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Summary of the National Advisory Committee on Immunization (NACI) Updated Guidance on Influenza Vaccination During Pregnancy

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Abstract

Background: Seasonal influenza infection can lead to serious complications and adverse outcomes for pregnant individuals, the developing fetus and infants younger than six months of age. This supplemental statement provides an evidence summary on the safety and effectiveness of influenza vaccination in pregnant individuals, and the benefits and risks to the pregnant person, the developing fetus and infants younger than six months of age.

Methods: A systematic review was conducted on the effectiveness and safety of influenza vaccination in pregnancy. The National Advisory Committee on Immunization (NACI)'s evidence-based process was used to assess the quality of eligible studies, summarize and analyze the findings, and apply an ethics, equity, feasibility and acceptability lens to develop recommendations.

Results: The evidence suggests that influenza vaccination during pregnancy is effective in reducing the risk of laboratory-confirmed influenza infection and hospitalization in both pregnant individuals and their infants up to six months postpartum. The evidence also suggests that influenza vaccination during pregnancy does not increase the risk of non-obstetric serious adverse events in pregnant persons, infant death, spontaneous abortion, stillbirth, preterm birth, small for gestational age, low birth weight and congenital anomalies.

Conclusion: Based on this body of evidence, NACI reaffirms the safety and importance of influenza vaccination during pregnancy. NACI recommends that individuals at any stage of pregnancy should receive an age-appropriate inactivated, unadjuvanted or recombinant influenza vaccine each influenza season. Influenza vaccination may be given at the same time as, or at any time before or after administration of another vaccine, including the coronavirus disease 2019 (COVID-19) or pertussis vaccines.

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Introduction

Pregnant individuals are at higher risk for severe influenza disease and related complications such as pneumonia, hospitalization and death, compared to non-pregnant individuals, because of pregnancy-related changes in anatomy and the immune and cardiovascular systems (1–3). Influenza infection during pregnancy can also impact the developing fetus and increase the risk of late-stage pregnancy loss, stillbirth, preterm birth and low birth weight (3,4). Furthermore, infants younger than six months of age are also at high risk for severe influenza disease and complications but are too young to be eligible for

influenza vaccination; however, passive transfer of antibodies from influenza vaccination during pregnancy can protect newborns during their first months of life. Therefore, the National Advisory Committee on Immunization (NACI) has identified pregnant individuals as a high-risk group for whom influenza immunization is particularly important, and strongly recommends immunizing pregnant persons against influenza to protect both them and their infants from severe disease. Despite pregnant people being prioritized to receive influenza vaccine, uptake remains lower than the non-pregnant population.

Literature continues to be published on influenza vaccination in pregnancy and NACI has taken this opportunity to review the safety, efficacy and effectiveness of influenza vaccines in pregnancy. NACI's *Updated Guidance on Influenza Vaccination During Pregnancy* statement (5) aims to synthesize key information and evidence to support provincial and territorial vaccine programs and frontline vaccinators in offering influenza vaccine to pregnant individuals. The statement supplements NACI's overarching recommendations for influenza vaccination, which are available in the NACI *Statement on Seasonal Influenza Vaccine for 2023–2024* (6).

Methods

The policy question addressed in this statement is: Should pregnant individuals, at any stage of pregnancy, continue to be listed among those who are particularly recommended to receive influenza vaccination? To address this question, a *de novo* systematic review was conducted to gather evidence to inform NACI's recommendations regarding the use of influenza vaccines during pregnancy. The methodology was specified *a priori* in a published protocol (7). For a comprehensive description of the review methods, including details on the study eligibility, literature search, study selection, data collection and statistical methods, please refer to Wolfe *et al.* (7). The review protocol and knowledge synthesis were developed and performed in collaboration with the Methods and Applications Group for Indirect Comparisons through the Drug Safety and Effectiveness Network (DSEN) and supervised by the NACI Influenza Working Group. An update to the literature search was completed by the NACI Secretariat in conjunction with a librarian from the Health Library of Health Canada and the Public Health Agency of Canada (PHAC). Methods related to the review update completed by the NACI Secretariat are reported in Appendix A of the supplemental statement. A health economic analysis was not conducted as it was not deemed necessary for this statement. In addition to critically appraising evidence on burden of disease and vaccine characteristics such as safety, efficacy, immunogenicity and effectiveness, NACI applied the Ethics, Equity, Feasibility, and Acceptability (EEFA) Framework with accompanying evidence-informed tools (Ethics Integrated Filters, Equity Matrix, Feasibility Matrix, Acceptability Matrix) to systematically consider these programmatic factors for the development recommendations (8). The NACI evidence-based process was used to assess the available evidence and develop updated recommendations.

Results

Vaccine efficacy/effectiveness

The DSEN systematic review assessed the effect of seasonal influenza vaccination during pregnancy against influenza-related infection and hospitalization in pregnant persons and/or their infants using findings from four randomized controlled trials (RCTs) (9–12) and two observational studies (13,14). Additional observational studies (n=6) were identified from the updated literature search, reporting data on influenza vaccine effectiveness in pregnant persons and/or their infants up to six months of age (15–20).

Benefits to the pregnant person: Vaccine efficacy/effectiveness

Overall, four studies reported data on laboratory-confirmed influenza (LCI) infection and three reported data on hospitalization due to LCI infection during pregnancy or up to six months post-partum.

A meta-analysis of the three RCTs suggested that seasonal influenza vaccination during pregnancy reduces the risk of LCI infection in pregnant persons prior to delivery and up to six months postpartum (pooled vaccine effectiveness [VE]=50%; 95% CI: 22–68, I^2=49%). One prospective cohort study conducted during the 2019–2020 influenza season in Greece also found a protective effect of seasonal IIV4 (quadrivalent inactivated influenza vaccine, IIV) against LCI infection in pregnant persons (adjusted vaccine effectiveness [aVE]=44%; 95% CI: 28–56) (15).

A meta-analysis of two test-negative studies suggested that seasonal influenza vaccination during pregnancy reduces the risk of hospitalization due to lab-confirmed influenza in pregnant persons prior to delivery and up to 42 days postpartum (pooled aVE=42%; 95% CI: 19–58, I^2=0%) (13,16).

One prospective cohort study reported vaccine effectiveness of 38% (95% CI: 14–55) against LCI hospitalization during pregnancy or up to two days after delivery (17).

Benefits to the infant: Vaccine efficacy/effectiveness

Overall, seven studies reported data on the effectiveness of influenza vaccination during pregnancy on infant LCI infection and five studies reported data on hospitalization due to LCI infection in infants up to six months of age.

A meta-analysis of the four RCTs demonstrated a protective effect of seasonal influenza vaccination during pregnancy against LCI in infants up to six months of age (pooled VE=37%; 95% CI: 22–49, I^2=0%) (9,11,12,21). Results from the RCTs suggest that the greatest effect of seasonal influenza vaccination during pregnancy against LCI infection in infants was found from birth up to two months of age (pooled $VE_{0 \text{ to } <2 \text{ months}}$=61%; 95% CI: 17–81, I^2=40%), following which the protective effect of vaccination during pregnancy waned as infant age increased (pooled $VE_{2 \text{ to } <4 \text{ months}}$=42%; 95% CI: −13–70, I^2=60%, and pooled $VE_{4 \text{ to } <6 \text{ months}}$=24%; 95% CI: −3–44, I^2=0%).

A meta-analysis of the three cohort studies demonstrated a protective effect of seasonal influenza vaccination during pregnancy against LCI infection in infants up to six months of age (pooled aVE=41%; 95% CI: 23–55, I^2=17%) (15,18,19).

A meta-analysis of the three test-negative studies demonstrated a protective effect of seasonal influenza vaccination during pregnancy against hospitalization due to LCI infection in infants up to six months of age (pooled aVE=42%; 95% CI: 16–59, I^2=71%) (14,16,20). Two cohort studies reported data on hospitalization due to LCI infection in infants up to six months of age, but only one demonstrated a significant protective effect of influenza vaccination during pregnancy (aVE=62%; 95% CI: 9–84 (18), and 21%; 95% CI: −18–47 (19)).

Vaccine safety

The DSEN systematic review on the safety of influenza vaccination during pregnancy evaluated non-obstetric serious adverse events (AE) in pregnant persons related to the administration of seasonal influenza vaccination during pregnancy using findings from three RCTs and three cohort studies. Additionally, the systematic review included four RCTs and 24 observational studies, including 20 cohort and four case-control studies, addressing other safety and/or pregnancy/birth related outcomes (i.e., infant death, spontaneous abortion [SAB], stillbirth, preterm birth, small for gestational age, low birth weight and congenital anomalies). Eleven additional observational studies were identified from the updated literature search.

Harms to the pregnant person

Two RCTs evaluated the risk of severe systemic reactions within seven days of seasonal influenza vaccination in pregnant people. No significant difference in the frequency of severe systemic reactions within seven days of seasonal influenza vaccination was observed within each individual study (RR 1.35; 95% CI: 0.78–2.34 (10), and RR 4.95; 95% CI: 0.24–102.95 (11)). The studies found either no difference in the occurrence of serious non-obstetric AEs, no AEs related to vaccination or no serious AEs. Finally, one cohort study and one case-series reported data on Guillain-Barré syndrome (GBS) following seasonal influenza vaccination during pregnancy. The cohort study identified no cases of GBS within 42 days of intervention in 75,906 vaccinated pregnant persons and one case in 147,992 unvaccinated pregnant persons in the United States (RR 0.65; 95% CI: 0.03–15.95) (22). The case series identified from the updated literature search reported one case (n=239) of GBS that occurred five days after IIV4 administration during the third trimester of pregnancy in a 29-year-old woman. The woman gave birth to a healthy baby while recovering and has fully recovered (23).

Harms to the infant

Four RCTs compared the effect of seasonal influenza vaccination to placebo (n=2) (9,10) or active comparators (n=2; meningococcal quadrivalent vaccine (11) or 23-valent pneumococcal vaccine (12)) during pregnancy on infant death up to six months of age. All RCTs were conducted in low-to-middle-income countries, and the control group infant death risk ranged from 1.1% to 2.8%. A meta-analysis of these RCTs did not demonstrate an association between seasonal influenza vaccination during pregnancy and infant death (pooled RR 1.14; 95% CI: 0.86–1.50, I^2=9%). Furthermore, no infant death was reported from a prospective cohort study conducted in Japan among infants diagnosed with fever from zero to six months of age born from vaccinated and unvaccinated pregnant people (n=0/36 IIV and n=0/47 unvaccinated) (24).

Three cohort studies and three observational studies evaluated the effect of IIV during pregnancy on SAB at less than 20 and 22 weeks gestational age. Two prospective cohort studies were included in a meta-analysis and no association between IIV and SAB was demonstrated (pooled aHR 0.77; 95% CI: 0.31–1.89, I^2=38%) (25,26). A third prospective cohort study found the same risk of SAB at less than 22 gestational weeks (0.4%) among unvaccinated and vaccinated pregnant people (first-trimester vaccination) (27).

