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Sexually Transmitted Infections (STI) Series

- **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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PHO Rounds: Sexually Transmitted Infections in Ontario: Chlamydia and Gonorrhea

Michael Whelan, Epidemiologist Lead

Jennifer Pritchard, Nurse Consultant

February 13, 2017

Ontario
Agency for Health Protection and Promotion
Agence de protection et de promotion de la santé

Context for STI Series

- Epidemiological changes
  - Sustained increases in cases and rates over time
  - Re-emergence of STIs among specific priority populations
  - Changes in geographic variation
  - Emergence of less well known STIs
- Variety of diagnostic methods are available at Public Health Ontario Laboratories and may evolve in the future
- Based on Ontario specific epidemiology, treatment recommendations for gonorrhea have been established

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Session Overview

- **Chlamydia & lymphogranuloma venereum (LGV)**
  - Background
  - Screening/testing considerations
  - Treatment
  - Epidemiology
- **Gonorrhea**
  - Background
  - Screening/testing considerations
    - Antibiotic resistance
  - Treatment
  - Epidemiology

CHLAMYDIA & LYMPHOGRANULOMA VENEREUM

Chlamydia

- **Causative agent**
  - *Chlamydia trachomatis*
- **Incubation period** ~ 7 – 21 days
- **Modes of transmission**
  - Sexual: oral, vaginal, anal
  - Vertical
- **Presentation**
  - Often asymptomatic in females (70%) and males
  - ♀ Females: cervicitis
  - ♂ Males: urethritis
- **Sequelae**
  - ♀ Females: pelvic inflammatory disease, infertility, ectopic pregnancy, chronic pelvic pain, arthritis
  - ♂ Males: epididymo-orchitis, arthritis

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link

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Chlamydia screening and testing

Site	Culture	NAAT
Urine specimen		✓
Vaginal swab	✓	
Urethral swab	✓	✓
Cervical swab	✓	✓
Pharyngeal swab	✓	*
Rectal swab	✓	*

* PHOL is working to offer NAAT testing for these sites in the future

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link
US Preventive Services Task Force. Recommendations for STI screening . Link

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Chlamydia screening

- Under screening identified as major gap in high risk males and females
- Sexually active individuals < 25 years of age *
- Pregnant females: screen at first prenatal visit
- Sexual assault victims

**Public Health Agency of Canada recommends screening in males and females <25 years of age; Center for Disease Prevention and Control and US Preventive Service Task Force recommends only females*

- Sexually active individuals with risk factors including:
  - Unprotected sexual contact
  - New sexual contact in last 2 months
  - Multiple sexual contact in last 6 months
  - Anonymous sex
  - History of STIs
  - Vulnerable populations
- Recommended rescreening 6 months post treatment

Chlamydia treatment and follow-up

Preferred treatment *	Alternative treatment
Azithromycin 1g PO in a single dose (safe in pregnancy)	**Ofloxacin** 300 mg PO bid x7 days
Doxycycline 100 mg PO bid x 7 days (contraindicated in pregnancy and lactating females)	**Erythromycin** 2g/day PO in divided doses for 7 days OR **Erythromycin** 1g/day PO in divided doses for 14 days

*For adults (non-pregnant non-lactating): urethral, endocervical, rectal conjunctival infection.

- **Follow up**
  - Test of cure 3-4 weeks after if alternative treatment used, pregnant, compliance questioned
  - Screen in 6 months
- **Contact tracing**
  - Last 60 days before symptoms or last partner if contact over 60 days prior
  - Offer empiric treatment for chlamydia to tested contacts (those who are current sexual contacts of case) consider expedited partner therapy if necessary

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link

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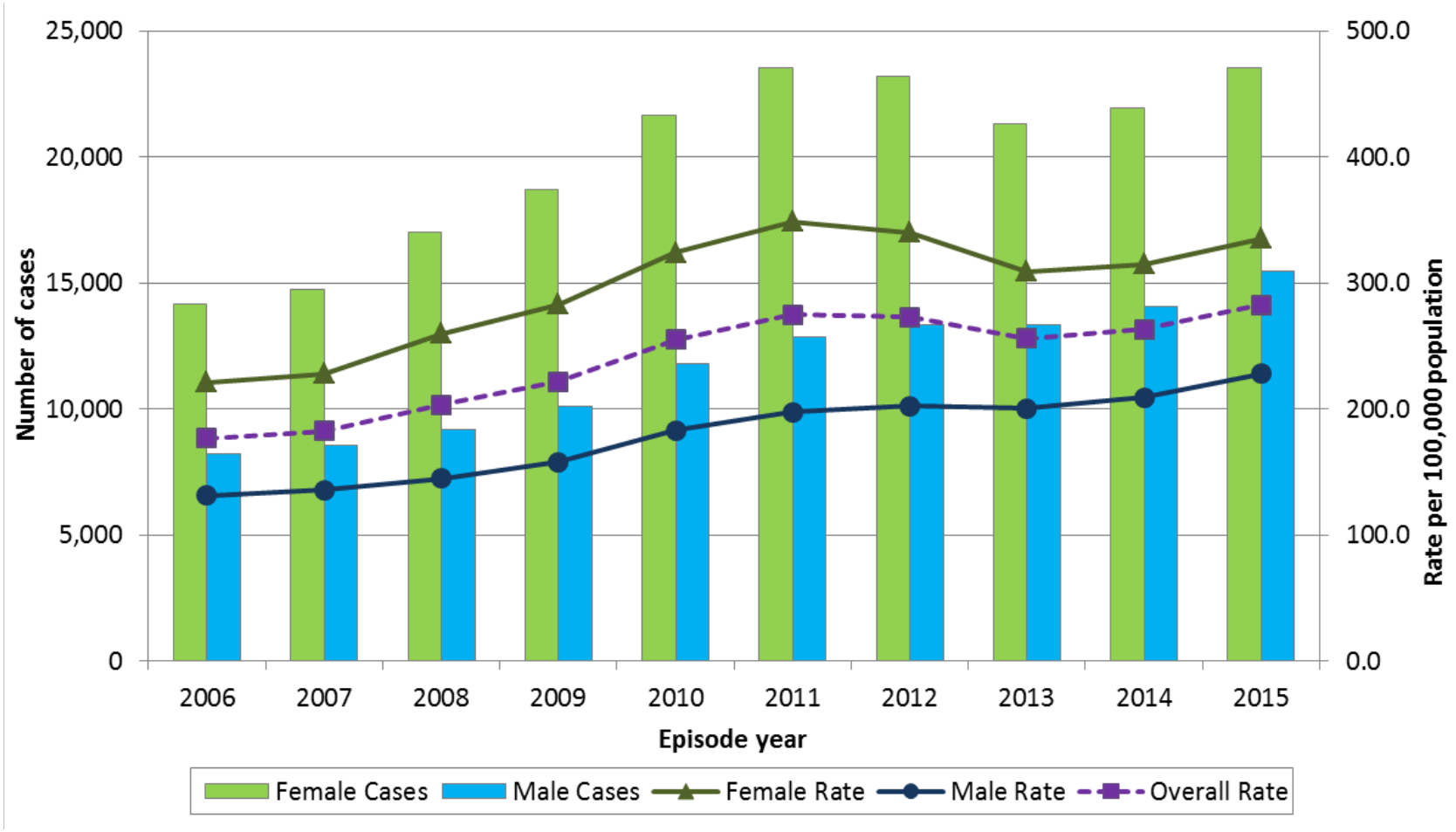
Reported incidence of chlamydia by year: Ontario, 2006-15



Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]; (Population data) Population Estimates and Projections, Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, dates received: 2005-11 [2014/07/03]; 2012-14 [2015/11/18]; 2015-16 [2015/03/13]

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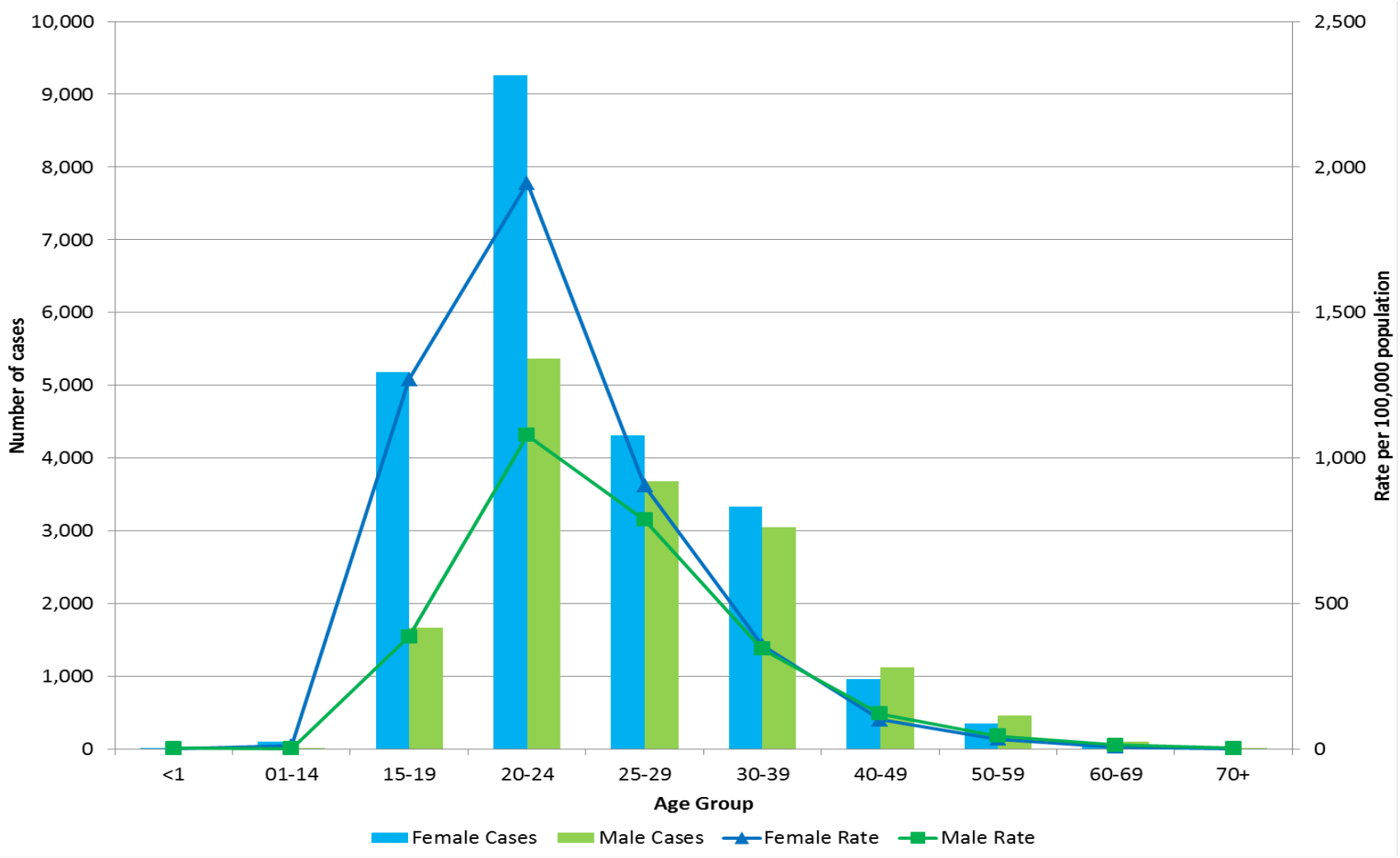
Reported incidence of chlamydia by age group and gender: Ontario, 2015



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WHAT ARE YOUR THOUGHTS?

Chlamydia trends

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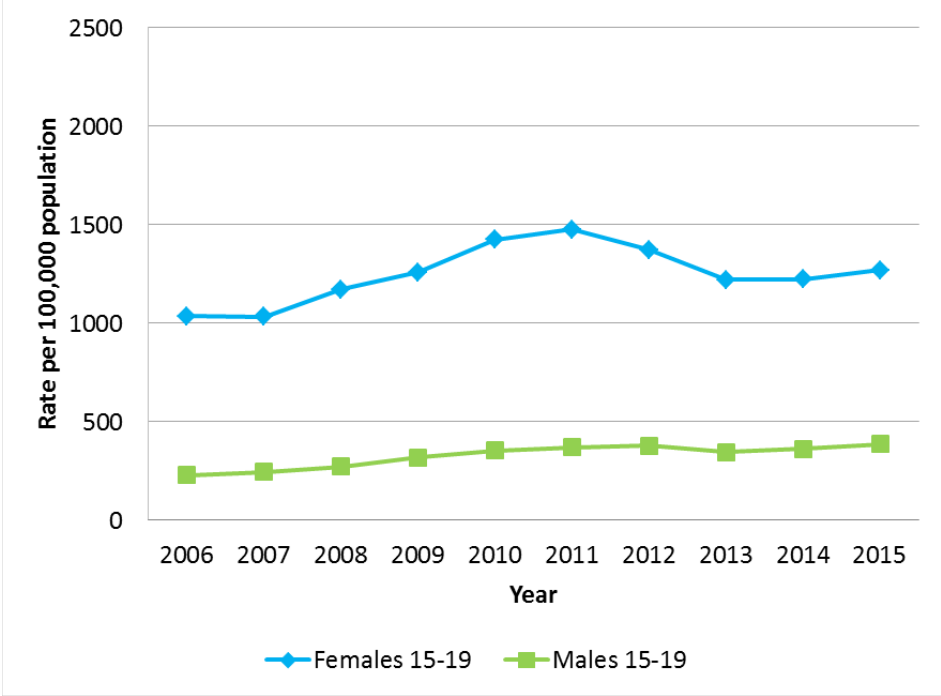
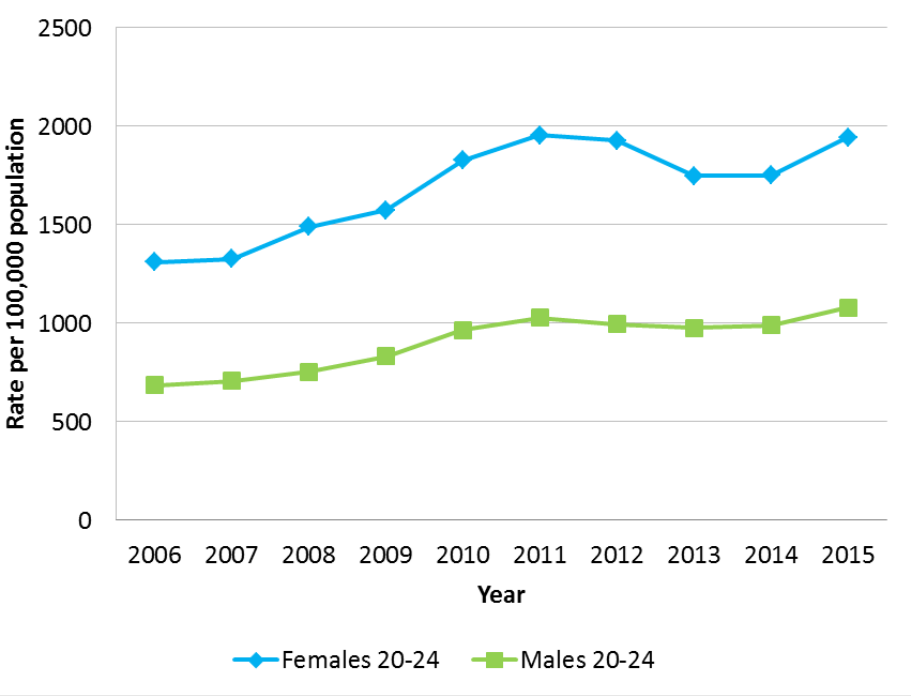
Reported incidence of chlamydia by gender and age group: Ontario, 2006-15





