CCDR | CANADA COMMUNICABLE DISEASE REPORT

canada.ca/ccdr

January 2025 - Volume 51-1

PERSONAL PROTECTIVE MEASURES

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

CCDR
CANADA COMMUNICABLE DISEASE REPORT

The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public health professionals, and policy-makers to inform policy, program development and practice.

The CCDR Editorial Board is composed of members based in Canada, United States of America, European Union and Australia. Board members are internationally renowned and active experts in the fields of infectious disease, public health and clinical research. They meet four times a year, and provide advice and guidance to the Editor-in-Chief.

Editorial Team

Indexed
in PubMed, Directory of Open Access (DOAJ)/Medicus

Available
in PubMed Central (full text)

Contact the Editorial Office

ccdr-rmtc@phac-aspc.gc.ca
613.301.9930

Photo credit

The cover photo represents a scientist in a laboratory using personal protective measures such as gloves, mask and goggles. The image was taken from Adobe Stock #17701808.

CCDR Editorial Board Members

ISSN 1481-8531 / Cat. HP3-1E-PDF / Pub. 240649

CCDR
CANADA COMMUNICABLE DISEASE REPORT

PERSONAL PROTECTIVE MEASURES

TABLE OF CONTENTS

Summary of the National Advisory Committee on Immunization (NACI) Statement—Updated guidance on Imvamune in the context of a routine immunization program

Nicole Forbes[1], Josh Montroy[1], Marina I Salvadori[1,2], Kristin Klein[3] on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: Mpox is a viral illness related to smallpox. It can cause flu-like symptoms and a rash, and in severe cases, can lead to hospitalization or death. The Imvamune® vaccine offers protection against mpox. Consistent with global trends, mpox cases in Canada have been reported primarily among men who have sex with men (MSM), with sexual contact as the predominantly reported mode of transmission. While the incidence of mpox in Canada has significantly declined since the fall of 2022, mpox remains an important public health concern with the potential for future resurgence.

Methods: The National Advisory Committee on Immunization (NACI) reviewed available evidence on the clinical benefits and risks of Imvamune. This evidence included studies assessing the vaccine effectiveness estimates from real-world evidence, as well as pre- and post-market licensure safety data. NACI has also considered additional factors including ethics, equity, feasibility and acceptability. Guidance on the use of Imvamune in the context of international travel was developed in collaboration with the Canadian Committee to Advise on Tropical Medicine and Travel (CATMAT).

Results: NACI concluded that available evidence supported the vaccine's effectiveness and safety in preventing mpox infection.

Conclusion: Building on previous interim guidance from NACI recommending the use of Imvamune for pre-exposure vaccination in the context of ongoing mpox outbreaks, NACI now recommends that Imvamune be used in the context of a focused routine immunization program. Individuals at high risk of mpox, including MSM who meet high-risk criteria such as having more than one sexual partner, should receive two doses of Imvamune administered by subcutaneous injection at least 28 days apart.

Affiliations

[1] Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, ON

[2] Department of Pediatrics, McGill University, Montréal, QC

[3] Department of Medicine, University of Alberta, Edmonton, AB

***Correspondence:**
naci-ccni@phac-aspc.gc.ca

Suggested citation: Forbes N, Montroy J, Salvadori MI, Klein K on behalf of the National Advisory Committee on Immunization (NACI). Summary of the National Advisory Committee on Immunization (NACI) Statement—Updated guidance on Imvamune in the context of a routine immunization program. Can Commun Dis Rep 2025;51(1):1–6. https://doi.org/10.14745/ccdr.v51i01a01
Keywords: National Advisory Committee on Immunization, mpox, Canada, Imvamune, vaccine guidance

Introduction

Mpox (previously known as monkeypox) is a viral disease that is typically mild and self-limited, but can lead to severe disease in some populations such as young children, pregnant women and pregnant people and immunocompromised individuals. While outbreaks primarily occur in Central and West Africa, where the monkeypox virus (MPXV) is endemic, a global outbreak occurred in 2022 among previously non-endemic countries, including Canada. Among countries previously non-endemic for the

disease prior to 2022, mpox has been primarily transmitted via sexual encounters (83.2%) and among men who have sex with men (MSM) (85.3%). Since 2022, the majority of cases in Canada were among males (96.4%) aged 18–44 years (79.4%), with a median age of 34 years. Non-sexual exposure settings included household contacts, large events/parties, tattoo parlours and the workplace (1,2). Among cases with known HIV status, 52.1% were living with HIV. Approximately 4.1% of cases reported to the World Health Organization (WHO) were in healthcare workers, most of whom were exposed in community settings (i.e., exposures not related to work) (1). Thirty-five mpox cases were reported among cisgender and transgender women and non-binary individuals assigned female sex at birth in the context of a multi-national case series (136 confirmed mpox cases among 15 countries; cases reported between May 11, 2022, and October 4, 2022) (3). Data on mpox cases among sex workers remains limited.

Monkeypox virus clades currently circulating in Europe, the United States (US) and Canada belong to clade II, specifically subclade IIb, which is associated with milder illness than clade I (4). Historically, clade I infections were not known to be associated with transmission through sexual contact; however, in March 2023, a cluster of sexually transmitted clade I mpox cases was confirmed in the Democratic Republic of the Congo (DRC). The index case was a man from the DRC who reported having multiple sexual encounters in both Europe and the DRC, which led to an additional five PCR-positive MPXV cases (5). This finding shows that mpox transmission through sexual contact extends beyond clade IIb and highlights the need for more routine screening in mpox-endemic and non-endemic regions.

In response to the outbreaks in Canada, the National Advisory Committee on Immunization (NACI) released interim guidance on the use of Imvamune® in the context of ongoing mpox outbreaks. NACI guidance was first limited to post-exposure vaccination (June 2022) (6), which was later updated to include interim guidance for pre-exposure vaccination for high-risk groups, primarily MSM with certain risk factors (September 2022) (7). Though the 2022 mpox outbreak has subsided, mpox remains a public health concern, both in Canada and internationally. In response to stakeholder feedback, NACI reconvened to discuss expanded use of Imvamune in the context of a targeted routine program (e.g., outside the context of an ongoing mpox outbreak). Updated guidance was released in May 2024 and is summarized below.

Methods

For this interim guidance, NACI reviewed key questions as proposed by the NACI mpox Working Group (WG), including on the burden of disease to be prevented and the population(s) with greatest disease burden, vaccine safety, vaccine efficacy/effectiveness, vaccine supply and other aspects of the overall immunization strategy. Knowledge synthesis was performed by the NACI Secretariat and supervised by the NACI mpox WG. Following critical appraisal of individual studies, summary tables with risk of bias assessments informed by Cochrane ROB 2.0 and ROBINS-I, as appropriate, were prepared. The NACI Secretariat provided the NACI mpox WG an assessment of the body of evidence using an Evidence to Decision framework, and proposed recommendations for WG input.

NACI considered feedback obtained during 2022 deliberations from stakeholder groups representing the communities and groups considered at high risk of mpox exposure. Input was also provided by the Public Health Ethics Consultative Group during a 2022 consultation, the Canadian Immunization Committee (CIC; August 2023) and the Public Health Agency of Canada. Guidance on the use of Imvamune in the context of international travel was developed in collaboration with the Canadian Committee to Advise on Tropical Medicine and Travel (CATMAT). The description of relevant considerations, rationale for specific decisions and knowledge gaps are described. NACI reviewed the available evidence and approved updated guidance on March 26, 2024.

Further information on NACI's evidence-based methods is available online.

Results

Effectiveness against mpox infection

Available evidence on the effectiveness of pre-exposure vaccination with Imvamune against mpox was limited to real-world vaccine effectiveness (VE) observational studies. To date, 10 studies have reported estimates of the effect of a single dose of Imvamune against mpox infection (8–17), four of which also evaluated the effect of a 2-dose series (13–16). One-dose VE against mpox infection ranged from 36% (95% confidence intervals [CI]: 22%–47%) to 86% (95% CI: 59%–95%), while 2-dose VE ranged from 66% (95% CI: 47%–78%) to 89% (95% CI: 44%–98%). All individual studies evaluated are summarized in the **Appendix**, **Figure A1**). Of note, evidence should be interpreted with caution, as studies were assessed to be at a serious risk of bias (largely due to concerns regarding confounding and the measurement of outcomes) or at a moderate risk of bias (Figure A1).

Effectiveness against moderate/severe mpox infection

Two studies provided an estimate of effect of Imvamune against moderate to severe mpox infection. Only Brousseau *et al.* provided an estimate of VE at 82% (95% CI: −50%–98%) for adjusted 1-dose VE. During the study period, 12 individuals had moderate to severe mpox disease, of which three were hospitalized. Only one of these 12 individuals received

Imvamune (8). A US-based study estimated odds of hospitalization due to mpox among those vaccinated versus those who were unvaccinated. Compared to unvaccinated individuals, the odds of hospitalization among those with mpox who received one or two doses of Jynneos® were 0.27 (95% CI: 0.08–0.65) and 0.20 (95% CI: 0.01–0.90), respectively. Among individuals with both mpox and HIV infections, the odds of hospitalization were 0.28 (95% CI: 0.05–0.91) for those who met the definition of having received one dose of Jynneos, compared to those who were unvaccinated (17). Of note, evidence should be interpreted with caution, as studies were assessed to be at a serious risk of bias (largely due to concerns regarding confounding and the measurement of outcomes) or at a moderate risk of bias (Appendix, **Figure A2**).

Vaccine safety

Both pre- and post-licensure safety data support the safety of Imvamune. According to Imvamune clinical trial data where approximately 13,700 doses were given to 7,414 participants, the most common adverse events reported by adults were injection-site reactions, such as pain, redness and swelling, and systemic reactions, including fatigue, headache and myalgia. Most were mild to moderate in intensity and resolved without intervention within seven days post-vaccination, and no unexpected adverse events were identified. Additionally, there were no confirmed cases of cardiac events such as myocarditis and/or pericarditis following vaccination. The safety profile of Imvamune was similar in both immunocompetent and immunocompromised individuals (18).

NACI recommendations on Imvamune in the context of a focused routine immunization program

Recommendation 1: NACI recommends that individuals at high risk of mpox should receive two doses of Imvamune administered at least 28 days (four weeks) apart. **(*Strong NACI recommendation*)**

At this time, individuals considered at high risk of mpox in Canada include:

- Men who have sex with men (MSM)* who meet one or more of the following criteria:
  - Have more than one partner; or
  - Are in a relationship where at least one of the partners has other sexual partners; or
  - Have had a confirmed sexually transmitted infection in the last year; or
  - Have engaged in sexual contact in sex-on-premises venues
- Sexual partners of individuals who meet the criteria above
- Sex workers regardless of gender, sex assigned at birth or sexual orientation
- Staff or volunteers in sex-on-premises venues where workers may have contact with fomites potentially contaminated with mpox
- Those who engage in sex tourism regardless of gender, sex assigned at birth or sexual orientation
- Individuals who anticipate experiencing any of the above scenarios

*For the purposes of this NACI guidance, MSM is defined as: Man or Two-Spirit identifying individual who has sex with another person who identifies as a man, including but not limited to individuals who self-identify as transgender, cisgender, Two-Spirit, gender-queer, intersex and non-binary.

Recommendation 2: NACI continues to recommend the use of Imvamune as a post-exposure vaccination (also known and referred to as post-exposure prophylaxis) to individuals who have had high risk exposure(s) to a probable or confirmed case of mpox, or within a setting where transmission is happening, if they have not received both doses of pre-exposure vaccination. **(*Strong NACI recommendation*)**

Additional guidance:

- Off-label use in pediatric populations is recommended for those meeting the criteria for post-exposure vaccination and may be offered at their clinician's discretion.
- Doses should be administered via subcutaneous injection. Dose sparing strategies involving intradermal administration are not recommended in the context of routine immunization.
- At this time, Imvamune is not routinely recommended for healthcare workers, including those serving populations at high risk of mpox, with the exception of post-exposure vaccination.
- Imvamune vaccination can be given concurrently (i.e., same day), or at any time before or after other live or non-live vaccines.

Conclusion

Due to evolving mpox epidemiology in Canada and emerging evidence on VE of Imvamune, NACI developed national guidance on pre-exposure vaccination in the context of a focused routine immunization program. This included identification of priority populations for pre-exposure vaccination and guidance on a recommended vaccine schedule (summarized below in Appendix, **Table A1**). Note this guidance should be considered interim guidance and will be re-evaluated as additional evidence emerges.

Authors' statement

NF — Writing–original draft, writing–review & editing
JM — Writing–review & editing
MS — Writing–review & editing
KK — Writing–review & editing

The *NACI Interim guidance on the use of Imvamune® in the context of a routine immunization program* was prepared by N Forbes, K Klein, J Montroy, M Salvadori, K Gusic X Yiao, V Dubey, R Harrison and MC Tunis, on behalf of the NACI mpox Working Group, and was approved by NACI.

Competing interests

None.

ORCID numbers

Nicole Forbes — 0000-0002-2645-695X
Joshua Montroy — 0000-0002-6611-0056
Marina Salvadori — 0000-0001-5371-6510
Kristin Klein — 0000-0002-4347-5626

Acknowledgements

NACI gratefully acknowledges the contribution of: M Tunis, K Young, A Tuite, A Howarth, L Coward and J Daniel.

NACI mpox Working Group Members: K Klein (Chair), N Brousseau, A Buchan, YG Bui, E Castillo, R Harrison, K Hildebrand, M Libman, D Tan, M Murti, A Rao, C Quach and B Petersen

NACI members: R Harrison (Chair), V Dubey (Vice-Chair), M Andrew, J Bettinger, N Brousseau, A Buchan, H Decaluwe, P De Wals, E Dubé, K Hildebrand, K Klein, M O'Driscoll, J Papenburg, A Pham-Huy, B Sander and S Wilson

Liaison representatives: L Bill/M Nowgesic (Canadian Indigenous Nurses Association), LM Bucci (Canadian Public Health Association), S Buchan (Canadian Association for Immunization Research and Evaluation), E Castillo (Society of Obstetricians and Gynaecologists of Canada), J Comeau (Association of Medical Microbiology and Infectious Disease Canada), M Lavoie (Council of Chief Medical Officers of Health), J MacNeil (Centers for Disease Control and Prevention, United States), D Moore (Canadian Paediatric Society), M Naus (Canadian Immunization Committee), M Osmack (Indigenous Physicians Association of Canada), J Potter (College of Family Physicians of Canada) and A Ung (Canadian Pharmacists Association).

Ex-officio representatives: V Beswick-Escanlar (National Defence and the Canadian Armed Forces), E Henry (Centre for Immunization and Respiratory Infectious Diseases [CIRID], Public Health Agency of Canada [PHAC]), M Lacroix (Public Health Ethics Consultative Group, PHAC), C Lourenco (Biologic and Radiopharmaceutical Drugs Directorate, Health Canada), S Ogunnaike-Cooke (CIRID, PHAC), K Robinson (Marketed Health Products Directorate, Health Canada), G Poliquin (National Microbiology Laboratory, PHAC) and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada).

Funding

The work of NACI is supported by the Public Health Agency of Canada.

References

1. World Health Organization. 2022–23 Mpox (monkeypox) Outbreak: Global Trends. Geneva, CH: WHO; 2024. [Accessed 2024 Mar 19]. https://worldhealthorg.shinyapps.io/mpx_global/

2. Viedma-Martinez M, Dominguez-Tosso FR, Jimenez-Gallo D, Garcia-Palacios J, Riera-Tur L, Montiel-Quezel N, Linares-Barrios M. MPXV transmission at a tattoo parlor. N Engl J Med 2023;388(1):92–4. DOI PubMed

3. Thornhill JP, Palich R, Ghosn J, Walmsley S, Moschese D, Cortes CP, Galliez RM, Garlin AB, Nozza S, Mitja O, Radix AE, Blanco JL, Crabtree-Ramirez B, Thompson M, Wiese L, Schulbin H, Levcovich A, Falcone M, Lucchini A, Sendagorta E, Treutiger CJ, Byrne R, Coyne K, Meyerowitz EA, Grahn AM, Hansen AE, Pourcher V, DellaPiazza M, Lee R, Stoeckle M, Hazra A, Apea V, Rubenstein E, Jones J, Wilkin A, Ganesan A, Henao-Martínez AF, Chow EJ, Titanji BK, Zucker JE, Ogoina D, Orkin CM; Share-Net writing group. Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series. Lancet 2022;400(10367):1953–65. DOI PubMed

4. Ulaeto D, Agafonov A, Burchfield J, Carter L, Happi C, Jakob R, Krpelanova E, Kuppalli K, Lefkowitz EJ, Mauldin MR, de Oliveira T, Onoja B, Otieno J, Rambaut A, Subissi L, Yinka-Ogunleye A, Lewis RF. New nomenclature for mpox (monkeypox) and monkeypox virus clades. Lancet Infect Dis 2023;23(3):273–5. DOI PubMed

5. Kibungu EM, Vakaniaki EH, Kinganda-Lusamaki E, Kalonji-Mukendi T, Pukuta E, Hoff NA, Bogoch II, Cevik M, Gonsalves GS, Hensley LE, Low N, Shaw SY, Schillberg E, Hunter M, Lunyanga L, Linsuke S, Madinga J, Peeters M, Cigolo JM, Ahuka-Mundeke S, Muyembe JJ, Rimoin AW, Kindrachuk J, Mbala-Kingebeni P, Lushima RS; International Mpox Research Consortium. Clade I-associated mpox cases associated with sexual contact, the Democratic Republic of the Congo. Emerg Infect Dis 2024;30(1):172–6. DOI PubMed

6. Public Health Agency of Canada. National Advisory Committee on Immunization. NACI Rapid Response: Interim guidance on the use of Imvamune in the context of monkeypox outbreaks in Canada. Ottawa, ON: PHAC; 2022. [Accessed 2024 Feb 27]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-imvamune-monkeypox.html

7. Public Health Agency of Canada. NACI Rapid Response: Updated interim guidance on use of Imvamune in the context of ongoing monkeypox outbreaks. Ottawa, ON: PHAC; 2022. [Accessed 2024 Mar 1]. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/rapid-response-updated-interim-guidance-imvamune-monkeypox-outbreaks.html

8. Brousseau N, Carazo S, Febriani Y, Padet L, Hegg-Deloye S, Cadieux G, Bergeron G, Fafard J, Charest H, Lambert G, Talbot D, Longtin J, Dumont-Blais A, Bastien S, Dalpé V, Minot PH, De Serres G, Skowronski DM. Single-dose effectiveness of mpox vaccine in Quebec, Canada: test-negative design with and without adjustment for self-reported exposure risk. Clin Infect Dis 2024;78(2):461–9. DOI PubMed

9. Navarro C, Lau C, Buchan SA, Burchell AN, Nasreen S, Friedman L, Okpokoro E, Austin PC, Tan DH, Gubbay JB, Kwong JC, Misra S; Canadian Immunization Research Network (CIRN). Effectiveness of one dose of MVA-BN vaccine against mpox infection in males in Ontario, Canada: A target trial emulation. medRxiv 2023;10.04.23296566. DOI

10. Bertran M, Andrews N, Davison C, Dugbazah B, Boateng J, Lunt R, Hardstaff J, Green M, Blomquist P, Turner C, Mohammed H, Cordery R, Mandal S, Campbell C, Ladhani SN, Ramsay M, Amirthalingam G, Bernal JL. Effectiveness of one dose of MVA-BN smallpox vaccine against mpox in England using the case-coverage method: an observational study. Lancet Infect Dis 2023;23(7):828–35. DOI PubMed

11. Fontán-Vela M, Hernando V, Olmedo C, Coma E, Martínez M, Moreno-Perez D, Lorusso N, Vázquez Torres M, Barbas Del Buey JF, Roig-Sena J, Pastor E, Galmés Truyols A, Artigues Serra F, Sancho Martínez RM, Latasa Zamalloa P, Pérez Martínez O, Vázquez Estepa A, García Rojas AJ, Barreno Estévez AI, Sánchez-Migallón Naranjo A, Pérez Martín JJ, Peces Jiménez P, Morales Romero R, Castilla J, García Cenoz M, Huerta Huerta M, Boone AL, Macías Ortiz MJ, Álvarez Río V, Rodríguez Recio MJ, Merino Díaz M, Berradre Sáenz B, Villegas-Moreno MT, Limia A, Diaz A, Monge S; Spanish MPOX Vaccine Effectiveness Study Group. Effectiveness of modified Vaccinia Ankara-Bavaria Nordic vaccination in a population at high risk of mpox: A Spanish cohort study. Clin Infect Dis 2024;78(2):476–83. DOI PubMed

12. Wolff Sagy Y, Zucker R, Hammerman A, Markovits H, Arieh NG, Abu Ahmad W, Battat E, Ramot N, Carmeli G, Mark-Amir A, Wagner-Kolasko G, Duskin-Bitan H, Yaron S, Peretz A, Arbel R, Lavie G, Netzer D. Real-world effectiveness of a single dose of mpox vaccine in males. Nat Med 2023;29(3):748–52. DOI PubMed

13. Deputy NP, Deckert J, Chard AN, Sandberg N, Moulia DL, Barkley E, Dalton AF, Sweet C, Cohn AC, Little DR, Cohen AL, Sandmann D, Payne DC, Gerhart JL, Feldstein LR. Vaccine effectiveness of JYNNEOS against mpox disease in the United States. N Engl J Med 2023;388(26):2434–43. DOI PubMed

14. Dalton AF, Diallo AO, Chard AN, Moulia DL, Deputy NP, Fothergill A, Kracalik I, Wegner CW, Markus TM, Pathela P, Still WL, Hawkins S, Mangla AT, Ravi N, Licherdell E, Britton A, Lynfield R, Sutton M, Hansen AP, Betancourt GS, Rowlands JV, Chai SJ, Fisher R, Danza P, Farley M, Zipprich J, Prahl G, Wendel KA, Niccolai L, Castilho JL, Payne DC, Cohn AC, Feldstein LR; CDC Multijurisdictional Mpox Case-Control Study Group. Estimated effectiveness of JYNNEOS vaccine in preventing mpox: A multijurisdictional case-control study - United States, August 19, 2022–March 31, 2023. MMWR Morb Mortal Wkly Rep 2023;72(20):553–8. DOI PubMed

15. Rosenberg ES, Dorabawila V, Hart-Malloy R, Anderson BJ, Miranda W, O'Donnell T, Gonzalez CJ, Abrego M, DelBarba C, Tice CJ, McGarry C, Mitchell EC, Boulais M, Backenson B, Kharfen M, McDonald J, Bauer UE. Effectiveness of JYNNEOS vaccine against diagnosed mpox infection - New York, 2022. MMWR Morb Mortal Wkly Rep 2023;72(20):559–63. DOI PubMed

16. Ramchandani MS, Berzkalns A, Cannon CA, Dombrowski JC, Brown E, Chow EJ, Barash E, Pogosjans S, Smith D, Golden MR. Effectiveness of the modified Vaccinia Ankara vaccine against mpox in men who have sex with men: a retrospective cohort analysis, Seattle, Washington. Open Forum Infect Dis 2023;10(11):ofad528. DOI PubMed

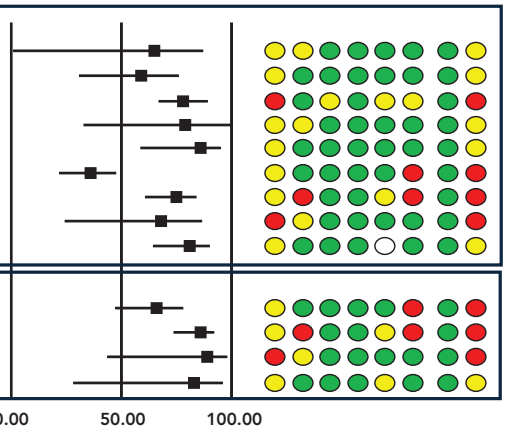
17. Schildhauer S, Saadeh K, Vance J, Quint J, Salih T, Lo T, Keinde A, Chojolan E, Gotlieb E, Ramos M, Chapman E, Peters P, Watson J, Johnson KA, Tang EC, Jacobson K, Snyder RE. Reduced odds of mpox-associated hospitalization among persons who received JYNNEOS vaccine — California, May 2022–May 2023. MMWR Morb Mortal Wkly Rep 2023;72(36):992–6. DOI PubMed

18. Bavarian Nordic A/S. Product Monograph Including Patient Medication Information. Imvamune®: Smallpox and Monkeypox Vaccine Modified Vaccinia Ankara-Bavarian Nordic® (live-attenuated, non-replicating). Copenhagen, DK: Bavarian Nordic; 2023. [Accessed 2024 June 24]. https://pdf.hres.ca/dpd_pm/00071931.PDF

Appendix

Figure A1: Vaccine effectiveness (and 95% confidence interval) against mpox infection[a,b]

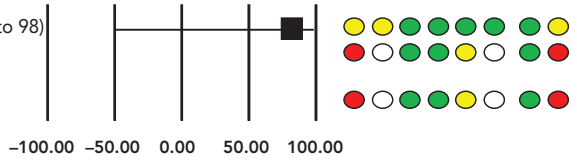
Study name	Study design	n, cases[b]	n, controls[b]	VE and 95% CI	Risk of bias (A B C D E F G H)
1 dose studies					
Brousseau *et al.* (Canada)	Case-control	231	301	65% (1 to 87)	
Navarro *et al.* (Canada)	Cohort study	3,204	3,204	59% (31 to 76)	
Bertran *et al.* (UK)	Case-coverage	362	N/A	78% (54 to 89)	
Fontan-Vela *et al.* (Spain)	Cohort study	5,660	5,660	79% (33 to 100)	
Sagy *et al.* (Israel)	Cohort study	1,037	1,017	86% (59 to 95)	
Deputy *et al.* (USA)	Case-control	2,193	8,319	36% (22 to 48)	
Dalton *et al.* (USA)	Case-control	309	608	75% (61 to 84)	
Rosenberg *et al.* (USA)	Case-control	252	255	68% (25 to 87)	
Ramchandani *et al.* (USA)	Cohort study	685	2,393	81% (64 to 90)	
2 dose studies					
Deputy *et al.* (USA)	Case-control	2,193	8,319	66% (47 to 78)	
Dalton *et al.* (USA)	Case-control	309	608	86% (74 to 92)	
Rosenberg *et al.* (USA)	Case-control	252	255	89% (44 to 98)	
Ramchandani *et al.* (USA)	Cohort study	1,152	2,393	83% (28 to 96)	



Abbreviations: CI, confidence interval; N/A, not applicable; UK, United Kingdom; USA, United States; VE, vaccine effectiveness
[a] Studies are stratified by the number of doses administered to participants. A pooled meta-analysis was not performed due to the significant heterogeneity observed across studies. The forest plot depicts estimated vaccine effectiveness (VE) and 95% confidence intervals (CI) of individual studies. Risk of bias legend: A) bias due to confounding; B) bias In selection of participants into the study; C) bias in classification of interventions; D) bias due to deviation from intended interventions; E) bias due to missing data; F) bias in measurement of outcomes; G) bias due to selection of reported result; H) overall risk of bias. Green represented a low risk of bias, yellow a moderate risk of bias, red a serious risk of bias and white represents no information
[b] Cohort studies are shown as n, vaccinated and n, unvaccinated

Figure A2: Vaccine effectiveness (and 95% confidence interval) against moderate to severe mpox infection[a,b,c,d]

Study name	Study design	No. mod/severe cases (%)	No. vaccinated (%)	VE and 95% CI	Risk of bias (A B C D E F G H)
1 dose studies					
Brousseau *et al.* (Canada)[b]	Case-control	12 (5.2%)	1 (8.3%)	82% (–50 to 98)	
Schildhauer *et al.* (US)[c,d]	Cohort study	250 (5.4%)	4 (1.6%)		
2 dose studies					
Schildhauer *et al.* (US)[c,d]	Cohort study	250 (5.4%)	1 (0.4%)		



Abbreviations: CI, confidence interval; mod, moderate; USA, United States; VE, vaccine effectiveness
[a] The forest plot depicts estimates vaccine effectiveness (VE) and 95% confidence intervals (CI) of individual studies. Risk of bias legend: A) bias due to confounding; B) bias in selection of participants into the study; C) bias in classification of interventions; D) bias due to deviation from intended interventions; E) bias due to missing data; F) bias in measurement of outcomes; G) bias due to selection of reported result; H) overall risk of bias. Green represented a low risk of bias, yellow a moderate risk of bias, red a serious risk of bias and white represents no information
[b] Define by mpox disease-related hospitalization, having had a complication or having received tecovirimat treatment
[c] Define as being hospitalized (inpatient hospitalization) for mpox disease
[d] No VE provided

Table A1: Immunization schedule for Imvamune® in the context of a focused interim routine immunization program

Dose number	Pre-exposure vaccination[a,b]	Post-exposure vaccination[a,b]
Dose 1	0.5mL, administered via subcutaneous injection (SC)	0.5mL, SC, within 4 days since exposure, can be considered up to 14 days
Dose 2	0.5mL, SC, administered ≥28 days after dose 1	0.5mL, SC, administered ≥28 days after dose 1 if MPXV infection did not develop

Abbreviations: MPXV, monkeypox virus; SC, subcutaneous injection
[a] Individuals recommended for Imvamune® pre-exposure vaccination should receive a 2-dose schedule regardless of previous vaccination with a live replicating first or second generation smallpox vaccine, immunocompromised status or age
[b] Pre-exposure or post-exposure vaccination is not indicated for individuals with a history of, or current infection with, MPXV

Is there sufficient evidence to inform personal protective equipment choices for healthcare workers caring for patients with viral hemorrhagic fevers?

