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PHO Rounds:

STI Series – Session 3: Infectious Syphilis

March 20, 2017

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Agency for Health Protection and Promotion
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STI series

- Session 1: Overview of bacterial STIs
  - January 23, 2017 – 12:00pm to 1:00pm
- Session 2: Chlamydia and gonorrhea
  - February 13, 2017 – 12:00pm to 1:00pm
- **Session 3: Infectious syphilis**
  - **March 20, 2017 – 12:00pm to 1:00pm**

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Context for STI series

- Epidemiological changes
  - Sustained increases in cases and rates over time
  - Changes in geographical distribution
  - Changes to priority populations
- Availability of new diagnostic methods and subsequent increases in testing volume
- Updated treatment recommendations

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Session outline

- Clinical overview
  - Staging and presentation
- Epidemiology of infectious syphilis in Ontario
  - Risk factors
- HIV co-infection
- Screening
- Testing and serologic interpretation
- Treatment and follow-up

What do you think?

Historical Figures with Syphilis

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BRIEF CLINICAL OVERVIEW

Syphilis – a brief description

- Etiologic agent: *Treponema pallidum*
- Primary modes of transmission:
  - Sexual (oral, vaginal, anal)
  - Vertical (congenital syphilis)
- Stages:
  - Infectious
    - Primary, secondary, early latent (<1 year)
    - Tertiary (infectious neurosyphilis)
  - Non-infectious
    - Late latent (≥ 1 year)
    - Tertiary (non-infectious neurosyphilis, cardiovascular, gumma)

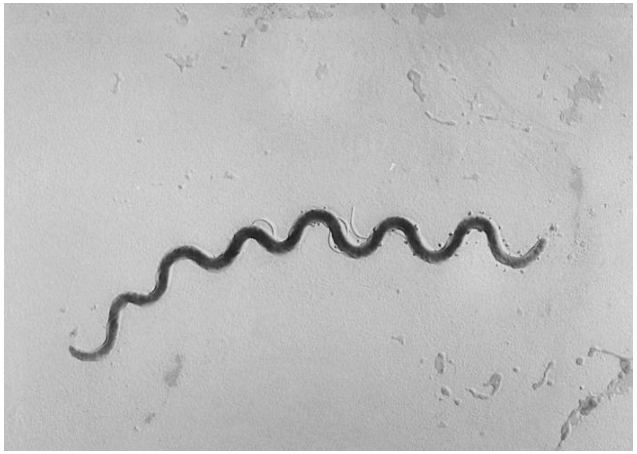


Image source: Centers for Disease Control and Prevention (CDC)/Susan Lindsley Public Health Image Library (PHIL) ID #19469

Primary syphilis

- Incubation period: 3 weeks (3 to 90 days)
- Chancre: 3mm to 3cm in diameter
- Initially a painless papule
  - Painless ulcer
  - Clean base
  - Rolled border
  - Associated regional lymphadenopathy

- Heals spontaneously in 1 to 12 weeks
- ~60% of those with secondary syphilis don't recall having a primary lesion

Image source: Centers for Disease Control and Prevention (CDC)/Robert Sumpter PHIL ID #12623

Secondary syphilis

- Incubation period: Usually 2 to 12 weeks after primary lesion
- Disseminated disease
- Symptoms include:
  - Maculopapular rash
  - Fever and malaise
  - Meningitis, headaches
  - Mucous patches
  - Condyloma latum
  - Patchy/diffuse alopecia
  - Lymphadenopathy
  - Rare: ocular and auditory symptoms, renal and hepatic involvement

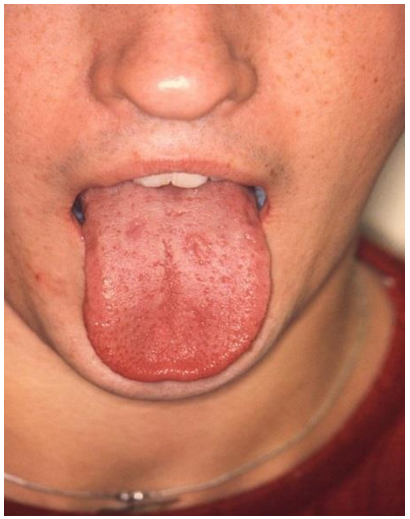


Image sources: Hands - CDC/Dr MF Rein PHIL ID #3476; Tongue - CDC/Susan Lindsley PHIL ID #15022

Tertiary syphilis

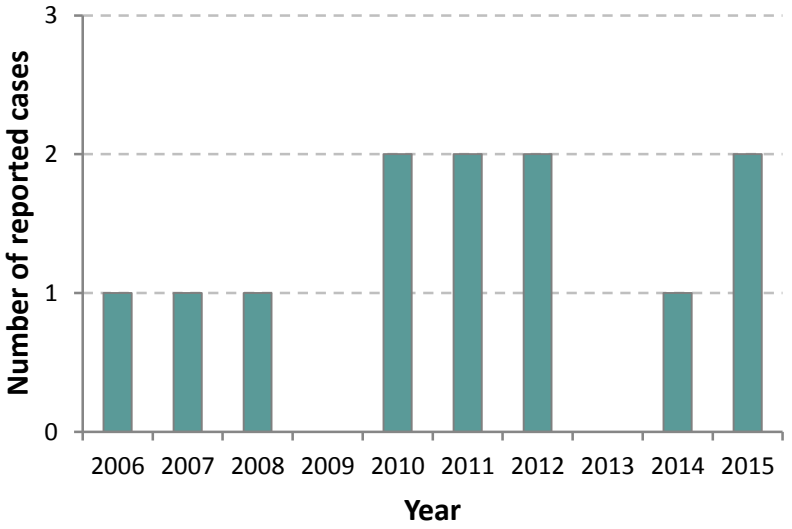
Manifestation	Clinical signs/symptoms	Incubation period
Cardiovascular	Aortic aneurysm Aortic regurgitation Coronary artery ostial stenosis	10 - 30 years
Gumma	Tissue destruction of any organ (depends on site involved)	1 - 46 years (most ~15 years)
Neurosyphilis	Potentially asymptomatic Headache, vertigo, personality changes, dementia, ataxia, Argyll-Robertson pupil	<2 - 20 years

Source: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

Congenital syphilis

- Transmitted from mother-to-infant during pregnancy or during delivery
  - Risk of transmission in untreated women with primary or secondary syphilis is 70%-100%
  - Up to 40% of infants born to mothers with untreated syphilis will be stillborn or die shortly after birth
- Symptoms may develop days/weeks or even years after birth, including:
  - Deformed bones, severe anemia, enlarged liver/spleen, jaundice, brain and nerve problems (blindness/deafness), meningitis or skin rashes
- Universal screening of pregnant women is crucial for prevention

Reported cases of congenital syphilis, Ontario: 2006-2015



Source: Centers for Disease Control and Prevention. Congenital syphilis – fact sheet. Available at: https://www.cdc.gov/std/syphilis/stdfact-congenital-syphilis.htm

