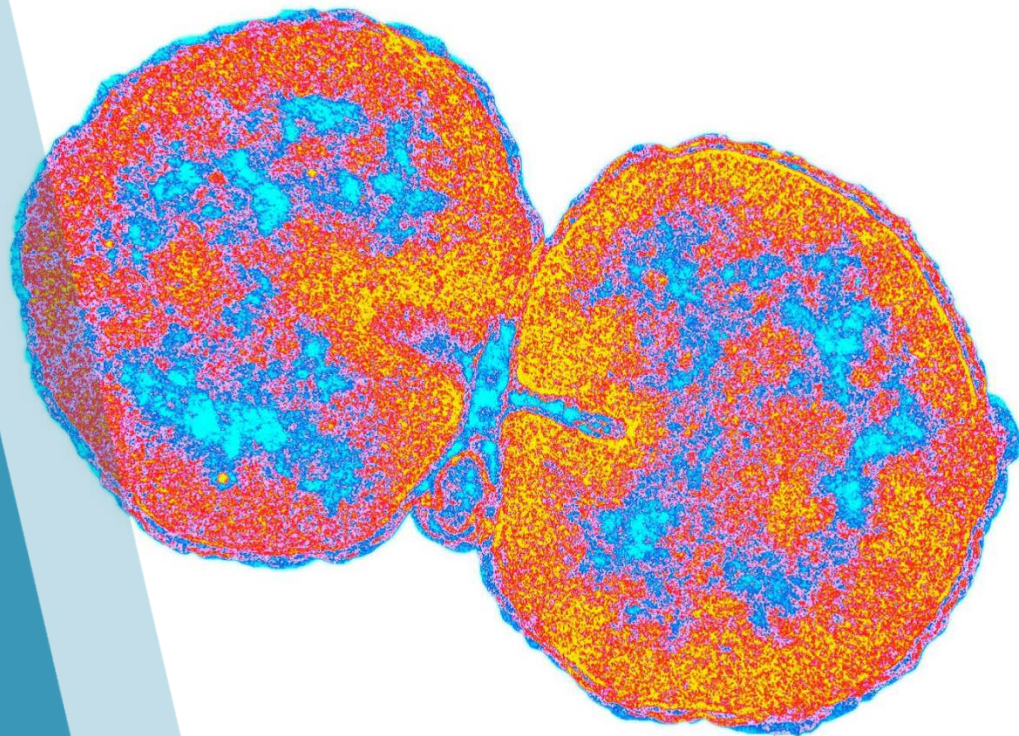


Treatment patterns among gonorrhea cases in Ontario, 2008 to 2014



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Abbreviations

AMR	Antimicrobial resistance
iPHIS	Integrated Public Health Information System
IM	Intramuscular
IV	Intravenous
MSM	Men who have sex with men
MIC	Minimum inhibitory concentration
NML	National Microbiology Laboratory
<i>N. gonorrhoeae</i>	<i>Neisseria gonorrhoeae</i>
NAAT	Nucleic acid amplification testing
PO	<i>Per os</i> (i.e., orally)
PHO	Public Health Ontario
PHOL	Public Health Ontario Laboratories
PHU	public health unit
MOHLTC	Ontario Ministry of Health and Long Term Care
STI	Sexually transmitted infection
WHO	World Health Organization

Executive Summary

Background

Gonorrhea is a sexually transmitted infection (STI) caused by the bacteria *Neisseria gonorrhoeae* (*N. gonorrhoeae*). Gonorrhea is a reportable disease in Ontario under the *Health Protection and Promotion Act*. It is the second most commonly reported STI in Ontario after chlamydia.

Over time, *N. gonorrhoeae* has developed antimicrobial resistance (AMR) to the mainstays of treatment for gonorrhea infections. This has resulted in repeated modifications to recommended antimicrobial treatments. Updated recommendations have been released in many jurisdictions in response to reduced susceptibility to third-generation cephalosporins, including but not limited to cefixime. The recommendations vary based on local context and epidemiology, but most jurisdictions now recommend a first line treatment of ceftriaxone and azithromycin (i.e., dual therapy). Public Health Ontario (PHO) formed a working group, in collaboration with the Ministry of Health and Long-Term Care (MOHLTC) and other stakeholders, to develop gonorrhea testing and treatment guidelines specific to Ontario. The result was the release of the *Guidelines for Testing and Treatment of Gonorrhea in Ontario* on April 30, 2013. The guidelines recommend first line treatment of gonorrhea infections with 250 milligrams (mg) ceftriaxone intramuscular (IM) injection plus 1 g azithromycin orally or *per os* (PO).

Objectives and methods

The primary objective of this analysis was to examine patterns of antimicrobial treatment received by confirmed cases of gonorrhea in Ontario, Canada. We looked at the period preceding and immediately following the release of Ontario's first provincial gonorrhea testing and treatment guidelines in April 2013. We extracted gonorrhea case data from the integrated Public Health Information System (iPHIS) for cases occurring from 2008 to 2014 and performed descriptive epidemiological analyses.

Results

- 94.8% (28,490/30,055) of gonorrhea cases 9 years of age or older had treatment data recorded.
- The percentage of gonorrhea cases in Ontario receiving cefixime declined from 2011 to 2014, while the percentage of cases receiving ceftriaxone increased. The percentage of cases receiving azithromycin also increased.
- The percentage of gonorrhea cases in Ontario receiving the recommended provincial first line treatment after the release of the provincial guidelines on April 30, 2013 increased from 47.9% (1,456/3,037) in the remainder of 2013 to 58.1% (3,301/5,677) in 2014.
- Month over month increases in the percentage of gonorrhea cases receiving the recommended provincial first line treatment were also observed, from 41.8% in May 2013 to 67.4% in December 2014.

- A higher percentage of male cases (57.2% [3,261/5,701]) than female cases (49.6% [1,488/3,003]) received the recommended provincial first line treatment from April 30, 2013 to December 31, 2014.
- Among male cases, the percentage of men who have sex with men (MSM) cases receiving the recommended provincial first line treatment was over 70% in most months (range: 66.7% - 85.2%) from May 2013 to December 2014. Over this time period, a lower percentage of non-MSM male cases (range: 26.1% - 67.7%) received the first line provincial treatment.
- Geographic variation in the percentage of cases receiving the recommended provincial first line treatment was observed. The public health units (PHU) with lower percentages of cases reported as receiving the recommended provincial first line treatment were mainly in southwestern Ontario.

Limitations

Potential limitations of the Ontario reportable disease data from iPHIS used for this analysis include the potential for variation in data entry at the local level. As iPHIS data offer a snapshot at a given point in time, any changes in gonorrhea treatment data (e.g., due to iPHIS data cleaning at the local level) after these data were extracted in 2015 would not have been captured. It was also beyond the scope of this analysis to examine receipt of first line treatment by provider type or setting, or to examine receipt of second line treatment as per the provincial guidelines.

Conclusions

Our findings highlight the temporal relationship between changes in gonorrhea treatment patterns in Ontario and the release of Ontario's first gonorrhea testing and treatment guidelines in 2013, as well as updates to federal guidelines in late 2011 and 2013. The percentage of cases receiving recommended provincial first line treatment increased from 2013 to 2014, but remained suboptimal. Reasons for this are likely multifactorial. Moving from oral monotherapy to dual therapy that includes an injectable antimicrobial (ceftriaxone via IM) may have reduced acceptability for patients and/or providers. Ongoing efforts to promote use of the Ontario guidelines should consider how to optimally support health care providers, particularly in PHUs with lower rates of first line treatment receipt.

Future analyses could explore linkages with laboratory data to examine treatment of gonorrhea cases by antimicrobial susceptibilities (e.g., minimum inhibitory concentrations [MICs]). Health administrative data could also be used to examine treatment by type of health care provider or clinical setting. Future research and evaluation could also explore the knowledge, attitudes and behaviours of Ontario patients and health care providers in relation to dual therapy with an injectable antimicrobial. Finally, consideration could be given to developing an ongoing sentinel surveillance system to monitor *N. gonorrhoeae* susceptibility and treatment patterns to ensure that timely AMR updates are available to Ontario PHU staff, health care providers and policy makers.

Background

Overview of *Neisseria gonorrhoeae*

Under the Ontario *Health Protection and Promotion Act*, gonorrhea is designated as a reportable disease.¹ Gonorrhea is the second most frequently reported sexually transmitted infection (STI) in Ontario after chlamydia.² Gonorrhea is caused by *Neisseria gonorrhoeae* (*N. gonorrhoeae*), which are gram negative diplococci bacteria.³ The clinical presentation of gonorrhea is well described.³ Often, females infected with *N. gonorrhoeae* do not experience symptoms. In females, serious reproductive complications can include pelvic inflammatory disease.³ Males are more likely to experience symptoms including painful urination and urethritis.³ Individuals can also have rectal or pharyngeal gonorrhea infections, though both are rarely associated with symptoms.³ Testing and treatment of both the index case and their sexual contacts are cornerstones of prevention and control of gonorrhea. This includes prompt empiric treatment of cases and contacts to reduce further transmission.⁴

Laboratory testing

Three testing modalities are available for *N. gonorrhoeae*:

- microscopy
- bacterial culture,
- nucleic acid amplification testing (NAAT).⁵

Today, the majority of individuals are tested for gonorrhea through NAAT, a highly sensitive testing modality able to detect the presence of *N. gonorrhoeae* from urine specimens.^{5,6} Historically, NAAT was preceded by culture, which is associated with a high specificity but a lower sensitivity compared to NAAT.⁵ Obtaining a specimen for culture is a more invasive procedure involving a cervical or urethral swab.⁵ Although there are identified benefits to NAAT, unlike culture, this testing method does not have the ability to determine the antimicrobial susceptibility of *N. gonorrhoeae*.⁵ In Ontario, most private and hospital laboratories perform testing for *N. gonorrhoeae* (i.e., microscopy, NAAT and/or culture). PHO laboratories (PHOL) offer all three types of tests to detect *N. gonorrhoeae*.⁵

Susceptibility is determined using the minimum inhibitory concentration (MIC). The MIC is the lowest concentration of antimicrobial required to prevent growth of the microorganism of interest. Increasing MICs are associated with reduced susceptibility and eventually the identification of antimicrobial resistance (AMR). Variation exists in the definitions of AMR for antimicrobials currently recommended for treating gonorrhea.⁵

Evolution of *N. gonorrhoeae* susceptibility and treatment

Beginning with resistance to sulphamides used to treat gonorrhea in the 1930s, *N. gonorrhoeae* has developed resistance to successive classes of antimicrobials. This includes antimicrobials from penicillin to tetracycline, quinolones (e.g., ciprofloxacin, ofloxacin), and more recently, third-generation

cephalosporins.⁷⁻⁹ As a result, treatment recommendations for gonorrhea have changed repeatedly over time. This has led to reliance on treatment with the last family of antimicrobials available, the cephalosporins, as well as the provision of dual antimicrobial therapy (i.e., a cephalosporin and azithromycin taken at the same time) to effectively treat gonorrhea.^{4,5,9,10}