Amanda Graham[1], Steven Ettles[1]*, Maureen McGrath[1], Toju Ogunremi[1], Jennifer Selkirk[1], Natalie Bruce[1]

Abstract

Background: Ugandan health authorities declared an outbreak of Ebola disease (EBOD), caused by the Sudan virus, in September 2022. A rapid review was conducted to update the Public Health Agency of Canada's guidelines for infection prevention and control measures for EBOD in healthcare settings to prepare for potential introduction of cases.

Objective: Summarize the available evidence on personal protective equipment (PPE) use by healthcare workers (HCWs) to prevent exposure to and transmission of viral hemorrhagic fevers (VHFs), including Ebola virus.

Methods: Electronic databases were searched to identify peer-reviewed evidence published from July 2014–October 2022. Peer-reviewed primary studies and literature reviews, in English or French, reporting on PPE for VHFs and filoviruses in the healthcare context were eligible for inclusion. Literature review processes were conducted by two reviewers using DistillerSR® systematic review software and the Public Health Agency of Canada's Infection Prevention and Control Critical Appraisal Toolkit. An environmental scan of grey literature was also conducted to inform the rapid review.

Results: The database search yielded 417 citations and 29 studies were considered eligible for critical appraisal. In total, 20 studies were included in the narrative synthesis of evidence. The evidence base was limited regarding comparative effectiveness of types of PPE for preventing exposure to and transmission of VHFs to HCWs. Four studies reported on exposure to and transmission of a VHF. Sixteen studies provided data on other relevant topics, such as simulated contamination and lab-based tests of PPE integrity.

Conclusion: There is limited evidence with which to draw conclusions on the comparative effectiveness of PPE to prevent exposure to and transmission of VHFs to HCWs. Additional research is required to determine the optimal PPE to protect HCWs from exposure to and transmission of VHFs.

Affiliation

[1] Centre for Communicable Disease and Infection Control, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
steven.ettles@phac-aspc.gc.ca

Suggested citation: Graham A, Ettles S, McGrath M, Ogunremi T, Selkirk J, Bruce N. Is there sufficient evidence to inform personal protective equipment choices for healthcare workers caring for patients with viral hemorrhagic fevers? Can Commun Dis Rep 2025;51(1):7–15. https://doi.org/10.14745/ccdr.v51i01a02

Keywords: personal protective equipment, PPE, healthcare worker, transmission, contamination, exposure, viral hemorrhagic fever, filovirus, Ebola

Introduction

Viral hemorrhagic fevers (VHFs) are a group of diseases caused by enveloped, single-stranded RNA viruses belonging to six taxa, namely Filoviruses (i.e., Ebola and Marburg virus), Arenaviruses, Flaviviruses, Hantaviruses, Nairoviruses and Phenuiviruses (1). Ebola disease (EBOD) was first described in 1976 in two simultaneous outbreaks in two different countries, South Sudan and the Democratic Republic of Congo, and comprises six species, four of which are pathogenic to humans (2,3). Prior to 2014, a total of 2,387 cases had been recorded in localized rural African outbreaks, with an overall crude mortality of 67% (1,2). In 2014, an outbreak that occurred in West Africa, which lasted for two years, showed intense urban transmission and resulted in over 28,000 cases, with multiple countries including Italy, Mali, Nigeria, Senegal, Spain, the United Kingdom and the United States reporting imported cases (4,5).

Human-to-human transmission of Ebola virus (EBOV) occurs by direct contact (i.e., through non-intact skin or mucous membranes) with the blood or other body fluids (e.g., stool, emesis, urine, saliva, semen and sweat) of an infected individual and/or by indirect contact with environmental surfaces and fomites contaminated with infected blood or other body fluids (1,2,4). The risk of transmission increases with the amount of infectious material to which the individual is exposed (5). Investigations conducted to date have not identified human-to-human transmission of EBOV in the absence of direct contact with an infected case (3,4).

The use of effective personal protective equipment (PPE) for healthcare workers (HCWs) providing care to patients with suspected or confirmed VHF is essential to prevent HCW infection and nosocomial transmission. Close contact with confirmed or suspected cases without adequate infection prevention and control (IPC) precautions in place can result in HCW infection and mortality. In Sierra Leone, Guinea and Liberia alone, 513 deaths out of a total of 881 infected HCWs have been reported as of 2015 (4). Currently, there is little consensus on the safest PPE ensembles to protect HCWs from exposure to EBOV, with frequent jurisdictional inconsistency in PPE recommendations. Despite the gap in global consensus, Canadian IPC recommendations are developed with a precautionary approach, designed to prioritize the health and safety of HCWs.

In September 2022, the Ugandan health authorities declared another outbreak of EBOD, caused by Sudan EBOV species, which led to 142 confirmed cases, 22 probable cases, 55 confirmed deaths and 87 recovered patients (2,6). No cases were reported in Canada. Given this evolving epidemiological situation, a rapid review of the literature was conducted to inform the update of the Public Health Agency of Canada's (PHAC) guidelines for IPC measures for EBOD in healthcare settings. This review summarizes the available evidence on PPE use by HCWs to prevent exposure to and transmission of VHFs, including EBOV.

Methods

Literature search and eligibility criteria

Electronic search strategies were developed by the authors in consultation with a Health Canada Library librarian. Embase, MEDLINE, Global Health and Scopus databases were searched in October 2022. Studies published in either English or French from July 2014 to October 2022 were considered in this review.

Our research aimed to answer the following question: What literature exists related to PPE use by healthcare staff to prevent transmission of and exposure to viral haemorrhagic fevers? Search terms utilized covered a wide variety of healthcare settings, professions and PPE items. Search terms and population, exposure, intervention, control and outcomes (PICO) criteria for the literature search can be found in **Table 1**.

Study selection and data extraction

Duplicate studies were identified and removed. A screening tool was developed in Excel® for initial screening to verify that parameters for inclusion were met. Additional title and abstract screening to assess study design/format and relevance to use of PPE was conducted by two independent reviewers in DistillerSR®. Due to the breadth of results, the scope of studies eligible for inclusion was narrowed to include only those directly relevant to the use of PPE in relation to the outcomes of interest, based on the informed opinion of the reviewer. News articles, editorials, commentaries, opinion pieces, guidelines, policy statements, cost analyses and articles with legal/ethical foci were excluded. Additionally, research focusing on protocol development, as well as heat exhaustion and comfort during PPE use, were also excluded.

As the review was primarily meant to inform national IPC guidance, studies were restricted to those conducted in G20 countries with the addition of New Zealand at full-text review to ensure applicability to the Canadian context.

A full-text screening tool (DistillerSR) was developed to exclude studies based on the exclusions noted above, and to retrieve relevant details on study design, methodology and qualitative and quantitative results regarding relevant PPE. Full-text screening was conducted by two independent reviewers. Conflicts were resolved via consensus-building discussion between reviewers, with a third reviewer providing input if consensus could not be reached.

Included articles were critically appraised using PHAC's Infection Prevention and Control Guidelines Critical Appraisal Toolkit (7).

Table 1: Population, exposure, intervention, control and outcomes search criteria for systematic review

PICO criteria	Search criteria
Populations	Personnel: Dietician, food services, emergency medical technician (EMT), licensed practical nurse (LPN), medical radiation technologist, medical laboratory technologist (MLT), midwife, nurse practitioner (NP), paramedic, physician, physician assistant, registered nurse (RN), registered nurse assistant (RNA), registered practical nurse (RPN), respiratory therapist (RT), environmental services, cleaning staff, phlebotomist, porters, transportation workers Type of care: Acute care, hospital care, emergency care, critical care, intensive care, ambulatory care, out-patient care, community care, home care, respite care, palliative care, long-term care, complex continuing care, rehabilitation care, pre-hospital care, convalescent care, mental healthcare
Exposures	Viral haemorrhagic fever, filoviruses, Ebola, Lassa, Marburg, Crimean-Congo virus, Ebola virus disease (EVD), Sudan virus disease (SVD)
Interventions	Personal protective equipment (PPE), gowns, gloves, respirators, N95, powered air purifying respirators (PAPR), face protection, masks, visors, eye protection, goggles, glasses, aprons, Tyvek, coverall, boots, boot covers, shoe covers, hood
Comparison	Not relevant at this time
Outcomes	Exposure (event) Transmission (event), spread Contamination, self-contamination

Abbreviations: EMT, emergency medical technician; EVD, Ebola virus disease; LPN, licensed practical nurse; MLT, medical laboratory technologist; NP, nurse practitioner; PAPR, powered air purifying respirators; PICO, population, exposure, intervention, comparison and outcomes; PPE, personal protective equipment; RN, registered nurse; RNA, registered nurse assistant; RPN, registered practical nurse; RT, respiratory therapist; SVD, Sudan virus disease

This suite of tools is used to grade evidence in a systematic manner across several domains, including assessments of the study population and sampling methods, internal and external validity, ethics and control of confounding and bias. A summary result was assigned to the study based on strength of design, overall quality of the study and directness of evidence.

Evidence synthesis

A narrative synthesis of the evidence was created to identify common study foci, areas of consensus and variation and gaps in the evidence base.

Results

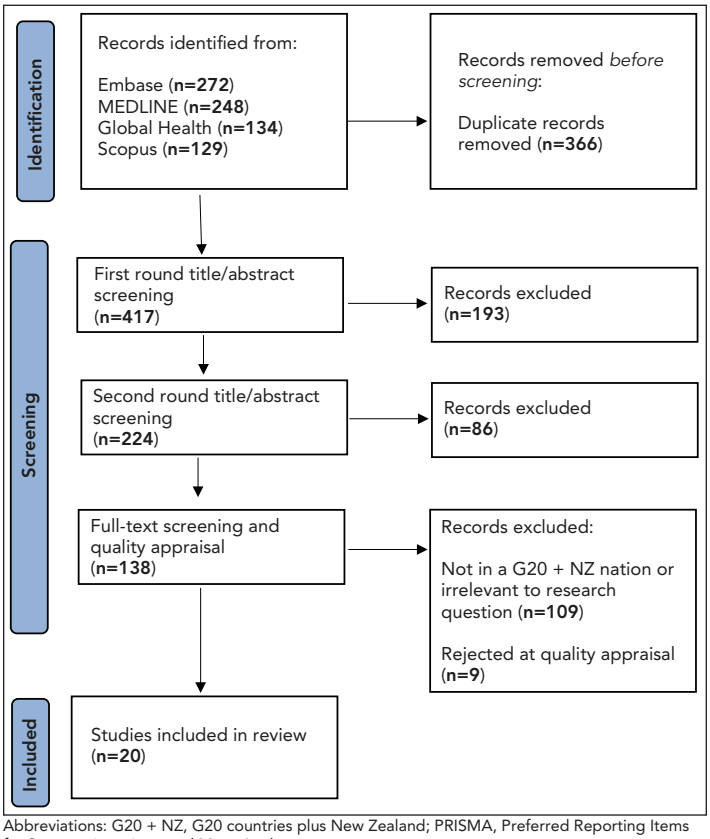
Overview of included studies

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) results can be found in **Figure 1**. Twenty studies were included in the analysis: eight laboratory studies, two randomized controlled trials, three non-randomized controlled trials, one cross-sectional study, four case reports and two literature reviews. A summary of the included evidence can be found as supplemental material in the **Appendix**.

Contamination by fluorescence

Three studies (8–10) assessed contamination using fluorescent surrogate viruses, simulating enveloped and non-enveloped viruses. In each study, participants donned a complete ensemble of PPE commonly used for high-consequence infectious diseases (HCID). In two studies conducted by Casanova *et al.*, researchers primarily sought to measure detectable contamination of PPE and of individuals, indicated by fluorescent markings (8,9). In both studies, there was no detection of the enveloped surrogate virus after doffing PPE, but several instances of contamination by non-enveloped virus, particularly on participants' inner gloves. Detection of contamination, on the inner gloves but not on the hands, suggested that hand hygiene steps in doffing processes were protective against self-contamination with enveloped and non-enveloped viruses.

Figure 1: PRISMA flow-chart of literature review process



Abbreviations: G20 + NZ, G20 countries plus New Zealand; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses

The study by Mumma *et al.* (10), conducted failure modes and effects analysis and fault tree analysis to identify and quantify the risk of errors in a doffing protocol. While participants completed simulated patient care activities and doffed Ebola-level PPE, risks of failure modes were identified and quantified. The extent to which errors contributed to self-contamination were delineated. Three groups of failure modes were found to have higher risk indices, characterized by their frequency and severity. These included hand hygiene-related errors, compromised PPE (especially at hands and wrists) and mishandling of PPE (especially the powered air purifying respirator [PAPR] hood and face shield). A subsequent study conducted by Mumma *et al.* (11) used similar methodology to identify potential errors in a PPE doffing process and their frequency. Corroborating the results of the previous study, hand hygiene and PAPR hood removal were associated with greater risk of error. Removal of the outermost garment and of boot covers also showed above-average risk of error in the PPE doffing process.

Comparing personal protective equipment ensembles

Chughtai *et al.* (12) tested ten established PPE protocols for EBOD. The rate of self-contamination among participants was lower for PPE protocols using gowns compared to protocols using coveralls. Powered air purifying respirators were observed to be more protective compared to N95 respirators, potentially due to lower risk of self-contamination with fewer items of PPE and the incorporation of assisted doffing.

A study by Suen *et al.* (13), which compared the efficacy of three PPE ensembles, reported some differences in contamination across the ensembles. Standard Ebola PPE (PPE1), which included neck-to-ankle coveralls, a water-resistant gown, double nitrile gloves and a hood, was compared to another Ebola PPE set (PPE2), which included front-zip coveralls, a plastic apron and double gloves. Both PPE1 and PPE2 used boots, a face shield and an N95 respirator, and were compared against a reference PPE ensemble used for routine practices and aerosol-generating procedures (PPE3). The study found less frequent contamination of participants' clothing in small patches during removal of PPE1 (median of 5.00 small patches of contamination), compared to PPE2 and PPE3 (median 7.00 patches). Additionally, less contamination overall for Ebola-specific PPE ensembles (PPE1, PPE2) was found compared to the reference PPE (PPE3).

Hall *et al.* (14) compared a basic PPE ensemble (surgical mask, standard length apron, one pair short gloves, own footwear) against established PPE protocols in use across HCID units in the United Kingdom. Across protocols, 1,584 contamination events were recorded after the completion of a simulation exercise, and twelve contamination events post-doffing. Identified breaches were related to protocol failure or complications in the doffing processes. In a follow-up study, Poller *et al.* (15) replicated the testing using a new PPE ensemble for HCIDs developed by an expert working group. While frequency of post-simulation contamination events was comparable to those observed by Hall *et al.*, no residual contamination was observed post-doffing with the new PPE ensemble. Notable features of the ensemble included use of a FFP3 respirator, anti-infection transfer hood, full face visor, rear-fastening reinforced and fluid-resistant surgical gown, wide and extra-long medium thickness plastic apron, three layers of gloves and surgical wellington boots.

A randomized controlled trial (16) utilized a single Ebola PPE ensemble but compared two different training packages to assess fluorescent contamination in each group after undergoing simulated contamination. Both groups received basic IPC and PPE training. The intervention arm received considerably more teamwork-focused training, including strategies, defined roles and responsibilities and a demonstration of the doffing process. Upon examination, self-contamination was observed to be significantly lower in the intervention group compared to controls.

Assessing personal protective equipment integrity

Gao *et al.* (17) tested thirteen brands of nitrile (n=8) and latex (n=5) gloves, examining tensile strength and ultimate elongation without (control) and with one to six applications of alcohol-based hand rub (ABHR). Overall, ethanol based ABHR had little to no effect on elongation of most gloves but resulted in decreased tensile strength for some nitrile gloves after up to six applications. Despite this, all but two relatively thin nitrile gloves continued to meet National Fire Protection Association standards for tension strength and elongation.

Nikiforuk *et al.* (18) measured environmental persistence of EBOV and viral RNA on various PPE materials. Ebola virus remained viable on all materials from 24–72 hours post-inoculation, except for on gloves (less than an hour) and goggles (less than 24 hours). Ebola virus penetration through PPE materials was measured using dry and phosphate-buffered saline-saturated samples of a hood, coveralls and respirator. Saturated samples were found to provide less protection compared to dry material. Similar results were observed when dry and saturated samples of a surgical mask and two respirators were tested. Overall, saturated PPE materials provided less protection compared to dry samples, with penetration of EBOV in seven of 21 saturated samples compared to one of 21 dry samples of the same materials.

Jaques *et al.* (19) conducted Elbow Lean Tests, using various levels of pressure, on isolation gowns and coveralls to measure resistance of the continuous and discontinuous regions of garments to penetration of simulated bodily fluids. Overall, higher pressure led to higher failure rates across all types of garments for both continuous and discontinuous regions. In discontinuous regions, coveralls that had high failure rates in seam regions and zippers were not protective, but heat-sealed

seams performed better. Only one garment model, a gown, demonstrated nearly 100% barrier protection for the whole garment, with one failure out of 42 tests.

Case reports

Four case reports were included, describing IPC measures taken for the care of patients under investigation, or confirmed to have EBOD or other VHFs (20–23). Reporting of specific PPE items and/or ensembles used in patient care was limited and few details were provided on the effectiveness of PPE in preventing exposure and transmission. Despite their limitations, these studies could not be reasonably excluded based on the established inclusion criteria and were therefore included in the analysis.

Literature reviews

Two literature reviews were included in the analysis.

Hersi *et al*. (24) assessed the benefits and harms of Ebola-specific PPE compared to potentially less robust PPE in the context of HCWs caring for patients with filoviruses. Despite comprehensive methodology, insufficient evidence was available to draw conclusions on the effectiveness and potential harms of robust PPE compared to the alternative.

Licina *et al*. (25) evaluated the effect of PAPRs for respiratory protection against highly virulent infectious diseases, including EBOD, compared to other devices such as N95/FFP2 respirators, on HCW infection rates and contamination. Equivalent rates of infection were demonstrated in cohorts using PAPRs compared to other appropriate respiratory protection. The review did identify some low-quality evidence pointing to the advantages of PAPRs, compared to alternative respiratory protection, for wearer protection from cross-contamination and in doffing simulation studies.

Quality appraisals

Twenty-nine studies underwent quality appraisal using PHAC's Critical Appraisal Toolkit (7). Nine studies were rejected for further inclusion at this stage due to a lack of relevance to our research question. Of the 20 included studies, 2 studies were appraised as being of high quality (17,18), 14 as being of medium quality and 4 as being low quality. For all studies, the directness of evidence was determined to be extrapolation, as results were related to a different research question, or were investigated under artificial conditions. Full quality appraisal results can be found in **Table 2**.

Table 2: Quality appraisal results of included studies

Study (reference)	Study design	Strength of design[a]	Directness of evidence	Overall quality of study
Andonian *et al*., 2019 (16)	RCT	Strong	Extrapolation	Medium
Bell *et al*., 2022 (26)	RCT	Strong	Extrapolation	Low
Barratt *et al*., 2015 (20)	Case report	Weak	Extrapolation	Medium
Casanova *et al*., 2018 (8)	Laboratory study	Strong	Extrapolation	Medium
Casanova *et al*., 2016 (9)	NRCT	Strong	Extrapolation	Low
Chughtai *et al*., 2018 (12)	Laboratory study	Strong	Extrapolation	Medium
Cummings *et al*., 2016 (21)	Case report	Weak	Extrapolation	Low
Drew *et al*., 2016 (27)	NRCT	Strong	Extrapolation	Medium
Gao *et al*., 2016 (17)	Laboratory study	Strong	Extrapolation	High
Hall *et al*., 2018 (14)	NRCT	Strong	Extrapolation	Low
Haverkort *et al*., 2016 (22)	Case report	Weak	Extrapolation	Medium
Hersi *et al*., 2015 (24)	Literature review	Not applicable[b]	Extrapolation	Medium
Jaques *et al*., 2016 (19)	Laboratory study	Strong	Extrapolation	Medium
Lehmann *et al*., 2017 (23)	Case report	Weak	Extrapolation	Medium
Licina *et al*., 2020 (25)	Literature review	Not applicable[b]	Extrapolation	Medium
Mumma *et al*., 2019 (11)	Cross-sectional study	Weak	Extrapolation	Medium
Mumma *et al*., 2018 (10)	Laboratory study	Strong	Extrapolation	Medium
Nikiforuk *et al*., 2017 (18)	Laboratory study	Strong	Extrapolation	High
Poller *et al*., 2018 (15)	Laboratory study	Strong	Extrapolation	Medium
Suen *et al*., 2018 (13)	Laboratory study	Strong	Extrapolation	Medium

Abbreviations: NRCT, non-randomized controlled trial; RCT, randomized controlled trial

[a] Strength of study design is determined based on rankings assigned in the Public Health Agency of Canada's Critical Appraisal Toolkit

[b] Literature reviews without meta-analyses are not assessed on study design. Quality of review methods used is captured under "overall quality of study"

Discussion

The review identified 20 relevant studies addressing PPE use in the context of VHFs, such as EBOD, in high-income country contexts. A quality appraisal of evidence was completed with most studies (19) ranking low-to-medium quality; unfortunately, the lower quality of many studies limited our ability to extrapolate to real world scenarios. We concluded that there was insufficient evidence to draw conclusions on the comparative effectiveness of PPE to prevent exposure to and transmission of VHFs, including EBOV, to HCWs. Given this gap in evidence on PPE effectiveness, the determination of PPE ensembles for EBOD should consider a precautionary approach.

Nine studies with varying methodologies involved detecting contamination by fluorescent markers. Two studies showed that use of HCID PPE resulted in no self-contamination, suggesting the ensembles were effective. Further, studies comparing EBOD/HCID-specific PPE ensembles against basic or routine practice PPE consistently showed that more robust PPE ensembles are significantly more protective against contamination (13–15). However, comparing efficacy of enhanced PPE combinations proves difficult due to heterogeneity of the ensembles compared between studies, methods used to simulate and record contamination, differences in reporting of contamination and variations in training and experience among participants. Due to the varied scope and methodology of the independent studies that met the inclusion criteria, a meta-analysis that would quantitatively summarize overall findings of the results was not possible. As such, it is difficult to draw conclusions on the protective effects of individual items or combinations of PPE. Most ensembles varied significantly with respect to body protection, gloving, head coverage and footwear. Other aspects of protocols (when reported) also varied, including hand hygiene and doffing assistance.

Three medium-to high-quality (17–19) laboratory studies using differing methodologies assessed the integrity of PPE items, examining degradation of PPE materials and penetration of EBOV, surrogate virus or simulated bodily fluids through samples. Personal protective equipment tested included gloves (17,18), gowns and coveralls (18,19) and surgical masks and respirators (18). These studies found that the PPE studied was generally resistant to ABHR degradation and that moisture-saturated PPE materials tended to provide less protection than dry materials, indicating the importance of avoiding body fluid contamination and excessive sweating while donned. Further work should be done to elucidate the comparative performance of other models of PPE to determine which provide the greatest protection in the event of moisture saturation and activity-induced pressure.

Despite a well-designed and comprehensive review methodology, Hersi *et al.* (24) were not able to reach a conclusion on the effectiveness of various forms of PPE for HCWs providing care to patients with VHFs, owing to similar issues with the body of evidence, such as low study quality and heterogeneity among PPE components and reporting. This result aligns with our findings.

When examining the role of PAPRs (25), investigators were unable to find differences in protection compared to other forms of respiratory protection. This result is inconsistent with the work by Chughtai *et al.* (12), which showed that PAPRs were observed to be more protective compared to N95 respirators. Though there were a number of limitations in the work by Chughtai *et al.*, further work is needed to determine the true safety of PAPR use, and its role in self-contamination, when caring for patients with VHFs.

Another issue that was noted was PPE reporting across studies was often inconsistent, with a number of studies citing PPE ensembles only as "high consequence" or "Ebola-specific" PPE, making it difficult to determine individual components and their comparability to PPE used in other studies. Additionally, steps for donning and doffing often were not reported, posing another barrier to compare results.

Strengths and limitations

One strength of this review was that it utilized a standardized screening and data extraction form within a reference management software, which helped to reduce bias and ensure data integrity via consistent collection and reporting. Results were also critically appraised to assess domains of bias, with some studies being excluded when methodology was deemed to be too poor. Another strength of this review was that search criteria excluded countries outside of the G20 and New Zealand, to ensure compatibility of findings with Canadian healthcare settings when drafting IPC practice recommendations. Further, the addition of multiple focus criteria during the screening process facilitated selection of studies that were more comparable and more relevant to the research question, thereby enhancing our analysis.

One weakness of this study is the limited number of studies included and the overall heterogeneity among the methodology and outcomes. Most studies were also limited by small sample sizes (fewer than 20 participants). Given these issues and the inability to conduct further statistical analysis, it was difficult to draw firm conclusions from the available data, impacting our ability to reach evidence-based conclusions.

Conclusion and future directions

To our knowledge, this is the first literature review conducted in Canada to address the research question: What literature exists related to PPE use by healthcare staff to prevent transmission of and exposure to viral haemorrhagic fevers in high-income contexts? This summary provides important insight into the state of knowledge of this topic as well as identifying areas needing further exploration.

Overall, there was limited evidence to draw conclusions on the comparative effectiveness of PPE to prevent exposure to and transmission of VHFs to HCWs. The current body of evidence would benefit from a more robust comparison of different PPE components and models, using standardized methods for data collection and reporting to ensure comparability amongst studies. There is a notable gap in strong study designs (such as randomized controlled trials and studies that involve large numbers of participants), which would produce more robust results and allow for statistical analysis and modelling. If feasible, conducting more studies during outbreaks of VHFs, or during actual care of EBOD patients, would provide greater insight into outcomes encountered in the real world compared to simulation studies.

Authors' statement

AG — Conceptualization, data curation, formal analysis, methodology, writing–original draft, writing–review & editing
SE — Conceptualization, data curation, formal analysis, methodology, writing–original draft, writing–review & editing
MM — Conceptualization, data curation, formal analysis, methodology, writing–original draft, writing–review & editing
TO — Conceptualization, writing–review & editing
JS — Conceptualization, data curation, formal analysis, methodology, writing–original draft, writing–review & editing
NB — Conceptualization, writing–review & editing

Competing interests

None of the authors have any conflicts of interest to declare.

ORCID numbers

None.

Acknowledgements

The authors would like to thank the librarians at the Health Canada and Public Health Agency of Canada Health Library for their contribution to the initial search results for this review.

Funding

The work for this review was supported by the Public Health Agency of Canada in pursuit of their mandate.