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EPIDEMIOLOGY OF INFECTIOUS SYPHILIS IN ONTARIO

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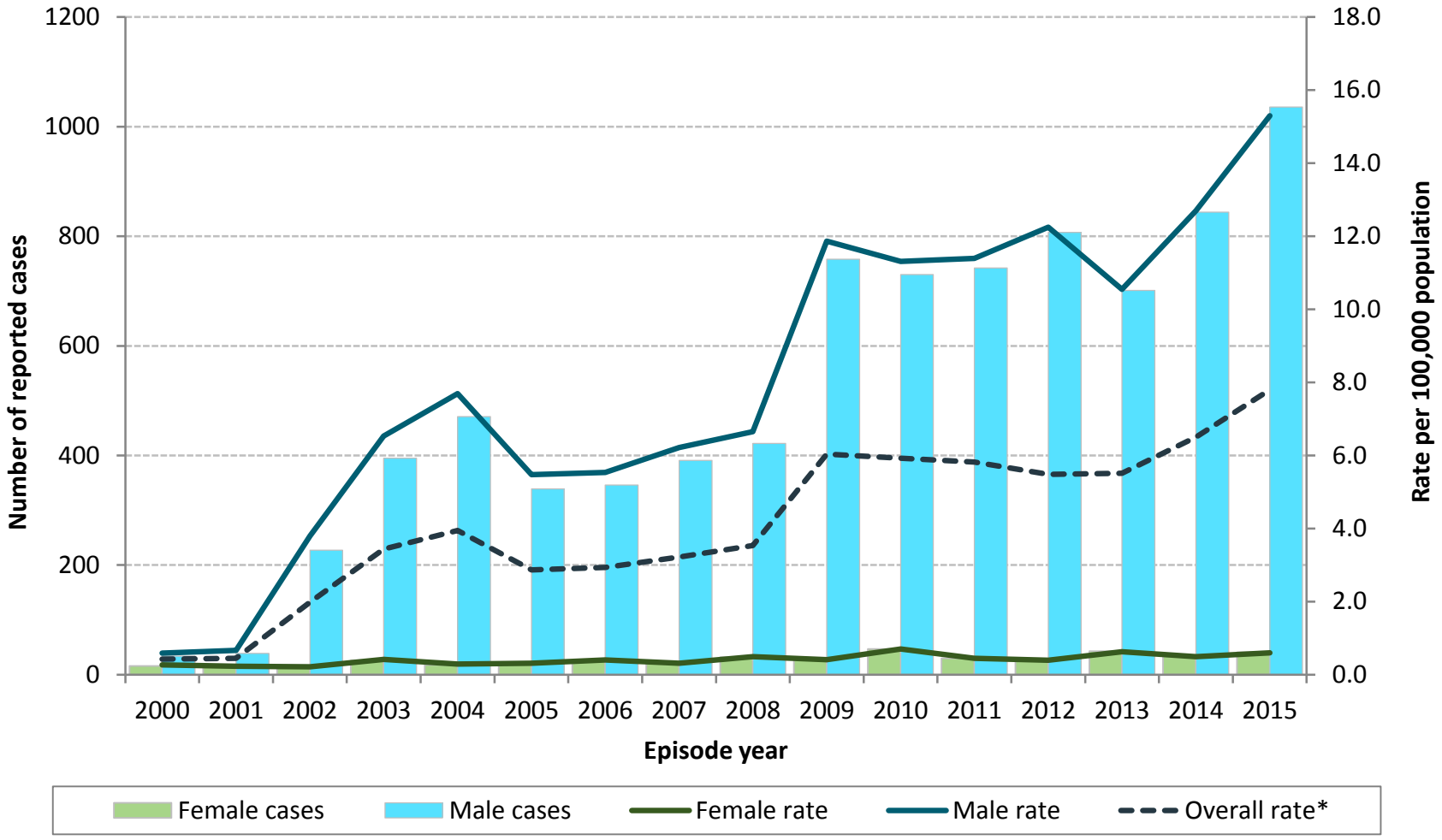
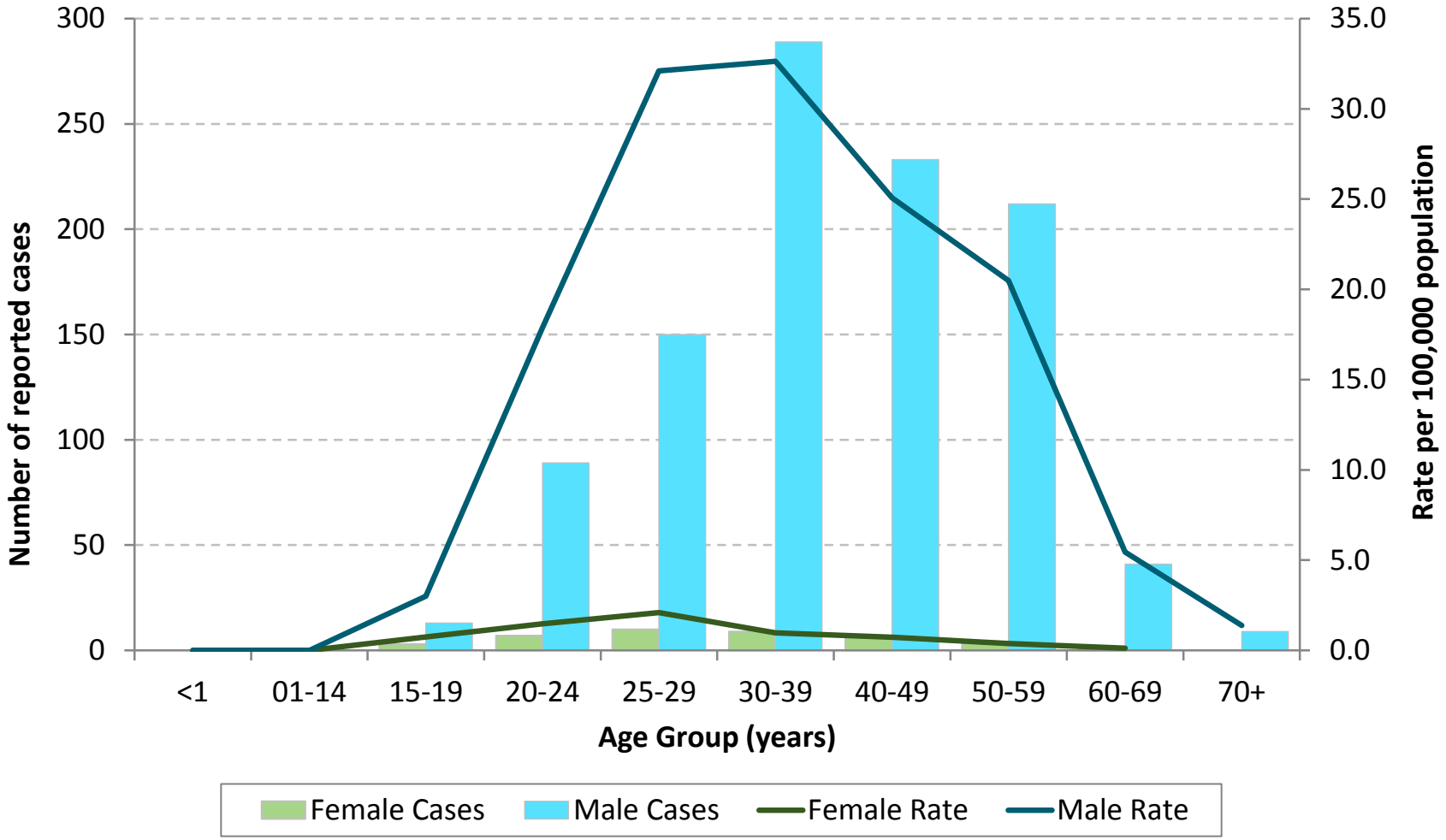
Infectious syphilis by year and sex: Ontario, 2000-2015



Ontario cases: Ontario Ministry of Health and Long-Term Care (MOHLTC), integrated Public Health Information System (iPHIS), extracted by Public health Ontario [2017/02/15].
Population estimates: 2000-2015: Ontario MOHLTC, intelliHEALTH ONTARIO, extracted by Public Health Ontario [2017/02/01].
***Note**: Overall rate includes cases that did not specify gender as male or female.

