STI Update

NBIMU

Dan Smyth

April 27, 2023

Disclosures:

- Gilead: research funding and advisory board (Hepatitis C)
- Merck: clinical trial participation, research funding and advisory board (HIV, Hepatitis C)
- Ferring: clinical trial participation, advisory board, expert testimony to third party (C. difficile)
- Off label drug use mentioned: Doxy for use as PEP

Objectives:

- At the end of this presentations, participants will be able to:

1. Discuss recent trends in STI incidence regionally and nationally
2. Review common STI's seen in clinical practice, including clinical manifestations and treatment
3. Acknowledge PREP as a safe and effective mechanism to reduce incident HIV cases and identify, evaluate, prescribe, and follow up patients eligible for PREP

A case

- 87 year old male with COPD seen January 2023
- Fall of 2022 progressive difficulty with gait/mobility, relatively rapid progression of cognitive impairment. Occasional visual hallucinations
- Admitted to hospital after fire in residence (left stove on). CT global atrophy only. Ultimately unable to safety return home and discharged to assisted living
  - Late in admission a diagnostic test is ordered….
- Social history: heavily tattooed, time in jail, remote IVDU
- Exam: pupils not reactive to light or accommodation, weak with mild intention tremor, loss of position and vibration sense in lower extremities, unable to complete heel shin testing. + Romberg. Palpable liver edge (firm) and dullness @ Castell’s with inspiration

- Syphilis Antibody + @ RPR 1:4
- HCV + GT 1a @ viral load 1,780,000 copies
- LP completed, protein 0.63, 15 WBC with no differential
    - Provided with two weeks high dose IV Penicillin
- Currently on 12 weeks SOF/VEL for treatment of HCV
- Continues to live in assisted care environment

New Brunswick STI/BBP (2020)

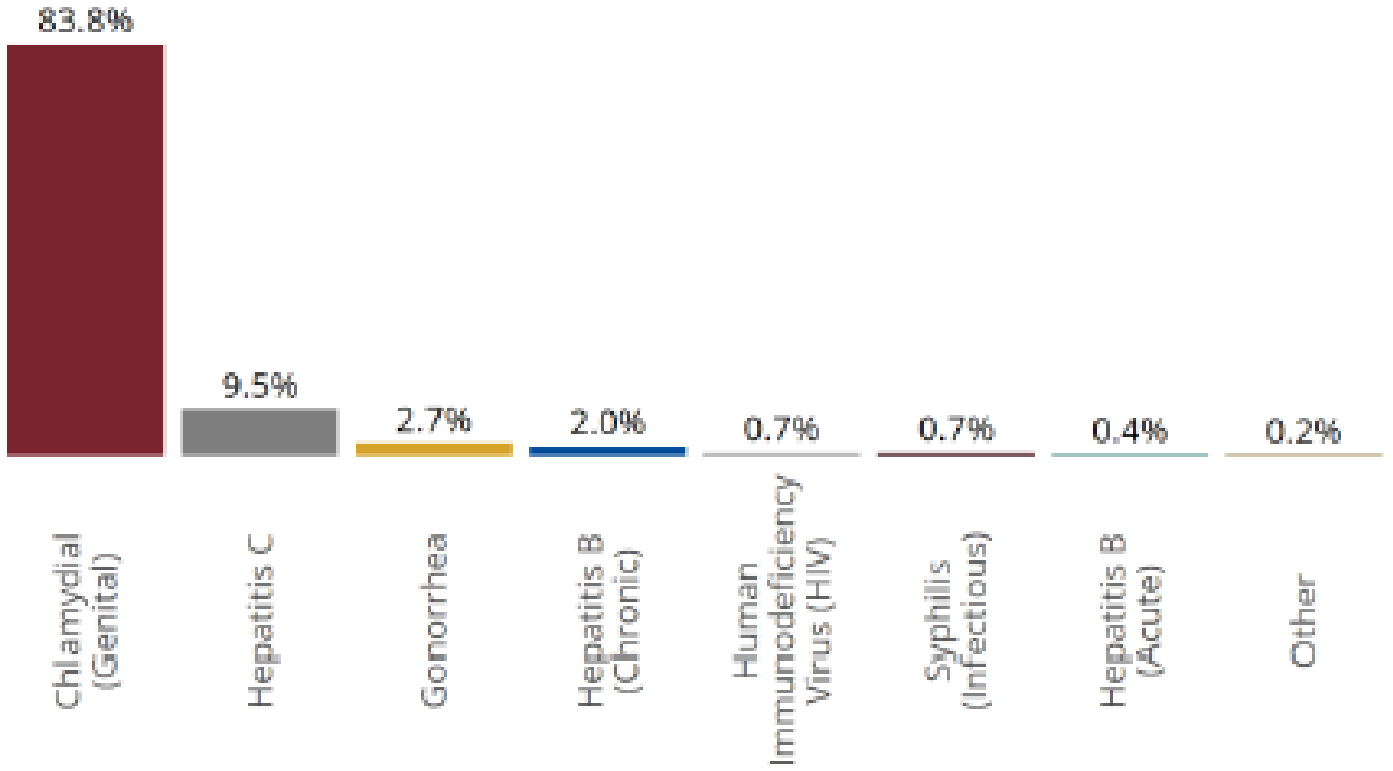
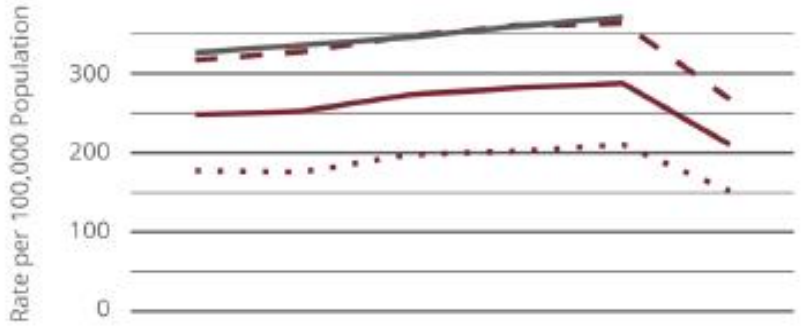


Figure 45: Percent Distribution of the most prevalent Sexually Transmitted and Blood Borne Infections in New Brunswick, 2020

Communicable Disease in NB Annual Report 2020, available online at https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/HealthProfessionals/Annual-report-CDC-branch-2020.pdf

Chlamydia (NB):

- Most common STI in NB
- 1642 cases in 2020
- 1056 female/586 male
- Incidence declining in 2020
  - Mayo clinic + CT cases down as much as 70% during pandemic year!
- Region 3 > 1 > 2
- Majority in 20-24 age group (705/43%)

