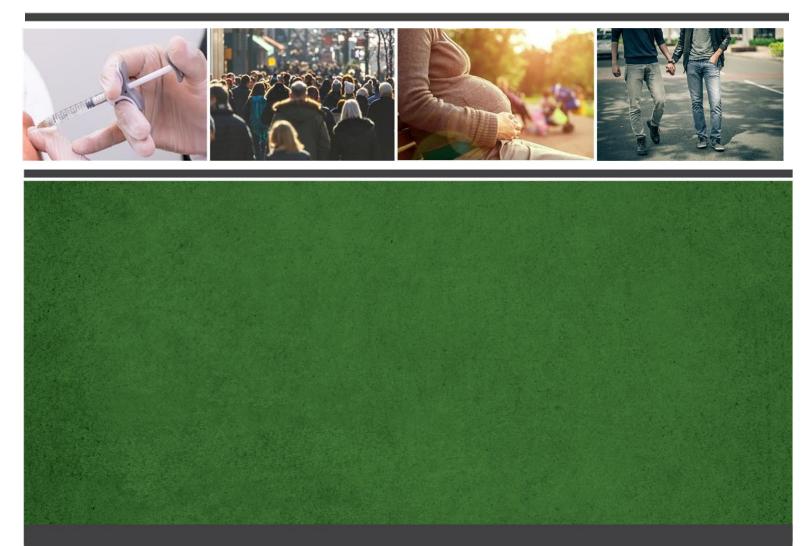
SYPHILIS IN CANADA

TECHNICAL REPORT ON EPIDEMIOLOGICAL TRENDS, DETERMINANTS AND INTERVENTIONS



PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH





TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

-Public Health Agency of Canada

Également disponible en français sous le titre : La syphilis au Canada, Rapport technique sur les tendances épidémiologiques, les déterminants et les interventions.

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Foreword

The Centre for Communicable Diseases and Infection Control at the Public Health Agency of Canada (PHAC) is pleased to present the report: *Syphilis in Canada, Technical Report on Epidemiological Trends, Determinants and Interventions.* The purpose of this report is to provide information to the public health sector, to clinicians and to policy makers about trends in syphilis cases and infection rates in Canada. This report was developed in response to the current rise of syphilis rates in Canada. It presents evidence on the current trends in rates of syphilis infection in Canada, associated risk factors, and some interventions that were implemented in response to the increase in cases of syphilis in Canada.

Syphilis is a notifiable disease in Canada. The report *Syphilis in Canada, Technical Report on Epidemiological Trends, Determinants and Interventions* is primarily based on surveillance data submitted to the Canadian Notifiable Disease Surveillance System (CNDSS) by provincial and territorial health authorities and also presents data published in provincial and territorial surveillance reports as well as information from the scientific literature and from the grey literature including media releases and international reports.

We welcome all comments and suggestions for improving future publications. We invite you to contact the staff of the Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada, at <u>phac.sti-hep-its.aspc@canada.ca</u>.

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Abbreviations

AB aOR aIRR ART BC BCCDC CDC CGSTI CI CIA CNDSS CSF CPHA DBS DFA-TP DNA ECDC EIA EMIS EU FTA-ABS gbMSM GHB HAV HBV HCV HIV	Alberta Adjusted odds ratio Adjusted incidence rate ratio Antiretroviral therapy British Columbia British Columbia Centre for Disease Control Centers for Disease Control and Prevention Canadian Guidelines for Sexually Transmitted Infections Confidence interval Chemiluminescence immunoassays Canadian Notifiable Disease Surveillance System Cerebrospinal fluid Canadian Public Health Association Dried blood spot [testing] Direct fluorescent antibody test for <i>T. pallidum</i> Deoxyribonucleic acid European Centre for Disease Prevention and Control Enzyme immunoassay (Treponemal screening test) The European Men-Who-Have-Sex-With-Men Internet Survey European Union Fluorescent treponemal antibody absorbed test (treponemal screening test) Gay, bisexual and other men who have sex with men Gamma-hydroxybutyrate Hepatitis A virus Hepatitis B virus Hepatitis B virus
HPV HPC	Human immunodeficiency virus Human papilloma virus Immunohistochemistry
IM	Intramuscular
LA	Long acting
LIA	Line immunoassay
MB	Manitoba
MBIA MLST	Microbead immunoassay
NAT	Multilocus sequence typing Nucleic acid test
NAAT	Nucleic acid amplification testing
NB	New Brunswick
NCCID	National Collaborating Centre for Infectious Diseases
NL	Newfoundland and Labrador
NS	Nova Scotia
NT	Northwest Territories
NU	Nunavut
OECD	Organization for Economic Co-operation and Development
ON	Ontario
OR	Odds ratio
PCR PE	Polymerase chain reaction Prince Edward Island
FE	

PEP PHAC POC Pap PT PrEP QC RNA RPR rRNA RSSS SIECCAN SMS SOICC ST STBBI STI STBBI STI SK TP-PA UK	Post-exposure prophylaxis Public Health Agency of Canada Point-of-care [testing] Papanicolaou [test] Provinces/Territories Pre-exposure prophylaxis Quebec Ribonucleic acid Rapid plasma reagin test (non-treponemal screening test) Ribosomal ribonucleic acid Reverse sequence screening for syphilis Sex Information and Education Council of Canada Short message service [text messaging] Syphilis Outbreak Investigation Coordination Committee Sequence type Sexually transmitted blood-borne infections Sexually transmitted infection Saskatchewan <i>T. pallidum</i> particle agglutination test (treponemal screening test) United Kingdom
US	United States [of America]
VDRL YT	Venereal disease research laboratory test (non-treponemal screening test) Yukon
WHO	World Health Organization

Executive summary

This report provides information on syphilis to public health professionals, clinicians and decisionmakers.

The report is organized around six thematic areas:

- 1. Syphilis: natural history, testing and treatment
- 2. Burden of syphilis and co-infections
- 3. Epidemiological trends of syphilis in Canada, 2009-2018
- 4. Determinants and risk factors of syphilis in Canada
- 5. Congenital syphilis: trends, determinants and response
- 6. Interventions and policy for syphilis prevention and control

The first two thematic areas are addressed by summarizing existing guidance from the <u>Canadian</u> <u>Guidelines for Sexually Transmitted Infections (CGSTI)</u> and clinical and laboratory literature. In order to describe syphilis trends in Canada, the third section uses surveillance data from the <u>Canadian Notifiable Disease Surveillance System (CNDSS)</u> from 1971 to 2017, along with preliminary 2018 data provided directly to PHAC by the provinces and territories. Wherever possible, Canadian trends are compared to international trends. The report also describes recent syphilis outbreaks across Canada, as well as the factors that have been associated with syphilis infection in studies conducted in Canada (<u>Section 4</u>). Lastly, interventions and policies proposed to support the control of syphilis in Canada are discussed in <u>Section 5</u> and <u>Section 6</u>.

1. Syphilis: natural history, testing and treatment

Syphilis is an infection caused by the bacteria *Treponema pallidum*. Syphilis is primarily transmitted sexually, although blood-borne transmission is possible. If left untreated, the infection can progress through four stages: primary, secondary, latent and tertiary. Individuals can transmit the infection during the early stages of infection (primary, secondary and early latent syphilis). Chancres and unspecific symptoms, such as fever, malaise or headaches, are among the most common symptoms in the early stages. Tertiary syphilis can cause severe neurological, cardiologic and musculoskeletal manifestations. The infection can also be transmitted from a mother to her fetus/child during pregnancy or at delivery, causing congenital syphilis. Congenital syphilis can lead to stillbirth, birth defects or infant death.

Guidelines for screening vary across the provinces and territories. The CGSTI recommends screening for any individual presenting with signs and symptoms or with risk factors, such as having engaged in condomless sex. Syphilis is usually diagnosed using serological tests on blood samples. Microscopic examination or Polymerase Chain Reaction (PCR) can also be used to detect *T. pallidum* or its deoxyribonucleic acid (DNA). Syphilis is usually treated with penicillin. Resistance of *T. pallidum* to penicillin has not been reported.

2. Burden of syphilis and co-infections

National rates of chlamydia, gonorrhea and syphilis have been increasing, with syphilis having the highest relative rate increase of all three over 2009 to 2018. Some populations, such as gay, bisexual and other men who have sex with men (gbMSM), have been more affected in the past few decades. However, over the past five years, infection rates have substantially increased in other populations including females of reproductive age. As a result, the highest number of

congenital syphilis cases observed in the last 25 years in Canada (17 cases) were reported in 2018. Though syphilis is not associated with high levels of mortality in Canada, it is associated with reduced functioning, a lowered quality of life as well as psychosocial repercussions. Specific populations are affected by overlapping epidemics, such as syphilis and Human Immunodeficiency Virus (HIV) infection, which exacerbate the burden of these infections for affected individuals and communities. Syphilis interacts with HIV to amplify the impacts of both infections, as one may lead to the acquisition of the other and intensify its progression.

3. Epidemiological trends of syphilis in Canada, 2009-2018

Following a sustained decline in the 1990s, syphilis rates began to increase in Canada once again in the early 2000s. In the past few years, rates in Canada have reached their highest point in decades. Similar trends can be found in other high-income countries, such as Australia, the European Union (EU), New Zealand, the United States (US), and the United Kingdom (UK).

In the 1990s, rates among males and females were similar, but beginning in the 2000s, rates among males began to increase rapidly. In 2012, syphilis rates among males were 18 times higher than among females. However, in 2018, preliminary data indicate a reduction in the male-to-female ratio of new syphilis infections from 8:1 in 2017 to 4:1 in 2018. In 2017, the highest rates were observed in the 25 to 29 year old age group and the 30 to 39 year old age groups. Female cases tend to be younger than male cases, as the proportion of male cases increases with age.

Between 2014 and 2018, most provinces and territories reported increases in their infectious syphilis rates. Outbreaks of syphilis have recently been reported in nine provinces and territories. The provinces and territories with the highest increases in rates over this time were Alberta (831%), Northwest Territories (550%), Manitoba (538%), and Saskatchewan (393%). Currently, the jurisdiction with the highest infectious syphilis rate is Nunavut with 261.1 cases per 100,000 population in 2018.

4. Determinants and risk factors of syphilis in Canada

Various social determinants of health and health behaviours shape the risk of acquiring syphilis. These include a broad range of underlying factors, such as age, sex and gender, socioeconomic factors, culture, norms, and health policies and programs, which influence individual-level risk factors, such as sexual activity, substance use, experiences of violence and discrimination and access to health care and services. There is a synergistic interaction at play between the concurrent epidemics of syphilis, other sexually transmitted and blood-borne infections (STBBI) and substance use, given their common risk factors and aggravating social forces.

5. Congenital syphilis: trends, determinants and response

As rates of syphilis increase among women of reproductive age, the number of early congenital syphilis (i.e., within two years of birth) cases is also rising in Canada. From 1993 (when congenital syphilis became notifiable) to 2017, between one and ten cases of congenital syphilis cases were reported each year in Canada. In 2018, 17 cases were reported, and over 50 cases are expected for 2019. The situation is particularly worrisome in the Prairies, which have reported the bulk of congenital syphilis cases in 2018 and 2019. Moreover, several provinces and territories have recently reported their first congenital syphilis case in years.

While there have been few studies examining the risk factors for congenital syphilis, findings from those that exist have reported inadequate prenatal care as one of the main reasons for the

occurrence of congenital syphilis. Pregnant women with syphilis who are not screened and treated in a timely manner are at high risk of transmitting the infection to their baby.

6. Interventions and policy for syphilis prevention and control

The <u>Pan-Canadian STBBI Framework for Action</u> identifies four pillars of action for addressing STBBI, including syphilis: prevention, testing, initiation of care and treatment, and ongoing care and support. The following section reviews the published literature on interventions and policy for syphilis prevention and control originating from Canada and abroad. Strategies to address syphilis are described according to the four pillars for action, starting with improving primary syphilis prevention to addressing underlying social determinants of health. This section also summarizes educational and clinical strategies to increase screening accessibility and uptake as well as approaches to ensure effective case management, and adapt surveillance practices to current epidemiologic case profiles. Areas for future research concerning the syphilis cascade of care, genomic analysis, and program evaluation are noted.

A note on language around sex and gender identity

Throughout the report, considerations of sex and gender are limited by data sources available. Syphilis trends and risk factors are presented according to sex (male, female), as these data are collected in most of the surveillance systems operating within Canada as well as most observational studies. Given that the multi-level determinants of syphilis infection can vary according to gender identity and experiences, discussion of influences of gender identity on how individuals perceive themselves or others, how they act, and how inequities are distributed across society have been included wherever possible throughout this report.

1. Syphilis: natural history, diagnosis and treatment

1.1 The Origins of Syphilis and Means of Transmission

Syphilis is a complex systemic illness caused by a bacterial infection. Specifically, it is caused by the spirochete bacterium *Treponema pallidum*, subspecies *pallidum*.

The origins of syphilis are unclear. Several hypotheses have been suggested, from a possible emergence in South-Western Asia around 3000 BC, to navigators from the Columbus fleet having brought back the disease from the New World - where it had existed in the pre-Columbian period - to the Old World in 1493¹.

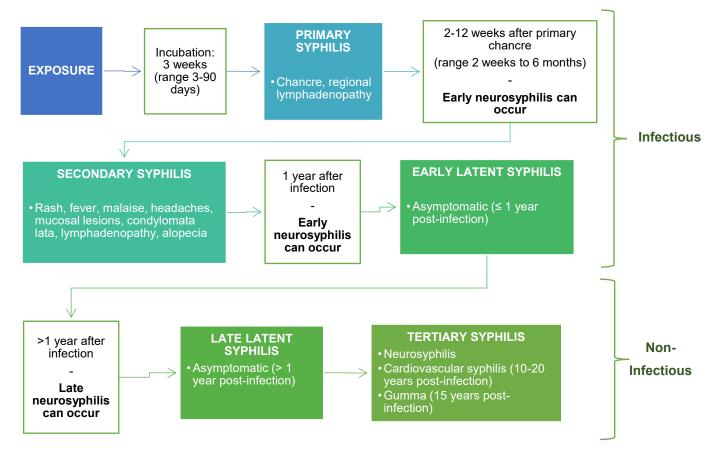
Syphilis is transmitted primarily via genital, anal, or oral sexual contact². Other routes of transmission, such as through kissing with exchange of saliva, blood transfusion and sharing of needles, are possible, but rare³. Congenital syphilis occurs mainly via vertical transmission during pregnancy, although transmission from mother to child can also happen due to contact with an active lesion at the time of delivery². Transplacental transmission can occur as early as nine weeks of gestation and the remainder of the pregnancy⁴. Syphilis in pregnancy can cause miscarriage, stillbirth or neonatal death. In 2012, syphilis resulted in 350,000 adverse pregnancy outcomes globally, including 143,000 early fetal deaths and stillbirths and 62,000 neonatal deaths⁵.

In Canada, syphilis has been a notifiable disease since 1924, and congenital syphilis has been notifiable since 1993⁶. However, reporting has been heterogeneous across provinces and territories (PTs) over time. Furthermore, for congenital syphilis cases, only cases diagnosed in infants less than two years of age are currently reportable nationally.

1.2 Infectious Syphilis Staging and Clinical Manifestations

If left untreated, syphilis infection can progress through four stages: primary, secondary, latent (early and late) and tertiary (stage progression described in <u>Figure 1</u>). However, reinfections are possible following treatment.

Figure 1. Summary of the natural history of untreated syphilis and its associated clinical manifestations



1.2.1 Primary Syphilis

Primary stage syphilis usually occurs after an incubation period of three weeks, on average. However, the incubation period can last between 3 and 90 days. At this stage, a lesion (chancre) may occur as well as regional lymphadenopathy. The chancre may not be readily apparent, as it may be internal (e.g., intra-anal, oral or on the internal genital tract in females), and therefore can frequently go unnoticed. This stage of syphilis is considered infectious with an estimated risk of transmission of approximately 60% per sexual partner².

1.2.2 Secondary Syphilis

After a secondary incubation period of two to 12 weeks (which can last up to six months), infectious syphilis may progress to the secondary stage. Symptoms at this stage can include rashes, fever, malaise, headaches, mucosal lesions, condylomata lata (wart-like lesions), lymphadenopathy, and patchy or diffuse alopecia, signs and symptoms of meningitis, uveitis/retinitis (e.g. blurred vision, eye redness, flashes or floaters) or otic symptoms (e.g.,

hearing loss, tinnitus). This secondary stage is also considered infectious, with an estimated risk of approximately 60% per sexual partner².

1.2.3 Latent Syphilis (Early, Late)

Without treatment, secondary syphilis can progress to the latent stage, during which no symptoms are present. Latent syphilis infections that occur within the first year following infection are considered "early" latent syphilis³. This stage is considered infectious because one in four cases can relapse to secondary stage manifestations⁷. An asymptomatic infection that persists over a year after the infection acquisition is considered "late" latent syphilis.

1.2.4 Neurosyphilis

At any stage of infection, *Treponema pallidum* can invade the central nervous system causing neurosyphilis. Neurosyphilis may be asymptomatic or may present with symptoms. Early neurosyphilis occurs within the first year of infection, and approximately 5% of cases experience symptoms, such as meningitis, cranial neuritis, ocular involvement and meningovascular disease⁸. Neurosyphilis is considered late if its onset is more than one year after infection. At this stage, 2-5% experience general paresis and 2-9% experience *tabes dorsalis* (loss of coordination of movement)⁸. Other signs and symptoms of neurosyphilis include ataxia, vertigo, dementia, headaches, personality changes, Argyll Robertson pupil, otic symptoms (e.g. tinnitus, hearing loss) and ocular symptoms (e.g. blurred vision, bright flashes, floating spots).

1.2.5 Tertiary Syphilis

Though rare, latent infections can progress to tertiary syphilis. Tertiary infections are not infectious. At this stage, the infection can affect several organs, including the brain, nerves, eyes, heart, blood vessels, liver, bones, and joints. Tertiary syphilis can manifest as neurosyphilis (described above). It can also manifest as to cardiovascular syphilis, which occurs ten to 30 years following initial exposure and can lead to development of aortic aneurysms or regurgitation, or coronary artery ostial stenosis. Although most cases will develop within 15 years, syphilis can manifest between one and 46 years following initial exposure, and can lead to gummatous lesions (gumma) on any organ, with clinical manifestations varying based on the site involved³.

1.2.6 Congenital Syphilis

The risk of vertical transmission varies depending on the stage of maternal syphilis, with the risk being over 50% if the pregnant woman has untreated primary or secondary syphilis^{9,10}. Congenital syphilis can lead to stillbirth. Early congenital syphilis occurs within the first two years of life. Manifestations can include fulminant disseminated infection, rhinitis (snuffles), mucocutaneous lesions, hepatosplenomegaly, anemia, osteochondritis and neurosyphilis. Symptom onset after two years is defined as late congenital syphilis. Symptoms include interstitial keratitis, lymphadenopathy, hepatosplenomegaly, anemia, bone involvement, dental abnormalities such as Hutchinson's teeth, and neurosyphilis.

1.2.7 Syphilis staging

Syphilis staging can be challenging, as infection stage cannot be determined by laboratory testing alone. Patient history and clinical presentation of disease are essential to determine syphilis stage and allow proper treatment. For primary and secondary stages, positive serology and clinical manifestation are needed to stage cases, as these stages can only be distinguished by signs and

symptoms. In the case of asymptomatic patients with positive serology, patient history is necessary to determine staging; those who previously tested negative in the last 12 months are most likely to be in the early latent stage of syphilis, while those without negative serology in the previous 12 months may be in the late latent stage. Neurosyphilis can manifest in early (infectious neurosyphilis) or late stages (non-infectious neurosyphilis) of syphilis infection. Similar to what was discussed above, patient history is pivotal, as only previous serology testing and the history of physical symptoms can distinguish infectious from non-infectious neurosyphilis cases. This distinction is important, as early stages and late stages will require different courses of treatment. Appendix A presents an algorithm of syphilis staging according to the CGSTI.

1.3 Syphilis Screening

1.3.1 Target Population for Screening

The Public Health Agency of Canada (PHAC) guidelines recommend that any individual presenting signs or symptoms compatible with syphilis and individuals presenting with risk factors for syphilis should be screened³. These risk factors include:

- Having sexual contact with someone who has received a syphilis diagnosis
- Being a man who has sex with men
- Being engaged in transactional sex
- Having experienced homelessness or street involvement
- Having used injection drugs
- Reporting multiple sexual partners
- Personal history of syphilis, HIV infection or other sexually transmitted infections (STIs)
- Being born to a mother diagnosed with infectious syphilis in pregnancy
- Having lived in a country or region with a high prevalence of syphilis
- Having a sexual partner with any of the above risk factors

Guidelines for screening vary across provinces and territories. Local, provincial and territorial recommendations should be followed.

1.3.2 Screening in Pregnancy

Given the rising rates of syphilis and congenital syphilis in Canada, universal screening of all pregnant women continues to be important and is the standard of care in all jurisdictions. Universal screening of pregnant women is recommended during the first trimester or at first prenatal visit¹¹. Repeat screening at 28-32 weeks (third trimester) and at delivery is recommended in areas with outbreaks and for women at high risk of acquiring syphilis. More frequent screening should be considered for women at high risk. It is also recommended that pregnant women with no history of prenatal care or testing be tested at delivery. Lastly, any person delivering a stillborn infant after 20 weeks gestation should be screened for syphilis.

1.3.3 Screening in Immigrants to Canada

Currently, syphilis testing is mandatory for all individuals aged 15 years and older who undergo an immigration medical exam¹². This medical exam is mandatory for all foreign nationals applying for permanent residency and for temporary resident applicants who intend to work in an occupation in which the protection of public health is essential (workers in the health sector field, for example)¹³. Cases that are positive must document appropriate treatment according to Canadian protocol by providing a completed Syphilis Treatment Form with the immigration medical exam content¹⁴.

1.4 Laboratory Diagnosis of Syphilis

Pathogenic treponemal bacteria include *Treponema pallidum* subspecies *pallidum* (subsequently referred to as *T. pallidum*) that causes venereal syphilis, *T. pallidum* subspecies *endemicum* that causes bejel or endemic syphilis, *T. pallidum* subspecies *pertenue* that causes yaws, and *T.*

Syphilis can be diagnosed using serological tests (treponemal or non-treponemal), microscopic examination or nucleic acid amplification tests (NAAT). Pointof-care testing is increasingly of interest for underserved populations, but is not yet licensed by Health Canada for use in Canada. carateum that causes pinta. Since the commonly used serological tests for the diagnosis of syphilis cannot differentiate between infection caused by *T*. *pallidum* and infections due to other pathogenic non-venereal treponemal agents, the differential diagnosis of skin lesions suspected of syphilis or other treponemal infection should therefore, include a careful clinical examination and consideration of the patient's background history including any travel to endemic areas for nonvenereal treponematosis.

1.4.1 Serological Diagnosis

Initial screening for syphilis can be conducted using a non-treponemal test or a treponemal test, both of which are applied on a serum sample. Once reactive, the treponemal test will most often remain so throughout the person's life, even in the presence of treatment². However, 15-25% will serorevert (non-reactive test result) if the individual is successfully treated while their infection is at the primary stage².

Non-Treponemal Antibody Test

Non-treponemal tests approved by Health Canada include the Rapid Plasma Reagin (RPR) and the Venereal Disease Research Laboratory (VDRL) tests. These tests detect non-specific antibodies to a complex mixture of cardiolipin, lecithin, and cholesterol. Both tests are flocculation tests (clumping of antigen mixture by positive test sample) and therefore, are subjective tests that require experience on the part of the test operator. Positive non-treponemal tests are indicative of active infection at the primary, secondary, or latent stages of infection; and when done quantitatively, they can be used to follow successful treatment of infection by observing a drop in the antibody titre³.

RPR is slightly more sensitive (86%) than VDRL (78%) for the detection of primary syphilis but both tests are 100% sensitive in secondary syphilis¹⁵. RPR can only be used on serum samples, while VDRL can be used to detect antibodies in serum and cerebrospinal fluid (CSF) and is the only approved non-treponemal serological test to be used on CSF for the diagnosis of neurosyphilis¹⁶. Interpretation of non-treponemal test results may be complicated by the prozone phenomenon, which occurs with very high titre samples that give negative results unless the test samples are diluted. Biological false positives, which may occur due to factors unrelated to treponemal infections, such as older age, some viral, bacterial, and parasitic infections, and some autoimmune diseases and pregnancy, may also interfere with the interpretation of nontreponemal test results.

Treponemal Antibody Test

Unlike non-treponemal tests, these tests use treponemal antigens to detect anti-treponemal antibodies. Since a positive treponemal antibody test result may remain positive for a very long time, treponemal antibody tests cannot be used to differentiate active infections from previous infections that have been treated in the past, nor can they be used to monitor and confirm success of treatment. There are many Health Canada approved serological tests that detect treponemal antibodies and these include amongst others, the fluorescent treponemal antibody absorption (FTA-ABS) test, *Treponema pallidum* particle agglutination (TP-PA) assay, various traditional enzyme immunoassays (EIAs), newer EIAs such as the chemiluminescence immunoassay (CIA) or the microbead immunoassay (MBIA), and the line immunoassay (LIA).

When the sensitivity and specificity of some of these treponemal antibody tests were compared, FTA-ABS has the lowest sensitivity in detecting both primary (78.2%) and secondary syphilis (92.8%) compared to other immunoassays (TP-PA, Trep-Sure, Inno-LIA, CIA and MBIA) that were found to be 100% sensitive in detecting secondary syphilis, while their sensitivities for primary syphilis were between 94.5% to 86.4%. The overall specificity was lowest for Trep-Sure (82.6%) and highest for TP-PA (100%), with FTA-ABS achieving a specificity of 98.0%¹⁷. False positive treponemal tests have been reported in patients with gingivitis and periodontitis due to cross-reactive antigens present on oral spirochete organisms¹⁸.

Algorithm of Syphilis Serology

Two types of serologic screening algorithms are currently used in Canada: traditional and reverse algorithms¹⁹. Traditionally, the serological detection of syphilis infection starts by screening with a non-treponemal antibody test. When positive, it is confirmed using a treponemal antibody test. For high risk individuals, both non-treponemal and treponemal antibody tests are done at the same time to detect possible latent infection when the non-treponemal antibody test may be negative²⁰.

The reverse sequence syphilis screening (RSSS) algorithm approach uses a treponemal test to screen and a quantitative non-treponemal test to confirm the positives. With increasing sample volumes for syphilis screening and the availability of automatic high-throughput platforms (such as CIA and MBIA) for performing treponemal antibody tests, many laboratories have opted for the reverse approach screening of syphilis, using high throughput treponemal antibody tests and confirming any positive findings with a non-treponemal antibody test. Presently, most provinces and territories favour the reverse algorithm³. In general, since the interpretation of serology results can be complex, and different algorithms may be employed across provinces and territories, consultation with public health laboratories regarding testing protocols is recommended.

When screening is done with the more sensitive treponemal test, discordant positive treponemal test results that cannot be confirmed by a non-treponemal test becomes a diagnostic and clinical issue²¹. For example, in a study involving over three million test samples in a major Canadian city, it was found that 2.2% of the samples screened positive for syphilis when CIA was used vs. only 0.6% positive when screening was done by RPR²². However, of the 2.2% that screened positive by CIA, 1.4% were RPR negative and only 0.6% of the samples having screened positive by CIA but negative by RPR were cases of early primary syphilis. These cases showed seroconversion to RPR positive, in a follow-up test sample. Therefore, under the RSSS algorithm, those who screened positive by EIA but who were RPR-negative may represent either early primary syphilis, treated past syphilis infection, latent syphilis of unknown duration, or false positive reaction. Consistent with this, in another study that examined the impact of the RSSS algorithm, an increase in the diagnosis of late latent syphilis was noted²³.

1.4.2 Other Methods of Detection

Microscopic Examination

The method of choice to detect *T. pallidum* may depend on the type of specimen taken for examination. Tissue specimens taken for histological examination can be used to examine the presence of *T. pallidum* using either silver staining or an immunohistochemistry (IHC) reaction. The former test relies on a morphological recognition of spirochetes in tissue samples made visible by the silver nitrate deposit or impregnation around the bacteria²⁴. The IHC method has enhanced sensitivity and specificity from the use of antibodies, such as monoclonal antibodies to *T. pallidum* and an enzyme reaction such as peroxidase reacting with an insoluble substrate to allow the antigen-antibody reaction to be visible under light microscopy²⁵. However, both methods are prone to potential false positives due to staining artifacts and the presence of cross-reacting bacteria²⁶.

Direct observation of *T. pallidum* in fresh specimens, such as serous fluids from genital, skin or mucous membrane lesions of primary and secondary syphilis cases, can be carried out by dark-field microscopy. This method requires a trained microscopist to recognize the live motile spirochetes. As a result, the test has to be performed at, or near, the location of specimen collection. It is not suitable for oral and anal lesion specimens due to the presence of other spirochete organisms whose morphology is indistinguishable from *T pallidum*. The use of microscopic examination is now limited in Canada, with only one provincial public health laboratory still using microscopy as a mean for laboratory diagnosis of primary syphilis, due to the difficulties in maintaining the technical expertise and methodological limitations of the technique.

Another method for detection of *T. pallidum* is the direct fluorescent antibody test for *T. pallidum* (DFA-TP). This method is now almost obsolete due to lack of a reliable source of direct fluorescent anti-*T. pallidum* antibody.

Nucleic Acid Amplification Test

Detection of *T. pallidum* nucleic acid by polymerase chain reaction (PCR) is a sensitive test capable of detecting ten to 100 copies of the target gene²⁷. PCR testing to detect DNA or ribonucleic acid (RNA) targets have been described^{28,29}. However, there is currently no Health Canada-licensed PCR test commercially available for use in Canada. As a result, many laboratories have developed their own in-house test or adopted methods described in academic journals. In the last two decades, the use of PCR for the diagnosis of syphilis has provided some information about its optimal use. PCR is most useful for the diagnosis of primary syphilis before seroconversion occurs^{30,31}. This method performs best in specimens taken from moist lesions in both primary and secondary syphilis. Its performance in blood specimens is only about 50%, except in neonates with congenital syphilis³². Positive PCR results have been reported with urine and semen specimens as well as in the oral cavity of secondary syphilis cases involving men who have sex with men, even without oral lesions³³⁻³⁵. Another use of PCR is in testing the involvement of *T. pallidum* in unusual pathology, such as lung abscess, tonsillitis or a non-healing oral ulcer that extends to the lower lip³⁶⁻³⁸.

1.4.3 Typing of T. Pallidum

Although various methods have been in use in the past, it appears likely that the recently proposed multi-locus sequencing typing (MLST) will become the widely adopted method of choice for the typing of *T. pallidum*³⁹. Since MLST has been used widely in the tracking of other bacterial pathogens like meningococci, pneumococci, methicillin-resistant *Staphylococcus aureus* and

many others, clinicians and public health officials are familiar with the method and the terminology used.

As of September 2018, 40 Sequence Types (STs) of *T. pallidum* have been documented, and they have been reported from Europe, North America, South America, and Asia. These STs can be grouped into two clonal complexes: the SSI4-like clonal complex and the Nichols-like clonal complex. Although not part of the MLST scheme, PCR amplification and sequencing of the 23S ribosomal RNA (rRNA) gene that encodes for macrolide resistance or susceptibility can identify resistant strains as well as the type of resistance. Mutations at positions 2058 or 2059, corresponding to the 23S rRNA gene of *Escherichia coli* (accession number V00331), results in an A to G substitution, which has been shown to cause macrolide resistance^{40,41}. The A2058G mutation causes azithromycin resistance, but not resistance to spiramycin, while the A2059G causes resistance to both antibiotics.

1.4.4 Point-of-care Test for Syphilis

Diagnostic testing conducted at or near the site of patient care, called point-of-care (POC) testing, can provide results to a clinician without time spent waiting for sample transport and laboratory processing⁴². While the World Health Organization (WHO) studies POC tests for syphilis and other STIs as a means for control in developing countries and in resource-limited settings, their use and need in high-income countries like Canada are less defined^{43,44}. Nevertheless, there is much interest in the role of POC tests for STIs (including syphilis) in STI clinics, remote regions, and underserved populations, particularly during outbreak situations. Currently there are no licensed POC test kits for the diagnosis of syphilis in Canada, although access to these tests might be possible through the Special Access Programme for Medical Devices⁴⁵. Field evaluations are currently underway to examine the diagnostic utilities of such POC tests across different settings, venues and populations who may benefit from such methods.

1.5 Syphilis Treatment

Syphilis is usually treated with penicillin, a treatment method that was established in 1943⁴⁶. A single dose (2.4 million units delivered through intra-muscular (IM) injection) of benzathine penicillin G-Long acting (LA) can render *T. pallidum* non-infectious within 24 hours for early syphilis infection⁴⁷. Infection of longer duration requires repeated dosing. There are limited data supporting the efficacy of alternate antibiotics, such as doxycycline or ceftriaxone, for patients

with penicillin allergies. These treatments may take longer to render a person non-infectious, so close patient follow-up is required. A more complete summary of treatment guidelines is available at: <u>https://www.canada.ca/en/public-</u> <u>health/services/infectious-diseases/sexual-healthsexually-transmitted-infections/canadian-</u> <u>guidelines/sexually-transmitted-infections/canadian-</u> <u>guidelines-sexually-transmitted-infections-27.html³</u>.

Syphilis is usually treated with penicillin. Resistance of *T. pallidum* to penicillin has not been reported.

Resistance of *T. pallidum* to penicillin (the drug of choice) has not been reported, however resistance to macrolide antibiotics — including azithromycin — has been reported in many parts of the world including Canada⁴⁸. Unless the *T. pallidum* strain has been tested and found to be sensitive, azithromycin is not recommended for the treatment of syphilis.

1.5.1 Treatment for People living with HIV

Though the literature on syphilis treatment for people living with HIV is limited, existing studies suggest that this population should receive the same penicillin treatment as people who are HIV-negative (single dose benzathine penicillin G-LA for treatment of early syphilis infection). It should be noted, however, that some experts suggest a higher dosage (three weekly doses of 7.2 million units IM) for people living with HIV³.

1.5.2 Treatment during Pregnancy

For early syphilis cases in pregnant women, a single penicillin dose is reported to be effective⁴⁹. However, given the difficulty in staging cases among pregnant women and the association between pregnancy and both lower plasma penicillin levels and modified pharmacokinetics of penicillin, some experts recommend infectious cases be treated with two doses of benzathine penicillin G-LA 2.4 million units one week apart, particularly in the third trimester⁵⁰. In general, treatment during pregnancy should be managed in collaboration with an obstetrician or maternal fetal medicine specialist.

1.5.3 Treatment of Newborns (Congenital Syphilis)

No newborn should be discharged from hospital without confirmation that either the mother or newborn infant has undergone syphilis serology testing during pregnancy or at the time of labour and delivery and that the results will be followed up according to local protocol¹¹. Treatment is recommended for all neonates and children who are symptomatic. Furthermore, all infants for whom adequate follow-up cannot be ensured including those for whom the non-treponemal test yielded a titre that was at least four-fold higher than that of the birthing parent, and those for whom the treatment of the birthing parent was inadequate, unknown, did not contain penicillin, or occurred in the last month of pregnancy, should also be treated¹⁰. Preferred penicillin treatments vary based on the age of the child (<1 month versus \geq 1 month of age) and presence of symptoms¹⁰.

KEY MESSAGES

- Syphilis is a notifiable disease caused by a bacterium, *Treponema pallidum*, and is transmitted primarily through genital, anal or oral sexual contact.
- Congenital syphilis occurs via vertical transmission mainly during pregnancy and can cause miscarriage, stillbirth or infant death shortly after birth.
- If left untreated, a primary syphilis infection can progress through secondary, latent and tertiary disease stages. Out of the four stages of syphilis, three are infectious: primary, secondary and early latent syphilis.
- PHAC's guidelines recommend that, any individual presenting signs or symptoms compatible with syphilis and any individual presenting with risk factors for syphilis be tested.
- Universal screening is recommended for pregnant women in the first trimester or at least once during pregnancy. Moreover, consideration should be given to repeat screening at 28-32 weeks of gestation and at delivery, particularly in areas experiencing outbreaks or for women at risk of syphilis acquisition.
- Syphilis is diagnosed most often using serologic tests and can be easily treated with penicillin.

2. Burden of syphilis and co-infections

2.1 Epidemiology of Syphilis in Canada

Following chlamydia and gonorrhea, syphilis is the third most commonly reported notifiable STI in Canada⁵¹. Canada, in 1998, announced a national goal of maintaining a syphilis rate below 0.5 per 100,000 population by the year 2000. However, since the early 2000s, rates of syphilis infection have been steadily increasing⁵². In recent years, many jurisdictions are experiencing a major surge in their number of syphilis cases (Section 3). Between 2008 and 2017, the rate of infectious syphilis increased nationally by 167%, the highest relative increase of all three STIs⁵¹. In 2017, the most recent year for which pan-Canadian syphilis data have been published, the rate of infectious syphilis in Canada was 11.2 cases per 100,000 population⁵¹. That year, the rate was 2.4 cases per 100,000 females, and 20.0 cases per 100,000 males⁵¹. Though the rate is lower among females, provincial reports suggest that up to 86% of female syphilis cases are among women of childbearing age (15 to 39 years), leading to a higher risk of congenital syphilis incidence⁵³. Provincial and territorial reports suggest that since 2017, rates of infectious and congenital syphilis have increased significantly, with a national rate of 17.0 in 2018, according to preliminary 2018 data (Section 5).

The risk of syphilis is not distributed evenly across the Canadian population. Certain populations, such as gbMSM, are known to experience high rates. Moreover, large increases in rates have been observed recently in other populations, especially women of reproductive age⁵⁴. As a result of this recent trend, Canada reported its highest number of congenital syphilis cases in past 25 years in Canada in 2018 (17 cases). <u>Section 4</u> of this report describes in detail social inequalities with regard to syphilis risk, highlighting the importance of considering health equity in syphilis prevention and control.

2.2 Burden of the Disease on those Affected

Among people diagnosed with syphilis in Canada, data on the distribution of staging is currently lacking. Most published studies do not distinguish between stages of infection in their reporting, and consistent staging data are not currently available across all provinces and territories⁵⁵. Studies that do detail staging indicate a broad distribution of cases across stages at diagnosis. Among 1,473 syphilis cases diagnosed between 1995 and 2005 in British Columbia, 50% were at primary or secondary stages, and 50% were early latent⁵⁶. In another study of a randomly selected set of 350 syphilis cases among gbMSM in British Columbia in 2013, 20% of cases were diagnosed at a primary stage, 25% were secondary, and 55% were early latent⁵⁷. In a Winnipegbased study of 151 infectious syphilis cases in 2014 and 2015, 41% were primary, 35% were secondary, and 21% were early latent⁵⁸. Additionally, in an Alberta-based review of retrospective cases from 1975 to 2016, 8,874 cases of syphilis were reported, of which 51% of cases were infectious (i.e. primary, secondary or early latent), while 49% were classified as non-infectious (i.e. primary, secondary or early latent), while 49% were classified as non-infectious (i.e. late latent or tertiary)⁵⁹. Of the 254 cases of neurosyphilis and tertiary syphilis identified in this review, 251 cases were neurosyphilis (52% early neurosyphilis and 46% late neurosyphilis) and three were cardiovascular syphilis.

In the same Winnipeg-based study referenced above, when comparing the distribution of stages among males and females, the authors found that although the proportions diagnosed at a primary stage were similar for both sexes (approximately 41%), female cases were diagnosed later (18% secondary and 35% early latent) than males (37% secondary and 19% early-latent)⁵⁸. Studies suggest that the higher rates of later-stage syphilis diagnosis among females may be due

to the fact that primary lesions may be less visible for females than males, thus making it more difficult for females to know to seek assessment and diagnosis². Other reported reasons for this difference include the fact that females may be less likely than males to be screened for syphilis when another STI is suspected, and they may be more likely to seek over-the-counter treatments, which may mask STI presence and delay diagnosis⁶⁰. Furthermore, while many health clinic programs and community-based organizations have conducted considerable outreach activities among gbMSM communities to promote access to sexual health resources and services, there have been fewer efforts geared towards women. Additionally, it has been reported in existing literature that cases of congenital syphilis usually occur because of absence or delays in access to prenatal care for pregnant women (Section 5). These disparities in the targeting of sexual health outreach may also contribute to delays in syphilis diagnosis among women. Overall, the large proportion of cases diagnosed at an early-latent phase may indicate gaps in syphilis screening and knowledge in the country. Inequalities in stage distribution represent an important health equity issue.

If left untreated, syphilis can progress from primary to subsequent stages, each associated with distinct clinical burdens for those affected². Available studies suggest that between 15% and 40% of untreated cases will experience complications associated with late stage syphilis, such as late neurosyphilis or tertiary syphilis². Late stage syphilis requires a more intensive treatment, with possible side effects and greater risk of treatment failure². Treatment failure is characterized by increasing or stable non-treponemal test titers at the recommended follow-up test one month after treatment.

