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Timing of Antibiotic Therapy for *Neisseria* *Gonorrhoeae* Infection

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Rapid Review

Key Messages

What Is the Issue?

- Gonorrhea is the second most prevalent sexually transmitted infection in Canada. It is caused by *Neisseria gonorrhoeae* and can be treated with antibiotic therapy. However, *N. gonorrhoeae* has developed antibiotic resistance, which may decrease the efficacy of current therapy.
- Antibiotic therapy can be administered after a positive *N. gonorrhoeae* test, but the turnaround time of laboratory testing may result in patients being lost to follow-up (i.e., not returning to the clinic after test results are available).
- Presumptive or empiric antibiotic therapy can be given before the laboratory confirmation of *N. gonorrhoeae* to individuals at high risk of gonorrhea or those with uncertain follow-up; however, such treatment may lead to overtreatment of those without *N. gonorrhoeae*, increasing the risk of antibiotic resistance and possible side effects to the individuals.
- It is important to understand the ideal timing of antibiotic therapy that balances concerns of antibiotic resistance and timely patient care.

What Did We Do?

- To inform decisions about timing of antibiotic therapy for the treatment of adults and adolescents with suspected uncomplicated *N. gonorrhoeae* infection, CADTH sought to identify and summarize literature comparing the clinical effectiveness and safety of delaying antibiotic therapy until confirmatory results of testing for *N. gonorrhoeae* infection are available, versus empiric treatment before test results are available.
- A research information specialist conducted a literature search of the peer-reviewed and grey literature published since January 1, 2013.

What Did We Find?

- We did not find any studies directly evaluating the clinical effectiveness and safety of delayed antibiotic treatment compared to presumptive treatment for uncomplicated *N. gonorrhoeae* infections in adult and adolescent populations. We included 2 nonrandomized studies that compared the rates of accurate treatment and overtreatment in individuals who received presumptive treatment and those who did not.
- In the 2 studies, *N. gonorrhoeae* test positivity rates in the presumptive treatment group were less than 50%, suggesting that less than half of the patients in this group received accurate presumptive treatment.

Key Messages

We also found high overtreatment rates, which were up to 90% in the included studies.

- The certainty of these findings is very low due to methodological limitations of the included studies.
- We also identified 5 single-arm studies that evaluated these outcomes in individuals who received presumptive therapy. The findings are generally consistent with the 2 included studies.

What Does It Mean?

- Available evidence points to high rates of overtreatment when presumptive antibiotics are given. Results also suggest that there is value in clinical assessment in detecting *N. gonorrhoeae* infections. The downstream clinical effectiveness implications of these results for antimicrobial resistance or increasing spread of *N. gonorrhoeae* are unclear.
- Contextual factors, such as the local prevalence of *N. gonorrhoeae* infection and potential barriers to care that could hinder post-test follow-up for certain individuals or groups, may also be useful considerations when making decisions about appropriate timing for *N. gonorrhoeae* antibiotic therapy.

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Abbreviations

CDC	Centers for Disease Control and Prevention
NAAT	nucleic acid amplification test
STI	sexually transmitted infection

Context and Policy Issues

What Is *Neisseria Gonorrhoeae* Infection?

Gonorrhea is a sexually transmitted infection (STI) caused by the bacterium *Neisseria gonorrhoeae*.¹ It is the second most reported bacterial STI in Canada.² In 2020, there were about 81 new cases per 100,000 individuals living in Canada; 63% of these cases were reported in male patients, and 37% of cases were reported in female patients.³ Uncomplicated gonorrhea infections are urogenital, anogenital, pharyngeal, and ocular gonococcal infections that are not associated with bacteremia or ascending spread of the pathogen to other organs.¹ Untreated gonorrhea can lead to serious complications regardless of the presence or severity of symptoms, such as epididymitis and pelvic inflammatory disease.¹

Accurate and timely gonorrhea case identification based on symptoms may be challenging because the symptoms may overlap with other disorders such as chlamydia (caused by *Chlamydia trachomatis*),⁴ which is the most common STI in Canada.³ For example, both gonorrhea and chlamydia can have genital or extragenital symptoms.⁴ Symptoms in female individuals (e.g., dysuria and increased vaginal discharge) are often mild and could be mistaken for a bladder or vaginal infection.⁵ Moreover, some people may have asymptomatic gonorrhea. For example, about 10% of gonococcal urethritis cases in males⁶ and nearly half of cervicitis cases in females caused by gonorrhea are asymptomatic.⁷ Asymptomatic rectal and pharyngeal infections are also common in males and females.⁸

What Is the Current Practice?