Recent gonorrhea treatment guidelines: the international context

The World Health Organization (WHO) outlines criteria that should be considered when recommending first line gonorrhea treatment, including the following:¹¹

- Highly effective
- Widely available
- Affordable
- Lacks toxicity
- Single dose
- Rapidly cures at least >95% of infected patients

Table 1 summarizes selected gonorrhea treatment guidelines in Australia, the European Union (EU), the United States of America (US), as well as in Canada and Ontario.^{4,5,10,12,13} A recent systemic review summarizes the recommendations of additional guidelines from the United Kingdom (UK), Australia, New Zealand, and the WHO.¹⁴

Dual therapy (treatment with a cephalosporin and azithromycin concurrently) has been recommended as a first line treatment for cases of gonorrhea in Europe, US, and Australia since the early 2010's, in the context of rapidly evolving resistance to cephalosporins.^{7,10} The recommended first line cephalosporin and dosage varies by jurisdiction.¹⁴ Dual therapy may have contributed to the recent increase in cephalosporin susceptibility in multiple jurisdictions.¹⁵⁻¹⁷

Based on the resistance patterns identified in Japan in 2006, the Japanese Society of Sexually Transmitted Infections' guidelines for gonococcal infection, as cited by Unemo and Shafer,¹⁸ began recommending monotherapy with 1 gram (g) ceftriaxone, which requires intravenous (IV) administration, (or cefodizime 1 g IV or spectinomycin 2 g via intramuscular (IM) injection) as the first line treatments for uncomplicated anogenital and pharyngeal cases of *N. gonorrhoeae*. This 1 g ceftriaxone IV monotherapy approach can eradicate *N. gonorrhoeae* strains exhibiting MICs for ceftriaxone up to 0.5 milligrams per litre (mg/L).¹⁹ It is postulated that this approach will provide only a short-term solution for effective treatment of gonorrhea.²⁰

Table 1: Summary of recommended selected recent gonorrhea treatment guideline recommendations

Jurisdiction	Recommended treatment: Uncomplicated gonococcal infections of the cervix, urethra and rectum	Date of most recent update
Australia ¹²	Ceftriaxone 500 mg IM plus azithromycin 1 g <i>per os</i> (PO)	2014
Canada ⁷	Ceftriaxone 250 mg IM plus azithromycin 1 g PO OR Cefixime 800 mg PO plus azithromycin 1 g PO (not applicable for men who have sex with men(MSM))	2013
European Union ¹³	Ceftriaxone 500 mg IM plus azithromycin 1 g PO	2012
Ontario ⁵	Ceftriaxone 250 mg IM plus azithromycin 1 g PO	2013
United States of America ¹⁰	Ceftriaxone 250 mg IM plus azithromycin 1 g PO	2015

Federal gonorrhea testing and treatment guidelines in Canada from 1998 to 2013

The federal STI guidelines (now the *Canadian Guidelines for Sexually Transmitted Infections*) recommended cefixime 400 mg orally or *per os* (PO) as a preferred (i.e., first line) treatment for uncomplicated gonorrhea from 1998 until 2011.²¹⁻²⁴ Quinolones were recommended as alternatives in selected circumstances.²¹⁻²⁴ In response to increasing AMR in *N. gonorrhoeae*, a December 21, 2011 notice updated the federal guidelines' preferred monotherapy to cefixime 800 mg PO or ceftriaxone 250 mg via IM injection. Ceftriaxone was the only preferred antimicrobial for uncomplicated gonorrhea in MSM.²⁵ The 2011 update retained quinolones, such as ciprofloxacin and ofloxacin, as acceptable alternatives in some circumstances.²⁵ In the absence of Ontario-specific guidelines at that time, health care providers treating gonorrhea in Ontario were encouraged to follow the federal guidelines. The *Canadian Guidelines for Sexually Transmitted Infections* also recommended and continue to recommend concurrent testing for chlamydia and gonorrhea infection, and prompt empiric treatment for chlamydia when gonorrhea is diagnosed without waiting for chlamydia test results (e.g., if pending), due to frequent co-infection; since 2006, azithromycin 1 g PO and doxycycline 100 mg PO twice daily for 7 days have been the preferred treatments for chlamydia.^{21,23,24,26}

Evolving Antimicrobial Resistance in *N. gonorrhoeae* in Ontario

In 2013, in the context of growing global concerns about antimicrobial resistance (AMR) in gonorrhea, a retrospective cohort study of 133 *N. gonorrhoeae* infections from a single clinic in Toronto, Ontario identified nine clinical treatment failures associated with the use of cefixime over a single year.²⁷ These clinical treatment failures represented 6.8% (9/133) of all individuals who returned for test of cure.

These clinical failures were the first to be reported in North America.²⁷ Additionally, the study documented clinical failures at MIC \geq 0.125 mg/L, which was an unexpected finding.²⁷ Although generalizability was potentially limited due to analysis of isolates from one urban clinic that primarily served MSM,²⁷ these findings had concerning implications for *N. gonorrhoeae* susceptibility in Ontario.

Release of the first provincial guidelines in Ontario

On April 30, 2013, PHO released the *Guidelines for Testing and Treatment of Gonorrhea in Ontario* (the Ontario or provincial guidelines).⁵ The Ontario guidelines provide recommendations to frontline health care providers on testing, treatment and follow up for gonorrhea cases, as well as their sexual contacts. They recommend dual therapy with 250 mg ceftriaxone IM plus 1 g azithromycin PO, for first line treatment of uncomplicated gonorrhea of the cervix, urethra and rectum.⁵ The guidelines state that the use of second line treatments should only be considered if first line treatments are not available, and that a test of cure must be performed.⁵

The Ontario guidelines recommend screening for gonorrhea among asymptomatic individuals with identified risk factors using urine NAAT.⁵ For symptomatic individuals, they recommend culture testing or NAAT testing.^{4,5} Receipt of samples for culture testing allows the PHOL to monitor antibiotic susceptibility among *N. gonorrhoeae* in Ontario.

Development and implementation of the Ontario guidelines

The [Ontario guidelines](#) were developed by PHO with a working group including representatives from PHUs and the Ontario Ministry of Health and Long Term Care (MOHLTC).⁵ These are the first Ontario-specific clinical practice guidelines for any STI, developed to address the changing epidemiology of gonorrhea AMR in Ontario.

To promote uptake and support implementation of the Ontario guidelines among frontline health care providers, PHO and MOHLTC engaged key stakeholders, including: the Society of Obstetricians and Gynecologists of Canada; the Ontario College of Family Practitioners; the Nurse Practitioner Association of Ontario; and, the Ontario Medical Association. Between April and May, 2013, several supplementary resources for PHUs and health care providers were produced to promote the Ontario guidelines. These included:

- A webinar for Ontario PHUs,
- PHO Rounds,²⁸
- An online training module for health care providers,²⁹
- A Quick Reference Guide for clinicians, highlighting key recommendations by sex for testing, first line treatment and follow up,³⁰ and
- A Frequently Asked Questions document.³¹

These resources are available on the [PHO website](#).

Updates to the Canadian Guidelines

On July 1, 2013, an updated gonorrhea diagnosis and treatment chapter in the federal guidelines was released, with a shift to dual therapy as the preferred approach.⁴ Preferred (i.e., first line) treatments are: ceftriaxone 250 mg IM plus azithromycin 1 g PO, or cefixime 800 mg PO plus azithromycin 1 g PO for uncomplicated anogenital infections in persons who do not identify as MSM.⁴ (See [Appendix A](#) for additional details.)

For MSM, the Ontario and 2013 federal first line recommendations are the same (i.e., ceftriaxone 250 mg IM and azithromycin 1 g PO).^{4,5} However, the updated federal guidelines differ from the Ontario guidelines and from other jurisdictions (e.g., Japan, Australia, the US, the EU), in continuing to recommend cefixime as a first line treatment option for treating gonorrhea for those who do not identify as MSM.^{14,18}

The federal guidelines recommend culture *and* NAAT for symptomatic individuals, unlike the Ontario guidelines, which recommend culture *or* NAAT testing. Both provincial and federal guidelines recommend test of cure in the case of alternative treatment provision; the Ontario guidelines recommend culture for test of cure.^{4,5}

Antimicrobial susceptibility patterns in the context of treatment guideline changes

A recent study analyzed the susceptibility of *N. gonorrhoeae* isolates submitted to Canada's National Microbiology Laboratory (NML) from 2010 to 2014, which accounted for 11.3% (6,728/59,400) of gonorrhea cases reported in Canada over this time period.¹⁶ NML isolates were from provincial reference laboratories, as well as laboratories that do not complete susceptibility testing. Breakpoints of MIC \geq 0.25 mg/L for decreased susceptibility to cefixime; MIC \geq 0.125 mg/L for decreased susceptibility to ceftriaxone; and MIC \geq 1.0 mg/L for resistance to azithromycin were used.¹⁶

Over the study period, *N. gonorrhoeae* isolates with reduced susceptibility to cefixime decreased from 4.2% in 2011 to 1.1% in 2014. Similarly, reduced susceptibility to ceftriaxone declined from 7.3% in 2010 to 2.7% in 2014. By contrast, azithromycin resistance increased from 0.4% in 2011 to 3.3% in 2014.¹⁶ The authors noted that the decrease in reduced susceptibility to cefixime and ceftriaxone coincided with the shift toward dual therapy (e.g., ceftriaxone and azithromycin) in treatment guidelines. The authors noted with concern that the increase in azithromycin-resistant isolates to 3.3% was close to the WHO's recommended 5% threshold for reviewing and changing national STI treatment guidelines. They also concluded that ongoing surveillance of antimicrobial susceptibilities in *N. gonorrhoeae* is critical for informing treatment recommendations.

Objectives and Scope

The primary objective of this analysis was to examine patterns of antimicrobial treatment received by confirmed cases of gonorrhea in Ontario, Canada, in the period preceding and immediately following the release of Ontario's first provincial gonorrhea testing and treatment guidelines in April 2013 (i.e., 2008 to 2014). Key outcomes of interest included:

- Percentage of confirmed gonorrhea cases who received the provincial first line treatment, overall and by age group, sex, risk factor status, reason for testing, and by PHU, from April 30, 2013 to December 31, 2014.
- Percentage of confirmed gonorrhea cases in Ontario who received selected individual antimicrobial agents from 2008 to 2014.

Our secondary objectives were to:

- Describe the epidemiology of confirmed gonorrhea cases reported in Ontario, Canada from 2008 to 2014.
- Examine receipt of first line treatment as per the evolving federal guidelines, among gonorrhea cases reported in Ontario, Canada from 2008 to 2014.

Methods

Data sources and case definitions

Case data for all confirmed cases of gonorrhea (per provincial case definitions) reported from 2008 to 2014 in Ontario were extracted from Ontario's integrated Public Health Information System (iPHIS), on June 22, 2015.³² Risk factor, treatment and reason for testing data for reported cases, where available, were also extracted from iPHIS. [Appendix B](#) summarizes key iPHIS data caveats and limitations. Annual population denominators were obtained from Statistics Canada, (2008 to 2014), through IntelliHEALTH Ontario and the Ontario Ministry of Health and Long-Term Care.³³

Receipt of first line treatment recommendation was defined based on the guideline(s) available on the treatment date entered in iPHIS for the case. Cases were defined as receiving the recommended federal and/or provincial first line treatment if:

- they received any of the recommended first line treatment(s), AND
- treatment doses met or exceeded the recommendation, AND,
- the two recommended antimicrobial agents for dual therapy were recorded in iPHIS as administered on the same date.

