HEALTH RISK ASSESSMENT

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CANADA COMMUNICABLE DISEASE REPORT

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TABLE OF CONTENTS

Estimating public health risks of infectious disease events: A Canadian approach to rapid risk assessment

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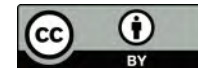
Abstract

Background: The COVID-19 pandemic highlighted the need for timely, evidence-based rapid risk assessments (RRA) of infectious disease events to inform public health action during rapidly evolving situations with high uncertainty. In 2022, the Public Health Agency of Canada established a coordinated approach to public health risk assessment, including a methodology for qualitative RRA of infectious disease threats.

Objective: To describe the RRA methodology and illustrate its use with examples from different infectious hazards of public health concern.

Methods: The RRA methodology employs the risk pathway to describe the sequence of events leading from a hazard's source to the adverse event of concern and subsequent impacts; define specific questions to be addressed; and identify relevant knowledge gaps, limitations and recommendations. Qualitative likelihood and impact estimates are derived through integration of evidence review and expert opinion and are communicated together with corresponding levels of uncertainty. The impacts of the event are based on an assessment of the most likely spread scenario within Canada, considering individual-level impact on affected individuals, the impact on the general population and, if relevant, sub-groups at higher risk.

Results: This RRA approach aligns with well-established international methods and provides flexibility to accommodate a broad range of risk questions. It has been implemented to estimate the risk of various threats of concern to Canada, including mpox, avian influenza A(H5N1) and measles.

Conclusion: Given the broad range and complexity of public health hazards, RRAs provide a timely, coordinated and systematic process for characterizing and communicating the risk to inform risk mitigation and decision-making and to guide appropriate public health response.

Introduction

The COVID-19 pandemic highlighted the need for a risk- and evidence-based approach to implementing public health measures in the context of a rapidly evolving situation with limited information and high uncertainty. Rapid risk assessments (RRAs) provide a systematic approach to gathering, assessing and documenting information about a public health hazard, to assign a level of risk to inform decision-making within a short timeframe (1,2). Rapid risk assessments are, therefore, crucial in the early response to a public health event as they provide risk managers with a timely and evidence-based assessment of the

risk and associated levels of uncertainty upon which to base risk management, surveillance and research recommendations (3,4). Additionally, RRAs can be updated, taking into account new information as an event evolves.

Based on recommendations from the Auditor General's Report on Pandemic Preparedness, Surveillance, and Border Control Measures (5) and the Global Public Health Intelligence Network Independent Review Panel (6), in 2022, the Public Health Agency of Canada (PHAC) consolidated risk assessment activities across PHAC to establish and coordinate an integrated risk assessment approach to RRA. The RRA process is initiated when a threat is identified (e.g., through signal detection or surveillance) for which an estimation of the associated risk is needed to inform public health preparedness and response. Due to the need for timely response and the limited information available during the early stages of an event, RRAs are typically qualitative in nature, involving a combination of evidence review and expert opinion. In this paper, we describe the development and methodology of PHAC's qualitative RRA approach and illustrate its use with different infectious hazards of public health concern as examples.

Rapid risk assessment methodology

Development
Four qualitative public health RRA approaches (1,2,7,8) were initially identified through an informal environmental scan of risk assessment approaches utilized by international public health organizations (e.g., UK Health Security Agency, European Centre for Disease Prevention [ECDC] and Control and World Health Organization [WHO]) as well as peer-reviewed publications, grey literature and expert input of threat and risk assessment frameworks and methodologies. The four approaches were subsequently tested in the Canadian context using scenarios and historical infectious disease events. Two approaches use an algorithm to determine the risk level posed by infectious disease events (1,7), while the other two involve development of specific questions to be addressed related to the likelihood and impact of the event of concern (2,8). The RRA approach described herein is largely based on the Joint Risk Assessment Operational Tool (JRA OT), developed by the Food and Agriculture Organization (FAO), the World Organization for Animal Health (WOAH) and the WHO (8), as a qualitative approach that can be conducted rapidly to inform decision-making for emerging events. The JRA OT was chosen based on its 1) flexibility to accommodate a wide range of risk questions, 2) high level of scientific validity by employing a risk pathway model as a framework to assess likelihood and impact, 3) ability to incorporate One Health considerations in the risk assessment process to address the many hazards that intersect human-animal-plant-ecosystem health and 4) ability to provide sufficient guidance material for implementation and adaptable tools to facilitate the RRA process (e.g., terms of reference

for committees). The iterative JRA process at-large has been adapted based on organizational mechanisms and structures in-place and informed by lessons learnt via internal pilot-testing with infectious disease events that occurred in 2022.

Overall process
When the RRA process is triggered, an event-specific steering committee is formed comprising decision-makers, senior staff in key program areas and relevant external partners. The steering committee's role is to determine if a RRA is needed, oversee the RRA process, define the scope and key objectives of the assessment, review findings and recommendations and communicate these to relevant decision-makers. In the execution phase, a multidisciplinary technical team comprising risk assessors and subject matter experts (SMEs) conducts the assessment by mapping a risk pathway; finalizing the risk question(s) to be addressed; gathering and synthesizing evidence; assigning likelihood, impact and uncertainty levels; identifying assumptions, limitations and knowledge gaps; and providing recommendations for risk mitigation, surveillance and research. These are summarized in a report that includes an overall risk statement and recommendations for risk management that are approved and communicated to relevant stakeholders in the dissemination phase (**Box 1**).

Box 1: Overall process for conducting a public health rapid risk assessment for infectious disease events[a]

1. Initiation phase: setting the stage
   - Establishing a steering committee and technical team
   - Risk framing and formulating risk question(s)

2. Execution phase: conducting the assessment
   - Diagramming risk pathway(s)
   - Finalizing risk question(s) and formulating pathway sub-questions
   - Gathering and synthesizing evidence
   - Assigning likelihood, impact and uncertainty levels
   - Identifying assumptions, limitations and knowledge gaps
   - Formulating risk statement and risk management recommendations

3. Closure phase: recommendations, communication and update
   - Reviewing and approving RRA findings and recommendations
   - Disseminating RRA outcomes and report
   - Developing triggers for re-assessment of risk
   - Monitoring emerging evidence and situational assessment
   - Updating the assessment as the event evolves

Abbreviation: RRA, rapid risk assessment
[a] This process is situation-dependent and not linear; it is often adapted to the hazard, scope, purpose and timelines, as established during risk framing

Initiation phase: setting the stage

Risk framing

The steering committee conducts a risk framing (problem formulation) exercise to determine whether a RRA is needed and outline the scope and key objectives of the assessment. This includes defining the following:

- The public health hazard (pathogen or other threat) that poses a potential risk
- The public health concerns related to the hazard
- The adverse event of concern (the event to be avoided or mitigated); e.g., introduction of an infectious individual with disease X into Canada
- The source of the hazard
- The at-risk population(s) of interest
- The timeframe over which the risk should be assessed
- The contextual factors that can influence the likelihood or impact of the event; e.g., conditions affecting exposure or transmission, available countermeasures and resources for risk mitigation
- The relevant stakeholders (including those whose expertise is required to conduct the assessment and those to whom the results of the assessment should be communicated)

- The risk management decisions that should be informed by the RRA; e.g., border health measures, infection prevention and control guidance

This risk framing aids in the formulation of the specific risk question(s) to be answered during the RRA (see **Table 1** for more examples).

Execution phase: conducting the assessment

Risk pathway

The risk framing informs the development of a risk pathway: a diagram describing the sequence of events leading from the hazard's source to the adverse event of concern and its resultant impacts. Each box (node) in the diagram represents a step along the risk pathway; arrows (edges) depict causal relationships, linking each event to its consequences (**Figure 1**). The likelihood of a specific event occurring is, therefore, conditional on preceding events. Typically, a risk pathway for an infectious disease hazard includes components describing the importation, if relevant, of the hazard (pathogen) from the source country, exposure to the hazard within Canada, human infection, the most

Table 1: Risk framing leading to the risk question for assessment for different infectious disease agents of public health concern

Hazard	Adverse event of concern	Source population(s)	At-risk populations	Timeframe	Risk question
VHF disease outbreak in Country X	Introduction of infected human into Canada	Immigrants resettling to Canada, travellers including tourists, Canadians visiting home countries or on business trips	Close contacts of infected individual, general population	4 weeks	What is the likelihood and impact of a VHF disease introduction into Canada from the outbreak in Country X within the next four weeks?
Avian influenza A(H5N1) clade 2.3.4.4b virus (9)	Human infection in Canada	Wild birds, domestic birds, wild mammals, domestic mammals	Individuals with higher-level exposure[a], individuals with lower-level exposure, general population	Current and up to the end of the next bird migratory season in Canada	What is the likelihood and impact of at least one human infection with avian influenza A(H5N1) clade 2.3.4.4b due to exposure to either birds or mammals in Canada up to the end of the 2023 fall bird migratory season?
Poliovirus outbreak in Country X	Infection of an un/under-vaccinated person in Canada	Immigrants resettling to Canada, travellers including tourists, Canadians visiting home countries or on business trips	Un/under-vaccinated close contacts, un/under-vaccinated communities	4 months	What is the likelihood and impact of poliovirus importation and transmission to un/under-vaccinated close contacts in Canada associated with the poliovirus outbreak in Country X within the next four months?
2022 global mpox outbreak (10)	Human-to-human transmission in Canada	Travellers to Canada from endemic regions at the start of the outbreak, limited clusters of domestic transmission	gbMSM, trans and gender-diverse people, sex workers in Canada, individuals with multiple sexual partners and their close contacts, general population	4 weeks	What is the likelihood and impact of mpox virus transmission among gbMSM with multiple sexual partners and their close contacts in Canada within the next month?

Abbreviations: gbMSM, gay, bisexual, and other men who have sex with men; VHF, viral hemorrhagic fever
[a] High intensity contact (within two meters and/or prolonged without use of personal protective equipment) with animals infected with avian influenza A(H5N1) clade 2.3.4.4b virus (i.e., wild birds, poultry or mammals), infected materials from these animals (e.g., feces, blood, secretions or tissues) or an environment highly contaminated by infected animals

likely spread scenario should infection occur and the resulting impacts. The adverse event of concern (the event to be avoided or mitigated) should be clearly defined, since this is the event for which the overall likelihood will be assessed. Other components such as potential interventions (e.g., vaccination, treatment) and monitoring points (e.g., surveillance systems) can be added to the pathway where relevant. Mapping out the risk pathway helps to formulate the risk question that is of key concern and the types of information that will be needed to address it.

Figure 1: Risk pathway diagrams depicting the steps from the source of infection to the adverse event of concern
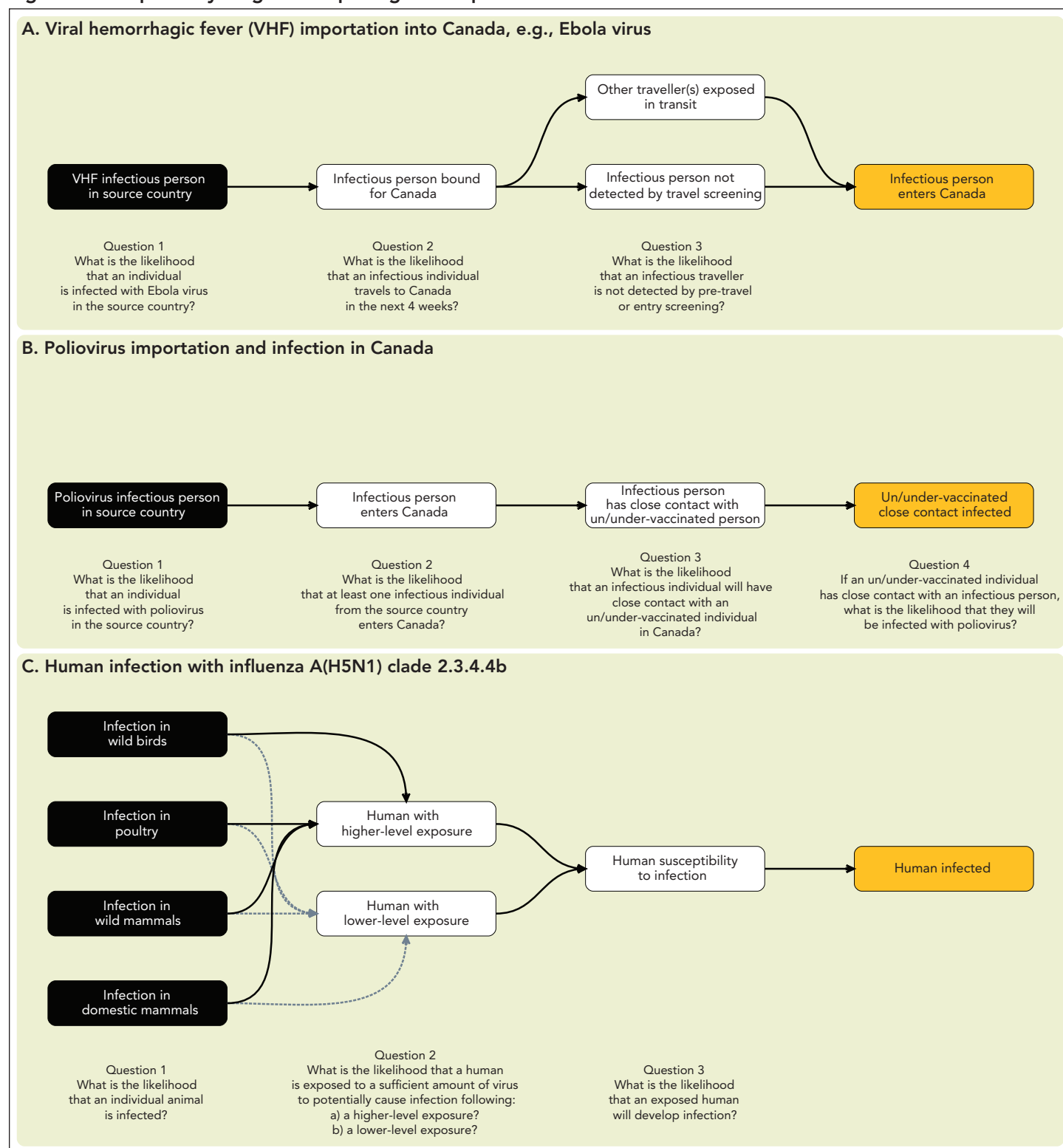
Risk pathways can vary in complexity depending on the hazard and risk question and individual components of the pathway can be expanded and assessed in greater detail or simplified as needed. For example, in considering the potential for importation of a non-endemic disease into Canada (e.g., Ebola virus) into Canada, measures such as pre-travel health screening could reduce the likelihood of importation by preventing symptomatic individuals in the source country from travelling (Figure 1A). With infectious diseases that mostly present as asymptomatic (e.g., poliovirus), such measures are unlikely to meaningfully influence the likelihood of importation; thus, the importation component of the risk pathway can be simplified, assuming that pre-travel health screening would not detect poliovirus infections (Figure 1B). The level of detail in a risk pathway are dependent on the time and resources, availability of information, complexity of the risk questions, risk management needs and sensitivity of the risk to specific steps in the pathway.

Similarly, the risk pathway approach allows for flexibility in incorporating components at the human-animal-ecosystem interface. For example, when assessing the risk of human infection with influenza A(H5N1) clade 2.3.4.4b viruses, the risk pathway can include the likelihood of infection in relevant animal species and the likelihood of human exposure and infection (Figure 1C); depending on the scope, the assessment could consider impacts on human health, the economy, wildlife and agriculture. Risk pathways are, therefore, useful for incorporating multi-sectoral perspectives within a One Health approach.

The risk pathway is used to develop specific sub-questions to be answered during the risk assessment. These sub-questions correspond to individual steps (nodes) in the pathway influencing the likelihood of the event of concern (likelihood sub-questions) and steps leading from the event of concern to the impacts being assessed (impact sub-questions). For infectious hazards, assessing the impacts typically requires an assessment of the most likely spread scenario(s) should the event of concern occur. It should be noted that the event of concern can differ depending on the context and the specific objectives of the assessment (Figure 1, orange nodes).

Risk pathways can be adapted to consider at-risk populations or settings within the RRA (**Figure 2**). For example, the risk pathway can capture the likelihood and impact of infection in defined sub-populations of concern, such as specific occupational, demographic or other relevant high-risk groups (Figure 2A). A further consideration is that the unit of analysis may differ depending on the context. Figure 1 and Figure 2A depict risk pathways related to the likelihood of an individual importing, transmitting or acquiring a pathogen. Figure 2B depicts a risk pathway in which the event of concern is the spread of a multidrug-resistant organism between healthcare facilities, making a healthcare facility a more appropriate unit of analysis.

Estimation of likelihood and impact

Once the risk pathway is complete, evidence to address each pathway sub-question is compiled, reviewed and appraised to produce qualitative estimates of likelihood and/or impact together with levels of uncertainty (see more on uncertainty below). Estimates are informed by a rapid review of relevant evidence, which can include scientific literature, published and unpublished technical reports and epidemiological investigations, event and case-based surveillance data, intelligence obtained through international networks and reporting systems and scientific expertise. As time and evidence can be limited during the early stages of an event, RRAs rely on expert knowledge and opinion. Subject matter experts in relevant areas can guide the estimation process by providing contextual or privileged

Figure 2: Risk pathways for mpox and multidrug-resistant organism transmission
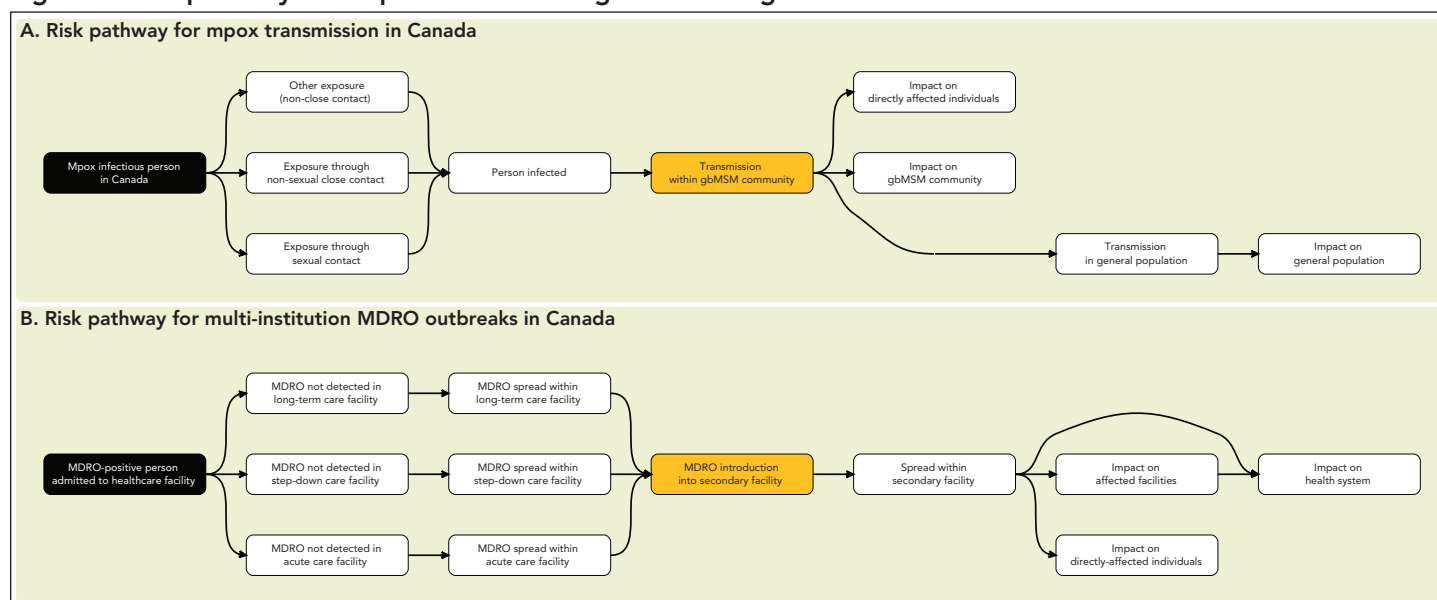
Abbreviations: gbMSM, gay, bisexual, and other men who have sex with men; MDRO, multidrug-resistant organism

information about the hazard being assessed, a nuanced interpretation of the evidence and expert judgement on the event of interest and surrounding context, such as relevant socialcultural factors and industry practices. Uncertainty is estimated based on the availability and quality of relevant evidence, SME opinion and degree of expert agreement. For each pathway sub-question, a qualitative estimate of the likelihood or impact is assigned using pre-defined, standardized scales describing how likely an event is to occur and what impact it is expected to have, both among directly affected individuals and the wider population. Each estimate is accompanied by a brief, focused rationale summarizing the evidence that supports the level assigned. Scales for likelihood and impact estimation available in existing risk assessment frameworks (2,8) can be adapted to suit the local and situational context (see RRAs of measles in Canada and influenza A(H5N1) clade 2.3.4.4b virus for current likelihood, magnitude of effect, impact and uncertainty scales (11,12).

Likelihood considerations

The overall likelihood is a qualitative statement of probability that the adverse event of concern will occur within the time period of interest. The overall likelihood for the adverse event is conditional on the likelihood estimates for preceding steps in the risk pathway and is derived in a manner analogous to the quantitative multiplication of probabilities. When multiplying conditional probabilities, the overall probability can never be higher than the lowest individual probability in the pathway. In the qualitative equivalent, the overall likelihood should not be higher than (and is thus determined by) the lowest likelihood estimate in the pathway (**Figure 3**) (13).

Considerations for assessing the likelihood of an infectious disease event depend on the context and the pathway sub-question (examples in **Appendix**, **Table A1**). For example, when considering the likelihood of importation of a disease, relevant factors include the prevalence of infection and epidemic trajectory in the source country, the volume of incoming travellers, health screening measures, the potential for

transmission of infection during transit, the case-to-infection ratio and incubation period (which influence the likelihood of infected individuals being detected by surveillance or screening) and the duration of infectiousness (which influences the likelihood of an individual being infectious at the time of travel). Similarly, an assessment of the likelihood of infection in Canada should consider the potential for exposure to infectious individuals, the intensity of exposure, pathogen infectivity and demographic, medical, social and other factors that may influence susceptibility to infection.

Impact considerations

The estimation of impact conveys the severity of consequences resulting from the adverse event of concern, should it occur. The PHAC RRA approach assesses impacts at the individual and population levels. Impacts on individuals affected by the hazard are informed by evidence regarding disease severity and associated sequelae, availability and efficacy of prophylaxis and treatment and intrusiveness of control measures (e.g., isolation, quarantine). Population-level impacts are additionally dependent on the most likely scenario for the extent and duration of spread.

The most likely spread scenario is influenced by the pathogen transmissibility (e.g., the reproduction number, *R*), speed of transmission (e.g., serial interval, epidemic doubling time) and effectiveness of public health measures (e.g., case detection, case isolation, contact tracing) and medical countermeasures (e.g., antimicrobials, vaccines). It is not necessarily a description of what will happen; in some situations, all spread scenarios may be unlikely to occur if they are contingent upon earlier steps in the risk pathway that are themselves unlikely. Conveying how likely a chosen spread scenario is to occur is useful for providing appropriate context for estimated impacts.

Public Health Agency of Canada's assessments typically focus on direct health impacts, but also consider additional impacts on wellbeing (e.g., mental health, long-term disability), impacts on the health system, impacts arising from implementation of public health measures or wider impacts using a social, technological,

Figure 3: Risk pathway for the importation of a viral hemorrhagic fever disease
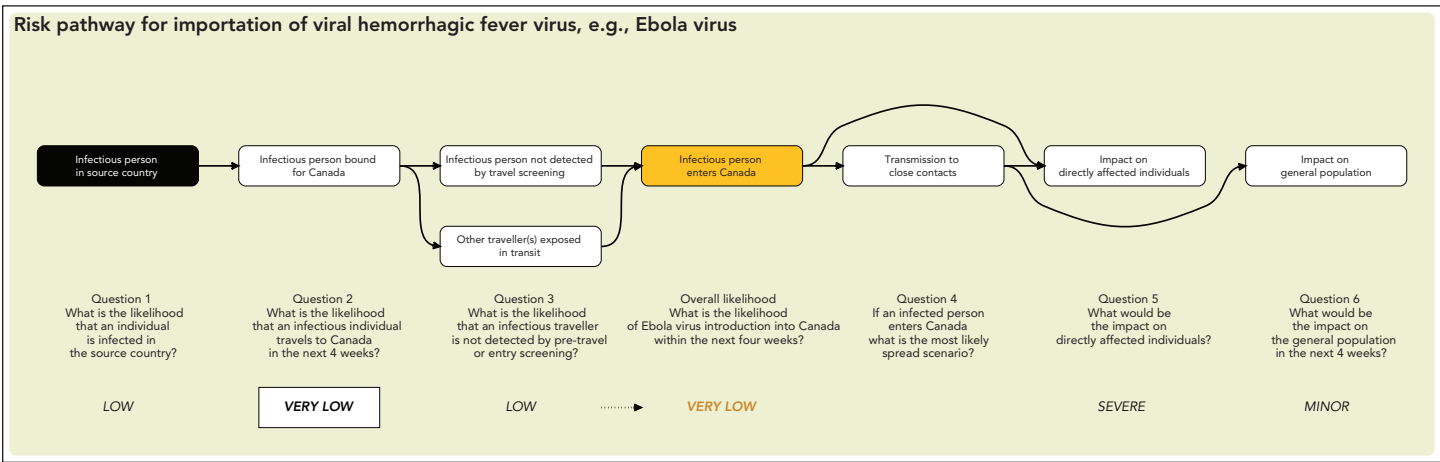
economic, environmental, political and regulatory and population and health system (STEEPP) framework depending on the risk framing (2,14). Balancing these different impacts is challenging and the prioritization of impacts to be assessed should be clarified at the outset, based on the needs of decision-makers and the risk framing exercise. For example, Ebola virus is likely to have severe consequences for infected individuals because of the high case fatality and the need for case isolation but could have minimal population consequences if little onward transmission is expected to occur. Conversely, seasonal influenza is not expected to cause severe illness in most infected individuals but could have major population consequences due to the large number of cases and resultant pressure on the health system.

Sub-populations with disproportionate impacts

The effects of an event may not be uniformly distributed across the population. Certain population sub-groups may be disproportionately affected due to shared risk factors, occupational exposures, demographics, medical vulnerabilities or socioeconomic circumstances. Infectious disease outbreaks that are highly concentrated in certain sub-groups may have minimal impact on the general population. Assessing only the general population impact may mask significant impacts on specific sub-groups and may have downstream health equity implications. Furthermore, it is important to distinguish between sub-groups that are disproportionately affected because of shared risk factors for infection and sub-groups that are more susceptible to severe consequences of infection, as these may not always be the same groups. For example, during the ongoing global outbreak of mpox, transmission has predominantly occurred among gay, bisexual and other men who have sex with men (15) despite high susceptibility to mpox in the general population. Consequently, the health impacts have overwhelmingly affected this sub-population, while the impact on the general population has been minimal (notwithstanding potential elevated risk of severe outcomes in certain sub-groups such as pregnant women) (16). In contrast, generalized community transmission of SARS-CoV-2 has been the norm throughout the COVID-19 pandemic, but the health impacts have been disproportionately high among the elderly, those with co-morbidities and under-vaccinated individuals, because of their higher susceptibility to severe illness. Assessing the differential impact on specific population sub-groups may, therefore, be necessary for certain hazards and this should be considered in the risk framing, risk pathway and assessment of likelihood, spread and impact.

