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HIV AND OTHER SEXUALLY TRANSMITTED AND BLOOD-BORNE INFECTIONS

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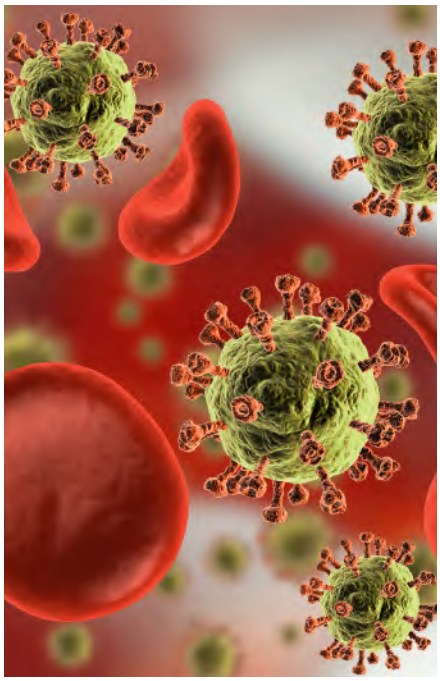

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RAPID COMMUNICATION

Risk of sexual transmission of HIV in the context of viral load suppression

Pascal Djiadeu[1]*, Housne Begum[1], Stacy Sabourin[1], Stephan Gadient[1], Chris Archibald[1], Marc-André LeBlanc[1], Andrea Chittle[1], Annie Fleurant[1], Joseph Cox[1]

Abstract

Background: In 2018, the Public Health Agency of Canada (PHAC) published a systematic review to calculate the risk of sexual transmission of human immunodeficiency virus (HIV) in the context of antiretroviral therapy (ART). In 2022, PHAC commissioned the Canadian Agency for Drugs and Technologies in Health (CADTH) to conduct a rapid review of evidence published since 2017. We undertook a meta-analysis of relevant studies from these two reviews.

Methods: Studies from the rapid review that adequately assessed exposure (HIV viral load) and outcome (HIV seroconversion) were included and assessed for risk of bias (RoB) and certainty of evidence. Results were pooled to estimate the risk of HIV transmission per 100 person-years.

Results: Three studies from the rapid review were eligible for inclusion and one was excluded after RoB assessment. In the remaining studies examining risk among people living with HIV who take ART and maintain a suppressed viral load (fewer than 200 copies/mL, measured every 4–6 months), no sexual transmissions of HIV were observed. The pooled incidence estimate based on these studies, and one from the 2018 PHAC review, was zero transmissions/100 person-years (95% CI: 0.00–0.10). No studies in the rapid review provided data on the risk of sexual transmission of HIV in situations of varying levels of viral load.

Conclusion: This update highlights the consistency of evidence since the 2018 PHAC review. There remains no evidence of HIV transmission to sexual partners when a person living with HIV is on ART and maintains a suppressed viral load.

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Keywords: HIV, viral load, sexual transmission, serodiscordance, viral suppression, gbMSM

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Introduction

Human immunodeficiency virus (HIV) is a retrovirus that progressively destroys CD 4+ lymphocytes, which are crucial to immune system functioning. If not treated, HIV can progress to acquired immunodeficiency syndrome (AIDS). Human immunodeficiency virus can be transmitted through exposure to blood, semen, vaginal fluid, rectal fluid and human milk (1,2). In Canada, the annual number of new diagnosed cases of HIV infection has remained relatively stable since 2012, with 1,472 cases reported in 2021 (3,4). As of 2020, an estimated 90% of persons living with HIV in Canada had been diagnosed and were aware of their infection. Of those diagnosed, 87% were estimated to be on treatment, and an estimated 95% of persons on treatment had a suppressed viral load of fewer than 200 copies/mL (4). Viral load is the measure of the amount of HIV ribonucleic acid circulating in the blood. In 2020, it was estimated that 77% of new HIV infections occurred through sexual transmission (4). Among people living with HIV, higher viral load levels are associated with increased risk of sexual transmission of HIV (5–8).

In 2018, the Public Health Agency of Canada (PHAC) published a systematic review to calculate the risk of sexual transmission of HIV (9). The 2018 PHAC review found that the overall risk of sexual transmission of HIV when the partner living with HIV was taking antiretroviral therapy (ART) with varying levels of viral load was 0.22 transmissions per 100 person-years (PY) (pooled

95% confidence interval [CI]: 0.14–0.33), across heterosexual and gay, bisexual and other men who have sex with men (gbMSM) serodiscordant couples. Furthermore, the review determined that the overall risk when a person living with HIV was taking ART and had a suppressed viral load (defined as fewer than 200 copies/mL measured every 4–6 months) was zero transmissions per 100 PY (pooled 95% CI: 0.00–0.28).

In 2022, PHAC commissioned the Canadian Agency for Drugs and Technologies in Health (CADTH) to carry out a rapid review of new evidence published since the 2018 PHAC review. The CADTH rapid review focussed on the risk of sexual transmission of HIV when a person living with HIV is taking ART (with varying levels of viral load) or is taking ART and has a suppressed viral load (10).

The CADTH rapid review identified 15 studies published between 2017 and 2022 that were relevant to the research questions, including one systematic review and 14 non-randomized studies (10). The rapid review did not evaluate the certainty of the evidence of each study, but rather described their strengths and limitations narratively. This rapid communication includes further analyses of studies included in the CADTH rapid review and provides an updated risk of sexual transmission of HIV when a person living with HIV is taking ART.

Methods

Relevant studies from the CADTH rapid review were first identified based on the use of valid measures of exposure (viral load testing) and outcome (phylogenetic linkage of observed seroconversions to the partner living with HIV). Included studies were further evaluated for risk of bias (RoB) and certainty of evidence using the Quality in Prognosis Studies instrument and Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria, respectively (11,12). Results from retained studies were pooled using a random-effects model to calculate pooled estimates of the risk of HIV transmission per 100 PY with 95% CIs. Analyses were done using R studio with the meta package: Meta-Analysis Package (v2.4-0) (13,14).

As in the 2018 PHAC review, HIV transmission risk was characterized using criteria defined by the Canadian AIDS Society (**Appendix**, **Table A1**) (15).

Results

Risk of bias and certainty of evidence of studies included in the CADTH rapid review

Regarding the risk of sexual transmission of HIV when a person living with HIV takes ART (with varying levels of viral load), only two studies were of potential relevance (Appendix, **Table A2**) (16,17).

The article by Nyombayire *et al.*, (16) had methodologic limitations, including a high RoB (Appendix, **Table A3**) and a very low certainty of evidence (Appendix, **Table A4**). The article by Bavinton *et al.*, (17) found no phylogenetically linked HIV transmissions when the partner living with HIV had varying levels of viral load and the partner did not use HIV pre-exposure prophylaxis (PrEP), but the article had only 5.8 PY of relevant follow-up. The certainty of evidence in this article was evaluated as very low (Appendix, **Table A5**). The RoB was high due to the lack of information on those who chose not to participate in the study, limited viral load reporting, no validation of ART adherence and considerable loss to follow up. In addition, not all reported transmissions were phylogenetically linked to the partner living with HIV. Given the above stated limitations, neither article was considered to add meaningful information to the 2018 PHAC review conclusions for this question.

Regarding the risk of sexual transmission of HIV when a person living with HIV takes ART and has a suppressed viral load (fewer than 200 copies/mL measured every 4–6 months), the CADTH rapid review found two observational studies among gbMSM (Table A2) that met the inclusion criteria, both of which were follow-up studies to work previously included in the 2018 PHAC review (17,18). The RoB was evaluated as moderate for the article by Bavinton *et al.*, (17) and low for Rodger *et al.*, (18) (Table A3), while the certainty of evidence on this question for both studies was evaluated as high (Table A5).

Public Health Agency of Canada analysis and pooled risk of sexual transmission of eligible studies

Two studies provided additional evidence regarding the risk of sexual transmission of HIV for gbMSM couples when the person living with HIV has a suppressed viral load. In these studies, no sexual transmissions of HIV that were phylogenetically linked were reported (17,18). The estimated incidence was zero transmissions/100 PY (95% CI: 0.00–0.23) for the article by Rodger *et al.*, (18) and zero transmissions/100 PY (95% CI: 0.00–1.59) for the article by Bavinton *et al.*, (17). Data from these studies were pooled to estimate an incidence of zero transmissions/100 PY (95% CI: 0.00–0.11) (Appendix, **Figure A1**).

The 2018 PHAC review included only one article (19) that provided data on the risk of HIV transmission for heterosexual couples where the partner living with HIV has a suppressed viral load. The estimated incidence was zero transmissions/100 PY (95% CI: 0.00–0.46) (9,19). No articles in the CADTH rapid review provided additional data for this population.

To update the 2018 PHAC review results for a combined (heterosexual and gbMSM) estimate of the risk of sexual transmission when a person living with HIV has a suppressed viral load, we pooled the results of Bavinton *et al.*, (17) and Rodger *et al.*, (18,19). This resulted in an incidence estimate of

zero transmissions/100 PY (95% CI: 0.00–0.10) (Figure A1). With additional data, there is more precision around the estimated incidence, so that the 95% CI of 0.00 to 0.28 documented in the 2018 PHAC review (9) is now 0.00 to 0.10.

Discussion

The 2023 PHAC analysis of relevant studies from the CADTH rapid review did not provide any new evidence to alter the conclusions from the 2018 PHAC review related to the risk of sexual transmission of HIV when a person living with HIV takes ART (with varying levels of viral load). Therefore, the risk of HIV transmission in this situation remains categorized as low, as per Canadian AIDS Society guidelines (Table A1). Future work is needed to determine more precise transmission risk estimates for situations involving varying levels of viral load.

Regarding the risk of sexual transmission of HIV when a person living with HIV takes ART and has a suppressed viral load of fewer than 200 copies/mL measured every 4–6 months, the CADTH rapid review found two updated studies among gbMSM. These studies, in addition to a single study on heterosexual couples, identified in the 2018 PHAC review, allowed an update of the meta-analysis from the 2018 PHAC review, resulting in more precision for the estimated risk of sexual transmission (zero transmissions/100 PY; 95% CI: 0.00–0.10). This updated review offers additional support to the conclusions of the 2018 PHAC review, further documenting no confirmed cases of sexual HIV transmission when a person living with HIV maintains a suppressed viral load. The risk of HIV transmission in this situation remains categorized as negligible, as per Canadian AIDS Society guidelines (Table A1). Communicating this message has the potential to reduce HIV-associated stigma and support increased engagement across the HIV care continuum, with benefits for individuals and communities.

Conclusion

This meta-analysis of updated articles derived a more precise estimate of the risk of sexual transmission of HIV when a person living with HIV is taking ART and maintains a suppressed viral load (fewer than 200 copies/mL, measured every 4–6 months). With five years of additional data, the conclusion of the 2018 PHAC review is strengthened. There remains no evidence of HIV transmission to sexual partners when a person living with HIV is on ART and maintains a suppressed viral load.

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Appendix

Table A1: Categories for assessing HIV transmission risk[a]

Category	Description	Criteria for determining level of risk	
No risk	None of the practices in this category have ever been demonstrated to lead to HIV infection. There is no potential for transmission since all the basic conditions for viral transmission are not present.	Potential for transmission	None
		Evidence of transmission	None
Negligible risk	All the practices assigned to this risk level present a potential for HIV transmission because they involve an exchange of bodily fluids (semen, pre-ejaculate, rectal fluid, vaginal fluid, blood, or breast milk). However, the amounts, conditions and media of exchange are such that the efficiency of HIV transmission appears to be greatly diminished. There are no confirmed reports of infection from these activities.	Potential for transmission	Yes
		Evidence of transmission	None
Low risk	All of the practices assigned this risk level present a potential for HIV transmission because they involve an exchange of bodily fluids (semen, pre-ejaculate, rectal fluid, vaginal fluid, blood, or breast milk). There are also a few reports of infection attributed to these activities (usually through individual case studies or anecdotal reports, and usually under certain identifiable conditions).	Potential for transmission	Yes
		Evidence of transmission	Yes (under certain conditions)
High risk	All of the practices assigned this risk level present a potential for HIV transmission because they involve an exchange of bodily fluids (semen, pre-ejaculate, rectal fluid, vaginal fluid, blood, or breast milk). In addition, a significant number of scientific studies have repeatedly associated the activities with HIV infection. Even when the exact mechanism of transmission is not completely clear, the results of such studies conclude that activities in this category are high risk.	Potential for transmission	Yes
		Evidence of transmission	Yes

Abbreviation: HIV, human immunodeficiency virus
[a] Adapted from the Canadian AIDS Society (15)

Table A2: Characteristics of new studies that align with questions of interest in this review[a]

Study, year, country	Study design, setting and period	Population characteristics	Exposure and comparator	Clinical outcome
Bavinton *et al.*, 2018 (17) Australia, Brazil, Thailand	Prospective cohort study Setting: 13 Australian clinics; 1 Brazilian clinic; 1 Thai clinic (no other information reported) Study period: May 2012–March 2016	HIV serodiscordant male same-sex couples/ sex partners Number of participant couples, n=343 Baseline characteristics (sex partner LWH): Age, median (IQR), years 34.4 (27,7, 43.9) Sex with outside partner(s), n (%): Any=136 (40%) CLAI=59 (17%) Viral load (measure NR) in the sex partner LWH, copies/mL, n (%): <200=267 (78%) ≥200=76 (22%) Daily PrEP use by the HIV-negative partner in the past 3 months, n (%): 26 (8%) ART use at baseline in sex partner LWH, n (%): 274 (80%) ≥90% adherence to ART in the past 3 months at baseline (among 274 sex partners LWH and taking ART), n (%): 241 (88%) Condom use/CLAI in the past 3 months, n (%): Always condoms/no CLAI=156 (45%) Some condoms/CLAI=126 (37%) Always CLAI=61 (18%) Any STI, n (%): Sex partner LWH=46 (13%) HIV-negative partner=39 (11%)	Exposure: Sex partners LWH were virally suppressed (most of whom were using ART) ART regimens: NR ART use in sex partner LWH during the follow-up, n (%): Never=6 (2%) Initiated during follow-up=85 (25%) Always=252 (73%) Viral load in sex partner LWH during the follow-up, n (%): Consistently <200 copies/mL=258 (75%) Variably >/<200 copies/mL=78 (23%) Consistently ≥200 copies/mL=7 (2%) Daily PrEP use by the HIV-negative partner anytime during the follow-up, n (%): 115 (34%) Comparator: None	Outcomes: Primary HIV seroconversion in the HIV-negative partner with viral load monitoring and phylogenetic linkage demonstrated Follow-up: At least 2 clinic visits per year Viral load monitoring was every 3–6 months Total couple years of follow-up=588.4 232 person-year (with suppressed viral load and no PrEP) 5.8 person-year (with varying viral load and no PrEP) Median follow-up/ couple (IQR)=1.7 (0.9, 2.2)

Table A2: Characteristics of new studies that align with questions of interest in this review[a] (*continued*)

Study, year, country	Study design, setting and period	Population characteristics	Exposure and comparator	Clinical outcome
Rodger *et al.*, 2019 (18) PARTNER2 UK (14 European countries)	Single arm prospective cohort study Setting: 75 sites across 14 European countries Study period: 2010–2017	Gay male HIV-serodiscordant couples Inclusion criteria: both partners were ≥18 years of age, had penetrative sex with or without condoms in the month prior to enrolment, expected to have sex together again after enrolment, consent of both partners obtained Exclusion criteria (for analysis): HIV negative partner using HIV PEP or PrEP, reported no condomless sex, viral load of the sex partner LWH >200 copies/mL, absence of viral load data, absence of HIV testing in the HIV negative partner Number of participants, n=782 couples (340 of whom were from PARTNER1) (19) Age, median (IQR), years: sex partner LWH=40.0 (33.3, 46.1) HIV negative partner=37.6 (30.9, 45.3) CD 4 cell count in the sex partner LWH, n (%): >350 cells/μL, n=730 (93%) ≤350 cells/μL, n=51 (7%) Number of participants with STIs, n (%): Sex partner LWH=214 (27%) HIV negative partner=185 (24%)	Exposure: Sex partner LWH takes suppressive ART and has viral load <200 copies/mL ART regimen: NR ART in sex partner LWH: Years on ART, median (IQR)=4.3 (1.8, 9.3) Self-reported ART adherence, n (%): ≥90%=739 (98%) <90%=14 (2%) Viral load in sex partner LWH at baseline: Undetectable viral load (<50 copies/mL), n (%): 754 (97%) Measured viral load: <200 copies/mL, n (%): 774 (99%) ≥200 copies/mL, n (%): 7 (<1%) Condom use: NR, only condomless acts were included in the analysis Use of HIV PrEP in HIV-negative partner: data for participants exposed to PrEP were removed from the analyses Comparator: None	Outcomes: Rate of phylogenetically linked HIV infections. (number of linked HIV infections/couple years of follow-up) Follow-up: 1,593 couple years Median follow-up/couple=2 years (IQR 1.1, 3.5 years) HIV negative partner: HIV testing baseline and every 6–12 months Sex partner LWH: Viral load tested baseline and every 6–12 months
Nyombayire *et al.*, 2021 (16) Rwanda	Prospective cohort Setting: Government clinics in Kigali Study period: 2010–2014	Heterosexual HIV-serodiscordant couples/sex partners Number of couples recruited n=3,777 Baseline characteristics: Number of couples with male sex partners LWH (M+/F-) n=1,947 Number of couples with female sex partners LWH (M-/F+) n=1,830 Age by sex overall, mean (SD), years: Male=35.3 (9.3) Female=29.6 (8.7) CD 4 of sex partners LWH mean (SD), (units NR)[b] M+/F-=472.5 (234.6) M-/F+=525.4 (269.7) Couples with current ART use in sex partner LWH at baseline, n (%): 1,684 (44.6) M+/F- couples with no contraceptive/condom use, n (%): 640 (80.7%) M-/F+ couples with no contraceptive/condom use, n (%): 570 (76.8%)	Exposure: Sex partner LWH receiving ART ART regimen: NR ART adherence: NR Viral load in sex partner LWH across follow-up: NR Duration of ART in sex partners LWH at baseline, mean (SD) years 3.1 (2.3) Use of HIV PrEP in HIV-negative partner: NR Comparator: Sex partner LWH not receiving ART	Outcomes: HIV seroconversion in the HIV-negative partner; virological linkage analysis (for most but not all couples with seroconversion in the HIV-negative partner) Follow-up: Quarterly clinic visits for HIV-negative partners Median (SD) follow-up, years=1.4 (1.2)

Abbreviations: ART, antiretroviral therapy; CD 4, cluster of differentiation 4; CLAI, condomless anal intercourse; HIV, human immunodeficiency virus; IQR, interquartile range; LWH, living with HIV; M+/F-, male partner positive, female partner negative; M-/F+, male partner negative, female partner positive; NR, not reported; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis; SD, standard deviation; STI, sexually transmitted infections

[a] Adapted from the 2023 CADTH review

[b] Data were available for 36% of sex partners LWH, only

Table A3: Risk of bias of new relevant studies to assess outcome of risk of HIV transmission[a]

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Overall risk of bias
Bavinton *et al.*, 2018, (17)	b	c	b	b	c	b	c
Rodger *et al.*, 2019, (18)	b	b	b	b	c	b	b
Rodger *et al.*, 2016, (19)	b	b	b	b	c	b	b
Nyombayire *et al.*, 2021, (16)	b	d	b	d	d	b	d

Abbreviation: HIV, human immunodeficiency virus
[a] To assess Risk of Bias, the Quality in Prognosis Studies (QUIPS) tool was used (12). It has six domains that critically appraise the validity and bias in included studies of prognostic factors. The domains are: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting
[b] Low risk of bias
[c] Moderate risk of bias
[d] High risk of bias

Table A4: GRADE summary of findings[a,b]

Certainty assessment							Number of couples/ person-years	Certainty of Evidence (GRADE)	Number of HIV transmission per 100 person-years (95% CI)
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias			
Outcomes: HIV incidence for unspecified sex acts (per person-years)									
Question 1: HIV incidence on ART[c]									
1[d] Cohort studies (16)	Observational studies (cohort and cross-sectional)	Very serious[d]	Very serious[e]	Serious[f]	Serious[g]	Undetected	3,777/2,867.4	Viral load of the Partner LWH was not reported Use of ART by Partner LWH was self-reported, and levels of adherence could not otherwise be validated Very high loss to follow up (i.e. 35%) Study power was not addressed Very low certainty of evidence (◯◯◯◯[e,f,g]) Excluded	0.63 (0.38–1.00)