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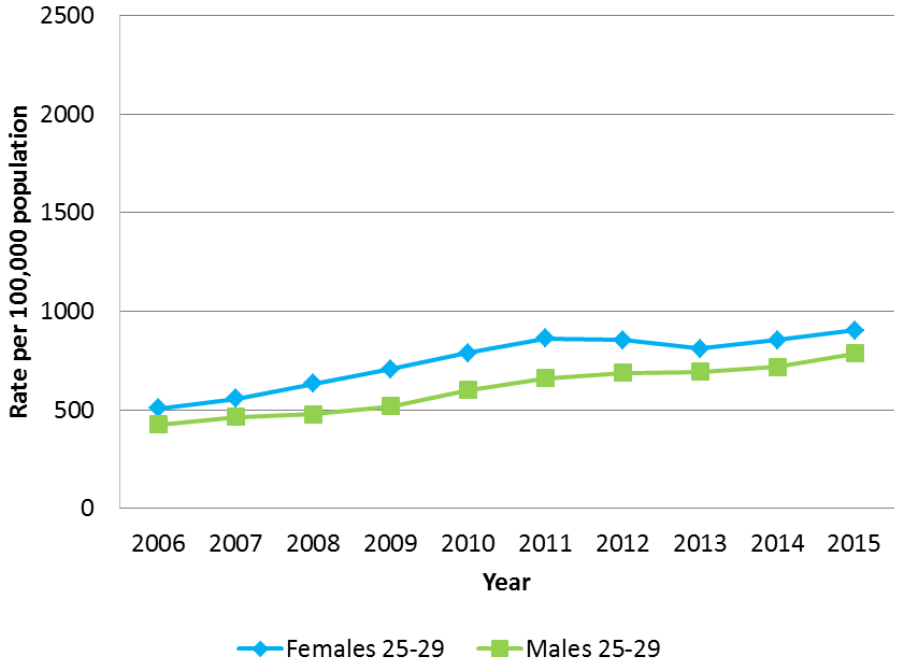
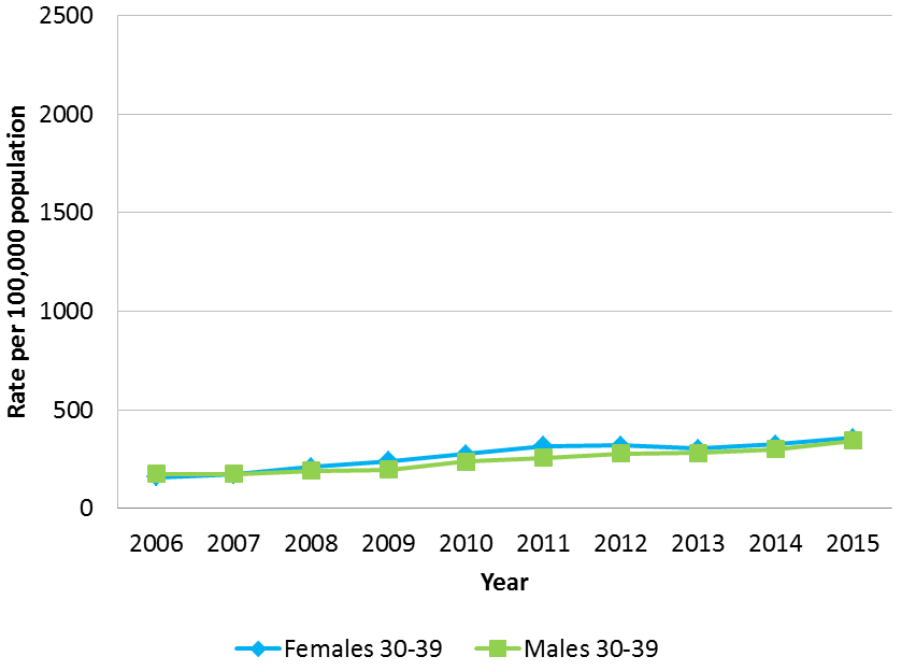
Reported incidence of chlamydia by gender and age group: Ontario, 2006-15





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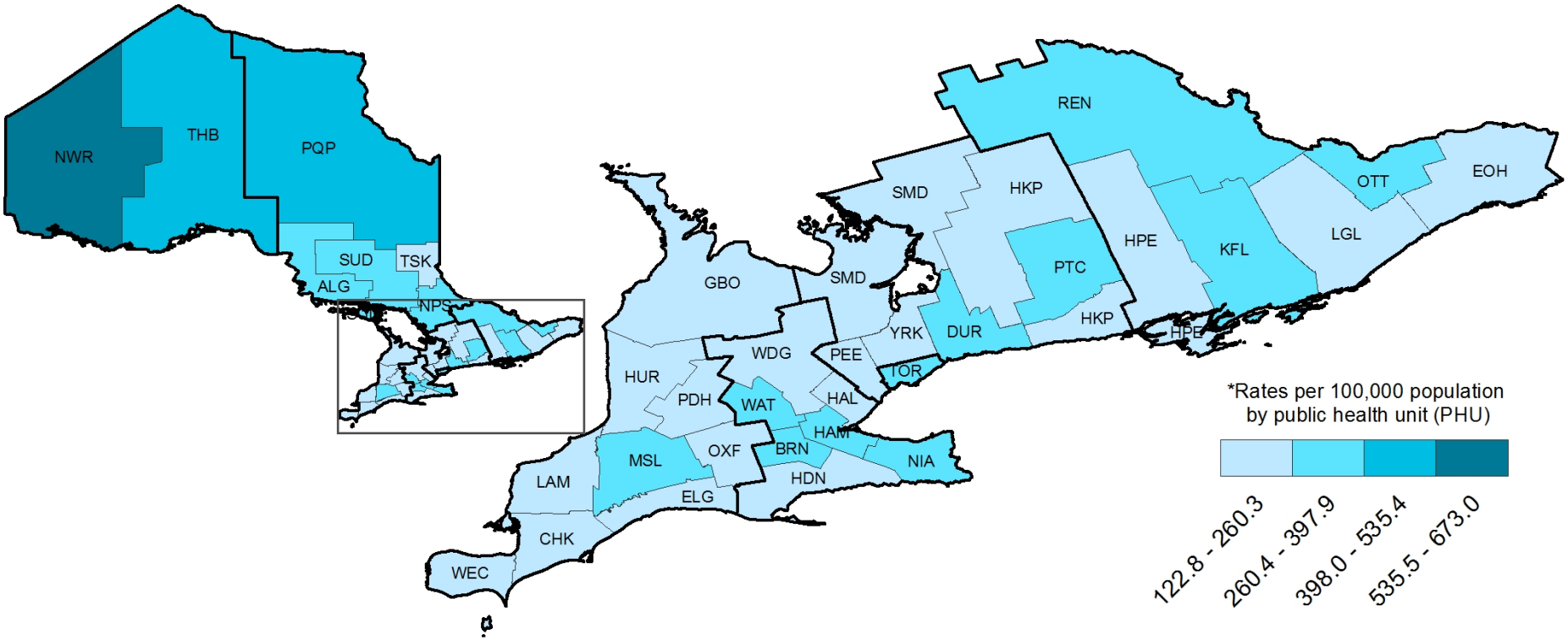
Reported incidence of chlamydia by gender and age group: Ontario, 2006-15

Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]; (Population data) Population Estimates and Projections, Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, dates received: 2005-11 [2014/07/03]; 2012-14 [2015/11/18]; 2015-16 [2015/03/13]

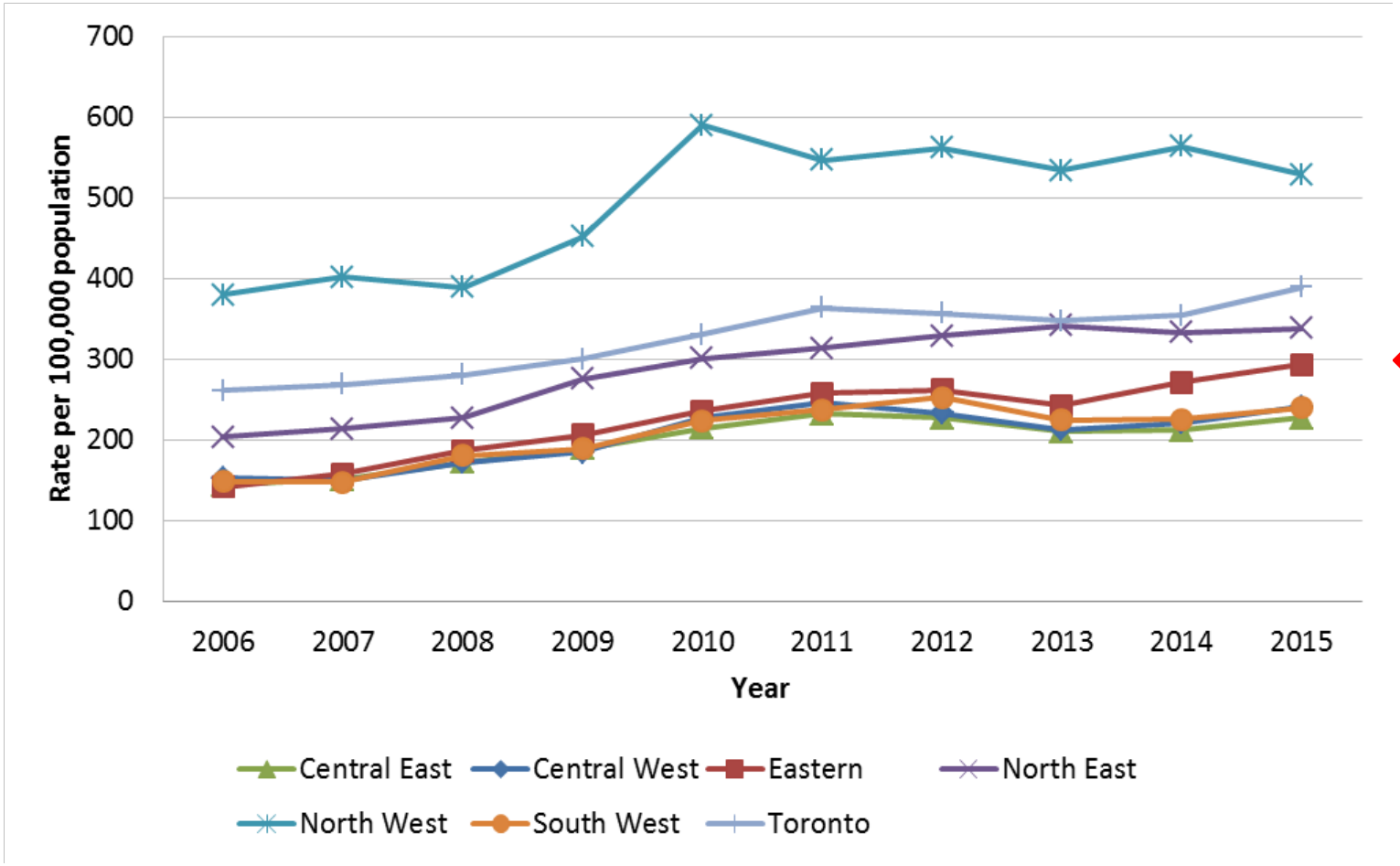
Reported incidence of chlamydia by public health unit: Ontario, 2015



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/10/03].

Population estimates and projections: Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, Dates Received: 2005-11 [2014/07/03], 2012-14 [2015/11/18], 2015 [2015/03/13].

Reported incidence of chlamydia by geographic region: Ontario 2006-15



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Summary of risk factors reported for cases of chlamydia: Ontario 2011-15

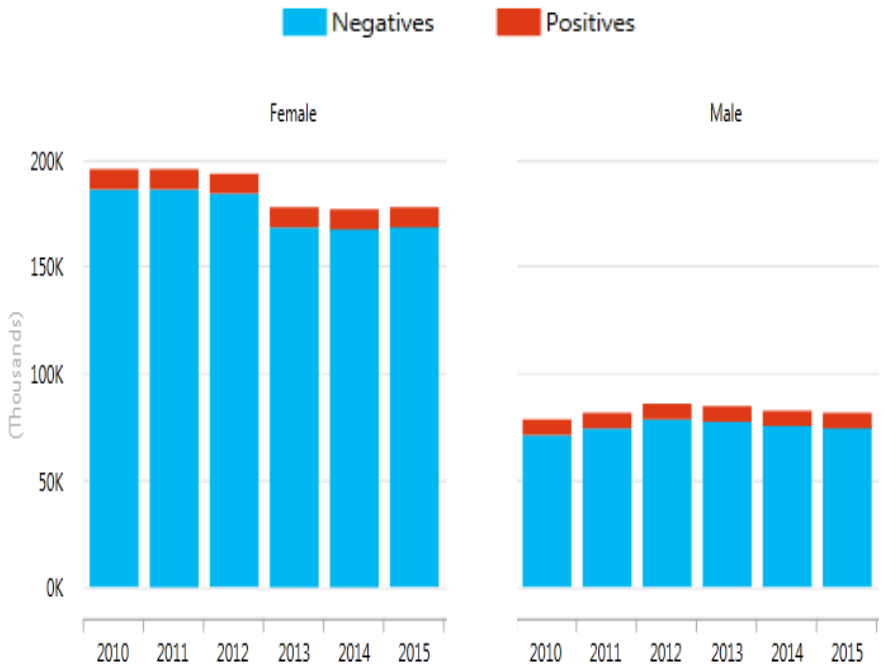
Risk factors reported in iPHIS*	2011	2012	2013	2014	2015	2011-15 trend
NO CONDOM USED	75.2%	72.8%	75.9%	73.7%	70.1%	↓
SEX WITH OPPOSITE SEX	51.1%	63.1%	67.9%	67.7%	64.9%	↑
NEW CONTACT IN PAST 2 MONTHS	16.5%	18.3%	18.6%	17.8%	19.8%	↑
MORE THAN ONE SEX CONTACT IN LAST 6 MONTHS	15.9%	15.2%	15.2%	16.4%	16.8%	↑
REPEAT STI	4.3%	5.5%	7.5%	8.1%	8.9%	↑
PREGNANT	5.7%	8.4%	9.9%	7.7%	4.2%	↓
MSM**	2.7%	2.8%	3.6%	3.7%	4.1%	↑
ANONYMOUS SEX	1.9%	2.1%	2.7%	3.0%	2.8%	↑
CONDOM BREAKAGE	4.3%	3.0%	3.0%	2.8%	2.6%	↓
JUDGEMENT IMPAIRED BY ALCOHOL/DRUGS	3.6%	2.9%	3.0%	2.8%	2.5%	↓
Percentage of cases reporting at least one risk factor	67.8%	72.3%	74.4%	75.3%	78.6%	↑

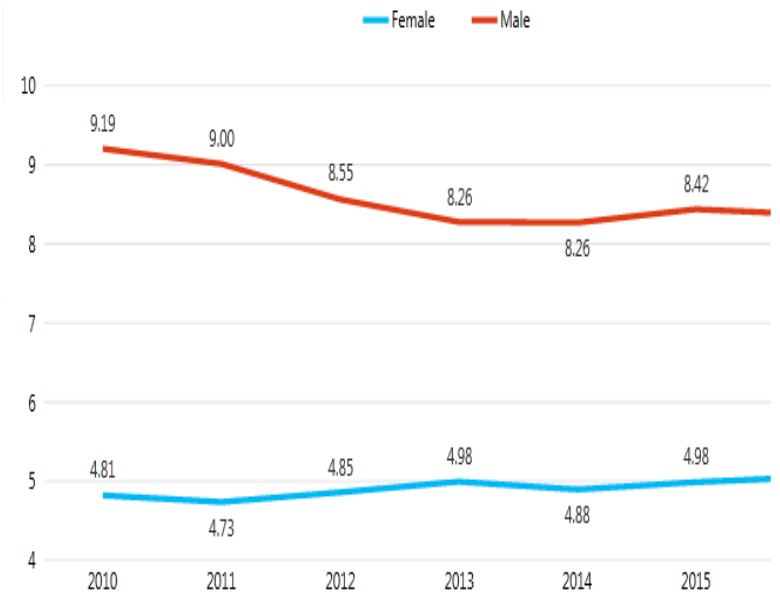
*Only the top ten risk factors reported by cases are shown

** Cases considered MSM if risk factor 'sex with same sex' = Y and client gender = male

Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]

Number of total tests and percent positivity for Chlamydia





*Nucleic Acid Amplification Tests performed on urine, urethral and cervical specimens

Source: Public Health Ontario Laboratory data – Laboratory Information Management System (LIMS) extracted [2017/01/30].

