

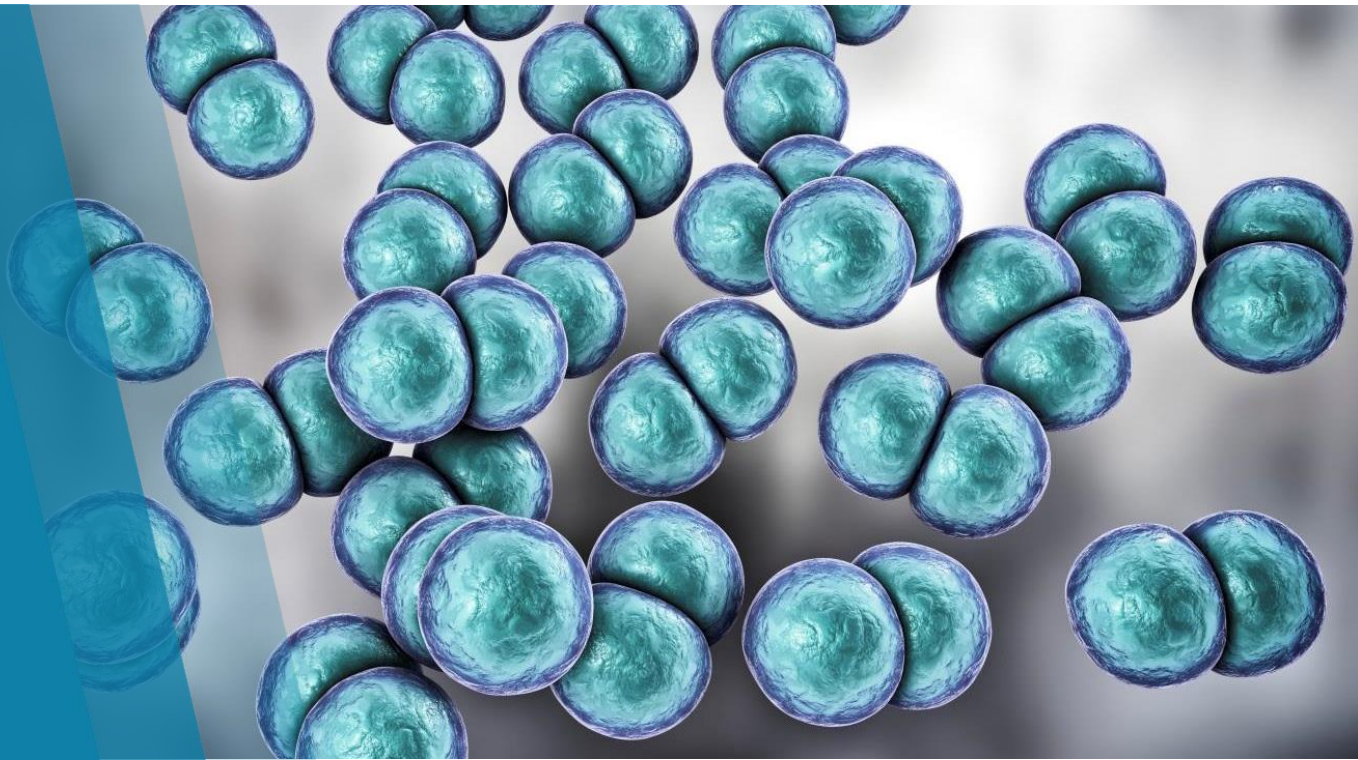
Notice

The Ontario Gonorrhoea Testing and Treatment Guidelines, 2nd edition is currently under review based on new scientific and technical information that has become available.

For updated testing recommendations regarding test of cure and use of culture, please refer to Public Health Ontario's [Chlamydia Trachomatis and Neisseria Gonorrhoeae - Nucleic Acid Amplification Testing](#) and [Test Information Pages for Gonorrhoea](#).

You can also refer to [Canadian Guidelines for Sexually Transmitted Infections](#).

Ontario Gonorrhoea Testing and Treatment Guide, 2nd Edition



Guide
November 2018

Public Health Ontario

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Disclaimer

This document was developed by Public Health Ontario (PHO). PHO provides scientific and technical advice to Ontario's government, public health organizations and health care providers. PHO's work is guided by the current best available evidence at the time of publication.

This document is intended to assist health care providers in clinical decision-making by describing a range of generally acceptable approaches for diagnosis and management of gonorrhoea cases. This document should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment regarding care of a particular patient must be made by the health care provider in light of the individual circumstances presented by the patient. The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

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Abbreviations

BASHH	British Association for Sexual Health and HIV
CDC	United States Centers for Disease Control and Prevention
CGSTI	Canadian Guidelines on Sexually Transmitted Infections
CLSI	Clinical Laboratories Standards Institute
HIV	Human Immunodeficiency Virus
iPHIS	Integrated Public Health Information System
IUSTI	International Union Against Sexually Transmitted Infections
MSM	Cisgender and transgender men who have sex with men, including males who identify as gay, bisexual, queer, two-spirit or other men who have sex with men ¹
MIC	Minimum inhibitory concentration
MOHLTC	Ministry of Health and Long-Term Care
NAAT	Nucleic acid amplification testing
NML	National Microbiology Laboratory
PHAC	Public Health Agency of Canada
PHO	Public Health Ontario
PID	Pelvic inflammatory disease
STBBIs	Sexually transmitted and blood-borne infections
STI	Sexually transmitted infections
WHO	World Health Organization

Summary of Recommendations

Testing Principles

When to Test

- Knowing an individual's sexual history is critical to informing testing decisions. Guidance on how to facilitate safe, respectful discussions about sexual health and reduce stigma is available from the [Canadian Public Health Association](#).
- All sexually active individuals who have signs and symptoms of gonorrhoea should be tested at the urogenital sites where they report unprotected sexual exposure and signs/symptoms.
- Offer screening to asymptomatic sexually active individuals with [risk factors](#) for gonorrhoea.
- Most rectal and pharyngeal gonococcal infections are asymptomatic. Testing at these sites is currently recommended among certain high risk groups when receptive sexual exposure has occurred. These groups are:
 - Men who have sex with men (MSM)
 - People who engage in sex work and their sexual contacts
 - Known sexual contacts of those infected with gonorrhoea
- Since a high proportion of individuals with gonorrhoea are at risk of co-infection with *Chlamydia trachomatis* (chlamydia), when testing for gonorrhoea, health care providers should concurrently test for chlamydia. Consider testing for other sexually transmitted and blood-borne infections (STBBIs), including Human Immunodeficiency Virus (HIV).

How to Test

- Nucleic acid amplification testing (NAAT):
 - NAAT is more sensitive than culture for gonorrhoea and chlamydia.
 - Urine NAAT is less sensitive than vaginal or cervical NAAT.
 - Most commercial NAAT assays test for gonorrhoea and chlamydia co-infection simultaneously with one specimen.
 - Antimicrobial susceptibility testing **cannot** be performed on NAAT specimens.

- Please contact your local laboratory to enquire if vaginal NAAT is available. As of the time of writing, Public Health Ontario offers urine, cervical and extragenital NAAT, but not vaginal NAAT.
- Culture:
 - Culture is recommended in specific clinical situations, e.g., test of cure, testing for medico-legal purposes ([see list for when culture is recommended](#)).
 - Culture can provide isolates to enable monitoring of local antimicrobial susceptibility trends.
 - Follow manufacturers' instructions for specimen collection.
 - Culture specimens should be received at the laboratory within 48 hours of collection for optimal specimen integrity; however, based on feasibility of transport, individual laboratories can decide to process delayed specimens. Public Health Ontario accepts specimens received up to 72 hours after collection.
 - Testing and screening of people who are transgender should be informed by current anatomy and sexual behaviours.

Urogenital Testing

SYMPTOMATIC INDIVIDUALS

Applies to adults and youth with symptoms compatible with gonorrhoea at urogenital sites and assumes concurrent testing for gonorrhoea and chlamydia.

Males

- If urethral discharge present:
 - **Urine NAAT (first-line)**
 - If testing by **urethral culture**, add **urine NAAT**, which will concurrently test for chlamydia, as well as provide a more sensitive test for gonorrhoea.
- If no urethral discharge:
 - **Urine NAAT**

Females, including pregnant females

- If a pelvic exam is not being conducted:
 - **Vaginal NAAT (first-line)**

- **Urine NAAT** is a second-line option because it is less sensitive than vaginal NAAT for gonorrhea.
- If a pelvic exam is being conducted:
 - **Cervical NAAT or vaginal NAAT (either is first-line)**
 - Urine NAAT is a second-line option because it is less sensitive than cervical NAAT or vaginal NAAT for gonorrhea.
 - If testing by **cervical culture**, **add any urogenital NAAT**, which will concurrently test for chlamydia, as well as provide a more sensitive test for gonorrhea.

ASYMPTOMATIC INDIVIDUALS

Screening asymptomatic patients is only recommended in individuals with [risk factors](#) for gonorrhea.

Males

- **Urine NAAT**

Females, including pregnant females

- If a pelvic exam is not being conducted:
 - **Vaginal NAAT (first-line)**
 - **Urine NAAT** is a second-line option because it is less sensitive than vaginal NAAT for gonorrhea.
- If a pelvic exam is being conducted:
 - **Cervical NAAT or vaginal NAAT (either is first-line)**
 - **Urine NAAT** is a second-line option because it is less sensitive than cervical NAAT or vaginal NAAT for gonorrhea.

Extragenital Testing

- **Rectal NAAT** and/or **pharyngeal NAAT** is recommended in the following individuals with receptive exposure at these sites, whether symptomatic or asymptomatic:
 - MSM
 - People who engage in sex work and their sexual contacts
 - Known sexual contacts of those infected with gonorrhea

- Rectal and/or pharyngeal testing in individuals who are not in the above risk groups may be considered in individual circumstances, based on clinical evaluation of symptoms, sexual behaviours and local epidemiology.
- A test of cure is recommended for laboratory-confirmed cases of pharyngeal gonorrhoea.

Treatment of Gonorrhoea

- Applies to individuals over nine years of age (including pregnant and breastfeeding females) with confirmed or suspected uncomplicated urogenital, rectal or pharyngeal gonorrhoea and their sex partners:

Recommended first line therapy: Ceftriaxone 250 mg intramuscularly (IM) plus azithromycin 1 g orally (PO) given at the same visit.

- First-line dual therapy is the strong preference due to compelling evidence of efficacy and current antimicrobial susceptibility patterns in Ontario.
- **Alternative therapeutic options** are only to be considered **if first-line therapy is not possible** and must be followed by a **test of cure**. These are:
 - Cefixime 400 mg PO plus azithromycin 1 g PO. First-line dual therapy with ceftriaxone is the strong preference because use of cefixime could potentially accelerate the development of resistance to ceftriaxone, which is the only remaining antimicrobial that is safe, well-tolerated and highly effective at all anatomic sites.
 - Gentamicin 240 mg in two separate 3mL IM injections of 40 mg/mL plus azithromycin 2 g PO. If IM is not feasible, gentamicin 240 mg intravenous (IV) infused over 30 minutes is an alternative route of administration.
 - Gemifloxacin 320 mg PO plus azithromycin 2 g PO (once available in the United States, will be accessible in Ontario through Health Canada's Special Access Program).
 - If the dual therapies listed above are not possible, azithromycin 2 g PO monotherapy may be used. This is the *least preferred option* due to reduced susceptibility of *N. gonorrhoeae* isolates to azithromycin in Ontario and evidence in support of dual therapy.
 - Please see [Treatment of Individuals with a History of Penicillin or Cephalosporin Allergy or Macrolide Allergy](#).
- Treatment of clinical failures if first-line therapy was used should include a higher dose of both ceftriaxone and azithromycin (1 g ceftriaxone IM + 2 g azithromycin PO) given at the same visit and a test of cure using culture at three to seven days post-treatment. If first-line treatment was not used initially when treatment failure is identified, first-line treatment should be used.

- Contact your [local public health unit](#) to obtain publicly-funded sexually-transmitted infection (STI) medications.
- Please refer to product monograph for potential adverse events for each medication.

Follow-Up of Gonorrhea Cases and Contacts

Reporting

- Gonorrhea is a [Disease of Public Health Significance](#) (i.e., a reportable disease) in Ontario. Positive gonorrhea laboratory test results are reported to the Medical Officer of Health of the health unit in which the case resides.
- Health care providers should **report all suspected or confirmed gonorrhea treatment failures** to the local public health unit in which the professional services were provided.
- The local public health unit should notify PHO of suspected or confirmed treatment failures as soon as possible to discuss any further public health action that may be required.

Contact Tracing

- A plan for contact tracing should be discussed. A 60-day trace back period should be used to identify sexual contacts for notification or the last sexual contact if the index gonorrhea case had no sexual contacts in the last 60 days.
- Sexual contacts are recommended to receive empiric treatment as soon as possible to reduce the risk of further transmission, along with appropriate STBBI testing.

Test of Cure

- A test of cure is recommended when first-line therapy is not used and in other specific clinical situations, including infection in pregnancy and pharyngeal gonorrhea ([see full list of indications for test of cure](#)).
- **Culture** is the first-line testing method for test of cure for gonorrhea and should be performed **three to seven days post-treatment**. If culture is not locally available, NAAT is a second-line option for test of cure, but should be performed two to three weeks post-treatment.