Infectious syphilis by age group and sex: Ontario, 2015



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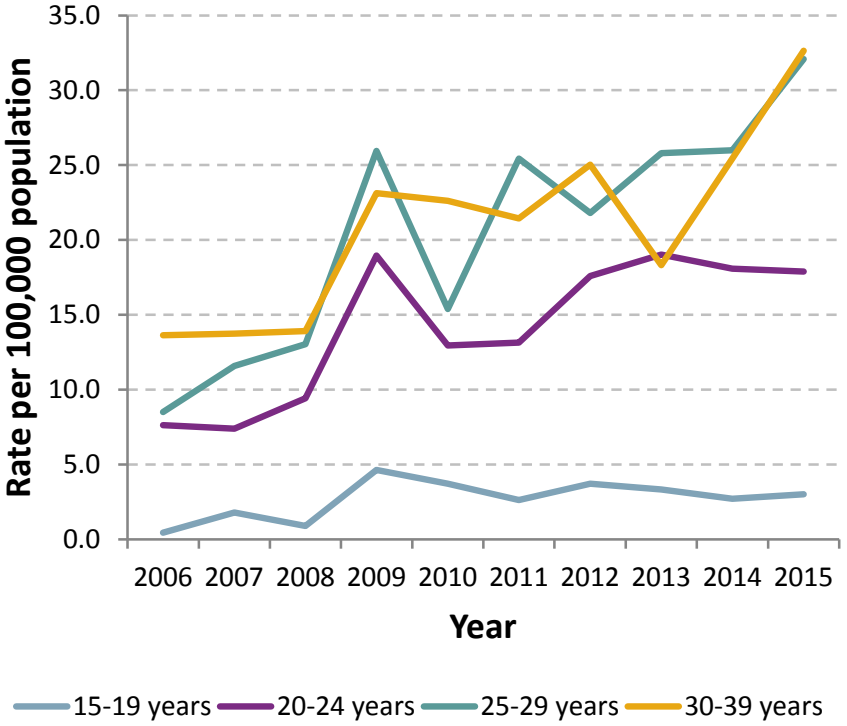
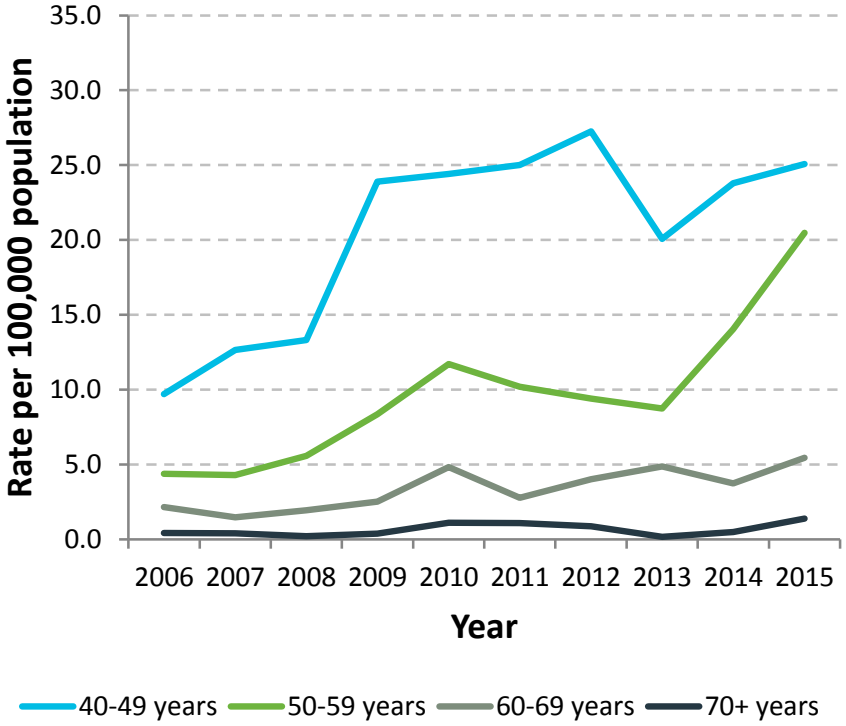
Population estimates: 2000-2015: Ontario MOHLTC, intelliHEALTH ONTARIO, extracted by Public Health Ontario [2017/02/01].

Infectious syphilis by year and age group - males: Ontario, 2006-2015





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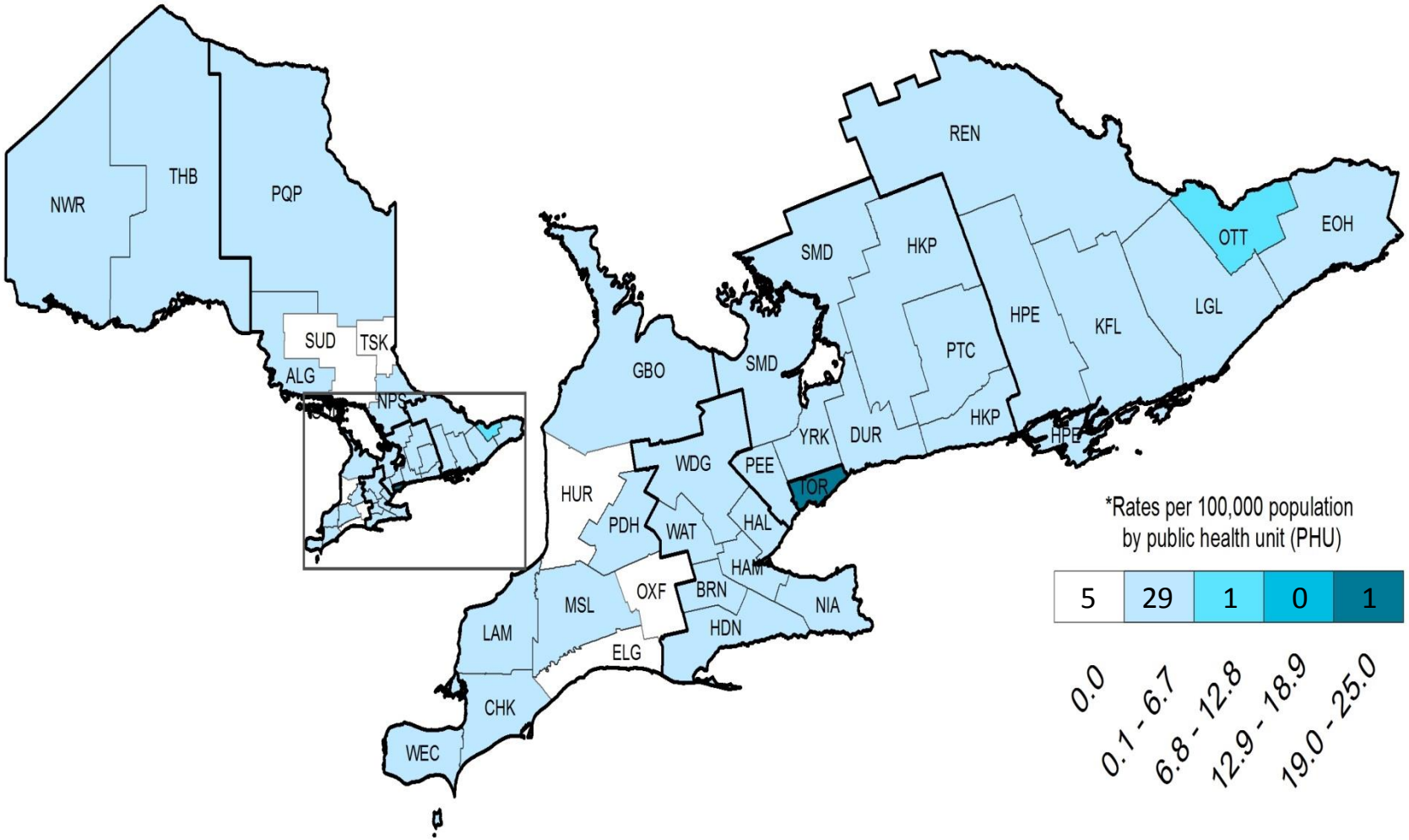
Infectious syphilis by public health unit: Ontario, 2015