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HIV, human immunodeficiency virus; LWH, living with HIV
Legend: ⊕⊕⊕⊕, High; ⊕⊕⊕◯, moderate; ⊕⊕◯◯, low; ⊕◯◯◯, very low
[a] Setting: Community
[b] Participants: Heterosexual
[c] Viral load could be any level (fewer than or more than 200 copies/ml)
[d] High risk of bias
[e] Downgraded for inconsistency because the viral load of partner living with HIV was not reported and use of ART by partner living with HIV was self-reported, and levels of adherence could not otherwise be validated
[f] Indirectness considered as serious because the study did not consistently account for condom use
[g] Imprecision: Total numbers did not meet the optimum sample size. Because of insufficient sample size and follow-up time (i.e. below 2,000 participants and 4,000 person-years), imprecision was rated as serious

Table A5: GRADE summary of findings[a,b]

Certainty assessment							Number of couples/ person-years	Certainty of Evidence (GRADE)	Number of HIV transmission per 100 person-years (95% CI)
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias			
Outcomes: HIV incidence for unspecified sex acts (per person-years)									
Question 1: HIV incidence on ART[c]									
1[d] Cohort study (17)	Cohort	Not serious	Not serious	Not serious	Very serious[d]	Undetected	NR/5.8	◯◯◯◯[e] Very low (Excluded)	0.00 (0.00–63.32)
Question 2: HIV incidence on ART + viral load suppression + no condom use[f]									
2[g] Cohort studies (17, 18)	Cohort	Not serious[g]	Not serious	Not serious	Serious[h]	Undetected	1,125/1,825.2	⊕⊕⊕⊕[e,i] High	0.00(0.00–0.11)

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HIV, human immunodeficiency virus; NR, number of participants not reported
Legend: ⊕⊕⊕⊕, High; ⊕⊕⊕◯, moderate; ⊕⊕◯◯, low; ⊕◯◯◯, very low
[a] Setting: Community
[b] Participants: gbMSM
[c] Viral load could be any level (fewer than or more than 200 copies/ml)
[d] Rated down because of the wide confidence interval crossing
[e] No downgrade for publication bias
[f] Viral load is suppressed at <200 copies/ml
[g] Risk of bias was assessed as low for one study and as moderate for the other. However, both studies reported consistent results
[h] Imprecision: Total numbers do not meet the optimum sample size. Because sample size and follow-up time were insufficient (i.e. below 2,000 participants and 4,000 person-years), imprecision was rated as serious
[i] Dose response gradient: there was a dose-response relationship between the viral load and the absolute risk of transmission (Baggaley *et al.*) (8), so rated up for a dose-response gradient

Figure A1: Pooled estimate of the risk of HIV transmission per 100 person-years among gbMSM and heterosexual serodiscordant couples[a,b]

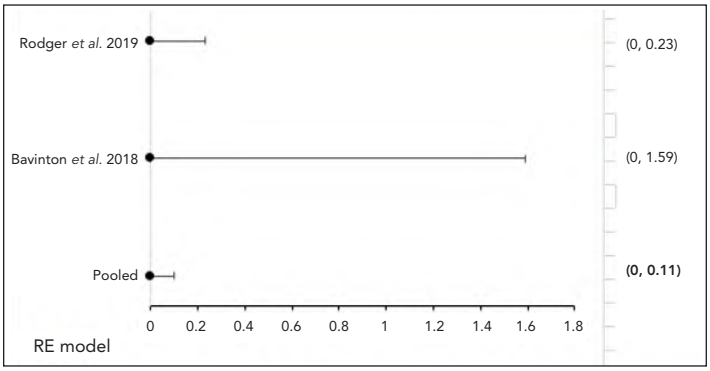
Question 1: The partner living with HIV is taking ART (with varying levels of viral load)

Updated evidence (2 studies) not applicable due to high risk of bias[a]

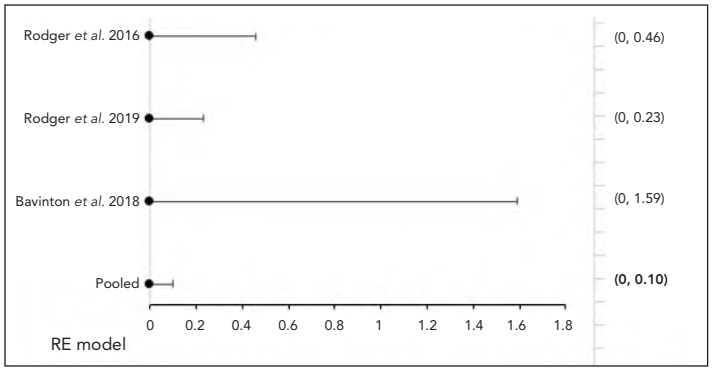
Question 2: The partner living with HIV is taking ART and has a suppressed viral load (fewer than 200 copies/mL measured every 4–6 months)

Outcome: Risk of HIV transmission

A1.1: Pooled gbMSM estimate: 0.00 (95% CI: 0.00–0.11)



A1.2: Pooled gbMSM and heterosexual estimate: 0.00 (95% CI: 0.00–0.10)[b]



Abbreviations: ART, antiretroviral therapy; CI, confidence interval; gbMSM, gay, bisexual and other men who have sex with men; HIV, human immunodeficiency virus; RE, random effect
[a] References Nyombayire *et al.* (16) and Bavinton *et al.* (17)
[b] The pooled estimate includes heterosexual partners from Rodger *et al.* (19) and gbMSM partners from Rodger *et al.* (18) and Bavinton *et al.* (17)

EPIDEMIOLOGIC STUDY

Estimation of the population size of gay, bisexual and other men who have sex with men in Canada, 2020

Justin Sorge[1]*, Sean Colyer[1,2], Joseph Cox[1], Abigail Kroch[2,3,4], Nathan Lachowsky[5,6], Nashira Popovic[1], Qiuying Yang[1]

Abstract

Background: Gay or bisexual (GB) and other men who have sex with men (MSM) are disproportionately affected by human immunodeficiency virus (HIV) globally and domestically in Canada. Reliable and recent population size estimates are necessary to allocate resources to meet prevention needs and for modelling the HIV epidemic. However, previous direct estimates did not account for GB men who would not reveal their sexual identity to a government survey, nor MSM not identifying as GB. The objective of this study was to develop two national population size estimates of gay, bisexual and other men who have sex with men (gbMSM) in 2020. First, GB men based on identity, regardless of sexual experience, and MSM who do not identify as GB but reported anal sex with a man in the past 1–5 years ("Identity-or-Behaviour" estimate). Second, an estimate of gbMSM who reported past 6–12 months anal sex with a man ("Behaviour-only" estimate).

Methods: Estimates for males aged 15 years and older were drawn from Statistics Canada's population size estimates, the Canadian Community Health Survey and the Community-Based Research Centre's Sex Now Survey. Estimated proportions of GB identity, those not likely to disclose GB identity and MSM who do not identify as GB but who reported past 1–5 years anal sex were applied. Past 6–12 months anal sex history was subsequently used to limit estimates to those sexually active anally.

Results: It was estimated that 3.5% of the male population in Canada aged 15 years and older identified as GB. Of GB males, 86.5% were likely to disclose their sexual identity to a government survey. A further 0.1% of non-GB identified males reported past year anal sex with a man. The national Identity-or-Behaviour gbMSM population size in 2020 was estimated at 669,613 people, equivalent to 4.3% of the Canadian male population aged 15 years and older. The estimate of Behaviour-only gbMSM was 412,186, representing 2.6% of the Canadian male population aged 15 years and older.

Conclusion: Using data from multiple sources, a model applied to estimate the population size of gbMSM, accounting for populations previously not included in prior estimates, has been described.

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Keywords: population size estimation, HIV, gay bisexual and other men who have sex with men, key populations

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Introduction

Nationally and globally, men who identify as gay or bisexual (GB) and other men who have sex with men (MSM) are overrepresented among people living with the human immunodeficiency virus (HIV) (1,2). Gay, bisexual and other men who have sex with men (gbMSM) account for approximately half of new HIV infections in Canada, despite representing only 2%–4% of adult males (2). Reliable population size estimates are necessary to inform resource allocation to meet prevention, testing and treatment needs and for modelling the HIV epidemic (3).

A nuanced understanding of the HIV epidemic among gbMSM has been limited by the challenges estimating this population size: lack of population sampling frame (4); small sample sizes in general population health surveys; stigma surrounding sexual orientation disclosure on health surveys (5,6); and inconsistent measurement of sexual orientation (7). The previous Canadian national estimate of 349,837 people (representing 2.4% of the male population aged 15 years and older), was published in 2014 and used for calculating population-specific estimates of HIV burden. This estimate was derived using direct estimation of self-identifying GB men who reported having sex with a man in the past 12 months on a population health survey. This estimate did not account for GB-identifying men who did not disclose their sexual orientation on a government survey, non-GB-identifying MSM or GB-identifying men who had not reached sexual debut (8). As such, previous estimates of this population size at national and subnational levels needed to be updated and made more comprehensive. Several other methods have been employed to estimate the population size at the local level. The "Wisdom of the Crowd" (WotC) method is based on the perceived size of the population by a sample of community members. The multiplier method estimates population size by triangulating information on group membership (e.g. HIV testers) with the proportion that report being a member of that group on a population survey. Successive/respondent-driven sampling methods utilize a Bayesian probability model and incorporate information on the sampling process. Mapping techniques enumerate community members in places where they congregate (9–11).

The primary objective of this study was to estimate the gbMSM population size in 10 provinces in Canada as of 2020. As gbMSM are both an identity and behavioural-based community, the aim was to calculate population size estimates based on three dimensions: 1) GB identity (regardless of sexual experience) 2) MSM who do not identify as GB but reported anal sex with a man in the past 1–5 years and, 3) an estimate of gbMSM reporting past 6–12 months anal sex with a man.

A secondary objective was to provide population size estimates 1) by region and 2) by rural areas and small population centres (small population areas defined as population size fewer than 30,000) versus medium and large urban population centres (large population areas defined as population size 30,000 or more).

Methods

Definitions

In an effort to be inclusive of all members of the population, efforts were taken to produce estimates incorporating both self-identity and recent anal intercourse as a risk for transmission of HIV and other sexually transmitted and blood-borne infections (STBBIs). Population size estimates of gbMSM were calculated for the following groups: 1) Identity-or-Behaviour—GB-identifying men, regardless of anal sex experience (identity), plus men who do not identify as GB but reported anal sex with a man in the past 1–5 years (behaviour); and 2) Behaviour-only—GB-identifying men who reported anal sex with a man in the past 6–12 months, plus men who do not identify as GB but who reported anal sex with a man in the past 6–12 months. Note, differing time frames (1 or 5 years and 6 or 12 months) is dependant on data source used, see below.

The Behaviour-only estimate was directly applicable to the development of policy, allocation of resources and modelling of diseases transmitted through anal sex, such as HIV and other STBBIs. An Identity-or-Behaviour estimate was derived that is inclusive of MSM community members who were previously excluded from estimation, regardless of sexual orientation. It was important to include MSM based on both anal sex experience and GB identity 1) for representativeness, 2) because it may be useful in primary prevention and health promotion efforts beyond sexual health and 3) in the context of sexual networks and potential bridges to populations outside existing gbMSM networks.

Data sources

Canadian Community Health Survey: The Canadian Community Health Survey (CCHS) is a national cross-sectional population survey of health status, healthcare utilization and health determinants. The CCHS, through a multistage probability sample allocation strategy, attempts to create a nationally representative sample of Canadians. Altogether, the CCHS sampling strategy covers 97% of Canadians aged 12 years and older (12,13). The CCHS collects data from the Canadian population via an interviewer-administered electronic questionnaire or computer-assisted telephone interview. The 2019–2020 cycles asked participants, "What is your sexual orientation?" Response options "heterosexual", "gay or lesbian", "bisexual" and "sexual orientation not elsewhere classified" dichotomized as "gay/bisexual" and "not elsewhere specified". Participants were also asked a separate, unlinked question: "In the past 12 months, have you had sex with a male?", which is defined in CCHS as "vaginal or anal" (yes/no). Statistics Canada provides users with bootstrap weights to estimate the sampling variance. The two cycles of CCHS data were combined as per the description by Thomas and Wannell (14). The CCHS analyses were restricted to male participants aged 15 years and older.

Sex Now Survey: Sex Now is Canada's largest community-based health survey specifically targeting Two Spirit, gay, bisexual, transgender and queer (2SGBTQ) men (15,16). Multiple recruitment methods were utilized to ensure the inclusion of a diverse pool of participants. Promotional material was shared through social media ad buys, prominent drag queen promotion, and ad buys on popular sex-seeking apps (Grindr, Squirt, Scruff, Jack'd), porn sites (PornHub) and 2SGBTQ-oriented media sites. Consenting participants were aged 15 years and older, lived in Canada, were capable of completing the survey in French or English, self-identified as a man or gender other than a woman, and identified as non-heterosexual or report sex with a man in the past five years. During November 2019 and February 2020, through an internet-based, self-administered survey, participants were asked, "How do you identify sexually?" Responses dichotomized as "gay/bisexual" and "other", which included "asexual", "straight", "pansexual", "queer" and "heteroflexible" identities. Past six-month anal sex experience among participants was based on non-zero responses to the following questions: 1) "In the PAST SIX MONTHS how many men have you had sex with?" and 2) "Of those, how many have you had ANAL sex with IN THE PAST SIX MONTHS?" The first question was used to quantify the denominator of respondents who received the nested question specifically about anal sex experience to calculate the proportion. The survey also asked, "How likely or unlikely would you be to reveal [your sexual orientation], if asked in a Statistics Canada survey (e.g., Census, [CCHS])?" Response options "very likely", "likely", "unlikely" and "very unlikely" dichotomized as "likely" and "unlikely."

Population size estimate

Statistics Canada provided custom postcensal Canadian 2020 population estimates for males aged 15 years and older for each province and stratified into small and large population areas. To estimate the Identity-or-Behaviour group, the proportion reporting GB-self-identity from CCHS was applied to the total male aged 15 years and older population count. This number was adjusted to also include those who would be unlikely to disclose GB identity on a Statistics Canada survey per the Sex Now results. To this, estimates of non-GB-identifying MSM were added, which was calculated separately as past 12 months anal sex with a man for CCHS data and past five years anal sex with a man from Sex Now.

To estimate the Behaviour-only group, the process is repeated among respondents reporting recent anal sex with a man (past six months Sex Now/past year CCHS) (17,18). Because the CCHS is a general population health survey, while Sex Now is a survey among 2SGBTQ men, analyses were treated differently. We developed separate models, as depicted below in equations 1 to 4:

Equation 1:

$$IB_{CCHS} = \left\{Pop_{count} * \left[\frac{GB_{CCHS\,prop}}{Disclosure_{SN\,prop}}\right]\right\} + \left(Pop_{count} * MSM_{CCHS\,prop}\right)$$

Where:

IB_{CCHS} is the Identity-or-Behaviour population size estimate of gbMSM estimated using CCHS data

Pop_{count} is the count of males aged 15 years and older population

$GB_{CCHS\,prop}$ is the proportion of CCHS respondents identifying as GB, relative to the sample

$Disclosure_{SN\,prop}$ is the proportion of GB Sex Now respondents likely to report their sexual orientation on a Statistics Canada survey, relative to GB respondents

$MSM_{CCHS\,prop}$ is the proportion of CCHS respondents who did not identify as GB and report past year sex with a man, relative to the sample

Equation 2:

$$IB_{SN} = \frac{\left\{Pop_{count} * \left[\frac{GB_{CCHS\,prop}}{Disclosure_{SN\,prop}}\right]\right\}}{GB_{SN\,prop}}$$

Where:

IB_{SN} is the Identity-or-Behaviour population size estimate of gbMSM estimated using Sex Now data

Pop_{count} is the count of males aged 15 years and older population

$GB_{CCHS\,prop}$ is the proportion of CCHS respondents identifying as GB, relative to the sample

$Disclosure_{SN\,prop}$ is the proportion of GB Sex Now respondents likely to report their sexual orientation on a Statistics Canada survey, relative to GB respondents

$GB_{SN\,prop}$ is the proportion of Sex Now respondents identifying as GB, relative to the sample

Equation 3:

$$B_{CCHS} = \left\{Pop_{count} * \left[\frac{GB_{CCHS\,prop\,p12m\,anal}}{Disclosure_{SN\,prop}}\right]\right\} + \left(Pop_{count} * MSM_{CCHS\,prop}\right)$$

Where:

B_{CCHS} is the Behaviour-only population size estimate of gbMSM estimated using CCHS data

Pop_{count} is the count of males aged 15 years and older population

$GB_{CCHS\ prop\ p12m\ anal}$ is the proportion of CCHS respondents identifying as GB and report past year anal sex with a man, relative to the sample

$Disclosure_{SN\ prop}$ is the proportion of GB Sex Now respondents likely to report their sexual orientation on a Statistics Canada survey, relative to GB respondents

$MSM_{CCHS\ prop}$ is the proportion of CCHS respondents who did not identify as GB and report past year sex with a man, relative to the sample

Equation 4:

$$B_{SN} = \frac{\left\{Pop_{count} * \left[\frac{GB_{CCHS\ prop}}{Disclosure_{SN\ prop}}\right]\right\} * GB_{SN\ prop\ p6m\ anal\ among\ GB}}{p6m\ Anal_{SN\ prop\ GB\ among\_all}}$$

Where:

B_{SN} is the Behaviour-only population size estimate of gbMSM estimated using CCHS data

Pop_{count} is the count of males aged 15 years and older population

$GB_{CCHS\ prop}$ is the proportion of CCHS respondents identifying as GB, relative to the sample

$Disclosure_{SN\ prop}$ is the proportion of GB Sex Now respondents likely to report their sexual orientation on a Statistics Canada survey, relative to GB respondents

$GB_{SN\ prop\ p6m\ anal\ among\ GB}$ is the proportion of Sex Now respondents identifying as GB and reporting past six months anal sex with a man, relative to the GB respondents

$p6m\ Anal_{SN\ prop\_GB\_among\_all}$ is the proportion of Sex Now respondents identifying as GB reporting past six months anal sex with a man, relative to all respondents reporting past six months anal sex with a man

This process was repeated at the regional-level and "small" and "large" population areas (see **Appendix**). Regions were defined as Atlantic (Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick), Québec, Ontario, Prairies (Manitoba, Saskatchewan, Alberta) and British Columbia.

Analysis

Analyses were done in SAS Enterprise Guide version 7.15 (19). Weighted estimation and bootstrap variance were used to calculate CCHS model inputs and 95% confidence intervals using the PROC SURVEYFREQ procedure. Sex Now model input 95% confidence intervals were calculated, unweighted, using the PROC FREQ procedure using binomial proportion. For the population size estimates, point estimates were calculated as the mean between CCHS- and Sex Now-derived estimates and upper and lower bounds were taken as Sex Now and CCHS estimates, respectively (17,18). Results are presented as counts (range) and percentage (range). Missing data were treated as non-response and excluded from analysis.

Results

The 2020 estimated male population of all Canadian provinces aged 15 years and older was 15,762,949. Direct weighted estimates of GB self-identity from CCHS totalled 496,594 people (3.5% of the male aged 15 years and older sample). Of 10,541 Sex Now participants beginning the questionnaire, 9,693 (92.0%) respondents self-identified as GB. Among 9,525 remaining GB participants who completed the question, 8,241 (86.5%) reported being likely to disclose their sexual orientation on a Statistics Canada survey. A further 21,380 (0.1% of the CCHS sample) of CCHS respondents who did not self-identify as GB reported anal sex with a man in the past year. In addition, the Sex Now sample included 848 (8.0%) of respondents identifying as a sexual orientation other than GB who reported sex with a man in the past five years.

A total of 218,705 (1.5% of the CCHS sample, 44.0% of GB respondents) self-identifying GB respondents reported anal sex with a man in the past year. Among the 5,791 remaining Sex Now GB participants, 4,561 (78.8%) reported anal sex with a man in the previous six months. While among the 460 remaining respondents identifying as a sexual orientation other than GB, 246 (53.5%) reported anal sex with a man in the previous six months. Among all respondents reporting past six months anal sex, 94.9% self-identified as GB. Note, due to survey dropout, crude counts become progressively lower across the survey and counts will not sum to the total sample of the 10,541 who initially completed the questionnaire for Sex Now. Estimation model inputs are presented in **Table 1**.

The national Identity-or-Behaviour gbMSM population size in 2020 was estimated at 669,613 (4.3% of the male aged 15 years and older population). Among these, an estimated 39,310 (0.2% of the male aged 15 years and older population) did not identify as GB and reported anal sex with a man in the past 1–5 years. The estimate of gbMSM reporting past 6–12 months anal sex with a man, the Behaviour-only estimate was 412,186, representing 2.6% of the male aged 15 years and older population in Canadian provinces and 61.6% of the above Identity-or-Behaviour estimate. The Behaviour-only estimate includes 25,129 (0.2% of the male aged 15 years and older population) men who did not identity as GB but reported past 6–12 months anal sex with a man (**Table 2**).