Re-Screening

- Gonorrhea cases should be re-screened **six months** after treatment. If re-screening at six months is not possible, cases should be re-screened when they next seek medical care within the next 12 months.
- For individuals at ongoing risk for STBBI, consider screening for gonorrhea, chlamydia, syphilis and HIV at three-month intervals.

Prevention

- Strategies for the primary prevention of gonorrhea, including counselling and risk reduction strategies can be found in the CGSTI; the Canadian Public Health Association's Discussing Sexual Health, Substance Use and STBIs; and, the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Diseases Treatment Guidelines.

Purpose and Scope

The Ontario Gonorrhoea Testing and Treatment Guide, 2nd Edition was completed to address:

- Discontinued manufacturing of spectinomycin
- Updates to the CGSTI alternative treatment guidance for gonorrhoea, released July 2017
- Changes in antimicrobial susceptibility patterns of *N. gonorrhoeae* isolates in Ontario

This document provides recommendations for Ontario health care providers to address the immediate threat of increasing antibiotic resistance in *N. gonorrhoeae*. It updates the evidence-informed recommendations on laboratory diagnosis and treatment of uncomplicated anogenital and pharyngeal gonorrhoea. Where recommendations differ from the CGSTI, rationale for the Ontario recommendations is provided. The CGSTI are available from the [Government of Canada](#).

The scope of the recommendations includes:

1. Laboratory testing recommendations, including when to perform a Gram stain, bacterial culture or NAAT
2. Treatment recommendations for uncomplicated anogenital and pharyngeal gonorrhoea
3. Follow-up of gonorrhoea cases, including public health reporting, testing and treatment of sexual contacts, test of cure and follow-up testing

This is an evergreen document and sections will be updated as needed. The recommendations within this document are based on the shared clinical and public health goals to facilitate access to appropriate laboratory diagnosis, timely and effective treatment and follow-up for cases and contacts, as well as slowing the emergence of extremely drug-resistant *N. gonorrhoeae* in Ontario.

This guide does not address other issues critical to reducing the burden of gonorrhoea in Ontario. These include strategies for the primary prevention of gonorrhoea, including counselling and risk reduction strategies, infections among specific populations (e.g., children) or co-infections. References for these topics include the CGSTI and the CDC Sexually Transmitted Diseases Treatment Guidelines.

1. Introduction

1.1 Antimicrobial Resistance in *N. gonorrhoeae*

Gonorrhea, caused by the Gram-negative bacteria *N. gonorrhoeae*, is the second most frequently reported bacterial STI in Ontario, after chlamydia.² Historically, gonorrhea was treated with penicillin and tetracyclines, until antimicrobial resistance to these antibiotics emerged in the 1980s.^{3,4} In the 1990s, fluoroquinolones, such as ciprofloxacin, were the treatment of choice for gonorrhea; however, due to the rapid emergence of resistance, ciprofloxacin has not been recommended for the empiric treatment of gonorrhea in Canada since 2008.⁵ Currently, third-generation cephalosporins, ceftriaxone or cefixime (depending on particular guidelines), are recommended as first-line treatment for gonorrhea;⁵⁻⁸ however, multi-drug resistance in *N. gonorrhoeae* is rapidly evolving, threatening the effectiveness of the third-generation cephalosporins. Clinical failures associated with the use of cephalosporins have been identified worldwide.⁹⁻¹³ The World Health Organization (WHO) recommends that medicines for the treatment of STIs have a cure rate of at least 95%.¹⁴

The potential for widespread multi-drug-resistant *N. gonorrhoeae* is a concern and could lead to increased rates of transmission, pelvic inflammatory disease (PID), urethritis, disseminated disease and neonatal ophthalmia. The number of documented clinical failures is most likely an underestimate because the ability to identify potential clinical failures is limited by the occurrence of asymptomatic infection,¹⁵⁻¹⁷ and the lack of routine test of cure. The identification of antimicrobial resistance and potential clinical failures is further complicated by an increasing reliance on NAAT rather than culture. NAAT is a more sensitive test than culture for the diagnosis of gonorrhea and can be performed on urine samples, facilitating easier specimen collection;¹⁸ however, NAAT does not allow for antimicrobial susceptibility testing, which precludes detection of those that are at highest risk of treatment failure.

1.2 Clinical Features

Transmission of *N. gonorrhoeae* most commonly occurs by direct contact from vaginal, anal or oral sex, but it can also be transmitted from mother to child during childbirth.¹⁹ The most frequent sites of infection include the urethra, endocervix, rectum and pharynx.

Common presentations of gonorrhea in men include acute urethral discomfort, urethral discharge and dysuria.^{5,14} Other symptoms may include: urethral itch; testicular pain and/or swelling; or rectal pain and discharge (if proctitis is present). In symptomatic men, the incubation period for *N. gonorrhoeae* is most commonly described as 2-5 days (range 1-10 days).²⁰

Common presentations of gonorrhea in women include: vaginal discharge, dysuria, abnormal vaginal bleeding, lower abdominal pain, pain and/or bleeding with intercourse; and/or rectal pain and discharge (if proctitis is present).^{5,14} Up to 50% of urogenital gonococcal infections in women and up to 10% in men are asymptomatic.¹⁵⁻¹⁷ Thus, the incubation period of gonorrhea is less well characterized in women than men. When present, urogenital symptoms develop in most women within 10 days of exposure.²¹

Rectal and pharyngeal infections are often asymptomatic,^{7,22} although proctitis can occur. Symptoms of proctitis include anal irritation, painful defecation, constipation, scant rectal bleeding, painless mucopurulent discharge, anal pruritus and tenesmus.²³

If left untreated, gonorrhoea can lead to a number of complications in both women (e.g., PID, infertility, ectopic pregnancy, chronic pelvic pain, Reiter syndrome or disseminated gonococcal infection) and men (e.g., epididymo-orchitis, Reiter syndrome, infertility or disseminated gonococcal infection). Gonorrhoea also increases the risk of HIV acquisition and transmission.²⁴⁻²⁶

1.3 Descriptive Epidemiology of Gonorrhoea in Ontario

The descriptive epidemiology was updated using provincial gonorrhoea case data reported in the integrated Public Health Information System (iPHIS)(extracted February 23, 2018) and 2017 Population Projection data from Statistics Canada (extracted October 24, 2017). Overall case counts include cases of gonorrhoea that did not specify male or female gender in 2017, which allows for cases that reported “Other,” “Transgender,” or “Unknown” to be captured in the denominator. Specific counts of cases reporting unknown gender and age have been specified.

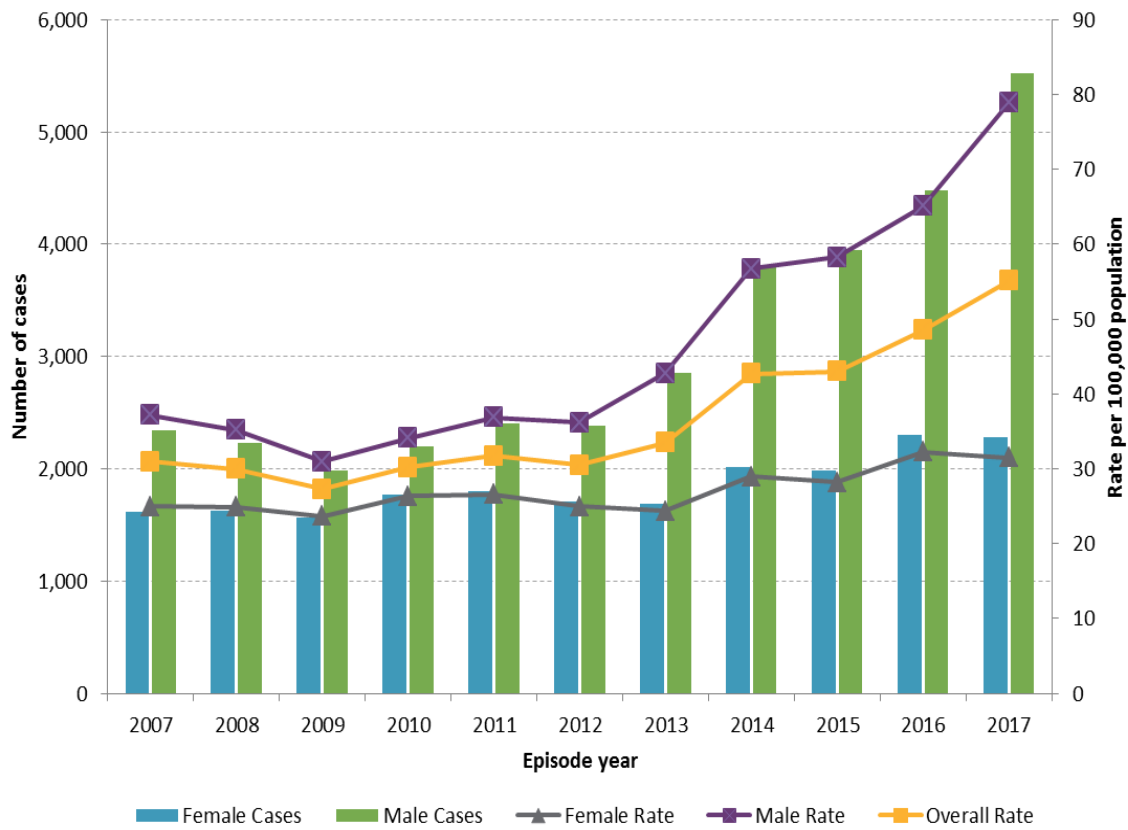
The overall incidence of gonorrhoea has increased over the past 10 years in Ontario ([Figure 1](#)). In 2017, 7,835 confirmed cases of gonorrhoea were reported, with males accounting for the majority of cases (5,523/7,835 or 70.5%). In 2017, the highest incidence rate for males was among 25- to 34-year-olds and the highest incidence rate for females was among 20- to 24-year-olds ([Figure 2](#)). Males 25 years and older made up the highest proportion of total gonorrhoea cases, at 53.0% (4,152/7,835), followed by females under 25-years old, at 14.5% (1,137/7,835). In 2017, two cases had an unknown age and 33 did not specify male or female gender.

The majority of gonorrhoea cases had defined risk factors for infection, with 87.9% (6,890/7,835) reporting at least one risk factor. Of those cases with at least one risk factor reported, the most common was “no condom use” (4,556/6,890 or 66.1%). Of males reporting at least one risk factor, 41.8% (2,071/4,957) reported “sex with same sex.” Of those, 80.7% (1,671/2,071) were 25 years and older.

For a geographical breakdown of the incidence rate of gonorrhoea in 2017 by public health unit jurisdiction, please refer to [Figure 3](#).

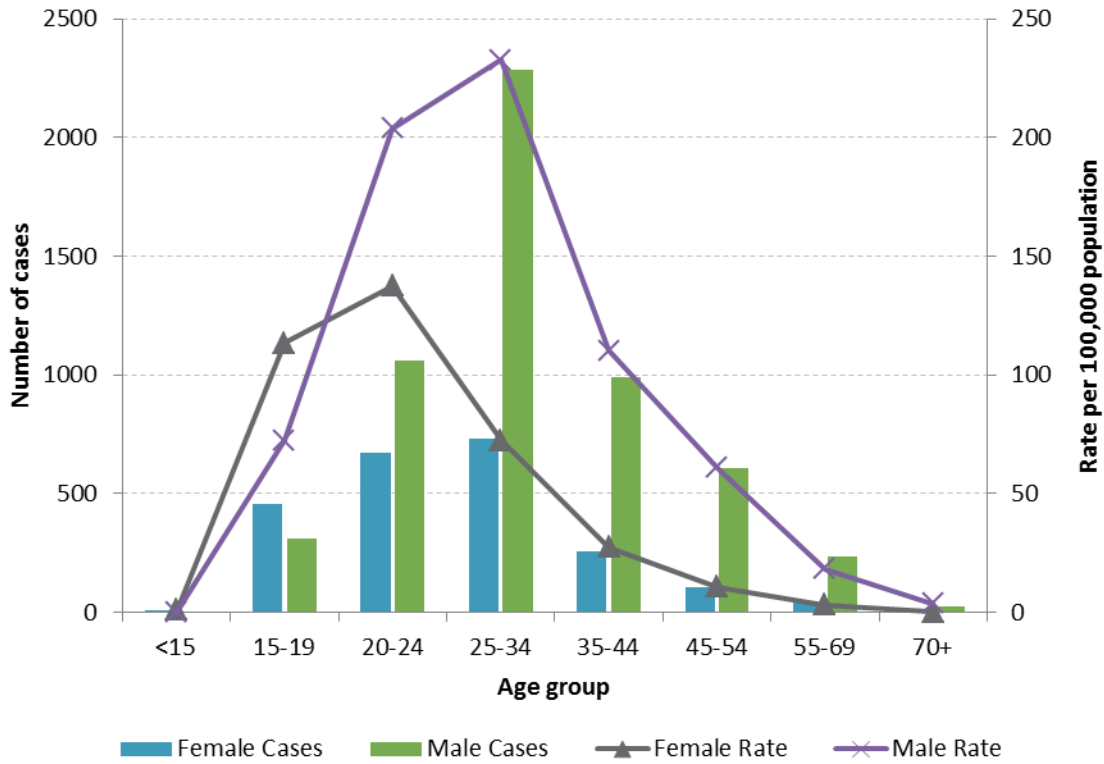
Recent data on the epidemiology of gonorrhoea in Ontario is available on [PHO’s Gonorrhoea website](#), as well as [PHO’s Reportable Disease Trends in Ontario website](#).

