

Intersecting Risk Factors Associated With High Syphilis Seroprevalence Among a Street-Involved Population in Canada

Syphilis has reemerged as a global public health concern, with a 340% increase in Ontario from 2013 to 2023. Women are the fastest-growing at-risk group for syphilis, many of whom report injection drug use and homelessness.

Data were collected from the SPRITE study, an outreach model of care implemented by eight Ontario public health units. A total of 630 participants were included, with a median age of 38; 42% being women. Syphilis seroprevalence was defined by reactive treponemal antibodies, and mixed-effects regression was used to evaluate associations between risk factors and seropositivity. The overall syphilis seroprevalence was 7.6% (95% CI 5.5–9.7), with significant variation across public health units. Seroprevalence was higher among those reporting three risk factors (19.2%) compared to one risk factor (4.8%). Women had a higher seroprevalence (9.8%) compared to men (6.0%). Individuals using illicit drugs had a seroprevalence of 9.4%, with crystal methamphetamine users showing the highest rates (aPR 2.88).

What this tells us

The findings highlight the burden of syphilis among street-involved populations, particularly women and those with overlapping risk factors. The SPRITE study emphasizes the need for targeted outreach models to address health inequities and improve access to care. The results align with global trends showing increased syphilis rates among women and those using methamphetamine. The findings underscore the urgent need for equity-oriented outreach models to address the rising syphilis rates among vulnerable populations. It calls for integrated community-based STI care to reduce transmission and address structural health inequities.



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Intersecting Risk Factors Associated With High Syphilis Seroprevalence Among a Street-Involved Population in Canada

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Background. Syphilis has reemerged as a global public health concern. In Ontario, Canada's most populous province, a 340% increase in infectious syphilis cases was observed between 2013 and 2023. This surge was accompanied by a demographic shift, with women emerging as the fastest-growing at-risk group. We examined intersecting risk factors associated with syphilis seropositivity among a street-involved population.

Methods. Data were collected from the Syphilis Point of Care Rapid Test and Immediate Treatment Evaluation (SPRITE) study—an outreach model of care implemented by 8 public health units (PHUs) across Ontario between 2023 and 2024. Reactive treponemal antibodies defined syphilis seroprevalence. A mixed-effects regression with a log-binomial distribution was used to evaluate the association between risk factors and seropositivity. Adjusted prevalence ratio (aPR) controlled for age and sex and clustering by PHUs.

Results. A total of 630 participants, 42% women, with a median age of 38, were included; 19.1% of participants reported having sexual risk factors, using illicit drugs, and being un(der)housed. Overall, syphilis seroprevalence was 7.6% (95% confidence interval 5.5–9.7), with significant heterogeneity across the province and higher among those reporting 3 risk factors (19.2% [11.2–29.7]) compared with 1 risk factor (4.8% [1.8–10.1]). Seropositivity was higher among women (aPR 1.62 [.94–2.80]) and people who use illicit drugs (aPR 2.30 [.93–5.50]), particularly those who use crystal methamphetamine (aPR 2.88 [1.31–6.33]).

Conclusions. Syphilis is heightened at the intersection of sexual risk factors, illicit drug use, and housing instability among equity-deserving populations. Targeted outreach models of care are necessary to reach this emerging at-risk population.

Keywords. people who use drugs; people who are unhoused; seroprevalence; street-involved population; syndemic; syphilis; women.

Syphilis is a curable, sexually transmitted and/or blood-borne infection (STBBI) caused by the bacterium *Treponema pallidum*. In Ontario, Canada's most populous province, the incidence of infectious syphilis increased from 5.3 to 20.9 cases per 100 000 people between 2013 and 2023 [1, 2]. This surge has been accompanied by demographic shifts. While syphilis has historically disproportionately affected men—particularly men who have sex with men (MSM)—women of reproductive

age (15–39 years) have emerged as the fastest-growing at-risk group [3]. These changes in epidemiology are even more pronounced in rural and smaller urban areas across Ontario [1]. Street-involved individuals [4]—including people who use illicit drugs (PWUD) and those who are un(der)housed—are also suspected to be disproportionately affected by syphilis [3, 5–7], yet prevalence estimates in this population vary widely [8–13]. Despite these concerning trends, much of the existing epidemiological research on syphilis among street-involved populations has focused on clinical cohorts in major urban centers [6, 7, 13, 14].

In response to the global resurgence of syphilis, the World Health Organization's 2022–2030 global health sector strategies on sexually transmitted infections set an ambitious target to reduce syphilis incidence by 90% by 2030 [15]. These strategies emphasize the importance of equity, context-specific action, and integrated service delivery. Evaluating syphilis seroprevalence among street-involved populations is therefore critical to addressing health inequities and informing effective public health interventions. To address this knowledge gap, we assessed the association of individual risk factors and the

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intersection of illicit drug use, sexual risk factors, and unstable housing status with syphilis seropositivity among street-involved individuals across small urban, rural, and remote public health units (PHUs) in Ontario.