References

1. Clément C, Adhikari NK, Lamontagne F. Evidence-Based Clinical Management of Ebola Virus Disease and Epidemic Viral Hemorrhagic Fevers. Infect Dis Clin North Am 2019;33(1):247–64. DOI PubMed

2. World Health Organization. Ebola Virus Disease. Geneva, CH: WHO; 2023. [Accessed 2023 Feb 20]. https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease#

3. Sivanandy P, Jun PH, Man LW, Wei NS, Mun NF, Yii CA, Ying CC. A systematic review of Ebola virus disease outbreaks and an analysis of the efficacy and safety of newer drugs approved for the treatment of Ebola virus disease by the US Food and Drug Administration from 2016 to 2020. J Infect Public Health 2022;15(3):285–92. DOI PubMed

4. World Health Organization. WHO: Ebola situation report 2 September 2015. Geneva, CH: WHO; 2015. [Accessed 2023 Feb 23]. https://apps.who.int/iris/handle/10665/183955

5. UK Health Security Agency. Ebola: overview, history, origins and transmission. London, UK: UK HAS; 2023. [Accessed 2023 Feb 21]. https://www.gov.uk/government/publications/ebola-origins-reservoirs-transmission-and-guidelines/ebola-overview-history-origins-and-transmission

6. World Health Organization. Ebola—Uganda, 2022. Geneva, CH: WHO; 2023. [Accessed 2023 Oct 19]. https://www.who.int/emergencies/situations/ebola-uganda-2022

7. Public Health Agency of Canada. Infection prevention and control guidelines: critical appraisal tool kit. Ottawa, ON: PHAC; 2016. [Accessed 2023 Mar 15]. https://publications.gc.ca/site/eng/470818/publication.html

8. Casanova LM, Erukunuakpor K, Kraft CS, Mumma JM, Durso FT, Ferguson AN, Gipson CL, Walsh VL, Zimring C, DuBose J, Jacob JT; Centers for Disease Control and Prevention Epicenters Program, Division of Healthcare Quality Promotion. Assessing Viral Transfer During Doffing of Ebola-Level Personal Protective Equipment in a Biocontainment Unit. Clin Infect Dis 2018;66(6):945–9. DOI PubMed

9. Casanova LM, Teal LJ, Sickbert-Bennett EE, Anderson DJ, Sexton DJ, Rutala WA, Weber DJ; CDC Prevention Epicenters Program. Assessment of self-contamination during removal of personal protective equipment for Ebola patient care. Infect Control Hosp Epidemiol 2016;37(10):1156–61. DOI PubMed

10. Mumma JM, Durso FT, Ferguson AN, Gipson CL, Casanova L, Erukunuakpor K, Kraft CS, Walsh VL, Zimring C, DuBose J, Jacob JT; Centers for Disease Control and Prevention Epicenters Program, Division of Healthcare Quality Promotion. Human Factors Risk Analyses of a Doffing Protocol for Ebola-Level Personal Protective Equipment: Mapping Errors to Contamination. Clin Infect Dis 2018;66(6):950–8. DOI PubMed

11. Mumma JM, Durso FT, Casanova LM, Erukunuakpor K, Kraft CS, Ray SM, Shane AL, Walsh VL, Shah PY, Zimring C, DuBose J, Jacob JT. Common Behaviors and Faults When Doffing Personal Protective Equipment for Patients With Serious Communicable Diseases. Clin Infect Dis 2019;69 Suppl 3:S214–20. DOI PubMed

12. Chughtai AA, Chen X, Macintyre CR. Risk of self-contamination during doffing of personal protective equipment. Am J Infect Control 2018;46(12):1329–34. DOI PubMed

13. Suen LK, Guo YP, Tong DW, Leung PH, Lung D, Ng MS, Lai TK, Lo KY, Au-Yeung CH, Yu W. Self-contamination during doffing of personal protective equipment by healthcare workers to prevent Ebola transmission. Antimicrob Resist Infect Control 2018;7:157. DOI PubMed

14. Hall S, Poller B, Bailey C, Gregory S, Clark R, Roberts P, Tunbridge A, Poran V, Evans C, Crook B. Use of ultraviolet-fluorescence-based simulation in evaluation of personal protective equipment worn for first assessment and care of a patient with suspected high-consequence infectious disease. J Hosp Infect 2018;99(2):218–28. DOI PubMed

15. Poller B, Tunbridge A, Hall S, Beadsworth M, Jacobs M, Peters E, Schmid ML, Sykes A, Poran V, Gent N, Evans C, Crook B; High Consequence Infectious Diseases Project Working Group. A unified personal protective equipment ensemble for clinical response to possible high consequence infectious diseases: A consensus document on behalf of the HCID programme. J Infect 2018;77(6):496–502. DOI PubMed

16. Andonian J, Kazi S, Therkorn J, Benishek L, Billman C, Schiffhauer M, Nowakowski E, Osei P, Gurses AP, Hsu YJ, Drewry D, Forsyth ER, Vignesh A, Oresanwo I, Garibaldi BT, Rainwater-Lovett K, Trexler P, Maragakis LL. Effect of an Intervention Package and Teamwork Training to Prevent Healthcare Personnel Self-contamination During Personal Protective Equipment Doffing. Clin Infect Dis 2019;69 Suppl 3:S248–55. DOI PubMed

17. Gao P, Horvatin M, Niezgoda G, Weible R, Shaffer R. Effect of multiple alcohol-based hand rub applications on the tensile properties of thirteen brands of medical exam nitrile and latex gloves. J Occup Environ Hyg 2016;13(12):905–14. DOI PubMed

18. Nikiforuk AM, Cutts TA, Theriault SS, Cook BW. Challenge of Liquid Stressed Protective Materials and Environmental Persistence of Ebola Virus. Sci Rep 2017;7(1):4388. DOI PubMed

19. Jaques PA, Gao P, Kilinc-Balci S, Portnoff L, Weible R, Horvatin M, Strauch A, Shaffer R. Evaluation of gowns and coveralls used by medical personnel working with Ebola patients against simulated bodily fluids using an Elbow Lean Test. J Occup Environ Hyg 2016;13(11):881–93. DOI PubMed

20. Barratt R. Infection prevention and control lessons learned from the management of the first suspected Ebola virus disease case admitted to a New Zealand hospital. Healthc Infect 2015;20:78–80. DOI

21. Cummings KJ, Choi MJ, Esswein EJ, de Perio MA, Harney JM, Chung WM, Lakey DL, Liddell AM, Rollin PE. Addressing Infection Prevention and Control in the First U.S. Community Hospital to Care for Patients With Ebola Virus Disease: Context for National Recommendations and Future Strategies. Ann Intern Med 2016;165(1):41–9. DOI PubMed

22. Haverkort JJ, Minderhoud AL, Wind JD, Leenen LP, Hoepelman AI, Ellerbroek PM. Hospital Preparations for Viral Hemorrhagic Fever Patients and Experience Gained from Admission of an Ebola Patient. Emerg Infect Dis 2016;22(2):184–91. DOI PubMed

23. Lehmann C, Kochanek M, Abdulla D, Becker S, Böll B, Bunte A, Cadar D, Dormann A, Eickmann M, Emmerich P, Feldt T, Frank C, Fries J, Gabriel M, Goetsch U, Gottschalk R, Günther S, Hallek M, Häussinger D, Herzog C, Jensen B, Kolibay F, Krakau M, Langebartels G, Rieger T, Schaade L, Schmidt-Chanasit J, Schömig E, Schüttfort G, Shimabukuro-Vornhagen A, von Bergwelt-Baildon M, Wieland U, Wiesmüller G, Wolf T, Fätkenheuer G. Control measures following a case of imported Lassa fever from Togo, North Rhine Westphalia, Germany, 2016. Euro Surveill 2017;22(39):17–00088. DOI PubMed

24. Hersi M, Stevens A, Quach P, Hamel C, Thavorn K, Garritty C, Skidmore B, Vallenas C, Norris SL, Egger M, Eremin S, Ferri M, Shindo N, Moher D. Effectiveness of personal protective equipment for healthcare workers caring for patients with filovirus disease: A rapid review. PLoS One 2015;10(10):e0140290. DOI PubMed

25. Licina A, Silvers A, Stuart RL. Use of powered air-purifying respirator (PAPR) by healthcare workers for preventing highly infectious viral diseases-a systematic review of evidence. Syst Rev 2020;9(1):173. DOI PubMed

26. Bell T, Smoot J, Patterson J, Smalligan R, Jordan R. Ebola virus disease: the use of fluorescents as markers of contamination for personal protective equipment. IDCases 2015;2(1):27–30. DOI PubMed

27. Drew JL, Turner J, Mugele J, Hasty G, Duncan T, Zaiser R, Cooper D. Beating the spread developing a simulation analog for contagious body fluids. Simul Healthc 2016;11(2):100–5. DOI PubMed

Appendix

Supplemental material is available upon request to the author: steven.ettles@phac-aspc.gc.ca

Surveillance of laboratory exposures to human pathogens and toxins, Canada, 2023

Abdulwadud Nafees[1], Audrey Gauthier[1], Antoinette N Davis[1]*, Emily F Tran[1], Christine Abalos[1], Christa M Girincuti[1], Samuel Bonti-Ankomah[1]

Abstract

Background: The Public Health Agency of Canada oversees the *Human Pathogens and Toxins Act* and *Human Pathogens and Toxins Regulations*, and monitors human pathogen and toxin incidents in licensed facilities to minimize exposure impact at the individual and population level.

Objective: To provide an overview of confirmed laboratory exposure incidents in Canada in 2023.

Methods: Confirmed exposure incident reports in 2023 were analyzed using R 4.2.2, Microsoft Excel and SAS.

Results: In 2023, 207 incident reports were received, including 63 confirmed exposure incidents that affected 85 individuals. The academic sector accounted for 50.8% (n=32) of the reported confirmed exposure incidents. Microbiology (n=33; 52.4%) was the predominant activity being performed, with the most common occurrence types being sharps-related (n=22; 27.2%) and procedure-related (n=16; 19.8%). Human interaction (n=36; 57.1%) and standard operating procedures (n=24; 38.1%) were the most frequent root causes cited, with corrective actions often directly addressing these causes. Most of the 85 affected individuals were technicians/technologists (n=55; 64.7%) and had a median of 11 years of laboratory experience. Sixty-seven human pathogens and toxins (HPTs) were implicated in the confirmed exposure incidents, with bacteria (n=36; 53.7%) being the most common biological agent type. The median time between the incident and the reporting date was six days.

Conclusion: The number of confirmed exposure incidents increased in 2023 compared to 2022. Microbiology was most often the activity being performed at the time of exposure, and occurrence-types, root causes and HPTs implicated in 2023 mirrored those cited in 2022.

Affiliation

[1] Regulatory, Operations and Emergency Management Branch, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
antoinette.davis@phac-aspc.gc.ca

Suggested citation: Nafees A, Gauthier A, Davis AN, Tran EF, Abalos C, Girincuti CM, Bonti-Ankomah S. Surveillance of laboratory exposures to human pathogens and toxins, Canada, 2023. Can Commun Dis Rep 2025;51(1):16–25. https://doi.org/10.14745/ccdr.v51i01a03

Keywords: Centre for Biosecurity, human pathogens and toxins, laboratory-acquired infections, laboratory exposures, laboratory incidents, Laboratory Incident Notification Canada, surveillance

Introduction

In the field of biosafety, the management of human pathogens and toxins (HPTs) is a matter of importance due to the potential for laboratory-acquired infections (LAIs) (1–6). Recognizing this risk, a rigorous approach to biosafety in facilities where controlled activities are conducted is necessary, including regulated safety practices and incident surveillance.

The backbone of Canada's regulatory framework in laboratory safety is the *Human Pathogens and Toxins Act* (HPTA) (7) and the *Human Pathogens and Toxins Regulations* (HPTR) (8), which are administered and enforced by the Public Health Agency of Canada's (PHAC's) Centre for Biosecurity. Since the enactment of the HPTA in 2009 and the HPTR in 2015, the HPTA/HPTR have set the standards for working with HPTs in various sectors such as hospitals, academic institutions and public or private institutions in Canada. There are four risk groups that classify HPTs based on their potential to harm individual and community health. For instance, risk group 1 (RG1) HPTs, like non-pathogenic

Escherichia coli, are not expected to cause disease in humans, while risk group 4 (RG4) HPTs, such as the Ebola virus, are known for their potential to cause life-threatening diseases that spread rapidly through the community (9). Also included amongst these regulated HPTs are a class of risk group 3 (RG3) and RG4 HPTs known as security sensitive biological agents (SSBAs) that are specified due to their potential for use as biological weapons and for bioterrorism (9).

The Centre for Biosecurity established the Laboratory Incident Notification Canada (LINC) surveillance system in late 2015 to oversee HPT incident reporting, identification, monitoring and analysis and ensure appropriate follow-up and support to licensed facilities with the goal of reducing the risk of recurrence (10) and minimizing the impact of exposures on the health and wellbeing of facility personnel and the general population. Compared to incident surveillance systems in other developed countries, LINC remains the most comprehensive in terms of its scope. For instance, both the Federal Select Agent Program (11) in the United States and the Security Sensitive Biological Agents Standards (12) in Australia were established to provide regulatory oversight for only SSBAs, with the former producing an annual report on its inspections, compliance actions, transfer of biological select agents and toxins as well as the theft, loss or release of biological select agents and toxins in order to improve understanding of their mandate (13). Operating under the HPTA and HPTR, LINC's scope includes a much broader range of HPTs and is not limited to SSBAs (14).

Under the HPTA, any facility working with risk group 2 (RG2) pathogens and above must obtain a pathogen and toxin licence to conduct controlled activities with HPTs (7,15). The licence requires facilities to adhere to the outlined safety protocols and reporting standards. Licensed facilities are mandated to report various types of incidents to LINC without delay, including exposure incidents, which involve potential or actual contact with pathogens, and non-exposure incidents, such as a missing, lost or stolen biological agent, the inadvertent possession, production or release of an HPT and SSBAs not received at the facility within their expected arrival time. Other incidents that must be reported without delay include changes to biocontainment and other biosafety-related occurrences that may not directly involve pathogen exposure but have significant implications for laboratory safety. The reporting of incidents involving agents in their natural environment is voluntary. Pathogens in their natural environment refer to those present in uncultured or unprocessed samples collected directly from humans or animals. Such biological materials may include blood, serum, saliva, milk or urine.

The year 2023 marked the eighth year of the LINC surveillance system. The program's duration has allowed for the meaningful analysis of incident data from more than 361 confirmed exposure reports (16), which provided insight into laboratory safety measures, highlighted areas of progress and ongoing challenges (10,14,17–21) and illuminated exposure incident trends such as the most common biological agent types (bacteria and virus) and leading root causes (standard operating procedures [SOPs] and human interaction).

This report summarizes exposure incidents in Canada that were reported to LINC in 2023 with the goal of enhancing awareness of the risks associated with handling HPTs, informing biosafety measures in facilities and comparing the incident data to those from previous years.

Methods

Data sources

Laboratory Incident Notification Canada is the Government of Canada's primary mechanism for collecting and monitoring incidents involving HPTs in licensed facilities across Canada under the HPTA and the HPTR. This system, which is accessible through an online Biosecurity Portal, facilitates the reporting of exposure, non-exposure and other types of incidents by licensed facilities. Once reported, these incidents are viewed and processed by LINC in the Integrated Suite of Tools for Operational Processes (iSTOP) of the Microsoft Customer Relationship Management system.

When a licensed facility reports an exposure incident, they are required to submit one or more follow-up reports in addition to their initial exposure report in order to provide further details and the most updated information regarding the incident.

Incidents reported between January 1, 2023, and December 31, 2023, were extracted from iSTOP on February 6, 2024, and analyzed. The analysis included incidents without a specified occurrence date, provided they were reported within this timeframe. Utilizing only the most recent follow-up reports ensured that the analysis was based on the latest and most accurate information pertaining to each incident. In cases where follow-up reports were not yet submitted to LINC, initial exposure report data were used. The extraction process involved examination for outliers and the removal of any duplicate entries to maintain the integrity of the data. The total number of active licences was extracted from the Customer Relationship Management on February 18, 2024, and additional filters were applied in iSTOP to obtain the number of active licences per sector. Some licences did not have a specified sector.

Report variables

The following variables were used to describe the confirmed exposure reports: the main activity being performed at the time of the exposure incident; sector affected; individuals, pathogens and toxins involved; root causes and corrective actions; occurrence types; and time delay in reporting. The definitions for the main activities are provided in **Appendix Table A1**. Sector variables include nine categories: academic; hospital; public health; veterinary/animal health; private industry/business; other government; environmental health; not specified;

and "do-it-yourself biology," where "do-it-yourself biology" refers to any individual not working in an institutionalized facility who is conducting their own experiments. Information about affected individuals, such as their role, years of experience and highest level of education, was also collected. Data on other characteristics, such as their age, gender and socioeconomic status, were not collected.

Data analysis

This report focuses on the confirmed exposure incidents reported to LINC in 2023. The classification of incidents into confirmed or ruled-out categories was based on a review of follow-up reports. Data were run in R 4.2.2 software for data wrangling, cleaning and generating descriptive statistics. Microsoft Excel and SAS 9.4 were used for data validation and to generate figures and tables. This dual approach allowed for cross-validation and ensured the quality of data for analysis. This year's analysis also re-examined data from 2016–2022 to account for any updates to previously submitted reports.

The exposure incident rate per 1,000 active licences was calculated by comparing the total number of reported exposure incidents against the total number of active licences during the surveillance period, multiplied by 1,000, to provide a standardized measure to assess trends over time and across different regulatory sectors.

Baseline establishment

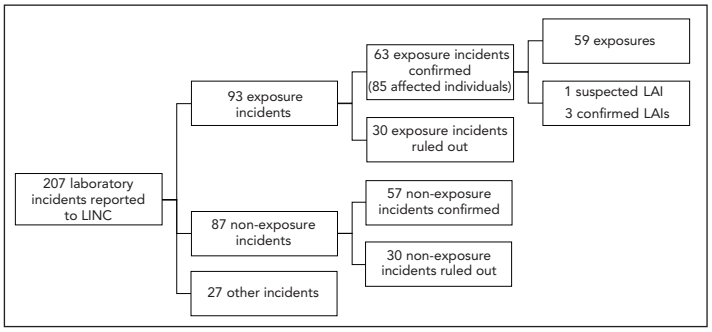
An annual and monthly average of exposure incidents from 2016–2022 was calculated along with 95% confidence intervals using Microsoft Excel. To establish an annual baseline incidence, data from 2016–2022 were pooled and the total number of confirmed exposure incidents from 2016–2022 was summed and divided by the total number of active licences from 2016–2022 and multiplied by 1,000 to obtain the annual baseline incidence of exposures per 1,000 active licences.

Results

Figure 1 depicts the 207 laboratory incident reports submitted to LINC from January 1, 2023, to December 31, 2023. Out of these, 93 (44.9%) were exposure reports, 87 (42.0%) were non-exposure reports and 27 (13.0%) were other reports. Thirty exposure reports and 30 non-exposure reports were ruled out, leaving 63 confirmed exposure incidents with 85 affected individuals in 2023. Amongst the confirmed exposure incidents, there was one suspected LAI and three confirmed LAIs.

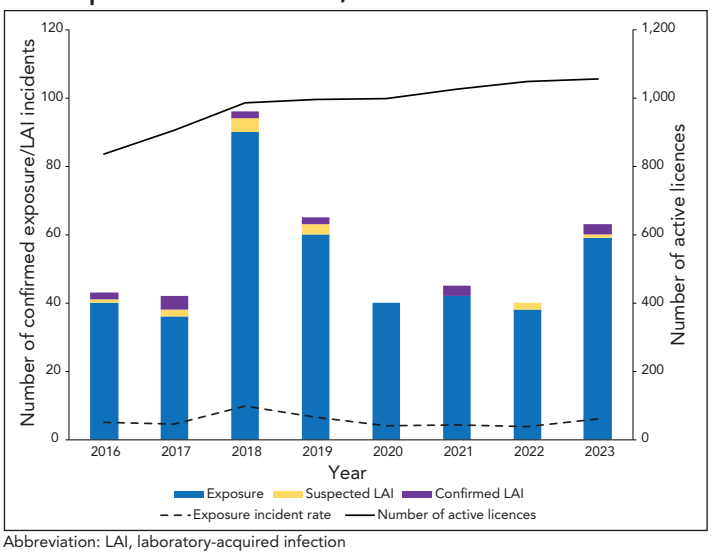
There was a total of 1,057 active licences (**Figure 2**) in 2023, including 981 licences for RG2 HPTs, 70 licences for RG3 pathogens, two licences for RG4 pathogens and four licences for SSBAs. The number of confirmed exposure incidents per 1,000 active licences (the exposure incident rate) was 60. From 2016–2022, there was an average of 53.0 (95% CI: 38.7–7.3) exposure incidents per year and a yearly baseline incidence of 54.6 exposure incidents per 1,000 active licences.

Figure 1: Incidents reported to Laboratory Incident Notification Canada, 2023



Abbreviations: LAI, laboratory-acquired infection; LINC, Laboratory Incidence Notification Canada

Figure 2: Confirmed exposure incidents, suspected and confirmed laboratory-acquired infections, active licences and exposure incident rate, 2016–2023



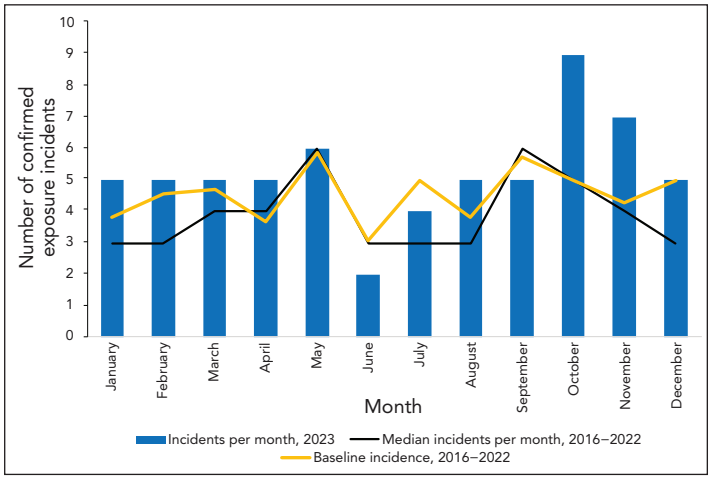
Abbreviation: LAI, laboratory-acquired infection

From 2016–2022, there was an average of 4.4 (95% CI: 3.8–5.0) exposure incidents per month. The number of confirmed exposure incidents remained relatively stable in 2023, with five confirmed exposure reports each month for seven of the 12 months (**Figure 3**). The lowest number of exposure reports occurred in June (n=2; 3.2%) and the highest occurred in October (n=9; 14.3%). In comparison, the baseline incidence per month per 1,000 active licences and the median from 2016–2022 peaked in May and September.

Exposure incidents by main activity and sector

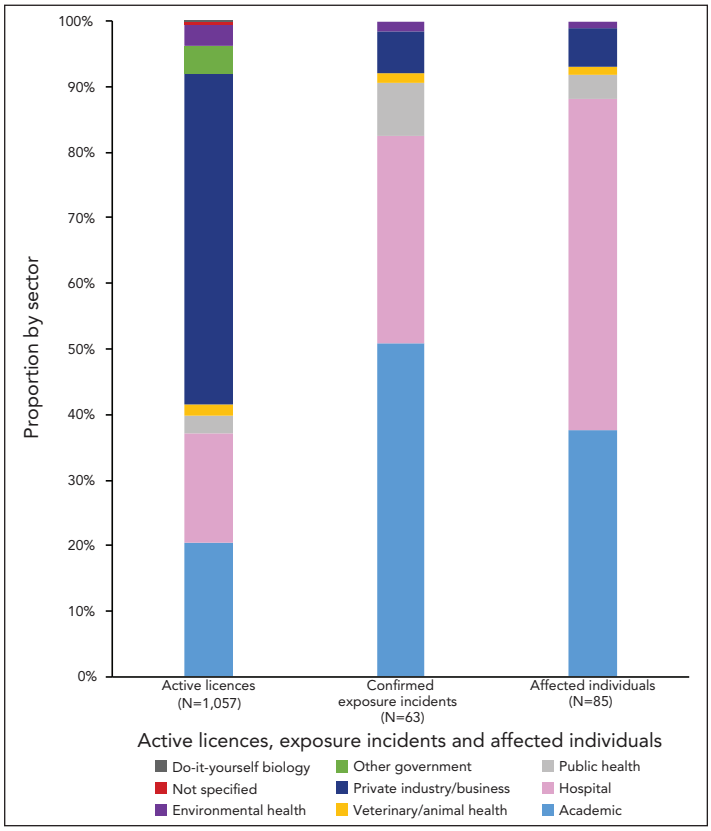
Microbiology and *in vivo* animal research were the most common main activities being performed at the time of the confirmed exposure incident (n=33; 52.4% and n=13; 20.6%, respectively) (data not shown). Other activities (n=6; 9.5%), cell culture (n=5; 7.9%), maintenance (n=3; 4.8%), microscopy (n=2; 3.2%) and education or training (n=1; 1.6%) were also mentioned as main activities being performed at the time of exposure.

Figure 3: Seasonality analysis using median confirmed exposure incidents per month and baseline incidence, 2016–2023



The largest number of confirmed exposure incidents were reported by the academic (n=32; 50.8%) and hospital (n=20; 31.7%) sectors, as shown on **Figure 4**. Only four confirmed exposures were reported from the private sector (6.3%). The active licences are distributed among multiple sectors, including academic, hospital, private and public health. Most licences in 2023 were held by private facilities (n=533; 50.7%), academic facilities (n=216; 20.5%) and hospitals (n=177; 16.8%).

Figure 4: Active licences, confirmed exposure incidents and affected individuals by sector, 2023

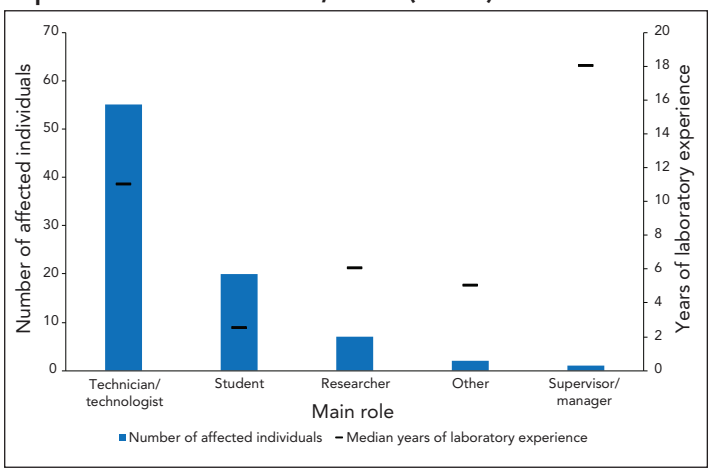


Affected individuals

An average of 1.57 persons were affected per confirmed exposure incident in 2023, with 85 individuals affected in total. Of these 85 individuals, 43 were affected through confirmed exposure incidents in hospital sector (50.6%), while 32 were affected through confirmed exposure incidents in the academic sector (37.6%), as shown in Figure 4. The veterinary/animal health and environmental health sectors each had one confirmed exposure (1.6%) with one affected individual (1.2%) in each.

The largest number of individuals affected in a single confirmed exposure incident (inhalation of *Brucella melitensis* caused by an inadvertent possession of the pathogen) was 11 in a hospital laboratory. The majority of individuals affected in confirmed exposure incidents in 2023 were technicians/technologists (n=55; 64.7%) with a median number of 11 years of experience working in a laboratory setting (**Figure 5**). Among the affected individuals, 20 were students (23.5%) with a median of 2.5 years of experience and seven were researchers (8.2%) with a median of six years of experience. In 2023, only one supervisor/manager was involved in a confirmed exposure incident (1.2%). That individual had 18 years of laboratory experience.

Figure 5: Affected individuals in confirmed exposure incidents reported by number of years of laboratory experience and main role, 2023 (N=85)



Implicated human pathogens and toxins

Sixty-seven HPTs were implicated in confirmed exposure incidents in 2023 (**Table 1**). Exposures were predominantly with non-SSBAs (n=57; 85.1%). Among the RG2 HPTs (n=48; 71.6%), the most common agent types were bacteria (n=30; 44.8%) and viruses (n=14; 20.9%). Other HPT agent types, such as fungus, parasite, prion and cell line, were each implicated in one exposure incident. For exposure incidents involving RG3 HPTs (n=15; 22.4%), the most common agent types were bacteria (n=6; 9.0%), fungus (n=5; 7.5%) and virus (n=3; 4.5%). The RG2 HPTs most frequently implicated in exposure incidents were *Neisseria meningitidis* (n=8; 16.7%) and *Staphylococcus aureus* (n=7; 14.6%), while among the RG3 agents, *B. melitensis* (n=3; 20%) as well as *Histoplasma capsulatum*

and *Mycobacterium tuberculosis* (n=2; 13.3% each) were most common. Only one exposure incident implicating SARS-CoV-2 was reported in 2023. Enterohemorrhagic *E. coli* and *Salmonella enterica* were implicated in two of the three confirmed LAIs, while the HPT implicated in the third confirmed LAI was unknown. Shiga toxin-producing *E. coli* (STEC) was implicated in the suspected LAI. There were no exposures to RG4 pathogens in 2023.

