COVID-19 Vaccine Surveillance Plan

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Ontario

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Contents

Background

Following the authorization of the first COVID-19 vaccines by Health Canada in late 2020[1], Ontario launched the first phase of its three-phased distribution plan[2] to implement Ontario's COVID-19 vaccine program. Phase One began on December 14, 2020 and prioritized high risk populations including residents, staff and essential care givers in long-term care and retirement homes, health care workers, and Indigenous adults in northern remote and higher risk communities (on-reserve and urban). Subsequent phases, including sequencing of population sub-groups for vaccination and additional delivery strategies have been facilitated with increases in vaccine supply.

Comprehensive surveillance plans are critical to all vaccine programs, but especially when these programs are incorporating new vaccine platforms, and in the current context of a mass immunization campaign that has the potential to influence a wide range of public health measures. Immunogenicity, safety, and efficacy data collected through clinical trials have all informed vaccine decision making. However, ongoing post-marketing surveillance (i.e., studying vaccines after market authorization and their incorporation into vaccine programs) is needed to ensure the ability to detect and respond to the potential for rare safety signals and to understand vaccine effectiveness in real world settings, including broader populations than those included in clinical trials. Ongoing vaccine program surveillance is also important in the context of the delayed second dose strategy, implemented in mid-March 2021 to maximize the number of individuals protected by the first dose of vaccine.

Given their multi-faceted nature, surveillance of vaccine programs is strengthened through initiatives that involve partnerships with other public health, governmental, and research organizations and across multiple levels (local, provincial, national).

Scan of other vaccine surveillance plans

The COVID-19 vaccine surveillance plan for Ontario was developed following the review of the existing Ontario vaccine program surveillance infrastructure and recent changes made in the setting of the COVID-19 vaccine program, as well as a review of COVID-19 vaccine surveillance plans and related documents including those from the US Centers for Disease Control and Prevention[3], the European Centre for Disease Prevention and Control[4,5], Public Health England[6], and the World Health Organization[7].

Vaccine program goals and surveillance objectives

Ontario's COVID-19 vaccine plan[2] has three objectives: 1) to prevent death; 2) to prevent illness, hospitalization, and Intensive Care Unit (ICU) admission; and 3) to reduce transmission, and is structured to align with the Ethical Framework for vaccine distribution. These objectives (described hereafter as vaccine program goals) are aligned with Canada's pandemic response goal, which has also been adopted by the National Advisory Committee on Immunization (NACI), which is "to minimize serious illness and overall deaths while minimizing societal disruption as a result of the COVID-19 pandemic".[8]

The Ontario vaccine surveillance plan is intended to inform and support Ontario's COVID-19 vaccine program in meeting these goals and to answer other key questions related to vaccine program implementation. These include: monitoring the impact of the program on serious illness and death, assessing the impact of COVID-19 vaccines on disease incidence, outbreaks and in relation to variants of concern (VOC), conducting robust vaccine safety monitoring, and monitoring for inequities in vaccine uptake and inequalities in outcome measures, and understanding public confidence in COVID-19 vaccines.

In order to answer these questions, this plan is organized into six surveillance areas:

1. Vaccine uptake and coverage
2. Vaccine safety

3. Program impact and vaccine effectiveness
4. Virus characterization of cases with vaccine history
5. Serosurveillance
6. Public confidence

Vaccine uptake and coverage

Vaccine coverage is a key indicator of program performance and refers to the proportion of the population that is vaccinated at a single point in time.

Ontario is using a single provincial information system, $COVax_{ON,}$ to document the administration of COVID-19 vaccines. In addition to detailed information about the vaccination event (location of administration, vaccine type, dose number, lot number, and reason for immunization), socio-demographic data, including sex, race and ethnicity, will be collected on a voluntary basis.

Vaccine coverage can be assessed using a variety of metrics, including uptake by product type and dose number, and by both individual-level (e.g., age, gender, reason for immunization) and population-level characteristics (e.g., geography). In order to estimate vaccine coverage, both the number of immunized individuals (the numerator), as well as the total number of both immunized and unimmunized individuals in a given population (the denominator) are required. Socio-demographic data and neighbourhood level analyses (i.e., by forward sortation area of postal codes) will be used to determine how well the vaccine program is reaching communities who have been disproportionately impacted by COVID-19.