For example, ≥ 250 mg ceftriaxone and ≥ 1 g azithromycin received on the same date was considered dual therapy received as per the Ontario guidelines' first line treatment recommendation.

Cases were not evaluated to determine whether they met the provincial second line treatment recommendations.

Data analysis

We described the epidemiology of gonorrhea in the Ontario population over the study period (i.e., 2008 to 2014), by case counts and incidence rates per 100,000 population overall and by sex.

We calculated the percentage of cases receiving any of the following individual antimicrobial agents:

- azithromycin
- cefixime
- ceftriaxone
- ciprofloxacin
- doxycycline

We described changes observed over the study period, before and after key guideline changes, including the release of the Ontario guidelines in April 2013.

We calculated the percentage of cases receiving first line treatment according to federal and provincial recommendations, using the total number of cases with treatment data available in iPHIS as the denominator. Similarly, we described changes observed in the percentage of cases receiving first line therapy over the study period, before and after key guideline changes, including the release of the Ontario guidelines. We examined the percentage of cases receiving first line provincial and federal treatments by PHU, age group, sex, by MSM status among males, and by the presence/absence of other STI risk factors. We also examined the percentage of cases receiving first line provincial treatment by reason for testing. Of note, federal and provincial gonorrhea treatment recommendations require weight-based dosing for children under the age of nine years. iPHIS does not have information on weight; therefore we excluded cases reported in children under the age of nine years from analysis of recommended first line treatment provision.

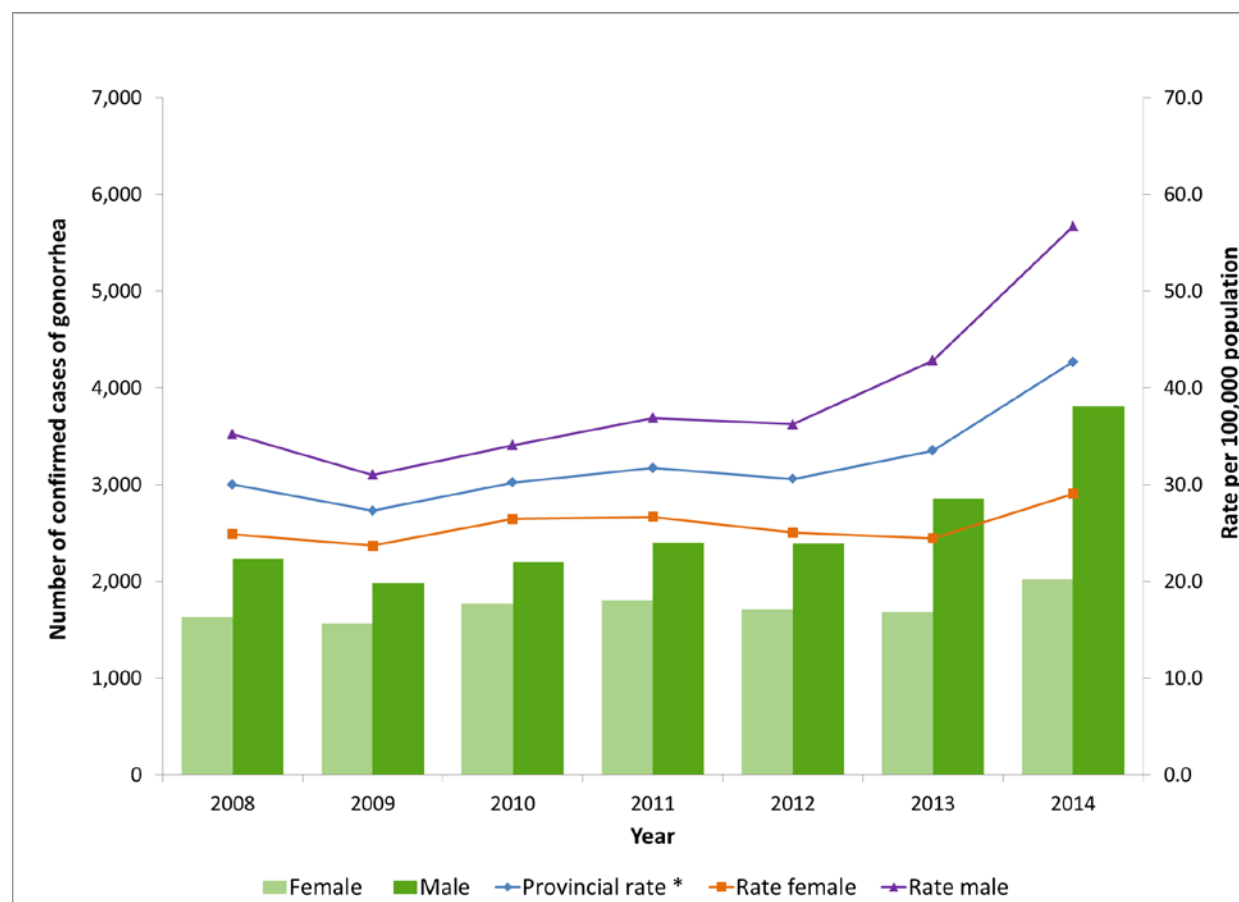
Data manipulation and analyses were conducted using SAS 9.3. This study received approval from Public Health Ontario's Ethics Review Board.

Results

Gonorrhea case counts and rates in Ontario, 2008 to 2014

From 2008 to 2014, there were 30,068 cases of gonorrhea reported in Ontario. While rates of reported cases per year fluctuated, there was a general increase from 2009 to 2014, with rates increasing from 27.3 to 42.7 cases per 100,000 population over that time period. The number of male cases reported and the corresponding rate was higher in every year than among females. Between 2009 and 2014, the reported gonorrhea rates in males increased from 31.0 to 56.7 cases per 100,000 population. From 2008 to 2013, the reported gonorrhea rates in females were fairly constant (ranging from 23.7 to 26.7 cases per 100,000 population) before increasing to 29.0 cases per 100,000 in 2014 (Figure 1). By 2014, the rate among males was 95.5% higher than the rate in females, compared to 30.8% higher in 2009.

Figure 1: Incidence of gonorrhea among males and females: Ontario, 2008-14



*Includes cases that did not have male or female gender specified

Availability of treatment data

Of the 30,068 cases, there were 13 cases reported in children under the age of nine. Of the remaining 30,055 cases, 94.8% (28,490 cases) had treatment data recorded in iPHIS. On an annual basis, more than 92% of cases had treatment data recorded in iPHIS every year from 2008 to 2014 (Table 2).

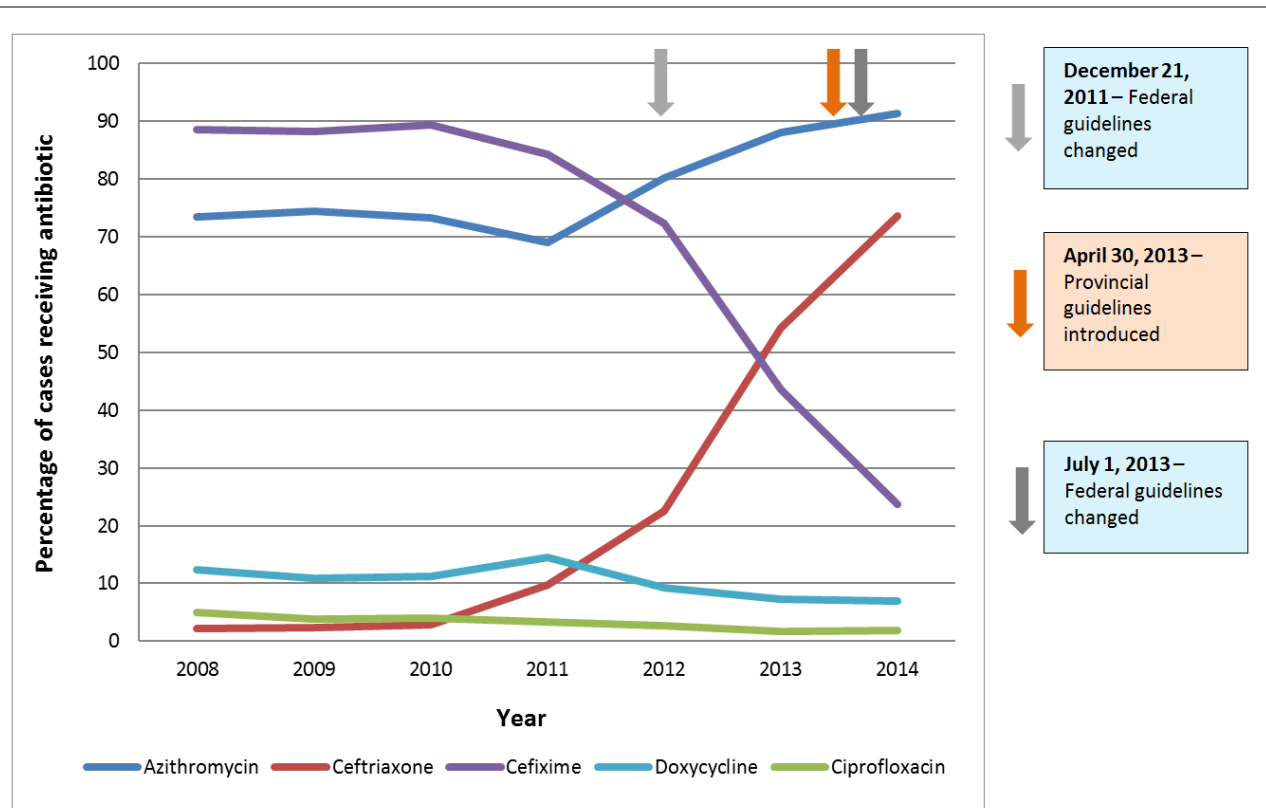
Table 2: Gonorrhea case information and treatment data availability: Ontario, 2008-14

Gonorrhea cases and treatment data	2008	2009	2010	2011	2012	2013	2014	Total
Cases	3,865	3,549	3,969	4,206	4,099	4,542	5,838	30,068
Cases (age ≥ 9)	3,864	3,546	3,969	4,206	4,097	4,542	5,831	30,055
Cases with treatment data (age ≥ 9)	3,688	3,267	3,656	3,949	3,907	4,346	5,677	28,490
Cases without treatment data (age ≥ 9)	176	279	313	257	190	196	154	1,565
Percentage with treatment info (age ≥ 9)	95.4%	92.1%	92.1%	93.9%	95.4%	95.7%	97.4%	94.8%

Use of individual antimicrobial agents over time

From 2010 to 2014, the percentage of cases receiving cefixime decreased from 89.4% (3,268/3,656) to 23.8% (1,349/5,677). The decline in treatment of gonorrhea cases with cefixime began in 2011, and accelerated in 2013 (Figure 2). Conversely, the percentage of cases receiving ceftriaxone increased from 2.8% (103/3,656) in 2010 to 73.5% (4,174/5,677) in 2014. This increase began in 2011, and accelerated in 2013. The percentage of cases receiving azithromycin increased from 69.0% (2,724/3,949) in 2011 to 91.3% (5,183/5,677) in 2014. From 2008 to 2014, some gonorrhea cases in Ontario continued to receive ciprofloxacin (from 1.7% to 5.0%) or doxycycline (from 7.0% to 14.6%) (Figure 2).