Suspected *N. gonorrhoeae* infection can be confirmed by microscopy of Gram-stained samples, bacterial cultures, or nucleic acid amplification tests (NAATs).¹ NAATs are highly sensitive for *N. gonorrhoeae*, but it may generate false-positive results due to potential cross-reaction with *Neisseria meningitidis* or other *Neisseria* species.⁹

All confirmed gonorrhea cases should be treated with antibiotics.¹⁰ However, gonorrhea has developed resistance to previously recommended treatment options including sulfonamides, penicillins, earlier generation cephalosporins, tetracyclines, macrolides, and fluoroquinolones.¹¹ Due to the potential risk of further antimicrobial resistance, the Public Health Agency of Canada currently recommends a combination antibiotic treatment of a third-generation cephalosporin (e.g., ceftriaxone, cefixime) plus either azithromycin or doxycycline, preferably given in a single dose.¹⁰ As azithromycin can be given in a single dose (thereby improving treatment adherence) and is effective against *C. trachomatis* infections, it is preferred over doxycycline.¹⁰ The 2020 Centers for Disease Control and Prevention (CDC) treatment guidelines for *N. gonorrhoeae* infection recommend a single 500 mg intramuscular dose of ceftriaxone. Combination therapy with doxycycline is recommended when *C. trachomatis* infection cannot be ruled out.¹²

In Canada, it is recommended to treat all confirmed cases, and to consider treatment in suspected cases, such as individuals at high risk of infection (e.g., partners of known cases, equivocal Gram stain results) or in those individuals with uncertain availability for follow-up.¹⁰

What Are Delayed and Presumptive Antibiotic Therapies?

Delayed antibiotic therapy refers to administering antibiotics only after the test results confirm the existence of *N. gonorrhoeae*. Laboratory testing for *N. gonorrhoeae* usually has a turnaround time of several days. For example, the turnaround time for NAATs is up to 3 days¹³ and for *N. gonorrhoeae* culture is up to 5 days from receipt at the Public Health Ontario laboratory.¹³ This turnaround time may result in delayed treatment and increase patient loss to follow-up (i.e., not returning to the clinic after test results are available). It could also result in spread to sexual partners in the meantime and pose a risk of developing complications (e.g., pelvic inflammatory disease and infertility in females), if left untreated.¹⁴

Presumptive or empirical antibiotic treatment refers to treating suspected *N. gonorrhoeae* infections with antibiotics before a positive laboratory test. This approach could lead to overuse of antibiotics contributing to antimicrobial resistance, and unnecessary adverse events in individuals who do not actually have an *N. gonorrhoeae* infection.

Why Is It Important to Do This Review?

Amid growing concerns of antimicrobial resistance globally, there is high interest in antimicrobial stewardship that promotes coordinated interventions to improve the judicious use of antibiotics including selection, dose, and duration of therapy. Considering increasing incidence of *N. gonorrhoeae* infection Canada,¹⁵ a focus on appropriate and effective treatment strategies, as well as a balance between unwanted treatments and timely patient care are important.

This same-day presumptive treatment could help avoid treatment delays, and minimize patient loss to follow-up.¹⁴ On the other hand, there are concerns that the presumptive treatment approach may lead to overtreating uninfected individuals, increasing the risk of adverse events such as allergic reactions¹⁴ and antibiotic resistance.^{16,17} It is unclear whether or not delaying antibiotic therapy until confirmatory results of testing are available may have better clinical effectiveness and safety outcomes compared to empiric treatment before test results are available.

Objective

We prepared this Rapid Review to summarize and critically appraise the evidence identified from medical databases and grey literature regarding clinical effectiveness of delayed antibiotic treatment compared to empiric or presumptive treatment for uncomplicated *N. gonorrhoeae* infection.

Research Question

What is the clinical effectiveness and safety of delaying antibiotic therapy until after confirmatory results of testing for *N. gonorrhoeae* infection are available versus empiric or presumptive treatment before test results are available in adults and adolescents with suspected uncomplicated *N. gonorrhoeae* infection?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE via Ovid, Embase via Ovid, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) via EBSCO, the Cochrane Database of Systematic Reviews, the International HTA Database, and the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were gonorrhoea (*N. gonorrhoeae*) and at least 1 synonym for either delayed treatment or presumptive treatment. No filters were applied to limit the retrieval by study type. Conference abstracts were excluded from the search results. Where possible, retrieval was limited to the human population. The search was completed on December 1, 2023, and limited to English-language documents published since January 1, 2013.