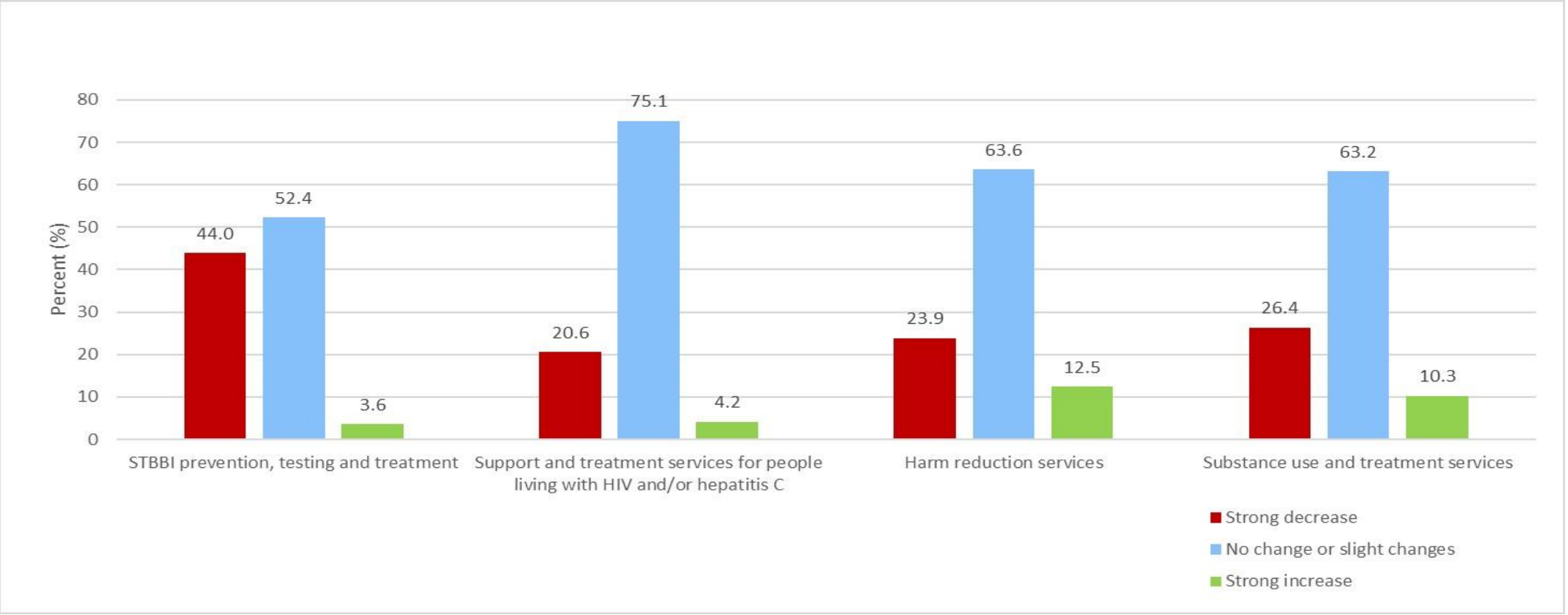


	2015	2016	2017	2018	2019	2020
No. of Cases (Males)	665	663	749	768	808	586
No. of Cases (Females)	1,215	1,264	1,345	1,402	1,426	1,056
No. of Cases	1,880	1,927	2,094	2,170	2,234	1,642
NB Rate (Males)	177.3	175.6	197.5	201.6	210.2	151.5
NB Rate (Females)	316.6	327.6	347.3	360.2	363.4	267.6
NB Rate	247.7	252.4	273.1	281.7	287.6	210.1
National Rate	326.1	335.7	345.6	359.2	370.8	-

Figure 47: Number of Reported Cases of Chlamydial (Genital) and Incidence Rates per 100,000 population, New Brunswick and Canada, 2015-2020

Communicable Disease in NB Annual Report 2020, available online at https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/HealthProfessionals/Annual-report-CDC-branch-2020.pdf

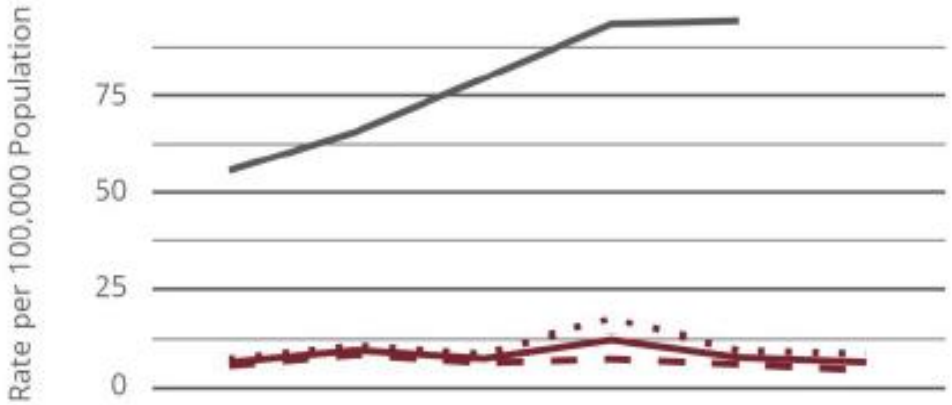
Proportion of STBBI service providers reporting changes in their organization's ability to provide STBBI-related services since the beginning of the COVID-19 pandemic (December 2020):



Survey on the impact of COVID-19 on the delivery of STBBI prevention, testing and treatment, including harm reduction services, in Canada. PHAC. Available at: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/survey-impact-covid-19-delivery-stbbi-prevention-testing-treatment.html

Gonorrhea (NB):

- 52 cases in 2020 (18 female, 34 male)
- NB much lower than national average
- Provincial outbreak declared April 2019. Region 1 > 2 > 3
- Highest in 25-29 males (50% gay/bisexual), 20-24 females, majority with casual or anonymous partner within 60 days
- 2019/2020 showed downtrend

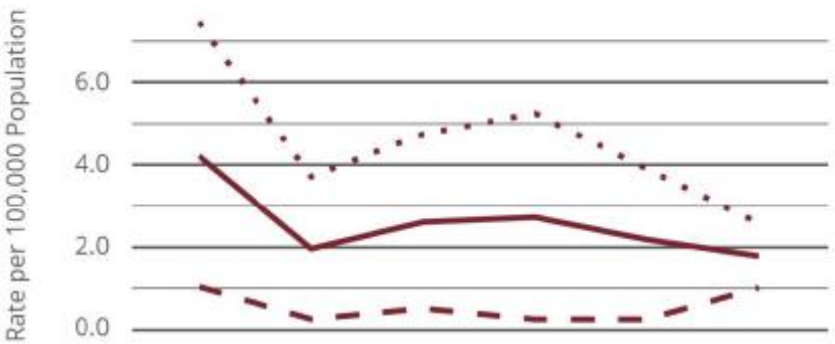


	2015	2016	2017	2018	2019	2020
No. of Cases (Males)	28	41	33	66	37	34
No. of Cases (Females)	22	33	25	29	24	18
No. of Cases	50	74	58	95	61	52
NB Rate (Males)	7.5	10.9	8.7	17.3	9.6	8.8
NB Rate (Females)	5.7	8.6	6.5	7.4	6.1	4.6
NB Rate	6.6	9.7	7.6	12.3	7.9	6.7
National Rate	55.5	65.6	79.4	93.5	94.3	-