Figure 2: Antimicrobials received by gonorrhea cases: Ontario, 2008-14*



*Cases treated with multiple antimicrobials are reflected in the percentages calculated for each of those antibiotics.

Changes to treatment guidelines' first line recommendations:

- Federal 2011 – dose for cefixime changed from 400 mg to 800 mg; 250 mg ceftriaxone added and was the only recommended first line treatment for MSM
- Provincial 2013 – 250 mg ceftriaxone and 1 g azithromycin was the only recommended first line treatment
- Federal 2013 – 250 mg ceftriaxone and 1 g azithromycin or 800 mg cefixime and 1 g azithromycin for uncomplicated anogenital infections in persons who do not identify as MSM

Receipt of first line treatment over time

Following a change in federal first line treatment recommendations in December 2011, the percentage of cases receiving first line treatment declined from 89.3% in 2010 to 46.7% in 2012. Following the release of the Ontario guidelines on April 30, 2013, 47.9% of cases received the provincial recommendations for first line treatment in the remainder of 2013. In 2014, the percentage of cases receiving the Ontario recommendations for first line treatment increased to 58.1% of cases (Figure 3, Table 3).

Figure 3: Percentage of gonorrhea cases over 9 years of age receiving recommended federal and provincial first line treatment by year: Ontario, 2008-14

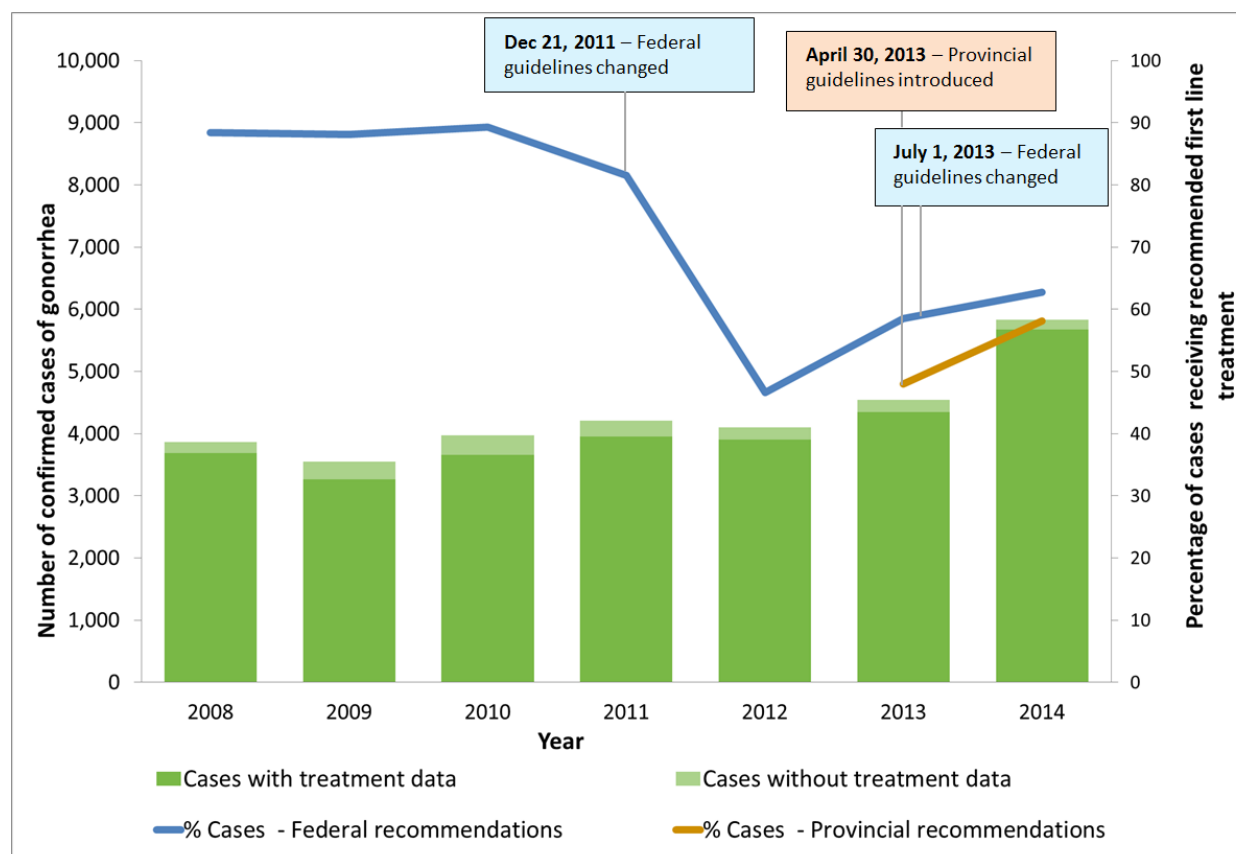


Table 3: Number and percentage of gonorrhea cases receiving recommended federal and provincial first line treatment by year: Ontario, 2008-14

Federal Guidelines

Confirmed cases (age ≥ 9)	2008	2009	2010	2011	2012	2013	2014
With treatment information	3,688	3,267	3,656	3,949	3,907	4,346	5,677
Receiving recommended first line treatment	3,262	2,879	3,266	3,220	1,823	2,545	3,561
Percent receiving first line treatment	88.4%	88.1%	89.3%	81.5%	46.7%	58.6%	62.7%

Provincial Guidelines

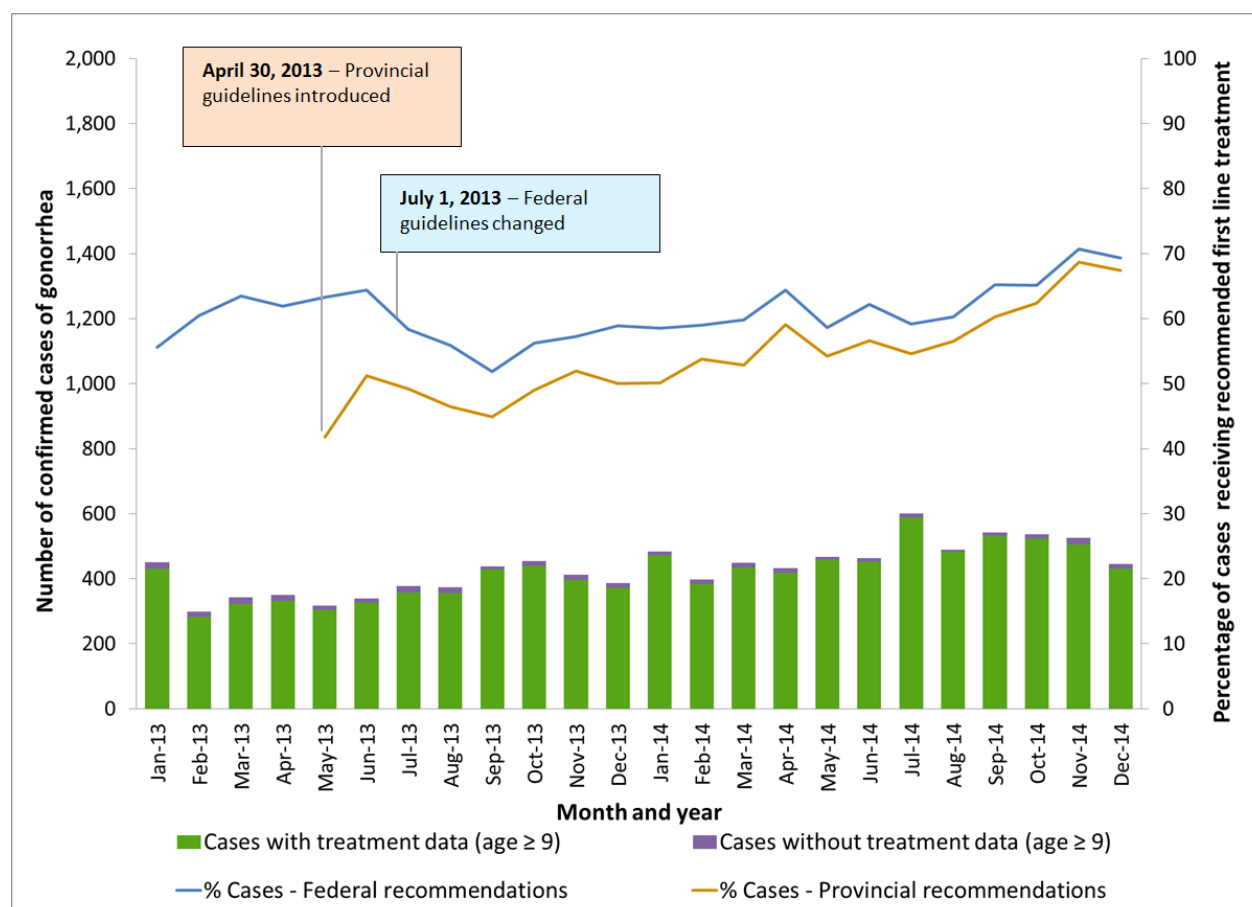
Confirmed cases (age ≥ 9)	2008	2009	2010	2011	2012	2013	2014
With treatment information						3,037*	5,677
Receiving recommended first line treatment						1,456	3,301
Percent receiving first line treatment						47.9%	58.1%

*From April 30, 2013 – December 31, 2013

Monthly increases in the percentage of cases receiving first line treatment according to both the provincial and federal guidelines were observed in 2013 and 2014. In the first month following the release of the provincial guidelines on April 30, 2013 (May 2013), 41.8% (127/304) of cases received recommended provincial first line treatment. The percentage of cases that received recommended provincial first line treatment increased over time. By December 2014, close to 70% (67.4%; 290/430 cases) of cases occurring in that month were receiving the provincially recommended first line treatment (Figure 4).

This compares to 58.4% (209/358) of cases in July 2013 receiving recommended federal first line treatment in the first month after the federal guidelines were updated. Following the July 2013 federal guidelines' change, a transient decline in the percentage of cases receiving the federally recommended first line treatment was observed from July to September 2013. However, rates of appropriate treatment increase after that time such that by December 2014, close to 70% (69.3%; 298/430 cases) of cases occurring in that month were receiving the federally recommended first line treatment (Figure 4).