Two retrospective case-control studies conducted by the same set of investigators in the United States assessed the association between SAB and vaccination within 28 days prior to SAB. The first study was conducted over two consecutive influenza seasons following the 2009 H1N1 pandemic (28). The authors observed an increased risk of SAB following IIV only in the first post-pandemic season (2010–2011 aOR 3.70; 95% CI: 1.40–9.40) but not the second (2011–2012 aOR 1.40; 95% CI: 0.60–3.30). *Post hoc* analyses of 2010–2011 data found that people who had been previously vaccinated in the 2009–2010 season with the H1N1 pandemic vaccine were at increased risk of SAB following IIV in the 2010–2011 season, which was not observed in those not vaccinated with the H1N1 pandemic vaccination in 2009–2010 but vaccination with IIV in 2010–2011.

The second study conducted over three consecutive influenza seasons (i.e., 2012–2013, 2013–2014 and 2014–2015) by Donahue *et al*. sought to confirm the association observed between SAB and history of influenza vaccination (29). No association was found between seasonal influenza vaccination during pregnancy and SAB within 28 days of vaccination

(aOR 0.80; 95% CI: 0.60–1.10), including among people vaccinated in the previous season. The authors state that the association of prior season vaccination found in the initial study may have been a spurious result due to residual confounding or random error, or it may have been due to differences in the time periods of the two studies. One cohort study identified from the updated literature search conducted in the United States over the 2008–2009 to 2013–2014 influenza seasons did not find an association between the history of pandemic H1N1-containing influenza vaccination and SAB within 28 days of vaccination (aHR 1.19; 95% CI: 0.97–1.46) (30).

An additional three single-arm cohort studies (31–33) and one case series (23) identified from the updated literature search reported data on SAB in persons vaccinated with IIV during pregnancy. Overall, from the three single-arm cohort studies and the case series study, no safety signals were identified among pregnant persons exposed to IIV.

No safety issues were identified regarding the administration of seasonal influenza vaccines during pregnancy, with respect to other adverse birth outcomes including stillbirth (18–22 gestational weeks or at least 500 g), preterm birth, small for gestational age birth, low birth weight and congenital anomalies identified at birth or up to six months of age. Evidence was derived from both RCTs and observational studies, including case-control studies and cohort studies.

Ethics, equity, feasibility and acceptability considerations

There were no distinct significant ethics or equity issues identified. Recommendations that allow vaccination at all gestational stages of pregnancy would reduce feasibility barriers in vaccination programs. Low vaccine uptake in pregnant individuals has been partly attributed to vaccine hesitancy, which is complex and multidimensional and can be influenced by individual, logistical, cultural and sociologic factors. A recommendation from a healthcare provider is the most important factor when deciding to be vaccinated; therefore, ensuring providers are well-informed of the most recent evidence and can communicate the importance of seasonal influenza vaccination during pregnancy is important for improving vaccine uptake.

Recommendations

1. NACI recommends that influenza vaccine should be offered to pregnant individuals. Recommended products include: IIV-SD, IIV-cc and RIV. (*Strong NACI Recommendation*)

- There has been no identified safety signal regarding the use of RIV during pregnancy, although published clinical data are limited.
- There has been no identified safety signal regarding the use of LAIV in pregnancy, although there are more data on the safety of other influenza vaccine products in pregnancy. There is also evidence that IIV has higher efficacy than LAIV in healthy adults. Note that vaccination with LAIV during pregnancy should not be considered a reason to terminate pregnancy.
- The only adjuvanted vaccine in Canada for the 2023/2024 influenza season is IIV3-Adj, which is authorized for infants 6 to 23 months (Fluad Pediatric®) and adults 65 years and older (Fluad®). There has been no identified safety signal regarding adjuvanted influenza vaccines in pregnancy; however, IIV3-Adj is not authorized for people of reproductive age.
- The only high-dose vaccine in Canada for the 2023/2024 influenza season is IIV4-HD (Fluzone® High-Dose Quadrivalent) which is authorized for adults 65 years and older. There has been no identified safety signal regarding high-dose influenza vaccines in pregnancy, however, IIV4-HD is not authorized for people of reproductive age.

2. NACI recommends that influenza vaccination should be offered at any stage of pregnancy (i.e., in any trimester). (*Strong NACI recommendation*)

- If an individual's pregnancy extends over two influenza seasons, that person may receive two doses of influenza vaccine (i.e., one dose in each season during the course of the pregnancy).

3. NACI recommends the inclusion of all pregnant individuals, at any stage of pregnancy, among those who are particularly recommended to receive influenza vaccination. (*Strong NACI recommendation*)

4. NACI reiterates its recommendation that influenza vaccination may be given at the same time as, or at any time before or after administration of another vaccine, including COVID-19 or pertussis vaccine. (*Strong NACI recommendation*)

- Every appropriate opportunity to immunize during pregnancy, with any immunization for which the pregnant person is eligible, should be taken.

A complete review of evidence and full NACI recommendations are published in the new NACI statement: *Updated Guidance on Influenza Vaccination During Pregnancy* (5).

Conclusion

Pregnant people and their fetuses and infants are at high risk of complications from influenza. The systematic review and meta-analysis conducted for this supplemental statement

examined current literature on the use of influenza vaccines during pregnancy. NACI concluded that the evidence continues to support the safety and effectiveness of influenza vaccination during pregnancy and recommends the use of either inactivated or recombinant influenza vaccines. Influenza vaccination reduces the risk of influenza and has no identified link to negative outcomes in pregnant individuals or their infants. NACI is committed to following vaccine safety information and efficacy/effectiveness data for pregnant individuals as they evolve and will update guidance as needed.

Authors' statement

WS — Writing, original draft, review, editing
AS — Writing, review, editing
JP — Review, editing

The NACI statement *Updated Guidance on Influenza Vaccination During Pregnancy* was prepared by P Doyon-Plourde, A Sinilaite, W Siu and J Papenburg, on behalf of the NACI Influenza Working Group, and was approved by NACI.

Competing interests

J Papenburg reports grants to his institution from MedImmune and Merck, and personal fees from AstraZeneca and Merck, all of which were outside of the submitted work.

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Innovations in public health surveillance: An overview of novel use of data and analytic methods

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Abstract

Innovative data sources and methods for public health surveillance (PHS) have evolved rapidly over the past 10 years, suggesting the need for a closer look at the scientific maturity, feasibility, and utility of use in real-world situations. This article provides an overview of recent innovations in PHS, including data from social media, internet search engines, the Internet of Things (IoT), wastewater surveillance, participatory surveillance, artificial intelligence (AI), and nowcasting.

Examples identified suggest that novel data sources and analytic methods have the potential to strengthen PHS by improving disease estimates, promoting early warning for disease outbreaks, and generating additional and/or more timely information for public health action. For example, wastewater surveillance has re-emerged as a practical tool for early detection of the coronavirus disease 2019 (COVID-19) and other pathogens, and AI is increasingly used to process large amounts of digital data. Challenges to implementing novel methods include lack of scientific maturity, limited examples of implementation in real-world public health settings, privacy and security risks, and health equity implications. Improving data governance, developing clear policies for the use of AI technologies, and public health workforce development are important next steps towards advancing the use of innovation in PHS.

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Introduction

Public health surveillance (PHS) is the ongoing, systematic collection, analysis, and interpretation of data, followed by the dissemination of information, for the purpose of guiding actions to prevent and control diseases or improve population health (1–3). Traditionally, PHS was conducted with a limited number of data sources from public health information systems, health care, and laboratory information systems, as well as questionnaire-based surveys, which often require substantial resources and time to process, analyze, and disseminate.

The digitization of health care and other sectors has reduced the time lag, cost and burden associated with conducting PHS, and enabled exploration of other sources of data to augment traditional sources (4). In addition, artificial intelligence (AI) has seen major advances over the past decade. Artificial intelligence-enabled methodologies that efficiently process large amounts of structured and unstructured data are increasingly used in PHS (5–7).

Many of these data sources and AI methods were used during the coronavirus disease 2019 (COVID-19) pandemic, where timely and complete information was crucial to understanding and responding to evolving pandemic risks (4). The rapid development of these innovative surveillance methods and use of novel data sources suggests the need to take a closer look at the scientific maturity, as well as the feasibility and utility of their use, in real-world applications (5,6,8). The objective of this paper is to highlight examples of the application of innovative methods

to PHS and provide insights for public health authorities on the potential benefits, risks, and challenges of using non-traditional data sources and methods in PHS.

This article provides an overview of PHS innovations in data and analytic methods published in the past five years, including any evidence of their application to real-world settings, ethical issues, and known health equity implications. Each innovation is described, including its level of scientific maturity and, where available, any evidence of its impact on surveillance practice or public health action. The results section starts by exploring novel data sources that have been applied to PHS, highlighting successful examples of their application to provide timely, accurate and reliable information to support public health action. It then focuses on innovative methods that have been developed to analyze surveillance data, including the development of AI to support the integration and analysis of large and/or non-traditional data sources and the application of advanced analytic methods to improve nowcasting of information.

Methods

Approach

This overview defines the term "innovative surveillance" broadly as the use of non-traditional data sources and/or analytic methods to detect and understand health events and determinants. The primary focus was on data sources and analytic methods; this overview does not provide detailed discussion of other components of the surveillance process (e.g., dissemination or evaluation strategies).

Relevant topic areas were identified for inclusion in this article by searching PubMed, Embase, Global Health, and Scopus in the spring of 2023. A detailed search strategy, developed with the support of a librarian, was restricted to peer reviewed articles published between January 1, 2013, and February 23, 2023, from member countries of the Organisation for Economic Co-operation and Development (OECD) and China, in English language only. Hand searching provided additional sources.

Results of the literature search were screened for relevance via title and abstract search and grouped into topic areas. Final selection of articles within each topic area was restricted to the past five years (January 1, 2018, to February 23, 2023) to ensure that articles were more reflective of current technological and methodological innovations. As the search yielded a large number of articles on analytic methods, decisions were made by the research team to exclude certain broad analytic topic areas (such as innovations in biostatistics, laboratory, or geospatial analytic methods), and focus on nowcasting and artificial intelligence, two areas that have been adopted by public health from other disciplines.

The authors focused this overview on a subset of articles that met the definition of "innovative surveillance", discussed steps taken to evaluate or validate the method or data source(s), described potential or actual improvements to the PHS system, and, where possible, showed application to real-world public health practice.

Results

Novel data sources and their applications

Overview of novel data sources

The rise of digital technologies has made new data sources available for disease surveillance. Commonly used digital data sources include social media and aggregate search query data, where initial surveillance applications date from the early 2000s, as well as participatory surveillance methods, such as repeated cross-sectional online surveys and crowdsourcing of photos or sample submissions (9). More recently, PHS applications of other digital technologies are being explored, such as mobility data and the Internet of Things (IoT), which includes wearable devices and other physical objects that connect and exchange data via the Internet (8). Digital data sources may have the potential to provide more timely information and capture populations that may not seek health care; although possible to use as an independent source of information, they are generally considered to be complementary to traditional surveillance data (9).