Communicable Disease in NB Annual Report 2020, available online at https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/HealthProfessionals/Annual-report-CDC-branch-2020.pdf

Syphilis (NB)

- 14 cases in 2020 (4 female 10 male)
- Most in regions 1 and 2
- Highest incidence in 20-24 and 15-19 age groups
- 7 primary/secondary, 7 latent
- 70% of the men identified as MSM



	2015	2016	2017	2018	2019	2020
No. of Cases (Males)	28	14	18	20	15	10
No. of Cases (Females)	4	1	2	1	1	4
No. of Cases	32	15	20	21	17	14
NB Rate (Males)	7.5	3.7	4.7	5.2	3.9	2.6
NB Rate (Females)	1.0	0.3	0.5	0.3	0.3	1.0
NB Rate	4.2	2.0	2.6	2.7	2.2	1.8
National Rate	-	-	-	-	-	-

Communicable Disease in NB Annual Report 2020, available online at https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/HealthProfessionals/Annual-report-CDC-branch-2020.pdf

Infectious syphilis and congenital syphilis in Canada*, 2021

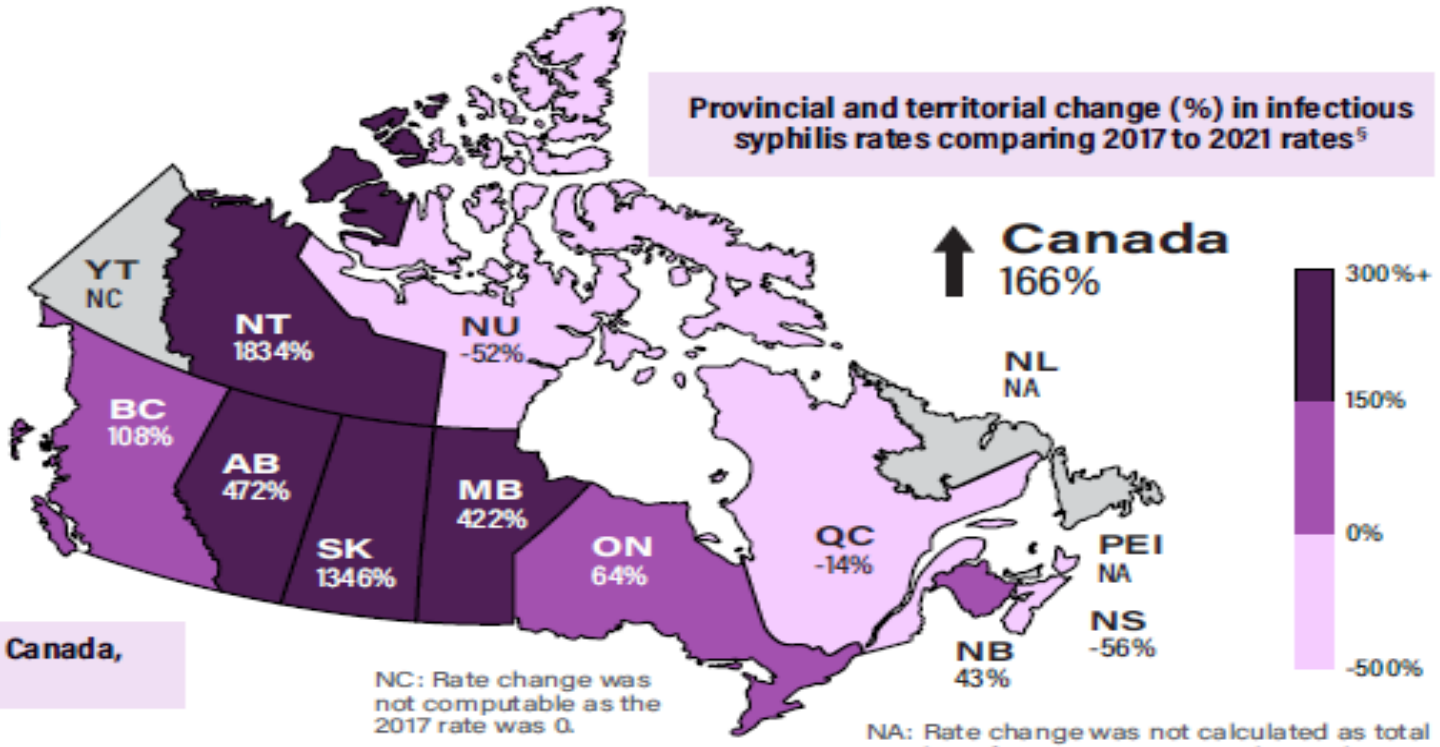
11,268 cases

of infectious syphilis† were reported in 2021, for a **rate of 30 per 100,000** population

Rate increased by ▲ **20%**

between 2020 and 2021 following a period of **decreased access to STBBI services** in the context of the COVID-19 pandemic ‡

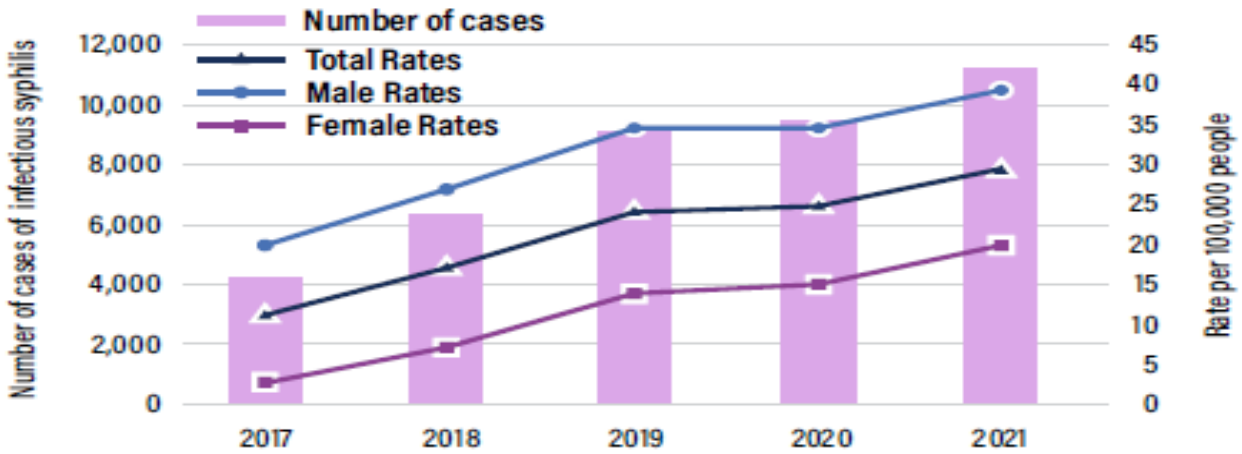
Provincial and territorial change (%) in infectious syphilis rates comparing 2017 to 2021 rates§



NC: Rate change was not computable as the 2017 rate was 0.

