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ABSTRACT

On November 18–19, 2019, the Immunity of Canadians and Risk of Epidemics (iCARE) Network convened a workshop in Toronto, Ontario, Canada. The objectives of the workshop were to raise the profile of sero-epidemiology in Canada, discuss best practice and methodological innovations, and strategize on the future direction of sero-epidemiology work in Canada. In this conference report, we describe the presentations and discussions from the workshop, and comment on the impact of the COVID-19 pandemic on serosurveillance initiatives, both in Canada and abroad.

1. Introduction

On November 18-19th, 2019 the Immunity of Canadians and Risk of Epidemics (iCARE) Network convened a workshop in Toronto, Ontario, Canada with participation from Canadian and international experts. The iCARE Network is a research group that seeks to answer questions related to population immunity to vaccine-preventable diseases. The objectives of the workshop were a) to raise the profile of sero-epidemiology in Canada, b) discuss best practice and methodological innovations, and c) strategize on the future direction of sero-epidemiology work in Canada. Workshop participants included Provincial and Federal public health officials, Canadian and other National Immunization Technical Advisory Group (NITAG) members, researchers, and representatives from industry and funding agencies. The workshop received financial support from the Canadian Association for Immunization Research and Evaluation, the Canadian Immunization Research Network, and the Canadian Institutes of Health Research. This report summarizes the workshop, including the case studies and examples that were presented by speakers, and participant discussion. It is notable that the COVID-19 pandemic erupted shortly after the workshop took place, further amplifying the importance of the serosurveillance themes that were discussed.

Sero-epidemiology is a multidisciplinary method used to estimate population immunity or exposure to infectious diseases [1]. Blood specimens are collected from a representative sample of a population and tested for antibodies to the pathogen being investigated. Epidemiological analyses, including prevalence proportions and regression models, and mathematical modelling can then be applied to the data [2]. Repeated or periodic sero-epidemiologic studies are often referred to as serosurveillance.

Serosurveillance can be used to monitor infectious disease trends and evaluate public health policies. It is commonly used to estimate population-level immunity to a wide range of vaccine-preventable diseases [2]. National serosurveillance programs have existed for several decades in some countries including the United Kingdom (UK), which was one of the first jurisdictions to implement a program in 1986/7; across Europe; in Australia and in the United States (US) [2]. The World Health Organization (WHO) recommends that regular serosurveys be performed for pathogens including hepatitis B, tetanus, diphtheria, dengue, measles and rubella [3–6]. Most recently, as part of the WHO Measles and Rubella Strategic Framework 2021–2030, serosurveys for measles and rubella were recommended as a potential action to improve surveillance and identify immunity gaps [7].

2. Use of sero-epidemiology

Speakers presented the infrastructure, priorities and funding models of sero-epidemiology programs in various jurisdictions, which were either considered core public health surveillance activities, or funded by research grants. Despite different funding sources and positioning within public health systems, these programs all shared the overall goals of measuring population immunity to infectious diseases (with a focus on vaccine-preventable diseases), evaluating interventions, and optimizing vaccine policy [2].

United Kingdom: The UK was one of the first jurisdictions to perform routine serosurveys and has used them since the 1980s to inform public health policy, evaluate the burden and changes in the epidemiology of disease, and gather data ahead of the introduction of vaccine programs [8,9]. The UK uses residual sera for its serosurveillance program, collecting specimens annually from National Health Service and UK Health Security Agency (formerly called Public Health England) laboratories that approximate the demographics of the general population. Participating laboratories collect aliquots of residual serum leftover from diagnostic testing, with accompanying age (or date of birth, if available), sex, and date of specimen collection [8,'10]. As early as the mid-1990 s, this program demonstrated its value when measles population serosurveys revealed substantial susceptibility in school-aged children [11]. This resulted in a large catch-up measles-mumps-rubella (MMR) vaccination campaign for all children aged 5–16 years in 1994, followed by the introduction of a second MMR dose in 1996 [9]. These activities substantially increased measles immunity in the birth cohorts of concern and may have mitigated a large outbreak [12]. Although the UK

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serosurveillance program was initially focused on measles, mumps and rubella, it was later extended to other infections of public health importance, including diphtheria, hepatitis A and B, and Herpes virus infections (varicella-zoster virus (VZV), herpes simplex virus 1 and 2, Epstein Barr virus), parvovirus B19 [9,13–16].

The Netherlands: Serosurveillance is one of the pillars of the Netherlands' National Immunization program. In contrast to the residual sera sampling approach in the UK, The Netherlands has been conducting serosurveys using a population-based study design since the 1990s, under the "Pienter" program [17–19]. This methodology utilizes a two-stage cluster sampling technique to draw a national sample representing all age-groups and regions, with oversampling of newcomers and in areas with known low vaccination coverage [20]. Individuals are recruited using an invitation letter. In addition to collecting data and serum specimens, participants can also consent to collection of other specimen types, additional data, and to the retrieval of medical history. The Pienter study has been conducted approximately decennially for every pathogen included in the National Immunization Program, in addition to other targets, depending on surveillance need. Results have been used to monitor the immunization program and inform the Dutch NITAG about insufficient herd immunity, duration of vaccine protection, and outbreak response. Examples of successful interventions include seroprevalence studies of VZV, which informed the initiation of a varicella immunization program in the Caribbean Netherlands [20,21] and a sero-epidemiology study that identified vulnerable age-groups for a catch-up human papilloma virus (HPV) vaccination in 2009 [22]. A measles serosurvey found that antibodies in infants born to vaccinated mothers dropped below the level of protection earlier than infants born to mothers immune through previous wild-type infection [23].

The European Sero-Epidemiology Network (ESEN): ESEN was initiated in 1996 as a time-limited endeavour funded by the European Union, with the aim of coordinating serological surveillance of vaccine-preventable diseases across Europe, and establishing methodologies to evaluate vaccine programs across borders [24,25]. ESEN initially included several Western European countries and covered measles, mumps, rubella, diphtheria and pertussis [26], expanding to 22 countries in 2001 for the ESEN2 survey, and also including varicella and hepatitis A and B [14]. Since countries used varying specimen collection and laboratory methods, ESEN validated standardization panels to allow the generation of standardization equations [14,24,27] to enable inter-country comparability.