Selection Criteria and Methods

One reviewer screened citations and selected studies. Titles and abstracts were reviewed in the first round of screening and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in [Table 1](#).

Table 1: Selection Criteria

Criteria	Description
Population	Adults and adolescents with suspected uncomplicated <i>Neisseria gonorrhoeae</i> infection, including partners of symptomatic individuals
Intervention	Delayed antibiotic therapy administered after confirmatory results of testing for <i>N. gonorrhoeae</i> infection are available
Comparator	Antibiotic therapy administered immediately with no initial definitive test results (i.e., empiric therapy, presumptive therapy)
Outcomes	Clinical effectiveness and safety (e.g., clinical cure, microbiological cure, medication adherence, unnecessary or inappropriate treatment, proportion of patients lost to follow-up, quality of life, harms [e.g., adverse events, allergic reactions, bacterial resistance])
Study designs	Randomized controlled trials, nonrandomized studies

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in [Table 1](#), they were duplicate publications, or they were published before 2013.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tool as a guide: the Downs and Black checklist¹⁸ for randomized and nonrandomized studies. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 688 citations were identified in the literature search. Following screening of titles and abstracts, 661 were excluded, and 27 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of the potentially relevant publications, 26 publications were excluded for various reasons. This report includes 2 nonrandomized studies.^{19,20} Study selection details are presented in [Appendix 1](#).

We also identified 5 noncomparative single-arm studies.²¹⁻²⁵ While these studies did not meet study design eligibility criteria for this report and were not formally included, they provided content relevant to the research question. The characteristics and findings of the single-arm studies are summarized in [Appendix 5](#).

[Appendix 6](#) presents additional references of potential interest related to *N. gonorrhoeae* and *C. trachomatis* screening and treatment. These additional studies include a previous CADTH report, single-arm studies of mixed populations with *N. gonorrhoeae* and *C. trachomatis* infection, review articles, and studies investigating perspectives of providers and patients.

Summary of Study Characteristics

We included 2 nonrandomized studies in this report.^{19,20} While we did not identify any studies that reported between-group statistical comparisons of delayed antibiotic treatment versus presumptive antibiotic therapy, the 2 included studies^{19,20} provided some relevant information about individuals who received presumptive treatment and those who did not.

One of the studies included patients tested for *C. trachomatis* or *N. gonorrhoeae* infections.¹⁹ Relevant to the current report, we have summarized the characteristics and findings related to the *N. gonorrhoeae* infections in the following sections. Additional details regarding the included publications are provided in [Appendix 2](#).

Study Design

The study by Shover et al. (2018)²⁰ was a cross-sectional study of medical records. Wilson et al. (2017)¹⁹ conducted a prospective cohort study as a part of a noninferiority trial comparing 2 diagnostic tests for *C. trachomatis* and *N. gonorrhoeae* infections.

Study Settings and Country of Origin

Both studies were conducted in the US.^{19,20}

Data for the study by Shover et al. (2018)²⁰ was collected from a community-based organization that provides services, including STI testing and treatment, to members of 2SLGBTQ+ communities. The study by Wilson et al. (2018)¹⁹ was conducted in an emergency department of an urban academic medical facility. The study periods for the studies were from 2015^{19,20} to 2016.¹⁹

Patient Population

Shover et al. (2018)²⁰ enrolled cisgender adult men who have sex with men (MSM) [wording from original source] who were tested for gonorrhea of the urethra, rectum, and/or pharynx. The units of analysis were patient clinic visits (hereafter reported as patients or participants in this report). Altogether, 9,141 visits (for 6,756 unique patients) were included in the study. They ranged from asymptomatic individuals with exposure to gonorrhea to those presenting with clinical signs and symptoms of *N. gonorrhoeae* infection. Most of the visits were by patients aged 30 years or older who identified as gay or homosexual [wording from original source]. The most commonly reported clinical feature was genitourinary symptoms (11% of visits), and about 11% were asymptomatic contacts.