NA: Rate change was not calculated as total number of cases per year was lower than 5

Number of cases and rates of infectious syphilis by sex in Canada, from 2017 to 2021

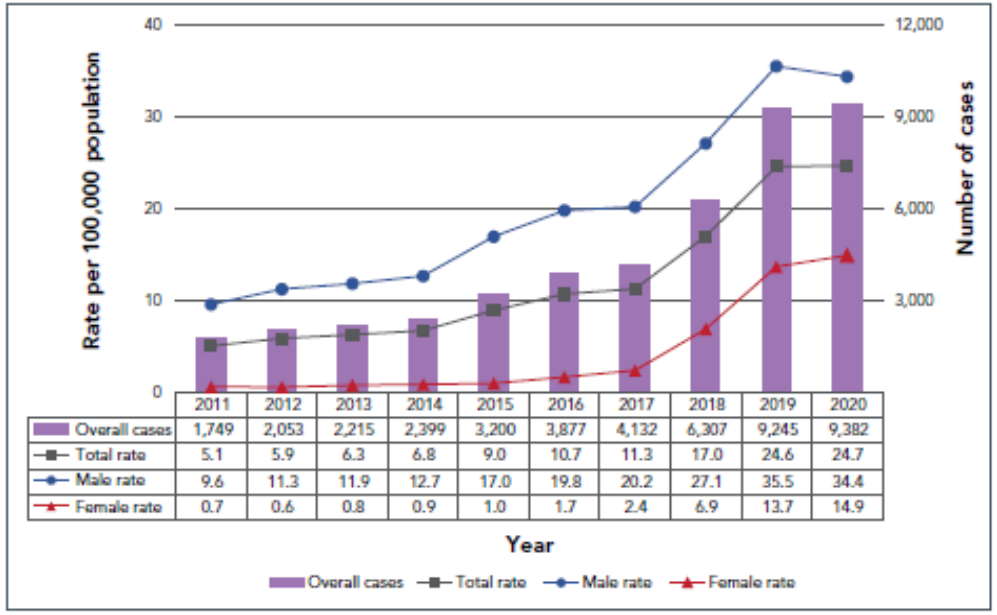


There were

96 CASES

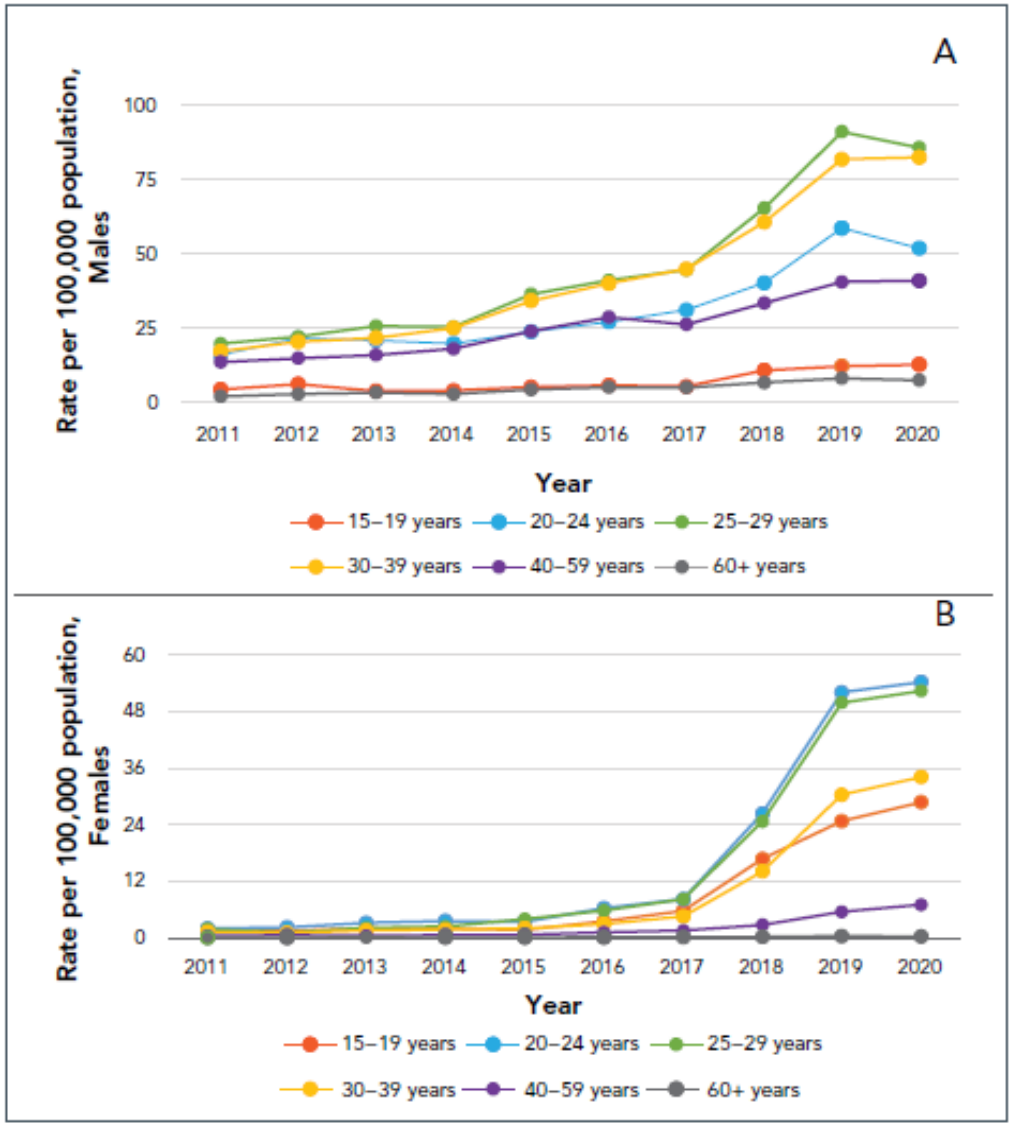
of confirmed early congenital syphilis† in 2021 compared to only 7 cases in 2017. An increase of 1271%.