United States: Like the Netherlands, the US utilizes a population-based study design conducted through the US National Health and Nutrition Examination Survey (NHANES), which uses multi-stage probability sampling to collect data and several types of biological specimens (blood, urine, cervicovaginal swabs and oral samples) from nationally representative cohorts [28]. Sero-epidemiology targets for these surveys are comprehensive, and have included measles, mumps, rubella, varicella, tetanus, diphtheria, viral hepatitis and sexually transmitted infections, among others [28–32]. One of the most significant accomplishments of the survey has been to uncover increased prevalence of hepatitis C antibody in persons born between 1945 and 1965 (baby boomers), directly resulting in policy change in 2012 with the addition of one-time screening for individuals in this age-group, in addition to already existing risk-based screening policy [33].

Canada: In Canada, sero-epidemiology studies have historically been supported by independent research, such that serosurveys are conducted on an *ad hoc* basis rather than programmatically. The iCARE Network has devoted considerable energy to validating antibody detection methods specific for vaccine-preventable diseases, including reference testing that was not previously available in Canada [34,35]. The first sero-epidemiology studies tested both provincial-level residual sera from Ontario as well as nationally representative sera obtained from the Canadian Health Measures Survey (CHMS), which is conducted biennially by Statistics Canada [36–38]. Specimens were tested for antibodies against measles and varicella. A comparison of results revealed similar estimates for both measles and varicella, suggesting that residual specimens, which are easier to access than CHMS specimens, are adequate for estimating population immunity to these diseases [38]. In addition to iCARE-led surveys, serosurveys were conducted through an academic partnership with the Public Health Agency of Canada using prenatal specimens, estimating immunity against rubella and pertussis [39,40]. Separately, Ontario and Alberta have conducted rubella serosurveys [41,42].

Low and Middle Income Countries (LMICs): In these settings, serosurveys serve both to inform supplementary immunization activities, and as an additional surveillance tool in areas with limited vaccine coverage data [43–45]. These roles were demonstrated by the Strengthening Immunization Systems through Serosurveillance group led by researchers at Johns Hopkins University, with studies in Northern Vietnam and Kenya [46,47]. This group also demonstrated the feasibility and utility of serosurveillance in LMICs to assess measles and rubella immunity gaps, evaluate vaccination campaigns, estimate outbreak risk and vaccine control strategies, and test alternative specimen types. For example, one study nested a serosurvey within a post-campaign evaluation survey and found that in Zambia, rubella seroprevalence estimates overall were 97.7%, but were lower than desired at 91.3% in adolescents and young adults [45]. The study also found that all estimates exceeded vaccine coverage estimates, likely due to immunity through wild type infection and underreporting of vaccination. Another study performed in Madagascar underscored the ability of serosurveys to identify immunity gaps in older populations in LMICs [43]. This is important because these groups are not always identified as susceptible by coverage data, which don't always focus on all age-groups. Furthermore, migration can result in historical coverage data becoming obsolete.

The Centers for Disease Control and Prevention (CDC) Centre for Global Health, Global Immunization Division has been instrumental in supporting LMICs in conducing serosurveys. A 2012 serosurvey in Cambodia included targets such as tetanus, measles, rubella, polio, and a variety of viral and parasitic pathogens amongst women of childbearing age. The survey found high (96%) measles seropositivity [48] which helped verify measles elimination, despite ongoing outbreaks [49]. However, tetanus immunity gaps in women age 15–24 in some regions of Cambodia were detected, informing Cambodia's 2015 maternal and neonatal tetanus elimination validation. Immunity gaps were also found for polio and rubella [48], and a seroprevalence of $>$ 45% was detected for *Strongyloides*, which was previously unknown [50]. The Bill and Melinda Gates Foundation has also been a driving force supporting serosurveys in LMICs. In collaboration with the CDC, it funded a serosurvey for neglected tropical diseases in Kenya, Tanzania and Mozambique. This survey found a tetanus immunity gap in adult men in Kenya and Tanzania, and less so in Mozambique [51]. This work contributed evidence to recommendations for tetanus risk mitigation and a change in the WHO-recommended tetanus vaccination schedule [52,53]. Although not specifically discussed in our meeting, other examples exist of serosurveys in sub-Saharan Africa to assess epidemic risk and inform public health programming [54,55].

3. Methodological considerations and innovations

The group discussed methodological considerations for designing and implementing serosurveys, including the target population(s), laboratory methods, specimen type and source, and data analysis considerations. These factors can also contribute substantially to study cost and feasibility. Although not specifically discussed at the iCARE meeting, it should be noted that a clear correlate of antibody-mediated protection may not be available for all pathogens, which presents a significant limitation on interpretation of serosurveys [56,57].

Specialized laboratory methods: Sero-epidemiology studies often use rapid and high throughput enzyme immunoassays (EIAs) for assessment of antibody titres. Recently, the use of multiplex bead-based EIAs has increased [34]. Although technical knowledge is required for assay

creation (if a commercial kit is not used) and validation, multiplexed bead-assays can test multiple antigens simultaneously using small volumes of specimen at a markedly reduced cost [58]. Countries are increasingly using multiplexed EIAs to obtain more useful data with fewer resources and to permit cost-sharing between programs. For example, the US has been using these assays for vaccine-preventable diseases, vector-borne diseases, and water and food borne diseases [58]. The CDC has been actively supporting technology transfer of multiplex bead assays to LMICs (as mentioned above) in Africa, Asia and The Americas [48,50,51]. The Netherlands has also used multiplex bead assays extensively, often multiplexing in a manner closely matched to vaccine programs (for example, combining measles-mumps-rubella and varicella, or diphtheria tetanus and pertussis). In Canada, the iCARE Network has implemented a multiplex bead assay for measles, mumps, rubella and varicella, after validating it for off-label use to provide quantitative antibody titres [34,59]. One challenge with laboratory studies is cold chain maintenance during collection, shipment and analysis of samples. This has driven interest in the development of so-called "point of care" diagnostics that can provide EIA results at the site of specimen collection. Lateral flow assays (LFA) have been a popular choice for this application [60,61], but there is growing interest in more sophisticated systems that can provide the same information with "laboratory-quality" results [62,63].