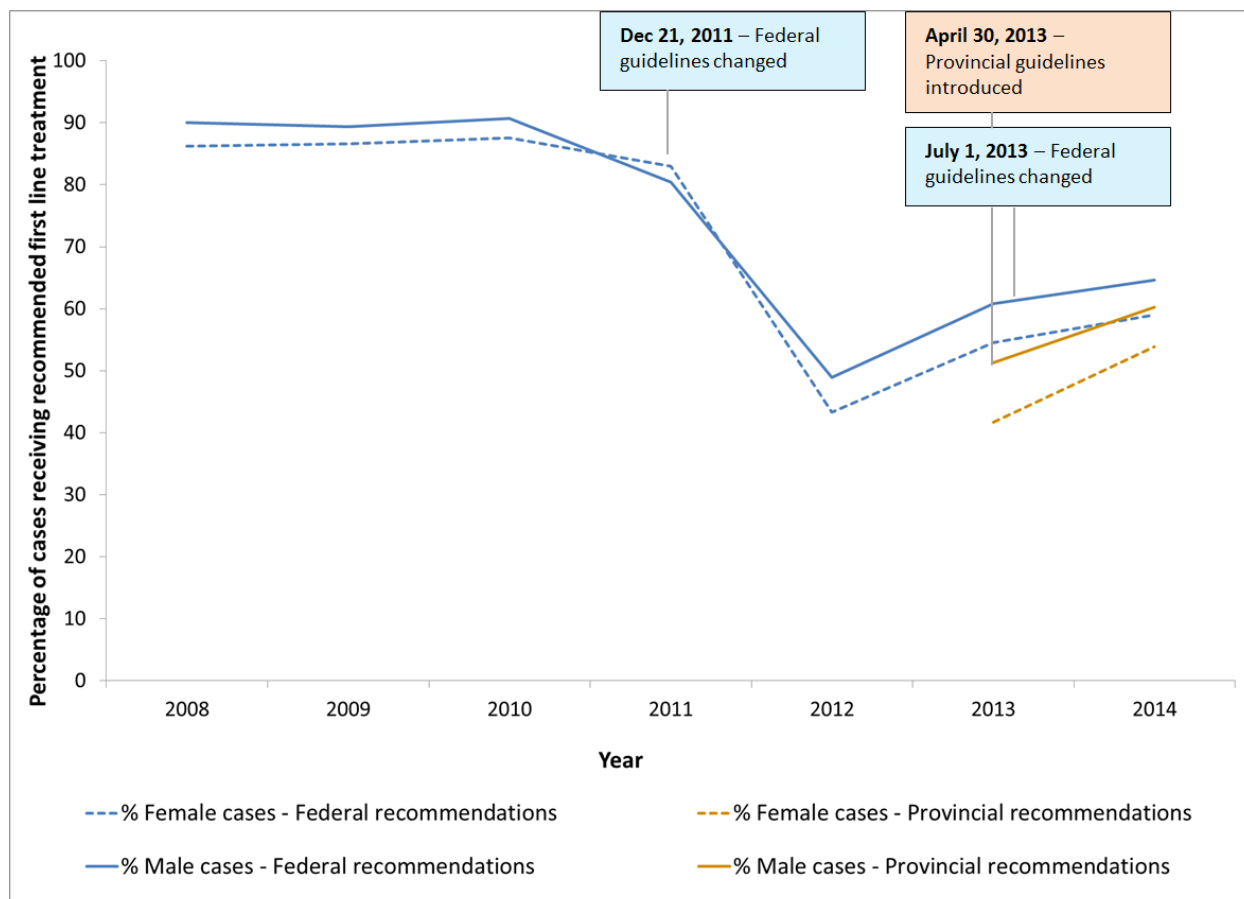
Figure 4: Percentage of gonorrhea cases receiving recommended federal and provincial first line treatment by month: Ontario, 2013-14



Receipt of first line treatment by sex

A higher percentage of male cases (57.2% [3,261/5,701]) than female cases (49.6% [1,488/3,003]) received the recommended provincial first line treatment from April 30, 2013 to December 31, 2014. Similarly, for most years from 2008 to 2014, a higher percentage of male cases than female cases received the first line treatment according to federal guidelines (Figure 5). A similar trend was seen by month (data not shown).

Figure 5: Percentage of gonorrhea cases over 9 years of age receiving recommended federal and provincial first line treatment by year and gender: Ontario, 2008-14



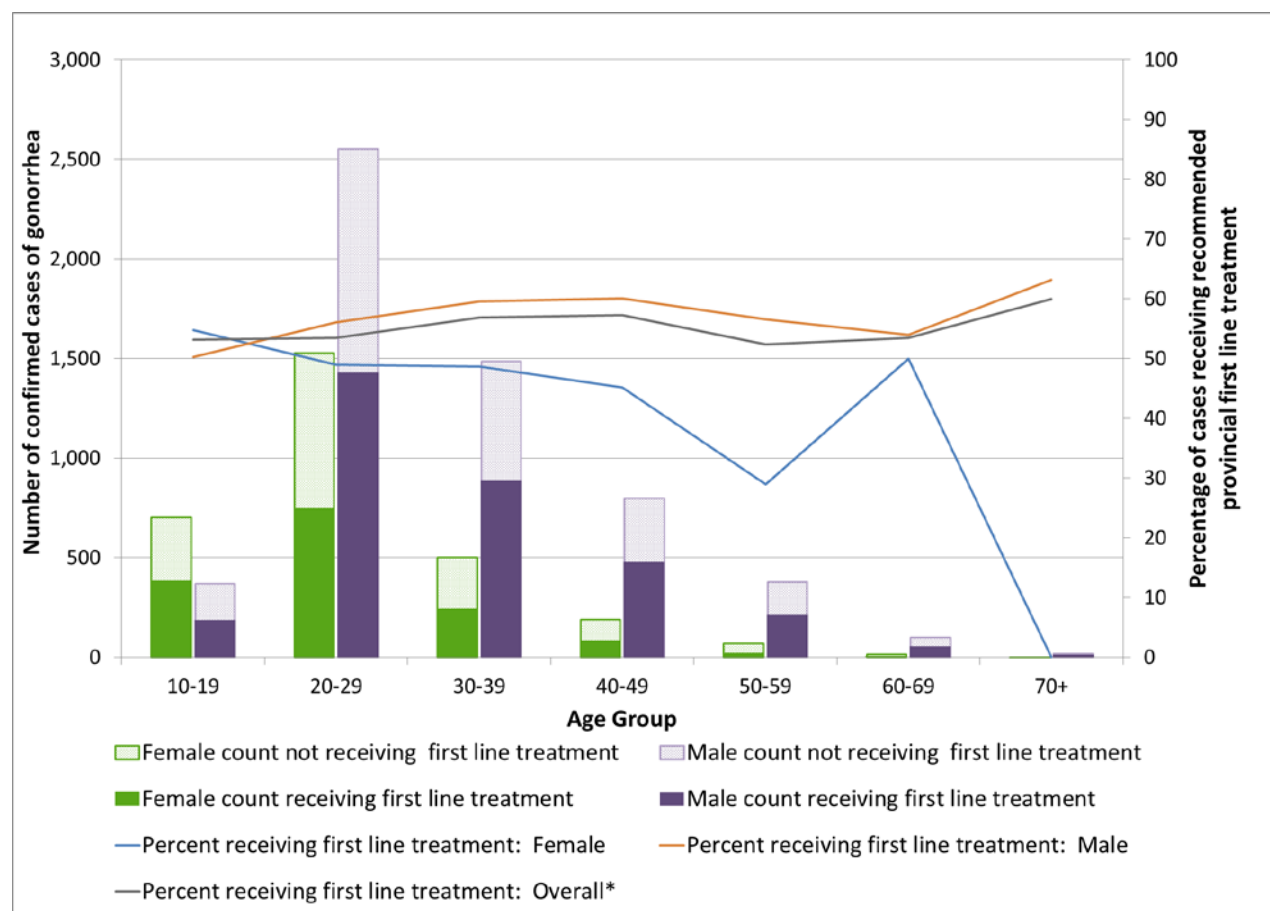
Receipt of first line treatment by age group and sex

In general, age did not appear to impact whether individuals received first line treatment. On average, cases receiving recommended provincial first line treatment were 30.6 years of age, compared to cases not receiving the first line treatment at 30.2 years of age. For males, the mean age was 32.8 year for those receiving first line treatment, compared to 32.1 years for those who did not. For female cases, the mean ages were 25.8 and 27.2 years for those receiving and not receiving recommended provincial first line treatment, respectively.

There were more male cases than female cases reported overall, and for every age group other than the 10-19 year-old age group. With the exception of 10-19 year-olds, a higher percentage of male cases than female cases received the recommended provincial first line treatment. The difference between the percentage of male and female cases receiving first line treatment grew with increasing age in those less than 60, and was most pronounced in the 40-49 and 50-59 age groups (

Figure 6).

Figure 6: Cases of gonorrhea by receipt of recommended provincial first line treatment by age group and gender: Ontario, April 30, 2013 - December 31, 2014



*Includes cases that did not have male or female gender specified

Receipt of first line provincial treatment overall and by PHU

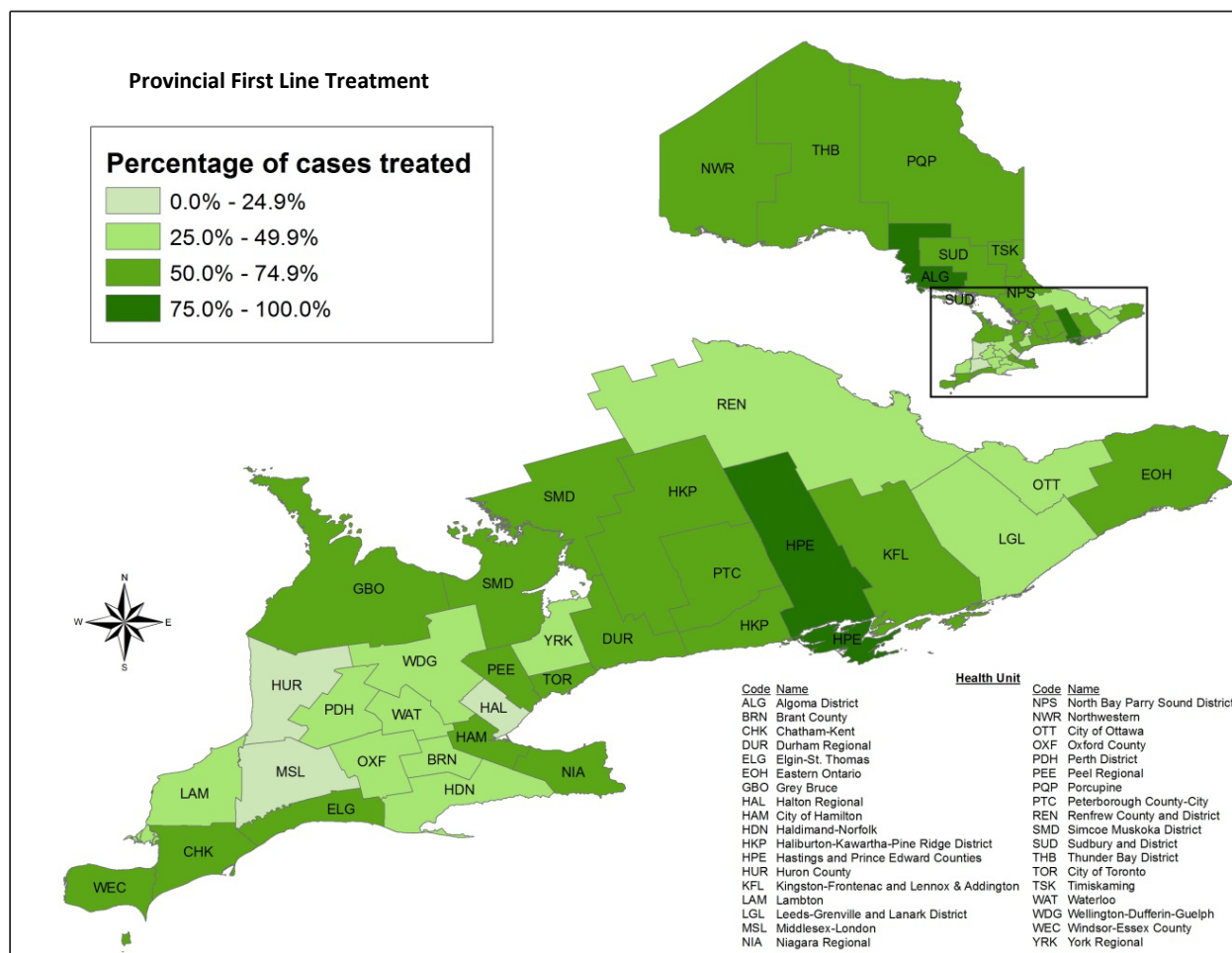
Among confirmed gonorrhea cases in Ontario from April 30, 2013 to December 31, 2014, 54.6% received the provincial first line recommended treatment. The percentage of cases receiving recommended provincial first line treatment by PHU ranged from 10.6% to 81.1%, with a median of 53.1% (Figure 7, Table 4). In 14 PHUs, fewer than 50% of cases received the recommended provincial first line treatment (Figure 7, Table 4). Further, eight of nine PHUs that had fewer than 40% of cases receiving the recommended provincial first line treatment were in southwestern Ontario.