Figure 1: Total number of cases and sex-specific rates of infectious syphilis in Canada by year, 2011–2020



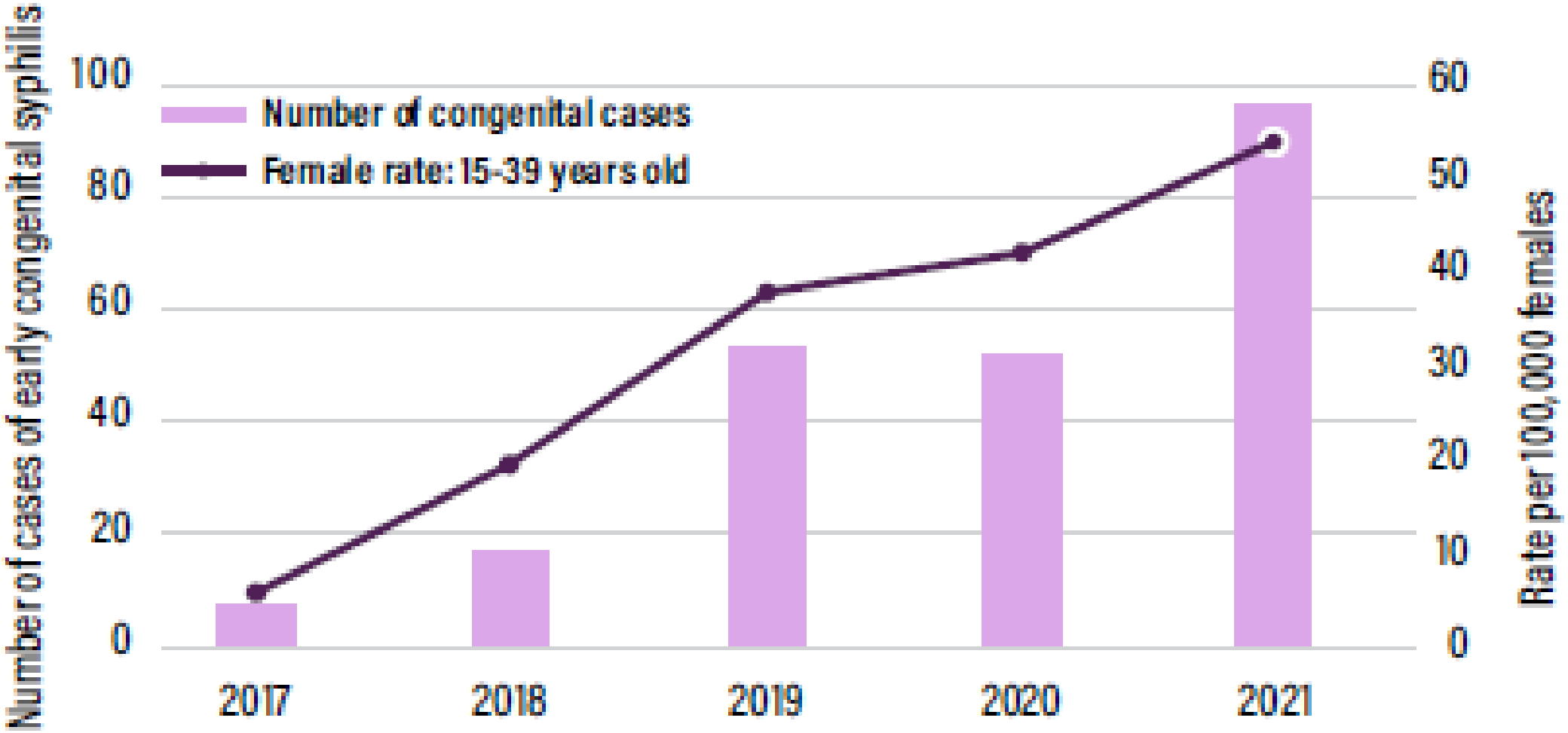
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Overall cases	1,749	2,053	2,215	2,399	3,200	3,877	4,132	6,307	9,245	9,382
Total rate	5.1	5.9	6.3	6.8	9.0	10.7	11.3	17.0	24.6	24.7
Male rate	9.6	11.3	11.9	12.7	17.0	19.8	20.2	27.1	35.5	34.4
Female rate	0.7	0.6	0.8	0.9	1.0	1.7	2.4	6.9	13.7	14.9

Figure 2: Rate of infectious syphilis in males and females per 100,000 by age group in Canada, 2011–2020[a,b]



[a] The rate for 2020 in Figure 2A (males) and Figure 2B (females) does not include data for Newfoundland and Labrador as they did not provide data stratified by sex AND age for this year
[b] Note that the scales of Figure 2A and 2B differ

Number of confirmed congenital syphilis cases and reported infectious syphilis rates among females aged 15-39 years in Canada, from 2017 to 2021



Screening

Guidelines for CT/GC **screening:**

- All sexually active persons < 25 years old
- Any person with risk factor for STI/BBP
- All pregnant women
- At least annually for MSM
  - Every 3-6 months if ongoing risk factors (multiple sexual partners)
- For those with HIV, at first screening and at least annually thereafter

Screening:

- HIV:
  - **PHAC: test if sexually active, especially if high risk, pregnancy.**
  - USPSTF: all pregnant, all adults 15-65
- Syphilis:
  - **PHAC: anyone presenting with risk factors, pregnancy**
  - USPSTF: **asymptomatic, non pregnant adolescents and adults who have ever been sexually active and are at increased risk for syphilis infection** should be screened. JAMA 2022; 328(12): 1243-1249
    - Caveat is it's physician discretion to determine who is at risk
  - All pregnant and symptomatic persons
    - **Universal first prenatal visit and strongly consider again at 28-32 weeks if any concern**
- HCV:
  - **Birth cohort (1945-1975) and those with risk factors.**
  - See Canadian Guidelines Shah et al CMAJ 2018 190 (22) E677-E687

Box 2: Populations for whom testing for hepatitis C virus (HCV) is recommended

Risk factor–based screening[24]

- History of current or past (even once) injection drug use*
- Received health care or personal services where there is a lack of infection prevention and control practices
- Received a blood transfusion, blood products or organ transplant before 1992 in Canada
- History of or current incarceration
- Born or resided in a region where hepatitis C prevalence is > 3%, such as:
  - Central, East and South Asia;
  - Australasia and Oceania;
  - Eastern Europe;
  - Subsaharan Africa;
  - North Africa or Middle East
- Born to a mother who is HCV-infected
- History of sexual contact or sharing of personal care items with someone who is HCV-infected*
- HIV infection, particularly men who have sex with men*
- Received chronic hemodialysis treatment
- Elevated alanine aminotransferase

Population-based screening[25]