METHODS

Data Source

Data were collected from the ongoing Syphilis Point of Care (POC) Rapid Test and Immediate Treatment Evaluation (SPRITE) study. A detailed overview of the study methods has been published elsewhere [16]. Briefly, this prospective community-based outreach study aims to evaluate a model of care that utilizes the INSTI® Multiplex HIV-1/HIV-2/Syphilis Antibody Test for syphilis screening, followed by immediate treatment of suspected cases. Outreach models include organized events at community-based organizations (ie, supervised consumption sites, shelters) and in the community (ie, routine harm reduction outreach using mobile units or visits to encampments) to reach the target street-involved population. The definition of street involved remained inclusive to describe an array of intersecting forces, accounting for both varying degrees of homelessness and a wide range of risk factors, including illicit drug use and survival sex. Therefore, it also included individuals who were not necessarily “homeless” but who were exposed to and experiencing the physical, mental, emotional, and social risks of street lifestyle [4]. Sociodemographic and risk factor data were self-reported and collected through public health intake forms during outreach encounters. Data for this analysis were restricted to 7 PHUs serving small urban, rural, and remote areas in Ontario from 23 June 2023 to 8 November 2024. Types of drugs used and past sex work were only collected beginning on 26 April 2024; therefore, a subset of the analytic sample includes this data.

Patient Consent Statement

Each participant consented to participate by providing verbal consent for their data to be used for research or evaluation purposes by outreach nurses administering the tests.

Ethics

This study was conducted in accordance with the Canadian Tri-Council Policy Statement Version 2 and the latest Seoul revision of the Declaration of Helsinki. Ethics approval was obtained from the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (file number 6039604). All data and documentation were managed according to the Personal Health Information Protection Act (PHIPA) and agency policies on safeguarding personal health information.

Risk Factors

Sociodemographic risk factors were chosen a priori and included sex (biological), age, sexual orientation (identifying as gay, bisexual, or an MSM [GBMSM]), and PHU. Illicit drug use included mode (injection vs inhalation) and drug type(s) (any nonprescription opioid, methamphetamine, cocaine, and psychedelics). We also categorized participants by the number of illicit drug types used. Sexual risk factors included reported anonymous sexual partners, multiple sexual partners, and current and/or past sex work. Un(der)housed was defined as being currently or recently homeless, staying in shelters or transitional housing, couch-surfing, or precariously housed. We developed a composite variable for the number of risk factors across 3 risk categories: (1) use of illicit drugs, (2) un(der)housed, and (3) any sexual risk factor.

Serology

As part of the SPRITE study, both POC and laboratory testing results are available. To align with other syphilis serosurveillance studies, we restricted our analysis to standard laboratory results. Syphilis seropositivity was defined as a reactive serological test based on chemiluminescent microparticle immunoassay, a qualitative immunoassay that detects treponemal antibodies (IgG and IgM) to *T. pallidum* [17]. Healthcare providers determined whether an individual had a prior syphilis infection or newly discovered/reinfection using a combination of results from the rapid plasma reagin and *T. pallidum* particle agglutination (TP.PA) tests, history, and examination of the patient [17]. Information on the clinical staging of syphilis infections is not available for this study. Positive HIV infections were defined based on testing positive for HIV-1/-2 antigen/antibody through the standard laboratory screening test for HIV in Ontario [18].

Statistical Analyses

Seroprevalence was presented overall and stratified by sex, age groups, PHU, drug use risk factors, housing status, sexual risk factors, and identifying as GBMSM. Secular trends were examined by quarter year. We used an exact binomial confidence interval (CI) for proportions due to low positive counts for some risk factors. The intersection of illicit drug(s), any sexual risk factor, and housing status was illustrated using an Euler diagram.

A mixed-effects regression model with a log-binomial distribution was used to evaluate the association between risk factors and seroprevalence [19]. Due to varying baseline prevalence, PHU was included as a random effect to account for this clustering. Models were adjusted for sex and age. We determined whether there was interaction on an additive scale using absolute excess risk due to interaction (AERI) between illicit drugs and an individual being un(der)housed. An additive interaction

was chosen as it is often considered the more relevant public health measure [20]. For interpretation, we used CIs in addition to the direction and magnitude of association in accordance with the *Statistical Analyses and Methods in the Published Literature (SAMPL) Guidelines* [21]. We did not interpret results solely based on dichotomous statistical significance in line with recent recommendations. Instead, we interpreted the strength of the association and presented all findings to

provide readers with a contextual understanding of our interpretation [22]. All statistical analyses were conducted using SAS version 9.4.