Social media and web-search data

Social media (e.g., Twitter/X) and web search (e.g., Google Trends) data have been used to support disease surveillance as a source of data for nowcasting, situational awareness, and outbreak detection (9). A recent systematic review focusing on communicable disease surveillance noted that the majority of included studies used data from Twitter/X, and that studies that used Twitter/X data showed higher overall reliability and validity than studies using data from other social media platforms (10). The review also noted that the majority of studies focused on influenza surveillance, and that additional research was needed to assess the effectiveness of social media for other disease areas (10). Other examples of the use of social media and/or web search data included retrospective analyses to evaluate the potential of these sources to predict cases of sexually transmitted and blood-borne infections (STBBIs) (11), prioritizing restaurant inspections based on foodborne outbreak information (12), drug utilization estimates (13), and early warning systems for e-cigarette/vaping-related lung injuries (14) and COVID-19 outbreaks (15).

One of the challenges with the use of digital media is the need to collect and process large quantities of information, either through manual monitoring or automation (16). The European Centre for Disease Prevention and Control (ECDC) released epitweetr, an R-based software library that collects, aggregates, detects, and disseminates information for early detection of public health threats using Twitter/X. An evaluation of the tool noted greater timeliness when compared to manual review (16). Artificial intelligence methods such as natural language processing, described later in this paper, are also increasingly being used to process and analyze digital information sources.

While the utility of social media and web search data for disease surveillance has been explored for nearly two decades, the validity, reliability, and stability of these data continue to present challenges to developing standardized approaches to using this information (9). For example, changes to the query algorithms of search engines, the use of different language styles, confounding search terms, and demographic biases in terms of who uses digital technologies, may impact the quality of information from these sources for PHS (9,17). A recent systematic scoping review also noted that most studies on digital surveillance did not utilize their results for public health action, and that more rigorous methods were needed to operationalize this information for public health decision-making (17). Surveillance platforms that combine social media, web search, and healthcare data may improve the accuracy of results (9,18).

Participatory surveillance data

Participatory surveillance involves the voluntary recruitment and engagement of members of the public to participate in repeated surveys or other crowdsourcing methods (9). This approach is sometimes used as an augment to traditional disease surveillance, to capture information in a timelier way, and to capture populations that may not seek health care for testing and diagnosis (8). Examples include Flu Near You in the United States, InfluenzaNet in Europe (9), and FluWatchers in Canada (19). Community surveillance using self-collected specimens has also been implemented and has enabled rapid assessment of community-level burden of influenza (20). Additionally, studies have explored participatory syndromic surveillance using social media and newspaper reports as a source of information during the COVID-19 pandemic that may be timelier and more accessible than official public health case reports (21,22).

Outside of respiratory pathogens, recent studies suggest current use of participatory approaches to support surveillance of potential disease carrying vectors or vector-borne disease. For example, platforms such as iNaturalist, eTick.ca, and Mosquito Alert use crowdsourced photos to identify the distribution and seasonal trends of specific species of ticks and mosquitos (23–26), and initiatives such as tickMAP in New York state used community-submitted tick specimens to track the emergence of tick-borne pathogens in near real time (27).

Participatory surveillance may be applied in a way that enables participation from equity-deserving populations that may otherwise be excluded from traditional surveillance systems. For example, in a rural Appalachian community, participatory surveillance via an online or phone-based symptom self-checking tool was used to identify at-risk individuals who may otherwise have not sought health care and link them to resources from the local health department (28). However, certain populations may be less likely to participate in participatory surveillance, including males, younger and older age groups (29), and those with lower income and education (9). This may introduce bias and potential health equity issues, particularly if groups that are more likely to experience illness are excluded.

New digital data sources

The use of digital data sources, such as mobile technologies, IoT and wearables, represent emerging areas for further exploration. For example, mobility data was used to explore the impact of COVID-19 and government policy on travel patterns. Health inequities were also noted, as socially disadvantaged populations were often unable to benefit from stay-at-home orders (30,31).

Wearable devices, such as smartwatches, have been used to collect individual-level data on variables linked to viral infection, such as resting heart rate, sleep, and mobility (32,33). As an example, a study noted that wearable technologies may improve nowcasting of influenza-like illness (ILI) rates in the United States (33). Various applications of IoT have emerged in the past few years. In one study, researchers placed thermal sensors and microphones in hospital waiting rooms to monitor coughing, which was then used to support ILI surveillance (34).

New digital data sources from mobility, wearables, and IoT represent an emerging field that requires greater evaluation and assessment (8,32), including careful consideration of privacy and ethical concerns (35). Like other digital data sources, these sources involve self-selected populations and exclude groups who do not have access to digital technologies. Privacy issues have also emerged with the use of new digital technologies and social media data; data ownership and the right to share data and use the data for secondary purposes may differ among the public sector (e.g., government), private sector (e.g., Twitter/X), and geopolitical jurisdictions (9,25). The need for upgraded infrastructure and investment to support the integration and analysis of information generated from new technologies may also present substantial barriers (8,36).

Wastewater

Wastewater surveillance (WWS) has evolved as a data source that now supports global surveillance of infectious diseases in a manner that is independent of health-seeking behaviour and healthcare system access (37,38). When coupled with small area socio-demographic data, WWS has the potential to forewarn and confirm clinical trends, address health inequities, fill reporting gaps due to waning clinical testing, and provide purpose-built

sentinel surveillance of communities with higher-risk profiles for specific pathogens (38–42). The deluge of WWS data during the COVID-19 pandemic led to novel analytic methods to help inform public health action. These include sophisticated machine learning algorithms that were applied to estimate sewage flow rates to allow for data normalization (43), and the application of simple statistical methods that were then tested to identify early warning signals in a user-friendly manner (44,45). New methods developed for WWS during the pandemic were validated by comparing wastewater signals to clinical case data and COVID-like illness syndromic data (38,40,41,45,46). Innovations in WWS have also benefited from other novel data linkages. In a recent study in Iceland, wastewater signals were compared with driving under the influence records to help distinguish trends of recreational drug use from increased drug dependencies, the latter of which may require enhanced public health action (47).

Wastewater surveillance of COVID-19, other infectious pathogens, and illicit substances, has identified limitations of this approach including the inability to distinguish reasons for signal increases/decreases, the degradation of the pathogen/substance in the wastewater before testing is performed, changing population denominators, and non-standardized sampling methods (47–49). Wastewater surveillance is also limited by the epidemiological indicators it can provide (i.e., incidence and prevalence) and the population it can monitor (e.g., includes only those in the sewer shed of a wastewater treatment facility) from the WWS data alone (45–49).

Innovative analytic methods

Artificial intelligence

Artificial intelligence, which includes natural language processing (NLP), machine learning, and deep learning, can integrate, process, and interpret multiple sources of information more efficiently and more consistently than humans (50). The recent growth in the use of AI-based technologies that can process unstructured text data has enabled the use of novel data sources, including those discussed in the previous sections, to be leveraged more effectively (7). Artificial intelligence has enormous potential to improve PHS, as it is capable of processing large amounts of data to identify anomalies that may pose a threat to public health (7), however, it is still an emerging field in which more real-world evaluations are needed. Some of the published innovations using AI for PHS still reside within academic collaborations. One such study from the Yale School of Medicine used NLP, which applies AI methods to the interpretation of human language, to provide real-time monitoring of population health by identifying symptoms mentioned on social media platforms (51).

Machine learning identifies complex patterns in data for classification and prediction (50). In New York City (NYC), machine learning, in combination with NLP, was tested to improve "pre-syndromic surveillance", which seeks to identify rare or previously unseen threats to health from clinical information (52). In this study, multidimensional semantic scan (MUSES) is a machine learning and NLP-based method developed to improve early detection of illness by eliminating the need for predefined case definitions and automatically clustering information by small geographies and/or demographics. MUSES was applied to historical free-text complaint data from NYC emergency departments and was found to identify more events of public health interest and a lower false positive rate than the current approaches used by the New York City Department of Health and Mental Hygiene (52). Natural language processing-based PHS has also been tested to improve the timeliness of overdose mortality reporting by eliminating the need for manual coding of free-text death certificates (53). The above examples show the potential of AI in PHS, but it remains unclear how many AI methods have been implemented into PHS. One real-world application by the Department of Veterans Affairs in the United States showed successful adaptation of an existing NLP-based PHS method early in the COVID-19 pandemic to monitor travel history in clinical records for public health follow-up (54).

Deep learning is a specialized type of machine learning that incorporates sophisticated neural networks that support classification using large amounts of text and are designed to work in a manner similar to a human brain. It has been increasingly used to support disease surveillance (7,55). The Centers for Disease Control and Prevention (CDC) tested neural networks and found that deep learning can interpret physician records to accurately predict the chief complaint, and potentially improve the timeliness and accuracy of information available for syndromic surveillance (56). Deep learning has also been applied to internet-based surveillance systems to support early warning, situational awareness, and nowcasting of infectious diseases. For example, Sentinel, an American surveillance system, uses deep learning to identify and classify health-related social media posts, news media, and CDC data to detect possible outbreaks and provide situational awareness (55).

The use of AI to support PHS is a new and emerging field that still needs evaluation of implementation into existing public health systems. Algorithms and machine learning models built with inaccurate, incomplete, or unrepresentative datasets, may both limit the accuracy of AI-based methods as well as bias results based on race, gender, or other characteristics (50,57). It is important to ensure that there is transparency in how AI models are built so that results are explainable, and that those who are interpreting the outputs of AI analyses are adequately skilled in PHS and can apply appropriate judgment. It is also important for public health professionals to understand AI methods, their applications, and their risks before applying it to public health practice (57).

Nowcasting

Nowcasting uses recent surveillance data to model the current situation (e.g., case counts) when real-time data are unavailable (58). In one study, nowcasting using a Bayesian approach accurately estimated COVID-19 rates to inform resource allocation in NYC, successfully overcoming delays between testing and reporting (59). Advances in nowcasting have also been adopted in One Health surveillance systems to help fill data gaps and help anticipate zoonotic outbreaks. For example, the Norwegian Institute of Public Health successfully applied nowcasting principals to respond to gastrointestinal illness outbreaks using *Campylobacter* testing data from poultry farms and meteorological data (60). While nowcasting can be useful to estimate current situational awareness during rapidly changing public health emergencies, it is limited by the quality of data and the clarity of the interpretations provided to decision makers (59,61).

Discussion

This review has explored innovations in PHS over the past decade and, where possible, described examples of their applications to PHS programs. Examples of the use of these novel sources to support PHS include providing novel information that improves estimates of disease, promoting early warning and identification of potential threats to health, and generating new information for public health action.

Despite these opportunities, there are substantial challenges to integrating innovations in PHS into practice. As new data sources and methods are added to the PHS toolbox, their risks and benefits should be considered with the goal of improving overall population health. Most of the areas explored in this paper are lacking in scientific maturity, and in many cases, are so novel that standard methods and best practices do not yet exist to help advance these fields reliably and responsibly (49,50,57). Many of the novel methods identified in this paper were tested in academic environments with no clear real-life implementation strategy (51,55). More evaluations of these interventions in real-world settings, which assess their utility in improving PHS and implications for public health action, are needed. These evaluations could be used to develop and disseminate guidance and standardized approaches to support public health organizations in implementing novel methods.