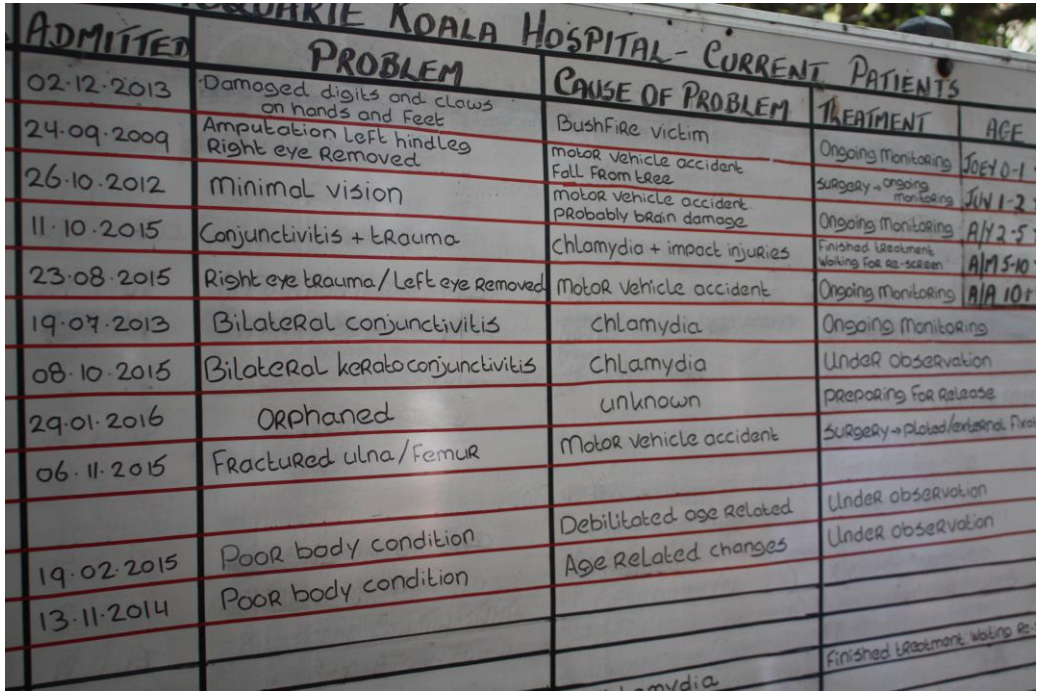
- Born between the years 1945 and 1975

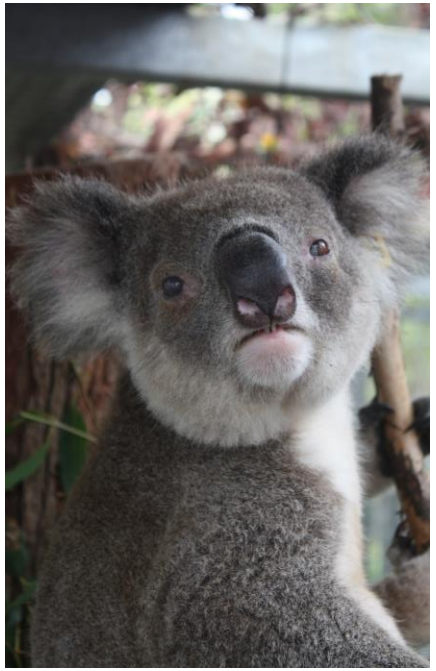
*Retesting should be performed at least once per year in those individuals who are engaged in ongoing high-risk activities and must be done with HCV RNA, as anti-HCV will remain positive even after achievement of sustained virologic response.

STI Clinical

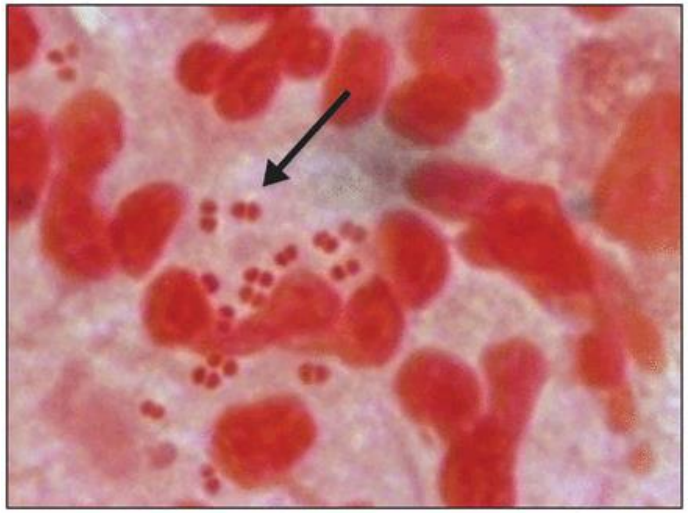
Chlamydia trachomatis:

- Most common bacterial STI
- Clinical:
  - Most asymptomatic
  - GU: urethritis, cervicitis, epididymitis, PID, PROM/pre term delivery in pregnancy
  - Non-GU: perihepatitis (FHC), conjunctivitis, pharyngitis/proctitis
  - Serovars L1, L2, L3: LGV: painless ulcer and regional LN
  - Infants born to infected mothers: conjunctivitis, pneumonia
- Treatment:
  - Anogenital and conjunctival: **DOXY 100 PO BID for 7 days or Azithromycin 1g PO X 1**
    - Doxy if rectal/pharyngeal infection and no adherence concerns
    - Azithromycin if pregnant
  - LGV: **Doxy 100 PO BID 21 days**
  - Test/treat partners, expedited partner therapy if partner is not available