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Repeat syphilis infections, 2011-2015

	2011	2012	2013	2014	2015
Annual number of reported cases	772	835	746	880	1,080
Number (%) with no previous infections†	595 (77.1)	602 (72.1)	573 (76.8)	655 (74.4)	786 (72.8)
Number (%) with previous infections†	**177 (22.9)**	**233 (27.9)**	**173 (23.2)**	**225 (25.6)**	**294 (27.2)**
Number (%) of previous infections†:					
1	120 (67.8)	158 (67.8)	118 (68.2)	156 (69.3)	195 (66.3)
2	45 (25.4)	57 (24.5)	36 (20.8)	49 (21.8)	75 (25.5)
≥3	12 (6.8)	18 (7.7)	19 (11.0)	20 (8.9)	24 (8.2)

† Includes infections reported within previous five-years and/or current year (e.g., for 2015, includes repeat infections reported between 2010-2015)

Source: Ontario Ministry of Health and Long-Term Care (MOHLTC), integrated Public Health Information System (iPHIS), extracted by Public health Ontario [2017/02/15].

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Reported risk factors among infectious syphilis cases, 2011-2015

Risk Factor	Male (%)	Female (%)
Sex with same sex	**85.1**	6.0
No condom used	61.5	78.5
≥ 1 contact in last 6 months	42.1	20.8
Co-infection	23.0	0.7
Anonymous sex	17.8	3.4
Repeat STI	15.0	8.1
New contact in last 2 months	14.6	14.8
Sex with opposite sex	9.9	**74.5**
Bath house	6.8	0.7
Met contact through internet	6.2	2.7
≥ 1 Risk Factor Reported	**93.4**	**85.6**

Source: Ontario Ministry of Health and Long-Term Care (MOHLTC), integrated Public Health Information System (iPHIS), extracted by Public health Ontario [2017/02/15].

Syphilis-HIV co-infection

- Syphilis may increase the risk of acquiring HIV
  - Higher risk if ulcerative lesions present in genital tract
- For those co-infected, syphilis infection may lead to:
  - Increased HIV viral loads resulting in increased infectiousness and subsequent risk of HIV transmission
  - Decreased CD4 counts influencing the progression and severity of clinical illness
- HIV-infected individuals may present with atypical clinical signs and symptoms of syphilis
- There may be additional considerations for diagnosis and management of syphilis-HIV co-infected cases

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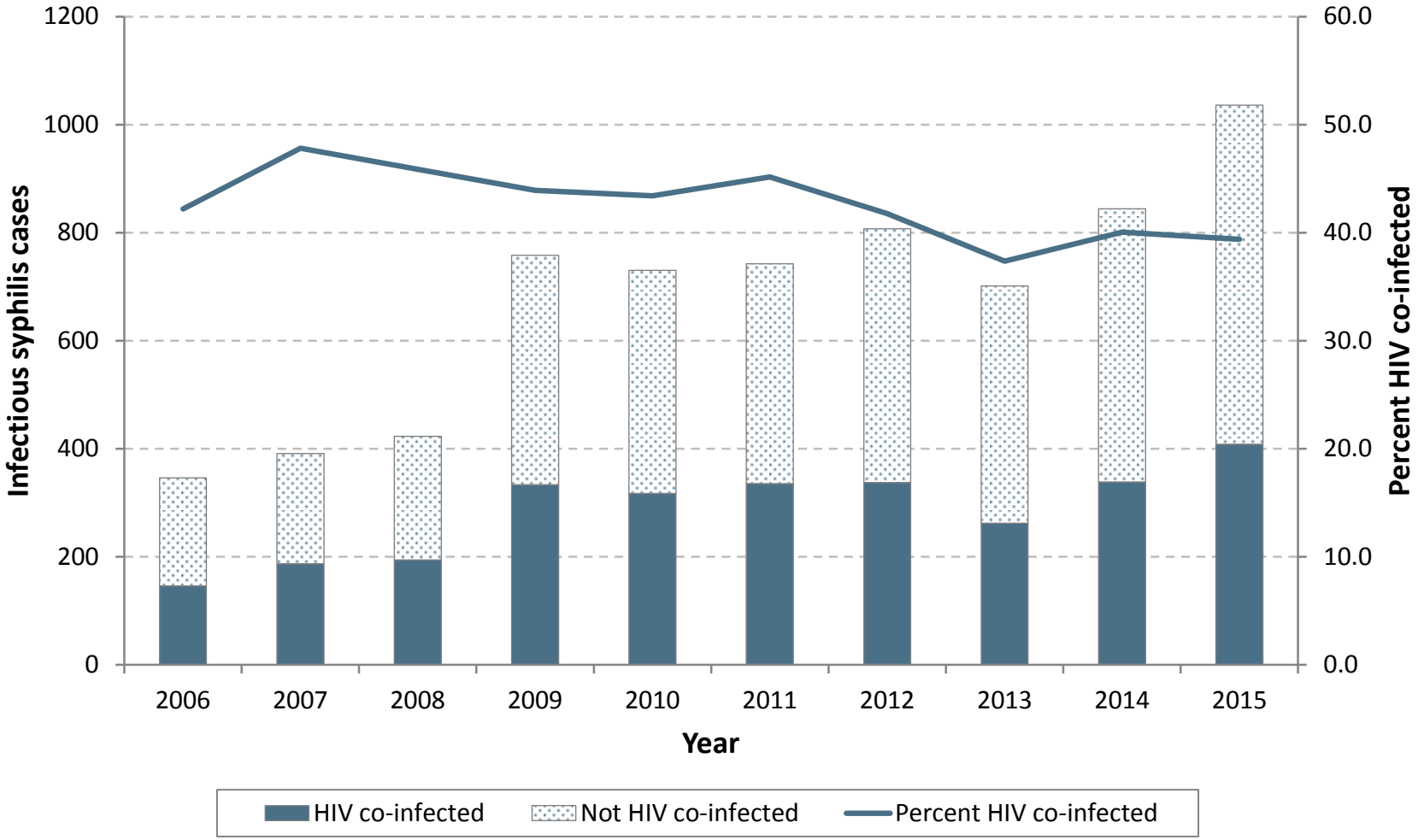
Syphilis-HIV co-infected cases among males: Ontario, 2006-2015