The use of digital technologies and AI in PHS also introduces challenges for privacy and security, data governance, and ethical considerations. For example, there is a need to balance between the benefits of having large quantities of granular information for analysis and the need to ensure individuals cannot be (re)identified. This is particularly true with AI methods, given the large quantity of information that is usually required to train the model (54,57,62,63). In the case of digital data, which may be publicly available, but where permission to use for surveillance purposes has not been acquired, it is not clear how/whether informed consent can or needs to be obtained. Particular care needs to be taken to ensure that data are anonymized and confidential information is not revealed (63). Protection of digital data and transparency in how and what data is acquired, stored, and used are key to maintaining public trust and ensuring the sustainability of these systems (57,64), and thus progress towards digital data governance is needed to fully operationalize these data sources. Ethical frameworks for the use of AI and social media data in research (63), and guidelines for the use of AI more broadly (65–67), have been developed to support responsible conduct and protection of individuals from whom data is collected.

Health equity is an important consideration in implementing new surveillance methods. This overview identified several examples of approaches that could be used to support health equity, as they include populations that may be missed in traditional surveillance. However, a recent review article noted that there were no studies that specifically focused on vulnerable populations in the use of digital PHS, and thus substantial work is needed to explore the health equity implications of its use (17). Furthermore, greater work is needed to explore, identify, and address biases in AI algorithms and in the data used to train AI algorithms to ensure that these methods are not perpetuating harmful outputs as a consequence of biased inputs (57).

Limitations

Limitations of this overview should be noted. This article was intended to provide a snapshot of recent innovations in PHS and explore examples of real-world application. As such, it is not intended to be an exhaustive list, and cannot provide detailed appraisal of the effectiveness of these innovations. The article focused on peer-reviewed literature only, and thus may have omitted articles from applied public health settings that were published as grey literature. The use of peer-reviewed literature may also have produced a positive publication bias, with studies noting negative results or unintended consequences potentially being under-represented. This is an important consideration given that non-traditional data sources may also be a source of public health misinformation (68), and thus require careful consideration and evaluation prior to use.

Conclusion

Novel data and methods for PHS have the potential to improve the quantity, accuracy, completeness, timeliness, and accessibility of information available for public health response; however, the evidence base to support their utility in the real-world, as opposed to academic, settings appears to be lacking. Substantial barriers prevent the implementation of novel data and methods in PHS, ranging from health equity, privacy, and ethical concerns to training and availability of data and technologies. Improving data governance mechanisms, developing clear policies

for ethical use of AI technologies in PHS, and training the public health workforce on the responsible use of innovative technologies are important next steps towards advancing greater use of novel methods and data sources.

Authors' statement

HR — Formal analysis, data analysis, writing–original draft, writing–review & editing
SS — Formal analysis, data analysis, writing–original draft, writing–review & editing
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Competing interests

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Commentary on the adoption of a test-based versus syndromic-based approach to outbreak declaration and management in hospital and institutional settings

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Abstract

At present, Ontario, like most other jurisdictions in Canada, uses a syndromic-based surveillance definition for acute respiratory infection (ARI) outbreaks in institutions and public hospitals. Confirmed outbreaks are defined as either two or more ARIs in 48 hours with any common epidemiological link and at least one that is laboratory-confirmed; or three cases of ARIs occurring within 48 hours with any common epidemiological link, and not necessarily with lab confirmation. However, with the adoption of broader test-based approaches for sick patients/residents throughout the pandemic, new challenges have surfaced regarding the declaration and management of ARI outbreaks with a variety of scenarios in respiratory testing results. Decisions, including the determination of epidemiological linkage when there are discordant/negative test results, have become more complicated with the addition of virus-specific test results for every sick individual. The ARI outbreak case definition and management guidance was updated in 2018. The purpose of this commentary is to highlight epidemiological trends in ARI outbreaks in Ontario over the 2022–2023 season compared to the 2018–2019 and 2019–2020 pre-pandemic seasons. This is followed by a discussion around some of the benefits and challenges of implementing a test-based versus syndromic-based approach to ARI outbreaks.

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Introduction

Respiratory infection (RI) outbreaks in hospitals and congregate care settings are common and can have serious implications (1,2). Impacts include increased morbidity and mortality, stresses on human health resources, psychological effects of isolation on patients/residents and their families, as well as higher healthcare costs. Not surprisingly, these factors can place a significant burden on an already strained healthcare system (1). Effective outbreak identification and management is essential to keep residents and staff safe while maintaining quality of life.

At present, Ontario, like most other jurisdictions in Canada, uses a syndromic-based surveillance definition for RI outbreaks in institutions and public hospitals (3–6). Confirmed outbreaks are defined as either two or more acute respiratory infections (ARIs) within 48 hours with any common epidemiological link and at least one that is laboratory-confirmed; or three cases of ARI occurring within 48 hours with any common epidemiological link, and not necessarily with lab confirmation (3). However, with the adoption of broader test-based approaches for sick patients/residents throughout the pandemic, new challenges have surfaced regarding the declaration and management of RI outbreaks with a variety of scenarios in respiratory testing results. Decisions, including the determination of epidemiological linkage when there are discordant/negative test results, outbreak attribution of cases, and declaring multiple concurrent outbreaks have become more complicated with the addition of virus-specific test results for every sick individual. The RI outbreak case definition and management guidance was updated in 2018.

The purpose of this commentary is to highlight epidemiological trends in RI outbreaks in Ontario over the 2022–2023 season compared to the 2018–2019 and 2019–2020 pre-pandemic seasons. This is followed by a discussion of issues and gaps in current outbreak management, with particular attention to considerations for syndromic-based versus test-based approaches to declaring and managing RI outbreaks in hospitals as well as congregate settings, specifically long-term care and retirement homes.

Results

Changes in the 2022–2023 season

There were a number of significant changes to the prevention, declaration, and management of institutional outbreaks throughout the coronavirus disease 2019 (COVID-19) pandemic. These include, among others: enhanced infection prevention and control (IPAC) measures (e.g., universal masking, increased use of alcohol-based hand rub); potential supports available from specialists in infectious diseases, medical microbiology, public health, and IPAC; regular and more frequent testing of staff; extended testing capacity through increased laboratory hours and personnel; and an increase in multi-pathogen testing in 2022–2023, as well as the routine use of rapid antigen tests (RATs) for COVID-19 (7,8). Taken together, these procedures and protocols may have impacted the overall size, attack rate, duration and/or frequency of RI outbreaks (7).

Of particular interest, an updated approach to testing likely had a significant contribution to the observed trends in mixed and unknown pathogen outbreaks. Historically, only the first four residents with ARI were eligible for multiplex respiratory virus PCR (MRVP) testing by Public Health Ontario's laboratory, with no routine testing on subsequently sick residents for that outbreak. However, throughout the COVID-19 pandemic, the province implemented routine COVID-19 testing for all symptomatic residents to ensure identification of all cases, but multiplex was still limited to the first four cases. Subsequently, the province expanded eligibility for RI outbreak testing in the fall of 2022, in addition to the first four individuals being eligible for MRVP, all subsequent symptomatic individuals were eligible for COVID-19, influenza, and respiratory syncytial virus (RSV) testing with a rapid turnaround time for results (9).

Respiratory infection outbreaks in the 2018–2020 seasons versus 2022–2023

Publicly available data from the Ontario Respiratory Virus Tool as of February 14, 2024, on RI outbreaks in institutions and public hospitals are summarized in **Table 1** (10).

In comparison to the pre-pandemic 2018–2019 and 2019–2020 (up to March 7, 2020) seasons, in 2022–2023, there was a significant increase in the proportion of outbreaks with "multiple pathogens." Similarly, in 2022–2023, there was a significant decrease in the proportion of outbreaks with "unknown pathogen" versus the comparable pre-pandemic seasons. An increase in outbreaks involving "multiple pathogens" is clinically relevant due to historically longer median duration of the outbreak when compared to those with only a single pathogen (1). Declines in "unknown pathogen" outbreaks are also clinically relevant, as virus-specific interventions (e.g., prophylaxis or application of virus-specific incubation periods when declaring an outbreak over) can be applied when there is a known causative virus.

Enhanced testing is the likely driver for the shift in trends in multiple and unknown pathogen outbreaks. However, enhanced testing may have also resulted in other trends in outbreaks for which data are not publicly available, such as changes to attack rates if inclusion of cases is based on test results instead of symptoms or if increased testing was applied to mildly symptomatic (non-ARI) individuals, and/or changes to outbreak duration if based on last laboratory-confirmed case versus last symptomatic case (7).

Table 1: Reported respiratory infection outbreaks in institutions and public hospitals[a] and a comparison of the outbreak proportions[b], for pre-pandemic seasons 2018–2020 versus 2022–2023[c]

Outbreak type	2018–2019	2019–2020	Combined 2018–2020	2022–2023	Uncorrected chi-square	*p*-value (two-tail)
Total outbreaks	1,643	1,018	2,661	1,679	N/A	N/A
Multiple pathogen outbreaks (proportion of total)	8 (0.5%)	53 (5.2%)	61 (2.3%)	135 (8.0%)	78.9	<0.001
Unknown pathogen outbreaks (proportion of total)	796 (48.4%)	353 (34.7%)	1,149 (43.2%)	193 (11.5%)	483.8	<0.001

Abbreviation: N/A, not applicable
[a] By total, multiple pathogen and unknown pathogen outbreaks
[b] Proportion of multiple and unknown pathogen outbreaks
[c] Dates ranges: 2018–2019 (August 26, 2018, to August 24, 2019), 2019–2020 (August 25, 2019, to March 7, 2020), Combined 2018–2020 (up to March 7, 2020, in 2019–2020), 2022–2023 (August 28, 2022, to August 26, 2023)
Note: This table does not include COVID-19 outbreaks, even for multiple pathogen outbreaks and unknown pathogen outbreaks

Discussion

Syndromic-based versus test-based respiratory infection outbreak management

The trends in the 2022–2023 season warrant a discussion on the issues and gaps of the current syndromic-based versus test-based outbreak definition and management approaches commonly used in Canada. First, in an ideal scenario, it enables the healthcare system to comprehensively identify and manage causative agents for all sick individuals in the outbreak. While historical multiplex testing of only initial cases in an outbreak (e.g., "first four" testing in Ontario) was sufficient for the majority of outbreaks, the decline in "unknown pathogen" outbreaks in institutions in 2022–2023 suggests that additional testing enables identification of a causative virus in a higher proportion of outbreaks. At an individual resident level, identification of influenza or COVID-19 allows for accurate initiation of oseltamivir or nirmatrelvir/ritonavir, respectively, which are both time-sensitive and life-saving interventions. Likewise, providers can more confidently initiate antiviral prophylaxis to suppress influenza outbreaks and avoid initiation/usage of antiviral prophylaxis for non-influenza outbreaks (11).

A second advantage of a test-based approach is the enhanced understanding of RI outbreak epidemiology for future vaccine and therapeutics programs, such as for RSV. For example, testing improves assessment of RSV prevalence in institution populations, to support consideration of an RSV vaccine program with forthcoming RSV vaccines (12). Third, existing syndromic-based approaches rely on the definition of ARI for inclusion of cases in an outbreak. Certain populations, such as the elderly, may not present with "classic" ARI symptoms. These cases may be missed if relying on a syndromic-based approach and not tested but would be captured if using a test-based approach (13). Of note, this argument becomes less pertinent when applying a more sensitive syndromic case definition, which includes non-respiratory symptoms such as a decrease in function or increased falls.