Table 1: Canadian provincial gay, bisexual, and other men who have sex with men population size estimation model inputs

Data source	Model input	n	%
		range	range
CCHS	Gay/bisexual identifying participants, among sample	496,594	3.5
		449,009–544,179	3.1–3.8
	Self-reported p12m anal sex with a man, gay/bisexual participants, among sample	218,705	1.5
		184,565–252,845	1.3–1.8
	Self-reported p12m anal sex with a man, participants identifying as another sexual identity[a], among sample	21,380[b]	0.1[b]
		12,146–30,613[b]	less than 0.1–0.2[b]
Sex Now[c]	Gay/bisexual identifying participants, among sample	9,693	92.0
		9,639–9,747	91.4–92.5
	Likely to disclose gay/bisexual identity on a government survey, among gay/bisexual participants	8,241	86.5
		8,175–8,307	85.8–87.2
	Self-reported p6m anal sex with a man, among gay/bisexual participants	4,561	78.8
		4,511–4,611	77.9–79.6
	Self-reported p6m anal sex with a man, participants identifying as gay/bisexual, among sample	4,561	94.9
		4,511–4,591	94.3–95.5
Statistics Canada	Canadian provincial 15 years of age and older male population count estimate	15,762,949	N/A
		N/A	N/A

Abbreviations: CCHS, Canadian Community Health Survey; N/A, not applicable; p6m, past 6 months; p12m, past 12 months
[a] Participants who do not identify as gay or bisexual
[b] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted
[c] Progressive respondent dropout/non-response and questionnaire skip logic have been accounted for in calculation of Sex Now proportions

Table 2: Canadian provincial gay, bisexual, and other men who have sex with men population size estimates, 2020

gbMSM definition	Population size estimate	% of male aged 15 years and older population
	range	range
Identity-or-Behaviour	669,613[a]	4.3[a]
	653,781[a]–685,446	4.2[a]–4.4
Behaviour-only	412,186[a]	2.6[a]
	301,070[a]–523,301	1.9[a]–3.3

Abbreviation: gbMSM, gay, bisexual and other men who have sex with men
[a] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted

By province, British Columbia (4.6% of the male aged 15 years and older population) was found to have the greatest proportion of gbMSM based on the Identity-or-Behaviour definition, with the Atlantic regions (3.3% of the male aged 15 years and older population) found to have the lowest. Using the Behaviour-only definition, Ontario had the largest proportion of gbMSM among the male aged 15 years and older population (2.9%) and the Atlantic region had the lowest proportion (1.8%). Regardless of anal sex experience, a greater proportion of gbMSM reside in large population size areas than the national estimate, with around 10% of gbMSM in Canadian provinces residing in small population areas. Estimates stratified by region and by small and large population areas are presented in the Appendix.

Discussion

In Canadian provinces during 2020, the gbMSM population size was estimated at 669,613 (representing 4.3% of the male aged 15 years and older population) based on our Identity-or-Behaviour definition. Among this, 94.1% self-identified as GB—regardless of sexual experience—and the remaining 5.9% did not identify as GB and reported past 1–5 years anal sex with a man. The Behaviour-only based estimate was 412,168 (representing 2.6% of the male aged 15 years and older population). This estimate comprises 93.9% self-identified GB individuals who reported past 6–12 months anal sex with a man and 6.1% men who did not self-identify as GB but who reported past 6–12 months anal sex with a man. These population estimates are invaluable in precise estimation of HIV incidence, prevalence, HIV testing and HIV pre-exposure prophylaxis uptake rates among gbMSM, which, in turn, are useful in program planning and resource allocation (2,3,20,21). These estimates will also be useful for inference at the population-level to quantify biobehavioural surveillance indicators among MSM.

Canada's previous national gbMSM estimate was published in 2014, producing a population size of 349,837 (representing 2.4% of the male aged 15 years and older population). This estimate was derived from a direct weighted measurement of men who self-identified as GB and reported any sex with a man in the past 12 months in the CCHS and Québec Population Health Survey (8). It should be noted that this estimate did

not include MSM who do not self-identify as GB, nor did it include an adjustment for nondisclosure on a governmental survey. While not directly comparable, the authors believe this previous estimate was likely an underestimate. Comparing to the present study's Identity-or-Behaviour estimate (669,613, 4.3% of the male aged 15 years and older population), the increase may be partially explained by the inclusion of groups previously unaccounted for. The literature base is sparse on analyses of gbMSM identity versus sexual behaviour, thus limiting comparison. However, recent analyses of CCHS data, the General Social Survey from the United States and polling suggest a growing proportion of North American populations identify as 2SLGBTQ+, particularly among younger age groups, despite same-sex behaviour increasing at a lower rate (22–24). This latter point may be reflected in this analysis, with the Behaviour-only estimate accounting for approximately 62% of the Identity-or-Behaviour estimate. It is important to note that, among a wide spectrum of sexual behaviours, these analyses account for only anal sex behaviour, as a risk for HIV transmission and other STBBIs. The Identity-or-Behaviour estimate may include unmeasured sexual behaviours other than anal sex, but as a limitation of the data this could not be determined. Incorporating more precise population size estimates in epidemiological modelling will lead to more accurate understanding of the HIV epidemic and comparison across jurisdictions and population groups.

While others have demonstrated success using WotC, multiplier method, successive/respondent-driven sampling and mapping estimation, lack of nationally representative data precluded such methods within this study. Further, WotC methods seem particularly suited to small-area estimation and tend to produce estimates on the lower range of plausibility (9,10,25).

Limitations

Sex Now and CCHS data, due to the self-report nature of their collection, are subject to measurement error, recall bias and reporting bias. However, due to the community-based nature of Sex Now, the authors believe sexual orientation reporting bias within CCHS is mitigated by our adjustment for non-disclosure. Additionally, Salway *et al.* show that assumed bias in non-probabilistic samples of sexual minority individuals may be overstated (26).

The data sources that were used to arrive at these estimates deserves some attention. It was found that 44.0% of GB-identifying CCHS respondents reported anal sex with a man in the past 12 months. Among GB-identifying Sex Now respondents, 78.8% reported past six months anal sex with a man. It is reasonable to suspect the CCHS sample, because of its interviewer-administration, to be subject to a greater amount of social desirability bias. While in contrast the Sex Now sample, given its promotion methods, may recruit a more sex-positive sample. Indeed, this was the impetus for taking the midpoint between these estimates as the main finding, resulting in the Behaviour-only estimate representing 62% of the Identity-behaviour estimate.

Some of the results from CCHS, as a limitation of a small sample size, are subject to high rates of sampling variability. This was evident in the national estimate of anal sex experience among men who do not self-identify as GB. Further, high sampling variability was particularly apparent in analyses stratified by region and population size area. Despite this, the authors believe the results to be plausible and provide them for interested readers.

These estimates, which incorporate sexual behaviour, have been limited to anal sex. It is important to note that many other STBBIs are readily transmitted through other routes, including oral sex. This is a limitation of CCHS data, which defines "sex" as vaginal or anal sex. As such, caution against the application of these estimates to other infections that are not transmitted through anal sex is warranted. Expanding the definition of sex within the CCHS to include oral sex, or including questions on other sex behaviours in future cycles is encouraged and may allow for population size estimation for broader STBBI considerations.

A limitation of CCHS data is the lack of information on sexual behaviours from residents in the northern Territories of Canada, which precluded estimation for these areas. Including this module of questions in future CCHS cycles may allow for more complete regional estimates. A gender-based analysis was unable to be applied to the data. However, Sex Now estimates account for gender diversity among respondents who do not identify as a woman.

Finally, estimates stratified by age were not produced in this study. With plans to update these estimates periodically, the authors hope to provide further stratification, including by age group, in future analyses.

Conclusion

Using data from multiple sources, models used to estimate the population size of gbMSM, accounting for community members previously not included in prior Canadian estimates have been described. Namely, models account for GB-identifying individuals who would not be willing to disclose their sexual orientation on a population health survey and men that do not identify as GB but report anal sex with a man. The Identity-or-Behaviour and Behaviour-only estimates allow data users and policymakers to apply the estimate that best fits their needs. Specifically the Identity-or-Behaviour estimate, which relates directly to community size, while the Behaviour-only estimate may be more relevant for HIV and other STBBIs transmitted through anal sex.

Authors' statement

JTS — Conceptualization, methodology, formal analysis, writing–original draft, writing–review and editing
SC — Conceptualization, methodology, writing–original draft, writing–review and editing
JC — Supervision, methodology, writing–original draft, writing–review and editing
AAK — Methodology, writing–original draft, writing–review and editing
NJL — Methodology, writing–original draft, writing–review and editing
NP — Supervision, conceptualization, methodology, writing–original draft, writing–review and editing
QY — Methodology, writing–original draft, writing–review and editing

Competing interests

None.

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Appendix

Table A1: Canadian provincial gay, bisexual, and other men who have sex with men population size estimation model inputs, by region

Data source	Model input	Region	n	%
			range	range
CCHS	Gay/bisexual identifying participants, among respective regional samples	Atlantic	24,690	2.7
			17,765–31,616	1.9–3.4
		Québec	122,155	3.7
			98,894–145,377	3.0–4.4
		Ontario	192,792	3.5
			160,889–224,694	2.9–4.0
		Prairies	81,754	3.1
			61,243–102,265	2.4–3.9
		British Columbia	75,243	3.9
			58,096–92,390	3.0–4.7
	Self-reported p12m anal sex with a man, gay/bisexual participants, among respective regional samples	Atlantic	7,411[a]	0.8[a]
			2,887–11,936[a]	0.3–1.3[a]
		Québec	37,986[a]	1.1[a]
			22,901–53,070[a]	0.1–1.6[a]
		Ontario	100,841	1.8
			78,072–123,609	1.4–2.2
		Prairies	42,766[a]	1.6[a]
			25,877–59,655[a]	1.0–2.3[a]
		British Columbia	29,701[a]	1.5[a]
			19,017–40,386[a]	1.0–2.1[a]
	Self-reported p12m anal sex with a man, participants identifying as another sexual identity[c], among respective regional samples	Atlantic	1,120[b]	0.1[b]
			0–2,502[b]	0.0–0.3[b]
		Québec	3,013[b]	0.1[b]
			0–6,247[b]	0.0–0.2[b]
		Ontario	13,435[a]	0.2[a]
			5,433–21,437[a]	0.1–0.4[a]
		Prairies	2,137[b]	0.1[b]
			163–4,111[b]	0.1–0.2[b]
		British Columbia	1,675[b]	0.1[b]
			72–3,278[b]	<0.0–0.2[b]
Sex Now[d]	Gay/bisexual identifying participants, among respective regional samples	Atlantic	802	90.0
			784–820	88.0–92.0
		Québec	2,199	92.9
			2,178–2,225	92.0–94.0
		Ontario	2,969	92.2
			2,939–3,000	91.3–93.2
		Prairies	1,984	90.8
			1,957–2,011	89.6–92.1
		British Columbia	1,793	92.5
			1,716–1,762	91.3–93.7

Table A1: Canadian provincial gay, bisexual, and other men who have sex with men population size estimation model inputs, by region (*continued*)

Data source	Model input	Region	n	%
			range	range
Sex Now[d] (*continued*)	Likely to disclose gay/bisexual identity on a government survey, gay/bisexual participants	Atlantic	680	86.5
			661–699	84.1–88.9
		Québec	1,962	90.8
			1,936–1,988	89.6–92.0
		Ontario	2,454	84.1
			2,416–2,492	82.8–85.4
		Prairies	1,643	83.7
			1,612–1,674	82.1–85.3
		British Columbia	1,502	88.5
			1,476–1,527	87.0–90.0
	Self-reported p6m anal sex with a man, among gay/bisexual participants	Atlantic	330	74.3
			315–345	70.9–77.8
		Québec	1,029	80.9
			1,006–1,052	79.0–82.7
		Ontario	1,367	77.3
			1,339–1,395	75.7–78.9
		Prairies	967	78.6
			945–989	76.8–80.4
		British Columbia	868	80.7
			847–889	78.8–82.6
	Self-reported p6m anal sex with a man, participants identifying as gay/bisexual, among sample	Atlantic	330	92.7
			320–340	90.0–95.4
		Québec	1,029	95.6
			1,016–1,042	94.4–96.9
		Ontario	1,367	94.2
			1,349–1,384	92.9–95.4
		Prairies	967	95.2
			954–980	93.9–96.5
		British Columbia	868	95.7
			856–880	94.4–97.0
Statistics Canada	Canadian Provincial male aged 15 years and older population count estimate	Atlantic	1,029,995	N/A
			N/A	N/A
		Québec	3,596,333	N/A
			N/A	N/A
		Ontario	6,119,281	N/A
			N/A	N/A
		Prairies	2,835,632	N/A
			N/A	N/A
		British Columbia	2,181,708	N/A
			N/A	N/A

Abbreviations: CCHS, Canadian Community Health Survey; N/A, not applicable; p6m, past 6 months; p12m, past 12 months
[a] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted
[b] Estimates are associated with a large amount of sampling variability (coefficient of variation: ≤35.0) and do not meet Statistics Canada's quality standards. Extreme caution in interpreting these data is warranted
[c] Participants who do not identify as gay or bisexual
[d] Progressive respondent dropout/non-response and questionnaire skip logic have been accounted for in calculation of Sex Now proportions

Table A2: Canadian provincial gay, bisexual, and other men who have sex with men population size estimates, by region, 2020

gbMSM definition	Region	Population size estimate	% of male aged 15 years and older population
		range	range
Identity-or-Behaviour	Atlantic	34,403[a]	3.3[a]
		33,255[a]–35,550	3.2[a]–3.5
	Québec	152,309[a]	4.2[a]
		148,390[a]–156,227	4.1[a]–4.3
	Ontario	270,604[b]	4.4[b]
		267,371[b]–273,837	4.4[b]–4.5
	Prairies	112,927[a]	4.0[a]
		108,728[a]–117,126	3.8[a]–4.1
	British Columbia	100,143[a]	4.6[a]
		97,217[a]–103,069	4.5[a]–4.7
Behaviour-only	Atlantic	18,259[a]	1.8[a]
		10,861[a]–25,657	1.1[a]–2.5
	Québec	85,590[a]	2.4[a]
		48,399[a]–122,781	1.4[a]–3.4
	Ontario	177,168[b]	2.6[b]
		146,910[b]–207,427	2.4[b]–3.3
	Prairies	72,937[a]	2.6[a]
		57,986[a]–70,797	2.0[a]–3.1
	British Columbia	59,938[a]	2.8[a]
		39,012[a]–80,364	1.8[a]–3.7

Abbreviation: gbMSM, gay, bisexual and other men who have sex with men
[a] Estimates are associated with a large amount of sampling variability (coefficient of variation: ≤35.0) and do not meet Statistics Canada's quality standards. Extreme caution in interpreting these data is warranted
[b] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted

Table A3: Canadian provincial gay, bisexual, and other men who have sex with men population size estimation model inputs, by area population size

Data source	Model input	Area population size	n	%
			range	range
CCHS	Gay/bisexual identifying participants, among sample	Large population area	418,516	3.3
			373,197–463,835	2.9–3.7
		Small population area	78,078	2.6
			64,063–92,092	2.1–3.0
	Self-reported p12m anal sex with a man, gay/bisexual participants, among sample	Large population area	189,522	1.5
			156,929–222,115	1.2–1.7
		Small population area	29,183[a]	0.9[a]
			18,587–39,779[a]	0.6–1.3[a]
	Self-reported p12m anal sex with a man, participants identifying as another sexual identity[b], among sample	Large population area	16,517[a]	0.1[a]
			7,832–25,202[a]	0.3–0.8[a]
		Small population area	4,863[a]	0.2[a]
			1,914–7,811[a]	0.1–0.3[a]

Table A3: Canadian provincial gay, bisexual, and other men who have sex with men population size estimation model inputs, by area population size (*continued*)

Data source	Model input	Area population size	n	%
			range	range
Sex Now[c]	Gay/bisexual identifying participants, among sample	Large population area	7,042	92.6
			6,995–7,086	92.0–93.2
		Small population area	1,326	91.0
			1,304–1,348	89.1–92.1
	Likely to disclose gay/bisexual identity, among gay/bisexual participants	Large population area	6,181	89.3
			5,958–6,235	88.6–90.1
		Small population area	1,054	81.0
			1,026–1,082	78.8–83.1
	Self-reported p6m anal sex with a man, among gay/bisexual participants	Large population area	3,947	79.9
			3,902–3,992	79.0–80.8
		Small population area	618	72.5
			597–639	70.1–75.0
	Self-reported p6m anal sex with a man, participants identifying as gay/bisexual, among sample	Large population area	3,947	95.3
			3,920–3,974	94.6–95.9
		Small population area	618	93.1
			605–631	91.1–95.0
Statistics Canada	Canadian Provincial male aged 15 years and older population count estimate	Large population area	12,703,406	N/A
			N/A	N/A
		Small population area	3,059,543	N/A
			N/A	N/A

Abbreviations: CCHS, Canadian Community Health Survey; N/A, not applicable; p6m, past 6 months; p12m, past 12 months
[a] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted
[b] Participants who do not identify as gay or bisexual
[c] Progressive respondent dropout/non-response and questionnaire skip logic have been accounted for in calculation of Sex Now proportions

Table A4: Canadian provincial gay, bisexual, and other men who have sex with men population size estimates, 2020

gbMSM definition	Area population size	Population size estimate	% of male aged 15 years and older population
		range	range
Identity-or-Behaviour	Large population area	618,482[a]	4.9[a]
		605,494[a]–631,470	4.8[a]–5.0
	Small population area	76,101[a]	2.5[a]
		74,205[a]–77,996	2.4[a]–2.6
Behaviour-only	Large population area	388,008[a]	3.1[a]
		285,475[a]–490,542	2.3[a]–3.9
	Small population area	42,511[a]	1.4[a]
		29,966[a]–55,056	1.0[a]–1.8

Abbreviation: gbMSM, gay, bisexual, and other men who have sex with men
[a] Estimates are associated with a moderate amount of sampling variability (coefficient of variation: 15.0<CV<35.0), and caution in interpreting these data is warranted

EPIDEMIOLOGIC STUDY

Mycoplasma genitalium infection among gay, bisexual and other men who have sex with men in Montréal, Canada

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Abstract

Background: The bacteria *Mycoplasma genitalium* has been identified as a causative agent of urethritis in men, especially in gay, bisexual and other men who have sex with men (gbMSM). Canadian clinic-based data have identified a high prevalence of *M. genitalium* and resistance to antibiotic treatments. This article estimates the prevalence of *M. genitalium* infections among Montréal gbMSM, explores correlates for *M. genitalium* infection and estimates the prevalence of mutations associated with antimicrobial resistance (AMR).

Methods: Engage Cohort Study is a multi-site longitudinal study on sexually active gbMSM, aged 16 years and older, recruited via respondent-driven sampling in Montréal, Toronto and Vancouver. Participants completed a questionnaire on behaviour and were tested for sexually transmitted and blood-borne infections at each visit. For this sub-study, Montréal participants with a follow-up visit that occurred between November 2018 and November 2019 were included.

Results: A total of 2,064 samples were provided by 716 participants. Prevalence of *M. genitalium* infection was 5.7% at rectal and/or urethral sites, 4.0% at rectal site and 2.2% at urethral site. Correlates for *M. genitalium* infection were younger age and reporting six or more sexual partners in the past six months. Prevalence of macrolide resistance associated mutations (MRAM), quinolone resistance associated mutations (QRAM) and either MRAM or QRAM, was 82%, 29% and 85%, respectively.

Conclusion: This first population-based study among gbMSM in Canada documents a high prevalence of urethral and rectal *M. genitalium* infection and high levels of AMR. Our results highlight the importance of access to testing and AMR detection when indicated.

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Keywords: *Mycoplasma genitalium*, gbMSM, sexually transmitted infections, azithromycin, moxifloxacin, resistance

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Introduction

Mycoplasma genitalium has been identified as a growing health concern for sexually active gay, bisexual and other men who have sex with men (gbMSM) by causing acute, persistent or recurrent urethritis (1–6). The data concerning *M. genitalium* as a causative agent of clinical proctitis are conflicting (4–8). *Mycoplasma genitalium* co-infection with other bacterial sexually transmitted infections (STIs) has been frequently reported in gbMSM (7,9).

Mycoplasma genitalium infection is not a notifiable condition in Canada (10,11) yet there are no published Canadian community-based studies concerning *M. genitalium* infection. Studies conducted in 2013 (Ontario), 2016 (Alberta) and 2019 (Saskatchewan), among men and women who had STI symptoms or sought medical attention for STI screening, have shown high rates of *M. genitalium* infection and macrolide resistance associated mutations (MRAM) and a significant presence of quinolone resistance associated mutations (QRAM) (12–14).

More detailed Canadian data are required to guide testing and treatment of *M. genitalium* infections in gbMSM. The objectives of this study are to 1) estimate the prevalence of *M. genitalium* infection and other selected bacterial STIs by anatomical site among Montréal gbMSM, 2) explore correlates of *M. genitalium* infection and 3) estimate the prevalence of MRAM and QRAM.