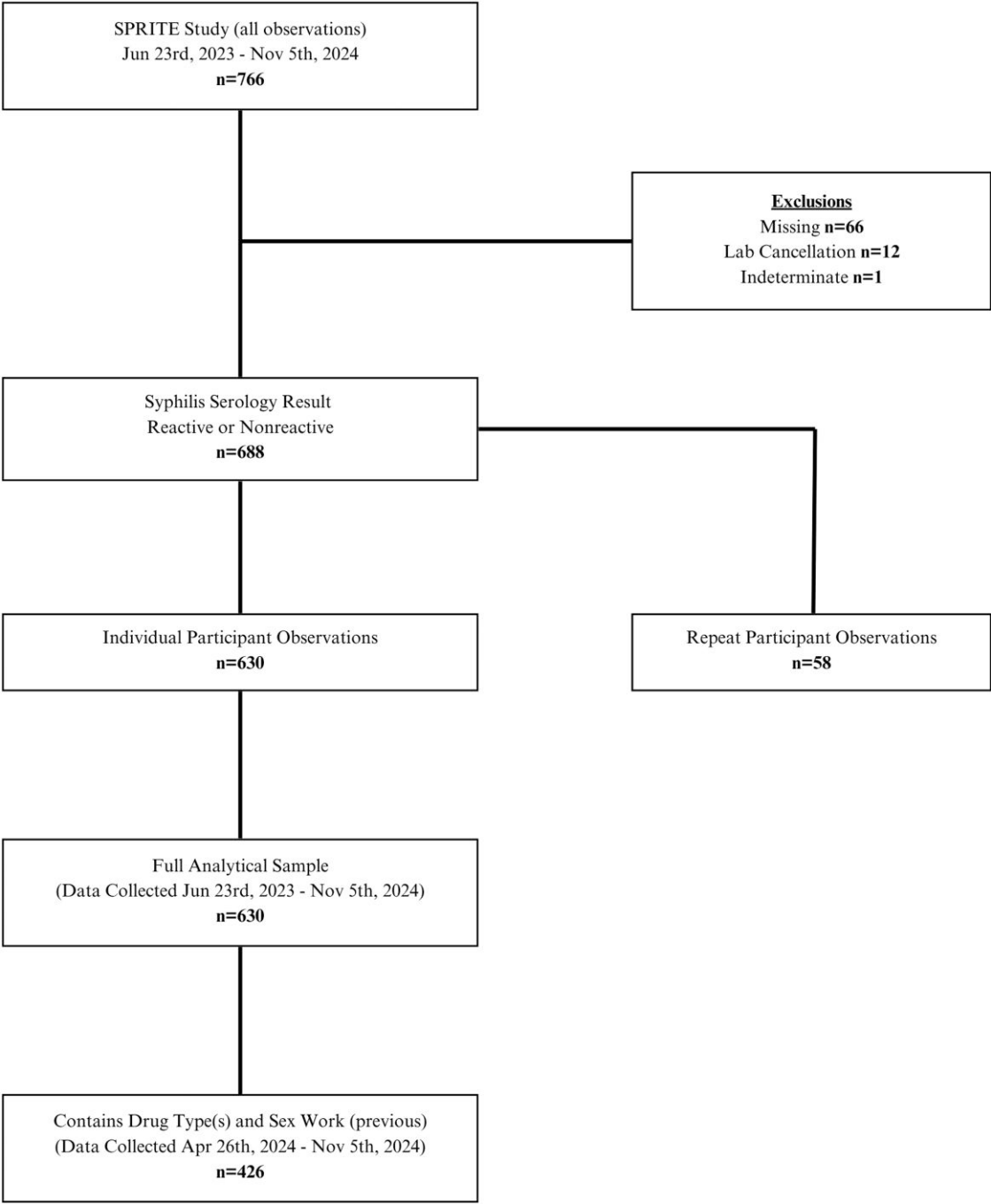


Figure 1. Dataset creation flowchart. For participants with repeat observations, we retained the last observation with a syphilis serology result.

Table 1. Baseline Characteristics of the Study Population

Characteristics	% (n) (n = 630)
Sex	
Female	42.1 (265)
Age	
Median (IQR)	38 (31–48)
Under 20	2.2 (14)
20–29	19.7 (124)
30–39	31.9 (201)
40–49	23.3 (147)
50–59	16.2 (102)
60+	6.7 (42)
Public Health Unit	
Algoma Public Health (APH)	4.9 (31)
Hastings Prince Edward Public Health (HPEPH)	14.4 (91)
Kingston, Frontenac and Lennox & Addington Public Health (KFL&APH)	38.4 (242)
Leeds Grenville & Lanark District Health Unit (LGLDHU)	5.2 (33)
Porcupine Health Unit (Porcupine HU)	2.2 (14)
Renfrew County District Health Unit (RCDHU)	9.0 (57)
Thunder Bay District Health Unit (TBDHU)	25.7 (162)
Un(der)housed	62.4 (393)
Gay, bisexual, or men who have sex with men (GBMSM)	6.5 (41)
Sexual risk factors	
Multiple sexual partners	26.9 (170)
Anonymous sexual partners	12.2 (77)
Sex trade work (current)	4.4 (28)
Sex trade work (previous) ^a	6.8 (29)
Any sexual risk factor (multiple, anonymous, current and/or past sex trade) ^a	34.5 (147)
Drug use	
Illicit drug (any) ^{a,b}	62.6 (255)
Intravenous drug use	28.3 (178)
Type of illicit drug(s) used ^{a,c}	
Crack and/or cocaine	29.1 (109)
Fentanyl	30.7 (115)
Opioid (other)	1.3 (5)
Crystal methamphetamine	31.8 (119)
Illicit drug (other)	1.1 (4)
Number of drugs used ^{a,c}	
None	40.6 (152)
Single type	29.7 (111)
2+ types	29.7 (111)
Measure of risk (counted across sexual, drug use, and housing risk factor categories) ^{a,b}	
0	12.0 (49)
1	30.7 (125)
2	38.1 (155)
3	19.2 (78)

^aCollected starting 26 April 2024, n = 426.^bMissing n = 19.^cMissing n = 52.