Although EIAs have become the backbone of sero-epidemiology programs, this method has well-known limitations. EIAs are usually designed for diagnostic purposes rather than for serosurveillance, such that they produce qualitative results (i.e. immune, non-immune, equivocal), and focus on specificity rather than sensitivity [34,64–66]. However, population immunity is often not bimodal, since individuals can have varying antibody levels depending on infection and/or vaccination status, and antibody waning [64,67]. Sero-epidemiology studies benefit from quantitative antibody measures to allow for a more nuanced characterization of immunity [34,64]. This is particularly true for specimens with low antibody levels, and therefore EIAs may have decreased accuracy when testing populations with a high proportion of equivocal or low-positive individuals, which is often the case with vaccinated populations [36]. To address these issues, EIAs used for serosurveillance are sometimes supplemented with reference testing. A commonly used reference method is the plaque reduction neutralization test. Although costly and labour intensive, the use of neutralization tests is an asset in populations with low or moderate antibody levels that are often reported as non-immune by EIAs, thus raising the reported level of immunity [36,38,68]. These additional testing considerations may be easy to implement in developed countries, but may not be feasible in underdeveloped countries. Moreover, EIA platforms may present maintenance challenges for developing countries, where support from manufacturers may be difficult to obtain.

Specimen sources: Specimens for sero-epidemiological studies can be obtained through population-based sampling using study volunteers (the US and The Netherlands [9,17]), which allows for the collection of additional information beyond basic demographic data. However, this method can be costly and may introduce a selection bias towards more affluent or healthy individuals [69], and study recruitment response rates are sometimes low [19]. Convenience sampling using residual specimens (used in the UK and some parts of Europe) is less labour-intensive and more cost-effective, but less information can be collected about participants, including individual-level vaccination status. Furthermore, residual specimens collected for occupational health or prenatal screening may be biased towards healthy individuals, while specimens collected for microbiological or biochemical testing may be biased towards those with comorbidities. Comparisons between specimen sources suggest that they can produce similar estimates, at least for infections which circulate widely or for which a considerable proportion of the general population has antibodies, such as measles, mumps, hepatitis B or varicella [70]. Studies of measles immunity in Ontario, Canada performed by the iCARE Network using these different approaches generated very similar estimates overall and by age-group [36].

Specimen type: While historically, serum specimens were used for sero-epidemiology studies, using alternative specimen types can be advantageous in some circumstances. For example, finger prick-based dry blood spots on filter paper are less invasive and stable for long periods of time, and are often comparable to results from venous blood specimens [71]. Oral fluid samples are another safe, non-invasive specimen type, that has a high patient acceptability profile [72]. Oral fluid samples have been shown to contain antibody levels at lower concentration than in serum, but have been proved useful and comparable to serum for measuring antibodies to human immunodeficiency virus (HIV), Human T-lymphotropic virus (HTLV), hepatitis A and B virus, rubella virus and parvovirus B19, although sensitivity depends on the antibody target and test used [72–74]. Oral fluid/saliva samples have been used both diagnostically and for surveillance purposes in the UK for measles by measuring IgM levels, which have been shown to have an adequate sensitivity of 92% compared to serum samples [75,76]. A study in Ethiopia aimed to assess whether oral fluid could replace serum in serosurveys by testing paired blood and oral fluid samples from 853 participants for antibodies against hepatitis B core antigen, rubella and measles [77]. Sensitivity and specificity were 43% and 87% for anti-hepatitis B core antigen, 79% and 90% for rubella, and 98% and 87% for measles. These results suggested that while oral fluid may be an adequate specimen source for serosurveillance in some circumstances, technical aspects including variation in assay performance and methods standardization needs further attention [77]. Since oral fluid/saliva sample quality can sometimes be inconsistent, commercial collection devices can facilitate more standardized specimen collection [71,72].

Mathematical modelling: Sero-epidemiological data has been used to parameterize mathematical models as part of jurisdictional sero-epidemiology surveillance activities and in stand-alone research [78,79]. In England, mathematical models using serological data indicated that the reproductive number of measles would increase above 1 in school-aged children by 1995, resulting in a resurgence of measles with a predicted 100,000 – 200,000 cases and 30–60 deaths [11]. This triggered a vaccination campaign for school-aged children later that year, and the policy decision to introduce a second vaccine dose in 1996. Cross sectional age-specific serosurvey data can also be used in a catalytic mathematical model to understand the current risk of susceptibility by age-group. For example, a time-varying catalytic model was used to assess measles immunity in China, taking into account changing force of infection due to supplemental vaccination activities, finding regional differences [80]. Del fava and colleagues used Bayesian mixture modelling to assess herd immunity to measles in Italy, and the impact of a catch-up vaccination campaign for school aged children in the Tuscany area in 2004 – 2005 [67], and to assess varicella susceptibility in Norway [64]. Mixture modelling is particularly useful for modelling population susceptibility to infections for which there is no reliable correlate of protection, such as mumps [9].

4. Measuring exposure to emerging pathogens

Several speakers presented results from ad-hoc serosurveys designed to evaluate exposure and/or immunity to emerging diseases are an important means of predicting the burden of disease. For example, during the 2009 influenza H1N1 pandemic, the UK performed large serosurveys before and after each pandemic wave to better understand age-specific background immunity to the pandemic strain, as well as seroprevalence after each pandemic wave. These findings were used to predict transmission patterns and inform optimal pandemic vaccine policy [81,82]. Similarly, in Canada, a mixture of residual specimens and a prospective cohort were used to measure seropositivity at points during the H1N1 pandemic in order to assess community transmission (as many cases were mild, and did not present for healthcare), identify risk factors for infection, and evaluate the antibody response in

vaccinated individuals [83]. Results from both countries indicated that, while children and younger adults were susceptible to the new pandemic strain, older adults had previous cross-protection.

Serosurveys were also useful in Northeastern Brazil during the Zika epidemic [84] using a combination of residual sera and prospective sampling. Testing revealed increasing seroprevalence of antibodies to Zika virus in 2015–2016, with a higher burden of disease in areas of low socio-economic status. Sera were also tested for antibody to dengue and Chikungunya viruses, allowing comparison of the spread of Zika virus to that of other arboviruses spread by the *Aedes* mosquito, which emerged in the Americas at roughly the same time. A study in the State of Rio de Janeiro in 2018 found that much of the population was still susceptible to Zika infection, although the test used in this study was not specific, making interpretation of results challenging [85]. Lastly, a seroprevalence study of Brazilian blood donors from the Northeast region of São Paulo State, was conducted before and after a 2016 Zika outbreak. The study used an EIA followed by PRNT confirmation of EIA positive samples, and found a seroprevalence of 5.3%, 12.8% and 13.2% in 2015, 2016 and 2017, respectively [86]. In addition to potential issues with representativeness due to the use of blood donor specimens, the authors pointed out the studied geographical region may have had lower Zika incidence compared to other areas in Brazil.