Conversely, there are also challenges with a test-based approach. First, decision-making is more challenging and time-consuming for outbreak management when performing a test on every symptomatic individual versus presuming their association with the outbreak and managing them accordingly. There may be a delay in initiation of treatment and prophylaxis if the outbreak management team must now wait for individual test results versus treating empirically. Second, although additional testing might optimize resource utilization in the long run, the upfront cost of these tests is not immaterial (14). Decision-makers for public health financing need to consider the costs versus benefits of adopting increased use of MRVP and/or COVID-19/influenza/RSV panel testing (15). Third, it is unclear if test-based approaches improve key outcomes, such as morbidity and mortality, for outbreaks. However, decreasing the frequency of "multiple pathogen" outbreaks could shorten outbreak duration and lessen restrictions on recreational programs, significantly enhancing residents' quality of life. Fourth, these proposed changes may actually result in fewer outbreaks reported as having "multiple pathogens." Rather, these might be considered as multiple concurrent outbreaks, increasing the total number of outbreaks reported. Fifth, this testing method could lead to an overemphasis on test outcomes by staff, overshadowing assessment of the whole patient. Lastly, test-based approaches need to address interpretation of negative test results and situations when individuals are not tested when a specific organism is identified in other patients/residents. For example, consider a situation of two epidemiologically linked patients with ARI, where one tested positive for influenza but the other tested negative. This would technically meet the current Ontario outbreak definition, hinging on the determined strength of the "epidemiological linkage" of the two cases and presumption that the negative test is a "false negative," possibly due to improper technique or timing of specimen collection. Historically, no additional testing would be conducted once the influenza outbreak was declared. It would then trigger initiation of antiviral chemoprophylaxis for the whole outbreak area, and initiation of antiviral treatment for all newly symptomatic individuals (8). However, if subsequently sick residents were all tested and also found to be negative (or to have a different virus), the influenza-based outbreak management could be deemed unnecessary and discontinued.

Conclusion

Respiratory infection outbreaks in hospital and institutional settings are common and can be severe. As a result of the COVID-19 pandemic, there were a number of changes to the identification and management of RI outbreaks in these settings following the last guidance update in 2018 (pre-pandemic) and the 2022–2023 respiratory season in Ontario. This commentary explores the benefits and challenges of adopting a more test-based approach to the outbreak declaration and management compared to one that is syndromic-based. More data and evaluation are needed to further assess whether the use of increased test-based approaches has a meaningful impact on outbreak management outcomes, and if it is cost-effective. For example, it would be important to stratify these impacts across different types of institutional settings, as well as an account for any differences in staff capabilities and patient populations. Ultimately, the exploration of test-based versus traditional syndromic-based methods underscores the need for a nuanced approach that not only enhances outbreak management effectiveness, but also significantly improves the quality of life for residents, resulting in better overall health outcomes.

Authors' statement

PG — Conceptualization, analysis, interpretation of data, writing–original draft, writing–review & editing
RM — Conceptualization, analysis, interpretation of data, writing–review & editing
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Competing interests

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Impact of the COVID-19 pandemic on inbound air travel to Canada

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Abstract

Background: Commercial air travel can result in global dispersal of infectious diseases. During the coronavirus disease 2019 (COVID-19) pandemic, many countries implemented border measures, including restrictions on air travel, to reduce the importation risk of COVID-19. In the context of inbound air travel to Canada, this study aimed to: 1) characterize travel trends before and during the pandemic, and 2) statistically assess the association between travel volumes and travel restrictions during the pandemic.

Methods: Monthly commercial air travel volume data from March 2017 to February 2023 were obtained from the International Air Transport Association (IATA). National and airport-level travel trends to Canada were characterized by inbound travel volumes, the number of countries contributing travellers and the ranking of the top ten countries contributing travellers across the study period, by six year-length subperiod groupings (three pre-pandemic and three pandemic). Using seasonal autoregressive integrated moving average (SARIMA) models, interrupted time series (ITS) analyses assessed the association between major travel restrictions and travel volumes by including variables to represent changes to the level and slope of the time series.

Results: The pre-pandemic inbound travel volume increased by 3% to 7% between consecutive subperiods, with three seasonal peaks (July–August, December–January, March). At the onset of the pandemic, travel volume decreased by 90%, with the number of contributing countries declining from approximately 200 to 140, followed by a slow recovery in volume and seasonality. A disruption in the ranking of countries that contributed travellers was also noticeable during the pandemic. Results from the ITS analysis aligned with the timing of travel restrictions as follows: implementation in March 2020 coincided with a sharp reduction in volumes, while the easing of major restrictions, starting with the authorization of fully vaccinated travellers from the United States to enter Canada in August 2021, coincided with an increase in the slope of travel volumes. Descriptive and statistical results suggest a near-return of pre-pandemic travel patterns by the end of the study period.

Conclusion: Study results suggest resilience in commercial air travel into Canada. Although the COVID-19 pandemic led to a disruption in travel trends, easing of travel restrictions appeared to enable pre-pandemic trends to re-emerge. Understanding trends in air travel volumes, as demonstrated here, can provide information that supports preparedness and response regarding importation risk of infectious pathogens.

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Keywords: travel volume, commercial air traffic, IATA, SARIMA, interrupted time series analysis, travel restrictions, Canada, COVID-19

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Introduction

Global air travel volumes and interconnectivity increased between 2010 and 2019 (1) and, prior to the coronavirus disease 2019 (COVID-19) pandemic, were expected to continue growing (2). While higher global connectivity increases international collaboration, trade, and the world's overall socioeconomic development, it also increases the spread of potential of infectious diseases (1,3), such as dengue (4), severe acute respiratory syndrome (SARS) (5), and influenza (6). More recently, the highly transmissible coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of the COVID-19, rapidly spread worldwide following its detection in Wuhan, China at the end of 2019. In response, travel restrictions were implemented by many countries to minimize spread.

On March 21, 2020, the Government of Canada introduced travel restrictions on foreign nationals entering Canada (7). Throughout the pandemic, other Canada-wide border measures for travellers coming to Canada were implemented to minimize COVID-19 importation risk, including flight suspensions from selected countries (8), pre-departure and on-arrival molecular testing for SARS-CoV-2, and a mandatory 14-day quarantine period for inbound travellers (9). Some travellers were exempt from these measures, given their reason for travel, which largely included delivery of essential services, supplies, and equipment (7). August 9, 2021, marked the beginning of easing of major travel restrictions with the authorization of non-essential fully vaccinated travellers from the United States to enter the country (9,10). The removal of all travel restrictions was completed by October 1, 2022, along with other border measures for testing, quarantine, and isolation (11).

In this study, the temporal trends in commercial air travel volumes into Canada from March 2017 to February 2023 were analyzed to gain a further understanding of the impact of the pandemic on inbound travel. The study objectives were to: 1) describe inbound travel patterns both before and during the COVID-19 pandemic, and 2) use an interrupted time series (ITS) analysis to statistically assess the association between inbound travel volumes and the implementation and removal of travel restrictions (as modelled by changes to the level and slope of the time series). The study results have implications for understanding the resilience of the air transportation system under the external stressor of a global pandemic.

Methods

Data

Commercial air passenger volume data, aggregated at the monthly level, were acquired from the International Air Transport Association (IATA) for March 2017 to February 2023. The IATA is the trade association for commercial airlines and provides analytics for their air traffic. The data, which are derived from approximately 300 airline companies, represent 83% of global air traffic from 2016 onwards (12). The data are presented as the number of passengers on each flight itinerary, which can include one to five stops between the origin and final destination airports. For this study, the IATA data were subset to inbound travel to Canada.

Descriptive analysis

Inbound air travel to Canada data were summarized at national and airport levels, with the latter consisting of the four largest Canadian airports as the final destination: Toronto Pearson International Airport, Montréal-Pierre Elliot Trudeau International Airport, Vancouver International Airport, and Calgary International Airport. The IATA data were divided into six year-length subperiods beginning in March, to align with the implementation of air travel restrictions. The pre-pandemic subperiods were March 2017 to February 2018 (subperiod −3), March 2018 to February 2019 (subperiod −2), and March 2019 to February 2020 (subperiod −1). The pandemic subperiods were March 2020 to February 2021 (subperiod 1), March 2021 to February 2022 (subperiod 2), and March 2022 to February 2023 (subperiod 3).

Data summaries included the travel volume for each subperiod and the percent change in the passenger volume between consecutive subperiods. To explore seasonal patterns in inbound air traffic, the travel volume and the total number of countries contributing to travel volume were summarized at the monthly level across the six subperiods. Finally, heat maps were generated at the national and airport levels to visually compare the ranking of the top 10 countries contributing to inbound travel during each subperiod. Countries were categorized into one of seven travel volume categories, which were determined by inspecting the distribution of total travel volumes into Canada.

Statistical analysis

An ITS analysis using seasonal autoregressive integrated moving average (SARIMA) models (13) was conducted to evaluate the association between major travel restrictions and inbound monthly travel volumes. For the purpose of this analysis, major travel restrictions are defined as traveller-level measures applicable to the majority of non-essential travellers (e.g., restrictions based on vaccination status). As such, we do not include Notices to Airmen (NOTAMs) in this definition, which, when used during the pandemic, were only applicable to a small proportion of travellers and were therefore not expected to have as big of an impact on travel volume.

Time series data are often serially dependent through time (known as autocorrelation). Seasonal autoregressive integrated moving average models have been used in air travel time series

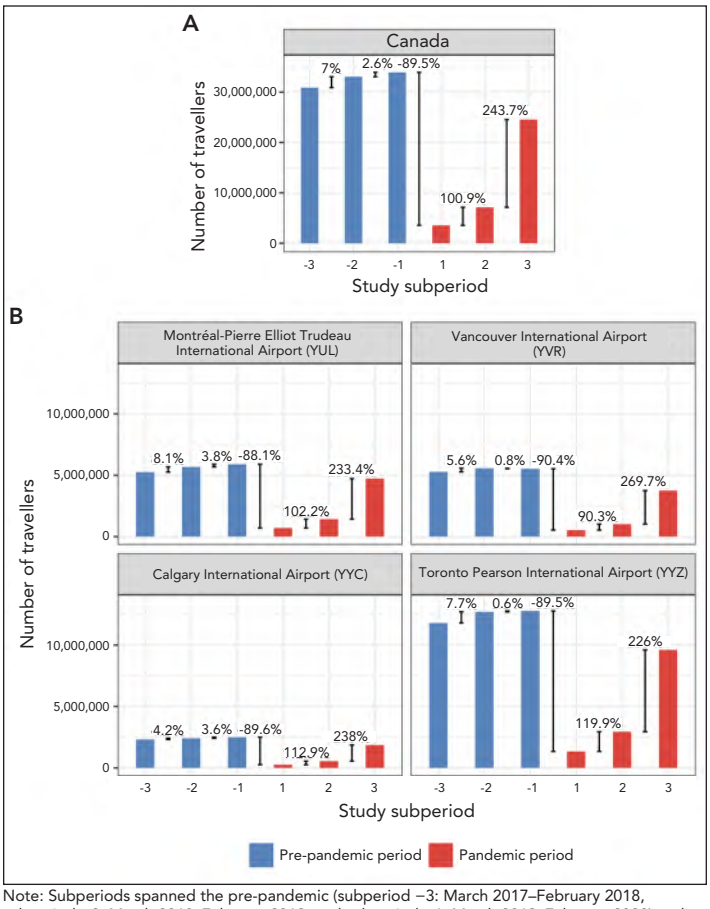
data analysis (14,15) as they have the advantage of accounting for seasonality and other autocorrelation. As such, an ITS analysis using the SARIMA modelling approach is robust for assessing the impact of an intervention on the outcome variable compared to the traditional segmented regression ITS, for which the assumption of independent observations is often violated. The model is expressed as SARIMA (p, d, q) × $(P, D, Q)_s$ where s refers to the number of observations per season, and parameters p, d, and q refer to the order of the autoregressive process, the degree of differencing, and the order of the moving average process, respectively. Additionally, P, D, and Q represent the analogous terms for the seasonal components.