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Fast Facts

Overall, rates of chlamydia have risen **59.7%** from 2006 to 2015

On average, **5** cases of chlamydia were reported **per hour** in 2015

Approximately **1 – 2 %** of all females and males age **20-24** in Ontario reported a case of chlamydia in 2015

Lymphogranuloma venereum

- **Causative agent**
  - *Chlamydia trachomatis* serovars L-1, L-2, L-3
- **Incubation period** ~ 3 – 30 days
- **Modes of transmission**
  - Sexual: oral, vaginal, anal
- **Presentation**
  - Primary: Painless, ulcerative papule; self-limited; often unnoticed
  - Secondary: Inguinal/femoral lymphadenopathy/buboes; systemic symptoms; acute hemorrhagic proctitis; 2-6 weeks post lesion
- **Sequelae**
  - Tertiary: Scarring, genital/rectal strictures/fistulae, esthiomene

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link

Lymphogranuloma venereum screening and testing

Screening & Testing Options

Site	Culture	NAAT
Cervical swab	✓	✓
Urine specimen		✓
Swab of lesion	✓	
Bubo aspirate	✓	
Rectal swab*	✓	
Urethral swab	✓	✓
Pharyngeal swab	✓	

MUST request LGV genotyping

***Positive rectal swabs are sent automatically sent to NML

Serology - Titres may be elevated, but not a definite test

Screening

- Identified contacts of LGV cases
- Patient history suggests possible or probable exposure
- Asymptomatic men who have sex with men (MSM) meeting the following criteria:
  - Positive for HCV, HIV or other STI

AND/OR

  - Unprotected anal or oral group sex

AND

  - History of travelling/residing in area with high LGV prevalence

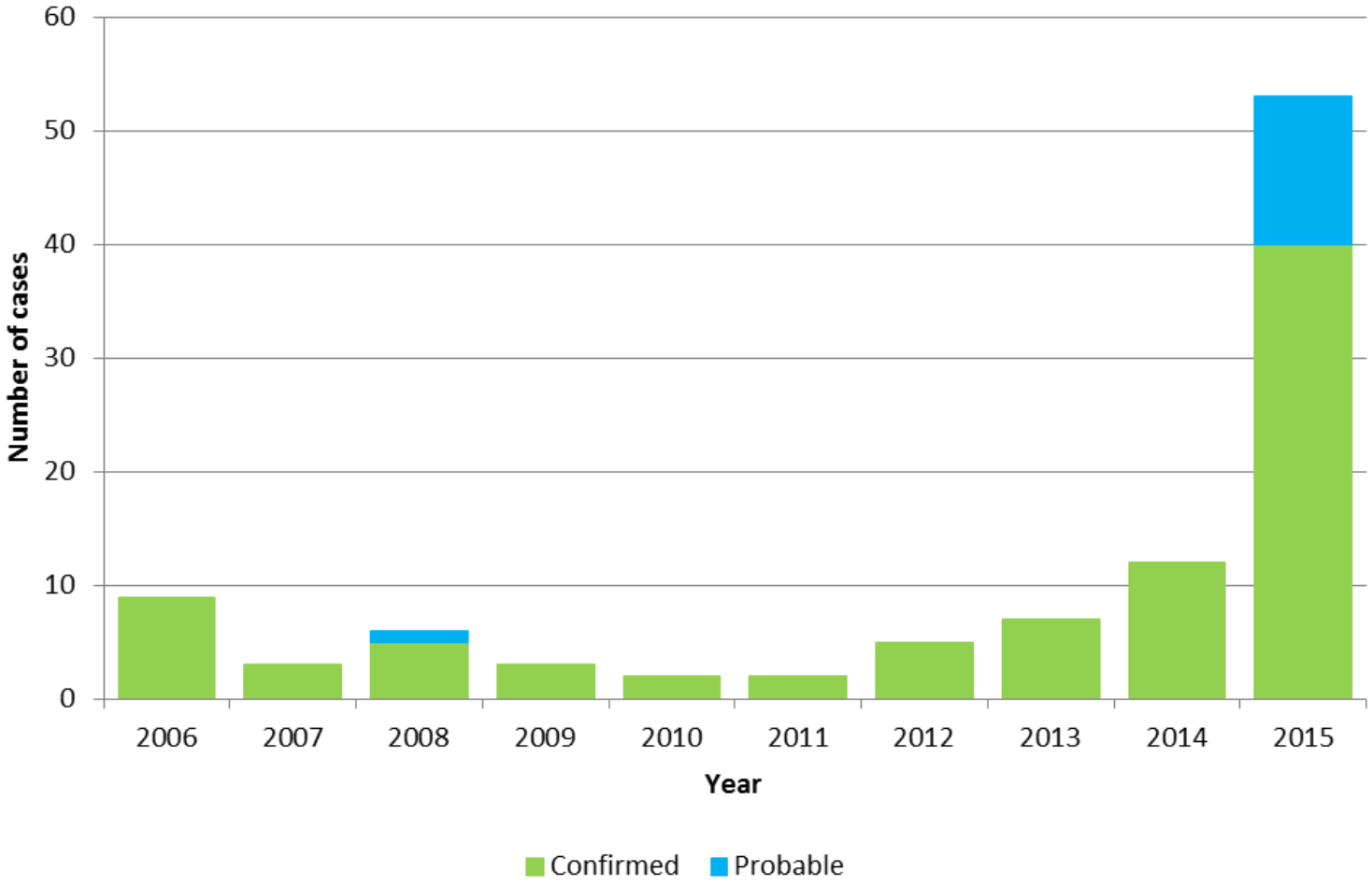
Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link
US Preventive Services Task Force. Recommendations for STI screening . Link

Lymphogranuloma venereum treatment & follow up

- **Recommended**
  - Doxycycline 100mg PO BID x 21 days
- **Follow up**
  - Test of cure 3-4 weeks after completed treatment
  - Continue follow up until symptoms resolve OR refer to specialist if complications require surgical repair
  - Consider further STI testing for HIV, syphilis, gonorrhea
- **Contact tracing**
  - Last 60 days before case's symptom onset or diagnosis date
  - Treat contacts empirically for chlamydia, if result indicates LGV provide LGV treatment

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link

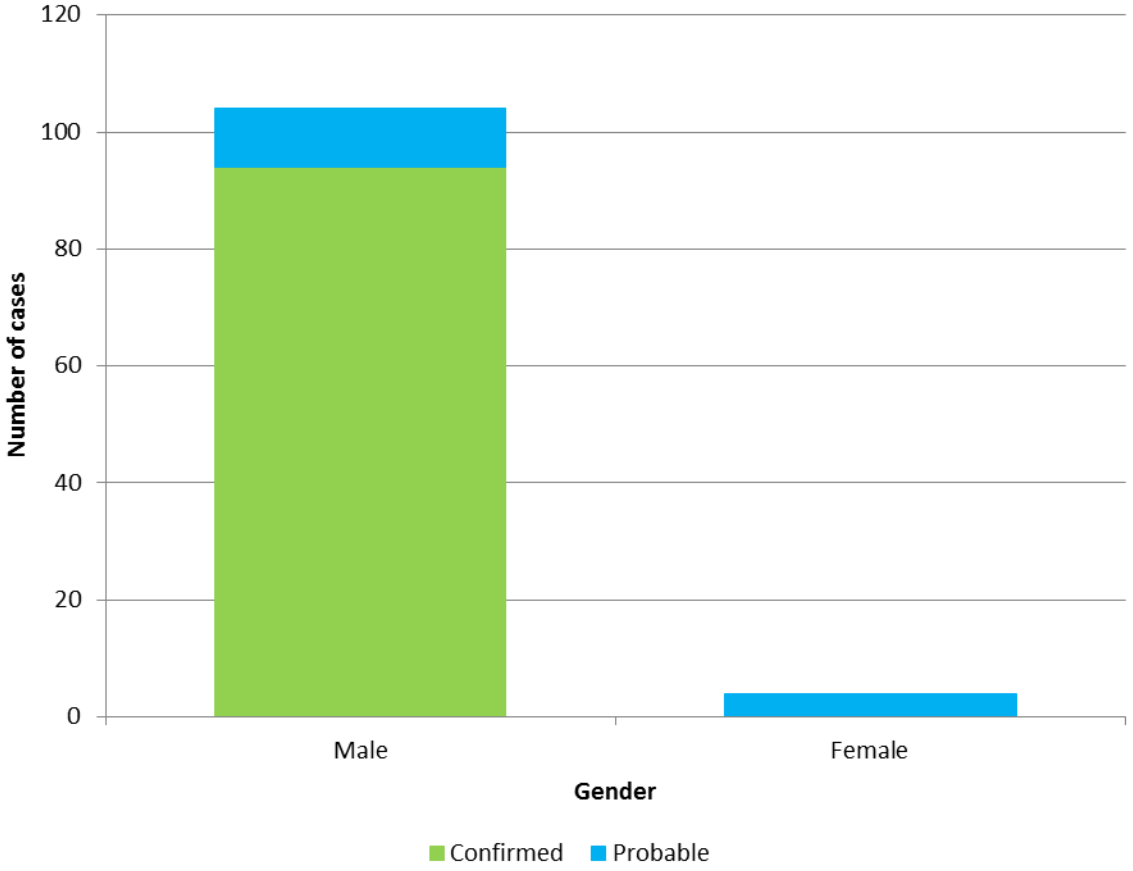
Reported cases of LGV by year: Ontario, 2006-15



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

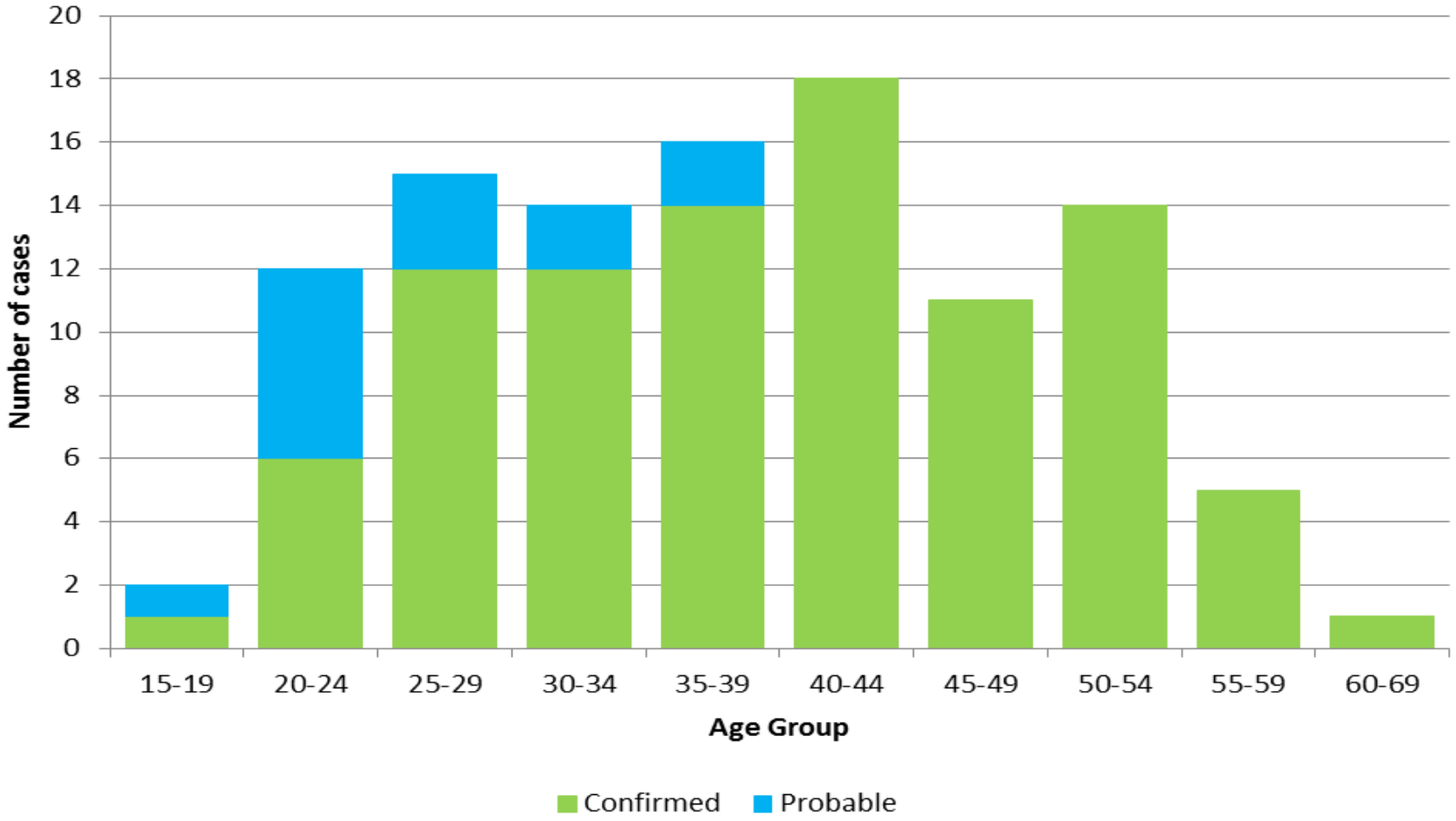
LGV by gender: Ontario 2006-15

- Of 94 confirmed cases all were male
- Of 14 probable cases
  - 71.4% (10/14) were male