Accurate numerator and denominator data are essential for assessments of vaccine program reach and coverage. Information on COVID-19 vaccine doses administered is also crucial for analyses of vaccine effectiveness and program impact as well as vaccine safety, as described further below.

Vaccine safety

The goals of vaccine safety surveillance include the early detection and timely response to real or perceived vaccine safety issues. Multiple complementary systems exist to support robust vaccine safety surveillance provincially and federally in Canada, many of which have been expanded to support the COVID-19 vaccine program.

Passive vaccine safety surveillance

Adverse Events Following Immunization

In Ontario, passive vaccine safety surveillance refers to the reporting of adverse events following immunization (AEFIs) by health care providers, vaccine recipients or their caregivers to local public health units (PHUs) for further investigation. Provincial surveillance of AEFIs is well established and is supported by legislation under the *Health Protection and Promotion Act*. AEFI reports received by PHUs are investigated, assessed and documented in the provincial database (Public Health Case and Contact Management Solution [CCM]) according to provincial surveillance guidelines.[9]

Vaccine safety surveillance is strengthened by collaboration across Canada. Ontario is participating in expedited COVID-19 AEFI surveillance organized by the Public Health Agency of Canada (PHAC) which involves reporting of COVID-19 AEFIs to PHAC for inclusion in the Canadian Adverse Event Following Immunization Surveillance System (CAEFISS), the national database for AEFIs reported from all provinces and territories in Canada. Ontario also participates in regular information sharing calls about vaccine safety with a pan-Canadian network called the Vaccine Vigilance Working Group (VVWG), coordinated by PHAC. Summarized Ontario AEFI and CAEFISS data are made publicly available on a weekly basis to support transparency in this important aspect of program monitoring.

Adverse Events of Special Importance

To support the COVID-19 vaccine program, the Ontario AEFI reporting form[10] has been revised to include Adverse Events of Special Importance (AESI). AESIs are

events that have been recommended by the Brighton Collaboration through the Safety Platform for Emergency vACcines (SPEAC) Project, to be included in vaccine safety surveillance systems for COVID-19 vaccines. As part of passive surveillance (described above), healthcare providers HCPs and PHUs are requested to report these AESIs for COVID-19 vaccines, in addition to the standard list of AEFIs reportable for all vaccines.

Signal detection

One of the goals of passive vaccine safety surveillance is rapid detection of vaccine safety signals for further assessment and public health action. Signals can be detected through daily reviews of AEFI reports, routinely examined AEFI counts, trends in serious and unexpected reports, clustering of reports (e.g., by time, place, lot number, etc.) or an increase in number or reporting rate of AEFIs compared to historical baseline or background rates. Ontario's protocol for signal detection and response includes rapid communication with VVWG and PHAC to determine if any signal that may be suggested in Ontario is observed elsewhere in Canada. Vaccine safety signals can also be identified through information sharing by international partners. Ontario is currently conducting enhanced surveillance for thrombosis with thrombocytopenia syndrome (TTS) following adenoviral vector vaccines through an enhanced surveillance directive issued by Public Health Ontario to PHUs and in collaboration with other partners, such as Ontario's Science Advisory Table, who have issued briefs on Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) to support clinician recognition and reporting of this rare event as an AEFI.

Public Health Ontario is collaborating with investigators at ICES who have received funding from the Canadian Immunization Research Network (CIRN) to assess background rates of AEFIs and AESIs in collaboration with other provinces and territories. Having Ontario-specific background rates (i.e., the incidence of particular health events unrelated to vaccine) assists in comparing observed events following vaccination to expected events (i.e., the background rate) in the vaccinated population.

Active vaccine safety surveillance

Active vaccine safety surveillance refers to the process of actively soliciting information on side effects and adverse events from vaccine recipients or searching for adverse events in clinical or administrative records.