Syphilis during pregnancy can lead to adverse outcomes for the fetus, including miscarriage, stillbirth and infant death. Although syphilis is not associated with high levels of mortality in Canada, it is associated with a reduction in functioning and poorer quality of life. A study conducted in Ontario reported that untreated syphilis was associated with the equivalent of 18 years of life lost due to reduced functioning, 94% of which was attributable to neurosyphilis⁶¹. However, given that there may be considerable under-diagnosis and under-reporting of syphilis, the authors note that it is possible that these estimates underestimate the true number of years of life lost⁶¹. Furthermore, beyond the physical health burden associated with syphilis infection, some studies also identify psychosocial repercussions of syphilis-related stigma^{62,63}.

2.3 Risk of Sexual Transmission

It is understood that the transmission rate of infectious syphilis (primary, secondary, and early latent stages) per sexual partner is approximately 64% for primary and secondary syphilis⁶⁴. There are few studies exploring the per-act transmission risk of syphilis⁶⁴. An American study that focused on transmission among gbMSM found that the probability of transmission is of 0.5% to 1.4% per sexual act during the primary and secondary syphilis stages, with lower probability in the early latent stage⁶⁴. Lastly, though few studies have explored possible sex differences in transmission probability, experts hypothesize that as with HIV and gonorrhea, transmission probabilities may be higher from men-to-women than from women-to-men⁶⁵.

In general, the probability of transmission is dependent on the susceptibility of the sexual partner that is exposed⁶⁴. Population-level risk of transmission is lower when pro-active screening occurs, cases are treated, cases' contacts are traced and treated, and preventive strategies, such as condoms, are employed⁶⁴. These factors, as well as other strategies to reduce transmission risk, are described in <u>Section 6</u> of this report.

2.4 Adverse Pregnancy Outcomes

As mentioned previously, the majority of female syphilis cases are among individuals of childbearing age (15 to 49 years, as defined by the WHO, although the PHAC STBBI surveillance team uses 15-39 years, in accordance with CNDSS age groups categories)^{51,53}.

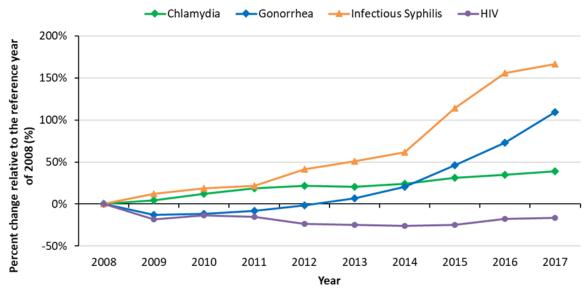
Studies on mother-to-child syphilis transmission risk are rare. In a systematic review, transmission rates ranging from 2.3% to 40.9% have been reported, with a pooled mother-to-child transmission rate of 15.5%⁶⁶.

Among pregnant women, the risk of transmission is dependent on the stage of the syphilis infection as well as the timing of infection, diagnosis, and treatment during the pregnancy. However, evidence indicates that vertical transmission can occur at any time during pregnancy^{64,67}. The risk of vertical transmission is highest when syphilis is acquired near term⁶⁷. Research suggests that the risk of vertical transmission is 70% to 100% during primary and secondary stages, and 40% in the early latent phase³. If untreated, approximately 77% of maternal syphilis cases will result in adverse outcomes, which could include pre-term birth, stillbirth, neonatal mortality or clinical manifestations of congenital syphilis^{64,68}. Risks of adverse outcomes are higher compared to uninfected pregnancies, even after treatment⁶⁹. As adverse pregnancy outcomes cause physical and psychological burdens both for the parent and the child, maternal syphilis and congenital syphilis are of significant public health concern.

2.5 Co-Infections and Syndemics

In recent years, the incidence of STIs has been increasing both in Canada and internationally (Figure 2 and Figure 5).





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

There is a trend with regard to co-infection of syphilis with HIV. The current epidemics of syphilis and other STIs have been described as a syndemic, given their concurrence (co-infections are common), interactions between these infections, associated health consequences, and shared underlying determinants (<u>Figure 3</u>)^{62,70,71}. National surveillance data do not track co-infections, but existing Canadian studies have reported the prevalence of syphilis among HIV-positive individuals to be around 8% to 11%^{72,73}.

Syphilis increases the risk of acquisition and transmission of HIV in several ways⁷⁴. First, syphilitic chancres provide an entry portal for the HIV virus⁷⁵. Secondly, the bacterium causing the syphilis infection, *T. pallidum*, has been observed to increase the expression of the CCR5 chemokine receptor—one of the principal receptors for macrophage-tropic viruses, such as HIV. This leads to a higher likelihood of HIV transmission⁷⁵.

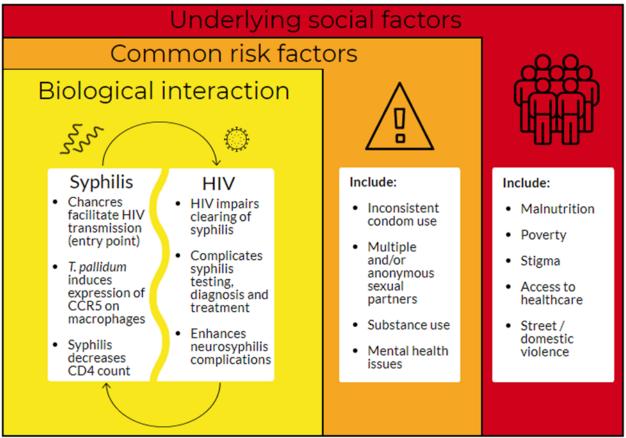


Figure 3. Factors contributing to the HIV-syphilis syndemic

Adapted from Jiang et al. (2017)⁷⁰, Yu et al. (2018)⁶², Singer and Clair (2003)⁷¹, Singer et al. (2006)⁷⁶, Lang et al. (2018)⁷², Remis et al. (2016)⁷³, Solomon et al. (2016)⁷⁴ and Karp G et al. (2009)⁷⁵.

In turn, people living with HIV are eight times more likely to be infected with syphilis compared to the general population⁷⁵. Several factors can explain the association between HIV and syphilis infection. First, the immune suppression associated with HIV is believed to impair clearance of syphilis⁷⁵. Further, HIV alters the natural evolution of syphilis, leading to more rapid progression through the disease stages —namely, to neurosyphilis and more aggressive and atypical signs of infection— and syphilis treatment complications have also been observed^{2,75,77}. Studies also indicate that it can be difficult to diagnose neurosyphilis in people living with HIV, insofar as CSF invasion-related symptoms can occur without syphilis infection². Lastly, due to the shared risk

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factors for both HIV and syphilis infections (including biological susceptibility and sexual behaviours), people living with HIV are more likely to have repeated syphilis infections following successful syphilis treatment^{64,78}.

Inconsistent condom use and sex with multiple or anonymous partners are major risk factors for both syphilis and HIV^{76,79}. Condom use is an effective prevention method to reduce the spread of STIs, but inconsistent or improper use decreases its effectiveness⁸⁰. A study conducted by Remis et al.⁷³ (n=442) showed that condomless anal and oral sex with casual partners was correlated with syphilis infection among gbMSM living with HIV in Toronto. Another study (n=194) identified syphilis co-infection in populations living with HIV and underlined a number of additional risk factors for syphilis co-infection, such as being a man who has sex with men, as well as alcohol and recreational substance use⁷².

Overarching adverse social conditions, such as malnutrition, poverty, stigma, discrimination and exposure to violence, can put individuals at risk for syndemics, exacerbating the likelihood of acquiring co-occurring infections^{71,76}. These inequalities all have an impact on health and can lead to adverse health outcomes in key populations and can limit access to healthcare and appropriate treatment^{62,80}.

KEY MESSAGES

- National rates of syphilis infection have had a higher relative increase between 2013 and 2018, compared to chlamydia and gonorrhea rates.
- Gay, bisexual and other men who have sex with men are the most affected population in past decades but high relative increases in rates have been observed in women of reproductive age in recent years.
- The female syphilis rate increase in recent years has translated to an increase in the number of congenital syphilis cases.
- Untreated syphilis is associated with a high burden of congenital cases and with reduced functioning for other cases.
- Trends of syphilis and other STIs have been described as a syndemic.

3. Epidemiological trends of syphilis in Canada, 2009-2018

3.1 Historical and Recent National Rates of Syphilis in Canada

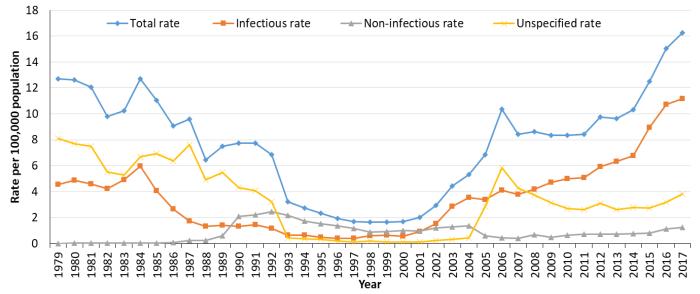
In Canada, syphilis has been nationally notifiable since 1924. In this section, Canadian syphilis CNDSS data covering the period of 1979 to 2017 are presented, along with preliminary data for 2018, provided directly by PTs. Current case definitions and details concerning data sources and analysis are described in <u>Appendix B</u> and <u>Appendix C</u>.

3.1.1 Historical Syphilis Trends in Canada

Canadian rates of syphilis were high until the 1940s, when they started to decrease significantly, a trend that continued until the 1980s. Rates remained low for most of the 1990s (Figure 4). This trend was also observed in other countries, such as the UK⁸¹. Following this period of decline, Canadian rates began to climb again in the early 2000s (Figure 4). A similar increase in incidence rates was observed in the UK and the US over this time (Figure 5)^{81,82}.

Several hypotheses have been proposed to explain the growing incidence of syphilis in Canada over the past decades. In the 1990s and 2000s, a number of significant events occurred, including the introduction of antiretroviral therapy (ART) for HIV treatment in the late 1990s. This was followed by the arrival of the Internet and online apps for meeting potential sexual partners, as well as an increase in the use of certain drugs, such as crystal methamphetamine for chemsex in the 2000s⁸³. The term "chemsex" (or Party and Play, "PnP") refers to the planned use of certain substances, including but not limited to methamphetamines, to extend the duration (hours to days) and intensity of sexual encounters (number of partners, types of practices)⁸⁴. While it is hypothesized that these ecological factors have shaped current STI incidence patterns in North America, no Canadian studies have confirmed the correlation between these population-level shifts and changes in syphilis incidence⁸³.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

Infectious syphilis rates have continued to increase in Canada (Figure 5) in the last decade. Similar increases have been observed in other Organisation for Economic Co-operation and Development (OECD) countries (Figure 5). Canadian rates tend to be similar to those of England and slightly higher than those reported in the US. Detailed rates of infectious syphilis for Canada and other selected OECD countries for the last decade are presented in <u>Appendix D</u>.

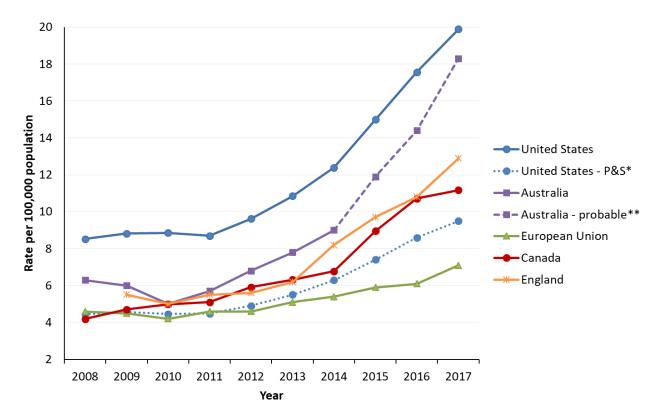


Figure 5. Comparison of rates of reported cases of infectious syphilis in OECD countries^a, 2008-2017

Note: Canada's definition of infectious syphilis includes confirmed cases of primary, secondary and early latent syphilis. Please note that some of the countries presented have slightly different definitions.

* The US includes confirmed primary and secondary stages only in its definition of infectious cases (US- P&S- blue dotted line). Confirmed early latent cases were added to primary and secondary cases to produce US rate estimates for the definition of infectious syphilis used in Canada (solid blue line).

** The dotted line for Australia represents the years for which the case definition included probable cases of infectious syphilis (in addition to confirmed cases of primary, secondary and early latent syphilis). In 2015, approximately 9% were reported as such.

The EU includes all cases of syphilis regardless of stage, although of the countries that provided staging information, 95% of cases were reported as either primary, secondary or early latent.

https://diseases.canada.ca/notifiable/charts-list, 2019.

England: Public Health England, Official Statistics, Sexually transmitted infections (STIs): annual data tables. Table 1 (b): Rates of new STI diagnoses in England by gender, 2008 – 2017, Rates per 100 000, Syphilis: primary, secondary, early latent, total. https://www.gov.uk/government/statistics/sexually-transmitted-infections-stis-annual-data-tables

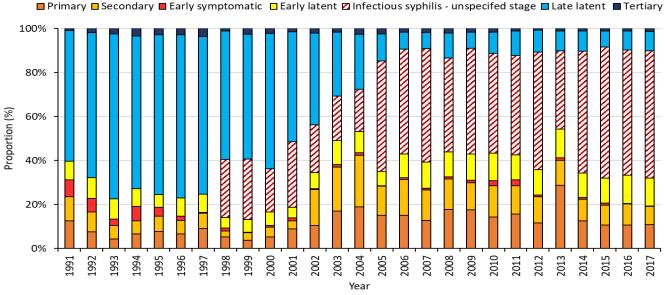
^a Sources: <u>Australia</u>: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. 2018. Australia's notifiable disease status, 2015: Annual report of the National Notifiable Diseases Surveillance System, NNDSS Annual Report working group. <u>https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance European Union:</u> European Centre for Disease Prevention and Control (ECDC). Syphilis - Annual epidemiological report for 2017. 12 July 2019. <u>https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2017</u>

<u>United States</u>: Centers for Disease Control and Prevention (CDC). Table 27. Primary and Secondary Syphilis — Reported Cases and Rates of Reported Cases by State/Area and Region in Alphabetical Order, United States and Outlying Areas, 2013–2017. 2018; Available at: https://www.cdc.gov/std/stats17/tables/27.htm. Accessed September 10, 2019.

Canada: Government of Canada. Canadian Notifiable Disease Surveillance System. 2018; Available at:

Over the past 25 years, the distribution of syphilis cases across the four stages of infection has evolved. Historically, the vast majority of cases were diagnosed in the late latent phase (Figure <u>6</u>). For example, in the 1990s, only 20% of cases for which a status was specified were diagnosed in the infectious stages. However, over time, cases have tended to be diagnosed earlier. Since 2006, primary, secondary and early latent cases now comprise at least 75% of the reported cases in Canada (Figure <u>6</u>) ⁸⁵⁻⁸⁸. This increase in the proportion of cases diagnosed during an infectious stage may be related to the introduction of PCR testing used in the diagnosis of syphilis, especially at early stages and for individuals without antibody response. Increased screening in key populations may also play a role. Few provinces, including British Columbia and Ontario, stopped reporting non-infectious cases in the late 1990s, which has affected the proportion of non-infectious over time holds even after excluding British Columbia and Ontario from the analysis. Reporting patterns by PT are presented in <u>Appendix B</u>.



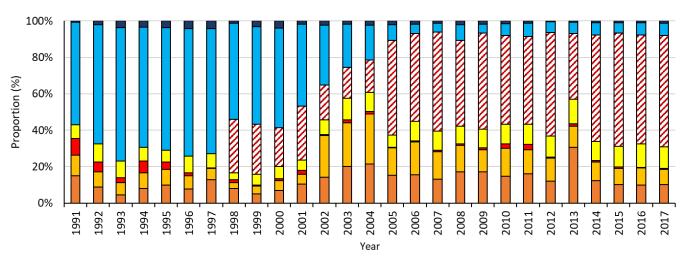


Note: Early symptomatic includes both primary and secondary cases. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

Slight variations in staging, according to sex, have been observed in Canada. Between 1991 and 2017, the proportion of infectious syphilis cases was higher amongst males (<u>Figure 7</u>) than females (

<u>Figure 8</u>) (case proportions by syphilis stage overall and sex are presented in <u>Appendix E</u>). Potential reasons for the difference in proportion of infectious syphilis by sex are presented in <u>Section 2.2</u>.

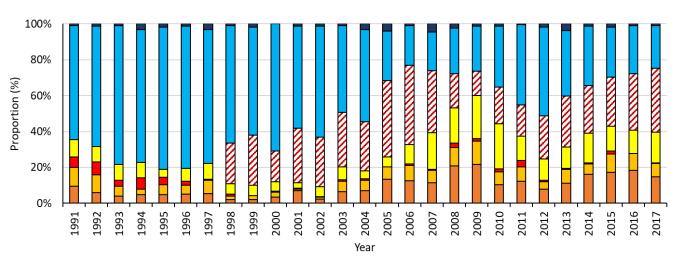
Figure 7. Proportion of reported cases of syphilis by stage of infection among males in Canada, 1991-2017



🗖 Primary 🗖 Secondary 🗖 Early symptomatic 🗖 Early latent 🖾 Infectious syphilis - unspecifed stage 🗖 Late latent 🔳 Tertiary

Note: Early symptomatic includes both primary and secondary cases. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

Figure 8. Proportion of reported cases of syphilis by stage of infection among females in Canada, 1991-2017



🗖 Primary 🗖 Secondary 🗖 Early symptomatic 🗖 Early latent 🖉 Infectious syphilis - unspecifed stage 🗖 Late latent 🗖 Tertiary

Note: Early symptomatic includes both primary and secondary cases. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

3.1.2 Infectious Syphilis Trends in Canada by Sex

<u>Figure 9</u> presents historical infectious syphilis trends by sex since 1991, the year when CNDSS began collecting information on sex at diagnosis. Between 1991 and the early 2000s, infectious syphilis rates were similar among males and females, with males experiencing slightly higher rates. The male-to-female rate ratio in the 1990s ranged from 1:1 to 2:1 (Figure 9). However, starting in 2002, rates among males began to increase more rapidly compared to female rates. By 2012, rates of syphilis were 18 times higher in males compared to females (male-to-female rate ratio of 18:1). This rapid increase was driven mainly by gbMSM cases, as outlined in <u>Section 4</u> of this report. According to preliminary data, in 2018, there was a major increase in both male and female rates (Figure 9). In that year, the number of female cases nearly tripled from what was observed in 2017, with outbreaks reported in heterosexual populations in several jurisdictions. This increase in the number of female cases resulted in a decrease in the male-to-female rate ratio from 8:1 in 2017 to 4:1 in 2018.

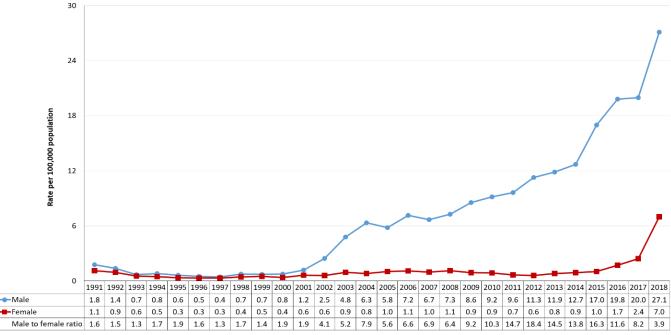


Figure 9. Rates of reported cases of infectious syphilis by sex in Canada, 1991-2018

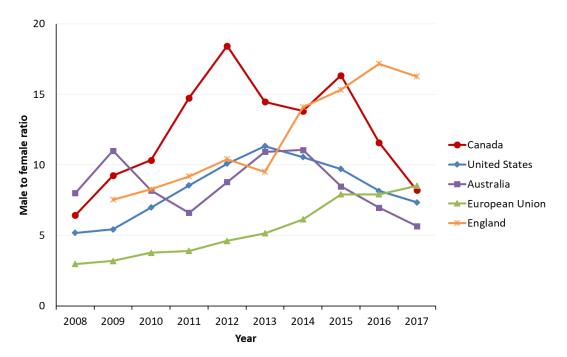
ear

Note: Age and Sex data for infectious syphilis began to be reported by PTs in 1991. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

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Between 2008 and 2017, the male-to-female rate ratio was generally higher in Canada than in other OECD countries (Figure 10). The subsequent decrease in male-to-female rate ratio observed in Canada has also been reported in other OECD countries (Figure 10)^{6,85-87}.





Note: Canada's definition of infectious syphilis includes confirmed cases of primary, secondary and early latent syphilis. Please note that some of the countries presented have slightly different definitions. The US includes confirmed primary and secondary stages only in its definition of infectious syphilis. In addition to confirmed primary, secondary and early latent cases, Australia include probable cases of infectious cases (approximately 9% were reported as such). The EU includes all cases of syphilis regardless of stage, although of the countries that provided staging information, 95% of cases were reported as either primary, secondary or early latent.

In 2017, Canada's ratio (8.2) was similar to those observed in the US (7.3) and the EU (8.5), and slightly higher than that of Australia (5.7) (Figure 10). Of countries with available data, England reported the highest male-to-female rate ratio in 2017 $(15.7)^{6,85-87}$.

https://diseases.canada.ca/notifiable/charts-list, 2019.

England: Public Health England, Official Statistics, Sexually transmitted infections (STIs): annual data tables. Table 1 (b): Rates of new STI diagnoses in England by gender, 2008 – 2017, Rates per 100 000, Syphilis: primary, secondary & early latent – total. https://www.gov.uk/government/statistics/sexually-transmitted-infections-stis-annual-data-tables

^b Sources: <u>Australia</u>: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. 2018. <u>https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance</u>

<u>European Union:</u> European Centre for Disease Prevention and Control (ECDC). Syphilis - Annual epidemiological report for 2017. 2019 12 July 2019. <u>https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2017</u>

<u>United States</u>: Centers for Disease Control and Prevention (CDC). Table 27. Primary and Secondary Syphilis — Reported Cases and Rates of Reported Cases by State/Area and Region in Alphabetical Order, United States and Outlying Areas, 2013–2017. 2018; Available at: <u>https://www.cdc.gov/std/stats17/tables/27.htm</u>. Accessed September 10, 2019.

Canada: Government of Canada. Canadian Notifiable Disease Surveillance System. 2018; Available at:

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<u>Figure 11</u> presents a comparison of rates of infectious syphilis by sex in selected OECD settings. Rates for both males and females tended to vary among countries. Canada reported higher rates among males compared to the US and the EU, although this should be interpreted with caution, as slightly different case definitions for infectious syphilis are used by each country. In contrast, female rates were higher in Canada than in all countries except Australia (<u>Figure 11</u>)^{6,85-87}.

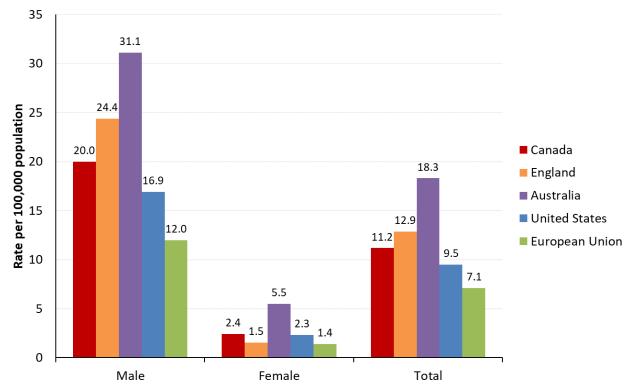


Figure 11. Rates of reported cases of infectious syphilis by sex in OECD countries^o, 2017

Note: Canada's definition of infectious syphilis includes confirmed cases of primary, secondary and early latent syphilis. Please note that some of the countries presented have slightly different definitions. The US includes confirmed primary and secondary stages only in its definition of infectious syphilis. In addition to confirmed primary, secondary and early latent cases, Australia include probable cases of infectious cases (approximately 9% were reported as such). The EU includes all cases of syphilis regardless of stage, although of the countries that provided staging information, 95% of cases were reported as either primary, secondary or early latent.

<u>United States</u>: Centers for Disease Control and Prevention (CDC). Table 27. Primary and Secondary Syphilis — Reported Cases and Rates of Reported Cases by State/Area and Region in Alphabetical Order, United States and Outlying Areas, 2013–2017. 2018; Available at: <u>https://www.cdc.gov/std/stats17/tables/27.htm</u>. Accessed September 10, 2019.

https://diseases.canada.ca/notifiable/charts-list, 2019.

England: Public Health England, Official Statistics, Sexually transmitted infections (STIs): annual data tables. Table 1 (b): Rates of new STI diagnoses in England by gender, 2008 – 2017, Rates per 100 000, Syphilis: primary, secondary & early latent – total https://www.gov.uk/government/statistics/sexually-transmitted-infections-stis-annual-data-tables

^C Sources: <u>Australia</u>: Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. 2018. <u>https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance</u>

European Union: European Centre for Disease Prevention and Control (ECDC). Syphilis - Annual epidemiological report for 2017. 12 July 2019. https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2017

Canada: Government of Canada. Canadian Notifiable Disease Surveillance System. 2018; Available at:

3.1.3 Infectious Syphilis Trends in Canada by Age Group

Infectious syphilis rates tend to vary by age. Since the 1990s, all age groups, with the exception of those under 15 years of age, have experienced increases in infectious syphilis rates (<u>Figure 12</u>). The largest increase has been observed in the 25 to 29 year age group, closely followed by the 30 to 39 year age group. Rates were also high in the 20 to 24 and 40 to 59 year age groups. The situation was similar in other OECD countries, with the highest rates reported among the 25 to 29 age group in Australia, England and the US (<u>Appendix D</u>).

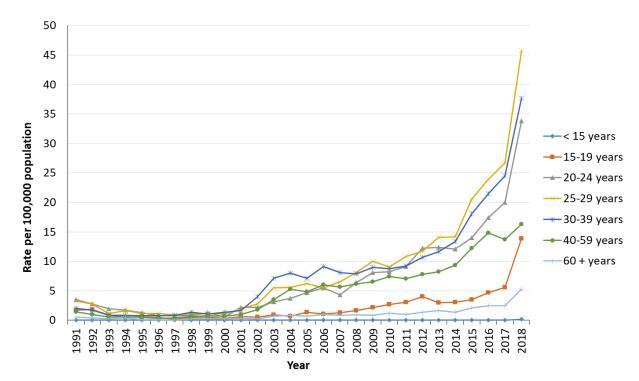


Figure 12. Rates of reported cases of infectious syphilis by age group in Canada, 1991-2018

Note: Age and sex data for infectious syphilis reporting by PTs began in 1991. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

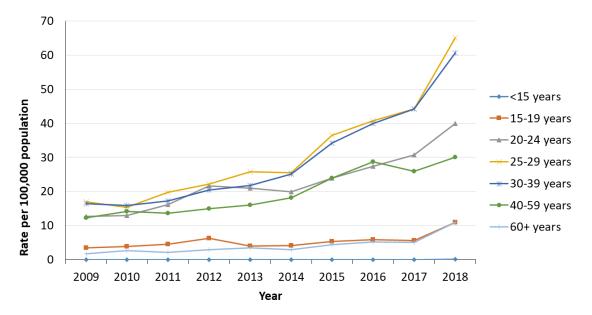
Description of cases under 15 years of age

The number of cases of syphilis has been low in those younger than 15 years of age. Since 1991, only 125 cases of syphilis were reported among those aged 15 years and younger. These cases were distributed almost equally among males and females. Only 14.4% (18 cases) of these 125 cases were infectious; 45 cases (36%) were congenital cases; four cases were non-infectious (3%); and 58 (46%) were of unspecified status. The large proportion of unspecified cases highlights the difficulty of obtaining staging information on syphilis cases that may be a result of congenital acquisition, sexual abuse or early sexual activity.

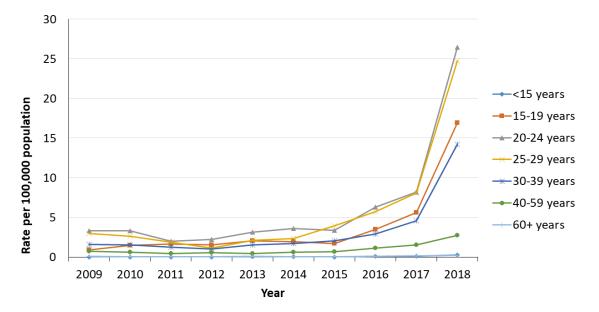
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There was a large increase in rates for all age groups in 2018, compared to previous years (Figure 12). When examining infectious rates among males between 2009 and 2018, the largest increases were observed among those in the 60+, the 25 to 29, and the 30 to 39 year age groups, with increases of 551%, 284% and 270%, respectively (Figure 13). In comparison, the largest increases in infectious rates among females were observed in the 15 to 19, the 30 to 39 and the 25 to 29 year age groups, with an increase of 1768%, 793% and 740%, respectively (Figure 14). In 2018, infectious syphilis rates for males were highest among the 25 to 29 and 30 to 39 year age group (65.1 and 60.6 per 100,000 respectively) while among females the rates were highest among the 20 to 24 and 25 to 29 year age groups (with rates of 26.4 and 24.7 per 100,000, respectively). Detailed rates of infectious syphilis by age group and sex from 2009 to 2018 are presented in Appendix F.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System Preliminary 2018 data received directly from provinces and territories.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

On average, male infectious syphilis cases tend to be older than female cases. In 2018, the proportion of infectious syphilis cases observed among females tended to decrease as age increased (Figure 15). Over half of the infectious syphilis cases (59%) in the 15-19 year age group were female, whereas only 2% of cases among those 60 years and above were female (Figure 15).

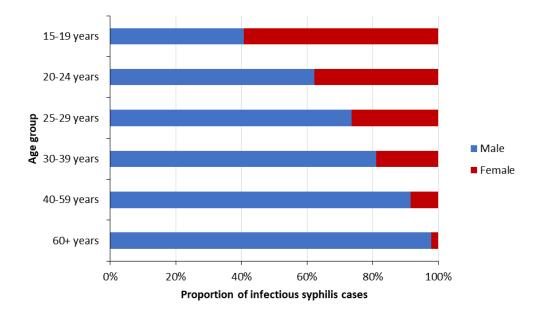


Figure 15. Proportion of reported cases of infectious syphilis by age group and sex in Canada, 2018

Source: Preliminary 2018 data received directly from provinces and territories.

KEY MESSAGES

- From the 1940s onwards, rates of infectious syphilis remained high in Canada. Then, after decades of high syphilis rates in Canada, rates of infectious syphilis began to decrease in the 1980s, and they remained low for most of the 1990s before beginning to climb again in the early 2000s.
- Similar increases were observed in other countries from the OECD.
- Syphilis mostly affects men, especially gbMSM. However, there has been a sharp increase in the number of female cases observed in recent years.
- Since the 1990s, all age groups with the exception of those under 15 years of age have experienced increases in infectious syphilis rates. The largest increases have been observed in the 25 to 29 year age group, closely followed by the 30 to 39 year age group.
- On average, male infectious syphilis cases tend to be older than their female counterparts.

3.2 Current Epidemiological Situation across Provinces and Territories

In <u>Section 3.1</u>, an overview of national syphilis data is presented. However, syphilis trends vary across the provinces and territories. In this section, rates of infectious syphilis reported to the CNDSS by provinces and territories from 2008 to 2017 are reported (detailed rates are presented in <u>Appendix G</u>). In addition, this section also features preliminary 2018 data sent to PHAC directly by the PTs and more recent numbers reported in provincial and territorial surveillance reports and media releases.

3.2.1 Overview of Provincial and Territorial Rates

<u>Figure 16</u> shows the most recent rates for PTs in CNDSS (2017), while <u>Figure 17</u> presents preliminary data reported by the PTs in 2018. From 2017 to 2018, all provinces and territories reported increases in rates, with the exception of Newfoundland and Labrador and Prince Edward Island.

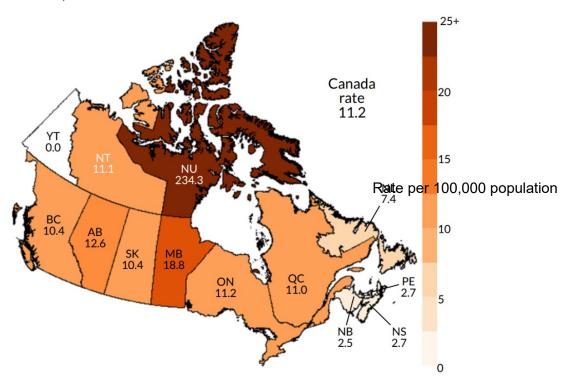


Figure 16. Rates of reported cases of infectious syphilis by province and territory in Canada, 2017

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

In 2017 and 2018, the highest rates of infectious syphilis were observed in Nunavut, followed by Manitoba and Alberta. The younger age structure of Nunavut might explain the higher infectious syphilis rates, as rates are usually higher in young adults. In order to test this hypothesis, a standardization by age was performed to assess the effect of the population age distribution on infectious syphilis rates. However, even after age-standardizing rates using the 2011 Canadian population as the reference population (for those 15 years of age and above), Nunavut's standardized rates remained the highest in the country (249.3 per 100,000 in 2017) (<u>Appendix F</u>). For other PTs, crude rates and age-standardized rates were largely similar.

According to preliminary 2018 data, rates of infectious syphilis in the PTs ranged from 2.6 per 100,000 population in Prince Edward Island to 260.6 per 100,000 per population in Nunavut (Figure 17). Northwest Territories rate more than doubled from 11.1 per 100,000 in 2017 to 24.7 per 100,000 in 2018. While there were no cases of infectious syphilis reported in 2017 in Yukon, its reported rate of infectious syphilis was 4.9 per 100,000 in 2018. Other provinces that have shown an increase in rates were British Columbia, Saskatchewan, Ontario and Nova Scotia. The other Atlantic provinces and Quebec remained relatively stable from 2017 to 2018.

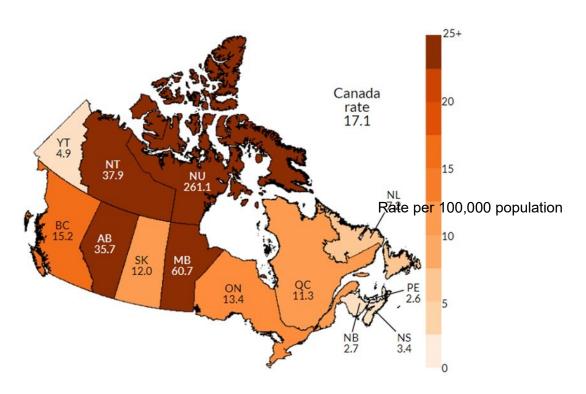
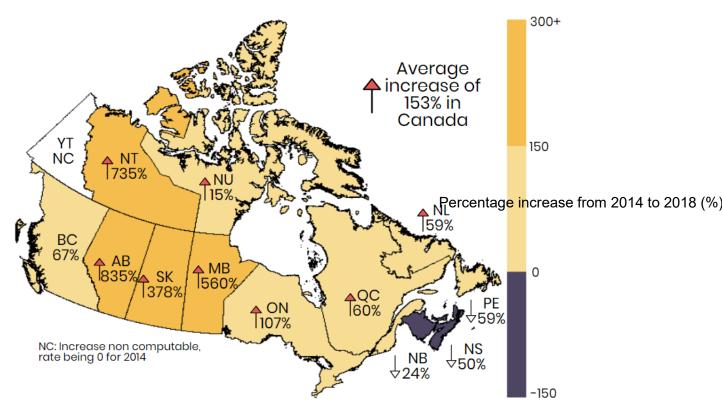


Figure 17. Reported rates of infectious syphilis by province and territory in Canada, 2018 (preliminary data)

Source: Preliminary 2018 data received directly from provinces and territories.

However, most PTs experienced increases in crude rates of infectious syphilis between 2014 and 2018 (Figure 18). The overall percentage change from 2014 to 2018 in Canada was a 153% increase in rates. PTs with the highest increases in rates were Alberta (835%), Northwest Territories (735%), Manitoba (560%), and Saskatchewan (378%). In 2018 and 2019, eight PTs (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, Northwest Territories and Nunavut) were experiencing jurisdiction-wide or regional syphilis outbreaks due to high increases in rates in the general population, new or increased number of congenital syphilis cases and shifts in populations affected. Nova Scotia declared a syphilis outbreak in January 2020⁸⁹.



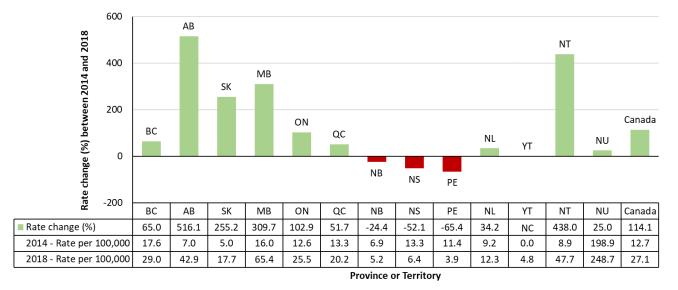


Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Provincial and territorial infectious syphilis rates for 2014 to 2018, including the associated percentage change are presented in <u>Appendix G</u>.

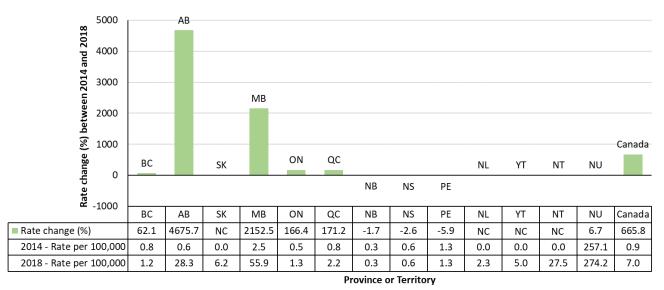
Overall, relative increases in rates from 2014 to 2018 were generally lower in males (<u>Figure 19</u>) than in females, except for Nunavut (<u>Figure 20</u>). In provinces experiencing a decrease in rates of infectious syphilis, this decrease was less pronounced in females than in males.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

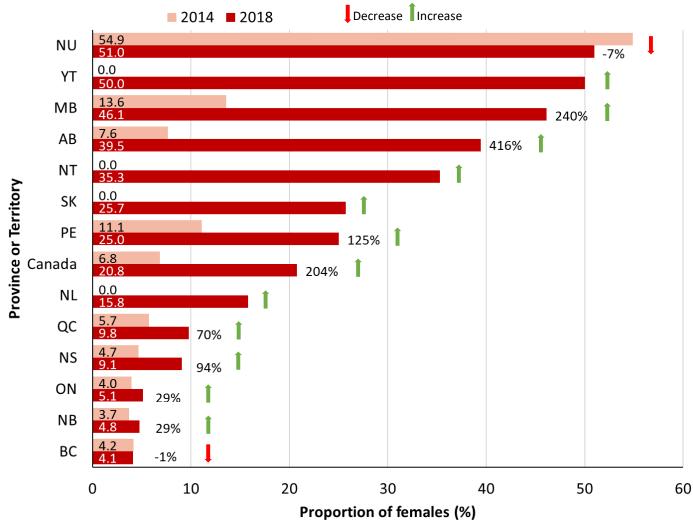




Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

From 2014 to 2018, almost every PT reported increases in the proportion of females, with an overall increase of 204% in Canada (Figure 21). The highest increase in the proportion of females was seen in Alberta and Manitoba, with a 416% and 240% increases, respectively. Both jurisdictions have recently reported heterosexual population outbreaks.





Note: Number of female cases in YT, NT, SK and NL was 0 in 2014. Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

KEY MESSAGES

- Between 2014 and 2018, most provinces and territories experienced increases in their infectious syphilis rates.
- In 2017 and 2018, the highest rates of infectious syphilis were observed in Nunavut, followed by Manitoba and Alberta.
- Other provinces that have reported increases in rates were British Columbia, Saskatchewan, Ontario and Nova Scotia. Quebec and the other Atlantic provinces remained relatively stable from 2017 to 2018.
- In 2018, large increases in the proportion of female cases were observed, especially in Alberta and Manitoba, with 415% and 239% increases, respectively. Both jurisdictions have recently reported outbreaks in the heterosexual population.

The next section presents the latest surveillance data and epidemiological information by PT.

3.2.2 Pacific Region: British Columbia

<u>Figure 22</u> presents the overall rate of infectious syphilis per 100,000 population in British Columbia, between 1979 and 2018. Following a period of high rates up until the late 1980s, rates decreased and remained low in the early 1990s, and then began climbing again in the late 1990s.

Barring a dip between 2009 and 2010, rates have increased since the late 1990s. In 2015, British Columbia experienced its highest rate of infectious syphilis since 1971 (12.7 per 100,000, 608 cases). In 2017, 510 cases of infectious syphilis were reported to CNDSS, corresponding to a rate of 10.4 per 100,000 population. In 2018, 919 cases of infectious syphilis were reported by the British Columbia Centre for Disease Control (BCCDC), corresponding to a rate of 18.4 per 100,000 population and a 33% increase from 2017⁹⁰. These are the highest rates of infectious syphilis reported in the region for the last 30 years.