Methods

Engage Cohort Study

Engage Cohort Study is a collaboration between researchers and community-based organizations to study the sexual health, including human immunodeficiency virus (HIV) and sexually transmitted and blood-borne infections (STBBIs), of gbMSM in Montréal, Toronto and Vancouver. Details for this cohort study were described elsewhere (15–17). In brief, participants were recruited using respondent-driven sampling (RDS), a survey method for sampling hard-to-reach populations deriving from chain referral sampling (18). Thus, enrolled participants recruited other eligible participants through their social networks. Eligibility criteria were as follows: French or English-speaking cisgender or transgender men; 16 years of age or older; and reporting at least one sexual encounter with a man in the prior six months. After recruitment, participants were invited every 6–12 months for subsequent visits at the community study site. At each visit, participants completed a self-administered computer-assisted questionnaire and provided biological samples, including first-pass urine, a pharyngeal and a rectal swab and a blood sample.

Sub-study in Montréal

Montréal recruitment into the Engage Cohort Study started in February 2017. For this one-time point sub-study, participants with a follow-up visit that occurred between November 2018 and November 2019 were included.

Biological specimen collection and laboratory testing

To detect *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, nucleic acid amplification tests were used (cobas® 4800; Roche Diagnostics, Branchburg, New Jersey). For *M. genitalium* detection, samples were kept at room temperature in the cobas® PCR Media (Roche Diagnostics) for a maximum of one year or as frozen eluates. Specimens were analyzed using the Allplex™ CT/NG/MG/TV assay (Seegene Inc.). *Mycoplasma genitalium*-positive samples were subsequently analyzed by real-time PCR to detect MRAM and QRAM by using the Allplex™ MG & AziR and Allplex™ MG & MoxiR assays, respectively.

Outcomes and correlates

Using current knowledge based on existing literature, variables were selected from the Engage Cohort Study questionnaire (19,20). Variables were grouped into the following categories: sociodemographic; sexual partners in the past six months (P6M); methods of finding sexual partners in the P6M; substance use in the P6M; and STBBIs in the P6M. The variable "chemsex" was defined as crystal methamphetamine, gamma-hydroxybutyrate (GBH), ecstasy/3,4-methylenedioxymethamphetamine (MDMA), ketamine, or poppers (i.e. alkyl nitrites) consumption in the two hours before or during sex with at least one of the last five sexual partners in the P6M. The variable "self-reported STI diagnosis" refers to a diagnosis by a healthcare professional in the P6M of *C. trachomatis*, *N. gonorrhoeae*, lymphogranuloma venereum (LGV) or syphilis. An individual was considered to have an *M. genitalium* infection if either their urine or their rectal sample was positive. Key mutations associated with azithromycin resistance (positions 2058 or 2059 in region V of the 23S ribosomal ribonucleic acid gene) and moxifloxacin resistance (S83I, S83R, S83N, D87N, or D87Y in *parC*) were used to define MRAM and QRAM, respectively.

Statistical analyses

Prevalence and odds ratios (OR) were estimated and adjusted for the recruitment method as well as censoring, using a combination of RDS-II weights (21) and inverse-probability-of-censoring weights (22). The RDS-II weights are inversely proportional to the participants' network size, meaning that data for individuals with large networks were weighted less. The 95% confidence intervals (CI) were calculated using robust (sandwich) variance estimation to account for the within-subject correlation induced by weighing (23). Prevalence data was not adjusted MRAM and QRAM since one individual with a larger weight could easily dominate the subsample within small subsamples (each MRAM and QRAM subsample had n fewer than 100 positive specimens). Logistic regression was used to predict *M. genitalium* infection among gbMSM. Since the aim was prediction, there was no need to consider confounding or effect modification. Predictive performance was assessed using Akaike information criterion (AIC).

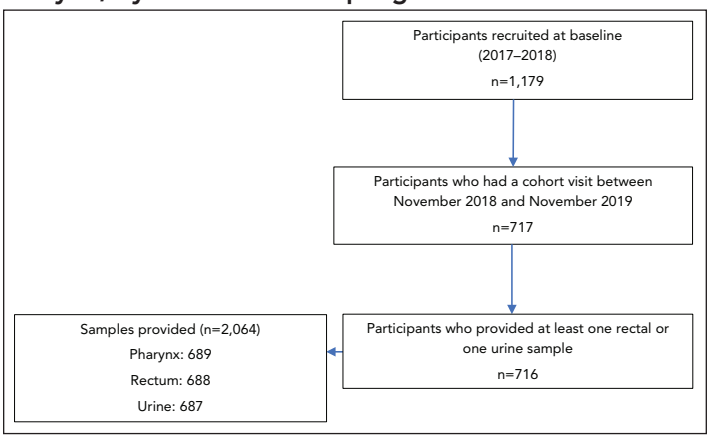
Ethics

Ethics approval was received from the Research Institute of the McGill University Health Centre.

Results

Between February 2017 and June 2018, 1,179 participants were recruited in Montréal. A follow-up study visit, during which samples were collected for *M. genitalium* testing, occurred for 717 participants. One participant was excluded from *M. genitalium* prevalence analyses because only a pharyngeal sample was provided. Overall, 716 participants provided a total of 2,064 samples (**Figure 1**).

Figure 1: Flow diagram of Engage Cohort Study in Montréal study participants and samples included in the analysis, by anatomical sampling sites



Most participants identified their ethnocultural identity as French or English Canadian (53.5%) and their sexual orientation as gay (82.2%). The majority reported having an education level higher than high school level (79.1%), a gross annual income of $30,000 or less (60.1%), being HIV-negative (84.9%) and having five or fewer male sexual partners in the P6M (67.6%) (**Table 1**).

Prevalence of *Mycoplasma genitalium* infection and other sexually transmitted infections

Mycoplasma genitalium prevalence was 5.7% (95% CI: 4.0–8.1) (rectal or urethral site) with anatomical site-specific prevalence being 4.0% (95% CI: 2.6–6.0) at the rectal site and 2.2% (95% CI: 1.2–4.0) at the urethral site (**Table 2**). The overall prevalence of *M. genitalium* was detected at the pharyngeal site in only two individuals (0.2%, 95% CI: 0.1–0.9). Prevalences of *C. trachomatis* and *N. gonorrhoeae* are detailed in Table 2. Among the individuals with urethral *C. trachomatis* infection, one of five were co-infected with *M. genitalium* (20%); among those with rectal *C. trachomatis* infection, two of 22 were co-infected with *M. genitalium* (9.1%) (**Table 3**). Among those with rectal *N. gonorrhoeae* infection, two of 12 were co-infected with *M. genitalium* (16.7%); no urethral *N. gonorrhoeae* infection was observed.

Table 1: Sociodemographic characteristics of the Engage Cohort Study in Montréal participants[a] who provided specimen(s) for *Mycoplasma genitalium* analysis, November 2018–November 2019, n=716

Characteristics	Adjusted proportion (%)[b]	95% CI
Age (years)		
29 or younger	30.2	24.5–36.7
30–45	38.5	31.6–45.8
46 or older	31.3	24.6–38.9
Education level		
High school degree or less	20.9	15.7–27.3
More than high school degree	79.1	72.7–84.3
Annual income (CAD)		
0–29,999	60.1	53.1–66.7
30,000–59,999	31.7	25.6–38.6
60,000 or more	8.2	6.1–11.0
Ethnocultural group		
French Canadian	45.0	37.9–52.4
English Canadian	8.5	5.6–12.5
European	12.7	9.1–17.4
Latin American	13.7	9.1–20.1
South or East Asian	4.9	2.1–11.2
Arab or North African	5.8	3.2–10.2
East or West African or Caribbean	3.5	1.7–7.1
Other[c]	5.9	3.4–10.1
Immigration		
Born in Canada	59.2	51.7–66.2
Moved to Canada in the past 2 years	5.1	2.7–9.3
Moved to Canada in the past 3 years or more	35.7	28.4–42.9
Gender identity		
Cisgender man	92.9	88.7–95.7
Transgender man	1.8	0.6–5.4
Other[d]	5.2	3.1–8.8
Sexual orientation		
Gay	82.2	76.6–86.7
Bisexual	9.2	6.0–13.8
Queer	4.6	2.6–8.2
Other[e]	4.0	2.1–7.3
Sexual behaviours P6M		
Any condomless anal sex	56.0	48.4–63.4
Any chemsex[f]	10.8	7.7–14.9
Number of male sexual partners		
5 or fewer	67.6	61.0–73.6
6–10	16.0	11.4–21.9
11 or more	16.4	12.5–21.2

Table 1: Sociodemographic characteristics of the Engage Cohort Study in Montréal participants[a] who provided specimen(s) for *Mycoplasma genitalium* analysis, November 2018–November 2019, n=716 (*continued*)

Characteristics	Adjusted proportion (%)[b]	95% CI
HIV status		
Living with HIV	15.1	11.0–20.3

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; P6M, past six months
[a] Montréal's Engage Cohort Study participants who had a follow-up visit in the window period between November 2018 and November 2019 and provided at least one rectal or urethral sample
[b] Adjusted for respondent-driven sampling recruitment and censoring
[c] Other ethnocultural group included Aboriginal or Indigenous
[d] Other sexual orientations included bisexual and queer
[e] Other gender identities included participants identifying as genderqueer, non-binary, or two-spirit
[f] Chemsex includes crystal methamphetamine, GHB (gamma-hydroxybutyrate), ecstasy/MDMA (3,4-methylenedioxymethamphetamine), or ketamine consumption in the two hours before or during sex with at least one of the last five partners participants reported having sex within the P6M (17). Poppers (i.e. alkyl nitrites) are included in the chemsex definition

Table 2: Prevalence of *Mycoplasma genitalium*[a] and of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections[b] by anatomical site, n=716

Type of sample (n)	Positive samples	Adjusted prevalence[c]	
	n	%	95% CI
Pharyngeal swab (n=688)			
M. genitalium	2	0.2	0.1–0.9
N. gonorrhoeae	15	1.5	0.8–2.6
C. trachomatis	7	0.8	0.2–3.0
Urethral swab (n=687)			
M. genitalium	23	2.2	1.2–4.0
N. gonorrhoeae	0	0.0	N/A
C. trachomatis	5	1.9	0.4–8.6
Rectal swab (n=688)			
M. genitalium	41	4.0	2.6–6.0
N. gonorrhoeae	12	1.4	0.6–3.3
C. trachomatis	22	2.6	1.2–5.5
Rectal or urethral swab (n=716)			
M. genitalium	61	5.7	4.0–8.1

Abbreviations: CI, confidence interval; *C. trachomatis*, *Chlamydia trachomatis*; *M. genitalium*, *Mycoplasma genitalium*; *N. gonorrhoeae*, *Neisseria gonorrhoeae*; N/A, not available
[a] Using Allplex™ CT/NG/MG/TV Assay
[b] Using the cobas® 4800 system
[c] Adjusted for respondent-driven sampling recruitment and censoring

Table 3: Co-infections of *Mycoplasma genitalium*, *Neisseria gonorrhoeae* and *Chlamydia trachomatis* by anatomical site, n=716

Type of sample (n)		*C. trachomatis*		*N. gonorrhoeae*	
		Negative	Positive	Negative	Positive
Urethral swab (n=672)					
M. genitalium	Negative	645	4	649	0
	Positive	22	1	23	0
Rectal swab (n=683)					
M. genitalium	Negative	622	20	632	10
	Positive	39	2	39	2

Abbreviations: *C. trachomatis*, *Chlamydia trachomatis*; *M. genitalium*, *Mycoplasma genitalium*; *N. gonorrhoeae*, *Neisseria gonorrhoeae*

Mycoplasma genitalium infection correlates

Younger age (29 years or younger) and the following factors (all reported in the past six months) were significantly associated in univariate analysis having more male sexual partners (6–10 partners and 11 or more partners compared to five or fewer); having at least one new sexual partner; reporting at least one condomless anal sex act (insertive or receptive) with another man; engaging in chemsex; and having received a diagnosis of an STI (**Table 4**). Living with HIV was not associated with *M. genitalium* infection. The best predictive regression model of *M. genitalium* infection included the following factors: younger age (29 years or younger) (OR: 2.5, 95% CI: 1.2–5.5); and declaring more male sexual partners P6M (6–10 partners and 11 or more partners) (respective OR: 3.3, 95% CI: 1.3–8.5, and OR: 5.7, 95% CI: 2.3–14.1) (**Table 5**).

Table 4: Correlates of *Mycoplasma genitalium* infection (urethral or rectal site) in univariate analyses (n=716)

Characteristics	aOR[a]	95% CI
Sociodemographics		
Age (years)		
46 or older		Reference
30–45	1.0	0.4–2.6
29 or younger	2.9	1.3–6.5
Born in Canada		
No		Reference
Yes	1.0	0.5–1.9
Ethnocultural group		
French Canadian		Reference
English Canadian	1.5	0.5–4.5
European	2.8	0.9–7.8
Latin American	0.5	0.1–2.0
South or East Asian	0.9	0.2–5.0
Other[b]	1.2	0.4–3.1
Education level		
Higher than high school degree		Reference
High school degree or less	0.5	0.2–1.4
Annual income (CAD)		
0–29,999		Reference
30,000–59,999	1.8	0.9–3.6
60,000 or more	2.9	1.0–7.5
Sexual orientation		
Gay		Reference
Other[c]	0.6	0.2–1.7
Gender identity		
Cisgender man		Reference
Transgender man	2.4	0.4–13.2
Other[d]	1.8	0.6–3.1
Living with HIV		
No		Reference
Yes	1.4	0.6–3.1

Table 4: Correlates of *Mycoplasma genitalium* infection (urethral or rectal site) in univariate analyses (n=716) (*continued*)

Characteristics	aOR[a]	95% CI
Sexual partners (P6M)		
Number of male sexual partners		
5 or fewer		Reference
6–10	3.9	1.5–10.3
11 or more	7.4	3.1–17.7
New sex partner		
No		Reference
Yes	3.9	1.5–10
Condomless anal sex acts with a man		
None		Reference
1 or more	3.3	1.3–8.6
Methods of finding sexual partners (P6M)		
Attending a bath house or sex club		
No		Reference
Yes	1.4	0.7–2.8
Attending a group sex event		
No		Reference
Yes	2.4	0.9–6.4
Substance use (P6M)		
Any chemsex[e]		
No		Reference
Yes	2.3	1.2–4.4
Crystal methamphetamine use		
No		Reference
Yes	2.0	0.8–4.9
Drug injection		
No		Reference
Yes	N/A[f]	N/A
STBBI (P6M)		
Self-reported sexually transmitted infection diagnosis[g]		
No		Reference
Yes	3.3	1.4–7.9
Co-infection with *C. trachomatis* or *N. gonorrhoeae*		
No		Reference
Yes	1.4	0.4–3.6

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; *C. trachomatis*, *Chlamydia trachomatis*; *N. gonorrhoeae*, *Neisseria gonorrhoeae*; N/A, not applicable; P6M, past six months; STBBI, sexually transmitted and blood-borne infections
[a] Adjusted for respondent-driven sampling recruitment and censoring
[b] Other ethnocultural groups included Arab or North African, East or West African or Caribbean and Aboriginal or Indigenous
[c] Other sexual orientations included bisexual and queer
[d] Other gender identities included participants identifying as genderqueer, non-binary, or two-spirit
[e] Chemsex includes crystal methamphetamine, GHB (gamma-hydroxybutyrate), ecstasy/MDMA (3,4-methylenedioxymethamphetamine) or ketamine consumption in the two hours before or during sex with at least one of the last five partners participants reported having sex within the P6M (17). Poppers (i.e. alkyl nitrites) are included here in chemsex definition
[f] Too few *M. genitalium* infections among participants who injected drugs to permit valid inference
[g] Self-reported STI (sexually transmitted infection) diagnosis by a healthcare professional in the P6M like *C. trachomatis*, *N. gonorrhoeae*, lymphogranuloma venereum (LGV) or syphilis

Table 5: Multivariable predictive model of *Mycoplasma genitalium* infection

Characteristics	aOR[a]	95% CI
Number of male sexual partners P6M		
5 or fewer		Reference
6–10	3.3	1.3–8.5
11 or more	5.7	2.3–14.1
Age (years)		
30 or older		Reference
29 or younger	2.5	1.2–5.5
Condomless anal sex at least once P6M		
No		Reference
Yes	2.1	0.8–5.4

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; *M. genitalium*, *Mycoplasma genitalium*; P6M, past six months
[a] Adjusted for respondent-driven sampling recruitment and censoring

Antimicrobial resistance of *Mycoplasma genitalium*

For the three participants who were infected at both the urethral and rectal sites, the results obtained from the urethral site were used to calculate the prevalence of antimicrobial resistance (AMR). Prevalence of MRAM was 82% (n=46/56) and prevalence of QRAM was 29% (n=16/55) (**Table 6**). Prevalence of either MRAM or QRAM was 85% (n=46/54), while prevalence of both MRAM and QRAM was 28% (n=15/54).

Table 6: Macrolide resistance and quinolone resistance-associated mutations detected by real-time polymerase chain reaction in *Mycoplasma genitalium*-positive specimens, n=61[a]

Resistance-associated mutations (genes)	Mutations	Real-time polymerase chain reaction results	
		n	%
MRAM (23S rRNA), n=56[b]	Wild type	10	18%
	A2058G	7	12%
	A2059G	39	70%
QRAM (*parC*[c]), n=55[b]	Wild type	39	71%
	S83I (G248T)	13	23%
	S83R (A247C)	2	4%
	D87Y (G259T)	1	2%

Abbreviations: *M. genitalium*, *Mycoplasma genitalium*; MRAM, macrolide resistance-associated mutations; QRAM, quinolone resistance-associated mutations; rRNA, ribosomal ribonucleic acid
[a] The 64 positive samples obtained from the urethral or rectal site were from 61 distinct individuals (three were infected at both sites). For the three participants who were infected at both the urethral and rectal site, the results obtained from the urethral site were used to calculate the prevalence of resistance
[b] An invalid result (amplification failure) was obtained in five cases for the macrolide assay and six cases for the quinolone assay
[c] No mutation in the *gyrA* gene, nor the S83N or the D87N mutations in *parC* was found

Discussion

This first Canadian community-based study estimates the prevalence of *M. genitalium* infection at 5.7% (urethral or rectal infection) among gbMSM. It is challenging to contextualize our data since population-based prevalence studies are lacking. Compared to Canadian STI clinic-based studies, the urethral *M. genitalium* prevalence in our study (2.2%) was lower than previous estimates among men in Ontario (4.5%, 2013), Alberta (5.3%, 2016) and Saskatchewan (6.2%, 2019) (12–14). In Australia, urethral *M. genitalium* prevalence among men who have sex with men (MSM) recruited in STI clinics ranged from 2.7–4.7% and prevalence of rectal infections (7.0%–8.9%) was higher than in our study (4.0%) (24,25). Consistent with our results (n=3/689; 0.4%), a very low number of pharyngeal *M. genitalium* infections among MSM were reported in Australia (n=0/508 to n=8/464; 2.0%) (9,25). We hypothesize that oral transmission is negligible, and we excluded *M. genitalium*-positive pharyngeal samples from our prevalence estimation. Rectal *M. genitalium* infection (4.0%) was more common than rectal *C. trachomatis* (2.6%) and *N. gonorrhoeae* (1.4%) infections. Urethral *M. genitalium* prevalence estimates were more similar to those of *C. trachomatis* infection (*M. genitalium*, 2.2%; *C. trachomatis*, 1,9%; *N. gonorrhoeae*, 0%). A United States cohort study conducted in 2018–2019 among young gbMSM and transgender women found that *M. genitalium* was more prevalent than other STIs in both rectal (*M. genitalium*, 21.7%; *C. trachomatis*, 8.8%; *N. gonorrhoeae*, 6.8%) and urine samples (*M. genitalium*, 8.9%; *C. trachomatis*, 1.6%; *N. gonorrhoeae*, 0.8%) (26). A 2017–2018 Australian study found that among asymptomatic MSM, *C. trachomatis* prevalence was comparable to *M. genitalium* in rectal samples (*M. genitalium*, 7.0%; *C. trachomatis,* 8.5%; *N. gonorrhoeae*, 6.2%) and urine samples (*M. genitalium*, 2.7%; *C. trachomatis*, 1.7%; *N. gonorrhoeae*, 0.7%). It also found that 9.2% of MSM that tested positive for rectal *C. trachomatis* were co-infected with *M. genitalium* while 6.1% of positive rectal *N. gonorrhoeae* samples demonstrated co-infection with *M. genitalium* (24). In our study, 9.1% of gbMSM that tested positive for *C. trachomatis* at the rectum were co-infected with *M. genitalium*, 16.7% of rectal *N. gonorrhoeae* infections showcased *M. genitalium* co-infection.