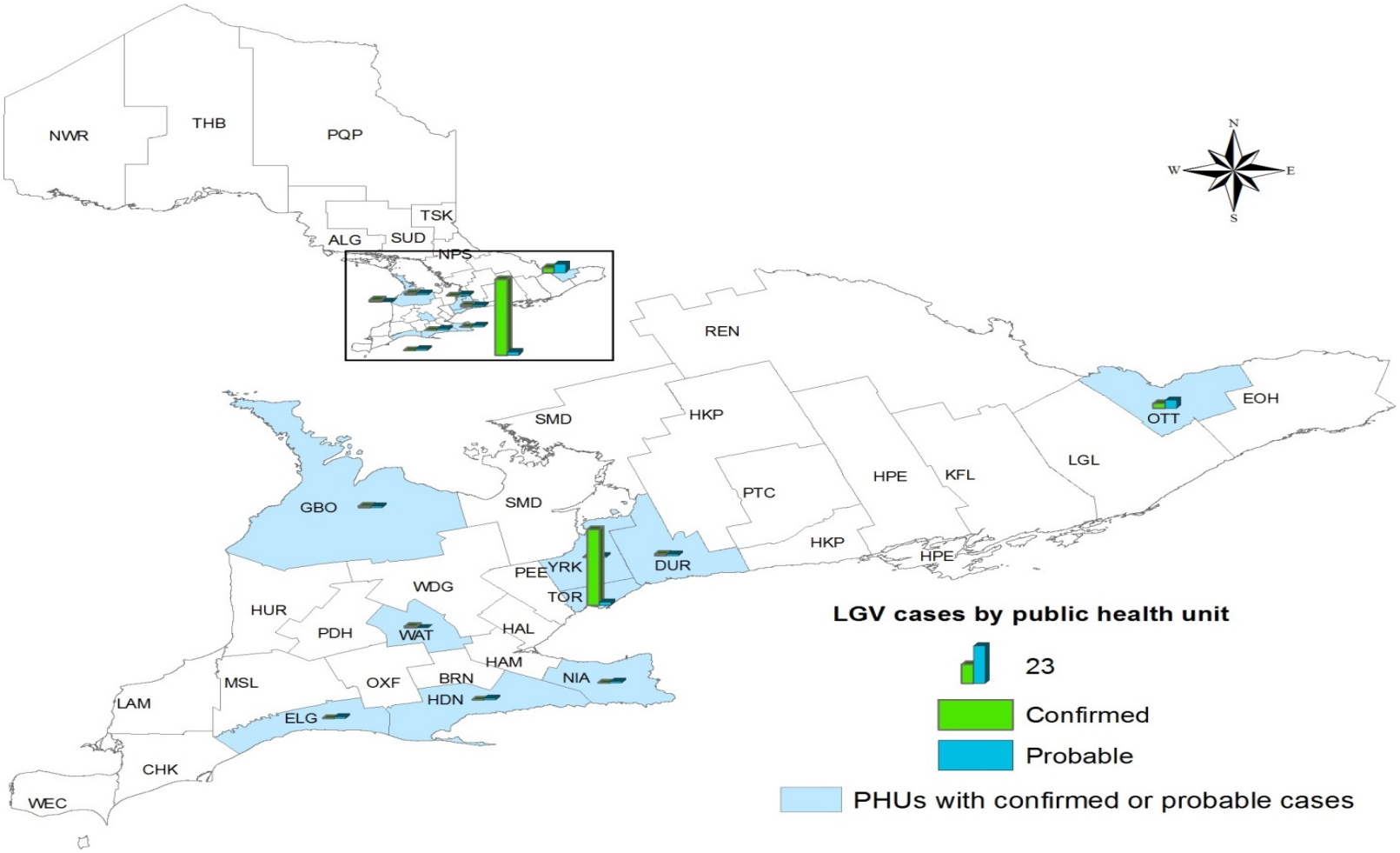
Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

Reported cases of LGV by age group: Ontario, 2006-15



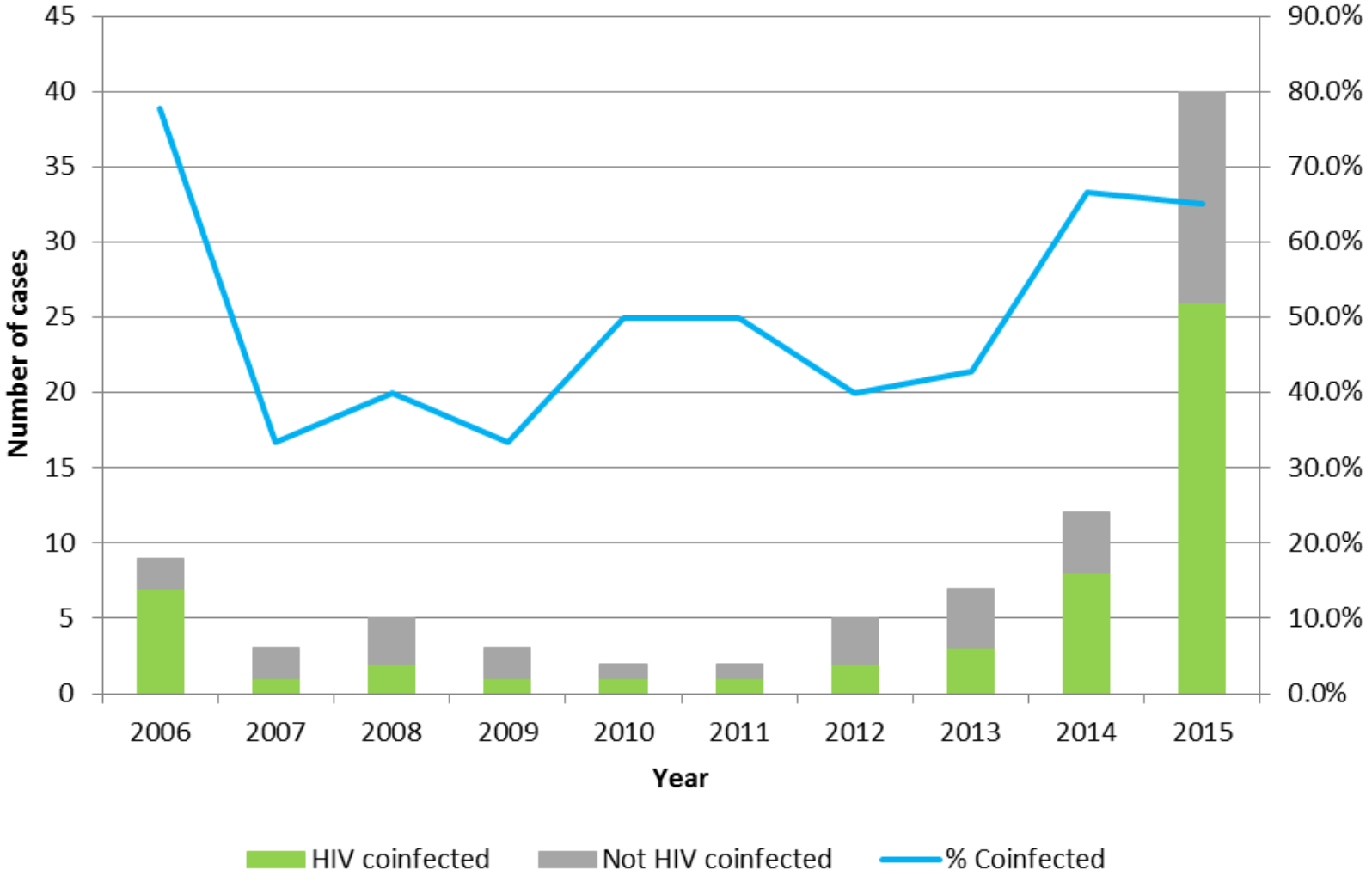
Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

Reported cases of LGV by public health unit: Ontario, 2014-15



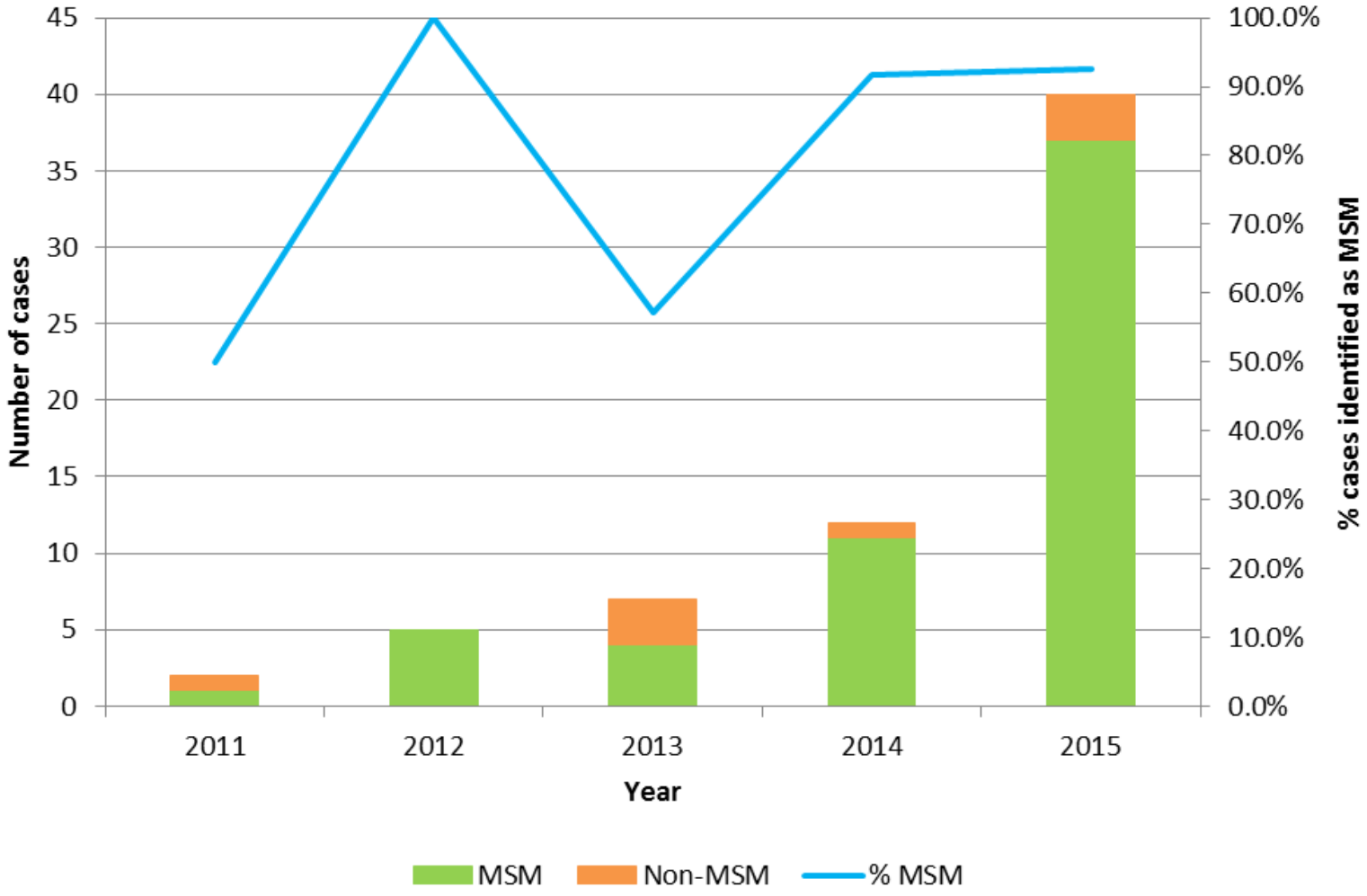
Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

HIV co-infection among confirmed LGV cases: Ontario 2006-15



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

Confirmed LGV cases that were MSM: Ontario 2011-15



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/06/01].

GONORRHEA

Gonorrhea

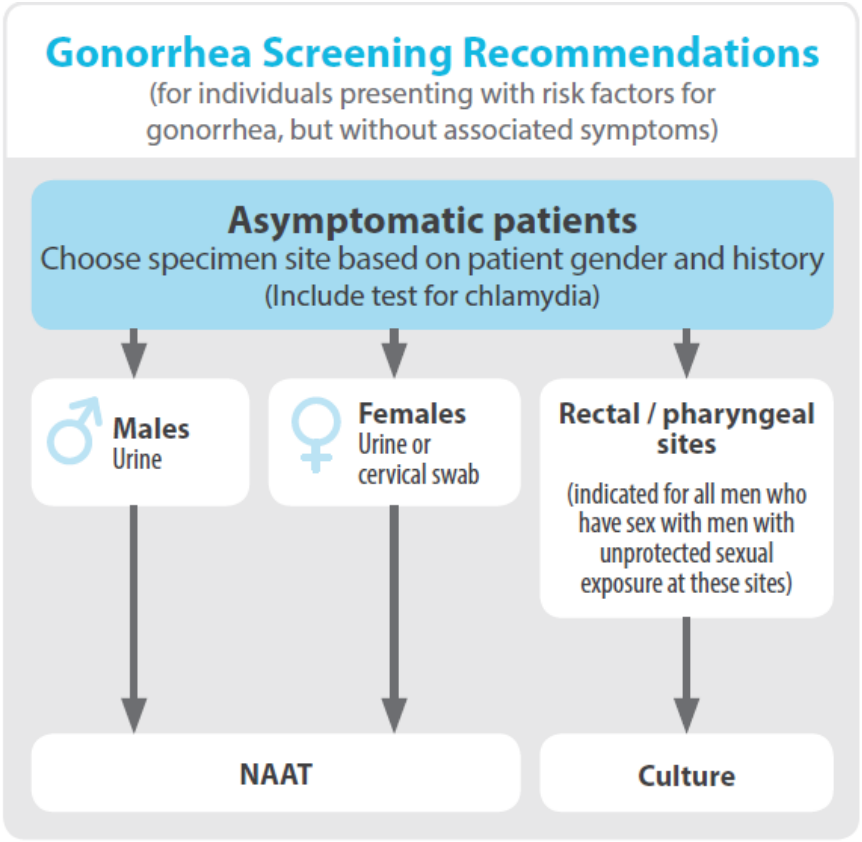
- **Causative agent**
  - *Neisseria gonorrhoeae*
- **Incubation period** ~ 1 – 14 days
- **Modes of transmission**
  - Sexual: oral, vaginal, anal
  - Vertical
- **Presentation**
  - ♂ Males: discharge, dysuria, testicular pain/swelling
  - ♀ Females: abnormal vaginal bleeding, discharge, dysuria
- **Sequelae**
  - infertility, arthritis, disseminated gonococcal infection
  - ♂ Males: epididymo-orchitis
  - ♀ Females: pelvic inflammatory disease, ectopic pregnancy

Source: Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections. Link

WHAT ARE YOUR THOUGHTS?