Table 1: Human pathogens and toxins implicated in reported exposure incidents by risk group level and biological agent security sensitive status, 2023 (N=67)

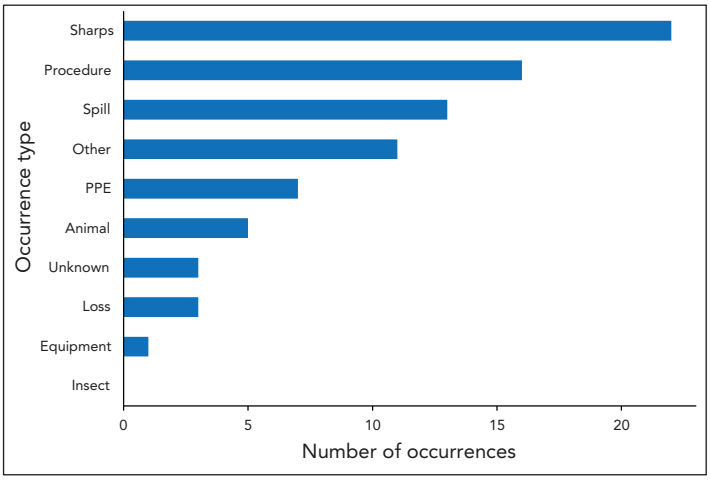
Biological agent type by risk group	Non-SSBA		SSBA		Unknown		Total	
	n	%	n	%	n	%	n	%
RG2	**48**	**71.6**	**0**	**0**	**0**	**0**	**48**	**71.6**
Bacteria	30	44.8	0	0	0	0	30	44.8
Fungus	1	1.5	0	0	0	0	1	1.5
Parasite	1	1.5	0	0	0	0	1	1.5
Prion	1	1.5	0	0	0	0	1	1.5
Toxin	0	0	0	0	0	0	0	0
Virus	14	20.9	0	0	0	0	14	20.9
Cell line	1	1.5	0	0	0	0	1	1.5
RG3	**9**	**13.4**	**6**	**9.0**	**0**	**0**	**15**	**22.4**
Bacteria	2	3.0	4	6.0	0	0	6	9.0
Fungus	4	6.0	1	1.5	0	0	5	7.5
Parasite	0	0	0	0	0	0	0	0
Prion	1	1.5	0	0	0	0	1	1.5
Toxin	0	0	0	0	0	0	0	0
Virus	2	3.0	1	1.5	0	0	3	4.5
Cell line	0	0	0	0	0	0	0	0
Unknown agents	**0**	**0**	**0**	**0**	**4**	**6.0**	**4**	**6.0**
Total	**57**	**85.1**	**6**	**9.0**	**4**	**6.0**	**67**	**100**

Abbreviations: RG2, risk group 2; RG3, risk group 3; SSBA, security sensitive biological agents

Occurrence types

More than one occurrence type could be selected for each of the 63 confirmed exposure incidents. Eighty-one occurrence types were identified in 2023 (**Figure 6**). The most frequently cited occurrence type was sharps-related (n=22; 27.2%). There were also 16 (19.8%) procedure-related occurrences, 13 (16.0%) spill-related occurrences and 11 (13.6%) occurrences categorized as "other." The "other" occurrence type included exposures due to work performed on an open bench and accidental ingestion. There were three (3.7%) unknown occurrence types. Definitions of the occurrence types are provided in Appendix **Table A2**.

Figure 6: Occurrence types involved in confirmed exposure incidents, 2023 (N=81)



Abbreviations: animal, animal-related; equipment, equipment-related; loss, loss of containment-related; PPE, personal protective equipment-related; procedure, procedure-related; sharps, sharps-related

Root causes and corrective actions

Many of the confirmed exposure incidents were associated with more than one root cause (**Table 2**), with a total of 131 root causes identified and an average of 2.08 per exposure incident. Human interaction was the root cause identified in 36 (57.1%) confirmed exposure incidents, while SOPs were identified as the root cause in 24 (38.1%) confirmed exposure incidents.

Corrective actions were compared with the root causes of each confirmed exposure incident (Table 2). The corrective actions that addressed the same root cause were related to SOPs (n=20; 83.3%), communication (n=12; 80.0%) and training (n=15; 78.9%). Only 50.0% of confirmed exposure incidents with an equipment-related root cause were addressed by corrective actions in this same area of concern (n=8).

Reporting delay to Public Health Agency of Canada

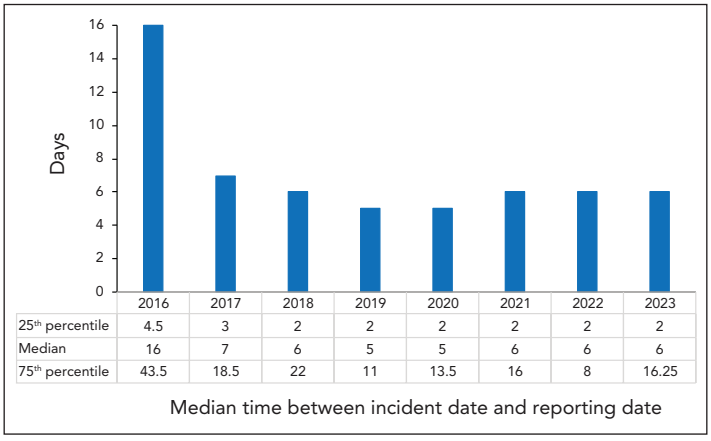
The reporting delay refers to the number of days between the date of the confirmed exposure incident's occurrence and the date on which it was first reported to PHAC via LINC. In 2023, the median reporting delay was six days, as was the median reporting delay in 2021 and 2022 (**Figure 7**). The 25th percentile for reporting delay was two days, consistent with the previous five years, while the 75th percentile was 16.25 days, more than double what it was in 2022 due to retrospective data entry of previously unreported exposure incident reports from 2016–2023 that were discovered during an on-site inspection.

Table 2: Root causes and corrective actions reported in follow-up reports of confirmed exposure incidents, 2023 (N=131)

Root cause	Examples of areas of concern	Citations		Corrective actions	
		n	%[a]	n[b]	%[c]
Human interaction	A violation (cutting a corner, not follow correct procedure, deviating from standard operating procedure)	36	57.1	22	61.1
	An error (a mistake, lapse of concentration or slip of any kind)				
Standard operating procedure (SOP)	Documents were followed as written but not correct for activity/task	24	38.1	20	83.3
	Procedures that should have been in place were not in place				
	Documents were not followed correctly				
Training	Training was not in place but should have been in place	19	30.2	15	78.9
	Training was not appropriate for task/activity				
	Staff were not qualified or proficient in performing task				
Management and oversight	Supervision needed improvement	17	27.0	11	64.7
	Lack of auditing of standards, policies and procedures				
	Risk assessment needed improvement				
Equipment	Equipment quality control needed improvement	16	25.4	8	50.0
	Equipment failed				
	Equipment was not appropriate for purpose				
Communication	Communication did not occur but should have	15	23.8	12	80.0
	Communication was unclear, ambiguous, etc.				
Other	Not applicable	4	6.3	0	0

[a] Percentage of exposure incidents that were associated with this root cause
[b] Number of exposures that were associated with this root cause, with the corrective action addressing the same area of concern
[c] Percentage of exposures that were associated with this root cause, with the corrective action addressing the same area of concern

Figure 7: Time between the date of the confirmed exposure incident and the date it was reported to Laboratory Incident Notification Canada, 2016–2023



	2016	2017	2018	2019	2020	2021	2022	2023
25th percentile	4.5	3	2	2	2	2	2	2
Median	16	7	6	5	5	6	6	6
75th percentile	43.5	18.5	22	11	13.5	16	8	16.25

Median time between incident date and reporting date

Discussion

In 2023, an increase in confirmed exposure incidents was observed in comparison with the preceding three years. While there are likely multiple contributing factors to this increase, one of the most significant may be the COVID-19 pandemic. The pandemic, which occurred between 2020 and 2022, significantly altered normal work practices in many fields by limiting the number of workers and changing the volume and type of laboratory activity conducted (22). The number of confirmed exposure reports in 2023 was similar to the pre-pandemic period. As seen in previous years (10,14,17–21) the academic and hospital sectors contributed the largest proportion of confirmed exposure incidents. The most common activities being performed during a confirmed exposure event were microbiology and *in vivo* animal research, and confirmed exposures due to sharps-, procedure- and spill-related occurrences were most often cited, with human interaction and SOPs as the most common root causes. Technicians/technologists made up the majority of affected individuals, while non-SSBAs were implicated most frequently in confirmed exposure incidents. Compared to 2021 and 2022, there was no change in the median reporting delay.

Corrective actions undertaken following a confirmed exposure incident

Understanding the underlying causes of incidents and developing strategies to prevent recurrence, especially for system-level failures rather than individual errors, is important (23,24). Part of the exposure incident follow-up process includes the reporting of corrective actions taken by regulated facilities. Corrective actions fall into the same categories as root causes, allowing for an assessment of incidents

based on the appropriateness of the applied corrective actions. In 2023, the root cause that was most frequently addressed through corrective actions following a confirmed exposure incident was SOP. Well-designed systems have just as much of an impact on safety as do individual-level capabilities and errors (23). This understanding drives SOP changes, which generally involve modifications to workflow or communication protocols. The higher rate of corrective action may reflect the tangible nature of these procedural improvements, which can be directly implemented and monitored (23). Training-related solutions were also frequently observed in 2023, aligning with literature that emphasizes the important role of continuous education in mitigating errors and enhancing safety (24). Training addresses immediate knowledge gaps and enhances skillsets (23). Efforts to improve communication through corrective actions, with 80.0% of related incidents addressed in 2023, emphasize the importance of effective communication channels in laboratory settings, which are foundational for error prevention and risk mitigation once an incident has already occurred (25).

Corrective actions were not reported for some root causes, like "other," which included unpredictable animal behaviour. This may indicate areas where solutions are more challenging to identify or implement. Corrective actions addressing equipment or "other" issues may require more resource-intensive solutions or reflect a lower perceived risk (25).

Non-security sensitive biological agents, risk group 2 and bacteria remain the most reported human pathogen and toxin types

Since the establishment of the LINC program and incident reporting, a large proportion of pathogens implicated in confirmed exposure incidents have consistently been RG2 non-SSBAs and, most commonly, bacterial agents (10,14,17–21). This trend continued in 2023, with non-SSBAs implicated in 85.1% of confirmed exposure incidents and RG2 HPTs accounting for 71.6% of HPTs identified. Almost 45% of agent types involved in exposure incidents were bacteria, which reflects the findings by Blacksell *et al.* (2024), where the predominant cause of exposure incidents that resulted in LAIs was a bacterial pathogen (1). The consistently high percentage of RG2 HPTs involved in confirmed exposure incidents reported to LINC is likely because the majority of active licences (92.8% in 2023) are held by facilities carrying out controlled activities with RG2 HPTs. Similarly, in 2023, the majority of facilities were licensed to work with non-SSBAs, with only 0.4% of active licences granted for SSBAs, thus explaining the higher proportion of non-SSBAs implicated in confirmed exposure incidents compared to SSBAs.

Sharps and procedure-related occurrences and support for licence holders

The leading occurrence-types cited in confirmed exposure incidents in 2023 were sharps (27.2%) and procedures (19.8%). This is consistent with annual report data from previous years (10,14,17–21). These occurrence types, sharps in particular, frequently occur in laboratories and have often resulted in exposure incidents (3,10). For example, a study using data of clinical laboratory workers from private and government health sectors in Al-Madinah, Saudi Arabia also found that sharps-related injuries were commonly experienced among the workers and were associated with a lack of biosafety training (26). As such, preventing needlestick and sharps-related injuries within laboratories remains crucial due to their potential to transmit pathogens (27).

To raise awareness of common causes of exposure incidents, mitigate the recurrence and encourage a culture of laboratory biosafety, LINC developed several new resources to support licence holders. These resources, which can be found online in the PHAC Training Portal, facilitate the dissemination of biosafety best practices and clarify reporting procedures using a variety of easily accessible formats, including videos, an e-learning course, webinars, downloadable and fillable forms and a podcast.

Strengths and limitations

A strength of this report is that it involved a comprehensive dataset, encompassing over eight years of data. The standardized reporting forms used as part of the incident reporting process ensured uniform data collection and ensured data reliability for trend analysis and identification of biosafety challenges.

This report has several limitations. Currently, individual-level data of all laboratory workers, such as their age, sex, experience and education background, income and other sociodemographic measures, are not collected. Such data could permit detailed analyses involving inferential statistics and hypothesis-based studies focused on potential variables associated with laboratory exposure incidents. Other limitations include the small sample size and the possibility of underreporting of laboratory exposure incidents, the extent of which remains unknown. It should also be noted that licensed facilities self-identify their sector when creating a user profile in the Biosecurity Portal as part of the licensing process, and they can only select one sector, though overlap with another sector may exist in actuality. For instance, a hospital may select the academic sector as their sector because they are affiliated with a university. This should be kept in mind when interpreting the results. Finally, a lack of comparable national incident reporting surveillance systems outside of Canada made it challenging to compare the findings and trends of this report with those of other countries.

Conclusion

In 2023, the number of confirmed exposure incidents rose and resembled levels seen prior to the COVID-19 pandemic. The most common occurrence-types, main activity being performed, root causes and HPTs implicated in confirmed exposure incidents in 2023 mirrored those cited in 2022. The natural baseline that was calculated will serve as an additional reference point for assessment in future years. Findings from this report can be used to inform biosafety practices and procedures in facilities to reduce the incidence of exposure to HPTs.

Authors' statement

AN — Methodology, data analysis, writing–original draft, writing–review & editing
AG — Conceptualization, incident monitoring, methodology, data analysis, data validation, writing–original draft, writing–review & editing
AND — Conceptualization, writing–original draft, writing–review & editing, supervision
CA — Incident monitoring, writing–original draft, writing–review & editing
EFT — Methodology, writing–original draft, writing–review & editing
CG — Writing–review & editing
SBA — Writing–review & editing

Competing interests

None.

ORCID numbers

Antoinette N. Davis — 0009-0002-5720-7742
Audrey Gauthier — 0009-0005-8729-3743
Christine Abalos — 0009-0009-5501-549X
Emily F. Tran — 0009-0005-0414-5025
Samuel Bonti-Ankomah — 0000-0002-7189-1643

Acknowledgements

Thank you to our licensed facilities for their ongoing compliance with incident notification and reporting.

Funding

This work was supported by the Public Health Agency of Canada as part of its core mandate.

References

1. Blacksell SD, Dhawan S, Kusumoto M, Le KK, Summermatter K, O'Keefe J, Kozlovac JP, Almuhairi SS, Sendow I, Scheel CM, Ahumibe A, Masuku ZM, Bennett AM, Kojima K, Harper DR, Hamilton K. Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review. Lancet Microbe 2024;5(2):e194–202. DOI PubMed

2. Haines CA, Gronvall GK. Improving U.S. Biosafety and Biosecurity: Revisiting Recommendations from the Federal Experts Security Advisory Panel and the Fast Track Action Committee on Select Agent Regulations. Appl Biosaf 2023;28(1):43–54. DOI PubMed

3. El Jaouhari M, Atchessi N, Edjoc R, Striha M, Bonti-Ankomah S. Multivariate analyses of risk factors associated with laboratory exposure incidents. Can Commun Dis Rep 2022;48(7/8):350–5. DOI PubMed

4. El Jaouhari M, Striha M, Edjoc R, Bonti-Ankomah S. Laboratory-acquired infections in Canada from 2016 to 2021. Can Commun Dis Rep 2022;48(7/8):303–7. DOI PubMed

5. Cornish NE, Anderson NL, Arambula DG, Arduino MJ, Bryan A, Burton NC, Chen B, Dickson BA, Giri JG, Griffith NK, Pentella MA, Salerno RM, Sandhu P, Snyder JW, Tormey CA, Wagar EA, Weirich EG, Campbell S. Clinical Laboratory Biosafety Gaps: Lessons Learned from Past Outbreaks Reveal a Path to a Safer Future. Clin Microbiol Rev 2021;34(3):e0012618. DOI PubMed

6. Singh K. Laboratory-acquired infections. Clin Infect Dis 2009;49(1):142–7. DOI PubMed

7. Public Health Agency of Canada. Human Pathogens and Toxins Act (HPTA). Ottawa, ON: PHAC; 2023. [Accessed 2024 Jan 17]. https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/human-pathogens-toxins-act.html

8. Justice Laws Website. Human Pathogens and Toxins Regulations (SOR/215–44). Ottawa, ON: Justice Laws Website; 2024. [Accessed 2024 Jan 25]. https://laws-lois.justice.gc.ca/eng/regulations/SOR-2015-44/index.html

9. Public Health Agency of Canada. Canadian Biosafety Guideline Pathogen Risk Assessment. Ottawa, ON: PHAC; 2018. [Accessed 2024 Sept 25]. https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/guidance/pathogen-risk-assessment/document.html

10. Abalos C, Gauthier A, Davis A, Ellis C, Balbontin N, Kapur A, Bonti-Ankomah S. Surveillance of laboratory exposures to human pathogens and toxins, Canada, 2022. Can Commun Dis Rep 2023;49(9):398–405. DOI PubMed

11. Centers for Disease Control and Prevention. About Us. Atlanta, GA: CDC; 2023. [Accessed 2024 Jan 17]. https://www.selectagents.gov/overview/

12. Department of Health and Aged Care. Security Sensitive Biological Agents (SSBA) Regulatory Scheme. Canberra, AU: DHAC; 2024. [Accessed 2024 Jan 24]. https://www.health.gov.au/our-work/ssba-regulatory-scheme

13. Centers for Disease Control and Prevention, Animal and Plant Health Inspection Service. 2022 Annual Report of the Federal Select Agent Program. Atlanta, GA/Riverdale, MD: CDC/APHIS; 2022. [Accessed 2024 Sept 27]. https://www.selectagents.gov/resources/publications/docs/FSAP_Annual_Report_2022_508.pdf

14. Pomerleau-Normandin D, Heisz M, Tanguay F. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2017. Can Commun Dis Rep 2018;44(11):297–304. DOI PubMed

15. Public Health Agency of Canada. Licensing program. Ottawa, ON: PHAC; 2024. [Accessed 2024 Jan 17]. https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/licensing-program.html

16. Balbontin N, Gauthier A, Abalos C, Davis AN, Lister M. Canadian laboratory incidents with human pathogens and toxins: an overview of reports, 2016−2022. Can Commun Dis Rep 2024;50(5):144–52. DOI PubMed

17. Atchessi N, Striha M, Edjoc R, Thompson E, El Jaouhari M, Heisz M. Surveillance of laboratory exposures to human pathogens and toxins, Canada 2020. Can Commun Dis Rep 2021;47(10):422–9. DOI PubMed

18. Lien A, Abalos C, Atchessi N, Edjoc R, Heisz M. Surveillance of laboratory exposures to human pathogens and toxins, Canada 2019. Can Commun Dis Rep 2020;46(9):292–8. DOI

19. Choucrallah D, Sarmiento L, Ettles S, Tanguay F, Heisz M, Falardeau E. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2018. Can Commun Dis Rep 2019;45(9):244–51. DOI PubMed

20. Bienek A, Heisz M, Su M. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2016. Can Commun Dis Rep 2017;43(11):228–35. DOI PubMed

21. Thompson ER, El Jaouhari M, Eltayeb N, Abalos C, Striha M, Edjoc R, Ayoo C, Bonti-Ankomah S. Surveillance of laboratory exposures to human pathogens and toxins, Canada, 2021. Can Commun Dis Rep 2022;48(10):484–91. DOI PubMed

22. Stenson MC, Fleming JK, Johnson SL, Caputo JL, Spillios KE, Mel AE. Impact of COVID-19 on access to laboratories and human participants: exercise science faculty perspectives. Adv Physiol Educ 2022;46(2):211–8. DOI PubMed

23. Kellogg KM, Hettinger Z, Shah M, Wears RL, Sellers CR, Squires M, Fairbanks RJ. Our current approach to root cause analysis: is it contributing to our failure to improve patient safety? BMJ Qual Saf 2017;26(5):381–7. DOI PubMed

24. Liu HC, Zhang LJ, Ping YJ, Wang L. Failure mode and effects analysis for proactive healthcare risk evaluation: A systematic literature review. J Eval Clin Pract 2020;26(4):1320–37. DOI PubMed

25. Wood LJ, Wiegmann DA. Beyond the corrective action hierarchy: A systems approach to organizational change. Int J Qual Health Care 2020;32(7):438–44. DOI PubMed

26. Khabour OF, Al Ali KH, Mahallawi WH. Occupational infection and needle stick injury among clinical laboratory workers in Al-Madinah city, Saudi Arabia. J Occup Med Toxicol 2018;13:15. DOI PubMed

27. Centers for Disease Control and Prevention. Sharps Safety Program Resources. Atlanta, GA: CDEC; 2024. [Accessed 2024 Mar 28]. https://www.cdc.gov/sharpssafety/index.html

Appendices

Table A1: Definitions of main activity

Main activity	Definition
Animal care	Activities such as attending to the daily care of animals and providing animals with treatment
Autopsy or necropsy	Post-mortem surgical examinations for purposes such as determining cause of death or to evaluate disease or injury for research or educational purposes
Cell culture	The process of growing cells under controlled conditions. It can also involve the removal of cells from an animal or plant
Education or training	Education or training of students and/or personnel on laboratory techniques and procedures
In vivo animal research	Experimentation with live, non-human animals
Maintenance	The upkeep, repair and/or routine and general cleaning of equipment and facilities
Microbiology	Activities involving the manipulation, isolation or analysis of microorganisms in their viable or infectious state
Molecular investigations	Activities involving the manipulation of genetic material from microorganisms or other infectious material for further analysis
Serology	Diagnostic examination and/or scientific study of immunological reactions and properties of blood serum
Hematology	Scientific study of the physiology of blood

Table A2: Definitions of occurrence types

Occurrence type	Definition
Spill	Any unintended release of an agent from its container
Loss of containment	Includes malfunction or misuse of containment devices or equipment and other type of failures that results in the agent being spilled outside of, or released from, containment
Sharps-related	Includes needle stick, cut with scalpel, blade or other sharps injury (i.e., broken glass)
Animal-related	Includes animal bites or scratches, as well as other exposure incidents resulting from animal behavior (i.e., animal movement resulting in a needle stick)
Insect-related	Includes insect bites
PPE-related	Includes either inadequate PPE for the activity or failure of the PPE in some way
Equipment-related	Includes failure of equipment, incorrect equipment for the activity or misuse of equipment
Procedure-related	Includes instances when written procedures were not followed, were incorrect for the activity or were inadequate or absent

Abbreviation: PPE, personal protective equipment

Burden of disease of respiratory syncytial virus in older adults and adults considered at high risk of severe infection

Elissa M Abrams[1,2,3]*, Pamela Doyon-Plourde[1], Phaedra Davis[1,4], Liza Lee[1], Abbas Rahal[1], Nicholas Brousseau[5], Winnie Siu[1,4], April Killikelly[1]

Abstract

Background: Availability of new vaccines for adults has increased interest in understanding Canada's respiratory syncytial virus (RSV) burden in older adults and adults considered at high risk of severe infection.

Objective: To characterize the burden of RSV disease in Canada by joint analysis of the published literature and hospitalization data from a healthcare administrative database.

Methods: Electronic databases of published literature were searched to identify studies and systematic reviews reporting data on outpatient visits, hospitalizations, intensive care unit (ICU) admissions and deaths associated with RSV infection in adults. For the hospitalization data analysis, hospital discharge records were extracted from the Canadian Institute of Health Information Discharge Abstract Database for all patients admitted to an acute care facility for RSV infection defined by ICD-10 codes from 2010 to 2020 and 2021 to 2023.

Results: Overall, 26 studies, including seven systematic reviews, were identified and summarized. Evidence suggests that medically attended RSV respiratory tract infections (RTI) are frequently causing 4.7%–7.8% of symptomatic RTI in adults 60 years of age and older. Incidence of RSV RTI increases with age and presence of underlying medical conditions. This trend was consistently observed across all RSV clinical outcomes of interest. Patients who reside in long-term care or other chronic care facilities have a higher likelihood of severe clinical outcomes compared to patients with other living situations upon hospital admission. Approximately 10% of older adults hospitalized with RSV infection require ICU admission. Although data are limited, the case fatality ratio (CFR) among those admitted to hospital varies between 5% and 10%. Some evidence suggests that RSV burden may be close to the influenza burden in older adults. In general, the results from the Canadian hospitalization data support the rapid review findings. Rates of hospitalization, ICU admission and death associated with RSV all increased with age, with 16% of hospitalizations resulting in ICU admission and with an in-hospital CFR of 9%.

Conclusion: In adults, the burden of severe RSV outcomes in general increases with age and presence of comorbidities.

Suggested citation: Abrams EM, Doyon-Plourde P, Davis P, Lee L, Rahal A, Brousseau N, Siu W, Killikelly A. Burden of disease of respiratory syncytial virus in older adults and adults considered at high risk of severe infection. Can Commun Dis Rep 2025;51(1):26–34. https://doi.org/10.14745/ccdr.v51i01a04

Keywords: respiratory syncytial virus, adults, burden of disease, surveillance, epidemiology

Affiliations

[1] Public Health Agency of Canada, Ottawa, ON

[2] Section of Allergy and Clinical Immunology, Department of Pediatrics, University of Manitoba, Winnipeg, MB

[3] Division of Allergy and Immunology, Department of Pediatrics, University of British Columbia, Vancouver, BC

[4] School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON

[5] Institut national de la santé publique du Québec, Québec, QC

***Correspondence:**

elissa.abrams@phac-aspc.gc.ca

Introduction

Respiratory syncytial virus (RSV) is commonly recognized as a significant respiratory pathogen mostly affecting young children under 24 months of age and older adults. Although the burden of disease in the older adult demographic can be substantial, with older adults experiencing more severe disease compared to younger populations, this is not as well described as it is in children and for other pathogens such as influenza. It has been estimated that globally, RSV is associated with approximately 336,000 hospitalizations and 14,000 in-hospital deaths each year in adults 65 years and older (1). Additionally, evidence suggests that younger adults living with underlying medical conditions, such as immunocompromising conditions and chronic cardiopulmonary disease, are at high risk of severe RSV infection and complications (2,3). Nonetheless, RSV remains generally underrecognized as a cause of severe respiratory tract infection (RTI) in adults.

The RSV vaccine landscape has evolved dramatically in the past year. While previously there were no vaccine products available for adults, there are currently three RSV vaccines being considered in Canada. As of February 2024, The GSK RSVPreF3 vaccine (Arexvy) and the Pfizer RSVpreF vaccine (Abrysvo) are approved by Health Canada for adults 60 years of age and older and the Moderna mRNA-1345 RSV vaccine is under review. As vaccination will be available to older adults for the first time, there is a need for a more nuanced understanding of the burden of RSV disease to inform risk and age-based vaccine recommendations especially in a Canadian context although comments on policy were out of scope for this document. Therefore, this rapid review aimed to evaluate RSV burden of disease in adults from high-income countries (Canada, United States, European countries, Australia). Additionally, hospitalization data from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) were analyzed to further describe RSV burden in Canada. This report compiles evidence derived from the literature and the Canadian discharge database in order to present a comprehensive picture of the RSV burden of disease to inform immunization guidance development in adults.

Methods

Rapid review

Search strategies: The search strategy was developed by a research librarian from Health Canada and the Public Health Agency of Canada. OVID Embase, MEDLINE, Global Health and ProQuest Public Health databases were searched from 1995 to November 2022, and again on September 1, 2023, to identify recent studies evaluating RSV burden of disease in adults (**Appendix**, Supplemental material S1–S6). Canadian respiratory virus surveillance experts were also contacted for any additional data. After removal of duplicates, references were uploaded in DistillerSR online software (Evidence Partners Inc., Ottawa, Ontario).

Study selection: Two reviewers screened titles and abstracts for study eligibility. Full texts of selected studies were then evaluated. A third independent reviewer assessed citations marked for exclusion, with disagreements resolved through discussion. Reference lists of included studies were also screened for relevant articles on RSV burden in high-income countries.

Eligibility criteria: Inclusion was limited to studies reporting data on RSV infection in adults, with a focus on adults 50 years of age and older and individuals 18 years of age and older with underlying medical conditions. The evaluation of RSV burden of disease focused on clinical outcomes of interest including medically attended RSV RTI, hospitalizations, intensive care unit (ICU) admissions, and death associated with RSV infection (Supplemental material S7). Observational studies, randomized controlled trials (RCTs) and systematic reviews (SRs) were included. Exclusion criteria were populations of other ages, and studies that did not report on outcomes of interest. The focus was on high-income countries, although studies from low- and middle-income countries were included.

Data extraction and data synthesis: One reviewer extracted data from each article, verified by a second reviewer. Disagreements were resolved through discussion. Data extracted included study design, study period, population characteristics, outcome definitions, sample size, number of events and effect measures. When reported in included studies, results comparing RSV and influenza burden of disease were extracted. Results were synthesized narratively based on the study population and outcomes. Subgroups of interest included long-term care (LTC) residents, adults with immunocompromising conditions and adults with chronic medical conditions.

Canadian hospitalization data

Data sources: Hospital discharge records were extracted from the CIHI DAD which contains data from acute care facilities from all provinces and territories, except Québec, representing 78% of the Canadian population (4). Population demographic data (i.e., age group) were obtained from the Statistics Canada website (5).

Respiratory syncytial virus hospitalizations were identified using the International Classification of Disease, Tenth Revision (ICD-10) codes J12.1, J20.5, J21.0 or B97.4. Respiratory syncytial virus hospitalizations were classified as one of the aforementioned ICD-10 codes recorded as anywhere from diagnosis 1 through 25. Hospitalizations were further stratified to determine the hospitalizations due to RSV, which was defined as one of the aforementioned ICD-10 codes recorded as diagnosis 1.