Integrating evidence and expert opinion

Evidence used to estimate likelihood and impact is triangulated with expert knowledge to support the overall assessment. Expert opinion is particularly valuable during a RRA when evidence is limited or conflicting, as well as to provide contextual information about the event based on prior experience. Additionally, expert input can help to identify key uncertainties and knowledge gaps in relation to the risk question. The overall

timeframe and number of SMEs involved in a RRA can vary depending on the event and the complexity of the issue. For events with less complexity, such as the risk associated with Ebola virus importation, a smaller group of SMEs may suffice and discussion with the aim to build consensus on risk estimates may be feasible. For more complex events, such as the risk associated with human infection with an influenza A(H5N1) clade 2.3.4.4b virus, experts from multiple sectors may be needed, including human and veterinary medicine, public health, virology, immunology, agriculture and environmental science. In such cases, different options can be considered to obtain balanced input from experts. Strategies can vary from requesting targeted input on sections most relevant to experts' field of knowledge to obtaining initial estimates of risk from experts through surveys ahead of group discussions, to help minimize biases and ensure that all relevant views are represented.

Levels and drivers of uncertainty and knowledge gaps

For each likelihood and impact level assessed, a level of uncertainty is assigned based on the availability and strength of relevant evidence, as well as expert opinion. As RRAs are typically conducted in the context of limited data, outlining the level of uncertainty for the likelihood or impact of different steps of the risk pathway is crucial for delineating the weight of evidence supporting individual estimates and provides important contextual information for decision-makers to guide appropriate actions (17). In addition to uncertainty levels, identifying drivers of uncertainty and variability is important for determining when actions based on the precautionary principle might be warranted and for defining triggers for re-evaluation of the risk, such as changes in epidemiology. For example, it is not possible to pinpoint which human-adaptive mutations will occur in influenza A(H5) strains within a given timeframe; this is inherently unknowable and will always be highly uncertain (i.e., has high variability). The uncertainty in the likelihood of a viral hemorrhagic fever disease importation, on the other hand, is influenced by availability of information on the extent of transmission, the specific groups in which transmission is occurring, the effectiveness of control measures and the expected volume of inbound travel from the source country. Identifying information gaps can inform surveillance and research recommendations. For example, during an assessment of the risk of human infection with avian influenza A(H5N1) clade 2.3.4.4b virus, gaps identified included lack of evidence regarding the infectious dose in humans and the types of exposures necessary for infection. Consequently, recommended actions included enhancing and integrating surveillance activities for avian influenza across the One Health spectrum in Canada to understand infection risk in human population groups with higher exposure (e.g., agricultural workers) and rapid information sharing of case detections (11).

Assumptions and limitations

During the assessment, certain assumptions may be necessary to make estimation possible in the face of limited information. For example, data on the frequency of and risk factors for severe illness following human infection with avian influenza A(H5N1) clade 2.3.4.4b virus are currently limited, given the small number of human infections that have been identified to date. Some similarity between this and other influenza A(H5) viruses in the propensity to cause severe illness may, therefore, need to be assumed. Any assumptions made during the assessment are described and any relevant limitations that could influence the outcome or limit the scope of the assessment are listed.

Closure phase: recommendations, communication and update

Summary statement and recommendations

The key findings of the RRA are described in a risk statement that summarizes the likelihood and impact estimates, main drivers influencing the estimates and key sources of uncertainty in the assessment. The risk statement, identified knowledge gaps and recommendations form the main outputs of the RRA report. Risk management decisions are outside the scope of RRA and may be based on factors other than assessed risk, including the level of risk tolerance, resource availability, cost-benefit analyses or acceptability of different control measures. However, providing recommended actions helps inform decision-makers, risk managers and relevant stakeholders on risk management options that are proportionate to the risk posed by a given public health hazard. These can include specific actions for response, such as surveillance, implementation of control measures or risk communication to mitigate risk at different levels (e.g., federal, provincial or territorial levels in Canada), as well as research to address knowledge gaps.

If there is considerable uncertainty regarding the likelihood and potential impact of an adverse event beyond the timeframe of the RRA (e.g., for pathogens with pandemic potential or for which the epidemic trajectory is highly uncertain), a description of plausible future scenarios or considerations influencing future risk can be included in the assessment to guide preparedness planning (11,12).

Updating the rapid risk assessment

As a public health event evolves and more information becomes available, a re-assessment of the risk and associated uncertainties may be required to ensure that ongoing risk management activities are appropriate. As part of the PHAC RRA process, monitoring indicators are defined that, if met, would indicate a worsening of the situation and trigger a reassessment of whether an updated RRA is needed. For example, increase in case counts, increased disease severity or case detections in new countries or regions of a given infectious disease outbreak could all trigger a re-evaluation of the risk. In future iterations of an RRA, the risk pathway and risk question(s) may need to be revised if the epidemiological situation changes significantly.

Discussion

We have demonstrated the application of a coordinated approach to public health RRA in the Canadian context, with a focus on infectious disease events. This method uses the risk pathway as a flexible framework to characterize the likelihood and impact of a public health event of concern, aligned with established international RRA frameworks (2,8). As part of the RRA, estimates of likelihood and impact are reported separately to adequately inform risk management decisions.

Alternative RRA frameworks, such as those used by the ECDC (1) and the UK Human Animal Infections and Risk Surveillance group (7) algorithms to guide risk assessors through a pre-determined decision process to derive estimates of likelihood and impact. Algorithm approaches have the advantage of using a standardized set of questions for every risk assessment and of being intuitively easier to understand for both risk assessors and decision-makers. In our experience, however, the risk pathway approach provides greater flexibility than a binary decision process when a more nuanced assessment is required and this approach may be easier to adapt for a broad range of hazards. This is primarily made possible with the ability to craft risk questions specific to the public health event being assessed to ensure that the RRA outputs are practical and relevant for the required risk management decisions under consideration by the steering committee.

Ongoing developments to PHAC's RRA methodology include enhancing approaches for rapid expert elicitation, broadening and improving assessment of impacts beyond health, potentially integrating qualitative and quantitative approaches to inform assessments, strengthening the assessment of quality of evidence, including variability in estimating uncertainty and exploring the possibility of expanding the methodology to hazards other than infectious diseases. Expert judgement, while critical for qualitative RRAs, is known to be prone to various biases (18). These can be mitigated through rigorous elicitation protocols and training of experts in subjective probability judgements, neither of which are easily implemented within the timeframe of a RRA. More work in rapid expert elicitation is required to develop flexible protocols and training material that can be implemented during RRAs.

Although the human health impacts of a public health event may be of primary concern in many risk assessments, in some situations, the economic and social impacts may be substantial. Examples include the economic impacts of highly pathogenic avian influenza on the agricultural sector and the wide-ranging impacts of the COVID-19 pandemic. Commonly used qualitative impact scales, such as that recommended in the JRA OT (8),

incorporate some of these dimensions, but can be difficult to use in practice because they require judgements about the relative importance of health and other impacts. The development of separate scales to capture impacts in different domains, such as impacts on health, the health system, the environment and wider society, could provide a more specific characterization of the types of impacts expected from both infectious and non-infectious hazards (14,19).

Increasingly, developments in mathematical modelling are being used to provide simulations and timely forecasts of likelihood of importation, epidemic spread and the impact of control measures to aid decision-making. Exploring how to integrate quantitative approaches into RRAs may help provide additional understanding of the potential impacts of an event, the key factors influencing those impacts and what public health actions should be prioritized to minimize impacts.

Risk assessment, an evolving field within public health, is important for informing timely and evidence-based decision-making. Given the broad range and complexity of public health hazards, RRA provides a coordinated approach to characterizing and communicating the level of risk to public health posed by an event of concern, to help prioritize and inform risk management activities. When the public health risks fall at the intersection of human-animal-plant-ecosystem health, a multisectoral One Health approach to risk assessment can reduce duplication of effort, improve timely sharing of information across sectors, enhance focus on upstream drivers of health risks and impacts across sectors and facilitate engagement of multiple sectors in risk management measures.

Authors' statement

SPA — Conceptualization, methodology, writing–original draft, writing–review & editing
CCT — Conceptualization, methodology, writing–original draft, writing–review & editing
SC — Conceptualization, methodology, writing–review & editing
DA — Methodology, writing–review & editing
LS — Methodology, writing–review & editing
IL — Methodology, writing–review & editing
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SPA and CCT contributed equally to this article.

Competing interests
None.

References

1. European Centres for Disease Prevention and Control. Operational tool on rapid risk assessment methodology - ECDC 2019. Solna, SE: ECDC; 2019. [Accessed 2023 July 26]. https://www.ecdc.europa.eu/en/publications-data/operational-tool-rapid-risk-assessment-methodology-ecdc-2019

2. World Health Organization. Rapid risk assessment of acute public health events. Geneva, CH: WHO; 2012. [Accessed 2023 July 26]. https://www.who.int/publications-detail-redirect/rapid-risk-assessment-of-acute-public-health-events

3. Morgan D, Kirkbride H, Hewitt K, Said B, Walsh AL. Assessing the risk from emerging infections. Epidemiol Infect 2009;137(11):1521–30. DOI PubMed

4. Palmer S, Jansen A, Leitmeyer K, Murdoch H, Forland F. Evidence-Based Medicine applied to the control of communicable disease incidents when evidence is scarce and the time is limited. Euro Surveill 2013;18(25):20507. DOI PubMed

5. Office of the Auditor General of Canada. Report 8—Pandemic Preparedness, Surveillance, and Border Control Measures. Ottawa, ON: OAG; 2021. [Accessed 2024 Apr 17]. https://www.oag-bvg.gc.ca/internet/English/parl_oag_202103_03_e_43785.html

6. Public Health Agency of Canada. Global Public Health Intelligence Network (GPHIN) Independent Review Panel Final Report. Ottawa, ON: PHAC; 2021. [Accessed 2024 May 3]. https://www.canada.ca/en/public-health/corporate/mandate/about-agency/external-advisory-bodies/list/independent-review-global-public-health-intelligence-network/final-report.html

7. UK Health Security Agency. Guidance: HAIRS risk assessment process. London, UK: UKHSA; 2023. [Accessed 2023 Oct 19]. https://www.gov.uk/government/publications/hairs-risk-assessment-process/hairs-risk-assessment-process

8. Food and Agriculture Organization of the United Nations. Joint Risk Assessment Operational Tool (JRA OT): An Operational Tool of the Tripartite Zoonoses Guide. Rome, IT: FAO/OIE/WHO; 2020. [Accessed 2023 July 26]. https://www.fao.org/documents/card/en/c/cb1520en/

9. World Health Organization. Influenza at the human-animal interface summary and assessment. Geneva, CH: WHO; 2023. https://www.who.int/publications/m/item/influenza-at-the-human-animal-interface-summary-and-assessment-3-march-2023

10. World Health Organization. Multi-country monkeypox outbreak in non-endemic countries. Geneva, CH: WHO; 2022. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385

11. Public Health Agency of Canada. Rapid risk assessment: Avian influenza A(H5N1) clade 2.3.4.4b. Ottawa, ON: PHAC; 2023. [Accessed 2023 Oct 19]. https://www.canada.ca/en/public-health/services/emergency-preparedness-response/rapid-risk-assessments-public-health-professionals/avian-influenza-a-h5n1-clade-2-3-4-4b.html

12. Public Health Agency of Canada. Rapid risk assessment: Measles in Canada, public health implications in 2024. Ottawa, ON: PHAC; 2024. [Accessed 2024 May 1]. https://www.canada.ca/en/public-health/services/emergency-preparedness-response/rapid-risk-assessments-public-health-professionals/rapid-risk-assessment-measles-public-health-implications-2024.html

13. Kelly L, Kosmider R, Gale P, Snary EL. Qualitative import risk assessment: A proposed method for estimating the aggregated probability of entry of infection. Microb Risk Anal 2018;9:33–7. https://www.sciencedirect.com/science/article/abs/pii/S2352352217301020 https://doi.org/10.1016/j.mran.2018.03.001

14. Goode EJ, Thomas E, Landeg O, Duarte-Davidson R, Hall L, Roelofs J, Schulpen S, De Bruin A, Wigenstam E, Liljedahl B, Waleij A, Simonsson L, Nyberg AG. Development of a Rapid Risk and Impact Assessment Tool to Enhance Response to Environmental Emergencies in the Early Stages of a Disaster: A Tool Developed by the European Multiple Environmental Threats Emergency NETwork (EMETNET) Project. Int J Disaster Risk Sci 2021;12(4):528–39. DOI

15. World Health Organization. Mpox (monkeypox). Geneva, CH: WHO; 2023. [Accessed 2023 Oct 19]. https://www.who.int/news-room/fact-sheets/detail/monkeypox

16. Ogoina D, Damon I, Nakoune E. Clinical review of human mpox. Clin Microbiol Infect 2023;29(12):1493–501. DOI PubMed

17. Benford D, Halldorsson T, Jeger MJ, Knutsen HK, More S, Naegeli H, Noteborn H, Ockleford C, Ricci A, Rychen G, Schlatter JR, Silano V, Solecki R, Turck D, Younes M, Craig P, Hart A, Von Goetz N, Koutsoumanis K, Mortensen A, Ossendorp B, Martino L, Merten C, Mosbach-Schulz O, Hardy A; EFSA Scientific Committee. Guidance on Uncertainty Analysis in Scientific Assessments. EFSA J 2018;16(1):e05123. DOI PubMed

18. Morgan MG. Use (and abuse) of expert elicitation in support of decision making for public policy. Proc Natl Acad Sci USA 2014;111(20):7176–84. DOI PubMed

19. Public Safety Canada. National Risk Profile: Strengthening Canada's All-Hazards Approach to Emergency Management. Ottawa, ON: PSC; 2024. [Accessed 2024 Jan 18]. https://www.publicsafety.gc.ca/cnt/mrgnc-mngmnt/ntnl-rsk-prfl/index-en.aspx

Appendix

Table A1: Examples of relevant considerations for different risk pathway steps and types of evidence and uncertainties informing the assessment

Example risk pathway steps	Example considerations	Types of evidence informing assessment	Uncertainty considerations
Infection in source country	What is the epidemiological situation? What is the geographic distribution of disease? Are specific population sub-groups being affected?	Case reports, event summaries, surveillance data, local and international risk assessments, intelligence from relevant agencies/organizations	Extent of under-ascertainment of cases, role of asymptomatic and pre-clinical infections in transmission, delays in reporting of cases and deaths through surveillance mechanisms, potential biases in case detection towards certain geographic regions (e.g., urban areas) or population sub-groups (e.g., children)
	How will the epidemic evolve over the period of assessment?	Information on the extent, speed and potential for epidemic spread; epidemic doubling time; evidence for widening of geographic range or population groups affected; immunization coverage (for vaccine-preventable diseases); effectiveness of public health control measures being implemented	Effectiveness of control measures over the period of assessment, changes in epidemiology and/or pathogen biology
Importation from source country	What is the expected volume of travel from the source country over the period of assessment?	Data on forecasted air passenger travel volumes over the period of assessment	Historical trends may not reflect travel patterns during period of assessment Limited information or travel by other routes (e.g., land, sea)
	Are potentially infectious individuals likely to travel to Canada?	Quantitative models of importation risk	Importation models may not accurately capture travel by specific population sub-groups of interest or through non-air travel routes
	Are infectious travellers likely to infect others during transit?	Epidemiological, microbiological and environmental studies and risk assessments of transmission risk during transit	The frequency and duration of potentially infectious exposure events during transit is likely to be unknown
	Will existing travel health screening and border measures reduce likelihood of importation?	Incubation period, duration of infectiousness, role of asymptomatic and pre-symptomatic infection in transmission, evidence of importation from similar events in the past	Information on what types of travel health screening and border measures are implemented in source, transit and destination countries and their effectiveness, may be limited
Exposure in Canada	What is the size of the population(s) at risk?	Census data, immunization coverage (for vaccine-preventable diseases), information on size of occupational groups, representative survey data on risk factor prevalence, spatio-temporal distribution of competent vectors (for vector-borne pathogens)	Information may not be available on the size and geographic distribution of specific population sub-groups of interest
	What is the frequency and intensity of exposure to infectious individuals or sources of infection?	Studies of population contact patterns or human-animal contact patterns (for zoonoses), information on types/categories of exposure	Detailed information on patterns of contact and other relevant exposures may not be available
	What is the availability and effectiveness of exposure-reduction measures (e.g., personal protective equipment)?	Epidemiological and other scientific studies of the effectiveness of exposure-reduction measures, information on adherence to and appropriate use of exposure-reduction measures	Scientific evidence may be limited, inconclusive or associated with high levels of uncertainty

Table A1: Examples of relevant considerations for different risk pathway steps and types of evidence and uncertainties informing the assessment (*continued*)

Example risk pathway steps	Example considerations	Types of evidence informing assessment	Uncertainty considerations
Susceptibility to infection	Is exposure likely to lead to infection?	Mode(s) of transmission, infectious dose, per-contact transmission probability, epidemiological studies of transmission in household and other contacts	The relative contribution of different routes of infection to transmission may be unclear, the infectious dose may not be well established, the probability of infection from different types of exposure may not be known
	Are there factors that influence the likelihood of infection in exposed individuals?	Epidemiological studies of risk factors for infection, studies of infection risk among exposed individuals with medical or other vulnerabilities, data on vaccine effectiveness in relevant population groups (for vaccine-preventable diseases), pathogen mutations/adaptations	Scientific evidence for the risk of infection in specific population sub-groups may be limited, the extent to which vaccination prevents infection (rather than disease) may be unclear, relevant pathogen mutations may not be well characterized
Likely spread scenario(s)	What would be the likely extent of transmission over the period of assessment?	Mode(s) of transmission; reproduction number (R); serial interval and epidemic doubling time; population contact patterns (including human-animal contacts for zoonoses); transmission patterns in specific population sub-groups or occupational/exposure groups; availability and effectiveness of public health measures and medical countermeasures, including vaccines and antimicrobials; seasonal factors influencing transmission patterns; experience from similar events in the past	For novel pathogens, data on relevant epidemiological parameters of transmissibility may be limited; the effectiveness of measures to control transmission may be unclear
Impact on directly-affected individuals	What would be the health consequences on infected individuals?	Information on case-to-infection, case-to-hospitalization and case-to-fatality ratios; epidemiological studies of risk factors for severe outcomes; information on the frequency of severe outcomes among infected individuals; availability and effectiveness of medical countermeasures; information on the frequency of long-term sequelae of infection and consequences of infection on well-being	For novel pathogens, illness severity and case fatality may be over-estimated early on if detection is biased towards severe cases; the frequency and impact of long-term sequelae may be unclear; risk factors for severe illness may not be well established
	What additional consequences could there be for infected individuals?	Evidence of financial or other impacts on affected individuals and their families, including stigma and discrimination; information on additional burdens on affected individuals and families resulting from control measures	Financial and other impacts may be dependent on individual circumstances
Population impact	What fraction of the population would be affected? Would large numbers of severe cases and deaths be expected? Would health impacts affect the general population or be restricted to specific sub-groups?	Disease incidence, hospitalization, mortality, speed and geographic extent of epidemic spread, population sub-groups affected, long-term consequences of infection	The scale of health impacts may be highly dependent on uncertainties in the most likely spread scenario
	Would there be impacts to the health system and/or wider society?	Impacts on the health system, including healthcare workforce; societal disruption and economic impacts resulting from epidemic and/or associated control measures; public anxiety, social unrest and discrimination resulting from epidemic and/or associated control measures; impacts of epidemic and/or associated control measures on health inequalities	The range and extent of indirect impacts may be difficult to predict

Public health contributions of entomological surveillance of West Nile virus (WNV) and other mosquito-borne arboviruses in a context of climate change

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Abstract

Background: Climate change is likely to increase the risk of human transmission of arboviruses endemic to Canada, including West Nile virus (WNV), Eastern equine encephalitis virus (EEEV) and California serogroup virus (CSV), calling for enhanced surveillance, including entomological surveillance targeting mosquito vectors. A scoping review was carried out to document the public health contributions of entomological surveillance of arboviruses of importance in Canada.

Methods: The Ovid® and EBSCO platforms and the grey literature were searched to identify documents published between 2009 and 2023, in English or French, dealing with entomological surveillance of arboviruses of interest, conducted annually for human health purposes under the aegis of a government authority, with specified public health objectives and actions.

Results: The 42 selected publications mainly reported two public health objectives of adult mosquito surveillance: early warning of viral circulation and assessment of the level of risk of human transmission. Recommended actions included clinical preparedness, risk communication, promotion of personal protection measures and vector control. The main objectives of immature mosquito surveillance were to identify sites with high larval densities, in order to reduce/eliminate them and target the application of larvicides.

Conclusion: In a context of climate change favouring the spread of arboviruses, this study highlights the potential public health contributions of regular entomological surveillance of endemic arboviruses of importance in Canada. It helps support concrete actions to protect the health of the population from the risks of arboviral transmission.
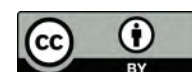
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Introduction

Increased ambient temperatures and variability in precipitation patterns associated with climate change are conducive to an expansion in the geographic range of mosquito vectors of arboviruses endemic to Canada, an increase in their local abundance and a reduction in the extrinsic incubation period, enabling them to become infectious earlier (1,2). This greater dispersion would contribute to an increased risk of human transmission, particularly of West Nile virus (WNV), Eastern equine encephalitis virus (EEEV) and California serogroup viruses (CSV) (1–3).

These changes call for enhanced surveillance of such arboviruses to better assess the health risks to the Canadian population (1) and target interventions more effectively. To the best of our knowledge, no synthesis of the public health objectives of entomological surveillance of mosquito-borne arboviruses has been published in Canada.

The aim of this scoping review was to document, as comprehensively as possible, the public health objectives of the entomological component of surveillance for arboviruses of interest, namely WNV, EEEV, Cache Valley virus (CVV) and the CSVs, including Jamestown Canyon virus (JCV) and Snowshoe Hare virus (SSHV). In other words, the aim was to show how entomological surveillance data can be used to support various actions designed to protect the population from the risk of arbovirus transmission. The purpose of this study is therefore to support thinking on the potential of surveillance of mosquito vectors of these arboviruses of importance in Canada by examining the relevance of such surveillance to concrete action by the authorities concerned, including the implementation of appropriate preventive measures and vector control.

Methods

Search strategy

A scoping review was conducted based on the methodological framework suggested by Arksey and O'Malley (4) and improved by Levac *et al.* (5). Its specific aims were 1) to synthesize the public health objectives targeted by entomological surveillance of mosquito-borne arboviruses under different arboviral transmission scenarios as detailed below and 2) to describe how the resulting data can help support actions to protect the population. The public health objective implies, in fact, that the entomological surveillances reported in the literature are carried out with the aim of supporting concrete actions.

The research question was: "What are the contributions of the entomological component in the surveillance of WNV, EEEV, CVV and the CSVs, including JCV and SSHV, in a context of climate change?". For this research, the term "surveillance" refers to any process of ongoing data collection, carried out under the aegis of a governmental authority, particularly a public health authority, in order to guide its decisions, policies and responses (6). The research question identified three major concepts that were combined as follows: "arboviruses transmitted by mosquitoes," "surveillance" and "mosquito vectors."

For each of these major concepts, a list of synonymous keywords was drawn up for searching the bibliographic databases of the Ovid® (Embase, Global Health and MEDLINE®) and EBSCO (CINAHL® Complete, Environment Complete and GreenFILE) platforms, as well as CAB Abstracts (CABI), Engineering Village, Pascal and Francis, PubMed and Web of Science. No

geographical restrictions were applied and the literature search covered the period from 2009 to 2023. A complementary search was carried out in the grey literature for the same time interval. It considered mainly Google and Google Scholar search engines, in addition to grey literature resources, including government websites, notably those of health agencies in Canadian provinces and US states, among which are those bordering Canada.

Relevant publications were selected initially by evaluating titles and abstracts, and then by reading the full text, where necessary. Inclusion and exclusion criteria required that publications 1) be written in English or French; 2) deal with entomological surveillance for human health purposes of our arboviruses of interest with field collection of mosquitoes; 3) be regularly conducted each year during the mosquito season and initiated, supervised, requested, required or supported by one or more government entity(ies); and 4) have explicit public health objectives and possible subsequent actions implemented or recommended. Publications dealing, for example, with pure research activities, such as the advancement of knowledge on the ecology of mosquito vectors or trapping techniques, without mentioning public health objectives/actions, were excluded.

Descriptive knowledge synthesis

A summary table was developed to report relevant data extracted from the selected publications. These data include the arboviruses and developmental stages targeted, the epidemiological situation during which entomological surveillance was carried out (i.e., no human cases, sporadic, endemic or epidemic human cases), the public health objectives targeted by this surveillance and the subsequent actions that can derive from the entomological data obtained.

The objectives identified were then classified according to four types of arboviral transmission scenarios based on the epidemiological situations described in the literature:

- **No arboviral transmission:** No human cases reported, no apparent arboviral transmission to the human population and low or unknown levels among reservoir hosts
- **Sporadic:** Human cases reported anecdotally, arboviral transmission considered sporadic, low level in the human population and among reservoir hosts
- **Endemic:** Human cases reported on a recurrent basis with no sign of sudden or rapid increase, arboviral transmission considered to be persistent in the human population and among reservoir hosts
- **Epidemic:** Sudden and rapid increase in human cases, arboviral transmission considered high and persistent in the human population and among reservoir hosts

Results

Figure 1 shows a flow chart illustrating the search and selection of relevant publications. Bibliographic database queries yielded 15,112 results. After removing duplicates, 7,392 scientific publications were evaluated by title and abstract. Only 121 were finally screened for eligibility by full text reading, including 10 literature reviews. These reviews were initially retained in an attempt to find relevant references not detected in the bibliographic databases. They were afterwards excluded. Of these 121 scientific publications, 23 were deemed eligible. Consultation of grey literature sources led to the addition of 18 documents, mainly recent entomological surveillance and intervention plans or reports. A grey literature document was also found in one of the accepted scientific articles. A total of 42 publications were included in the knowledge synthesis. The scientific articles are mainly from European countries, while the grey literature is more from North America. Most of these publications focused on two or even three mosquito-borne arboviruses. However, the vast majority of cases involved WNV (n=38), with the remainder involving EEEV (n=12) and JCV (n=3). No relevant documents on SSHV or CVV were identified (n=0).

A summary of the public health objectives of entomological surveillance of arboviruses of interest is presented in **Table 1** (adult mosquitoes) and **Table 2** (immature forms of mosquitoes). Surveillance of these different developmental stages is usually carried out concomitantly in order to consider the entire vector lifecycle (7–20). The two tables also include the number of publications reporting on each of the public health objectives, the arboviral transmission scenarios concerned and the arbovirus(es) of interest targeted per scenario, as well as examples of entomological indicators that help to achieve the targeted objectives.