Figure 1. Reported gonorrhoea cases and rates by year and gender Ontario, 2007–2017



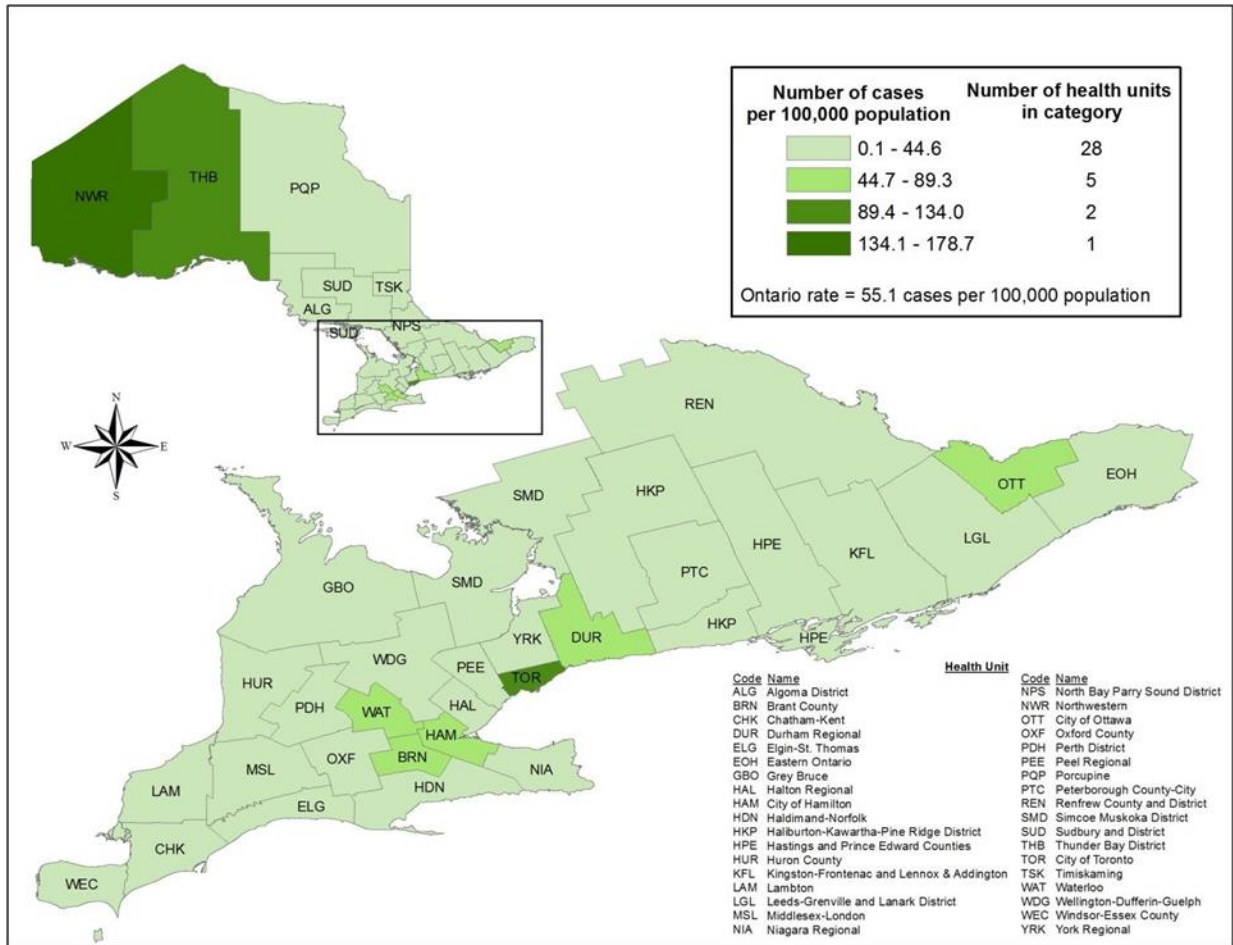
Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by PHO February 23, 2018. Population data: Population projections 2017-2018. Ontario. Ministry of Health and Long-Term Care, IntelliHEALTH Ontario. Date extracted October 24, 2017. Note: Overall rates include cases that did not specify male or female (2007-17: n=92).

Figure 2. Reported gonorrhoea cases and rates by age and gender: Ontario, 2017



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by PHO February 23, 2018. Population data: Population projections 2017-2018. Ontario. Ministry of Health and Long-Term Care, IntelliHEALTH Ontario. Date extracted October 24, 2017. Note: Does not include two cases of unknown age and 33 cases that did not specify female or male gender.

Figure 3. Reported rate of gonorrhoea by health unit: Ontario, 2017



Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by PHO February 23, 2018. Population data: Population projections 2017-2018. Ontario. Ministry of Health and Long-Term Care, IntelliHEALTH Ontario. Date extracted October 24, 2017.

2. Methods

The recommendations in this guide were informed by the following:

- A literature search and synthesis of recent evidence on laboratory diagnosis and treatment of gonorrhea
- A jurisdictional scan of Canadian gonorrhea testing and treatment guidelines and guidelines from other selected high-income jurisdictions
- Descriptive analysis of recent antimicrobial susceptibilities of *N. gonorrhoeae* isolates in Ontario
- Expert consultation with members of the Working Group for Updates to the Ontario Gonorrhea Testing and Treatment Guide

In addition, implementation considerations, such as availability of specific laboratory tests in Ontario, were considered. Patient acceptability was considered from a clinician perspective via the Working Group participants, but patient values and preferences were not solicited.

Literature Search and Synthesis: Diagnosis and Testing

To identify recently published evidence on methods for the diagnosis of gonorrhea, a focused literature scan was conducted using MEDLINE (PubMed) on March 9, 2018 using the search terms: ((gonorrhea) AND neisseria) AND test* AND diagno*. The literature scan was conducted by one reviewer. Results were limited to English language publications from the last five years (2013 to 2018). Studies were eliminated if they described treatment, therapy, antimicrobial susceptibility or case descriptions. There were 125 citations for screening. The reference lists of relevant articles were hand-searched for additional relevant articles. Studies were included if they reported laboratory methods for the diagnosis of gonorrhea. A total of 13 studies were considered to inform the evidence synthesis on methods for the diagnosis of gonorrhea ([Appendix A](#)).

The body of synthesized diagnosis and testing evidence was assessed for overall quality by one reviewer, considering the following across studies: risk of bias, inconsistency, indirectness of outcome measures, imprecision, publication bias, effect size, dose response and whether plausible confounding would change the effect.²⁷ Findings were summarized in tables.

Literature Search and Synthesis: Treatment

For gonorrhea treatment, we systematically searched and appraised peer-reviewed literature that has emerged since the literature review performed for the 2013 Ontario Guidelines for Testing and Treatment of Gonorrhea in Ontario,²⁸ i.e., published from 2012 to early 2018. Search strategies were developed by a PHO Library Information Specialist experienced in systematic review searching. The MEDLINE strategy was peer-reviewed by members of the PHO Library Services team using a

collaborative quality assurance process²⁹ and all required revisions were implemented before it was translated and executed in secondary databases. MEDLINE, CINAHL, Embase, SCOPUS were searched on December 19, 2017 and February 21, 2018 using the search terms: (Gonorrhoea/ or Neisseria gonorrhoeae/ or gonorrh*) AND (Drug Therapy/ or Anti-Infective Agents/ or Anti-Bacterial Agents/ or Drug Prescriptions/ or Prescription Drugs/ or Drug Resistance/ or Drug Resistance, Microbial/ or Drug Resistance, Bacterial/ or Drug Resistance, Multiple/ or Drug Resistance, Multiple, Bacterial or drugs used to treat gonorrhoea by generic name), limited to English language publications and excluding animal studies. Please see [Appendix B](#) for the MEDLINE search strategy as an example. After removing duplicates, there were 1,678 citations for screening. Please see [Appendix C](#) for a flow diagram outlining the screening steps.

The first level of screening (Level 1) for gonorrhoea treatment literature involved screening titles and abstracts and was conducted by one reviewer. A second reviewer checked every 25th article for agreement with the first reviewer's decision to include or exclude the study. Any discrepancies were resolved through discussion. Studies passed Level 1 screening if they met any of the following criteria: referred to effectiveness of a gonorrhoea treatment, treatment failures, treatment guidelines, resistance trends, empiric treatment, new treatments and commentaries. A total of 138 studies passed Level 1 screening. Level 2 involved screening the full-text and was conducted by two reviewers in parallel. Studies were included if they met any of the following criteria: reported gonorrhoea treatment failures or reported the effectiveness of drugs to treat uncomplicated gonorrhoea, but limited to drugs available or intended for the treatment of gonorrhoea in Canada. A total of 22 studies were included in the evidence synthesis on treatment ([Appendix A](#)).

Included treatment studies were critically appraised individually by one reviewer using the Meta Quality Appraisal Tool.³⁰ No studies were excluded from the treatment evidence synthesis on the basis of quality.

The body of the synthesized treatment evidence was then assessed for overall quality by considering the following across studies: risk of bias, inconsistency, indirectness of outcome measures, imprecision, publication bias, effect size, dose response and whether plausible confounding would change the effect.²⁷ The quality of the body of synthesized evidence on treatment was assessed by two reviewers in parallel and any discrepancies were resolved through discussion. Findings were summarized in tables.

The study summaries and critical appraisals were reviewed by the Working Group during the expert consultation process (see Expert Consultation Process below).

Jurisdictional Scan

We performed a jurisdictional scan of gonorrhoea treatment recommendations that consisted of the CGSTI, British Association for Sexual Health and HIV (BASHH), the United States CDC, the European Guidelines on The Diagnosis and Treatment of Gonorrhoea in Adults and the WHO Guidelines for the Treatment of Gonorrhoea.^{5-8,14}

Descriptive Analysis of Ontario Antimicrobial Susceptibility Trends

For antimicrobial susceptibility trends, the number and proportion of Ontario *N. gonorrhoeae* isolates with resistance or reduced susceptibility to ceftriaxone, cefixime, azithromycin, tetracycline and ciprofloxacin submitted for culture to Public Health Ontario were compiled for 2013 to 2017, by site of infection, using thresholds established by the Clinical Laboratories Standards Institute (CLSI) and the Gonococcal Isolate Surveillance Project.

Expert Consultation Process

To ensure this guide was informed by expert consideration of the available evidence and expert opinion where gaps in evidence exist, PHO formed the Working Group for Updates to the Ontario Gonorrhoea Testing and Treatment Guide (the Working Group). The Working Group included representation from PHO, MOHLTC, local public health units and a diverse range of health care providers, including family physicians and specialists with clinical expertise in STI management. The appraised literature ([Appendix C](#)), jurisdictional scan ([Appendix D](#)) and antimicrobial susceptibility patterns ([Appendix E](#)) were summarized and presented to the Working Group and discussed at a meeting on March 16, 2018. These discussions were used to inform updates to the 2013 Guidelines for Testing and Treatment of Gonorrhoea in Ontario. The draft updated guide was reviewed by the Working Group and discussed at a meeting on May 1, 2018.

The strength of each recommendation for diagnosis and testing and treatment was informed by available evidence and the expert opinion of consulted Working Group members (see Expert Consultation Process below) and was characterized as follows:

- For diagnosis and testing recommendations, testing methods were characterized as either “first-line” or “second-line,” taking into account patient sex and gender, whether the patient is symptomatic/asymptomatic and anatomic testing site.
- For treatment recommendations, recommended treatment regimens were characterized as the recommended “first-line” therapy or “alternative” options.

Additional details on the systematic literature searches, evidence syntheses, quality appraisal and terms of reference for the Working Group are available upon request.

3. Laboratory Diagnosis

Summary

Testing Principles

WHEN TO TEST

- Knowing an individual's sexual history is critical to informing testing decisions. Guidance on how to facilitate safe, respectful discussions about sexual health and reduce stigma is available from the [Canadian Public Health Association](#).
- All sexually active individuals who have signs and symptoms of gonorrhoea should be tested at the urogenital sites where they report unprotected sexual exposure and signs/symptoms.
- Offer screening to asymptomatic sexually active individuals with [risk factors](#) for gonorrhoea.
- Most rectal and pharyngeal gonococcal infections are asymptomatic. Testing at these sites is currently recommended among certain high risk groups when receptive sexual exposure has occurred. These groups are:
 - MSM^{16,22,31,32}
 - People who engage in sex work and their sexual contacts^{33,34}
 - Known sexual contacts of those infected with gonorrhoea^{32,35}
- Since a high proportion of individuals with gonorrhoea are at risk of co-infection with *Chlamydia trachomatis* (chlamydia), when testing for gonorrhoea, health care providers should concurrently test for chlamydia. Consider testing for other STBBIs, including HIV.

HOW TO TEST

- NAAT:
 - NAAT is more sensitive than culture for gonorrhoea and chlamydia.^{17,36}
 - Urine NAAT is less sensitive than vaginal or cervical NAAT.^{37,38}
 - Most commercial NAAT assays test for gonorrhoea and chlamydia co-infection simultaneously with one specimen.
 - Antimicrobial susceptibility testing **cannot** be performed on NAAT specimens.