RESULTS

Study Population

Between 23 June 2023, and 8 November 2024, 630 individuals were included in this analysis (Figure 1). The median age of our

study population was 38 (interquartile range [IQR] 31–48), 42.1% were women, 62.4% were un(der)housed, 32.9% had at least 1 sexual risk factor, and 28.3% reported using intravenous drugs (Table 1). Risk factors varied by PHU; median age ranged from 29 to 40 years, proportion reporting being un(der)housed from 6.1% to 72.5%, and illicit drug use from 33.3% to 100%.

Among the subset of the population with the illicit drug use variable (n = 426), 62.6% reported illicit drug use, of whom 46.7% reported using crystal methamphetamine, 45.1% fentanyl, 42.7% crack and/or cocaine, and 43.5% reported using more than 1 type of illicit drug (Table 1). Sociodemographic and risk factors were similar between the full sample and this subset (Supplementary Table 1).

Seroprevalence

The overall syphilis seroprevalence was 7.6% (95% CI 5.5–9.7; Table 2). This level remained stable across the study period, ranging from 5.3% (95% CI 2.2–10.6) in January–March 2024 to 12.2% (95% CI 3.4–28.2) in July–September 2023. New/re-infection accounted for half of the prevalent cases (3.8% [95% CI 2.6–5.6]) and population was similar to the overall prevalent population (Supplementary Table 2). Seroprevalence varied by geography, ranging from 0% in Leeds, Grenville & Lanark District Health Unit (LGLDHU), Porcupine Health Unit (Porcupine HU) and Renfrew County District Health Unit (RCDHU) to 16.1% in Algoma Public Health (Figure 2). This mirrored the heterogeneity of population-level infectious syphilis rates between these regions (Supplementary Table 3) [2]. This variation may be partly attributable to differences in the characteristics of the populations that were being sampled. LGLDHU and RCDHU had among the lowest proportion of un(der)housed individuals (6.1% and 38.6%, respectively) and individuals who reported any illicit drug use (33.3% and 50.0%, respectively). While Porcupine HU had baseline characteristics similar to those observed in regions with higher syphilis seroprevalence, due to the low sample size (n = 14), these results should be interpreted with caution. The overall seroprevalence of HIV was 1.7% (95% CI .9–3.1).

Syphilis Seroprevalence by Sex

Seropositivity was higher among women (9.8% [95% CI 6.5–14.0]) compared with men (6.0% [95% CI 3.8–8.9]; Table 2; adjusted prevalence ratio [aPR] of 1.62 [95% CI .94–2.80]; Table 3). There were considerable sex differences in 2 PHUs: Kingston, Frontenac and Lennox & Addington Public Health (KFL&APH; 13.5% women vs 6.5% men) and Thunder Bay District Health Unit (TBDHU; 11.4% vs 6.0%; Table 2).

Among women participants, the highest syphilis seroprevalence was seen among the 40–49 age group (17.5% [95% CI 9.0–29.1]), followed by 20–29 (11.7% [95% CI 4.8–22.6]), and closely by 30–39 (8.3% [95% CI 3.4–16.4]). Women who were un(der)housed had higher burden (11.6% [95% CI 7.0–17.7])