Gonorrhea testing

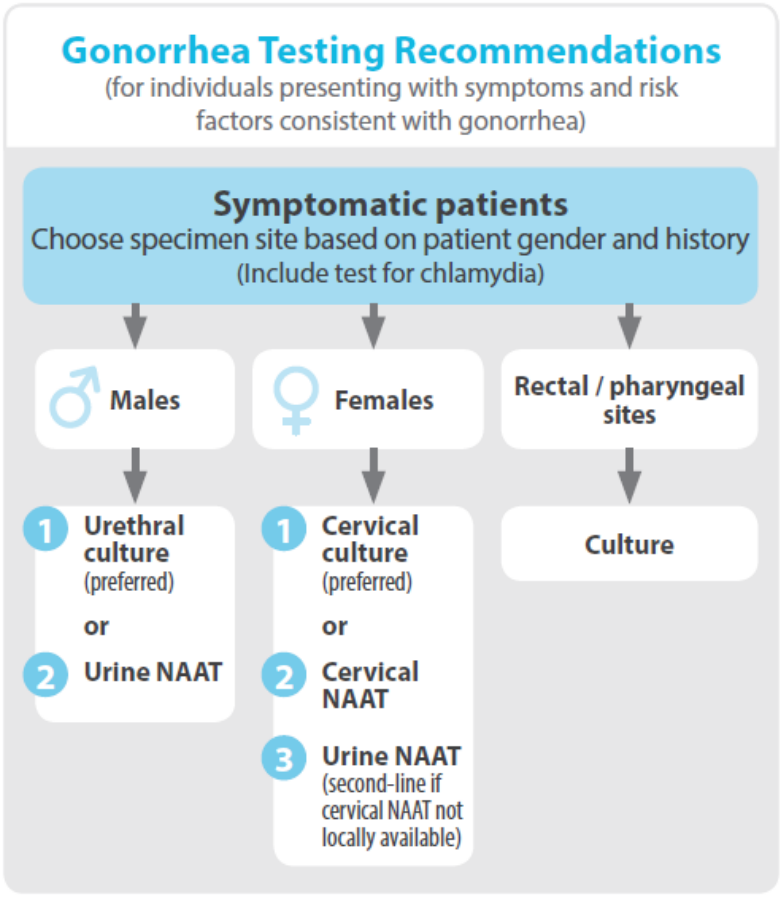
Screening Recommendations



- Sexually active individuals < 25 years of age
- New sexual partner in last 2 months
- Multiple sexual partners in last 6 months
- Contact of a case
- History of previous gonorrhea infection or other STI
- Sexually active males who have unprotected sex with men
- Sex work exposure
- Street-involved youth

Source: Public Health Ontario. Guidelines for testing and treatment of gonorrhea in Ontario, 2013. Link

Testing Recommendations (for Symptomatic Patients)



- NAAT testing does not allow for susceptibility testing
- Culture critical for improved monitoring of antibiotic resistance
- Culture necessary to determine any shifts in minimum inhibitory concentration

Source: Public Health Ontario. Guidelines for testing and treatment of gonorrhea in Ontario, 2013. Link

Two Primary Challenges for the Treatment of *N. gonorrhoeae*

1) Antibiotic resistance

- Loss of sulfa based compounds, penicillin, tetracyclines and ciprofloxacin as empiric therapy due to high rates of resistance
- Risk of losing cephalosporins (cefixime and ceftriaxone) the last reliable class of antibiotics

2) Change in number of positive culture specimens vs. positive NAAT specimens at Public Health Ontario Laboratory

- No susceptibility data available for non-culture specimens

Source: Allen, V & Whelan, M. PHO: Grand Rounds: Neisseria gonorrhea: The Ontario perspective. May 5, 2015. Link

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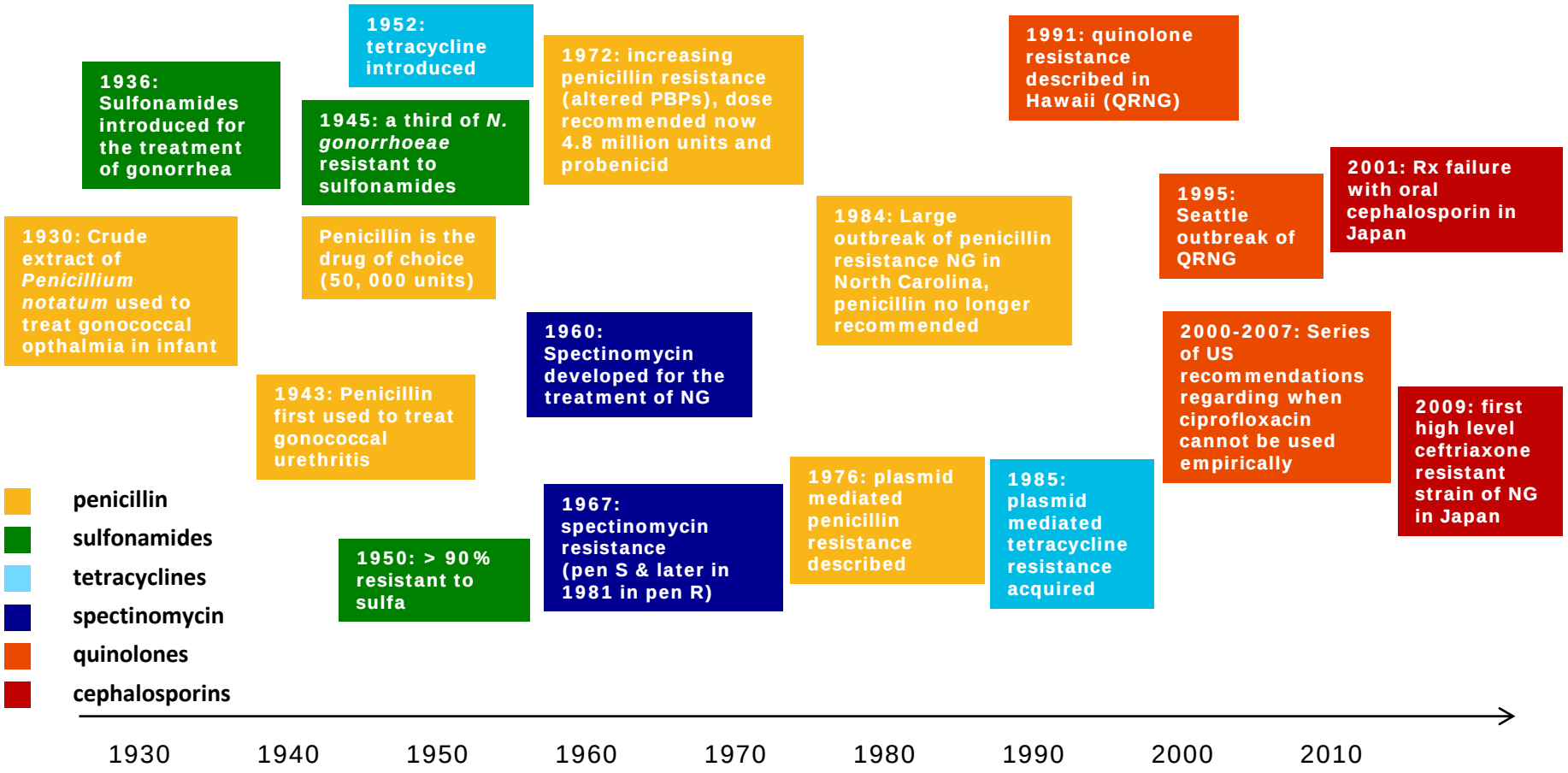
History of Antimicrobial Resistance in *Neisseria gonorrhoeae*



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Neisseria gonorrhoeae Treatment Failure and Susceptibility to Cefixime in Toronto, Canada

Vanessa G. Allen, MD, MPH
Leo Mitterni
Christine Seah, MLT
Anuradha Rebbapragada, PhD
Irene E. Martin, BSc
Colin Lee, MD

Importance Although cephalosporins are the cornerstone of treatment of *Neisseria gonorrhoeae* infections, cefixime is the only oral antimicrobial option. Increased minimum inhibitory concentrations (MICs) to cefixime have been identified worldwide and have been associated with reports of clinical failure.

Objective To assess the risk of clinical treatment failure of *N gonorrhoeae* infections associated with the use of cefixime.

Design, Setting, and Population A retrospective cohort study of culture-

- **Nine clinical failures with cefixime (9/133, 6.77%)**
- **Urethral, pharyngeal and rectal sites of infection**
- **MSM, MSW, women**
- **Two cases initially treated with cefixime 800 mg**

juvant azithromycin or doxycycline is recommended for treatment of gonorrhea.[1-5] Cefixime is the only oral cephalosporin recommended for gonorrhea treatment, critical to the success of expedited partner therapy. An increase in the minimum inhibitory concentration (MIC) of *N gonorrhoeae* to cefixime, and to a lesser extent, an intramuscularly administered cephalo-

have experienced cefixime treatment failure, involving urethral (n=4), pharyngeal (n=2), and rectal (n=3) sites. The overall rate of clinical treatment failure among those who had a test of cure was 6.77% (95% CI, 3.14%-12.45%; 9/133). The rate of clinical failure associated with a cefixime MIC of 0.12 μg/mL or greater was 25.0% (95% CI, 10.69%-44.87%; 7/28) compared with 1.90% (95% CI, 0.23%-6.71%; 2/105) of infections with cefixime MICs less than 0.12 μg/mL, with a relative risk of 13.13 (95% CI, 2.88-59.72; $P < .001$).

Conclusion and Relevance The rate of clinical failure following treatment of *N gonorrhoeae* infections with cefixime was relatively high at a Toronto clinic and was associated with elevated MICs.

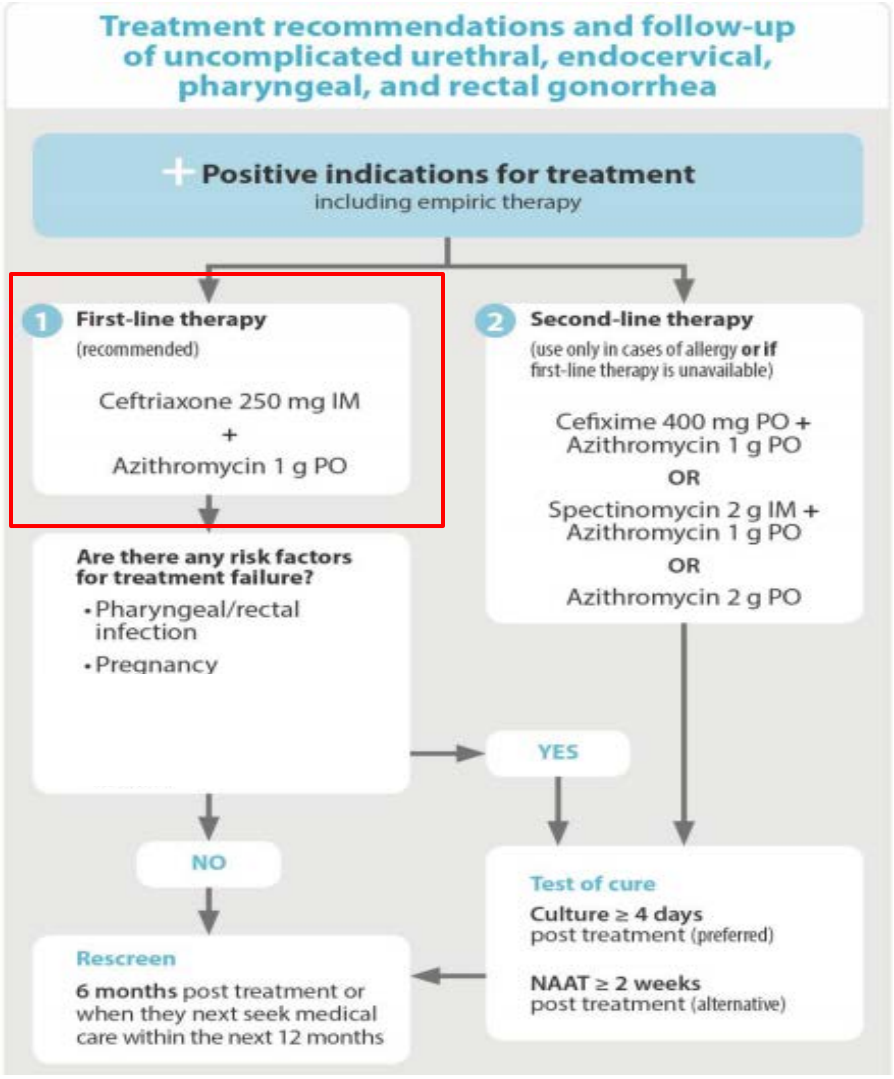
JAMA. 2013;309(2):163-170 www.jama.com

Source: Allen, V & Whelan, M. PHO: Grand Rounds: Neisseria gonorrhea: The Ontario perspective. May 5, 2015. Link

WHAT ARE YOUR THOUGHTS?