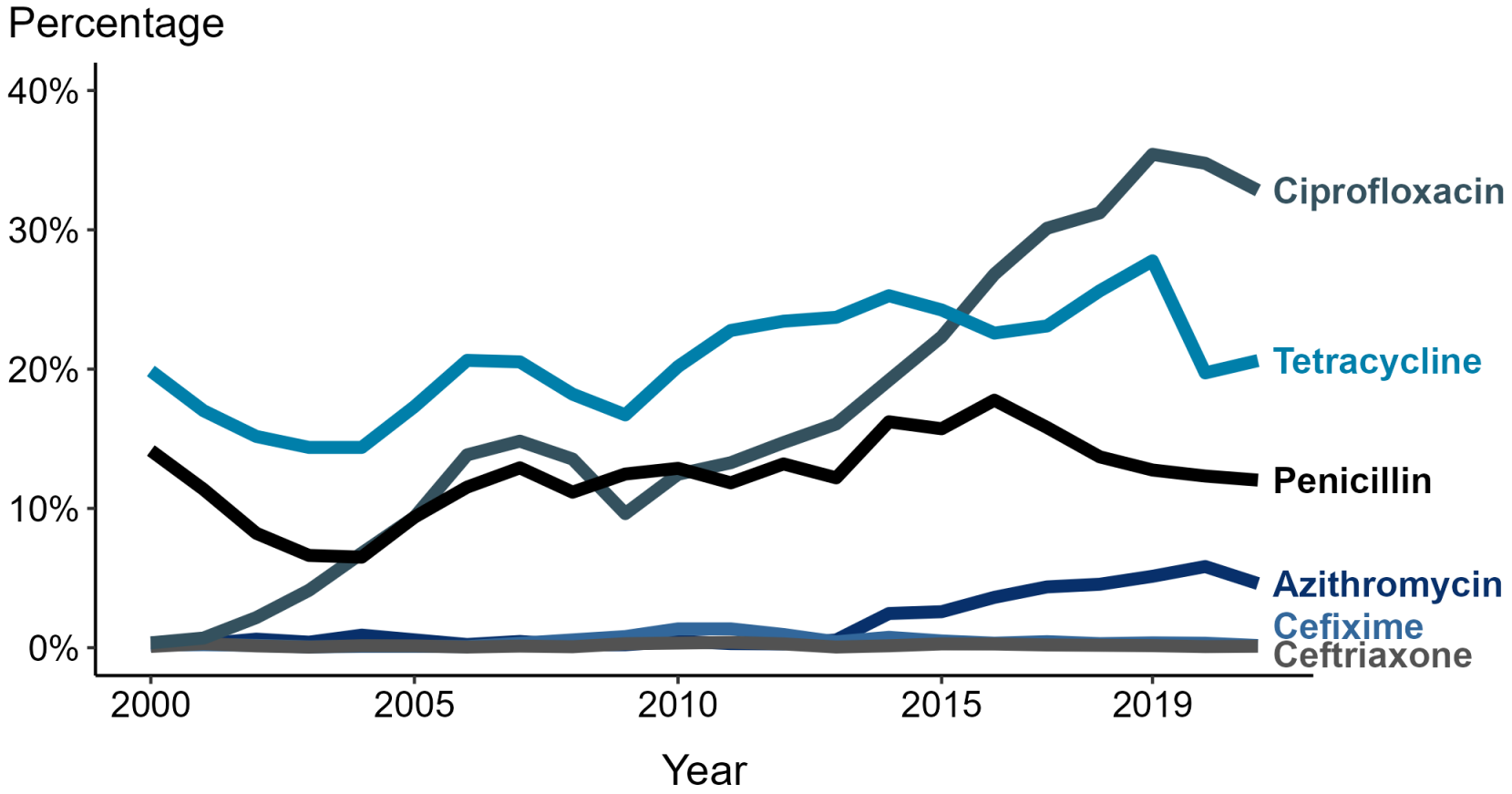
Gonorrhea



- Asymptomatic in up to 70%
- Incubation 2-10 days.
- Clinical symptoms:
  - Urogenital: cervicitis, urethritis, PID
  - Extragenital: oropharynx, proctitis, ocular – often asymptomatic and more likely in MSM
  - Disseminated: septic arthritis, tenosynovitis, meningitis, bloodstream infection, endocarditis
  - Pregnancy: PROM, preterm birth, spontaneous abortion.
    - 30-50% vertical transmission rate.
- Diagnosis: NAAT Sens > 90% spec > 98% first catch urine or vaginal, anal, pharyngeal swab.
- Treatment:
  - **Progressive development of resistance to all antibiotics used for treatment**
  - Urogenital, pharyngeal, rectal infection:
    - **USA/CDC: Ceftriaxone 500 IM x 1**
    - **Canada/PHAC: Ceftriaxone 250 IM + Azithromycin 1g PO. For anogenital infection only can use Cefixime 800 + Azithromycin 1g PO**
  - Disseminated: Ceftriaxone IV
  - **Obtain test of cure for all positive sites**
- Pearls:
  - Exclude concurrent STI/BBP (many are CT co infected!, treat if no negative test)
  - Treat all partners from past 60 days
  - No condomless sex for 7 days after treatment
  - Positive NAT > 14 days after treatment = reinfection or treatment failure

Image: CMAJ, 185(5) 414-415

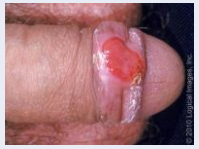
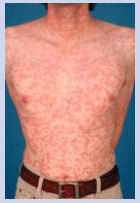
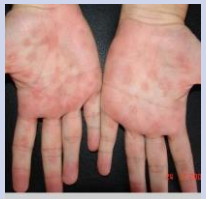
Neisseria gonorrhoeae — Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2021



* Resistance: Ciprofloxacin: MIC ≥ 1.0 µg/mL; Penicillin: MIC ≥ 2.0 µg/mL or Beta-lactamase positive; Tetracycline: MIC ≥ 2.0 µg/mL

† Elevated MICs: Azithromycin: MIC ≥ 1.0 µg/mL 29 (2000–2004); ≥ 2.0 µg/mL (2005–2020); Ceftriaxone: MIC ≥ 0.125 µg/mL; Cefixime: MIC ≥ 0.25 µg/mL

NOTE: Cefixime susceptibility was not tested in 2007 and 2008.

Syphilis	Incubation	Symptoms	Treatment	Alternative Treatment
Primary (contagious!) 	3-90 days Median 3 weeks	Chancre at site of inoculation. This is clean/painless! +/- Regional LN. = Local replication	IM BP 2.4M X 1	DOXY 100 PO BID 14 days
Secondary (contagious!)  	2-12 weeks Median 6 weeks	Fever, LN, macular rash, myalgias, sore throat, +/- aseptic meningitis, uveitis, hepatitis, immune complex GN = Dissemination (CNS, Neuro!)	IM BP 2.4M X 1	DOXY 100 PO BID 14 days
Latent Syphilis (contagious only early on)	Early latent < 1 year	Generally no symptoms	Early latent: IM BP 2.4 M X 1	DOXY 100 PO BID 14 days
	Late latent > 1 year		Late latent: IM BP 2.4M weekly X 3	DOXY 100 PO BID 28 days
Tertiary Syphilis (not contagious)	10-30 years	Aorta: aortitis, AI CNS: neurosyphilis, Tabes dorsalis, otitis/otosyphilis Soft tissue: gummas	IM BP 2.4M X 3 Neuro: Pen IV 14 days	DOXY 100 PO BID 28 days IV Ceftriaxone

PREP

PREP: HIV epidemiology and acquisition:

- > half of incident HIV infections in Canada in gay and bisexual MSM
- HIV incidence also high in persons who inject drugs, persons from HIV endemic countries, and Indigenous persons
- **PREP = Pre exposure prophylaxis:** Use of anti retroviral medications by HIV uninfected person who are at high or ongoing risk of HIV acquisition, beginning before and continuing after a potential HIV exposure

Table 2: Risk of HIV transmission per act by exposure type from an HIV-positive source[5]

Level	Exposure type	Estimated risk per act, %
High	Anal (receptive)	1.38 (1.02–1.86)
	Needle sharing	0.63 (0.41–0.92)
Moderate	Anal (insertive)	0.11 (0.04–0.28)
	Vaginal (receptive)	0.08 (0.06–0.11)
	Vaginal (insertive)	0.04 (0.01–0.14)
Low	Oral sex (giving)	Precise estimates not available
	Oral sex (receiving)	
	Oral–anal contact	
	Sharing sex toys	
	Blood on compromised skin	

CMAJ 2017 November 27;189:E1448-58. doi: 10.1503/cmaj.170494

- PREP is recommended for:
  - Individuals at high risk of HIV acquisition including:
    - **Condomless sex with HIV+ partner with substantial risk* of transmissible HIV or where HIV status is unknown.**
      - **Especially if high risk (inconsistent condom use, sex for drugs or money, etc)**
    - **Other STI – especially if Syphilis or rectal bacterial STI within past year**
    - **Recurrent use of non occupational PEP**
  - IVDU:
    - **Consider in IVDU if sharing drug paraphenalia with persons know to be positive or at high risk of transmissible HIV infection.**
- PREP is not recommended in stable closed relationship with single partner with negligible/no risk of having transmissible HIV.