In addition to informing public health as new pathogens emerge, studies can also be performed to estimate the burden of infections with unknown or changing epidemiology. For example, the burden of Lyme disease in Canada is unknown and rapidly changing as the climate warms. An analysis of seroprevalence in Nova Scotia, Canada, of antibodies against Borrelia burgdorferi, the bacteria that causes Lyme disease, found a seroprevalence of 0.14% using specimens collected in 2012 [87]. Another example is hepatitis. In addition to the above-mentioned US NHANES serosurvey, Canadian study groups have performed several hepatitis B and C serosurveys. An Ontario study of hepatitis C antibody in baby-boomers demonstrated higher seroprevalence in individuals born between 1950 and 1964 compared to younger and older adults [88], and a national CHMS hepatitis B and C serosurvey found lower seroprevalence overall, albeit in a study population that is likely not representative of those infected [89]. A study of hepatitis E in England conducted using specimens collected in 1991 and 2004 found a seroprevalence estimate of 13.0% and 13.5% for each time period, respectively [90]. Seropositivity increased with age, and was associated with being male and living in the South of England.

5. Future plans and recommendations

The meeting also included strategic planning for the iCARE Network, and discussion of strategies to raise the profile of sero-epidemiology in Canada. While in some jurisdictions sero-epidemiology studies are a core part of infectious disease surveillance, serosurveys have historically been viewed as research in Canada. This is in contrast with WHO recommendation to conduct serosurveys for a variety of pathogens. The lack of familiarity with sero-epidemiology in some Canadian research or public health circles has led to chronic underfunding of serosurveys. However, Workshop members agreed that the iCARE Network has demonstrated that sero-epidemiology studies are valuable from both research and surveillance perspectives in Canada. In addition, the iCARE Network has built a national infrastructure to carry out serosurveys, and has tackled methodological questions related to specimen sourcing and laboratory assays required to carry out studies in the Canadian context. Recently, the Network has developed a methodology to link data from individuals' residual sera to health administrative databases to explore variables such as vaccination status, socio-economic status, and immigration status, among others. This approach allows the use of residual sera while still obtaining plentiful individual subject-level data.

Serosurvey programs in many other jurisdictions are core funded by public health programs, allowing them to perform work pre-emptively and not reactively, and contribute to public health policy. The group agreed that this would be optimal in Canada, too, and a single funding source would be ideal. To raise the profile of sero-epidemiology nationally, the Network should continue to make efforts to engage stakeholders and leverage interest in serosurveys. These stakeholders include Provincial and Territorial public health agencies and/or Ministries of Health; the Federal Public Health Agency of Canada; Funding bodies such as the Canadian Institutes of Health Research; and Industry. In particular, there would be value in underscoring the benefits of sero-epidemiology studies for public health, and the opportunity for Canada to be innovators in this field. One challenge that was identified was that, since healthcare in Canada is a provincial/territorial prerogative rather than federal, there are many stakeholders, each with its own set of priorities and limitations.

6. Epilogue

Since the conclusion of our meeting in November 2019, we have weathered the COVID-19 pandemic and a resulting shift in the scope, interpretation, and value of serological data for understanding and controlling the spread of infectious diseases. Shortly after the iCARE Workshop, many participants mobilized in 2020 to conduct SARS-SoV-2 serosurveys in their jurisdictions, either by leveraging and extending on existing infrastructure like in the Netherlands [91], or with new serosurvey infrastructure like the US [92,93]. Unlike countries with pre-existing infrastructure, SARS-CoV-2 serosurveillance efforts in Canada were highly reactive. De-novo serosurveys were funded by the COVID-19 Immunity Task Force, the Canadian Institutes of Health Research, and others using new specimen sources that were previously untapped.

Canadian serosurveillance data were instrumental to assessing the impact of the COVID-19 pandemic on Canadians, and to evaluating the public health pandemic response. It demonstrated that public health restrictions were effective in curbing COVID-19 transmission in the first wave [93,94], and that racialized groups and those experiencing material deprivation were disproportionality affected by SARS-CoV-2 than other population groups [95]. During the Omicron wave, restricted PCR testing eligibility [96–98] resulted in difficulties assessing population-level infection incidence. This made serosurveillance data even more valuable for understanding the population burden of infection. Serosurveillance data was also useful to model the pandemic and predict future transmission trends [99]. Despite these successes, the reactive nature of these initiatives impacted the timeliness of results, which often lagged behind reporting from jurisdictions like the UK, where routine serosurveillance systems were in place pre-pandemic.

These efforts underscore the need for programmatic serosurveillance funding in Canada. It has become clear that a serosurveillance program with sustained funding would provide great value in supporting public health surveillance, both routinely and in a pandemic. Leveraging the lessons learned from COVID-19, there is great opportunity to highlight the strengths of serological data and sero-epidemiological studies, and leverage pandemic-era advancements in the Canadian serosurvey landscape towards routine and sustainable surveillance post-pandemic.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: MS has been an investigator on projects funded by GlaxoSmithKline, Merck, Pfizer, Moderna, Sanofi-Pasteur, Seqirus, Symvivo and VBI Vaccines. All funds have been paid to his institute, and he has not received any personal payments. Other authors have no conflicts to declare.

Data availability

No data was used for the research described in the article.