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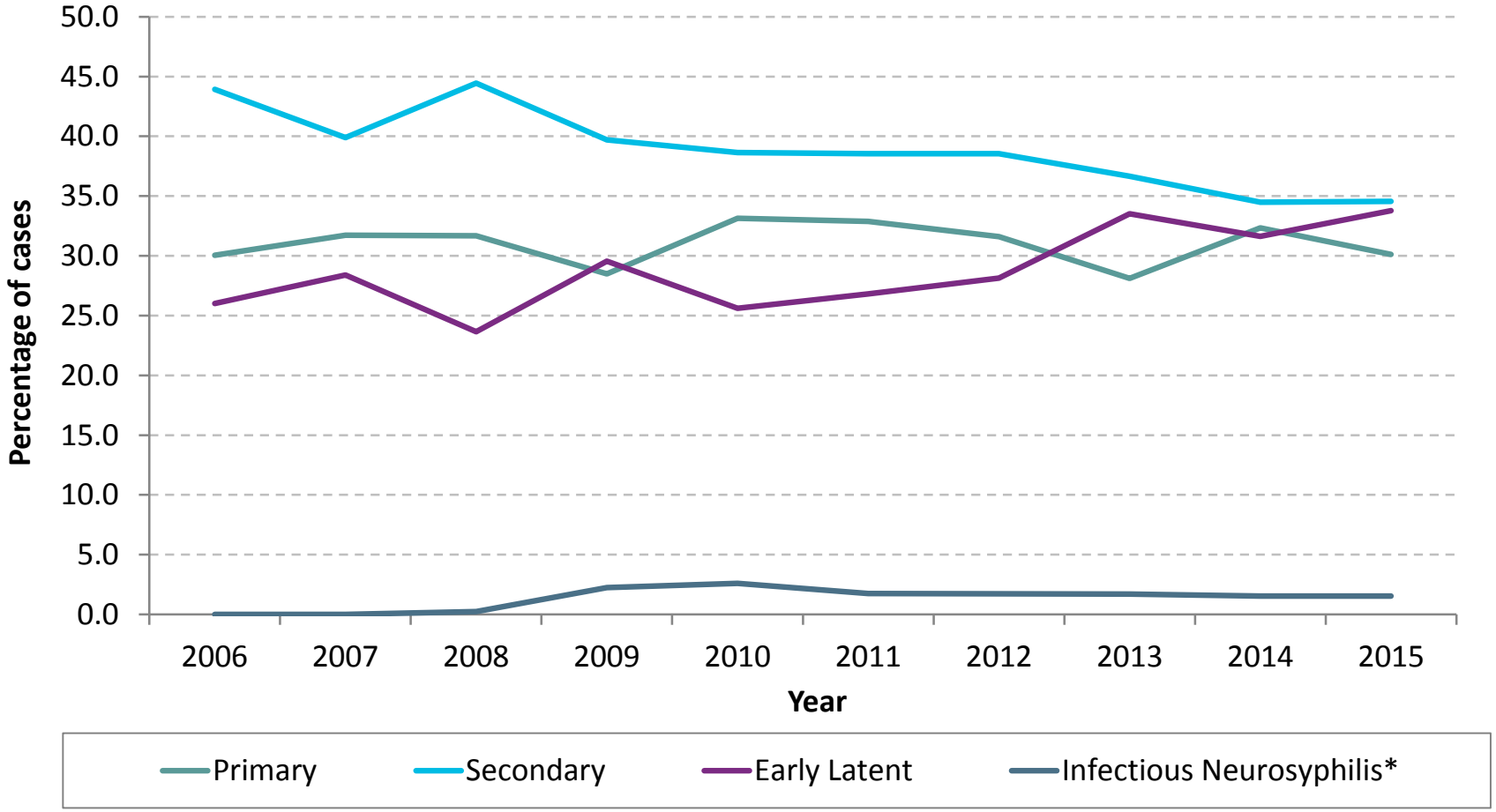
Staging of infectious syphilis cases by year (males): Ontario, 2006-2015



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***Note**: Infectious neurosyphilis added to provincial case definition in April 2009.

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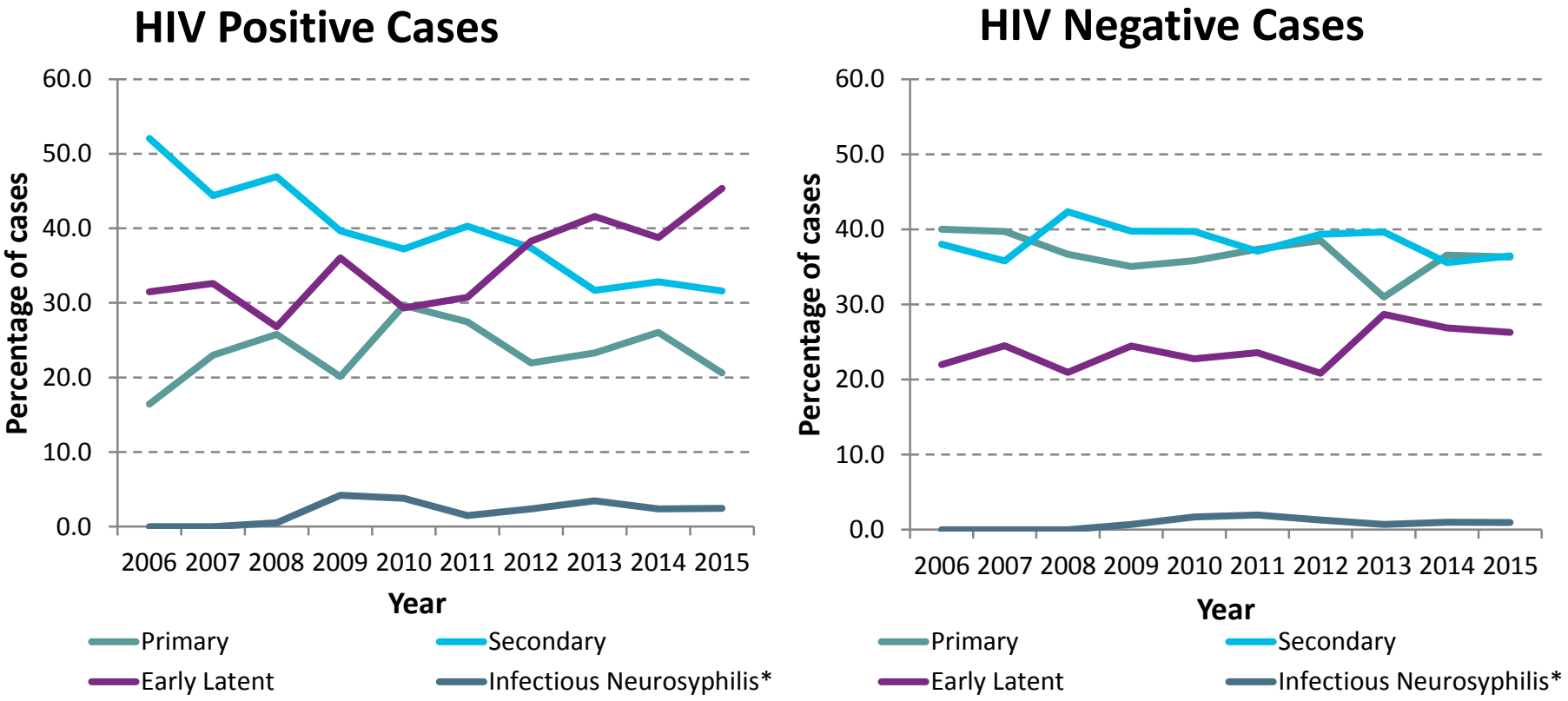
Staging of infectious syphilis cases by year and HIV status (males): Ontario, 2006-2015