Figure 1: Flow chart illustrating the various stages in the search for and selection of relevant publications[a,b]
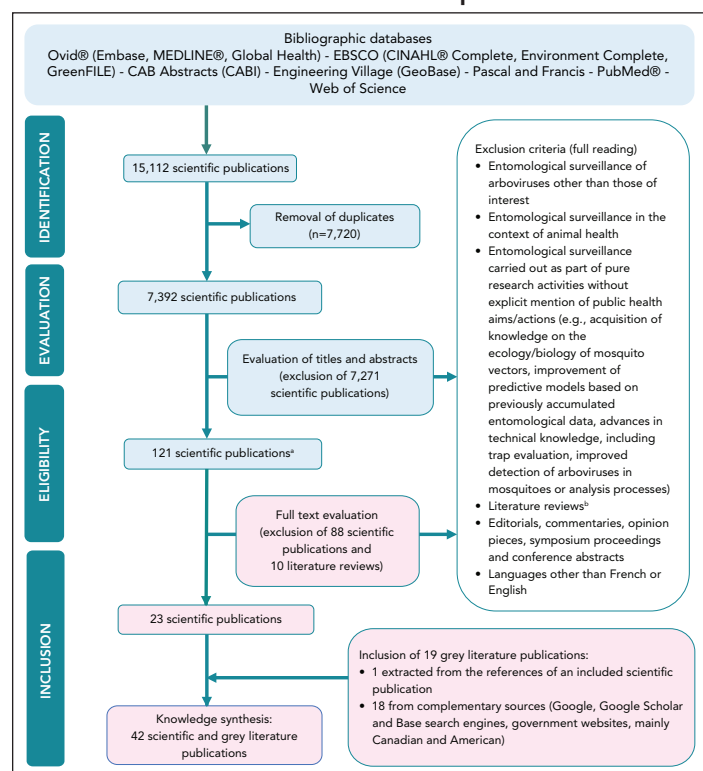
[a] The 121 articles retained following title and abstract evaluation included 111 to be assessed for eligibility by full text review and 10 literature reviews in an attempt to find any relevant publications not detected in the bibliographic databases
[b] Literature reviews were excluded after extracting 13 scientific publications which were not retained after reading of the full text
Restrictions used: from 2009 to 2023; no geographical restrictions were applied for document searches

Table 1: Public health objectives of entomological surveillance of arboviruses of interest by arboviral transmission scenario of adult mosquito surveillance

Public health objectives		n[a]	Arboviral transmission scenarios concerned				Example of entomological indicators used
			None	Sporadic	Endemic	Epidemic	
Early warning of viral circulation before the first human cases appear		20	WNV	WNV	WNV, EEEV, JCV	-	First positive mosquito pools for one and/or another of the arboviruses (7,9–11,14,18,19,21–33)
Human risk assessment	Assessing the level of risk of human transmission[b]	22	WNV	WNV	WNV, EEEV, JCV	-	Spatiotemporal distribution and abundance of mosquitoes by identified species, number of mosquitoes per trap, number of positive mosquito pools, number of traps with positive mosquitoes, species type of positive mosquitoes (more ornithophilic or more that feed on mammals, including mosquitoes that feed on humans), number of weeks with positive mosquito pools, infection rate[c], vector index[d] (7–19,21,32,34–40)
	Mapping levels of viral circulation intensity	3	-	-	WNV	-	Mosquito infection rate (maximum likelihood estimation and minimum infection rate)[c] (22–24)
	Predicting an outbreak of human cases	2	-	-	WNV	-	Proportion of positive mosquito pools, minimum infection rate, vector index (22,33)
Assessing resistance to insecticides used in vector control		7	-	-	WNV, EEEV, JCV	WNV	Mosquito abundance before and after insecticide treatment, presence and frequency of mutation genes (9,11,16,17,20,41,42)

Table 1: Public health objectives of entomological surveillance of arboviruses of interest by arboviral transmission scenario of adult mosquito surveillance (*continued*)

Public health objectives	nª	Arboviral transmission scenarios concerned				Example of entomological indicators used
		None	Sporadic	Endemic	Epidemic	
Real-time monitoring and support for efforts to reduce human transmission	3	-	-	-	WNV, EEEV	Mosquito abundance, number of positive mosquito pools, vector index, minimum infection rate (43–45)
Contribution to the declaration of a health emergency linked to arboviruses	1	-	-	WNV, EEEV	-	Proportion of positive mosquito pools (health emergency declared as soon as 10% of bridge vectorᵉ mosquito pools tested positive for WNV or EEEV) (14)
Controlling the spread of the *Culex* population from flooded areasᶠ	1	-	-	WNV	-	Abundance of *Culex* species per trap (35)
Update of the list of potential vector species	1	-	-	WNV	-	Adult mosquito abundance by identified species, minimum infection rate (46)
Documentation of WNV transmission and overwintering mechanisms in competent vectorsᵍ	1	-	-	WNV	-	Presence of WNV in hibernating mosquitoes (9)
Documenting the intensity of viral circulation during an epidemic year at international airportsʰ	1	-	-	-	WNV	Mosquito abundance by identified species, minimum infection rate (47)
Warning of a potentially increased risk of arboviral transmission for next year's mosquito seasonⁱ	1	-	-	-	WNV	Mosquito abundance by identified species, minimum infection rate (48)

Abbreviations: EEEV, Eastern equine encephalitis virus; JCV, Jamestown Canyon virus; WNV, West Nile virus; -, not applicable
ª n is the number of publications having documented the public health objective. The same publication could report on several public health objectives. The sum of these numbers is therefore greater than 42
ᵇ Also known as the probability of locally acquired human diseases in the states of Massachusetts and Rhode Island, or the probability of human illness in the state of New Hampshire. Risk levels for human transmission are generally classified as low, moderate, high or very high
ᶜ The infection rate corresponds to the number of infected mosquitoes per 1,000 tested. It can be expressed using two indicators: maximum likelihood estimation, which assumes that one or more mosquitoes are infected in a pool tested positive for the targeted arbovirus, or minimum infection rate, which is a simple approximation of the prevalence of infected mosquitoes, since it assumes that only one mosquito is positive in each positive pool
ᵈ The vector index, or risk index, is the estimated proportion of infected mosquitoes of a particular species in a specific area. It corresponds to the product of the number of mosquitoes collected and their infection rate
ᵉ A bridge vector mosquito is capable of carrying the pathogen and transmitting it to another species (including humans) other than the one involved in the enzootic cycle
ᶠ *Culex* mosquitoes are strongly influenced by temperature, precipitation and humidity
ᵍ Based on the hypothesis that some *Culex pipiens* may survive the winter as adults while infected. Adult mosquitoes are collected during the off-season (from November to the end of March)
ʰ During epidemic years, the ecological habitats of airports can favour WNV transmission and increase the risk of mosquitoes and/or viruses spreading to non-endemic regions
ⁱ This higher risk is associated with a milder winter combined with the ability of the main infected mosquito vectors to spend the winter season in the geographical area where entomological surveillance takes place

Table 2: Public health objectives of entomological surveillance of arboviruses of interest by arboviral transmission scenario of immature mosquito surveillance

Public health objectives	nª	Arboviral transmission scenarios concerned				Example of entomological indicators used
		None	Sporadic	Endemic	Epidemic	
Identifying larval breeding sitesᵇ and determining high larval density areas	16	WNV	WNV	WNV, EEEV, JCV	-	Presence of eggs, larvae and pupae; abundance (or density) by identified species and developmental stageᶜ (7–20,32,37)
Mapping of breeding sitesᵈ	6	-	-	WNV, EEEV, JCV	-	Presence of breeding sites (12,15,17–20)

Abbreviations: EEEV, Eastern equine encephalitis virus; JCV, Jamestown Canyon virus; WNV, West Nile virus; -, not applicable
ª n is the number of publications having documented the public health objective. The same publication could report on both of the public health objectives described. The sum of these numbers is therefore greater than 16
ᵇ The location of artificial and natural breeding sites is linked to the specific ecology of each mosquito vector
ᶜ The abundance of immature mosquitoes is an early indicator of the density of the future adult population
ᵈ The collection and examination of topographical maps, aerial photographs, geographic information systems (GIS) technology and local expertise can be used to map breeding sites

The majority of public health objectives identified in the consulted literature concern the scenario of arboviral transmission at endemic level. Those most documented for adult mosquito surveillance, and common to WNV, EEEV and JCV, are:

- Early warning of viral circulation (n=20) before the first human cases appear and thanks to the first positive mosquito vectors pools for one and/or another of the arboviruses under surveillance.

- Assessment of the level of risk of human transmission (n=22) based on, among others, entomological indicators such as mosquito abundance, infection rate of arbovirus in mosquito population and vector index. These risk levels are generally described as low, moderate, high or very high.

The main objectives reported for surveillance of immature forms of the vectors of one and/or another of these three arboviruses are the identification of artificial and natural breeding sites and the determination of areas with high larval densities (n=16).

Table 3 and **Table 4** summarize the main public health actions that can derive from adult and immature mosquito surveillance data, respectively. These actions are presented for each surveillance objective. For adult forms, they include:

- Clinical preparedness to strengthen human surveillance, particularly through greater vigilance in recognizing and diagnosing illnesses linked to these three arboviruses, as well as increased laboratory resources for confirmatory testing of human cases.
- Real-time risk communication by the responsible authorities to local authorities, healthcare providers, the media and the general public.

- Ongoing education/awareness campaigns, using a variety of communication channels to increase outreach efforts, aimed at the general population and healthcare professionals. These campaigns focus mainly on personal protection measures (e.g., long-sleeved clothing, mosquito nets, use of repellents) and participation in source reduction efforts by eliminating peridomestic stagnant water (e.g., emptying artificial containers, recovering used tires, swimming pool maintenance).
- Vector control, including the ground-based and/or aerial application of larvicidal treatments or even of adulticides, when the level of risk of human transmission is deemed high or critical.

Public health actions guided by data from immature forms surveillance essentially include source reduction aimed at eliminating/reducing natural and artificial larval breeding sites (e.g., elimination of stagnant water and vegetation management), targeted larvicidal treatments focusing on areas of high larval density and evaluation of the effectiveness of such treatments.

Table 3: Public health actions that can derive from adult mosquito surveillance data

Surveillance objectives		Public health actions			
		Clinical preparedness[a]	Risk communication[b]	Ongoing awareness/ education campaigns[c]	Vector control[d]
Early warning of viral circulation before the first human cases appear		X[e]	X[e]	X[e]	X[e]
Human risk assessment	Assessment of the level of risk of human transmission	X[e]	X[e]	X[e]	X[e]
	Mapping levels of viral circulation intensity	-	-	-	X[e]
	Predicting an outbreak of human cases	-	-	-	X[e]
Evaluation of resistance to insecticides used in vector control[f]		-	-	-	X[e]
Real-time monitoring and support for efforts to reduce human epidemic transmission[g]		X[e]	X[e]	X[e]	X[e]
Contribution to the declaration of a health emergency linked to arboviruses[h]		-	X[e]	X[e]	X[e]
Controlling the spread of the *Culex* population from flooded areas		-	X[e]	X[e]	X[e]
Update of the list of potential vector species[f]		-	-	-	X[e]
Documentation of WNV transmission and overwintering mechanisms in competent vectors		-	-	-	X[e]
Documenting the intensity of viral circulation during an epidemic year at international airports		-	-	-	X[e]
Warning of a potentially increased risk of arboviral transmission for next year's mosquito season[i]		-	X[e]	X[e]	-

Abbreviations: WNV, West Nile virus; -, not applicable
[a] Includes increased vigilance in the recognition and diagnosis of arboviruses, an expansion of technical laboratory resources for confirmatory testing of human cases, the strengthening of veterinary surveillance and the activation of the procedure guaranteeing the safety of blood transfusions
[b] Includes real-time, regular and constantly updated communication of the levels of risk of human transmission to local authorities, health care providers, the media (e.g., publication of national press releases) and the general public
[c] Includes awareness-raising and ongoing education of human healthcare providers and the general population, especially those at risk, on personal protection measures (e.g., long-sleeved clothing, mosquito nets, use of repellents) and source reduction by eliminating peridomestic and urban stagnant water (e.g., emptying of artificial containers, recovery of used tires, swimming pool maintenance), while multiplying communication platforms (e.g., websites of health authorities and other relevant government entities, press releases in local newspapers, interviews on various cable channels, social networks, information leaflets in different languages in schools and community organizations, workshops in retirement homes) to increase outreach efforts
[d] Includes source reduction, ground and/or aerial application of larvicides and even of adulticides, when the level of risk of human transmission have been deemed high or even critical
[e] For each of the adult mosquito surveillance objectives, the coloured cells designate the public health actions that can be derived from the surveillance data
[f] Public health action involves updating vector control programs where necessary
[g] Public health action consists of an increase in confirmatory testing of human cases and an intensification of risk communication strategies, personal protection awareness/education campaigns and vector control in the most at-risk areas
[h] Public health actions can include the creation of a panel of experts and the setting up of an emergency operations centre for coordinated, faster and more effective responses
[i] Public health actions consist of a sustained, ongoing education/awareness campaign for the general population and risk communication to public health authorities in neighbouring states and regions

Table 4: Public health actions that can derive from immature mosquito surveillance data

Surveillance objectives	Public health actions			
	Source reduction[a]	Targeted larvicidal treatments[b]	Evaluation of larvicidal treatments[c]	Real-time monitoring of larvicide deployment[d]
Identifying larval breeding sites and determining high larval density areas	X[e]	X[e]	X[e]	-
Mapping of breeding sites[f]	-	-	-	X[e]

Abbreviation: -, not applicable
[a] Includes elimination of stagnant water (e.g., percolation, recirculation, drainage), vegetation management (e.g., controlling algae growth) and saltmarsh water management
[b] Involves targeting priority areas with high larval densities
[c] Includes evaluation of duration and efficacy of larvicidal treatments
[d] Involves checking the suitability of larvicidal treatments in priority areas with high larval densities
[e] For each of the immature mosquito surveillance objectives, the coloured cells designate the public health actions that can be derived from the surveillance data
[f] Enables improved surveillance of breeding sites for the following year's mosquito season by allowing the responsible authorities to decide where to concentrate this surveillance

Discussion

Entomological surveillance of mosquito-borne arboviruses: a valuable contribution to public health

This literature review has documented the public health objectives that can be achieved through entomological surveillance of arboviruses of interest, as well as the subsequent actions that can derive from the resulting data. These objectives were reported by developmental stage monitored, i.e., adult and immature mosquitoes, and by arboviral transmission scenario. This strategic breakdown of public health objectives/actions according to various scenarios offers some avenues for reflection to carry out mosquito surveillance. Any authority concerned could then, according to its priorities, opt for the appropriate objective(s) in line with the arboviral transmission scenario prevailing in the region targeted for entomological surveillance of mosquito-borne arboviruses.

The major finding of this study is that mosquito surveillance can help support the implementation of actions to protect human health from the risk of arboviral transmission. Real-time exploitation of entomological data from adult mosquito surveillance provides useful and rapid information to the authorities concerned by contributing to early warning of viral circulation and by helping to assess the level of risk of human transmission to support more prompt and informed management. The aim is to decrease arboviral transmission and limit human cases by implementing a range of preventive public health actions, including vector control. The latter intends to reduce the abundance of infected or potentially infected vectors, thereby lowering the environmental viral load.

Early warning of viral circulation is based on the detection of the first positive mosquito pools for the arboviruses under surveillance, which usually occur a few days or even several weeks before human cases appear (9,22,23,26,30,31,42). In New York City, for example, data collected between 2000 and 2022 showed that WNV was detected in mosquitoes weeks before any risk of human transmission became significant (9). The main purpose of this alert is to rapidly initiate clinical preparedness activities, as described above, risk communication, coordination and training of local health officials and personnel involved in entomological surveillance, as well as the development of materials for public awareness/education campaigns on preventive measures. Early warning also enables vector control to be initiated, including source reduction, to limit the spread of infected mosquitoes to densely populated areas (7–9,14,17–19,21–33).

The level of risk of human transmission is assessed throughout the mosquito season using real-time entomological data from the current year, often combined with those from previous years (10–13,16–18). These data are most often also combined with other parameters, as no single indicator can provide an accurate measure of risk (10,18). These parameters include (9,11,13,14,16–18,35):

- Immature mosquito surveillance data, including type and location of breeding sites and their proximity to the human population at risk and larval abundance
- Human and animal surveillance data (wild birds, chickens, horses, etc.)
- The time of year
- Current and projected local weather conditions (degree-day accumulation, precipitation, wind speed, etc.)
- The density of the human population at risk, particularly those close to larval breeding sites

The use of entomological data to estimate the level of risk of human transmission is justified by the statistically positive correlation between mosquito abundance, vector index and/or mosquito infection rate, on the one hand, and the number of human cases, on the other. This correlation has been well documented for WNV in Canada (49,50) and elsewhere in the world (33,44,51,52).

This risk level assessment helps guide the rapid implementation and gradual, targeted and proportionate intensification of public health actions, including regular risk communication and updates, education/awareness-raising through public outreach campaign on preventive measures and vector control. The focus is put on a gradual reinforcement of personal protection measures for humans and source reduction measures, or even a possible restriction of outdoor activities to decrease exposure risks (10,13,16–18,34–38). The states of Massachusetts (10), Vermont (17), New Hampshire (18) and Rhode Island (38) have, in fact, developed guidelines revealing the entomological data, combined or not with other parameters, that define levels of risk of human transmission and the subsequent public health responses.

Outbreak risk assessment is generally based on the vector index, which predicts an increase in the number of human cases over the following two to three weeks (33,43,50). This predictive effort can be used to guide vector control strategies in order to prioritize areas identified as being most at risk (32,33).

Other public health objectives were identified in the consulted literature. Although few publications have reported on them, they remain relevant. One example is the assessment of resistance to insecticides used in vector control, which is essential for evidence-based strategy revision. Another example would be the contribution to the declaration of a health emergency linked to arboviruses, prompting the creation of a panel of experts (epidemiologists, veterinarians, vector control experts, biologists, local representatives) and the setting up of an emergency operations centre for coordinated, faster and more effective public health interventions (14).

Finally, surveillance of immature mosquitoes is essential, as it enables targeted larvicidal treatments to help reduce the adult mosquito population, particularly when the level of risk of human transmission is deemed high (11,17). Detailed documentation of the presence and abundance of immature mosquitoes, the developmental stages treated by larvicides, the size of breeding sites and the effectiveness of vector control is considered of great value in continuously estimating the likely size of future adult mosquito populations (10,14,18).

Optimal conditions for more effective entomological surveillance

The literature review also identified relevant information on the optimal conditions for strengthening the efficiency of entomological surveillance strategies for adult mosquitoes to achieve the main public health objectives documented.

As an early warning tool for viral circulation

As reported for WNV, early warning of viral circulation depends on certain operational modalities, in particular:

- Intensive trapping to increase the number of mosquitoes to be collected and tested, as this parameter is crucial for the sensitivity of early arbovirus detection (21,28,30). This condition implies a substantial number of mosquito traps located in "hot spots," selected according to a multifactorial approach (e.g., presence of wetlands and other water bodies, human population density, meteorological parameters) (21,30). Thomas-Bachli *et al.* (53) demonstrated that increasing the number of traps in Ontario, combined with shifting their locations to areas where WNV had been detected in previous years, improved detection times for arbovirus in mosquitoes, which became similar to or even shorter than those associated with dead corvid surveillance (53). A judicious choice of the type of mosquito traps and their wide deployment also enhances the ability of entomological surveillance to provide early warning of viral circulation (25).
- Rapid acquisition, ideally within a few days, of results of WNV screening in mosquito population (9,26,27).
- Maintain regular surveillance on an annual basis, preferably from May until the end of the mosquito season (usually late September), in order to improve strategy and refine early detection capabilities and sensitivity (24).
- Collaboration between veterinary and human health services, as well as between medical entomologists and ornithologists, in addition to coordination and data management at national, regional and local levels (24).
- Regular updating of the entomological surveillance program in line with available data (results from the previous year and those obtained from research studies) and funding opportunities (24,27).

As a tool for assessing the level of risk of human transmission

The development of appropriate models for assessing human transmission risk levels, using entomological data, also requires ongoing surveillance carried out every year during the mosquito season. It also calls for rapid processing and analysis of entomological data, so that the necessary preventive measures can be implemented without delay (27,50). It is also strongly recommended that monitoring programs include permanent traps placed at fixed stations, with a long-term perspective, in order to develop a historical baseline for detecting spatiotemporal trends in mosquito abundance and arbovirus prevalence within their populations. In fact, the assessment of the level of risk of human transmission generally incorporates the results of mosquito surveillance from previous years. The constant accumulation of entomological data, year after year, also offers the opportunity to improve the robustness of predictive models for more accurate estimates of human risk,

including the occurrence of outbreaks (10,14,18,19,24,27). In New York City, comprehensive vector and human surveillance data collected over the years 2006 to 2022 enabled health authorities to develop a more sensitive protocol for assessing the level of WNV activity and human disease risk across the entire city (9). In Massachusetts, routine seasonal data collection over a period of several years also considerably improved the accuracy of assessing the level of risk of human transmission at the municipal level (10).

Karki *et al.* (54) have demonstrated, for the state of Illinois, that the power of predictive models based on vector index increases in regions with abundant entomological data. The authors also highlighted their usefulness, when collected over the long term, for developing risk assessments at specific times and in specific regions to guide an appropriate public health response (54).

On the other hand, Kilpatrick and Pape (52) warned against the loss of data resulting from discontinuous entomological surveillance. Thus, a pronounced decline in the predictive power of the models used is expected in the absence of arbovirus prevalence and mosquito abundance data for the surveillance year. Moreover, the decline in predictive power is exacerbated by delays in processing and analyzing entomological data (52).

Finally, it should be noted that the consulted literature also highlighted the importance of sharing roles and responsibilities for the smooth running of entomological surveillance programs, including the operational aspect (e.g., selection of locations and installation of mosquito traps), the assessment of the level of risk of human transmission and the resulting public health responses, particularly the application of larvicides and adulticides. Mosquito surveillance programs can therefore involve various levels of health authorities, as well as other government bodies, notably from the agricultural and environmental sectors, and local administrations such as municipalities (14,16,17,19,38,45).

Strengths and limitations

The main strength of this work lies in the inclusion of publications dealing with entomological surveillance carried out annually, on a regular and uninterrupted basis, while involving government authorities at the national, regional or local level. This approach lent greater weight to the public health objectives of this surveillance and subsequent actions documented in the literature. Furthermore, the surveillance programs described are still underway in the countries/regions concerned, as they are considered to be relevant, which further strengthens this knowledge synthesis. However, this review cannot claim to be exhaustive, as additional results could have been identified with less stringent inclusion criteria. In addition, there have been few publications on EEEV and the CSVs and no relevant literature on SSHV or CVV has been identified. These factors could make it harder to infer about these arboviruses, which, however, are likely to grow in importance in the coming years. Beyond these limitations, we are confident in the relevance and significance of

the results obtained and believe that this review remains a first description of the synthesis of the objectives of entomological surveillance of arboviruses of public health interest and endemic to Canada.

Conclusion

In a context of climate change conducive to the spread of arboviruses, this knowledge synthesis supports the usefulness and relevance of entomological surveillance of arboviruses of interest in Canada, namely WNV, EEEV and JCV. Its contribution to public health is nevertheless grounded in a regular annual deployment during the mosquito season, according to the objectives pursued by the authorities concerned, while using a judicious number and locations of mosquito traps. For optimum benefit, it is also vital that entomological data are analyzed and shared rapidly to support effective actions, integrating clinical preparedness, real-time and ongoing risk communication as well as timely implementation of preventive measures. Entomological surveillance of arboviruses of public health importance should be maintained and strengthened, taking into consideration expected changes, due to climate variations, in mosquito populations and the diseases they carry in Canada.