References

[1] Dimech W, Mulders MN. A review of testing used in seroprevalence studies on measles and rubella. Vaccine 2016;34:4119–22. S0264-410X(16)30405-4 [pii].
[2] Wilson SE, Deeks SL, Hatchette TF, Crowcroft NS. The role of seroepidemiology in the comprehensive surveillance of vaccine-preventable diseases. CMAJ 2012;184:E70.
[3] World Health Organization. Documenting the Impact of Hepatitis B Immunization: best practices for conducting a serosurvey.
[4] World Health Organization. Guidance on conducting serosurveys in support of measles and rubella elimination in the WHO European Region.
[5] World Health Organization. Informing vaccination programs: a guide to the design and conduct of dengue serosurveys. vol. WHO/IVB/17. Geneva; 2020.
[6] World Health Organization. Surveillance standards for vaccine-preventable diseases. 2nd ed. Geneva PP - Geneva: World Health Organization.
[7] Measles and rubella strategic framework 2021–2030. Geneva; 2020.
[8] Osborne K, Gay N, Hesketh L, Morgan-Capner P, Miller E. Ten years of serological surveillance in England and Wales: methods, results, implications and action. Int J Epidemiol 2000;29:362–8.
[9] Vyse AJ, Gay NJ, White JM, Ramsay ME, Brown DW, Cohen BJ, et al. Evolution of surveillance of measles, mumps, and rubella in England and Wales: providing the platform for evidence-based vaccination policy. Epidemiol Rev 2002;24:125–36.
[10] Health Protection Agency. Seroepidemiology Unit User Guide.
[11] Ramsay M, Gay N, Miller E, Rush M, White J, Morgan-Capner PBD. The epidemiology of measles in England and Wales: rationale for the 1994 national vaccination campaign. Commun Dis Report 1994;4:R141–56.
[12] Gay N, Ramsay M, Cohen B, Hesketh L, Morgan-Capner P, Brown DME. The epidemiology of measles in England and Wales since the 1994 vaccination campaign. Commun Dis Rep CDR Rev 1997;7:R17–21.
[13] Gay N. Analysis of serological surveys using mixture models: application to a survey of parvovirus B19. Stat Med 1996;15:1567–73.
[14] Kafatos G, Andrews N, Nardone A. Model selection methodology for inter-laboratory standardisation of antibody titres. Vaccine 2005;23:5022–7. https://doi.org/10.1016/j.vaccine.2005.05.030.
[15] Morris MC, Edmunds WJ, Hesketh LM, Vyse AJ, Miller E, Morgan-Capner P, et al. Sero-epidemiological patterns of epstein-barr and herpes simplex (HSV-1 and HSV-2) viruses in England and Wales. J Med Virol 2002;67:522–7. https://doi.org/10.1002/jmv.10132.
[16] Talukder YS, Kafatos G, Pinot de Moira A, Aquilina J, Parker SP, Crowcroft NS, et al. The seroepidemiology of varicella zoster virus among pregnant Bangladeshi and white British women in the London Borough of Tower Hamlets, UK. Epidemiol Infect 2007;135:1344–53. https://doi.org/10.1017/S0950268807008497.
[17] De Melker HE, Conyn-van Spaendonck MA. Immunosurveillance and the evaluation of national immunization programmes: a population-based approach. Epidemiol Infect 1998;121:637–43.
[18] van der Klis FRM, Mollema L, Berbers GAM, de Melker HECHA. Second national serum bank for population-based seroprevalence studies in the Netherlands. Neth J Med 2009;67:301.
[19] Verberk JDM, Vos RA, Mollema L, van Vliet J, van Weert JWM, de Melker HE, et al. Third national biobank for population-based seroprevalence studies in the Netherlands, including the Caribbean Netherlands. BMC Infect Dis 2019;19:470. https://doi.org/10.1186/s12879-019-4019-y.
[20] de Greeff SC, de Melker HE, van Gageldonk PG, Schellekens JF, van der Klis FR, Mollema L, et al. Seroprevalence of pertussis in The Netherlands: evidence for increased circulation of Bordetella pertussis. PLoS One 2010;5:e14183.
[21] Vos RA, Mollema L, van Boven M, van Lier A, Smits G, Janga-Jansen AVA, et al. High varicella zoster virus susceptibility in Caribbean island populations: Implications for vaccination. Int J Infect Dis 2020;94:16–24. https://doi.org/10.1016/j.ijid.2020.02.047.
[22] Kramer M, Mollema L, Smits G, Boot H, de Melker H, van der Klis F. Age-specific HPV seroprevalence among young females in The Netherlands. Sex Transm Infect 2010; 86: 494 LP – 499. 10.1136/sti.2009.041210.
[23] Waaijenborg S, Hahne SJ, Mollema L, Smits GP, Berbers GA, van der Klis FR, et al. Waning of maternal antibodies against measles, mumps, rubella, and varicella in communities with contrasting vaccination coverage. J Infect Dis 2013;208:10–6. https://doi.org/10.1093/infdis/jit143 [doi].
[24] de Ory F, Echevarria JM, Kafatos G, Anastassopoulou C, Andrews N, Backhouse J, et al. European seroepidemiology network 2: Standardisation of assays for seroepidemiology of varicella zoster virus. J Clin Virol 2006;36:111–8. https://doi.org/10.1016/j.jcv.2006.01.017.
[25] Tischer A, Andrews N, Kafatos G, Nardone A, Berbers G, Davidkin I, et al. Standardization of measles, mumps and rubella assays to enable comparisons of seroprevalence data across 21 European countries and Australia. Epidemiol Infect 2007;135:787–97. https://doi.org/10.1017/S0950268807008266.
[26] Osborne K, Weinberg JME. The European Sero-Epidemiology Network. Eurosurveillance 1997;2:167.
[27] Kafatos G, Andrews N, Mcconway K, Anastassopoulou C, Barbara C, Manchón F, et al. Estimating seroprevalence of vaccine-preventable infections: Is it worth standardizing the serological outcomes to adjust for different assays and laboratories? Epidemiol Infect Epidemiol 2014; 1–10. 10.1017/S095026881400301X.
[28] Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey Biospecimen Program n.d. https://www.cdc.gov/nchs/nhanes/biospecimens/biospecimens.htm (accessed June 11, 2021).
[29] Oliver SE, Unger ER, Lewis R, McDaniel D, Gargano JW, Steinau M, et al. Prevalence of Human Papillomavirus Among Females After Vaccine Introduction-National Health and Nutrition Examination Survey, United States, 2003–2014. J Infect Dis 2017;216:594–603. https://doi.org/10.1093/infdis/jix244.