The premise of an ITS approach is to assess whether the observed values diverge from model-fitted values when accounting for the effect of an intervention. For the present analyses, it was hypothesized that intervention effects from travel restrictions could be modelled by two types of dummy variables—step change and ramp (13). Two step changes were used to capture the sharp drop in travel volumes during March and April 2020, respectively. Two step changes were required because travel restrictions implemented on March 21, 2020, only partially impacted the total travel volume that month. A ramp was used to capture rebounding travel volumes starting in August 2021, to coincide with the first instance of easing major travel restrictions, with the authorization of non-essential fully vaccinated travellers from the United States to enter the country. The ITS model was compared with a null hypothesis (H_0) model that did not include the step and ramp variables. The models were fit using the auto.arima function from the R forecast package to find the best-fitting SARIMA terms accounting for autocorrelation (16,17). Residuals from the fitted models were assessed for normality, absence of heteroscedasticity, and autocorrelation using a plot through time, a histogram, an autocorrelation function plot and the Ljung-Box test for autocorrelation. The *p*-values below 0.05 were considered statistically significant for all statistical tests. The ITS and H_0 models were compared by their fit to the observed data using root mean square error (RMSE) and mean absolute error (MAE) (18). All analyses were conducted using the R statistical software environment, version 4.2.1 (19).

Results

Prior to the COVID-19 pandemic, the overall inbound commercial air travel to Canada increased over time with a 7% increase from pre-pandemic subperiod −3 to subperiod −2, and a 3% increase from pre-pandemic subperiod −2 to subperiod −1. By pre-pandemic subperiod −1, there were over 33.9 million travellers arriving in Canada. The onset of the COVID-19 pandemic resulted in a 90% decrease in air traffic volume, with fewer than 4 million travellers entering Canada in pandemic subperiod 1. The travel volume subsequently increased throughout the remainder of the study period (a 101% increase from pandemic subperiod 1 to subperiod 2, and a 244% increase from pandemic subperiod 2 to subperiod 3), allowing a slow recovery to near pre-pandemic levels by pandemic subperiod 3 (24.5 million travellers; **Figure 1**). Similar trends were observed at the airport level, where most travellers (38%–41% per year) landed at Toronto Pearson International Airport, followed by Montréal-Pierre Elliot Trudeau International Airport (17%–20% per year), Vancouver International Airport (14%–17% per year), and, finally, Calgary International Airport (7%–8% per year).

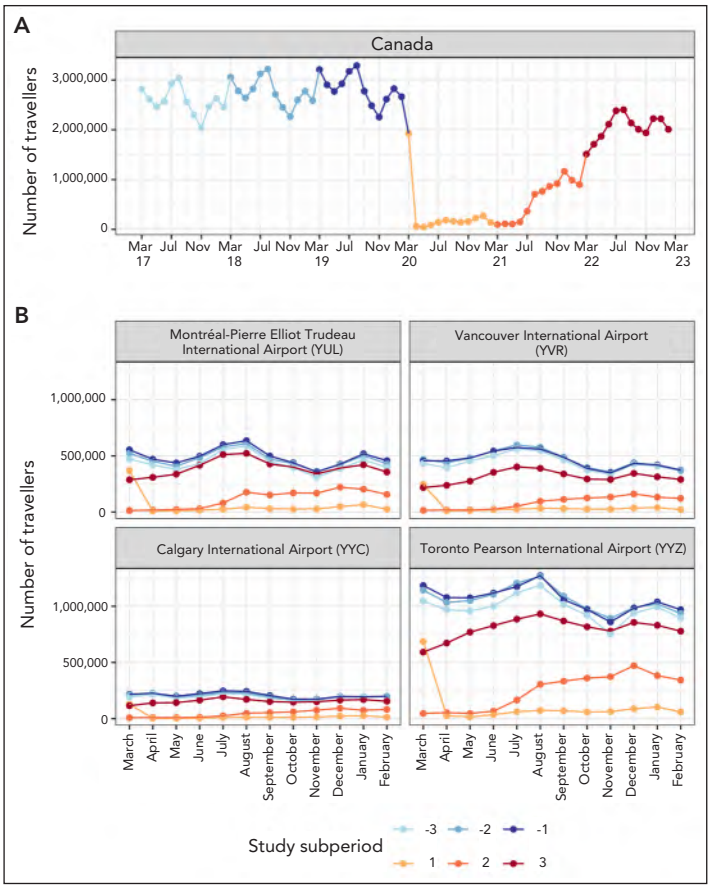
Figure 1: Total incoming travel volumes per study subperiod and percent change between consecutive subperiods for A) Canada and B) each of the four largest Canadian airports as the final destination



Note: Subperiods spanned the pre-pandemic (subperiod −3: March 2017–February 2018, subperiod −2: March 2018–February 2019, and subperiod −1: March 2019–February 2020) and pandemic (subperiod 1: March 2020–February 2021, subperiod 2: March 2021–February 2022, and subperiod 3: March 2022–February 2023) study period

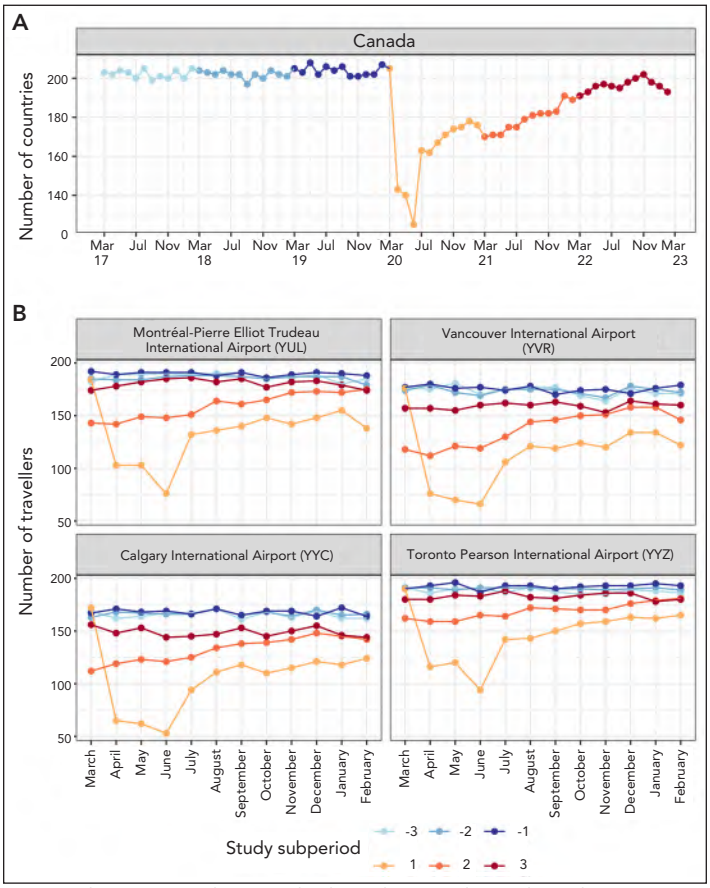
Throughout the pre-pandemic subperiods, the overall and airport-level monthly inbound travel volume was cyclical, with peaks in summer (July–August), winter (December–January), and late winter/early spring (March). Although highly dampened, these trends appear by visual assessment to continue throughout the pandemic, with a rise in travel volume noticeable especially during the summer and the winter months. Similar trends were observed at the airport level (**Figure 2**).

Figure 2: Incoming travel volume to A) Canada and B) each of the four largest Canadian airports as the final destination stratified by month and study subperiod



Note: The study period was divided into six subperiods: pre-pandemic (subperiod −3: March 2017–February 2018, subperiod −2: March 2018–February 2019, and subperiod −1: March 2019–February 2020) and pandemic (subperiod 1: March 2020–February 2021, subperiod 2: March 2021–February 2022, and subperiod 3: March 2022–February 2023)

Figure 3: The number of countries with travellers arriving in Canada each month, reported for A) Canada and B) the four largest Canadian airports as the final destination



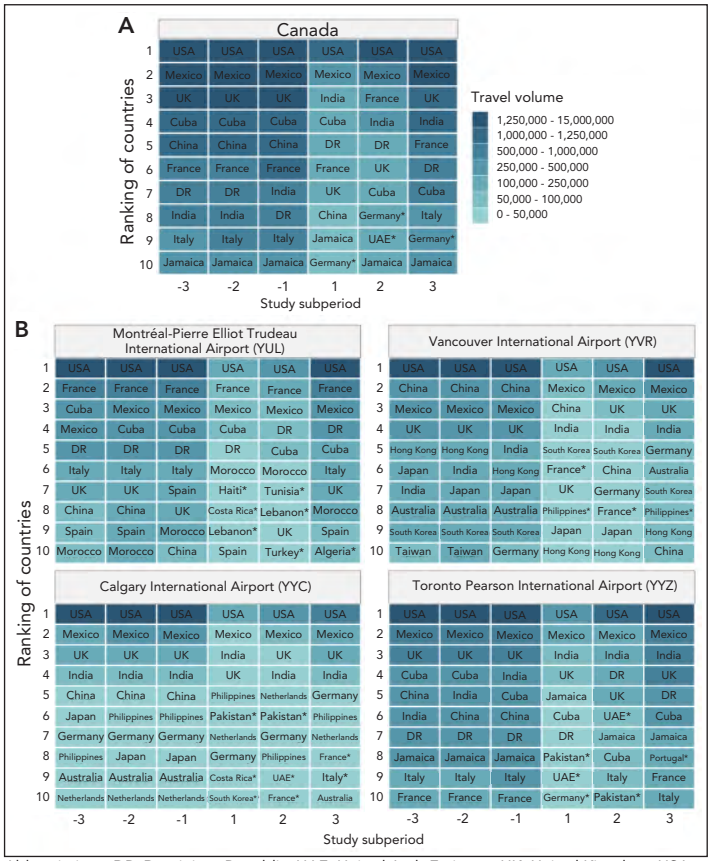
Note: Trends were compared across study subperiods: pre-pandemic (subperiod −3: March 2017–February 2018, subperiod −2: March 2018–February 2019, and subperiod −1: March 2019–February 2020) and pandemic (subperiod 1: March 2020–February 2021, subperiod 2: March 2021–February 2022, and subperiod 3: March 2022–February 2023)

In contrast to travel volume, seasonal patterns were not evident when data were summarized as the number of countries contributing travellers to Canada. Prior to the COVID-19 pandemic, travellers from approximately 200 countries contributed to inbound travel to Canada each month, decreasing to approximately 140 countries in April and approximately 125 countries in June 2020. The number of contributing countries continued to trend upward from June 2020 onward, reaching pre-pandemic levels during pandemic subperiod 3 at the national level and for all airport destinations, except Calgary and Vancouver international airports (**Figure 3**).