In univariate analyses, multiple risk factors for STI transmission, such as chemsex P6M, new sexual partners P6M and a STI diagnosis P6M, were identified. Younger age and having multiple male sexual partners were retained in our predictive model. These findings are consistent with studies that identified younger age (24,27,28) and multiple sexual partners (19,20,29,30) as correlates of *M. genitalium* infection. While a United Kingdom study documented a higher prevalence of *M. genitalium* among gbMSM living with HIV (31), HIV infection was not associated with *M. genitalium* infection in our study. More studies are needed to clarify the role of *M. genitalium* in HIV acquisition or transmission among gbMSM as it has been identified as a risk factor of HIV infection, especially in MSM (32,33).

The very high prevalence of MRAM (82%; n=46/56) and QRAM (29%; n=16/55) found among the Engage Cohort Study Montréal's gbMSM is a worrisome finding. This prevalence is higher than previous Canadian MRAM estimates (men in Alberta in 2016, 64%; women and men in Saskatchewan in 2019, 63% and men in Ontario in 2013, 63%) (12–14). Treatment failure with azithromycin has been well described with single nucleotide polymorphisms at positions 2058 and 2059 in region V of the 23S ribosomal ribonucleic acid (34). For QRAM, S83 in the *parC* gene is significantly associated with moxifloxacin resistance (34). While several single nucleotide polymorphisms contribute to quinolone resistance, none are as strong predictors of treatment failure than macrolide resistance with 23S ribosomal ribonucleic acid single nucleotide polymorphisms (34,35). Previous Canadian studies found a QRAM prevalence of 11%–20% among men and women (12–14). A meta-analysis compiling studies from 2010–2019 estimated MRAM and QRAM prevalence at 52% and 10%, respectively, in the Americas region (2). A 2017–2018 United States clinic-based study among men with urethritis found MRAM and *parC* QRAM prevalence levels of 64% and 12%, respectively (28). Being infected with a macrolide-resistant *M. genitalium* is more likely in gbMSM than in women and men with female partners only (1,36,37). This could be explained by transmission in closely-knit sexual networks and increased exposure to antibiotics (37). The increasing azithromycin resistance could be explained by its widespread use for the treatment of certain STIs (2,7,38–40). In our study, 28% of *M. genitalium*-positive samples had both MRAM and QRAM. Dual resistance has already been reported in gbMSM on HIV PrEP and those living with HIV (36,41).

Implications for research and practice

In our study, we identified a high prevalence of *M. genitalium* infections among gbMSM, especially among younger individuals and those reporting multiple male sexual partners. Although most current guidelines state that routine screening for *M. genitalium* infection is not recommended (as it would contribute to selection pressure of resistant strains), they vary in terms of testing indications and timing in symptomatic individuals (42–44): at the time of initial presentation of urethritis (concomitantly with *N. gonorrhoeae* and *C. trachomatis* testing) (42–44), only for recurrent non-gonococcal urethritis (4) or only for non-chlamydial non-gonococcal persistent or recurrent urethritis, following empiric treatment for *N. gonorrhoeae* and *C. trachomatis* and when pretreatment nucleic acid amplification tests or follow-up test of cure are negative for *C. trachomatis* and *N. gonorrhoeae* (45). Regarding rectal screening, some clearly state it is not recommended (4) or do not mention extra genital testing (46). The high prevalence of *M. genitalium* infection among gbMSM with *C. trachomatis* or *N. gonorrhoeae* infection demonstrates the need for clinicians to remain highly vigilant of a possible co-infection in the case of persistent symptoms after adequate treatment. Our findings of 4.0% prevalence of rectal *M. genitalium* among gbMSM in Montréal, being almost two-fold the prevalence of urethral *M. genitalium* infection (2.2%),

and much higher than *N. gonorrhoeae* rectal infection (1.4%) or *C. trachomatis* infection (2.6%), may add to epidemiologic evidence in the process of updating the Canadian guidelines (45). Finally, the most recent guidelines touching upon the management of *M. genitalium* infection recommend AMR-guided therapy (4,42,44). This approach has demonstrated potential in reducing treatment failures (47,48). Based on the identified susceptibility profile, doxycycline is used as initial empiric treatment and is followed by either azithromycin or moxifloxacin (49). Because of limited availability of tests in Canada and according to the current Canadian guidelines, treatment initiation for *M. genitalium* should occur in the context of syndromic management of persistent or recurrent urethritis (10). Recommended treatment consists of azithromycin and moxifloxacin as first and second lines of treatment (45). The high AMR observed in our study supports the need for *M. genitalium* detection and AMR testing in a short turnaround time (42,44,47). It also highlights the need, when both QRAM and MRAM are detected, for an easier and quicker access to alternative treatments such as pristinamycin, which can currently be requested through the Health Canada's special access program (42,46,50).

Limitations

The small sample size limited our ability to identify correlates of infection or AMR. Data regarding STI-related symptoms was not collected in the study questionnaire which was designed prior to the initiation of this sub-study and was focused on societal and community contexts, social relationships and sexual behaviour. Hence, we could not evaluate the prevalence of *M. genitalium* in association with clinical presentation. Despite using the RDS method for recruitment, some subgroups of the gbMSM population may be over- or under-represented. Potential biases related to RDS were attenuated by adhering to recommended recruitment procedures, having a large sample size with long recruitment chains and adjusting with RDS-II weights. The AMR data were not RDS-adjusted because they were obtained from too small a subsample. Our prevalence findings might not be generalizable to non-urban Canadian gbMSM populations. We did not find comparison studies analyzing the performance of the Allplex CT/NG/MG/TV Assay, which limited our appreciation of potential information biases. Le Roy *et al.* calculated an overall agreement of 94.6% between in-house real-time PCR and the Allplex MG & AziR Assay (51). The assay, however, showed low sensitivity for macrolide resistance compared to sequencing (sensitivity of 74.5%, specificity of 97.6%).

Conclusion

This first population-based study among Canadian gbMSM documented a high prevalence of urethral and rectal *M. genitalium* infection. The observed levels of AMR, which exceed the 5% threshold at which a change in empirical treatment is recommended by the World Health Organization, supports the need for AMR-guided therapy (52). Efforts should be made to facilitate targeted *M. genitalium* detection and AMR testing when indicated.

Authors' statement

ASL — Methodology, data interpretation, visualization, writing–drafting
ACL — Conceptualization, methodology, data interpretation, visualization, writing–review and editing, supervision
AF — Methodology, data curation, formal analysis, data interpretation, writing–review and editing
MD — Methodology, formal analysis, writing–review and editing
JC — Manuscript review and editing, project administration, funding acquisition
CF — Conceptualization, investigation, writing–review and editing
IM — Writing–review and editing
DG — Writing–review and editing
TAH — Writing–review and editing
DMM — Writing–review and editing
GL — Conceptualization, methodology, investigation, formal analysis, data interpretation, writing–review and editing, project administration, funding acquisition, supervision

All authors revised the manuscript critically for important intellectual content, approved the final version to be published and agreed to be accountable for all aspects of the work.

Competing interests

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Establishing Pandemic Influenza Severity Assessment (PISA) parameters and thresholds for Canada's FluWatch program

FluWatch Team[1]*

Abstract

Background: The World Health Organization (WHO) developed a structured framework to enable countries to rapidly assess the severity of an influenza pandemic. This framework, the Pandemic Influenza Severity Assessment (PISA), is intended to be performed weekly during seasonal epidemics so that assessing influenza severity during a pandemic can be done with greater ease and efficiency.

Objective: Using influenza surveillance indicators within Canada's FluWatch program from seasons 2014–2015 to 2018–2019, national PISA thresholds were developed and assessed against seasonal data for seasons 2019–2020 to June of 2022–2023.

Outcomes: Canada developed thresholds for each required indicator (transmissibility, seriousness of disease and impact) for multiple WHO-recommended parameters. The thresholds were assessed against four seasons, and it was determined that there was a good agreement between the PISA assessments and the characterization of the season by FluWatch epidemiologists.

Conclusion: With confidence in the validity of the PISA thresholds, the FluWatch program will begin to share PISA assessments weekly through the FluWatch report in the 2023–2024 seasons to help characterize influenza activity in Canada and inform responses to the seasonal influenza epidemic.

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Keywords: seasonal influenza, severity, FluWatch, PISA, thresholds

Introduction

One of the major gaps of the 2009 H1N1 pandemic was the ability of Member States of the World Health Organization (WHO) to rapidly assess the severity of the pandemic. To address this gap and to better prepare for future influenza pandemics, the WHO developed a structured framework to assess influenza severity, known as the Pandemic Influenza Severity Assessment (PISA) (1).

From 2014 to 2016, Canada participated in a WHO pilot that assessed the interim framework for PISA, and this framework was further refined based on the results from this pilot. In 2017, an official PISA guidance document was published by the WHO for Member States to implement PISA in their respective regions. Assessments are meant to be performed weekly during seasonal epidemics, and outputs are shared with the WHO and used in routine seasonal influenza situational assessments and reports. The goal is for a country to use PISA during seasonal epidemics so that assessing severity during a pandemic can be done with greater ease and efficiency.

In this article, the implementation of PISA into Canada's national influenza surveillance program, FluWatch, is summarized. In addition to implementing PISA for influenza indicators, PISA was also applied to respiratory syncytial virus (RSV) to determine whether PISA thresholds could be developed for viruses other than influenza.

Methods

Data sources

FluWatch is a long-standing national surveillance system that monitors the spread of influenza and influenza-like illness (ILI) in Canada. FluWatch is a composite surveillance system consisting of virological surveillance, influenza and ILI activity level surveillance, syndromic surveillance, outbreak surveillance, severe outcome surveillance, and vaccine monitoring (2). All the data that was considered for PISA originated from the FluWatch surveillance system.

Indicators and parameters for assessment are outlined in the PISA guidance document (1) and in subsequent refinements that were shared among the Member States at working group meetings (3). A list of each recommended parameter and associated indicator is found in **Table 1**. The PISA framework defines influenza severity through the use of three indicators: Transmission, Seriousness, and Impact. Each indicator consists of multiple parameters that countries can use. It is not required for each country to have every parameter listed by the WHO and it is up to each country to decide which parameters to monitor:

Transmissibility: how many people in a population get sick from influenza on a weekly basis

Seriousness: how severely sick individual people get when infected with the influenza virus

Impact: how the influenza epidemic or pandemic affects the healthcare system and society. As of 2023, Impact is split into two indicators: morbidity and mortality, and impact on healthcare capacity

It is recommended that historical data considered for PISA captures at least five seasons and, when possible, thresholds by age are developed.

To develop the thresholds, data for the seasons 2014–2015 to 2018–2019 from the identified FluWatch surveillance indicators in Table 1 were used. The calculated thresholds were assessed against four seasons: 2019–2020, 2020–2021, 2021–2022, and 2022–2023 (to June). In the 2022–2023 season, the epidemic started and ended early (4). Any activity occurring from June to the end of the surveillance season (August 26, 2023) would not have affected the season assessment.

Two methods were used to determine the thresholds: Moving Epidemic Method (MEM) and the WHO method. The MEM method was developed by Vega *et al.* and is recommended by the WHO for Transmissibility and Impact parameters (1,5). The WHO has developed an online MEM tool (6). The FluWatch program used the online MEM tool to calculate the thresholds.

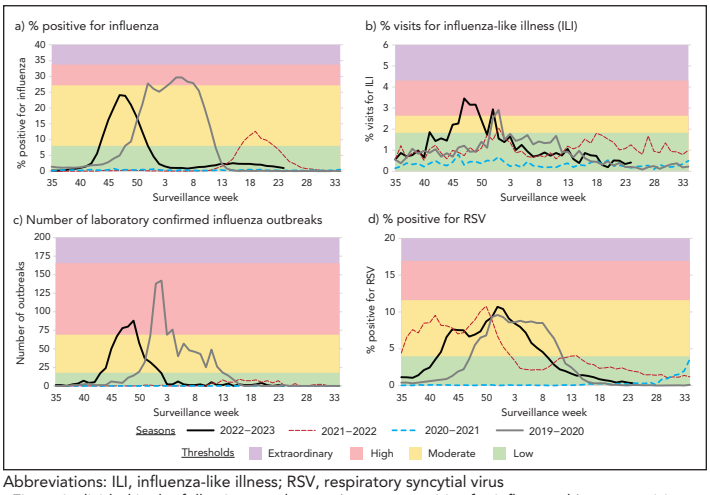
The WHO method is recommended for calculating thresholds for Seriousness (1). To determine the thresholds for moderate, high, and extraordinary Seriousness, the mean, mean plus 1 standard deviation, and mean plus 3 standard deviations of end-of-season values, respectively, were used. Any value below the mean would be considered low Seriousness. The Seriousness and Impact thresholds were developed using Excel 365 (Microsoft Corp., Redmond, United States).

Results

Transmissibility

Percentage of tests positive for influenza: The thresholds for moderate, high and extraordinary were determined to be 8.0, 27.2 and 34.0 (**Figure 1**, a). Any value below 8.0 was considered low. Two seasons (2021–2022 and 2022–2023) peaked at moderate Transmissibility, one season peaked at high Transmissibility (2019–2020) and one season (2020–2021) remained at low Transmissibility for the whole season.

Figure 1: Influenza Transmissibility parameters and thresholds by FluWatch indicator[a], assessed against data for season 2019–2020 to June 2022–2023 season, Canada



Abbreviations: ILI, influenza-like illness; RSV, respiratory syncytial virus

[a] Figure is divided in the following quadrants: a) percent positive for influenza; b) percent visits for influenza-like illness (ILI); c) number of laboratory confirmed influenza outbreaks; d) percent positive for RSV

Percentage of visits for ILI: The thresholds for moderate, high and extraordinary percentage of visits for ILI were determined to be 1.8, 2.6 and 4.3 (Figure 1, b). Any value below 1.8 was considered low. Two seasons (2019–2020 and 2022–2023) peaked at high Transmissibility, one season peaked at moderate Transmissibility (2021–2022), and one season (2020–2021) remained at low Transmissibility for the whole season.

Number of laboratory-confirmed influenza outbreaks: The thresholds for moderate, high and extraordinary were determined to be 18, 69 and 166 (Figure 1, c). Any value below 18 was considered low. Two seasons (2019–2020 and 2022–2023) peaked at high Transmissibility and the other two seasons remained at low Transmissibility for the whole season.

Table 1: WHO PISA parameters, FluWatch indicators and data sources used, Canada, season 2014–2015 to 2018–2019

WHO recommended parameter	FluWatch indicator	FluWatch data source
Transmissibility		
Weekly ILI or MAARI cases as a proportion of total visits or incidence rate	% visits for ILI	Sentinel Primary Care Provider ILI Surveillance Program
Composite (product) of weekly ILI or MAARI rates and weekly percentage positivity for influenza	N/A	Data not available (ILI rates and percentage positivity data from FluWatch indicators do not come from the same sites)
Percentage positivity from specific syndromic presentations (e.g., ILI, ARI, MAARI)	% positive for influenza % positive for RSV	Respiratory Virus Detection Surveillance System (RVDSS)
Number of influenza or respiratory outbreaks reported in care facilities housing elderly or other susceptible groups	Number of laboratory-confirmed influenza outbreaks	Outbreak surveillance
Other healthcare system usage for mild respiratory illness	N/A	Data not available
Data from participatory surveillance	% FluWatchers participants reporting cough and fever	FluWatchers[a]
Seriousness		
Cumulative death: hospitalization ratio	Number of in-hospital influenza deaths (all cases and by ages 0–19, 20–64 and 65+) Number of influenza hospitalizations (all cases and by ages 0–19, 20–64 and 65+)	Provincial and Territorial Severe Outcome Surveillance (PTSOS)
Cumulative ICU: hospitalization ratio	Number of influenza ICU admissions (all cases and by ages 0–19, 20–64 and 65+) Number of influenza hospitalizations (all cases and by ages 0–19, 20–64 and 65+)	PTSOS
SARI:ILI or SARI:ARI ratios	N/A	Data not available
Impact – Morbidity and Mortality		
Weekly number of hospital or ICU admissions for influenza/SARI/respiratory illness, or rate per unit population	Number of influenza hospitalizations (all cases and by ages 0–19, 20–64 and 65+)[b] Number of influenza ICU admissions	PTSOS
SARI proportion or influenza-confirmed SARI proportion of all hospital or ICU admissions	N/A	Data not available
Number of patients currently in hospital or ICU with influenza/SARI/respiratory illness, or rate per unit population	N/A	Data not available
Composite (product) of weekly SARI rate and weekly percentage positivity rates of SARI cases for influenza	N/A	Data not available
Weekly excess pneumonia and influenza or all-cause mortality	N/A	Data not available
Number of hospitalizations for influenza/SARI/respiratory illness requiring oxygen support	N/A	Data not available
Impact – Healthcare Capacity		
Proportion of all (occupied and available) hospital or ICU beds currently occupied for influenza/SARI/respiratory illness or all causes	N/A	Data not available
Proportion of beds with oxygen support occupied for influenza/SARI/respiratory illness or all causes	N/A	Data not available
Healthcare workforce absenteeism	N/A	Data not available
Saturation of primary healthcare capacity	N/A	Data not available

Abbreviations: ARI, acute respiratory infection; ICU, intensive care unit; ILI, influenza-like illness; MAARI, medically attended acute respiratory infection; N/A, not applicable; PISA, Pandemic Influenza Severity Assessment; PTSOS, Provincial and Territorial Severe Outcome Surveillance; RVDSS, Respiratory Virus Detection Surveillance System; RSV, respiratory syncytial virus; SARI, Severe Acute Respiratory Infection; WHO, World Health Organization

[a] FluWatchers data are excluded from the analysis, as data is only available for seasons 2016–2017 onwards (3 seasons)

[b] Rate per unit population can be calculated; however, to keep thresholds consistent with ICU admissions (where rates cannot be calculated), weekly number of hospitalizations will be used

Percentage of tests positive for RSV: The thresholds for moderate, high and extraordinary were determined to be 4.0, 11.6 and 16.9 (Figure 1d). Any value below 4.0 was considered low. Three seasons (2019–2020, 2021–2022 and 2022–2023) peaked at moderate Transmissibility and one season (2020–2021) remained at low Transmissibility for the whole season.

Seriousness

Mid-season (week 8) and year end (week 34) values are recommended for measuring Seriousness indicators. Mid-season values were the same as the year-end values for each included season. Thresholds for low, moderate, high and extraordinary are outlined in **Table 2** and **Table 3**.

Table 2: Cumulative ICU in hospitalization ratio thresholds (Seriousness indicator), by age groups, seasons 2019–2020 to 2022–2023, Canada

Season and age group (years)	Threshold level (ratio range)			
All ages	**Low (0–0.11)**	**Moderate (0.12–0.19)**	**High (0.20–0.33)**	**Extraordinary (0.34+)**
2022–2023	X	-	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-
0–19	**Low (0–0.09)**	**Moderate (0.10–0.16)**	**High (0.17–0.29)**	**Extraordinary (0.30+)**
2022–2023	X	-	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-
20–64	**Low (0–0.18)**	**Moderate (0.19–0.31)**	**High (0.32–0.57)**	**Extraordinary (0.58+)**
2022–2023	X	-	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	X	-	-	-
65+	**Low (0–0.08)**	**Moderate (0.09–0.12)**	**High (0.13–0.21)**	**Extraordinary (0.22+)**
2022–2023	X	-	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-

Abbreviations: ICU, intensive care unit; -, threshold not reached

Table 3: Cumulative death in hospitalization ratio thresholds (Seriousness indicator), by age groups, seasons 2019–2020 to 2022–2023, Canada

Season and age group (years)	Threshold level (ratio range)			
All ages	**Low (0–0.04)**	**Moderate (0.05–0.07)**	**High (0.07–0.12)**	**Extraordinary (0.13+)**
2022–2023	-	X	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-
0–19	**Low (0–0.005)**	**Moderate (0.006–0.013)**	**High (0.014–0.029)**	**Extraordinary (0.030+)**
2022–2023	-	X	-	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-
20–64	**Low (0–0.03)**	**Moderate (0.04–0.06)**	**High (0.07–0.11)**	**Extraordinary (0.12+)**
2022–2023	-	X	-	-
2021–2022	-	X	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-
65+	**Low (0–0.06)**	**Moderate (0.07–0.10)**	**High (0.11–0.17)**	**Extraordinary (0.18+)**
2022–2023	-	-	X	-
2021–2022	X	-	-	-
2020–2021	X	-	-	-
2019–2020	-	X	-	-

Abbreviation: -, threshold not reached

Cumulative intensive care unit: Hospitalization ratio

All ages: Seasons 2020–2021, 2021–2022 and 2022–2023 were classified as low Seriousness. Season 2019–2020 was classified as moderate Seriousness.

0–19 years: Seasons 2020–2021, 2021–2022 and 2022–2023 were classified as low Seriousness. Season 2019–2020 was classified as moderate Seriousness.

20–64 years: All seasons were classified as low Seriousness.

65+ years: Seasons 2020–2021, 2021–2022 and 2022–2023 were classified as low Seriousness. Season 2019–2020 was classified as moderate Seriousness.