Table 2. Syphilis Seroprevalence Stratified by Sex

	Overall (n = 630) (95% CI)	Female (n = 265) (95% CI)	Male (n = 365) (95% CI)
Overall	7.6% (5.5–9.7)	9.8% (6.5–14.0)	6.0% (3.8–8.9)
New or reinfection (overall)	3.8% (2.6–5.6)	5.3% (2.9–8.7)	2.7% (1.3–5.0)
Age			
Under 20	7.1% (.2–33.9)	0.0%	20.0% (.5–71.6)
20–29	7.3% (3.4–13.3)	11.7% (4.8–22.6)	3.1% (.4–10.8)
30–39	8.5% (5.0–13.2)	8.3% (3.4–16.4)	8.6% (4.2–15.2)
40–49	10.2% (5.8–16.3)	17.5% (9.0–29.1)	4.8% (1.3–11.7)
50–59	4.9% (1.6–11.1)	2.6% (.1–13.5)	6.3% (1.8–15.5)
60+	2.4% (.1–12.6)	0.0%	3.1% (.1–16.2)
Public Health Unit			
APH	16.1% (5.4–33.7)	16.7% (2.1–48.4)	15.8% (3.4–39.6)
HPEPH	7.7% (3.1–15.2)	7.9% (1.7–21.4)	7.6% (2.1–18.2)
KFL&APH	9.1% (5.8–13.4)	13.5% (7.2–22.4)	6.5% (3.2–11.7)
LGLDHU	0.0%	0.0%	0.0%
Porcupine HU	0.0%	0.0%	0.0%
RCDHU	0.0%	0.0%	0.0%
TBDHU	8.6% (4.8–14.1)	11.4% (5.3–20.5)	6.0% (2.0–13.5)
Risk factors (other)			
Un(der)housed	9.2% (6.5–12.5)	11.6% (7.0–17.7)	7.6% (4.5–11.7)
GBMSM	12.2% (4.1–26.2)	15.8% (3.4–39.6)	9.1% (1.1–29.2)
Sexual risk factors			
Multiple sexual partners	12.3% (7.8–18.3)	11.7% (5.5–21.0)	12.9% (6.8–21.4)
Anonymous sexual partners	15.6% (8.3–25.6)	15.1% (5.1–31.9)	15.9% (6.6–30.1)
Sex trade work (current)	10.7% (2.3–28.2)	8.3% (.0–27.0)	25.0% (.6–80.6)
Sex trade work (previous) ^a	24.1% (10.3–43.5)	22.2% (8.6–42.3)	50% (1.3–98.7)
Drug use risk factors			
Any illicit drug ^{a,b}	9.4% (6.1–13.7)	11.9% (6.7–19.1)	7.3% (3.6–13.1)
Intravenous drug use	9.5% (5.6–14.8)	11.9% (5.6–21.3)	7.8% (3.4–14.9)
Type of illicit drug(s) used ^{a,c}			
Crack and/or cocaine	7.3% (3.2–13.9)	8.8% (2.9–19.3)	5.8% (1.2–15.9)
Fentanyl	9.6% (4.9–16.5)	8.5% (2.8–18.7)	10.7% (4.0–21.9)
Crystal methamphetamine	12.6% (7.2–19.9)	14.0% (5.8–26.7)	11.6% (5.1–21.6)
Number of drugs used ^{a,c}			
None	3.9% (1.5–8.4)	4.2% (1.1–10.3)	3.6% (.4–12.3)
Single type	7.2% (3.1–13.7)	13.3% (5.0–26.8)	3.0% (.4–10.5)
2 + types	10.8% (5.7–18.1)	8.8% (2.9–19.3)	12.9% (5.4–24.9)
Measure of risk ^{a,b}			
0	2.0% (.1–10.8)	0%	3.6% (.09–18.2)
1	4.8% (1.8–10.1)	7.32% (1.5–19.9)	3.6% (.7–10.1)
2	5.2% (2.2–9.9)	10.3% (4.2–20.1)	1.15% (.03–6.24)
3	19.2% (11.2–29.7)	13.6% (5.2–27.3)	26.5% (12.9–44.4)

Abbreviations: APH, Algoma Public Health; HPEPH, Hastings Prince Edward Public Health; CI, confidence interval; HU, Health Unit; KFL&APH, Kingston, Frontenac and Lennox & Addington Public Health; LGLDHU, Leeds Grenville & Lanark District Health Unit; RCDHU, Renfrew County District Health Unit; TBDHU, Thunder Bay District Health Unit.

^aCollected starting 26 April 2024, n = 426.

^bMissing n = 19.

^cMissing n = 52.

than men who were un(der)housed (7.6% [95% CI 4.5–11.7]) and, among those who use illicit drugs, women also experienced higher burden than men (11.9% [95% CI 6.7–19.1] vs 7.3% [95% CI 3.6–13.1]; Table 2).

Risk Factors Associated With Syphilis Seroprevalence

Individuals reporting sexual risk factors had higher syphilis seroprevalence compared with those without such risk factors. Those reporting multiple sexual partners had a seroprevalence of 12.3% (95% CI 6.8–21.4) (aPR of 2.25 [95% CI 1.28–3.92]), and those reporting anonymous sexual partners had a seroprevalence of 15.6% (95% CI 6.6–30.1) (aPR of 2.74 [95% CI 1.49–