Results were presented in two groups: hospitalizations due to RSV and hospitalizations associated with RSV. Hospitalizations due to RSV provides data on direct burden of RSV in the

hospitalized population as it includes only patients where RSV was coded as the most responsible diagnosis or condition for the patient's stay in a facility (RSV-related ICD-10 code as diagnosis 1). Hospitalizations associated with RSV provide a general sense of the prevalence of RSV in the hospitalized population as it includes both patients where RSV was identified as the condition considered the most responsible for the stay in a facility and where it was diagnosed or present in the patient during their stay in the facility (RSV-related ICD-10 code found anywhere from diagnosis 1 through 25).

Analytic cohort

All patients admitted to an acute care facility with RSV between September 2010 to August 2020 and September 2021 to August 2023 (12 respiratory virus seasons spanning September through August of the following year) were included in the analysis. Due to public health measures enacted for the COVID-19 pandemic, there was almost no RSV activity in the 2020–2021 season (6); therefore, this season was excluded from the analysis as it did not reflect normal seasonal activity.

Data on ICU admissions and in-hospital deaths were also extracted. Diagnosis codes were not available specifically for ICU admissions and deaths; therefore, their classifications (associated with or due to RSV) were based on whether the initial hospitalization was associated with or due to RSV.

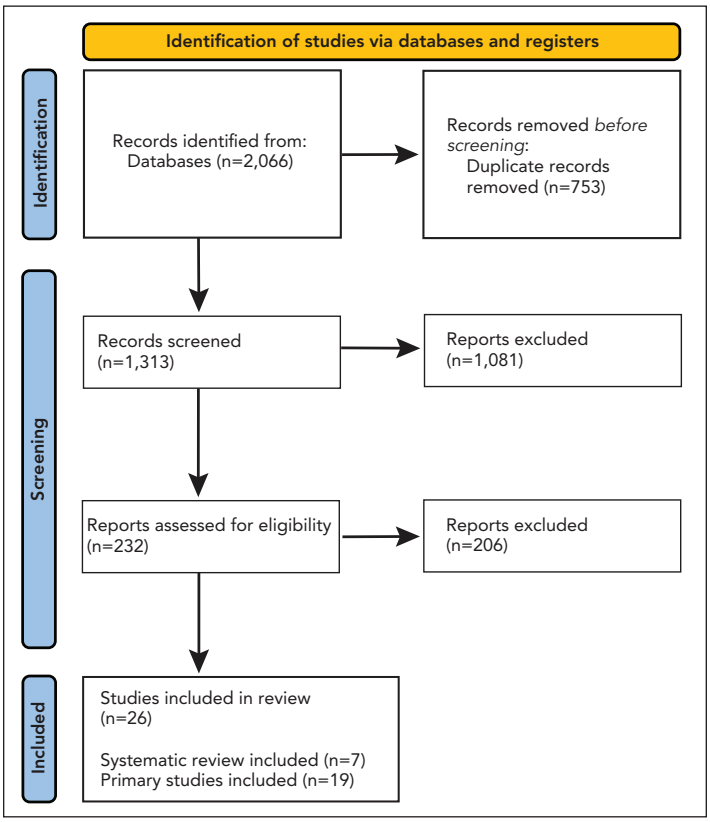
Risk factors of interest were also determined by diagnosis information based on ICD-10 classification codes and were chosen based on prior known associations with severe RSV outcomes. Diagnosis codes were considered mutually exclusive (i.e., one individual hospitalized for RSV with multiple risk factors of interest were counted in each individual risk factor category). All diagnoses and conditions that are present on a patient's record from diagnosis 1 through 25 were included in determining their risk factors. Risk factors of interest for the Canadian hospitalization data analysis included RTI, chronic obstructive pulmonary disease (COPD), immunocompromising conditions, cardiovascular disease, diabetes and chronic kidney disease. The list of ICD-10 codes used to define a risk factor is found in Supplemental material S8.

Data synthesis: The number of hospitalizations, ICU admissions and in-hospital death analyses were both aggregated and stratified by season and age groups where appropriate. Hospitalizations were also presented as rates aggregated by season and stratified by age groups (50–59 years, 60–69 years, 70–79 years and ≥80 years). Moreover, ICU admission rates and case fatality ratios (CFR) were presented by age group aggregated across the study period. The population of all provinces and territories, except Québec, by age groups was used to calculate rates per 100,000 population. The 18–49 years age group was included in the analysis for risk factors of interest. Data on risk factors were aggregated across age groups and seasons. Descriptive data analyses were performed in SAS 9.4 and figures were produced using Microsoft Excel. The results from the analysis of Canadian hospitalization data were compared with the evidence from the rapid review. Results from both sources are presented and summarized by outcome of interest, except for medically attended RSV RTI for which data was only available from the rapid review.

Results

After deduplication, 1,313 references were screened for study eligibility in the rapid review (**Figure 1**). Overall, 26 articles, including 7 SRs, were incorporated into the narrative synthesis of RSV burden of disease in adults (Supplemental material S9).

Figure 1: Study selection PRISMA flow diagram



Abbreviation: PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses

Between September 2010 to August 2020 and September 2021 to August 2023, there were a total of 19,436 recorded hospitalizations associated with RSV among adults 50 years of age and older, of which 6,314 were due to RSV (**Table 1**).

Medically attended respiratory syncytial virus respiratory tract infection

Rapid review: Seven SRs and six observational studies describing the incidence of medically attended RSV RTI in older adults as well as adults with underlying medical conditions were

Table 1: Total hospitalizations, intensive care unit admissions and in-hospital deaths associated with and due to respiratory syncytial virus, adults aged 50 years of age and older, seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b]

Season	Hospitalizations		Rate of hospitalizations per 100,000 population		ICU admissions		In-hospital deaths	
	Associated with RSV[c]	Due to RSV[d]	Associated with RSV[c]	Due to RSV[d]	Associated with RSV[c]	Due to RSV[d]	Associated with RSV[c]	Due to RSV[d]
2010–2011	238	90	3	1	51	13	28	11
2011–2012	179	53	2	1	41	4	19	1
2012–2013	591	211	6	2	113	30	49	13
2013–2014	663	251	7	3	149	38	59	20
2014–2015	1,342	402	14	4	247	42	120	20
2015–2016	921	317	9	3	177	43	77	23
2016–2017	2,225	695	22	7	393	85	190	49
2017–2018	2,338	706	22	7	374	69	205	45
2018–2019	2,891	928	27	9	482	90	232	52
2019–2020	2,213	753	20	7	333	70	193	48
2021–2022	1,330	469	12	4	188	40	118	34
2022–2023	4,505	1,439	39	13	636	118	378	81
Total	19,436	6,314	-	-	3,184	642	1,668	397
Average/season	1,620	526	16	5	265	54	139	33

Abbreviations: ICU, intensive care unit; RSV, respiratory syncytial virus; -, not applicable
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] Hospitalizations associated with RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4, found anywhere from diagnosis 1 through 25
[d] Hospitalizations due to RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4, recorded as diagnosis 1

identified; some included Canadian data (n=3), but none were restricted to Canada (Supplemental material S9). Some specific findings are specified here; full details of all studies are included in Supplemental material S9. In adults 60 years of age and older, a SR of developed countries, including Canada, found that RSV caused between 4.7% and 7.8% of symptomatic respiratory infections (7). Overall, the incidence of medically attended RSV RTI increased with age (8,9). For instance, a SR and meta-analysis (MA) found that rates of medically attended RSV RTI among adults from the United States (US) increased from 934 per 100,000 population in adults 18–49 years of age to 1,519 per 100,000 population in adults 65 years of age and older (10). Factors associated with severe RSV infection in adults 65 years of age and older included age and the presence of underlying medical conditions (i.e., cardiorespiratory disease, diabetes and immunocompromising conditions). In a prospective US cohort study of adults 60 years of age and older, incidence was almost two times higher among adults with chronic cardiopulmonary disease compared to those without (incidence rate ratio [IRR] of 1.89; 95% confidence interval [CI]: 1.44–2.48) (11). Although evidence was limited, studies suggest that RSV incidence is high in younger adults (i.e., 18–59 years) with certain medical conditions and is somewhat similar to adults 65 years of age and older. A cross-sectional study from the US of the annual incidence of medically attended RSV found that incidence was highest in adults 85 years of age and older, followed by adults 65 years of age and older, and then followed closely by adults 18–59 years of age considered at high risk of severe RSV including those with cardiorespiratory disease or immunocompromising conditions (3).

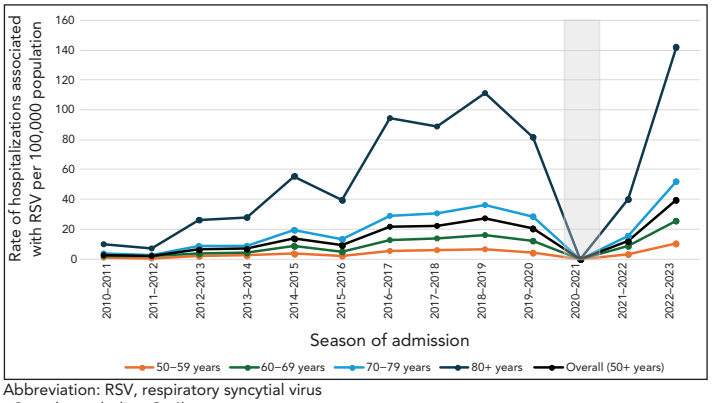
Hospitalization associated with respiratory syncytial virus infection

Rapid review: Six SRs and 15 observational studies, including four Canadian studies, described the incidence of hospitalization associated with RSV infection. In general, studies found that the incidence increased consistently with age. For instance, a prospective Canadian population-based surveillance study found the following average seasonal RSV hospitalization incidence rates per 100,000 population between 2012 and 2015:13.9 (95% CI: 9.9–17.9) in adults aged 50–59 years, 43.7 (95% CI: 34.2–51.2) in adults aged 60–69 years, 88.6 (95% CI: 71.0–106.1) in adults aged 70–79 years and 282.5 (95% CI: 238.2–326.8) in adults 80 years of age and older (2). A SR found that depending on age and risk factors, adults 18 years of age and older with chronic medical conditions have higher rates of hospitalization associated with RSV compared to those without the condition (10). The authors reported rates ranging from 1.2–1.3 times higher for adults with obesity to 27.6 times higher for those 20–39 years of age with congestive heart failure (CHF) (10). Similarly, a retrospective cohort study from Ontario found that among adults 18 years of age and older who had a hospitalization associated with RSV between September 2010 and August 2017, 35.4% had CHF, 44.7% had COPD, 32.2% had asthma and

38.4% had immunocompromising conditions; in addition, hospitalizations associated with RSV increased from 2010–2011 to 2018–2019 (12). Another Canadian study found that of adults 50 years of age and older who had a hospitalization associated with RSV over the 2012–2015 seasons, almost all (98.1%) had at least one comorbidity with the most frequent being vascular (71.3%), cardiac (55.5%), pulmonary (48.2%), renal (48.2%) and endocrine (33.2%) conditions; 26.8% were immunocompromised (2).

Canadian hospitalization data: Rates of hospitalizations associated with RSV among older adults in Canada were generally increasing between seasons 2011–2012 and 2017–2018 across all age groups until RSV activity was interrupted by the COVID-19 pandemic between seasons 2019–2020 to 2021–2022 (**Figure 2**). Overall, the average rate of hospitalization associated with RSV among adults 50 years of age and older was 16 per 100,000 population and the average rate of hospitalization associated with RSV per 100,000 population by age groups were the following: 4 in adults 50–59 years old, 10 in adults 60–69 years old, 22 in 70–79 years and 63 in adults 80 years of age and older. The rates of hospitalizations due to RSV among older adults in Canada followed the same trend; however, rates were much lower (**Figure 3**). Rates of hospitalization associated with and due to RSV increased with age (6,13).

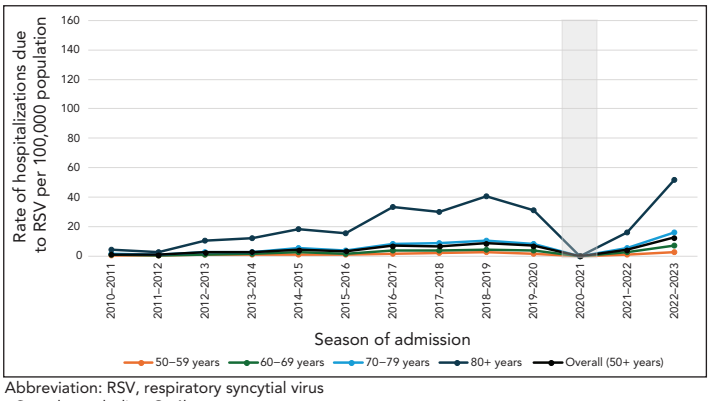
Figure 2: Rate of hospitalizations associated with respiratory syncytial virus, by age group (years), seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b,c,d]



Abbreviation: RSV, respiratory syncytial virus
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] The shaded area represents the 2020–2021 season where RSV hospitalizations were low due to public health measures enacted during the COVID-19 pandemic. The 2020–2021 season was excluded from other analyses
[d] Hospitalizations associated with RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4, found anywhere from diagnosis 1 through 25

A total of 21,258 hospitalizations associated with RSV among adults 18 years of age and older were reported across the 12 seasons (**Table 2**). Of these hospitalizations, 76.4% were reported to have at least one risk factor of interest, 34.6% were reported to have at least two of these risk factors and 9.1% were reported to have at least three of these risk factors. Among these 21,258 hospitalizations, 30.0% reported having COPD, 29.6% had diabetes, 23.4% had cardiovascular disease, 16.8% had an immunocompromising condition, 15.8% had a respiratory tract infection and 6.3% had chronic kidney disease.

Figure 3: Rate of hospitalizations due to respiratory syncytial virus, by age group (years), seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b,c,d]



Abbreviation: RSV, respiratory syncytial virus
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] The shaded area represents the 2020–2021 season where RSV hospitalizations were low due to public health measures enacted during the COVID-19 pandemic. The 2020–2021 season was excluded from other analyses
[d] Hospitalizations due to RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4, recorded as diagnosis 1

Table 2: Number and percent hospitalizations associated with respiratory syncytial virus with a risk factor of interest, adults aged 18 years of age and older, seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b]

Risk factor of interest	Number of hospitalizations[c]	Percentage (%)[d]
Chronic obstructive pulmonary disease	6,360	30.0
Diabetes	6,276	29.6
Cardiovascular disease	4,965	23.4
Immunosuppressive conditions	3,564	16.8
Respiratory tract infection	3,344	15.8
Chronic kidney disease	1,336	6.3
Total number of hospitalizations associated with RSV[e]	21,258	-
Total number of risk factors of interest		
At least 1	16,250	76.4
2 or more	7,345	34.6
3 or more	1,928	9.1
4 or more	297	1.4

Abbreviations: RSV, respiratory syncytial virus; -, not applicable
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] Number of hospitalizations by risk factor will not equal 21,258 hospitalizations as one patient may have multiple risk factors and the occurrence of each risk factor was considered mutually exclusive
[d] Percentage of hospitalizations will exceed 100% as one patient may have multiple risk factors and the occurrence of each risk factor was considered mutually exclusive
[e] Hospitalizations associated with RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4, found anywhere from diagnosis 1 through 25

Intensive care unit admission associated with respiratory syncytial virus infection

Rapid review: Two SRs and nine observational studies, including three Canadian studies, reported data on ICU admission associated with RSV infection. Full results are listed in Supplemental material S9. A few specific studies are highlighted below. A Canadian prospective population-based surveillance study found that among adults 50 years of age and older hospitalized with RSV, 13.7% required ICU admission and 6.4% required mechanical ventilation (similar to influenza) between 2012 and 2015 (2). As with other clinical outcomes, risk increased with age and the presence of comorbidities although data was more limited by specific age groups (7,14). A SR from developed countries (North America, Europe, Western Pacific) found a higher proportion of adults 18 years of age and older considered at risk of complications of infection was admitted to the ICU (26.7% vs. 5.0%), required oxygen use (23.8%–50.0% vs. 13.6%–14.8%), and was discharged to care (4.2%–17.3% vs. <1%) compared to adults 60 years of age and older (7). A Canadian prospective cohort study found that among adults 50 years of age and older with a history of COPD hospitalized with RSV during the winter seasons of 2011 to 2015, 17.9% required ICU admission, 9.0% were mechanically ventilated, and 23.6% needed non-invasive ventilation (15). A surveillance study from the US found that patients who resided in LTC or other chronic care facilities had a 4.43 (95% CI: 2.23–8.82) times higher likelihood of severe clinical outcomes (i.e., ICU admission, receiving mechanical ventilation and/or death) compared to patients with other living situations at admission (16).

Canadian hospitalization data: Across 12 seasons, among the 19,436 hospitalizations associated with RSV, 3,184 (16%) required ICU admission and among the 6,314 hospitalizations due to RSV, 642 (10%) required ICU admission. The average rate of ICU admissions associated with RSV among adults 50 years of age and older across the 12 seasons were 2.6 per 100,000 population and increased with age (1.1 in adults 50–59 years, 2.4 in 60–69 years, 4.3 in 70–79 years, and 6.0 in adults 80 years of age and older) (**Table 3**). Rates of ICU admissions due to RSV in Canadian older adults followed the same trend; however, rates were much lower.

Regardless of the type of RSV hospitalization (associated with or due to), the number and rate of ICU admissions increased with age but the proportion of hospitalizations requiring ICU admissions decreased with age.

Death associated with respiratory syncytial virus infection

Rapid review: Five SRs and eleven observational studies, including four Canadian studies, reported data on death associated with RSV infection. Full results are listed in Supplemental material S9. A few specific studies are highlighted below. Although evidence is more limited than for other clinical outcomes, in general the CFR among adults admitted to hospital is approximately 5%–10% which increases with age and the presence of one or more comorbidities. A SR of developed countries found an overall RSV-related CFR of 8.2% (95% CI: 5.5–11.9%) among adults 60 years of age and older and 9.9% (95% CI: 6.7%–14.4%) among adults 18 years of age and older considered at higher risk (7). Another systematic review and meta-analysis found that the in-hospital case fatality rate was higher in adults 65 years of age and older than adults 50–64 years of age (1). Similarly, two studies from Ontario found that among patients hospitalized with RSV, 30-day all-cause mortality rates increased with age (12,17). A US prospective cohort study found that the CFR was higher in adults admitted from LTC facilities (38%) than in those admitted from the community (3%, $p<0.001$) (18).

Table 3: Number and rate of intensive care unit (ICU) admissions associated with and due to respiratory syncytial virus (RSV), percentage of RSV hospitalizations resulting in an ICU admission, by age groups (years), seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b]

Age group (years)	Among hospitalizations associated with RSV[c]			Among hospitalizations due to RSV[d]		
	Number of ICU admissions	Rate per 100,000 population[e]	% of hospitalizations requiring ICU	Number of ICU admissions	Rate per 100,000 population[e]	% of hospitalizations requiring ICU
50–59	504	1.1	26	101	0.2	17
60–69	896	2.4	23	155	0.4	14
70–79	969	4.3	19	174	0.8	12
80+	815	6.0	9	212	1.5	7
Total[f]	3,184	2.6	16	642	0.5	10

Abbreviations: ICU, intensive care unit; RSV, respiratory syncytial virus
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] Hospitalizations associated with RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4 found anywhere from diagnosis 1 through 25
[d] Hospitalizations due to RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4 recorded as diagnosis 1
[e] Aggregated rate by age group was calculated by averaging the number of ICU by age group, by season and dividing by the average population of that age group across the study period
[f] Total column values were calculated by aggregating ICU across all seasons in the study period. The average population of each season during the study was used to calculate rates

Canadian hospitalization data: Across 12 seasons, 1,668 in-hospital deaths among RSV associated hospitalizations were reported in adults 50 years of age and older, corresponding to an in-hospital CFR of 9% (**Table 4**). Among these in-hospital deaths, 397 were among those hospitalized due to RSV, corresponding to an in-hospital CFR of 6%. The average rate of in-hospital deaths associated with RSV in adults 50 years of age and older across the 12 seasons was 1.4 per 100,000 population and increased with age (the rates of in-hospital deaths in hospitalizations associated with RSV per 100,000 population by age groups were the following: 0.2 in adults 50–59 years old, 0.6 in 60–69 years, 1.7 in 70–79 years, and 6.7 in adults 80 years of age and older). The rates of in-hospital deaths among older adults hospitalized due to RSV in Canada followed the same trend; however, rates were much lower.

Regardless of the type of RSV death (in hospitalizations associated with or due to RSV), both the number and rates of death and CFR increased with age.

Discussion

The rapid review offers insight into the burden of RSV disease in older adults and adults with underlying medical conditions, with a focus on high-income countries such as Canada, the US and European countries. This review is also supported with hospitalization data to further describe RSV burden of disease in Canada.

Evidence from the rapid review suggests that medically attended RSV infections in high-income countries are frequent in older adults and those with underlying medical conditions. The incidence of RSV RTI increases with age as well as the presence of comorbidities, including cardiorespiratory disease, diabetes and immunocompromising conditions. While the incidence of hospitalization varies between studies, risk of hospitalization associated with RSV increases consistently with age. Depending on age and risk factors, adults 18 years of age and older with underlying medical conditions are more likely to have a hospitalization associated with RSV infection than those without. Patients who reside in LTC or other chronic care facilities have a higher likelihood of severe clinical outcomes compared to patients with other living situations upon hospital admission. Moreover, ICU admission associated with RSV increases with age and presence of comorbidities, with approximately 10% of older hospitalized older adults requiring ICU admission. There were more limited data on deaths associated with RSV. The CFR among those admitted to hospital varied between studies but is approximately 5%–10% and increases with age.

Canadian administrative hospitalization data generally support the findings of the rapid review. Over 12 respiratory seasons between August 2010 and September 2023, it was found that RSV-associated hospitalization rates increased with age and that finding was consistent for each season. The average rates of hospitalization associated with RSV in adults 50 years of age and older was estimated at 16 per 100,000 population. Overall, 16% of hospitalizations associated with RSV resulted in an ICU admission corresponding to an average rate of 2.6 per 100,000 population for adults 50 years of age and older. Rate of hospitalization associated with RSV resulting in ICU admissions increased with age; however, the proportion of hospitalizations requiring ICU admission decreased with age. The average CFR among adults 50 years of age and older was 9% and in-hospital death among hospitalizations associated with RSV increased with age. Hospitalizations, ICU admissions and deaths due to RSV followed the same trend; however, calculated values were lower than those associated with RSV.

Although there is general alignment between the rapid review and Canadian hospitalization data analysis, with increasing risk with age and specific conditions, some differences can be noted. Findings from the Canadian hospitalization data were usually

Table 4: Number and rate of in-hospital deaths associated with and due to respiratory syncytial virus, case fatality rate, by age groups (years), seasons 2010–2011 to 2019–2020 and 2021–2022 to 2022–2023[a,b]

Age group (years)	Among hospitalizations associated with RSV[c]			Among hospitalizations due to RSV[d]		
	Number of in-hospital deaths	Rate per 100,000 population[e]	CFR (%)	Number of in-hospital deaths	Rate per 100,000 population[e]	CFR (%)
50–59	110	0.2	6	18	0.0	3
60–69	244	0.6	6	44	0.1	4
70–79	390	1.7	8	72	0.3	5
80+	924	6.7	11	263	1.9	8
Total[f]	1,668	1.4	9	397	0.3	6

Abbreviations: CFR, case fatality rate; RSV, respiratory syncytial virus
[a] Canada, excluding Québec
[b] Canadian Discharge Abstract Database
[c] Hospitalizations associated with RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4 found anywhere from diagnosis 1 through 25
[d] Hospitalizations due to RSV were identified using ICD-10 codes J12.1, J20.5, J21.0 or B97.4 recorded as diagnosis 1
[e] Aggregated rate by age group was calculated by averaging the number of deaths by age group, by season and dividing by the average population of that age group across the study period
[f] Total column values were calculated by aggregating deaths across all seasons in the study period. The average population of each season during the study was used to calculate rates

lower than what is reported in the literature. Discrepancies can be explained by differences in methodology used between studies. Individual study characteristics such as study population, case definitions, study period, and data source can lead to discrepancies between the observed incidence rates. Few studies reported data on Canadian adults and heterogeneity between study results limits the generalizability of the findings. Another limitation of the rapid review is the inclusion of RSV infection not limited to laboratory confirmed infection potentially leading to an overestimation of RSV incidence.

Currently, Canada has limited enhanced national RSV surveillance data and leveraging administrative health data from CIHI DAD helped address those evidence gaps to supplement the evidence on RSV burden of disease in adults to inform the development of immunization recommendation. However, known limitations of healthcare administrative data are expected to lead to underestimation of RSV incidence especially due to limits in viral identification and undertesting in patients (19). Of note, rates from CIHI DAD were higher in the more recent period, which could be partly due to more frequent testing. Other limitations of the Canadian hospitalization data include the exclusion of Québec data, a large Canadian province, differing coding practices between hospitals and changes in testing and admission practices during the study period, especially in respiratory season following the COVID-19 pandemic.

The descriptive analyses provided information on general trends of severe outcomes of RSV RTI in older adults (19). Although the rapid review and healthcare administrative data analysis methodologies each have their drawbacks, the combination of these analyses provides an interdisciplinary view of the burden of RSV in older adults to support vaccine program decision-making. Enhanced national surveillance programs for RSV are in development where timely data variables of interest can be collected specifically for surveillance activities and to support policy and decision-making. These analyses may be revisited as additional data becomes available from the literature or from the Canadian surveillance landscape.

Authors' statement

EMA — Conceptualization, formal analysis, data interpretation, writing–original draft
PDP — Formal analysis, data interpretation, writing–original draft
PD — Formal analysis, data interpretation, writing–review & editing
AR — Formal analysis, data interpretation
LL — Data interpretation, writing–original draft
NB — Writing–review & editing
WS — Conceptualization, writing–review & editing
AK — Conceptualization, writing–original draft

Competing interests

None.

ORCID numbers

Elissa M Abrams — 0000-0003-3433-1986
Abbas Rahal — 0000-0003-2816-4501
Nicholas Brousseau — 0000-0001-6042-3177

Acknowledgements

The authors wish to acknowledge the NACI Secretariat team, Matthew Tunis, Kelsey Young, Mona Hersi, Adrienne Stevens, Anastassia Howarth, Su Hyun Lim, the Health Canada Library (Shannon Hayes) and the NACI RSV Working Group.

Funding

None.