Cumulative deaths: Hospitalization ratio

All ages: Seasons 2020–2021 and 2021–2022 were classified as low Seriousness. Seasons 2019–2020 and 2022–2023 were classified as moderate Seriousness.

0–19 years: Seasons 2020–2021 and 2021–2022 were classified as low Seriousness. Seasons 2019–2020 and 2022–2023 were classified as moderate Seriousness.

20–64 years: Season 2020–2021 was classified as low Seriousness. Seasons 2019–2020, 2021–2022 and 2022–2023 were classified as moderate Seriousness.

65+ years: Seasons 2020–2021 and 2021–2022 were classified as low Seriousness. Season 2019–2020 was classified as moderate Seriousness and 2022–2023 was classified as high Seriousness.

Impact

The thresholds for Impact were calculated using the WHO method.

Number of weekly hospitalizations

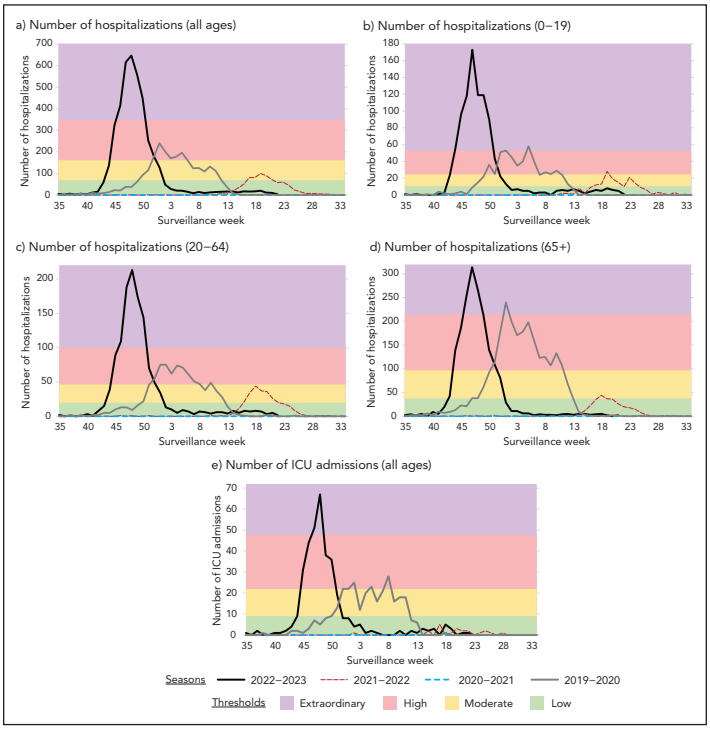
All ages: The thresholds for moderate, high and extraordinary were determined to be 68, 160 and 346 (**Figure 2**, a). Any value below 68 was considered low. The 2022–2023 season peaked at extraordinary Impact. The 2019–2020 season peaked at high Impact. The 2021–2022 season peaked at moderate Impact. The 2020–2021 season remained at low Impact for the whole season.

0–19 years: The thresholds for moderate, high and extraordinary were determined to be 10, 25 and 53 (Figure 2, b). Any value below 10 was considered low. The 2022–2023 and 2019–2020 seasons peaked at extraordinary Impact. The 2021–2022 season peaked at high Impact. The 2020–2021 season remained at low Impact for the whole season.

20–64 years: The thresholds for moderate, high and extraordinary were determined to be 68, 160 and 346 (Figure 2, c). Any value below 68 was considered low. The 2022–2023 season peaked at extraordinary Impact. The 2019–2020 season peaked at high Impact. The 2021–2022 season peaked at moderate Impact and the 2020–2021 season remained at low Impact for the whole season.

65+ years: The thresholds for moderate, high and extraordinary were determined to be 37, 97 and 214 (Figure 2, d). Any value below 37 was considered low. The 2022–2023 and 2019–2020 seasons peaked at extraordinary Impact. The 2021–2022 season peaked at moderate Impact. The 2020–2021 season remained at low Impact for the whole season.

Figure 2: Influenza Impact parameters and thresholds by age group (years, where available) and FluWatch indicator[a], assessed against data for season 2019–2020 to June 2022–2023 season, Canada



Abbreviation: ICU, intensive care unit

[a] Figure is divided in the following quadrants: a) number of hospitalizations (all ages); b) number of hospitalizations (0–19); c) number of hospitalizations (20–64); d) number of hospitalizations (65+); e) number of ICU admissions (all ages)

Number of weekly intensive care unit admissions

Due to the small weekly numbers, it was determined that measuring intensive care unit (ICU) admissions by age group was not feasible. Instead, ICU admissions were measured as an aggregate of all age groups. The thresholds for moderate, high and extraordinary were determined to be 9, 22 and 48 (Figure 2, e). Any value below 9 was considered low. The 2022–2023 season peaked at extraordinary Impact. The 2019–2020 season peaked at high Impact. The 2019–2020 and 2021–2022 seasons remained at low Impact for the whole season.

Discussion

The indicators chosen for PISA are reliable, timely and of high quality. With the exception of the healthcare capacity (Impact) indicator, Canada's FluWatch program has data to support parameters within each indicator, with age-specific parameters for the Seriousness and Impact indicators.

The thresholds resulting from this work allow Canada to assess influenza severity at a national level during both seasonal epidemics and pandemics. PISA is a standardized assessment that is used globally, which allows for country-to-country comparisons and enables Canada to contribute to the WHO's global severity assessment for influenza.

The Transmissibility indicator has the greatest number of unique parameters (percent positive for influenza, number of laboratory-confirmed outbreaks, percent visits for ILI). The weekly percentage of tests positive for influenza is currently used to determine the start and the end of a seasonal epidemic in Canada; therefore, it is used as the main parameter for Transmissibility. The others will be used as supporting parameters to monitor Transmissibility in different populations (outbreaks—in congregate settings, percent ILI—in the community among those seeking medical care). With additional surveillance seasons available, data from participatory surveillance (FluWatchers) could be added to the Transmissibility indicator as a measure in a population that does not seek medical care.

Two FluWatch indicators (cumulative ICU to hospitalization ratio and cumulative death to hospitalization ratio) were used to assess Seriousness, each stratified by age group (0–19 years, 20–64 years and 65+ years). The availability of age-specific data will allow the FluWatch program to monitor the Seriousness for influenza in different age groups. This indicator requires cumulative data and would be used to assess the season at the midpoint and at the end.

Two FluWatch indicators (number of weekly hospital admissions, number of weekly ICU admissions) were used to assess Impact in the population overall and for three age groups 0–19 years, 20–64 years and 65+ years) for hospitalizations only. The availability of age-specific data in the hospitalization parameter will allow the FluWatch program to monitor impact in different age groups.

The separation of healthcare capacity within the Impact indicator was a recent change in 2023, resulting from the coronavirus disease 2019 (COVID-19) pandemic. Healthcare capacity was an important measure during the COVID-19 pandemic and will likely be an important measure during a future pandemic. Determining a reliable source of data and the accumulation of historical data will be required for the development of this parameter.

The 2019–2020 season was the last pre-pandemic season included in this assessment. The 2019–2020 season peaked at high Transmissibility and Impact, while Seriousness was considered moderate. These assessments are supported by the characterization of the season by the FluWatch program, where the concurrent circulation of all seasonal influenza types and subtypes resulted in higher than average numbers of influenza detections and hospitalizations (7). With concurrent circulation of all types and subtypes of influenza, all age groups were affected during that season, which is supported by the moderate levels reported in at least one of the parameters within the Seriousness indicator for each age group.

Due to public health measures implemented for the COVID-19 pandemic, no community circulation of influenza occurred in the 2020–2021 season (8). This was evident in the low PISA assessments for the season. Community circulation of influenza returned briefly in the spring of the 2021–2022 season (9). This season peaked at moderate Transmissibility while both Impact and Seriousness indicators remained low.

The 2022–2023 season was the first season since the 2019–2020 season where influenza began to return to pre-pandemic circulation patterns. The season started early, with reports of higher than usual influenza-associated hospitalizations, ICU admissions, and deaths (10). It peaked at high Transmissibility and extraordinary Impact, while Seriousness was considered both low (for ICU to hospitalization ratio) and moderate (for death to hospitalization ratio). Hospitalization rates were highest among the 65+ and the 0–4 age groups (10), wherein high and moderate Seriousness assessments were recorded, respectively.

Transmissibility thresholds within PISA were also developed for RSV. The Transmissibility threshold for RSV will enable the FluWatch program to characterize RSV activity for each season. RSV surveillance has historically been limited to laboratory data; however, there are efforts to expand Canada's national respiratory surveillance program to include enhanced surveillance indicators for RSV. As RSV surveillance indicators are developed, additional PISA parameters for RSV can also be established. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could also be another candidate for PISA, as historical endemic/non-pandemic surveillance data accumulates.

The PISA thresholds were developed using pre-pandemic data, which might have an effect on the interpretability and applicability of the thresholds going forward. Upcoming work will include the internal monitoring of the effects of the pandemic on influenza trends and calculated thresholds, as well as determining the appropriateness of including the most recent season's data (2022–2023) into threshold assessments for future seasons.

Conclusion

Canada has internally monitored PISA thresholds for the past four seasons. It has been determined that there is good agreement between the PISA assessments and the characterization of the season by FluWatch epidemiologists. The FluWatch program will begin to share PISA assessments in the 2023–2024 FluWatch reports to characterize influenza activity in Canada and to help inform public health responses to seasonal influenza epidemics.

Authors' statement

MBM — Data curation, formal analysis, review and editing
SB — Data curation, review and editing
LL — Original draft, review and editing
AR — Data curation, formal analysis, review and editing
KS — Data curation, review and editing

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The authors have no competing interests.

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Does the Australian influenza season predict the Canadian influenza season? A qualitative comparison of seasons, 2014–2020

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Abstract

A commonly held belief by the Canadian media and public is that the Australian influenza season is a fairly reliable indicator of what the Canadian influenza season that follows might be like. However, this claim is not well substantiated with epidemiological evidence. Therefore, the objective of this work was to qualitatively compare the timing of the onset, peak, and intensity of influenza activity, the dominant circulating influenza strains, and the seasonal vaccine and vaccination policies from 2014 to 2020 between Canada and Australia, using a combination of FluNet data and influenza surveillance reports and publications. Across the epidemiological indicators considered, the epidemics between Canada and Australia often differ. While vaccination policies and coverage are similar between the two countries, vaccine composition and vaccine effectiveness estimates also differ. Ultimately, there are many differences and confounding variables between the Australian and Canadian influenza seasons across numerous indicators that preclude the use of the Australian influenza season as the sole predictor of the Canadian influenza season. However, the availability of global surveillance data and robust national and sub-national surveillance data can provide lead time and inform within-season resource and capacity planning, as well as mitigation measures, for seasonal influenza epidemics.

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Keywords: influenza, surveillance, seasonality, epidemiology, vaccine

Introduction

Seasonal influenza primarily circulates in the winter months. In Australia, the influenza season typically occurs during the months of May to October, while in Canada, the influenza season typically occurs during the months of October to May. A commonly held belief by the Canadian media and public is that the Australian influenza season is a fairly reliable indicator of what the Canadian influenza season that follows might be like (1–4) The origin of this belief is unknown, but likely became widespread after the severe influenza seasons in both the Southern and Northern Hemispheres in 2017 (2).

As of December 2021, only one empirical study has been published on whether Australian influenza data can predict influenza activity in the Northern Hemisphere (the United States, United Kingdom, and China). Zhang *et al.* applied a multivariate seasonal autoregression integrated moving average model and found that using World Health Organization (WHO) FluNet surveillance data from 2010 to 2018 for the Southern Hemisphere, in combination with local data from internet queries, nominally improved prediction of the influenza positive incidence in these three Northern Hemisphere countries (5). Beyond this, the claim that the Australian influenza season can be used to predict the Canadian influenza season is not well investigated nor substantiated by epidemiological evidence.

The objective of this commentary is to compare the timing of the onset, peak, and intensity of influenza activity, the dominant circulating influenza strains, and the seasonal vaccine and vaccination policies from 2014 to 2020 between Canada and Australia to determine whether there is sufficient evidence to support whether the seasonal influenza epidemic in Australia can be used as a predictor of the Canadian influenza season.

Scope and methods

Data from seven consecutive seasons (Northern Hemisphere seasons 2014–2015 to 2020–2021 and corresponding Southern Hemisphere seasons 2014 to 2020) were used for qualitative comparison. The WHO FluNet data were used to determine the dominant circulating subtype and to calculate and generate the influenza A and B percent positivity epidemiological curves for Australia and Canada from January 2014 to August 2021 (6). To enable the comparison of seasons, start and end, epidemiological week 35 of a Canadian season was aligned to week 1 of an Australian season and periods. Australia does not set a threshold to call the start and end to their seasonal epidemic; therefore, to enable a direct comparison, Canada's threshold of two consecutive weeks of ≥5% influenza test positivity was used to define a seasonal influenza epidemic (7). Epidemiological curves were compared and analyzed. All analyses were done in R software (8) and figures were produced in Excel.

Hospitalizations, while an important surveillance indicator for severity, were excluded from this comparison, as hospitalization data between the two countries were not comparable. Data used for the comparison of epidemiological trends and vaccination recommendations were limited to official surveillance reports and immunization handbooks and statements published by the Government of Canada and the Australian Government. Information on seasonal influenza vaccine composition was obtained from the meeting reports published by the WHO. Vaccine effectiveness (VE) results were obtained from published journal articles that were collected, collated and saved as part of active surveillance of global VE results by Canada's national influenza surveillance program (FluWatch).

Key findings

Virologic

Influenza A was the dominant circulating virus type in both Canada and Australia across seasons, with the exception of the 2015 season in Australia, where influenza A and B circulated in similar proportions (**Table 1**). Over the seven seasons compared, in only three did the dominant Australian influenza A subtype correspond to the following season's dominant Canadian influenza A subtype (2016/2016–2017 [A(H3N2)], 2017/2017–2018 [A(H3N2)] and 2018/2018–2019 [A(H1N1)] seasons). While strain information on the influenza A subtypes in circulation were unavailable in the Australian surveillance reports, dominant influenza A subtype in circulation in Australia during the three seasons were determined to be well matched, reasonably well matched, or antigenically similar to the vaccine components, respectively (9–11). This suggests that the dominant circulating strains of influenza A subtypes were similar to those in Canada during these three seasons (12–14).

During this period, both Canada and Australia had seasons with influenza B circulation, but the seasons with higher influenza B incidence had no correspondence (2015 in Australia vs. 2017–2018 and 2019–2020 in Canada). Across most seasons, Canada had a large wave of influenza A followed by a smaller wave of influenza B, except in seasons 2017–2018 and 2019–2020, where influenza B co-circulated with influenza A (**Figure 1**). In Australia, influenza A and B generally co-circulated in all seasons, with influenza B circulating at lower levels. Due to the coronavirus disease 2019 (COVID-19) pandemic and public health response measures, both Australia and Canada had minimal circulating influenza in 2020–2021.

Table 1: Number and proportion of Influenza detections by type, Australia and Canada, 2014–2020[a]

Season	Country	Total influenza detections	Influenza A		Influenza B		Among subtyped influenza A detections			
							Influenza H1N1		Influenza H3N2	
			n	%	n	%	n	%	n	%
2014/2014–2015	Australia	3,473	**3,011**	**86.7**	462	13.3	**1,701**	**60.2**	1,124	39.8
	Canada	45,048	**36,428**	**80.9**	8,620	19.1	104	0.8	**13,168**	**99.2**
2015/2015–2016	Australia	3,625	1,825	50.3	1,800	49.7	244	13.7	**1,533**	**86.3**
	Canada	39,449	**28,495**	**72.2**	10,954	27.8	**11,168**	**90.5**	1,172	9.5
2016/2016–2017	Australia	6,705	**5,566**	**83.0**	1,139	17.0	588	16.9	**2,893**	**83.1**
	Canada	39,512	**35,001**	**88.6**	4,511	11.4	176	1.0	**17,524**	**99.0**
2017/2017–2018	Australia	10,509	**7,684**	**73.1**	2,825	26.9	507	18.4	**2,248**	**81.6**
	Canada	64,250	**36,039**	**56.1**	28,211	43.9	1,274	10.3	**11,074**	**89.7**
2018/2018–2019	Australia	4,264	**3,869**	**90.7**	395	9.3	**2,058**	**74.8**	695	25.2
	Canada	47,763	**45,240**	**94.7**	2,523	5.3	**10,981**	**67.9**	5,196	32.1
2019/2019–2020	Australia	14,002	**12,035**	**86.0**	1,967	14.0	674	12.8	**4,586**	**87.2**
	Canada	53,789	**30,986**	**57.6**	22,803	42.4	**4,956**	**69.1**	2,215	30.9
2020/2020–2021	Australia	949	**876**	**92.3**	73	7.7	**267**	**80.7**	64	19.3
	Canada	72	**49**	**68.1**	23	31.9	5	38.5	**8**	**61.5**

[a] Dominant circulating type and influenza A subtype by country and season are indicated in bold

Figure 1: Historical comparison of influenza percent positivity in Canada and Australia, by surveillance week and season

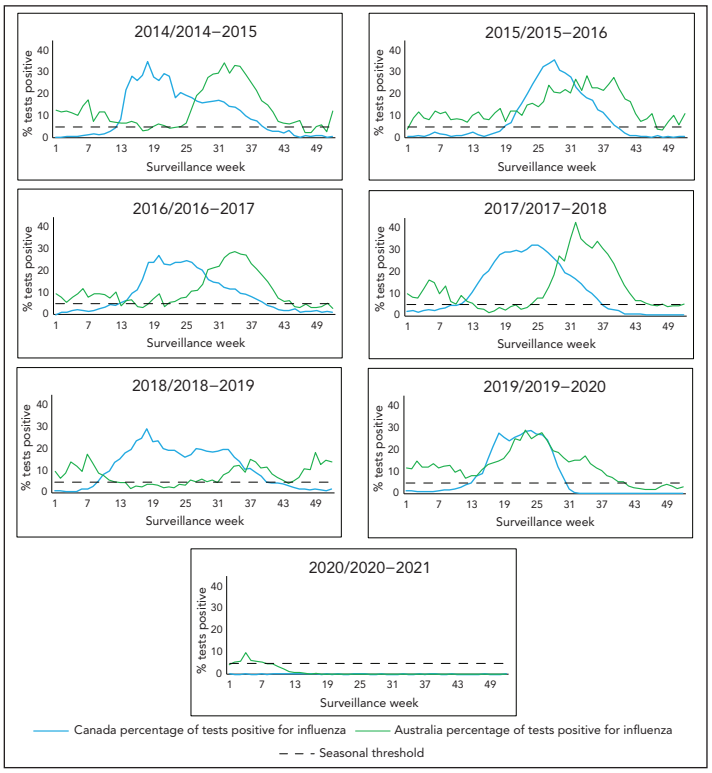
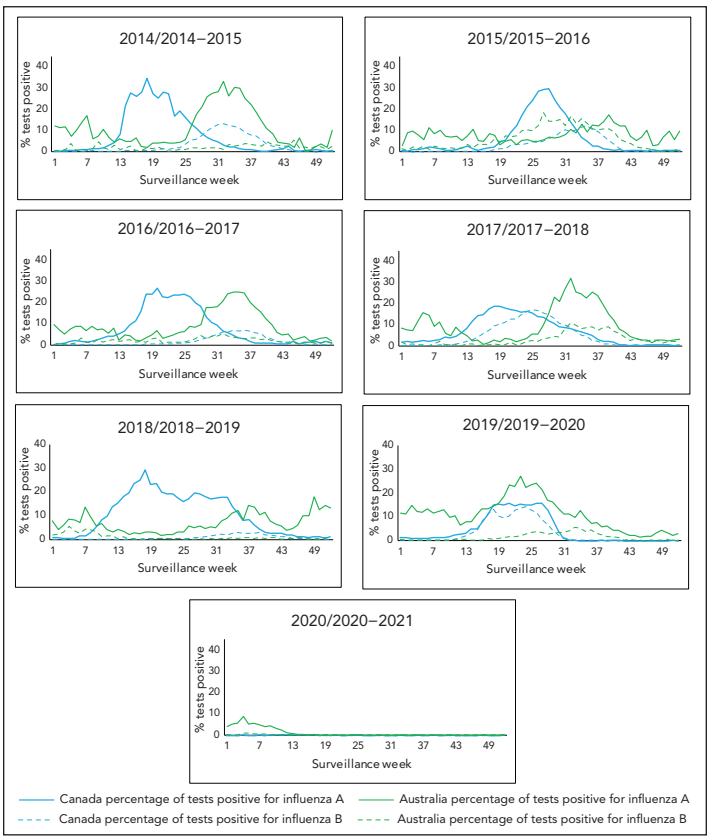


Figure 2: Historical comparison of influenza A and B percent positivity in Canada and Australia by surveillance week and season



Influenza activity

Australia and Canada also show different seasonal dynamics and differ from one season to another (**Figure 2**). Using Canada's thresholds for seasonal influenza epidemics (at least two consecutive weeks where ≥5% of tests are positive for influenza) as a marker for epidemic activity, Australia appears to experience a short and less intense epidemic period of influenza activity in most seasons before experiencing the main, larger epidemic, while Canada usually experiences one continuous period of epidemic activity. Excluding the Canadian 2019–2020 and 2020–2021 seasons and the Australian 2020 season due to the COVID-19 pandemic, the average epidemic length in Canada was 27 weeks (range: 22–31 weeks) and 31 weeks in Australia (range: 23–45 weeks). Excluding the seasons affected by the COVID-19 pandemic, Australia sees an average of 40 weeks where at least 5% positivity was reported, compared to Canada's average of 27 weeks.