Wilson et al. (2017)¹⁹ included all patients (at any age) who tested for suspected *C. trachomatis* or *N. gonorrhoeae* infection. A total of 1,162 patients were included in the study, of which 96% (n = 1,112) were female and 4% (n = 50) were male. Among them, 30% were pregnant (n = 338). The mean age of patients was 26 years (standard deviation [SD] not reported). For each patient, presence of symptoms and signs such as dysuria or urethral or vaginal discharge, cervicitis, or uterine tenderness on exam were assessed; however, no data were reported. About 4% of the patients were asymptomatic.

Interventions and Comparators

Both studies reported outcomes in patients who received presumptive antibiotic treatment and those who did not.^{19,20}

Presumptive Antibiotic Therapy

In the study by Shover et al. (2018),²⁰ empiric or presumptive antibiotic treatment was given according to CDC's gonorrhea treatment guidelines of 2015 (dual therapy of azithromycin and ceftriaxone). They were given to patients with clinical signs and symptoms of *C. trachomatis* or *N. gonorrhoeae* infection and to those with known exposure. Patients with pharyngitis, who reported condomless oral sex with a partner of unknown STI status were also given the presumptive antibiotic treatment. The details of presumptive antibiotic therapy were not reported in the second study.¹⁹

No Presumptive Antibiotics

The comparator group in both studies consisted of patients who did not receive presumptive antibiotic treatments.^{19,20} Neither study described the number of patients who received delayed treatment within that group.

In the study by Shover et al.,²⁰ the comparator group included patients who tested positive and received subsequent delayed treatment, as well as those who tested negative. The proportion of patients who received the delayed treatment was not reported.

Patients in the study by Wilson et al.¹⁹ were not followed beyond the emergency department encounter to determine if those who tested positive for *N. gonorrhoeae* in this group had subsequent follow-up or delayed treatment.

Testing Method

Both studies used NAATs to detect possible *N. gonorrhoeae* infection.^{19,20} While urethral, rectal, and pharyngeal swabs were collected in 1 study,²⁰ cervical or urethral swabs were used in the other.¹⁹

Outcomes

Outcomes assessed in the 2 nonrandomized studies included:

- accurate presumptive treatment,^{19,20} defined as the proportion of presumptively treated patients who tested positive for *N. gonorrhoeae*
- overtreatment,¹⁹ defined as the proportion of patients with presumptive treatment who tested negative for *N. gonorrhoeae*
- missed treatment,¹⁹ defined as the proportion of patients without presumptive treatment who tested positive for *N. gonorrhoeae*.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in [Appendix 3](#).

The study objectives and methods were clearly described in both studies.^{19,20} The outcomes of interest were described along with their definitions, which were appropriate. Patients in both intervention and control groups were recruited from the same population and over the same period of time. All eligible visits during the study periods were included in the studies, without any sampling.

The included studies had several important limitations that could lower the internal and external validity of the results.^{19,20} Because both studies were observational studies (retrospective chart review²⁰ and prospective observational¹⁹), no randomization of patients was performed. Patients were grouped based on the intervention received, as per the clinical assessment by the health care providers. Thus, treatment and comparator groups were not similar at baseline, making between-group comparison of outcomes challenging. There was no blinding of the patients or the researchers measuring the outcomes. However, because the intervention and outcome measures were objective, the effect of this limitation on the results could be minimal. Another major limitation of the studies was in how the comparator group was defined. In both studies, patients who were not given the presumptive antibiotic treatment were grouped into the control group. However, it was unclear how many patients within that group went on to receive delayed treatment, were lost to follow-up and treatment, or tested negative. In the study by Shover et al.,²⁰ the unit of analysis in the study was “visits,” rather than individual patients. If an individual had multiple visits, they would be considered as separate patient visits and thus counted multiple times. There were 9,141 visits by 6,756 individuals included in the study. It was unclear if individuals who attended the clinic multiple times for the same episode of infection were counted separately. The outcomes relevant to the current report were descriptive, except for the *N. gonorrhoeae* test positivity rate outcome. Effect estimates or confidence

intervals were not reported in the comparative results relevant to the current report. Regional prevalence of *N. gonorrhoeae* was not accounted for in either study while interpreting the findings.^{19,20}

Accuracy of presumptive treatment was an outcome of interest in both studies.^{19,20} The studies defined it as the proportion of patients who received presumptive treatment and tested positive for *N. gonorrhoeae*. The “accuracy” was estimated based on NAAT results of samples collected from the patients. The sensitivity and specificity of NAATs were not factored in while measuring the accuracy of treatment. Because NAATs may have false-positive results,²⁶ it is possible that the true accurate treatment rates could be lower than what was measured in the studies.