Two PHUs, Toronto Public Health and Peel Public Health, which represent approximately one third of Ontario's population,³³ represented 59.5% (5,188/8,714) of Ontario's gonorrhea cases reported from April 30, 2013 to December 31, 2014. In Toronto, 57.5% of cases and 61.5% of cases in Peel received the recommended provincial first line treatment. Table 4 summarizes case counts and percentage receiving first line treatment by PHU.

Receipt of first line federal treatment overall and by PHU

Between January 1, 2008 and July 1, 2013, 76.6% (15,645/20,421) of confirmed gonorrhea cases in Ontario received the federal first line treatment recommended at the time, compared to 60.9% of cases that received the federal first line recommended treatment after July 1, 2013. The percentage of cases receiving the recommended federal first line treatment by PHU from July 1, 2013 to December 31, 2014 ranged from 14.6% to 87.5% with a median of 59.7% (Table 4).

Figure 7: Percentage of gonorrhea cases receiving recommended provincial first line treatment by PHU: Ontario, April 30, 2013 - December 31, 2014



* Please see Appendix B for detailed iPHIS data caveats.

Table 4: Number and percentage of gonorrhea cases receiving recommended first line treatment by PHU and guideline: Ontario, April 30, 2013 - December 31, 2014

Public health unit	First Line – Provincial (April 30, 2013 – Dec. 31, 2014)				First Line – Federal (Jul. 1, 2013 – Dec. 31, 2014)			
	No	Yes	Total	% Y	No	Yes	Total	% Y
Algoma	12	51	63	81.0	9	48	57	84.2
Brant County	59	26	85	30.6	50	28	78	35.9
Chatham-Kent	6	9	15	60.0	4	6	10	60.0
City Of Hamilton	132	172	304	56.6	114	165	279	59.1
City of Ottawa	254	243	497	48.9	220	248	468	53.0
Durham Region	143	164	307	53.4	118	167	285	58.6
Eastern Ontario	25	29	54	53.7	17	31	48	64.6
Elgin-St. Thomas	6	9	15	60.0	6	9	15	60.0
Grey Bruce	11	17	28	60.7	10	18	28	64.3
Haldimand-Norfolk	22	12	34	35.3	17	14	31	45.2
Haliburton, Kawartha, Pine Ridge	15	21	36	58.3	10	22	32	68.8
Halton Region	128	34	162	21.0	103	42	145	29.0
Hastings & Prince Edward Counties	7	30	37	81.1	7	29	36	80.6
Huron County	8	1	9	11.1	6	3	9	33.3
Kingston, Frontenac and Lennox & Addington	34	38	72	52.8	27	41	68	60.3
Lambton County	16	6	22	27.3	14	6	20	30.0
Leeds, Grenville and Lanark District	12	10	22	45.5	9	11	20	55.0
Middlesex-London	135	16	151	10.6	123	21	144	14.6
Niagara Region	83	134	217	61.8	76	129	205	62.9
North Bay Parry Sound District	11	14	25	56.0	7	16	23	69.6
Northwestern	9	9	18	50.0	9	9	18	50.0
Oxford County	14	5	19	26.3	10	9	19	47.4
Peel Region	389	621	1,010	61.5	293	646	939	68.8
Perth District	11	9	20	45.0	10	10	20	50.0
Peterborough County-City	12	20	32	62.5	11	20	31	64.5
Porcupine	4	4	8	50.0	2	5	7	71.4
Renfrew County and District	9	4	13	30.8	7	6	13	46.2
Simcoe Muskoka District	79	84	163	51.5	62	92	154	59.7

Public health unit	No	Yes	Total	% Y	No	Yes	Total	% Y
Sudbury & District	17	48	65	73.8	15	48	63	76.2
Thunder Bay District	21	33	54	61.1	21	31	52	59.6
Timiskaming	3	5	8	62.5	1	7	8	87.5
Toronto	1,776	2,402	4,178	57.5	1,336	2,502	3,838	65.2
Waterloo Region	183	168	351	47.9	165	163	328	49.7
Wellington-Dufferin-Guelph	48	31	79	39.2	43	32	75	42.7
Windsor-Essex County	42	60	102	58.8	30	54	84	64.3
York Region	221	218	439	49.7	196	223	419	53.2
Total	3,957	4,757	8,714	54.6	3,158	4,911	8,069	60.9

Receipt of first line treatment by STI risk factors, including among MSM

Of the 8,714 cases with treatment data reported after the release of the provincial guidelines, 86.6% (7,547) of these cases also had risk factor data reported. The most common risk factors were lack of condom use (75.0%; 5664/7547), and sex with the opposite sex (50.4%; 3801/7547). Among male cases reporting risk factors, 42.8% (2148/5020) identified as MSM. The highest percentage of cases receiving recommended first line provincial treatment was observed among cases that identified as MSM at 73.7%. Of cases reporting sex with opposite sex, 52.0% received first line provincial treatment (Table 5).

Table 5: Percentage of cases of gonorrhea receiving first line provincial treatment among cases by reported risk factors: Ontario April 30, 2013 – December 31, 2014*

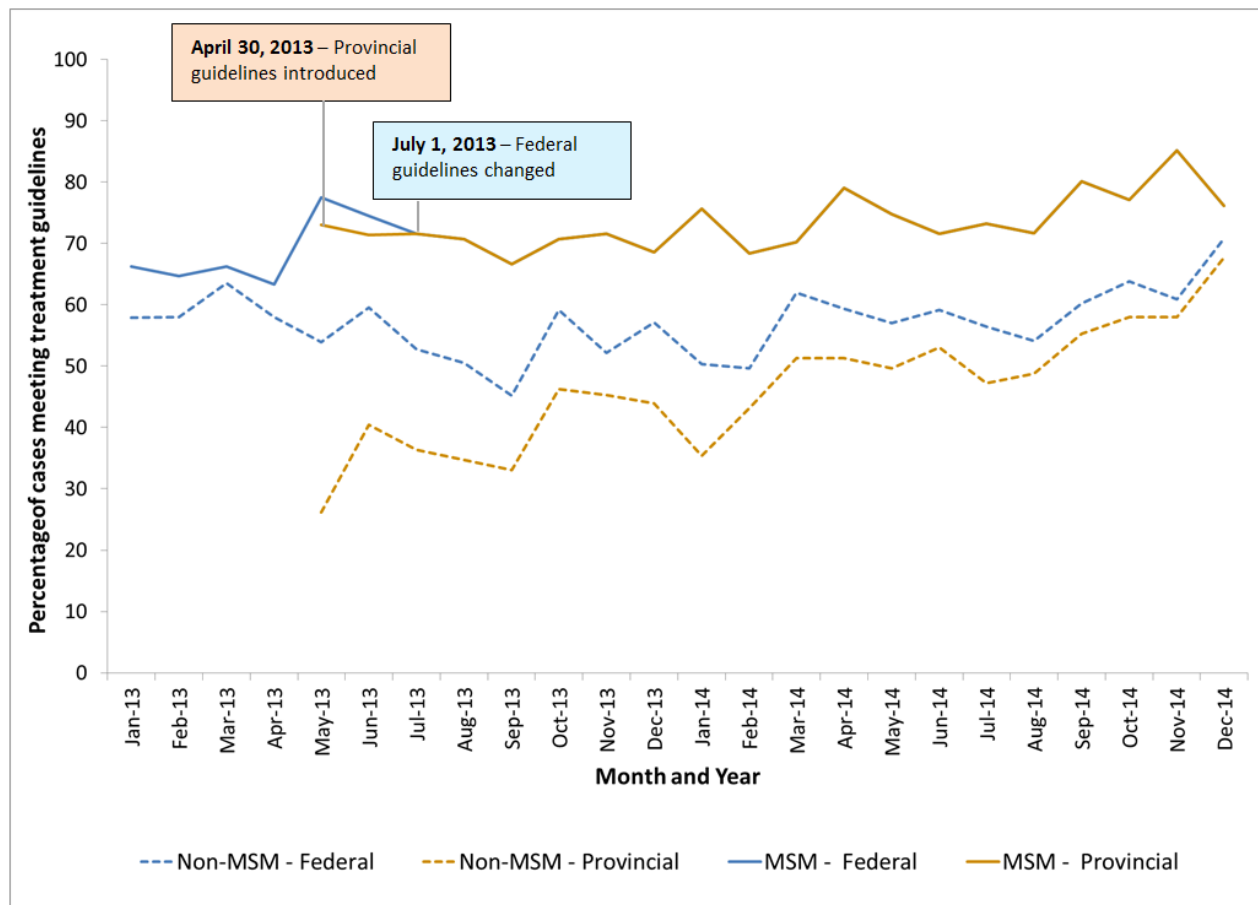
Risk factor	Number (%) of cases receiving first line provincial treatment	Total
MSM**	1,584 (73.7%)	2,148
Multiple sex contacts in the last six months	1,103 (62.2%)	1,773
No condom used	3,302 (58.3%)	5,664
Anonymous Sex	355 (56.2%)	632
New contact in the past two months	867 (52.5%)	1,650
Sex with opposite sex	1,975 (52.0%)	3,801

*Cases may have more than one risk factors selected and therefore may be reflected in more than one row in the table

**Male cases only.

Among male cases, the percentage of MSM cases receiving the recommended provincial first line treatment was over 70% in all but three months (range: 66.7% - 85.2%), from May 2013 to December 2014 (Figure 98). Over this time period, a lower percentage of non-MSM male cases (range: 26.1% - 67.7%) and female cases (range: 31.8% - 67.1%) received the first line provincial treatment.