[30] Petrosky EY, Hariri S, Markowitz LE, Panicker G, Unger ER, Dunne EF. Is vaccine type seropositivity a marker for human papillomavirus vaccination? National Health and Nutrition Examination Survey, 2003–2010. Int J Infect Dis 2015;33:137–41. https://doi.org/10.1016/j.ijid.2015.01.010.
[31] Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey.
[32] Lebo EJ, Kruszon-Moran DM, Marin M, Bellini WJ, Schmid S, Bialek SR, et al. Seroprevalence of measles, mumps, rubella and varicella antibodies in the United States population, 2009–2010. Open Forum. Infect Dis 2015;2:ofv006. https://doi.org/10.1093/ofid/ofv006 [doi].
[33] Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, et al. Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. MMWR Recomm Rep 2012;61:1–32.
[34] Hatchette TF, Scholz H, Bolotin S, Crowcroft NS, Jackson C, McLachlan E, et al. Calibration and Evaluation of Quantitative Antibody Titers for Measles Virus by Using the BioPlex 2200. Clin Vaccine Immunol 2017;24:e00269–316.
[35] McLachlan E, Scholz H, Bolotin S, Crowcroft NS, Hatchette TF, Jackson C, et al. Calibration and Evaluation of Quantitative Antibody Titers for Varicella-Zoster Virus by Use of the BioPlex 2200. J Clin Microbiol 2019; 57: 10.1128/JCM.00296-19. Print 2019 Aug. e00296-19 [pii].
[36] Bolotin S, Severini A, Hatchette T, McLachlan E, Savage R, Hughes SL, et al. Assessment of population immunity to measles in Ontario, Canada: A Canadian Immunization Research Network (CIRN) Study. HumVaccin Immunother 2019.
[37] Statistics Canada. Canadian Health Measures Survey (CHMS); 2021. https://www.statcan.gc.ca/eng/survey/household/5071.
[38] Osman S, Crowcroft N, McLachlan E, Hatchette T, Perez-Iratxeta C, Joh E, et al. Population immunity to measles in Canada using Canadian Health Measures survey data – A Canadian Immunization Research Network (CIRN) study. Vaccine 2022 [In Press].
[39] Brooks JI, Bell CA, Rotondo J, Gilbert NL, Tunis M, Ward BJ, et al. Low levels of detectable pertussis antibody among a large cohort of pregnant women in Canada. Vaccine 2018;36:6138–43. https://doi.org/10.1016/j.vaccine.2018.08.066.
[40] Gilbert NL, Rotondo J, Shapiro J, Sherrard L, Fraser WD, Ward BJ. Seroprevalence of rubella antibodies and determinants of susceptibility to rubella in a cohort of pregnant women in Canada, 2008–2011. Vaccine 2017;35:3050–5. https://doi.org/10.1016/j.vaccine.2017.04.057.
[41] Lai FY, Dover DC, Lee B, Fonseca K, Solomon N, Plitt SS, et al. Determining rubella immunity in pregnant Alberta women 2009–2012. Vaccine 2015;33:635–41. https://doi.org/10.1016/j.vaccine.2014.12.022 [doi].
[42] Lim GH, Harris T, Desai S, Crowcroft NS, Mazzulli T, Kozlowski T, et al. Rubella immunity among prenatal women in Ontario, 2006–2010. BMC Infect Dis 2013;13:362. https://doi.org/10.1186/1471-2334-13-362.
[43] Winter AK, Wesolowski AP, Mensah KJ, Ramamonjiharisoa MB, Randriamanantena AH, Razafindratsimandresy R, et al. Revealing Measles Outbreak Risk With a Nested Immunoglobulin G Serosurvey in Madagascar. Am J Epidemiol 2018;187:2219–26. https://doi.org/10.1093/aje/kwy114.
[44] Gong W, Hayford K, Taighoon Shah M, Iqbal J, Moss WJ, Moulton LH, et al. Using Serosurvey Data Triangulation for More Accurate Estimates of Vaccine Coverage: Measured and Modeled Coverage From Pakistan Household Surveys. Am J Epidemiol 2019;188:1849–57.
[45] Hayford K, Mutembo S, Carcelen A, Matakala HK, Munachoonga P, Winter A, et al. Measles and rubella serosurvey identifies rubella immunity gap in young adults of childbearing age in Zambia: The added value of nesting a serological survey within a post-campaign coverage evaluation survey. Vaccine 2019;37:2387–93. https://doi.org/10.1016/j.vaccine.2019.02.037.
[46] Choisy M, Trinh S, Nguyen T, Nguyen T, Mai Q, Pham Q, et al. Sero-prevalence surveillance to predict vaccine-preventable disease outbreaks; a lesson from the 2014 measles epidemic in Northern Vietnam. Open Forum Infect Dis n.d.; 6.
[47] Mburu CN, Ojal J, Chebet R, Akech D, Karia B, Tuju J, et al. The importance of supplementary immunisation activities to prevent measles outbreaks during the COVID-19 pandemic in Kenya. BMC Med 2021;19:35. https://doi.org/10.1186/s12916-021-01906-9.
[48] Mao B, Chheng K, Wannemuehler K, Vynnycky E, Buth S, Soeung SC, et al. Immunity to polio, measles and rubella in women of child-bearing age and estimated congenital rubella syndrome incidence, Cambodia, 2012. Epidemiol Infect 2015;143:1858–67.
[49] Hagan JE, Kriss JL, Takashima Y, Mariano KML, Pastore R, Grabovac V, et al. Progress Toward Measles Elimination - Western Pacific Region, 2013-2017. MMWR Morb Mortal Wkly Rep 2018; 67: 491–5. 10.15585/mmwr.mm6717a3.
[50] Priest JW, Jenks MH, Moss DM, Mao B, Buth S, Wannemuehler K, et al. Integration of Multiplex Bead Assays for Parasitic Diseases into a National, Population-Based Serosurvey of Women 15–39 Years of Age in Cambodia. PLoS Negl Trop Dis 2016;10:e0004699–. https://doi.org/10.1371/journal.pntd.0004699.
[51] Scobie HM, Patel M, Martin D, Mkocha H, Njenga SM, Odiere MR, et al. Tetanus Immunity Gaps in Children 5–14 Years and Men ≥ 15 Years of Age Revealed by Integrated Disease Serosurveillance in Kenya, Tanzania, and Mozambique. Am J Trop Med Hyg 2017;96:415–20. https://doi.org/10.4269/ajtmh.16-0452.
[52] World Health Organization. Tetanus vaccines: WHO position paper- February 2017.
[53] World Health Organization. WHO Informal Consultation on Tetanus and Voluntary Medical Male Circumcision.
[54] Njenga SM, Kanyi HM, Arnold BF, Matendechero SH, Onsongo JK, Won KY, et al. Integrated cross-sectional multiplex serosurveillance of IgG antibody responses to