Substantial Risk = HIV positive and viremic

CMAJ 2017 November 27;189:E1448-58. doi: 10.1503/cmaj.170494

Prep in clinical practice:

- The drug: Truvada (Tenofovir disoproxil fumarate, emtricitabine).
- Dosing: one tablet daily, or “on demand” (take two pills 2-24 hours prior to exposure ad one pill daily for 48 hours after last exposure).
- Baseline workup: HIV negative within one month of starting PREP, full STI workup (HBV, HCV, Syphilis, CT/GC), CBC, lytes, SCR.
- Vaccinate everyone against HBV and confirm immunity. Be careful if HBV positive at baseline (ID consult).
- Q3 months repeat of above blood work while eon treatment, sooner if symptoms of STI or drug toxicity.
- Discuss potential renal and bone toxicity if relevant.

CMAJ 2017 November 27;189:E1448-58. doi: 10.1503/cmaj.170494

Table 3: Suggested evaluation at baseline and during pre-exposure prophylaxis

Assay type	Baseline	30 d	Q 3 mo	Q 12 mo
Laboratory evaluation				
HIV testing*	X	X	X	
Hepatitis A immunity (hepatitis A total antibody)†	X			
Hepatitis B screen (surface antigen, surface antibody, core antibody)†‡	X			X†
Hepatitis C antibody	X			X
Screening for gonorrhea and chlamydia§ (urine nucleic acid amplification test, throat and rectal swabs for culture or nucleic acid amplification; test anatomic sites depending on type of sexual activity reported)	X		X	
Syphilis serology§	X		X	
Complete blood count	X			
Creatinine	X	X	X	
Urinalysis	X			
Pregnancy test (as appropriate)	X		X	
Clinical evaluation				
Symptoms of HIV seroconversion	X	X	X	
PrEP adherence		X	X	
Indication for PrEP	X	X	X	
Use of other HIV and STI prevention strategies	X	X	X	
Presence and management of syndemic conditions	X	X	X	

Note: PrEP = pre-exposure prophylaxis, STI = sexually transmitted infection.
*Preferred HIV test is a 4th-generation antibody/antigen combo assay. Those with signs or symptoms of acute HIV should also undergo HIV RNA or pooled nucleic acid amplification test.
†Hepatitis A and/or B vaccine should be initiated in unvaccinated individuals. Those who remain nonimmune to hepatitis B virus should be rescreened annually.
‡Individuals with chronic active hepatitis B should be managed in consultation with an expert on hepatitis B virus according to Canadian guidelines.
§Individuals who have STIs should be offered standard therapy and follow-up as per local guidelines.

CMAJ 2017 November 27;189:E1448-58. doi: 10.1503/cmaj.170494

- PREP is provided as a component of a combination preventative strategy that includes:
  - Behavioral interventions: ongoing condom use, partner reduction
  - Biomedical interventions: identification and treatment of HIV/STI infected individuals
  - Addressing other conditions that may lead to high risk behaviors (mental health and substance use disorders)

This should be a regular component of counselling for persons presenting to your practice who are HIV negative and at risk of acquisition.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

- Who: MSM and transgender women, living with HIV (PLWH) or on PREP for prevention, condomless anal/oral sex with a man within one year and with a case of CT, NG, or Syphilis in past year.
- What: open label randomized study, 200 mg of DOXY within 72 hours after condomless sex versus standard of care.
- Outcome: STI incidence quarterly follow up visits.
- Result: 327 on PREP, 174 PLWH:
  - PREP: STI in 10.7% DOXY versus 31.9% standard of care.
    - **For PREP NNT 4.7 for one STI per quarter.**
  - PLWH: 11.8 % in DOXY group versus 30.5% in standard of care group.
  - For PREP group, RR of 0.45 for NG, 0.12 for CT, and 0.13 for Syphilis.
- Conclusion: **combined incidence of NG/CT/Syphilis 2/3 lower with DOXY PEP.**
- Concerns: ? resistance, higher risk behaviors.

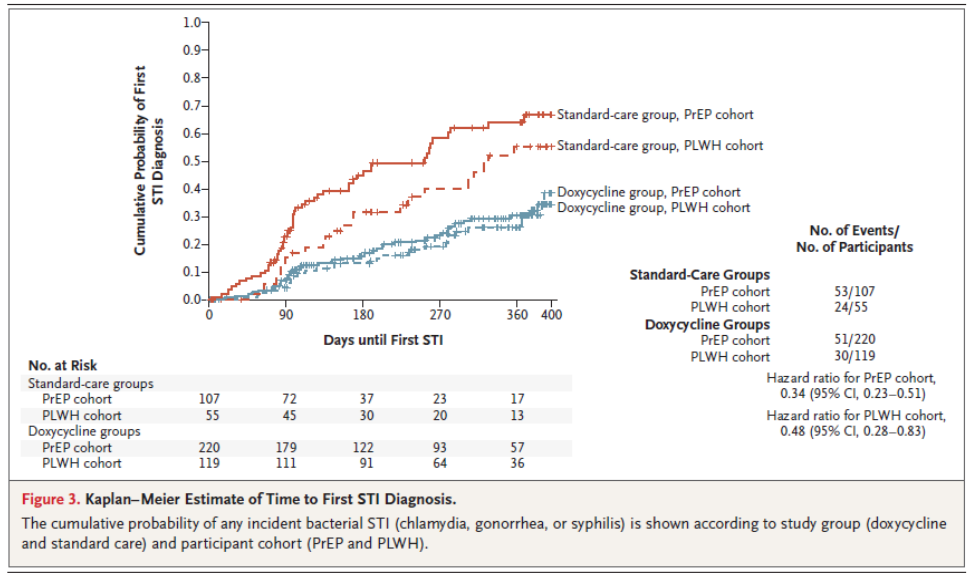


Figure 3. Kaplan–Meier Estimate of Time to First STI Diagnosis.
The cumulative probability of any incident bacterial STI (chlamydia, gonorrhea, or syphilis) is shown according to study group (doxycycline and standard care) and participant cohort (PrEP and PLWH).

N ENGL J MED 388;14 NEJM.ORG APRIL 6, 2023

Objectives:

- At the end of this presentations, participants will be able to:

1. Discuss recent trends in STI incidence regionally and nationally
2. Review common STI's seen in clinical practice, including clinical manifestations and treatment
3. Acknowledge PREP as a safe and effective mechanism to reduce incident HIV cases and identify, evaluate, prescribe, and follow up patients eligible for PREP

Thanks!