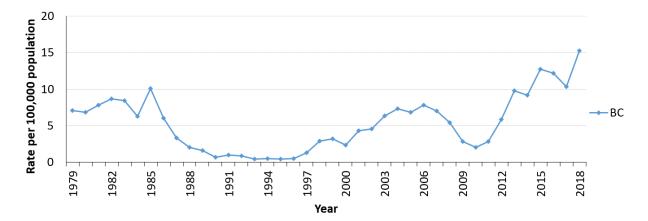


Figure 22. Rates of reported cases of infectious syphilis cases in British Columbia, Canada, 1979-2018

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

From 2009 to 2018, rates of reported infectious syphilis cases in British Columbia were substantially higher among males than females (Figure 23). Rates among males increased by 437% between 2009 and 2018 (from 5.4 to 29.0 per 100,000 population), while rates among females increased by 300% (from 0.3 to 1.2 per 100,000 population). In 2018, the rate of infectious syphilis was 24.2 times higher in males compared to females. This male-to-female ratio was much higher than the observed 2018 Canadian average of 3.9:1 (Figure 9). While there were only 16 cases of infectious syphilis reported among females in British Columbia in 2017, there were 54 cases reported among females in 2018, accounting for 6% of the province's total number of infectious syphilis cases⁹¹.

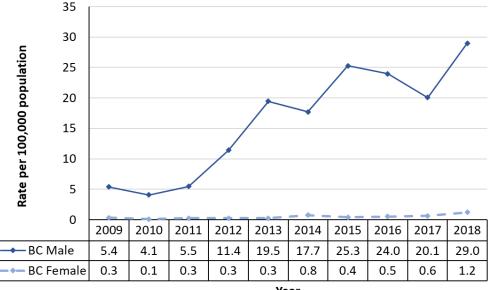


Figure 23. Rates of reported cases of infectious syphilis by sex in British Columbia, Canada, 2009-2018

Year

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Detailed sociodemographic data of the most recent cases in British Columbia are available through the BCCDC's 2016 detailed STI report, 2017 summary report and 2018 data available in the BCCDC dashboard⁹¹⁻⁹³. Insofar as the BCCDC reports both confirmed and probable cases, the province's reported case numbers and rates tend to be much higher (approximately 40% of reported cases are probable cases) than the confirmed case numbers provided to the CNDSS.

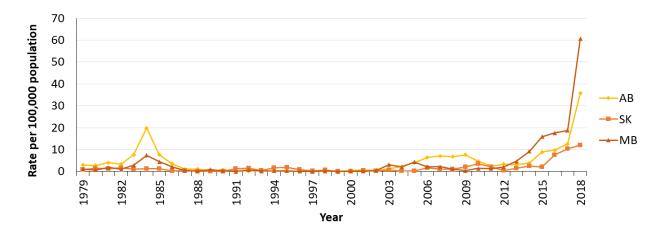
Provincial data suggest that from 2016 to 2018, the incidence of infectious syphilis was highest among the 25 to 29 year age group, followed closely by the 30 to 39 year age group⁹¹⁻⁹³. Among females, rates tended to be higher in those of reproductive age (the highest rates were found in the 20 to 24 year age group). Concurrent with data available through the CNDSS, the majority of reported cases in the province were among males (725 of 759 cases diagnosed in 2016 (95%) and 849 of 919 cases diagnosed in 2018 (92%)). In 2016, almost half of the male cases self-identified as Caucasian (47%), while the remaining cases self-identified as Asian (7%), Hispanic (5%), Indigenous (2%), South Asian (3%), Black (1%) or Arab/West Asian or other/mixed ethnicity $(1\%)^{92}$. Ethnicity was unknown for 34% of the male cases. In 2016, most of the 33 female cases self-identified as either Caucasian (15%), Asian (15%), South Asian (6%) or Indigenous (6%). Ethnicity data were not available for 58% of female cases.

In 2016, the majority of cases occurred among gbMSM (655 of 725 male cases (90%); 86% of all cases). Of the 635 gbMSM cases with known HIV status, 43% were living with HIV at the time of their syphilis diagnosis, a decrease since 2015 (52%). The majority of female cases identified as heterosexual. Overall, the proportion of heterosexual cases (male or female) without other risk factors increased slightly between 2015 (86 cases, 11% of all cases) and 2016 (95 cases, 13% of all cases)⁹².

From 2007 to 2018, most of the infectious syphilis cases and the highest overall rates of infectious syphilis in British Colombia were identified in the urban region of Vancouver (Vancouver Coastal Health Authority; 70.9 per 100,000). Rates were also high in South Vancouver Island (home to the urban centre of Victoria and Central Vancouver Island; 18.4 and 14.4 per 100,000, respectively), and Richmond (12.9 per 100,000)⁹¹.

3.2.3 Prairies Region: Alberta, Manitoba and Saskatchewan

<u>Figure 24</u> presents the overall rate of infectious syphilis per 100,000 population in Alberta, Saskatchewan and Manitoba, between 1979 and 2018. Rates were high in the early to mid-1980s in Alberta and Manitoba, before decreasing significantly. For more than a decade, from 1987 to 2002, rates for all three provinces remained low before increasing in the early 2000s and peaking after 2012, with the highest rates observed in Manitoba in 2018. According to 2017 CNDSS data, there were 251 cases reported in Manitoba, corresponding to a rate of 18.8 per 100,000 and 535 cases of infectious syphilis reported in Alberta, corresponding to a rate of 12.6 per 100,000. In comparison, Saskatchewan reported 120 cases, corresponding to a rate of 10.4 per 100,000. Preliminary 2018 data indicate an increase in rates for all three provinces (60.7 per 100,000 for Manitoba, 35.7 per 100,000 for Alberta and 12.0 per 100,000 for Saskatchewan (<u>Appendix F</u>).

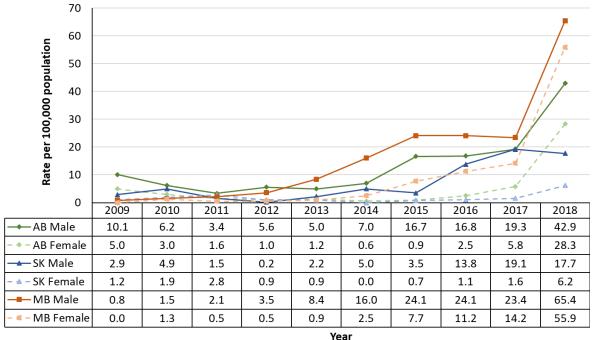




Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Between 2009 and 2012, male and female rates were generally low in all three provinces, with male rates generally higher than female rates (<u>Figure 25</u>). Starting in 2013, rates among males began to increase at a more rapid pace than female rates, which led to an increase in the male-to-female rate ratio in all three provinces. Nonetheless, female rates have also been on the rise in all three provinces. In 2018, female rates were especially high in Manitoba (55.9 per 100,000 females), much higher than the Canadian national female rate of 7.0 per 100,000 that year.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Alberta

Recent case numbers and rates are available through the province's 2018 STI and HIV report⁹⁴. In 2018, there were 1,536 cases of infectious syphilis in Alberta, corresponding to a rate of 35.7 cases per 100,000 population⁹⁴. This represents a 187.1% increase in case numbers from 2017 (n=535)⁹⁴. Similar to 2017 data (Figure 25), males were the most affected population in 2018, representing 60% of all reported cases, of which 31% were in the 20 to 29 year age group. The highest incidence was observed among the 25 to 29 year age group. Information on sexual orientation and ethnicity was not available in the 2018 report. However, in 2016, 73% of male cases reported same sex partners⁹⁵. According to preliminary data for 2019, 1,958 cases of infectious syphilis were reported in Alberta⁹⁶. As a result of this sharp rise in the number of cases, the province declared a provincial outbreak on July 16th 2019.

In 2018, the highest incidence of infectious syphilis was observed in the urban zone of Edmonton (977 cases; 65% of all provincial cases; 70 cases per 100,000). The second highest rate was observed in the northern region of the province (North health zone; 43.5 cases per 100,000), which also observed the greatest infectious syphilis rate increase of all of the province's five zones since 2017 (321.5%). The other three regions (Central, Calgary and South zones) reported rates of infectious syphilis ranging from 10.1 to 18.5 per 100,000⁹⁴. Cases reported in 2019 were also primarily located in Edmonton zone and North zone.

Saskatchewan

Available provincial surveillance products reported 120 cases of infectious syphilis in the province in 2017 (corresponding rate of 10.4 per 100,000 population), which is similar to the Canadian average rate that year⁹⁷. In 2019, Saskatchewan Ministry of Health reported 381 cases of syphilis compared to just 140 in 2018, an increase of 172%^{98,99}.

From 2017 to 2018, gbMSM were the group most affected by syphilis⁹⁷. However, the proportion of female cases is increasing in Saskatchewan. In 2017, 92% of reported cases were among males. According to preliminary data, this proportion dropped to 70% in 2018 and to 57% in 2019^{97,99}. In 2018, 95% of female cases were of reproductive age (15 to 45 years of age)⁹⁷. From 2012 to 2016, the most important risk factors for syphilis incidence in the Saskatoon Health Region (the region that saw the largest proportion of cases in 2017) included condomless sex with a same-sex partner, having a new partner within the previous three months, having met partner(s) on the Internet, and having an unknown or anonymous partner¹⁰⁰.

Most of the 2017 cases in the province (77%) were diagnosed in the urban regions of former Regina and Saskatoon regional health authorities⁹⁷. In 2019, the Saskatchewan Health Authority declared a syphilis outbreak in the regions of Battleford and Lloydminster, in the west central region of the province, following a surge of 42 cases in the first six months of the year¹⁰¹. A syphilis outbreak was also declared in First Nations on-reserve communities, with 80% of cases occurring among the 15 to 29 year age group¹⁰². In 2018, the average reported rate in First Nations communities in the province was 25.7 per 100,000, almost three times higher than the provincial average¹⁰³. According to media outlets, rates reached 83 per 100,000 in the affected First Nations communities during the outbreak in 2019¹⁰⁴. Crystal methamphetamine use seems to be a driver in the current 2019 outbreak⁹⁹.

Manitoba

While the last comprehensive surveillance report from the province describes data up to 2014, other summary reports and news publications for more recent years have been produced¹⁰⁵. In 2015, a syphilis outbreak was declared across the province¹⁰⁶. As in previous years, rates in 2015

were highest among men, and gbMSM were the most affected population⁵³. Nonetheless, rates among females have been steadily increasing. In 2017, the female rate was 14.2 per 100,000, and the male rate was 23.4 per 100,000 (Figure 25). Approximately 48% of all cases diagnosed in 2018 were female, up from 22% in 2015. This was one of the highest proportion of female cases of all PTs, giving rise to a female rate of 55.9 per 100,000, according to preliminary data (Figure 25)^{6,53}. The highest rate of reported cases was among the 20 to 24 (45.7 per 100,000) and 25 to 29 year age groups (65.3 per 100,000).

In 2018, approximately 15% of the cases were people living with HIV, and 50 to 60% of patients identified themselves as Indigenous^{107,108}. Preliminary data suggest that heterosexual transmission is prominent in the province in 2019¹⁰⁹. Risk factors within the urban region of Winnipeg include use of crystal methamphetamine¹¹⁰.

In 2012, a syphilis outbreak was declared in the urban region of Winnipeg (Winnipeg Health Regional Authority) which continued into 2019¹⁰⁵. In 2018, the infectious syphilis rate reached 87 per 100,000 in Winnipeg, nearly five times greater than it was in 2017 (18 per 100,000)¹¹⁰. As of 2019, a large proportion of cases have also been identified in the more rural northern region of the province (Northern Health Region), which is home to 26 First Nation communities^{109,111}.

3.2.4 Central Region: Ontario and Quebec

In the 1980s, high rates were observed in both Ontario and Quebec. Significant decreases in rates occurred in the 1990s (Figure 26). Rates began to gradually increase in the 2000s and have peaked in recent years. In 2018, rates for both provinces were similar to or lower than the Canadian average for that year (25.5 per 100,000 for Ontario and 20.2 per 100,000 for Quebec, while the Canadian average was 27.1 per 100,000) (Appendix G).

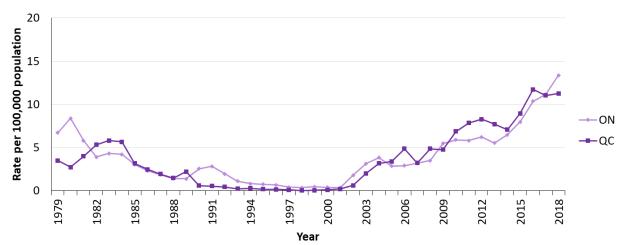
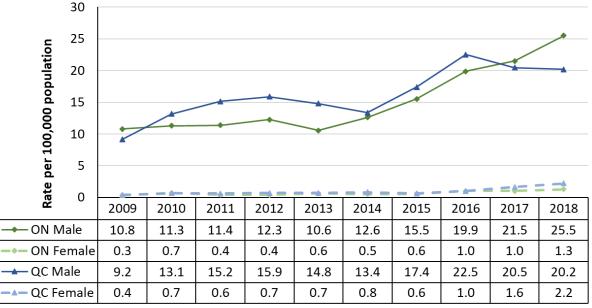


Figure 26. Rates of reported cases of infectious syphilis in Ontario and Quebec, Canada, 1979-2018

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

In both provinces, the reported rates among males are substantially higher than the corresponding rates for females (<u>Figure 27</u>). Rates among males gradually increased between 2009 and 2018, while female rates have slightly increased since 2014 in both provinces. In 2018, the rate of infectious syphilis in Ontario was 19.6 times greater in males than females, while for Quebec, it was 9.2 times greater in males than in females.





Year

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Ontario

According to CNDSS data, there were 1,571 cases of infectious syphilis in Ontario in 2017, corresponding to a rate of 11.2 per 100,000. Overall, 95% of cases reported by the province were male, and the highest rates were observed in the 25 to 39 year age groups (approximately 26 per 100,000).

In 2018, 1,800 cases of infectious syphilis were reported, corresponding to a rate of 12.5 per 100,000, a slight increase from the 2017 rate, and a large increase since 2015 (1,068 cases; 7.7 per 100,000)^{112,113}. After releasing a first notice in October 2018, the Ontario Northwestern Health Unit declared a syphilis outbreak in 2019, following the detection of 48 cases from August 1st, 2018 to July 30th, 2019^{114,115}. During this period, the rate of reported cases was 58.6 per 100,000. Of the 48 cases, 50% occurred among males (24 cases), primarily in the 25 to 29, 35 to 39 and 65 to 69 year age groups. The other 50% occurred among females (24 cases), most of which affected the 20 to 24 year age group. Risk factor information at the time of reporting was available for more than two-thirds of the cases (33 of the 48). The most common risk factors included condomless sex (85% of cases), heterosexual sex (67%), injection drug use (61%) and being under-housed/homeless (46%)¹¹⁴. Concurrent condomless sex and injection drug use were reported by a majority (72%) of the cases. More than 30% of the cases had undergone testing as a result of contact tracing¹¹⁴. Case investigations suggest that this outbreak is linked to the Winnipeg Regional Health Authority outbreak referenced above^{116,117}.

The Middlesex-London Health Unit also reported a syphilis outbreak in 2019¹¹⁸. Since 2014, the number of cases reported to the Health Unit has more than tripled to 113¹¹⁸. Previous data reported by this Health Unit suggested the rise in cases was occurring mainly among gbMSM¹¹⁸. However, more recent data show increases among heterosexuals and in those engaged in the sale or purchase of sex¹¹⁸.

The City of Peterborough also declared an outbreak in January 2020, following a surge in the number of cases in 2019 compared to 2018 (15 vs 9 cases)¹¹⁹. In Ottawa, the number of cases increased from 30 to 159 between 2013 and 2018^{120} .

Quebec

In 2017, the province of Quebec reported 915 cases to CNDSS, corresponding to a rate of 11.0 per 100,000 population, similar to the Canadian average. In 2018, 938 infectious syphilis cases were identified (11.1 cases per 100,000 population), and 1,141 cases are projected for 2019 (based on the number of cases reported during the first 222 days of the year), corresponding to a rate of 13.3 per 100,000 population¹²¹. In 2017 and 2018, the majority of cases (92% and 89%, respectively) were found in males^{121,122}. The age group reporting the highest rates shifted from those in the 30 to 34 year age group (25.5 per 100,000 in 2017), to those in the 20 to 29 year age group (26.3 per 100,000 population in 2018) ^{121,122}. GbMSM continue to be the most affected population¹²². However, the province also noted an increase of cases among women, most of which (89%) occurred in women of reproductive age (15 to 49 years of age).

The Montreal region continues to be one of the most affected regions of the province, contributing to 53% of all Quebec cases in 2018, a rate of 24.4 per 100,000 population¹²¹. However, rates were highest (116.5 per 100,000) in Nunavik, a northern Inuit region, where a syphilis outbreak has been ongoing since 2016¹²¹. In 2017, the majority of cases reported in Nunavik were in the 15 to 34 year age group, of which 59% (19/32 cases) were female¹²².

3.2.5 Atlantic Region: New Brunswick, Newfoundland and Labrador, Nova Scotia and Prince Edward Island

The overall rates of infectious syphilis per 100,000 population for the provinces of New Brunswick, Newfoundland and Labrador, Nova Scotia and Prince Edward Island from 1979 to 2018 are presented in Figure 28. Throughout the 1980s and 1990s, the rates of infectious syphilis for all four provinces varied slightly, but were generally low, especially between 1995 and 2002. In the mid-to-late 2000s, the rates began increasing. Despite these increases, rates in the region continue to be lower than the Canadian average each year.

According to the New Brunswick Communicable Disease 2017 Annual Surveillance Report, there were 20 cases of infectious syphilis in the province in 2017, corresponding to a rate of 2.6 per 100,000 population¹²³. CNDSS data for the province of Nova Scotia reported 26 cases, corresponding to a rate of 2.7 per 100,000. Four cases were reported in Prince Edward Island, for a rate of 2.7 per 100,000. Newfoundland and Labrador had both the highest number of cases (39 cases) and the highest rate (7.4 per 100,000).

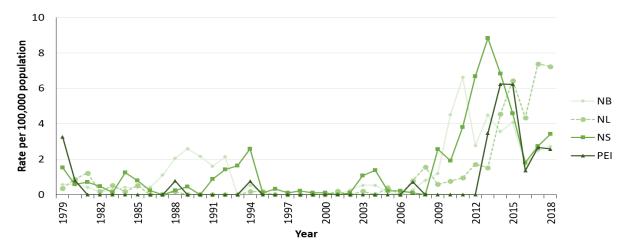
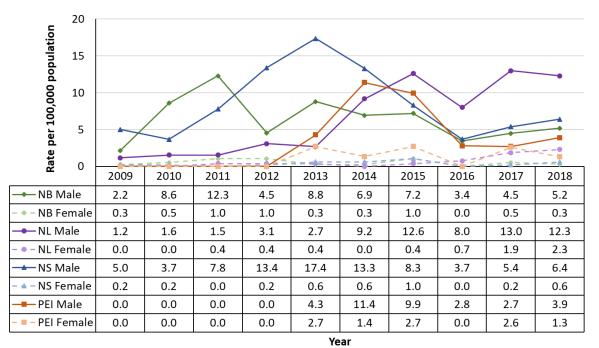


Figure 28. Rates of reported cases of infectious syphilis in New Brunswick, Newfoundland and Labrador, Nova Scotia and Prince Edward Island, Canada, 1979-2018

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

<u>Figure 29</u> presents the male and female rates of infectious syphilis per 100,000 population in New Brunswick, Newfoundland and Labrador, Nova Scotia and Prince Edward Island from 2009 to 2018. Male rates have generally been higher than female rates in all four provinces. The largest male-to-female rate ratio in the region was observed in New Brunswick in 2018, where the infectious syphilis rate was 17.3 times greater among males than females. Female rates have generally been low for all provinces through time.





Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

New Brunswick

From November 2009 to December 2012, New Brunswick experienced a syphilis outbreak, which resulted in 121 cases of infectious syphilis. The outbreak began in the Moncton region at the end of 2009 and affected all regions of the province. The cities of Moncton, Fredericton and Saint John were the most affected cities. Most cases occurred among males (92%), of which three quarters self-identified as gbMSM (75%). Rates were highest among the 15 to 24 year age group (12.4 per 100,000)¹²⁴.

In 2017 as in previous years, most cases occurred among males (18/20 cases, 4.8 per 100,000), and the highest incidence rates were observed among the 30 to 39 year age group (13.3 per 100,000). All of the male cases self-identified as gbMSM¹²³. Moreover, the province's most recent published report on STBBI risk factors (2016) reported other risk factors for infectious syphilis. For the 14 cases reported in 2016, these included condomless sex (69%), past-year substance use (50%), having casual or anonymous sexual contacts (46%), having two or three sexual partners (36%), and having had five or more sexual partners in the last 12 months (27%). Furthermore, three of the cases (21%) had concurrent STI infections (co-infections)¹²⁵.

In 2017, cases were reported in different regions of the province¹²³. The largest proportion of cases (40%) was identified in the southeastern region surrounding the urban area of Moncton (Region 1).

Newfoundland and Labrador

The province declared a provincial outbreak of infectious syphilis in October 2014. The majority of cases occurred in the urban region of St. John's and among gbMSM¹²⁶.

At the same time, an outbreak of infectious syphilis was declared in the Eastern Health region of Newfoundland and Labrador. From January 2014 to December 2016, there were 82 cases of outbreak-related syphilis, of which 77 were infectious syphilis cases. At the peak of the outbreak, the rate of infectious syphilis reached 11.3 cases per 100,000. By comparison, the Eastern Health rate of infection was 1.9 per 100,000 in pre-outbreak 2013. During this time, 92% of all syphilis cases occurred among males¹²⁷. HIV co-infection was reported in 21% of the 82 outbreak-related cases.

According to preliminary data, in Newfoundland and Labrador in 2018, the rate of infectious syphilis cases (7.2 per 100,000) represented a 59% increase from the rate reported in 2014 (4.5 per $100,000)^6$.

Nova Scotia

In 2017, there were 26 reported cases of infectious syphilis in Nova Scotia, corresponding to a rate of 2.7 per 100,000—well below the Canadian average. According to the province's 2017 Notifiable Disease Surveillance Report, most cases occurred among males (96%) (25/26 cases; 5.3 per 100,000) and overall, the highest rates were reported among the 25 to 39 year age group (13.5 per 100,000 males; 1.1 per 100,000 females)¹²⁸. The majority of these cases were from to the Central Zone of Nova Scotia (which encompasses the urban area of Halifax). Prior to 2019, the last syphilis outbreak reported in the province was declared in September 2008 in Nova Scotia's Central Zone and occurred mainly among men in Halifax. This outbreak peaked in 2013, where there were 84 cases of infectious syphilis reported in the province^{128,129}.

In 2018, Nova Scotia reported 50 cases of syphilis, two thirds of which were infectious⁸⁹. Preliminary 2019 data has indicated a 70% increase in the number of syphilis cases from 2018:

82 infectious and non-infectious cases have been reported to-date in 2019. Preliminary analysis of the 2019 syphilis cases has indicated a greater proportion of female syphilis cases reported in 2019 (20%), relative to previous years (approximately 10% female in 2018, approximately 5% female in 2017)^{89,130}.

Prince Edward Island

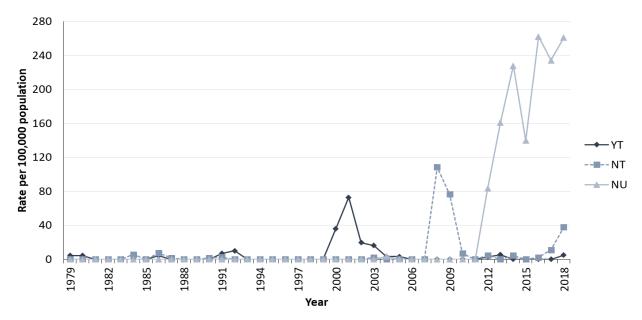
Overall, the rate of infectious syphilis has remained stable and low in Prince Edward Island over the last 10 years¹³¹. In 2017, four infectious syphilis cases were reported in Prince Edward Island, corresponding to a rate of 2.7 per 100,000—well below the Canadian average¹³¹. In 2017, infectious syphilis cases were evenly distributed among males and females (50% respectively)⁶. Prior to 2014, most individuals diagnosed with syphilis had acquired it in other provinces or countries; however, local transmission is now more common¹³². In 2018, the rate of infectious syphilis in Prince Edward Island was 2.6 per 100,000 according to preliminary data.

3.2.6 Northern Region: Yukon, Northwest Territories and Nunavut

<u>Figure 30</u> presents the rate of reported infectious syphilis cases per 100,000 population in the Yukon and the Northwest Territories from 1979 to 2018, and in Nunavut, from the time of its creation in 1999 to 2018. Despite some spikes in cases in the 2000s, rates in both the Northwest Territories and Yukon have remained low and stable. Conversely, after low rates for multiple years, Nunavut has seen increases in cases since 2011.

According to CNDSS data, there were no cases of infectious syphilis reported in Yukon in 2017. In comparison, five cases were reported in Northwest Territories, corresponding to a rate of 11.1 per 100,000 population, and 88 cases were reported in Nunavut, a rate of 234.3 per 100,000. From 2017 to 2018, substantial increases in rates have been reported in all three territories (Figure 17 and Figure 18).

Figure 30. Rates of reported cases of infectious syphilis in Yukon, Northwest Territories and Nunavut, Canada, 1979-2018

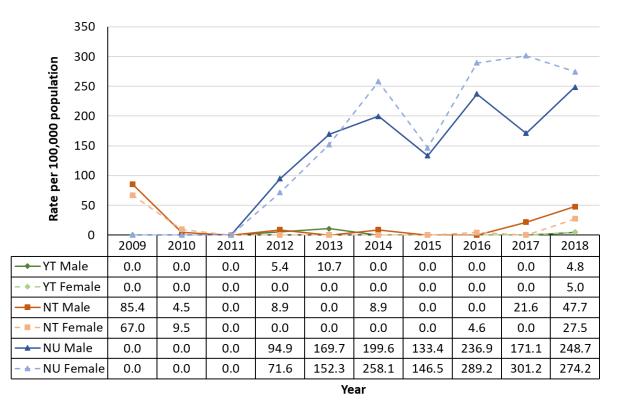


Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

56 Syphilis in Canada, 2009-2018

Between 2009 and 2018, Yukon reported very few cases of infectious syphilis in both males and females (Figure 31). In the Northwest Territories, both male and female rates were high in 2008 and 2009, before decreasing in subsequent years. Between 2016 and 2018, rates in males began to increase again. In Nunavut, following the territory's outbreak in 2012, a considerable increase in both male and female rates of syphilis was observed, with female rates exceeding male rates since 2014 (Figure 31).

Figure 31. Rates of reported cases of infectious syphilis by sex in Yukon, Northwest Territories and Nunavut, Canada, 2009-2018



Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Yukon

In Yukon, rates increased in 2000, decreased in 2004, and have remained low and stable since then. Less than five cases were reported from 2010 to 2014, and zero cases of infectious syphilis were reported in 2017 (Figure 31). There have not been any recent outbreaks in the territory¹³³. However, a few cases have been reported in 2018.

Northwest Territories

In 2008, the Northwest Territories' syphilis rates spiked due to an outbreak, which mainly affected the smaller communities in the Territory and a transient population in the urban centre of Yellowknife¹³⁴. The outbreak was resolved by 2010¹³⁴. Since then, the number of reported cases has been low, until a recent resurgence of cases in late 2017, which carried over into 2018^{135,136}. In 2017, five cases were reported, corresponding to a rate of 11.1 per 100,000 population. It should be noted that due to these small numbers, an increase by a few cases is likely to have a large impact on computed rates. An outbreak of syphilis was declared in the Northwest Territories on August 22nd 2019, following a surge of 28 cases of syphilis, including one case of congenital

syphilis, the first since 2009. Approximately 70% of these cases were reported in Yellowknife^{135,137}.

Nunavut

The first infectious syphilis case reported in Nunavut since the territory's creation in 1999 occurred in 2004 (one case). Rates were low until 2012⁶. In 2012, Nunavut's syphilis rates increased significantly following an outbreak that year, and have remained high since then. In the 2012 outbreak, a slightly higher proportion of cases occurred among females (55% of cases) compared to males (45%)¹³⁸. In the 15 to 19 year age group, most cases were reported among females¹³⁹. Risk factors observed during the 2012 outbreak included not using a condom (96% of cases), reported alcohol or substance use (74% of cases; frequency or intensity of consumption was not specified); and having had another STI in the previous year (71% of cases)¹³⁹.

The 2012 outbreak began in the Qikiqtaaluk region (northern-most Baffin region) and was later reported in other regions, affecting five communities. Between 2007 and 2014, 98% of all syphilis cases reported in the territory were from the Qikiqtaaluk region.

Nunavut's outbreak is ongoing. In 2015, there were 51 infectious syphilis cases reported (139.8 per 100,000), 97 in 2016 (262.3 per 100,000) and 88 in 2017 (234.3 per 100,000). Since 2014, a larger number of cases were reported among females than males⁵⁴. In 2017, 63% of cases reported by the territory to CNDSS were female, while preliminary 2018 data showed the proportion of female cases to be 51%. In 2017, the highest rate was observed among those aged 15 to 19 years (788.4 per 100,000), followed by those 20 to 24 year of age (680.5 per 100,000) and 25 to 29 years of age (447.8 per 100,000).

4. Determinants and risk factors of syphilis in Canada

4.1 Proposed Conceptual Framework of the Determinants of Infectious Syphilis

It has been well established that many factors can affect or influence health. Determinants of health include personal, social, economic and environmental factors, such as gender, culture, race, education, employment, physical environments, healthy behaviors and access to health services^{140,141}. Several researchers have proposed conceptual frameworks of the determinants of either health behaviours that may place individuals or populations at higher risk of sexually transmissible infections or of the determinants of infectious disease outcomes¹⁴²⁻¹⁴⁵. Figure 32 below is an adaptation of existing frameworks. It summarizes categories of underlying and proximate determinants of syphilis transmission dynamics, infection and disease outcomes.

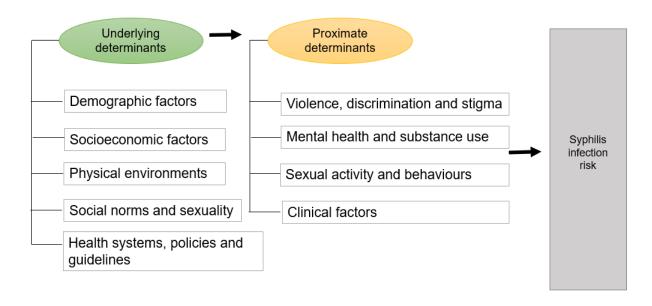


Figure 32. Conceptual framework of syphilis infection in Canada

Adapted from frameworks proposed by Boerma and Weir (2005)¹⁴⁴, Aral (2002)¹⁴³, Galea et al. (2003)¹⁴², Government of Canada (2019)¹⁴¹, Public Health Agency of Canada (2016)¹⁴⁶, and the British Columbia Centre for Disease Control (2016)¹⁴⁵, and based on existing published Canadian literature.

Within this framework, factors considered to be "underlying" are those that tend to operate beyond the individual level. They shape the contexts in which individuals live and behave¹⁴⁴. These underlying determinants influence individuals' exposure to or adoption of more proximate determinants of syphilis infection and transmission. Thus, proximate determinants tend to be experienced at an individual level, with ties to either behaviour or biology¹⁴⁴. This section summarizes the underlying and proximate determinants of syphilis infection documented in the Canadian literature mainly, as well as in the international literature. Gaps in knowledge and research are highlighted.

4.2 Underlying Determinants of Syphilis in Canada

4.2.1 Demographic Factors

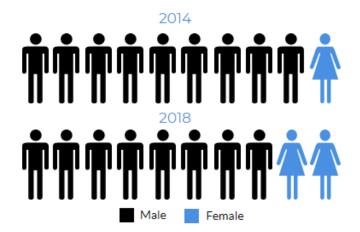
Sex and gender identity

Federal surveillance and studies conducted across Canada on infectious syphilis trends from 2003 to 2017 note significantly higher rates among males compared to females, with males representing the vast majority of cases (over 90%)^{55,58,147-149}. In

Canada, similar to the US, most male syphilis cases are among gbMSM¹⁵⁰.

As indicated in <u>Section 3</u>, in the 1990s and 2000s, infectious syphilis rates increased at a greater pace for males than for females^{55,149}. However, in recent years, rates of infectious syphilis have risen considerably in females, thereby reducing the male-to-female rate ratio. This is especially true for the provinces of Alberta, Saskatchewan and Manitoba, as well as for certain northern communities in other parts of Canada^{53,94,97,151}. As epidemics shift into heterosexual populations, rates appear to be increasing in both heterosexual females and males in certain jurisdictions¹⁵¹.

Gender roles, ideologies and norms are key social determinants of STI vulnerability.



The proportion of reported cases of infectious syphilis among females in Canada is on the rise

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System

Biological sex is a particularly relevant determinant of syphilis staging, as primary lesions may be less visible for females than males, thus making it more difficult for females to know to seek early testing and diagnosis^{2,58}. However, though sex differences in syphilis risk have been observed in Canada, literature suggests that these are likely mostly attributable to gender-based differences in risk behaviours rather than biological risk.

Gender roles, ideologies and norms are key social determinants of STI vulnerability¹⁵²⁻¹⁵⁴.For instance, for women, especially in young adulthood, internalization of 'femininity ideologies', associated with passivity, compliance, and altruism, can be associated with difficulties in

communicating needs or boundaries in sexual relationships¹⁵⁵. This can interfere with sexual agency and protective sexual practices and compromise health¹⁵⁵.

Among heterosexual women, research has documented that STI risk can be determined by their partner's behaviours (number of other partners their partner has, etc.) rather than their own behaviours¹⁵⁶. In a study conducted in the province of Quebec between 2010 and 2011 (n=51), 51% of female cases reported a recent sexual contact with a partner who was at higher risk of syphilis, either because of their history of substance use, being gbMSM, engagement in sex work, having multiple partners, or having sexual relations outside of Canada¹²². Sexual violence can also put women at significantly higher risk of STIs¹⁵⁷.

Additionally, women's experiences of STI screening and care can also differ from men's experiences. Specifically, research conducted in the US in 1999, has documented instances where physicians are less likely to recommend syphilis screening for women when an STI is suspected compared to men¹⁵⁸. More recent Canadian research on STI screening inequities is currently not available.

For men, societal pressures to perform according to masculine norms and ideals can be a considerable source of stress¹⁵⁹. For example, masculine gender norms can include peer pressure to have multiple sexual partners¹⁶⁰. In younger members of the gbMSM population, condomless sexual intercourse has been reported as a normative component in certain settings, as it is associated with a desire for greater intimacy and spontaneity¹⁶¹. Condomless sex is, however, a frequent occurrence among heterosexual partners as well. A pan-Canadian survey of adults aged 16 years and older (n=2,452), the majority of which self-identified as heterosexual, noted that 63% of respondents reported inconsistent condom use¹⁶². Among the 15% of respondents who reported never using condoms, the four most frequent reasons given were trust in their partner (25%), a dislike for condom use (17%), a lack of perceived pregnancy risk when not using condoms (11%), and finding that condoms were not easy to obtain or were too costly (9%)¹⁶².

All told, factors pertaining to sexuality, gender, partnership status, and related power dynamics can influence risk-taking behaviours⁷⁶. Though not commonly documented in Canadian literature, these factors likely contribute to observed sex differences in syphilis-related outcomes.

Age

Recent Canadian research and surveillance data suggest that younger age is associated with a higher risk of syphilis incidence. Overall, CNDSS data suggest that syphilis incidence has been increasing for most age groups. According to preliminary data provided by the provinces and territories, in 2018, the largest proportion of male cases was observed in the 25 to 39 year age group (48%), while the largest proportion of cases in women—over half (61%)—was observed in the 15 to 29 year age group. These proportions vary slightly across provinces and territories, and across sub-populations^{58,122,163}.

It should also be noted that among cases aged 15 years and younger, syphilis infection could occur due to vertical transmission from mother to child. However, syphilis acquired post-natally can also indicate sexual abuse, which has implications for reporting requirements and follow-up recommendations¹⁶⁴. In addition, early onset of sexual behaviors (before the age of 15) has been associated with a higher risk of STI. However, high levels of support (from family, school and community) are associated with delayed first intercourse¹⁶⁵. <u>Section 3.1.3</u> summarizes infectious syphilis trends in Canada by age group¹⁶⁶.

Ethnicity and cultural background

Published Canadian studies suggest that certain ethnocultural groups may be more vulnerable to syphilis than others. Much of the research exploring the association between ethnocultural identity and syphilis infection has been focused specifically on male populations. In such instances, most cases were reported among Caucasian men^{57,148,167,168}.

Several studies observed no differences in syphilis incidence risk across racial or ethnic groups. This was the case in two large studies of gbMSM in Canada^{163,169}. Others indicate that although racial and ethnic minorities represent smaller proportions of cases overall, syphilis incidence has at times been observed to be proportionally higher among these populations than in Caucasians. However, findings vary by geographic location, sex, and subgroup populations. For instance, Quebec reports disproportionately higher rates of infectious syphilis in its northern region of Nunavik, in which 83% of the population are Inuit, compared to other regions^{122,170}. In another study looking at infectious syphilis among 362 females in the Winnipeg Health Region from 2003 to 2015, 67% of reported cases self-identified as Indigenous, a number of cases disproportionate to the size of the Indigenous population in the city (12% of the population)^{58,170}. These findings echo those from previous outbreaks in the late 1980s and early 2000s in Alberta, in which at least half of female cases identified as First Nations, Métis or Inuit^{171,172}. Inuit were also overrepresented in an outbreak in Manitoba in the late 1980s¹⁷³.

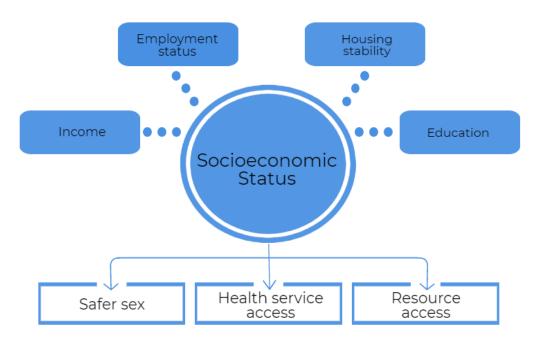
Canadian literature has documented that Indigenous Peoples often face syndemic conditions pertaining stigma and discrimination, violence, mistrust of health care systems, and higher rates of concurrent health issues and problematic substance use, all of which are tied to legacies of colonization and structural disenfranchisement¹⁷⁴. Additionally, lack of information and awareness on sexual health, taboos related to sex, and intergenerational unresolved trauma that is linked with violence, alcohol and substance use, place Indigenous communities at higher risk for experiencing STBBI. These factors indicate a need to consider a syndemic-informed approach designed and led by Indigenous Peoples, to mitigate syphilis risk in First Nations, Inuit and Métis communities^{174,175}.

Immigration

Syphilis infections can be acquired abroad through exposure in regions of high incidence. A Canadian study published in 1998 (n=890) determined that approximately 20% of total syphilis cases diagnosed between 1990 and 1994 were identified during immigration screening. Syphilis screening is a component of Canada's immigration medical assessment¹⁷⁶. From 2000 and 2004, a period where Canada received just over two million immigration applications, the average rate of syphilis (infectious and non-infectious) was 110 cases per 100,000 applicants to Canada¹². Some of the latter cases were identified (and treated) prior to arrival. Among refugees, whose screening was only upon arrival in Canada, the average rate was 286 cases per 100,000 applicants¹². However, recent studies of syphilis rates among immigrants are limited. One study found that in a sample of 442 gbMSM living with HIV in Toronto between 2010 and 2012, those born in Canada or the US had lower odds of syphilis infection (adjusted odds ratio (aOR)=0.41, 95% confidence interval (CI): 0.20, 0.84) than those born in other countries⁷³. Due to the limited number of published studies or reports on the topic, it remains unclear as to what proportion of cases recently diagnosed in Canada may be attributable to infections acquired abroad, or to a heightened risk of infection experienced by immigrants once they arrived in the country.

4.2.2 Socioeconomic Factors

Socioeconomic status is considered to be one of the most important social determinants of sexual health-related outcomes¹⁷⁷. Income, employment status, housing stability, and education shape access to resources needed for health-promoting behaviours, such as healthy sexual practices, as well as access to and use of health care services¹⁷⁷.



Socioeconomic factors influence STI risk factors

Currently missing from the Canadian literature is an understanding of the potential differences in socioeconomic determinants of syphilis incidence across genders. Additional research in this area will be valuable, as these factors may influence the effectiveness of surveillance and prevention activities.