Figure 8: Percentage of MSM and non-MSM male cases of gonorrhea receiving recommended provincial or federal first line treatment by month: Ontario 2013-14*



*After the federal guideline changed in 2013 the federal and provincial guideline for MSM is the same and represented by MSM-Provincial

Receipt of first line treatment by reason for testing

Of the 28,490 cases of gonorrhea with treatment information between 2008 and 2014, 87.6% (24,963) had information reported on reason for testing. The majority of these cases (63.8%; 15,924/24,963) were tested due to the presence of symptoms. Among males, 76.6% (11,742/15,325) of cases were tested due to the presence of symptoms compared with 43.3% (4,164/9,614) of females. Among females, 34.2% (4,604/9,614) of cases were identified through routine screening, compared with 8.6% (1,317/15,325) among males. We noted a decline in the percentage of cases identified through routine screening, from 20.7% (732/3,534) in 2012 to 15.3% (786/5,126) in 2014.

Individuals tested for gonorrhea through contact tracing efforts were the most likely to be treated according to the first line provincial treatment (59.0%). Additionally, over half of cases identified through routine screening (57.6%) or the presence of symptoms (54.6%) were treated according to the first line provincial treatment. Female cases identified through prenatal screening were the least likely of the various reasons for testing to receive the first line provincial treatment, with 48.9% receiving the first line provincial treatment (Table 6).

Table 6: Cases of gonorrhea by reason for testing and treatment status: Ontario April 30, 2013 – December 31, 2014*

Reason for testing	Number of cases receiving first line provincial treatment	Number of cases not receiving first line provincial treatment	Total	Percentage of cases receiving first line provincial treatment
Symptoms	2,845	2,367	5,212	54.6
Contact tracing	679	472	1,151	59.0
Prenatal screening**	43	45	88	48.9
Routine screening	727	536	1,263	57.6

*Cases may have more than one reason for testing selected and therefore may be reflected in more than one row in the table

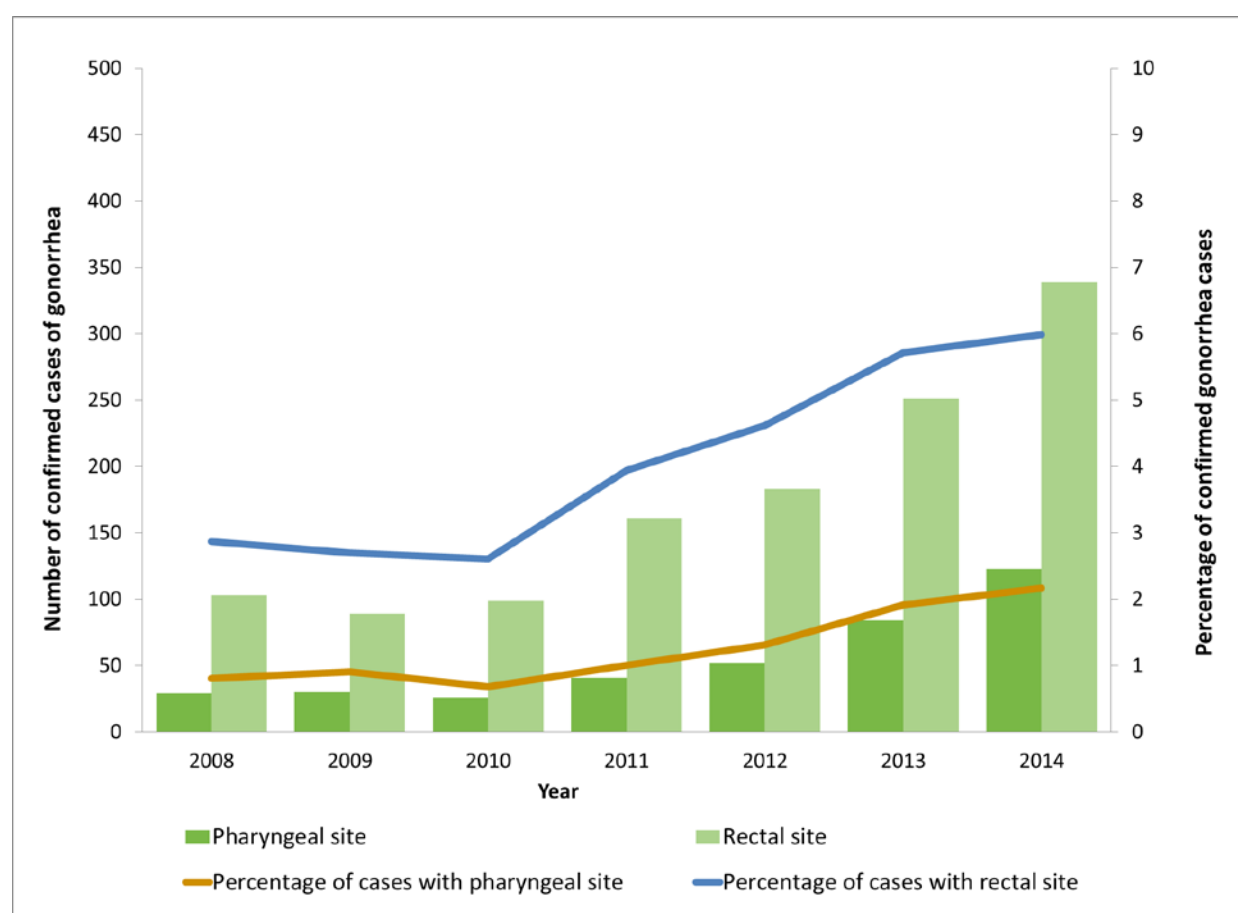
**Female cases only.

Analysis of laboratory data reported for cases in iPHIS

Laboratory data recorded in iPHIS for cases were examined to determine whether cases were being tested according to the provincial guidelines (culture testing is recommended for individuals presenting with symptoms associated with gonorrhea). There were 8,721 cases of gonorrhea with test data occurring after the release of the gonorrhea guidelines on April 30, 2013. Of the cases with laboratory test data available in iPHIS, only 17.8% (915/5,141) of cases tested because of symptoms had an appropriate sample tested via culture recorded in iPHIS.

From 2008 to 2014, 95.8% (28,781/30,055) of gonorrhea cases had laboratory data recorded in iPHIS, with the majority of cases having laboratory data from genital specimens. However, the number and proportion of gonorrhea cases associated with pharyngeal and rectal infections increased over time (Figure 9). Overall between 2008 and 2014 1.3% (385/28,781) of gonorrhea cases were associated with pharyngeal infections and 4.3% (1,225/28,781) of cases were associated with rectal infections (Figure 9). In 2008, 0.8% (29/3,585) of gonorrhea cases was associated with pharyngeal infections compared to 2.2% (123/5,666) in 2014. In 2008, 2.9% (103/3,585) of gonorrhea cases were associated with rectal infections, compared to 6.0% (339/5,666) in 2014 (Figure 9).

Figure 9: Number and percentage of gonorrhea cases with positive tests from rectal or pharyngeal samples, as recorded in iPHIS: Ontario, 2008-14



Discussion

Evolving gonorrhea treatment patterns in the context of guideline changes

Our findings show changes over time in antimicrobial treatment patterns for gonorrhea cases reported in Ontario from 2008 to 2014. They highlight the temporal relationship between these treatment changes and the release of Ontario's first gonorrhea testing and treatment guidelines in 2013, as well as updates to federal guidelines in late 2011 and 2013.

Receipt of first line treatment among gonorrhea cases in Ontario peaked at 89.3% in 2010, when federal guidelines recommended 400 mg of oral cefixime as the first line monotherapy. In 2011, before any guideline changes, we started to observe a reduction in receipt of cefixime and an increase in receipt of ceftriaxone and azithromycin among cases of gonorrhea reported in Ontario. In 2012, following a federal guideline shift toward monotherapy with ceftriaxone or higher dose cefixime, receipt of first line treatment declined to 46.7% in Ontario cases.

The new 2013 Ontario gonorrhea testing and treatment guidelines and the 2013 update to the federal guidelines shifted to dual therapy. Both recommend ceftriaxone plus azithromycin as a first line treatment option. Notably, the federal guidelines also identify 800 mg of cefixime plus azithromycin as a first line option for uncomplicated anogenital infections that do not occur in MSM. Following these guideline changes, we observed a more rapid increase in the percentage of Ontario gonorrhea cases receiving ceftriaxone, and a more rapid decline in percentage of cases receiving cefixime. In 2014, 23.8% of all cases received cefixime, 73.5% of cases received ceftriaxone, and 91.3% of cases received azithromycin.

Overall in 2014, 58.1% of cases of gonorrhea received treatment that met the provincial first line recommendation of 250 mg ceftriaxone plus 1 g azithromycin. By comparison, 62.7% of Ontario gonorrhea cases received treatment that met the federal guidelines first line recommendation in 2014. Our findings show that the receipt of first line treatment associated with the current Ontario and federal guidelines is much lower than with past guidelines. However, the results of our analysis by month also demonstrate a consistent increase over time in the percentage of cases receiving provincial and federal first line treatment in 2013 and 2014. By December 2014, 67.4% of gonorrhea cases received treatment according to the provincial guidelines, and 69.3% received first line treatment as per the federal guidelines.

The reasons for the marked reduction in receipt of first line gonorrhea treatment after 2011 compared to the pre-2011 era in Ontario are likely multifactorial. Historically, gonorrhea had been successfully treated with monotherapy with an oral cephalosporin. Challenges related to promoting awareness of multiple changes to clinical guidelines between 2011 and 2013, and the shift to first line treatment with dual therapy and to recommended use of an injectable drug for empiric treatment were likely

contributing factors. Other potential reasons for not receiving first line treatment may include specific drug allergies or medical contraindications. Exploring this was beyond the scope of this analysis. Factors affecting provider and patient acceptability of provincial first line treatment (including delivering or receiving ceftriaxone injection) and potential health systems barriers and facilitators merit further consideration.^{34,35}

The difference in the receipt of first line treatment between the provincial and federal guidelines in 2014 (e.g., 58.1% versus 62.7%) is not surprising. This difference is due to the 260 cases of uncomplicated anogenital gonorrhea infections in non-MSM in 2014 who received the additional first line option recommended in the federal guidelines but not in the provincial guidelines (dual therapy with oral cefixime and azithromycin).

Potential reasons for the gap between the percentage of cases who received each specific antimicrobial drug included in first line recommendations (as shown in Figure 2) and the percentage who received treatment as per provincial and/or federal guidelines (as shown in Figure 3) include:

- receipt of only one of the recommended antimicrobials;
- receipt of a lower dose than recommended;
- receipt of the recommended antimicrobials more than a day apart (i.e., not concurrently); or,
- variation in data entry, including data entry errors.

Of note, prior to the release of the provincial guidelines and throughout the study period, some gonorrhea cases were receiving azithromycin or doxycycline; this may reflect the recommendation in the federal guidelines for concurrent empiric treatment of chlamydia with those antimicrobials for those with gonorrhea.