parasitic diseases and vaccines in coastal Kenya. Am J Trop Med Hyg 2020;102: 164–76. https://doi.org/10.4269/ajtmh.19-0365.
[55] Manigart O, Trotter C, Findlow H, Assefa A, Mihret W, Moti Demisse T, et al. A Seroepidemiological study of Serogroup A meningococcal infection in the african meningitis belt. PLoS One 2016;11:e0147928–. https://doi.org/10.1371/journal.pone.0147928.
[56] Plotkin SA. Correlates of protection induced by vaccination. Clin Vaccine Immunol 2010;17:1055–65. https://doi.org/10.1128/CVI.00131-10 [doi].
[57] World Health Organization. Correlates of vaccine-induced protection: methods and implications, vol. WHO/IVB/13. Geneva, Switzerland: WHO; 2013.
[58] Pan American Health Organization. Towards a better surveillance in Public Health: Multiplex Bead Assay. 9th Global Health Conference "Innovative Research, Global Solutions," n.d.
[59] Serhir B, Dagenais C, Ogee-Nwankwo A, Lamirande R, Hatchette T, Crowcroft N, et al. Validation of a Plaque Reduction Neutralization Test for Rubella: Performance Comparison with Virus-Specific IgG EIAs. Canadian Association for Clinical Microbiology and Infectious Diseases Annual Conference, Victoria BC, Canada 2014.
[60] Fu E, Liang T, Spicar-Mihalic P, Houghtaling J, Ramachandran S, Yager P. Two-dimensional paper network format that enables simple multistep assays for use in low-resource settings in the context of malaria antigen detection. Anal Chem 2012; 84:4574–9. https://doi.org/10.1021/ac300689s.
[61] Lafleur L, Stevens D, McKenzie K, Ramachandran S, Spicar-Mihalic P, Singhal M, et al. Progress toward multiplexed sample-to-result detection in low resource settings using microfluidic immunoassay cards. Lab Chip 2012;12:1119–27. https://doi.org/10.1039/C2LC20751F.
[62] C. NAH, Ryan F, Christian F, Julian L, G. RD, Aimee S, et al. A digital microfluidic system for serological immunoassays in remote settings. Sci Transl Med 2018; 10: eaar6076. 10.1126/scitranslmed.aar6076.
[63] Tassaneewan L, W. GT, Samiksha N, A. SA, Shi X, O. OO, et al. A smartphone dongle for diagnosis of infectious diseases at the point of care. Sci Transl Med 2015; 7: 273re1-273re1. 10.1126/scitranslmed.aaa0056.
[64] Del Fava E, Rimseliene G, Flem E, Freiesleben de Blasio B, Scalia Tomba G, Manfredi P. Estimating Age-Specific Immunity and Force of Infection of Varicella Zoster Virus in Norway Using Mixture Models. PLoS One 2016; 11: e0163636. 10.1371/journal.pone.0163636 [doi].
[65] Cohen BJ, Parry RP, Doblas D, Samuel D, Warrener L, Andrews N, et al. Measles immunity testing: Comparison of two measles IgG ELISAs with plaque reduction neutralisation assay. J Virol Methods 2006;131:209–12. https://doi.org/10.1016/j.jviromet.2005.08.001.
[66] Ratnam S, Gadag V, West R, Burris J, Oates E, Stead F, et al. PMC228046; Comparison of commercial enzyme immunoassay kits with plaque reduction neutralization test for detection of measles virus antibody. J Clin Microbiol 1995;33:811–5.
[67] Del Fava E, Shkedy Z, Bechini A, Bonanni P, Manfredi P. Towards measles elimination in Italy: Monitoring herd immunity by Bayesian mixture modelling of serological data. Epidemics 2012;4:124–31. https://doi.org/10.1016/j.epidem.2012.05.001.
[68] Cho HK, Lee H, Kim HW, Kim SS, Kang HJ, Kim IT, et al. Seroprevalences of Specific IgG Antibodies to Measles, Mumps, and Rubella in Korean Infants. J Korean Med Sci 2016;31:1957–62. https://doi.org/10.3346/jkms.2016.31.12.1957 [doi].
[69] Nummela O, Sulander T, Helakorpi S, Haapola I, Uutela A, Heinonen H, et al. Register-based data indicated nonparticipation bias in a health study among aging people. J Clin Epidemiol 2011;64:1418–25. https://doi.org/10.1016/j.jclinepi.2011.04.003 [doi].
[70] Kelly H, Riddell MA, Gidding HF, Nolan T, Gilbert GL. A random cluster survey and a convenience sample give comparable estimates of immunity to vaccine preventable diseases in children of school age in Victoria, Australia. Vaccine 2002;20: 3130–6.
[71] Prosperi C, Kaduskar O, Bhatt V, Hasan AZ, Vivian Thangaraj JW, Kumar MS, et al. Diagnostic Accuracy of Dried Blood Spots Collected on HemaSpot HF Devices Compared to Venous Blood Specimens To Estimate Measles and Rubella Seroprevalence. MSphere 2021;6:e0133020–. https://doi.org/10.1128/mSphere.01330-20.
[72] Vyse A, Cohen B, Ramsay M. A comparison of oral fluid collection devices for use in the surveillance of virus diseases in children. Public Health 2001;115:201–7. https://doi.org/10.1038/sj/ph/1900751.
[73] Archibald DW, Zon LI, Groopman JE, McLane MF, Essex M. Antibodies to human T-lymphotropic virus type III (HTLV-III) in saliva of acquired immunodeficiency syndrome (AIDS) patients and in persons at risk for AIDS. Blood 1986;67:831–4.
[74] Parry JV, Perry KR, Mortimer PP. Sensitive assays for viral antibodies in saliva: an alternative to tests on serum. The Lancet 1987; 330: 72–5. 10.1016/S0140-6736(87)92737-1.
[75] Brown DW, Ramsay ME, Richards AF, Miller E. Salivary diagnosis of measles: a study of notified cases in the United Kingdom, 1991–3. BMJ 1994;308:1015–7. https://doi.org/10.1136/bmj.308.6935.1015.
[76] Warrener L, Slibinskas R, Chua K, Nigatu W, Brown K, Sasnauskas K, et al. A point-of-care test for measles diagnosis: Detection of measles-specific igM antibodies and viral nucleic acid. Bull World Health Organ 2011;89:675–82. https://doi.org/10.2471/BLT.11.088427.