Income

An ecological study conducted in British Columbia between 2005 and 2016 observed a correlation between the proportion of low-income households in an area and increased rates of infectious syphilis among men in that area¹⁷⁸. These results aligned with findings from a large ecological study conducted in the US (n=4,472)¹⁷⁹. However, few studies in Canada have explored the association at an individual level, and results from those have reported mixed results. For example, one pan-Canadian study conducted among 7,872 gbMSM, and another which focused specifically on 2,280 gbMSM living with HIV in Ontario, found no association between income and syphilis diagnosis^{163,167}. In contrast, a Toronto-based study of 442 HIV-negative gbMSM found that individuals with a household income less than \$20,000 were more likely to report a syphilis infection than those earning higher incomes (aOR=6.41, 95% CI: 1.84-22.40)⁷³.

Education

Mixed results have been reported for the association between educational attainment and syphilis incidence in Canada. The pan-Canadian gbMSM study mentioned above did not find an association between level of education and having a recent syphilis diagnosis (n=7,872)¹⁶³. On the other hand, a study of gbMSM living with HIV in Ontario, found a positive association between

individuals with university education level and having a first diagnosis of syphilis compared to those who had completed high school education or less¹⁶⁷.

Housing stability

Several jurisdictions across Canada have noted that housing instability and homelessness may be contributing to current syphilis outbreaks^{114,180}. A study comparing reported syphilis cases among heterosexuals in Winnipeg, Manitoba, in 2017-2018, to those diagnosed in 2011-2012, noted that the prevalence of cases reporting no fixed address was higher in more recent years than in the past (15% in 2017-2018 vs. 2% in 2011-2012)¹⁵¹. These results aligned with findings from the US, wherein social vulnerability, due to homelessness or precarious housing, has been associated with higher risk of maternal syphilis¹⁸¹.

4.2.3 Physical Environments

<u>Section 3</u> of the report covers the case and rate distribution of infectious syphilis per province and territory in Canada. As was noted, considerable variability in rates have been observed across Canada, with the territories and Prairie Provinces most affected. The lowest rates were observed in the Atlantic Provinces. Beyond provincial and territorial distribution of syphilis infection, reports have also explored geographic heterogeneity in case distribution within jurisdictions. Though the highest levels of incidence have largely been observed in urban settings across the country, some rural areas have seen high rates as well. For example, in their reporting of infectious syphilis cases across regions in British Columbia, in 2018, the BCCDC described how rates varied from 2 cases per 100,000 population in the more rural interior and northern regions of the province to 70.9 per 100,000 in Vancouver⁹¹. In Alberta, rates vary from 10.1 per 100,000 population in the southern health region of the province, up to 70 per 100,000 in the region of Edmonton¹⁸². Rates were also high in the rural, northern part of Alberta (43.5 per 100,000 population)¹⁸². In 2017 in Quebec, although cases were observed in all regions of the province, the highest rates were observed in the northern region of Nunavik (236.3 per 100,000)¹²².



Typically identified in urban centres, syphilis is on the rise in certain rural communities

Detailed analyses of the association between rural or urban residence and syphilis risk are currently lacking in Canada. One cross-sectional pan-Canadian study of gbMSM (n=7,872) noted no association between area of residence (urban vs. suburban and rural) and odds of recent syphilis diagnosis after adjustment for other sociodemographic factors¹⁶³. No recent studies have explored potential differences in risk associated with area of residence in women. Recent studies are also lacking on the role of mobility within or across provinces. In the early 2000s, a study of 102 reported syphilis cases in Ottawa noted that movement between major cities in Quebec and Ontario were common among the gbMSM population, which likely contributed to parallel rises of cases in both provinces¹⁸³. Early evidence suggests that interprovincial mobility may also be contributing to transmission dynamics in northern Manitoba and Ontario in 2018 and 2019¹⁸⁴. Lastly, to a smaller extent, population mobility between provinces, as well as between cities and

more rural areas, and between Indigenous communities and off-reserve communities, also present an additional challenge for syphilis outbreak control in Canada^{116,185}

Incarceration

In Canada, there is a paucity of studies assessing the association between an individual's experience of incarceration, or their partner's experience of incarceration, and syphilis risk. In a study conducted in the US found that among congenital syphilis cases, mothers with personal experiences of incarceration or having a partner who experienced incarceration may have places them at higher risk of syphilis¹⁸¹. Some jurisdictions across Canada have noted a potential correlation between the incarceration of index patients or their partners and increased syphilis risk¹⁸⁵. A study comparing heterosexual syphilis cases identified in Winnipeg, Manitoba, in 2017-2018, to those diagnosed in 2011-2012, found that the prevalence of cases reporting a history of incarceration was higher in more recent years than in the past (36% in 2017-2018 vs. 14% in 2011-2012)¹⁵¹.

4.2.4 Social Norms and Sexuality

With the advent of hormonal contraception in the 1960s during the sexual revolution, changes in sexual behaviors and shifts in population-level sexual culture and norms worldwide are believed to have influenced STI risk¹⁸⁶. Although findings on the association between oral hormonal contraception use and reported number of partners and condom use are mixed, studies have noted that women who have a regular partner are more likely to use hormonal contraception without barrier methods because of the low risk of unintended pregnancy, as well as low STI risk perception¹⁸⁷.

Among the most important secular changes observed globally since the 2000s has been the growing uptake of internet-based dating apps and websites⁸³. In the 2017 European Men-Who-Have-Sex-With-Men Internet Survey (EMIS), which surveyed 6,059 Canadian gbMSM respondents, 54% reported using a mobile phone app for partner finding, and 74% reported having met their current non-steady partner online¹⁸⁸. However, it should be noted that the latter findings are likely over-estimations due to the survey's reliance on websites and apps for respondent sampling. For reference, a 2013 phone survey in Canada, 50% of 1,830 gbMSM interviewed noted that they had used internet sites to meet partners in the previous six months¹⁸⁹. Nonetheless, the frequency of use for dating apps and websites has been noted to vary according to the population's age, gender, and ethnicity¹⁹⁰.

The rise in the use of dating apps and websites marks a shift in social norms and sexuality in Canadian society. Among gbMSM communities in particular, these changes highlight a shift in norms between age cohorts. For example, a qualitative study of 31 gbMSM in Toronto noted that compared to peers who lived through the 1980s and 1990s, a time during which there was a higher perceived risk associated with anal sex, younger cohorts had different views. These younger cohorts described current social expectations of condomless sex and greater concerns for having "good sex", rather than reducing STI risk¹⁹¹. The use of dating apps and platforms among gbMSM has been associated with greater numbers of reported sexual partners and higher odds of inconsistent condom use^{192,193}.

Among women, evidence suggests that dating app or website use is correlated with a higher number of sexual partners¹⁹⁴. In a study of 362 reported syphilis cases in the Winnipeg Health Region, a statistically significant higher proportion of female cases (n=52) indicated having met partners on websites or online in 2014-2015 (18%) compared to 2003-2005 (0%)⁵⁸.

Although these platforms are associated with certain behaviours that may place individuals at higher risk for syphilis, they also represent sites for potential social marketing for STBBI prevention, and have indeed been leveraged for such purposes by public health actors in Canada and abroad¹⁸⁹.

Lastly, many studies report that certain social or cultural understandings of syphilis may also be contributing to its emergence in several settings in Canada. For example, two qualitative studies with small samples have documented how, for many gbMSM, syphilis can be viewed as something that is more treatable and manageable than HIV, making it of lesser concern in sexual health decision-making^{62,191}.

4.2.5 Health Systems, Policy and Guidelines

In addition to shifts in culture and norms, elements of health policy and systems are also believed to influence STBBI risk at a population level.

Screening guidelines

The implementation of, or changes to, screening guidelines for STBBI can influence screening uptake. For example, in 2012, cervical cancer screening guidelines changed recommendations to a lower frequency of Papanicolaou (Pap) testing in Canada– shifting from screening every year to every three years after becoming sexually active or after reaching the age of 21 years¹⁹⁵. Since then, it has been documented that screening for chlamydia and gonorrhea has decreased¹⁹⁶⁻¹⁹⁸. Screening rates declined the most among females 15 to 19 years of age, following the change in guidelines, since it results in fewer opportunities for health professionals to screen for STIs¹⁹⁸. A study carried out at a Toronto, Ontario hospital, which looked at 200 women aged 19 to 25, found that they had lower odds of being tested for syphilis after the release of the updated guidelines compared to before¹⁹⁶. Despite a limited number of studies exploring the effects of such guideline changes, researchers have recommended that clinicians be vigilant to identify higher risk individuals and recommend STBBI testing when patients present themselves to clinical settings^{198,199}.

Other factors influence STI screening uptake. For example, HIV screening barriers can occur at the patient level (e.g., low risk perception, fear, difficulty accessing services), the healthcare provider level (e.g., lack of time, staff, knowledge) and at the institutional/policy level (e.g., cost of testing delivery and access, impact on other medical services). In addition to screening guidelines, interventions to increase the availability of STI tests and to introduce testing into new settings (e.g., making HIV testing available as a routine service at the healthcare provider and institutional level), as well as improve awareness and knowledge about STIs, should be promoted²⁰⁰⁻²⁰².

Sexual education

In Canada, sexual education is within provincial jurisdiction, and is believed to be a key determinant in population-level knowledge of STBBI risk factors and risk reduction methods^{203,204}. Indeed, in a 2002-2003 survey of 3,536 Canadian high school students, 51% of boys and 41% of girls indicated that school was their main source of information about human sexuality and sexual health²⁰⁵. In another survey of 2,310 teenagers and their mothers in 2005, school was also noted as one of the most valuable providers of sexual health-related information²⁰⁶. However, studies also note limits to the effectiveness of current sexual health curriculums in informing teenagers about STI risk factors and transmission methods in Canada, and propose that these educational gaps may be contributing to high STI prevalence among younger adults in the country²⁰⁶. Recent studies of the effects of sexual education reform in Canada on STI risk, and particularly on syphilis risk, are not available and remain an area of interest for future policy planning. The Sex

Information and Education Council of Canada (SIECCAN) leads a series of project activities to increase the capacity of the education sector to provide effective sexual health education, including the revision and dissemination of the <u>Canadian Guidelines for Sexual Health</u> <u>Education²⁰⁴</u>.

4.3 Proximate Determinants of Syphilis in Canada

4.3.1 Violence, Discrimination and Stigma

Though the body of existing research is limited, it does suggest that an individual's experience of violence and discrimination may affect their risk of acquiring a syphilis infection. In a national study of 7,872 gbMSM in Canada, intimate partner violence, defined as being threatened, emotionally abused, or physically assaulted by a partner, boyfriend, or sexual partner, was reported by 13% of respondents¹⁶³. Those who experienced intimate partner violence had more than two times the odds of reporting a recent syphilis diagnosis, after adjustment for individual-level sociodemographic characteristics and HIV status (aOR=2.3, 95% CI: 1.7-3.1) compared to those who did not. This finding is consistent with research conducted outside of Canada in women experiencing intimate partner violence who have been shown to experience higher STI risk^{207,208}. Experiences of intimate partner violence can be a barrier to individuals' self-efficacy in negotiating condom use, thereby placing individuals at higher risk of STI infection.

In the same pan-Canadian gbMSM study referenced above, participants were also asked if they had experienced homophobic discrimination in the health care system within the last 12 months. Of the 7,872 survey respondents, 3% reported having experienced health care discrimination. These individuals had four times higher odds of reporting a recent syphilis diagnosis (aOR=4.1, 95% CI: 2.4-7.0)¹⁶³. Discrimination in health care settings can shape individuals' likelihood of undergoing regular STI screening. Conversely, researchers have noted the potential importance of emergency room departments as sites of screening and other programs pertaining to STIs and intimate partner violence, given their importance for individuals with limited health care access or who use health care services infrequently²⁰⁸. Improving the cultural competency of health professionals to minimize discrimination and bias for sexual minorities and other groups has also been identified as an area for potential intervention to address STI risk and transmission^{163,174}.



Those who experienced **intimate partner violence** had over **two times** the odds of reporting a recent syphilis diagnosis (Ferlatte, 2018)



Those who experienced **health care discrimination** had over **four times** the odds of reporting a recent syphilis diagnosis (Ferlatte, 2018)

Experience of violence and discrimination increases the likelihood of recent syphilis diagnosis

As recognized by the Truth and Reconciliation Commission Report, experiences of discrimination and stigma are common among Indigenous Peoples accessing health care services in Canada. These are a direct result of historical colonial policies, including the Residential School system^{174,209}. These elements represent important structural barriers to health-promotion services including STI testing²¹⁰. Harm reduction practices that do not stigmatize substance use, and that integrate components of mental, spiritual, and emotional health, have been identified as promising strategies to address the latter barriers²¹⁰.

4.3.2 Mental Health and Substance Use

Mental health

Similarly to experiences of violence and discrimination, mental health issues, such as anxiety and depression, have been associated with lower self-esteem and self-efficacy in negotiating condom use¹⁵⁹. In Canada overall, there remains a paucity of studies exploring the association between mental health issues and increased syphilis risk. What has been documented, however, is the high prevalence of affective symptomatology among populations who are typically at higher risk of syphilis. For example, in a 2014-2015 study of 7,872 gbMSM in Canada, participants were ask if they had mental health issues in the last 12 months¹⁶³. Among them, 19% reported having suicidal thoughts or ideations and 30% reported depressive or anxiety symptoms.

In addition, a few studies have focused on the association between substance use and syphilis risk, as mental health issues have been, at time, correlated with substance use-related issues. Substances, such as alcohol or other drugs, are sometimes used to self-medicate against affective symptomatology, and their consumption can sometimes lead to dependence and substance use issues²¹¹.

Alcohol

Regarding syphilis risk specifically, a study of 194 people living with HIV attending a sexual health clinic in Alberta between 2006 and 2016, found that individuals with a history of problematic alcohol use (>14 drinks per week or binge drinking) were more likely to have tested positive for a syphilis infection compared to those who did not report such behavior⁷². The latter findings are consistent with those from a Winnipeg Health Region study in 2014-2015 that found that 21% of 362 cases of infectious syphilis reported alcohol use (without specification of frequency or quantity)⁵⁸. In that study, females with infectious syphilis were more likely to report alcohol use than their male counterparts (53% vs. 18%, *p* value<0.001)⁵⁸. Problematic alcohol use continues to be an issue across several populations. A Canadian study of 7,872 gbMSM in 2014-2015, noted that at least 7% of participants reported binge drinking in the past year¹⁶³.

Injection and non-injection drug use

In a study of 442 gbMSM who were HIV-negative in Toronto, injection drug use was more common in individuals with syphilis infections than those without (21% vs. 2%)⁷³. Additionally, in the US, among primary and secondary syphilis cases, the proportion of women that reported using injection drugs increased from 4.0% to 10.5% between 2013 and 2017, while it increased from 2.8% to 6.3% in men who have sex with women²¹². Injection drug use was stable among gbMSM for the same time period. Existing studies suggest that non-injection drug use may be a more common risk factor than injection drug use. For example, among 164 infectious syphilis cases identified in Winnipeg in 2014-2015, 2% of cases reported injection drug use and 18% reported non-injection drug use⁵⁸. Though the latter study did not provide information on the type of drug or frequency of use, it noted that the prevalence of non-injection drug use has been increasing over time among female infectious syphilis cases (4% reported use in 2003-2005, 13% in 2006-

2013, and 29% in 2014-2015)⁵⁸. In the US, Kidd et al. also observed that although there were increases in heroin use from 0.8 to 1.7% between 2013 and 2017, the prevalence of methamphetamine use was the highest, among drugs included in the study $(7.9\% \text{ in } 2013 \text{ to } 9.6\% \text{ in } 2017)^{212}$. This increase in methamphetamine use was observed in women and in men who have sex with women (from 6.2% to 16.6% and from 5.0% to 13.3%, respectively) and not in gbMSM, suggesting that a substantial proportion of heterosexual syphilis transmission occurs in persons who use these drugs.

In a study of 7,872 gbMSM in Canada in 2014-2015, 16% reported substance use (cocaine, crystal methamphetamine, ecstasy, gamma-hydroxybutyrate (GHB), ketamine, or crack cocaine), and substance use was independently associated with having a recent syphilis diagnosis after adjustment for demographic and socioeconomic characteristics (aOR=2.4, 95% CI: 1.8-3.2)¹⁶³. Such substances may be used recreationally for their ability to reduce inhibitions and increase pleasure²¹³. In the context of sexual relations, especially among gbMSM, the term "chemsex" (or Party and Play. "PnP") refers to the planned use of certain substances to extend the duration (hours to days) and intensity of sexual encounters (number of partners, types of practices)⁸⁴. More recently, increases in crystal methamphetamine (crystal meth) and Viagra® consumption, have been noted as potential contributing risk factors to STBBI outbreaks, especially among gbMSM¹⁹³. In the 2017 EMIS study (n=6,059), 6% of Canadian gbMSM respondents reported engaging in chemsex in the four weeks preceding the survey¹⁸⁸. In a Montreal-based sample of the crosssectional Engage survey of 2017-2018, nearly one-in-ten respondents (9% of 1,179 gbMSM respondents) had consumed a psychoactive drug (GHB, methamphetamine, ketamine, cocaine, or ecstasy) with at least one of his last five sexual partners, in a recreational chemsex context²¹⁴. Cocaine use was more prevalent (25% had sniffed or inhaled cocaine in the previous six months and 12% had consumed cocaine in the context of chemsex).

While chemsex has predominantly been described as a phenomenon in the gbMSM community, more widespread recreational substance use has been observed across other population subgroups. Overall in Canada, self-reported lifetime methamphetamine use appears to be increasing for those aged 25 years and over (e.g. from 2.5% in 2015 to 4% in 2017)²¹⁵. Overall, substance use has been associated with higher likelihoods of having condomless sex and of being at higher risk of experiencing STIs²¹⁶.

Historically, consumption of substances, such as crack cocaine, was noted as a determinant of past syphilis outbreaks during the 1990s in both Canada and the US^{217,218}. Crack cocaine use often intersects with experiences of transactional sex, namely as a source of income to support continued substance use²¹⁸. Researchers studying past syphilis outbreaks in British Columbia noted how dense sexual networks of concurrent partnerships were tied to crack cocaine use, transactional sex and limited condom use, and led to an increase of syphilis transmission and risk in both gbMSM and heterosexual populations in the late 1990s²¹⁸. In the latter contexts, partner notification was impeded by index cases' unwillingness or inability—due to ongoing substance use or due to the anonymity of transactional sex clients—to name their sexual partners²¹⁸.

Early data from 2018 and 2019 suggest that substance use may be a contributing factor to syphilis risk in certain areas of Canada^{219,220}. A study comparing heterosexual syphilis cases identified in Winnipeg, Manitoba, in 2017-2018 to those diagnosed in 2011-2012, noted crystal methamphetamine use was more prevalent in the more recent cases (30% in 2017-2018 versus 3% in 2011-2012)¹⁵¹. The intersection between mental health, illicit substance use, and syphilis risk merits attention in future Canadian research and surveillance activities.

Alcohol	Problematic alcohol use in relation to sexual contact has been associated with increased syphilis risk
Crack cocaine	Past syphilis outbreaks in Canada were associated with a combination of factors such as crack cocaine use and sex work. However, scientific data suggests these factors may not play a prominent role in current outbreaks
Injection drug use	Injection drug use has been associated with syphilis risk in Canada for the past decade
Crystal meth	Consumption of stimulants such as crystal meth appears to be a growing risk factor across both gbMSM and heterosexual populations in several jurisdictions in Canada

4.3.3 Sexual Activity and Behaviors

Condom use and number of partners

Risk of syphilis transmission tends to be higher among those who have a greater number of partners and those who do not use physical barriers, such as condoms, consistently, given that both risk factors increase likelihood of syphilis exposure and infection. Indeed, syphilis outbreak investigations in Canada have consistently noted the association between condomless sex, multiple sex partners and syphilis infection across provinces^{58,73,148,163,221}. Though these risk factors are relevant for both male and female cases, gbMSM appear to be at particularly high risk of syphilis, due in part to a high prevalence of multiple sexual partners and the risk associated with condomless sex^{73,163,221,222}. Though multiple reasons can explain inconsistent condom use, including low perceived STI risk, the 2017 EMIS survey noted that 22% of Canadian gbMSM respondents did not consistently use condoms due to issues of availability and access¹⁸⁸. Population-level gaps in access to condoms remain a public health issue in Canada.

Sex in Public venues

Certain studies note that the venues in which sexual activities are engaged in can also be correlated with higher syphilis risk, mainly due to their associations with inconsistent use of condoms or a higher number of sexual partners¹⁸⁸. For example, Canadian studies note an association between attendance at sex venues or cruising locations, such as bathhouses and saunas and syphilis risk, especially among gbMSM⁵⁸. Following a spatial network investigation of a syphilis outbreak in Toronto between 2006 and 2010, researchers identified certain bathhouses as sites contributing to syphilis transmission in the network of gbMSM in the city, even if only 6% of surveyed cases had indicated having met sexual partners at the bathhouses in question²²¹. Attending bathhouses was also reported by 6 of 17 cases surveyed in a social network investigation of a 2009-2010 Ottawa syphilis outbreak¹⁴⁸. Though public venues such as saunas, sex clubs, or bars are not as commonly used for sex by gbMSM as private dwellings, group sex or sex with multiple partners tend to be more common in public sites, as is consumption of substances, such as nitrite inhalants (poppers) or erectile dysfunction medications^{58,188}. For these reasons and for accessibility reasons, venues such as bathhouses and saunas remain of particular importance for targeted STBBI prevention efforts. The 2017 EMIS survey indicated that 46% of Canadian gbMSM respondents reported that they obtained condoms in targeted locations. including bars or saunas in the previous year¹⁸⁸. They also represent potential sites for targeted STI screening²²³.

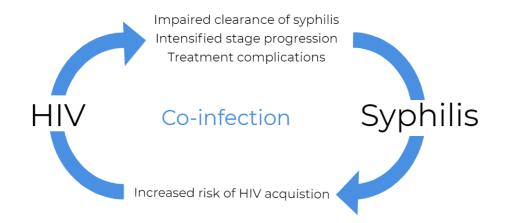
Transactional sex

Lastly, while the sale or purchase of sex was associated with syphilis risk in past outbreaks in Canada, it does not appear to be a driving factor behind syphilis emergence in more recent years²¹⁸. In the few studies that explore history of transactional sex among syphilis cases since 2008, it was noted that the majority of male and female cases were not engaging in the sale or purchase of sex⁵⁸. However, though few recent publications explore the potential association between transactional sex and syphilis infection, risk remains, especially if other concurrent factors such as substance use are present. For example, the Middlesex-London Health Unit recently declared a syphilis outbreak and reported that increases in the number of cases are also being seen among people who have sex with the opposite sex and people engaging in transactional sex¹¹⁸. From another perspective, human trafficking for sexual exploitation in Canada, in which women and girls are most often victims, is a context where sexual abuse and violence is common^{224,225}. Both of these determinants are well known to increase the risk of STI and HIV^{71,76,224,225}.

4.3.4 Clinical Factors

HIV co-infection

Historically, syphilis incidence has been correlated with incidence of other STBBI, especially HIV since the 1980s²²². The concurrence of STBBI infections, such as HIV, is an important determinant of syphilis incidence for reasons noted previously in <u>Section 2</u>. That is, HIV infection can impair syphilis clearance, lead to more rapid progression through the disease stages, and result in complicated treatment^{2,75,148,221}.



Across Canadian provinces and territories, studies have documented syphilis and HIV coinfections^{78,226}. A study investigating a syphilis outbreak in Ottawa (n=72) looked at the characteristics of infectious syphilis cases and noted that 26% had a coinfection with HIV¹⁴⁸. In a cross-sectional study of syphilis cases among Toronto males between 2006 and 2010, 47% of cases occurred in people living with HIV²²¹. Among 119 ocular syphilis cases identified in Montreal, Quebec between 2000 and 2015, approximately 48% were living with HIV²²⁷. In recent years, HIV and syphilis co-infection have tended to be more prevalent among gbMSM populations in Canada, compared to other populations^{57,73,163,167,169}. Recent Canadian studies suggest that younger (less than 30 years of age) gbMSM who report higher numbers of partners, condomless anal intercourse, and injection drug use or problematic alcohol use, are at particularly high risk of HIV and syphilis co-infection^{72,73,167}. In a British Colombia study, all individuals who reported more than three infectious syphilis diagnoses between 2005 and 2014 (n=30) identified as gbMSM, and a majority (96%) were living with HIV⁷⁸. HIV infection and its associated risk factors appears to represent a risk factor for both syphilis infection and re-infection in Canada.

It should be noted that the association between HIV and syphilis infection does not hold true for every population. A 2009-2010 cross-sectional study that looked specifically at STI co-infections among 126 HIV-positive and 291 HIV-negative African-Caribbean women recruited in downtown Toronto, found that syphilis prevalence did not significantly differ by HIV status (0.8% vs. 0.3%)⁷³. Similarly, in a Winnipeg-based study, all of the female infectious syphilis cases in 2014-2015 (n=17) were HIV-negative individuals⁵⁸. The few small studies that focus on female syphilis cases suggest that female cases may be at higher risk of co-infection with other STIs, such as chlamydia compared to male syphilis cases⁵⁸. However, associations between HIV, syphilis, and both gonorrhea and chlamydia infections have been reported in both males and females in Canada⁷².

Lastly, there were no notable associations found in Canadian studies that have assessed the impacts of HIV antiretroviral therapy or viral load suppression on syphilis risk among people living with HIV^{72,167}.

HIV pre-exposure prophylaxis (PrEP)

Concerns have been raised suggesting that the use of pre-exposure prophylaxis (PrEP) could lead individuals to engage in condomless sexual practices due to their perception of a decreased risk of HIV acquisition. However, very few Canadians studies have looked at the relationship between the use of HIV PrEP and the risk of syphilis. Furthermore, measuring such associations is challenged by various sources of bias. For example, insofar as PrEP therapy requires regular STI screening, those on PrEP are more likely than their peers to be screened for other STIs. One Montreal-based study conducted on 195 gbMSM observed a significant association between the prescription of PrEP and the number of all STI cases (chlamydia, gonorrhea, and syphilis) reported among gbMSM in the subsequent year, compared to the year prior to prescription²²⁸. However, after adjustment for frequency of screening visits during the 12 months before and after PrEP prescription, the association between PrEP use and STI infection was not significant (adjusted incidence rate ratio (aIRR)=1.4, 95% CI: 0.98-1.96). Similarly, this relationship did not hold when looking at the risk of syphilis acquisition, specifically (aIRR=1.5, 95% CI: 0.6-3.4)²²⁸.

Similarly, a longitudinal Australian study following 2,981 gbMSM who received daily PrEP was found that STI incidence increased from before- to after- commencing PrEP with the increase greatest for chlamydia infection (adjusted incidence rate ratio=1.12, 95% CI: 1.02-1.23). However, after adjusting for testing frequency between periods, no significant change in syphilis incidence was observed in the group of participants²²⁹. Although these studies have not been able to show an association, it should be noted that other studies have shown that PrEP use was associated with condomless sex and increases in STIs^{230,231}. In communities in which PrEP was widely used, condom use decreased even in gbMSM not using PrEP^{231,232}. Similarly, a higher incidence of STIs and faster time to first symptomatic STI was observed in a US longitudinal study among gbMSM on PrEP (n=365) compared to gbMSM not using PrEP (n=730)²³³. The adjusted IRR for early syphilis was 2.9 (95% CI: 1.5-5.6), comparing PrEP users to nonusers. Time to first symptomatic STI was of 120 days (95% CI: 77-171) among PrEP users compared to 185 days (95% CI: 163-256) among non-users.

Other STBBI co-infection

Beyond HIV, associations between syphilis and chlamydia and gonorrhea risk have also been explored in Canada. A British Columbia study of 133,264 individuals who were diagnosed with either chlamydia or gonorrhea between 2006 and 2017, found that individuals who subsequently received a syphilis diagnosis were more likely to be men, to live with HIV or have a history of lymphogranuloma venereum²³⁴. Among a sample of female infectious syphilis cases in Winnipeg between 2003 and 2015, 24% had concomitant chlamydia infection, while few presented with HIV (7%) or gonorrhea (4%)⁵⁸. Recent studies suggest that syphilis, chlamydia and gonorrhea co-infections may be on the rise in certain populations in Canada. For example, a study comparing heterosexual syphilis cases identified in Winnipeg, Manitoba, in 2017-2018, to those diagnosed in 2011-2012, noted that chlamydia was more prevalent in recent cases (23% co-infection in 2017-2018 vs. 10% in 2011-2012), as was gonorrhea (21% vs. 3%)¹⁵¹.

Lastly, a study conducted between 2005 to 2018 among 4,139 gbMSM in Montreal found no association between HCV infection and higher likelihood of current or lifetime syphilis infection²³⁵. However, this form of co-infection remains understudied.

KEY MESSAGES

- Experience of violence and discrimination increase the likelihood of recent syphilis diagnosis.
- Mental health issues such as anxiety and depression have been associated with lower self-esteem and self-efficacy in negotiating safer sex practices.
- Crystal methamphetamine consumption has been noted as a potential contributing factor to increased syphilis rates, especially among gbMSM.
- Inconsistent condom use and multiple sex partners have been consistently associated with syphilis outbreaks in Canada.

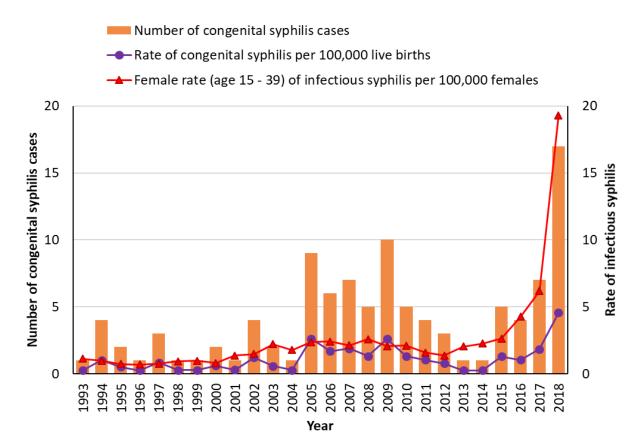
5. Congenital syphilis: trends, determinants and response

5.1 Congenital Syphilis Trends in Canada over the Past 25 years

According to CNDSS data, from 1993 to 2004, the number of confirmed congenital syphilis cases reported was low, ranging from one to four cases per year, corresponding to a rate of 0.3 to 1.2 cases per 100,000 live births (Figure 33). Since 2004, the number of cases reported yearly has fluctuated, with the highest number of cases reported in 2009 (ten cases). The number of congenital syphilis cases dipped between 2013 and 2014, but has been on the rise ever since. There were seven confirmed congenital syphilis cases in 2017 (1.9 cases per 100,000 live births). In 2018, the number of cases more than doubled to reach 17 confirmed cases (4.6 per 100,000 live births). It is expected that the number of cases in 2019 will exceed 50 cases. Further details on recent congenital syphilis trends are described in <u>Section 5.2</u> below.

The WHO defines women of reproductive age as 15 to 49 years of age. However, as CNDSS uses different age groupings, the computation of rates for this age group is not possible. Instead, the CNDSS age grouping of 15 to 39 years of age is used to capture females of reproductive age, although this will underestimate the true number of females of reproductive age. Over time, the rate of congenital syphilis has loosely followed the rate of infectious syphilis among females of reproductive age, which while relatively low in the 1990s, has increased steadily until peaking in 2018 with 19.0 cases per 100,000 females, more than triple the 2017 rate of 6.2 cases per 100,000 females (Figure 33, Appendix G). The overall female rate in 2018 reached 7.0 cases per 100,000 females, compared to only 2.4 cases per 100,000 females in 2017. These data highlight the increased population-level risk for vertical transmission of syphilis infections.

Figure 33. Number and rates of reported cases of congenital syphilis and rates of reported cases of infectious syphilis among females of reproductive age (15 to 39 years of age), Canada, 1993-2018



Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

5.2 Epidemiological situation across Provinces and Territories

Over time, congenital syphilis incidence in Canada has varied across provinces and territories. Between 2016 and 2019, seven provinces and one territory published reports that included information relating to congenital syphilis cases. Of these, two provinces—Manitoba and Quebec—described maternal risk factor information. No congenital syphilis information was publicly available for Saskatchewan, Nova Scotia, Prince Edward Island, Yukon and Nunavut. Note that national surveillance data only present confirmed cases. Several probable cases have been reported in various jurisdictions (Alberta, Saskatchewan, Manitoba and Quebec all have probable case definitions for early congenital syphilis). PHAC will begin work on the revision of the national syphilis case definitions in 2020.

5.2.1 Pacific Region: British Columbia

From 2008 to 2017, five cases of congenital syphilis were reported to CNDSS by British Columbia. The BCCDC's 2016 STI report indicated that the number of prenatal syphilis tests performed each year was steadily increasing and that 51,377 prenatal syphilis tests were conducted in 2016, resulting in the identification of eight maternal syphilis cases that did not lead to congenital

cases⁹². In 2019, two cases of congenital syphilis were reported in British Columbia, making these cases the first reported since 2013²³⁶.

5.2.2 Prairie Region: Alberta, Saskatchewan and Manitoba

In Alberta, between 2015 and 2016, one confirmed congenital syphilis case was reported to CNDSS. In 2017, four confirmed cases of early congenital syphilis and three probable cases of congenital syphilis were reported by the province⁹⁴. By 2018, the number of confirmed and probable cases in Alberta doubled (eight confirmed cases—one of whom was stillborn—and six probable cases). According to preliminary data, in 2019, 40 cases, including confirmed, probable and stillborn cases of congenital syphilis were reported in the province—more than 30 of which were identified in the Edmonton region²³⁷. Some of the risk factors associated with these cases included homelessness, insecure housing and substance use²³⁸. Most women had not received prenatal care or did not receive it early enough to prevent vertical transmission of the infection.

From 2008 to 2017, Saskatchewan reported one case of congenital syphilis to CNDSS. According to 2019 Saskatchewan news releases, recent cases of syphilis were reported in pregnant women; however, cases received medical treatment, which prevented the vertical transmission of the infection, and no congenital cases of syphilis were reported in the first five months of 2019²³⁹.

In 2015, the Manitoba government reported one case of congenital syphilis, the first case in the province in over 30 years^{53,240}. In 2017, another case was identified²⁴¹. On February 25th, 2019, the government of Manitoba informed health care providers that at least ten infants had been treated for congenital syphilis in the previous six months, and that substance use and lack of prenatal care were risk factors associated with identified cases¹⁰⁹. So far, in 2019, the number of congenital syphilis cases reported by Manitoba is among the highest of all the Canadian provinces and territories.

5.2.3 Central Region: Ontario and Quebec

From 2008 to 2017, Ontario reported ten confirmed cases of congenital syphilis to CNDSS. One case was reported in 2018, followed by two additional cases identified between January and August 2019^{112,242,243}. Although the Ontario Northwestern Health Unit, which borders Manitoba, experienced an outbreak of infectious syphilis in 2019, no cases of congenital syphilis were reported in this region between January and March 2019^{184,244}.

From 2008 to 2017, five confirmed cases of congenital syphilis were reported to CNDSS from Quebec. Most recent available provincial reporting suggests that three cases of congenital syphilis were reported in 2016, followed by one case in 2017, one in 2018 and two in 2019^{121,122}. Lack of prenatal care or delayed prenatal care and treatment was a factor identified in most cases diagnosed between 2016 and 2018.

5.2.4 Atlantic Region: New Brunswick, Nova Scotia, Prince Edward Island and Newfoundland and Labrador

Overall, Nova Scotia, Prince Edward Island and Newfoundland and Labrador did not report any cases of congenital syphilis to CNDSS from 2008 to 2017. In the same time period, New Brunswick reported two cases of congenital syphilis to CNDSS, one of which occurred in 2017¹²³. In 2018, one case of congenital syphilis was identified by the Eastern Health authority of Newfoundland and Labrador²⁴⁵.

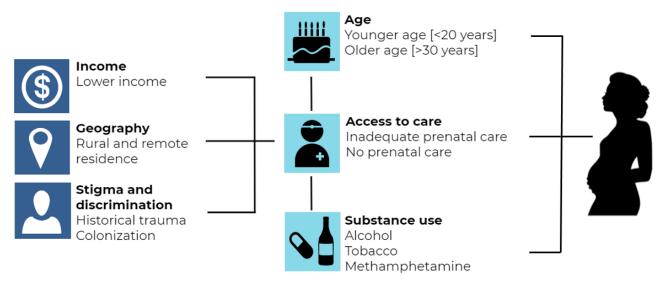
5.2.5 Northern Region: Yukon, Northwest Territories and Nunavut

From 2008 to 2017, neither Yukon nor Nunavut reported any congenital syphilis cases, while the Northwest Territories reported two cases to CNDSS during that period. In 2019, the Northwest Territories Health and Social Services reported another case of congenital syphilis—the same year for which the territory declared a pan-territorial syphilis outbreak^{135,137}.

5.3 Factors associated with Canadian Trends

Very few publications in Canada have reported on the determinants and risk factors associated with maternal or congenital syphilis, or on the characteristics of women seeking or not seeking prenatal care. Current publications from British Columbia, Alberta, Manitoba, Ontario and Quebec, offer some indications of the potential determinants of congenital syphilis in Canada. However, evidence remains limited and might not be representative of the whole country. In consequence, the following section, which summarizes what has been published in peer-reviewed and grey literature between 2009 and 2019, should be interpreted with caution. Figure 34 summarizes documented risk factors for maternal and congenital syphilis in Canada.

Figure 34. Most commonly reported risk factors associated with maternal syphilis and related congenital syphilis in the Canadian literature



Note: Existing studies and reports published from 2009 to 2019 in British Columbia, Alberta, Manitoba, Ontario and Quebec.

5.3.1 Access to Care

PHAC's CGSTI recommends universal screening in pregnancy. The initial syphilis screen should be performed in the first trimester or at the first prenatal visit. In areas experiencing a resurgence of syphilis or for women at ongoing risk of syphilis, consideration should be given to repeating the screening in the third trimester (28 to 32 weeks) and again at delivery¹¹. Lastly, any person delivering a stillborn infant after 20 weeks gestation should be screened for syphilis. It is important to note that provincial and territorial screening guidelines may vary across jurisdictions, and take precedence over the CGSTI recommendations.

Access to appropriate prenatal care, including syphilis screening and timely and effective treatment, have been identified as key resources to prevent maternal and congenital syphilis²⁴⁶. Indeed, lack of access to care is among the most commonly reported risk factors for congenital syphilis incidence. The occurrence of congenital cases might indicate missed opportunities for prevention.

A British Columbia study on prenatal syphilis screening uptake and case detection in a cohort of women aged 16 to 45 years of age (n=233,203), found that between 2007 and 2011, uptake of prenatal screening for syphilis was high in the province (over 90% of pregnant individuals were tested at least once, which was consistent with provincial guidelines) and improved annually^{236,247}. In 2011, 96% (n=44,614) of the women who received any prenatal tests were tested for syphilis, a statistically significant increase from 2007 (91% tested, n=42,154, *p* value<0.001)²⁴⁷. Of interest is the fact that 41% (n=19) of maternal syphilis cases detected between 2010 and 2016 in the province (n=46) were diagnosed in the second or third trimester or at delivery²⁴⁸, highlighting the potential importance of repeat screening during pregnancy or at delivery.

In 2009, Alberta implemented syphilis screening guidelines which recommended universal, repeated screening throughout pregnancy (at first trimester, mid-gestation and delivery). In a study of all pregnancies resulting in a live or stillborn infant between 2010 and 2011 in Alberta (n=99,609), 1.5% of pregnant individuals received no syphilis screening at all, and 98.5% had received at least one prenatal syphilis test. Of these, 1.5% had received screening only at the time of delivery²⁴⁶. Only 20.7% (n=20,624) of all pregnant individuals had received prenatal syphilis screening tests at all three recommended time points²⁴⁶. Compared to women who had received screening for syphilis at all three recommended time points, women who were underscreened were more likely to not have received any prenatal care, or to have received prenatal care through a midwife only or through a combination of midwifery and physician-based care alone). The authors suggest that the observed association between midwifery-based prenatal care and lower likelihood of repeat syphilis screening may be due to midwives' or their patients' lower perceived risk of syphilis infection, or due to the clientele's potential reluctance to undergo screening, as one of many health care procedures²⁴⁶.

In Quebec, for one of the three cases confirmed in 2016, the mother had not received prenatal care. For another, the mother tested negative for syphilis at the beginning of her pregnancy and was not tested a second time, as she did not present syphilis-related symptoms nor did she report any new partners. For the latter case, both mother and child tested positive for syphilis one month post-delivery. For the third, the mother tested positive for syphilis at the start of her pregnancy, but only underwent treatment two weeks prior to delivery¹²². For the 2017 case, the mother did not receive any prenatal care. In 2018, the mother of the case received no prenatal care prior to the 31st week of pregnancy, and only underwent syphilis screening during the 35th week of pregnancy. For the 2019 cases, one mother had not received prenatal care, and diagnosis occurred at delivery, while the other mother had received a negative syphilis result early in pregnancy, but had not presented to subsequent prenatal visits¹²¹.