Gonorrhea treatment

Treatment recommendations



- Combination therapy
- Consider risk factors for treatment failure
- Provide counselling including information about treatment failure
- Provide test of cure & rescreen as appropriate
- Suspected treatment failures should be investigated with culture

Source: Public Health Ontario. Guidelines for testing and treatment of gonorrhea in Ontario, 2013. Link

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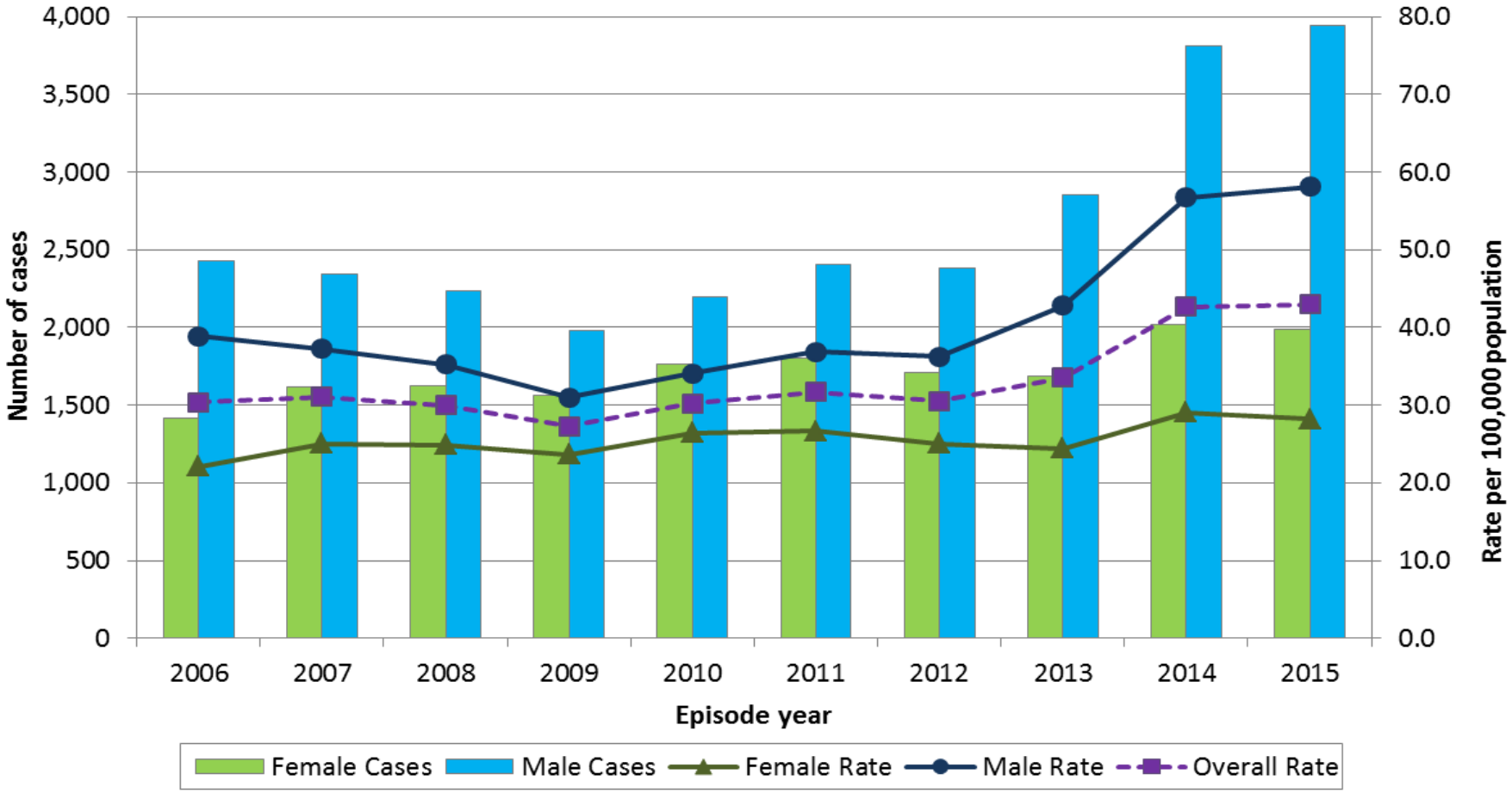
Reported incidence of gonorrhea by year: Ontario, 2006-15



Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]; (Population data) Population Estimates and Projections, Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, dates received: 2005-11 [2014/07/03]; 2012-14 [2015/11/18]; 2015-16 [2015/03/13]

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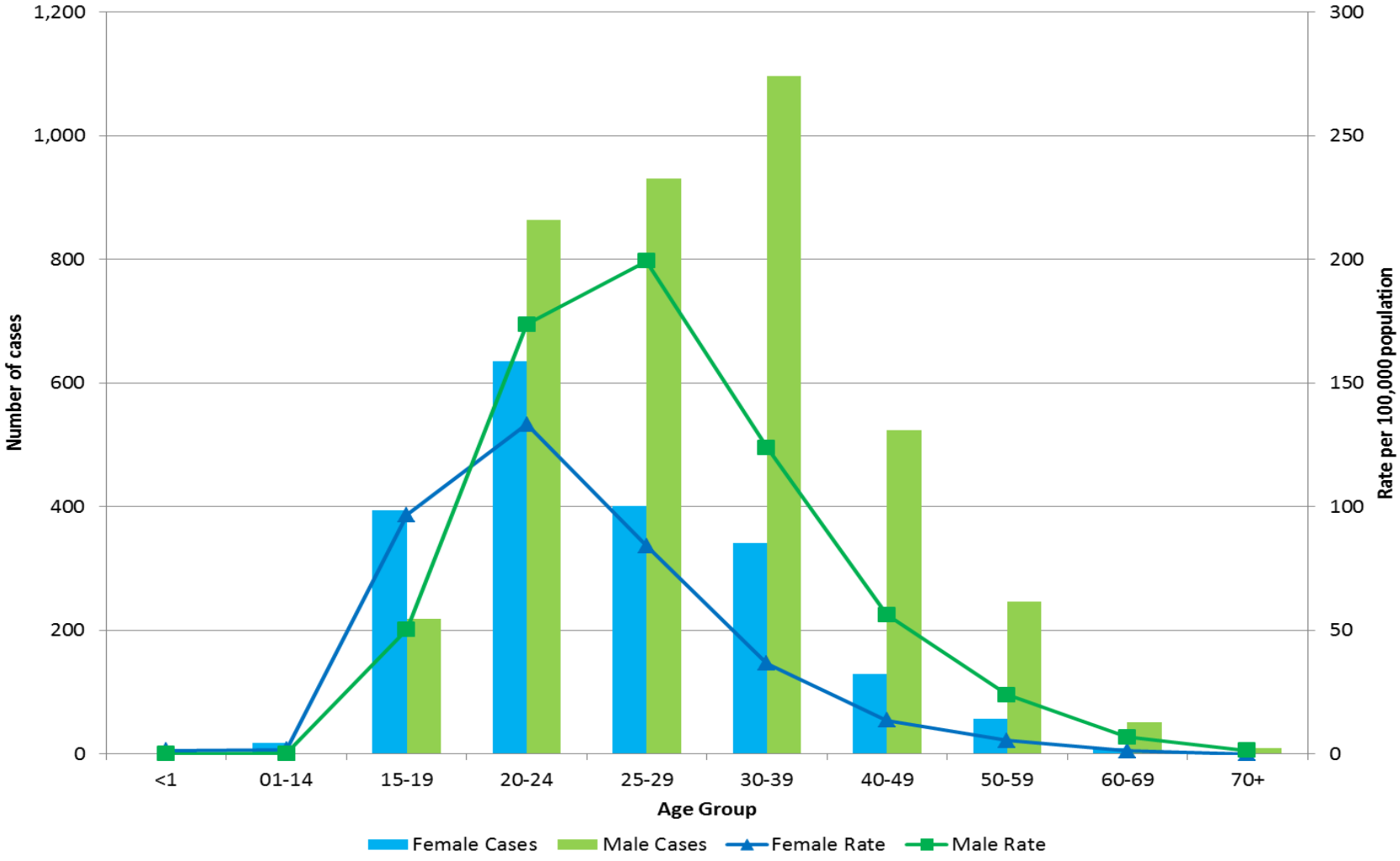
Reported incidence of gonorrhea by age group and gender: Ontario, 2015

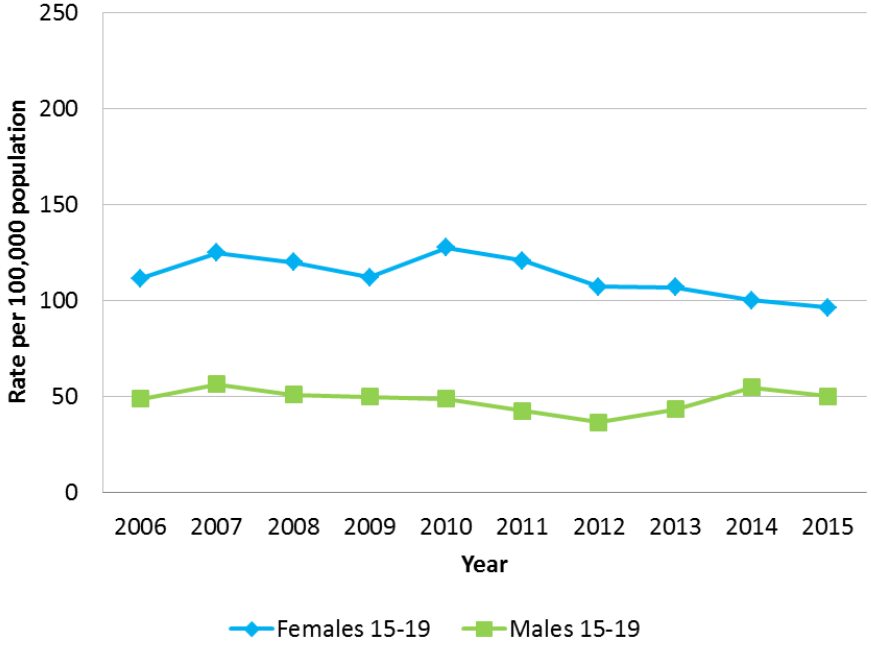


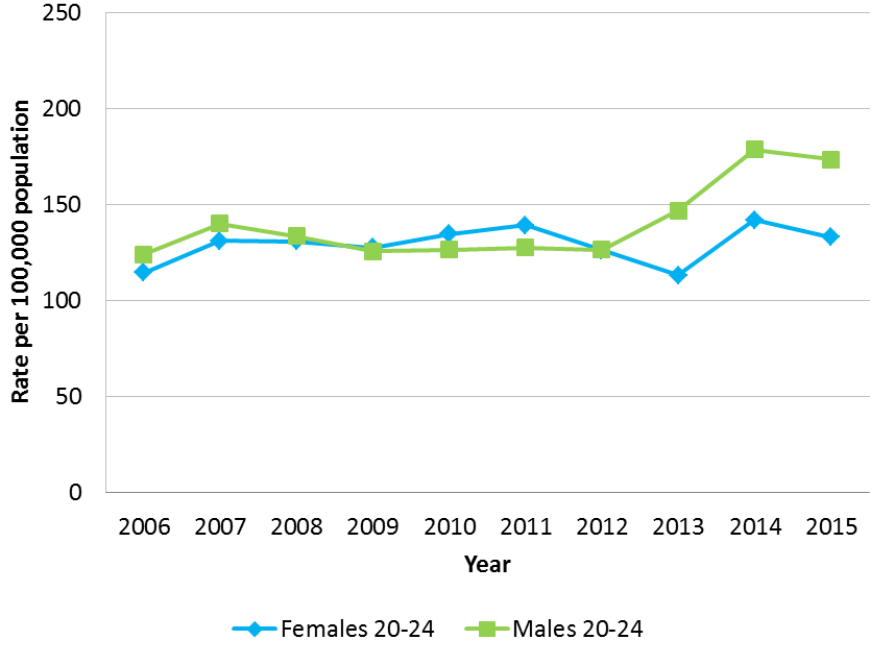
Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]; (Population data) Population Estimates and Projections, Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, dates received: 2005-11 [2014/07/03]; 2012-14 [2015/11/18]; 2015-16 [2015/03/13]

WHAT ARE YOUR THOUGHTS?

Gonorrhea trends

Reported incidence of gonorrhea by gender and age group: Ontario, 2006-15





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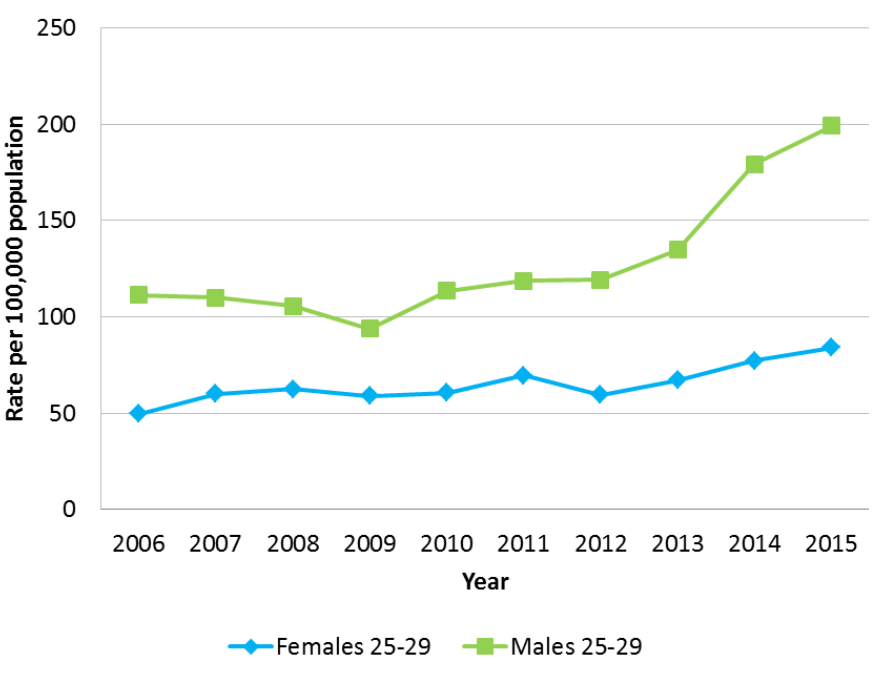
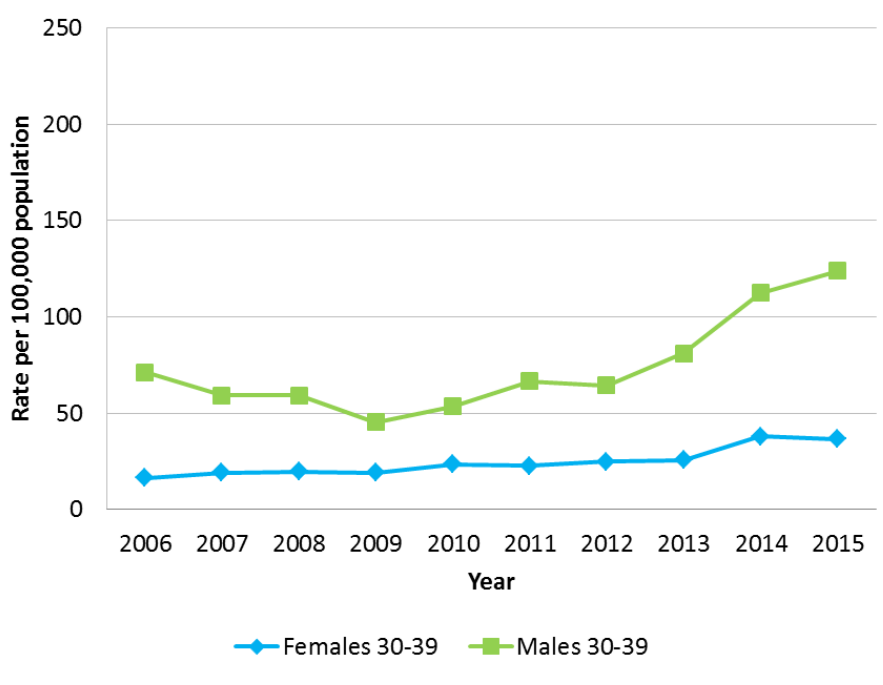
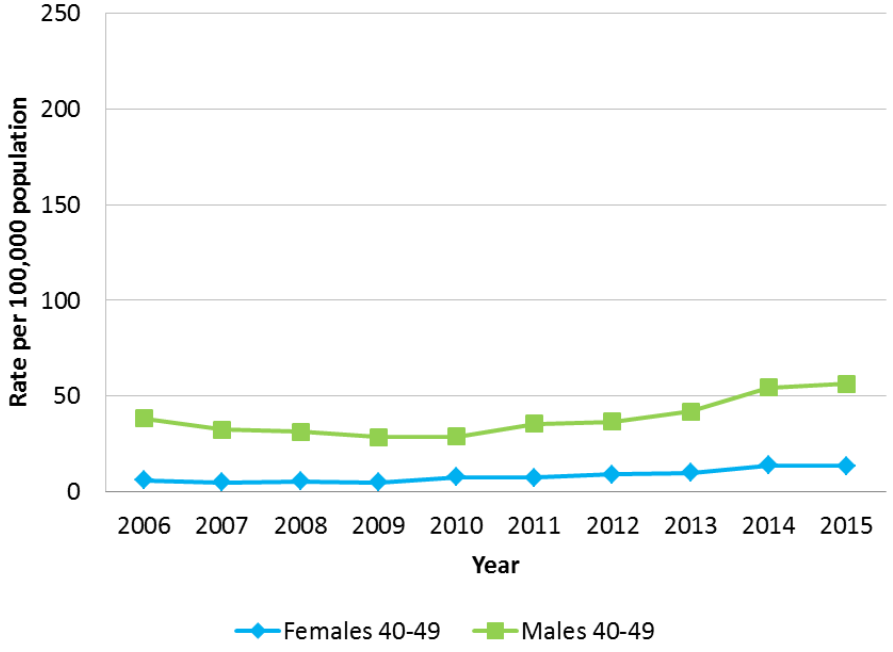
Reported incidence of gonorrhea by gender and age group: Ontario, 2006-15