[77] Nokes DJ, Enquselassie F, Nigatu W, Vyse AJ, Cohen BJ, Brown DW, et al. Has oral fluid the potential to replace serum for the evaluation of population immunity levels? A study of measles, rubella and hepatitis B in rural Ethiopia. Bull World Health Organ 2001;79:588–95.
[78] Brisson M, Gay NJ, Edmunds WJ, Andrews NJ. Exposure to varicella boosts immunity to herpes-zoster: implications for mass vaccination against chickenpox. Vaccine 2002; 20: 2500–7. S0264410X02001809 [pii].
[79] Brisson M, Melkonyan G, Drolet M, De Serres G, Thibeault R, De Wals P. Modeling the impact of one- and two-dose varicella vaccination on the epidemiology of varicella and zoster. Vaccine 2010;28:3385–97. https://doi.org/10.1016/j.vaccine.2010.02.079.
[80] Li S, Ma C, Hao L, Su Q, An Z, Ma F, et al. Demographic transition and the dynamics of measles in six provinces in China: A modeling study. PLoS Med 2017;14: e1002255–. https://doi.org/10.1371/journal.pmed.1002255.
[81] Hardelid P, Andrews NJ, Hoschler K, Stanford E, Baguelin M, Waight PA, et al. Assessment of baseline age-specific antibody prevalence and incidence of infection to novel influenza A/H1N1 2009. Health Technol Assess 2010;14:115–92.
[82] Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 2010;375:1100–8. https://doi.org/10.1016/S0140-6736(09)62126-7 [doi].
[83] Achonu C, Rosella L, Gubbay JB, Deeks S, Rebbapragada A, Mazzulli T, et al. Seroprevalence of pandemic influenza H1N1 in Ontario from January 2009-May 2010. PLoS One 2011;6:e26427.
[84] Netto EM, Moreira-Soto A, Pedroso C, Hoser C, Funk S, Kucharski AJ, et al. High Zika Virus Seroprevalence in Salvador, Northeastern Brazil Limits the Potential for Further Outbreaks. MBio 2017; 8: 10.1128/mBio.01390-17. e01390-17 [pii].
[85] Périssé ARS, Souza-Santos R, Duarte R, Santos F, de Andrade CR, Rodrigues NCP, et al. Zika, dengue and chikungunya population prevalence in Rio de Janeiro city, Brazil, and the importance of seroprevalence studies to estimate the real number of infected individuals. e0243239–e0243239 PLoS One 2020;15. https://doi.org/10.1371/journal.pone.0243239.
[86] Slavov SN, Guaragna Machado RR, Ferreira AR, Soares CP, Araujo DB, Leal Oliveira DB, et al. Zika virus seroprevalence in blood donors from the Northeastern region of São Paulo State, Brazil, between 2015 and 2017. J Infect 2020;80:111–5. https://doi.org/10.1016/j.jinf.2019.10.002.
[87] Hatchette T, Johnston BL, Schleihauf E, Mask A, Haldane D, Drebot M, et al. Epidemiology of Lyme Disease, Nova Scotia, Canada, 2002–2013. Emerg Infect Dis J 2015;21:1751. https://doi.org/10.3201/eid2110.141640.
[88] Bolotin S, Feld JJ, Garber G, Wong WWL, Guerra F, Mazzulli T. Population-based estimate of hepatitis C virus prevalence in Ontario, Canada. PLoS One 2018; In Press.
[89] Rotermann, Michelle, Langlois, Kellie, Andonov, Anton, Trubnikov M. Seroprevalence of hepatitis B and C virus infections: Results from the 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey. Statistics Canada, Catalogue No 82-003-X • Health Reports 2013;24:3–13.
[90] Ijaz S, Vyse AJ, Morgan D, Pebody RG, Tedder RS, Brown D. Indigenous hepatitis E virus infection in England: More common than it seems. J Clin Virol 2009;44: 272–6. https://doi.org/10.1016/j.jcv.2009.01.005.
[91] den Hartog G, Vos ERA, van den Hoogen LL, van Boven M, Schepp RM, Smits G, et al. Persistence of Antibodies to Severe Acute Respiratory Syndrome Coronavirus 2 in Relation to Symptoms in a Nationwide Prospective Study. Clin Infect Dis 2021; 73:2155–62. https://doi.org/10.1093/cid/ciab172.
[92] Havers FP, Reed C, Lim T, Montgomery JM, Klena JD, Hall AJ, et al. Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. JAMA Intern Med 2020. https://doi.org/10.1001/jamainternmed.2020.4130.
[93] Bolotin S, Tran V, Deeks SL, Peci A, Brown KA, Buchan SA, et al. Assessment of population infection with SARS-CoV-2 in Ontario, Canada, March to June 2020. Euro Surveill 2021;26:2001559. https://doi.org/10.2807/1560-7917.ES.2021.26.50.2001559.
[94] Skowronski DM, Sekirov I, Sabaiduc S, Zou M, Morshed M, Lawrence D, et al. Low SARS-CoV-2 sero-prevalence based on anonymized residual sero-survey before and after first wave measures in British Columbia, Canada, March-May 2020. MedRxiv 2020:2020.07.13.20153148. 10.1101/2020.07.13.20153148.
[95] Candian Blood Services COVID-19 Seroprevalence Report: March 18, 2021 2021. https://www.covid19immunitytaskforce.ca/wp-content/uploads/2021/04/COVID-19-Report_January-2021_18March2021.pdf.
[96] BC Centre for Disease Control: When to get a COVID-19 test 2022. http://www.bccdc.ca/health-info/diseases-conditions/covid-19/testing/when-to-get-a-covid-19-test.
[97] Government of Alberta: Symptoms and testing; 2022. https://www.alberta.ca/covid-19-testing-in-alberta.aspx.
[98] Updated Eligibility for PCR Testing and Case and Contact Management Guidance in Ontario 2022. https://news.ontario.ca/en/backgrounder/1001387/updated-eligibility-for-pcr-testing-and-case-and-contact-management-guidance-in-ontario.
[99] Dick DW, Childs L, Feng Z, Li J, Röst G, Buckeridge DL, et al. COVID-19 Seroprevalence in Canada Modelling Waning and Boosting COVID-19 Immunity in Canada a Canadian Immunization Research Network Study. Vaccines (Basel) 2021; 10:17. https://doi.org/10.3390/vaccines10010017.

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