The United States consistently contributed the majority of air travellers at both the national and airport levels throughout the study period. Before the COVID-19 pandemic, the order of the top ten countries contributing to inbound travel was relatively consistent between subperiods, though the ranking varied between airports. At the onset of the pandemic, there was a large decrease in travel volume per country of origin, as well as a disruption in the ranking of the top ten contributing countries to travel volume at the national and airport levels throughout the pandemic period. For example, some airports had new countries entering the top ten (e.g., United Arab Emirates for the Toronto Pearson International Airport) and some countries moved higher in their rank of contribution (e.g., Netherlands for the Calgary International Airport) (**Figure 4**).

The best fit H_0 and ITS models were SARIMA (0,1,1) x $(1,0,0)_{12}$ and SARIMA (2,0,0) x $(2,1,0)_{12}$, respectively. In the ITS, variables included to model the impact of the implementation of travel restrictions on inbound air travel volumes to Canada were statistically significant (i.e., two step changes estimating a reduction in travellers for March 2020 and April 2020). Also statistically significant was an increase in the slope of travellers in August 2021 compared with what was expected in the absence of travel restrictions (Supplemental material). Both the H_0 and ITS models passed the Ljung-Box tests (Q*=7.6141, df=12, lag=14, *p*-value=0.815; Q*=7.2782, df=10, lag=14, *p*-value=0.699), however, the additional variables in the ITS model intended to capture changes in travel restrictions resulted in better model performance metrics for RSME (H_0: 303,353.2, ITS: 124,124.6)

Figure 4: Ranking of incoming travel volume by origin country for incoming travel volume to A) Canada and B) each of the four largest Canadian airports as the final destination



Abbreviations: DR, Dominican Republic; UAE, United Arab Emirates; UK, United Kingdom; USA, United States of America

Notes: The rankings were stratified by study subperiod (pre-pandemic: subperiod −3: March 2017–February 2018, subperiod −2: March 2018–February 2019, and subperiod −1: March 2019–February 2020; and pandemic: subperiod 1: March 2020–February 2021, subperiod 2: March 2021–February 2022, and subperiod 3: March 2022–February 2023) Asterisks indicate countries that were found within the top ten contributors of incoming travel volume during the pandemic subperiods but not the pre-pandemic subperiods

and MAE (H_0: 198,609.5, ITS: 82,132.2). Residual assessments of the H_0 model suggest that it did not account for the effect of travel restrictions, as expected, and as observed by the stark drop in residuals during March 2020 and April 2020. On the other hand, residuals for the ITS model show that the model does not adequately account for differences in the magnitude of seasonal patterns between the pre-pandemic and pandemic periods. Details for model diagnostics are included in the supplemental material.

Discussion

This study analyzed temporal trends in inbound commercial air travel volumes into Canada before and during the COVID-19 pandemic and included a statistical assessment of COVID-19 travel restrictions on travel volumes. While the initial disruption was biggest at the onset of the pandemic during the strictest border measures, descriptive and ITS analysis results show that travel volume and seasonal patterns gradually returned to pre-pandemic trends as travel restrictions were eased. Conversely, the ranking of countries by incoming volume did not return to pre-pandemic levels to the same extent as the other measures.

Using the COVID-19 pandemic as a case study, the present analyses highlight the impact that an international crisis can pose on travel patterns (volume, seasonality, ranking of contributing countries). Air travel has been shown to be an important factor in the dispersion of infectious diseases worldwide (20), and such radical changes in air traffic are likely to have direct implications on the importation risk of infectious pathogens into Canada. For instance, the risk of importation depends on the travel volume from high-incidence source countries, as previously reported for COVID-19 and other infectious diseases (21,22). Similarly, we would expect that a change in the ranking of countries that contribute travellers would alter the overall importation risk if the countries differed by disease incidence. The present study results have also shown a gradual return of travel volume patterns to pre-pandemic levels as travel restrictions were eased, demonstrating the resilience of inbound air travel in Canada. Thus, during future outbreaks of emerging and re-emerging infectious diseases, if current or projected air travel volume data are unavailable, "business as usual" patterns (i.e., through historical data under usual circumstances) can still be relevant for informing situational awareness and intervention strategies.

The present ITS analysis was a simple approach to assess for the effect of travel restrictions on travel volumes into Canada using basic intervention impact shapes. Results from this analysis suggest that the implementation of the first travel restrictions on the entry of foreign nationals into Canada (9) in March 2020, in response to the global increase in cases (23), catalyzed the initial downtrend in travel volume observed at that time, as found elsewhere in the world (24). Following that, the easing of travel restrictions in Canada in August 2021 coincided with a significant increase in inbound travel volume during the COVID-19 pandemic period. Even though the modelled effects were statistically significant, other factors not included in the model could be associated with observed trends in travel volumes during the pandemic period. For instance, other border measures, such as testing, and quarantine requirements can act as major disincentives for people to travel. Furthermore, NOTAMs that were implemented over short periods to ban travellers from specific countries from entering Canada (e.g., the United Kingdom [December 2020 to January 2021 (25)], Pakistan [April to June 2021 (26)], India [April to September 2021 (27)], Mexico and Caribbean countries [January to April 2021 (28)], and Morocco [August to October 2021 (8,9)]) likely contributed to reducing travel volumes transiently. Global travel can also be impacted by complex and interconnected factors related to economic production, trade, and tourism (29), as well as people's willingness to travel given risk perceptions of COVID-19 (30). Given the complexity of the air travel system during the

pandemic, future research could benefit from exploring more complex models, for example using transfer functions to better capture the observed effect (13) or applying alternative methods to adequately adjust for changes in seasonal patterns, as observed during the pandemic (31). Furthermore, a future extension of the study could involve investigating the potential impact of air travel restrictions on COVID-19 importation rates to assess for their effectiveness.

Limitations

There are other limitations within the study data and analysis. First, the IATA data does not include all global air traffic (12). Although the majority of travel volume data (83%) was available for the analysis, it is possible that some trends may have been overestimated, underestimated, or missed. Furthermore, it is important to note that the study results are in the context of the COVID-19 experience in Canada. It is intuitive to expect that travel restrictions implemented for future pandemics would cause a decrease in travel volumes, dampening of seasonal patterns, and re-ordering of the ranking of countries that contribute travellers, as demonstrated in this study. The nature of these impacts, however, will depend on the context of the air travel interactions with Canada given trade, personal travel (e.g., tourism, education, visits to family), the epidemiology of the disease, and the potential for the implementation of travel restrictions.

Conclusion

In this study, a method is presented to help understand how inbound air travel patterns can be impacted by travel restrictions, as demonstrated in the context of the COVID-19 pandemic in Canada. The approach characterizes the behaviour of the system during standard and unusual circumstances, as shown descriptively by trends in travel volume, seasonality and contributions from countries, and statistically as significant impacts in the implementation and removal of disruptions. While study results indicate that interventions implemented in response to the pandemic have the capacity to disrupt inbound travel patterns at both national and arrival airport levels, they also suggest a gradual return to expected travel patterns and, hence, resilience of the air travel system to major disruptions. Frequent monitoring of air travel patterns, during "business as usual" and disruptive global events, can help public health professionals better inform emergency preparedness and response efforts aimed at reducing importation risk. The study opens avenues for future research in the intersecting fields of air transportation and public health.

Authors' statement

VG-R — Conceptualization, formal analysis, analysis performance, writing–review & editing
ER — Conceptualization, formal analysis, writing–review & editing
AR — Analysis performance, writing–review & editing
RMM — Conceptualization, formal analysis, writing–review & editing

Both VG-R and ER share first authorship.

Competing interests

The authors declare no competing interests.

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Supplemental material

These documents can be accessed on the Supplemental material file.

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Microbiology of bloodstream infections in Ontario, Canada during COVID-19 pandemic

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Abstract

Background: Bloodstream infections (BSI) caused by a wide range of bacterial and fungal pathogens are associated with high rates of morbidity and mortality. Based on an estimate in 2017, the number of BSI incidences in Ontario is 150 per 100,000 population. The epidemiology of BSIs may be affected by many factors, including the social and travel restrictions and increased rates of hospitalizations in Ontario during the coronavirus disease 2019 (COVID-19) pandemic.

Objectives: This study aimed to assess the changes in the microbiology of BSIs in Ontario during the COVID-19 pandemic compared to the pre-pandemic period.

Methods: Retrospective blood culture data (n=189,106) from LifeLabs Ontario (July 2018 to December 2021) were analyzed. Blood culture positivity rates for common bacterial pathogens were compared between pre-COVID-19 (July 2018 to March 2020) and COVID-19 (April 2020 to December 2021) periods in community and hospital settings, using the chi-square test for significance.

Results: During the COVID-19 period, blood culture positivity rates in the community remained the same, while hospital rates increased by approximately threefold (p=0.00E-00). In the community, the isolation rates of most bacterial species remained unchanged, except for an increase in *Enterococcus* spp. and a decrease in *Salmonella* spp. The rates of antibiotic-resistant organisms (AROs) also significantly decreased in the community. In hospitals, all bacterial species, including AROs, showed significant increases in isolation rates during the COVID-19 period.

Conclusion: The study revealed shifts in the microbiology of BSIs and suggests changes in the epidemiology of BSIs during the COVID-19 pandemic in Ontario, both in hospitals and in the community.

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Introduction

Bloodstream infections (BSIs) have a considerable impact on healthcare settings and communities because of high rates of morbidity and mortality associated with such infections (1). In hospitals, they are among the most common healthcare-associated infections. Studies have reported varying incidence rates, ranging from 1.5 to 4.0 cases per 1,000 patient days. The incidence of community-acquired BSIs is lower but still significant, affecting individuals outside of healthcare facilities (2). In Ontario, based on a population-wide retrospective cohort study of BSIs in 2017, there were 150 BSI episodes per 100,000 population with a 30-day mortality rate of 17% (3).

The causative agents of BSIs vary depending on the setting, patient population, and regional factors. Gram-positive bacteria are commonly implicated, with *Staphylococcus aureus*, including methicillin-resistant strains (MRSA), being a leading cause. Coagulase-negative staphylococci, such as *Staphylococcus epidermidis*, are also frequently isolated. Gram-negative

bacteria, including *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, contribute significantly to BSIs, particularly in healthcare settings. Fungal pathogens, such as *Candida* spp., are an important cause of BSIs in immunocompromised individuals. The emergence and spread of antimicrobial resistance pose additional challenges in managing BSIs. Methicillin-resistant *Staphylococcus aureus* and extended-spectrum beta-lactamase (ESBL) producing gram-negative bacteria have been associated with increased mortality and healthcare costs (1,3).