As for the external validity of the results, in the Wilson et al. study,¹⁹ it was unclear whether patients were representative of the recruited population. The study was conducted among the patients of a larger study that required urine samples. Patients who did not provide a urine specimen were excluded from the larger trial and therefore not included in the Wilson et al. study.¹⁹ It is unclear how many were excluded for this reason, and whether the excluded patients were systematically different from the study participants.¹⁹ Additionally, 96% of the study population were female,¹⁹ whereas in Canada, more than half of newly diagnosed *N. gonorrhoeae* cases are in males.²

In both studies, it was unclear whether the staff, locations, and facilities where the patients were treated were representative of the treatment most patients receive.^{19,20} One was conducted in a sexual health clinic serving primarily gay men, bisexual men, and other MSM,²⁰ and the other in an urban academic emergency department.¹⁹ The former study primarily included members of the 2SLGBTQ+ community²⁷ and the setting of the latter study may not reflect clinical practice in Canada, where STI testing is mostly conducted in sexual health clinics, local public health units, and walk-in clinics, or by primary health care providers.²⁸ It was reported in the study by Shover et al.²⁰ that patients were presumptively treated based on CDC treatment guidelines at the time (2015), which were comparable to current Canadian recommendations.¹⁰ Details of the treatment given were not described in the study by Wilson et al.;¹⁹ therefore, we were unable to determine if it was generalizable to current Canadian clinical settings.

Summary of Findings

[Appendix 4](#) presents the main study findings.

Clinical Effectiveness of Delayed Antibiotic Treatment

N. Gonorrhoeae Test Positivity Rates

Shover et al.²⁰ reported that the *N. gonorrhoeae* test positivity rates in the presumptive treatment and no presumptive treatment groups were 31% and 9%, respectively. The probability of testing positive was statistically significantly higher in patients who received presumptive treatment ($P < 0.01$). However, presumptive treatment was given based on clinical assessment of signs and symptoms (in addition to the medical and sexual history), which were more prevalent in the presumptive group. For example, compared to 11% in the control group, 52% of visits in the presumptive treatment group included patients reporting genitourinary symptoms.

In the study by Wilson et al. (2017),¹⁹ 4% of total patients (n = 52 out of 1,162) were *N. gonorrhoeae*-positive. Among female patients, the test positivity rates were 8% and 1% in the presumptive treatment and no presumptive treatment groups, respectively. While 9% of male patients and 7% of pregnant patients who received presumptive treatment were *N. gonorrhoeae*-positive, no male or pregnant patients who did not receive same-day treatment had positive test results.

Accurate Presumptive Treatment

Accurate presumptive treatment was defined in the studies as the proportion of patients who tested positive for *N. gonorrhoeae* among all the patients who received presumptive treatment.

Across the included studies,^{19,20} the accurate presumptive treatment rate varied. It was 31% in the study by Shover et al.,²⁰ while in the Wilson et al. study,¹⁹ it was 8% for male patients and 9% for female patients. Among patients who were pregnant, 7% who received presumptive treatment were *N. gonorrhoeae*-positive.²⁰

Overtreatment

Overtreatment was defined in the studies as the proportion of patients who received presumptive treatment but tested negative in the laboratory test.

Results from the study by Wilson et al.¹⁹ showed that most of the patients who received presumptive treatment tested negative for *N. gonorrhoeae*, and were thus overtreated. The unnecessary treatment rates were 91% in males, 92% in females, and 93% in individuals who were pregnant.

Missed Treatment

Missed treatment was defined in 1 included study¹⁹ as the population who did not receive presumptive treatment but tested positive. It constituted the subset of patients in the “no presumptive treatment” group who tested positive.

In the Wilson et al. study,¹⁹ missed treatment rates were low. Out of 640 female patients who did not receive presumptive treatment, 1% (n = 9) tested positive for *N. gonorrhoeae* and therefore missed treatment, as per the study definition. Since the patients were not followed up, it is unknown whether these patients received subsequent treatment based on their lab results. There were no male or pregnant patients in the “no presumptive treatment” group who tested positive.