Authors' statement

BB — Conceptualization, writing–original draft, revision & critical review
AIC — Conceptualization, revision & critical review
AL — Revision & critical review
MRR — Revision & critical review
CT — Revision & critical review
ID — Revision & critical review
AAP — Conceptualization, revision & critical review

The contents and opinions expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

References

1. Ludwig A, Zheng H, Vrbova L, Drebot MA, Iranpour M, Lindsay LR. Increased risk of endemic mosquito-borne diseases in Canada due to climate change. Can Commun Dis Rep 2019;45(4):91–7. DOI PubMed

2. Ogden NH, Gachon P. Climate change and infectious diseases: What can we expect? Can Commun Dis Rep 2019;45(4):76–80. DOI PubMed

3. Rosenkrantz L, National Collaborating Centre for Environmental Health. Impacts of Canada's changing climate on West Nile Virus vectors. Vancouver, BC: NCCEH; 2022. https://ncceh.ca/sites/default/files/Mosquito_EvidenceReview_Nov1_EN.pdf

4. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International journal of social research methodology. Int J Soc Res Methodol 2005;8(1):19–32. DOI

5. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010;5(69):69. DOI PubMed

6. Lussier MT, Richard C, Bennett TL, Williamson T, Nagpurkar A. Surveillance or research: what's in a name? Can Fam Physician 2012;58(1):117. PubMed

7. Osório HC, Zé-Zé L, Amaro F, Alves MJ. Mosquito surveillance for prevention and control of emerging mosquito-borne diseases in Portugal - 2008-2014. Int J Environ Res Public Health 2014;11(11):11583–96. DOI PubMed

8. Medlock JM, Guillem R, Johnston C, Gandy S, Findlay-Wilson S, Desoisa K, Schaffner F, Vaux AG. The first 6 years of surveillance of Aedes albopictus (Diptera: Culicidae) in Gibraltar. J Eur Mosq Control Assoc 2022;40:23–35. https://doi.org/10.52004/JEMCA2022.0001

9. Bajwa W, Slavinski S, Shah Z, Zhou L, Herbert V. Comprehensive Mosquito Surveillance and Control Plan. New York City Department of Health and Mental Hygiene; 2023. p. 41. https://www.nyc.gov/assets/doh/downloads/pdf/wnv/2023/wnvplan2023.pdf

10. Brown CM, DeMaria A Jr, Gallagher GR, Osborne M, Stinson C, Smole S, Werner BG. Massachusetts Arbovirus Surveillance and Response Plan. Bureau of infectious Disease and Laboratory Sciences, Massachusetts Department of Public Health; 2023. https://www.mass.gov/lists/arbovirus-surveillance-plan-and-historical-data

11. California Department of Public Health. California Mosquito-borne Virus Surveillance & Response Plan. Mosquito & Vector Control Association of California; 2023. https://westnile.ca.gov/pdfs/CAMosquitoSurveillanceResponsePlan.pdf

12. City of Fort Collins. West Nile Virus Program Manual. Fort Collins, CO: City of Fort Collins; 2014. https://www.fcgov.com/westnile/pdf/wnv_program_manual.pdf

13. Government of Saskatchewan. West Nile Virus (WNV). Saskatoon, SK: Government of Saskatchewan; 2023. https://www.saskatchewan.ca/residents/health/diseases-and-conditions/west-nile-virus

14. Maine Department of Health and Human Services/Maine Center for Disease Control and Prevention. Arboviral (Mosquito-Borne) Illness, Surveillance, Prevention, and Response Guidance for Maine Towns and Communities. Augusta, ME: Maine DHHS; 2021. https://www.maine.gov/dhhs/mecdc/infectious-disease/epi/vector-borne/documents/2022-Arbo-Plan.pdf

15. Manitoba Health. West Nile Virus Program 2023: Planning Documents for Municipalities. I. Provincial West Nile Viruses Program Information. Winnipeg, MB: Manitoba Health; 2023. https://www.gov.mb.ca/health/wnv/docs/wnv_program_information_2023.pdf

16. Ontario Ministry of Health. West Nile Virus Preparedness and Prevention Plan. Toronto, ON: King's Printer for Ontario; 2023. https://files.ontario.ca/moh-ophs-ref-west-nile-virus_plan-2023-en.pdf

17. Vermont Agency of Agriculture, Food, and Markets/Vermont Department of Public Health. State of Vermont. Arbovirus Surveillance and Response Plan. Vermont, NH: Vermont Department of Public Health; 2022. https://www.healthvermont.gov/sites/default/files/documents/pdf/HS-ID-Arbovirus-Surveillance-Response-Plan.pdf

18. State of New Hampshire. Arboviral Illness Surveillance, Prevention and Response Plan. Department of Health and Human Services, Division of Public Health Service; 2023. https://www.dhhs.nh.gov/sites/g/files/ehbemt476/files/documents/2021-11/arboviralresponse.pdf

19. New York State Department of Health. Mosquito Borne Illness Surveillance & Response Plan. New York, NY: New York State Department of Health; 2012. https://www.health.ny.gov/diseases/west_nile_virus/docs/2012_mosquito_borne_illness_surveillance_and_response_plan.pdf

20. Saginaw County Mosquito Abatement Comission. Surveillance Biology. Saginaw County, MI: Saginaw County Mosquito Abatement Comission; 2024. https://www.saginawmosquito.com/programs/surveillance

21. Pautasso A, Radaelli MC, Ballardini M, Francese DR, Verna F, Modesto P, Grattarola C, Desiato R, Bertolini S, Vitale N, Ferrari A, Rossini I, Accorsi A, Mosca A, Monaco F, Savini G, Prearo M, Mignone W, Chiavacci L, Casalone C. Detection of West Nile and Usutu Viruses in Italian Free Areas: Entomological Surveillance in Piemonte and Liguria Regions, 2014. Vector Borne Zoonotic Dis 2016;16(4):292–4. DOI PubMed

22. Calzolari M, Angelini P, Bolzoni L, Bonilauri P, Cagarelli R, Canziani S, Cereda D, Cerioli MP, Chiari M, Galletti G, Moirano G, Tamba M, Torri D, Trogu T, Albieri A, Bellini R, Lelli D. Enhanced West Nile Virus Circulation in the Emilia-Romagna and Lombardy Regions (Northern Italy) in 2018 Detected by Entomological Surveillance. Front Vet Sci 2020;7:243. DOI PubMed

23. Petrović T, Šekler M, Petrić D, Lazić S, Debeljak Z, Vidanović D, Ignjatović Ćupina A, Lazić G, Lupulović D, Kolarević M, Plavšić B. Methodology and results of integrated WNV surveillance programmes in Serbia. PLoS One 2018;13(4):e0195439. DOI PubMed

24. Petrović T, Šekler M, Petrić D, Vidanović D, Debeljak Z, Lazić G, Lupulović D, Kavran M, Samojlović M, Ignjatović Ćupina A, Tešović B, Lazić S, Kolarević M, Labus T, Djurić B. Intensive West Nile Virus Circulation in Serbia in 2018-Results of Integrated Surveillance Program. Pathogens 2021;10(10):1294. DOI PubMed

25. Verna F, Modesto P, Radaelli MC, Francese DR, Monaci E, Desiato R, Grattarola C, Peletto S, Mosca A, Savini G, Chianese R, Demicheli V, Prearo M, Chiavacci L, Pautasso A, Casalone C. Control of Mosquito-Borne Diseases in Northwestern Italy: Preparedness from One Season to the Next. Vector Borne Zoonotic Dis 2017;17(5):331–9. DOI PubMed

26. Papa A, Gewehr S, Tsioka K, Kalaitzopoulou S, Pappa S, Mourelatos S. Detection of flaviviruses and alphaviruses in mosquitoes in Central Macedonia, Greece, 2018. Acta Trop 2020;202:105278. DOI PubMed

27. Patsoula E, Vakali A, Balatsos G, Pervanidou D, Beleri S, Tegos N, Baka A, Spanakos G, Georgakopoulou T, Tserkezou P, Van Bortel W, Zeller H, Menounos P, Kremastinou J, Hadjichristodoulou C. West Nile Virus Circulation in Mosquitoes in Greece (2010-2013). BioMed Res Int 2016;2016:2450682. DOI PubMed

28. Tsioka K, Gewehr S, Pappa S, Kalaitzopoulou S, Stoikou K, Mourelatos S, Papa A. West Nile Virus in Culex Mosquitoes in Central Macedonia, Greece, 2022. Viruses 2023;15(1):224. DOI PubMed

29. Alba A, Allepuz A, Napp S, Soler M, Selga I, Aranda C, Casal J, Pages N, Hayes EB, Busquets N. Ecological surveillance for West Nile in Catalonia (Spain), learning from a five-year period of follow-up. Zoonoses Public Health 2014;61(3): 181–91. DOI PubMed

30. Calzolari M, Bonilauri P, Bellini R, Albieri A, Defilippo F, Maioli G, Galletti G, Gelati A, Barbieri I, Tamba M, Lelli D, Carra E, Cordioli P, Angelini P, Dottori M. Evidence of simultaneous circulation of West Nile and Usutu viruses in mosquitoes sampled in Emilia-Romagna region (Italy) in 2009. PLoS One 2010;5(12):e14324. DOI PubMed

31. Calzolari M, Monaco F, Montarsi F, Bonilauri P, Ravagnan S, Bellini R, Cattoli G, Cordioli P, Cazzin S, Pinoni C, Marini V, Natalini S, Goffredo M, Angelini P, Russo F, Dottori M, Capell G, Savini G. New incursions of West Nile virus lineage 2 in Italy in 2013: the value of the entomological surveillance as early warning system. Vet Ital 2013;49(3):315–9. DOI PubMed

32. Saginaw County Mosquito Abatement Commission. Annual Report. Saginaw County, MI: Saginaw County Mosquito Abatement Commission; 2022. https://www.saginawmosquito.com/news/publications/annualreport

33. Gobbi F, Capelli G, Angheben A, Giobbia M, Conforto M, Franzetti M, Cattelan AM, Raise E, Rovere P, Mulatti P, Montarsi F, Drago A, Barzon L, Napoletano G, Zanella F, Pozza F, Russo F, Rosi P, Palù G, Bisoffi Z; Summer Fever Study Group. Human and entomological surveillance of West Nile fever, dengue and chikungunya in Veneto Region, Italy, 2010-2012. BMC Infect Dis 2014;14:60. DOI PubMed

34. City of Fort Collins. Program Response Guidelines to Mosquito-Borne Arboviral Activity. Fort Collins, CO: City of Fort Collins; 2018. https://www.fcgov.com/westnile/pdf/WNV_Response_Plan_March_2018.pdf?1568214777

35. Kansas Department of Health and Environment. Arboviral Disease Surveillance. Kansas, KS: Kansas Department of Health and Environment; 2019. https://www.kdhe.ks.gov/DocumentCenter/View/23922/Arboviral-Surveillance-Report-2019-PDF

36. Kansas Department of Health and Environment. West Nile Virus. Kansas, KS: Kansas Department of Health and Environment; 2023. https://www.kdhe.ks.gov/1519/West-Nile-Virus

37. Ginsberg HS, Gettman A, Becker E, Bandyopadhyay AS, Lebrun RA. Environmental management of mosquito-borne viruses in Rhode Island. R I Med J 2013;96(7):37–41. http://www.rimed.org/rimedicaljournal/2013/07/2013-07-37-cont-mosquitos.pdf PubMed

38. Rhode Island Department of Health. Guidelines for Phased Response to Eastern Equine Encephalitis (EEE) Surveillance Data. Division of Preparedness, Response, Infectious Disease, and EMS Center for Acute Infectious Disease Epidemiology. Rhode Island, RI: Rhode Island Department of Health; 2019. https://health.ri.gov/publications/guidelines/PhasedResponseToEEESurveillanceData.pdf

39. Oliver J, Lukacik G, Kokas J, Campbell SR, Kramer LD, Sherwood JA, Howard JJ. Twenty years of surveillance for Eastern equine encephalitis virus in mosquitoes in New York State from 1993 to 2012. Parasit Vectors 2018;11(1):362. DOI PubMed

40. Public Health Ontario. Why Is It Important to Monitor Ontario's Mosquitoes? Ottawa, ON: PHO; 2018. https://www.publichealthontario.ca/en/about/news/2017/monitor-mosquitoes

41. Fotakis EA, Mavridis K, Kampouraki A, Balaska S, Tanti F, Vlachos G, Gewehr S, Mourelatos S, Papadakis A, Kavalou M, Nikolakakis D, Moisaki M, Kampanis N, Loumpounis M, Vontas J. Mosquito population structure, pathogen surveillance and insecticide resistance monitoring in urban regions of Crete, Greece. PLoS Negl Trop Dis 2022;16(2):e0010186. DOI PubMed

42. Mavridis K, Fotakis EA, Kioulos I, Mpellou S, Konstantas S, Varela E, Gewehr S, Diamantopoulos V, Vontas J. Detection of West Nile Virus - Lineage 2 in Culex pipiens mosquitoes, associated with disease outbreak in Greece, 2017. Acta Trop 2018;182:64–8. DOI PubMed

43. Kretschmer M, Ruberto I, Townsend J, Zabel K, Will J, Maldonado K, Busser N, Damian D, Dale AP. Unprecedented Outbreak of West Nile Virus - Maricopa County, Arizona, 2021. MMWR Morb Mortal Wkly Rep 2023;72(17):452–7. DOI PubMed

44. Martinez D, Murray KO, Reyna M, Arafat RR, Gorena R, Shah UA, Debboun M. West Nile Virus Outbreak in Houston and Harris County, Texas, USA, 2014. Emerg Infect Dis 2017;23(8):1372–6. DOI PubMed

45. Quilliam DN, Gosciminski M, Bandy U. Eastern Equine Encephalitis Surveillance and Response, Rhode Island, 2019. R I Medicine 2020;103(3):68–70. PubMed

46. Noden BH, Coburn L, Wright R, Bradley K. An Updated Checklist of the Mosquitoes of Oklahoma Including New State Records and West Nile Virus Vectors, 2003-06. J Am Mosq Control Assoc 2015;31(4):336–45. DOI PubMed

47. Bakran-Lebl K, Camp JV, Kolodziejek J, Weidinger P, Hufnagl P, Cabal Rosel A, Zwickelstorfer A, Allerberger F, Nowotny N. Diversity of West Nile and Usutu virus strains in mosquitoes at an international airport in Austria. Transbound Emerg Dis 2022;69(4):2096–109. DOI PubMed

48. Kemenesi G, Krtinić B, Milankov V, Kutas A, Dallos B, Oldal M, Somogyi N, Németh V, Bányai K, Jakab F. West Nile virus surveillance in mosquitoes, April to October 2013, Vojvodina province, Serbia: implications for the 2014 season. Euro Surveill 2014;19(16):20779. DOI PubMed

49. Giordano BV, Kaur S, Hunter FF. West Nile virus in Ontario, Canada: A twelve-year analysis of human case prevalence, mosquito surveillance, and climate data. PLoS One 2017;12(8):e0183568. DOI PubMed

50. Albrecht L, Kaufeld KA. Investigating the impact of environmental factors on West Nile virus human case prediction in Ontario, Canada. Front Public Health 2023;11:1100543. DOI PubMed

51. Bolling BG, Barker CM, Moore CG, Pape WJ, Eisen L. Seasonal patterns for entomological measures of risk for exposure to Culex vectors and West Nile virus in relation to human disease cases in northeastern Colorado. J Med Entomol 2009;46(6):1519–31. DOI PubMed

52. Kilpatrick AM, Pape WJ. Predicting human West Nile virus infections with mosquito surveillance data. Am J Epidemiol 2013;178(5):829–35. DOI PubMed

53. Thomas-Bachli AL, Pearl DL, Berke O, Parmley EJ, Barker IK. A comparison of West Nile virus surveillance using survival analyses of dead corvid and mosquito pool data in Ontario, 2002-2008. Prev Vet Med 2015;122(3):363–70. DOI PubMed

54. Karki S, Westcott NE, Muturi EJ, Brown WM, Ruiz MO. Assessing human risk of illness with West Nile virus mosquito surveillance data to improve public health preparedness. Zoonoses Public Health 2018;65(1):177–84. DOI PubMed

Human echinococcosis incidence in Canada: A retrospective descriptive study using administrative hospital and ambulatory visit data, 2000–2020

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Abstract

Background: Echinococcosis is a zoonotic disease caused by the ingestion of tapeworm eggs shed by canids. The potential recent establishment of a more virulent European-type strain may be impacting human echinococcosis in Canada, yet information is limited.

Objective: Administrative hospital and ambulatory visit data were used to provide a baseline of human echinococcosis cases in Canada between 2000–2020.

Methods: Canadian Institute of Health Information's Discharge Abstract Database, Hospital Morbidity Database and National Ambulatory Care Reporting System were combined to identify cases. Risk ratios (RR) by demographic factors and cumulative incidences (CIN) over place and time were calculated.

Results: A total of 806 echinococcosis cases were identified in Canada between 2000–2020, for a mean annual CIN of 1.3 cases per million population. Over the two decades, the mean annual CIN of cases increased nationally (1.3–1.4 cases per million), in the Northwest Territories (6.3–9.1 cases per million), in Alberta (1.5–2.4 cases per million) and in the Atlantic provinces (0.2–0.6 cases per million). Those from the Territories had the highest risk of echinococcosis (RR 17.1; 95% confidence interval: 8.7–33.7).

Conclusion: Though explanations are multifactorial, the new European-type strain may have a role in the small absolute increase in echinococcosis CIN in Canada observed over the study period. The CIN is likely underestimated and the validity of administrative data for analyzing zoonoses warrants investigation. Though this study contributes important awareness and a baseline, improved data are needed to clarify the effects of the new strain and inform public health response.

Introduction

Echinococcosis is a rare zoonotic disease caused by infection with larval *Echinococcus* tapeworms (1). Tapeworm eggs are excreted in the feces of infected canids and can be ingested by humans through contaminated food, water or soil, or from close contact with infected animals (1). Compared to the general population, those who have frequent contact with canids, such as dog owners, can face increased risk of echinococcosis (2). Some

Indigenous Peoples in Canada, Alaska, Russia and Siberia north of the Arctic Circle who practise traditional cultural activities, such as using sled dogs, hunting, fishing and gathering, may also face increased risk (3–5). In isolated areas, use of untreated surface water as a potable water source and inaccessible medical services can compound risk and contribute to more severe health outcomes (5).

Echinococcosis in humans occurs in two major forms. Cystic echinococcosis (CE), caused by *Echinococcus granulosus,* leads to hydatid cysts in organs, often the liver and lungs, that can impair physiological function (1). Alveolar echinococcosis (AE), caused by *Echinococcus multilocularis*, produces a tumour-like polycystic mass in organs, most often in the liver, that can infiltrate adjacent organs and tissues to produce distant metastases (1). Treatment generally requires surgical removal or chemotherapy (1). Echinococcosis is frequently under or misdiagnosed because the disease is rare, awareness is limited, both AE and CE have long incubation periods ranging 5–15 years and up to 60% of cases are asymptomatic (1).

While both AE and CE have been reported in Canada, AE was historically limited to the North American *E. multilocularis* strain and found almost exclusively in wildlife (6). In 2009, a new *E. multilocularis* strain more closely related to European strains was detected in a dog from British Columbia with no travel history outside of the province (7). Local canid transmission was identified thereafter in British Columbia as well as Alberta, Manitoba and Ontario (8–11). The first human case of AE with the European-type *E. multilocularis* strain was confirmed in Alberta in 2013 (12). Of six subsequent human cases in Alberta, molecular typing was available for five, all indicating the presence of the European-type strain (13).

European *E. multilocularis* strains have greater virulence and zoonotic potential than North American strains (8). Due to the potential establishment of the European-type strain in animal hosts, climate change, urbanization and anthropogenic activities, human AE is considered an emerging disease threat in Canada (4,8). Yet, knowledge about human echinococcosis in the country is limited. While AE is a provincially notifiable disease in Alberta, Ontario, Nunavut and the Northwest Territories, it is currently not nationally notifiable (14).

Absence of information on echinococcosis among people in Canada, exacerbated by limited awareness and underdiagnosis, as well as increasing evidence of emergence due to the detection of a more virulent strain, necessitates the use of alternative nationwide data sources to describe echinococcosis. This study leveraged administrative hospital and ambulatory visit data to provide a baseline for human echinococcosis in Canada between 2000–2020, relevant for increasing awareness and informing public health guidelines. Risk ratios (RRs) by demographic factors and incidences over place and time of echinococcosis cases were estimated. The authors hypothesized a higher incidence in 2011–2020 than 2000–2010, especially in isolated northern areas, due to the European-type *E. multilocularis* strain detected in 2009.

Methods

Data sources
To identify echinococcosis cases, three Canadian Institute for Health Information (CIHI) databases were combined: the Discharge Abstract Database (DAD), Hospital Morbidity Database (HMDB) and National Ambulatory Care Reporting System (NACRS). These databases collect data on an annual basis corresponding to the fiscal year (April 1 of one year to March 31 of the following year) (15). The DAD and HMDB databases similarly capture national administrative, clinical and basic demographic information on hospital inpatient events, however, the DAD does not include data from Québec (15). The NACRS contains complete or partial data on hospital-based and community-based ambulatory care from Alberta, British Columbia, Manitoba, Nova Scotia, Ontario, Prince Edward Island, Québec, Saskatchewan and Yukon (15).

Eligibility criteria
Diagnoses in CIHI databases use the ninth or tenth revision of the World Health Organization's International Classification of Diseases (ICD-9 and ICD-10) (16,17). Cases were defined as patients visiting hospital or ambulatory care for whom the main responsible diagnosis or one of the first five discharge diagnoses was echinococcosis (ICD-9 codes 122.0 to 122.9; ICD-10 codes B67.0 to B67.9).

To derive the echinococcosis cases dataset, the available DAD, HMDB and NACRS data were first merged. Records of cases in years with incomplete data due to collection on a fiscal year basis were removed. Then, duplicates and records describing readmissions for echinococcosis for the same case were removed to align with the goal of estimating incidence. Specifically, the first chronological record was retained, regardless of which database it came from and subsequent records were excluded. The CIHI databases contain encrypted health card numbers that were used to find records for the same case. The SAS Enterprise Guide® 7.1 software for Microsoft Windows was used to merge data.

Data analysis
Descriptive analyses were used to characterize echinococcosis cases by infecting *Echinococcus* species, sex, age group and region and province/territory (P/T) of health card issuance. Bivariate analyses were used to determine the RR, with 95% confidence intervals (CI), of echinococcosis by sex, age group, region and P/T. Québec was excluded from RR calculations to avoid skewed comparisons, as data from the province were only available from the HMDB for the first half of the study period (2000–2010). Population estimates from Statistics Canada's 2011 Census of Population were used as denominators to compute RRs (18).

The cumulative incidence (CIN) of echinococcosis cases over 2000–2020 at the national, regional and P/T levels was calculated using annual population estimates (fourth quarter) from Statistics Canada as denominators (19). The mean annual CIN was calculated by taking an average of the yearly CIN of echinococcosis cases. Québec was excluded from CIN calculations. Data were analyzed using R Statistical Software (v4.1.1; R Core Team 2021) and QGIS Geographic Information System 3.8 was used to map CIN.

Results

Characteristics and risk ratios

The final dataset comprised 806 records of incident echinococcosis cases in Canada between 2000–2020 (**Figure 1**). The demographic characteristics of cases and RRs are presented in **Table 1**. Of the 806 cases, most were unspecified (n=669; 82.3%), followed by *E. granulosus* (n=111; 13.7%) and *E. multilocularis* (n=33; 4.1%). The largest proportion of cases (n=371; 46.0%) were from Ontario. Females comprised over half of cases (n=501; 62.2%) and were at 1.6 (95% CI: 1.4–1.8) times higher risk of echinococcosis compared to males. While most cases were aged 35–54 years (n=265; 32.9%), those over 75 years of age had the highest risk, at 5.6 (95% CI: 3.9–8.0) times higher than those aged 0–14 years.

Figure 1: Flow diagram of incident human echinococcosis hospital and ambulatory care visits, as cases, record selection, Canadian Institute for Health Information, 2000–2020
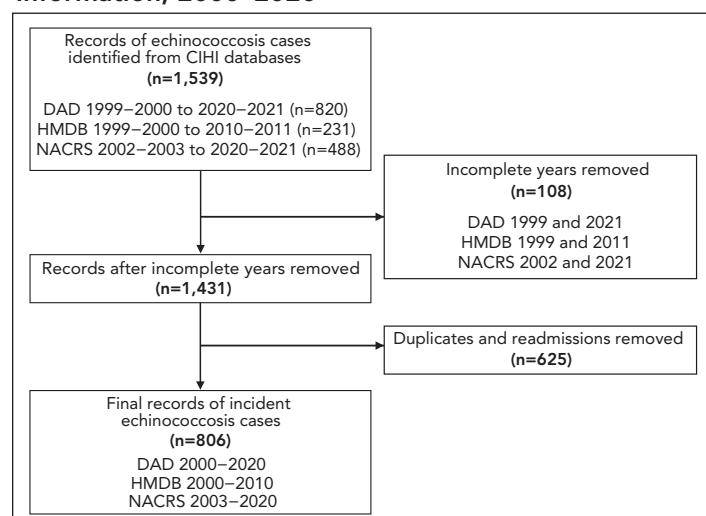
Abbreviations: CIHI, Canadian Institute for Health Information; DAD, Discharge Abstract Database; HMDB, Hospital Morbidity Database; NACRS, National Ambulatory Care Reporting System

Table 1: Characteristics and risk ratios of echinococcosis hospital and ambulatory care visits, as cases, in Canada, Canadian Institute for Health Information[a], 2000–2020 (n=806)

Characteristics	Echinococcosis cases	
	n (%)	Risk ratios (95% CI)
***Echinococcus* species[b]**		
E. multilocularis	33 (4.1)	N/A
E. granulosus	111 (13.7)	N/A
Unspecified	669 (82.3)	N/A
Sex		
Male	305 (37.8)	1.0
Female	501 (62.2)	1.6 (1.4–1.8)
Age group		
0–14 years	42 (5.2)	1.0
15–34 years	193 (23.9)	3.0 (2.1–4.1)
35–54 years	265 (32.9)	3.6 (2.6–5.0)
55–74 years	211 (26.2)	4.0 (2.9–5.6)
≥75 years	95 (11.8)	5.6 (3.9–8.0)
Geography		
Atlantic region	**19 (2.4)**	**1.0**
Prince Edward Island	1 (0.1)	1.0
New Brunswick	7 (0.9)	1.3 (0.2–10.3)
Newfoundland and Labrador	5 (0.6)	1.3 (0.2–11.3)
Nova Scotia	6 (0.7)	0.9 (0.1–7.4)
Eastern region	**436 (54.1)**	**3.5 (2.2–5.6)[c]**
Ontario	371 (46.0)	3.9 (0.6–27.9)
Québec	65 (8.1)	N/A[c]
Western region	**336 (41.7)**	**4.0 (2.5–6.4)**
Alberta	155 (19.2)	5.8 (0.8–41.3)
British Columbia	102 (12.7)	3.2 (0.4–22.6)
Manitoba	37 (4.6)	4.2 (0.6–30.3)
Saskatchewan	42 (5.2)	5.5 (0.8–40.1)
Territories region	**15 (1.9)**	**17.1 (8.7–33.7)**
Northwest Territories	7 (0.9)	22.9 (2.8–186.4)
Nunavut	4 (0.5)	17.0 (1.9–152.4)
Yukon	4 (0.5)	16.0 (1.8–143.4)

Abbreviations: CI, confidence interval; *E.*, *Echinococcus*; N/A, not applicable
[a] Including the Discharge Abstract Database (2000–2020), Hospital Morbidity Database (2000–2010) and National Ambulatory Care Reporting System (2003–2020)
[b] Seven cases reported with multiple diagnoses of echinococcosis in the same record. Therefore, *Echinococcus* species sums to 813 cases
[c] Québec excluded, as data for the province were unavailable between 2011–2020

Cases with a health card issued from the Territories region (Northwest Territories, Nunavut and Yukon) had a much higher risk of echinococcosis (RR 17.1; 95% CI: 8.7–33.7) compared to the Atlantic region (New Brunswick, Newfoundland and Labrador, Nova Scotia and Prince Edward Island). Cases from the Northwest Territories had the highest risk of echinococcosis in the country, at 22.9 (95% CI: 2.8–186.4) times that of Prince Edward Island. Among provinces, cases from the Western region (Alberta, British Columbia, Manitoba and Saskatchewan) (RR 4.0; 95% CI: 2.5–6.4), compared to the Atlantic region, had the highest risk of echinococcosis.

Cumulative incidence

As shown in **Table 2**, the mean annual CIN of echinococcosis cases in Canada between 2000–2020 was 1.3 cases per million population. There was a slight absolute increase over the two decades nationally, from 1.3 cases per million between 2000–2010 to 1.4 cases per million between 2011–2020. The mean annual CIN of cases diagnosed as *E. multilocularis* increased very slightly over the two decades (0.05–0.06 cases per million), while cases diagnosed as *E. granulosus* decreased very slightly (0.19–0.18 cases per million). Detailed count and CIN by *Echinococcus* species, geography and year is provided in the **Appendix** as Supplemental material.