Canadian Vaccine Safety Network (CANVAS)

Ontario is conducting active vaccine safety surveillance for COVID-19 vaccines through the Canadian National Vaccine Safety Network (CANVAS). CANVAS has conducted active vaccine safety surveillance for new vaccines and seasonal influenza vaccine for many years.

Everyone vaccinated against COVID-19 in Ontario is asked whether they consent to receive email communications about research. Those who provide consent receive an email from COVax$_{ON}$ that provides a link to the CANVAS website (www.CANVAS-COVID.ca) where they can enrol in CANVAS's active vaccine surveillance program.

CANVAS participants receive an online survey after each vaccine dose and six months after the vaccination series is complete. The surveys gather demographic and health status information, as well as information on any symptoms following vaccination, work absenteeism, or medically attended events (e.g., outpatient or emergency department visits, hospitalization). CANVAS contacts participants who have a medically attended event for further assessment and reports medically attended AEFIs to PHO who refer the event to the appropriate PHU for further follow-up and reporting into the provincial passive surveillance system.

CANVAS shares their safety data regularly with vaccine stakeholders including PHO and the Ontario Ministry of Health, VVWG and NACI. Results are also shared with the public via the CANVAS website.

Immunization Monitoring Program Active (IMPACT)

IMPACT is a paediatric hospital-based national active surveillance network for adverse events following immunization and selected infectious diseases that are vaccine preventable. IMPACT will contribute to active vaccine safety surveillance

monitoring among children and adolescents as the age indications for current and future COVID-19 vaccines expand.

Vaccine safety investigations using administrative data

With the establishment of a single source of COVID-19 vaccine information, linkage of immunization records within $COVax_{ON}$ to Ontario's health administrative datasets will allow for complementary analytic approaches to assess vaccine safety in specific sub-populations who have been excluded from COVID-19 vaccine clinical trials (e.g., individuals who are pregnant, immunosuppressed). In addition, hypothesis driven studies can be undertaken with linked health administrative data using study designs such as the self-controlled case series design. In Ontario, these analyses will be led by ICES as part of a multi-provincial project also involving British Columbia, Alberta, Manitoba, and Quebec, and with funding support from CIRN and the Vaccine Surveillance Reference Group of the COVID-19 Immunity Task Force (CITF).

Specialist referral following AEFIs and Special Studies

Lastly, the Special Immunization Clinic Network (SIC), has recently expanded to include additional adult sites in Ontario. The SIC Network is a Canadian network of paediatric and adult infectious disease specialists and allergists with expertise in the assessment and management of patients who have experienced a complex AEFI. In addition to its role in the clinical assessment of individuals, investigators in the SIC network enroll patients following informed consent, in studies that aim to improve the understanding of complex AEFIs, including their risk of recurrence.

Program impact and vaccine effectiveness

Program impact

The overall population impact of the vaccine program on trends in cases and outbreaks and measures of clinical severity will be assessed. The impact of a vaccine program may benefit both vaccinated and unvaccinated individuals, due to indirect effects of vaccines, which will also be examined.

Assessments of program impact will include monitoring the incidence of COVID-19 cases, hospitalizations, and deaths over time, including among specific populations such as long-term care home residents. Ecological analyses comparing incidence in periods before and after vaccines were introduced will allow for an understanding of how effective vaccine programs are at reducing cases, outbreaks and severe outcomes at a population level. Understanding any indirect effects offered by vaccine may also be possible by comparing incidence in priority groups (i.e., age), to understand if vaccinating one group has effects beyond direct protection, such as reducing incidence across other groups as well.

Vaccine effectiveness

Vaccine clinical trials are conducted in defined populations and often exclude key populations such as those with immunosuppression, pregnant women and children. For COVID-19 vaccines, the pivotal trials examined a primary endpoint of virologically confirmed symptomatic disease within a relatively short follow-up period. In the setting of 'real world' program implementation which includes the immunization of some groups excluded from trials (i.e., LTC residents, immunosuppressed and pregnant individuals) and the incorporation of an extended second dose interval (with some exceptions), it is essential to evaluate the performance of COVID-19 vaccines as part of post-implementation surveillance.