Epidemic activity rises more quickly in Canada (with seasons peaking on average during? 10.4 weeks in Canada [range: 8–15 weeks] vs. 17 weeks for Australia [range: 9–33 weeks]) from the time where 5% positivity is reached in the main epidemic curve. The intensity, as indicated by the magnitude of the peak, differed between Canada and Australia for most seasons. There was only one season (2016/2016–17), where the peak percent positivity in Canada and Australia was within 5%. There was no discernable peak pattern, as peak percent positivity ranged from 15.1%–42.9% in Australia and 27.1%–36.0% in Canada.

Vaccine policy and coverage

Vaccine policies are relatively similar between Australia and Canada. The Australian Immunisation Handbook and the Canadian Immunization Guide both outline similar groups recommended for seasonal influenza vaccination. For both countries, all individuals aged ≥6 months should be offered the seasonal influenza vaccine with a focus on groups that include individuals at high risk of influenza-related complications or hospitalization, individuals capable of transmitting influenza to those at high risk, individuals who provide essential community services and commercial poultry (both Canada and Australia), and swine workers (Australia only) during an outbreak of avian or swine influenza (15,16).

In the 2020/2020–2021 season, vaccine coverage in both countries was also relatively similar. Vaccine coverage was highest among individuals aged 65+ (62% in Australia and 70% in Canada) (17,18). Adults also had similar coverage in both countries (in Australia 23% and 35% of individuals aged 15 to ≤49 years and 50 to ≤64 years respectively were vaccinated and in Canada, 29% in individuals aged 18–64 years in Canada) (17,18). Vaccination coverage is relatively stable year to year in both countries.

Influenza vaccine composition and vaccine effectiveness

Vaccine strain recommendations were identical between Australia and Canada from 2014 to 2017, with both countries providing both trivalent and quadrivalent vaccines. The recommended B strains differed in 2018, 2019 and 2020 and A strains differed in 2019 and 2020 (19).

Vaccine effectiveness estimates generated using similar test negative case control designs for comparable seasons and intervals are summarized in **Table 2**. For three out of the four seasons where the vaccines were identical, Australia's VE estimate was higher than that of Canada's (with the exception of the 2016–2017 season); however, the confidence intervals overlapped in all but the 2014–2015 season, where the VE in Canada was 9% vs. 44% in Australia).

Discussion

Australia and Canada have different seasonal dynamics and overall activity differs from one season to another. The Canadian influenza season appears to be more concentrated with activity peaking more quickly than that of the Australian influenza season. The dominant circulating type and subtype can have an effect on the burden and severity of a season. The dominant circulating type and subtype, length, intensity and activity of an influenza season are core surveillance indicators in Canada. Our comparison showed that these indicators are often different between the countries from season to season.

Vaccine policy and coverage are similar between the countries and among the seasons, with comparable vaccine components. No distinct VE estimate trends were found between the two countries. More recently, the composition of the Northern and Southern Hemispheres seasonal influenza vaccine began to differ, which limits the comparability and usefulness of the Australian VE estimates as a predictor of Canadian VE estimates. Differences and similarities in vaccine composition, policy and VE are other limitations that must be considered when comparing the influenza activity of the two countries and using one as a predictor of activity for the other.

In addition to the differences in seasonal activity, climatic and demographic factors are well-established factors that influence influenza disease dynamics (32,33). Both similarities and differences exist between Canada and Australia in climate and population. The climate of the two countries is different, with sub-zero degrees Celsius winter temperatures in Canada and above zero degrees Celsius in Australia. The population distribution, however, in 2020 by age and sex are similar between the two countries (34,35).

Confounding issues in the side-by-side analysis of standard surveillance indicators is a major limitation of this analysis. For example, laboratory-confirmed influenza is a nationally notifiable disease in both Australia and Canada; however, there can be differences in the populations being tested and testing practices between the countries. This is evidenced by the differences in the number of influenza detections reported between Canada and Australia. In some seasons, Canada has greater than 10 times the influenza detections; however, it is unknown whether this is due to differences in testing and reporting practices or actual differences in the number of detections (illness). Canada leans towards testing more severe disease in patients; however, Australia's testing strategy may differ from Canada. The metadata to assess data comparability and potential threats to validity are often unavailable in routine surveillance reports or from the underlying surveillance systems.

Table 2: Summary of published vaccine effectiveness estimates (interim or final) against medically attended influenza, Australia and Canada, seasons 2014 to 2020

Season (references)	Australia VE estimate (95% CI)	Canada VE estimate (95% CI)	Notes on VE estimate[a]
2014/2014–2015 (20,21)	44% (31–55)	9% (−14 –57)	VE against medically attended influenza (all types)
2015/2015–2016 (22,23)	54% (42–63)	46% (32–57)	VE against medically attended influenza (all types)
2016/2016–2017 (24,25)	40% (18–56)	44% (30–55)	VE against medically attended influenza (all types)
2017/2017–2018 (26,27)	55% (17–46)	42% (25–55)	Interim VE against medically attended influenza (all types)
2018/2018–2019[b] (28,29)	68% (47–67)	68% (55–77)	Interim VE against medically attended influenza (all types)
2019/2019–2020[c] (30,31)	A(H1N1): 62% (39–78) A(H3N2): 37% (24–49) B: 63% (45–74)	A(H1N1): 44% (26–58) A(H3N2): 62% (37–77) B: 69% (57–77)	Interim VE against medically attended influenza (by type/subtype)
2020/2020–2021[d]	N/A	N/A	N/A

Abbreviations: CI, confidence interval; N/A, not applicable; VE, vaccine effectiveness
[a] The most up-to-date comparable estimates available were used: If only interim estimates were available for one country, the interim estimates for both countries were used for the comparison
[b] The 2018 Southern Hemisphere and 2018–2019 Northern Hemisphere vaccine had a different influenza B Victoria component
[c] The 2019 Southern Hemisphere and 2019–2020 Northern Hemisphere vaccine had different influenza A(H1N1) and A(H3N2) components
[d] The 2020 Southern Hemisphere and the 2020–2021 Northern Hemisphere vaccine had different influenza A(H1N1) and A(H3N2) components

Influenza activity is notoriously hard to predict. The attraction of using the seasonal influenza experience that occurred just months before in one country to predict the activity of another country is understandable from a planning perspective. The Australian influenza surveillance reports are available online and they have robust surveillance indicators; however, there are many important considerations outlined in this article that should be taken into account when interpreting the data and applying it to Canada.

Conclusion

This comparison is the first season-by-season comparison of Canadian and Australian influenza data to our knowledge, and it brings to light the challenges and limitations with using Australia's data to predict Canada's influenza season. Based on this comparison, the use of key indicators from the Australian season to predict trajectory, intensity or duration characteristics of the Canadian influenza season is unsupported by evidence. While we are not discounting the use of Australian influenza surveillance data, the data should be treated the same way as surveillance data obtained from any other country and used together as global intelligence to inform influenza trends and activity that could occur in Canada. Timely and robust national and sub-national surveillance data is a great asset in aiding the development of within-season predictions that can provide lead time and inform within-season resource and capacity planning, as well as mitigation measures (36).

Authors' statement

DC — Conception, analysis, writing–original draft, writing–review and editing
LL — Conception, revising of writing, critical review
CB — Conception, revising of writing, critical review

Competing interests

None.

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Syndromic surveillance performance in Canada throughout the COVID-19 pandemic, March 1, 2020 to March 4, 2023

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic has highlighted the need for robust surveillance of respiratory viruses. Syndromic surveillance continues to be an important surveillance component recommended by the World Health Organization (WHO). While FluWatchers, Canada's syndromic surveillance system, has been in place since 2015, the COVID-19 pandemic provided a valuable opportunity to expand the program's scope and underlying technology infrastructure. Following some structural changes to FluWatchers syndromic questionnaire, participants are now able to contribute valuable data to the non-specific surveillance of respiratory virus activity across Canada. This article examines the performance of FluWatchers' syndromic surveillance over the three years of the COVID-19 pandemic in Canada. More specifically, this article examines FluWatchers' performance with respect to the correlation between the FluWatchers influenza-like illness (ILI) and acute respiratory infection (ARI) indicators and total respiratory virus detections (RVDs) in Canada, including influenza, respiratory syncytial virus (RSV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and other respiratory viruses.

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Keywords: syndromic surveillance, participatory surveillance, influenza, respiratory viruses

Introduction

FluWatchers is a participatory syndromic surveillance system that has been in place in Canada since 2015. This crowdsourced system, which relies on volunteers in Canada to report influenza-like illness (ILI) symptoms on a weekly basis, was initially implemented to monitor influenza as part of the FluWatch program (1). Respiratory viruses, including both influenza and non-influenza viruses such as respiratory syncytial virus (RSV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and others place a substantial burden on global healthcare systems (2,3). In Canada alone, influenza is estimated to cause 12,200 hospitalizations and 3,500 deaths each year, based on pre-pandemic data (3). Readily available and robust surveillance data facilitates response and assists public health authorities in coordinating the implementation of public health measures, such as seasonal vaccination campaigns, to reduce the stress on the healthcare system. The collection of syndromic data aims not only to facilitate the early detection of epidemics and allow for the detection of unexpected circulation patterns, but also to pivot toward non-specific disease surveillance. Participatory syndromic surveillance has been internationally accepted as a robust supplement to traditional respiratory virus surveillance systems for over a decade. Programs similar to FluWatchers are in place across the globe, including FluTracking in Australia, and CoughWatchSA in South Africa (4,5). The InfluenzaNet network in Europe, in place since 2003, gathers and reports data from several European countries (6). A 10-year review of the system found that syndromic surveillance data for these countries correlated well with ILI incidence reported by the European Centre for Disease Prevention and Control (7). Notably, international syndromic surveillance systems also seem to be shifting toward non-specific respiratory infection surveillance. For instance, Outbreaks Near Me, formerly known as Flu Near You and COVID Near You, is a system in place in the United States that pivoted toward non-specific respiratory infection surveillance in December 2020 (8).

Valid surveillance-based indicators are essential to informing emerging infectious disease readiness and responses, by allowing the detection of signals of unusual or unexpected activity and the observation of epidemic dynamics in real time, notably in a post-pandemic context. Syndromic surveillance systems in the context of ILI and related illnesses must be adaptable and exhibit the potential for scalability in response to global epidemiological events. FluWatchers had long been known to be successful in its original intent of tracking influenza activity in Canada (9). However, throughout the COVID-19 pandemic, crowdsourced data had been assessed as a potential mitigation tool (10). As such, the program pivoted toward the inclusion of COVID-19 related data. With the increasing push toward integrative surveillance (11), FluWatchers could demonstrate potential to expand toward the non-specific syndromic surveillance of respiratory viruses in Canada. This approach might offer valuable insights into the prevalence and trends of such viruses while allowing for a broader perspective on health monitoring.

This descriptive surveillance study aimed to examine trends in syndromic indicators of ILI as compared to laboratory-confirmed respiratory virus detections (RVDs), including SARS-CoV-2, influenza, RSV, and all other respiratory viruses (ORVs) throughout the three years of the COVID-19 pandemic. This study also aimed to provide insight on FluWatchers population characteristics, in order to facilitate inferences on community circulation trends and assess how the population's evolution may contribute to syndromic surveillance performance.

Methods

FluWatchers consists of an open cohort of volunteer participants located in Canada, who can both enroll and unsubscribe from participating at any time. Individuals within the Canadian population can enroll to participate online (12). Participants are eligible if they provide a valid Canadian postal code (first three digits) and a valid email address. At the time of enrolment, participants are also invited to enroll and report on behalf of their household members (13).

FluWatchers data collection

FluWatchers data consists of self-reported weekly episodes of cough and/or fever. At enrolment, participants self-report their year of birth, their gender, the first three digits of their postal code of residence, their email address, and, if they choose, household members (13). Each week, participants receive an emailed invitation to participate in an online survey that asks whether they have experienced a cough or a fever in the previous week. Participants are also asked to provide input on their annual influenza vaccination status. Each weekly questionnaire must be responded to in full by each participant choosing to respond in a given week, and incomplete questionnaires are automatically excluded from that week's data. The number of questions a participant must respond to is dependent on whether the participant has reported a cough or a fever in a given week.

With the progression of the COVID-19 pandemic and the acquisition of additional evidence on its modes of transmission and symptomology, additional COVID-19-related questions were added to the follow-up questions (1), namely to capture the following COVID-19-related symptoms: shortness of breath (week of March 29, 2020), headache (week of April 19, 2020), skin rash, and runny/stuffy nose, loss of taste or smell (week of October 4, 2020). As of February 28, 2021, the following COVID-19 vaccination question was included: "Between December 2020 and now: Did you receive vaccination for COVID-19? [Yes/No]." Prior to April 2022, additional questions about other symptoms of illness experienced, absenteeism from work or school, and healthcare utilization were only asked from participants who reported cough and fever. Due to the variety of symptoms reported early in the COVID-19 pandemic, the questionnaire was modified to collect additional data from participants reporting only cough and/or fever. These substantial changes were swiftly executed in collaboration with the Canadian Network for Public Health Intelligence (CNPHI) team, the platform behind FluWatchers. Leveraging the technology's inherent agility and foresight, the evolution involved meticulous adjustments to the questionnaire and data handling processes. This ensured seamless integration for surveillance objectives while upholding user-friendliness.

In the spring of 2020, in response to the COVID-19 pandemic, the FluWatchers program initiated a campaign to increase participant enrolment. Additional participants were recruited via social media beginning on April 3, 2020. This recruitment consisted of five posts to the Healthy Canadians Facebook page, 23 posts to the Health Canada and Public Health Agency of Canada (PHAC) Twitter account (@GovCanHealth), and 14 posts to Canada's Chief Public Health Officer's official Twitter account (@CPHO_Canada). Furthermore, through an email campaign, existing participants were encouraged to invite others to participate in the FluWatchers program. These recruitment efforts, as well as the ability of participants to share links, resulted in an increase of 330% over a one year period, from 4,895 to 21,040 registered participants.

Laboratory-based respiratory virus data

Data from FluWatchers was compared against laboratory-confirmed SARS-CoV-2, influenza and other seasonal respiratory viruses (adenovirus, coronavirus, enterovirus/rhinovirus, human metapneumovirus [hMPV], parainfluenza and RSV). Data on the number of tests positive for SARS-CoV-2 at a national level are collected by the Public Health Agency of Canada through reports by health authorities in the provinces and territories (14). The SARS-CoV-2 data used for this analysis were extracted from the PHAC COVID-19 Health InfoBase and contained information on cases with onset up to March 4, 2023, based on data reported up to June 21, 2023. Data on the number of tests positive for influenza and ORV are collected through PHAC's Respiratory

Virus Detection Surveillance System (RVDSS) (15), which RVDSS collects weekly nucleic acid testing results from provincial, regional, and some hospital labs across Canada. Case data are subject to possible reporting delays between time of case notification to the provincial/territorial public health authority and time of reporting to PHAC.

Measures

For each week, the weekly percentage of FluWatchers participants reporting either A) cough and fever, or B) cough or fever among all participants was calculated. For the purposes of this analysis, reports of cough and fever are referred to as ILI, and reports of cough or fever are referred to as acute respiratory infection (ARI), as they are intended to mimic simplified versions of the World Health Organization (WHO) syndromic case definitions (4). Specifically, ILI and ARI percentages were calculated as the number of reports of cough and/or fever in a given week divided by the total number reports received by participants for that same week. The weekly total RVDs count is defined as the sum of the number of positive tests for all respiratory viruses (influenza, SARS-CoV-2, RSV, and the aggregated sum of adenovirus, coronavirus, enterovirus/rhinovirus, hMPV, and parainfluenza) in a given week. The SARS-CoV-2 case numbers are available by week using the earliest date between onset date, specimen collection date, laboratory testing date, date reported to province or territory, or date reported to PHAC (14).

Statistical analysis

Spearman correlation coefficients were calculated to compare self-reported ILI and self-reported ARI against the weekly total RVD count and the weekly total RVD count excluding SARS-CoV-2 detections. These were calculated over the entire study period and for the time periods of March 1, 2020, to March 6, 2021; March 7, 2021, to March 5, 2022; and March 6, 2022, to March 4, 2023. Pearson correlation coefficients were unsuitable for these datasets, due to the high proportion of outliers in total RVDs. Furthermore, Shapiro-Wilk tests indicated that the populations were not normally distributed.

Results

Participants

Between March 1, 2020, and March 4, 2023, FluWatchers consisted of 25,326 participants. The average response rate per week over the entire study period was 45% and ranged from 13% to 51%. However, the average weekly response rates per individual year (March 2020 to March 2021, March 2021 to March 2022, and March 2022 to March 2023) were 51%, 65%, and 65% respectively. Throughout the entire study period, a total of 10,716 participants (42%) had a response rate of 75% or greater; 3,121 participants (12%) had a response rate between 50%–74%; 5,907 participants (23%) had a response rate between 10%–49%; and 5,582 (22%) had a response rate of less than 10%. The majority of FluWatchers participants were female (63%), and less than 1% identified as gender diverse. FluWatchers participants were mainly located in Ontario (47%) and Québec (19%). The median year of birth of FluWatchers was 1977 (interquartile range, IQR=1963–1989). While the demographic characteristics of FluWatchers remained more or less similar throughout the study period, epidemiological trends varied year-by-year (**Table 1**). For instance, the proportion of FluWatchers reporting an absence from work or school increased from 24.4% in 2020–2021 to 47.5% in 2022–2023. The proportion of FluWatchers reporting healthcare-seeking behaviour varied throughout the study period, increasing from 25.2% to 40.7% between 2020–2021 and 2021–2022, before sharply decreasing to 18.3% in 2022–2023.

Table 1: FluWatchers participation profile

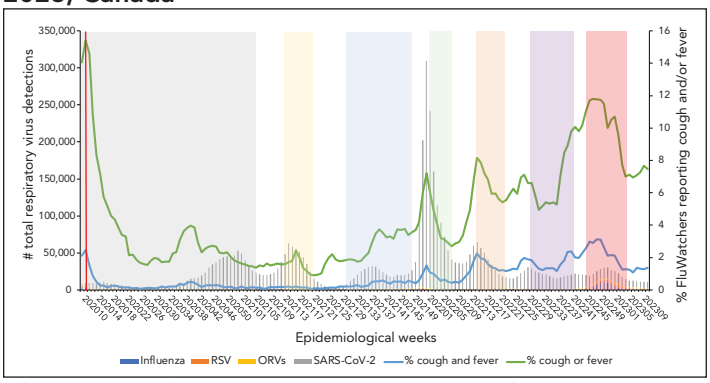
FluWatchers characteristics	2020–2023	2020–2021	2021–2022	2022–2023
Total number of participants	25,326	21,005	19,026	17,066
Average weekly response rate (%)	44.7 (12.5–51.9)	51.1 (15.1–61.5)	64.9 (58.4–69.1)	64.8 (58.2–70.9)
Average weekly absenteeism rate (%)	38.4 (2.1–62.1)	24.4 (2.1–42.4)	43.9 (31.5–55.7)	47.5 (37.8–62.1)
Average weekly healthcare utilization rate (%)	27.9 (2.3–53.8)	25.2 (2.3–41.5)	40.7 (22.3–53.4)	18.3 (9.2–53.8)
Proportion of participants responding to >75% of surveys (%)	42	56	63.5	58.5
Proportion participants reporting in <10% of surveys (%)	22	10	8.6	10.4
Average ILI (%)	0.8	0.3	0.4	1.7
Average ARI (%)	4.6	3.5	2.7	7.6
Median year of birth (IQR)	1977 IQR=1963–1989	1977 IQR=1963–1989	1974 IQR=1961–1987	1973 IQR=1960–1986
Proportion of female (%)	62.6	62.6	63.1	63.5
Proportion of male (%)	36.9	37.2	36.5	36
Proportion gender diverse (%)	0.5	0.2	0.4	0.5
Influenza vaccination rate (%)	61.3	68.5	62.1	69.8

Abbreviations: ARI, acute respiratory infection; ILI, influenza-like illness; IQR, interquartile range

Seasonal respiratory virus pattern

The temporal pattern in the proportion of FluWatchers respondents reporting ILI, ARI, and the weekly RVD count over the three years of the pandemic (March 2020 to March 2023) is shown in **Figure 1**.