Table 2: Mean annual cumulative incidence, per million population, of echinococcosis hospital and ambulatory care visits, as cases, over place and time in Canada, Canadian Institute for Health Information[a], 2000–2020 (n=741)

Geography	Mean annual CIN (per million population)		
	Overall (2000–2020)	First decade (2000–2010)	Second decade (2011–2020)
National	**1.3**	**1.3**	**1.4**
E. multilocularis	0.06	0.05	0.06
E. granulosus	0.20	0.19	0.18
Unspecified	1.1	1.1	1.1
Atlantic region	**0.4**	**0.2**	**0.6**
New Brunswick	0.4	0.4	0.5
Newfoundland and Labrador	0.5	0.4	0.6
Nova Scotia	0.3	0.1	0.5
Prince Edward Island	0.3	0	0.6
Eastern region	**1.3[b]**	**1.4[b]**	**1.3[b]**
Ontario	1.3	1.4	1.3
Québec	N/A[b]	N/A[b]	N/A[b]
Western region	**1.6**	**1.6**	**1.6**
Manitoba	1.4	1.4	1.5
Saskatchewan	1.9	2.0	1.8
Alberta	1.9	1.5	2.4
British Columbia	1.1	1.4	0.8
Territories region	**6.2**	**6.8**	**5.6**
Northwest Territories	7.6	6.3	9.1
Nunavut	5.8	8.6	2.6
Yukon	5.2	5.3	5.1

Abbreviations: CIN, cumulative incidence; *E.*, *Echinococcus*; N/A, not applicable
[a] Including the Discharge Abstract Database (2000–2020), Hospital Morbidity Database (2000–2010) and National Ambulatory Care Reporting System (2003–2020)
[b] Québec excluded as data for the province were unavailable between 2011–2020

The Territories region had the absolute highest mean annual CIN of echinococcosis cases overall, at 6.2 cases per million (Table 2). Though case counts were low, over the two decades, there was an increase in the Northwest Territories (6.3–9.1 cases per million) but decreases in Nunavut (8.6–2.6 cases per million) and Yukon (5.3–5.1 cases per million) (**Figure 2**), resulting in a regional absolute decrease in mean annual CIN from 6.8 to 5.6 cases per million.

Figure 2: Map of the mean annual cumulative incidence, per million population, of echinococcosis hospital and ambulatory care visits, as cases, by province and territory in Canada between 2000–2010 (n=364) and 2011–2020 (n=377), Canadian Institute for Health Information[a]
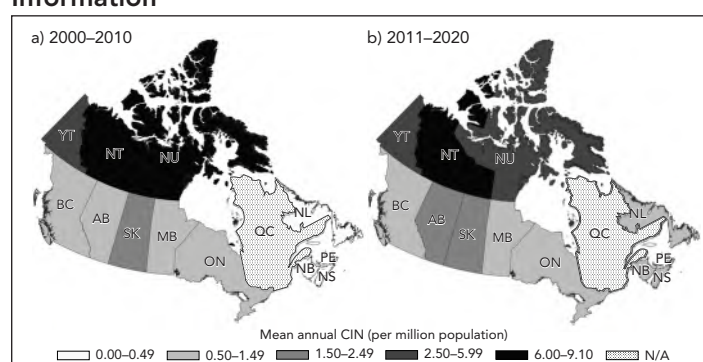
Abbreviations: CIN, cumulative incidence; N/A, not applicable because Québec was excluded due to unavailable data between 2011–2020
[a] Including the Discharge Abstract Database (2000–2020), Hospital Morbidity Database (2000–2010) and National Ambulatory Care Reporting System (2003–2020)

Among provinces, the Western region had the absolute highest mean annual CIN of echinococcosis cases, at 1.6 cases per million (Table 2). In Alberta, the mean annual CIN increased over the two decades from 1.5 to 2.4 cases per million (Figure 2). The Eastern region, which only included Ontario due to limited data from Québec, had the second absolute highest mean annual CIN of echinococcosis cases overall, at 1.3 cases per million. In the Atlantic region, the mean annual CIN was low overall at 0.4 cases per million. However, though case counts were low, each province in the Atlantic region experienced an increase in the mean annual CIN of cases over the two decades, resulting in a regional absolute increase from 0.2 to 0.6 cases per million.

Discussion

This study used administrative data to describe echinococcosis incidence and risk in Canada between 2000–2020. The mean annual CIN of echinococcosis in Canada over the study period was rare at 1.3 cases per million, which was slightly lower than the 1.5 cases per million reported by the European Surveillance System in 2020 (20). Between 2001–2005 in Canada, Gilbert *et al.* (21) found a lower mean incidence than this study, at 0.72 echinococcosis hospitalizations per million.

Schurer *et al.* (22) found a median annual incidence between 2002–2011 of 1.4 echinococcosis hospital and ambulatory visits per million. The Gilbert *et al.* (21) estimate may be lower because they only used HMDB and restricted to cases with only a first or second discharge diagnosis of echinococcosis. Schurer *et al.* (22) used the DAD and NACRS and included cases with an echinococcosis diagnosis in any of the 25 available discharge diagnoses. This study's use of the DAD, HMDB and NACRS may have been beneficial for capturing hospital and ambulatory visits more completely.

The results indicated an absolute increase, though small, in the mean annual CIN of echinococcosis cases in Canada between 2011–2020 compared to 2000–2010. Whether this was due to the European-type *E. multilocularis* strain first detected in Canada in 2009 remains unclear, as the species-level diagnosis for most cases was unspecified. Distinguishing *E. multilocularis* from *E. granulosus* in humans is not only an epidemiological but also a clinical necessity, as there are differences in prognosis, treatment, intermediate hosts and regional prevalence (1). Species-level diagnosis is complex, involving imaging, microscopy and serology (1). Serology is required for early stages of infection, while later stages may be diagnosed through histopathology (23). For people in Canada, confirmatory diagnosis of *E. multilocularis* demonstrating larval tapeworms in histopathology samples can require species-specific polymerase chain reaction (PCR) or serologic testing in some provinces (24). While this PCR is done at a limited number of laboratories across North America, approved serologic testing is only performed at the Institute of Parasitology in Switzerland (23). Studies have recommended that accessible and standardized testing optimized for circulating species of *Echinococcus* and increased awareness of clinical signs among physicians and veterinarians in endemic regions, would help improve prognosis and surveillance in Canada (12,22).

Over the two decades, there was a notable absolute increase in mean annual CIN of echinococcosis cases in the Northwest Territories. Having a health card from any of the three Territories also posed the highest risk of echinococcosis. The overall mean annual CIN for the Territories region (6.2 cases per million) was closer to that which has been recorded in European countries considered endemic for echinococcosis, like Luxembourg (4.8 cases per million) (20,25). Northern parts of Canada may be at higher risk of echinococcosis due to some populations hunting, consuming untreated surface water, keeping dogs as pets and working animals and harvesting potentially contaminated food (5,21,22).

There was also an absolute increase in the mean annual CIN of echinococcosis cases in Alberta over the two decades. Alberta had the second-highest number of cases diagnosed as *E. multilocularis* following Ontario despite having a substantially smaller population. Between 2013–2020, 17 cases of human AE were identified in Alberta, all likely locally acquired and all five of the cases with molecular typing results showing presence of

the European-type strain (13). Among coyotes in urban areas of Alberta, studies have highlighted an increasing prevalence of *E. multilocularis,* ranging from 25% between 2009–2011 (26) to 65% between 2016–2018 (8), with histology results from the region often confirming the presence of the European-type strain (9,27).

The Atlantic region had the lowest mean annual CIN of echinococcosis cases, but it increased slightly over the two decades. In the past 30 to 40 years, coyotes have reportedly expanded their range from the Great Lakes region of southern Canada into eastern Canada (28). A recent study recorded the first ever instances of *E. canadensis,* a subtype of *E. granulosus,* in free-ranging wildlife in Atlantic Canada (one coyote and four moose), suggesting that coyote natural range expansion has a role in enabling the lifecycle of *Echinococcus* tapeworms in the region (28).

Similar to previous Canadian literature, females in this study had a significantly higher risk of echinococcosis compared to males, warranting further investigation (21,22). Older age was also associated with a significantly higher risk of echinococcosis; however, this may be due to the long incubation period preceding clinical manifestations of the disease (1).

In the absence of national reporting and surveillance of echinococcosis in Canada, CIHI databases were explored as an option for monitoring cases of this potentially increasing zoonosis. Administrative data are useful for investigating disease epidemiology, as they are population-based, timely, accessible, provide large sample sizes and have broad jurisdictional coverage. However, administrative data are not collected for research purposes and may have quality and reliability issues (29). There is value in prioritizing future studies to examine the validity of administrative data sources for studying zoonoses in the future.

Limitations

There are some limitations of this study. Though it was the only available nationwide data source for echinococcosis, using hospital and ambulatory data to estimate incidence likely resulted in an underestimation. Echinococcosis is rare with a long incubation period, increasing the chance of under or misdiagnosis and most, but not all, symptomatic infections require medical attention (1). The incidence is also likely underestimated, both overall and for the Eastern region especially, because data for Québec were unavailable between 2011–2020 and Québec contributed 15% of all cases between 2000–2010.

Administrative data can have quality and reliability concerns and often lack information on potentially relevant indicators. For example, we did not have data on travel history and as echinococcosis has a long incubation period, this may have been relevant for understanding local disease acquisition. Additionally, not all P/Ts have mandated reporting to NACRS; those with mandated reporting may have contributed more echinococcosis cases than those without.

The RRs of echinococcosis for the Territories had wide CIs, likely because of small population sizes and indicate imprecision. Due to the small population sizes, the CIN for the Territories were also unstable.

Conclusion

This study fills an important gap by contributing a baseline for human echinococcosis in Canada between 2000–2020. Although echinococcosis is rare, there was a small absolute increase in the mean annual CIN of cases nationally between 2011–2020 compared to 2000–2010. Further research is needed to determine the role of the new European-type *E. multilocularis* strain, in addition to climate change, urbanization and anthropogenic activity, on disease burden. Improved and complete data are needed to understand differences across provinces and territories, in order to inform engagement with and guidelines for, public health partners, key risk groups and the general public. Research investigating the validity of administrative data for zoonoses is also warranted.

Authors' statement

AK — Conceptualization, methodology, formal analysis, writing–original draft, writing–review & editing
PKM — Supervision, conceptualization, methodology, writing–review & editing
DAJ — Validation, writing–review & editing

Competing interests

None.

Acknowledgements

Funding

References

1. World Health Organization/World Organisation for Animal Health. WHO/OIE manual on echinococcosis in humans and animals: A public health problem of global concern. Paris, FR: WHO/OIE; 2001. [Accessed 2022 Oct 1]. https://www.who.int/publications/i/item/929044522X

2. Schmidberger J, Uhlenbruck J, Schlingeloff P, Maksimov P, Conraths FJ, Mayer B, Kratzer W. Dog ownership and risk for alveolar echinococcosis, Germany. Emerg Infect Dis 2022;28(8):1597–605. DOI PubMed

3. Hotez PJ. Neglected infections of poverty among the indigenous peoples of the arctic. PLoS Negl Trop Dis 2010;4(1):e606. DOI PubMed

4. Jenkins EJ, Castrodale LJ, de Rosemond SJ, Dixon BR, Elmore SA, Gesy KM, Hoberg EP, Polley L, Schurer JM, Simard M, Thompson RC. Tradition and transition: parasitic zoonoses of people and animals in Alaska, northern Canada, and Greenland. Adv Parasitol 2013;82:33–204. DOI PubMed

5. Davidson RK, Lavikainen A, Konyaev S, Schurer J, Miller AL, Oksanen A. Echinococcus across the north: current knowledge, future challenges. Food Waterborne Parasitol 2016;4:39–53. DOI

6. Santa MA, Umhang G, Klein C, Grant DM, Ruckstuhl KE, Musiani M. It's a small world for parasites: evidence supporting the North American invasion of European Echinococcus multilocularis. Proc Biol Sci 2023;290(1994):20230128. DOI

7. Peregrine AS, Jenkins EJ, Barnes B, Johnson S, Polley L, Barker IK, De Wolf B, Gottstein B. Alveolar hydatid disease (Echinococcus multilocularis) in the liver of a Canadian dog in British Columbia, a newly endemic region. Can Vet J 2012;53(8):870–4. PubMed

8. Luong LT, Chambers JL, Moizis A, Stock TM, St Clair CC. Helminth parasites and zoonotic risk associated with urban coyotes (Canis latrans) in Alberta, Canada. J Helminthol 2020;94:e25. DOI PubMed

9. Gesy K, Hill JE, Schwantje H, Liccioli S, Jenkins EJ. Establishment of a European-type strain of Echinococcus multilocularis in Canadian wildlife. Parasitology 2013;140(9):1133–7. DOI PubMed

10. Samuel WM, Ramalingam S, Carbyn LN. Helminths in coyotes (Canis latrans Say), wolves (Canis lupus L.), and red foxes (Vulpes vulpes L.) of southwestern Manitoba. Can J Zool 1978;56(12):2614–7. DOI PubMed

11. Kotwa JD, Isaksson M, Jardine CM, Campbell GD, Berke O, Pearl DL, Mercer NJ, Osterman-Lind E, Peregrine AS. Echinococcus multilocularis Infection, Southern Ontario, Canada. Emerg Infect Dis 2019;25(2):265–72. DOI PubMed

12. Massolo A, Liccioli S, Budke C, Klein C. Echinococcus multilocularis in North America: the great unknown. Parasite 2014;21:73. DOI PubMed

13. Houston S, Belga S, Buttenschoen K, Cooper R, Girgis S, Gottstein B, Low G, Massolo A, MacDonald C, Müller N, Preiksaitis J, Sarlieve P, Vaughan S, Kowalewska-Grochowska K. Epidemiological and clinical characteristics of alveolar echinococcosis: an emerging infectious disease in Alberta, Canada. Am J Trop Med Hyg 2021;104(5):1863–9. DOI PubMed

14. Public Health Agency of Canada. Case definitions: Nationally notifiable diseases. Ottawa, ON: PHAC; 2022. [Accessed 2022 Oct 1]. https://diseases.canada.ca/notifiable/diseases-list

15. Canadian Institute for Health Information. Data holdings. Toronto, ON: CIHI; 2022. [Accessed 2022 May 1]. https://www.cihi.ca/en/access-data-and-reports/data-holdings

16. World Health Organization. International Classification of Diseases Manual of the international statistical classification of diseases, injuries, and causes of death. 9th revision, 1975 edition. Geneva, CH: WHO; 1977.

17. World Health Organization. International Classification of Diseases Manual of the international statistical classification of diseases and related health problems. 10th revision, 2016 edition. Geneva, CH: WHO; 2015.

18. Statistics Canada. 2011 Census of Population. Ottawa, ON: StatCan; 2011. [Accessed 2022 May 1]. https://www12.statcan.gc.ca/census-recensement/2011/dp-pd/index-eng.cfm

19. Statistics Canada. Population estimates, quarterly. Ottawa, ON: StatCan; 2022. [Accessed 2022 May 1]. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901

20. European Centre for Disease Prevention and Control. Echinococcosis - Annual Epidemiological Report for 2020-2022. Solna, SE: ECDC; 2022. [Accessed 2022 Oct 1]. https://www.ecdc.europa.eu/en/publications-data/echinococcosis-annual-epidemiological-report-2020

21. Gilbert NL, Dare OK, Libman MD, Muchaal PK, Ogden NH. Hospitalization for trichinellosis and echinococcosis in Canada, 2001-2005: the tip of the iceberg? Can J Public Health 2010;101(4):337–40. DOI PubMed

22. Schurer JM, Rafferty E, Farag M, Zeng W, Jenkins EJ. Echinococcosis: An Economic Evaluation of a Veterinary Public Health Intervention in Rural Canada. PLoS Negl Trop Dis 2015;9(7):e0003883. DOI PubMed

23. Public Health Ontario. Ontario public health standards: Requirements for programs, services, and accountability. Appendix 1: Case Definitions and Disease-Specific Information. Disease: Echinococcus multilocularis infection. Toronto, ON: PHO; 2022. [Accessed 2022 Oct 1]. https://files.ontario.ca/moh-ophs-echinococcus-multilocularis-infection-en-2022.pdf

24. Alberta Health. Alberta Public Health Disease Management Guidelines - Echinococcosis (Alveolar). Edmonton, AB: Alberta Health; 2022. [Accessed 2022 Oct 1]. https://open.alberta.ca/dataset/140a7c4a-d7bd-4909-b02f-24c7b35afc63/resource/65528d86-2571-42cd-a821-f4f93cbfaa9d/download/health-phdmg-echinococcus-2021-11.pdf

25. Martini M, Dumendiak S, Gagliardo A, Ragazzini F, La Rosa L, Giunchi D, Thielen F, Romig T, Massolo A, Wassermann M. Echinococcus multilocularis and other taeniid metacestodes of muskrats in Luxembourg: Prevalence, risk factors, parasite reproduction, and genetic diversity. Pathogens 2022;11(12):1414. DOI PubMed

26. Catalano S, Lejeune M, Liccioli S, Verocai GG, Gesy KM, Jenkins EJ, Kutz SJ, Fuentealba C, Duignan PJ, Massolo A. Echinococcus multilocularis in urban coyotes, Alberta, Canada. Emerg Infect Dis 2012;18(10):1625–8. DOI PubMed

27. Kolapo TU, Hay A, Gesy KM, Frey CF, Rothenburger JL, Joffe DJ. Canine alveolar echinococcosis: an emerging and costly introduced problem in North America. Transbound Emerg Dis 2023;2023:1. DOI

28. Priest JM, McRuer DL, Stewart DT, Boudreau M, Power JW, Conboy G, Jenkins EJ, Kolapo TU, Shutler D. New geographic records for Echinococcus canadensis in coyotes and moose from Nova Scotia, Canada. Int J Parasitol Parasites Wildl 2021;16:285–8. DOI PubMed

29. Butler AL, Smith M, Jones W, Adair CE, Vigod SN, Lesage A, Kurdyak P. Multi-province epidemiological research using linked administrative data: a case study from Canada. Int J Popul Data Sci 2018;3(3):443. DOI

Appendix

Supplemental material is available upon request to the author: ayisha.khalid@mail.utoronto.ca

Aggregated case count and incidence by *Echinococcus* species, geography and year

Prevalence and correlates of oral antibiotic use in Canada

Glenys Smith[1], Anna-Louise Crago[1]*, Stephanie Alexandre[1], Denise Gravel-Tropper[1], Melissa Isada[1], Braden Knight[1], Jami Mackenzie[1], Jayson Shurgold[1]

Abstract

Background: Antimicrobial use (AMU) is a known driver of antimicrobial resistance. Insight into prevalence and correlates of AMU can help identify health inequities and areas for targeted action. To better understand sociodemographic and medical dimensions of AMU in Canada, the Public Health Agency of Canada, in partnership with Statistics Canada, developed a Rapid Response Module questionnaire on self-reported oral antibiotic use, to be administered as part of the 2018 Canadian Community Health Survey (CCHS).

Objective: To provide data on the proportion of people in Canada that self-report the use of antibiotics and sociodemographic and health factors associated with use.

Methods: This cross-sectional study used data from the CCHS, a national survey of 24,176 people with a clustered multi-stage stratified random sampling design. In 2018, an antibiotic use module was administered to CCHS participants.

Results: Among respondents 18 years and older, 26% reported receipt of at least one oral antibiotic over the past year. Several sociodemographic and health factors had higher adjusted odds of receiving an antibiotic prescription, including those aged 18 years compared to aged 48 years (mean), women compared to men, immigrants compared to non-immigrants (excluding Indigenous), current and former smokers compared to those who have never smoked, and those with comorbidities (asthma, chronic obstructive pulmonary disease, arthritis, heart disease, cancer, bowel disorder and urinary incontinence).

Conclusion: Variations in AMU across different key populations and sociodemographic groups highlight the need to improve our understanding of different drivers of AMU and for tailored interventions to reduce inequitable risks of antimicrobial resistance.
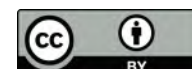
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Introduction

Antimicrobial resistance (AMR) is an increasing threat to global health (1). In Canada, resistance is increasing for most human pathogens of concern (2). Antibiotic use is associated with the development of antibiotic resistance at the individual, community, and country levels, making it imperative to identify and reduce use that is unnecessary or inappropriate (3,4). While there are no national-level data, studies in Ontario and Alberta have found that 15.4% and 39.2% of antibiotics were

inappropriately prescribed, respectively (5,6). For older adults (over the age of 65 years), evidence from Ontario and British Columbia suggests that 50% of antibiotics in the community are prescribed for conditions not requiring antibiotics (7).

There is robust evidence of sociodemographic differences in antibiotic use in high-income countries, with a dominant trend of higher use among the elderly, people with underlying medical

conditions, women, people with a low income, people with low formal education and various ethnic groups (8). This suggests differential drivers of antibiotic use some of which may be linked to health inequities such as disparities in the burden of infection among different population groups or differential rates of inappropriate prescriptions.

While national surveillance of human antimicrobial use (AMU) in Canada reports on the tonnage of antibiotics and number of antibiotic prescriptions dispensed by Canadian pharmacies (2), this study provides self-reported data on the proportion of people in Canada reporting use of antibiotics and sociodemographic and health factors associated with AMU. These data are key to elucidating drivers of AMU, developing strategies for community-based antibiotic stewardship and preventing AMR health inequities.

Methods

Data source, study design and sample population

This cross-sectional study used data from the Canadian Community Health Survey (CCHS), a voluntary national survey with a clustered multi-stage stratified random sampling design that collects information on health status, determinants of health and healthcare utilization (9). There are certain limitations to the sampling methodology, as it excludes those living on reserves or other Indigenous settlements, institutionalized populations (e.g., residents of healthcare facilities, prisons, convents), full-time members of the Canadian Forces, children living in foster care and residents of the remote Québec regions of Nunavik and Terres-Cries-de-la-Baie-James (9). Altogether, these exclusions represent less than 3% of the Canadian population aged 12 years and over (9).

Along with the core questions of the CCHS, the rapid response component is offered to organizations interested in national estimates on an emerging or specific issue related to the population's health (9). To gain further insights into antibiotic use in humans within Canada, the Public Health Agency of Canada, in partnership with Statistics Canada, developed a Rapid Response Module questionnaire on AMU. Between January 2 and June 30, 2018, a nine-question antimicrobial use Rapid Response Module with a focus on antibiotics was administered to 24,176 consenting CCHS participants from all provinces (the territories were excluded). We excluded participants who responded with "don't know", "not stated", or "refused" when asked if they had received antibiotic prescriptions in the past year (n=250), resulting in a final total of 23,926 Canadians aged 18 years and older. Relevant information, including prescribing facility, whether guidance on use was provided, adherence, type of non-adherence, medical reason for prescription and the fate of leftover antibiotics was associated with each outcome. For the

complete list of the AMU Rapid Response Module items, please refer to **Appendix**.

Outcome variable

The outcome for the logistic regression was receipt of one or more outpatient oral antibiotic medication prescription(s) in the 12 months prior to survey administration, regardless of whether the participant filled the prescription.

Exposure variables

Pre-selected sociodemographic exposure variables were chosen based on clinical plausibility and previous literature. They included age, sex, highest household level of education, household income, smoking status, marital status and specific chronic medical conditions captured in the CCHS (9). Body mass index, immigrant/Indigenous status, receipt of previous year influenza vaccination, access to a regular healthcare provider and insurance for prescription medications was also explored. Perceived physical and mental health, as well as perceived stress were also assessed.

Statistical analysis

Descriptive statistics were used to summarize responses from the AMU Rapid Response Module. Adjusted and unadjusted multivariable logistic regression analyses were performed to evaluate the association between previous year AMU and the pre-selected exposure variables. Age was defined using a five-knot restricted cubic spline (10) and all other variables were treated as categorical. Each variable was included in a separate logistic regression model to examine its unadjusted effect on AMU in the previous 12 months. A final model, with all predefined exposure variables, was used to determine which factors maintained their association with AMU in the previous 12 months, adjusting for all other variables. The model included the following variables: sex, age, highest level of education, smoking status, Indigenous status (off-reserve), immigrant status, total household income (in thousands), perceived health, perceived life stress, having asthma, having chronic obstructive pulmonary disease, having arthritis, having high blood pressure, having high blood cholesterol/lipids, having heart disease, ever having been diagnosed with cancer, having a bowel disorder (Crohn's disease, ulcerative colitis, irritable bowel syndrome, incontinence), having urinary incontinence, usual place for immediate care for minor problems, regular provider type, province of residence, marital status, body mass index, type of drinker, level of physical activity, insurance for prescription medications, language most often spoken at home, perceived mental health, having received a seasonal flu shot, having had a stroke, having diabetes, having a mood disorder and having an anxiety disorder. Statistical significance was set at a *p*-value of ≤0.05.

Given the complex sampling strategy of the CCHS, participants had unequal probabilities of being selected for the survey. To account for this, the logistic regression applied sampling

weights provided by Statistics Canada to extrapolate the results to the overall Canadian population represented by the CCHS. Bootstrapping weights were used to estimate 95% confidence intervals through a bootstrap variance estimation method (1,000 replications).

All analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute, Cary, North Carolina, United States). To allow for the proper application of the sampling and bootstrap replicate weights, SAS survey analysis procedures were used.

Results

Among the CCHS survey respondents 18 years of age or older who completed the 2018 AMU Rapid Response Module (n=23,926, representing a weighted national population of 29,020,553), 26.0% (95% CI: 24.96%–26.99%) reported receipt of at least one oral antibiotic during the previous year (**Table 1**). Of these, 38.2% (95% CI: 36.16%–40.21%) reported receiving more than one prescription. The majority of patients received their antibiotic prescription from community physician clinics (81.8%, 95% CI: 78.19%–85.36%). The reason for prescription

Table 1: Responses to antimicrobial use questions asked in the Canadian Community Health Survey

Responses	Unweighted		Weighted	
	Frequency	Percent (%)	Frequency	Percent (%)
Did you receive a prescription for antibiotics in the past 12 months (oral antibiotic)?				
Yes	6,407	26.78	7,537,172 (7,243,253–7,831,091)	25.97 (24.96–26.99)
Did not fill prescription[a]	61	0.95	49,548 (33,225–65,872)	0.66 (0.44–0.88)
Still taking it	189	2.95	200,614 (153,032–248,195)	2.66 (2.04–3.29)
No	17,519	73.22	21,483,380 (21,189,461–21,777,300)	74.03 (73.01–75.04)
Did you receive more than one prescription in the past 12 months?				
Yes	2,541	39.66	2,878,101 (2,691,207–3,064,995)	38.19 (36.16–40.21)
No, just one	3,866	60.34	4,659,071 (4,420,023–4,898,120)	61.81 (59.79–63.84)
Why were you given a prescription for antibiotics?				
Chest infection	1,430	21.90	1,617,409 (1,445,932–1,788,885)	21.46 (19.41–23.51)
Ear/nose/throat/sinus/eye infection	1,467	22.90	1,750,049 (1,604,002–1,896,095)	23.22 (21.41–25.02)
Urinary tract infection	978	15.26	1,122,468 (1,002,702–1,242,234)	14.89 (13.39–16.39)
Skin infection	484	7.55	608,859 (502,866–714,851)	8.08 (6.72–9.43)
Gastrointestinal infection	253	3.95	325,678 (259,782–391,573)	4.32 (3.46–5.18)
Other	1,822	28.44	2,112,711 (1,948,239–2,277,183)	28.03 (26.1–29.96)
Where did you receive the prescription?				
Walk-in/doctor's office	4,227	65.97	5,243,770 (4,986,062–5,501,478)	69.57 (67.47–71.67)
Outpatient clinic	991	15.47	919,754 (799,370–1,040,139)	12.2 (10.72–13.69)
Inpatient	272	4.25	263,550 (213,118–313,982)	3.5 (2.83–4.17)
Dentist	745	11.63	877,336 (770,540–984,133)	11.64 (10.27–13.01)
Another place	172	2.68	232,762 (170,137–295,387)	3.09 (2.26–3.92)

[a] Weighted frequencies have limited interpretation due to small response rates

was most commonly for infections of the upper respiratory tract (nose, throat or sinus), ear and eye (23.2% combined, 95% CI: 21.41%–25.02%), followed by chest infections (21.5%, 95% CI: 19.41%–23.51%).