There do exist inequities in access to prenatal care by ethnicity. In Alberta, in 2010 and 2011, First Nations women were more likely to have not received the three recommended prenatal syphilis screening tests compared to women who did not report being First Nations (aOR=1.78, 95% CI: 1.62-1.96, n=99,609)²⁴⁶. Of the 17 confirmed and three probable congenital syphilis cases born in the Edmonton Health Zone of Alberta between 2002 and 2010, 65% (n=13) were born to mothers who identified as First Nations, Métis or Inuit²⁴⁹. Syphilis outbreaks in Winnipeg, an especially hard-hit city, have seen a disproportionate number of cases in Indigenous women²¹⁰.

Colonization has contributed to the health inequities Indigenous peoples face today through systemic discrimination across the social, criminal justice, health care and employment environment²⁵⁰. As mentioned in <u>Section 4.2</u>, due to legacies of colonization and structural disenfranchisement, Indigenous peoples in Canada often face stigma, discrimination, violence, mistrust of health care systems, and concurrent health issues, such as HIV and problematic subtance use, which place them at higher risk for experiencing STBBI¹⁷⁴. The unequal power dynamics created by colonization and reinforced by ongoing colonialism are important drivers of stigma. The discriminatory interpersonal behaviour of health professionals, along with Eurocentric health professionnal training have led to the reduced seeking, or avoidance, of healthcare services and poorer quality of services received by Indigenous peoples²⁵¹. The gendered impacts of colonization along with patriarchal systems and inequitable education opportunities have led to the marginalisation of Indigenous women and their increased risk for sexually transmitted infections²¹⁰. In consequence, factors associated with higher risk of syphilis infection, such as methamphetamine use and survival sex, have been observed among Indigenous women²¹⁰.

Studies also indicate that delays in maternal syphilis treatment following diagnosis may contribute to congenital syphilis risk. An Alberta study of the management of positive prenatal syphilis serologies in a Calgary STI clinic from 2009 to 2010 (n=48 charts reviewed) noted that while the average time needed to contact and inform patients of their diagnosis was fairly short (one or two days), the average time to receive the first dose of treatment was longer (nine to 20 days on average), highlighting the need to improve the follow-up and support of affected patients²⁵². Another study in Alberta, in the Edmonton Health Zone, noted that of the 17 confirmed and three probable congenital syphilis cases born between 2002 and 2010, 30% of cases (n=6) were born to mothers who received syphils treatment before delivery, but in whom the treatment was deemed to be inadequate—and 70% (n=14) received postnatal treatment only²⁴⁹.

5.3.2 Age

Three existing studies from Alberta and British Columbia suggest that both youngest and oldest reproductive age groups included in their studies may be at highest risk for maternal syphilis, and thereby vertical transmission. A study conducted in British Columbia (n=233,203), the highest maternal diagnosis rates were observed in the youngest (16 to 20 years of age and oldest (41 to 45 years of age) age groups; however, these differences were not statistically significant²⁴⁷. Similarly, Alberta has seen a statistically significant increase in the proportion of positive syphilis specimens collected through prenatal screening among women aged 30 years and oldest (≥40 years of age) pregnant women in 2010 to 2011 were significantly less likely to have received syphilis screening at all three of the time periods recommended by the province (at first and third trimester and at delivery) (n=99,609)²⁴⁶.

5.3.3 Income

Though few studies have explored the relationship between lower income and likelihood of prenatal syphilis screening uptake and thereby congenital syphilis risk, evidence from Alberta suggests that lower income may be associated with lower likelihood of receiving repeated prenatal screening (at first and third trimester and at delivery) when universal repeated screening is recommended (n=99,609)²⁴⁶. This is consistent with findings from a study conducted in Ontario (n=264,737), which found that lower income, particularly living in lower-income areas, has been associated with lower likelihood of prenatal screening uptake for publicly insured screening tests²⁵⁴.

5.3.4 Geography

Information on the risk of maternal and congenital syphilis among individuals living in urban vs. rural areas is limited. Evidence from Alberta suggests that that living in rural areas may be associated with lower likelihood of receiving repeated prenatal screening when universal repeated screening is recommended. The odds of not having received all three tests was approximately four times higher among rural and remote areas compared to those living in metropolitan areas (n=99,609, aOR=3.61, 95% CI: 3.10-4.20)²⁴⁶. This is consistent with findings from Ontario (n=264,737) indicating that living in more rural or remote areas has been associated with lower likelihood of prenatal screening uptake for publicly insured screening tests²⁵⁴.

5.3.5 Ethnicity

Ethnic disparities were also observed in British Columbia. In a study of maternal syphilis cases in British Columbia between 2010 and 2016, almost half of all cases (46%) did not identify as Caucasian. Of all maternal syphilis cases identified in the latter period (n=45), 20% identified as Asian, 13% identified as Indigenous, 11% identified as South Asian, and 2% identified as Black; compared to 24% who identified as Caucasian²⁴⁸. Data were missing for 30% of all cases. This overrepresentation of women of ethnic minorities among maternal syphilis cases is distinct from what has traditionally been observed for male cases in Canada. In fact, among the latter, a majority of infectious syphilis cases (40% to 70%) have been reported to occur among males who identify as Caucasian^{92,167}. However, ethnicity data are rarely collected for STBBI by most jurisdictions. As described in the access to care section above, due to legacies of colonization and structural disenfranchisement, Indigenous people have limited access to quality care. This might explain why Indigenous women seem to be disproportionately affected by maternal syphilis or congenital syphilis in their infants^{210,251}.

5.3.6 Immigration status

The evidence related to immigration status and congenital syphilis risk is sparse. Evidence from British Columbia between 2010 and 2016 suggests that up to one third (29%, n=13) of maternal syphilis cases were either born outside of Canada or had a partner in a developing country⁹². This is aligned with preliminary data from Quebec, which suggests that sexual contact with a partner who may be having sexual partnerships abroad may be a contributing risk factor to female syphilis risk in the province¹²².

5.3.7 Sexual Partnerships

For pregnant individuals, partnership status appears to be an important correlate of screening follow-through. A study in Alberta from 2010 to 2011 reported that women who were not married were more likely to be under-screened for syphilis, as defined by the province's recommendation of universal screening in the first and third trimester and at delivery (aOR=1.09, 95% CI: 1.04-1.13, n=99,609)²⁴⁶.

Though a higher reported number of sexual partners and casual sex are known risk factors for syphilis risk in general, very few studies describe the potential role of these factors in determining maternal or congenital syphilis risk. Among maternal syphilis cases identified in British Columbia between 2010 and 2016 (n=45), 13% (n=6) reported having two or more partners in the previous year, and two thirds (n=4) reported engaging in casual sex with more than four partners in the previous year²⁴⁸. Thus, though these behaviours may be associated with higher risk, they are not highly prevalent among reported cases.

Lastly, concerning sexual practices and partnerships, it is important to consider the extent to which pregnant individuals' risk may be attributable to their partners' behaviours and exposures. For example, in Quebec, it was estimated that between 2010 and 2011 (n=51), the most common risk factor reported by female syphilis cases (51% of cases) was having had sexual contact with a partner who was at risk. Partner's risk level was determined based on whether they were a man who had sex with other men, reported use of substances, were engaging in sex work, had multiple other partners or had sexual relations abroad¹²².

5.3.8 Sex Work

Few available studies reported on sex work as a potential risk factor for maternal or congenital syphilis. In British Columbia between 2010 and 2016, only 2% (n=1) of maternal syphilis cases reported transactional sex²⁴⁸. No information was provided regarding the type of transactional sex activities or the frequency of transactional sex. Though engagement in sex work was a known risk factor during past outbreaks in Canada, existing evidence does not suggest that it plays as important a role in the current epidemiologic context²¹⁸.

5.3.9 Substance Use

Preliminary reports from Manitoba suggest that substance use may be a contributing factor to the province's observed congenital syphilis cases in 2019^{109,255}. In fact, of the 16 confirmed and the 12 probable cases of congenital syphilis reported in Manitoba from January 2015 to July 2019, substance use, including crystal methamphetamine, was identified in 50% of mothers²⁵⁶. Since questions on substance use are not always asked, it is probable that substance use among pregnant women with syphilis may be underestimated. In Alberta, homelessness, insecure housing and a history of substance use were associated with most of the 40 cases of congenital syphilis reported in the province in 2019²³⁸. Substance use may be a relevant determinant of congenital syphilis in part due to its correlation with lower prenatal testing uptake. In Alberta, women who reported smoking or alcohol consumption during pregnancy were more likely to report no prenatal syphilis testing or late testing²⁴⁶. The hesitancy to present for prenatal care might be even higher for people who use substances. People who use drugs often face stigma in health care settings due to a lack of training in harm reduction among health care professionals. This stigma has led to decreased health care use and poorer quality of health and social services for people who use drugs²⁵¹.

The prevalence of substance use as a risk factor appears to vary according to jurisdictions, however. For example, in British Columbia, only 9% (n=4) of maternal syphilis cases identified between 2010 and 2016, reported substance use²⁴⁸.

5.4 How do Recent Trends in Canada Compare to those in other Countries?

5.4.1 Australia

In Australia, the rate of congenital syphilis has fluctuated in the past decade. Unlike Canada, Australia's case definition for congenital syphilis includes all cases of congenitally acquired syphilis among infants and children, as well as syphilitic stillbirths. Overall, 44 cases of congenital syphilis were reported between 2008 and 2017, of which the majority (60%, n=26) were born to mothers who identified as Indigenous (i.e. Aboriginal and Torres Strait Islander population). In 2017, specifically, 71% of cases (5/7 cases) were born to mothers who identified as Indigenous, corresponding to a rate of 26.9 cases per 100,000 live births in that population. Among non-Indigenous mothers, three congenital cases were confirmed, corresponding to a rate of one case

per 100,000 live births. From 2008 to 2017, the congenital syphilis rates among the Australian non-Indigenous population were slightly lower than the average Canadian rate of congenital syphilis (1.9 cases per 100,000 live births in 2017)⁸⁵. Both countries are similar in their observation of inequities in maternal and congenital syphilis risk according to Indigenous ancestry^{85,246,257}. Aboriginal and Torres Strait Islander people are disproportionately impacted by STIs compared to non-Indigenous populations, due to a lack of access to testing and treatment and to being more frequently exposed to environments and situations where there is an increased risk of exposure to STIs⁸⁵.

In 2017, the infectious syphilis rate for females of all ages reached 5.5 cases per 100,000 females in Australia. Recent (2015-2017) female infectious syphilis rates are therefore slightly higher in Australia than in Canada, where a rate of 2.4 cases per 100,000 females was observed in 2017. However, Australian rates include both probable and confirmed infectious syphilis cases, which is not the case in Canada, where only confirmed cases are reported⁸⁵.

5.4.2 European Union

Overall, congenital syphilis rates among the EU and European Economic Area countries have decreased since 2005, and are mostly comparable to rates in Canada²⁵⁸. In 2017, 36 cases of congenital syphilis were reported in the EU and European Economic Area, from a total of 23 member states, corresponding to a crude rate of 1.1 cases per 100,000 live births. It should be noted that these values might be an underestimation as information was missing from eight countries. It should also be noted that case definitions vary across European countries. Although the majority of countries reported syphilis data according to EU case definitions during the last data collection, five countries used national case definitions, EU congenital syphilis case definitions were used. Similarly to Canadian case definitions, EU congenital syphilis case definitions do not include stillbirths, abortions or fetal deaths and only include cases under two years of age²⁵⁸. In 2017, confirmed cases were reported in Bulgaria (n=14), Romania (n=6), Portugal (n=4), Germany (n=3), Hungary (n=3), Spain (n=2), Czech Republic (n=1), Ireland (n=1), Lithuania (n=1) and Poland (n=1). These case numbers corresponded to rates of congenital syphilis that ranged from 0.3 cases per 100,000 live births (Poland) to 21.5 cases per 100,000 live births (Bulgaria)²⁵⁸.

Overall, infectious syphilis rates among females of all ages have also been decreasing in the EU and European Economic Area since 2005²⁵⁸. In 2015, the female rate was 1.3 cases per 100,000 females, before increasing slightly to 1.4 cases per 100,000 females in 2017²⁵⁹. As such, the 2017 EU and European Economic Area female infectious syphilis rates were lower than the Canadian average for that year (2.4 cases per 100,000 females).

In Europe, risk factors associated with maternal syphilis included: (1) high-risk sexual behaviour and/or drug use, (2) history of incarceration, (3) low income and younger age, (4) east-European ethnicity and (5) factors related to the healthcare system capacity to identify and treat syphilis infection during pregnancy²⁵⁸.

5.4.3 United Kingdom

In the UK, the number of cases of congenital syphilis has been increasing since 2011. Between 2010 and 2017, 21 cases of congenital syphilis were reported in England, including six cases in 2016-2017. Of these cases, 57% (12/21 cases) had not received prenatal syphilis screening. Of those who did receive screening (43% of all cases, 9/21 cases), 77% (7/9 cases) had received a

negative test result during their first trimester, suggesting that these mothers acquired the infection later in their pregnancy.

Between 2010 and 2015, the number of cases reported corresponded to a yearly incidence rate that varied between 0.1 to 1.5 cases per 100,000 live births, slightly lower than the Canadian average²⁶⁰. In 2017, the rate of infectious syphilis among all females in England was 1.5 per 100,000 females – lower than the Canadian average that year (2.4 per 100,000 females)²⁶¹. Comparisons between Canadian and UK rates should be interpreted with caution, as there were no publicly available syphilis case definitions from the UK at the time this report was written.

5.4.4 United States

The CDC case definition for congenital syphilis used for reporting purposes includes cases of congenitally acquired syphilis among infants and children, as well as syphilitic stillbirths. Additionally, infants born to a mother who was untreated or inadequately treated for syphilis are counted as probable cases of syphilis, regardless of their signs or symptoms. In the US, the rates of reported congenital syphilis have been increasing since 2012²⁶². After noting a rate of 16.2 cases per 100,000 live births in 2016, a 44% rate increase was observed between 2016 and 2017. In 2017, 918 cases of congenital syphilis were confirmed, corresponding to a rate of 23.3 per 100,000 live births (compared to the Canadian rate of 1.9 per 100,000 live births). Of the cases diagnosed in 2017, there were 64 syphilitic stillbirths and 13 infant deaths²⁶². In 2018, the number of reported congenital syphilis cases reached 1,306 (33.1 per 100,000 live births), a 40% increase from 2017²⁶³. In 2018, 78 of the cases were syphilitic stillbirths and 16 resulted in infant deaths. Like in Canada, congenital syphilis trends in the US have largely been correlated with the increasing trend of primary and secondary syphilis among females, which reached a rate of 3.0 cases per 100,000 females in the US in 2018.

Rates of congenital syphilis varied considerably according to ethnicity. In 2018, the highest rates of congenital syphilis were observed among cases whose mothers identified as Black (86.6 cases per 100,000 live births), followed by those identifying as Indigenous (79.2 cases per 100,000 live births—double the 2017 rate of 35.5 cases per 100,000 live births in this group), Hispanic (44.7 cases per 100,000 live births), White (13.5 cases per 100,000 live births), and Asian/Pacific Islander (9.2 cases per 100,000 live births—also double the 2017 rate of 4.3 cases per 100,000 live births among this group)²⁶².

In 2018 as in previous years, the geographical distribution of rates varied across the country. Rates were highest in the West (48.5 cases per 100,000 live births), followed by the South (44.7 cases per 100,000 live births), the Midwest (12.4 cases per 100,000 live births) and the Northeast (8.5 cases per 100,000 live births)²⁶³.

Previous CDC reports have indicated that late or limited prenatal care is associated with congenital syphilis incidence²⁶². Similar to Canadian guidelines, the CDC recommends universal screening of pregnant women at the first trimester and at delivery if the woman had not been screened before or if she delivered a stillborn child²⁶⁴. Screening in the third trimester (between 28 and 32 weeks) and at delivery are also recommended for women at high risk of syphilis acquisition or those living in regions that experience a significant increase in the number of cases²⁶⁴. Even among those receiving prenatal care, syphilis is often detected or treated too late during the pregnancy to prevent vertical transmission. Non-adherence to prenatal syphilis screening test can contribute to vertical transmission of infection²⁶². In the US, every state's Medicaid program is mandated to cover prenatal care for lower-income females (i.e., those

reporting incomes below 133% of the federal poverty level)²⁶⁵. However, it was estimated that up to 25% of reproductive-age women were uninsured, at least at some point in the year, and that neither private health insurance nor Medicaid covered 10% of pregnant individuals, during the early 2010 decade.²⁶⁶. Though the Affordable Care Act led to a reduction in the estimated proportion of uninsured women of all ages, in 2017, approximately 11% of all women in the US remained uninsured²⁶⁷. The proportion of uninsured women of all ages was highest among non-citizens (32% uninsured), Hispanic (22% uninsured) and Black (12% uninsured) women, as well as women whose income was 200% lower than the federal poverty line in 2017 (i.e. reporting an individual yearly income of \$24,100) (20% uninsured)²⁶⁷. According to the CDC, the fact of being uninsured or underinsured for women, as well as substance use, increase the risk of receiving inadequate or no prenatal care²⁶⁸.

5.5 What can be done to Address Congenital Syphilis in Canada

Although research on effective interventions to reduce congenital syphilis incidence is limited, certain countries have implemented various interventions in order to control the growing number of cases.

5.5.1 Using adequate screening guidelines

Canadian guidelines recommend universal testing for syphilis in the first trimester of pregnancy, and further screening at third trimester (between 28 and 32 weeks) and at d for individuals at high risk³. The guidelines also note that consideration should be given to re-screening all pregnant individuals, regardless of risk profile, in areas experiencing heterosexual outbreaks of syphilis or where congenital syphilis cases have been reported in pregnant individuals with no personal risk factors for syphilis³.

Given epidemiologic shifts observed in syphilis cases in Canada, especially towards heterosexual populations, as well as the emergence of congenital syphilis cases, several jurisdictions in Canada have recommended repeat screening in the third trimester and/or at delivery for all pregnant individuals, in addition to universal screening during the first trimester. For example, in 2019 British Columbia developed interim guidelines that added a recommendation of universal screening at delivery²⁶⁹. In 2019, Manitoba issued a recommendation for universal third trimester screening (completing additional screening at delivery for higher risk individuals)¹⁰⁹. In Ontario, in 2019, the Northwestern Health Unit recommended universal screening for all pregnant individuals in the region both during the third trimester and at delivery¹⁸⁴. This is aligned with recommendations in northern Quebec, Nunavut, and Alberta. After experiencing high rates of syphilis, the northern Nunavik region of Quebec has recommended universal screening at the first visit for pregnancy, at 28 weeks and at 36 weeks of pregnancy (or at the time of delivery if not performed at 36 weeks) since 2017²⁷⁰. Universal screening during the first and third trimester and at delivery has been recommended since 2013 in Nunavut and as an interim measure during an outbreak between 2009 and 2011 in Alberta^{246,271,272}. Since then, Alberta recommended screening in the first trimester and at delivery with additional testing suggested for individuals with ongoing risks.

In the US, universal repeat testing during pregnancy is recommended for women who live in highprevalence areas²⁷³. Historically, CDC guidance has suggested that universal screening at delivery be considered in areas where infectious syphilis incidence among women of reproductive age is of four to five cases per 100,000 population²⁷⁴. It remains up to individual states to define high-prevalence thresholds after which universal screening in the third trimester be considered²⁷⁴. As of 2018, 12 states required universal screening during the third trimester, and three required universal screening at delivery for all pregnant individuals²⁷⁵. Among states that recommended third trimester screening for all pregnant individuals, incidence rates for females of reproductive age ranged from 0.7 (Connecticut) to 7.8 (Louisiana) per 100,000 population in 2017²⁷⁶.

Seven countries in Europe currently recommend universal screening in the first and third trimester of pregnancy (Czech Republic, Estonia, Latvia, Lithuania, Romania, Slovakia and Spain)²⁷⁷.

5.5.2 Evaluating screening guidelines

Overall, few evaluations on the acceptability and feasibility of universal guideline changes, as well as their effectiveness in increasing screening uptake during pregnancy have been performed. One Canadian study based in Alberta explored the effects of recommending universal screening in the first and third trimester and at delivery²⁴⁶. Out of the of 99,609 pregnancies that occurred in Alberta in 2010-2011, 99% had at least one prenatal screening for syphilis, but just 21% had all three recommended tests (first trimester, mid-gestation and at delivery)²⁴⁶. A smaller proportion of pregnant individuals (2%, n=1,494) were screened only at delivery of childbirth, and the same proportion received no screening. The women that were more at risk of not having the three recommended screenings were those registered as First Nations or Inuit (aOR=1.78, 95% CI: 1.62-1.96), those living in a remote rural area (aOR=3.61, 95% CI: 3.10-4.20), and those receiving prenatal care only from a midwife (aOR=13.70, 95% CI: 9.20-20.39). Thus, despite an increase in recommended screening frequency, which was documented in other subsequent studies, social and structural barriers appeared to persist in the province, limiting the effectiveness of interventions related to changes in guidelines alone²⁵³. Ensuring compliance with recommended screening guidelines and increasing health provider awareness are therefore essential to reducing congenital syphilis cases in Canada. Evaluating screening guidelines frequently is necessary to ensure that they align with the epidemiological situation.

5.5.3 Increasing access to care

As mentioned in <u>Section 5.3</u>, lack of access to care has been identified as a major obstacle for women at risk of transmitting syphilis vertically and has contributed to the increase of congenital syphilis cases in Canada. Testing facilitates entry to care and provides opportunities for health promotion, disease prevention and linkage to treatment²⁷⁸. Considering congenital syphilis is preventable, vigilant follow-up of patients undergoing treatment is essential to reduce the growing number of cases.

Certain researchers and public health experts have expressed the need to consider innovative strategies to promote prenatal syphilis testing. Potential strategies proposed have included testing pregnant individuals if they present to emergency rooms throughout their pregnancy, or encouraging syphilis screening for individuals who present to clinical settings for other concerns, such as symptoms of pelvic inflammatory disease²⁷⁹.

Additionally, ensuring access to care to populations such as Indigenous women with a suboptimal access to quality care is paramount. To achieve this, working on upstream factors that put women at higher risk for syphilis, and in consequence at higher risk of vertical transmission, are necessary to prevent congenital syphilis. This requires direct actions to address structural barriers. For cases born to Indigenous mothers, peer-education, provision of harm reduction services, and prevention interventions led and developed by Indigenous organisations, are therefore crucial to address the growing number of congenital cases in these communities²⁸⁰. The stigma, racism and discrimination that Indigenous women have historically and currently face, contributes to their mistrust of health care providers, and in consequence, their reduced access to health care. In

April 2019, PHAC, Health Canada and the British Columbia First Nation Health Authority signed the *Declaration of Commitment to Advance Cultural Safety and Humility in Health and Wellness Services and Organizations*²⁵¹. The aim of this declaration is to identify opportunities to reduce the systemic barriers and harms that Indigenous peoples experience, raise awareness about existing systemic discrimination, and address inequities in outcomes for Indigenous peoples²⁵¹. These actions are essential in addressing the structural barriers Indigenous women face when accessing health care. As mentioned in the Government of Canada's five-year action plan on STBBI, STBBI testing facilitates entry to care and provides opportunities for health promotion and prevention²⁷⁸. Reaching individuals by providing supportive and stigma-free testing environments facilitates dialogue on sexual health, mental health and substance use²⁷⁸. It will in turn allow improved health outcomes through sustained engagement with culturally safe health and social services²⁷⁸. Supporting women by eliminating stigma associated with sex and substance use, engaging them in their own care, and building trust is essential to increasing access to health care, and in consequence, reducing the number of congenital syphilis cases^{210,280}.

5.5.4 Identifying and addressing missed opportunities for diagnosis and treatment

In the case that congenital syphilis occurs, identifying the upstream factors that led to the vertical transmission of the disease is important to prevent new cases. Review boards have been implemented in the US to identify missed opportunities to prevent congenital syphilis cases. In a Canadian context, review boards would connect provincial and local health authorities along with representatives of key specialized programs such as harm reduction units to contribute to identifying and addressing opportunities to prevent congenital syphilis. In fact, according to a review board of all congenital syphilis cases reported from January 2016 to July 2017 in Louisiana (n=79), 59% (n=47) of congenital cases were deemed preventable or somewhat preventable if patients had received adequate prenatal care²⁸¹. Among these cases, lack of adherence to screening recommendations, lack of follow-up treatment, and delayed treatment, were listed as associated factors. In fact, CDC's Call to Action regarding syphilis outbreaks identifies the immediate treatment of women infected with syphilis and the confirmation of syphilis testing at delivery as key actions for the control of congenital syphilis²⁸². Review of congenital syphilis cases by the means of review boards and the identification of missed opportunities of care and prevention have also been ongoing in New Zealand and are included in their National Syphilis Action Plan²⁸³. By reviewing cases, it would be possible to identify gaps in access to care and improve the quality of care.

KEY MESSAGES

- From 1993 to 2017, the number of confirmed congenital syphilis cases reported was relatively low, ranging from one to ten cases per year.
- In 2018, the number of cases reached 17 confirmed cases (rate of 4.56 per 100,000 live births), and it is expected that the number of cases in 2019 will exceed 50 cases.
- Over time, the rate of congenital syphilis has loosely followed the rate of infectious syphilis among females of reproductive age, which was relatively low in the 1990s and increased steadily afterwards.
- Other countries have experienced similar increases in the number of congenital cases.
- Access to appropriate prenatal care, including syphilis screening and timely and effective treatment, have been identified as key interventions to prevent congenital syphilis.
- Ensuring compliance with screening guidelines, identifying gaps in access to care, and tackling upstream factors that lead to congenital syphilis, is essential to reduce the growing number of cases.

6. Interventions and policy for syphilis prevention and control

KEY MESSAGES

- Condoms are effective at reducing the risk of syphilis transmission.
- School-based sexual education initiatives can be effective in promoting sexual risk reduction strategies, including condom use.
- Programs or interventions that address the underlying social determinants of syphilis infection (such as addressing structural barriers to basic needs, managing co-infections, using culturally adapted approaches, and considering traumatic life experiences as determinants of health) may help curb outbreaks in Canada.
- Although educational social media campaigns around testing have been shown to be feasible, the evaluation of their effectiveness still appears limited.
- Syphilis testing in emergency departments may be a way to detect syphilis in vulnerable populations who do not have access to or avoid routine primary care.
- Online screening services have also been found to promote screening among harder-to-reach populations.
- Partner notification led by a health care professional may be a more effective strategy to ensure those contacted pursue appropriate screening and treatment than compared to partner notification led by the individual. However, patient-initiated notification may be a useful community-based tool to ensure outbreak surge capacity.

Given the shifts in the epidemiology of infectious and congenital syphilis cases across Canada in recent years, and the known social determinants of syphilis incidence, pressing questions remain concerning the best strategies to employ in order to prevent and respond to syphilis outbreaks in the country, as well as addressing the social inequities in syphilis incidence.

The <u>Pan-Canadian STBBI Framework for Action</u> identifies four pillars of action to address STBBI, including syphilis: prevention, testing, initiation of care and treatment, and ongoing care and support. In this section, we review published literature in Canada and abroad, and describe strategies to address syphilis in accordance with these pillars for action, starting with improving primary syphilis prevention, promoting access and uptake of timely syphilis testing, and ensuring effective case management and surveillance.

6.1 Primary Prevention

6.1.1 Healthy Sexuality Practices

Condoms are effective at reducing the risk of syphilis transmission⁶⁴. For example, in a study conducted by Ferlatte et al., in a pan-Canadian sample of 7,872 gbMSM observed that the odds of receiving a syphilis diagnosis were almost two times higher among those who did not use condoms during anal intercourse, compared to those who did, after adjustment for sociodemographic factors (aOR=1.9, 95% CI: 1.3-2.6)¹⁶³. Similar observations were made in other study settings, where syphilis diagnosis was associated with infrequent condom use^{148,221}. Female condoms can also prevent syphilis transmission⁶⁴. Studies conducted outside of Canada have also assessed the use of targeted condom distribution programs. Though organized condom distribution programs appear feasible, only a few studies have assessed the effectiveness of such programs in increasing condom use and reducing the risk of syphilis transmission²⁸⁴.

This section provides an overview of approaches to promoting the use of condoms for the prevention of syphilis, including education-based initiatives and educational resources for service providers.

Education-based initiatives

Though only a few studies in Canada have studied the effectiveness of interventions that promote safer sex practices in reducing syphilis incidence, studies conducted outside of Canada suggest that certain education-based initiatives to promote risk reduction strategies may be effective²⁸⁵. A literature review was conducted, which analyzed 62 non-Canadian studies of pedagogical group-based risk reduction interventions (which lasted an average of 15 hours and were delivered in school or community settings and delivered by a trained adult)²⁸⁶. These interventions were associated with reduced odds of condomless sexual activity (Odds ratio [OR]=0.70, 95% CI: 0.60-0.82) and higher odds of condom use (OR=1.49, 95% CI: 1.20-1.74) in adolescents²⁸⁶. They were also associated with reduced odds of STI diagnosis (OR=0.65, 95% CI: 0.47-0.90). Unfortunately, odds estimation pertaining specifically to syphilis risk reduction was not available. For youth, educational programs that address both pregnancy and STBBI prevention as well as distribute condoms appears to be effective in decreasing self-reported condomless sex^{285,287}.

The Sex Information and Education Council of Canada has recently released guidelines to help develop sexual health education programs targeting different sexual health issues²⁰⁴. The guidelines use established theoretical models to create the foundation of education programs²⁰⁴. In an intervention aimed to increase condom use, the Information-Motivation-Behavioural Skills Model was used to target three key areas to help encourage behavioural change: information, motivation, and behavioural skills²⁰⁴. The information component included aspects such as increasing knowledge of STIs, the effectiveness of condom use in preventing STIs and pregnancy, as well as where contraception can be accessed and how to use it. The information also addressed how to discuss contraception use with their partner, amongst other subjects²⁰⁴. The motivation aspect involved discussion of specific individual benefits to using condoms, vulnerability to STIs, personal responsibility, sexual scripts and gender norms, attitudes and norms of contraception use or non-use²⁰⁴. Finally, the behavioural skills portion helped participants practice and apply practice knowledge of how to access condoms and other barriers, how to negotiate condom use with partner, how to use condoms, how to engage in other forms of sex if condoms are unavailable, as well as scripting unilateral use of a condom amongst other

things²⁰⁴. These education programs help to increase the understanding of effective condom use as well as increase self-efficacy with regards to condom use²⁰⁴.

International organizations, such as the US CDC and the US National Institute for Health Care Excellence have also provided recommendations to support condom use promotion. Both institutions recommend providing condom distribution schemes or programs at structural levels to help change the environment and promote condom use^{204,288}. These interventions can include a variety of different projects, such as the distribution of free condoms, the use of social media campaigns, as well as policy change²⁸⁸.

Beyond condom use, researchers have also explored the importance of promoting healthy sexual relationships as a way to improve the uptake of safe sex practices. Given that gender socialization influences factors, such as age of first sexual contact, number of partners, as well as relative comfort levels in discussing and negotiating safer sex practices, including condom use, women can be at higher risk of experiencing domestic violence and face resistance in negotiating safer sex practices⁶⁰. Empowerment-based pedagogical interventions as well as interventions to improve financial independence between partners have been identified as upstream strategies to promote safer sex practices and prevent bacterial STI incidence in Canada⁶⁰. An example includes Quebec's northern region of Nunavik Good Touch/Bad Touch Program, which teaches body-safety and addresses the topic of abuse²⁸⁹. However, the need remains for rigorous studies on such interventions for reducing syphilis risk.

Lastly, researchers have also commented on the potential effectiveness of media-based educational initiatives in promoting safer sex practices for syphilis prevention. Following an analysis of the interventions implemented during Vancouver's syphilis outbreak in the late 1990s—which included a media-based campaign through mainstream media outlets, as well as street-level communications—researchers suggested that educational messages alone might prove insufficient to modify the behaviors that place certain individuals at higher risk of syphilis infection²¹⁸. Social marketing campaigns may also have a more limited effect on long-term condom use²⁹⁰. Researchers have noted that products and services designed to support the behavioural changes promoted by these campaigns may be relevant. These include extended clinic hours, free or low-cost testing options, including convenient testing sites, expedited testing processes, or subsidized transportation initiatives²⁹¹.

Resources for health care providers

Health professionals play a key role in educating sexually active patients on the risks of various sexual behaviours³. For this reason, PHAC's CGSTI offer several resources for health professionals, including motivational interviewing scripts about condom use and guiding questions for STI risk assessments to be used when providing counselling on safer sex²⁹². Given time constraints, concerns about patient privacy, and difficulties in asking patients questions pertaining to sex and sexual health, studies have explored the use of computer-generated consultation aids for primary care practitioners, and various institutions have proposed resources to guide discussions with adolescents or adults^{293,294}.

Fuzzel et al. interviewed 40 heterosexual teens and teens belonging to sexual minority groups (lesbian, gay, bisexual, pansexual, etc.), endeavouring to better understand their experiences of communicating with Canadian physicians about sexuality²⁹⁵. Both groups of teens noted that sexuality was not sufficiently discussed. Participants made a number of suggestions to address this gap in services, such as providing a welcoming environment for sexual minorities and using various tools to help teens educate themselves about sexuality (social media, websites, etc.).

Participants also noted that educational resources regarding sexual minorities might help clinicians to gain a better understanding of the issues and challenges faced by this population.

In response to observed structural barriers to health care and institutional stigma faced by sexual minorities, the Canadian Public Health Association (CPHA) has developed training and awareness workshops on stigma in sexual health services for health professionals. Evaluation of these materials by way of pilot workshops with health professionals in 14 Canadian cities was conducted throughout 2015 and 2016. The workshops focused on various forms of stigma and sought to make people more comfortable discussing issues around sexuality and STBBI²⁹⁶. The CPHA has developed a guide for service providers on methods to discuss sexual health, substance use, and STBBI, which is available free-of-charge online in both French and English²⁹⁷. PHAC has also developed resources to promote inclusive healthcare practice in the prevention of STBBI among ethno-cultural minorities, which are also available online²⁹⁸.

In the Chief Public Health Officer's latest Report on the State of Public Health in Canada (2019) entitled "Addressing Stigma – Towards a more inclusive Health System", an Action Framework for Building an Inclusive Health System was developed²⁵¹. The Action Framework provides direction on developing multi-level and comprehensive approaches that respect differences across stigma experiences, while offering potential lasting effects across these various experiences. For example, it includes approaches related to "cultural safety," which move away from a focus on differences in culture to a view of the health system environment as a site for change. Institutional-level cultural safety interventions include building partnerships with communities, creating safe and welcoming physical spaces reflective of the populations they serve (e.g., signage in Indigenous languages, sacred spaces in hospitals), institutional commitments to cultural safety, and hiring and supporting Indigenous healthcare providers. Healthcare organizations can also change internal policies to support cultural safety, such as creating flexibility in appointment scheduling to increase responsiveness, while building trusting relationships²⁵¹.

6.1.2 Pre-Exposure Prophylaxis

Syphilis can be treated using penicillin, the treatment of choice, or alternative antibiotics, such as doxycycline (for those who are allergic to penicillin)²⁹⁹. PrEP can be administered to individuals deemed to be at high risk of contracting infections and consists of daily intake of antimicrobials in order to reduce the risk of contracting disease. Currently, no Canadian studies have assessed the effectiveness of antibacterial PrEP on the acquisition of syphilis. At the time this report was drafted, exploratory research to assess the acceptability, feasibility, effectiveness, and potential antimicrobial resistance related to this strategy, was ongoing in British Columbia³⁰⁰. Previously, a 2018 study of 424 gbMSM in Toronto and Vancouver, documented that 44% of participants indicated willingness to use syphilis PrEP (60% were willing to use syphilis post-exposure prophylaxis if it was available)³⁰¹. Those most likely to indicate willingness to use syphilis PrEP were those who had previously or were currently using HIV PrEP, and those who reported being "very concerned" with STI acquisition³⁰¹. Additionally, a pilot study- the Dual Daily HIV and Syphilis PrEP (DuDHS) Study in Canada- is currently underway and is examining concurrent daily HIV PrEP (Truvada ®) and doxycycline PrEP in gbMSM without HIV. Fifty participants will take part in the study and will be randomized to immediate doxycycline PrEP vs. delayed initiation after six months; all participants will receive one year of HIV PrEP. The acceptability, adherence, and tolerability of daily HIV PrEP and doxycycline PrEP, as well as STI incidence and sexual behaviours of participants, will be examined³⁰².

A randomized, controlled pilot trial in the US studied the association between pre-exposure doxycycline use and syphilis incidence among a sample of high-risk gbMSM who live with HIV and who had had syphilis at least two times since receiving their HIV diagnosis. The authors found that doxycycline PrEP was associated with overall lower odds of infection of any STI (gonorrhea, chlamydia, and/or syphilis) after 48 weeks of follow-up (OR=0.27, 95% CI: 0.09-0.83). However, the association was not significant when considering syphilis acquisition alone (OR=0.24, 95% CI: 0.04-1.33, *p* value:0.10) possibly due to the small sample size (n=30)³⁰³. A qualitative US study conducted among 19 adult gbMSM who were diagnosed with early syphilis at least twice within the previous five years observed that PrEP was considered an acceptable intervention. However, respondents raised some concerns regarding potential side effects, development of antibiotic resistance (a topic which is explored in greater detail in section 6.3.8 below), and difficulties in following daily treatment protocols³⁰⁴.

It remains to be seen whether pre-exposure prophylaxis for syphilis prevention represents a feasible and effective strategy for outbreak prevention in Canada. Looking at the example of HIV PrEP in Canada, public health officials may face some challenges in promoting syphilis PrEP uptake. According to the 2017 EMIS report, approximately 8% of the 6,059 survey respondents from Canada reported currently being on HIV PrEP, despite 25% reporting condomless intercourse with non-steady partners of unknown HIV status in the past year, among other risk factors¹⁸⁸. The authors noted that general understanding of HIV PrEP was lacking, and recommended community-based education initiatives be used to promote knowledge to high risk groups¹⁸⁸. The same strategy may be needed for syphilis PrEP, if it is to be promoted in Canada.

6.1.3 Addressing Social Determinants of Health

Beyond clinical risk factors, several Canadian studies have documented underlying social determinants of syphilis infection (see <u>Section 4</u>). However, few Canadian studies have assessed how potential modifications of social or economic exposures may help reduce syphilis incidence.

Structural barriers

One Canadian narrative review summarized elements of conceptual frameworks related to potential action pathways to reduce health inequities, using an Indigenous health lens¹⁷⁴. Elements of successful interventions summarized in the review included the importance of addressing structural barriers such as access to food, water, and housing, managing STBBI co-infections, protecting patients' confidentiality, using culturally adapted approaches, and considering traumatic life experiences as both the determinants of health and of health services use¹⁷⁴. These elements are echoed in other Indigenous-led efforts, such as the Inuit Women of Canada's 2018 Ikajurniq Inuit Cascade of Care Framework for STBBI³⁰⁵. These frameworks and summaries express how strategies to address STI-related syndemics can be implemented at the patient care-, clinic-, and community-levels.

Health service-related actions

At a patient-care level, promising practices include asking patients about social challenges they are facing or ensuring that patient are referred to local resources, benefits programs, and support services¹⁷⁴. At the clinic level, use of patient navigators (individuals who guide patients through the healthcare system) or peer educators have been identified as a way to increase the uptake of health care services^{174,305}. Studies have also explored the use of an integrated sexual health care approach for service delivery³⁰⁶. Models in the UK, for example, have explored provision of services pertaining to contraception and reproductive health, infection care, sexual well-being, education, and partner notification, within a single clinic setting³⁰⁶. These types of integrated

approaches to general practice tend to be appreciated by patients seeking sexual health care services³⁰⁷.

Furthermore, insofar as adverse childhood experiences and experiences of interpersonal or sexual violence can influence the likelihood of seeking medical care, many scholars have promoted the importance of trauma-informed care³⁰⁸. The final report from the National Inquiry into Missing and Murdered Indigenous Women and Girls has also outlined the importance of developing a continuum of care grounded in a trauma-informed approach, which takes into account an understanding of trauma in all aspects of service delivery³⁰⁹. Several resources have been developed in Canada to support healthcare providers in creating safe environments (summarized namely by the Canadian Centre on Substance Abuse), including checklists to support organizational change^{310,311}.

Community-level actions

At the community level, cooperation with community groups and local leaders can help ensure that STI-related stigma is reduced, and that health inequalities are addressed or mitigated^{174,305,312}. An example of such practices observed outside of Canada was noted in a UK-based study of the modernization of a health clinic aimed to promote sexual health services for gbMSM. The clinic collaborated with charitable organizations and drug and alcohol support services to publicize their new clinical services³¹³. In Canada, examples of partnerships include those between First Nations communities, provincial health ministries and federal departments, such as Indigenous Services Canada, Health Canada, and PHAC. What remains to be seen is how specific examples of such approaches may successfully reduce syphilis incidence or help curb outbreaks in Canada.

6.1.4 Vaccination

Currently, no syphilis vaccine exists. Researchers have noted that an effective syphilis vaccine would provide a valuable contribution to syphilis prevention efforts, given that challenges exist in relation to the clinical diagnosis of the disease, and to effective treatment of infections (due to barriers in health care access, follow-up, and potential limitations in penicillin supplies)³¹⁴. Early Canadian evidence suggests that a vaccine may likely be acceptable to populations at high risk of infection. For example, a recent study of 293 sexual health clinic patients in British Columbia noted that 87% respondents would be interested in receiving an STI vaccine³¹⁵.