- Please contact your local laboratory to enquire if vaginal NAAT is available. As of the time of writing, Public Health Ontario offers urine, cervical and extragenital NAAT, but not vaginal NAAT.
- Culture:
 - Culture is recommended in specific clinical situations, e.g., test of cure, testing for medico-legal purposes ([see list for when culture is recommended](#)).
 - Culture can provide isolates to enable monitoring of local antimicrobial susceptibility trends.
 - Follow manufacturers' instructions for specimen collection.
 - Culture specimens should be received at the laboratory within 48 hours of collection for optimal specimen integrity;^{17,39} however, based on feasibility of transport, individual laboratories can decide to process delayed specimens. Public Health Ontario accepts specimens received up to 72 hours after collection.
 - Testing and screening of people who are transgender should be informed by current anatomy and sexual behaviours.

Urogenital Testing

SYMPTOMATIC INDIVIDUALS

Applies to adults and youth with symptoms compatible with gonorrhoea at urogenital sites, and assumes concurrent testing for gonorrhoea and chlamydia.

Males

- If urethral discharge present:
 - **Urine NAAT (first-line)**⁴⁰⁻⁴²
 - If testing by **urethral culture**, add **urine NAAT**, which will concurrently test for chlamydia, as well as provide a more sensitive test for gonorrhoea.
- If no urethral discharge:
 - **Urine NAAT**

Females, including pregnant females

- If a pelvic exam is not being conducted:
 - **Vaginal NAAT (first-line)**³⁷

- **Urine NAAT** is a second-line option because it is less sensitive than vaginal NAAT for gonorrhea.³⁸
- If a pelvic exam is being conducted:
 - **Cervical NAAT or vaginal NAAT (either is first-line)**³⁷
 - **Urine NAAT** is a second-line option because it is less sensitive than cervical NAAT or vaginal NAAT for gonorrhea.³⁸
 - If testing by **cervical culture, add any urogenital NAAT**, which will concurrently test for chlamydia, as well as provide a more sensitive test for gonorrhea.

ASYMPTOMATIC INDIVIDUALS

Screening asymptomatic patients is only recommended in individuals with [risk factors](#) for gonorrhea.

Males

- **Urine NAAT**

Females, including pregnant females

- If a pelvic exam is not being conducted:
 - **Vaginal NAAT (first-line)**³⁷
 - **Urine NAAT** is a second-line option because it is less sensitive than vaginal NAAT for gonorrhea.³⁸
- If a pelvic exam is being conducted:
 - Cervical NAAT or vaginal NAAT (either is first-line)³⁷
 - Urine NAAT is a second-line option because it is less sensitive than cervical NAAT or vaginal NAAT for gonorrhea.³⁸

Extragenital Testing

- **Rectal NAAT and/or pharyngeal NAAT** is recommended in the following individuals with receptive exposure at these sites, whether symptomatic or asymptomatic:⁴³⁻⁴⁶
 - MSM^{16,22,31,32}
 - People who engage in sex work and their sexual contacts^{33,34}
 - Known sexual contacts of those infected with gonorrhea^{32,35}

- Rectal and/or pharyngeal testing in individuals who are not in the above risk groups may be considered in individual circumstances, based on clinical evaluation of symptoms, sexual behaviours and local epidemiology.³²
- A test of cure is recommended for laboratory-confirmed cases of pharyngeal gonorrhoea.^{5,12,47-52}

3.1 What Laboratory Test Methods Are Available for the Diagnosis of Gonorrhoea?

- Most Ontario laboratories offer testing for the detection of *N. gonorrhoeae* using microscopy, NAAT and/or culture, depending on the laboratory. Please contact your local laboratory to determine the testing methods available and ideal collection and transport media. Details for testing at Public Health Ontario can be found in the PHO Lababstracts.⁵³⁻⁵⁵

Microscopy

- The identification of intracellular Gram-negative diplococci by microscopy has a relatively high sensitivity and specificity for the diagnosis of gonorrhoea in men, with a sensitivity > 90% in symptomatic men, a sensitivity of 50% to 75% in asymptomatic men and a specificity of > 90% for both symptomatic and asymptomatic men ([Table 1](#)). Microscopy for *N. gonorrhoeae* in women is not recommended due to low sensitivity and specificity in this population.^{56,57}
- The primary advantage of microscopy for the diagnosis of gonorrhoea in men is the rapid turn-around time particularly when performed in the clinical setting. For improved sensitivity, it is recommended that all specimens tested by microscopy be supplemented by an additional specimen for culture or NAAT. If *N. gonorrhoeae* is identified by microscopy, culture is preferred in order to obtain antimicrobial susceptibility results.

Culture

- Bacterial culture for *N. gonorrhoeae* has a test specificity of more than 99%, the highest of the three testing methods and is the only diagnostic method that enables antimicrobial susceptibility testing ([Table 1](#)). The sensitivity of culture for the detection of *N. gonorrhoeae* ranges from 50% to 92% and is reduced with suboptimal transport times (i.e. exceeding 24 to 48 hours).^{17,39} Culture can be used for testing of all potentially infected anatomic sites, including urethral, cervical, pharyngeal, rectal, conjunctiva, joint fluid and blood. Culture can provide the isolates for antimicrobial susceptibility testing, which is critical both for targeted antibiotic therapy (e.g., when culture as test of cure is performed for suspected treatment failure) and for the surveillance of *N. gonorrhoeae* resistance. Samples for culture obtained less than 48 hours after exposure may give false negative results.⁵

Nucleic Acid Amplification Testing (NAAT)

- NAAT for *N. gonorrhoeae* was introduced in the late 1990s and has become the predominant method of testing due to ease of collection of specimens, high sensitivity and the ability to test for chlamydia and gonorrhea in the same sample. The sensitivity of NAAT for the detection of *N. gonorrhoeae* is higher than bacterial culture ([Table 1](#)).^{17,36} The high sensitivity of NAAT for *N. gonorrhoeae* is unaffected by suboptimal sample transport times and conditions, which can affect organism viability for culture. The high sensitivity also means testing could be considered right after high risk unprotected exposure, but if NAAT is negative when tested within two days after exposure and no antibiotic was given, follow-up testing should be submitted in five to seven days to rule out a false negative due to early infection.^{20,21} NAAT specificity (96.1% to 99.8%) is slightly lower than bacterial culture leading to a slightly higher risk of false positive results.
- NAAT is licensed for testing of *N. gonorrhoeae* in urine, cervical, vaginal and urethral samples. Urine testing by NAAT has the advantage of being less invasive than cervical and urethral swabs obtained for culture and/or NAAT; however, when testing women, urine NAAT for *N. gonorrhoeae* is less sensitive than cervical and vaginal NAAT.^{37,38} At the time of writing, vaginal NAAT was not available at Public Health Ontario. Please contact your local laboratory to enquire if such testing is available.
- The primary disadvantage of NAAT is that it cannot provide antimicrobial susceptibility results, which can currently only be performed on cultured isolates. NAAT is not ideal for test of cure, as it can result in false positive results from samples that contain DNA from dead bacteria, sometimes up to two weeks post-treatment.⁵⁸ In contrast, culture method for test of cure can be done three to seven days post-treatment as all living organisms should be eradicated with effective antimicrobial therapy by this time.⁵⁹
- NAAT for *N. gonorrhoeae* is not licensed for pharyngeal or rectal sites; however, since data have shown that NAAT can increase the detection of extragenital *N. gonorrhoeae* infection, many jurisdictions (CDC, BASHH, Australasian Sexual Health Alliance (ASHA)) have included NAAT as the recommended test method for rectal and pharyngeal specimens, as long as validation is performed by the laboratories to be in compliance with accreditation regulations. The revised Laboratory Diagnosis of Sexually Transmitted Infections Chapter of the CGSTI suggested NAAT as a test method for specimens from pharyngeal and rectal sites depending on local laboratory capacity.⁵⁹ [Public Health Ontario accepts rectal and pharyngeal NAAT specimens.](#)

Self-Collected Vaginal Swabs

- Changes to Ontario cervical cancer screening guidelines have resulted in less frequent and later initiation of routine pelvic exams and are associated with reduced chlamydia testing in females.⁶⁰ The evidence indicates that self-collection of vaginal specimens for STI testing is acceptable to patients;⁶¹⁻⁶³ however, specimen quality may differ between self-collection in a clinic versus at-home and more evidence is needed to assess any differences in accuracy

between vaginal specimens collected in these two settings.^{64,65} As well, for commonly used commercial assays (e.g. the Hologic® Aptima® Combo 2 Assay used at Public Health Ontario), the vaginal swab specimen collection kit is not United States Food and Drug Administration (FDA) or Health Canada approved for home use. At this time, Public Health Ontario does not accept vaginal specimens, including self-collected specimens, for gonorrhoea testing. Please contact your local laboratory to enquire if such specimens are accepted.

Table 1. Sensitivity, specificity and other characteristics of laboratory tests for *N. gonorrhoeae*

Test	Sensitivity	Specificity	Susceptibility Testing	Specimen Collection Details (Please contact your testing lab for specific requirements)
Gram stain (microscopy)	Men: Symptomatic: >90% Asymptomatic: 50%–75% Women: < 50%	Men: >90% Women: <90%	No	Most commonly performed from slide or Amies charcoal swab
Bacterial culture	50%–92% Sensitivity decreases with long transport times and asymptomatic infection	>99%	Yes	Most commonly performed from Amies charcoal swab
Nucleic acid amplification testing (NAAT)	92%–97.2%	96.1%–99.8%	No	Proprietary collection kits specific to commercial assays or urine containers

3.2 Recommended Populations Who Should be Tested for *N. gonorrhoeae*

Knowing an individual's sexual history is critical to informing testing decisions. Guidance on how to facilitate safe, respectful discussions about sexual health and reduce stigma is available from the [Canadian Public Health Association](#). All sexually active individuals who have signs and/or symptoms of urogenital gonorrhea should be tested for gonorrhea. Since a high proportion of individuals with gonorrhea are at risk of co-infection with chlamydia, when testing for gonorrhea, practitioners should concurrently test for chlamydia.⁵

Offer screening of asymptomatic sexually active individuals with risk factors (below) for gonorrhea based on sexual history-taking, local epidemiology and clinical judgement. The CGSTI do not recommend a particular testing interval for asymptomatic sexually active persons.

In Ontario, risk factors for gonorrhea of particular importance among those with unprotected sexual exposure include:

- Sexually active women under 25 years of age, as they represented 49.9% (1,137/2,279) of infections in women in Ontario in 2017 (extracted by PHO on March 23, 2018).
- Sexually active MSM, as they represented 41.8% (2,071/4,957) of all gonorrhea diagnoses in men in Ontario in 2017 (extracted by PHO on March 23, 2018).

The CGSTI risk factors and at-risk populations for gonorrhea include but are not limited to:⁵

- People who have had sexual contact with a person with proven infection or compatible symptoms
- People who have a history of a previous STI, including gonorrhea
- People who engage in sex work and their sexual contacts
- Men who have unprotected sex with men
- Sexually active youth <25 years of age
- Street-involved youth and other people who are homeless or under-housed
- People who have had sex with multiple partners
- Travellers who have had unprotected sexual exposure with a resident of an area with high gonorrhea burden and/or high risk of antimicrobial resistance

In 2018, there were reports of extremely-drug resistant (XDR) gonorrhea in the United Kingdom and Australia associated with travel to countries within Asia.⁶⁶⁻⁶⁸ Antimicrobial susceptibility data and travel-

associated STI data are often of low completeness and limited external validity and subject to change given the propensity of gonorrhoea to spread. Safer sex counselling should be considered for travellers who intend to or may have new sexual contacts when abroad.¹³

Pregnant Women

Pregnant women should be screened for gonorrhoea early in pregnancy due to potential complications from an undiagnosed infection.^{5,69} In alignment with the [Ontario Perinatal Record](#), for pregnant women at on-going risk of acquiring gonorrhoea, re-screening is recommended in each trimester.⁶⁹ Test of cure is recommended for all pregnant females diagnosed with gonorrhoea.

Testing/Screening People Who Are Transgender

Testing of people who are transgender should be informed by current anatomy and sexual behaviours and should use an individualized approach. For resources to inform testing/screening in people who are transgender, please see the [Transgender people and sexually transmitted infections \(STIs\) chapter](#) of the University of California's [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#) and Sherbourne Health Centre's [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#) and the 519 Church Street Community Centre's [Brazen: Trans Women's Safer Sex Guide](#), which is a client-centred resource.