The mean age of respondents was 48.1 years old, which served as the reference for the logistic regression models. After adjusting for all other exposure variables, those aged 18 years had much higher odds, 1.70 (95% CI: 1.29–2.23) compared to those aged 48 years (Table 2). Adults aged 30 years had odds of 1.42 (95% CI: 1.23–1.63); at age 60, the odds were 1.01 (95% CI: 0.88–1.16) and at age 80, the odds were 1.11 (95% CI: 0.89–1.37) compared to those aged 48 years (see Figure 1 for unadjusted odds and Figure 2 for adjusted odds).

Table 2: Characteristics associated with receiving an antibiotic prescription in the previous 12 months

Characteristics	Unweighted		p-value	Odds ratio	
	Frequency	Percent (%)		Unadjusted	Adjusted
Age (years)					
Mean (SEM)		48.11 (48.0–48.22)	<0.0001	See Figure 1 and Figure 2	
18–29	5,472,681 (5,303,207–5,642,156)	18.86 (18.27–19.44)	-	Not included in model, age was treated as continuous	
30–39	5,255,468 (5,017,771–5,493,165)	18.11 (17.29–18.93)			
40–49	4,668,792 (4,508,772–4,828,812)	16.09 (15.54–16.64)			
50–59	5,013,909 (4,856,837–5,170,981)	17.28 (16.74–17.82)			
60–69	4,698,262 (4,497,236–4,899,288)	16.19 (15.5–16.88)			
70–79	2,693,963 (2,572,919–2,815,007)	9.28 (8.87–9.7)			
80+	1,217,479 (1,125,974–1,308,983)	4.2 (3.88–4.51)			
Sex				<0.0001	
Female	14,742,425 (14,742,424–14,742,426)	50.8 (50.8–50.8)	-	1.65 (1.49–1.83)	1.55 (1.38–1.72)
Male	14,278,128 (14,278,127–14,278,128)	49.2 (49.2–49.2)			Ref.
Highest level of education				0.0029	
High school	10,333,492 (9,999,596–10,667,387)	35.61 (34.46–36.76)	-	0.91 (0.79–1.05)	0.77 (0.66–0.89)
Diploma	10,371,261 (10,058,907–10,683,616)	35.74 (34.66–36.82)		0.95 (0.84–1.07)	0.88 (0.77–1.01)
University	8,315,800 (7,987,390–8,644,210)	28.65 (27.52–29.79)			Ref.
Smoking status				0.0063	
Current	4,872,020 (4,617,655–5,126,385)	16.79 (15.91–17.67)	-	1.31 (1.13–1.51)	1.3 (1.11–1.53)
Experiment	3,914,117 (3,696,472–4,131,761)	13.49 (12.74–14.24)		1.11 (0.94–1.29)	1.14 (0.97–1.34)
Former	7,704,652 (7,421,722–7,987,581)	26.55 (25.57–27.53)		1.2 (1.06–1.36)	1.22 (1.06–1.4)
Never	12,529,764 (12,185,432–12,874,096)	43.18 (41.99–44.36)			Ref.
Indigenous (off-reserve)/immigrant status				0.1067	
Indigenous (off-reserve)	978,508 (870,556–1,086,460)	3.37 (3.0–3.74)	-	1.2 (0.94–1.53)	1.04 (0.81–1.34)
Immigrant	7,492,618 (7,126,684–7,858,551)	25.82 (24.56–27.08)	-	0.94 (0.82–1.08)	1.21 (1.01–1.45)
Non-Indigenous/non-immigrant	20,549,427 (20,193,939–20,904,9150	70.81 (69.58–72.04)	-		Ref.

Table 2: Characteristics associated with receiving an antibiotic prescription in the previous 12 months (*continued*)

Characteristics	Unweighted		p-value	Odds ratio	
	Frequency	Percent (%)		Unadjusted	Adjusted
Total household income (thousands)					0.7555
<50	7,588,111 (7,288,500–7,887,721)	26.15 (25.11–27.18)	-	1.11 (0.93–1.31)	0.94 (0.78–1.14)
50–100	9,303,183 (9,011,645–9,594,722)	32.06 (31.05–33.06)		0.99 (0.84–1.16)	0.92 (0.78–1.09)
100–149	6,033,084 (5,772,751–6,293,418)	20.79 (19.89–21.69)		0.97 (0.82–1.15)	0.92 (0.77–1.09)
>150	6,096,174 (5,804,118–6,388,231)	21.01 (20.00–22.01)			Ref.
Perceived health					<0.0001
Poor/fair	3,487,551 (3,276,377–3,698,725)	12.02 (11.29–12.75)	-	2.82 (2.36–3.38)	1.89 (1.45–2.46)
Good	8,341,719 (8,033,243–8,650,196)	28.74 (27.68–29.81)		1.75 (1.51–2.04)	1.47 (1.22–1.75)
Very good	10,588,084 (10,279,864–10,896,303)	36.48 (35.42–37.55)		1.47 (1.27–1.7)	1.34 (1.14–1.57)
Excellent	6,603,198 (6,323,648–6,882,749)	22.75 (21.79–23.72)			Ref.
Perceived life stress					0.0003
Not at all stressful	3,957,912 (3,760,455–4,155,369)	13.64 (12.96–14.32)	-		Ref.
Not very stressful	6,783,011 (6,515,591–7,050,432)	23.37 (22.45–24.3)		1.35 (1.13–1.61)	1.29 (1.07–1.55)
A bit stressful	11,999,017 (11,679,691–12,318,343)	41.35 (40.24–42.45)		1.61 (1.36–1.91)	1.42 (1.18–1.72)
Stressful	6,280,612 (5,995,955–6,565,269)	21.64 (20.66–22.62)		2.05 (1.68–2.51)	1.62 (1.29–2.04)
Chronic medical condition(s)					
Has asthma	2,413,833 (2,237,478–2,590,188)	8.32 (7.71–8.93)	0.0001	1.88 (1.58–2.24)	1.44 (1.2–1.74)
Has chronic obstructive pulmonary disease	838,936 (743,407–934,466)	2.89 (2.56–3.22)	<0.0001	2.83 (2.23–3.59)	1.92 (1.45–2.53)
Has arthritis	5,790,867 (5,564,474–6,017,260)	19.95 (19.17–20.74)	0.0001	1.57 (1.4–1.75)	1.29 (1.13–1.47)
Has high blood pressure	5,326,295 (5,092,116–5,560,473)	18.35 (17.55–19.16)	0.0249	1.08 (0.96–1.21)	0.85 (0.74–0.98)
Has high blood cholesterol/lipids	3,686,570 (3,491,111–5,560,473)	12.7 (12.03–13.38)	0.4780	1.21 (1.06–1.39)	1.06 (0.9–1.25)
Has heart disease	1,382,509 (1,248,851–1,516,167)	4.76 (4.3–5.23)	0.0004	1.72 (1.43–2.07)	1.45 (1.18–1.79)
Ever been diagnosed with cancer	2,175,846 (2,030,344–2,321,349)	7.5 (7.0–8.0)	0.0157	1.41 (1.22–1.62)	1.23 (1.04–1.46)
Has a bowel disorder (Crohn's disease, ulcerative colitis, irritable bowel syndrome, incontinence)	1,558,896 (1,431,507–1,686,285)	5.37 (4.93–5.81)	0.0080	1.91 (1.63–2.24)	1.27 (1.07–1.52)
Has urinary incontinence	1,146,488 (1,028,631–1,265,228)	3.95 (3.54–4.36)	0.0265	1.85 (1.5–2.27)	1.31 (1.03–1.67)
Usual place for immediate care for minor problems					<0.0001
Community health centre	1,146,488 (1,030,584–1,262,392)	3.95 (3.55–4.35)	-	0.77 (0.6–0.98)	0.78 (0.6–1.02)
Doctor's office	14,534,280 (14,210,494–14,858,067)	50.08 (48.97–51.2)			Ref.

Table 2: Characteristics associated with receiving an antibiotic prescription in the previous 12 months (*continued*)

Characteristics	Unweighted		p-value	Odds ratio	
	Frequency	Percent (%)		Unadjusted	Adjusted
Usual place for immediate care for minor problems (*continued*)					<0.0001
Emergency room	1,944,944 (1,792,576–2,097,311)	6.7 (6.18–7.23)	-	0.91 (0.74–1.11)	1 (0.8–1.23)
Hospital outpatient	725,183 (642,555–807,811)	2.5 (2.21–2.78)		0.82 (0.64–1.06)	0.83 (0.63–1.08)
Walk-in clinic	6,889,707 (6,603,742–7,175,672)	23.74 (22.75–24.73)		0.99 (0.87–1.13)	1.1 (0.95–1.26)
No usual place of care	3,779,951 (3,566,350–3,993,551)	13.03 (12.29–13.76)		0.56 (0.46–0.66)	0.66 (0.54–0.8)
Regular provider type					0.0004
FP/GP	23,941,588 (23,683,672–24,199,503)	82.5 (81.61–83.39)	-		Ref.
Non-FP/GP	732,110 (605,057–859,163)	2.52 (2.08–2.96)		0.87 (0.62–1.23)	0.84 (0.58–1.23)
No usual provider	4,346,855 (4,123,637–4,570,073)	14.98 (14.21–15.75)		0.61 (0.53–0.71)	0.71 (0.6–0.84)

Abbreviations: FP, family practitioner; GP, general practitioner; Ref., reference; SEM, standard error of the mean
Note: These additional covariates were also included in the model: province of residence, marital status, body mass index, type of drinker, physical activity, insurance for prescription medications, language most often spoken at home, perceived mental health, seasonal flu shot, stroke, diabetes, mood disorder and anxiety disorder. Adjusted and unadjusted results for these covariates can be found in the Appendix

Figure 1: Unadjusted odds ratio for oral antibiotic use in the past 12 months by age
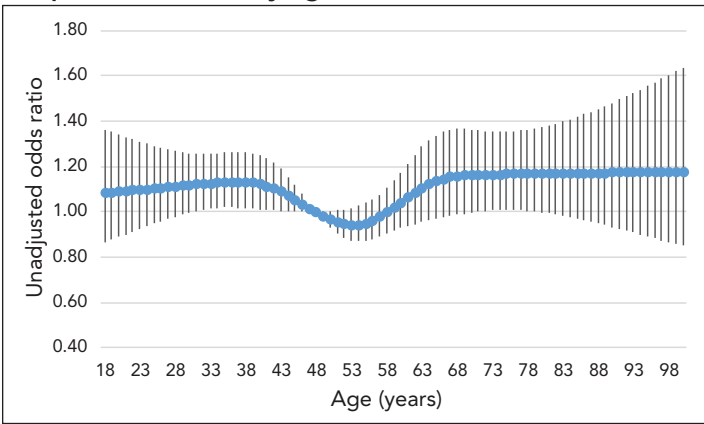
Figure 2: Adjusted odds ratio for oral antibiotic use in the past 12 months by age
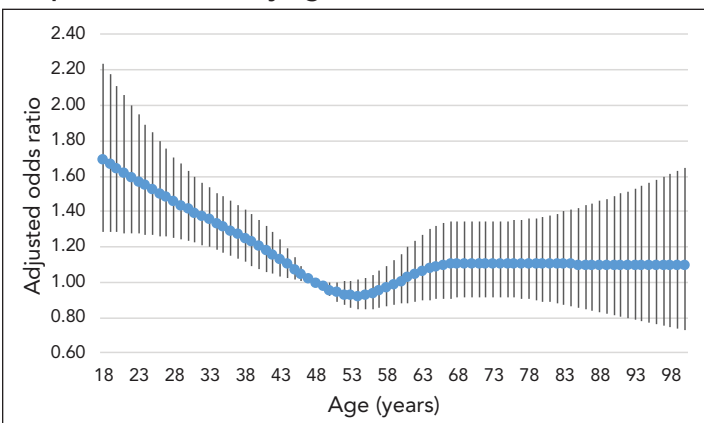
In the adjusted model, women had higher odds of reporting receipt of an antibiotic prescription in the previous 12 months compared to men (OR 1.55; 95% CI: 1.38–1.72) (Table 2). Using the adjusted logistic regression model, immigrants were 1.21 (95% CI: 1.01–1.45) times more likely than those who were both non-Indigenous and non-immigrants to report receiving an antibiotic prescription. For Indigenous respondents (off-reserve), the odds were 1.04 (95% CI: 0.81–1.34) times higher, however, it was not possible to determine if this difference was significant due to the small number of Indigenous respondents (3.37%).

Respondents who reported having no usual place of care for minor medical problems (OR 0.66; 95% CI: 0.54–0.80) or no regular healthcare provider (OR 0.71; 95% CI: 0.60–0.84) were less likely to receive an antibiotic prescription after adjusting for all other covariates (Table 2).

Those who self-reported less than excellent health and perceived life stress had greater odds of receiving an antibiotic prescription. Both current and former smokers had higher odds compared to those who had never smoked. Asthma, chronic obstructive pulmonary disease, arthritis, heart disease, cancer, bowel disorders and urinary incontinence were associated with an increased odds of receiving a prescription. Hypertension was associated with lower odds. The frequency of responses was too low to include receipt of seasonal influenza vaccination in the model.

Discussion

This study revealed that about one-quarter of Canadians (26.0%) received at least one systemic (oral) antibiotic prescription over a one-year period, of whom 38% received more than one. One in five of these prescriptions (21.5%) was reported to be for a chest infection. This is concerning given that bronchitis has been found to be associated with high levels of unnecessary antibiotic prescribing in other research (52% in British Columbia (11); 53% in Ontario) (5). The high proportion of reported prescriptions for ear/nose/throat/sinus/eye infections (23.2%) is similarly notable, given that previous research has found a high rate of unnecessary prescribing for sinus infections (48% in British Columbia; 48% in Ontario), throat infections (42% in British Columbia) and ear infections (39% in Ontario) (5,11).

After controlling for medical conditions, the odds of those aged 18 years and those aged 30 years having received a prescription were higher than those aged 48 years, 60 years and 80 years. It is expected for antibiotic use to rise with age and for much of it to be attributable to greater morbidity, however, it is unclear what underpins young adults' odds of use such that it surpasses the odds for middle-age and older adults when controlling for medical conditions. Younger adults may be more likely to have a faulty understanding of what constitutes an oral antibiotic. As well, this survey does not capture the frailest older adults, such as long-term care residents or those in hospital, possibly eliminating a large portion of antibiotic use in these disproportionately elderly groups. Population usage metrics show a greater burden of antibiotic use among older age groups (2). Taken together, these different measures might also indicate that those older adults who use antibiotics use a high quantity (by tonnage or by prescription) while young adults may have more evenly distributed use across their age groups or shorter prescriptions. These findings are similar to those of other surveys on antibiotic use in Canada that found high reported use among young adults (12,13). Younger age groups also have a much higher burden of conditions that are frequently treated with antibiotics that were not controlled for in our study, such as sexually transmitted infections (14) and acne (15). The widespread and intensive use of systemic antibiotics for acne, particularly among young adults, has notably been challenged in recent scientific literature and guidelines have been changed in many regions to reduce their use to limit AMR (16–19). Young adults may also be parents and are more likely to be exposed to respiratory infections through their children (20,21). In some contexts, young adults have a higher rate of inappropriate prescriptions for upper respiratory tract infections than other adult age groups (22,23).

In line with previously published findings in the literature and Canadian dispensation data (2,8), antibiotic use is higher among women. This may be for reasons linked to biology (e.g., a higher risk of urinary tract infections) or gendered social dynamics (e.g., a higher likelihood to seek medical care (24)

and very high representation in work with exposure to patients, children or food-labour sectors associated with higher rates of infections (25)).

Contrary to other studies from high-income countries, neither income nor education were significant in either adjusted or unadjusted analyses (8). This may be because we were able to control for other variables that are often co-linear with socioeconomic status such as comorbidities (positively associated with use) and low levels of access to regular medical care (negatively associated with use).

We found very slightly higher use among Indigenous populations off-reserve. This contrasts with other studies that have found high dispensation rates of antibiotics to Indigenous populations on-reserve and in the Arctic (26,27). However, it is in line with studies that have found that antibiotic use is not highly different in regions with higher Indigenous populations, though the latter studies also appear to have excluded on-reserve dispensations, potentially skewing regional use and its associations (28,29).

The finding of higher use among immigrant populations in Canada departs from a study that found that regions in Ontario with a higher proportion of immigrants had neither higher nor lower use (28).

In accordance with many other findings, several medical conditions were associated with higher antibiotic use, which is potentially explained by the need for invasive devices with elevated risk of infection, depressed immunity, symptoms of unclear etiology or frequent interactions with medical care. The finding that hypertension was associated with lower odds of prescriptions may be explained by known contraindications of blood pressure medications with use of certain antibiotics (30,31).

Limitations
The results are based on self-reported survey data, and responses may reflect recall bias or social desirability bias. Respondents may also have a faulty understanding of what an antibiotic is. This is a common and well-known limitation in surveys of antibiotic use (32–35). While restricting participation to respondents who demonstrate knowledge of antibiotic use could mitigate this issue, it would introduce selection bias (32).

These results do not include the Territories or residents of the remote Québec regions of Nunavik and Terres-Cries-de-la-Baie-James, Indigenous communities, institutionalized populations (e.g., residents of healthcare facilities, long-term care, prisons, convents) and full-time members of the Canadian Armed Forces. This survey does not include unprescribed antibiotic use, which in other contexts has been found to be higher among certain demographics, including migrant workers, men who have sex with men and people who inject drugs (22,36). Additionally, telephone surveys may not capture the frailest community-

dwelling adults and will not capture people without a phone, which may both be key populations for high antibiotic use (8). As well, recent research has highlighted very elevated levels of antibiotic prescribing to gay, bisexual, and other men who have sex with men in an urban sexual health clinic (37), to people living in Arctic communities (27) and to First Nations individuals accessing health care at nursing stations on-reserve in Canada (26). Further research should further inquire into levels of AMU among these populations at a national level.

Conclusion

These results suggest that efforts to reduce unnecessary antibiotic use through stewardship and policy initiatives need to target the whole age spectrum. More data are necessary to understand and address the drivers of antibiotic use and to elucidate why young people have higher odds of being prescribed an antibiotic than those in middle-age when controlling for other factors, similar to what has been seen in other studies (12,13). Medical record data may help elucidate why certain comorbidities are associated with higher antibiotic use and help capture if it is appropriate or not to better tailor stewardship interventions.

In order to best tailor interventions on antibiotic use for immigrant communities, further research is necessary to identify which ethnocultural and linguistic groups are most affected. As well, more research and better data are needed on key populations not included in this study of AMU, including Indigenous people on-reserve and in the Arctic, individuals in long-term care establishments, two-spirit, gay, and bisexual men who have sex with men, transgender populations, incarcerated populations and people who use drugs, particularly by injection.

Notably, just over a quarter of respondents reported having taken systemic oral antibiotics, most frequently for indications for which close to half of prescriptions are known to be inappropriate. This points to the need for better education of prescribers and Canadians on the role of judicious AMU in protecting individual health and the health of the community.

Authors' statement

GS — Writing–original draft, formal analysis, writing–review & editing
A-LC — Writing–original draft, formal analysis, writing–review & editing
SA — Writing–review & editing, formal analysis, supervision, project administration
DG-T — Conceptualization, supervision
MI — Writing–review & editing
BK — Formal analysis, writing–review & editing
JM — Writing–original draft
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Competing interests

None.

Acknowledgements

References

1. Murray CJ, Ikuta KS, Sharara F; Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022;399(10325):629–55. DOI PubMed

2. Public Health Agency of Canada. Canadian Antimicrobial Resistance Surveillance System (CARSS). Report 2022. Ottawa, ON: PHAC; 2022. DOI

3. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096–2096. DOI PubMed

4. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infect Dis 2014;14(1):13. DOI PubMed

5. Schwartz KL, Langford BJ, Daneman N, Chen B, Brown KA, McIsaac W, Tu K, Candido E, Johnstone J, Leung V, Hwee J, Silverman M, Wu JH, Garber G. Unnecessary antibiotic prescribing in a Canadian primary care setting: a descriptive analysis using routinely collected electronic medical record data. CMAJ Open 2020;8(2):E360–9. DOI PubMed

6. Leslie M, Fadaak R, Lethebe BC, Szostakiwskyj JH. Assessing the appropriateness of community-based antibiotic prescribing in Alberta, Canada, 2017-2020, using ICD-9-CM codes: a cross-sectional study. CMAJ Open 2023;11(4):E579–86. DOI PubMed

7. Saatchi A, Reid JN, Povitz M, Shariff SZ, Silverman M, Morris AM, Reyes RC, Patrick DM, Marra F. Appropriateness of outpatient antibiotic use in seniors across two Canadian provinces. Antibiotics (Basel) 2021;10(12):1484. DOI PubMed

8. Schmiege D, Evers M, Kistemann T, Falkenberg T. What drives antibiotic use in the community? A systematic review of determinants in the human outpatient sector. Int J Hyg Environ Health 2020;226:113497. DOI PubMed

9. Statistics Canada. Canadian Community Health Survey (CCHS). Ottawa, ON: StatCan; 2023. https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&Id=1496481

10. Harrell FE. Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. Springer Series in Statistics. Springer International Publishing; 2015. https://warin.ca/ressources/books/2015_Book_RegressionModelingStrategies.pdf

11. Saatchi A, Yoo JW, Schwartz KL, Silverman M, Morris AM, Patrick DM, McCormack J, Marra F. Quantifying the gap between expected and actual rates of antibiotic prescribing in British Columbia, Canada. Antibiotics (Basel) 2021;10(11):1428. DOI PubMed

12. Crago AL, Alexandre S, Abdesselam K, Tropper DG, Hartmann M, Smith G, Lary T. Understanding Canadians' knowledge, attitudes and practices related to antimicrobial resistance and antibiotic use: results from public opinion research. Can Commun Dis Rep 2022;48(11/12):550–8. DOI PubMed

13. Lorcy A, Quakki M, Dubé É. Étude Sur Les Connaissances, Attitudes et Perceptions de La Population Québécoise Sur l'utilisation Des Antibiotiques : 2019. 2020. [Accessed 2023 Dec 5]. https://www.inspq.qc.ca/publications/2690

14. Public Health Agency of Canada. Notifiable Disease Charts. Ottawa, ON: PHAC; 2024. https://diseases.canada.ca/notifiable/charts-list

15. Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol 2013;168(3):474–85. DOI PubMed

16. Sinnott SJ, Bhate K, Margolis DJ, Langan SM. Antibiotics and acne: an emerging iceberg of antibiotic resistance? Br J Dermatol 2016;175(6):1127–8. DOI PubMed

17. Walsh TR, Efthimiou J, Dréno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. Lancet Infect Dis 2016;16(3):e23–33. DOI PubMed

18. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, Bowe WP, Graber EM, Harper JC, Kang S, Keri JE, Leyden JJ, Reynolds RV, Silverberg NB, Stein Gold LF, Tollefson MM, Weiss JS, Dolan NC, Sagan AA, Stern M, Boyer KM, Bhushan R. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016;74(5):945–73.e33. DOI PubMed

19. Nast A, Dréno B, Bettoli V, Bukvic Mokos Z, Degitz K, Dressler C, Finlay AY, Haedersdal M, Lambert J, Layton A, Lomholt HB, López-Estebaranz JL, Ochsendorf F, Oprica C, Rosumeck S, Simonart T, Werner RN, Gollnick H. European evidence-based (S3) guideline for the treatment of acne - update 2016 - short version. J Eur Acad Dermatol Venereol 2016;30(8):1261–8. DOI PubMed

20. Byington CL, Ampofo K, Stockmann C, Adler FR, Herbener A, Miller T, Sheng X, Blaschke AJ, Crisp R, Pavia AT. Community surveillance of respiratory viruses among families in the Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study. Clin Infect Dis 2015;61(8):1217–24. DOI PubMed

21. Seibold MA, Moore CM, Everman JL, Williams BJ, Nolin JD, Fairbanks-Mahnke A, Plender EG, Patel BB, Arbes SJ, Bacharier LB, Bendixsen CG, Calatroni A, Camargo CA Jr, Dupont WD, Furuta GT, Gebretsadik T, Gruchalla RS, Gupta RS, Khurana Hershey GK, Murrison LB, Jackson DJ, Johnson CC, Kattan M, Liu AH, Lussier SJ, O'Connor GT, Rivera-Spoljaric K, Phipatanakul W, Rothenberg ME, Seroogy CM, Teach SJ, Zoratti EM, Togias A, Fulkerson PC, Hartert TV; HEROS study team. Risk factors for SARS-CoV-2 infection and transmission in households with children with asthma and allergy: A prospective surveillance study. J Allergy Clin Immunol 2022;150(2):302–11. DOI PubMed

22. Grigoryan L, Zoorob R, Shah J, Wang H, Arya M, Trautner BW. Antibiotic prescribing for uncomplicated acute bronchitis is highest in younger adults. Antibiotics (Basel) 2017;6(4):22. DOI PubMed

23. Malo S, Bjerrum L, Feja C, Lallana MJ, Moliner J, Rabanaque MJ. Compliance with recommendations on outpatient antibiotic prescribing for respiratory tract infections: the case of Spain. Basic Clin Pharmacol Toxicol 2015;116(4):337–42. DOI PubMed

24. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. BMC Fam Pract 2016;17(1):38. DOI PubMed

25. Morales-Suárez-Varela M, Kaerlev L, Zhu JL, Llopis-González A, Gimeno-Clemente N, Nohr EA, Bonde JP, Olsen J. Risk of infection and adverse outcomes among pregnant working women in selected occupational groups: A study in the Danish National Birth Cohort. Environ Health 2010;9(1):70. DOI PubMed

26. Jeong D, Nguyen HN, Tyndall M, Schreiber YS. Antibiotic use among twelve Canadian First Nations communities: a retrospective chart review of skin and soft tissue infections. BMC Infect Dis 2020;20(1):118. DOI PubMed

27. Williams K, Colquhoun A, Munday R, Goodman KJ; CANHelp Working Group. Antibiotic dispensation rates among participants in community-driven health research projects in Arctic Canada. BMC Public Health 2019;19(1):949. DOI PubMed

28. Schwartz KL, Achonu C, Brown KA, Langford B, Daneman N, Johnstone J, Garber G. Regional variability in outpatient antibiotic use in Ontario, Canada: a retrospective cross-sectional study. CMAJ Open 2018;6(4):E445–52. DOI PubMed

29. Marra F, Mak S, Chong M, Patrick DM. The relationship among antibiotic consumption, socioeconomic factors and climatic conditions. Can J Infect Dis Med Microbiol 2010;21(3):e99–106. DOI PubMed

30. Wright AJ, Gomes T, Mamdani MM, Horn JR, Juurlink DN. The risk of hypotension following co-prescription of macrolide antibiotics and calcium-channel blockers. CMAJ 2011;183(3):303–7. DOI PubMed