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Population estimates: 2000-2015: Ontario MOHLTC, intelliHEALTH ONTARIO, extracted by Public Health Ontario [2017/02/01].
***Note**: Infectious neurosyphilis added to provincial case definition in April 2009.

SCREENING

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Who to screen or test for syphilis

- Anyone with signs/symptoms compatible with syphilis

  AND/OR

- Any of the following populations identified as priorities:
  - Sexual contacts of known syphilis case
  - Those with increased STI rates (sexually active <25 years of age; MSM)
  - Those engaging in high risk behaviours and/or practices
    - Unprotected sex, multiple/new sexual partner(s), anonymous sex
    - Injection drug use
  - Those with previous STI history (repeat, co-infection)
  - Pregnant women
  - Those involved in sex work
  - Street-involved or homeless/underhoused

Source: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

Syphilis screening in pregnancy

- **Universal prenatal screening:**
  - ***In first trimester*** (seeks to prevent transmission of syphilis to fetus)
- **Additional screening for women at high risk:**
  - ***At 28-32 weeks*** (seeks to prevent transmission to fetus)
  - ***At delivery*** (primarily seeks to detect early congenital cases)
- **Screening after delivery:**
  - Any woman delivering a hydropic or stillborn infant at ≥20 weeks
  - Infants presenting with signs/symptoms compatible with early congenital syphilis (even if mother seronegative at delivery)
  - Infants with no confirmation of syphilis serology performed during pregnancy and/or at time of labour/delivery

Source: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

What do you think?

Syphilis Screening

DIAGNOSTIC TESTING

Benefits of diagnosing and treating syphilis infection

- **For individual clinical decisions:**
  - Prevention of symptoms and sequelae related to disease
  - Decrease risk of HIV transmission and acquisition
  - Decrease risk of late (tertiary) complications
- **For public health protection:**
  - To reduce transmission to others via:
    - Sexual (limited to primary, secondary, and early syphilis)
    - Mother-to-child (can occur at early and later stages of disease)

Source: Whelan M. and Allen VG. Syphilis in Ontario: Impact of changes in diagnostic testing. Public Health Ontario Rounds – October 23, 2012.

Syphilis diagnostic testing methods

- Diagnosis based on a combination of history, clinical and laboratory findings
- Testing methods:
  - **Direct detection** (e.g., dark-field microscopy, PCR)
    - Direct visualization of spirochete ('Gold Standard')
    - Only possible if lesions (primary/secondary) are present
  - **Antibody detection**
    - Cerebral spinal fluid (CSF) – for diagnosing neurosyphilis
    - ***Serology is the primary laboratory testing method***
  - *Treponema pallidum* cannot be cultured routinely

Source: Whelan M. and Allen VG. Syphilis in Ontario: Impact of changes in diagnostic testing. Public Health Ontario Rounds – October 23, 2012.

Syphilis serological tests

- Serological tests used to diagnose, assess stage of infection, and monitor response to treatment
- Diagnosis best made on results of two blood tests performed 2-4 weeks apart
- Treponemal and non-treponmenal tests

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Key differences: non-treponemal and treponemal syphilis serology tests

Test	Non-Treponemal Tests	Treponemal Tests
Characteristics	• Simple, inexpensive; often used to screen • False +ves (syphilis non-specific) • NT test alone insufficient for diagnosis • If reactive → treponemal test to confirm • Convert to non-reactive over time • Quantitative titre results (can be used to monitor therapy)	• More sensitive early in infection • Fewer false +ves (syphilis specific) • If reactive → non-treponemal test (quantitative titre) to confirm • Usually reactive for life • Qualitative (cannot be used to monitor therapy)
Examples	• Rapid plasma reagin (RPR) • Venereal disease research laboratory (VDRL)	• Enzyme immunoassay (EIA) • Chemiluminescent immunoassay test (CLIA) • Treponema particle agglutination (TPPA) • Fluorescent treponemal antibody absorbed (FTA-ABS)

Source: Whelan M. and Allen VG. Syphilis in Ontario: Impact of changes in diagnostic testing. Public Health Ontario Rounds – October 23, 2012.