Experts have noted that vaccination programs targeted towards key populations, such as gbMSM, may be particularly effective in reducing syphilis incidence³¹⁶. Challenges in vaccine development include the need to ensure vaccine safety and effectiveness for pregnant individuals as well as individuals on HIV PrEP, or those who live with HIV³¹⁶. In 2019, the US National Institutes of Health awarded funds to researchers at the University of Connecticut to formulate and test candidate antigens for the eventual development of a syphilis vaccine³¹⁷.

Vaccination of higher risk individuals remains an important STBBI prevention strategy for other sexually transmitted infections, such as hepatitis A (HAV) and B viruses (HAV and HBV respectively), and human papilloma virus (HPV), which can co-occur in sexually active individuals³¹⁸.



Areas for Prevention

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Using condoms during vaginal, anal, and oral sex



Tackling stigma related to gender and sexuality in health care settings



Having trauma-informed and culturally adapted health care practices

Ensuring access to key resources such as housing and other social determinants of health

Areas for Future Research



Syphilis vaccine is currently unavailable



Syphilis PrEP effectiveness has yet to be determined in Canada



Syphilis prevention with an integrated approach has yet to be evaluated for feasibility and effectiveness

6.2 Screening – Methods to Increase Access and Uptake

As described in <u>Section 1</u>, regular screening for syphilis is recommended for individuals at higher risk of infection and for pregnant women. It is also mandatory for all individuals 15 years and over who undergo a medical exam for immigration¹⁴. Infection risk should be determined by consulting local guidelines and referring to the latest surveillance reports that describe risk factors.

Screening is an important strategy to detect infections earlier and identify individuals who require treatment³¹⁹. However, screening is accompanied by certain risks and costs, which must be weighed when considering changes to screening guidelines or policies. Possible harms of syphilis screening include the possibility of inaccurate results, unnecessary stress for the patient, and potential consequences related to unnecessary antimicrobial treatment³²⁰. However, existing estimates suggest that the reverse screening algorithm that is currently favored in most Canadian jurisdictions has a sensitivity, specificity, and validity of over 99%³²¹.

Published literature has explored interventions to either promote screening uptake among certain key populations, increase the frequency of testing, or reduce the time between testing and notification. Key findings are summarized below.

6.2.1 Educational Social Media Campaigns

Education-based initiatives and social marketing campaigns have been identified as potential areas of intervention to increase population-wide knowledge and uptake of syphilis testing. However, Canadian literature studying the effectiveness of education-based initiatives at improving testing uptake is limited. Available studies suggest that educational initiatives may have little impact on increasing public knowledge or promoting uptake of testing for syphilis, especially over the longer term.

One Winnipeg-based study evaluated the effectiveness of an advertisement-based intervention on social media and dating sites (the Gay ad Network, Facebook, Grindr and Squirt) to promote syphilis screening among gbMSM³²². They compared the number of syphilis tests ordered before and after the campaign's implementation and studied the number of "clicks" elicited by the advertisements. The month-long intervention generated 2,166 clicks (0.3% of the over 808,200 ad appearances) and led to no statistically significant change in the number of tests ordered in the city. Unfortunately, no data on the effects of the intervention among gbMSM, specifically, were available. Though this type of intervention appeared acceptable and feasible, its effectiveness appeared limited. In another example, a 2017 syphilis awareness campaign implemented in Vancouver ("Syphistory"), included the use of posters in gbMSM community spaces (physical spaces and online) as well as a website³²³. Of a sample of patients at STI clinics in Vancouver who were tested on their knowledge of syphilis before (n=137) and after (n=266) the campaign, no statistically significant difference in mean knowledge scores was observed pre- or post-campaign³²³.

These studies' null findings are similar to those from studies conducted outside of Canada. For example, an Australia-based study targeting 761 gbMSM found that their campaigns were not associated with a reduction of the time elapsed between infection and treatment³²⁴. Another study of a media campaign based in Florida, involving posters, cards, ads, and TV/radio public service announcements targeting gbMSM, found no significant change in knowledge of 851 participants about syphilis, clinic visits, or syphilis testing or treatment during the 6-month study period³²⁵. It has been noted that the integration of an evaluation phase in the planning of social marketing campaigns is critical, insofar as it may allow public health jurisdictions to adjust and adapt messaging and dissemination strategies²⁹⁰.

6.2.2 Integration of Syphilis into Other Routine STI Screening

Syphilis Testing During Routine STI Screening

Syphilis screening can be achieved opportunistically when individuals present themselves to health centres for regular STI testing or other health issues³²⁶. Though many Canadian PTs have embraced an integrated STBBI screening approach—once such example is Saskatchewan's "Test One, Test All" strategy, which promotes comprehensive STBBI testing, and is also currently employed by Manitoba—few studies have assessed the effectiveness of integrated screening strategies in Canada^{106,327}.

Outside of Canada, interventions have been explored to adapt screening guidelines to increase screening uptake and reduce rates of STIs. For example, in Australia, in 2002, screening guidelines for gbMSM were updated (these were later revised in subsequent years) to

recommend that all men who have had any type of sex with another man in the previous year be tested for multiple STIs (including syphilis) every year. A study of gbMSM attending a sexual health clinic in Sydney reported that 61% of patients were screened for the complete list of STIs, following the guideline implementation, compared to 46% before implementation (p<0.05) (n=559)³²⁸. In the 2014 version of Australia's guidelines, all gbMSM who had had any condomless sex, had more than ten sexual partners in the previous six months, participated in group sex, used recreational drugs during sex, or who were living with HIV, were recommended to be screened for all designated STIs (including syphilis) up to four times per year³²⁹.

Syphilis Testing During Routine HIV Clinical Monitoring (among People Living with HIV)

In Canada, early evaluations have explored the effects of integrating routine syphilis screening in HIV testing or monitoring programs. A study of 3,893 HIV-positive men in Ontario found that the inclusion of syphilis serological testing with HIV load testing led to a small, but statistically non-significant, increase in detection of new cases of infectious syphilis (2.5 cases per 100 person-years of follow-up in treated vs.1.5 cases in controls receiving provider-initiated syphilis testing)³²⁶. Outside of Canada, an Australian study compared testing-related outcomes 18 months before and after a sexual health centre in Melbourne implemented a policy to include syphilis screening with every routine blood sample collected from gbMSM patients who were HIV-positive³³⁰. The authors observed an increase in the median number of syphilis tests and in the proportion of asymptomatic syphilis infections diagnosed³³⁰. A US study (n=245) identified a higher syphilis detection rate (16%) after syphilis testing was included in routine clinic-based HIV monitoring compared to the pre-intervention rate (7% detection rate)³³¹. An Australian study also noted that increasing testing coverage in gbMSM living with HIV via opt-out syphilis testing during routine HIV monitoring was associated with a reduction in the proportion of syphilis cases detected at a secondary stage³¹⁹.

Frequency of syphilis testing among higher risk groups

Few studies have explored the frequency at which syphilis screening should occur for populations at higher risk of infection. A US study assessed various screening frequencies (quarterly, semiannually, and symptom-based) and their association with early syphilis detection in a sample of gbMSM and transgender women using HIV PrEP (n=557))^{259,332}. The results indicated that 20% of detected syphilis cases would have been missed without guarterly testing. Furthermore, a mathematical modeling study conducted in Winnipeg noted that focused screening every three months for gbMSM who had a high number of partners (i.e., using existing evidence, authors estimated that approximately 20% of all gbMSM had approximately ten or more partners in the preceding six months) could potentially avert 59% of incident cases and reduce syphilis prevalence by 95%³³³. Enhanced quarterly screening of gbMSM with a prior diagnosis of syphilis could reduce incident cases by 52% and prevalence by 89%³³³. Manitoba's Winnipeg Regional Health Authority currently encourages ongoing STBBI testing every three months for gbMSM³²⁷. In the context of Winnipeg, gbMSM represented 80% of infectious syphilis cases diagnosed between 2011 and 2015 (171 of 213 cases), and the estimated size of the gbMSM population in the city was approximately 7,100 (3% of the city's estimated 237,760 men in 2011)³³³. However, the proportion of syphilis cases who are female has consistently increased in Manitoba since then (Section 3.2). It is possible that these high frequency, targeted testing strategies may be less relevant in contexts with different demographic profiles or in which most syphilis cases are heterosexual.

Although quarterly testing may be ideal in some epidemiologic circumstances, it may be difficult to achieve. Since 2005-2006, Australia has recommended opt-out quarterly syphilis testing in men living with HIV as part of routine HIV monitoring. The change in screening guideline was

associated with an increase in syphilis testing. However, only 41% of individuals succeeded in undergoing quarterly testing³³⁴.

6.2.3 Outreach Screening Activities

Venue-based targeted outreach screening interventions have been identified as a potential strategy to increase syphilis screening uptake among more vulnerable populations. These interventions can occur in spaces that are frequented for sex, such as saunas and commercial sex venues, events linked to sexual activity, such as adult lifestyle conferences, or clinical spaces, such as emergency departments.

Community spaces (bars, hotels, drop-in centres)

To date, the effectiveness of place-based screening interventions to promote screening uptake and case finding has rarely been studied in Canada. One descriptive study of Vancouver's syphilis outbreak in the late 1990s noted that in the 30 months between July 1997 and December 1999, outreach workers provided syphilis testing in bars, hotels, and community spaces frequented by sex workers. However, despite these concerted place-based screening efforts, few new cases were identified. The number of tests conducted and cases diagnosed was not provided. The researchers posited that low diagnosis might have been due to low overall prevalence of the disease, even in the outbreak context, and that those most vulnerable may not have frequented the selected locations²¹⁸.

Saunas and commercial sex venues

Studies have also documented interventions in sex-based venues. In the UK, following an increase in syphilis incidence in Walsall, England, a survey on risk-taking behaviour and syphilis screening was administered at a local sauna frequented by gbMSM. The survey identified four of the 51 cases (8%) diagnosed between 2003 and 2004, and 73% of the study's 142 respondents indicated that they would use screening services if they were provided in a community setting, such as the sauna³³⁵. In Brisbane, Australia, a survey (n=1,653) was administered at two outreach clinics that were located at private male saunas and a mainstream health clinic³³⁶. The sauna-based clinics drew a higher proportion of gbMSM to testing, and identified five of the 16 (31%) syphilis diagnoses during the study period, despite a lower number of visits compared to the mainstream clinic³³⁶. These findings led the authors to conclude that targeted health clinics in male saunas may be an effective strategy for promoting syphilis screening and case identification.

Events

While many STI testing kiosks and events have been implemented in Canada, especially around HIV Testing Day (June 27th), or Pride events across the country, few Canadian studies have assessed the effectiveness of event-based screening initiatives in increasing screening uptake^{337,338}. Outside of Canada, one UK-based study assessed the merits of STI screening outreach in a National Health Service health bus at two adult sexuality and lifestyle events and exhibitions (London's Erotica 2013 and Sexpo 2015 events)³³⁹. A total of three syphilis cases were identified among the 381 individuals screened at the events (of over 20,000 attendees). Though the proportion of attendees who accessed the screening services was low, the authors observed that many of those screened had never been screened in their lifetime (31% had never had an HIV test before).Thus, the event may have helped screen populations that have limited access to care³³⁹. Another example was an evaluation of a syphilis and STI testing tent set up at the annual Sydney Gay and Lesbian Mardi Gras Fair Day in Australia. The tent's services were restricted to gbMSM who had had sex with another man in the past year. Very few of the fair's total participants were estimated to have frequented the tent (approximately 0.23% to 0.26%),

and the cost of running the service was relatively high³⁴⁰. Moreover, in contrast to the previous study's findings, only 18% of these participants had never been tested for STIs in their lifetime³⁴⁰. This initiative identified only one infectious syphilis case.

Emergency departments

Emergency departments have been identified as a potential relevant site for targeted syphilis screening for two main reasons. First, for populations who do not have access to, or are less likely to use routine primary care services, emergency departments can represent a more accessible clinical setting³⁴¹. Second, identifying cases within hospital settings can facilitate treatment follow-up³⁴². Outside of Canada, a US-based study assessed the feasibility and effectiveness of using syphilis POC testing in emergency departments on men aged 18 to 34 during a syphilis outbreak that was occurring among gbMSM living with HIV in Detroit³⁴². Among 871 patients tested, six (0.7%) active syphilis diagnoses were identified³⁴². The authors concluded that the implementation of emergency-department syphilis screening was feasible to detect new syphilis cases. Currently in Canada, Saskatchewan and some areas of Alberta are exploring ways to promote screening in emergency departments.

Correctional facilities

Few Canadian studies have explored opportunities for syphilis screening outreach in provincial or federal correctional facilities in Canada. A study of STBBI testing between 2012 and 2015 in three provincial correctional facilities in Alberta found that syphilis prevalence was 3.2% overall (n=5,135)³⁴³. Prevalence was significantly higher in adult facilities (remand and mixed long-term and remand; 3% to 4.1% prevalence) compared to youth facilities (0.4% prevalence), and higher in female compared to male facilities (5.4% versus 2.4% prevalence, respectively)³⁴³. The authors propose that an "opt-out" screening strategy—through which patients would be routinely screened for syphilis and all other STBBI unless a patient refuses—be considered for correctional facilities³⁴³. The province of Alberta followed that recommendation and implemented an STBBI opt-out testing in provincial correctional facilities in 2019.

Door-to-Door visits

Although this approach may not be feasible in all areas or jurisdictions, a pilot of systematic doorto-door visits was implemented in Quebec's northern Nunavik region to promote STBBI screening for all without singling out specific settings or households¹⁸⁵. Community residents expressed appreciation for the home visits, given their hesitancy in visiting local health clinic because of privacy and stigma concerns¹⁸⁵. Although most new STI cases identified were of chlamydia and gonorrhea, at least five syphilis cases were identified¹⁸⁵.

6.2.4 Communications (SMS) Reminder Systems

One of the strategies explored to promote syphilis screening uptake among higher-risk groups was the use of texting-based (i.e. Short Message Service (SMS)-based) reminder messaging³²⁶. To date, Canadian studies have yet to explore this area of intervention. Evidence from other countries suggest that although this strategy is feasible, evidence on its acceptability is mixed. For example, one US-based study examined the acceptability of quarterly SMS STI testing reminders (using 2SMS software), offered to (n=4,087) gbMSM who had been diagnosed with syphilis, gonorrhea or chlamydia ^{344,345}. The SMS content was: "It's time for your follow-up testing at Harborview" (Harborview was the largest hospital in the county). Of those offered the SMS reminders, only 13% accepted (80% refused, 7% received some other form of SMS reminder). Among those who refused, 37% used no other form of reminder (i.e. no reminder from medical providers, no testing during routine physicals, no smartphone app or calendar reminders, etc.)³⁴⁵.

A qualitative US study of 19 adult gbMSM diagnosed with early syphilis at least twice within the previous five years, noted that though most respondents viewed automated text or email-based reminders favourably, they also expressed two areas of concern. First, participants feared that the message content could be viewed by someone else (a partner, parent) who may look at their phone. Second, participant expressed concerns about redundancy, given that they already had mechanisms in place to remind themselves to be tested regularly³⁰⁴.

Studies on the effectiveness of these interventions for increasing the likelihood of repeated screening obtained mixed results. One US study found no statistically significant difference in STI screening re-attendance between intervention and control groups (all of which were high-risk patients) following the implementation of a SMS reminder system (intervention group n=274, control group n=266)³⁴⁶. In contrast, an Australia study of SMS reminders used to promote STI retesting among gbMSM found that those receiving the text messages had four times higher odds of re-testing compared to the study's comparison group³⁴⁷. It remains to be seen how this type of intervention would affect re-screening in Canada.

Automated reminder systems have also been designed to target health care professionals during healthcare consultations. For example, researchers in Australia studied the use of a computer alert system that reminded health professionals of the recommended frequency of syphilis screening for higher-risk gbMSM, and found that it was associated with an increase in syphilis screening uptake in the latter population (n=6,789 consultations before intervention; n=8,036 consultations after intervention)³⁴⁸. Studies of such interventions in Canada have yet to be conducted.

6.2.5 Express Testing and Triage Systems

As a way to promote the accessibility, feasibility and acceptability of syphilis and STI screening, researchers and health settings have explored ways to streamline STI screening among certain groups. Various strategies fall under the rubric of "express" testing. These interventions, typically implemented in primary care settings, are designed to shorten wait-times for testing for a predefined sub-group of patients. Strategies include the offering of a walk-in screening system for high-risk groups, or the possibility for low-risk groups to skip physical examinations and pass directly to specimen collection^{313,349}. These have been implemented in Alberta and in Quebec's northern Nunavik region^{185,349}.

A study based in Edmonton assessed the impact of express testing for 4,789 low-risk patients on total visit time and the number of STIs diagnosed³⁴⁹. Individuals who were asymptomatic, had not had contact with a person with an STI, had not had receptive anal intercourse since their last testing visit, had no history of sexual assault in the last two weeks, and had no involvement in transactional sex in the previous six months were considered low-risk. These patients were given the option to forgo a complete physical examination and pass directly to specimen sampling for STBBI testing³⁴⁹. This clinical policy change was implemented as a strategy to curb wait times and reduce the number of patients who were being turned away from the clinic. The authors observed that visit times with a registered nurse were reduced by a median of 13 minutes per low-risk female visit and 9 minutes per low-risk male visit³⁴⁹. Though the absolute number of visits associated with a syphilis diagnosis was higher post-intervention (67 post- vs. 22 pre-intervention), the proportion of visits resulting in diagnosis of syphilis was smaller post-intervention (0.1% post- vs. 0.2% pre-intervention) (*p* value=0.03)³⁴⁹. The authors also noted that a higher proportion of high-risk patients was diagnosed with STIs following the policy change. Though this increase in the number of visits post-intervention may be due to increasing secular trends in STI

rates over the study period, the authors posit that the increase may also be attributable to higher overall testing capacity made possible by time saved through express testing³⁴⁹.

6.2.6 Online Screening Services

Among the strategies to link individuals to testing are web-based interventions through which patients answer sexual history questions online and can then receive a test requisition form to use at a local laboratory. In 2014, the BCCDC launched its GetCheckedOnline website, which surveys users on their sexual history, generates a test requisition, and links them to designated specimen collection centres in Vancouver²⁷¹. The website also links to an online appointment booking system to make an appointment for sample collection³⁵⁰. Results are communicated online via the GetCheckedOnline account. Between September 2014 and December 2015, 868 users created accounts on the platform. Of these, 43% were gbMSM, and 13% were tested for STIs for the first time. A total of 37% submitted specimens and 3% received a positive STI diagnosis²⁷¹. Researchers evaluating the intervention concluded that *GetCheckedOnline* is an acceptable and feasible intervention, with the capacity to promote screening among populations that traditionally may have been under-screened²⁷¹. Based on these results, *GetCheckedOnline* was expanded to selected communities in Vancouver Island and Interior BC in March 2016³⁵¹. A later study of the platform, comparing 1,093 clients using the website to the 18,404 STI clinic clients in the province between 2014 and 2017, found that GetCheckedOnline clients were more likely to be women or men who have sex with women (compared to gbMSM), have a history of STI diagnosis, and to have a partner living with HIV³⁵². GetCheckedOnline clients also demonstrated a higher rate of repeat testing, suggesting the interface may facilitate repeated testing if the latter is needed³⁵².

Results from British Columbia are aligned with findings of studies conducted outside of Canada, including a study conducted in the UK (n=2,072), which also reported higher rates of completion rates of STI testing in groups receiving online screening services³⁵³.

Despite the latter strengths, a qualitative evaluation with 39 respondents prior to BC's GetCheckedOnline implementation reported certain concerns with internet-based testing that could prevent participation in online screening services. These include reluctance to share personal data online, mistrust of data protection mechanisms, and concern over inadequate preor post-test counseling³⁵⁴. Mitigation strategies to address these concerns include strategies to ensure data privacy and security, and provide sufficient resources and referrals for counseling and support services³⁵⁴.

6.2.7 Incentive-Based Screening

One of the strategies proposed to promote screening uptake is to use financial incentives (e.g., cash payments, conditional cash transfers, vouchers). Though there is evidence that STI health clinics in Canada have used incentives, such as the use of gift cards or lunches —namely, in Saskatchewan and Alberta—to promote STI screening and treatment, the effectiveness of these incentive-based strategies has not been widely studied³²⁷. In Edmonton, Alberta, an intervention was implemented, which offered a \$10 gift card for STI testing, including syphilis testing, and another gift card of the same amount for returning to obtain results and treatment. This intervention was targeted at individuals who resided in subsidized housing locations, were street-involved, or who frequented community-based organizations³⁵⁵. Among the 342 individuals who participated, 34 individuals tested positive for syphilis (11% seropositivity rate). Most participants (60%) reported substance use, 19% reported injection drug use, and 6% reported involvement in transactional sex³⁵⁵. The authors conclude that incentivized testing may be an effective approach

for improving STI testing among populations who may be less likely to access regularly primary health care³⁵⁵.

Outside of Canada, a qualitative US study of 19 gbMSM adults diagnosed with early syphilis at least twice within the previous five years, asked participants if they would take advantage of getting paid for syphilis testing, and if so, what amount they would want to receive³⁰⁴. Most participants were favorable to financial incentives, and monetary amounts preferred ranged from \$0 to \$100, with at least one of the 19 participants expressing an interest in receiving compensation for transportation to the clinic and hours missed at work³⁰⁴. These findings should be interpreted with caution, however, given the small sample size and distinct health service context of the study.

6.2.8 Point-Of-Care Testing

POC testing refers to medical diagnostic testing used outside of a clinical setting. POC testing for syphilis has been proposed as a strategy to increase the accessibility of screening in populations that may be more hesitant or unable to access traditional screening.

Rapid point-of-care testing

Rapid POC testing allows for a rapid sample collection, testing, and results, which can all be communicated in a single session by a health professional, with the possibility of follow-up sessions as needed (for confirmatory results communication and post-test counseling).

There are two main types of POC syphilis tests: (1) Immunochromatographic strip tests, which react to whole blood or serum when antibodies are present, and (2) particle agglutination tests, wherein treponemal antigen-coated gelatin particles clump together when in contact with whole blood or serum, in which antibodies against *Treponema* are present³⁵⁶. These tests cannot differentiate between a new or previous infection, and require additional confirmation using quantitative non-treponemal testing³⁵⁶. Due to these limitations, researchers have indicated that rapid POC tests would be of most benefit in areas with low but rising rates of infectious syphilis or low rates of screening and testing^{356,357}.

Although there exist over a dozen rapid POC syphilis tests to detect treponemal antibodies, to date, no rapid POC syphilis tests have been approved for use in Canada³⁴². While POC tests for syphilis are not routinely used in Canada, they have been used in research studies. For example, an Edmonton-based study assessed the acceptability and field performance of rapid POC tests for syphilis (SD Bioline 3.0 test) in key populations (gbMSM, people engaged in the sale or purchase of sex, persons who inject drugs, Indigenous people, etc.) in clinical and community settings (n=1,183)³⁵⁸. Acceptability of the test was high, as 82% of individuals approached agreed to be screened. Testing performed at places frequented by gbMSM (e.g., saunas, etc.) had the highest acceptance rate (91% tested), followed by drug rehabilitation facilities (89%), detention centres (80%), healthcare facilities (74%), and community organizations (70%). High acceptance may have been attributable to the sample, insofar as tests were being offered to a group of people who had largely been screened previously. Nonetheless, findings are aligned with qualitative evidence outside of Canada that indicated the high level of acceptability of POC testing^{304,359}. A study funded by the Canadian Institutes of Health Research will commence shortly in the Arctic communities of Nunavut and Nunavik to evaluate the acceptability, performance and utility of a point-of-care test for syphilis³⁶⁰.

Another international multi-site study with a study arm based in Montreal, Quebec, assessed the feasibility and impact of a multiplex rapid POC syphilis test, which could also test for HIV, Hepatitis

C virus (HCV) and HBV (Miriad Rapid TP/HBV/HIV/HCV Antibody Test) in a sample of at-risk individuals (n=375 in Mumbai, n=119 in Montreal)³⁵⁷. They found that 92% of individuals agreed to testing, and that 97% of respondents preferred the multiplex test to conventional testing, and 99% would recommend it to others³⁵⁷.

Though evidence shows that POC testing appears highly acceptable, regulatory approvals, clinical guidelines, and accompanying screening and quality assessment policies are necessary to ensure how and where POC testing can have a meaningful impact on halting transmission of infections³⁶¹.

Dried blood spot testing

Although not a form of rapid POC testing, dried blood spot (DBS) testing for syphilis has been proposed as a complementary alternative to standard syphilis testing³⁶². DBS samples do not require refrigeration, are very stable, and can be collected by non-medical professionals, making them particularly useful for populations who may be hesitant to seek screening services due to systemic barriers and stigma, or communities in remote areas^{362,363}. DBS samples can also be transported via novel technological methods, such as drones, to microbiology laboratory sites³⁶⁴.

Interventions using DBS testing are currently implemented in Canada, namely in Alberta, Saskatchewan, Ontario and Prince Edward Island^{363,365}. Preliminary evidence from a DBS testing implementation in a First Nations community in Ontario indicated that DBS testing is highly feasible and acceptable³⁶³. However, some concerns remain in relation to the communication of results back to participants, and time required to adequately perform the tests³⁶³. These preliminary Canadian results are aligned with those from other countries, which indicate high feasibility and acceptability in higher risk groups, such as gbMSM and people living with HIV and HBV³⁶⁶.

6.3 Case Management

6.3.1 Partner Elicitation and Identification

Identifying partners depends on an individual's willingness and ability to disclose information on sexual partners. Life course histories of discrimination or anticipated stigma can lead individuals to fear disclosing contacts. Indeed, a study by Lukac et al. conducted in 2017 (n=491) found that gbMSM living with HIV were less likely than gbMSM who were HIV-negative to disclose their sexual partners to the public health nurse (70% vs. 80%)³⁶⁷. Other documented barriers of partner elicitation in Canada include mental health or substance use issues, which prevent cases from being able to complete interviews, as well as partners being anonymous and unidentifiable²¹⁸.

Social network elicitation questions

Various strategies have been detailed in the literature to encourage partner elicitation. In Canada, some public health units have adapted how they inquire about sexual contacts, namely by asking broader question such as "Who do you hang out with?" rather than asking individuals to name their sexual partners³⁶⁸. It remains to be assessed whether using alternative questions during partner elicitation interviews represent more effective strategies for partner identification than traditional approaches.

Use of communicable disease investigators

A literature review conducted by the BCCDC noted that several existing studies have observed that the use of Communicable Disease Intervention Specialists (non-medical staff specialized in

communicable disease follow-up activities) placed in outbreak sites and health departments, has been associated with greater success in eliciting contacts compared to conventional public health or health care providers³⁶⁹. Communicable Disease Intervention Specialists have been utilized predominantly outside of Canada, especially in the US³⁷⁰. Their strength is a specialization in finding and providing supportive services for patients diagnosed with STIs and their contacts^{369,370}.

Targeted elicitation interviews

BCCDC's literature review also noted that existing literature supports targeting elicitation interviews and partner notification to higher risk groups when faced with limited resources³⁶⁹. These groups include partners who are more vulnerable to negative health outcomes, including STI transmission, those who themselves may have more partners and are more likely to contribute to onward community transmission, and those who may be more hesitant or less likely to access STI testing and care services³⁶⁹. The need for assessment of the effectiveness of targeted partner elicitation and notification practices in Canada remains.

6.3.2 Partner Notification

The notifying of partners is a secondary prevention measure to identify sexual partners of confirmed syphilis cases so they can be offered testing and treatment, and thus reduce the risk of infection in the original patient or others²⁹². PHAC's STI guidelines recommend that all sexual or perinatal contacts of primary syphilis cases be notified within a 3-month trace-back period (i.e., the time prior to symptom onset or date of specimen collection if asymptomatic). Additionally, the trace-back period is six months for secondary syphilis, one year for early latent syphilis. All long-term partners and children of individuals diagnosed with late latent and tertiary syphilis should also be notified²⁹². Various approaches designed for successful notification of partners are presented below.

Patient or health professional-led notification

Partner notification may be completed directly by the patient receiving the syphilis diagnosis or can be carried out by a health professional. Though more costly and resource-intensive, existing Canadian literature suggests that notification led by health professionals may be a more effective strategy to ensure a patient contacts pursue appropriate screening and treatment^{371,372}. For example, in a Canadian study of partner notification outcomes among gbMSM in British Columbia from 2010 to 2013 (n=350), researchers observed that a greater proportion of partners was tested for syphilis when notified by a health professional (54%) than when notified by the patient (21%)⁵⁷. These findings align with those observed outside of Canada³⁷³. Furthermore, in certain circumstances when protection of anonymity is paramount, such as when an index patient may have experienced sexual assault or may be concerned about the potential emotional or physical consequences of referring a partner, professional-led notification remains an important method^{371,372}.

However, patient-initiated partner notification remains a useful approach. Many patients prefer having the option to communicate directly with their sexual partners about potential exposure to an STI³⁷². Furthermore, the growing number of syphilis cases across several jurisdictions in Canada continues to place pressure on front-line workers, especially public health nurses, to keep up with partner notification. Ensuring appropriate availability of human and financial resources to appropriately identify and contact partners is already a challenge for several jurisdictions³⁶⁹. A recent study from British Columbia documented that of the 648 infectious syphilis cases confirmed among gbMSM in the province between 2006 and 2016, 42% of first-diagnosed and 62% rediagnosed cases chose patient-initiated partner notification (rather than provider-initiated)³⁷⁴. Among those with a first diagnosis of syphilis (73% of gbMSM cases), patient-initiated partner

notification led to a 19 percentage-point higher proportion of partners' notified (89%), compared to provider-initiated cases (70% partners notified)³⁷⁴. Patient-initiated partner notification is a valuable strategy, especially during outbreaks.

Cluster notification

Enhanced syphilis contact tracing and notification using a cluster-based approach may be useful, and it has been carried out previously in Canada (e.g., to investigate an HIV outbreak in Saskatchewan, or in response to a syphilis outbreak in British Columbia)^{375,376}. In this approach, index patients are asked to identify others in their social networks or community whom they believe may benefit from counseling and testing (e.g. "Who do you think should be tested for syphilis?"³⁷⁵⁻³⁷⁷. Though this approach may result in a smaller proportion of positive cases compared to one based solely on contacting sexual contacts, it remains a potentially useful approach in areas with high infectious syphilis rates, and can additionally provide useful information for social network analysis³⁷⁸.

Internet-based notification

In Canada and abroad, given the increased use of dating apps and websites, strategies have been explored to find and notify contacts of cases via web-based channels. Though these approaches may be perceived as more impersonal, they are especially relevant when partners meet and communicate online, and when contact information traditionally used to trace contacts is more challenging to obtain³⁷¹.

A recent Canadian literature review summarizes two broad types of approaches for internet-based partner notification (those applied through social networking sites and those contacting cases via email), as well as potential challenges that may occur when applying such strategies³⁷⁹. The review found that most partner notification strategies applied via social networking sites required public health entities to have a profile on the site in question, and communicate with the profiles provided by index cases³⁷⁹. Outside of Canada, published studies suggest partner notification via social networking sites is largely feasible and acceptable, including with certain key populations, such as gbMSM³⁸⁰⁻³⁸⁷. It has also been associated with an increase in the number of partners notified and screened^{380,384}. Given the paucity of Canadian evidence, whether such interventions would be effective in Canadian contexts remains to be assessed. The provinces of Alberta, Saskatchewan, and Newfoundland and Labrador are currently exploring innovative approaches to partner notification via social media and dating apps.

Another internet-based notification strategy has been the use of websites to facilitate anonymous email contact notification. In Canada, these include British Columbia's CheckHimOut site, which allows for anonymous contact notification through email or text message and provides information about local sexual health clinics for testing³⁸⁸. Another similar website is InSpot.org, which allows individuals to notify partners in Ottawa, Toronto, or in British Columbia that they may have been exposed to an STI. Outside of Canada, sites include Australia's Let Them Know and the Netherlands' Suggest a Test platforms^{389,390}. Studies evaluating these types of programs are limited. Those that exist suggest that website-based contact notification is largely acceptable, especially for those in more casual relationships³⁹¹. However, despite advertising campaigns to promote the use of sites, uptake tends to be low^{392,393}. Website-based approaches face an additional challenge if potential users do not have the email addresses of their contacts³⁷⁹.

6.3.3 Treatment

Early, successful treatment of syphilis remains an important strategy for outbreak management and secondary prevention. Treatment reduces the duration of infectivity and transmission efficiency¹⁴⁴. Current Canadian STI guidelines recommend that non-pregnant adults with infectious syphilis be treated with a 2.4 million units of benzathine penicillin G, as a single dose administered intra-muscularly³. Suggested treatments vary slightly for non-infectious syphilis, for pregnant individuals and infants with congenital syphilis³. Currently, the CGSTI recommend that all sexual and perinatal contacts be located, tested and treated if serology is reactive³. The guidelines also note that if follow-up cannot be assured, it may be appropriate to administer a post-exposure prophylaxis for infectious syphilis³. In general, clinicians are advised to consult with their provincial and territorial guidelines to guide their prescription practices.

Decreasing delays in treatment

Few Canadian studies have assessed potential strategies to reduce delays between syphilis diagnosis and treatment. Among the strategies used outside of Canada are SMS-based test result communication strategies³⁹⁴. A US-based study (n=4,081) used a text-messaging strategy to convey STI test results and found that over half of the study participants (57%) who received the intervention were treated within one to four days, compared to 41% in the control group³⁹⁴. Researchers noted that in the study context, up to 50% of patients were offered presumptive treatment the day of testing, and these cases were therefore excluded from the analyses. In contrast, a UK-based study of an online screening and SMS messaging intervention (n=2,072) found no statistically significant difference in time to treatment between treated and control groups³⁵³. However, the latter study did not provide treatment delays by STI type. Results from these two studies are difficult to compare given differences in the operationalization of their outcomes measures. The first study presents differences in the proportions of cases treated one to four days after receiving results (versus eight or more days or never)³⁹⁴, while the second study presents differences in mean time to treatment³⁵³. Given the heterogeneity in study measures and limited available evidence, it remains unclear whether such communication-based interventions could contribute to reducing treatment delays in Canada. Therefore, further research is required.

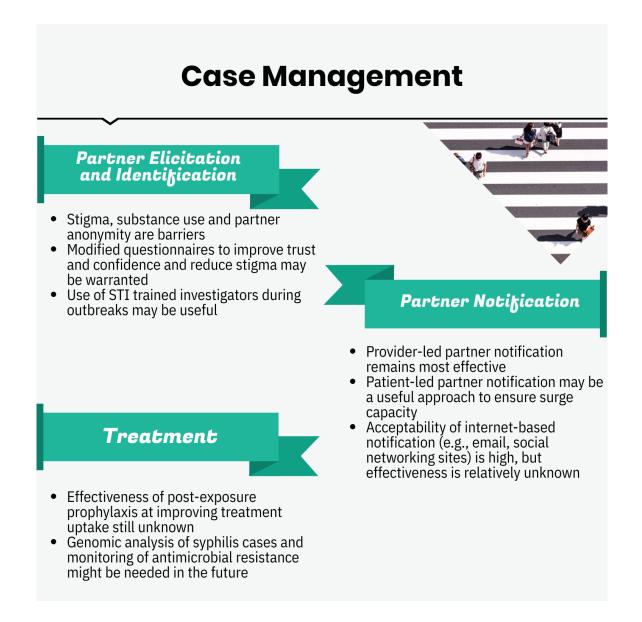
Post-exposure prophylaxis

Currently, no Canadian studies have assessed the effectiveness of antibacterial post-exposure prophylaxis (PEP) on the acquisition of syphilis. However, use of the latter may represent a potential strategy to reduce syphilis incidence in higher-risk populations³⁹⁵. A randomized controlled trial conducted in France assessed the effectiveness of PEP with doxycycline at reducing risk of a first episode of syphilis among 232 HIV-negative men who have condomless sex with men and who were currently using PrEP for HIV prevention³⁹⁶. The study observed a statistically significantly lower risk of syphilis acquisition among those receiving PEP compared to those who were not (Hazard ratio=0.27, 95% CI: 0.07-0.98)³⁹⁶.

A recent study (2018) of 424 gbMSM in Toronto and Vancouver documented that 60% of participants indicated willingness to use syphilis PEP if it was available. It remains to be seen whether syphilis PEP represents a feasible and effective strategy for outbreak control and prevention in Canada³⁰¹. Looking to the example of HIV PEP, challenges may occur if such a treatment strategy is promoted in Canada, including issues of general awareness of syphilis PEP and barriers to access. For example, according to the 2017 European Men-Who-Have-Sex-With-Men Internet Survey, 26% of the Canadian sample of 6,059 gbMSM remained unaware of HIV PEP, and almost half (47%) were not confident they could access PEP¹⁸⁸. The findings suggest that visible and accessible services as well as community education initiatives are among the strategies that could increase PEP awareness and use. A similar strategy may be needed for syphilis PEP if ever it is to be promoted¹⁸⁸.

Antimicrobial resistance

Existing studies have begun to document the emergence of antimicrobial-resistant syphilis infections, and to predict whether resistance will become a global issue³⁹⁷. For example, macrolide- (alternative antibiotics to penicillin) resistant T. *pallidum* strains have been observed in Canada, China, Europe, and the US^{48,398,399}. These have been associated with a specific mutation in the pathogen (mutations in the *T. pallidum* 23S rRNA genes)³⁹⁸. Specific mutations and *T. pallidum* strains known to have antimicrobial resistance can be identified by genomic analysis. Experts recommend that all syphilis patients who receive macrolides be closely followed, clinically and serologically, to identify instances of resistance³⁹⁸. In addition to treatment failures of HIV co-infections or other clinical issues, the risk of increased antimicrobial resistance is among one of the reasons why some scientists continue to advocate for the need to develop a syphilis vaccine³¹⁴.



6.4 Surveillance

Syphilis is a notifiable disease in Canada, and therefore passive surveillance of reported cases is conducted via CNDSS. In addition to this standard passive syphilis surveillance, other surveillance strategies have been employed in Canada to track syphilis trends and inform outbreak management.

6.4.1 Enhanced Surveillance

Enhanced federal surveillance activities

At the federal level, in collaboration with PT partners, community organizations and academic researchers, PHAC has designed and launched the Tracks enhanced surveillance system⁴⁰⁰⁻⁴⁰³. The Tracks involves periodic, cross-sectional surveys at sentinel sites across Canada of key populations (gbMSM, people who inject drugs, people born in countries where HIV is endemic, youth who are living on the streets, and Indigenous peoples)⁴⁰¹⁻⁴⁰⁵. Given its non-random sampling methods, Tracks surveillance findings may not be generalized to the entire Canadian population. Enhanced survey-based surveillance offers important opportunities to identify risk factors and determinants of syphilis incidence and related outcomes. In July 2019, PHAC established a Syphilis Outbreak Investigation Coordination Committee (SOICC) to support the coordination of the Canadian response in dealing with the rise in the number of syphilis cases and jurisdictionally declared outbreaks. All of the provinces and territories have collected and shared with PHAC preliminary 2018 and 2019 enhanced syphilis surveillance data on gbMSM status, pregnancy status and substance use, in addition to age and sex. PHAC published an infographic, using the preliminary reported data, focusing on infectious syphilis cases in Canada from 2009 to 2018⁵⁴. SOICC members continue to discuss the collection of enhanced syphilis surveillance data on an ongoing basis.

Enhanced provincial and territorial surveillance activities

In Canada, enhanced provincial syphilis surveillance activities have been implemented in some provinces and territories, each varying in scope and timeframe of application, based on local contexts. For example, in New Brunswick, following a resurgence of syphilis cases, a standardized enhanced surveillance investigation form was implemented in 2011-2012 to collect information on cases, their sexual contacts and risk factors, as a response to the outbreak. In 2016, the province implemented routine enhanced surveillance. This form is used by the province's public health staff when following up on each new infectious syphilis case. The data collected provided information necessary for social network analysis of cases and their contacts. Manitoba has also developed enhanced surveillance protocols, which were implemented in 2004 in partnership with the province's Stop Syphilis campaign⁴⁰⁶. The province's strategy included aggressive case-finding initiatives, and the delegation of syphilis testing and treatment provision to Public Health Nurses⁴⁰⁶.

Following increases in infectious syphilis incidence in the province, enhanced syphilis surveillance was also initiated in Quebec. The province collected, pooled, and analysed additional information on infectious cases that occurred between 2004 and 2005⁴⁰⁷. The same was done for female infectious syphilis cases that occurred between 2009 and 2012⁴⁰⁸.

In Toronto, in 2010, an online monitoring tool was tested for 27 men with infectious syphilis⁴⁰⁹. Respondents were asked to complete a self-administered survey on the number of sexual partners they had and on the venues they frequented when seeking to meet sexual partners.

