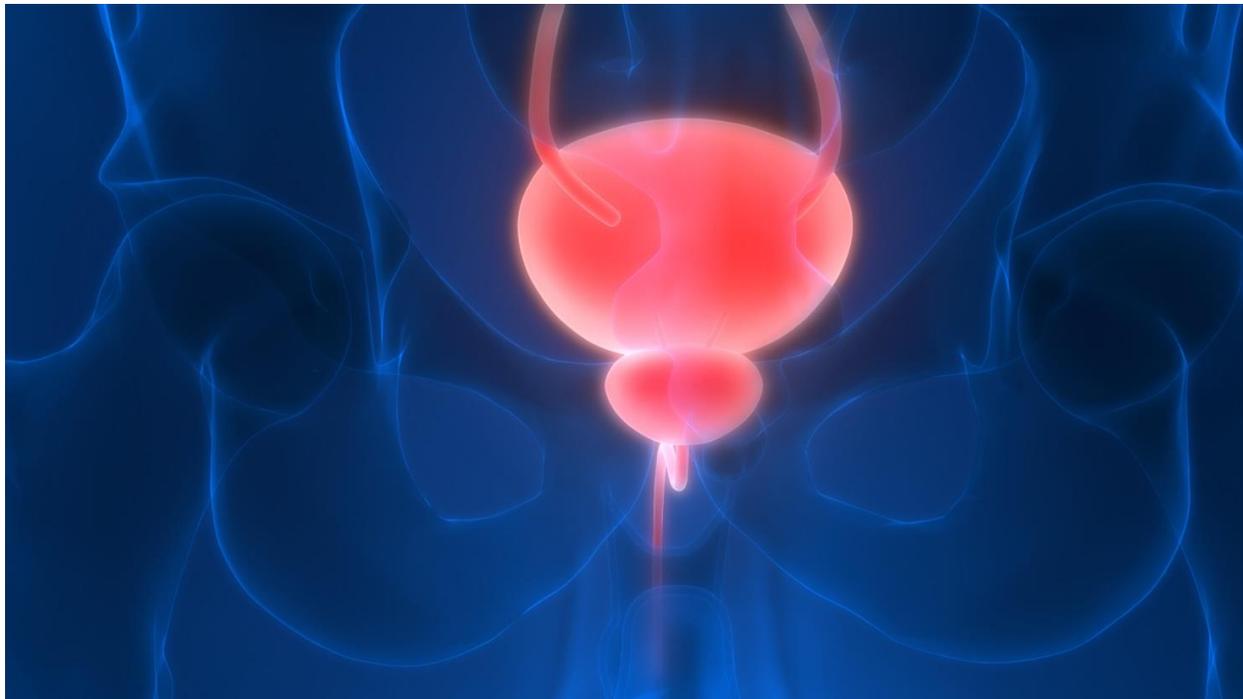


## EVIDENCE BRIEF

# Duration of Antibiotic Treatment for Uncomplicated Urinary Tract Infection in Long-Term Care Residents



October 2018

## Key Messages

- Recent evidence suggests that short courses of antibiotics (7 days or less) are appropriate for older adults with uncomplicated lower urinary tract infections.
- There are several advantages to short course antibiotic therapy when compared to longer durations, including less side effects,<sup>1,2</sup> less risk of antibiotic-resistant organisms<sup>3,4</sup> and less risk of *C. difficile* infection.<sup>5</sup>

## Issue and Research Question

Overuse of antimicrobial therapy in the long term care (LTC) setting is common and leads to patient harm.<sup>6</sup> Seventy eight (78) % of Ontario LTC residents will receive at least one course of antimicrobial therapy over the course of a year. Of these prescriptions, one third are prescribed for urinary indications. At least one-third of these prescriptions are for asymptomatic bacteriuria, a condition that does not benefit from antimicrobial treatment in older adults.<sup>7</sup>

Sixty three (63) % of prescribed courses of antibiotic treatment in LTC are longer than 10 days. Duration of therapy varies drastically based on prescriber, but not patient characteristics.<sup>8</sup> This overall long duration and prescriber variability persists when examining management of urinary tract infections. This data suggests that habit and experience play a large role in antibiotic prescribing patterns in long-term care, particularly for urinary tract infections.