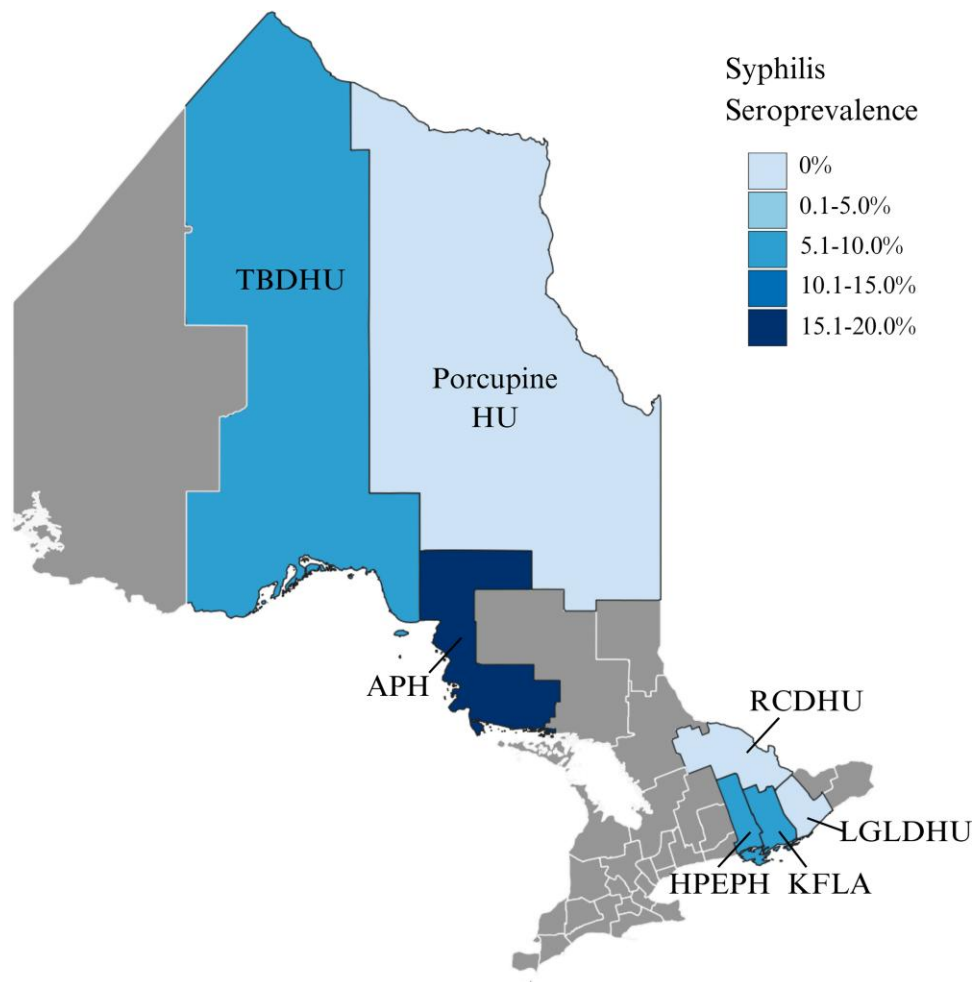


Figure 2. Map of Ontario segmented by Public Health Units (PHUs), highlighting the locations of participating PHUs and their respective study seroprevalence.

5.05]; [Table 3](#)). One in 4 participants who reported previously engaging in sex work were seropositive (aPR 3.55 [95% CI 1.52, 8.28]). Individuals who reported being un(der)housed had a seroprevalence of 9.2% (95% CI 6.5–12.5) (aPR 1.80 [95% CI .93–3.52]; [Table 3](#)). Among men, GBMSM seroprevalence was 9.1% (95% CI 1.1–29.2) and among women, identifying as gay or bisexual seroprevalence was 15.8% (95% CI 3.4–39.6; [Table 2](#)).

Individuals who reported illicit drug use had a seroprevalence of 9.4% (95% CI 6.1–13.7), 2.26 (95% CI .93–5.50) times higher compared with those not reporting illicit drug use ([Tables 2 and 3](#)). Similarly, among people who inject drugs (PWIDs), the seroprevalence was 9.5% (95% CI 5.6–14.8). Of all illicit drugs reported, those who reported crystal methamphetamine use had the highest syphilis seroprevalence compared with other drugs, with an aPR of 2.88 (95% CI 1.31–6.33) compared with those who did not report crystal methamphetamine use ([Table 3](#)).

There was a notable overlap of risk factors among this population: 19.1% of participants reported having sexual risk factors, illicit drug use, and being un(der)housed, and 38.1% reported any 2 of the risk factor groups ([Figure 3A](#)). Seroprevalence was substantially higher among those who reported all 3 risk factor groups (19.2% [95% CI 11.2–29.7]; [Figure 3B](#)) in comparison with each individually (4.8% [95% CI 1.8–10.1]; aPR of 4.41 [95% CI 1.76–11.03]), or an overlap of any 2 (5.2% [95% CI 2.2–9.9]; [Table 3](#)). The interaction on an additive scale between being un(der)housed and reporting any illicit drug use was not significant (AERI 2.7% [95% CI –6.9, 12.0]).

DISCUSSION

Our findings highlight a disproportionately high syphilis burden among a diverse street-involved population in Ontario, Canada. Women, PWUD, and those with sexual risk factors experienced

Table 3. Association Between Risk Factors and Syphilis Seroprevalence

Covariate	Univariate PR (95% CI)	Adjusted PR (95% CI)
Sex		
Male	Reference	...
Female	1.67 (.97–2.89)	1.62 (.94–2.80)
Age		
Under 20	0.72 (.10–5.10)	0.62 (.08–4.50)
20–29	0.84 (.38–1.82)	0.82 (.38–1.79)
30–39	Reference	...
40–49	1.29 (.58–2.18)	1.14 (.59–2.19)
50–59	0.53 (.20–1.39)	0.54 (.21–1.42)
60+	0.26 (.03–1.9)	0.28 (.04–1.05)
Risk factors (other)		
Un(der)housed	1.69 (.87–3.28)	1.80 (.93–3.52)
GBMSM	1.93 (.79–4.68)	1.81 (.75–4.40)
Sexual risk factors		
Multiple sexual partners	2.40 (1.40–4.12)	2.24 (1.28–3.92)
Anonymous sexual partners	2.98 (1.64–5.44)	2.74 (1.49–5.05)
Sex trade work (current)	1.41 (.46–4.29)	1.03 (.33–3.23)
Sex trade work (previous) ^a	3.99 (1.90–8.40)	3.55 (1.52–8.28)
Drug use risk factors		
Illicit drug (any) ^{a,b}	2.45(1.01–5.90)	2.26 (.93–5.50)
Intravenous drug use	1.37 (.77–2.44)	1.24 (.70–2.20)
Type of illicit drug(s) used^{a,c}		
Crack and/or cocaine	1.12 (.46–2.71)	1.00 (.40–2.51)
Fentanyl	1.63 (.77–3.46)	1.29 (.59–2.83)
Crystal methamphetamine	3.08 (1.41–6.75)	2.88 (1.31–6.33)
Number of drugs used^{a,c}		
None	Reference	...
Single type	1.84 (.65–5.19)	1.83 (.65–5.16)
2 + types	2.73 (1.04–7.12)	2.24 (.84–5.99)
Measure of risk^{a,b}		
0	0.42 (.05–3.43)	...
1	Reference	...
2	1.11 (.39–3.14)	...
3	4.41 (1.76–11.03)	...