3.3 Testing at Rectal or Pharyngeal Sites

The majority of rectal and pharyngeal gonococcal infections are asymptomatic.⁷⁰⁻⁷² Hence, testing for rectal and pharyngeal sites is risk-based and recommended for certain high-risk groups with receptive sexual exposure at these sites. From a public health perspective, individuals who are high-risk for gonorrhoea infection and likely to transmit to a large number of sexual contacts play critical roles in the spread of antimicrobial resistant gonorrhoea.^{31,35,73} Evidence that exchange of genetic material between *Neisseria* species in the pharynx can lead to circulating drug-resistant strains of gonorrhoea, underscores the importance of identifying and treating these infections in high-risk groups likely to transmit to a large number of sexual contacts.^{74,75}

Populations Who Should Be Tested

Rectal and/or pharyngeal NAAT is recommended for individuals in the following risk groups with receptive rectal or oral exposure:⁴³⁻⁴⁶

- MSM^{16,22,31,32}
- People who engage in sex work and their sexual contacts^{33,34}
- Known sexual contacts of those infected with gonorrhoea^{32,35}

At minimum, annual rectal and/or pharyngeal screening can be considered for asymptomatic MSM with receptive rectal or pharyngeal sexual exposures.^{5,6} Rectal and/or pharyngeal testing in individuals who

are not in the aforementioned risk groups (**not** MSM, or people who engage in sex work and their sexual contacts or sexual contacts of those infected with gonorrhoea) may be considered in individual circumstances based on clinical evaluation of symptoms, sexual behaviours and local epidemiology.³²

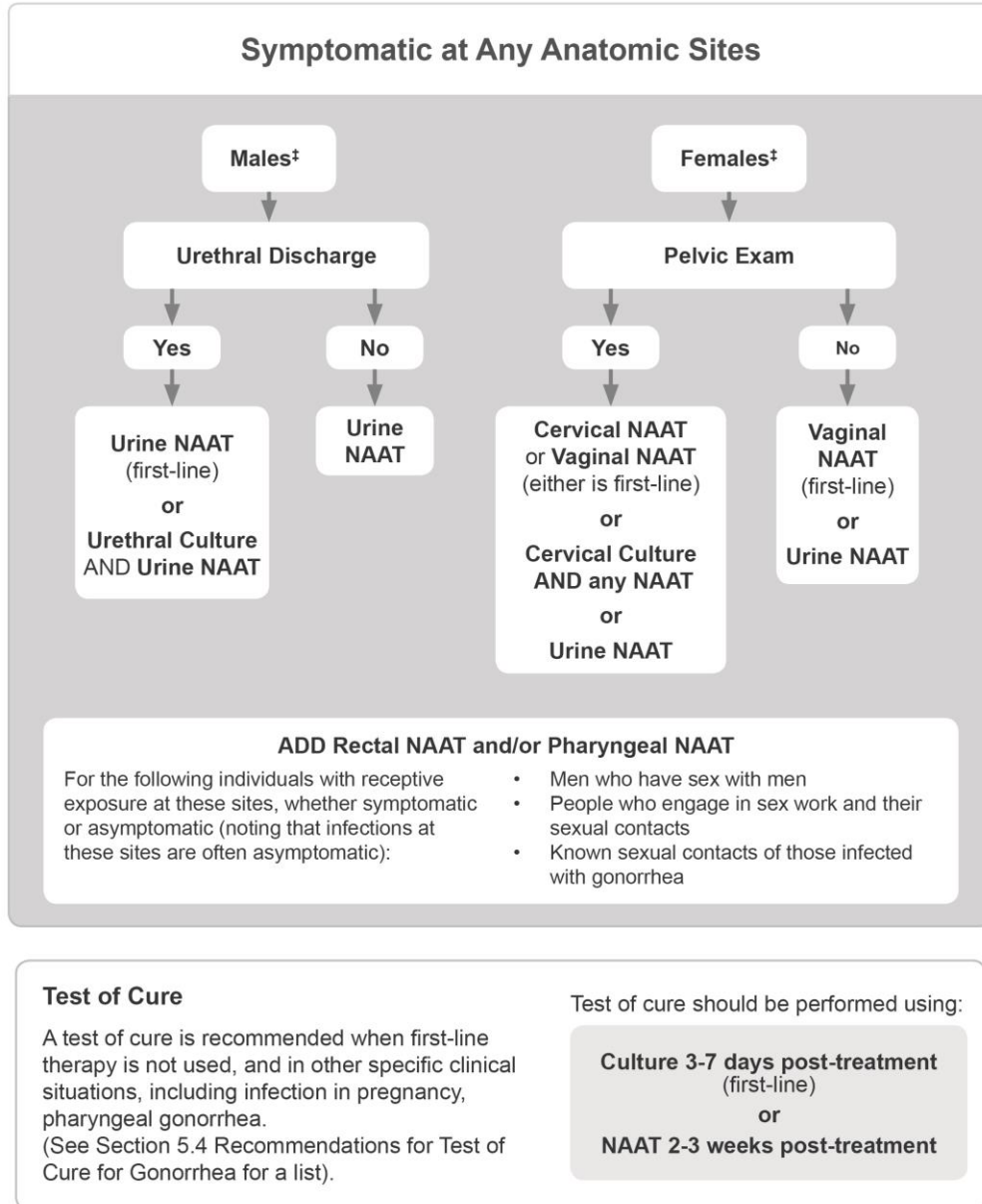
How to Test

- The first-line testing method at rectal or pharyngeal sites are rectal NAAT or pharyngeal NAAT, respectively, because of the higher sensitivity of NAAT compared to culture.⁴³⁻⁴⁶
- A test of cure is recommended for positive cases of pharyngeal gonorrhoea.^{5,12,47-52}

3.4 Recommended Methods for Testing Symptomatic Individuals for Gonorrhoea

See Figure 4 for a testing algorithm for symptomatic individuals. While not examined in the published literature, symptomatic persons infected with *N. gonorrhoeae* are likely to have a larger bacterial load. In such cases, the sensitivity of culture is postulated to be closer to that of NAAT. Nonetheless, NAAT is still recommended if culture is done to ensure optimal sensitivity.

Figure 4. Testing algorithm for symptomatic individuals



Medico-legal Considerations

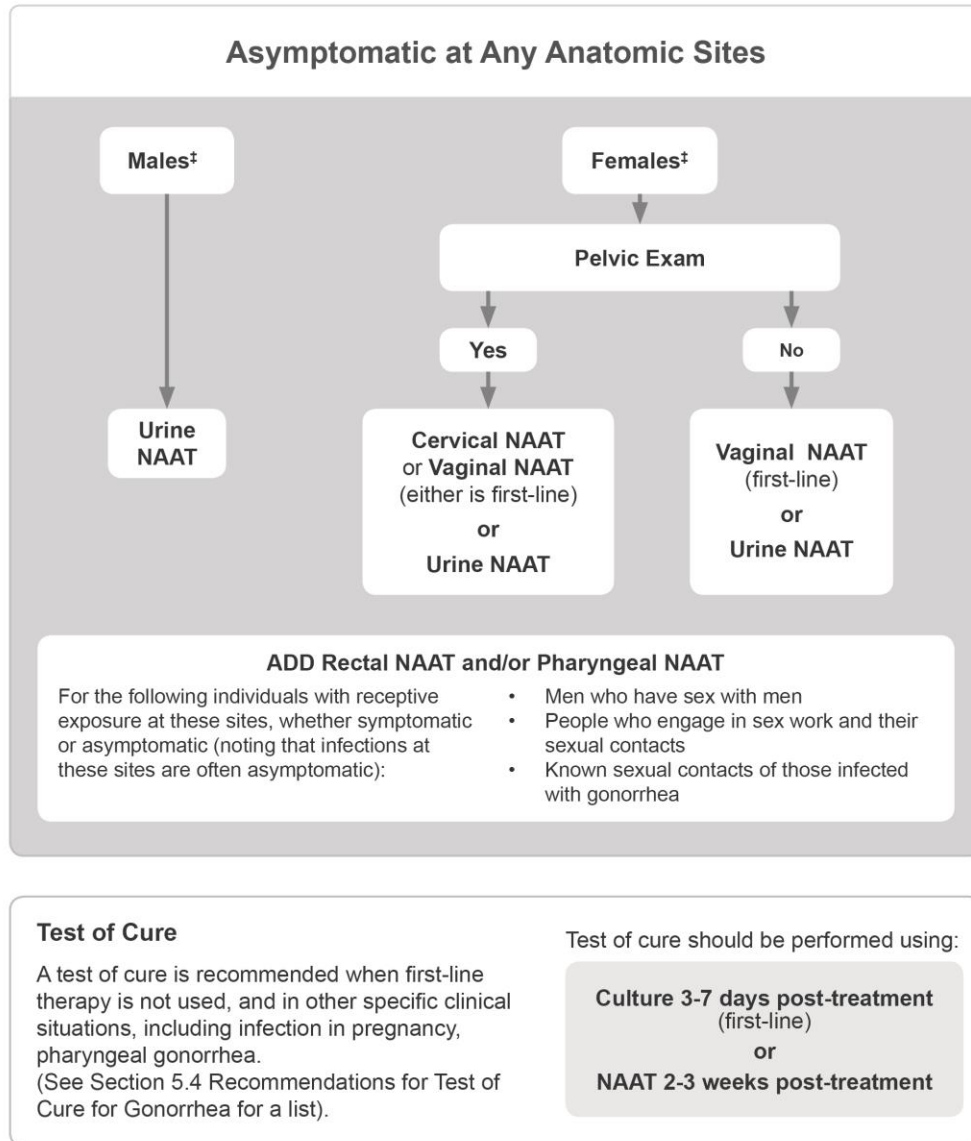
Culture is the preferred testing method for sexual abuse in children. Culture AND NAAT is preferred for sexual assault in postpubertal children/adolescents/adults. NAAT alone may be used for medico-legal purposes if a positive NAAT result is confirmed by another NAAT using a second set of primers.

Note: †Testing of people who are transgender should be informed by current anatomy and sexual behaviours.

3.5 Recommended Methods for Screening Asymptomatic Individuals for Gonorrhea

See Figure 5 for a testing algorithm for asymptomatic individuals.

Figure 5. Testing algorithm for asymptomatic individuals



Medico-legal Considerations

Culture is the preferred testing method for sexual abuse in children. Culture AND NAAT is preferred for sexual assault in postpubertal children/adolescents/adults. NAAT alone may be used for medico-legal purposes if a positive NAAT result is confirmed by another NAAT using a second set of primers.

Note: ‡Testing of people who are transgender should be informed by current anatomy and sexual behaviours.

3.6 Additional Considerations for Using Culture to Diagnose Gonorrhea

Note that similar to the recommendations in the CGSTI, culture testing is also recommended in the following situations:⁵

- Test of cure (e.g., pregnancy, suspected treatment failure, see [Recommendations for Test of Cure for Gonorrhea](#))
- If antimicrobial susceptibility testing is otherwise required (e.g., contact of a treatment failure or infection acquired overseas or in areas with recognized antimicrobial resistance)
- Sexual abuse of children (rectal, pharyngeal, vaginal). Although culture is the preferred method for medico-legal purposes, NAAT may be used for medico-legal purposes if a positive NAAT result is confirmed by another NAAT using a second set of primers.⁷⁶
- Sexual assault. Culture and NAAT is the preferred method for medico-legal purposes. NAAT alone may be used for medico-legal purposes if a positive NAAT result is confirmed by another NAAT using a second set of primers.^{5,76,77}
- Presumed treatment failure with ongoing signs and/or symptoms
- Evaluation of PID

4. Treatment of Gonorrhoea

Summary

- Applies to individuals over nine years of age (including pregnant and breastfeeding females) with confirmed or suspected uncomplicated urogenital, rectal or pharyngeal gonorrhoea and their sex partners:

Recommended first-line therapy: Ceftriaxone 250 mg intramuscularly (IM) plus azithromycin 1 g orally (PO) given at the same visit.^{14,78-80}

- First-line dual therapy is the strong preference due to compelling evidence of efficacy and current antimicrobial susceptibility patterns in Ontario.
- Alternative therapeutic options are only to be considered if first-line therapy is not possible and must be followed by a test of cure. These are:
 - Cefixime 400 mg PO plus azithromycin 1 g PO. First-line dual therapy with ceftriaxone is the strong preference because use of cefixime could potentially accelerate the development of resistance to ceftriaxone, which is the only remaining antimicrobial that is safe, well-tolerated and highly effective at all anatomic sites.^{9,47,80}
 - Gentamicin 240 mg in two separate 3mL IM injections of 40 mg/mL plus azithromycin 2 g PO. If IM is not feasible, gentamicin 240 mg intravenous (IV) infused over 30 minutes is an alternative route of administration.⁸¹⁻⁸³
 - Gemifloxacin 320 mg PO plus azithromycin 2 g PO (once available in the United States, will be accessible in Ontario through Health Canada's Special Access Program).^{83,84}
 - If the dual therapies listed above are not possible, azithromycin 2 g PO monotherapy may be used.^{51,85,86} This is the least preferred option due to reduced susceptibility of *N. gonorrhoeae* isolates to azithromycin in Ontario and evidence in support of dual therapy;⁸⁷
 - Please see [Treatment of Individuals with a History of Penicillin or Cephalosporin Allergy, or Macrolide Allergy](#).
- Treatment of clinical failures if first-line therapy was used should include a higher dose of both ceftriaxone and azithromycin (1 g ceftriaxone IM + 2 g azithromycin PO) given at the same visit and a test of cure using culture at three to seven days post-treatment. If first-line treatment was not used initially when treatment failure is identified, first-line treatment should be used.
- Contact your [local public health unit](#) to obtain publicly-funded STI medications.
- Please refer to product monograph for potential adverse events.

4.1 Changing Antimicrobial Susceptibility Patterns

The minimum inhibitory concentration (MIC) is used in laboratories to measure the lowest possible concentration of antibiotics that is required to inhibit the growth of bacteria. Reduced susceptibility is identified when higher concentrations of antibiotic are needed to stop the growth of bacteria. *N. gonorrhoeae* resistance thresholds have not yet been defined to the cephalosporins or azithromycin in North America.