Due to the increased susceptibility to UTIs in older individuals, a function of reduced immune response and altered bladder function, elderly are often treated with longer antibiotic courses than younger patients.<sup>9</sup> However, there is a lack of data that support the concept that longer courses are superior in this population. Additionally, older individuals are more prone to adverse drug events, drug interactions and the collateral damage of antimicrobial resistance.

Uncertainty exists regarding the appropriate management of symptomatic urinary tract infections in residents of LTC homes, particularly with respect to the appropriate duration of therapy. Additionally, there is controversy in North American guidelines with respect to the appropriate duration of treatment for these infections. This document will summarize the literature pertaining to treatment of uncomplicated lower UTI in LTC residents, with a focus on optimal duration of therapy.

## Methods

An initial Cochrane Database search was performed to determine if there were any relevant systematic reviews. Following this, a full primary literature search was performed. On November 8, 2016, Public Health Ontario (PHO) Library Services performed a literature search of articles published since 2008 using three databases (MEDLINE, Embase, CINAHL). The search included the concepts “urinary tract infection,” “elderly,” “antibiotic” and “duration.” Both primary literature and review articles were searched to comprehensively capture all relevant literature. English-language articles retrieved by the searches were assessed for eligibility by PHO staff. Articles were included if they were interventional studies comparing short course (<7 days) to longer courses (≥ 7 days) for treatment of uncomplicated lower UTI in elderly individuals. Single-dose studies were excluded.

## Main Findings

A Cochrane database search on the topic of “urinary tract infection” revealed 35 reviews, with one relevant to this question. The initial literature search for articles published between May 6, 2008 and November 8, 2016 retrieved 2,236 references. After title and abstract screening, no eligible studies were found on this topic.

A 2008 Cochrane Review (includes all primary literature up until May 6, 2008) examined 15 studies including 1,644 elderly women comparing duration of antibiotic treatment for uncomplicated urinary tract infection (UTI).<sup>10</sup> The authors found that single dose antibiotic therapy was inferior to short or long courses of treatment.

**Short course antibiotic therapy (less than 7 days) results in similar outcomes compared to long durations (7-10 days) for cystitis.**

However, short course antibiotic therapy (3-6 days) had similar efficacy to long durations (7-14 days).<sup>10</sup> Examining the pooled data, no differences were found in terms of clinical failure with short vs. long treatment (risk ratio: 0.98, 95% confidence interval; 0.62 to 1.54), microbiological persistence (risk ratio: 0.85, 95% confidence interval; 0.54 to 1.32) or discontinuation due to adverse events (risk ratio: 0.11, 95% confidence interval; 0.01 to 1.97). However, one study found a higher risk of adverse effects in elderly that received 7 days compared to a 3 day course of treatment.<sup>11</sup>

Appendix A includes a table summarizing all studies comparing short course (3-6 days) to long course (7-14 days) of antibiotics for treatment of uncomplicated urinary tract infections in older patients.<sup>11,21-25</sup>

## Discussion and Conclusions

There is a lack of data examining the optimal duration of antibiotic treatment for uncomplicated lower UTI in LTC residents. However, there are several studies in older adults, summarized in a Cochrane review,<sup>10</sup> showing that shorter courses of antibiotics (3-6 days) have similar efficacy to longer courses (7-14 days).

Limitations of this data include:

- Most data is from sub-populations of older adults, resulting in wide confidence intervals, with low precision.
- Majority of RCTs are not designed as non-inferiority analyses and may be underpowered.
- The bulk of studies focus on fluoroquinolones for short course therapy, agents that are no longer considered first line.