31. Gandhi S, Fleet JL, Bailey DG, McArthur E, Wald R, Rehman F, Garg AX. Calcium-channel blocker-clarithromycin drug interactions and acute kidney injury. JAMA 2013;310(23):2544–53. DOI PubMed

32. Kosiyaporn H, Chanvatik S, Issaramalai T, Kaewkhankhaeng W, Kulthanmanusorn A, Saengruang N, Witthayapipopsakul W, Viriyathorn S, Kirivan S, Kunpeuk W, Suphanchaimat R, Lekagul A, Tangcharoensathien V. Surveys of knowledge and awareness of antibiotic use and antimicrobial resistance in general population: A systematic review. PLoS One 2020;15(1):e0227973. DOI PubMed

33. Vanden Eng J, Marcus R, Hadler JL, Imhoff B, Vugia DJ, Cieslak PR, Zell E, Deneen V, McCombs KG, Zansky SM, Hawkins MA, Besser RE. Consumer attitudes and use of antibiotics. Emerg Infect Dis 2003;9(9):1128–35. DOI PubMed

34. Parimi N, Pinto Pereira LM, Prabhakar P. The general public's perceptions and use of antimicrobials in Trinidad and Tobago. Rev Panam Salud Publica 2002;12(1):11–8. DOI PubMed

35. Barah F, Gonçalves V. Antibiotic use and knowledge in the community in Kalamoon, Syrian Arab Republic: a cross-sectional study. East Mediterr Health J 2010;16(5):516–21. DOI PubMed

36. O'Halloran C, Croxford S, Mohammed H, Gill ON, Hughes G, Fifer H, Allen H, Owen G, Nutland W, Delpech V, Saunders JM. Factors associated with reporting antibiotic use as STI prophylaxis among HIV PrEP users: findings from a cross-sectional online community survey, May-July 2019, UK. Sex Transm Infect 2021;97(6):429–33. DOI PubMed

37. Vanbaelen T, Tsoumanis A, Kenyon C. Total Antimicrobial Consumption in Doxycycline Postexposure Prophylaxis Cohorts and the Intensity of Screening for Bacterial Sexually Transmitted Infections. Clin Infect Dis 2024;78(3):803–5. DOI PubMed

Appendix

Table A1: Characteristics associated with receiving an antibiotic prescription in the previous 12 months with all variables

Characteristics	Weighted		Odds ratio	
	Frequency	Percent (%)	Unadjusted	Adjusted
Age (years)				
Mean (SEM)		48.11 (48.0–48.22)	See Figure 1	
18–29	5,472,681 (5,303,207–5,642,156)	18.86 (18.27–19.44)	Not included in model, age was treated as continuous	
30–39	5,255,468 (5,017,771–5,493,165)	18.11 (17.29–18.93)		
40–49	4,668,792 (4,508,772–4,828,812)	16.09 (15.54–16.64)		
50–59	5,013,909 (4,856,837–5,170,981)	17.28 (16.74–17.82)		
60–69	4,698,262 (4,497,236–4,899,288)	16.19 (15.5–16.88)		
70–79	2,693,963 (2,572,919–2,815,007)	9.28 (8.87–9.7)		
80+	1,217,479 (1,125,974–1,308,983)	4.2 (3.88–4.51)		
Sex				
Female	14,742,425 (14,742,424–14,742,426)	50.8 (50.8–50.8)	1.65 (1.49–1.83)	1.55 (1.38–1.72)
Male	14,278,128 (14,278,127–14,278,128)	49.2 (49.2–49.2)		Ref.
Marital status				
Married/common-law	18,199,194 (17,888,721–18,509,667)	62.71 (61.64–63.78)		Ref.
Single	7,070,640 (6,828,042–7,313,238)	24.36 (23.53–25.2)	1.03 (0.89–1.18)	0.95 (0.8–1.14)
Widowed/separated/divorced	3,750,719 (3,567,739–3,933,700)	12.92 (12.29–13.56)	1.11 (0.97–1.26)	0.94 (0.8–1.09)
Highest level of education				
High school	10,333,492 (9,999,596–10,667,387)	35.61 (34.46–36.76)	0.91 (0.79–1.05)	0.77 (0.66–0.89)
Diploma	10,371,261 (10,058,907–10,683,616)	35.74 (34.66–36.82)	0.95 (0.84–1.07)	0.88 (0.77–1.01)
University	8,315,800 (7,987,390–8,644,210)	28.65 (27.52–29.79)		Ref.
Body mass index				
Underweight	420,444 (330,287–510,601)	1.45 (1.14–1.76)	0.98 (0.6–1.61)	0.79 (0.46–1.33)
Normal weight	9,389,187 (9,068,169–9,710,205)	32.35 (31.25–33.46)		Ref.
Overweight	10,036,834 (9,720,884–10,352,785)	34.59 (33.5–35.68)	0.91 (0.8–1.03)	0.97 (0.84–1.11)
Obese I	4,724,310 (4,496,430–4,952,190)	16.28 (15.49–17.07)	1.07 (0.92–1.23)	1.03 (0.88–1.21)
Obese II	1,645,989 (1,503,982–1,787,997)	5.67 (5.18–6.16)	1.38 (1.13–1.69)	1.24 (1.0–1.54)
Obese III	897,816 (788,814–1,006,819)	3.09 (2.72–3.47)	1.49 (1.14–1.95)	1.18 (0.89–1.56)
Unknown	1,905,972 (1,730,180–2,081,763)	6.57 (5.96–7.17)	0.99 (0.79–1.23)	0.84 (0.66–1.07)

Table A1: Characteristics associated with receiving an antibiotic prescription in the previous 12 months with all variables (*continued*)

Characteristics	Weighted		Odds ratio	
	Frequency	Percent (%)	Unadjusted	Adjusted
Smoking status				
Current	4,872,020 (4,617,655–5,126,385)	16.79 (15.91–17.67)	1.31 (1.13–1.51)	1.3 (1.11–1.53)
Experiment	3,914,117 (3,696,472–4,131,761)	13.49 (12.74–14.24)	1.11 (0.94–1.29)	1.14 (0.97–1.34)
Former	7,704,652 (7,421,722–7,987,581)	26.55 (25.57–27.53)	1.2 (1.06–1.36)	1.22 (1.06–1.4)
Never	12,529,764 (12,185,432–12,874,096)	43.18 (41.99–44.36)		Ref.
Type of drinker (last 12 months)				
Never	6,098,171 (5,786,026–6,410,317)	21.01 (19.94–22.09)		Ref.
Occasional	4,861,665 (4,609,049–5,114,282)	16.75 (15.88–17.62)	1.04 (0.88–1.22)	1.0 (0.84–1.19)
Regular	18,060,716 (17,708,394–18,413,038)	62.23 (61.02–63.45)	0.93 (0.81–1.06)	1.0 (0.86–1.15)
Physical activity				
Active	10,675,829 (10,346,693–11,004,965)	36.79 (35.65–37.92)		Ref.
Moderately active	4,926,604 (4,685,618–5,167,590)	16.98 (16.14–17.81)	1.15 (0.99–1.34)	1.08 (0.93–1.26)
Somewhat active	6,472,529 (6,191,847–6,753,211)	22.3 (21.33–23.27)	1.14 (1.0–1.31)	1.05 (0.91–1.21)
Sedentary	6,945,590 (6,672,435–7,218,745)	23.93 (22.99–24.88)	1.14 (1.0–1.3)	1.0 (0.86–1.16)
Indigenous (off-reserve)/immigrant status				
Indigenous (off-reserve)	978,508 (870,556–1,086,460)	3.37 (3.0–3.74)	1.2 (0.94–1.53)	1.04 (0.81–1.34)
Immigrant	7,492,618 (7,126,684–7,858,551)	25.82 (24.56–27.08)	0.94 (0.82–1.08)	1.21 (1.01–1.45)
Non-Indigenous/non-immigrant	20,549,427 (20,193,939–20,904,915)	70.81 (69.58–72.04)		Ref.
Language most often spoken at home (first answer)				
English	18,759,089 (18,414,234–19,103,944)	64.64 (63.45–65.83)		Ref.
French	5,915,950 (5,767,569–6,064,331)	20.39 (19.87–20.9)	0.97 (0.87–1.08)	1.05 (0.82–1.35)
Other	4,345,514 (3,998,878–4,692,150)	14.97 (13.78–16.17)	0.82 (0.69–0.98)	0.89 (0.7–1.12)
Total household income (thousands)				
<50	7,588,111 (7,288,500–7,887,721)	26.15 (25.11–27.18)	1.11 (0.93–1.31)	0.94 (0.78–1.14)
50–100	9,303,183 (9,011,645–9,594,722)	32.06 (31.05–33.06)	0.99 (0.84–1.16)	0.92 (0.78–1.09)
100–149	6,033,084 (5,772,751–6,293,418)	20.79 (19.89–21.69)	0.97 (0.82–1.15)	0.92 (0.77–1.09)
>150	6,096,174 (5,804,118–6,388,231)	21.01 (20.0–22.01)		Ref.
Province of residence				
Alberta	3,319,229 (3,319,228–3,319,229)	11.44 (11.44–11.44)	1.02 (0.87–1.2)	1.05 (0.89–1.24)

Table A1: Characteristics associated with receiving an antibiotic prescription in the previous 12 months with all variables (*continued*)

Characteristics	Weighted		Odds ratio	
	Frequency	Percent (%)	Unadjusted	Adjusted
Province of residence (*continued*)				
British Columbia	3,867,378 (3,867,377–3,867,378)	13.33 (13.33–13.33)	1.02 (0.87–1.19)	1.07 (0.9–1.27)
Manitoba	977,254 (977,254–977,254)	3.37 (3.37–3.37)	0.99 (0.8–1.22)	1.11 (0.88–1.39)
New Brunswick	603,559 (603,559–603,560)	2.08 (2.08–2.08)	1.1 (0.87–1.38)	1.12 (0.87–1.44)
Newfoundland and Labrador	428,946 (428,946–428,947)	1.48 (1.48–1.48)	1.27 (1.0–1.6)	1.42 (1.1–1.84)
Nova Scotia	768,501 (768,501–768,501)	2.65 (2.65–2.65)	1.19 (0.98–1.44)	1.17 (0.94–1.45)
Ontario	11,377,324 (11,377,324–11,377,324)	39.2 (39.2–39.2)		Ref.
Prince Edward Island	120,209 (120,209–120,209)	0.41 (0.41–0.41)	1.29 (1.0–1.67)	1.39 (1.04–1.86)
Québec	6,712,348 (6,712,347–6,712,348)	23.13 (23.13–23.13)	0.99 (0.87–1.13)	1.1 (0.86–1.42)
Saskatchewan	845,805 (845,805–845,805)	2.91 (2.91–2.91)	1.07 (0.87–1.33)	1.12 (0.89–1.41)
Perceived health				
Poor/fair	3,487,551 (3,276,377–3,698,725)	12.02 (11.29–12.75)	2.82 (2.36–3.38)	1.89 (1.45–2.46)
Good	8,341,719 (8,033,243–8,650,196)	28.74 (27.68–29.81)	1.75 (1.51–2.04)	1.47 (1.22–1.75)
Very good	10,588,084 (10,279,864–10,896,303)	36.48 (35.42–37.55)	1.47 (1.27–1.7)	1.34 (1.14–1.57)
Excellent	6,603,198 (6,323,648–6,882,749)	22.75 (21.79–23.72)		Ref.
Perceived mental health				
Poor/fair	2,103,157 (1,926,551–2,279,763)	7.25 (6.64–7.86)	2.01 (1.64–2.48)	1.03 (0.79–1.33)
Good	7,680,865 (7,390,689–7,971,041)	26.47 (25.47–27.47)	1.45 (1.26–1.67)	1.07 (0.91–1.26)
Very good	10,430,576 (10,111,131–10,750,020)	35.94 (34.84–37.04)	1.08 (0.95–1.22)	0.9 (0.78–1.03)
Excellent	8,805,955 (8,505,460–9,106,450)	30.34 (29.31–31.38)		Ref.
Perceived life stress				
Not at all stressful	3,957,912 (3,760,455–4,155,369)	13.64 (12.96–14.32)		Ref.
Not very stressful	6,783,011 (6,515,591–7,050,432)	23.37 (22.45–24.3)	1.35 (1.13–1.61)	1.29 (1.07–1.55)
A bit stressful	11,999,017 (11,679,691–12,318,343)	41.35 (40.24–42.45)	1.61 (1.36–1.91)	1.42 (1.18–1.72)
Stressful	6,280,612 (5,995,955–6,565,269)	21.64 (20.66–22.62)	2.05 (1.68–2.51)	1.62 (1.29–2.04)
Had a seasonal flu shot (current/last year)	56,010 (36,132–75,888)	0.19 (0.12–0.26)	Frequency too low to include in model	
Chronic medical condition(s)				
Has asthma	2,413,833 (2,237,478–2,590,188)	8.32 (7.71–8.93)	1.88 (1.58–2.24)	1.44 (1.2–1.74)

Table A1: Characteristics associated with receiving an antibiotic prescription in the previous 12 months with all variables (*continued*)

Characteristics	Weighted		Odds ratio	
	Frequency	Percent (%)	Unadjusted	Adjusted
Chronic medical condition(s) (*continued*)				
Has chronic obstructive pulmonary disease	838,936 (743,407–934,466)	2.89 (2.56–3.22)	2.83 (2.23–3.59)	1.92 (1.45–2.53)
Has arthritis	5,790,867 (5,564,474–6,017,260)	19.95 (19.17–20.74)	1.57 (1.4–1.75)	1.29 (1.13–1.47)
Has high blood pressure	5,326,295 (5,092,116–5,560,473)	18.35 (17.55–19.16)	1.08 (0.96–1.21)	0.85 (0.74–0.98)
Has high blood cholesterol/lipids	3,686,570 (3,491,111–3,882,029)	12.7 (12.03–13.38)	1.21 (1.06–1.39)	1.06 (0.9–1.25)
Has heart disease	1,382,509 (1,248,851–1,516,167)	4.76 (4.3–5.23)	1.72 (1.43–2.07)	1.45 (1.18–1.79)
Suffers from the effects of a stroke	376,726 (310,763–442,688)	1.3 (1.07–1.53)	1.36 (0.95–1.94)	0.88 (0.58–1.33)
Has diabetes	2,221,519 (2,062,356–2,380,683)	7.65 (7.11–8.2)	1.3 (1.11–1.53)	1.08 (0.9–1.29)
Ever been diagnosed with cancer	2,175,846 (2,030,344–2,321,349)	7.5 (7.0–8.0)	1.41 (1.22–1.62)	1.23 (1.04–1.46)
Has a bowel disorder (Crohn's disease, ulcerative colitis, irritable bowel syndrome, incontinence)	1,558,896 (1,431,507–1,686,285)	5.37 (4.93–5.81)	1.91 (1.63–2.24)	1.27 (1.07–1.52)
Has urinary incontinence	1,146,930 (1,028,631–1,265,228)	3.95 (3.54–4.36)	1.85 (1.5–2.27)	1.31 (1.03–1.67)
Has a mood disorder (depression, bipolar, mania, dysthmia)	2,620,823 (2,425,021–2,816,626)	9.03 (8.36–9.71)	1.85 (1.57–2.18)	1.15 (0.93–1.42)
Has an anxiety disorder (phobia, obsessive compulsive disorder, panic disorder)	2,615,767 (2,424,766–2,806,769)	9.01 (8.35–9.67)	1.68 (1.44–1.97)	1.02 (0.86–1.22)
Usual place for immediate care for minor problems				
Community health centre	1,146,488 (1,030,584–1,262,392)	3.95 (3.55–4.35)	0.77 (0.6–0.98)	0.78 (0.6–1.02)
Doctor's office	14,534,280 (14,210,494–14,858,067)	50.08 (48.97–51.2)		Ref.
Emergency room	1,944,944 (1,792,576–2,097,311)	6.7 (6.18–7.23)	0.91 (0.74–1.11)	1.0 (0.8–1.23)
Hospital outpatient	725,183 (642,555–807,811)	2.5 (2.21–2.78)	0.82 (0.64–1.06)	0.83 (0.63–1.08)
Walk-in clinic	6,889,707 (6,603,742–7,175,672)	23.74 (22.75–24.73)	0.99 (0.87–1.13)	1.1 (0.95–1.26)
No usual place of care	3,779,951 (3,566,350–3,993,551)	13.03 (12.29–13.76)	0.56 (0.46–0.66)	0.66 (0.54–0.8)
Regular provider type				
FP/GP	23,941,588 (23,683,672–24,199,503)	82.5 (81.61–83.39)		Ref.
Non-FP/GP	732,110 (605,057–859,163)	2.52 (2.08–2.96)	0.87 (0.62–1.23)	0.84 (0.58–1.23)
No usual provider	4,346,855 (4,123,637–4,570,073)	14.98 (14.21–15.75)	0.61 (0.53–0.71)	0.71 (0.6–0.84)
Insurance for prescription medications (all or part coverage)	22,877,375 (22,616,076–23,138,674)	78.83 (77.93–79.73)	1.27 (1.11–1.45)	1.15 (1.0–1.32)

Abbreviations: FP, family practitioner; GP, general practitioner; Ref., reference; SEM, standard error of the mean

Epidemiology of sporadic and outbreak-associated hepatitis A infections in Ontario, Canada: A descriptive summary, 2015–2022

Katherine Paphitis[1]*, Janica A Adams[1], Christine Navarro[1]

Abstract

Background: Hepatitis A is a disease of public health significance that typically causes acute, self-limiting infection. Understanding the risk factors and demographics associated with individual infections and outbreaks can guide public health communication and interventions.

Objective: To assess the number of hepatitis A cases and outbreaks in Ontario from January 1, 2015, to November 22, 2022, and to identify common risk factors associated with sporadic and outbreak-associated infections in Ontario.

Methods: Confirmed and probable hepatitis A cases reported between January 1, 2015, and November 22, 2022, were extracted from the Ontario electronic reporting system. Descriptive analyses were used to summarize and compare risk factors reported by sporadic and outbreak-associated hepatitis A cases. Annual rates of infection for individual public health units were calculated using annual population estimates for Ontario health regions.

Results: During the study period, 938 cases of hepatitis A were reported in Ontario (an average annual rate of 0.9 cases per 100,000 population), with 31.3% (n=294) of cases linked to one of 18 unique outbreaks of hepatitis A. Four of 13 local outbreaks were associated with elementary school settings. Reported risk factors differed between sporadic cases (predominantly travel-related) and cases linked to known outbreaks (anal-oral contact, illicit drug use, diapering/assisting in toileting, close contact with a case). Rates of sporadic infection differed across public health units in Ontario over the study period.

Conclusion: Public health interventions that aim to increase awareness of hepatitis A risk factors and increase vaccine uptake among those at increased risk of exposure could help to reduce the incidence of both locally acquired and travel-related sporadic infections and outbreaks.
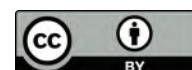
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Introduction

Hepatitis A is typically spread via the fecal-oral route and through direct or indirect contact (including anal-oral contact) or ingestion of contaminated food, typically causing acute, self-limiting infection in those who are infected (1). Following exposure to hepatitis A virus (HAV), signs and symptoms typically develop within 28–30 days, although symptoms may occur 15–50 days following exposure (1). Transmission of infection can occur from two weeks prior to symptom onset and up to seven days after onset of jaundice; thus, transmission of infection may occur before a case is aware they are ill (1). While children under six years of age are usually asymptomatic, severity of infection increases with age (1–4).

Hepatitis A incidence is low in developed countries, such as Canada, where most individuals have access to clean water and adequate sanitation (3). Individuals considered to be at increased risk of exposure to hepatitis A in developed countries include men who have sex with men (MSM), people who use drugs

(including people who inject drugs), household or sexual contacts of a confirmed case, individuals experiencing homelessness, individuals anticipating close contact with international adoptees and travellers to HAV endemic areas (3,5–7). Hepatitis A virus exposure may also occur through the ingestion of contaminated food, including ready-to-eat foods, shellfish and foods imported from areas with high hepatitis A endemicity (1,3,8–11).

In Ontario, all confirmed and probable cases of hepatitis A are reported to local public health units (PHUs) for investigation (12). Through case interviews using a standardized questionnaire, PHUs collect information on symptoms, medical and behavioural risk factors and relevant exposures during the incubation period (13). Confirmed cases are those with laboratory confirmation of infection (a serum or plasma sample positive for HAV IgM antibody) without recent vaccination for hepatitis A and either acute symptomatic illness or an epidemiologic link to a confirmed case (1). Probable cases are those with acute illness and an epidemiologic link to a confirmed case, but without laboratory confirmation of infection (1). Where two or more cases share a common exposure, an outbreak may be declared. Multijurisdictional outbreaks involve more than one PHU and in some situations, for example, outbreaks linked to consumption of a widely distributed food product, a national outbreak may be declared.

Case management of confirmed and probable cases includes providing education on disease transmission and prevention, excluding cases who work in high-risk settings (such as food handlers, childcare staff and healthcare workers) from work until 14 days after symptom onset or seven days after the onset of jaundice and recommending post-exposure prophylaxis for household and close contacts of HAV cases to minimize risk of transmission (1).

In Ontario, HAV vaccination is not part of the routine childhood immunization schedule but is available to travellers (for a fee) and is publicly funded for individuals at high risk of exposure or severe outcomes, including MSM, people who inject drugs and individuals with chronic liver disease, including hepatitis B and C (14). While individuals at high risk of exposure to hepatitis A are eligible to receive two doses of publicly funded vaccine as a means of primary prevention, a single dose of vaccine may be offered to contacts of cases as post-exposure prophylaxis (1,14,15).

This study aimed to assess the number of reported hepatitis A cases and outbreaks in Ontario from January 1, 2015, to November 22, 2022, and to identify and to compare demographics and reported risk factors for sporadic and outbreak-associated cases. Awareness of specific risk factors associated with sporadic infections and outbreaks can help to target public health communication and interventions aimed at disease prevention.

Methods

Cases meeting the confirmed or probable case definition for hepatitis A infection in Ontario and reported via the integrated Public Health Information System (iPHIS) by local PHUs from January 1, 2015, to November 22, 2022, were extracted for analyses. Data for 2022 were incomplete as data extraction was performed on November 22, 2022, in response to an internal data request and reanalyzed as a convenience sample. Where case onset date was unavailable, the episode date was used as a proxy per the following hierarchy: onset date, followed by specimen collection date, then laboratory test date, then reported date. Cases were categorized by the reporting PHU as outbreak-confirmed if a common exposure or contact with an infectious case of hepatitis A was known to have occurred, or as sporadic if no linkages to other cases or common exposures were identified at the time of initial case investigation. Outbreak-associated case counts were compared to published outbreak summaries for known outbreaks and, where observed to be misclassified as sporadic in the surveillance system, cases were reassigned to the correct outbreak.

Descriptive analyses were performed using SAS Enterprise Guide 8.2 (SAS Institute Inc., Cary, North Carolina) and Microsoft Excel 2013 (Redmond, Washington). Case data included age, gender (reported as male, female, transgender or unknown), risk factor/exposure information and PHU (based on home address). Annual rates of hepatitis A per 100,000 population were calculated for each PHU using annual population estimates for health regions in Ontario (16). Infection rates were calculated for each PHU (by year and averaged over the study period) to determine which PHUs had the highest rates of sporadic hepatitis A infections. Responses for individual risk factors were assessed separately for sporadic and outbreak-associated cases to explore associations between age or gender and individual risk factors. The Wilcoxon-Mann-Whitney test, Fisher's exact test or Mantel-Haenszel chi-square test were used to assess the significance of differences between outbreak-confirmed and sporadic hepatitis A cases and case demographics or risk factors (as applicable). Statistical significance for all analyses was 5% (α=0.05).

Research ethics committee approval was not required for this project as the activities described here are considered routine surveillance at Public Health Ontario.

Results

Hepatitis A cases and outbreaks
A total of 938 hepatitis A cases (n=917 confirmed, n=21 probable) were reported from all 34 PHUs in Ontario between January 1, 2015, and November 22, 2022, representing an average annual rate of 0.9 cases per 100,000 population.
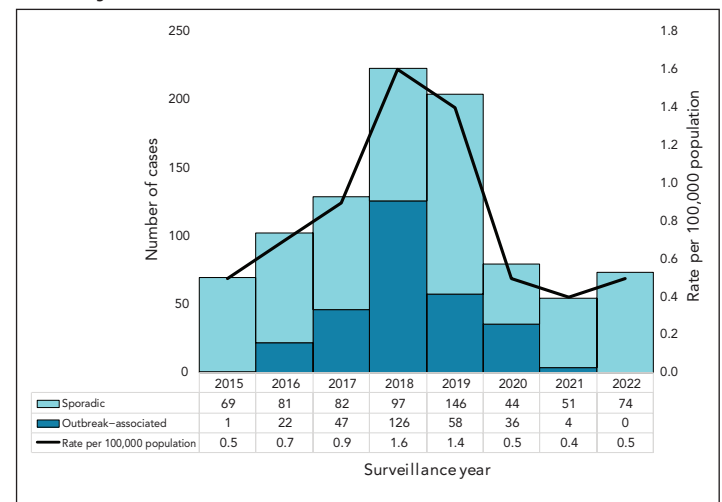
Of the reported cases, 39 cases that were entered into iPHIS as sporadic but known to be linked to an outbreak of hepatitis A were reassigned to the correct outbreak number. Subsequent analyses were based on corrected sporadic and outbreak-associated case counts. Most cases (68.7%, n=644) were reported as sporadic by the investigating PHU and 31.3% (n=294) were linked to an outbreak of hepatitis A. The number of sporadic and outbreak-associated cases generally increased each year prior to the COVID-19 pandemic (**Figure 1**). The number of reported outbreaks also generally increased each year, with one outbreak in each of 2015 and 2016, three in 2017, two in 2018 and five in each of 2019 and 2020 before declining during pandemic-impacted years.

There was a significant association between sporadic versus outbreak-associated cases and age group (*p*<0.0001). Almost two thirds of sporadic cases were younger than 30 years of age (n=421, 65.4%) compared to 36.7% (n=108) of outbreak-associated cases (**Table 1**).

Sporadic cases ranged in age from one to 96 years, with a median of 24.3 years (Table 1). Just over half (54.4%, n=350) of sporadic cases were male. Sporadic cases were significantly more likely than outbreak-associated cases to report travel outside of Ontario 15–50 days prior to symptom onset (*p*<0.0001) (**Table 2**).