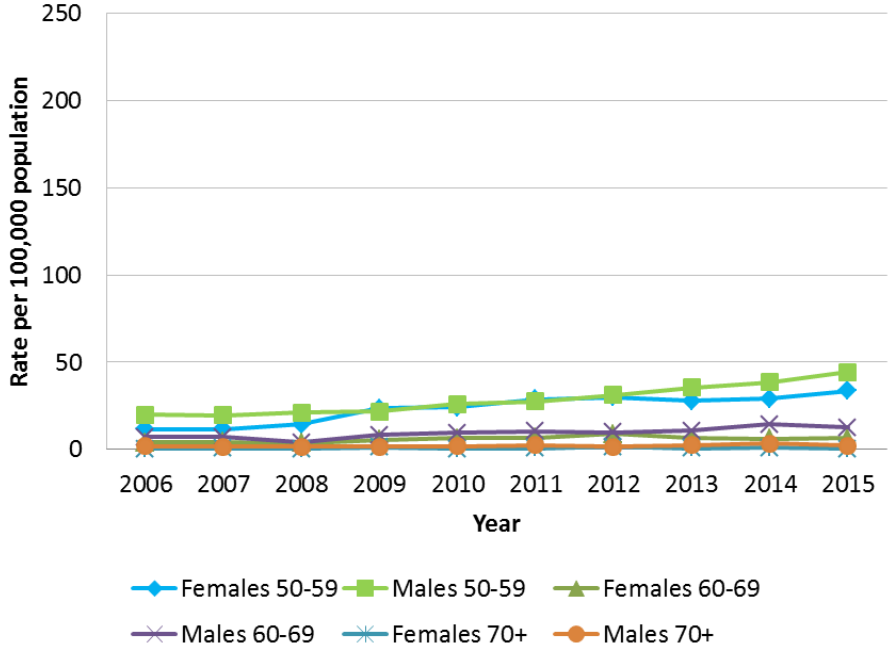




Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]; (Population data) Population Estimates and Projections, Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, dates received: 2005-11 [2014/07/03]; 2012-14 [2015/11/18]; 2015-16 [2015/03/13]

Reported incidence of gonorrhea by gender and age group: Ontario, 2006-15





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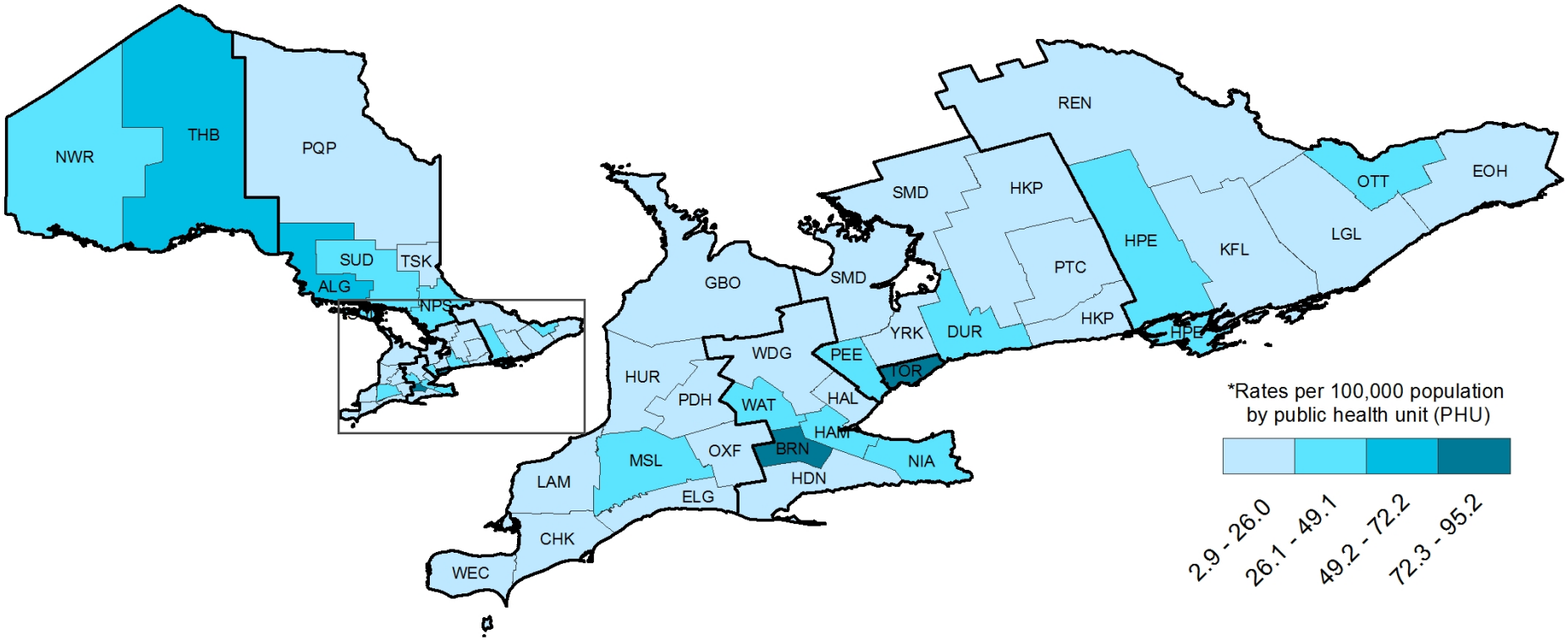
Reported incidence of gonorrhea by public health unit: Ontario, 2015



Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2016/10/03].
Population estimates and projections: Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, Dates Received: 2005-11 [2014/07/03], 2012-14 [2015/11/18], 2015 [2015/03/13].

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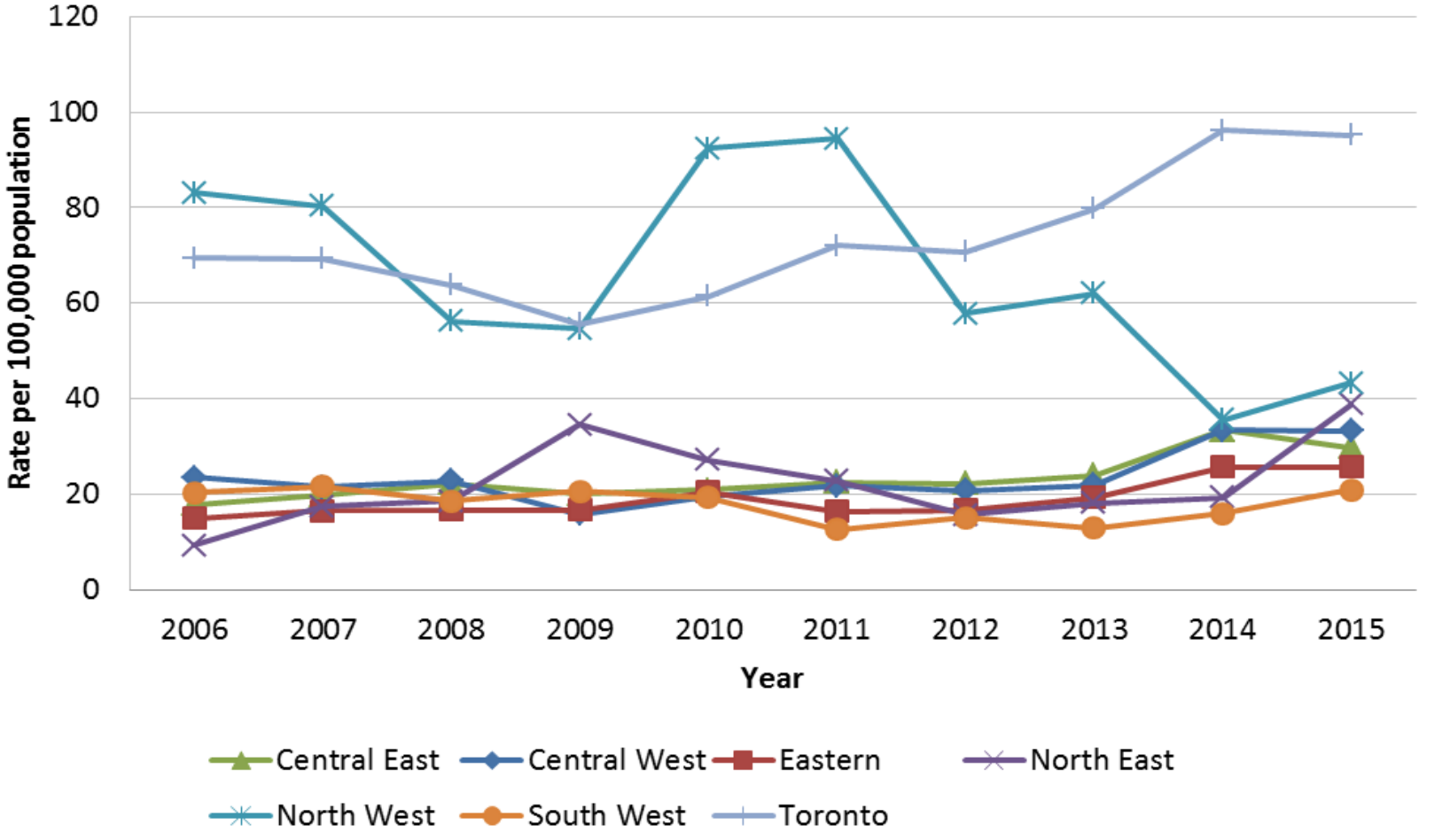
Reported incidence of gonorrhea by geographic region: Ontario 2006-15



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Summary of risk factors reported for cases of gonorrhea: Ontario 2011-15

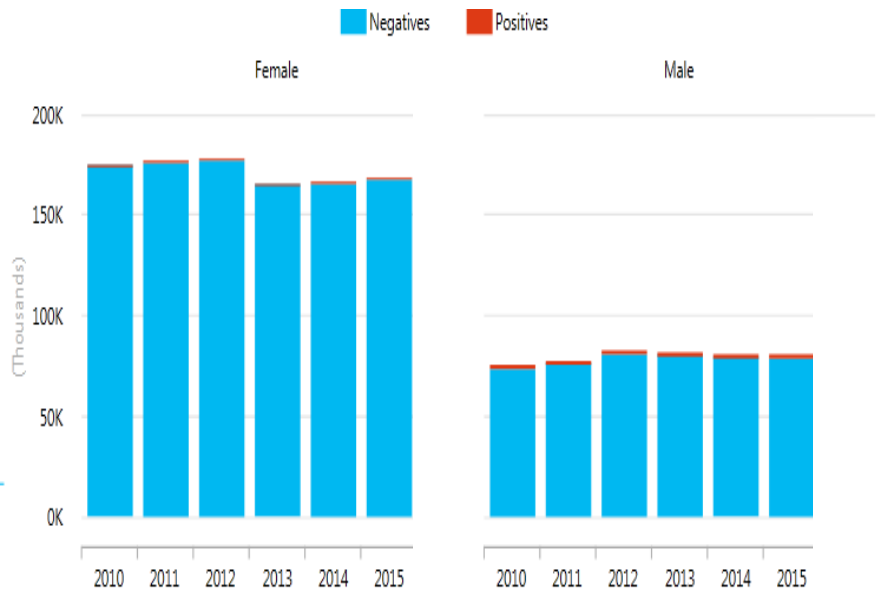
Risk factors reported in iPHIS*	2011	2012	2013	2014	2015	2011-15 trend
NO CONDOM USED	73.8%	73.0%	76.9%	73.4%	71.2%	↓
SEX WITH OPPOSITE SEX	36.7%	45.9%	51.1%	49.9%	47.9%	↑
MSM**	24.1%	24.2%	29.0%	27.1%	27.7%	↑
NEW CONTACT IN PAST 2 MONTHS	17.2%	23.6%	22.6%	21.4%	23.5%	↑
MORE THAN ONE SEX CONTACT IN LAST 6 MONTHS	25.1%	23.7%	23.8%	23.2%	23.4%	↓
REPEAT STI	5.7%	7.5%	10.2%	11.3%	14.9%	↑
ANONYMOUS SEX	5.2%	6.4%	7.1%	8.7%	8.6%	↑
CO-DIAGNOSIS/CO-INFECTION WITH EXISTING STI	1.8%	2.5%	4.7%	4.4%	4.4%	↑
JUDGEMENT IMPAIRED BY ALCOHOL/DRUGS	3.8%	3.8%	3.6%	3.9%	3.5%	↓
CONDOM BREAKAGE	5.1%	4.2%	3.7%	3.5%	3.2%	↓
Percentage of cases reporting at least one risk factor	74.9%	80.6%	82.8%	86.3%	87.3%	↑

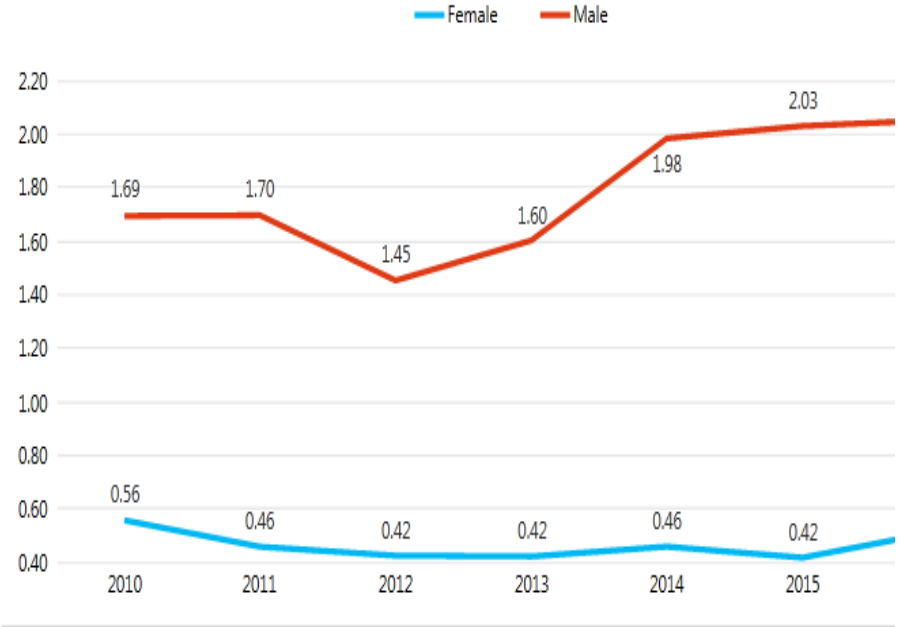
*Only the top ten risk factors reported by cases are shown