Although the Vogel study<sup>11</sup> examines the use of fluoroquinolones, it overcomes most of the above limitations. It includes only women over the age of 65 and a subset of hospitalized patients (23%). The study design is a non-inferiority analysis and is adequately powered. Based on this study, it is reasonable to recommend short courses of antibiotics for older residents of LTC homes, particularly when using fluoroquinolones.

A Cochrane review comparing 3 days to 5-10 days of therapy for uncomplicated lower UTI in those aged 18-65 found similar results. Pooled data from 32 trials (9,605 patients) showed no difference in symptomatic failure between short and long course therapy for both short-term (RR 1.06, 95% CI 0.88

to 1.28) and long-term (RR 1.09, 95% CI 0.94 to 1.27) follow-up. Although the longer treatment course was associated with a lower risk of bacteriological failure, the clinical significance of this finding is not clear. No differences were found when looking at subgroups of antibiotic classes (quinolones, sulfonamides, beta-lactams).<sup>1</sup>

However, the use of short course beta-lactam treatment in UTI is controversial. A RCT published after this analysis indicated that 3 days of beta-lactam (amoxicillin-clavulanate) therapy was inferior to 3 days of ciprofloxacin.<sup>12</sup> This is in keeping with an older review showing that 5 days of beta-lactam therapy is superior to 3 days of therapy.<sup>13</sup> This concern is echoed by the Infectious Diseases Society of America (IDSA) Urinary Tract Infection Guidelines that highlight that beta-lactam agents have inferior efficacy compared to other first-line agents and may require a course of 5-7 days to improve efficacy.<sup>14</sup>

Neither the Cochrane review in younger nor older patients examined short course nitrofurantoin for uncomplicated UTI; however, there is robust data to support a duration as short as 5 days of nitrofurantoin in these patients.<sup>15</sup>

In addition, there are several risks to prolonged courses of antimicrobial therapy. Due to physiological changes associated with aging, older adults are more susceptible to the negative consequences of antibiotics, including adverse effects<sup>13,16</sup> and drug interactions.<sup>21</sup> The Cochrane review in patients aged 18-65 with UTI also found an increased risk of adverse effects (gastrointestinal, dermatological) in those with prolonged therapy compared to the shorter duration group. Prolonged antimicrobial therapy has been shown in many studies to result in a greater risk of acquiring antibiotic resistant organisms.<sup>5,6</sup> Additionally, longer durations of antimicrobial therapy are associated with increased risk of *C. difficile* infection (CDI).<sup>7</sup> Older adults are already more susceptible to CDI and more likely to suffer morbidity and mortality from this infection.<sup>17</sup>

While this review focused on uncomplicated cystitis, there is evidence that shorter courses (7 days) are adequate in men with non-prostatic lower UTI and those with catheter-associated UTIs.<sup>18-20</sup> On the other hand, prolonged courses (10-14 days) are still recommended in residents with pyelonephritis, bacteremia or deep-seated infection (e.g., peri-nephric abscess). Even in these scenarios there is emerging evidence that 7 days of treatment might be sufficient.<sup>26,27</sup>

Given the lack of proven efficacy with longer courses, in combination with the risks associated with prolonged antibiotic therapy, short course treatment (7 days or less) should be used whenever possible for management of uncomplicated UTI in LTC home residents.

**Treatment of asymptomatic bacteriuria in LTC residents is not recommended, as it does not improve outcomes and can lead to harm. For more information on preventing treatment of asymptomatic bacteriuria, see Public Health Ontario's [UTI Program](#).**