Table 2. Minimum inhibitory concentration (MIC) thresholds as specified by Clinical Laboratories Standards Institute, in µg/mL⁸⁸

Drug	Susceptible, ≤	Intermediate	Resistant, ≥	Comments
Tetracycline	0.25	0.5–1.0	2.0	N/A
Ciprofloxacin	0.06	0.12–0.5	1.0	N/A
Azithromycin	N/A	N/A	N/A	<ul style="list-style-type: none"> Resistance has not been defined in North America. MIC ≥2 µg/mL are generally considered non-susceptible.
Cefixime	0.25	N/A	N/A	<ul style="list-style-type: none"> Resistance has not been defined in North America. Clinical failures have been associated with cefixime MIC >0.12 µg/mL.
Ceftriaxone	0.25	N/A	N/A	<ul style="list-style-type: none"> Resistance has not been defined in North America.
Gentamicin	N/A	N/A	32.0	N/A

Summary of Susceptibility Patterns in Ontario

For current antimicrobial susceptibility patterns analyzed by health unit, gender, age group and specimen site, and a table summarizing current thresholds used to determine susceptibility, please see PHO's online [STI Laboratory Tool](#) or contact your [local health unit](#). Trends toward reduced susceptibility are of great concern because they indicate an increasing risk of treatment failure. The WHO recommends the discontinuation of empiric use of an antibiotic once 5% of locally acquired isolates of *N. gonorrhoeae* demonstrate resistance.¹¹ The reason cefixime was removed as a first-line treatment option in the 2013 Guidelines for Testing and Treatment of Gonorrhoea in Ontario was because over 10% of culture isolates from July 20, 2010 to October 24, 2012 had decreased susceptibility to cefixime.²⁸ From May 2013 to January 2015, the proportion of gonorrhoea cases in Ontario receiving ceftriaxone and azithromycin concurrently (the recommended first-line treatment option in the 2013 Guidelines for Testing and Treatment of Gonorrhoea in Ontario) increased from under 40% to approximately 70% and has remained between 65% and 76% per month from January 2015 until December 2017.

Limitations to consider when evaluating the susceptibility data of *N. gonorrhoeae* isolates from Ontario include the fact that susceptibility testing for *N. gonorrhoeae* can only be performed on specimens positive by culture and therefore represents a subset of all gonorrhoea diagnoses; some populations and health units may be over or under-represented in these data due to variability in routine use of culture for gonorrhoea testing. Please see [Appendix E](#) for antimicrobial susceptibility for Ontario *N. gonorrhoeae* culture specimens, 2013 to 2017.

Ceftriaxone

Since 2013, the per cent of *N. gonorrhoeae* culture isolates submitted to PHO with ceftriaxone MICs ≥ 0.125 $\mu\text{g}/\text{mL}$, which is the Alert Value used by the Gonococcal Isolate Surveillance Project (GISP) in the United States to monitor resistance to ceftriaxone, has decreased from 3.2% (45/1,403) in 2013 to 0.2% (4/2,276) in 2017 ([Appendix F](#)).

Azithromycin

From 2014 to 2017, the per cent of *N. gonorrhoeae* culture isolates meeting the National Medical Laboratory (NML) threshold for non-susceptible (i.e., MIC ≥ 2 $\mu\text{g}/\text{mL}$) ranged from 3.5% to 4.0% and a greater proportion of isolates required higher concentrations of antibiotic to inhibit growth in vitro, i.e., the proportion of isolates with susceptibility at lower thresholds demonstrated a dramatic decline ([Appendix F](#)).

Gentamicin

As of March 2018, there were no Ontario-specific data on gentamicin susceptibility, but this testing was being done nationally at the NML. In July 2017, the Public Health Agency of Canada (PHAC) reported no resistance to gentamicin in Canada based on a breakpoint of MIC ≥ 32 $\mu\text{g}/\text{mL}$, though 95% of isolates exhibited intermediate susceptibility based on a range of MIC 8–16 $\mu\text{g}/\text{mL}$.^{84,89}

Cefixime

Since 2013, the per cent of *N. gonorrhoeae* culture isolates submitted to PHO with cefixime MICs ≥ 0.125 $\mu\text{g}/\text{mL}$ has decreased from 8.1% (114/1,403) in 2013 to 1.6% (37/2,276) in 2017 and could be attributable to the use of ceftriaxone and azithromycin dual therapy for the treatment of most cases later in this time period ([Appendix F](#)). The improved susceptibility to cefixime is a favourable development; however, the mechanism of *N. gonorrhoeae* resistance to all cephalosporins is the same (namely mosaic penicillin binding protein). As lower drug concentrations are achievable using cefixime compared to ceftriaxone, cefixime use may lead to sub-therapeutic drug concentrations and selection of cephalosporin resistance threatening the effectiveness of both cefixime and ceftriaxone.

Tetracycline (proxy for doxycycline)

From 2013 to 2015, resistance to tetracycline increased from 33.8% (474/1,403) in 2013 to 55.9% (987/1,767) in 2015 and then decreased to 37.0%, 843/2,276 in 2017 ([Appendix F](#)).

Ciprofloxacin

From 2013 to 2017, resistance to ciprofloxacin has increased each year, from 32.4% (455/1,403) in 2013 to 54.9% (1,249/2,276) in 2017 ([Appendix F](#)).

4.2 Comparison of Gonorrhea Treatment

Recommendations

The WHO recommends the discontinuation of empiric use of an antibiotic once 5% of locally acquired isolates of *N. gonorrhoeae* demonstrate resistance.¹⁴ To address the issue of increasing cefixime resistance, the CGSTI, the CDC, the European chapter of the International Union against Sexually Transmitted Infections (IUSTI) and BASHH all revised their treatment recommendations.⁵⁻⁷ Dual therapy with cephalosporins plus azithromycin provided concurrently is the preferred regimen in all of these guidelines ([Appendix D](#)). The WHO retains monotherapy as an option if recent local resistance data confirm susceptibility to the antimicrobial; however, these data are missing or of poor quality in most settings.¹⁴ Treatment of gonorrhea with two antimicrobials is recommended on the theoretical basis that dual therapy may potentially improve treatment effectiveness and thereby reduce the likelihood of transmission of resistant strains and having two antibiotics with different mechanisms of action should in theory hinder the development of resistant strains; however, the evidence to support these theories is limited to laboratory studies and case series.^{10,51,90,91} Dual therapy for pharyngeal gonorrhea is supported by studies demonstrating poor cephalosporin penetration of the pharynx.^{73,91}

The 2015 CDC guidelines, the 2011 BASHH guidelines and the 2012 European guidelines all recommend ceftriaxone as the first-line cephalosporin agent for all gonorrhea infections, given in combination with azithromycin (Please see [Appendix D](#) for a table).⁶⁻⁸ The 2011 BASHH and 2012 European guidelines recommend ceftriaxone 500 mg IM and oral cefixime is not recommended as first-line therapy. The 2015 CDC guidelines recommend ceftriaxone 250 mg IM plus azithromycin 1 g orally as the only first-line therapy. In Canada, the CGSTI 2013 gonorrhea guidelines recommend ceftriaxone 250 mg IM plus azithromycin 1 g orally and recommend cefixime 800 mg and azithromycin 1 g as a potential first-line cephalosporin agent in non-pharyngeal infections in the non-MSM populations.⁵ The 2011 BASHH guidelines provide first-line treatment options specifically for pharyngeal gonorrhea, including ceftriaxone and azithromycin dual therapy or ciprofloxacin or ofloxacin if there is susceptibility to quinolones.

In terms of dose of azithromycin in first-line dual therapy, the 2013 CGSTI, 2012 BASHH, 2015 CDC and 2016 WHO guidelines recommend 1 g azithromycin. The 2012 European guidelines recommend 2 g azithromycin in first-line dual therapy. There is much greater variability in dosage of azithromycin in alternate or second line treatment options across jurisdictions. The 2016 WHO, 2012 European and the 2013 CGSTI gonorrhea guidelines recommend 2 g azithromycin for second-line dual treatment options. In contrast, the 2012 BASHH recommends 1 g azithromycin for first-line and alternate dual therapy and the 2015 CDC guideline recommends 1 g azithromycin as dual treatment with cefixime, but 2 g azithromycin as dual treatment with gentamicin or gemifloxacin, possibly because clinical trials only assessed those regimens. The July 2017 CGSTI alternative treatment guidance statement, which was released in response to the discontinuation of spectinomycin, also includes 2 g azithromycin as dual treatment with gentamicin or gemifloxacin, which are also alternative treatment options in this guide.⁸⁴

4.3 Indications for Treatment of Gonorrhea

Indications for treatment:

- Identification of Gram-negative intracellular diplococci by microscopy in male urethral samples
- Confirmed culture or NAAT specimen for *N. gonorrhoeae*
- Epidemiological link to a gonorrhea case
- Based on clinical assessment and/or risk behaviours following testing, but before results are available
- Following sexual assault
- Mother of neonate with confirmed gonorrhea

4.4 Rationale for the Recommended Treatment for Gonorrhea in Ontario

See [Figure 6](#) for a treatment algorithm.

The dual goals of the recommendations are optimal treatment for individuals, as well as slowing the emergence of extremely drug-resistant *N. gonorrhoeae* in Ontario. Given the propensity of *N. gonorrhoeae* to develop antimicrobial resistance, the current treatment recommendations may be revised with larger doses or different antimicrobials in the future.

PHO recommends a first-line treatment approach similar to the 2015 CDC, 2011 BASHH and 2012 European guidelines by recommending one first-line option: **ceftriaxone 250 mg IM and azithromycin 1 g PO, given at the same visit.**^{6-8,14,78-80} In addition to ceftriaxone and azithromycin, the CGSTI recommends cefixime and azithromycin as first-line in certain circumstances. Although antimicrobial susceptibility to cefixime has improved in Ontario, use of cefixime could potentially accelerate the development of resistance to ceftriaxone, which is the only remaining antimicrobial that is safe, well-tolerated and highly effective at all anatomic sites. Therefore, cefixime remains an alternative option in Ontario if first-line is not used, and must be followed by a test of cure, as is the requirement for all alternative treatment options.

In line with the WHO and CGSTI recommendations,^{5,14} dual therapy is recommended in Ontario. The only exceptions to dual therapy in Ontario are ceftriaxone 250 mg IM monotherapy in the case of macrolide allergy and azithromycin 2 g PO monotherapy in the case of a severe reaction to penicillin (defined as risk of anaphylaxis) or any allergic reaction to the cephalosporins and if azithromycin and gentamicin or gemifloxacin (if available) dual therapy is not an option. The CGSTI alternative treatment guidance states that azithromycin should not be used as monotherapy due to resistance.⁸⁴ From 2014 to 2017, the percentage of *N. gonorrhoeae* culture isolates in Ontario meeting the NML threshold for non-susceptibility to azithromycin ranged from 3.5% to 4%, which is close to the 5% cut-off established by the WHO for empiric treatment. Hence, although azithromycin is included as an alternative treatment option in this guide, it is the least preferred option. Ciprofloxacin is no longer recommended as empiric therapy for gonorrhea in Ontario. In 2017, 54.9%, 1,249/2,276 of *N. gonorrhoeae* culture isolates tested at PHO were resistant to ciprofloxacin (MIC \geq 1.0 μ g/mL). Ciprofloxacin is only recommended if treatment is guided by a culture isolate of *N. gonorrhoeae* demonstrating susceptibility to this drug. Similarly, doxycycline is not recommended as empiric therapy for gonorrhea due to high rates of tetracycline-resistant *N. gonorrhoeae*. In 2017, 37%, 843/2,276 of *N. gonorrhoeae* culture isolates tested at PHO were resistant to tetracycline, which is a proxy for doxycycline (MIC \geq 2.0 μ g/mL).

In the event of confirmed or suspected co-infection with chlamydia, where azithromycin cannot be administered, doxycycline 100 mg oral dose twice daily for seven days should be given to treat chlamydia and should be followed by a test of cure.

For information regarding preparation, dosage, administration, storage and contraindications, please refer to the product monograph for the drug you are administering.

4.5 Treatment of Individuals with a History of Penicillin or Cephalosporin Allergy or Macrolide Allergy

Beta-lactams, which include penicillins and cephalosporins (such as cefixime and ceftriaxone), are generally very safe and only a small number of patients who are told that they have a penicillin allergy will have any reaction if they take one of these drugs. The estimated rate of severe reactions to the administration of a cephalosporin to an individual with a history of a penicillin allergy are between 0.0001% and 0.1%.^{92,93}

Patients with a history of a severe reaction to penicillin (defined as risk of anaphylaxis) or any allergic reaction to the cephalosporins should be prescribed a non-cephalosporin based regimen for any suspected or confirmed gonorrhea infection. Therapies to consider in this context include gentamicin 240 mg in two separate 3-mL IM injections of 40 mg/mL plus azithromycin 2 g PO, gemifloxacin 320 mg PO plus azithromycin 2 g PO or azithromycin 2 g PO monotherapy (Figure 8),⁸⁴ both of which require a test of cure. Dual therapy is the strong preference.