Limitations

In the absence of studies that specifically compared delayed antibiotic treatment to presumptive antibiotic treatment, we included studies that compared presumptive treatment with no presumptive treatment. While the “no presumptive treatment” group could include the subset of patients who received “delayed treatment,” the studies included in this review did not provide information about this subset. No randomized studies were identified. None of the included studies evaluated key clinical effectiveness outcomes such as time to treatment, clinical cure, or quality of life, and focused instead on outcomes that related to *N. gonorrhoeae*

test result proportions in various subsets of the study populations. No safety outcomes were reported. We did not identify specific evidence regarding the effectiveness of delayed or presumptive treatment in the adolescent population. Apart from the methodological limitations of the included studies, as described in the Summary of Critical Appraisal section, the external validity of results was low. Both studies were conducted in the 2015 to 2016 period, and 1 study reported that their presumptive treatment was based on the CDC guidelines from 2015. The guidelines have since changed in the US. Moreover, since none of the studies were conducted in Canada, the generalizability to current Canadian clinical settings is unclear.

Conclusions and Implications for Decision- or Policy-Making

Summary of Evidence

This report aimed to summarize the evidence regarding the clinical effectiveness and safety of delayed antibiotic treatment compared to presumptive or empiric antibiotic treatment among adults and adolescents with suspected uncomplicated *N. gonorrhoeae* infection. We included 2 nonrandomized studies^{19,20} that provided rates of *N. gonorrhoeae* test positivity, accurate presumptive treatment, and overtreatments or undertreatments among groups of patients that either received presumptive treatment or no presumptive treatment. We also identified 5 single-arm studies²¹⁻²⁵ that reported similar outcomes in presumptively treated patients and have summarized them separately in [Appendix 5](#).

We did not identify comparative evidence (randomized or nonrandomized) regarding relevant clinical effectiveness outcomes such as clinical cure, time to treatment, medication adherence, and quality of life, or safety outcomes between presumptive treatment and delayed antibiotic treatment. We did not identify specific evidence regarding the effectiveness of delayed or presumptive treatment in the adolescent population.

The test positivity rates were numerically higher in the presumptive treatment group than in the no presumptive treatment group,^{19,20} suggesting that the clinical assessment of signs and symptoms, as well as an assessment of medical and sexual history, is helpful in identifying possible *N. gonorrhoeae* infections. The positive predictive value of clinical assessment was estimated as high as 56% for genitourinary signs ([Table 5](#)).²⁰ However, it should be noted that the positive predictive value of a diagnostic test or clinical assessment is linked to population prevalence of *N. gonorrhoeae* in the population. In the 2 included studies,^{19,20} the proportion of patients who were given presumptive treatment and tested positive for *N. gonorrhoeae* infection (i.e., accurate treatment rates) was reported as less than 10%¹⁹ or 31%,²⁰ suggesting that less than half individuals who received presumptive treatment for NG actually required it. In the single-arm studies, the accurate treatment rates similarly ranged from 0%²³ to 46.1%.²⁵ One included study reported overtreatment rates of 90%.¹⁹ The rates of overtreatment were higher across the single-arm studies as well (68%²⁵ to 100%²³). While interpreting these results, it should be noted that factors such as the regional prevalence of *N. gonorrhoeae* and the diagnostic accuracy of NAATs were not considered in the studies. It is possible that some results were false positives or false negatives, lowering the validity of the results. Furthermore, it was unclear from some studies whether the patients had other STIs with similar clinical

presentation (such as *C. trachomatis*) warranting presumptive treatment, as per the guidelines at the time of the studies.

Among the patients who did not receive presumptive antibiotic treatment, the positivity rates were reported as less than 1%¹⁹ and 9%.²⁰ While these studies did not further report on outcomes in patients in the no presumptive treatment group, we identified 1 single-arm study²² reporting that, out of 31 individuals who did not receive presumptive treatment but subsequently tested positive for *N. gonorrhoeae* infection, 41.9% (n = 13) did not receive treatment.¹⁹

Implications for Clinical Practice

In individuals with suspected uncomplicated *N. gonorrhoeae* infection, the limited evidence identified for this report suggests that overtreatment rates are high. The test positivity rates in the presumptively treated group were numerically higher than in those not presumptively treated, highlighting the value of clinical assessment in detecting *N. gonorrhoeae* infections. However, the implications of these observations on clinical effectiveness downstream remains undetermined. There is a lack of comparative evidence comparing clinical outcomes between delayed antibiotic treatment and presumptive antibiotic treatment. The subsets of those who received delayed treatment within the no presumptive treatment groups were not reported in the studies.^{19,20} Overall, due to the methodological limitations in the available studies (e.g., no between-group statistical comparisons, descriptive results only, insufficient details about the treatment given), the certainty of the evidence is very low.