References

1. Shi T, Denouel A, Tietjen AK, Campbell I, Moran E, Li X, Campbell H, Demont C, Nyawanda BO, Chu HY, Stoszek SK, Krishnan A, Openshaw P, Falsey AR, Nair H; RESCEU Investigators. Global disease burden estimates of respiratory syncytial virus-associated acute respiratory infection in older adults in 2015: A systematic review and meta-analysis. J Infect Dis 2020;222 Suppl 7:S577–83. DOI PubMed

2. ElSherif M, Andrew MK, Ye L, Ambrose A, Boivin G, Bowie W, David MP, Gruselle O, Halperin SA, Hatchette TF, Johnstone J, Katz K, Langley JM, Loeb M, MacKinnon-Cameron D, McCarthy A, McElhaney JE, McGeer A, Poirier A, Pirçon JY, Powis J, Richardson D, Semret M, Smith S, Smyth D, Trottier S, Valiquette L, Webster D, McNeil SA, LeBlanc JJ; Serious Outcomes Surveillance (SOS) Network of the Canadian Immunization Research Network (CIRN) and the Toronto Invasive Bacterial Diseases Network (TIBDN). Leveraging influenza virus surveillance from 2012 to 2015 to characterize the burden of respiratory syncytial virus disease in Canadian adults ≥50 years of age hospitalized with acute respiratory illness. Open Forum Infect Dis 2023;10(7):ofad315. DOI PubMed

3. Mesa-Frias M, Rossi C, Emond B, Bookhart B, Anderson D, Drummond S, Wang J, Lefebvre P, Lamerato LE, Lafeuille MH. Incidence and economic burden of respiratory syncytial virus among adults in the United States: A retrospective analysis using 2 insurance claims databases. J Manag Care Spec Pharm 2022;28(7):753–65. DOI PubMed

4. Canadian Institute for Health Information. Discharge Abstract Database (DAD) metadata. Ottawa, ON: CIHI; 2023. [Accessed 2023 Nov 27]. https://www.cihi.ca/en/discharge-abstract-database-dad-metadata

5. Statistics Canada. Table 17-10-0005-01 Population estimates on July 1, by age and gender. Ottawa, ON: StatCan; 2024. [Accessed 2024 Feb 16]. DOI

6. Public Health Agency of Canada. Respiratory virus report, week 34 - ending August 28, 2021. Ottawa, ON: PHAC; 2021. [Accessed 2024 Feb 16]. https://www.canada.ca/en/public-health/services/surveillance/respiratory-virus-detections-canada/2021-2022/week-34-ending-august-28-2021.html

7. Nguyen-Van-Tam JS, O'Leary M, Martin ET, Heijnen E, Callendret B, Fleischhackl R, Comeaux C, Tran TM, Weber K. Burden of respiratory syncytial virus infection in older and high-risk adults: a systematic review and meta-analysis of the evidence from developed countries. Eur Respir Rev 2022;31(166):220105. DOI PubMed

8. Wilkinson T, Beaver S, Macartney M, McArthur E, Yadav V, Lied-Lied A. Burden of respiratory syncytial virus in adults in the United Kingdom: A systematic literature review and gap analysis. Influenza Other Respir Viruses 2023;17(9):e13188. DOI PubMed

9. Johannesen CK, van Wijhe M, Tong S, Fernández LV, Heikkinen T, van Boven M, Wang X, Bøås H, Li Y, Campbell H, Paget J, Stona L, Teirlinck A, Lehtonen T, Nohynek H, Bangert M, Fischer TK; RESCEU Investigators. Age-specific estimates of respiratory syncytial virus-associated hospitalizations in 6 European countries: A time series analysis. J Infect Dis 2022;226 Suppl 1:S29–37. DOI PubMed

10. McLaughlin JM, Khan F, Begier E, Swerdlow DL, Jodar L, Falsey AR. Rates of medically attended RSV among US adults: A systematic review and meta-analysis. Open Forum Infect Dis 2022;9(7):ofac300. DOI PubMed

11. Belongia EA, King JP, Kieke BA, Pluta J, Al-Hilli A, Meece JK, Shinde V. Clinical features, severity, and incidence of RSV illness during 12 consecutive seasons in a community cohort of adults ≥60 years old. Open Forum Infect Dis 2018;5(12):ofy316. DOI PubMed

12. Mac S, Shi S, Millson B, Tehrani A, Eberg M, Myageri V, Langley JM, Simpson S. Burden of illness associated with Respiratory Syncytial Virus (RSV)-related hospitalizations among adults in Ontario, Canada: A retrospective population-based study. Vaccine 2023;41(35):5141–9. DOI PubMed

13. Public Health Agency of Canada. Respiratory Virus Report, Week 34 - ending August 27, 2022. Ottawa, ON: PHAC; 2022. [Accessed 2024 Jan 17]. https://www.canada.ca/en/public-health/services/surveillance/respiratory-virus-detections-canada/2021-2022/week-34-ending-august-27-2022.html

14. Colosia AD, Yang J, Hillson E, Mauskopf J, Copley-Merriman C, Shinde V, Stoddard J. The epidemiology of medically attended respiratory syncytial virus in older adults in the United States: A systematic review. PLoS One 2017;12(8):e0182321. DOI PubMed

15. Mulpuru S, Andrew MK, Ye L, Hatchette T, LeBlanc J, El-Sherif M, MacKinnon-Cameron D, Aaron SD, Alvarez GG, Forster AJ, Ambrose A, McNeil SA; Serious Outcomes Surveillance and Canadian Immunization Research Network (CIRN) Investigators. Impact of respiratory viral infections on mortality and critical illness among hospitalized patients with chronic obstructive pulmonary disease. Influenza Other Respir Viruses 2022;16(6):1172–82. DOI PubMed

16. Goldman CR, Sieling WD, Alba LR, Silverio Francisco RA, Vargas CY, Barrett AE, Phillips M, Finelli L, Saiman L. Severe clinical outcomes among adults hospitalized with respiratory syncytial virus infections, New York City, 2017–2019. Public Health Rep 2022;137(5):929–35. DOI PubMed

17. Hamilton MA, Liu Y, Calzavara A, Sundaram ME, Djebli M, Darvin D, Baral S, Kustra R, Kwong JC, Mishra S. Predictors of all-cause mortality among patients hospitalized with influenza, respiratory syncytial virus, or SARS-CoV-2. Influenza Other Respir Viruses 2022;16(6):1072–81. DOI PubMed

18. Falsey AR, Hennessey PA, Formica MA, Cox C, Walsh EE. Respiratory syncytial virus infection in elderly and high-risk adults. N Engl J Med 2005;352(17):1749–59. DOI PubMed

19. Schanzer DL, Saboui M, Lee L, Nwosu A, Bancej C. Burden of influenza, respiratory syncytial virus, and other respiratory viruses and the completeness of respiratory viral identification among respiratory inpatients, Canada, 2003–2014. Influenza Other Respir Viruses 2018;12(1):113–21. DOI PubMed

Appendix

Supplemental material is available upon request to the author: elissa.abrams@phac-aspc.gc.ca

The prevalence of HIV pre-exposure prophylaxis (HIV-PrEP) use and HIV-PrEP-to-need ratio in nine Canadian provinces, 2018–2021

Nashira Popovic[1]*, Qiuying Yang[1], Laurence Campeau[1], Janelle Elliott[1], Anson Williams[1], Viviane D Lima[2,3], Paul Sereda[2], Joseph Cox[4]

Affiliations

[1] Centre for Communicable Disease and Infection Control, Public Health Agency of Canada, Ottawa, ON

[2] BC Centre for Excellence in HIV/AIDS, Vancouver, BC

[3] Department of Medicine, University of British Columbia, Vancouver, BC

[4] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, QC

***Correspondence:**
nashira.popovic@phac-aspc.gc.ca

Abstract

Background: Measuring trends in HIV pre-exposure prophylaxis (HIV-PrEP) uptake is important to inform planning for prevention programs and policies. The HIV-PrEP-to-need ratio (PnR) is a construct used by public health organizations to explore disparities in the provision of HIV-PrEP across geographic areas and demographic categories (e.g., age, sex).

Methods: This is a retrospective database review study using administrative pharmacy data, containing limited demographic information, from nine Canadian provinces. Annual estimates of persons taking HIV-PrEP and PnR were generated using data from the company IQVIA and the BC Centre for Excellence on HIV/AIDS. Data on new HIV diagnoses were obtained from the National HIV Surveillance System. The PnR was defined as the number of HIV-PrEP users divided by the number of new HIV diagnoses annually and is interpreted as the number of HIV-negative people using HIV-PrEP each year for every person newly diagnosed with HIV.

Results: In 2021, an estimated 23,644 individuals were prescribed HIV-PrEP, corresponding to an HIV-PrEP prevalence of 66.9 per 100,000 persons. This represents a 1.8-fold increase since 2018. The overall PnR was 16.8, meaning that for every person newly diagnosed with HIV, 17 HIV-negative individuals were taking HIV-PrEP. There were disparities between provinces (PnR range: 1.5/100,000–37.7/100,000) and between males and females (PnR 22.6 and 1.2, respectively). Females, individuals aged 0–19 years, and those in Manitoba, Saskatchewan and Prince Edward Island, had lower levels of HIV-PrEP use relative to epidemic need.

Conclusion: In Canada, the use of HIV-PrEP increased from 2018 to 2021 and uptake varied by age, sex and province. HIV-PrEP-to-need ratio is a useful measure to assess uptake of HIV-PrEP as a prevention strategy and could be used to explore disparities in provision across provinces and available demographic categories. However, PnR could be improved with more information on key populations and other attributes, such as race/ethnicity, socioeconomic status and residence of city/rural area.

Suggested citation: Popovic N, Yang Q, Campeau L, Elliott J, Williams A, Lima VD, Sereda P, Cox J. The prevalence of HIV pre-exposure prophylaxis (HIV-PrEP) use and HIV-PrEP-to-need ratio in nine Canadian provinces, 2018–2021. Can Commun Dis Rep 2025;51(1):35–42. https://doi.org/10.14745/ccdr.v51i01a05
Keywords: HIV, pre-exposure prophylaxis (PrEP), epidemiology, prevention, HIV-PrEP use, HIV-PrEP-to-need ratio (PnR)

Introduction

HIV pre-exposure prophylaxis (HIV-PrEP) is highly effective and has the potential to make a significant contribution to reducing Canada's HIV incidence (1). In 2016, Health Canada approved the drug combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for use as HIV-PrEP, and in July 2017, lower-cost generic versions became available in Canada (1,2).

The Government of Canada has endorsed global health sector strategies on HIV, viral hepatitis and sexually transmitted infections for the period of 2022–2030. This includes ensuring continued engagement of people living with HIV in treatment and care services and leveraging innovations, such as new treatment regimens and new prevention approaches (3–6). Canadian National Surveillance data shows that new HIV diagnoses have been decreasing for several years (7) and mathematical modelling suggests that HIV incidence is decreasing overall in Canada (8). The estimated annual number of new HIV infections in Canada has decreased from about 4,000 per year in the mid-1980s to around 2,000–2,500 in the 2000s, following the introduction of antiretroviral therapy (ART), with a further decrease to 1,520 in 2020 (8). Although HIV incidence appears to be declining nationally, this overall trend does not account for the heterogeneity in HIV infections across Canada, as incidence appears to be increasing within some jurisdictions.

Previous studies showed that when adherence is maintained, daily HIV-PrEP use reduced HIV transmission by 36% to 99% in people who inject drugs (PWID), heterosexual individuals, and gay, bisexual, and other men who have sex with men (gbMSM) (9–12). Murchu *et al.* (13) conducted a systematic review and meta-analysis of randomized controlled trials of the effectiveness and safety of oral HIV-PrEP to prevent HIV. They found that HIV-PrEP is effective in gbMSM (RR 0.25; 95% CI: 0.1–0.61) and PWID (RR 0.51; 95% CI: 0.29–0.92), but not in heterosexuals (RR 0.77; 95% CI 0.46–1.29).

Reducing new HIV infections by 2030 will require multi-pronged strategies to support combination prevention, including condom promotion and educational programs (14), testing and the use of both post-exposure prophylaxis (PEP) and HIV-PrEP in high-risk populations.

HIV-PrEP-to-need ratio (PnR) is defined as the ratio of HIV-PrEP users per new HIV diagnoses. A higher level of PnR indicates more HIV-PrEP users relative to estimated need (15). Tan *et al.* (2021) (16) found that PnRs were highest in those 30–39 years of age, males, Toronto and the Central East and West regions of Ontario. Siegler *et al.* (2020) (15) found that Medicaid expansion and HIV-PrEP drug assistance programs in the United States were associated with higher HIV-PrEP use in states that adopted those policies, after controlling for potential confounders. Thus, to reduce HIV-PrEP disparities, public health strategies must be developed to reach those most in need, especially historically disadvantaged communities (17). These studies suggested that PnR is useful for future assessments of HIV prevention strategy uptake.

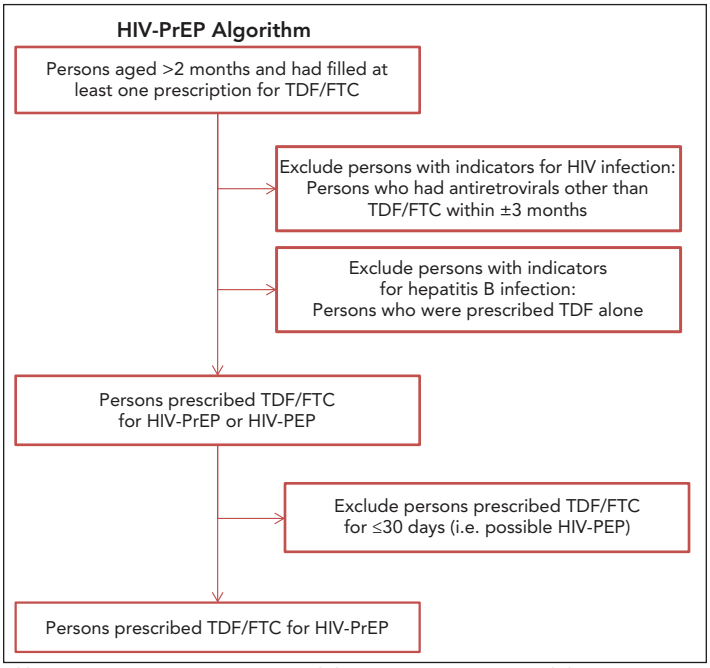
This study updated a previous analysis of HIV-PrEP uptake in Canadian provinces (2), and estimated HIV-PrEP-use prevalence and PnR for nine Canadian provinces from 2018–2021, by sex, age group and province. This information could be used to identify groups and populations with lower HIV-PrEP uptake, or higher HIV-PrEP need, thus informing policymakers and program planners.

Methods

Prevalence of HIV-PrEP users

Annual estimates of persons using HIV-PrEP in Canada were generated for 2018–2021 from a prescription database held by the company IQVIA. A validated algorithm (18) was used to distinguish users of TDF/FTC for HIV-PrEP from those using TDF/FTC for HIV or hepatitis B treatment or post-exposure prophylaxis (**Figure 1**). The algorithm was adapted from the validated United States Centers for Disease Control algorithm (18,19) and modified to fit the Canadian context (2).

Figure 1: Algorithm to assign HIV-PrEP treatment indication



Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PEP, post-exposure prophylaxis; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine

Briefly, in a given year, persons older than two months of age who had one or more TDF/FTC prescriptions were included. Since TDF/FTC is also used to treat HIV or hepatitis B infections and as HIV PEP, several exclusion criteria were applied: 1) persons who were prescribed antiretrovirals other than TDF/FTC within ±3 months (persons on HIV treatment); 2) persons who were prescribed with TDF alone (for hepatitis B treatment); and 3) persons who were prescribed TDF/FTC for less than or equal to 30 days (PEP users). In any given year, persons prescribed TDF/FTC who were not excluded with our algorithm were considered HIV-PrEP users.

All ages were taken into account when IQVIA extracted the data and estimated the number of projected patients by indication; however, the results for patients younger than 15 years of age were omitted due to small counts. Prevalence of HIV-PrEP users was defined as the number of HIV-PrEP users in a calendar year, divided by the total population in that year. It is expressed as HIV-PrEP users per 100,000 population.

Data sources

Data on new HIV diagnoses were obtained from the National HIV Surveillance System (7). These data include only people diagnosed with HIV for the first time in Canada and do not include individuals who were previously diagnosed with HIV in another country and then emigrated to Canada.

Data on antiretroviral drug prescriptions dispensed in eight provinces (Manitoba [MB], Ontario [ON], New Brunswick [NB], Newfoundland and Labrador [NL], Nova Scotia [NS], Prince Edward Island [PE], Québec [QC] and Saskatchewan [SK]) between January 1, 2018, and December 31, 2021, were extracted by IQVIA from the company's geographical prescription monitor dataset. Data from Alberta (AB) are not included in IQVIA's dataset, since coverage within this province does not meet the threshold for reporting projected patient counts. The HIV-PrEP use number in British Columbia (BC) was provided by the BC Centre for Excellence in HIV/AIDS (BC-CfE) (20). These nine provinces represented 88.1% of the Canadian population in 2021. Population size estimates were obtained from Statistics Canada (21).

The IQVIA database includes Canadian aggregate dispensed prescription data projected from a sample of approximately 6,000 pharmacies in eight provinces, representing close to 60% of all retail pharmacies in Canada. Patient counts were then projected from this sample of pharmacies to extrapolate for the entire province.

In January 2018, BC implemented an HIV-PrEP program as part of a comprehensive Treatment as Prevention strategy, within which BC residents are eligible to receive publicly funded HIV-PrEP via the BC-CfE HIV-PrEP program. The BC-CfE HIV-PrEP program database is a centralized clinical registry, which stores data from various sources relating to demographic and behavioural information, clinical outcomes (laboratory results) and antiretroviral medication dispensation data (20).

HIV-PrEP-to-need ratio (PnR)

HIV-PrEP-to-need ratio was defined as the ratio of the number of HIV-PrEP users to the number of people newly diagnosed with HIV in the same year (15,16,19). New HIV diagnoses were used as an epidemiological proxy for HIV incidence from 2018–2021. HIV-PrEP-to-need ratio was used to describe HIV-PrEP coverage overall and per province and demographic subgroups (sex and age group) relative to new HIV diagnoses in the same year. The PnR attempts to assess and compare how well-targeted HIV-PrEP coverage is to the groups and populations that can benefit from it the most and can be understood as the number of people using HIV-PrEP each year for every person newly diagnosed with HIV. A PnR of 2.0 means that for every person newly diagnosed with HIV in a year, two HIV-negative people were using HIV-PrEP.

Analyses

The two outcomes (HIV-PrEP uptake and PnR) were calculated for nine Canadian provinces from 2018–2021 and stratified by sex, age group and province over this time period. Chi-square tests were performed among sex, age groups and provinces. Cochran-Armitage trend tests were conducted to determine whether HIV-PrEP prevalence and PnR changed significantly over time. Analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute).

Results

Overall trends

In 2021, a total of 23,644 individuals were estimated to be on TDF/FTC for HIV-PrEP in nine Canadian provinces (BC, MB, ON, NL, NB, NS, PE, QC and SK), resulting in an estimated HIV-PrEP prevalence of 69.9 per 100,000 persons. The estimated number of HIV-PrEP users increased over the four-year period (**Table 1**), showing a 1.8-times increase from 13,222 in 2018 to 23,644 in 2021 (p trend<0.001). The PnR was 16.8 in 2021, meaning that for every person newly diagnosed with HIV, 17 HIV-negative individuals were using HIV-PrEP (Table 1). From 2018–2021, annual HIV-PrEP use prevalence increased while reported HIV incidence declined, leading to a 2.3-times increase in PnR (p trend<0.001) (Table 1, **Figure 2**).

Table 1: HIV-PrEP users and HIV-PrEP-to-need ratio by year in nine Canadian provinces, for both sexes

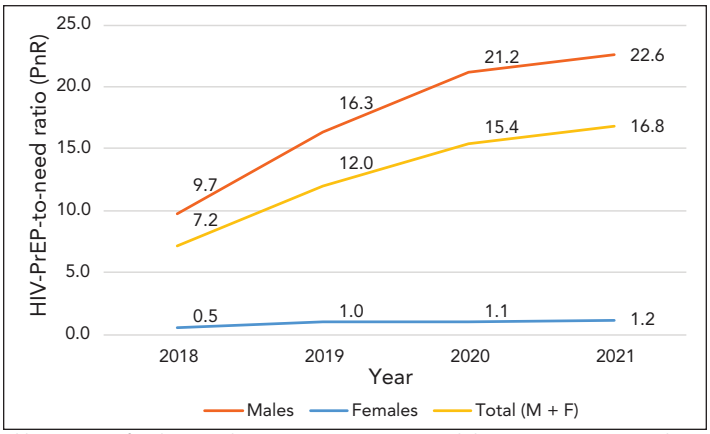
Year	HIV-PrEP use		New HIV diagnoses		PnR
	Count	Prevalence (n/100,000)	Count	Rate of new HIV diagnoses (n/100,000)	
2018	13,222	40.3	1,839	5.6	7.2
2019	19,689	59.1	1,646	4.9	12.0
2020	20,771	62.0	1,351	4.0	15.4
2021	23,644	69.9	1,406	4.2	16.8

Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

Trends by sex

HIV-PrEP use was much greater among males than females, with almost all (98.0%) HIV-PrEP users being males during the four-year period (p chi-square<0.001). In 2021, the PnR for males was 22.6, meaning that for every male newly diagnosed with HIV, 23 HIV-negative males were using HIV-PrEP. Among males, the number of HIV-PrEP users was 1.8 times higher in 2021 than in 2018 (p trend<0.001), HIV-PrEP use prevalence was 1.7 times higher in 2021 than in 2018 (p trend<0.001) and PnR was 2.3 times higher in 2021 than in 2018 (p trend<0.001) (Figure 2, **Table 2**).

Figure 2: HIV-PrEP-to-need ratio by sex in nine Canadian provinces, 2018–2021



Abbreviations: F, females; M, males; HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

Table 2: HIV-PrEP users and HIV-PrEP-to-need by year in nine Canadian provinces, males only

Year	HIV-PrEP use		New HIV diagnoses		PnR
	Count	Prevalence (n/100,000)	Count	Rate of new HIV diagnoses (n/100,000)	
2018	12,947	79.6	1,335	8.2	9.7
2019	19,234	116.4	1,178	7.1	16.3
2020	20,351	122.5	962	5.8	21.2
2021	23,195	138.1	1,028	6.1	22.6

Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

In 2021, the PnR for females was 1.2. Among females, the number of HIV-PrEP users was 1.6 times higher in 2021 than in 2018 (p trend<0.001), HIV-PrEP use prevalence was 1.5 times higher in 2021 than in 2018 (p trend<0.001) and PnR was 2.4 times higher in 2021 than in 2018 (p trend<0.001) (**Table 3**, Figure 2).

Table 3: HIV-PrEP users and HIV-PrEP-to-need by year in nine Canadian provinces, females only

Year	HIV-PrEP use		New HIV diagnoses		PnR
	Count	Prevalence (n/100,000)	Count	Rate of new HIV diagnoses (n/100,000)	
2018	275	1.7	504	3.0	0.5
2019	455	2.7	468	2.8	1.0
2020	420	2.5	389	2.3	1.1
2021	449	2.6	378	2.2	1.2

Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

Trends by age

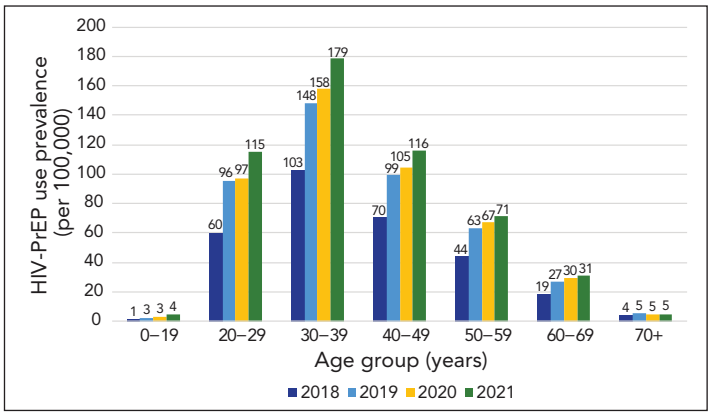
In 2021, HIV-PrEP use and PnR were highest among people aged 30–39 years (HIV-PrEP users: 8,337; HIV-PrEP use prevalence: 179.1/100,000; PnR: 19.3) and were lowest among individuals aged 0–19 years and 70+ years (p chi-square<0.001) (**Table 4**). Between 2018–2021, the annual prevalence of HIV-PrEP use increased among all age groups (p trend<0.01) and the PnR increased in all age groups (p trend<0.01), except those aged 60–69 years (p trend=0.11) (**Figure 3** and **Figure 4**).

Table 4: HIV-PrEP users and HIV-PrEP-to-need ratio by age group, nine Canadian provinces, 2021

Age group (years)	HIV-PrEP use		New HIV diagnoses		PnR
	Counts	Prevalence (n/100,000)	Counts	Rate of new HIV diagnoses (n/100,000)	
0–19	301	4.3	27	0.4	11.1
20–29	5,216	115.2	352	7.8	14.8
30–39	8,337	179.1	431	9.3	19.3
40–49	4,957	116.0	263	6.2	18.8
50–59	3,250	71.5	195	4.3	16.7
60–69	1,356	31.1	114	2.6	11.9
70+	227	5.1	24	0.5	9.5

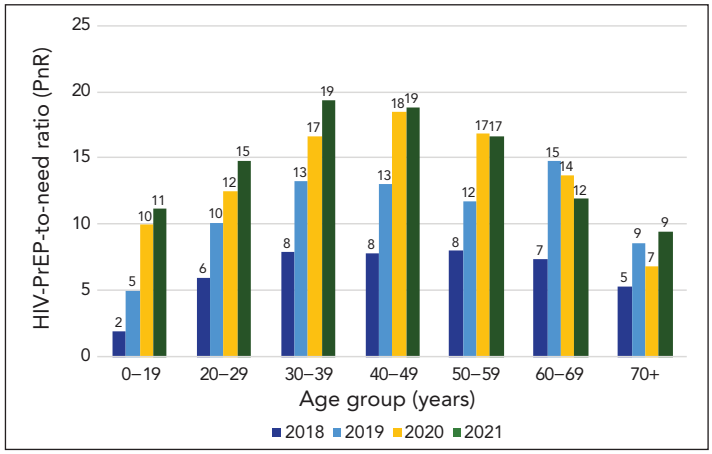
Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

Figure 3: Annual HIV-PrEP use prevalence (per 100,000 persons) by age group, nine Canadian provinces, males and females, 2018–2021



Abbreviation: HIV-PrEP, pre-exposure prophylaxis

Figure 4: HIV-PrEP-need ratio by age group, males and females, nine Canadian provinces, 2018–2021

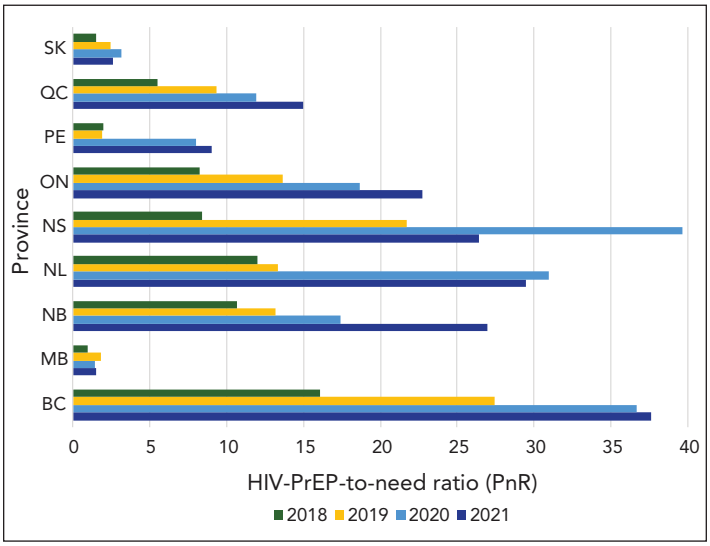


Abbreviation: HIV-PrEP, pre-exposure prophylaxis

Geographical trends

Provincial HIV-PrEP use prevalence in 2021 ranged widely from 15.9–107.6 per 100,000 persons (average: 69.9/100,000) (*p* chi-square<0.001). The provincial PnR also ranged widely from 1.5–37.7 (average: 16.8) (*p* chi-square<0.001) (**Table 5**). HIV-PrEP use prevalence in 2021 was the highest in BC, ON, QC and SK; however, given the higher rates of new HIV diagnoses, the PnR was lowest in MB and SK (Table 5). From 2018–2021, patterns of HIV-PrEP use varied. Trend test was significant in all provinces (*p* trend<0.01) except for NL (*p* trend=0.13) and MB (*p* trend=0.05), and decreasing in SK, NS and NL between 2020–2021 (**Figure 5**).

Figure 5: HIV-PrEP-to-need ratio by province, 2018–2021



Abbreviations: BC, British Columbia; HIV-PrEP, pre-exposure prophylaxis; MB, Manitoba; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; QC, Québec; SK, Saskatchewan

Discussion

An estimated 23,644 individuals were prescribed TDF/FTC for HIV-PrEP across nine Canadian provinces in 2021, corresponding to an estimated HIV-PrEP prevalence of 66.9 per 100,000 persons, representing a 1.8-fold increase since 2018. HIV-PrEP uptake varied by age, sex and province. The overall PnR in Canada was 17; however, females, individuals aged 0–19 years, and those in MB, SK and PE had lower levels of HIV-PrEP use relative to epidemic need.

HIV-PrEP use is much higher among males, likely, in part, due to the high uptake of HIV-PrEP among gbMSM. For example, among the 511 individuals accessing HIV-PrEP in AB at sexually transmitted infection, sexual and reproductive health clinics and private family practitioner offices, 98.4% were men and 89.8% were gbMSM (22). In addition, challenges encountered by clinicians in identifying women who have HIV-PrEP indications may contribute to lower uptake among females (18).