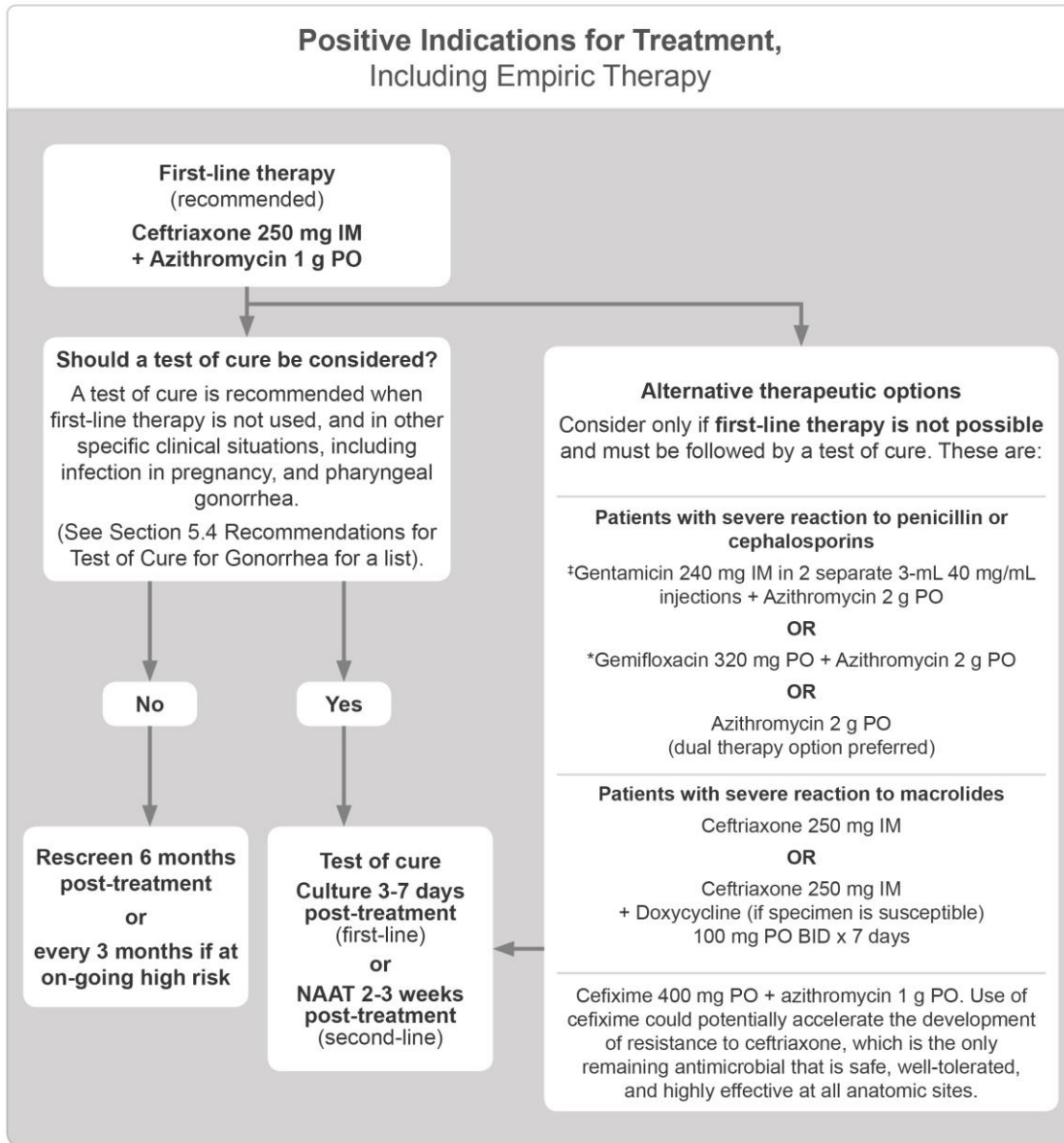
Patients with a history of allergy to macrolides such as azithromycin should be prescribed a non-macrolide-based regimen for any suspected or confirmed gonorrhea infection. An alternative therapeutic option in the case of macrolide allergy is ceftriaxone 250 mg IM monotherapy, followed by a test of cure.^{10,14,80,85,94} Doxycycline 100 mg PO BID x seven days plus ceftriaxone 250 mg IM is an alternative treatment option in the context of macrolide allergy, only if a specimen culture indicates sensitivity to doxycycline. Both of these treatments require a test of cure.

In addition to receiving a safe and effective treatment option, it is recommended that any patient with a reported penicillin, cephalosporin or macrolide allergy be referred to a drug allergy clinic or allergist for assessment.

4.6 Treatment of Individuals with Pharyngeal Gonorrhea

Pharyngeal infections present a more challenging treatment dilemma and several cases of clinical failure with the use of cefixime, ceftriaxone and azithromycin have been described.^{12,47,50,95} Similarly in a review of 178 cases of pharyngeal gonorrhea from 1995 to 2007, 9% of these infections had evidence of ongoing infection at test of cure.⁷⁵ The MICs were not provided in all of these studies, but several of the case reports suggest that pharyngeal infection treatment failures can occur even among susceptible strains, possibly due to poor drug penetration in the pharynx and transfer of genetic material between *Neisseria* species in the pharynx that are resident and *N. gonorrhoeae*, leading to reduced susceptibility.^{11,12,43,48-50,74,75,96,97} Test of cure is therefore recommended for pharyngeal gonorrhea.

Figure 6. Treatment algorithm



Note:

Treatment of **clinical failures** if first line therapy was used should include a higher dose of ceftriaxone and azithromycin (1 g ceftriaxone IM + 2 g azithromycin PO) given at the same visit and a test of cure using culture at three to seven days post-treatment. If first line treatment is not used initially, first line treatment should be used.

‡If IM is not feasible, gentamicin 240 mg intravenous (IV) infused over 30 minutes is an alternative route of administration.

*Once available in the United States, will be accessible through Health Canada's Special Access Program.

5. Follow-Up of Gonorrhea Cases and Contacts

Summary

Reporting

- Gonorrhea is a [Disease of Public Health Significance](#) (i.e., a reportable disease) in Ontario.⁹⁸ Positive gonorrhea laboratory test results are reported to the Medical Officer of Health of the health unit in which the case resides.⁹⁹
- Health care providers should **report all suspected or confirmed gonorrhea treatment failures** to the local public health unit in which the professional services were provided.⁹⁹
- The local public health unit should notify PHO of suspected or confirmed treatment failures as soon as possible to discuss any further public health action that may be required.

Contact Tracing

- A plan for contact tracing should be discussed. A 60-day trace back period should be used to identify sexual contacts for notification, or the last sexual contact if the index gonorrhea case had no sexual contacts in the last 60 days.⁵
- Sexual contacts are recommended to receive empiric treatment as soon as possible to reduce the risk of further transmission, along with appropriate STBBI testing.⁵

Test of Cure

- A test of cure is recommended when first-line therapy is not used, and in other specific clinical situations, including infection in pregnancy and pharyngeal gonorrhea (see [full list of indications for test of cure](#)).
- Culture is the first-line testing method for test of cure for gonorrhea and should be performed **three to seven days post-treatment**.⁵ If culture is not locally available, NAAT is a second-line option for test of cure, but should be performed two to three weeks post-treatment.⁵

Re-Screening

- Gonorrhea cases should be re-screened **six months** after treatment. If re-screening at six months is not possible, cases should be re-screened when they next seek medical care within the next 12 months.
- For individuals at ongoing risk for STBBI, consider screening for gonorrhea, chlamydia, syphilis and HIV at three-month intervals.

Prevention

- Strategies for the primary prevention of gonorrhoea, including counselling and risk reduction strategies, can be found in the CGSTI; the Canadian Public Health Association's Discussing Sexual Health, Substance Use and STBBI; and, the CDC Sexually Transmitted Diseases Treatment Guidelines.^{5,6,100}

5.1 Reporting and Notification

Gonorrhoea is a disease of public health significance in Ontario.⁹⁸ Pursuant to Section 29 (1) of the *Health Protection and Promotion Act* (1990),⁹⁹ the operator of a laboratory is required to notify the medical officer of health of the health unit in which the person from whom the specimen was taken resides. Each case of a positive laboratory finding in respect to a disease of public health significance must be reported as soon as possible after the making of the finding. Physicians and identified health care providers are also required under Section 25 (1) of the *Health Protection and Promotion Act* (1990) to report to the Medical Officer of Health of the health unit for the jurisdiction which the professional services are provided any patients (except for patients receiving hospital care who are reported by the hospital) that they believe have a disease of public health significance.^{5,99} Once notified of a Disease of Public Health Significance, such as gonorrhoea, local boards of health are often able to assist with contact tracing and referrals for evaluation, testing, treatment and education. PHAC notes that case finding and contact tracing are critical to maintaining control of gonococcal infections; as a result, such infections are reportable across the country.

5.2 Reporting of Clinical Failures

Gonorrhoea treatment failures are defined as individuals with confirmed gonorrhoea who are treated, but have a positive test of cure (culture or NAAT), taken at the correct interval post-treatment (three to seven days for culture and two to three weeks for NAAT) in the absence of risk of reinfection (i.e. patient denies potential sexual re-exposure).¹⁰¹

Health care providers should report all suspected or confirmed gonorrhoea treatment failures to their local public health unit.

Once a local health unit has been notified of a suspect or confirmed case of gonorrhoea treatment failure, the local public health unit should work with the responsible health care practitioner to complete the PHO enhanced surveillance form for gonorrhoea clinical failures (available from the PHO Communicable Disease Unit, cd@oahpp.ca). The local health unit should notify PHO of the suspected or confirmed clinical failure as soon as possible to discuss any further clinical and public health action that may be required.

5.3 Recommended Testing and Treatment of Sexual Contacts

All individuals who have had sexual contact with the index case within 60 days prior to symptom onset or date of specimen collection should be notified for the purposes of evaluation, testing, and treatment. If the index case had no sexual contacts during the 60-day trace-back period, the last sexual contact should be notified.

It is recommended that sexual contacts of cases should be evaluated, counselled, tested and treated for gonorrhoea and other STBBI as appropriate. Regardless of clinical findings and without waiting for the test results, the sexual partners are recommended to receive empiric treatment as per the treatment recommendations as soon as possible to reduce the risk of further transmission. For sexual contacts of cases, the recommended testing method is as per Figures 4 or 5, as appropriate (algorithms for testing symptomatic and asymptomatic individuals).

5.4 Recommendations for Test of Cure for Gonorrhoea

The CGSTI list of circumstances in which a test of cure is particularly recommended includes, but is not limited to the following:⁵

- First-line treatment is not used.
- Pharyngeal infection
- Pregnancy
- Suspected or confirmed gonorrhoea clinical treatment failure or sexual contact of a suspected or confirmed clinical failure.
- Infection with *N. gonorrhoeae* with reduced susceptibility to the cephalosporins (defined as an ceftriaxone or cefixime MIC of ≥ 0.12 $\mu\text{g}/\text{mL}$ based on culture results) or sexual contact of person infected with *N. gonorrhoeae* isolate with reduced susceptibility to the cephalosporins.
- Treatment failure has occurred previously.
- There is a re-exposure to an untreated partner after treatment.
- PID or disseminated gonococcal infection is diagnosed.
- Women receiving a therapeutic abortion who are positive for a diagnosis of gonorrhoea and therefore at increased risk of PID.
- Children <12 years of age

Test of cure is reported to be one of the most effective strategies to prevent increased gonorrhea prevalence due to antimicrobial resistance.¹⁰² For test of cure, regardless of presence or absence of symptoms, the first-line testing method is culture. Test of cure using culture should be performed three to seven days post-treatment. If culture is not locally available, NAAT is a second-line option, but should be performed two to three weeks post-treatment.

5.5 Recommended Repeat Testing/Re-screening of Individuals Diagnosed With Gonorrhea

The CGSTI recommends re-screening for all who are diagnosed with gonorrhea six months after treatment, as they are at high risk for a reinfection, which is supported by the Ontario data.⁵ If re-screening at six months is not possible, cases should be re-screened when they next seek medical care within the next 12 months.

For individuals at on-going risk of STBBI based on local epidemiology and sexual behaviours, consider screening for gonorrhea, chlamydia, syphilis and HIV at three-month intervals.

From 2008 to 2012, 11% of gonorrhea cases in Ontario reported at least one prior infection within the same five-year period. Of the repeat infections, 16% occurred between one and three months of the initial infection, 37% occurred between one and six months, with 61% of repeat infections occurring between one month and less than one year of the initial infection. Males accounted for 61.8% of repeat infections and of males with repeat infection who reported risk factors, 51.8% identified sex with same sex (e.g. MSM).

Conclusion

The Ontario Gonorrhoea Testing and Treatment Guide, 2nd Edition, 2018 was completed primarily to address changes to the availability of antibiotics used to treat gonorrhoea in Ontario, as well as changes in antimicrobial susceptibility patterns of *N. gonorrhoeae* isolates in Ontario. The second edition prioritized updating the evidence on laboratory diagnosis and treatment of uncomplicated anogenital and pharyngeal gonorrhoea. This document is guided by a testing, screening and treatment approach based on the shared clinical and public health goals to facilitate access to appropriate laboratory diagnosis, timely and effective treatment and follow-up for cases and contacts, as well as slowing the emergence of extremely drug-resistant *N. gonorrhoeae* in Ontario. PHO recommends a first-line treatment approach similar to many international guidelines by recommending ceftriaxone 250 mg IM and azithromycin 1 g PO concurrently.^{6-8,51} In line with the WHO 2016 and CGSTI recommendations, dual therapy is recommended. Ciprofloxacin and doxycycline are not recommended as empiric therapy for gonorrhoea in Ontario due to high rates of resistance. Given the propensity of *N. gonorrhoeae* to develop antimicrobial resistance, the current treatment recommendations may be revised with larger doses or different antimicrobials in the future, as new evidence becomes available.