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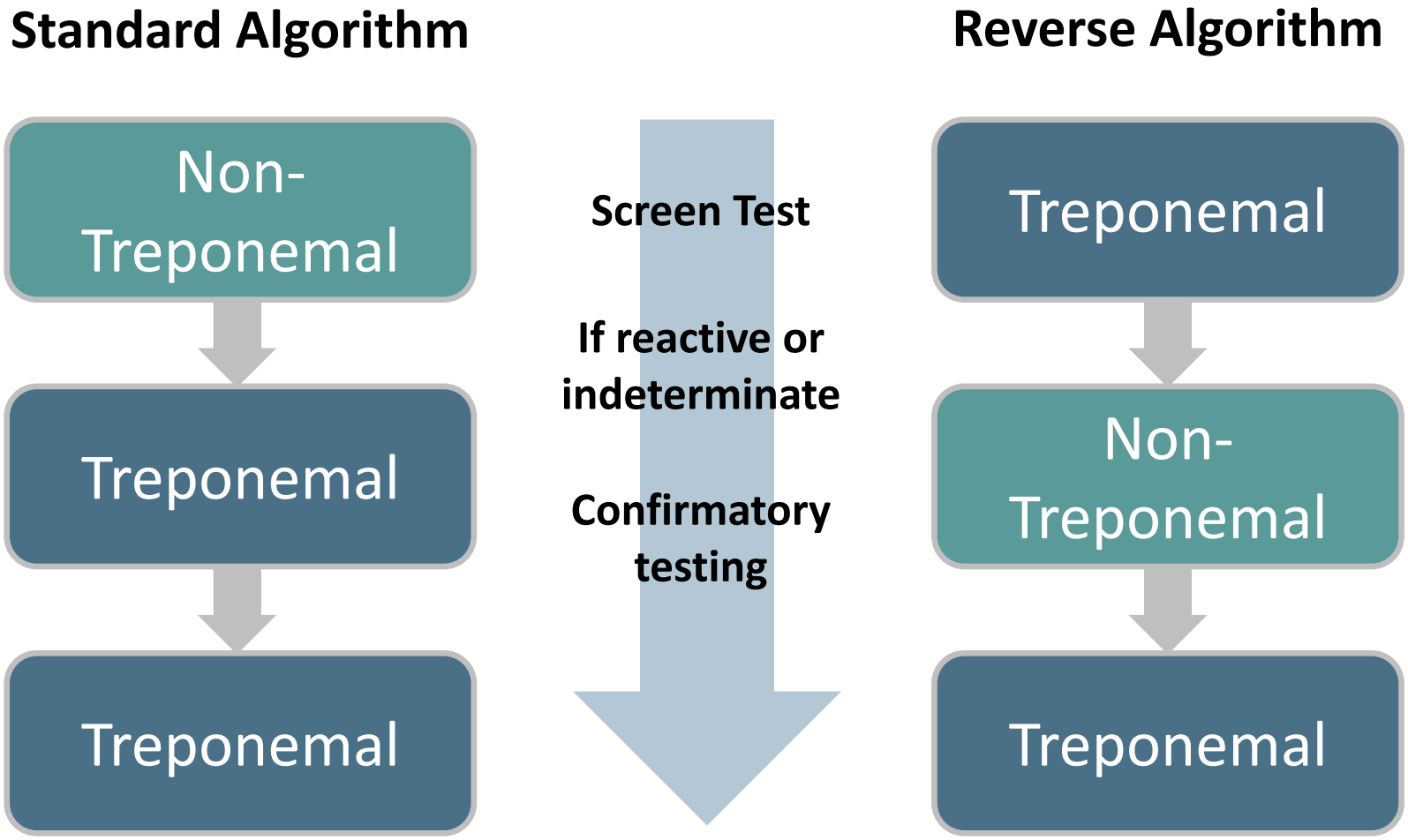
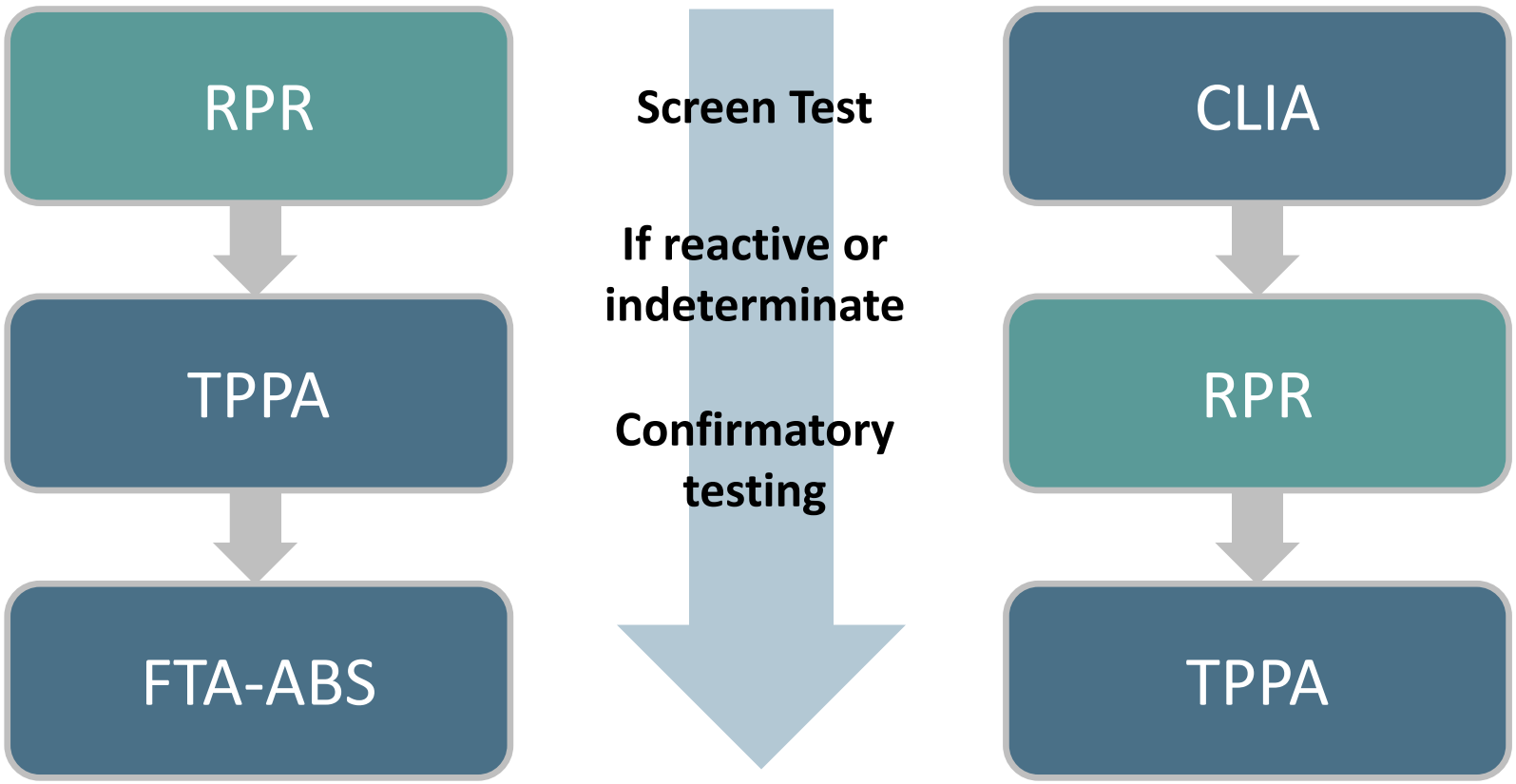
ALGORITHMS FOR SYPHILIS SEROLOGY TESTING AND INTERPRETATION