Abbreviations: APH, Algoma Public Health; CI, confidence interval; HPEPH, Hastings Prince Edward Public Health; HU, Health Unit; KFL&APH, Kingston, Frontenac and Lennox & Addington Public Health; LGLDHU, Leeds Grenville & Lanark District Health Unit; PR, prevalence ratio; RCDHU, Renfrew County District Health Unit; TBDHU, Thunder Bay District Health Unit

^aCollected starting 26 April 2024, n = 426.

^bMissing n = 19.

^cMissing n = 52.

higher seroprevalence. Additionally, we found evidence that overlapping risk factors compound the disease burden.

Compared with previous global and regional estimates, our study's overall syphilis seroprevalence and new/re-infection rate fall within the mid-to-upper range of values, though notably lower than estimates from high-risk subpopulations, such as those co-infected with HIV or engaging in transactional sex [10, 12]. Estimates of syphilis prevalence vary widely over different populations and study settings. A systematic review examining lifetime syphilis prevalence among PWUD in low- and middle-income countries estimates prevalence to be 11.1% (IQR 6.3%–15.3%) [9]. In the United States, syphilis

prevalence among PWUD also shows considerable variation, with a recent finding of 4.8% among PWID [23] and ranging from 1.8% among veterans [8] to 17.1% among women living with HIV [10]. In a review of STBBI rates among homeless youth in the United States, syphilis rates were reported between 0.2% and 3.5% [11]. In Canada, among individuals deemed at-risk of HIV using a risk assessment algorithm, 3.5% self-reported a previous syphilis infection [24] and, in Manitoba, among individuals recently diagnosed with HIV, syphilis prevalence was 38% among those who were unhoused, 30.6% among individuals reporting methamphetamine use, and 29.5% among (PWID) [13].

In our study, women exhibited higher seroprevalence than men, particularly among those of reproductive age (20–40 years). This disparity was most pronounced in KFL&APH and TBDHU, 2 PHUs with the highest rates of congenital syphilis in Ontario in 2022 [3]. This finding is critical in the context of congenital syphilis and reflects the shifting epidemiology of syphilis in Ontario. While men still represent most syphilis cases in Ontario, the rate of increase among women has been more rapid. Between 2013 and 2022, cases among women tripled, shifting the men-to-women case ratio from 26:1 in 2015 to 5:1 in 2022 [3]. Similar shifts in the gender distribution of syphilis cases have been observed elsewhere in North America [7, 14, 25].

Although men still constitute the majority of syphilis cases at the population level, studies in Canada and internationally have consistently found that, among street-involved individuals, a more significant proportion of syphilis cases occur in women, aligning with our findings [13, 26]. One hypothesized explanation for this trend is the increased prevalence of drug use, particularly methamphetamine, among women. Between 2013 and 2017, rates of methamphetamine, injection drug, and heroin use increased among women with primary or secondary syphilis in the United States [27]. There also appears to be a disproportionate effect of drug use on women. In 2019, Brookmeyer et al [28] reported that among PWID, syphilis was higher among women compared with men (7.0% vs 3.3%), potentially due to more sexual partners, forced sex, and lower rates of condom use. The intersection of gender, sexual risk factors, housing instability, and illicit drug use likely contributes to this trend. We highlight significant associations between sexual risk factors, including multiple sexual partners, anonymous sexual partners, and previous engagement in sex work and seropositivity, consistent with previous reports among street-involved individuals engaged in survival sex work and other high-risk sexual behaviors [11, 12, 27, 29, 30]. In Ontario, among those newly diagnosed with syphilis, homelessness was an identified risk factor, particularly among women (12.7% compared with 1.5% among men). Engaging in sex trade work was reported by 10.9% of women versus only 1% of men, and survival sex was reported by 5.5% compared with just 0.1% of men [3].