Using linked data at ICES, Ontario will assess the effectiveness of COVID-19 vaccines against a range of outcomes and in subgroups of interest (e.g., age group, comorbidities). This work will estimate how effective vaccines are against laboratory PCR-confirmed COVID-19 infection (symptomatic and asymptomatic) and against measures of clinical severity such as hospitalization and death. Vaccine effectiveness (VE) assessments will also allow for an examination of the effectiveness following one and two vaccine doses, and examine VE against SARS-CoV-2 subtypes (i.e., variants of concern).

Virus characterization among cases with a vaccine history

Genomic surveillance and characterization of SARS-CoV-2 is being led by the Public Health Ontario Laboratory in partnership with other laboratory partners. These efforts include screening for mutations and utilization of whole genome sequencing, which allow for the identification of new and existing variants of concern (VOC) and mutations of interest for those who develop SARS-CoV-2 following COVID-19 vaccination.

Efforts to characterize the prevalence of circulating VOC and mutations of interest will allow for the estimation of VE against specific variants. Whole genome sequencing will help to identify cases of primary vaccine failure and vaccine escape, which may be a result of a mutation for which vaccines have reduced effectiveness.

Serosurveillance

Serosurveillance combines cross-sectional antibody assays with epidemiological analysis to understand the impact of public health interventions on population immunity. Serosurveillance is particularly important for evaluating the impact of vaccines on population-level immunity (i.e., herd immunity).[11]

During the first year of the COVID-19 pandemic, Public Health Ontario used serosurveillance to estimate the proportion of the population who had been infected with the SARS-CoV-2 virus and to identify population groups who had been most impacted. In the vaccine era, the utility of anonymized serosurveys is evolving, because data on vaccination status is important for serosurvey interpretation. As our data streams and understanding of the COVID-19 antibody response evolve, serosurveillance in the COVID-19 vaccine program era could aim to differentiate those with with SARS-CoV-2 antibodies due to infection, from those with antibodies from vaccination and in the longer-term, will be used to monitor the impact of the vaccination program on trends in population immunity, including antibody durability[12]. Work in this area will involve collaborations with both Canadian and international experts in serosurveillance.

Public confidence

Global attitudes towards COVID-19 vaccines have steadily improved since November 2020, with interest growing among Canadians.[13] Understanding attitudes and enablers of vaccine confidence is essential to support Canadians' decision-making in pursuit of the high vaccine uptake needed to achieve SARS-CoV-2 herd immunity.

Through the COVID-19 Health Behaviour Surveillance Study, the Ontario Ministry of Health is conducting sequential telephone and online surveys to understand Ontarians' views on COVID-19 public health measures, and to monitor confidence in the COVID-19 vaccination program. These data are central to discerning existing enablers and barriers to vaccine uptake in order to tailor program strategies and messaging accordingly.

Partnerships with community organizations and academic partners will accelerate the understanding of vaccine confidence in Ontario. One such example is the Behavioural Science Working Group (BSWG) of the Ontario COVID-19 Science Advisory Table, that brings together behavioural scientists and public health officials to synthesize available behavioural science evidence in the context of COVID-19 and COVID-19 vaccines and highlights how information can be actioned by public health organizations. The BSWG's first brief described which behavioural science principles can be used to support vaccine confidence and uptake in healthcare workers and how they can be operationalized.[14] This group is focussing their attention to increasing vaccine confidence and uptake in the general population in recognition of the vast and multidisciplinary nature of this work. In addition to vaccine confidence work at the provincial and national level, there are many initiatives led by PHUs and community partners to inform tailored strategies at the local level.

Conclusion

Ontario's COVID-19 vaccine surveillance plan provides a comprehensive framework to evaluate the delivery of the program and to better understand drivers of vaccine

confidence, to conduct ongoing safety monitoring of COVID-19 vaccines and to understand the impact of the vaccine program on trends in COVID-19 epidemiology. The outcomes and results of the surveillance plan's various domains will be made available through publicly available reports, dashboards, manuscripts and presentations, and will assist in providing in evidence for decision-making for both the vaccine program and public health measures in the longer-term.

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