## Appendix A

### Studies comparing duration of antibiotic therapy for uncomplicated cystitis in older patients

Study	Design	Patients	Intervention	Comparator	Outcomes
Vogel, 2004 <sup>11</sup>	Randomized (Non-inferiority, margin=10%) Double blind Multi-center	Uncomplicated lower UTI in women $\geq$ 65, hospitalized or ambulatory  n=183	Ciprofloxacin 250 mg PO bid x 3 days	Ciprofloxacin 250 mg PO bid x 7 days	Bacterial Eradication: (after therapy) 3 days: 98% 7 days: 93% RR=1.05 (0.93-1.07)  Clinical failure (after therapy) 3 days: 0% 7 days: 3% RR=0.36 (0.02-8.63)
Guibert J, 1997 <sup>21</sup> (French)	Randomized Open Label Multi-center	Recurrent uncomplicated lower UTI in ambulatory women $\geq$ 18 years n=421  Subgroup $\geq$ 50 years n=92	Lomefloxacin 400 mg PO daily x 3 days	Norfloxacin 500 mg PO bid x 10 days	Patient acceptability (little or not satisfied with treatment) 3 days: 4% 10 days: 12%  RR 0.35 (0.07-1.72)
Piipo T, 1990 <sup>22</sup>	Randomized Double blind Multi-center	Uncomplicated lower UTI in ambulatory women 18-80 years n=400  Subgroup $\geq$ 65 years n=65	Norfloxacin 400 mg PO bid x 3 days	Norfloxacin 400 mg PO bid x 7 days	Microbiological failure: 3 days: 17% 7 days: 7%  RR= 2.57 (0.56-11.81)
Raz R, 1996 <sup>23</sup>	Randomized Open Label	Uncomplicated lower UTI in ambulatory	Ofloxacin 200 mg PO daily x 3 days	Cephalexin 500 mg PO bid x 7 days	Microbiological failure (after therapy)

Study	Design	Patients	Intervention	Comparator	Outcomes
	Single-center	post-menopausal women  n=223			3 days: 23% 7 days: 37% RR= 0.62 (0.41 - 0.94)  Clinical failure (after therapy) 3 days: 23% 7 days: 23% RR = 0.98 (0.61 - 1.59)  Symptom recurrence (at 28 days) 3 days: 24% 7 days: 33% RR = 0.75 (0.49 -1.13)
Stein, 1992 <sup>24</sup>	Randomized Double Blind Multi-center	Uncomplicated lower UTI in women ≥ 18 years n=404  Subgroup ≥65 years n=81	Temafloxacin 400 mg PO daily x 3 days	Ciprofloxacin 250 mg PO bid x 7 days	Clinical failure (after therapy) Nil in both groups
van Merode, 2005 <sup>25</sup>	Randomized Single blind Multi-center	Uncomplicated lower UTI in women 13-77 n=129  Subgroup ≥60 years n=26	Trimethoprim PO x 3 days (dose not specified)	Trimethoprim PO x 5 days (dose not specified)	Microbiological failure (after therapy) 3 days: 58% 5 days: 21% RR=2.72 (0.9-8.27)  Clinical failure (after therapy) 3 days: 25% 5 days: 21% RR=1.17 (0.29-4.74)

## Specifications and Limitations of Evidence Brief

The purpose of this Evidence Brief is to investigate a research question in a timely manner to help inform decision making. The Evidence Brief presents key findings, based on a systematic search of the best available evidence near the time of publication, as well as systematic screening and extraction of the data from that evidence. It does not report the same level of detail as a full systematic review. Every attempt has been made to incorporate the highest level of evidence on the topic. There may be relevant individual studies that are not included; however, it is important to consider at the time of use of this brief whether individual studies would alter the conclusions drawn from the document.