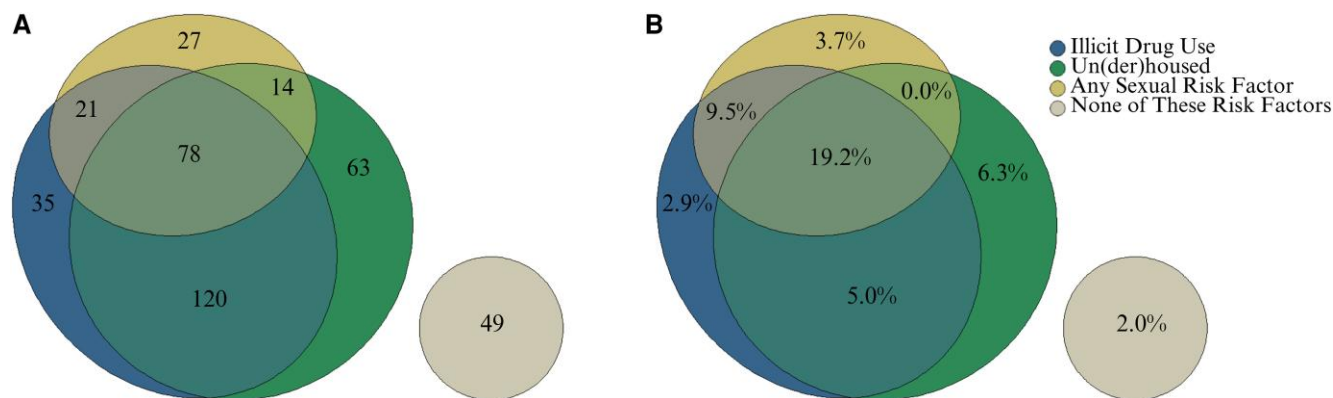


Figure 3. A, The number (*N*) of participants by self-reported risk factors, reflected by circle size. B, Syphilis seroprevalence (%) by risk factor(s).

Our findings also support the hypothesis that illicit drug use, in particular crystal methamphetamine, is a strong correlate with the rapidly rising syphilis rates, reinforcing patterns observed in previous syphilis outbreaks in both the United States and Canada [31]. Methamphetamine use is increasing in Canada [32], and US surveillance data show that the proportion of incident syphilis cases involving methamphetamine has doubled between 2013 and 2017 among women and men who have sex with women in the general population [27] and tripled between 2012 and 2016 among pregnant women [33]. Prior studies have reported higher syphilis prevalence among those who use methamphetamine in equity-deserving populations, such as those living with HIV [10, 13], and those with substance use disorder [34]. Villamagna et al [34] examined Veterans Health Administration data in the United States and found that individuals with substance use disorder who used nonco-caine stimulants (eg, methamphetamine) had syphilis rates twice as high as those with alcohol use disorder, 1.6 times higher than those with cocaine use disorder, and 3 times higher than those with opioid use disorder.

The considerable overlap between illicit drug use and sexual risk factors may explain the association between drug use and syphilis transmission, which is likely mediated by sexual risk factors. The use of crystal methamphetamine is associated with having multiple partners [6, 27, 35–39], condomless sex [27, 36–38, 40], casual or anonymous partners [6, 35–37], being sexually active [35–37], anal sex [35, 38, 39], and having a partner who injects drugs [35]. Research also indicates that individuals who use illicit drugs, including methamphetamine, are more likely to engage in transactional sex [6, 27, 28, 35] and report experiences of forced sex [28, 35].

The World Health Organization's 2022–2030 global health sector strategies on sexually transmitted infections emphasize the importance of equity, context-specific action, and integrated service delivery [15]. Our results illustrate how the SPRITE outreach model of care can reach a high-risk population [16] with

new/reinfections syphilis rates nearly 80 times higher than the 2022 national average [41]. A strength of this study is its community-based outreach model, which extends surveillance beyond clinic-based STI testing, thereby improving representativeness. Unlike traditional STI studies that focus on healthcare-seeking individuals, this approach captures hidden populations that may not engage with formal healthcare systems.

Our study has several limitations. Given sample size constraints, we could not evaluate risk factors based solely on new or re-infections. While we report risk factors individually associated with higher syphilis seroprevalence, they cannot be considered in isolation. Each risk factor interacts with others and operates within broader social, structural, and historical contexts with interlocking systems of oppression and power that create these social inequities and maintain health disparities [42]. This intersection is evident in our findings, where reports of being un(der)housed, using illicit drugs, and reporting any sexual risk factor were associated with significantly higher seroprevalence compared with those with any single risk factor alone.

All sociodemographic and risk factor variables were self-reported, which may have led to misclassification. We hypothesize that any misclassification was likely nondifferential, thereby potentially biasing effects toward the null and reducing the magnitude of the observed effect. This study did not include certain key risk factors identified in existing literature, such as mental health status [43] and sexual networks [44], both of which may influence syphilis seroprevalence. Our study's cross-sectional design prohibits the assessment of causal relationships.

CONCLUSIONS

This study highlights a high burden of syphilis among street-involved populations in Ontario, particularly for those at the intersection of drug use, sexual risk, and housing instability. By identifying key overlapping risk factors and documenting the disproportionate impact on women, our findings

underscore the urgent need for targeted, equity-oriented outreach models. These results can inform clinical practice by guiding risk-based screening strategies and supporting policy development to scale integrated, community-based STI care to reduce transmission and address structural health inequities.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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