The epidemiology of BSIs has been changing in recent decades, driven by many factors, such as changing population demographics, healthcare delivery methods, and increasing globalization (1). Most recently, BSI epidemiology in the community and hospitals may have been impacted by mobility restrictions and increased rates of hospitalizations associated with coronavirus disease 2019 (COVID-19). In this study, we assessed the microbiology of BSIs in Ontario during the COVID-19 pandemic and compared it to the pre-pandemic period.

Methods

In this retrospective observational study, data from blood cultures (n=189,106) performed by LifeLabs medical laboratories in Ontario from July 2018 to December 2021 were utilized; the cultures were collected from patients attending primary care facilities and 36 hospitals across the province. For hospitals, more than 90% of blood cultures were from five general community hospitals in the Hamilton Niagara Haldimand Brant Local Health Integration Network (LHIN) that have 100 or more patient beds. For the blood cultures from communities, more than 70% were from urban communities. Data were retrieved without any patient identifying information, according to the LifeLabs code of ethics policy. Blood culture positivity rates for all pathogens and for most frequently isolated bacterial pathogens were compared between the pre-COVID-19 period (July 2018 to March 2020) and the COVID-19 period (April 2020 to December 2021) for both community and hospital settings. The chi-square test was used to determine if the differences in proportions were significantly different.

Results

In the 21 months before the COVID-19 restrictions were put in place in Ontario, overall blood culture positivity rates in the community and in hospitals were 2.8% and 8.06%, respectively. During the 21 months of COVID-19 restrictions, overall blood culture positivity rates for the community remained the same but significantly increased (approximately three-fold; p=0.00E-00) for hospitals as compared to the preceding pre-pandemic period (**Table 1** and **Table 2**).

During the pre-pandemic period, the most frequently isolated bacterial species in blood cultures from the community were coagulase-negative staphylococci (CoNS), *E. coli*, viridans streptococci, *Salmonella* spp., *Staphylococcus aureus*, and *Enterococcus* spp. Both *S. pneumoniae* and *H. influenzae* were rarely isolated in BSIs from the community, perhaps reflecting widespread vaccination coverage for both species in Ontario. For the community, isolation rates of most bacterial species remained the same or changed very little during the COVID-19 pandemic, except in the cases of *Enterococcus* spp. and *Salmonella* spp. The rates of *Enteococcus* spp. increased about two-fold (p=0.0003) during the COVID-19 pandemic. The reason for this is not clearly understood, but may be attributed to changes in gut microbiome favouring *Enterococcus* spp. and increased intestinal permeability in COVID-19 patients, which have been recently described (4). On the other hand, the rates of *Salmonella* spp. in BSIs declined drastically (p=0.0000) in the community, which is likely associated with travel restrictions and physical distancing during the COVID-19 pandemic. Perhaps for the same reasons, the rates of antibiotic-resistant organisms (AROs) such as *Serratia*, *Pseudomonas*, indole-positive *Proteus*, *Citrobacter*, and *Enterobacter* (SPICE) organisms; ESBL/AmpC-producing Enterobacterales; and MRSAs also significantly (p<0.05) decreased in the community (5). Among the positive blood cultures from the community, the relative proportions of several bacterial species changed significantly during the COVID-19 pandemic. The proportions of CoNS, viridans streptococci, and *Enterococcus* spp. increased significantly (p≤0.05), while the proportions of *Salmonella* spp. and SPICE organisms decreased significantly (p≤0.001) (**Figure 1**).

For hospitals, the most frequently isolated bacterial species during the pre-COVID-19 period were *E. coli*, CoNS, *S. aureus*, other streptococci, *Klebsiella* spp., and *Enterococcus* spp. The isolation rates for all organism groups, including AROs, increased significantly (two to three-fold) during the COVID-19 pandemic, even though the total number of blood cultures was less than half than that reported during the pre-pandemic period. These results are consistent with higher incidence rates of hospital onset BSIs in other populations as well (6–8) and may be related to a higher rate of admission of COVID-19 patients to intensive care units. In the hospitals, the relative proportions of pathogens recovered from positive blood cultures were not significantly different for most pathogens, except for a significant increase in the proportion of positive blood cultures with CoNS (p≤0.0001) and a significant decrease in the proportion of positive blood cultures with *S. pneumoniae* (p≤0.0001) (Figure 1). A small but significant (p≤0.05) increase in the proportion of positive blood cultures with *Klebsiella* spp. was also noted during the COVID-19 period.

Table 1: Blood culture positivity rates in community settings by bacterial pathogens

Organisms	Pre-COVID-19 period[a]		COVID-19 period[a]		*p*-value[b]
	n	%	n	%	
Total blood cultures	32,411	100.00	25,860	100.00	-
All organisms	907	2.80	687	2.66	0.2971
CoNS	275	0.85	247	0.96	0.1746
Escherichia coli	118	0.36	69	0.27	0.0392
Viridans streptococci	97	0.30	97	0.38	0.1145
Salmonella spp.	89	0.27	13	0.05	0.0000
Staphylococcus aureus	57	0.18	32	0.12	0.1094
Enterococci	41	0.13	66	0.26	0.0003
Klebsiella spp.	38	0.12	37	0.14	0.3875
Other streptococci	15	0.05	15	0.06	0.5354
Pseudomonas spp.	12	0.04	4	0.02	0.1187
Yeast	10	0.03	13	0.05	0.2410
Streptococcus pneumoniae	5	0.02	5	0.02	0.7205
Other	41	0.13	52	0.20	0.0250
Anaerobe	56	0.17	26	0.10	0.0208
ESBL/AmpC	35	0.11	11	0.04	0.0052
SPICE	34	0.10	7	0.03	0.0004
MRSA	18	0.06	2	0.01	0.0020

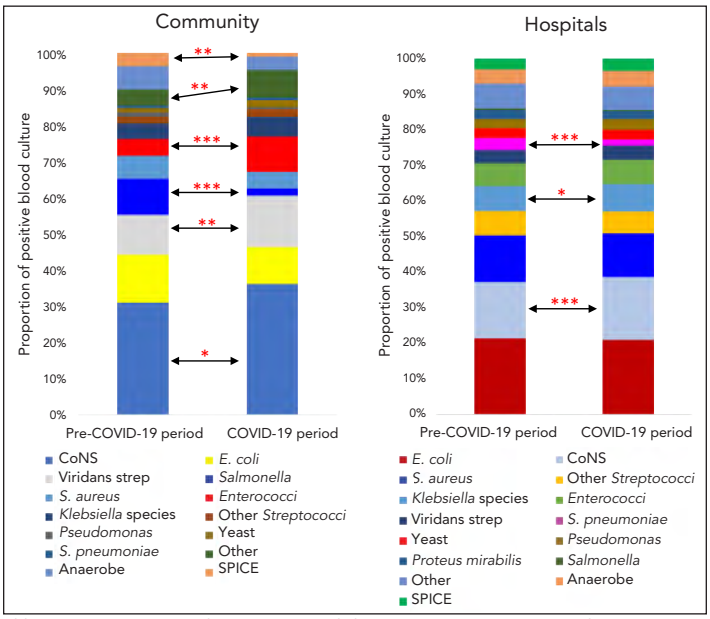
Abbreviations: AmpC, AmpC beta-lactamases; CoNS, coagulase-negative staphylococci; ESBL, extended-spectrum beta-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*; SPICE, *Serratia*, *Pseudomonas*, indole-positive *Proteus*, *Citrobacter*, and *Enterobacter*
[a] Pre-COVID-19 period: July 2018 to March 2020; COVID-19 period: April 2020 to December 2021
[b] *p*-value obtained from chi-square tests

Table 2: Blood culture positivity rates in the hospitals by bacterial pathogens

Organisms	Pre-COVID-19 period[a]		COVID-19 period[a]		*p*-value[b]
	n	%	n	%	
Total blood cultures	88,170	100.00	42,665	100.00	-
All organisms	7,105	8.06	10,197	23.90	0.00E-00
Escherichia coli	1,410	1.60	2,026	4.75	1.6E-244
CoNS	1,045	1.19	1,698	3.98	6.6E-240
Staphylococcus aureus	860	0.98	1,200	2.81	3.3E-138
Other streptococci	461	0.52	593	1.39	8.88E-61
Klebsiella spp.	455	0.52	745	1.75	4E-106
Enterococci	424	0.48	648	1.52	6.98E-85
Viridans streptococci	245	0.28	376	0.88	4.02E-50
Streptococcus pneumoniae	221	0.25	176	0.41	6.03E-07
Yeast	182	0.21	255	0.60	1.34E-30
Pseudomonas spp.	170	0.19	286	0.67	5.89E-43
Proteus mirabilis	164	0.19	224	0.53	4.03E-26
Salmonella spp.	27	0.03	39	0.09	4.43E-06
Other	459	0.52	624	1.46	1.48E-69
Anaerobe	260	0.29	420	0.98	1.89E-59
ESBL/AmpC	182	0.21	171	0.40	2.1E-10
SPICE	215	0.24	348	0.82	1.22E-49
MRSA	507	0.58	539	1.26	3.06E-39

Abbreviations: AmpC, AmpC beta-lactamases; CoNS, coagulase-negative staphylococci; ESBL, extended-spectrum beta-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*; SPICE, *Serratia*, *Pseudomonas*, indole-positive *Proteus*, *Citrobacter*, and *Enterobacter*
[a] Pre-COVID-19 period: July 2018 to March 2020; COVID-19 period: April 2020 to December 2021
[b] *p*-value obtained from chi-square tests

Figure 1: Relative proportion of pathogens recovered from positive blood cultures from the community or hospitals during the COVID-19 period compared to the pre-COVID-19 period[a]



Abbreviations: CoNS, coagulase-negative staphylococci; COVID-19, coronavirus disease 2019; *E. coli*, *Escherichia coli*; *S. aureus*, *Staphylococcus aureus*; *S. pneumoniae*, *Streptococcus pneumoniae*; SPICE, *Serratia*, *Pseudomonas*, indole-positive *Proteus*, *Citrobacter*, and *Enterobacter*; viridans strep, viridans streptococci

[a] *p*-values calculated from two proportion Z-test; *$p \leq 0.05$; **$p \leq 0.001$; ***$p \leq 0.0001$

Discussion

Limitations

This study has several limitations. Although the study shows blood culture positivity rates for a representative Ontario population, it does not represent the accurate incidence of BSIs in Ontario because data were analyzed based on unique specimen accession numbers instead of patient identifiers. Also, because records of hospital admission dates were not available, the count of blood cultures received from hospitals may include a fraction that was community-acquired. It is likely that a small proportion of positive blood cultures, most commonly with CoNS and viridans streptococci, were reported as potential contaminants. However, this data could not be retrieved from the LifeLabs blood culture database.

Conclusion

The blood culture data on overall and species-wise positivity rates for a large representative population suggest that there were shifts in BSI epidemiology in Ontario during the COVID-19 pandemic, both in hospitals and in the community.

Authors' statement

MRH — Conceptualization, methodology, data analysis, writing–original draft
YMV — Methodology, data analysis, writing–review & editing
DL — Methodology, data analysis, writing–review & editing
HA — Methodology, data analysis, writing–review & editing

All authors have read and approved the final manuscript.

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Competing interests

The authors have declared no conflicts of interest.

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