During the study period, five multijurisdictional outbreaks (four national outbreaks, one Ontario-only outbreak) and 13 local (single PHU) outbreaks were reported. These ranged in size from three to 166 cases with a median of four cases. Outbreak-

Figure 1: Number of sporadic and outbreak-associated cases of hepatitis A and rates of infection (per 100,000 population) in Ontario, Canada (n=938), January 1, 2015, to November 22, 2022

	2015	2016	2017	2018	2019	2020	2021	2022
Sporadic	69	81	82	97	146	44	51	74
Outbreak–associated	1	22	47	126	58	36	4	0
Rate per 100,000 population	0.5	0.7	0.9	1.6	1.4	0.5	0.4	0.5

associated cases ranged in age from younger than one year to 80 years, with a median of 33.5 years. Most outbreak-associated cases (28.9%) were aged 30–39 years and most (62.2%) were male (Table 1). One of the five multijurisdictional outbreaks was linked to consumption of a nationally distributed, contaminated frozen fruit product (2016, n=19 Ontario cases) and one large Ontario-only outbreak (2017–2019, n=166 cases linked through HAV genotyping and genetic sequencing; 92% of cases occurring in four PHUs) was linked through case interviewing and outbreak

Table 1: Age and gender distribution for confirmed and probable cases of hepatitis A reported in Ontario, Canada, January 1, 2015, to November 22, 2022

Characteristics	Outbreak-associated cases (number, %)	Sporadic cases (number, %)	Total cases (number, %)	*p*-value
Age (years), median (IQR[a])	33.5 (23.5)	24.3 (25.9)	27.1 (27.4)	N/A
Age group				**<0.0001[b]**
Younger than 10 years	34 (11.6)	110 (17.1)	144 (15.4)	N/A
10–19 years	22 (7.5)	139 (21.6)	161 (17.2)	N/A
20–29 years	52 (17.7)	172 (26.7)	224 (23.9)	N/A
30–39 years	85 (28.9)	64 (9.9)	149 (15.9)	N/A
40–49 years	44 (15.0)	40 (6.2)	84 (9.0)	N/A
50–59 years	37 (12.6)	41 (6.4)	78 (8.3)	N/A
60 years or older	20 (6.8)	78 (12.1)	98 (10.5)	N/A
Total	294 (100.0)	644 (100.0)	938 (100.0)	N/A
Gender				**0.02[b,c]**
Male	183 (62.2)	350 (54.4)	533 (56.8)	N/A
Female	109 (37.1)	289 (44.9)	398 (42.4)	N/A
Transgender/unknown	2 (0.7)	5 (0.8)	7 (0.8)	N/A
Total	294 (100.0)	644 (100.0)	938 (100.0)	N/A

Abbreviations: IQR, interquartile range; N/A, not applicable
[a] Interquartile range from the 25th to 75th percentile
[b] Significant at *p*<0.05
[c] Chi-square value determined using "male" and "female" responses only

Table 2: Individual risk factors reported by sporadic and outbreak-associated cases of hepatitis A in Ontario, Canada, January 1, 2015, and November 22, 2022

Risk factor	Outbreak-associated cases (%)[a]	Sporadic cases (%)[a]	*p*-value
Anal-oral contact	60 (26.8)	22 (5.4)	<0.0001[b]
Close contact with case	72 (37.1)	61 (14.7)	<0.0001[b]
Diapering a child, or assisting a child or adult with bathroom use	32 (16.1)	37 (8.9)	0.008[b]
Illicit drug use[c]	123 (48.6)	16 (3.6)	<0.0001[b]
Travel outside of Ontario during the incubation period	33 (13.9)	413 (70.4)	<0.0001[b]

[a] Of those with a "yes" or "no" response available for each risk factor
[b] Significant at *p*<0.05
[c] Illicit drug use includes but is not limited to injection drug use

investigation by local PHUs to illicit drug use (reported by 67% of cases), MSM (15%) and person-to-person transmission among individuals experiencing homelessness (27%), in various settings utilized by the under-housed population, including shelters and drop-in centres. The remaining three outbreaks did not have an identified source; however, one was suspected to be associated with a contaminated food product.

Of the 13 locally occurring outbreaks, four (30.8%) were reported to be associated with elementary school settings, three (23.1%) were linked to a food handler or food premises, with the remaining six (46.2%) either having an unspecified source or linked to various settings, including private homes and local group home or shelter settings. Outbreak-associated cases,

particularly those older than 18 years, were significantly more likely than sporadic cases to report anal-oral contact, close contact with a case of hepatitis A, illicit drug use and diapering a child or assisting an individual with bathroom use (Table 2). Female outbreak-associated cases were significantly more likely to report diapering a child or assisting with bathroom use compared to males (*p*=0.04). Comparatively, males were significantly more likely to report illicit drug use compared to females (*p*=0.04).

Of 459 cases with a "yes" or "no" response available, 47 (10.2%) reported asymptomatic hepatitis A infection. Of those individuals who reported being asymptomatic, 21.3% were children younger than 10 years of age and 21.3% were aged 60 years or older, with the remainder aged 10–59 years. Of 775 cases with a "yes" or "no" response available, most cases (86.6%, n=671) reported jaundice as a symptom. Of 701 cases with a "yes" or "no" response available, most cases (75.6%; n=530) reported being unimmunized for hepatitis A at the time of case interview.

Geographic distribution

Rates of sporadic infection varied by PHU, with the highest rates observed in predominantly urban areas (**Table 3**). Peel Public Health and Toronto Public Health had high rates of infection, above the provincial average, across all study years, with the Region of Waterloo Public Health and Paramedic Services and Middlesex-London Health Unit also having high rates in some years (**Figure 2**). While rates of reported infection in Porcupine Health Unit, located in northern Ontario, were below the provincial average for most years examined, this PHU had the highest rate of sporadic hepatitis A infections in 2018 (Figure 2).

Table 3: Annual rates of sporadic hepatitis A infection per 100,000 population, by public health unit and compared to the provincial average, January 1, 2015, to November 22, 2022

Public health unit	Annual rates of sporadic hepatitis A infection (per 100,000 population)								
	2015	2016	2017	2018	2019	2020	2021	2022	Public health unit average
Algoma Public Health	0.0	1.7	0.0	1.7	0.0	0.0	0.0	0.0	0.4
Brant County Health Unit	0.0	0.0	0.0	0.0	1.3	1.3	0.0	0.0	0.3
Chatham-Kent Public Health	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1
City of Hamilton Public Health Services	0.2	0.0	0.4	0.4	0.7	0.2	0.2	0.3	0.3
Durham Region Health Department	0.2	0.8	0.9	0.7	0.9	0.3	0.1	0.0	0.5
Eastern Ontario Health Unit	0.5	0.0	0.0	0.0	0.9	0.0	0.9	0.5	0.4
Grey Bruce Health Unit	0.0	0.6	1.8	0.6	0.6	0.0	0.0	0.0	0.5
Haldimand-Norfolk Health Unit	0.0	1.8	0.0	0.0	0.0	0.0	0.0	0.0	0.2
Haliburton, Kawartha, Pine Ridge District Health Unit	0.0	0.0	0.0	0.5	0.0	0.0	0.5	0.0	0.1
Halton Region Public Health	0.2	0.5	0.2	0.7	1.0	0.5	0.3	0.6	0.5
Hastings Prince Edward Public Health	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.0	0.1
Huron Perth Public Health	0.0	0.7	0.0	0.0	0.0	0.0	0.7	0.0	0.2
Kingston, Frontenac and Lennox & Addington Public Health	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.5	0.1

Table 3: Annual rates of sporadic hepatitis A infection per 100,000 population, by public health unit and compared to the provincial average, January 1, 2015, to November 22, 2022 (*continued*)

Public health unit	Annual rates of sporadic hepatitis A infection (per 100,000 population)								
	2015	2016	2017	2018	2019	2020	2021	2022	Public health unit average
Lambton Public Health	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Leeds, Grenville & Lanark District Health Unit	0.0	0.0	0.6	0.0	0.0	0.0	0.0	0.5	0.1
Middlesex-London Health Unit	0.2	0.0	1.5	0.4	1.2	1.0	0.6	1.1	0.8
Niagara Region Public Health	0.4	0.2	0.0	0.2	0.4	0.2	0.2	0.4	0.3
North Bay Parry Sound District Health Unit	0.0	0.0	0.0	0.0	1.5	0.0	0.0	0.0	0.2
Northwestern Health Unit	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ottawa Public Health	0.5	0.3	0.4	0.5	1.0	0.2	0.8	0.5	0.5
Peel Public Health	1.2	1.3	1.5	0.9	2.0	0.6	0.6	1.6	1.2
Peterborough Public Health	0.0	0.0	0.0	2.0	0.0	0.7	0.0	0.0	0.3
Porcupine Health Unit	1.2	0.0	0.0	3.5	1.2	0.0	0.0	0.0	0.7
Public Health Sudbury & Districts	1.0	0.0	0.0	0.5	0.0	0.0	0.0	0.5	0.3
Region of Waterloo Public Health and Emergency Services	0.2	0.7	0.4	1.7	2.2	0.0	0.2	0.8	0.8
Renfrew County and District Health Unit	0.9	0.0	0.0	1.9	0.0	0.0	0.0	0.0	0.4
Simcoe Muskoka District Health Unit	0.0	0.2	0.0	0.5	0.5	0.0	0.2	0.2	0.2
Southwestern Public Health	0.0	1.0	0.0	0.5	0.9	0.0	0.0	0.4	0.4
Thunder Bay District Health Unit	0.6	0.0	0.0	0.0	0.0	0.0	1.3	0.6	0.3
Timiskaming Health Unit	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Toronto Public Health	0.9	0.9	0.9	0.8	1.7	0.3	0.5	0.4	0.8
Wellington-Dufferin-Guelph Public Health	0.7	0.7	0.0	1.0	0.3	0.3	0.0	0.3	0.4
Windsor-Essex County Health Unit	0.2	0.7	0.0	0.5	0.2	1.2	0.2	0.9	0.5
York Region Public Health	0.5	0.5	0.7	0.6	0.3	0.2	0.1	0.1	0.4
Provincial (Ontario) average	**0.5**	**0.6**	**0.6**	**0.7**	**1.0**	**0.3**	**0.3**	**0.5**	**0.6**

Figure 2: Annual rates of sporadic hepatitis A per 100,000 population, by public health unit and compared to the provincial average, January 1, 2015, to November 22, 2022
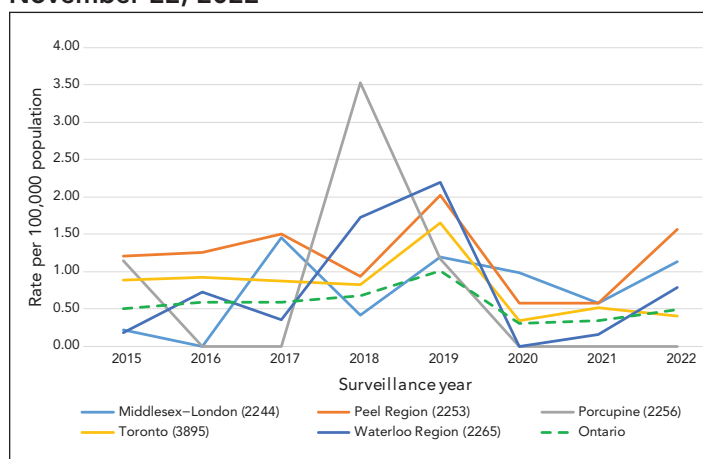
Discussion

Since 2015, reported cases of hepatitis A in Ontario have increased each year, with the exception of 2020–2022 when case reporting for all diseases of public health significance was impacted by the COVID-19 pandemic (17). Interestingly, almost one third of local outbreaks were associated with an elementary school setting and female outbreak-associated cases were significantly more likely to report diapering a child or assisting an individual with bathroom use. Predominance of females employed in childcare or elementary school settings may have contributed to the observed association between gender and diapering or toileting as a risk factor; however, data regarding case occupation was not available. Children may be more likely to transmit hepatitis A in communal settings such as schools and daycares due to poor hand hygiene and the tendency of infants and younger children to mouth objects (18). Children, including those attending childcare settings, have been linked to the spread of hepatitis A, with attendees and their contacts/relatives at increased risk of infection (4,15,19). The

EPIDEMIOLOGIC STUDY

United States Advisory Committee on Immunization Practices recommends HAV vaccination for children aged 12–23 months and unvaccinated children and youth aged two to 18 years (20). Routine vaccination of children in the United States has resulted in HAV infections being rare (20). Currently, Québec is the only jurisdiction in Canada that offers hepatitis A (combined with hepatitis B) vaccine at 18 months of age as part of their routine childhood immunization program (21).

Most cases in our study (76%) were unimmunized for hepatitis A at the time of case interview. Hepatitis A vaccination is not part of the routine immunization schedule in Ontario, however, it is recommended by the National Advisory Committee on Immunization for individuals aged six months and older who are at high risk of exposure or severe outcomes, including travellers to hepatitis A endemic countries, MSM, people who use intravenous drugs and individuals with chronic liver disease (22). Similar to the current literature (5–7,20,23,24), our study found that illicit drug use, close contact with a confirmed case and anal-oral contact were commonly reported risk factors among outbreak-associated cases, potentially indicating suboptimal vaccine uptake by eligible individuals. The finding that male outbreak-associated cases were more likely to report illicit drug use than female outbreak-associated cases was likely influenced by the large Ontario-only outbreak that occurred during the study period (2017–2019), for which illicit drug use was a predominant risk factor and many of the cases (almost two thirds) were male. The United States Advisory Committee on Immunization Practices also recommends routine HAV vaccination for persons experiencing homelessness (20), another important risk factor related to outbreak-associated cases in Ontario.

Sporadic cases were significantly more likely to report travel outside Ontario during the exposure period, with infection in many cases likely acquired during travel. From 2020 to 2022, there was a significant decrease in the number of hepatitis A cases reported in Ontario and elsewhere, with restrictions on travel likely having a substantial impact on travel-associated hepatitis A acquisition rates (25). The World Health Organization considers several regions to be endemic for hepatitis A, including most countries in South Asia, South America, Africa, the Middle East and Oceania, with unvaccinated travellers to these areas at increased risk of exposure (22,26). Outbreaks of hepatitis A have previously occurred in Canada and elsewhere following travel to endemic regions (27,28), or due to consumption of contaminated food (10,29); for example, in 2016, 25 cases of hepatitis A linked to consumption of a frozen fruit product were identified from three provinces (30).

Compared to sporadic cases, only a small proportion of outbreak-associated cases reported travel outside of Ontario, indicating local acquisition of infection. Previous studies have explored the under-reporting of hepatitis A in non-endemic countries, including in Canada (27), and noted around 15%

of cases may be asymptomatic, contributing to missed opportunities for diagnosis and case reporting, particularly as up to 70%–90% of children younger than six years of age may be asymptomatic (4,31,32). Under-reporting may also occur if symptomatic individuals do not seek medical care or testing. Asymptomatic infections can contribute to undetected transmission of infection and may result in outbreaks, particularly in susceptible populations where most individuals are unimmunized for hepatitis A.

The finding that the highest overall rates of sporadic infection disproportionately occurred within Peel Region and the City of Toronto was likely influenced by the proportion of new immigrants that reside in these areas (33). According to the 2016 census, about 76% of new immigrants to Ontario from 2011 to 2016 settled within the Toronto census metropolitan area, one of the most culturally diverse areas in Canada (33). Additionally, municipalities within Toronto, Peel Region and the Kitchener-Cambridge-Waterloo areas were among the top 10 census metropolitan areas in Canada with the highest proportion of the population being foreign-born (33). Although reported cases of hepatitis A in Ontario are not explicitly asked about recent immigration, those who arrived in Ontario within the 50 days prior to symptom onset would likely have been captured as having travelled during the incubation period. Individuals whose parents or grandparents previously immigrated to Canada from a hepatitis A-endemic country may also be more likely to return to these countries to visit friends and family, increasing their risk of hepatitis A acquisition, particularly if they are not vaccinated for hepatitis A (31). Prince Edward Island is currently the only Canadian province that identifies immigrants from endemic areas as eligible for publicly funded HAV vaccine (34).

The unusually high rate of sporadic hepatitis A infections in Porcupine Health Unit in 2018 was driven by a small number of cases (fewer than five) in this PHU, which has a small population size compared to other PHUs in Ontario. The high rate of sporadic hepatitis A infections in Middlesex-London Health Unit over the study period was unexpected and was above the provincial average for most years examined. Further investigation may be warranted to ascertain local or other factors that may contribute to observed rates in this region.

Limitations

This study had several limitations. The data only represented cases reported in iPHIS. As a result, all counts could be subject to varying degrees of under-reporting due to several factors, such as the presence and severity of symptoms, access to health care and healthcare seeking behaviours. Similarly, data for certain risk factors and symptoms may have been incomplete or missing for some cases due to individual case investigator and PHU interviewing and data entry practices. The proportion of cases who were under-housed or homeless or who recently immigrated to Canada are likely underestimated in the dataset as these risk factors are not routinely asked of cases or reported by PHUs.

Due to the impact of the COVID-19 pandemic on testing and reporting of diseases of public health significance in Ontario, cases may have been under-ascertained and data for 2020 and 2021 should be interpreted with caution. The standardized questionnaire for hepatitis A only asks cases to self-report if they were "unimmunized" for hepatitis A at the time of infection, which may be subject to recall bias. For those who report previous vaccination, no information is obtained regarding the number of doses received, date(s) of administration or the reason for vaccination (e.g., post-exposure prophylaxis, anticipated travel). Hepatitis A vaccination data is not routinely entered into a provincial immunization registry; thus, vaccination status could not be verified. Lastly, as this study was intended to be descriptive in nature, analyses were not adjusted to control for potential confounding or effect modification.

Conclusion

Asymptomatic infection among children and youth in Ontario may be an important contributor to local transmission of HAV within settings such as schools, daycares and private households. While travel to endemic areas for hepatitis A infection increases the risk of sporadic illness, various risk factors, including being under-housed or homeless, using drugs and self-identifying as MSM, may also increase the risk of both acquisition and transmission of infection. Interventions that increase awareness of risk factors and vaccine uptake among individuals at high risk of exposure, including consideration for publicly funded vaccine programs for additional populations (e.g., under-housed persons) and universal vaccination of children, could help to reduce the incidence of hepatitis A infections in Ontario.

Authors' statement

KP — Conceptualization, methodology, formal analysis, interpretation, writing–original draft, writing–review & editing
JA — Conceptualization, methodology, formal analysis, interpretation, writing–original draft, writing–review & editing
CN — Interpretation, writing–review & editing

All named authors read and approved the final manuscript. KP and JA contributed equally to this manuscript.

The views expressed in this manuscript are those of the authors and do not necessarily reflect those of Public Health Ontario or the Ministry of Health.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

The authors declare that they have no competing interests.

Acknowledgements

References

1. Ontario Ministry of Health. Infectious Disease Protocol. Appendix 1: Case definitions and disease-specific information. Disease: Hepatitis A. Toronto, ON: Government of Ontario; 2022. [Accessed 2023 Nov 23]. https://files.ontario.ca/moh-ophs-hepatitis-a-en-2022.pdf

2. Shenoy B, Andani A, Kolhapure S, Agrawal A, Mazumdar J. Endemicity change of hepatitis A infection necessitates vaccination in food handlers: an Indian perspective. Hum Vaccin Immunother 2022;18(1):1868820. DOI PubMed

3. World Health Organization. Position paper on hepatitis A vaccines—June 2012. Geneva, CH: WHO; 2012. [Accessed 2023 Nov 24]. https://apps.who.int/iris/bitstream/handle/10665/241938/WER8728_29_261-276.PDF;jsessionid=1846D0A5AEEA44B43DA222ADFA369FF1?sequence=1

4. Royal College of Physicians of Ireland. NIAC Immunization Guidelines. Chapter 08. Hepatitis A. Dublin, IE: NIAC; 2022. [Accessed 2023 Nov 23]. https://rcpi.access.preservica.com/uncategorized/IO_950e5299-ead9-4db1-8c75-e8313f59ad7a/

5. Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2019. Atlanta, GA: CDC; 2021. [Accessed 2023 Dec 5]. https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm

6. Castaneda D, Gonzalez AJ, Alomari M, Tandon K, Zervos XB. From hepatitis A to E: A critical review of viral hepatitis. World J Gastroenterol 2021;27(16):1691–715. DOI PubMed

7. Pisano MB, Giadans CG, Flichman DM, Ré VE, Preciado MV, Valva P. Viral hepatitis update: progress and perspectives. World J Gastroenterol 2021;27(26):4018–44. DOI PubMed

8. Shukla S, Cho H, Kwon OJ, Chung SH, Kim M. Prevalence and evaluation strategies for viral contamination in food products: risk to human health-a review. Crit Rev Food Sci Nutr 2016;58(3):405–15. DOI PubMed

9. Cuthbert JA. Hepatitis A: old and new. Clin Microbiol Rev 2001;14(1):38–58. DOI PubMed

10. Collier MG, Khudyakov YE, Selvage D, Adams-Cameron M, Epson E, Cronquist A, Jervis RH, Lamba K, Kimura AC, Sowadsky R, Hassan R, Park SY, Garza E, Elliott AJ, Rotstein DS, Beal J, Kuntz T, Lance SE, Dreisch R, Wise ME, Nelson NP, Suryaprasad A, Drobeniuc J, Holmberg SD, Xu F, Hepatitis A; Hepatitis A Outbreak Investigation Team. Outbreak of hepatitis A in the USA associated with frozen pomegranate arils imported from Turkey: an epidemiological case study. Lancet Infect Dis 2014;14(10):976–81. DOI PubMed

11. Hu X, Collier MG, Xu F. Hepatitis A Outbreaks in Developed Countries: Detection, Control, and Prevention. Foodborne Pathog Dis 2020;17(3):166–71. DOI PubMed

12. Government of Ontario. Ontario Regulation 135/18: Designation of diseases. Toronto, ON: Government of Ontario; 2023. [Accessed 2023 Dec 5]. https://www.ontario.ca/laws/regulation/180135

13. Public Health Ontario. Ontario Investigation Tools. Toronto, ON: PHO; 2019. [Accessed 2023 Dec 6]. https://www.publichealthontario.ca/en/diseases-and-conditions/infectious-diseases/ccm/oit

14. Ontario Ministry of Health. Publicly Funded Immunization Schedules for Ontario – June 2022. Toronto, ON: OMH; 2022. [Accessed 2023 Dec 5]. https://www.ontario.ca/files/2024-01/moh-publicly-funded-immunization-schedule-en-2024-01-23.pdf

15. Public Health Ontario. Provincial Infectious Diseases Advisory Committee. Hepatitis A Post-exposure Prophylaxis. Toronto, ON: PHO; 2013. [Accessed 2023 Dec 5]. https://www.publichealthontario.ca/-/media/documents/H/2013/hepa-post-exposure-prophylaxis.pdf

16. Statistics Canada. Archived - Population estimates, July 1, by health region and peer group, 2018 boundaries, inactive. Ottawa, ON: StatCan; 2023. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710013401

17. Public Health Ontario. Infectious disease trends in Ontario, 2022: Technical Notes. Toronto, ON: PHO; 2023. [Accessed 2023 Dec 5]. https://www.publichealthontario.ca/-/media/Documents/I/2019/idto-technical-notes.pdf

18. Sockett PN, Rodgers FG. Enteric and foodborne disease in children: A review of the influence of food- and environment-related risk factors. Paediatr Child Health 2001;6(4):203–9. DOI PubMed

19. O'Connor L, McGovern E, O'Meara M, Dean J, Ward M, O'Connor M. Extensive hepatitis A outbreak in an urban childcare facility in Ireland, associated with considerable adult morbidity. Epidemiol Infect 2018;146(6):705–11. DOI PubMed

20. Nelson NP, Weng MK, Hofmeister MG, Moore KL, Doshani M, Kamili S, Koneru A, Haber P, Hagan L, Romero JR, Schillie S, Harris AM. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR Recomm Rep 2020;69(5):1–38. DOI PubMed

21. Public Health Agency of Canada. Provincial and territorial routine and catch-up vaccination schedule for infants and children in Canada. Ottawa, ON: PHAC; 2023. [Accessed 2023 Dec 5]. https://www.canada.ca/en/public-health/services/provincial-territorial-immunization-information/provincial-territorial-routine-vaccination-programs-infants-children.html

22. Public Health Agency of Canada. Hepatitis A vaccines: Canadian Immunization Guide. Ottawa, ON: PHAC; 2023. [Accessed 2023 Dec 5]. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-6-hepatitis-a-vaccine.html

23. Migueres M, Lhomme S, Izopet J. Hepatitis A: Epidemiology, high-risk groups, prevention and research on antiviral treatment. Viruses 2021;13(10):1900. DOI PubMed

24. Hofmeister MG, Gupta N. Preventable deaths during widespread community Hepatitis A outbreaks - United States, 2016-2022. MMWR Morb Mortal Wkly Rep 2023;72(42):1128–33. DOI PubMed

25. European Centre for Disease Prevention and Control. Hepatitis A: annual epidemiological report for 2021. Stockholm, SE: ECDC; 2022. [Accessed 2023 Dec 5]. https://www.ecdc.europa.eu/sites/default/files/documents/HEPA_AER_2021.pdf

26. World Health Organization. Hepatitis A, countries or areas at risk. Geneva, CH: WHO; 2012. [Accessed 2023 Dec 5]. https://www.who.int/images/default-source/maps/global_hepa_ithriskmap.png

27. Savage RD, Rosella LC, Brown KA, Khan K, Crowcroft NS. Underreporting of hepatitis A in non-endemic countries: a systematic review and meta-analysis. BMC Infect Dis 2016;16:281. DOI PubMed

28. Sane J, MacDonald E, Vold L, Gossner C, Severi E; Outbreak Investigation Team. Multistate foodborne hepatitis A outbreak among European tourists returning from Egypt--need for reinforced vaccination recommendations, November 2012 to April 2013. Euro Surveill 2015;20(4):21018. DOI PubMed

29. Swinkels HM, Kuo M, Embree G, Andonov A, Henry B, Buxton JA; Fraser Health Environmental Health Investigation Team. Hepatitis A outbreak in British Columbia, Canada: the roles of established surveillance, consumer loyalty cards and collaboration, February to May 2012. Euro Surveill 2014;19(18):20792. DOI PubMed

30. Public Health Agency of Canada. Public Health Notice: Outbreak of hepatitis A infections; consumers advised not to eat Nature's Touch Organic Berry Cherry Blend frozen fruit. Ottawa, ON: PHAC; 2016. [Accessed 2023 Dec 5]. https://www.canada.ca/en/public-health/services/public-health-notices/2016/public-health-notice-outbreak-hepatitis-a-infections-consumers-advised-nature-s-touch-organic-berry-cherry-blend-frozen-fruit.html

31. Michaelis K, Poethko-Müller C, Kuhnert R, Stark K, Faber M. Hepatitis A virus infections, immunisations and demographic determinants in children and adolescents, Germany. Sci Rep 2018;8(1):16696. DOI PubMed

32. Hadler SC, Webster HM, Erben JJ, Swanson JE, Maynard JE. Hepatitis A in day-care centers. A community-wide assessment. N Engl J Med 1980;302(22):1222–7. DOI PubMed

33. Government of Ontario. Immigration (Fact Sheet 8: 2016 census highlights). Toronto, ON: Government of Ontario; 2022. [Accessed 2023 Dec 5]. https://www.ontario.ca/document/2016-census-highlights/fact-sheet-8-immigration

34. National Collaborating Centre for Infectious Diseases. Hepatitis A Immunization and High-Risk Populations in Canada and Internationally. Winnipeg, MB: NCCID; 2022. [Accessed 2023 Dec 5]. https://nccid.ca/publications/hepatitis-a-immunization-and-high-risk-populations-in-canada-and-internationally/

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