Lastly, British Columbia's sentinel surveillance system uses administrative medical databases from specific STI clinics to assess social and demographic determinants of syphilis incidence in the province¹⁶⁹. The latest reported data from British Columbia were published in 2015 (data from 2000-2013)¹⁶⁹. In 2016, BCCDC established additional data collection procedures to assess determinants of viral load at and around the time of syphilis diagnosis, and HIV co-infection¹⁴⁵.

6.4.2 Social Network Analysis

Once data are obtained on cases, their sexual contacts, and locations frequented, an analysis of sexual networks can help public health professionals prevent and screen for syphilis. Social network analysis helps to shed light on how syphilis is transmitted, the role of meeting and gathering places, as well as the role that individuals who have acquired the infection and their sexual contacts, may play in outbreaks.

In the late 1990s, social network analysis helped to identify a link between female transactional sex, crack cocaine use, and increased syphilis transmission, in British Columbia²¹⁸. More recently, social network analysis has been conducted in several settings in Canada. For example, a social network study of 52 STI clinic patients in Alberta identified a network of 94 gbMSM⁴¹⁰. Within this network, there were 18 individuals with infectious syphilis linked to 76 sexual contacts through 21 meeting places⁴¹⁰. Just over three-quarters of participants (77%) said they had met a sexual partner in a social venue, and sexual partners were often met online⁴¹⁰. The authors suggested that web venues could therefore be targeted for future primary or secondary syphilis prevention efforts. In Toronto, following the implementation of an online monitoring tool for patients diagnosed with infectious syphilis, a social network analysis (n=27) was conducted⁴⁰⁹. The study identified six meeting places linked to the cases (three websites, two saunas and one bar)⁴⁰⁹. Most participants found their sexual partners online (88%) and in bathhouses (60%). This information allowed public health officials to glean where future public health messaging and case finding efforts should be focused. In New Brunswick, a social network analysis (n=56) identified that gbMSM aged 18 to 55 were at highest risk of syphilis infection in the province, and often met partners through websites, bars, and saunas⁴¹¹. These findings led the province to target media content through identified websites and meeting places⁴¹¹. In Ontario, at the request of the Ontario Ministry of Health, PHAC's Canadian Field Epidemiology Program helped conduct an enhanced social network analysis of syphilis cases diagnosed between 2009 and 2010¹⁴⁸. Information on cases, contacts and social venues was plotted, connecting many of the single individuals and dyads and allowing for identification of potential venues for targeted sexual-health messaging.

Surveillance

Enhanced Federal Surveillance

- TRACKS surveillance system uses periodic cross-sectional surveys at sentinel sites of key populations of interest to help identify risk factors and outcomes for infectious syphilis in response to increasing syphilis rates.
- Enhanced surveillance data on syphilis are sent to PHAC by all provinces and territories in order to provide additional information related to populations affected.

Enhanced Provincial Surveillance

• Various provinces and territories have implemented their own enhanced surveillance systems in response to growing concerns about the syphilis epidemic.

Social Network Analysis

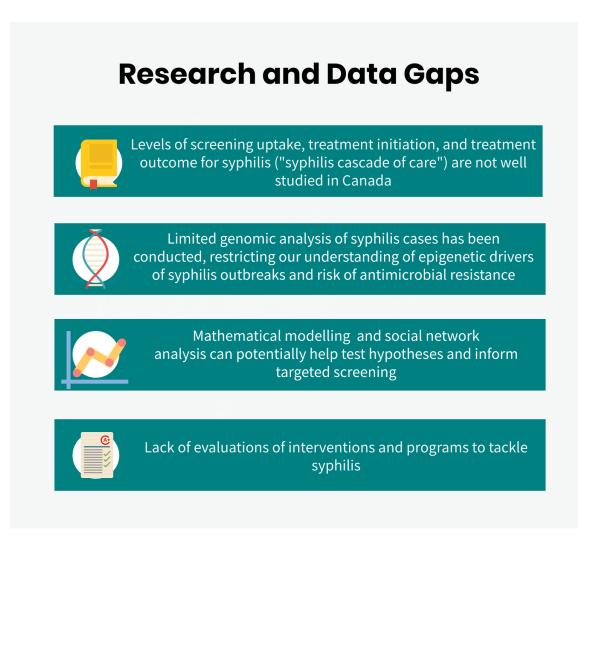
• Social network analyses can help highlight transmission patterns during outbreaks as well as bring attention to areas and populations to target for screening and prevention

6.5 Gaps in Research and Data

Throughout this section, a number of gaps in Canadian syphilis research have been identified and potential areas for future research are discussed. First, some have highlighted that knowledge is missing on the "cascade of care" for syphilis in Canada, including testing coverage, access to treatment, and cure^{3,363}. Although attempts have been made to estimate outcomes of the cascade of care for HIV and HCV in Canada—from screening uptake, to treatment initiation and follow-up—little has been done on the subject of syphilis. Second, researchers have also identified that very little genomic analysis of *T. pallidum* has been conducted, which limits our epidemiologic understanding on the epigenetic drivers of syphilis outbreaks, and of the risk of potential antimicrobial resistance^{48,397}. Third, an area of future syphilis research is in the domain of mathematical modeling, which can allow public health units to test hypotheses and can provide evidence to inform targeted screening strategies, among other interventions⁴¹². Similarly, network analysis of current outbreaks may help guide areas of intervention²¹⁸.

Effective research requires data. Provinces such as British Columbia have developed a data governance model that allows for data linkage, which provides opportunities for research and analysis into the determinants of syphilis outbreaks in the province. Linked vital statistics, STBBI case data, laboratory data, enhanced surveillance data on cases and their contacts, and other sources of clinical data (e.g., prescriptions) provide resources for policy planning in the province³²⁷.

Overall, one of the most important gaps in the syphilis and STBBI literature resides in the lack of evaluation of implemented programs, interventions and policies. Rigorous evaluation design, using data on both pre- and post-intervention periods, among intervention and control groups, is needed, in order to expand our scientific understanding on the effectiveness of interventions for syphilis prevention and control²⁹¹. Other evaluation methods can also be used, as required.



6.6 Strategic Policy and Planning

6.6.1 Canada's Response

In June 2018, federal, provincial and territorial Ministers of Health jointly released a <u>Pan-Canadian</u> <u>STBBI Framework for Action</u>. The Framework provides a common vision, strategic goals, and guiding principles to support cohesive action to address STBBI, including syphilis. The Framework envisions a Canada where STBBI are rare and people living with these infections receive the care and support they need. The Framework outlines how Canada will contribute to reaching the global targets set by WHO for the year 2030 for HIV, viral hepatitis, and STIs (specifically syphilis, gonorrhea and HPV). Canada has endorsed these global targets. WHO's global targets for syphilis for the year 2030 are as follows:

- 90% reduction of *T. pallidum* incidence globally;
- Fifty or fewer cases of congenital syphilis per 100,000 live births in 80% of countries.

In response to the <u>Pan-Canadian STBBI Framework for Action</u>, the Government of Canada launched its five-year action plan for these infections in July 2019 titled "<u>Accelerating our response: Government of Canada five-year action plan on sexually transmitted and blood-borne infections</u>"²⁷⁸. The Action Plan aims to help address health inequalities and build more supportive environments for Canadians affected by STBBI, such as the syphilis outbreaks currently experienced in the country. In order to reduce the public health impact of STBBI, like syphilis, and support Canada's contributions to meeting the global STBBI targets outlined above, the Action Plan aims to accelerate Canada's efforts to prevent, diagnose and treat STBBI, and address barriers to care through the identification of seven priority areas:

- 1) Moving toward truth and reconciliation with First Nations, Inuit and Métis Peoples;
- 2) Addressing stigma and discrimination;
- 3) Promoting community innovation—putting a priority on prevention;
- 4) Reaching the undiagnosed—increasing access to STBBI testing;
- 5) Providing prevention, treatment and care to populations that receive health services or coverage of health care benefits from the federal government;
- 6) Leveraging existing knowledge and targeting future research; and
- 7) Measuring impact—monitoring and reporting on trends and results.

In addition, as described in <u>Section 6.4</u>, SOICC was established in July 2019 in Canada in response to the increase in syphilis rates across the country. This committee includes representatives from all PTs, in particular those reporting current outbreaks, as well as representatives from various federal agencies (including PHAC, Indigenous Services Canada, Immigration, Refugees and Citizenship Canada, Department of National Defense). The committee, coordinated by PHAC, aims to share data on current syphilis outbreaks as well as best practices and lessons learned.

6.6.2 Planning in Other OECD Countries

Outside of Canada, several countries have developed national strategies for syphilis elimination.

In Australia, the *Fourth National STI Strategy* aims to reduce the transmission, morbidity and mortality associated with all STIs in the country²⁵⁷. Given outbreaks in Aboriginal and Torres Strait Islander communities, the National Strategy aims to eliminate the negative impact of stigma, discrimination and human rights issues on people's health, as well as minimize the personal and social impacts of STIs. It also aims to reduce the prevalence of chlamydia, gonorrhea and infectious syphilis and eliminate congenital syphilis by 2022. Their priority areas include

prevention education, testing and treatment, equitable access to care with a focus on innovative and emerging models of service delivery, such as peer-based testing and peer support, community-based testing and online testing. It also includes increasing the health workforce, addressing stigma, improving data quality and implementing enhanced surveillance.

In England, substantial increases of infectious syphilis diagnoses between 2008 and 2018 demonstrated a need to strengthen public health measures to reduce transmission²⁶¹. England's response for syphilis control and prevention emphasizes four prevention pillars: increasing testing frequency of high-risk gbMSM and re-testing cases after treatment, increasing the quality of partner notification, maintaining high antenatal screening coverage and vigilance for syphilis throughout antenatal care and sustaining targeted health promotion.

Following concerns raised about the increase of syphilis in the EU, the ECDC published a technical report, which included a range of response options²⁵⁹. The proposed interventions were enhanced screening of key populations during routine testing or clinical monitoring, expanding testing outreach in venues, appropriate and effective partner notification, prevention education directed at the general population, and education of healthcare providers. In order to sustain low rates of congenital syphilis in the EU, prevention measures include universal early prenatal screening, retesting women at risk of acquiring syphilis during pregnancy, testing all women at delivery if they had not been tested before, collecting surveillance data in order to identify gaps in prevention, and the harmonization of congenital case definitions across the EU.

Ireland responded to STI and HIV outbreaks among gbMSM by identifying effective prevention interventions from the best available evidence and the resources required to implement them in an Irish setting²⁸⁴. According to their evidence review, the interventions with the strongest evidence base include interventions aiming to increase condom use, peer-led group interventions, peer outreach within the gbMSM community, and in the case of HIV, universal coverage of antiretroviral treatment and treatment as prevention.

New Zealand identified priority actions under four key action areas, with the aim of covering the full spectrum of syphilis prevention and care²⁸³. The first priority action is prevention and health promotion through promoting a healthy sexuality culture, which includes improving knowledge and awareness of syphilis, and promoting condom use and regular STI testing. The second priority, testing and management, is needed to ensure availability and access to syphilis testing, by increasing health professional awareness and understanding of syphilis, improving contact tracing, and ensuring the availability of sexual health specialists. The third priority is the prevention of congenital syphilis through antenatal testing and appropriate treatment of syphilis during pregnancy. Lastly, high quality surveillance and monitoring aims to improve the understanding of risk factors, and planning and evaluation of prevention and control activities.

Finally, faced with a growing syphilis epidemic in the 1990s, the US published <u>The National Plan</u> to <u>Eliminate Syphilis from the US⁴¹³</u>. The US' plan supported activities in several areas, including sustained STBBI prevention programs, a commitment to multi-sectoral partnerships, a comprehensive health communication plan, a systematic approach to quality assurance and evaluation of screening, treatment, and surveillance systems, as well as, training, planning and priority-setting for research⁴¹³. The CDC has recently published a call to action detailing what can be done in specific populations to reduce syphilis transmission²⁸². These specific populations include pregnant women, gbMSM, health-care providers, decision-makers, biomedical scientists and more. This call to action highlights the need to create new tools to detect and treat syphilis, to increase testing, to control the further spread of syphilis, and to improve electronic medical records in order to improve patient outcomes.

7. Conclusion

This report on syphilis provides a comprehensive overview of the latest infectious and congenital syphilis epidemiological trends in Canada, associated risk factors, and interventions that can be implemented in an effort to reduce the burden of disease in affected populations, The report highlights the complexity of the disease, in terms of its natural history, screening and diagnosis, as well as epidemiology and prevention.

Syphilis is a complex, multi-stage sexually and vertically transmitted infection. Some symptoms are unspecific and, as a result, it is easy for syphilis to go undetected. Testing is also challenging; the wide variety of tests that are currently in use for diagnosing and staging syphilis can make the interpretation of testing results complex, and may require the insights of an experienced clinician. If syphilis goes undetected and is left untreated, the infection can cause serious health consequences in babies, youth and adults.

The epidemiology of syphilis has changed markedly over the past few decades in Canada, a trend that has been paralleled in numerous high-income countries. Following years of low and stable rates of syphilis in the 1990s, rates began to increase in the 2000s, mainly among gbMSM. Since then, in the past three years, rates have increased significantly in other populations, such as women and heterosexual men, although gbMSM remain the most affected population. Risk factors of infectious syphilis vary across these populations, making it difficult to apply a one-size-fits-all intervention. Determinants of health, such as socioeconomic factors, physical environment, sexual behaviours, experiences of discrimination and stigma, as well as health policy and programs, are examples of broader social determinants, which shape an individual's risk of syphilis acquisition.

Syphilis is a preventable and treatable disease. Condom use, as well as education-based initiatives and educational resources on healthy sexuality for both patients and service providers, can be effective primary prevention measures. Interventions designed to make accessing testing more comfortable, convenient and responsive to the needs of particular populations, such as gbMSM, can help ensure quicker access to care and improved linkage to treatment. It is recommended that pregnant women undergo screening at first trimester, at 28-32 weeks (3rd trimester) and at delivery, particularly in areas at high risk of transmission. Among harder-to-reach populations, several initiatives, such as syphilis testing in emergency departments, as well as online screening services, have been found to promote higher rates of screening. Another proposed strategy for improving linkage to care is POC testing, which is designed to increase the accessibility of screening in populations that may be more hesitant or who may experience barriers to accessing traditional screening. Addressing structural barriers and adopting culturally adapted approaches is of paramount importance to all syphilis prevention and control efforts. Moreover, collaboration between clinicians, public health professionals, community-based organizations and researchers is key to successfully prevent and control syphilis in Canada.

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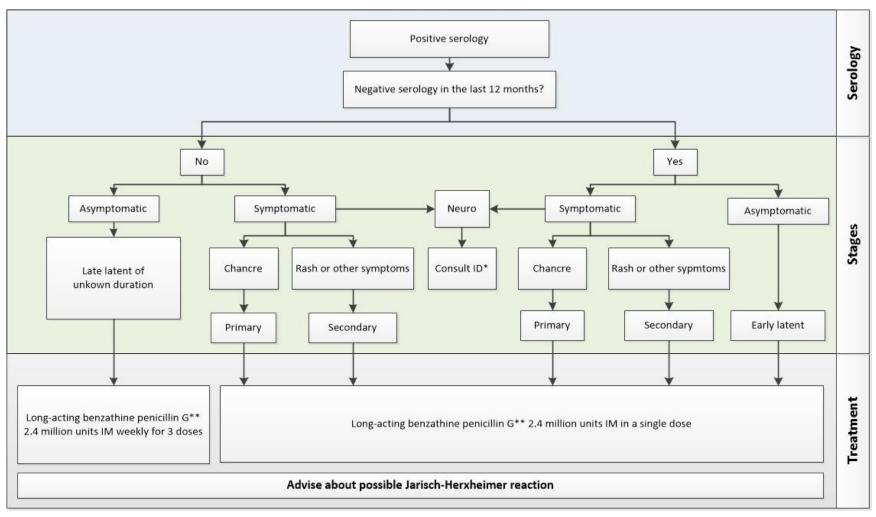
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Appendix A: Clinical algorithm for syphilis staging and treatment



* Infectious Disease Specialist

** Alternative treatment to be considered in case of penicillin allergy.

This staging diagram was kindly shared by Dr Troy Grennan, Clinical Lead, HIV/STI Program Medicine (Division of Infectious Diseases), University of British Columbia, BC Centre for Disease Control, British Columbia and by Dr. Todd F. Hatchette, Chief of Service, Division of Medical Microbiology, Department of Pathology and Laboratory Medicine, Capital District Health Authority, Nova Scotia.

Appendix B: Case definitions of syphilis used in Canada

B.I Federal case definitions^d

Confirmed case—Early congenital syphilis (within two years of birth)

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody or equivalent examination of material from nasal discharges, skin lesions, placenta, umbilical cord or autopsy material of a neonate (up to four weeks of age); OR
- reactive serology (non-treponemal and treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory or radiographic evidence of congenital syphilis whose mother is without documented evidence of adequate treatment; OR
- detection of *T. pallidum* DNA in an appropriate clinical specimen.

Confirmed case—Primary syphilis

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, nucleic acid testing (NAT), or equivalent examination of material from a chancre or a regional lymph node; OR
- presence of one or more typical lesions (chancres) and reactive treponemal serology, regardless of non-treponemal test reactivity, in individuals with no previous history of syphilis; OR
- presence of one or more typical lesions (chancres) and a fourfold or greater increase in the titre over the last known non-treponemal test in individuals with a past history of syphilis treatment.

Confirmed case—Secondary syphilis

Laboratory evidence of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, NAT or equivalent examination of mucocutaneous lesions, condylomata lata and reactive serology (non-treponemal and treponemal); OR
- presence of typical signs or symptoms of secondary syphilis (e.g. mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise or splenomegaly) AND either a reactive serology (nontreponemal and treponemal OR a fourfold or greater increase in titre over the previous known non-treponemal test.

^d Public Health Agency of Canada. Case Definitions for Communicable Diseases under National Surveillance. *Canada Communicable Disease Report* CCDR 2009, 35S2: 1 – 123.

Confirmed case—Early latent syphilis (< one year after infection)

Laboratory confirmation of infection:

- An asymptomatic patient with reactive serology (treponemal and/or non-treponemal) who, within the previous 12 months, had one of the following:
 - non-reactive serology
 - o symptoms suggestive of primary or secondary syphilis
 - o exposure to a sexual partner with primary, secondary or early latent syphilis.

Confirmed case—Late latent syphilis (> one year after infection or of unknown duration) Laboratory confirmation of infection:

• An asymptomatic patient with persistently reactive treponemal serology (regardless of non-treponemal serology reactivity) who does not meet the criteria for early latent disease and who has not been previously treated for syphilis.

Confirmed case—Neurosyphilis

Infectious (< one year after infection):

Laboratory confirmation of infection:

- Fits the criteria of primary, secondary OR early latent syphilis above AND one of the following:
 - reactive CSF-VDRL in non-bloody CSF
 - clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes.

Non-infectious (> one year after infection):

Laboratory confirmation of infection:

- Reactive treponemal serology (regardless of non-treponemal serology reactivity) AND one of the following:
 - reactive CSF-VDRL in non-bloody CSF
 - clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes.

Confirmed Case—Tertiary syphilis other than Neurosyphilis

Laboratory confirmation of infection:

- Reactive treponemal serology (regardless of non-treponemal test reactivity) together with characteristic late abnormalities of the cardiovascular system, bone, skin or other structures, in the absence of other known causes of these abnormalities (*T. pallidum* is rarely seen in these lesions although, when present, it is diagnostic); AND
- no clinical or laboratory evidence of neurosyphilis.

B.II Provincial and territorial case definitions for congenital syphilis

Differences between national and provincial/territorial congenital syphilis case definitions are described below. Currently, seven jurisdictions use the national case definition for early congenital syphilis or have similar definitions (Alberta, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Northwest Territories and Nunavut). Five jurisdictions use a different case definition than the national early congenital syphilis case definition (British Columbia, Saskatchewan, Manitoba, Ontario and Quebec). British Columbia, Saskatchewan and Manitoba have the additional option of diagnosing according to non-treponemal test titre. However, these provinces do not use these tests in the same way. In British Columbia, a fourfold higher titre in the newborn than in the mother in combination with a confirmatory treponemal test and clinical evidence is sufficient to confirm a case. Whereas, Saskatchewan and Ontario do not take into consideration maternal status in their confirmed case definition. In Quebec, the case definition is similar to the national definition, but Quebec requires the addition of two serology tests with at least one treponemal test. At the time this report, case definitions for the Yukon were not available publicly or upon request.

Lastly, additional case definitions for early congenital syphilis are used in five provinces (British Columbia, Alberta, Saskatchewan, Manitoba and Quebec). These additional case definitions include a maternal syphilis definition, probable early congenital syphilis, clinically confirmed early congenital syphilis, syphilitic stillbirth, probable syphilitic stillbirth, and late congenital syphilis.

Province/ Territory	Comparison with national early congenital syphilis case definition	Additional case definitions
BC ¹	Differs	Maternal syphilis Late congenital syphilis
AB ²	\checkmark	Probable early congenital syphilis Syphilitic stillbirth (confirmed, probable)
SK ³	Differs	Early congenital syphilis (laboratory confirmed, clinically confirmed, probable) Syphilitic stillbirth (confirmed, probable)
MB ⁴	Differs	Early congenital syphilis (laboratory confirmed, clinically confirmed, probable) Syphilitic stillbirth (confirmed, probable)
ON ⁵	Differs	
QC ⁶	Differs	Probable early congenital syphilis
NB	\checkmark	
NS	✓	
PE	✓	
NL	√	
YT	NA	
NT	✓	
NU	\checkmark	

Table 1. Provincial and territorial comparison to the national case definition for congenital syphilis

Note: A check mark (\checkmark) indicates a match with the national case definition. "NA" indicates that the information were not available publicly or upon request at the time this report was drafted.

¹ British Columbia^e

Confirmed case—Early congenital syphilis

A stillbirth, neonate or older case with clinical presentation compatible with congenital syphilis, onset less than two years of age and one of the following:

- titre greater than maternal titre and positive treponemal confirmatory test
- detection of *T. pallidum* clinical specimens, (e.g., lesions, placenta, umbilical cord, autopsy) through dark-field microscopy, direct fluorescent antibody assay or PCR
- mother with untreated or inadequately treated syphilis (i.e., primary, secondary, early or late latent syphilis) during pregnancy or at birth.

Confirmed case—Late congenital syphilis

A stillbirth, neonate or older case with clinical presentation compatible with congenital syphilis, onset at two or more years of age and one of the following:

- titre greater than maternal titre and positive treponemal confirmatory test
- detection of *T. pallidum* clinical specimens, (e.g., lesions, placenta, umbilical cord, autopsy) through dark-field microscopy, direct fluorescent antibody assay or PCR
- mother with untreated or inadequately treated syphilis (i.e., primary, secondary, early or late latent syphilis) during pregnancy or at birth.

Confirmed case—Maternal syphilis

A woman who meets the case definition of infectious syphilis (i.e., primary, secondary, early latent syphilis) OR late latent syphilis, AND one of the following:

- syphilis serology conducted as part of prenatal blood screening
- known to have given birth to an infant (live or stillborn) with congenital syphilis
- clinical presentation of infectious syphilis during pregnancy.

² Alberta^f

Probable case—Early congenital syphilis

Reactive serology (non-treponemal and treponemal) from venous blood (not cord blood) in an infant/child without clinical, nor laboratory, nor radiographic evidence of congenital syphilis whose mother had untreated or inadequately treated syphilis at delivery.

Confirmed case—Syphilitic stillbirth

- A fetal death that occurs after 20 weeks gestation where the mother had unrelated or inadequately treated syphilis at delivery; AND
- laboratory confirmation of infection (i.e., detection of *T. pallidum* DNA in an appropriate clinical specimen, fluorescent antibody or equivalent examination of material from placenta, umbilical cord or autopsy material).

^f <u>Alberta</u>: Alberta Health. Public Health Notifiable Disease Management Guidelines: Congenital Syphilis. 2012. Available at: <u>https://open.alberta.ca/dataset/e341ccf6-c0dc-45aa-9b4c-2e7b53769340/resource/29aeea4c-2903-4bff-8c3d-e577851398e6/download/Guidelines-Congential-Syphilis-2012.pdf</u>, Accessed June 17, 2020.

^e <u>British Columbia</u>: BCCDC. Syphilis: Case Definition. 2020. Available at: <u>http://www.bccdc.ca/health-professionals/clinical-resources/case-definitions/syphilis</u>, Accessed June 17, 2020.

Probable case—Syphilitic stillbirth

A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated infectious syphilis at delivery with no other cause of stillbirth established.

³ Saskatchewan^g

Confirmed case—Early congenital syphilis (within two years of birth)

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark field microscopy, fluorescent antibody or detection of *T. pallidum* DNA in an appropriate clinical specimen, or equivalent examination of material from nasal discharges, skin lesions, placenta, umbilical cord or autopsy material of a neonate (up to four weeks of age); OR
- reactive serology (non-treponemal and treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory or radiographic evidence of congenital syphilis, but who has one or both of the following, regardless of maternal treatment status;
 - rising syphilis serologic titres upon follow-up where there is evidence that the mother had a syphilis infection during pregnancy
 - titres greater than or equal to fourfold those of the mother's when collected at the same time or on the same day, in the immediate postnatal period;

OR

 a child who does not meet the above criteria but has persistently reactive treponemal serology between 18 and 24 months of age (regardless of maternal treatment status and infectious status).

Confirmed case—Early congenital syphilis (within two years of birth)

Clinical confirmation of infection:

- Reactive serology (non-treponemal and treponemal) from a venous blood (not cord blood) in an infant/child with clinical, laboratory, or radiographic evidence consistent with congenital syphilis whose mother:
 - was seropositive or PCR positive for syphilis during pregnancy or at delivery; AND
 - had inadequate treatment (i.e., no documented evidence of adequate treatment);
 OR
 - demonstrated to have evidence of reinfection or relapse in pregnancy following appropriate therapy.

Probable case—Early congenital syphilis (within two years of birth)

Reactive serology (non-treponemal and treponemal) from a venous blood (not cord blood) in an infant/child without clinical nor other laboratory, nor radiographic evidence of congenital syphilis whose mother had untreated or inadequately treated syphilis at delivery.

Confirmed case—Syphilitic stillbirth

 A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated syphilis at delivery; AND

^g <u>Saskatchewan</u>: Saskatchewan Ministry of Health. Disease Control Manual: Sexually Transmitted Infections, Section 5-70-Syphilis. 2019. Available at: <u>https://www.ehealthsask.ca/services/Manuals/Documents/Section-5-Dec-2019.pdf</u>, Accessed June 17, 2020.

• laboratory confirmation of infection (e.g., detection of *T. pallidum* DNA in an appropriate clinical specimen, fluorescent antibody or equivalent examination of material from placenta, umbilical core of autopsy material).

Probable case—Syphilitic stillbirth

A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated infectious syphilis at delivery with no other cause of stillbirth established.

⁴ Manitoba^h

Confirmed Case—Early congenital syphilis (within two years of birth)

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, or detection of *T. pallidum* – specific nucleic acid (using NAT, e.g., PCR) in an appropriate clinical specimen, or equivalent examination of material from nasal discharges, skin lesions, placenta or umbilical cord, or autopsy material of a neonate (up to four weeks of age); OR
- reactive serology (treponemal and non-treponemal) from venous blood (not cord blood) in an infant/child with or without clinical, laboratory, or radiographic evidence consistent with congenital syphilis but who has one or both of the following:
 - rising syphilis serologic titres upon follow-up where there is evidence that the mother had a syphilis infection during pregnancy
 - titres greater than or equal to fourfold higher than those of the mother when collected at the same time or on the same day, in the immediate post-natal period;
 OR
- a child who does not meet the above criteria but has persistently reactive treponemal serology between 18 and 24 months of age (regardless of maternal treatment status and infectious status).

Note: A nasopharyngeal swab should be taken for syphilis PCR, as many of the cases are positive by this relatively non-invasive method. The specimen collection procedure is the same as the Cadham Provincial Laboratory respiratory virus detection available at:

https://www.gov.mb.ca/health/publichealth/cpl/docs/nasopharyngeal_collection.pdf;

Clinical confirmation of infection:

- Reactive serology (treponemal and non-treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory, or radiographic evidence consistent with congenital syphilis whose mother:
 - was seropositive or PCR positive for syphilis during pregnancy or at delivery; AND
 - had inadequate treatment (i.e., no documented evidence of adequate treatment);
 OR
 - demonstrated to have evidence of reinfection or relapse in pregnancy following appropriate therapy.

^h <u>Manitoba</u>: Manitoba Health, Seniors and Active Living. Communicable Disease Management Protocol. 2019. Available at: <u>https://www.gov.mb.ca/health/publichealth/cdc/protocol/syphilis.pdf</u>, Accessed June 17, 2020

Probable Case—Early congenital syphilis (within two years of birth)

Reactive serology (treponemal and non-treponemal) from venous blood (not cord blood) in an infant/child without clinical, laboratory, or radiographic manifestations of congenital syphilis whose mother had untreated or inadequately treated syphilis at delivery.

Note: A persistent treponemal serologic reaction at 18-24 months of age confirms the diagnosis of congenital syphilis. An absent serologic reaction (treponemal and non-treponemal) at 18-24 months of age excludes the case (i.e., it is no longer probable or confirmed). Inadequate treatment consists of any non-penicillin therapy or penicillin administered during pregnancy, but less than 30 days before delivery.

Confirmed case—Late congenital syphilis (greater than two years after birth)

Laboratory Confirmation of Infection:

- Reactive treponemal serology (regardless of non-treponemal test reactivity) along with characteristic late manifestations of congenital syphilis in a child whose mother was known or considered to be seropositive for syphilis during pregnancy, without documented evidence of adequate treatment; AND
- no other known source of exposure (i.e., infection must have occurred in utero).

Confirmed Case—Syphilitic stillbirth:

Laboratory Confirmation of Infection:

- A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated syphilis at delivery; AND
- laboratory confirmation of infection (i.e., detection of *T. pallidum* DNA in an appropriate clinical specimen, fluorescent antibody or equivalent examination of material from placenta, umbilical cord or autopsy material).

Probable Case—Syphilitic stillbirth:

A fetal death that occurs after 20 weeks gestation where the mother had untreated or inadequately treated infectious syphilis at delivery with no other cause of stillbirth established.

⁵ Ontarioⁱ

Confirmed case—Early Congenital Syphilis (within two years of birth)

Laboratory confirmation of infection:

- Identification of *T. pallidum* by dark-field microscopy, direct fluorescent antibody microscopy, NAAT or equivalent examination of material from nasal discharges, skin lesions, placenta, umbilical cord or autopsy material of a newborn (up to four weeks of age);
 - OR
- reactive serology (non-treponemal and treponemal) from venous blood (not cord blood) in an infant/child with clinical, laboratory or radiographic evidence of congenital syphilis; OR

Ontario : Ministry of Health and Long-Term Care. Infectious Disease Protocol, Appendix B: Provincial Case Definitions for Diseases of Public Health Significance, Disease: Syphilis, 2019. Available at:

http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/syphilis_cd.pdf, Accessed June 17, 2020.

• detection of *T. pallidum* DNA in an appropriate clinical specimen (whose mother is without documented evidence of adequate treatment is excluded).

⁶ Quebec^j

Confirmed case—Congenital Syphilis

In an infant or stillbirth:

• Detection of nucleic acids of *T. pallidum* or observation by microscopic examination with appropriate staining or using fluorescent antibodies (DFA-TP) of *T. pallidum* in a clinical specimen (placental, umbilical cord, nasal exudate or skin lesions) or autopsy material.

In a newborn or infant:

- Serological detection of *T. pallidum* infection by two recognized tests, including at least one treponemal test in venous blood (not umbilical cord blood); AND
- clinical, biochemical or radiological manifestations of congenital syphilis compatible with the cardiovascular, bone or skin system in the absence of other causes; AND
- mother with untreated or inadequately treated syphilis.

Probable Case—Congenital syphilis

In a newborn or infant, in the absence of clinical, biochemical or radiological manifestations of congenital syphilis, the following two conditions are present:

- serological detection of *T. pallidum* infection by two recognized tests, including at least one treponemal test in venous blood (not umbilical cord blood)
- mother with untreated or inadequately treated syphilis.

^j <u>Quebec</u>. Ministère de la santé et services sociaux. Surveillance des maladies à déclaration obligatoire au Québec-Définitions nosologiques-Maladies d'origine infectieuse-12^e édition, 2019. Available at : <u>https://publications.msss.gouv.gc.ca/msss/fichiers/2019/19-268-05W.pdf</u>, Accessed June 17, 2020.

B.III Other provincial and territorial syphilis case definitions

Differences between national and provincial/territorial syphilis case definitions are described below. Currently, four jurisdictions use the national case definitions for all stages of syphilis (Saskatchewan, New Brunswick, Prince Edward Island and Northwest Territories), two jurisdictions have case definitions that are similar to the national case definition for all stages of syphilis (Nova Scotia and Nunavut), and six jurisdictions have at least one case definition that differs from the national case definition (British Columbia, Alberta, Manitoba, Ontario, Quebec and Newfoundland and Labrador). At the time of this report, information on case definitions used in Yukon as well as case definitions for late latent, neurosyphilis and tertiary syphilis used in British Columbia, were not available either publicly or upon request. Saskatchewan has additional suspect case definitions for ocular syphilis and unspecified syphilis stage. Quebec is the only province who has a different case definition for every stage of syphilis, but this is mainly due to their definitions reflecting their testing algorithm, as they specify that two serological tests are required, with at least one being treponemal.

Secondary syphilis and neurosyphilis are the two stage case definitions with the most variability between the provinces and territories. Three provinces have differences in their confirmed secondary syphilis definitions. Contrary to the federal case definition, British Columbia and Quebec do not require serology testing in addition to direct testing (by microscopy or fluorescent antibody detection or NAT). In Alberta, detection of syphilis DNA by PCR (polymerase chain reaction) is sufficient on its own to confirm secondary syphilis. In the case of neurosyphilis, all provinces except Quebec and Newfoundland and Labrador distinguish between infectious neurosyphilis from non-infectious neurosyphilis. In provinces that do distinguish between these two forms of neurosyphilis, only Alberta and Manitoba have slight differences from the federal case definition.

Beyond the latter differences, minor differences can also be observed in relation to early latent syphilis and late latent syphilis definitions used across jurisdictions.

In the case of early latent syphilis, the national case definition requires treponemal or nontreponemal serology in asymptomatic patients. British Columbia and Quebec's definitions differ slightly in that British Columbia requires both tests or a four-fold increase in titres, while Quebec requires two tests with at least one being a treponemal test. Further, in British Columbia's case definition, in addition to criteria of (1) non-reactive serology or (2) the presence of symptoms or (3) reported history of being exposed to syphilis in the previous 12 months, an individual considered to be "at risk" or an individual presenting a titre higher than 1:16 can also fit the criteria of early latent syphilis. In Quebec, an individual meeting one of those first three criteria, or having had a previous episode of syphilis and having been treated, can fit the case definition for early latent syphilis.

Two provinces have differences in their definitions for late latent syphilis. The national case definition requires persistent treponemal serology, while Ontario and Quebec only require positive serology. Ontario requires treponemal or non-treponemal serology, while Quebec requires two tests with at least one being treponemal. For Ontario, the national definition's requirement that the individual was not previously treated for syphilis is replaced by the requirement that the individual was not adequately treated for syphilis or has an increase in titre. For Quebec, the province specifies that the individual must not have been at risk for syphilis acquisition in the past 12 months.

Province			National case classification								
or			Early	Late	Neuros	syphilis					
Territory	Primary	Secondary	Latent	Latent	Infectious	Non- infectious	Tertiary				
BC	\checkmark	Differs ⁸	Differs ⁸	NA	NA	NA	NA				
AB	✓	Differs ⁹	\checkmark	\checkmark	Differs ⁹	✓	\checkmark				
SK	✓	\checkmark	✓								
	+	+	+	\checkmark	\checkmark	\checkmark	\checkmark				
	suspect ¹⁰	suspect ¹⁰	suspect ¹⁰								
MB	\checkmark	\checkmark	\checkmark	\checkmark	Differs ¹¹	\checkmark	\checkmark				
ON	\checkmark	\checkmark	\checkmark	Differs ¹²	\checkmark	\checkmark	\checkmark				
QC	Differs ¹³	Differs ¹³	Differs ¹³	Differs ¹³	Diffe	ers ¹³	Differs ¹³				
NB	√	~	\checkmark	~	~	\checkmark	\checkmark				
NS	✓	✓	✓	\checkmark	\checkmark	✓	✓				
PE	✓	✓	✓	✓	✓	✓	\checkmark				
NL	✓	✓	✓	✓	Diffe	ers ¹⁴	\checkmark				
ΥT	NA	NA	NA	NA	NA	NA	NA				
NT	✓	\checkmark	✓	\checkmark	\checkmark	✓	\checkmark				
NU	✓	✓	\checkmark	✓	\checkmark	✓	\checkmark				

Table 2. Provincial comparison of the national case definition of primary, secondary, early latent, late latent, neurosyphilis and tertiary syphilis

Note: A check mark (✓) indicates a match with the national case definition. "NA" indicates that the information were not available publicly or upon request at the time this report was drafted. "Suspect" indicates the presence of a case definition for suspect cases. "Differs" indicates an instance in which the PT case definition differs from the national case definition.

⁸ British Columbia^k

Confirmed case—Secondary syphilis

Clinical presentation compatible with secondary syphilis (e.g., rash, fever, malaise, lymphadenopathy, mucus lesions, condylomata lata, alopecia, meningitis, headaches, uveitis, retinitis, recent hearing impairment), and one of the following:

- identification of *T. pallidum* in clinical specimens (e.g., from chancre, regional lymph node) by dark-field microscopy, direct fluorescent antibody, or NAAT
- reactive serology (non-treponemal and treponemal) in individuals with no previous history of syphilis
- significant (i.e., fourfold or greater) increase in titre over the last known non-treponemal test.

Confirmed case—Early latent syphilis

An individual without symptoms of primary or secondary syphilis but has a reactive serology (nontreponemal and treponemal) or fourfold increase in titre over the last known non-treponemal test, and one of the following within the previous 12 months:

- non-reactive serology
- symptoms suggestive of primary or secondary syphilis
- exposure to a sexual partner with primary, secondary, early latent syphilis
- is a member of (or has had sexual partners in the previous 12 months from) groups at known increased risk of syphilis infection in BC

^k <u>British Columbia</u>: BCCDC. Syphilis: Case Definition. 2020. Available at: <u>http://www.bccdc.ca/health-professionals/clinical-resources/case-definitions/syphilis</u>, Accessed June 17, 2020.

• has a titre of >=1:16.

Confirmed case—Ocular syphilis

- Meets the case definition for any stage of syphilis; OR
- reactive treponemal serology (regardless of non-treponemal serology reactivity); AND

clinical presentation of uveitis, retinitis or optic neuropathy in the absence of other known causes.

Syphilis Stage Unspecified

- Reactive treponemal serology (regardless of non-treponemal serology reactivity) in an individual either with no previous history of syphilis or four-fold or greater increase in titre over the last known non-treponemal test; AND
- follow-up to determine staging of syphilis is not complete.

⁹ Alberta¹

Confirmed case—Secondary syphilis

Laboratory evidence of infection:

- Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody or equivalent examination of mucocutaneous lesions, condylomata lata and reactive serology (nontreponemal and treponemal); OR
- detection of *T. pallidum* nucleic acid (e.g., PCR) in an appropriate clinical specimen; OR
- presence of typical signs or symptoms of secondary syphilis (e.g., mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise or splenomegaly) AND either:
 - reactive serology (non-treponemal and treponemal); OR
 - a fourfold or greater increase in titre over the last known non-treponemal test.

Confirmed case—Infectious neurosyphilis

Laboratory confirmation of infection:

- Fits the criteria of a confirmed case of primary, secondary or early latent syphilis AND one or more of the following:
 - reactive CSF-VDRL in non-bloody CSF
 - o detection of *T. pallidum* nucleic acid (e.g., PCR) in CSF or vitreous humor
 - clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes.

¹ <u>Alberta</u> : Alberta Health. Public Health Notifiable Disease Management Guidelines : Syphilis. 2012. Available at: <u>https://open.alberta.ca/dataset/e234483d-fc2d-4bbf-a248-e0442808187e/resource/244eaccc-c0ac-4933-9347-a908cbbc45f0/download/Guidelines-Syphilis-2012.pdf</u>, Accessed June 17, 2020.

¹⁰ Saskatchewan^m

Suspect case—Primary syphilis

- A reactive serological test (both treponemal and non-treponemal); OR
- presence of one or more typical lesions (chancres) during the past three months regardless of treponemal serology or non-treponemal test reactivity; AND
- sexual contact with a lab-confirmed or suspect infectious stage syphilis partner during the past six months.

Suspect case—Secondary syphilis

- Presence of typical signs or symptoms of secondary syphilis (e.g., mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise or splenomegaly); AND
- reactive non-treponemal serology titre greater than or equal to four; OR
- sexual contact with a lab-confirmed or suspect infectious stage partner in the past nine months.

Note: Nine months allows for sexual contact during a three-month incubation (transmission) period after first contact with a source person plus an ensuing six-month infected period of the case being reported.