## Additional Resources

- [Duration of Antibiotic Treatment for Pneumonia in Long-Term Care Residents](#) (Evidence Brief)
- [Shorter is Smarter: Reducing Duration of Antibiotic Treatment for Common Infections in Long-Term Care](#) (Fact Sheet)
- [Shorter is Smarter: Reduce Duration of Antibiotic Therapy in Long-Term Care](#) (Infographic)
- [Duration of Antibiotic Treatment for Uncomplicated Urinary Tract Infection in Long-Term Care Residents](#) (Evidence Brief)
- [Duration of Antibiotic Treatment for Uncomplicated Cellulitis in Long-Term Care Residents](#) (Evidence Brief)

## References

1. Milo G, Katchman EA, Paul M, Christiaens T, Baerheim A, Leibovici L. Duration of antibacterial treatment for uncomplicated urinary tract infection in women. *Cochrane Database Syst Rev.* 2005;(8):CD004682.
2. Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, Rochette L. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial. *CMAJ.* 2004;170(4):469-73. Available from: <http://www.cmaj.ca/content/170/4/469.long>
3. Chastre J, Wolff M, Fagon JY, Chevret S, Thomas F, Wermert D, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. *JAMA.* 2003;290(19):2588-98. Available from: <https://jamanetwork.com/journals/jama/fullarticle/197644>
4. Goessens WH, Verbrugh HA. [Antibiotic resistance: epidemiological developments and preventive measures]. *Ned Tijdschr Geneeskd.* 2007;151(13):748-52.
5. Owens RC Jr, Donskey CJ, Gaynes RP, Loo VG, Muto CA. Antimicrobial-associated risk factors for *Clostridium difficile* infection. *Clin Infect Dis.* 2008;46 Suppl 1:S19-31. Available from: [https://academic.oup.com/cid/article/46/Supplement\\_1/S19/455084](https://academic.oup.com/cid/article/46/Supplement_1/S19/455084)
6. Daneman N, Bronskill SE, Gruneir A, Newman AM, Fischer HD, Rochon PA, et al. 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. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2337257>
7. Mody L, Crnich C. Effects of excessive antibiotic use in nursing homes. *JAMA Intern Med.* 2015;175(8):1339-41. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4626211/>
8. Daneman N, Gruneir A, Bronskill SE, Newman A, Fischer HD, Rochon PA, et al. Prolonged antibiotic treatment in long-term care: role of the prescriber. *JAMA Intern Med.* 2013;173(8):673-82. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1669102>
9. Reid G, Zorzitto ML, Bruce AW, Jewett MA, Chan RC, Costerton JW. Pathogenesis of urinary tract infection in the elderly: the role of bacterial adherence to uroepithelial cells. *Curr Microbiol.* 1984;11(2):67-72.
10. Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. *Cochrane Database Syst Rev.* 2008;(3):CD001535.
11. Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, Rochette L. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial. *CMAJ.* 2004;170(4):469-73. Available from: <http://www.cmaj.ca/content/cmaj/170/4/469.full.pdf>

12. Hooton TM, Scholes D, Gupta K, Stapleton AE, Roberts PL, Stamm WE. Amoxicillin-clavulanate vs ciprofloxacin for the treatment of uncomplicated cystitis in women: a randomized trial. *JAMA*. 2005;293(8):949-55. Available from: <https://jamanetwork.com/journals/jama/fullarticle/200414>
13. Norrby SR. Short-term treatment of uncomplicated lower urinary tract infections in women. *Rev Infect Dis*. 1990;12(3):458-67.
14. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103-20. Available from: <https://academic.oup.com/cid/article/52/5/e103/388285>
15. Gupta K, Hooton TM, Roberts PL, Stamm WE. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. *Arch Intern Med*. 2007;167(20):2207-12. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/413431>
16. Faulkner CM, Cox HL, Williamson JC. Unique aspects of antimicrobial use in older adults. *Clin Infect Dis*. 2005;40(7):997-1004. Available from: <https://academic.oup.com/cid/article/40/7/997/373878>
17. Miller M, Gravel D, Mulvey M, Taylor G, Boyd D, Simor A, et al. Health care-associated *Clostridium difficile* infection in Canada: patient age and infecting strain type are highly predictive of severe outcome and mortality. *Clin Infect Dis*. 2010;50(2):194-201. Available from: <https://academic.oup.com/cid/article/50/2/194/328758>
18. Drekonja DM, Rector TS, Cutting A, Johnson JR. Urinary tract infection in male veterans: treatment patterns and outcomes. *JAMA Intern Med*. 2013;173(1):62-8. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1470563>
19. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(5):625-63.
20. Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary tract infection and asymptomatic bacteriuria in older adults. *Infect Dis Clin North Am*. 2017;31(4):673-88. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5802407/>
21. Guibert J, Herman H, Capron MH. [Treatment of uncomplicated recurrent cystitis in women: lomefloxacin versus norfloxacin]. *Contracept Fertil Sex*. 1997;25(1):79-84.
22. Piippo T, Pitkääjärvi T, Salo SA. Three-day versus seven-day treatment with norfloxacin in acute cystitis. *Curr Ther Res*. 1990;47(4):644-53.
23. Raz R, Rozenfeld S. 3-day course of ofloxacin versus cefalexin in the treatment of urinary tract infections in postmenopausal women. *Antimicrob Agents Chemother*. 1996;40(9):2200-1. Available from: <http://aac.asm.org/content/40/9/2200.long>