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Appendices

Appendix A: Reference List of Literature Used in Diagnosis and Treatment Evidence Syntheses

Methods of Gonorrhea Diagnosis

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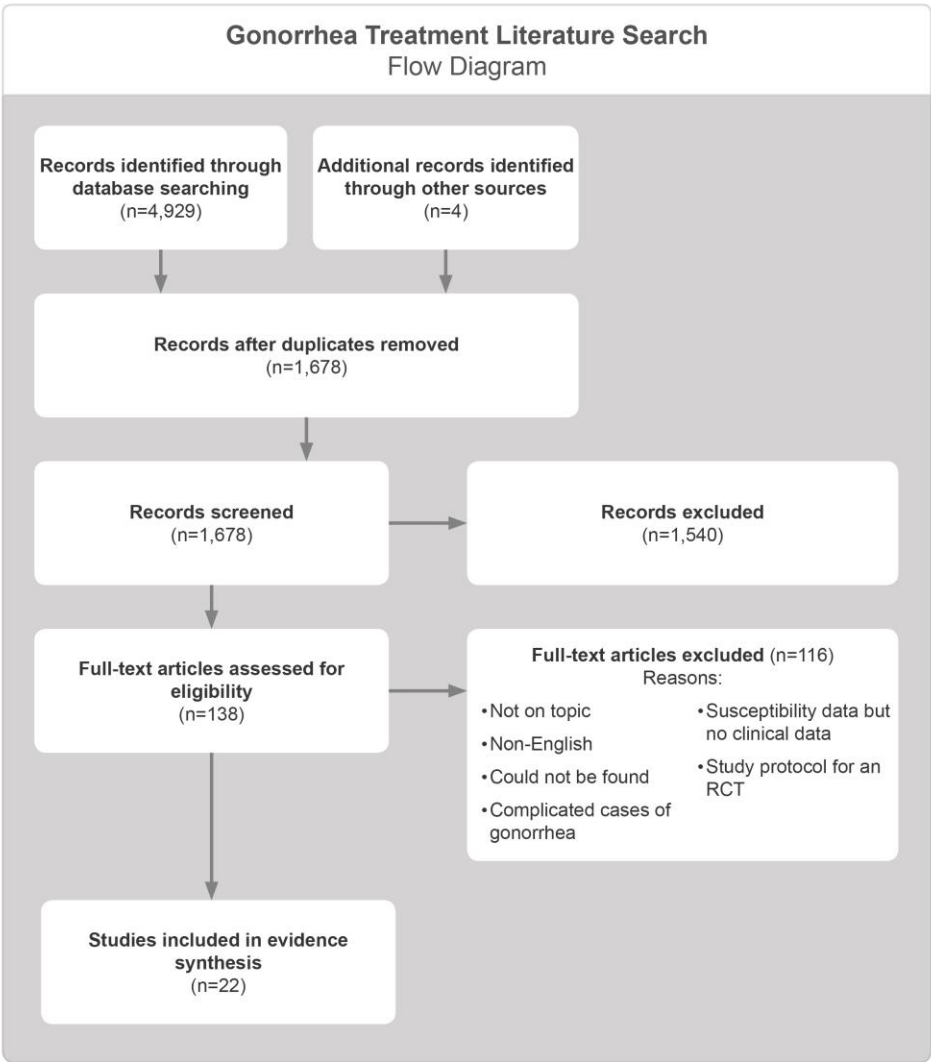
Appendix B: Sample Search Strategy for Treatment Evidence in Medline

Table 1. Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches	Results
1	exp Gonorrhea/ or Neisseria gonorrhoeae/ or gonorrh*.ti,ab,kf,kw.	24695
2	*Gonorrhea/dt or Drug Therapy/ or Anti-Infective Agents/ or Anti-Bacterial Agents/ or Drug Prescriptions/ or Prescription Drugs/ or Drug Resistance/ or Drug Resistance, Microbial/ or Drug Resistance, Bacterial/ or Drug Resistance, Multiple/ or Drug Resistance, Multiple, Bacterial/ or Gentamicins/ or Azithromycin/ or Doxycycline/ or Ceftriaxone/ or Cefixime/ or Quinolones/ or Cephalosporins/ or Tetracycline/ or Tetracycline Resistance/ or (((drug* or multidrug or multi-drug or antibiotic* or antimicrobial or anti-biotic* or anti-microbial* or anti-infective* or prescription* or prescribe* or combination) adj2 (treatment* or therapy or therapies or resist* or susceptib*)) or (gentamicin or gemifloxacin or azithromycin or doxycycline or ceftriaxone or cefixime or quinolone or cephalosporin* or tetracycline)).ti,ab,kf,kw.	876760
3	1 and 2	6918
4	3 not (Animals/ not (Animals/ and Humans/))	6820
5	limit 4 to (yr="2016 -Current" and english)	397
6	remove duplicates from 5	340

Appendix C: Flow Diagram for Gonorrhoea Treatment Literature Search

Figure 1. Flow chart of gonorrhoea treatment literature search and screening results.



Appendix D: Summary of Gonorrhoea Treatment Guidelines from Other Jurisdictions.^{5,7,8,14,84}

Table 2. Summary of gonorrhoea treatment recommendations in other jurisdictions

Resource	First-Line Treatment
Public Health Ontario, Guidelines for Testing and Treatment of Gonorrhoea in Ontario, 2013	<p>Urogenital, rectal or pharyngeal</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p>
CGSTI: Gonococcal Infections Chapter, July, 2013 & Supplement: Treatment of <i>N. gonorrhoeae</i> in response to the discontinuation of spectinomycin: Alternative treatment guidance statement, 2017	<p>Urethral, endocervical, vaginal, rectal</p> <p>Non-MSM, adults and youth ≥9 years:</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p> <p>OR</p> <p>Cefixime 800 mg PO + azithromycin 1 g PO</p> <p>MSM:</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p> <p>Pharyngeal</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p>
British Association for Sexual Health and HIV, 2011	<p>Anogenital</p> <p>Ceftriaxone 500 mg IM + azithromycin 1 g PO</p> <p>Pharyngeal</p> <p>Ceftriaxone 500 mg IM + azithromycin 1 g</p> <p>OR</p> <p>Ciprofloxacin 500 mg PO if <i>N. gonorrhoeae</i> known to be quinolone sensitive</p> <p>OR</p>

Resource	First-Line Treatment
	Ofloxacin 400 mg PO if <i>N. gonorrhoeae</i> known to be quinolone sensitive
Centers for Disease Control and Prevention, USA, 2015, Sexually Transmitted Diseases Treatment Guidelines, Gonococcal Infections	<p>Anogenital, pharyngeal</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p>
European Guidelines on the Diagnosis and Treatment of Gonorrhoea in Adults, 2012	<p>Anogenital</p> <p>Ceftriaxone 500 mg IM + azithromycin 2 g PO</p>
WHO Guidelines For the Treatment of Gonorrhoea, 2016	<p>Anogenital</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p> <p>OR</p> <p>Cefixime 400 mg PO + azithromycin 1 g PO</p> <p>OR</p> <p>Ceftriaxone 250 mg IM</p> <p>OR</p> <p>Cefixime 400 mg PO</p> <p>OR</p> <p>Spectinomycin 2 g IM</p> <p>Pharyngeal</p> <p>Ceftriaxone 250 mg IM + azithromycin 1 g PO</p> <p>OR</p> <p>Cefixime 400 mg PO + azithromycin 1 g PO</p> <p>OR</p> <p>Ceftriaxone 250 mg IM</p>

Appendix E: Antimicrobial Susceptibility for Ontario *N. gonorrhoeae* Culture Specimens, 2013 to 2017

MIC – minimum inhibitory concentration. Includes all sites of infection and isolates with unknown age and gender.

Table 3. Number and percentage of *N. gonorrhoeae* culture specimens at Public Health Ontario by ceftriaxone MIC threshold and year, 2013 to 2017

Ceftriaxone MIC	2013	2014	2015	2016	2017
≤0.03 µg/mL	91.4% (1283/1403)	94.2% (1683/1786)	91.6% (1619/1767)	96.6% (1788/1851)	97.4% (2216/2276)
0.06 µg/mL	5.3% (75/1403)	5.3% (95/1786)	6.4% (114/1767)	2.9% (54/1851)	2.5% (56/2276)
0.125 µg/mL	2.9% (41/1403)	0.4% (8/1786)	1.9% (33/1767)	0.5% (9/1851)	0.2% (4/2276)
0.25 µg/mL	0.3% (4/1403)	0.0% (0/1786)	0.1% (1/1767)	0.0% (0/1851)	0.0% (0/2276)

Table 4. Number and percentage of *N. gonorrhoeae* culture specimens at Public Health Ontario with azithromycin MIC ≥2.0 µg/mL, by year, 2013 to 2017

2013	2014	2015	2016	2017
1.3%	4.0%	3.7%	3.5%	3.5%
(18/1403)	(71/1786)	(66/1767)	(64/1851)	(80/2276)

Table 5. Number and percentage of *N. gonorrhoeae* culture specimens at Public Health Ontario by cefixime MIC threshold and year, 2013 to 2017

Cefixime MIC	2013	2014	2015	2016	2017
≤0.03 µg/mL	85.7% (1203/1403)	81.9% (1463/1786)	81.6% (1442/1767)	89.9% (1665/1851)	92.5% (2106/2276)
0.06 µg/mL	6.1% (86/1403)	8.0% (143/1786)	9.9% (175/1767)	6.7% (125/1851)	5.8% (133/2276)
0.125 µg/mL	6.1% (85/1403)	9.4% (168/1786)	5.8% (103/1767)	2.9% (54/1851)	1.4% (32/2276)
0.25 µg/mL	2.0% (28/1403)	0.6% (10/1786)	2.7% (47/1767)	0.4% (7/1851)	0.2% (5/2276)
≥ 0.5 µg/mL	0.1% (1/1403)	0.1% (2/1786)	0.0% (0/1767)	0.0% (0/1851)	0.0% (0/2276)

Table 6. Number and percentage of *N. gonorrhoeae* culture specimens at Public Health Ontario with tetracycline MIC ≥2.0 µg/mL, by year, 2013 to 2017

2013	2014	2015	2016	2017
33.8%	42.7%	55.9%	43.2%	37.0%
(474/1403)	(755/1786)	(987/1767)	(800/1851)	(843/2276)

Table 7. Number and percentage of *N. gonorrhoeae* culture specimens at Public Health Ontario with ciprofloxacin MIC \geq 1.0 $\mu\text{g/mL}$, by year, 2013 to 2017

2013	2014	2015	2016	2017
32.4%	40.8%	47.1%	46.1%	54.9%
(455/1403)	(728/1786)	(832/1767)	(853/1851)	(1249/2276)

Appendix F: Testing Instructions by Site of Specimen

Collection of Specimens:¹⁰³

CERVIX

1. Insert a speculum to view the cervix.
2. Remove overlying vaginal secretions and cervical exudate.
3. Insert a sterile swab 1 to 2 cm into the endocervical canal, rotate 180 degrees and withdraw for collection of columnar epithelial cells for diagnosis of *C. trachomatis* and *N. gonorrhoeae*.

NOTES:

- The choice of swab should be based on the type of testing being done; consult with the laboratory providing the service; and follow the swab package instruction.
- Obtain a specimen for *N. gonorrhoeae* before taking a specimen for *C. trachomatis* if culture is the testing method.
- If a culture is to be performed for *N. gonorrhoeae*, directly inoculate the culture tube or plate, or place the swab in the transport medium. If NAAT is to be performed, place the swab in a nucleic acid amplification transport tube.

Consideration: For women who have had a hysterectomy, collect first void urine or vaginal swab for NAAT.

PHARYNX

1. Swab the posterior pharynx and the tonsillar crypts.
2. Use the swab to directly inoculate the appropriate culture medium or place it in a transport medium.

NOTE: Specify that the swab should be tested for *N. gonorrhoeae* on the requisition form.

RECTUM

Specimens may be obtained blindly or through an anoscope. Specimens with stool are not acceptable; specimens without stool are easier to obtain using an anoscope which allows for direct visualization. The anoscope is preferred for symptomatic patients.

1. For blind swabbing, insert 2 to 3 cm into the anal canal.
2. If using an anoscope, use only tap water for lubrication.
3. Press laterally to avoid fecal material and, in the case of *C. trachomatis* or *N. gonorrhoeae*, to obtain columnar epithelial cells.

NOTE: If there is visible fecal contamination, discard the swab and obtain another specimen.

URETHRA

1. Warn the patient that specimen collection may be painful, that the next urination may be painful and that increasing fluid intake may help to decrease urine concentration and therefore discomfort.
2. Use a thin, swab with a flexible wire shaft. Moistening the swab with water before insertion may help reduce discomfort.
3. Introduce the swab slowly (3 to 4 cm in males), rotate slowly and withdraw gently.
4. The swab can be used to prepare a smear by slowly unrolling the secretions onto a slide; then, directly inoculate the appropriate culture medium or place the swab in a transport medium.

NOTES:

- If a NAAT is used, follow the manufacturer's instructions.
- Ideally, the patient should not have voided for at least two hours, as voiding reduces the amount of exudate and may decrease the ability to detect organisms; but having done so does not preclude testing.

Consideration: Having the patient "milk" the penis three or four times from the base to the glans enhances the ability to detect otherwise unapparent urethral discharge.

URINE (FIRST VOID)

1. Provide the patient with a sterile leak-proof container.

NOTE: The patient should not have voided for at least two hours, but having done so does not preclude testing.

2. Ask the patient to collect only the first 10 to 20 mL of urine into the container and to cap it tightly.

VAGINA

Please contact your local laboratory to enquire if vaginal NAAT is available. As of the time of writing, Public Health Ontario offers urine, cervical and extragenital NAAT, but not vaginal NAAT.

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