In the absence of clear clinical effectiveness evidence, prevalence of *N. gonorrhoeae* infections, and the facilitators and barriers to accessing timely testing, treatment, and follow-up as needed, are important decision-making factors. It is important to balance the concerns about antimicrobial resistance and possible adverse effects of unwanted treatment in suspected individuals, as well as the repercussions of not providing timely care to those who need it. Development of accurate point-of-care diagnostic tests could alleviate some of these concerns by eliminating the time between testing and treatment.²⁹

Considerations for Future Research

Well-designed cohort studies with adequate follow-up periods could investigate potential harms associated with delayed treatment – such as missed treatment, loss to follow-up, and spread to contacts – and those of presumptive treatment, such as adverse events and antibiotic resistance. Research focused on equity-deserving groups who may face barriers in accessing follow-up treatments is important.

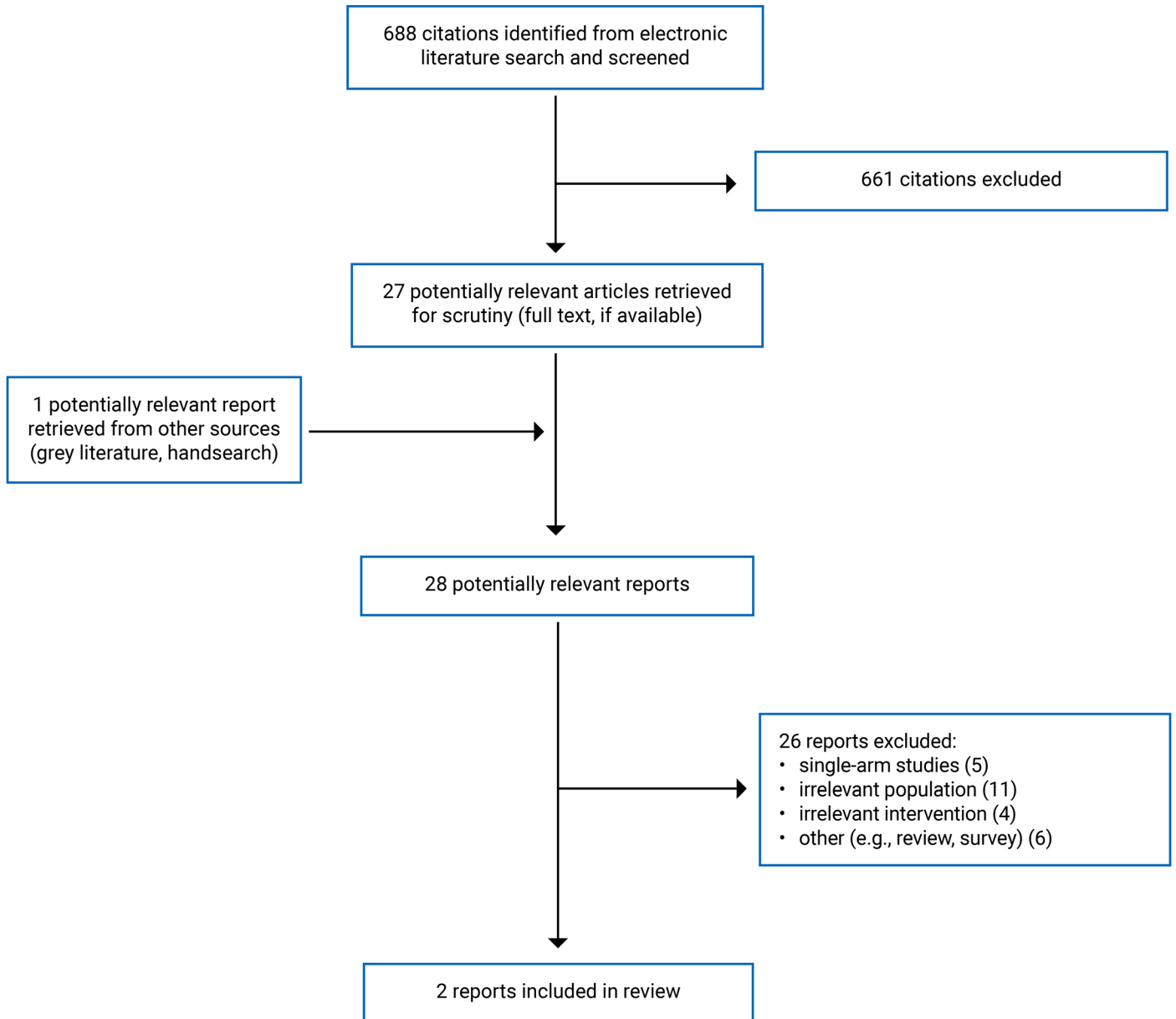
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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design, setting	Population characteristics	Intervention and comparator, testing method	Clinical outcomes
Shover et al. (2018) ²⁰ Country: US Funding source: University of California, Los Angeles Postdoctoral Fellowship Training Program, National Institutes of Health/ National Institute of Allergy and Infectious Diseases	Cross-sectional study of medical records Setting: A community-based organization, between February and July 2015	Cisgender MSM (aged 18 years or older) tested for gonorrhea of the urethra, rectum, and/or pharynx (The units of analysis were visits.) Total number of visits, N = 9,141 (for 6,756 unique patients) Presumptive treatment, n = 1,677 visits (for 1,514 unique patients) No presumptive treatment, n = 7,464 ^a visits Age in years, n (%): <ul style="list-style-type: none"> • < 25: 1,723 (19) • 25 to 29: 2,540 (28) • 30 to 39: 2,829 (31) • 40 or older: 2,049 (22) Race/ethnicity, ^b n (%): <ul style="list-style-type: none"> • White: 4,315 (47) • Hispanic: 2,861 (31) • Black or African American: 727 (8) • Other: 1,231 (13) • Unknown/unreported: 7 (0.1) Sexual orientation, n (%): <ul style="list-style-type: none"> • Gay/homosexual: 7,774 (85) • Bisexual: 1,129 (12) • Other: 218 (2) • Unknown/unreported: 20 (0.2) • Signs/symptoms at visits,^c n (%) 	Intervention: Presumptive same-day antibiotic therapy (dual therapy of azithromycin and ceftriaxone), based on clinical assessment Comparator: No presumptive treatment (wait for lab results and treatment determined accordingly) All patients were asked to provide self-collected rectal and urine samples for gonorrhea and chlamydia testing. Pharyngeal samples were collected by clinical staff Testing method: NAAT performed using APTIMA Combo 2 assay	Accurate presumptive treatment (proportion of presumptively treated patients who tested positive), PPV of treating <i>N. gonorrhoeae</i> infection based on clinical assessment