Suspect case—Early latent syphilis

- An individual without symptoms of primary or secondary syphilis; AND
- has evidence of having acquired the infection within the previous 12 months based on one or more of the following criteria:
 - reactive serology (non-treponemal and treponemal) tests from a person whose only exposure occurred within the preceding 12 months;
 - documented seroconversion or fourfold or greater increase in the titre of a nontreponemal test during the previous 12 months;
 - has a RPR titre of ≥ 1:16 and is a member of (or has had sexual partners in the previous 12 months from) groups at known increased risk of syphilis infection;

OR

- an individual who has had symptoms of primary or secondary syphilis within the past 12 months regardless of treponemal serology or non-treponemal test reactivity; AND
- is a member of (or has had sexual partners in the previous 12 months from) groups at known increased risk of syphilis.

^m <u>Saskatchewan</u>: Saskatchewan Ministry of Health. Disease Control Manual: Sexually Transmitted Infections, Section 5-70-Syphilis. 2019. Available at: <u>https://www.ehealthsask.ca/services/Manuals/Documents/Section-5-Dec-2019.pdf</u>, Accessed June 17, 2020.

¹¹ Manitobaⁿ

Provincial case definitions are slightly different than national definitions; however, differences are minor and would not likely alter the reported rate of syphilis at the national level. First, the province specifies NAT as TP-specific NAT (e.g., PCR). Second, Early latent syphilis may be referred to as incubating syphilis, which is reported as early latent syphilis. Lastly, the provincial Infectious neurosyphilis definition includes the following additional statement, underlined below:

- "Laboratory confirmation of infection fits the criteria of primary, secondary OR early latent syphilis above AND one of the following:
 - reactive CSF-VDRL in non-bloody CSF followed by reactive treponemal-specific antibodies on CSF
 - clinical evidence of neurosyphilis AND either elevated CSF leukocytes OR elevated CSF protein in the absence of other known causes."

¹² Ontario^o

Confirmed case—Late latent syphilis

An asymptomatic patient with reactive serology (treponemal and/or non- treponemal) who does not meet the criteria for early latent disease AND one of the following:

- who has not been previously treated adequately for syphilis
- has a prior history of syphilis and a significant (i.e., fourfold or greater) rise in titre of a nontreponemal test > 12 months ago.

¹³ Quebec^p

Confirmed case—Primary syphilis

- Identification of *T. pallidum* by dark-field microscopy or fluorescent antibody from a chancre or a regional lymph node; OR
- detection of *T. pallidum* nucleic acids in a sample from a chancre; OR
- presence of one or more typical lesions (chancres) and reactive serology by two tests with at least one being treponemal, in individuals with no previous history of syphilis; OR
- presence of one or more primary typical lesions (chancres) and a fourfold or greater increase in the titre over the last known non-treponemal test in individuals with a past history of syphilis treatment.

Confirmed case—Secondary syphilis

 Identification of *T. pallidum* by dark-field microscopy or fluorescent antibody testing of mucocutaneous lesions or condylomata lata; OR

^o <u>Ontario</u> : Ministry of Health and Long-Term Care. Infectious Disease Protocol, Appendix B: Provincial Case Definitions for Diseases of Public Health Significance, Disease: Syphilis, 2019. Available at:

ⁿ <u>Manitoba</u>: Manitoba Health, Seniors and Active Living. Communicable Disease Management Protocol. 2019. Available at: <u>https://www.gov.mb.ca/health/publichealth/cdc/protocol/syphilis.pdf</u>, Accessed June 17, 2020

<u>http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/syphilis_cd.pdf</u>, Accessed June 17, 2020.

^p <u>Quebec</u>. Ministère de la santé et services sociaux. Surveillance des maladies à déclaration obligatoire au Québec-Définitions nosologiques-Maladies d'origine infectieuse-12^e édition, 2019. Available at : <u>https://publications.msss.gouv.gc.ca/msss/fichiers/2019/19-268-05W.pdf</u>, Accessed June 17, 2020.

- detection of *T. pallidum* nucleic acids in a sample from a mucocutaneous lesion or condylomata lata;
 OR
- presence of the following two conditions:
 - typical signs or symptoms of secondary syphilis (e.g., mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise or splenomegaly)
 - reactive serology (by two tests with at least one being treponemal) or a fourfold or greater increase in titre over the previous known non-treponemal test.

Confirmed case—Early latent syphilis

Presence of the following three conditions:

- absence of clinical manifestations of syphilis
- serological detection of a *T. pallidum* infection by two recognized tests, including at least one treponemal test
- at least one of the following four situations:
 - non-reactive serology or a fourfold decrease in titre for a non-treponemal test done in the last 12 months
 - symptoms suggestive of primary or secondary syphilis in the last 12 months and has not been treated
 - exposure to a sexual partner with primary, secondary or early latent syphilis in the last 12 months and has not been treated
 - an adequately treated anterior infection where the only cause of the persistence of elevated titre can be explained by a new infection.

Confirmed case—Late latent syphilis

Presence of the following four conditions:

- serological detection of a *T. pallidum* infection by two recognized tests, including at least one treponemal test
- absence of clinical manifestations of syphilis
- no previous treatment for syphilis
- absence of situations suggesting the acquisition of *T. pallidum* infection in the past 12 months (mentioned in point 3 of the case definition of early latent syphilis).

Confirmed case—Neurosyphilis

Does not differentiate between Infectious and Non-infectious Neurosyphilis

Serological detection of a *T. pallidum* infection by two recognized tests, including at least one treponemal test in a person who has one of the following three conditions:

- a VDRL using a specific validated method reactive on a non-bloody CSF
- clinical manifestations compatible with neurosyphilis (meningo-vascular syphilis, generalized paresis or *tabes dorsalis*, for example) and pleiocytosis on the CSF in the absence of other causes
- clinical manifestations compatible with neurosyphilis (meningo-vascular syphilis, generalized paresis or *tabes dorsalis*, for example) and proteinorachia on the CSF in the absence of other causes.

Confirmed case—Tertiary Syphilis

Serological detection of a *T. pallidum* infection by two recognized tests, including at least one treponemal test, with at least one of the following:

- characteristic late abnormalities of the cardiovascular system, bone, skin or other structures, in the absence of other known causes of these abnormalities
- no clinical or laboratory evidence of neurosyphilis

¹⁴ Newfoundland and Labrador^q

The methods (such as NAT) for identifying *T. pallidum* are not specified for primary, secondary or early latent syphilis.

Confirmed case—Neurosyphilis

The provincial case definition does not differentiate between infectious and non-infectious Neurosyphilis. Instead, the provincial definition is a combination of the two and does not include the prefacing statement of "Fits the criteria of primary, secondary OR early latent syphilis above" which can be found in the national definition.

^q <u>Newfoundland and Labrador</u>: Department of Health and Community Services. Newfoundland and Labrador Disease Control Manual- Section 5: Sexually Transmitted Infections and Blood-Borne Pathogens, 2016. Available at: <u>https://www.health.gov.nl.ca/health/publications/diseasecontrol/s5 sexually transmitted and bloodborne pathogens</u>.<u>pdf</u>, Accessed June 17, 2020.

B.IV Provincial reporting to CNDSS from 2008 to 2017

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
BC ¹⁵	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
AB	\checkmark	\checkmark	\checkmark	\checkmark	√16	√16	√16	√16	√ 16	√16
SK	\checkmark	\checkmark	\checkmark	\checkmark	√17	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
MB	\checkmark	✓	✓	\checkmark	\checkmark	✓	✓	✓	✓	✓
ON18	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
QC	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
NB ¹⁹	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
NS	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
PE						√20	√20	√20	√20	√20
NL ²¹	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	√22	\checkmark	\checkmark
ΥT					√23	√24				
NT	\checkmark	\checkmark	√ ²⁵		√ ²⁶			√ ²⁵		√ ²⁵
NU					\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark

Provincial reporting of infectious syphilis (primary, secondary, early latent)

Note: A check mark (\checkmark) indicates that the PT reported syphilis data on that given year

¹⁵British Columbia: Did not specify case stages (primary, secondary or early latent) from 2008 to 2017

¹⁶Alberta: Did not specify case stages (primary, secondary or early latent) from 2012 to 2017

¹⁷Saskatchewan: No reported cases of early latent syphilis that year

¹⁸Ontario: Did not specify case stages (primary, secondary or early latent) from 2008 to 2017

¹⁹New Brunswick: Did not distinguish primary from secondary syphilis when reporting from 2008 to 2017

²⁰Prince Edward Island: Did not specify case stages (primary, secondary or early latent) from 2013 to 2017

²¹Newfoundland and Labrador: No reported cases of secondary syphilis from 2008 to 2017

²²Newfoundland and Labrador: No reported cases of secondary or early latent syphilis that year

²³Yukon Territory: No reported cases of primary or early latent syphilis that year

²⁴Yukon Territory: No reported cases of early latent syphilis that year

²⁵Northwest Territories: No reported cases of secondary or early latent syphilis that year

²⁶Northwest Territories: No reported cases of secondary syphilis that year

Provincial reporting of non-infectious syphilis (late latent and tertiary syphilis)

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
BC										
AB	\checkmark	\checkmark	\checkmark	\checkmark						
SK		√27	√28	√28	√28	\checkmark			√27	√27
MB	\checkmark	√ ²⁹			√ ²⁹		√ ²⁹	√ ²⁹	\checkmark	√ ²⁹
ON										
QC	\checkmark									
NB ³⁰		\checkmark								
NS	√31	√ 31	\checkmark	\checkmark	√31	√31	\checkmark	\checkmark	√31	\checkmark
PE										
NL	√ ³²	√ ³³	\checkmark	√ ³³	√ ³³	√ ³³	\checkmark	\checkmark	\checkmark	\checkmark
ΥT			√ ³⁴	√ ³⁴	√ ³⁴	\checkmark	√ ³⁴	√ ³⁴	√ ³⁴	√ ³⁴
NT	\checkmark	\checkmark	√ ³⁵	√ ³⁵	√ ³⁵	√ ³⁵				√ ³⁵
NU					√ ³⁶		√ ³⁶	√ ³⁶	√ ³⁶	\checkmark

Note: A check mark (\checkmark) indicates that the PT reported syphilis data on that given year

²⁷Saskatchewan: No reported cases of late latent syphilis that year

²⁸Saskatchewan: No reported cases of tertiary syphilis that year

²⁹Manitoba: No reported cases of late latent syphilis that year

³⁰New Brunswick: No reported cases of tertiary syphilis from 2008 to 2017

³¹Nova Scotia: No reported cases of tertiary syphilis that year

³²Newfoundland and Labrador: No reported cases of late latent syphilis that year

³³Newfoundland and Labrador: No reported cases of tertiary syphilis that year
 ³⁴Yukon Territory: No reported cases of tertiary syphilis that year
 ³⁵Northwest Territory: No reported cases of tertiary syphilis that year
 ³⁶Nunavut: No reported cases of tertiary syphilis that year

Appendix C: Data and methods

C.I. Syphilis Surveillance Data

Data Sources

Numerator data

Provincial and territorial health authorities provide non-nominal data on laboratory-confirmed cases to PHAC via CNDSS. Data from January 1, 1971 to December 31, 2017, were available from all provinces and territories as per their reporting history (<u>Table 2</u>) and were extracted from CNDSS in April and May 2019. Syphilis has been notifiable since 1924, while congenital syphilis became notifiable in 1993. Reported cases adhere to the national case definitions (see <u>Appendix B – Case definitions</u>). Variables submitted along with the diagnosis include stage of syphilis, sex, age at time of diagnosis, year of diagnosis and province/territory of diagnosis. CNDSS began to collect information on these variables at various times; stage of syphilis and province/territory has been reported since 1971, while age and sex has been reported since 1991. Preliminary syphilis surveillance data for 2018-2019, stratified by age and by sex were received directly from the provinces and territories. All data received were validated in collaboration with the corresponding province or territory.

Denominator data

Population estimates from Canada between 1979 and 2018 were extracted from Statistics Canada census (2018). The data includes the total Canadian population, as well as provincial population stratified by both age (0-100+) and sex (Male, Female, Both). As per the Statistics Canada data extraction, estimates are adjusted for under coverage and postcensal estimates are based on the 2016 census. Population estimates for the Northwest Territories and Nunavut were not separately provided prior to July 1991. To calculate rates of congenital syphilis, the number of live births, by place of residence of mother, was extracted from Statistics Canada data between 1993 and 2017^r. The total for "Canada, place of residence of mother" was used, and the total for "Place of residence of mother outside Canada" was excluded. For data pertaining to live births within women of childbearing age only, data were extracted from Statistics Canada between 1993 and 2017 from the "Live births, by age of mother" table.^s

^r Statistics Canada. Table 13-10-0414-01 Live births, by place of residence of mother **DOI:** <u>https://doi.org/10.25318/1310041401-eng</u>

^s Statistics Canada. Table 13-10-0416-01 Live births, by age of mother

DOI: https://doi.org/10.25318/1310041601-eng

Province/Territory	Reporting history
British Columbia	Began to report on syphilis cases in 1939.
	Only reported on infectious cases from 1998 to 2016.
Alberta	Began to report on syphilis cases in 1931.
	Only reported on infectious cases since 2006.
Manitoba	Began to report on syphilis cases in 1938.
Saskatchewan	Began to report on syphilis cases in 1931.
	Only reported on infectious cases from 2005 to 2011 and in 2016.
Ontario	First reported in 1924 and then each year since 1927.
	Has only reported on infectious cases since 2005.
Quebec	Began to report on syphilis cases in 1944.
New Brunswick	Began to report on syphilis cases in 1931.
Nova Scotia	Began to report on syphilis cases in 1925.
Prince Edward Island	Began to report on syphilis cases in 1931.
Newfoundland and	Joined the confederation in 1949.
Labrador	Began to report on syphilis cases in 1949.
Nunavut	Established as a territory in 1999.
	Preliminary data reported as of 2015.
Northwest Territories	Began to report on syphilis cases in 1959.
Yukon	Began to report on syphilis cases in 1956.

Table 3. Reporting of syphilis across provinces and territories through time in Canada

Note: These details were obtained from: <u>https://diseases.canada.ca/notifiable/charts?c=pd</u>

Data Analysis

Data analysis was performed using Microsoft Excel and RStudio version 3.6.0. All stages of syphilis are notifiable, but infectious stages (primary, secondary, and early latent) form the majority of content presented in this report. National annual rates of reported cases of infectious syphilis were computed using the number of cases from the CNDSS as numerators, and Statistics Canada July 2018 yearly population estimates as denominators. Age group, sex and province/territory-specific incidence rates were also calculated. For all years, incidence rates were given per 100,000 population. For congenital syphilis, rates were reported per 100,000 live births. Rates, percentages, and change in rates were calculated using unrounded numbers. No statistical procedures were used for comparative analyses.

Previous reports may present different rates for some years due to reporting delays, data being updated from provinces and territories, or improvements in data cleaning and validation.

Rates of infectious syphilis by age group and sex over time can be retrieved from the Notifiable Disease Online website: <u>https://diseases.canada.ca/notifiable/charts-list</u>

Data Source and Analysis for OECD Countries

Data for figures comparing rate values from OECD countries were obtained from the most recent reports from the following institutions: CDC (US), The Kirby Institute (Australia), ECDC (Europe) and Public Health England. Tables were generated using reported data for each country between the years of 2008 and 2017.

International Syphilis Response Environmental Scan

International responses to syphilis were analyzed from the following organizations: Institute of Public Health in Ireland, Public Health England, CDC, Australian Government Department of Health, and the ECDC from August 12, 2019 to August 30, 2019. Searches were performed in their respective public health websites with the following key words: "syphilis" AND "intervention" OR "response" OR "evaluation" OR "campaign". From the resulting selected resources, the following data items were extracted: location/setting, outcome to be modified, intervention, evaluation method, and results.

C.II Literature Review

Research Strategy: A PHAC reference librarian used the Medline, Embase, ProQuest Public Health and Scopus databases to search for articles on the topic of syphilis in Canada published between January 2009 and December 2018. The search was completed on December 18, 2018. To ensure references were up to date for the purposes of this report, another search was conducted in September 2019.

Using the Boolean operator "OR", the terms employed to capture articles pertaining to syphilis were: syphilis, neurosyphilis, *Treponema pallidum*, and Great Pox. Terms used to identify Canadian publications were: Canada, Canadian, *Canadien*, Ottawa, British Columbia, *Colombie-Britannique*, Vancouver, Alberta, Edmonton, Calgary, Saskatchewan, Regina, Saskatoon, Manitoba, Winnipeg, Ontario, Toronto, Quebec, Quebecois, Montreal, New Brunswick, *Nouveau Brunswick*, Fredericton, Nova Scotia, *Nouvelle-Écosse*, Halifax, Prince Edward Island, *Île-du-Prince-Édouard*, Charlottetown, Newfoundland, *Terre-Neuve*, Yukon, Whitehorse, Northwest Territories, *Territoires du Nord-Ouest*, Nunavut, Yellowknife, and Iqaluit. These two sets of terms were combined using the Boolean operator "AND". Additional publications were identified using a snowball-based approach, based on relevant publications' reference lists.

Inclusion and Exclusion Criteria

Works were included in the literature review if they covered the topic of the epidemiology of syphilis in Canada, the risk factors associated with the rise of syphilis rates in Canada, or the public health efforts to reduce syphilis rates in Canada. Studies were included if they used data from 2009 to 2019. Scientific peer-reviewed articles, governmental reports, conference and article abstracts, and scientific posters were all included. No language restrictions were applied.

Works were excluded if they did not address the aforementioned topics of syphilis or if they were based outside of Canada. Furthermore, clinical case studies, research notes, and articles on sampling techniques, molecular characterization, and economic evaluations of public health interventions were excluded. When multiple publications by the same author explored a similar topic (e.g., repeat publications), only the most recent work was included. Finally, publications that were not available online or via the PHAC Health Library were excluded from the review.

Study Selection and Data Extraction

To select relevant, non-duplicative works, one researcher reviewed the publication's titles, and then subsequently reviewed the retained abstract summaries, followed by the retained full-text works. A second researcher independently reviewed a sample of the identified full-text works to validate the initial selection approach. Where divergence in opinions occurred between the two reviewers, consensus was reached between the first two reviewers and a third researcher. From the final selection of works, two researchers extracted the following data items for narrative synthesis: title, author, year, setting, design, objectives, years of data collection, study population, sample size, syphilis stage, syphilis measure, co-infection measure, risk factors, type of analysis, primary results, challenges identified during the intervention, secondary results, and study limitations.

Additional searches were conducted in a targeted way in the international scientific evidence when Canadian studies were limited on specific themes.

C.III Outbreak Data

National Outbreak Environmental Scan

All resources included in the the outbreak environmental scan were published after January 1, 2005, were restricted to Canada, included the keywords "syphilis" and "outbreak," and" were collected from February 2019 to September 2019. Publically available resources included media sources (Canadian Broadcasting Corporation News, Canadian Television Network, Maclean's, Global News, The Western Star, etc.), provincial and municipal websites (Ontario Public Health, Government of Northwest Territories, Vancouver Coastal Health, etc.), alerts from the International Society for Infectious diseases (Pro-MED), peer-reviewed articles (PubMed, Google Scholar), and articles and podcasts from the National Collaborating Centre for Infectious Diseases (NCCID). Internal resources, including PowerPoint slide decks from the NCCID Knowledge Exchange Forum on Syphilis, were also incorporated if they matched the inclusion criteria. Overall, over 100 resources were found which met the stated criteria.

From the selected resources, the following data items were extracted: location, date of outbreak, number of cases, proportion of infectious cases, profile of cases, detailed description of the outbreak, outbreak evolution, female to male ratio, main risk factors, main interventions, and additional information of interest.

Outbreak time periods were estimated based on the following:

- The beginning of an outbreak time period was determined by sources which indicated that an outbreak was declared at a certain time or the earliest sources available which indicate that a syphilis outbreak is occurring in that region
- The end of an outbreak time period was determined by sources which indicated that a syphilis outbreak was declared over at a certain time or the latest available sources which indicate that a syphilis outbreak is occurring

In some cases, multiple syphilis outbreaks were found in one region in the post-2005 time period. This was determined if a source was found which indicated that multiple outbreaks had occurred post-2005, or if a source was found which referred to an older outbreak in the past tense.

The environmental scan was used to complement the scientific literature review, given lags in publication, and to allow for the presentation of a more up-to-date picture, by jurisdiction.

Appendix D: Rates of infectious syphilis per 100,000 population by sex in countries of the Organization for Economic Co-operation and Development, 2008-2017

Year	ar Canada			United States				England		Australia			European Union		
	Male	Female	Ratio	Male	Female	Ratio	Male	Female	Ratio	Male	Female	Ratio	Male	Female	Ratio
2008	7.3	1.1	6.4	7.5	1.5	5.2	NA	NA		11.2	1.4	8.0	-	-	3.0
2009	8.6	0.9	9.2	7.8	1.4	5.4	9.8	1.3	7.5	11	1	11.0	-	-	3.2
2010	9.2	0.9	10.3	7.9	1.1	7.0	9.1	1.1	8.3	9	1.1	8.2	-	-	3.8
2011	9.6	0.7	14.7	8.1	1.0	8.5	10.1	1.1	9.2	9.9	1.5	6.6	-	-	3.9
2012	11.3	0.6	18.4	9.2	0.9	10.1	10.4	1.0	10.4	12.3	1.4	8.8	-	-	4.6
2013	11.9	0.8	14.5	10.2	0.9	11.3	11.4	1.2	9.5	14.2	1.3	10.9	-	-	5.1
2014	12.7	0.9	13.8	11.6	1.1	10.5	15.5	1.1	14.1	16.6	1.5	11.1	-	-	6.1
2015	17.0	1.0	16.3	13.6	1.4	9.7	18.4	1.2	15.3	21.2	2.5	8.5	-	-	7.9
2016	19.8	1.7	11.6	15.5	1.9	8.2	20.6	1.2	17.2	25.1	3.6	7.0	-	-	7.9
2017	20.0	2.4	8.2	16.9	2.3	7.3	24.4	1.5	16.3	31.1	5.5	5.7	12.0	1.4	8.5

Note: Data for England was available starting 2009

Data was retrieved online from the Surveillance Atlas of Infectious Diseases

(https://atlas.ecdc.europa.eu/public/index.aspx). To calculate the Male to Female ratio, reported syphilis cases from 2008 to 2017 were extracted. Rates before 2017 were not available, so the ratio was calculated by comparing the male to female total number of confirmed cases and the proportion of male to female cases (distribution by gender) for the EU.

United States data sources

Centers for Disease Control and Prevention, Sexually Transmitted Disease Surveillance 2017, Table 28. Primary and Secondary Syphilis among women – reported cases and rates of reported cases by State/Area and Region in Alphabetical order, US and Outlying Areas, 2013 – 2017

Centers for Disease Control and Prevention, Sexually Transmitted Disease Surveillance 2017, Table 29. Primary and Secondary Syphilis among men – reported cases and rates of reported cases by State/Area and Region in Alphabetical order, US and Outlying Areas, 2013 – 2017

CDC Wonder, Selected Sexually Transmitted Diseases by Age, Race/Ethnicity, and Gender, 1996-2014 Request, Primary and Secondary Syphilis, Male AND Female, All ages, All races/ethnicities, 2008 – 2013

Australia data source

HIV, viral hepatitis and sexually transmissible infections in Australia, Annual surveillance report 2018. Chapter 4, Section 4.3 – Syphilis. Data retrieved from Figure 4.3.1 Infectious syphilis notification rate per 100 000 population, 2008 – 2017, by sex.

England data source

Public Health England, Official Statistics Sexually Transmitted infections (STIs): annual data tables. Table 1 (b): Rates of new STI diagnoses in England by gender, 2008 – 2017 Rates per 100 000, Syphilis: primary, secondary & early latent – total

European Union data source

European Center for Disease Prevention and Control, Surveillance Atlas of Infectious Diseases. Criteria: Syphilis, confirmed cases, reported cases, Export: Reported cases, Distribution by gender, 2008 – 2017

European Center for Disease Prevention and Control, Syphilis – Annual Epidemiological Report for 2017, Gender, Figure 2. Syphilis, male-to-female ratio in 27 EU and European Economic Area countries, 2017

Appendix E: Proportion of cases by syphilis stage overall and by sex in Canada, 1991-2017

Proportion of Male Cases by Stage

Year	Primary	Secondary	Early symptomatic	Early latent	Infectious syphilis - unspecified stage	Late latent	Tertiary
1991	15.0%	11.2%	9.3%	7.4%	0.0%	56.2%	0.9%
1992	8.9%	8.2%	5.4%	9.9%	0.0%	65.4%	2.2%
1993	4.4%	6.8%	2.6%	9.4%	0.0%	73.1%	3.7%
1994	8.1%	8.4%	6.6%	7.6%	0.0%	65.9%	3.4%
1995	10.0%	8.4%	4.0%	6.5%	0.0%	67.3%	3.7%
1996	7.8%	7.1%	1.8%	9.2%	0.0%	69.9%	4.3%
1997	12.8%	6.2%	0.4%	7.8%	0.0%	68.7%	4.1%
1998	7.9%	3.3%	1.7%	3.7%	29.5%	52.7%	1.2%
1999	5.1%	4.3%	0.4%	5.9%	27.5%	53.7%	3.1%
2000	6.8%	5.4%	1.1%	6.8%	21.2%	54.7%	4.0%
2001	10.4%	5.5%	2.0%	5.8%	29.7%	45.0%	1.7%
2002	14.1%	23.1%	0.3%	8.2%	19.0%	32.8%	2.4%
2003	20.1%	24.0%	1.5%	11.9%	17.0%	23.7%	1.8%
2004	21.5%	27.5%	1.3%	10.6%	17.6%	19.1%	2.4%
2005	15.4%	14.9%	0.3%	6.7%	52.0%	8.7%	2.0%
2006	15.6%	17.8%	0.6%	10.9%	48.1%	5.1%	1.8%
2007	13.0%	15.1%	0.8%	10.4%	54.6%	4.7%	1.3%
2008	17.2%	14.6%	0.7%	9.8%	47.1%	8.6%	2.0%
2009	17.0%	12.2%	1.0%	10.2%	52.9%	4.9%	1.7%
2010	14.7%	15.3%	2.4%	10.8%	48.8%	6.3%	1.7%
2011	16.0%	13.4%	2.7%	11.1%	48.2%	7.3%	1.2%
2012	12.1%	12.6%	0.7%	11.5%	56.7%	5.9%	0.5%
2013	30.6%	11.7%	1.2%	13.4%	36.3%	6.1%	0.8%
2014	12.3%	10.2%	0.8%	10.6%	58.4%	6.6%	1.1%
2015	10.1%	9.1%	0.7%	11.3%	62.2%	5.4%	1.1%
2016	9.8%	9.5%	0.3%	13.0%	59.8%	6.5%	1.1%
2017	10.2%	8.5%	0.4%	12.0%	61.0%	6.8%	1.2%

% of infectious syphilis cases by stage

0	25	50	75	100

Proportion of Female Cases by Stage (Primary, Secondary, Early Latent, Late Latent and Tertiary)

Year	Primary	Secondary	Early symptomatic	Early latent	Infectious syphilis - unspecified stage	Late latent	Tertiary
1991	9.6%	10.5%	5.8%	9.6%	0.0%	63.7%	0.9%
1992	5.8%	10.0%	7.2%	8.4%	0.0%	67.1%	1.4%
1993	4.1%	5.4%	3.2%	8.9%	0.0%	77.3%	1.1%
1994	4.8%	2.9%	6.5%	8.7%	0.0%	73.9%	3.2%
1995	4.9%	5.3%	4.2%	4.5%	0.0%	79.2%	1.9%
1996	5.0%	5.0%	2.1%	7.1%	0.0%	79.4%	1.3%
1997	5.3%	7.6%	0.4%	8.9%	0.0%	74.7%	3.1%
1998	2.0%	2.0%	1.0%	6.0%	22.5%	65.5%	1.0%
1999	1.9%	2.4%	0.0%	5.8%	27.9%	60.1%	1.9%
2000	3.3%	2.9%	0.5%	5.3%	17.2%	70.8%	0.0%
2001	7.0%	0.8%	0.4%	3.3%	30.2%	57.0%	1.2%
2002	2.3%	1.1%	0.4%	5.4%	27.6%	62.1%	1.1%
2003	6.5%	5.8%	0.7%	7.2%	30.5%	48.3%	1.0%
2004	7.0%	5.9%	0.7%	4.5%	27.3%	51.4%	3.1%
2005	13.4%	6.9%	0.0%	5.7%	42.5%	27.5%	4.0%
2006	12.4%	8.6%	0.9%	10.7%	44.2%	22.3%	0.9%
2007	11.5%	6.9%	0.5%	20.6%	34.4%	21.6%	4.6%
2008	20.9%	10.3%	2.3%	19.8%	19.0%	25.5%	2.3%
2009	21.6%	13.1%	1.4%	23.9%	13.6%	24.9%	1.4%
2010	10.2%	7.2%	1.7%	25.1%	20.4%	34.0%	1.3%
2011	12.1%	8.3%	3.4%	13.6%	17.5%	44.7%	0.5%
2012	7.8%	4.1%	0.9%	11.9%	24.2%	49.3%	1.8%
2013	11.2%	7.9%	0.4%	12.0%	28.5%	36.4%	3.7%
2014	16.0%	6.0%	0.4%	16.8%	26.4%	33.2%	1.2%
2015	17.4%	10.2%	1.5%	14.0%	27.2%	27.9%	1.9%
2016	18.3%	9.5%	0.0%	12.8%	31.6%	26.9%	0.9%
2017	14.8%	7.4%	0.2%	17.1%	35.8%	23.7%	1.0%

	% of infectious syphilis cases by stage									
0		25		50			75			100

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

Appendix F: Rates of reported cases of infectious syphilis per 100,000 population by age group and sex in Canada, 2009-2018

Rates of Infectious Syphilis per 100,000 Population in Males by Age Group in Canada

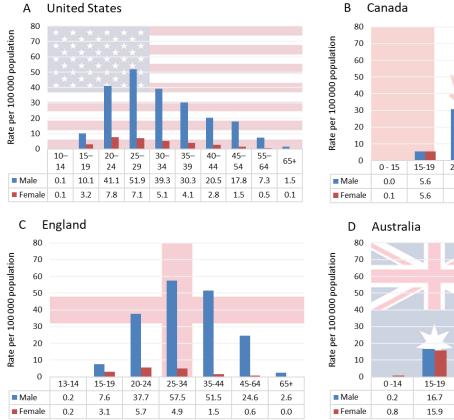
		Age group										
Year	<15	15 to 19	20 to 24	25 to 29	30 to 39	40 to 59	60+					
2009	0.0	3.4	12.7	17.0	16.4	12.3	1.7					
2010	0.0	3.9	12.9	15.4	15.9	14.2	2.6					
2011	0.0	4.5	16.1	19.8	17.3	13.6	2.1					
2012	0.0	6.3	21.6	22.2	20.5	15.0	2.9					
2013	0.0	4.0	20.9	25.7	21.8	16.0	3.4					
2014	0.0	4.1	19.9	25.5	25.0	18.1	2.9					
2015	0.0	5.3	23.9	36.5	34.2	24.0	4.4					
2016	0.0	5.9	27.4	40.8	39.9	28.7	5.2					
2017	0.0	5.6	30.7	44.2	44.2	26.0	5.1					
2018	0.1	11.0	40.0	65.1	60.6	30.0	10.9					

Rates of Infectious Syphilis per 100,000 Population in Females by Age Group in Canada

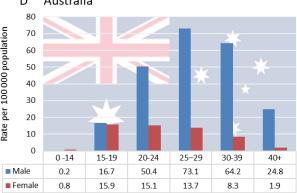
		Age group										
Year	<15	15 to 19	20 to 24	25 to 29	30 to 39	40 to 59	60+					
2009	0.0	0.9	3.3	2.9	1.6	0.7	0.1					
2010	0.0	1.5	3.3	2.6	1.5	0.6	0.1					
2011	0.0	1.7	2.0	1.9	1.2	0.4	0.0					
2012	0.0	1.5	2.2	1.1	1.0	0.5	0.0					
2013	0.0	2.0	3.1	2.1	1.5	0.4	0.1					
2014	0.0	2.0	3.6	2.4	1.7	0.6	0.0					
2015	0.0	1.7	3.4	3.9	2.0	0.6	0.0					
2016	0.1	3.5	6.3	5.7	2.9	1.1	0.1					
2017	0.1	5.6	8.2	8.1	4.5	1.5	0.1					
2018	0.3	16.9	26.4	24.7	14.2	2.7	0.2					

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

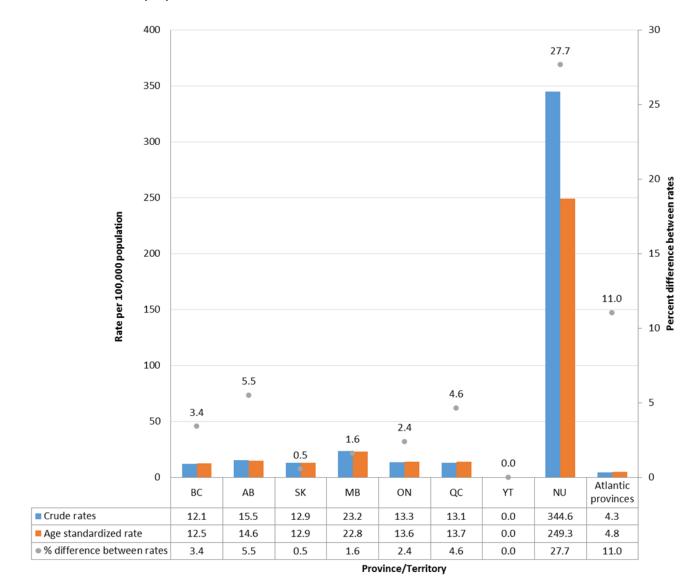
Rates of Reported Cases of Infectious Syphilis by Sex and Age per 100,000 Population in selected OECD Countries, 2017



60+ 40-59 20-24 25-29 30-39 30.7 44.2 44.2 26.0 5.1 8.2 8.1 4.5 1.5 0.1



Crude and age-standardized rates of reported cases of infectious syphilis for those 15 years of age and over, by province and territory, using the 2011 Canadian population as a reference, Canada, 2017



Note: Crude rates presented vary from the ones presented in Figure 17 because of the fact that the <15 year age group was excluded from the age-standardization procedure due to low counts of cases.

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System.

Appendix G: Rates of reported cases of infectious syphilis by province/territory and by sex in Canada, 2009-2018

Change in rates of reported cases of infectious syphilis by province and territory in Canada, 2014-2018



Province or Territory

Rate of Infectious Syphilis by Province/Territory in Canada, 2009-2018

	Province/Territory										Canada			
Year	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	ΥT	NU	NT	rate
2009	2.9	7.6	2.0	0.4	5.5	4.8	1.2	2.6	0.0	0.6	0.0	0.0	76.5	4.7
2010	2.1	4.6	3.4	1.4	5.9	6.9	4.5	1.9	0.0	0.8	0.0	0.0	6.9	5.0
2011	2.8	2.5	2.2	1.3	5.8	7.8	6.6	3.8	0.0	1.0	0.0	0.0	0.0	5.1
2012	5.8	3.3	0.6	2.0	6.2	8.3	2.8	6.7	0.0	1.7	2.8	83.6	4.6	5.9
2013	9.8	3.1	1.5	4.7	5.5	7.7	4.5	8.8	3.5	1.5	5.5	161.3	0.0	6.3
2014	9.2	3.8	2.5	9.2	6.5	7.1	3.6	6.8	6.2	4.5	0.0	228.0	4.6	6.7
2015	12.7	8.9	2.1	15.9	8.0	9.0	4.1	4.6	6.2	6.4	0.0	139.8	0.0	8.9
2016	12.2	9.7	7.5	17.7	10.4	11.7	1.7	1.8	1.4	4.3	0.0	262.3	2.2	10.7
2017	10.4	12.6	10.4	18.8	11.2	11.0	2.5	2.7	2.7	7.4	0.0	234.3	11.1	11.1
2018	15.2	35.7	12.0	60.7	13.4	11.3	2.7	3.4	2.6	7.2	4.9	261.1	37.9	17.1

	Province/Territory									Canada				
Year	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	ΥT	NU	NT	rate
2009	5.4	10.1	2.9	0.8	10.8	9.2	2.2	5.0	0.0	1.2	0.0	0.0	85.4	8.6
2010	4.1	6.2	4.9	1.5	11.3	13.1	8.6	3.7	0.0	1.6	0.0	0.0	4.5	9.2
2011	5.5	3.4	1.5	2.1	11.4	15.2	12.3	7.8	0.0	1.5	0.0	0.0	0.0	9.6
2012	11.4	5.6	0.2	3.5	12.3	15.9	4.5	13.4	0.0	3.1	5.4	94.9	8.9	11.3
2013	19.5	5.0	2.2	8.4	10.6	14.8	8.8	17.4	4.3	2.7	10.7	169.7	0.0	11.9
2014	17.7	7.0	5.0	16.0	12.6	13.4	6.9	13.3	11.4	9.2	0.0	199.6	8.9	12.7
2015	25.3	16.7	3.5	24.1	15.5	17.4	7.2	8.3	9.9	12.6	0.0	133.4	0.0	17.0
2016	24.0	16.8	13.8	24.1	19.9	22.5	3.4	3.7	2.8	8.0	0.0	236.9	0.0	19.8
2017	20.1	19.3	19.1	23.4	21.5	20.5	4.5	5.4	2.7	13.0	0.0	171.1	21.6	20.0
2018	29.0	42.9	17.7	65.4	25.5	20.2	5.2	6.4	3.9	12.3	4.8	248.7	47.7	27.1

Rate of Infectious Syphilis in Males by Province/Territory in Canada, 2009-2018

Rate of Infectious Syphilis in Females by Province/Territory in Canada, 2008 – 2018

	Province/Territory									Canada				
Year	BC	AB	SK	MB	ON	QC	NB	NS	PE	NL	ΥT	NU	NT	rate
2009	0.3	5.0	1.2	0.0	0.3	0.4	0.3	0.2	0.0	0.0	0.0	0.0	67.0	0.9
2010	0.1	3.0	1.9	1.3	0.7	0.7	0.5	0.2	0.0	0.0	0.0	0.0	9.5	0.9
2011	0.3	1.6	2.8	0.5	0.4	0.6	1.0	0.0	0.0	0.4	0.0	0.0	0.0	0.7
2012	0.3	1.0	0.9	0.5	0.4	0.7	1.0	0.2	0.0	0.4	0.0	71.6	0.0	0.6
2013	0.3	1.2	0.9	0.9	0.6	0.7	0.3	0.6	2.7	0.4	0.0	152.3	0.0	0.8
2014	0.8	0.6	0.0	2.5	0.5	0.8	0.3	0.6	1.4	0.0	0.0	258.1	0.0	0.9
2015	0.4	0.9	0.7	7.7	0.6	0.6	1.0	1.0	2.7	0.4	0.0	146.5	0.0	1.0
2016	0.5	2.5	1.1	11.2	1.0	1.0	0.3	0.0	0.0	0.7	0.0	289.2	4.6	1.7
2017	0.6	5.8	1.6	14.2	1.0	1.6	0.5	0.2	2.6	1.9	0.0	301.2	0.0	2.4
2018	1.2	28.3	6.2	55.9	1.3	2.2	0.3	0.6	1.3	2.3	5.0	274.2	27.5	7.0

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.

Appendix H: Number of cases and rates of congenital syphilis, rates of infectious syphilis among women aged 15 – 39 and rates of infectious syphilis among females, 1993-2018

Year	Number of congenital syphilis cases	Rate of congenital syphilis per 100,000 live births	Female rate (age 15 - 39) of infectious syphilis per 100,000 females	Total female rate of infectious syphilis per 100,000 females
1993	1	0.3	1.1	0.6
1994	4	1.0	1.0	0.5
1995	2	0.5	0.7	0.3
1996	1	0.3	0.7	0.3
1997	3	0.9	0.8	0.3
1998	1	0.3	0.9	0.4
1999	1	0.3	1.0	0.5
2000	2	0.6	0.8	0.4
2001	1	0.3	1.4	0.6
2002	4	1.2	1.5	0.6
2003	2	0.6	2.2	0.9
2004	1	0.3	1.8	0.8
2005	9	2.6	2.4	1.0
2006	6	1.7	2.4	1.1
2007	7	1.9	2.1	1.0
2008	5	1.3	2.6	1.1
2009	10	2.6	2.1	0.9
2010	5	1.3	2.1	0.9
2011	4	1.1	1.6	0.7
2012	3	0.8	1.4	0.6
2013	1	0.3	2.1	0.8
2014	1	0.3	2.3	0.9
2015	5	1.3	2.6	1.0
2016	4	1.0	4.3	1.7
2017	7	1.9	6.2	2.4
2018	17	4.6	19.3	7.0

Source: Public Health Agency of Canada (2019). Canadian Notifiable Disease Surveillance System. Preliminary 2018 data received directly from provinces and territories.