24. Stein GE, Philip E. Comparison of three-day temafloxacin with seven-day ciprofloxacin treatment of urinary tract infections in women. *J Fam Pract.* 1992;34(2):180-4.
25. van Merode T, Nys S, Raets I, Stobberingh E. Acute uncomplicated lower urinary tract infections in general practice: clinical and microbiological cure rates after three-versus five-day treatment with trimethoprim. *Eur J Gen Pract.* 2005;11(2):55-8.
26. Yahav D, Turjeman A, Babitch T, Koppel F, Bitterman R, Neuberger A, et al. Seven versus 14 antibiotic days for the treatment of Gram-negative bacteraemia: non-inferiority randomized controlled trial. Paper presented at: European Congress of Clinical Microbiology and Infectious Diseases. 2018 April 21-24; Madrid.
27. Sandberg T, Skoog G, Hermansson AB, Kahlmeter G, Kuylenstierna N, Lannergård A, et al. Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial. *Lancet.* 2012;380(9840):484-90.

## Authors

Bradley Langford, Antimicrobial Stewardship Pharmacist Consultant, Infection Prevention and Control, Public Health Ontario.

## Contributors

Rita Ha, Antimicrobial Stewardship Pharmacist Consultant, Infection Prevention and Control, Public Health Ontario.

Nick Daneman, Scientist and Physician, Infection Prevention and Control , Public Health Ontario

Kevin Schwartz, Scientist and Physician, Infection Prevention and Control , Public Health Ontario

## Reviewers

Dan Dalton, Pharmacist, Medical Pharmacies Group Ltd.

Carrie Heer, Nurse Practitioner, St. Joseph's Health Centre, Guelph

Justin Lin, Pharmacist, Medical Pharmacies Group Ltd.

Heidi Wittke, Director, Clinical, Medisystems Pharmacy

Louis Kennedy, Hospitalist, Providence Care Hospital, Medical Director, Arbour Heights LTC

Allan Grill, Lead Physician, Markham Family Health Team

## Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Duration of antibiotic treatment for uncomplicated urinary tract infection in long-term care residents. Toronto, ON: Queen's Printer for Ontario; 2018.

ISBN: 978-1-4868-2516-5

©Queen's Printer for Ontario, 2018

## Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario's government, public health organizations and health care providers. PHO's work is guided by the current best available evidence at the time of publication.

The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

This document may be reproduced without permission for non-commercial purposes only and provided that appropriate credit is given to PHO. No changes and/or modifications may be made to this document without express written permission from PHO.

## For Further Information

Antimicrobial Stewardship Program, Infection Prevention and Control

Email: [ASP@oahpp.ca](mailto:ASP@oahpp.ca)

## Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit [publichealthontario.ca](http://publichealthontario.ca).



Public Health Ontario acknowledges the financial support of the Ontario Government.