** Cases considered MSM if risk factor ‘sex with same sex’ = Y and client gender = male

Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2016/10/03]

Number of total tests and percent positivity for gonorrhea



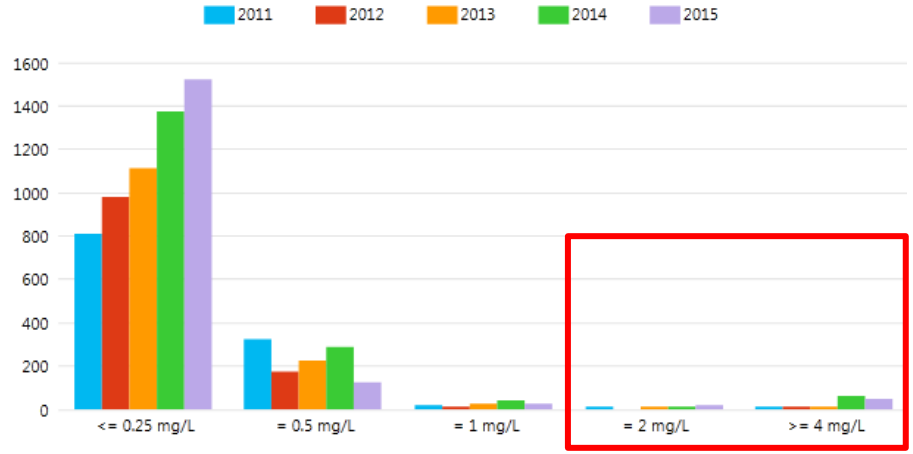


*Nucleic Acid Amplification Tests performed on urine, urethral and cervical specimens

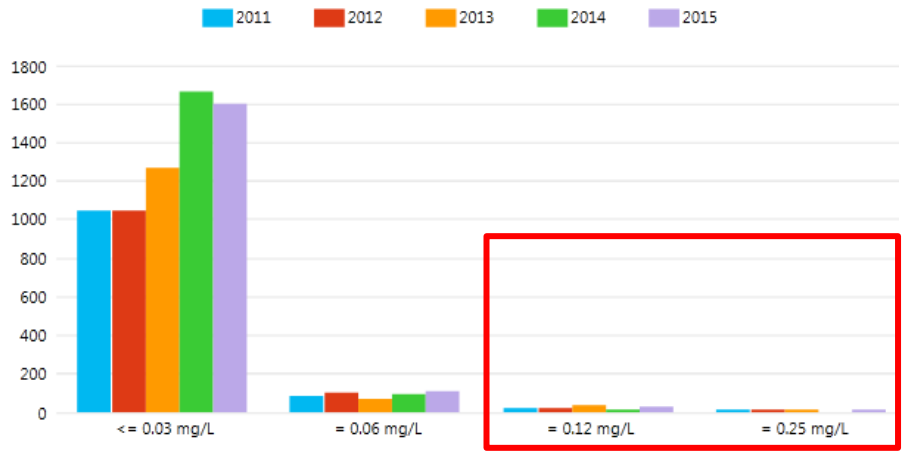
Source: Public Health Ontario Laboratory data – Laboratory Information Management System (LIMS) extracted [2017/01/30].

Gonorrhea antibiotic susceptibility by minimum inhibitory concentration: Ontario, 2011-15

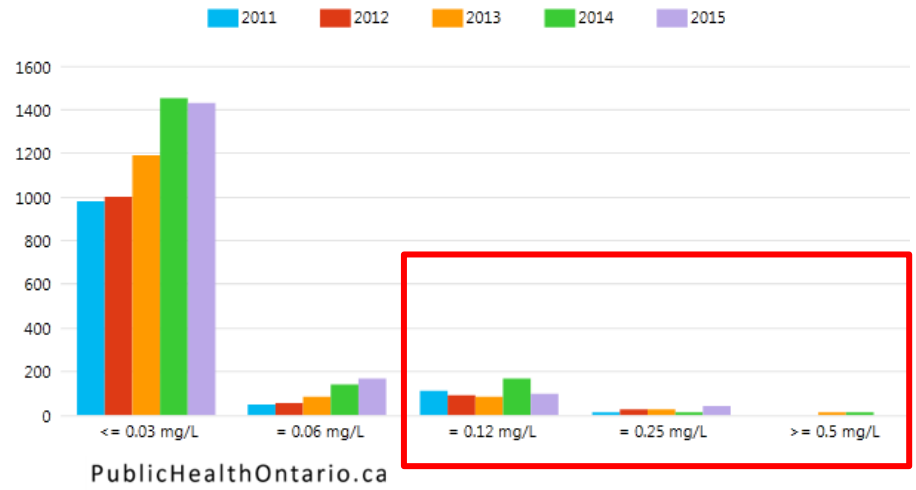
Azithromycin



Ceftriaxone



Cefixime



- There are no North American definitions of resistance to azithromycin, ceftriaxone and cefixime
- Treatment failure has been associated with cefixime ≥0.12mg/L

Source: Public Health Ontario Laboratory data – Laboratory Information Management System (LIMS) extracted [2016/10/17].

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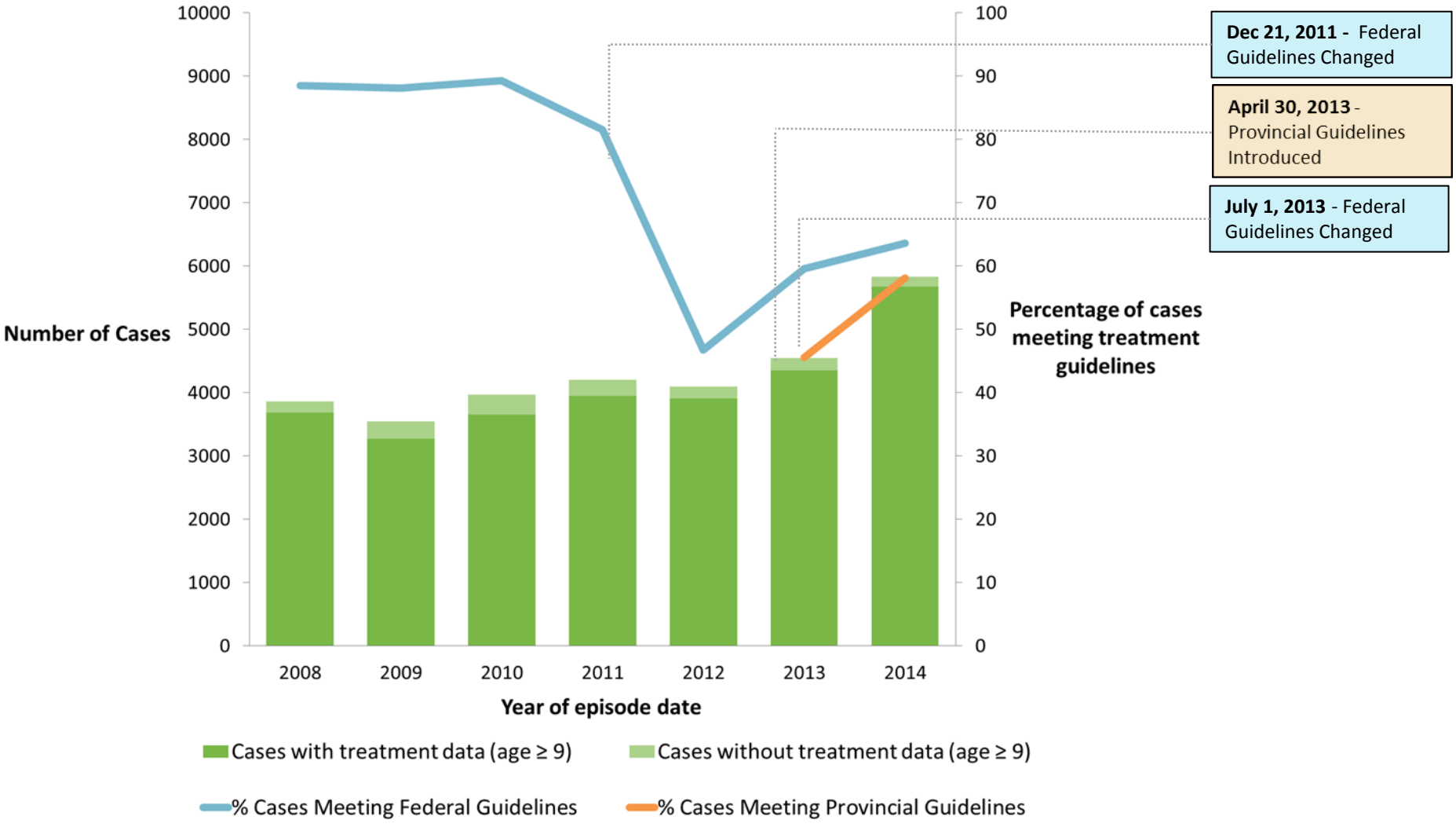
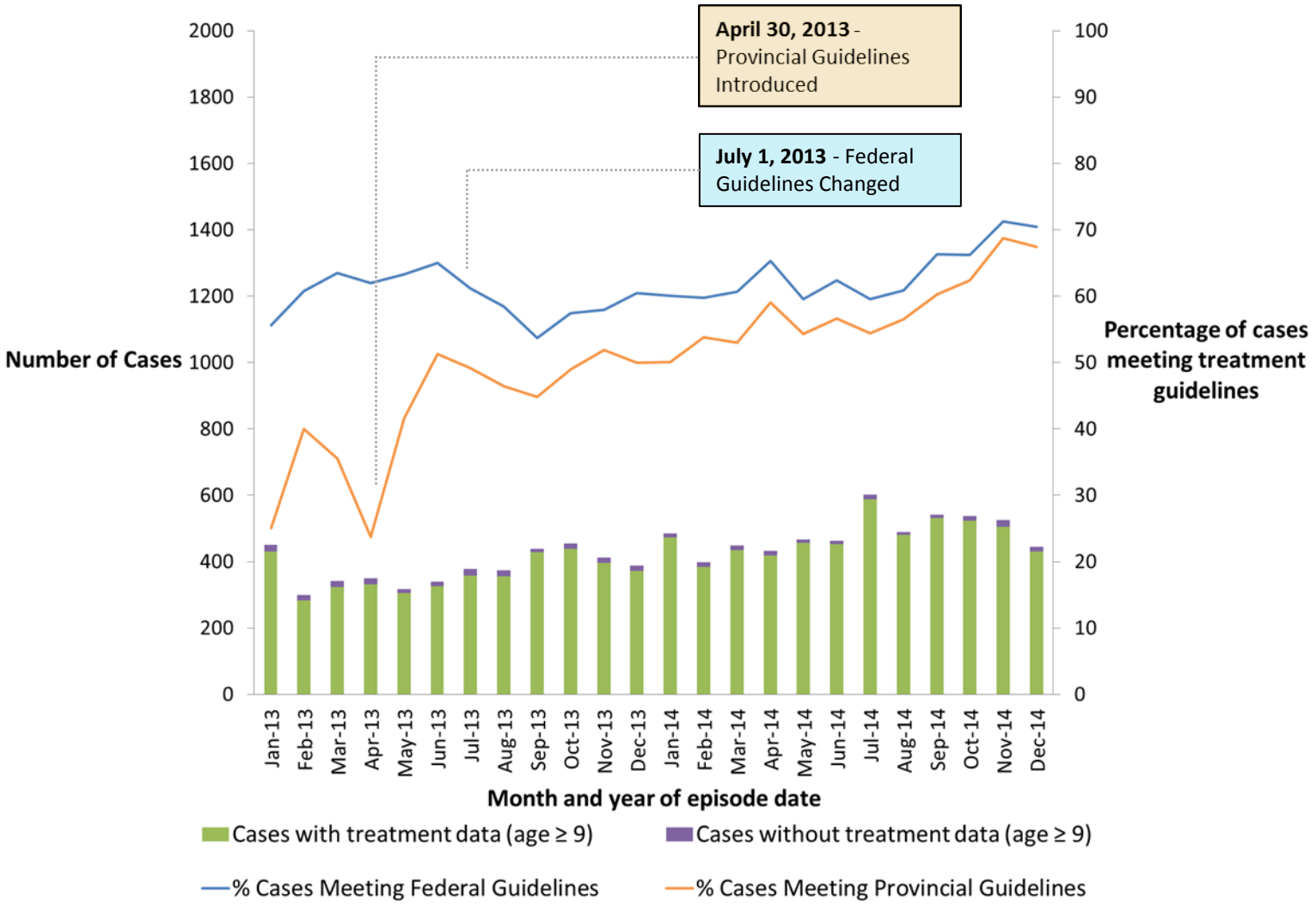
Gonorrhea cases meeting treatment guidelines by year: Ontario, 2008-14



Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/06/22].

Gonorrhea cases meeting provincial first line treatment recommendations: Ontario, 2013-14



Source: (Case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/06/22].

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Fast Facts

Overall, rates of gonorrhea have risen **41.5%** from 2006-2015

On average, **16** cases of gonorrhea were reported **per day** in 2015

In 2015, the highest rates of gonorrhea were seen in females age **20-24** and in males age **25-29**

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Considerations and next steps

- Potential causes for the increase in reported rates of chlamydia and gonorrhea
  - Likely multifactorial
- Current and future Public Health Ontario STI initiatives
  - On-going monitoring of the epidemiology of bacterial STIs in the province
  - Bacterial STI webinar series
  - Working collaboratively with the MOHLTC to develop an STI work plan
  - Analyze risk factors associated with bacterial STI

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Resources

Public Health Ontario:

- Guidelines for Testing and Treatment of Gonorrhea in Ontario, 2013
- Testing directory
- Labstracts

Public Health Agency of Canada:

- Canadian Guidelines on Sexually Transmitted Infections

Centers for Disease Control and Prevention:

- Sexually Transmitted Diseases – STD & HIV Screening Recommendations
- US Preventive Service Task Force Recommendations for STI Screening

Acknowledgements

A large thank you goes out to the following:

- Christina Renda
- Vanessa Allen
- Stacie Carey
- Ontario's Public Health Units

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Sexually Transmitted Infections (STI) Series

- Session 3: Infectious syphilis
  - March 20, 2017 – 12:00pm to 1:00pm

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Thank you