Figure 1: Total respiratory virus detections vs. influenza-like illness and acute respiratory infection reported by FluWatchers, March 1, 2020, to March 4, 2023, Canada[a,b,c,d,e,f,g,h]



Abbreviations: ORV, other respiratory viruses; RSV, respiratory syncytial virus; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2

[a] The red dotted line represents the onset of public health measures related to COVID-19

[b] The grey shaded area (epidemiological weeks 2020-10 to 2021-04) represents the first wave of the COVID-19 pandemic

[c] The yellow shaded area (epidemiological weeks 2021-14 to 2021-21) represents the Alpha, Beta, and Gamma variant predominance period of the COVID-19 pandemic

[d] The blue shaded area (epidemiological weeks 2021-30 to 2021-48) represents the Delta variant predominance period of the COVID-19 pandemic

[e] The green shaded area (epidemiological weeks 2022-01 to 2022-07) represents the Omicron BA.1 variant predominance period of the COVID-19 pandemic

[f] The orange shaded area (epidemiological weeks 2022-14 to 2022-22) represents the Omicron BA.2 variant predominance period of the COVID-19 pandemic

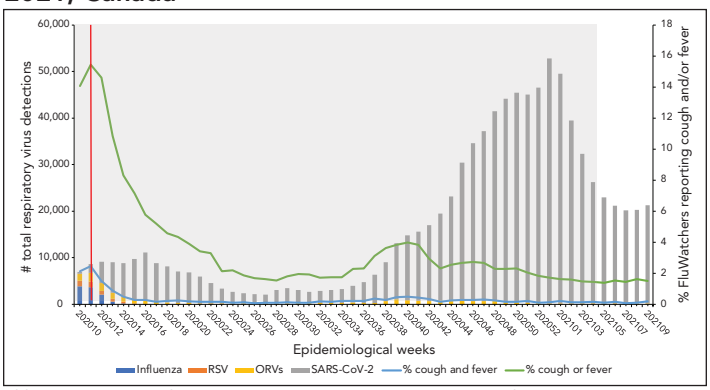
[g] The purple shaded area (epidemiological weeks 2022-29 to 2022-41) represents the Omicron BA.5 variant predominance period of the COVID-19 pandemic

[h] The red shaded area (epidemiological weeks 2022-44 to 2023-03) represents the 2022–2023 influenza season

The number of laboratory tests positive for seasonal respiratory viruses (influenza, adenovirus, coronavirus, enterovirus/rhinovirus, hMPV, parainfluenza, and RSV) demonstrated a rapidly declining end-of-season wave from March 8, 2020, to April 18, 2020, concurrent with the increase of the first epidemic wave of SARS-CoV-2.

The SARS-CoV-2 case counts demonstrated that Canada experienced two epidemic waves over the first year of the COVID-19 pandemic (**Figure 2**). The first occurred in the spring of 2020, with case counts peaking mid-April, and the second in the autumn/winter of 2020–2021, with case counts peaking the last week of December. During the second year of the COVID-19 pandemic, Canada experienced three more epidemic waves (**Figure 3**). The first occurred in the spring of 2021, with case counts peaking around April 2021. The second wave began late in the summer of 2021, lasting until December 2022. This wave was quickly followed by the third epidemic wave of the second year of the pandemic, occurring in the early months of 2022 and marked by the predominant circulation of the Omicron BA.1 variant. During the third year of the COVID-19 pandemic, Canada experienced two final consecutive epidemic waves, mainly attributable to the circulation of Omicron variants (BA.2 and BA.5) (**Figure 4**). Both took place between March 2022 and October 2022, with the first peaking early in April, and the second peaking early in July. This year was also marked by the return of the circulation of ORVs. An early and intense resurgence of influenza A occurred in the fall of 2022, before subsiding shortly after January 2023 (16).

Figure 2: Total respiratory virus detections vs. influenza-like illness and acute respiratory infection reported by FluWatchers, March 1, 2020, to March 6, 2021, Canada[a,b]

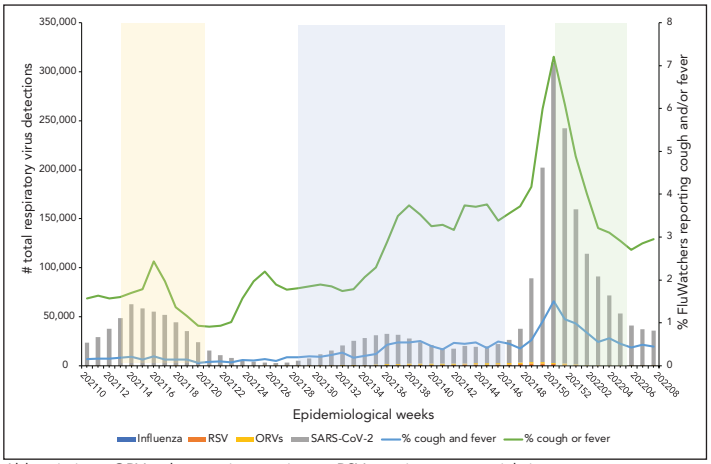


Abbreviations: ORV, other respiratory viruses; RSV, respiratory syncytial virus; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2

[a] The grey shaded area (epidemiological weeks 2020-10 to 2021-04) represents the first wave of the COVID-19 pandemic

[b] The red dotted line represents the onset of public health measures related to COVID-19

Figure 3: Total respiratory virus detections vs. influenza-like illness and acute respiratory infection reported by FluWatchers, March 7, 2021, to March 5, 2022, Canada[a,b,c]



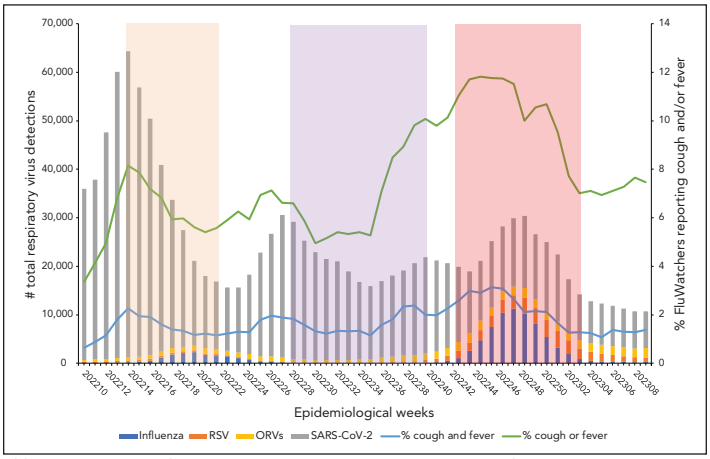
Abbreviations: ORV, other respiratory viruses; RSV, respiratory syncytial virus; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2

[a] The yellow shaded area (epidemiological weeks 2021-14 to 2021-21) represents the Alpha, Beta, and Gamma variant predominance period of the COVID-19 pandemic

[b] The blue shaded area (epidemiological weeks 2021-30 to 2021-48) represents the Delta variant predominance period of the COVID-19 pandemic

[c] The green shaded area (epidemiological weeks 2022-01 to 2022-07) represents the Omicron BA.1 variant predominance period of the COVID-19 pandemic

Figure 4: Total respiratory virus detections vs. influenza-like illness and acute respiratory infection reported by FluWatchers, March 6, 2022, to March 4, 2023, Canada[a,b,c]



Abbreviations: ORV, other respiratory viruses; RSV, respiratory syncytial virus; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2
[a] The orange shaded area (epidemiological weeks 2022–14 to 2022–22) represents the Omicron BA.2 variant predominance period of the COVID-19 pandemic
[b] The purple shaded area (epidemiological weeks 2022–29 to 2022–41) represents the Omicron BA.5 variant predominance period of the COVID-19 pandemic
[c] The red shaded area (epidemiological weeks 2022–44 to 2023–03) represents the 2022–2023 influenza season

Association between self-reported influenza-like illness and acute respiratory infection and laboratory-confirmed respiratory virus detections

The FluWatchers syndromic surveillance indicator—the percentage of participants meeting the ILI and the ARI case definitions—showed a similar pattern to that of respiratory virus detections. Both the ILI and ARI rates mirrored the sharp decline in percentage positive observed for seasonal respiratory viruses. No deceleration in the decline (or increase) corresponding to the rise in SARS-CoV-2 during the first epidemic wave (epidemiological weeks 2020-10 to 2020-24; March 2020 to June 2020) was observed.

The ILI rate remained flat during the typical inter-seasonal period during which influenza, other respiratory viruses, and SARS-CoV-2 curves were lower, with a mild signal/increase in the early fall (weeks September 6, 2020, to October 11, 2020) corresponding to an increase predominantly consisting of rhinovirus/enterovirus (17). The ILI rate fluctuated through the second and third waves of SARS-CoV-2 (November 2020 to June 2021) and the FluWatchers ARI rate captured trends in RVD case counts. The FluWatchers ARI tracked laboratory-confirmed RVDs accurately as of epidemiological week 2021-11. Self-reported ILI began to demonstrate accurate overlap with laboratory-confirmed RVDs as of September 2021. During the fourth wave of SARS-CoV-2 activity, self-reported ILI peaked around the same time as RVDs. The same applies to all subsequent RVDs spikes.

Despite these visual trends, there is insufficient statistical evidence of a significant correlation between self-reported ILI and the total RVDs including SARS-CoV-2 over the entire study period [ρ=0.16 (−0.0015, 0.30); *p*=0.05], as well as during the isolated period of March 2020 to March 2021 [ρ=0.18 (−0.11, 0.30); *p*=0.21] (**Table 2**). However, self-reported ILI showed a moderate correlation with total RVDs from March 2021 to March 2022 [ρ=0.51 (0.27, 0.69); *p*=1.02e-04] and a low correlation from March 2022 to March 2023 [ρ=0.34 (0.07, 0.57); *p*=0.01]. The same trends apply to self-reported ARI, where there was also no statistical evidence of a significant correlation between self-reported ARI and the total RVDs, including SARS-CoV-2, over the entire study period [ρ=−0.03 (−0.18, 0.13); *p*=0.72], and from March 2020 to March 2021 and from March 2022 to March 2023. However, from March 2021 to March 2022, self-reported ARI demonstrated a stronger correlation with total RVDs [ρ=0.40 (0.13, 0.61); *p*=3.53e-03] (Table 2).

When SARS-CoV-2 detections are excluded from the total RVD counts, the correlation coefficients with self-reported ILI over the entire study period [ρ=0.87 (0.82, 0.90); *p*=3.12e-51] and for the first two isolated years of the pandemic are strong and statistically significant. Over the period of March 2022 to March 2023, the correlation between self-reported ILI and total RVDs excluding SARS-CoV-2 is moderate [ρ=0.37 (0.10, 0.59); *p*=7.47e-03]. However, self-reported ARI exhibits a strong and statistically significant correlation with total RVDs excluding SARS-CoV-2 over the entire study period [ρ=0.88 (0.83, 0.91); *p*=5.17e-54] and over each isolated year of the pandemic (**Table 3**).

Table 2: Spearman correlation results, influenza-like illness and acute respiratory infection reported by FluWatchers vs. total respiratory virus detections, including SARS-CoV-2

Year	ILI		ARI	
	ρ (95% CI)	*p*-value	ρ (95% CI)	*p*-value
2020–2023	0.16 (−0.0015, 0.30)	0.05	−0.03 (−0.18, 0.13)	0.72
2020–2021	0.18 (−0.11, 0.43)	0.21	−0.09 (−0.36, 0.19)	0.51
2021–2022	0.51 (0.27, 0.69)	1.02e-04	0.40 (0.13, 0.61)	3.53e-03
2022–2023	0.34 (0.07, 0.57)	0.01	0.01 (−0.27, 0.29)	0.92

Abbreviations: ARI, acute respiratory infection; CI, confidece interval; ILI, influenza-like illness

Table 3: Spearman correlation results, influenza-like illness and acute respiratory infection reported by FluWatchers vs. total respiratory virus detections, excluding SARS-CoV-2

Year	ILI		ARI	
	ρ (95% CI)	*p*-value	ρ (95% CI)	*p*-value
2020–2023	0.87 (0.82, 0.90)	3.12e-51	0.88 (0.83, 0.91)	5.17e-54
2020–2021	0.84 (0.74, 0.91)	2.20e-15	0.85 (0.75, 0.91)	7.37e-16
2021–2022	0.83 (0.71, 0.90)	4.36e-14	0.88 (0.80, 0.93)	7.53e-18
2022–2023	0.37 (0.10, 0.59)	7.47e-03	0.70 (0.53, 0.82)	6.60e-09

Abbreviations: ARI, acute respiratory infection; CI, confidece interval; ILI, influenza-like illness

Discussion

Overall, ILI and ARI rates followed a similar pattern as total RVDs throughout the study period, including throughout specific epidemic waves. The correlation between self-reported ILI and ARI and total RVDs, including SARS-CoV-2, was not statistically significant in the early pandemic but became moderate or low in subsequent years. However, when SARS-CoV-2 detections were excluded from the total respiratory virus counts, the correlation between self-reported ILI and total RVDs became strong and statistically significant for the entire study period and the early pandemic years. Self-reported ARI exhibited a strong and statistically significant correlation with total RVDs when SARS-CoV-2 was excluded, both for the entire study period and each isolated year of the pandemic.

Since its inception in 2015, the main objective of the FluWatchers program was to track the spread of influenza in Canada (1). However, over the years, program improvements have enabled the system to track the spread of other respiratory viruses, such as SARS-CoV-2, RSV, and others. This analysis provides valuable insight into how FluWatchers acts as a complement to traditional surveillance systems for non-specific respiratory virus surveillance. At the time of writing, this paper is the first known publication comparing the performance of a participatory syndromic surveillance program's ILI data against laboratory detections of SARS-CoV-2, influenza, RSV, and other seasonal respiratory viruses over the three years of the COVID-19 pandemic.

The COVID-19 pandemic has highlighted the need for robust surveillance of respiratory viruses. The WHO mosaic framework for the surveillance of respiratory viruses of epidemic and pandemic potential has stated that it is "impossible to address the many complex needs of respiratory virus surveillance with a single surveillance system" (11), and as such, multiple systems need to function together in order to achieve specific surveillance objectives and targets. The framework specifies three main domains to classify surveillance approaches, and within each domain, both core and enhanced surveillance approaches are recommended. Most notably, syndromic surveillance is included as an enhanced surveillance approach in domains 1 and 2, and participatory surveillance is included as a surveillance innovation in all three domains (11).

- Domain 1: detection and assessment of an emerging or re-emerging respiratory virus
- Domain 2: monitor epidemiological characteristics of respiratory viruses in interpandemic periods
- Domain 3: informing use of human health intervention

Participatory surveillance is particularly touted for its ability to complement traditional surveillance by capturing information from individuals who may not seek care (12,18). Additionally, participatory surveillance may be able to identify peaks of respiratory virus activity earlier than sentinel or laboratory surveillance (18). This can be highlighted through visual assessment of Figure 1, wherein peaks in RVDs are typically preceded by peaks in self-reported ILI. For instance, during the 2022–2023 influenza season (Figure 4), total RVDs peaked in epidemiological week 2022-50 (week ending December 17, 2022), whereas self-reported ILI through FluWatchers peaked three to four weeks sooner (week 2022-48, ending December 3, 2022). Participatory surveillance is also useful in its ability to gather additional information on both healthcare seeking, testing, and vaccination behaviours in the population (11). FluWatchers collects valuable data, including whether an individual took time off work or school, or whether they consulted a healthcare professional in a given week (13). Additionally, FluWatchers is one of the only national programs that collects data on rapid antigen testing for COVID-19, including both numerator and denominator data. Despite the fact that participatory surveillance populations are typically not representative of the general population, which is the case in the FluWatchers population, their data provides great insight over periods of time (9). Participatory surveillance offers the advantage of effectively identifying and tracking community respiratory circulation.

This analysis is limited by various factors. A known weakness of participatory surveillance systems is the bias associated with participant self-selection into the program, as those who choose to participate are systematically different than those who do not (19). As such, participant populations in participatory syndromic surveillance systems tend to differ from the population they are intended to represent. The FluWatchers population differs from the Canadian population in terms of gender, age, and geographical distribution. This limits the extent to which age and geography-specific trends can be discussed. Paediatric

population and elderly populations are underrepresented in FluWatchers data. These populations are often marked by particular community circulation trends, which may not be reflected in Canada's participatory syndromic surveillance. Additionally, the two populations being compared are fairly distinct. Those who seek testing for respiratory viruses, and therefore would be included in the total RVD dataset, are typically individuals who are already sick and seeking care. However, FluWatchers typically represent a subset of relatively healthy members of the general population (12). This can be demonstrated by the results obtained in the year one correlation analysis (March 2020 to March 2021). In the first year of the pandemic, total RVDs showed increases at several points, however, no associated increases in the percentage of FluWatchers reporting a cough and a fever were present. The SARS-CoV-2 cases in the first year of the pandemic were concentrated in outbreaks primarily occurring in long-term care facilities (20). The FluWatchers population is not adequately representative of this segment of the population (13), and thus FluWatchers data was not able to capture these spikes in SARS-CoV-2 activity. A large majority of Canadians were subject to public health measures during this phase in the pandemic (21). Due to the FluWatchers population's higher likelihood to engage in health promoting behaviours, there was a high probability that FluWatchers participants were adhering to these public health measures, thus limiting their exposure to SARS-CoV-2 and respiratory viruses in general. In the following year, namely throughout the Omicron wave, the community spread of SARS-CoV-2 increased sharply. The FluWatchers population appeared to have captured these spikes in activity (Figure 3 and Figure 4 and Spearman correlation results [ρ=0.51 [0.27, 0.69]; p=1.02e-04]).

Another limitation to address is the fact that total RVDs are sensitive to policy changes, most notably changes in testing practices. In the case of SARS-CoV-2 detections, asymptomatic testing for SARS-CoV-2 was a global common practice into the second year of the pandemic (22). FluWatchers is a syndromic surveillance system and would not capture asymptomatic cases, so this may have been a factor in the poor correlation during the first year of the pandemic. Additionally, a shift toward the use of rapid antigen tests after December 2021 in Canada and a reduction of widespread polymerase chain reaction (PCR) testing availability across many jurisdictions lead to a decline in the number of reported cases, which was likely not reflective of the actual prevalence of SARS-CoV-2 in the community (14,23). This artificial decline in SARS-CoV-2 detections may have contributed to the poor correlation with FluWatchers' self-reported ILI and ARI indicator, as FluWatchers data was still able to capture community circulation of all respiratory viruses, including SARS-CoV-2. This can be further demonstrated through the analysis of the correlation results excluding SARS-CoV-2. During the COVID-19 pandemic, testing eligibility for influenza and ORV did not change as frequently, nor as significantly, as those for SARS-CoV-2, as PCR testing for these viruses is most commonly performed among symptomatic individuals. This may explain why the Spearman correlations between total RVDs excluding SARS-CoV-2 and the self-reported ILI indicator were positive and statistically significant over the entire study period and in each individual year.

Influenza-like illness has been a long-standing syndromic case definition for influenza surveillance. While the WHO recommends ILI surveillance for COVID-19 syndromic surveillance (24), COVID-19 may present with a greater variety of symptoms other than cough or fever (25). Self-reported symptoms vary not only over the course of infection but also between individual cases and different age groups (26). Much remains to be understood about COVID-19, its symptomatology, and its extended impacts, notably encompassing long COVID and post-COVID symptoms. This may challenge the use of ILI or ARI case definitions for capturing COVID-19 community activity. The establishment of an optimal syndromic case definition will become a pertinent consideration once COVID-19 seasonality is established. This is especially true if ILI and ARI exhibit shortcomings in accurately capturing COVID-19 activity in the future.

Conclusion

In summary, despite the correlation results obtained in the analysis, FluWatchers remains a valuable component of Canada's influenza monitoring strategy and will remain an important component in an integrative program for non-specific respiratory virus surveillance. FluWatchers self-reported ILI showed a moderate to strong correlation with total RVDs, and while this correlation decreased in strength and significance with the addition of SARS-CoV-2 data, a trend that is both expected and explained as discussed above, the association between the two data sources still existed. The concordance between respiratory detections and the proportion of FluWatchers reporting a cough and a fever is clearly demonstrated in the visual trends (Figure 1). FluWatchers data provides a point-in-time estimate of non-specific respiratory virus activity in the community, and can be used to detect periods of high or unusual circulation in near-real time within a respiratory season.

Authors' statement

MB — Conceptualization, methodology, writing–original draft, writing–review & editing, formal analysis, visualization
AR — Writing–original draft, writing–review & editing, formal analysis
LL — Conceptualization, writing–original draft, writing–review & editing
SM — Writing–review & editing, data curation, software

Competing interests

None.

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