Considering health care in Canada is distributed provincially, coverage of HIV-PrEP remains complex, with different policies between provinces. Several provinces (e.g., BC, SK, AB, MB and PE) offer HIV-PrEP at no cost for those who meet eligibility guidelines and have applicable residence and citizenship status. However, implementation of these programs occurred at different times, and increases in HIV-PrEP uptake and PnR may vary according to increased accessibility to HIV-PrEP. For example, BC has the highest HIV-PrEP prevalence and PnR, and this may be because the HIV-PrEP program is free of charge and has been operating since 2018 (23,24). Other provinces provide HIV-PrEP coverage through multiple programs, which sometimes include eligibility criteria and co-payments. This could

Table 5: HIV-PrEP users and HIV-PrEP to need ratio by province, 2021

Province	HIV-PrEP use		New HIV diagnoses		PnR
	Count	Prevalence (n/100,000)	Count	Rate of new HIV diagnoses (n/100,000)	
British Columbia	5,650	107.6	150	2.9	37.7
Manitoba	221	15.9	145	10.5	1.5
New Brunswick	216	27.2	8	1.0	27.0
Newfoundland and Labrador	118	22.6	4	0.8	29.5
Nova Scotia	423	42.3	16	1.6	26.4
Ontario	11,045	74.1	485	3.3	22.8
Prince Edward Island	36	21.7	4	2.4	9.0
Québec	5,307	61.5	354	4.1	15.0
Saskatchewan	628	53.2	240	20.3	2.6

Abbreviations: HIV-PrEP, pre-exposure prophylaxis; PnR, HIV-PrEP-to-need ratio

potentially be contributing to low HIV-PrEP prevalence and PnR, since individuals need to pay for part or all of the entire cost of treatment if they do not have private insurance (25). These policy differences between provinces, which are difficult to measure, may account for differences in HIV-PrEP uptake and resulting PnR. This could include the organization and delivery of HIV-PrEP programs, the number of HIV-PrEP providers and access to linguistically and culturally appropriate care (26). In addition to these policy differences, further work is needed to examine province-specific challenges in HIV-PrEP uptake.

Limitations

There are several limitations in our study. The results do not reflect the complete national picture of HIV-PrEP use in Canada, although these nine provinces represented 88.1% of the Canadian population in 2021 (21). The addition of information from AB and three territories would provide a more representative overview of HIV-PrEP uptake in Canada. IQVIA data only included prescriptions that were acquired from a community pharmacy. Dispensations from hospital pharmacies, medications provided at no cost and medications purchased online were not included. The dispensation data from IQVIA covered approximately 60% of all retail pharmacies in Canada. Patient counts from participating pharmacies were projected to the whole population of each province by IQVIA and the algorithm used to project dispensations is proprietary. Dispensation data do not include information on medical indication; therefore, an algorithm was used to assign a treatment indication to each dispensation. Although the algorithm for classifying TDF/FTC users as HIV-PrEP users has been validated using data from the United States, it is possible that some dispensations may have been misclassified, and the algorithm may not perform the same in the Canadian context. Not all dispensed prescription drugs are consumed, as some people may have filled a prescription but may not have consumed the medication. These limitations could result in an under- or over-estimate of HIV-PrEP use. This study could not control potential confounders or consider effect modifiers because the database only included limited demographic information. The COVID-19 pandemic has reduced demand for and access to services and has an impact on HIV-PrEP uptake and new HIV diagnoses.

The calculation of PnR was based on new HIV diagnoses, which does not necessarily represent all incident HIV cases. For the PnR, the numerator (number of HIV-PrEP users) could influence the denominator (new HIV diagnoses). Change in overall HIV incidence has been found to be correlated with an increase in PnR (27). However, modelling data showed that this impact is likely limited (28). Compared to a baseline scale-up scenario of 10% HIV-PrEP coverage, a scale-up scenario of 30% HIV-PrEP coverage reduces HIV incidence over a ten-year period by an estimated 25% (28). Modest provision of HIV-PrEP has little substantial impact on new HIV diagnoses. However, if HIV-PrEP is brought to a greater scale, the PnR calculation may need further refinement, such as inclusion of HIV incidence, rather than diagnoses (19).

To determine the need for HIV-PrEP use in a particular group of individuals, the World Health Organization uses a 'substantial risk' threshold at the group level. Groups with an HIV incidence greater than 3 per 100 person-years are considered at risk and should be recommended for HIV-PrEP (29). Unfortunately, the additional sociodemographic variables are not available through the IQVIA administrative pharmaceutical dataset used to estimate HIV-PrEP update and, therefore, could not estimate PnR by key populations disproportionately impacted by HIV in Canada.

Conclusion

In Canada, the use of HIV-PrEP increased from 2018–2021, however, uptake varied by age, sex and geography. The PnR attempts to provide an opportunity for comparisons regarding whether HIV-PrEP coverage reflects the need for prevention (20). HIV-PrEP-to-need ratio may be a useful measure to report on the use of HIV-PrEP as a prevention strategy and can be used to explore disparities in provision across jurisdictions and available demographic categories. As well, this type of measure could be used to help inform program planning and policies for other similar diseases (e.g., Doxy-HIV-PrEP for bacterial sexually transmitted diseases).

Authors' statement

NP — Methodology, data interpretation, writing–original draft
QY — Methodology, formal analysis, interpreted results
LC — Writing–review & editing
JE — Writing–review & editing
AW — Writing–review & editing
VDL — Data curation, writing–review & editing
PS — Data curation, writing–review & editing
JC — Writing–review & editing

All authors approved the final version of the manuscript.

Competing interest

None.

ORCID numbers

None.

Acknowledgements

We thank the non-co-author members of the National Routine HIV Surveillance team at the Public Health Agency of Canada and provincial/territorial public health authorities for their contribution to national HIV surveillance.

Funding

This work was supported by the Public Health Agency of Canada.

References

1. Tan DH, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, Kille J, Baril JG, Cox J, Giguere P, Harris M, Hughes C, MacPherson P, O'Donnell S, Reimer J, Singh A, Barrett L, Bogoch I, Jollimore J, Lambert G, Lebouche B, Metz G, Rogers T, Shafran S; Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ 2017;189(47):E1448–58. DOI PubMed

2. Popovic N, Yang Q, Archibald C. Trends in HIV pre-exposure prophylaxis use in eight Canadian provinces, 2014–2018. Can Commun Dis Rep 2021;47(56):251–8. DOI PubMed

3. World Health Organization. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Geneva, CH: WHO; 2022. https://www.who.int/publications/i/item/9789240053779

4. Joint United Nations Programme on HIV and AIDS. 90-90-90 An Ambitious Treatment Target to Help End the AIDS Epidemic. Geneva, CH: UNAIDS; 2014. https://www.unaids.org/en/resources/documents/2017/90-90-90

5. Centre for Communicable Diseases and Infection Control. A summary of the Pan-Canadian framework on sexually-transmitted and blood-borne infections. Can Commun Dis Rep 2018;44(7/8):179–81. DOI PubMed

6. Public Health Agency of Canada. Accelerating our response: Government of Canada five-year action plan on sexually transmitted and blood-borne infections. Ottawa, ON: PHAC; 2019. https://www.canada.ca/en/public-health/services/reports-publications/accelerating-our-response-five-year-action-plan-sexually-transmitted-blood-borne-infections.html

7. Public Health Agency of Canada. HIV in Canada Surveillance Report to December 31, 2020. Ottawa, ON: PHAC; 2023. https://www.canada.ca/en/public-health/services/publications/diseases-conditions/hiv-canada-surveillance-report-december-31-2020.html

8. Public Health Agency of Canada. Estimates of HIV incidence, prevalence and Canada's progress on meeting the 90-90-90 HIV targets, 2020. Ottawa, ON: PHAC; 2022. https://www.canada.ca/en/public-health/services/publications/diseases-conditions/estimates-hiv-incidence-prevalence-canada-meeting-90-90-90-targets-2020.html

9. Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, McMahan V, Bushman LR, Casapía M, Montoya-Herrera O, Veloso VG, Mayer KH, Chariyalertsak S, Schechter M, Bekker LG, Kallás EG, Grant RM; iPrEx Study Team. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. Sci Transl Med 2012;4(151):151ra125. DOI PubMed

10. Martin M, Vanichseni S, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, Chiamwongpaet S, Curlin ME, Na-Pompet S, Warapronmongkholkul A, Kittimunkong S, Gvetadze RJ, McNicholl JM, Paxton LA, Choopanya K; Bangkok Tenofovir Study Group. The impact of adherence to preexposure prophylaxis on the risk of HIV infection among people who inject drugs. AIDS 2015;29(7):819–24. DOI PubMed

11. Hanscom B, Janes HE, Guarino PD, Huang Y, Brown E, Chen YQ, Hammer SMD, Gilbert PB, Donnell DJ. Preventing HIV-1 Infection in Women using Oral Pre Exposure Prophylaxis: A Meta-analysis of Current Evidence. Journal of acquired immune deficiency syndromes 2016;73(5):606–8. https://journals.lww.com/jaids/fulltext/2016/12150/brief_report__preventing_hiv_1_infection_in_women.17.aspx

12. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, Sullivan AK, Clarke A, Reeves I, Schembri G, Mackie N, Bowman C, Lacey CJ, Apea V, Brady M, Fox J, Taylor S, Antonucci S, Khoo SH, Rooney J, Nardone A, Fisher M, McOwan A, Phillips AN, Johnson AM, Gazzard B, Gill ON. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. Lancet 2016;387(10013):53–60. DOI PubMed

13. Murchu EO, Marshall L, Teljeur C, Harrington P, Hayes C, Moran P, Ryan M. Oral pre-exposure prophylaxis (PrEP) to prevent HIV: a systematic review and meta-analysis of clinical effectiveness, safety, adherence and risk compensation in all populations. BMJ Open 2022;12(5):e048478. DOI PubMed

14. Sullivan PS, Giler RM, Mouhanna F, Pembleton ES, Guest JL, Jones J, Castel AD, Yeung H, Kramer M, McCallister S, Siegler AJ. Trends in the use of oral emtricitabine/tenofovir disoproxil fumarate for pre-exposure prophylaxis against HIV infection, United States, 2012–2017. Ann Epidemiol 2018;28(12):833–40. DOI PubMed

15. Siegler AJ, Mehta CC, Mouhanna F, Giler RM, Castel A, Pembleton E, Jaggi C, Jones J, Kramer MR, McGuinness P, McCallister S, Sullivan PS. Policy- and county-level associations with HIV pre-exposure prophylaxis use, the United States, 2018. Ann Epidemiol 2020;45:24–31.e3. DOI PubMed

16. Tan DH, Dashwood TM, Wilton J, Kroch A, Gomes T, Martins D. Trends in HIV pre-exposure prophylaxis uptake in Ontario, Canada, and impact of policy changes: a population-based analysis of projected pharmacy data (2015–2018). Can J Public Health 2021;112(1):89–96. DOI PubMed

17. Doherty R, Walsh JL, Quinn KG, John SA. Association of Race and Other Social Determinants of Health With HIV Pre-Exposure Prophylaxis Use: A County-Level Analysis Using the PrEP-to-Need Ratio. AIDS Educ Prev 2022;34(3):183–94. DOI PubMed

18. Wu H, Mendoza MC, Huang YA, Hayes T, Smith DK, Hoover KW. Uptake of HIV Preexposure Prophylaxis Among Commercially Insured Persons-United States, 2010–2014. Clin Infect Dis 2017;64(2):144–9. DOI PubMed

19. Siegler AJ, Mouhanna F, Giler RM, Weiss K, Pembleton E, Guest J, Jones J, Castel A, Yeung H, Kramer M, McCallister S, Sullivan PS. The prevalence of pre-exposure prophylaxis use and the pre-exposure prophylaxis-to-need ratio in the fourth quarter of 2017, United States. Ann Epidemiol 2018;28(12):841–9. DOI PubMed

20. British Columbia Centre for Excellence in HIV/AIDS. HIV Pre-exposure prophylaxis (HIV-PrEP) Semi Annual Report. Vancouver, BC: BCCFE; 2022. https://bccfe.ca/wp-content/uploads/2023/12/prep_qmr_report_q2_2022-updated.pdf

21. Statistics Canada. Table 17-10-0009-01 Population estimates, quarterly. Ottawa, ON: StatCan; 2024. DOI

22. Candler E, Naeem Khan M, Gratrix J, Plitt S, Stadnyk M, Smyczek P, Anderson N, Carter J, Sayers S, Smith D, Ugarte-Torres A, Shukalek C, Singh AE. Retrospective audit of a convenience cohort of individuals on HIV pre-exposure prophylaxis in Alberta, Canada. J Assoc Med Microbiol Infect Dis Can 2022;7(4):350–63. DOI PubMed

23. British Columbia Centre for Excellence in HIV/AIDS. Vancouver, BC: BCCFE; 2020. https://paninbc.ca/wp-content/uploads/2018/11/BCCfE-PrEP-DrJunineToy-PAN-Fall-Mtg-2018.pdf

24. British Columbia Centre for Excellence in HIV/AIDS. Guidance for the use of pre-exposure prophylaxis (PrEP) for the prevention of HIV acquisition in British Columbia. Vancouver, BC: BCCFE; 2019. https://bccfe.ca/wp-content/uploads/2023/12/prep_guidelines_17-jun-2020.pdf

25. Virgilio L. Navigating Current Social and Economic Barriers for Pre-Exposure Prophylaxis (PrEP) Accessibility in Canada. McMaster University 2020. https://macsphere.mcmaster.ca/bitstream/11375/25479/1/ANTHROP%204S03_LVirgilio.pdf

26. Gaspar M, Tan D, Lachowsky N, Hull M, Wells A, Sinno J, Javier Pico Espinosa O, Grace D. HIV pre-exposure prophylaxis (HIV-PrEP) should be free across Canada to those meeting evidence-based guidelines. Can J Hum Sex 2022;31(3):309–13. DOI

27. Bunting SR, Hunt B, Boshara A, Jacobs J, Johnson AK, Hazra A, Glick N. Examining the Correlation Between HIV-PrEP Use and Black:White Disparities in HIV Incidence in the Ending the HIV Epidemic Priority Jurisdictions. J Gen Intern Med 2023;38:382–9. DOI PubMed

28. Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, Sullivan P. Impact of the Centers for Disease Control's HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. J Infect Dis 2016;214(12):1800–7. DOI PubMed

29. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. Geneva, CH: WHO; 2016. [Accessed 2022 Dec 13]. https://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf

EPIDEMIOLOGIC STUDY

Using behavioural science to improve antibiotic stewardship in Canadian long-term care homes: Protocol for a multi-center cluster randomized quality improvement study

Tyler Good[1]*, Jorida Cila[1], Rhiannon Mosher[1], Klajdi Puka[1,2], Shaghig Reynolds[3], Barbara Catt[3], Aboubakar Mounchili[3], Denise Gravel-Tropper[3], Patrick Quail[4], Allison McGeer[5], Andrea Moser[6,7], Madeleine Ashcroft[8], Peter Daley[9,10], Katrina Piggott[11,12], Jerome Leis[11,12], Mark Morrissey[1]

Affiliations

See Appendix C

***Correspondence:**
tyler.good@phac-aspc.gc.ca

Abstract

Background: Antimicrobial resistance (AMR) is associated with significant human and financial costs, particularly among vulnerable populations like older adults living in long-term care homes (LTCHs). Urinary tract infection (UTI) is the leading indication for antibiotic use in this population, with some estimates suggesting that up to 70% of these prescriptions may be avoidable.

Objective: The purpose of this study is to develop and test novel behavioural science-informed antimicrobial stewardship (AMS) quality improvement strategies in Canadian LTCHs, which aim to decrease unnecessary testing and treatment for residents who lack the minimum clinical signs and symptoms of UTI.

Intervention: The quality improvement strategy is a two-pronged approach that includes 1) targeted education for essential care providers (family and friends of LTCH residents) about UTI and benefits of AMS, which strives to outline a positive role for this group in UTI management, and 2) monthly feedback to LTCH staff on their facility's urine culture ordering rates.

Outcomes: The protocol was piloted in a single LTCH; a process evaluation of the pilot implementation served to refine the research protocol, which is being implemented in eight LTCHs across Canada using an eight-month stepped wedge randomized cluster design.

Conclusion: This protocol represents a behavioural science-informed intervention to improve AMS across LTCHs. If successful, this model of care could be scalable across Canadian LTCHs, offering an inclusive approach that aims to empower clinicians, non-regulated healthcare staff, residents and their family and friends to improve health outcomes as antibiotic stewards.

Suggested citation: Good T, Cila J, Mosher R, Puka K, Reynolds S, Catt B, Mounchili A, Gravel-Tropper D, Quail P, McGeer A, Moser A, Ashcroft M, Daley P, Piggott KL, Leis JA, Morrissey M. Using behavioural science to improve antibiotic stewardship in Canadian long-term care homes: Protocol for a multi-center cluster randomized quality improvement study. Can Commun Dis Rep 2025;51(1):43–53. https://doi.org/10.14745/ccdr.v51i01a06
Keywords: antimicrobial resistance, antimicrobial stewardship, education, essential care provider, long-term-care home, audit and feedback, urinary tract infection, urine culture order

Introduction

The World Health Organization has identified antimicrobial resistance (AMR) as one of the top ten threats to global public health (1), with serious human and financial costs (2). Some Canadian estimates indicate that up to 50% of antibiotic prescriptions in outpatient settings (3), and nearly 25% in hospital settings (4), are avoidable. Residents of long-term care homes (LTCHs) are increasingly frail and particularly vulnerable to high rates of antibiotic use and antimicrobial-resistant infections (5,6), risk of adverse outcomes linked to avoidable antibiotic use (7) and relatively less developed antimicrobial stewardship (AMS) programs compared to other sectors (8). The leading indication for antibiotic use in LTCHs is urinary tract infections (UTI) (9), as it makes up over half of antibiotics prescribed in this sector (10), with up to 70.5% of these prescriptions considered clinically unnecessary (9). At the core of this challenge is the occurrence of asymptomatic bacteriuria, which is remarkably prevalent, being present in up to 50% of LTCH residents (5,11). Asymptomatic bacteriuria is the expected presence of bacteria in an appropriately collected urine specimen, in absence of clinical symptoms of UTI. Positive urine cultures that identify asymptomatic bacteriuria are frequently attributed to UTI for many non-specific presentations, which underscores the importance of limiting urine culture collection to situations where minimum clinical symptoms are present. An upstream focus on the judicious use of urine cultures is known to result in significant reductions in antibiotic use of asymptomatic bacteriuria (12,13) and may significantly improve AMS in LTCHs.

Evidence suggests that AMS interventions in LTCH can reduce antibiotic prescribing, especially for the treatment of UTI (14–16), including a recent meta-analysis showing a 14% overall reduction in antimicrobial use (8). Upstream interventions targeting urine culture, known as diagnostic stewardship interventions, may be most effective at reducing unnecessary antibiotic prescriptions for UTI (10,12,13,17–20). Importantly, a recent systematic review found AMS interventions did not increase risk of hospital admission or death, indicating that these programs did not lead to under-treatment of infection (21).

Behavioural science offers a useful lens for addressing antimicrobial resistance (22). Behavioural science frameworks have been used to understand the drivers and barriers affecting stewardship behaviours (23), as foundation for AMS interventions (24–28). In the current work, findings from an initial literature review (29) were synthesized with stakeholder interview results into a series of mapping exercises that narrowed from a systems, to behaviour, to cognitive map. In this way, we formalized our understanding of how prescribing decisions are influenced by the context of the individual resident, their caregivers, the clinical environment, the healthcare system and the surrounding culture. We then used a barrier prioritization exercise with a working group of experts to identify barriers for our quality improvement (QI) strategies to address. This resulted in development of a two-pronged QI strategy for reducing diagnostic testing and antibiotic treatment of UTI when not clinically indicated. The first strategy consists of targeted education for essential care providers (ECPs; someone who provides important care for a resident and who is not on the medical team, e.g., family member or friend) to address ECP expectations for testing and treatment of UTI when not warranted. The second QI strategy consists of facility-level, monthly feedback about urine culture usage and reminders of guidelines, which will be given to LTCH staff to address the barrier of perceived risk of negative outcomes when choosing non-testing/treatment. Both QI strategies do not require explicit changes to work processes of LTCH staff, an important and advantageous consideration at a time when the Canadian healthcare sector faces human resource challenges.

The effectiveness of the QI strategies will be evaluated by assessing expected reductions in urine culture orders and antibiotic prescriptions for UTI. Whenever possible, we will also examine the proportion of urine cultures aligned with guidelines before and after intervention. A mixed-methods approach will evaluate the success of the study, with qualitative data helping contextualize quantitative findings.

The purpose of this study is to test novel behavioural AMS interventions in support of optimizing testing and treatment of UTI in LTCHs. The primary quantitative research questions are as follows: 1) What is the baseline usage of urine cultures in participating LTCHs?; and 2) Does implementation of the proposed QI strategies reduce the rates of a) urine cultures, b) antibiotic prescriptions for UTI and c) overall antibiotic prescriptions? Exploratory research questions will examine the baseline proportion of urine cultures aligned with guidelines and what risk factors are associated with collection of urine cultures when not aligned with guidelines. Qualitative data will also be collected to nuance quantitative findings.

Methods

Study overview

The study will be conducted in two stages. In the Pilot Stage, the protocol was implemented in a single LTCH for process evaluation (see **Appendix A: Protocol refinements**). The Trial Stage involves implementation in eight other LTCHs across Canada, with the main objective being an outcomes evaluation. The Trial Stage is designed as a stepped-wedge cluster randomized quality improvement study (**Table 1**) using a mixed-method approach. Quantitative data will evaluate the effectiveness of the protocol at reducing both testing and treatment for UTI, and qualitative data will contextualize the findings. Long-term care homes will be randomized to different starting times for the crossover from the control to intervention

Table 1: Overview of the stepped-wedge design

LTCH	Cluster	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8
a	1	C	C	T	I	I	I	I	I
b	1	C	C	T	I	I	I	I	I
c	2	C	C	C	T	I	I	I	I
d	2	C	C	C	T	I	I	I	I
e	2	C	C	C	T	I	I	I	I
f	3	C	C	C	C	T	I	I	I
g	4	C	C	C	C	C	T	I	I
h	4	C	C	C	C	C	T	I	I

Abbreviations: C, Control Phase (usual care is given); I, Intervention Phase (implementation of intervention); LTCH, long-term care home; T, Transition Phase (initiation of intervention)

phases, with staff and residents blinded to their allocation sequence. Here, we present the final protocol, including changes informed by Pilot Stage findings. For a complete list of refinements made to the protocol following the Pilot Stage, refer to Appendix A: Protocol refinements.

Sample characteristics

A purposive sampling strategy was used to recruit large (approximately 200 residents) LTCHs across Canada. To be eligible, LTCHs had to provide long-term (permanent placement) residential care with 24-hour monitoring and medical assistance. Sample size calculations using Hemming and Taljaard's approach (30) indicated that eight LTCHs across four clusters, observed for a total of eight months, would be sufficient to detect a clinically meaningful 20% reduction in rate of urine culture ordering (6.5 to 5.2 urine cultures per 1,000 resident days) at greater than 80% power and 5% significance level. The effect size is in line with previous studies that observed greater than 25% reduction in urine culture ordering (31,32) and is more conservative than 25% reduction used in sample size calculations for a similarly designed trial (33).

Two limitations of this trial are its smaller sample size and the purposive sampling technique, which will not provide a representative sample of LTCHs across Canada. However, this is the first pilot study of a novel intervention, so the smaller more homogenous sample will provide initial evidence on the effectiveness of the strategies, which will allow for improvement of the processes and materials.

Pilot Stage

The Pilot Stage took place in a single LTCH from May to August 2023, starting with retrospective data collection (for the period February 2022 to January 2023), continuing with a transition phase where the QI strategies were brought online and concluding with a one-month intervention phase. The main output from the Pilot Stage was a process evaluation to gather exploratory and evaluative insights to validate study materials, check assumptions, identify gaps in the interventions and evaluate in-field processes. A series of semi-structured interviews with LTCH staff (n=3), a focus group with ECPs (n=2), voluntary online surveys (n=10) and direct observation of the materials deployed in the home informed the process evaluation. In addition to these targeted sources of information input from the frontline workers of the Local Implementation Team was valuable to ground and validate our analytical interpretations in a deeper understanding of the local context of the home (34–36).

Fewer ECPs participated in the focus group than anticipated and this was likely at least partially due to the necessary timing of the pilot during the summer months, especially as the regular touchpoint of the resident family and friends council was on hiatus. However, even these few responses provided a valuable level of nuance regarding ECPs' perceptions of the educational materials and of UTI treatment best practices that helped to identify areas for consideration and improvement for the stepped-wedge trial.

Retrospective data collection

Facility and demographic data will be collected along with proposed outcomes metrics for a retrospective one-year period to provide historical insight, contextualize these data with home demographics and serve as true baseline for comparison with intervention phase data. Participating LTCHs will be provided detailed data dictionaries and template data entry forms to ensure consistency.

Control Phase

The Control Phase will last between two and five months, depending on cluster number (Table 1). During the Control Phase, usual care will be given to the LTCH residents, and minimum and additional data elements (such as the number of urine cultures ordered and catheter use) will be collected on a monthly basis, as necessary, to answer both the primary and exploratory research questions. The complete list of variables is provided in **Appendix B: Outcome metrics**.

Transition Phase

During the one-month Transition Phase, the research team will liaise with each LTCH to coordinate education and delivery of the interventions. The goals of the Transition Phase are to 1) provide level-setting foundational AMS knowledge and practices to help standardize the intervention across participating LTCHs and 2) coordinate the implementation of the intervention. To further

ensure alignment, the research team will offer to connect the medical leadership of each LTCH with a physician member of the study working group for an optional peer-to-peer conversation about the guidelines and their experience with implementation within their practice.

During this phase the research team will deliver brief education sessions for LTCH staff (nurses, physicians, non-regulated healthcare staff, pharmacists) about the overprescribing of antibiotics, a reminder of when it is and is not appropriate to test for and treat UTI in older adults (37,38) and practices that can contribute to this problem. These sessions will be delivered in-person or by webinar at the discretion of the LTCHs. A recording will be made available for new staff and those unable to attend the synchronous sessions.

Intervention Phase

The Intervention Phase will consist of two primary strategies: 1) ECP education and 2) monthly feedback letters to LTCH staff about facility urine culture ordering.

Essential care providers education: Although educational components are common in AMS interventions within LTCHs (14,18,38–46), they typically target physicians and/or nurses. Fewer studies have provided education for ECPs (11), despite ECPs' influence on testing and treatment decisions (16,47–49). We designed these educational resources to increase understanding of AMS and the harms of unnecessary antimicrobial use among ECPs, and to outline a positive advocacy role for ECPs in UTI management.

Drawing on lessons learned from the Pilot Stage, taking a multi-modal approach to ECP education will help reach a broader audience among this diverse target population. Brief education sessions will be delivered in-person by a LTCH staff trained by the research team and asynchronously by leveraging digital communications and in-home communications (e.g., UTI best practice posters in common areas). In-person and live virtual sessions will be offered monthly, with exact frequency to reflect each LTCH's unique needs, and delivered within regularly occurring events (e.g., monthly LTCH town halls). Educational materials will also be distributed to ECPs through videos, posters, newsletters and physical handouts made available at the LTCH. We hypothesize that this intervention will reduce urine culture ordering and antibiotic prescribing by increasing ECPs' knowledge about AMS and, therefore, decreasing caregiver expectations for these tests and treatments when not clinically indicated.

Feedback letter: This strategy consists of monthly feedback given to LTCH staff (i.e., nurses, non-regulated healthcare staff, pharmacists, physicians) that shows the rate of urine cultures ordered by their facility in the past month relative to their previous data (retrospective, Control, Transition and previous Intervention Phase when relevant). Audit and feedback on antibiotic prescription use have been embraced for use with physicians (50). Feedback to nurses and non-regulated healthcare staff, however, has not been used as an intervention strategy in LTCHs, yet these professionals play particularly important roles in LTCHs. They collaborate with physicians in making these decisions typically by assessing the resident and communicating their observations to the physician and, in some cases, collecting a urine sample before the physician has assessed the resident (49,51-53). Comparing recent with past performance acts as a self-comparison, which can motivate recipients by establishing personal norms (54) and has been effective in other contexts (55). Feedback will also indicate the proportion of urine cultures aligned with best practice guidelines (for LTCHs able to collect signs and symptoms data), which is a more specific measure of stewardship than overall ordering rate alone (56). We hypothesize that the feedback strategy will increase institutional awareness and reduce perceived risk of negative outcomes of urine culture avoidance, ultimately leading to a decrease in urine cultures and antibiotic prescriptions.

Feedback will be provided to all LTCH staff (nurses, non-regulated healthcare staff, pharmacists, physicians) starting after the first month of the Intervention Phase, for a total of two to five cycles of feedback depending on the cluster number. The LTCH implementation team will work with the research team to identify appropriate medium(s) for this feedback (e.g., central communications location on the floor, email, bulletin boards, regular staff meetings). The feedback letter will also include reminders regarding urine culture ordering decision guidelines (37,38) and links to additional resources.

Study measures

De-identified quantitative data will be collected monthly during the Control, Transition and Intervention Phases. Minimum data elements needed to answer the primary research questions include number of urine cultures ordered, antibiotic prescriptions for UTI, total antibiotic prescriptions and total days of residence. Additional data elements are necessary to answer the exploratory research questions and include signs and symptoms prompting urine culture orders, resident demographic characteristics, chronic conditions and functional status.

To contextualize the quantitative findings with the perspectives of the end users (LTCH staff and ECPs), we will additionally 1) conduct semi-structured interviews with 3–6 staff members from each LTCH after the Intervention Phase; 2) hold 2–3 focus groups with 4–6 ECPs each, within two months of the end of the intervention phase; and 3) collect qualitative data on perceptions and experience with the study through voluntary online questionnaires available to all LTCH staff and ECPs throughout the study. As with the Pilot Stage, qualitative data collection and validation will be supported by Local Implementation Teams.