Variation in treatment patterns among male and female cases

Over time, receipt of first line provincial treatment increased among MSM, non-MSM and females. The percentage of MSM cases who received the first line provincial treatment ranged from 66.7% to 85.2% between May 2013 and December 2014. This was consistently higher than the percentage of non-MSM male cases receiving the first line provincial treatment (range: 26.1% - 67.7%), and females receiving first line provincial treatment (range: 31.8% - 67.1%) over the same time period. If health care providers are following the federal guidelines, which provide a second preferred option for selected non-MSM patients, this may contribute to the lower percentage of cases among non-MSM and females receiving the first line provincial treatment. As well, health care providers treating MSM may be more aware of the recommended use of ceftriaxone for treating gonorrhea in MSM, because it has been recommended in the federal guidelines since 2011.

Interestingly, the percentage of female cases receiving the first line provincial treatment from April 30, 2013 to December 31, 2014 declines in older age groups (i.e., 40-49 and 50-59 years). This merits further exploration, including but not limited to understanding whether awareness among health care providers serving older females may be a contributing factor.

Variation in testing patterns in male and female gonorrhea cases

A higher percentage of male cases was tested due to symptoms while more female cases were tested as part of routine screening. As males are more likely to experience symptoms associated with gonorrhea infections, and females are more likely to have screening as part of cervical cancer prevention, this observed discrepancy between males and females is expected.

Our analysis also identified a decline in the percentage of gonorrhea cases tested via routine screening after the 2012 release of updated Ontario cervical cancer screening guidelines, which recommend Papanicolaou (Pap) testing less frequently and initiating testing at an older age.³⁶ Of note, over this time period, a study in Toronto, Ontario compared the rate of STI screening in females aged 19 to 25 years at one academic family practice unit, before and after the release of the 2012 cervical cancer screening guidelines.³⁷ After the release of the cervical screening guidelines, a 50% decrease in STI screening was observed.³⁷ Additional investigation into the reason individuals were tested and the treatment they received is warranted, including the potential for a decrease in opportunistic gonorrhea screening in the context of less frequent Pap testing.

Variation in treatment patterns by PHU

Considerable variation by PHU was observed, with some geographic clustering of lower receipt of provincial first line treatment in southwestern Ontario. Some of this variation may reflect variation in data entry between different PHUs (e.g., with respect to antimicrobials prescribed, dose sizes given or timing of receipt of antimicrobials). Of note, PHUs may have updated their data in iPHIS after extraction for this analysis took place and any subsequent changes (e.g., due to data cleaning and validation) would not be captured here. However, some of the variation between PHUs may also reflect differing prescribing practices among health care providers. To better understand this finding, this geographical and regional variation merits further exploration.

Uptake of recent clinical practice guidelines in other jurisdictions

Our findings are generally consistent with emerging evidence from Canada and other jurisdictions that have introduced similar changes to gonorrhea treatment recommendations.³⁰⁻³² A recent cross-sectional study³⁸ asked a convenience sample of 625 physicians from across Canada about gonorrhea treatment prescribing practices. Of physician respondents, 30% indicated that they would prescribe their patients monotherapy and 30 to 35% did not provide any treatment information in response to questions based on several clinical scenarios. The findings suggest that suboptimal knowledge, awareness and/or uptake of recommended dual therapy for gonorrhea among Canadian physicians may be influencing gonorrhea treatment prescribing.

Over a six month period in 2015, 65% of gonorrhea cases in Auckland, New Zealand received a treatment that was considered guideline compliant (which includes receipt of ceftriaxone and azithromycin, ceftriaxone and doxycycline, azithromycin alone, ciprofloxacin and azithromycin), with 57.6% receiving a combination therapy of ceftriaxone and azithromycin.³¹ Although generalizability is limited due to cases residing in only one New Zealand city, the overall finding with respect to ceftriaxone and azithromycin dual therapy was consistent with the Ontario experience. Further, in the Auckland study, 89% of cases tested at sexual health services received the recommended treatment, compared with 56% of cases seen in hospital and 52% of cases seen by general practitioners and other community practitioners.³⁹

As of 2012, the US Centers for Disease Control and Prevention (CDC) updated their gonorrhea treatment recommendations to include 250 mg ceftriaxone IM, as well as dual therapy. Between 2011 and 2013, a retrospective cohort study examined adherence to the CDC recommendations in gonorrhea cases at one US academic urban health care institution with multiple clinical settings.⁴⁰ Adherence was 76% with the 2010 guidelines and 88% with the 2012 guidelines overall. In 2012, specialty clinics provided 94% of their gonorrhea cases with treatment according to the CDC recommendation, compared to 78% at non-specialty clinics. It was beyond the scope of our analysis to examine receipt of first line gonorrhea treatment in Ontario by provider type or health care setting type; however, future analyses in the Ontario population could include consideration of health care provider and setting characteristics to help guide efforts to promote provincial treatment guidelines.

In a US pediatric emergency setting, researchers used a cross sectional, anonymous, scenario-based internet survey to determine physicians' knowledge and practice compared to the recommended gonorrhea screening and testing recommendations.⁴¹ In this study, 85.6% of 231 respondents selected a screening approach for asymptomatic patients consistent with the recommendations. For symptomatic patients, only 37.4% of physicians indicated the appropriate testing approach.⁴¹ In comparison to our Ontario analysis, only 17.8% (915/5141) of those tested because of symptoms reported having a sample tested via culture (as recommended in the Ontario guidelines) recorded in iPHIS.

Potential limitations

Several potential limitations should be considered when interpreting the findings of this analysis. The routine surveillance data from iPHIS used in these analyses have a number of limitations including under-reporting, as well as data completion and quality issues (see [Appendix B](#) for a detailed list of iPHIS data caveats). Although iPHIS user guides exist to promote consistent and complete data entry, a key limitation with respect to these reportable disease data is the potential introduction of reporting biases due to inconsistent or incomplete data entry at the local level.

Our analysis did not examine patient adherence to treatment recommendations. In addition, we did not assess receipt of second line treatment recommendations. Patients receiving second line treatments and a test of cure would meet provincial treatment recommendations.⁵ However, negative results are not typically received by PHUs nor recorded in iPHIS, so assessing test of cure was not possible. In addition, our analysis examined the receipt of first line treatment regardless of whether other

antimicrobials were provided prior to the recommended first line treatment. The result is that the percentage of cases receiving recommended first line treatment includes cases who were treated with other antimicrobials prior to the recommended first line treatment. Future analyses may benefit from comparing cases that received only recommended first line treatment versus cases receiving another treatment first.

Our analysis of key outcomes in relation to STI risk factors was limited by gaps in reported risk factor data in iPHIS, as well as the introduction of a new iPHIS user guide for risk factors in 2011. Given the limitations of data in iPHIS on health care setting, provider type, and laboratory susceptibility testing, an examination of treatment provision in relation to these factors was beyond the scope of this analysis. However, over 94.8% of gonorrhea cases had treatment data reported in iPHIS, suggesting that our treatment data are representative of gonorrhea cases in Ontario.

Finally, although we observed temporal relationships between gonorrhea treatment patterns in Ontario cases and changing testing and treatment guidelines, the ecological design of our analysis precludes inferences about causality. Despite these potential limitations, our findings reflect the most representative population-based data on gonorrhea cases and treatment in Ontario.

Conclusions

The percentage of cases receiving recommended provincial first line treatment following the 2013 Ontario guidelines and updates to federal guidelines improved over time from 2013 to 2014, but remained suboptimal. Reasons for this are likely multifactorial and merit further exploration. Moving from an oral monotherapy to a dual therapy that includes an injectable antimicrobial may have reduced acceptability for patients and/or providers. Ongoing efforts to promote use of the Ontario guidelines should consider how to optimally support health care providers, particularly in PHUs with lower rates of first line treatment provision.

Future analyses could explore linkages with laboratory data to examine treatment of gonorrhea cases by antimicrobial susceptibilities (e.g., MICs), or with health administrative data to examine treatment by type of health care provider or clinical setting. Future research and evaluation could also explore the knowledge, attitudes and behaviours of Ontario patients and health care providers in relation to dual therapy with an injectable antimicrobial. Finally, consideration could be given to developing an ongoing sentinel surveillance system to monitor *N. gonorrhoeae* susceptibility and treatment patterns, to ensure that timely AMR updates are available to Ontario PHU staff, health care providers and policy makers.

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Appendix A: Provincial and Canadian treatment guidelines

The treatment guidelines for PHAC and Ontario are available online:

- [2008-2010 Canadian Guidelines on Sexually Transmitted Infections](#)
- [2011 Public Health Agency of Canada Notice](#)
- [2013 Public Health Agency of Canada Summary](#)
- [2013 Ontario Guidelines](#)

Appendix B: Technical notes and data caveats

There are a number of caveats with respect to the data presented in this report, these are as follows:

- **Case data:**

iPHIS is a dynamic disease reporting system which allows ongoing updates to data previously entered. As a result, data extracted from iPHIS represent **a snapshot at the time of extraction** and may differ from previous or subsequent reports.

 - The data for this report were based on information entered in the Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database as of June 22, 2015.
- **Ontario Population data:**
 - Population estimates [2008-2011], Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, Date Received: [2014/07/03].
 - Population Estimates [2012-2014], Ontario Ministry of Health and Long-Term Care, Health Analytics Branch, Date Received: [2015/11/18]
- The data only represent cases reported to public health and recorded in iPHIS. As a result, the counts are subject to **underreporting**. For example, persons with asymptomatic gonorrhea infections may not be tested and therefore would not be reported.
- Case counts were assigned to PHUs based on the PHU of residence at the time of illness onset and not necessarily the location of exposure. Cases for which the case's PHU of residence was reported as MOHLTC (to signify a case that is not a resident of Ontario) or Muskoka Parry Sound (a health unit that no longer exists) were excluded.

- Cases are classified in iPHIS according to the (MOHLTC) surveillance **case definitions**, available online as part of the Infectious Diseases Protocol (for details, please see the [provincial gonorrhea case definition](#)). Please note that the case definitions available online represent the most recent versions and cases reported in prior years may have slightly different case definitions.
- Cases in this dataset are reported based on the earliest of 'Episode Date' and 'Reported Date' to correct for potential data entry irregularities. In order to determine 'Episode date', the following hierarchy is used for iPHIS data entry depending on which date is available: Onset Date > Specimen Collection Date > Lab Test Date > Reported Date.
- Cases for which the 'Encounter Status' was reported as ENTERED IN ERROR, DUPLICATE-DO NOT USE, or any variation on these values were excluded.
- Risk factors were based on information reported in iPHIS and may not be fully captured for every case.
 - Cases may have multiple risk factors reported, no hierarchy was applied to these data, and each risk factor was kept for the analyses.
 - Cases were determined to be MSM if the risk factor sex with same sex was selected and the gender of the cases was reported as male.
- In 2011, a user guide was released to aid with the entry of risk factor data into iPHIS. Some risk factor variables were added at this time, such as anonymous sex. These changes make comparisons of risk factor data before and after the release of the guide difficult.

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