Comparison of syphilis testing algorithms

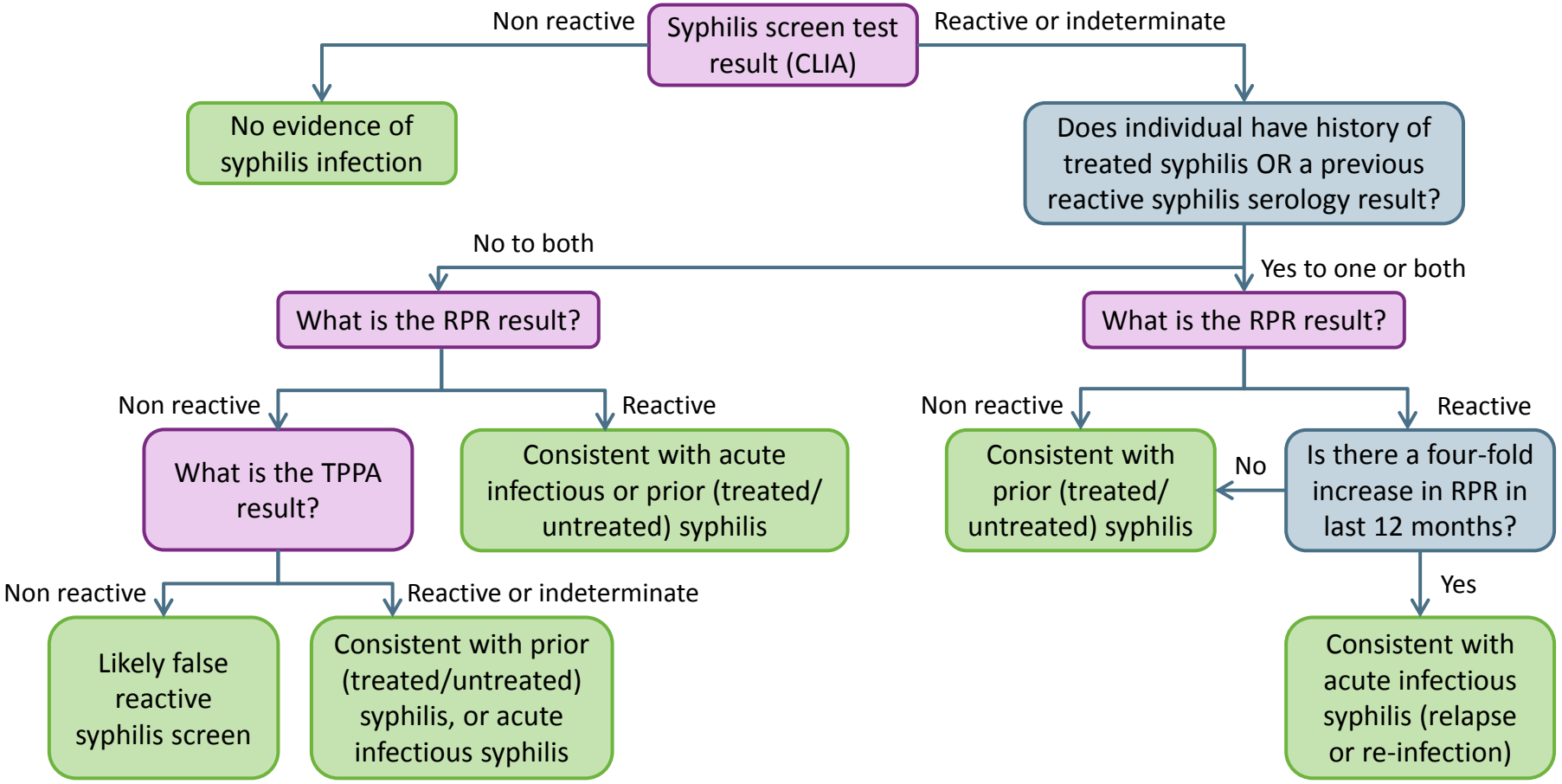


Source: Whelan M. and Allen VG. Syphilis in Ontario: Impact of changes in diagnostic testing. Public Health Ontario Rounds – October 23, 2012.

Comparison of syphilis testing algorithms: example



Interpretation of syphilis serology testing performed in adults



Adapted from: Public Health Ontario (2012). Labstract: Syphilis (*Treponema pallidum*) Serology Testing and Interpretation – Update. Available at: http://www.publichealthontario.ca/en/eRepository/LAB_SD_057_Syphilis_Treponema_pallidum_serology_testing.pdf

What do you think?

Interpreting Syphilis Serology

TREATMENT AND FOLLOW-UP

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Syphilis treatment

Stage		Preferred treatment
Non-pregnant adults	Primary, secondary, early latent (<1 year)	Benzathine penicillin G 2.4 million units IM as a single dose*
	Late latent, latent unknown duration, tertiary (excluding neurosyphilis)	Benzathine penicillin G 2.4 million units IM weekly for 3 doses*
	HIV positive (syphilis of any stage)	
Pregnant women	Primary, secondary, early latent (<1 year)	Benzathine penicillin G 2.4 million units IM weekly for 1-2 doses*
	Late latent, latent unknown duration, tertiary (excluding neurosyphilis)	Benzathine penicillin G 2.4 million units IM weekly for 3 doses*
Neurosyphilis		Penicillin G 3-4 million units IV q 4 h (16-24 million units/day) for 10-14 days

* Benzathine penicillin G (Bicillin) 2.4 million units comes divided with 2mL in each pre-loaded syringe therefore one dose = 2 injections

- NOTE: Congenital syphilis: complex, additional considerations; consult specialist PHAC guidelines and Canadian Pediatric Society

Source: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

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Alternative treatment options if penicillin-allergic

Stage		Alternative (if penicillin-allergic)
Non-pregnant adults	Primary, secondary, early latent (<1 year)	Doxycycline 100mg PO BID x 14 days
	Late latent, latent unknown duration, tertiary (excluding neurosyphilis)	Consider penicillin desensitization OR give Doxycycline 100mg PO BID x 28 days
	HIV positive (syphilis of any stage)	
Pregnant women	Primary, secondary, early latent (<1 year)	Strongly consider penicillin desensitization, then treat with penicillin (No satisfactory alternative to penicillin)
	Late latent, latent unknown duration, tertiary (excluding neurosyphilis)	
Neurosyphilis		Strongly consider penicillin desensitization, then treat with penicillin OR ceftriaxone 2g IV or IM daily x 10 days

Source: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

What do you think?

Syphilis Treatment

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Contact follow up considerations

Syphilis stage	Trace-back period for sexual, perinatal contacts
Primary	4 months + 1 week (17 weeks)
Secondary	8 months (34 weeks)
Early latent	1 year
Late latent / tertiary	Assess long-term partners, others (e.g. children) as appropriate
Congenital	Assess mother and mother's sexual partner(s)
Stage undetermined	Assess/consult with colleague

- Considerations for extending trace-back: if no partners during recommended period; if all traced partners test negative

Sources: Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections, Section 5 – Management and Treatment of Specific Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/section-5-10-eng.php

Ministry of Health and Long-Term Care. Sexual health and sexually transmitted infections prevention and control protocol, 2013 (revised). Available at: http://www.health.gov.on.ca/en/pro/programs/publichealth/oph_standards/docs/sexual_health_sti.pdf

Additional management considerations

- HIV co-infection: may require longer treatment and follow-up
- Syphilis follow-up serology (to monitor treatment success)
  - **Primary, secondary and early latent:** 3, 6, and 12 months post-treatment
  - **Late latent and tertiary:** 12 and 24 months post-treatment
  - **Neurosyphilis:** 6, 12, and 24 months post-treatment.
  - **HIV-infected (any stage):** 3, 6, 12, 24 months post-treatment; yearly after
  - Pregnant and congenital cases: additional considerations (see PHAC Guidelines); consider consulting specialist

What do you think?

Syphilis Follow-up

Acknowledgements

- Public Health Units and their staff
- Public Health Ontario and Public Health Ontario Laboratory:
  - Dr. Doug Sider
  - Dr. Vanessa Allen
  - Michael Whelan
  - Stacie Carey

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THANK YOU.