Data analysis

A series of descriptive (continuous variables) and frequency analyses (categorical variables) will be conducted to get a global sense of the sample responses.

Analysis will be done at the level of the LTCH as an intention-to-treat analysis. To evaluate research question 1, rate of urine culture (per 1,000 resident days) will be calculated for the retrospective data period. To evaluate research question 2a, a generalized linear mixed-effects model will be used to assess whether or not the intervention has an effect on the rate of urine culture (per 1,000 resident days). The model will include categorical, fixed effects for phase (control/intervention) and for each month to account for secular trends, as well as a random effects for LTCH. Data from the Transition Phase will be excluded from these analyses as we do not consider these data to be clearly Control or Intervention Phase data. To evaluate research questions 2b and 2c, a similar model will be used with the outcome measures rate of antibiotic prescriptions for UTI and total antibiotic prescriptions per 1,000 resident days. Exploratory analyses will use a similar model to evaluate the potential effect of the intervention on rate of urine cultures not aligned with guidelines. Alignment with guidelines will be estimated by comparing the signs and symptoms prompting each urine culture to meet the modified Loeb minimum criteria for UTI for a catheterized or non-catheterized resident (37,38).

Thematic analysis will be guided by ethnographic methods and Normalization Process Theory. Taking an iterative approach that draws on Grounded Theory (35), open-ended codes will be applied alongside selected evaluative codes developed from a Normalization Process Theory perspective (57,58). Ethnographic data reduction techniques will be applied to surface focused insights to support the overarching research questions for the study (34,36,59).

Refinements to intervention based on Pilot Stage

A series of key observations drawn from the suite of qualitative methods employed were noted during the Pilot Stage: most staff who participated in interviews and ECPs who participated in the questionnaire and/or focus group viewed UTI guidelines as only relevant to residents without dementia, despite the guidelines' validation in LTCHs with residents with and without dementia (37,38). To address this challenge, two adjustments were made to the protocol: 1) the addition of an optional peer-to-peer conversation between the medical leadership of the LTCH and a physician member of the study's expert working group and 2) the revision of educational materials to highlight validation of guidelines in LTCHs and share experience in management of residents with dementia, including those that are non-communicative. For a full accounting of revisions in response to preliminary findings, see Appendix A.

Findings from the questionnaire, focus group and observations by staff interviewees and the Local Implementation Team indicated that the educational component of the intervention was generally appreciated by the ECPs, seeing it as relevant to their role as caregiver. However, it was observed across our qualitative data that ECPs constituted a heterogenous group and scheduling was, at times, challenging. Therefore, we increased our flexibility to offer multimodal delivery of educational materials (i.e., poster, handout, in-person session, video).

Regarding the feedback letter, members of the Local Implementation Team and all interviewed staff (n=3) expressed uncertainty about the intended use and action. Some concerns regarding the peer-comparison were also raised, highlighting the challenge of inter-home comparisons. To address these challenges, the following changes to the protocol were made: 1) inclusion of an estimate of proportion of urine cultures aligned with guidelines to provide a more actionable metric, 2) shift from peer-comparison to self-comparison to emphasize continual self-improvement and 3) highlighting links to additional supports and resources.

Conclusion

This study will rigorously evaluate the impact of a behavioural science-informed intervention to improve AMS across LTCHs. If successful, this model of care could be scalable across Canadian LTCHs, offering an inclusive approach that aims to empower clinicians, non-regulated healthcare staff, residents and their family and friends to improve health outcomes as antibiotic stewards.

Authors' statement

TG — Conceptualization, methodology, writing–original draft, writing–review & editing, investigation, data curation & analysis, project administration
JC — Methodology, writing–original draft, writing–review & editing
RM — Methodology, writing–original draft, writing–review & editing, investigation, data curation & analysis, project administration
KPuka — Methodology, writing–review & editing, data curation & analysis
SR — Methodology, writing–review & editing, project administration
BC — Methodology, writing–review & editing, project administration
AMounchili — Methodology, writing–review & editing
DG-T — Conceptualization, methodology, writing–review & editing
PQ — Conceptualization, methodology, writing–review & editing
AMcGeer — Methodology, writing–review & editing
AMoser — Conceptualization, methodology, writing–review & editing
MA — Conceptualization, methodology, writing–review & editing
PD — Conceptualization, methodology, writing–review & editing

KPiggott — Conceptualization, methodology, writing–review & editing
JL — Conceptualization, methodology, writing–review & editing
MM — Conceptualization, methodology, writing–review & editing, investigation, project administration

Competing interests

Dr. Leis reports support from Choosing Wisely Canada for a leadership role in the Using Antibiotics Wisely campaign. Dr. Moser is a board member of the Canadian Society for Long-Term Care and Ontario Long Term Care Clinicians and is also in a contracted role as the Corporate Medical Director for the City of Toronto's Senior Services and Long-Term Care Division and by the Institute for Safe Medication Practices. Madeleine Ashcroft sits on the Infection Prevention and Control Canada Board as Director of Standards and Guidelines. Dr. Piggott has a leadership role on Choosing Wisely Canada Geriatric Medicine.

ORCID numbers

Tyler Good — 0000-0002-4153-3917
Jorida Cila — 0000-0001-8741-0683
Rhiannon Mosher — 0000-0001-9230-2740
Klajdi Puka — 0000-0001-7763-988X
Patrick Quail — 0000-0002-9745-0993
Allison McGeer — 0000-0001-5647-6137
Andrea Moser — 0009-0001-5871-9785
Peter Daley — 0000-0001-7068-8056
Katrina Piggott — 0000-0001-7039-0436
Jerome Leis — 0000-0003-2250-4894
Mark Morrissey — 0000-0002-3300-162X

Acknowledgments

No.

Funding

The Public Health Agency of Canada, through the Antimicrobial Resistance Task Force is the funder of this research. Compensation will be provided directly to each participating home.

References

1. EClinicalMedicine. Antimicrobial resistance: a top ten global public health threat. EClinicalMedicine 2021;41:101221. DOI PubMed

2. Public Health Agency of Canada. Canadian Antimicrobial Resistance Surveillance System Report—Update 2020. Ottawa, ON: PHAC; 2020. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-2020-report.html

3. 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

4. Public Health Agency of Canada. Pan-Canadian Action Plan on Antimicrobial Resistance. Ottawa, ON: PHAC; 2023. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/pan-canadian-action-plan-antimicrobial-resistance.html

5. Eze N, Cecchini M, Hashiguchi TC. Antimicrobial resistance in long-term care facilities. OECD Health Working Papers. No. 136. OECD 2022. DOI

6. van Buul LW, van der Steen JT, Veenhuizen RB, Achterberg WP, Schellevis FG, Essink RT, van Benthem BH, Natsch S, Hertogh CM. Antibiotic use and resistance in long term care facilities. J Am Med Dir Assoc 2012;13(6):568.e1–13. DOI PubMed

7. Daneman N, Bronskill SE, Gruneir A, Newman AM, Fischer HD, Rochon PA, Anderson GM, Bell CM. Variability in Antibiotic Use Across Nursing Homes and the Risk of Antibiotic-Related Adverse Outcomes for Individual Residents. JAMA Intern Med 2015;175(8):1331–9. DOI PubMed

8. Wu JH, Langford BJ, Daneman N, Friedrich JO, Garber G. Antimicrobial Stewardship Programs in Long-Term Care Settings: A Meta-Analysis and Systematic Review. J Am Geriatr Soc 2019;67(2):392–9. DOI PubMed

9. Penney C, Boyd SE, Mansfield A, Dalton J, O'Keefe J, Daley PK. Antimicrobial use and suitability in long-term care facilities: A retrospective cross-sectional study. JAMMI 2018;3(4):209–16. DOI

10. Pulia M, Kern M, Schwei RJ, Shah MN, Sampene E, Crnich CJ. Comparing appropriateness of antibiotics for nursing home residents by setting of prescription initiation: a cross-sectional analysis. Antimicrob Resist Infect Control 2018;7:74. DOI PubMed

11. Brown KA, Chambers A, MacFarlane S, Langford B, Leung V, Quirk J, Schwartz KL, Garber G. Reducing unnecessary urine culturing and antibiotic overprescribing in long-term care: a before-and-after analysis. CMAJ Open 2019;7(1):E174–81. DOI PubMed

12. Trautner BW, Grigoryan L, Petersen NJ, Hysong S, Cadena J, Patterson JE, Naik AD. Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria. JAMA Intern Med 2015;175(7):1120–7. DOI PubMed

13. Smith MA, Puckrin R, Lam PW, Lamb MJ, Simor AE, Leis JA. Association of Increased Colony-Count Threshold for Urinary Pathogens in Hospitalized Patients With Antimicrobial Treatment. JAMA Intern Med 2019;179(7):990–2. DOI PubMed

14. Nace DA, Hanlon JT, Crnich CJ, Drinka PJ, Schweon SJ, Anderson G, Perera S. A Multifaceted Antimicrobial Stewardship Program for the Treatment of Uncomplicated Cystitis in Nursing Home Residents. JAMA Intern Med 2020;180(7):944–51. DOI PubMed

15. Rehan Z, Pratt C, Babb K, Filier B, Gilbert L, Wilson R, Daley P. Modified reporting of positive urine cultures to reduce treatment of asymptomatic bacteriuria in long-term care facilities: a randomized controlled trial. JAC Antimicrob Resist 2022;4(5):dlac109. DOI PubMed

16. Scales K, Zimmerman S, Reed D, Beeber AS, Kistler CE, Preisser JS, Weiner BJ, Ward K, Fann A, Sloane PD. Nurse and Medical Provider Perspectives on Antibiotic Stewardship in Nursing Homes. J Am Geriatr Soc 2017;65(1):165–71. DOI PubMed

17. Lohfeld L, Loeb M, Brazil K. Evidence-based clinical pathways to manage urinary tract infections in long-term care facilities: a qualitative case study describing administrator and nursing staff views. J Am Med Dir Assoc 2007;8(7):477–84. DOI PubMed

18. Pasay DK, Guirguis MS, Shkrobot RC, Slobodan JP, Wagg AS, Sadowski CA, Conly JM, Saxinger LM, Bresee LC. Antimicrobial stewardship in rural nursing homes: impact of interprofessional education and clinical decision tool implementation on urinary tract infection treatment in a cluster randomized trial. Infect Control Hosp Epidemiol 2019;40(4):432–7. DOI PubMed

19. Stagg A, Lutz H, Kirpalaney S, Matelski JJ, Kaufman A, Leis J, McCready J, Powis J. Impact of two-step urine culture ordering in the emergency department: a time series analysis. BMJ Qual Saf 2018;27(2):140–7. DOI PubMed

20. Vaughn VM, Gupta A, Petty LA, Malani AN, Osterholzer D, Patel PK, Younas M, Bernstein SJ, Burdick S, Ratz D, Szymczak JE, McLaughlin E, Czilok T, Basu T, Horowitz JK, Flanders SA, Gandhi TN. A Statewide Quality Initiative to Reduce Unnecessary Antibiotic Treatment of Asymptomatic Bacteriuria. JAMA Intern Med 2023;183(9):933–41. DOI PubMed

21. Crespo-Rivas JC, Guisado-Gil AB, Peñalva G, Rodríguez-Villodres Á, Martín-Gandul C, Pachón-Ibáñez ME, Lepe JA, Cisneros JM. Are antimicrobial stewardship interventions effective and safe in long-term care facilities? A systematic review and meta-analysis. Clin Microbiol Infect 2021;27(10):1431–8. DOI PubMed

22. Sirota M, Habersaat KB, Betsch C, Bonga DL, Borek A, Buckel A, Butler R, Byrne-Davis L, Caudell M, Charani E, Geiger M, Gross M, Hart J, Kostopoulou O, Krockow EM, Likki T, Lo Fo Wong D, Santana AP, Sievert ED, Theodoropoulou A, Thorpe A, Wanat M, Böhm R. We must harness the power of social and behavioural science against the growing pandemic of antimicrobial resistance. Nat Hum Behav 2023;8(1):11–3. DOI PubMed

23. Crayton E, Richardson M, Fuller C, Smith C, Liu S, Forbes G, Anderson N, Shallcross L, Michie S, Hayward A, Lorencatto F. Interventions to improve appropriate antibiotic prescribing in long-term care facilities: a systematic review. BMC Geriatr 2020;20(1):237. DOI PubMed

24. Chappell N, Gerard C, Gyani A, Hamblin R, Jansen RM, Lawrence A, Mackay J, Minko N, Roberts S, Shuker C, Te Karu L, White J. Using a randomised controlled trial to test the effectiveness of social norms feedback to reduce antibiotic prescribing without increasing inequities. N Z Med J 2021;134(1544):13–34. PubMed

25. Australian Government. Department of the Prime Minister and Cabinet. Nudge vs Superbugs: A behavioural economics trial to reduce the overprescribing of antibiotics. Canberra, AU: Australian Government; 2017. https://behavioraleconomics.pmc.gov.au/projects/nudge-vs-superbugs-behavioural-economics-trial-reduce-overprescribing-antibiotics

26. Hallsworth M, Chadborn T, Sallis A, Sanders M, Berry D, Greaves F, Clements L, Davies SC. Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial. Lancet 2016;387(10029):1743–52. DOI PubMed

27. Meeker D, Linder JA, Fox CR, Friedberg MW, Persell SD, Goldstein NJ, Knight TK, Hay JW, Doctor JN. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices a randomized clinical trial. JAMA 2016;315(6):562–70. DOI PubMed

28. Parzen-Johnson S, Kronforst KD, Shah RM, Whitmer GR, Scardina T, Chandarraju M, Patel SJ. Use of the Electronic Health Record to Optimize Antimicrobial Prescribing. Clin Ther 2021;43(10):1681–8. DOI PubMed

29. Vyas N, Good T, Cila J, Morrissey M, Tropper DG. Antibiotic prescribing and antimicrobial stewardship in long-term care facilities: past interventions and implementation challenges. Can Commun Dis Rep 2022;48(11/12):512–21. DOI PubMed

30. Hemming K, Taljaard M. Sample size calculations for stepped wedge and cluster randomised trials: a unified approach. J Clin Epidemiol 2016;69:137–46. DOI PubMed

31. Jump RL, Olds DM, Seifi N, Kypriotakis G, Jury LA, Peron EP, Hirsch AA, Drawz PE, Watts B, Bonomo RA, Donskey CJ. Effective antimicrobial stewardship in a long-term care facility through an infectious disease consultation service: keeping a LID on antibiotic use. Infect Control Hosp Epidemiol 2012;33(12):1185–92. DOI PubMed

32. Zabarsky TF, Sethi AK, Donskey CJ. Sustained reduction in inappropriate treatment of asymptomatic bacteriuria in a long-term care facility through an educational intervention. Am J Infect Control 2008;36(7):476–80. DOI PubMed

33. Jokanovic N, Haines T, Cheng AC, Holt KE, Hilmer SN, Jeon YH, Stewardson AJ, Stuart RL, Spelman T, Peel TN, Peleg AY; START Trial Group. Multicentre stepped-wedge cluster randomised controlled trial of an antimicrobial stewardship programme in residential aged care: Protocol for the START trial. BMJ Open 2021;11:e046142. https://bmjopen.bmj.com/content/bmjopen/11/3/e046142.full.pdf

34. Ladner, S. Mixed methods: A short guide to mixed methods. Sam Ladner; 2019.

35. Charmaz K. Grounded Theory. Approaches to Qualitative Research: A Reader on Theory and Practice. Oxford University Press 2004;496–521.

36. Sangaramoorthy T, Kroeger KA. Rapid Ethnographic Assessments: A Practical Approach and Toolkit for Collaborative Community Research. London: Routledge; 2020.

37. Loeb M, Bentley DW, Bradley S, Crossley K, Garibaldi R, Gantz N, McGeer A, Muder RR, Mylotte J, Nicolle LE, Nurse B, Paton S, Simor AE, Smith P, Strausbaugh L. Development of minimum criteria for the initiation of antibiotics in residents of long-term-care facilities: results of a consensus conference. Infect Control Hosp Epidemiol 2001;22(2):120–4. DOI PubMed

38. Loeb M, Brazil K, Lohfeld L, McGeer A, Simor A, Stevenson K, Zoutman D, Smith S, Liu X, Walter SD. Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial. BMJ 2005;331(7518):669. DOI PubMed

39. Cooper DL, Titler M, Struble L, Redman R. A multifaceted, evidence-based program to reduce inappropriate antibiotic treatment of suspected urinary tract infections. Ann Longterm Care 2017;25(2):36–43. https://www.hmpgloballearningnetwork.com/site/altc/articles/multifaceted-evidence-based-program-reduce-inappropriate-antibiotic-treatment-suspected

40. Fleet E, Gopal Rao G, Patel B, Cookson B, Charlett A, Bowman C, Davey P. Impact of implementation of a novel antimicrobial stewardship tool on antibiotic use in nursing homes: a prospective cluster randomized control pilot study. J Antimicrob Chemother 2014;69(8):2265–73. DOI PubMed

41. McMaughan DK, Nwaiwu O, Zhao H, Frentzel E, Mehr D, Imanpour S, Garfinkel S, Phillips CD. Impact of a decision-making aid for suspected urinary tract infections on antibiotic overuse in nursing homes. BMC Geriatr 2016 Apr;16:81. DOI PubMed

42. Monette J, Miller MA, Monette M, Laurier C, Boivin JF, Sourial N, Le Cruguel JP, Vandal A, Cotton-Montpetit M. Effect of an educational intervention on optimizing antibiotic prescribing in long-term care facilities. J Am Geriatr Soc 2007;55(8):1231–5. DOI PubMed

43. Naughton BJ, Mylotte JM, Ramadan F, Karuza J, Priore RL. Antibiotic use, hospital admissions, and mortality before and after implementing guidelines for nursing home-acquired pneumonia. J Am Geriatr Soc 2001;49(8):1020–4. DOI PubMed

44. Pettersson E, Vernby A, Mölstad S, Lundborg CS. Can a multifaceted educational intervention targeting both nurses and physicians change the prescribing of antibiotics to nursing home residents? A cluster randomized controlled trial. J Antimicrob Chemother 2011;66(11):2659–66. DOI PubMed

45. van Buul LW, van der Steen JT, Doncker SM, Achterberg WP, Schellevis FG, Veenhuizen RB, Hertogh CM. Factors influencing antibiotic prescribing in long-term care facilities: a qualitative in-depth study. BMC Geriatr 2014;14:136. DOI PubMed

46. Zimmerman S, Sloane PD, Bertrand R, Olsho LE, Beeber A, Kistler C, Hadden L, Edwards A, Weber DJ, Mitchell CM. Successfully reducing antibiotic prescribing in nursing homes. J Am Geriatr Soc 2014;62(5):907–12. DOI PubMed

47. Kistler CE, Zimmerman S, Scales K, Ward K, Weber D, Reed D, McClester M, Sloane PD. The Antibiotic Prescribing Pathway for Presumed Urinary Tract Infections in Nursing Home Residents. J Am Geriatr Soc 2017;65(8):1719–25. https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/jgs.14857

48. Laur C, Sribaskaran T, Simeoni M, Desveaux L, Daneman N, Mulhall C, Lam J, Ivers NM. Improving antibiotic initiation and duration prescribing among nursing home physicians using an audit and feedback intervention: a theory-informed qualitative analysis. BMJ Open Qual 2021;10(1):e001088. DOI PubMed

49. Schweizer AK, Hughes CM, Macauley DC, O'Neill C. Managing urinary tract infections in nursing homes: a qualitative assessment. Pharm World Sci 2005;27(3):159–65. DOI PubMed

50. Schwartz KL, Xu AX, Alderson S, Bjerrum L, Brehaut J, Brown BC, Bucher HC, De Sutter A, Francis N, Grimshaw J, Gunnarsson R, Hoye S, Ivers N, Lecky DM, Lindbæk M, Linder JA, Little P, Michalsen BO, O'Connor D, Pulcini C, Sundvall PD, Lundgren PT, Verbakel JY, Verheij TJ. Best practice guidance for antibiotic audit and feedback interventions in primary care: a modified Delphi study from the Joint Programming Initiative on Antimicrobial resistance: Primary Care Antibiotic Audit and Feedback Network (JPIAMR-PAAN). Antimicrob Resist Infect Control 2023;12(1):72. DOI PubMed

51. Ramly E, Tong M, Bondar S, Ford JH 2nd, Nace DA, Crnich CJ. Workflow Barriers and Strategies to Reduce Antibiotic Overuse in Nursing Homes. J Am Geriatr Soc 2020;68(10):2222–31. DOI PubMed

52. Russell J, Gallen D. Influencing factors on antibiotic prescribing in nursing homes. Prim Health Care Res Dev 2003;4(1):69–75. DOI

53. Fleming A, Bradley C, Cullinan S, Byrne S. Antibiotic prescribing in long-term care facilities: a meta-synthesis of qualitative research. Drugs Aging 2015;32(4):295–303. DOI PubMed

54. Proman M, Brunswicker S. Affordances Of Eco-Feedback Design in Home Energy Context. American Conference on Information Systems. 2017. https://aisel.aisnet.org/amcis2017/GreenIS/Presentations/7/

55. Otaki Y, Honda H, Ueda K. Historical Self-Comparison of Water Consumption as a Water Demand Management Tool. Water 2019;11(4):844. DOI

56. Chung GW, Wu JE, Yeo CL, Chan D, Hsu LY. Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes. Virulence 2013;4(2):151–7. DOI PubMed

57. Kousgaard MB, Olesen JA, Arnold SH. Implementing an intervention to reduce use of antibiotics for suspected urinary tract infection in nursing homes - a qualitative study of barriers and enablers based on Normalization Process Theory. BMC Geriatr 2022;22(1):265. DOI PubMed

58. May C, Finch T. Implementation, embedding, and integration: An outline of Normalization Process Theory. Sociology 2009;43(3):535–54. DOI

59. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol 2013;13:117. DOI PubMed

Appendices

Appendix A: Protocol refinements

The following table summarizes changes made to the protocol following the Pilot Stage. The protocol described in the paper reflects these changes.

Change	Change made	Description
1	Addition of an optional peer-to-peer conversation between physician member of the study expert working group and medical leadership at each home at the beginning of the Transition Phase	A goal of our Transition Phase is level-setting (getting everyone on the same page) about foundational AMS knowledge and practices. To facilitate this, we meet with the implementation team at each LTCH and review current practices and alignment with guidelines. To strengthen this, the protocol now includes an optional peer-to-peer conversation between a physician member of the working group and the medical leadership at each LTCH (i.e., Medical Director, Physician Chief). The intention is for these conversations to cover the evidence supporting the guidelines and the experiences the working group member had in implementing them in their practice.
2	Explicit inclusion of clinical pharmacists and personal support workers	The protocol now calls for clinical pharmacists employed by the home and non-regulated healthcare staff (sometimes referred to as personal support workers or nursing assistants) to attend the introductory education session provided during the Transition Phase, along with nursing staff and physicians. Previously these groups were not explicitly named in our protocol, despite being likely to interact with study materials present in staff areas (e.g., a monthly feedback report at the nursing station). This change appropriately includes them as important members of the clinical team that a portion of the responsibility for AMS.
3	Increased flexibility in delivery of staff introductory education session	The duration of the introductory education session was reduced to 5–10 minutes and the protocol calls for it to be presented in-person, by webinar or via recorded video at the discretion of the LTCH. This increased flexibility is intended to allow for the adaption to the unique circumstances and procedures of staff training at each LTCH. The session is now provided to nurses, physicians, clinical pharmacists and non-regulated healthcare staff (personal support workers, nursing assistants, etc.), as per change 2.
4	Narrowing of prospective data collection	The protocol now includes collection of signs and symptoms prompting all urine culture orders during the Control, Transition and Intervention Phases. This allows an estimation of the proportion of cultures that are aligned with guidelines. A measure of alignment with guidelines will allow for a more precise measure of AMS compared to rate of urine culture alone. Alignment with guidelines will be used as an exploratory evaluation of the success of the trial (pre-post comparison) as well as a component of the feedback report. To balance the additional workload to LTCHs collecting this data, the protocol also limits the previously required monthly facility-level demographic data from all residents of the LTCH to only those who received a urine culture. The previous monthly facility-level demographics provided little additional value to the cross-sectional demographic data collected with the retrospective data. If some LTCHs are unable to provide signs and symptoms data, we will 1) report this finding, which will highlight an important knowledge gap, 2) remain adequately powered to evaluate the study using rate of urine culture order and 3) antibiotic prescription for UTI as previously planned.
5	Updates to feedback letter content	The protocol now calls for the feedback letter to provide a self-comparison of LTCH urine culture order rate over time, as well as an estimate of the proportion of urine culture orders that were aligned with guidelines. Previously, the protocol called for a peer-comparison of urine culture order rate between the LTCHs included in the Trial Stage, as well as comparison with historical data. The change avoids limitations of inter-home comparisons and allows for a focus on self-comparison in the spirit of continual improvement.
6	Increased opportunity for qualitative engagement with staff	The protocol calls for a minimum of three, but opportunity for six semi-structured interviews at each LTCH. This is a change from the previous protocol which required three interviews, with no opportunity for more. The protocol also includes a voluntary online questionnaire available to LTCH staff. This mirrors the questionnaire provided to ECPs, asking about LTCH staff's experience with our study and suggestions for improvements. Together, these changes provide opportunity to supplement qualitative findings from a previously small number of interviews, only if there is interest and capacity at each LTCH. The online questionnaire provides a mechanism for all LTCH staff to share feedback, if they choose to do so.

Abbreviations: AMS, antimicrobial stewardship; ECP, essential care provider; LTCH, long-term care home; UTI, urinary tract infection

Appendix B: Outcome metrics

The intervention study will be collecting data on the following key outcomes:

1. Outcomes related to urine culture orders
   a. Baseline prevalence of urine cultures for diagnosis of urinary tract infections (UTIs)
   b. Effect of intervention on decreasing rate of urine culture orders
   c. Effect of intervention on decreasing rate of urine culture orders aligned with guidelines

2. Outcomes related to antibiotic use
   a. Baseline usage of antibiotics
   b. Effect of intervention on reducing incidence of antibiotic prescriptions written for suspected UTIs
   c. Effect of intervention on reducing duration of written urinary antibiotic prescriptions
   d. Effect of intervention on reducing incidence of total antibiotic prescriptions
   e. Effect of intervention on duration of total antibiotic prescriptions

3. Outcomes related to essential care provider (ECP) education
   a. Long-term care home (LTCH) staff perceptions on whether ECP education reduced pressure from ECPs to collect urine cultures for testing when not clinically indicated
   b. LTCH staff perceptions on whether ECP education reduced pressure from ECPs for antibiotic treatment of UTIs when not clinically indicated

4. Outcomes related to feedback letter
   a. LTCH staff perceptions on whether the feedback letter reduced their perceived risk of negative outcomes when not ordering diagnostic testing or treatment for UTIs when not clinically indicated

In addition to the above, we will also be collecting data on additional outcomes to test some exploratory research questions (e.g., result of urine culture; antibiotic dosage, duration and route of administration; catheter use; ethnicity; sex; age; chronic conditions).

Appendix C: Affiliations

[1] Data, Surveillance and Foresight Branch, Public Health Agency of Canada, Ottawa, ON

[2] Impact & Innovation Unit, Privy Council Office, Ottawa, ON

[3] Infectious Diseases and Vaccination Programs Branch, Public Health Agency of Canada, Ottawa, ON

[4] Department of Family Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB

[5] Department of Laboratory Medicine & Pathobiology, University of Toronto, Toronto, ON

[6] Department of Family and Community Medicine, University of Toronto, Toronto, ON

[7] City of Toronto Senior Services and Long-Term Care Division, Toronto, ON

[8] Trillium Health Partners, Toronto, ON

[9] Newfoundland and Labrador Health Services, Memorial University of Newfoundland, St. John's, NL

[10] Memorial University of Newfoundland, St. John's, NL

[11] Sunnybrook Health Sciences Centre, Toronto, ON

[12] Department of Medicine and Centre for Quality Improvement and Patient Safety, Temerty Faculty of Medicine, University of Toronto, Toronto, ON

CCDR

CANADA COMMUNICABLE DISEASE REPORT

Public Health Agency of Canada
130 Colonnade Road
Address Locator 6503B
Ottawa, Ontario K1A 0K9
ccdr-rmtc@phac-aspc.gc.ca

To promote and protect the health of Canadians through leadership, partnership, innovation and action in public health.

Public Health Agency of Canada

Published by authority of the Minister of Health.

This publication is also available online at

https://www.canada.ca/ccdr

Également disponible en français sous le titre :
Relevé des maladies transmissibles au Canada