Study citation, country, funding source	Study design, setting	Population characteristics	Intervention and comparator, testing method	Clinical outcomes
		<ul style="list-style-type: none"> • Genitourinary signs: 234 (3) • Genitourinary symptoms: 964 (11) • Rectal signs: 20 (0.2) • Rectal symptoms: 177 (2) • Pharyngitis: 77 (1) • Asymptomatic: 992 (11) 		
Wilson et al. (2017) ¹⁹ Country: US Funding source: No funding source	Prospective observational study, some as part of a noninferiority trial comparing 2 diagnostic tests for <i>C. trachomatis</i> and <i>N. gonorrhoeae</i> . Setting: Level 1 trauma ED, between April 2015 and March 2016	All patients (any age) tested for <i>C. trachomatis</i> and <i>N. gonorrhoeae</i> Patients who did not provide a urine sample, or not assessed within 24 hours were excluded. Total number of participants, N = 1,162 Presumptive treatment, n = 512 (44%) Average age: 26 years Sex, n (%) All population: <ul style="list-style-type: none"> • Female: 1,112 (96%) • Male: 50 (4%) Presumptive treatment: <ul style="list-style-type: none"> • Female: 470 of 512 (91%) • Male: 42 of 512 (8.2%) Pregnant people, n (%): <ul style="list-style-type: none"> • Total population: 338 of 1,152 (30%) • Presumptive treatment: 58 of 512 (11.3%) 	Intervention: Presumptive treatment (for <i>N. gonorrhoeae</i> and <i>C. trachomatis</i>), additional details NR Comparator: No presumptive treatment ^d Testing method: NAAT (APTIMA Unisex assay) for both <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> , using cervical or urethral swabs	Accurate treatment: Defined as antibiotic treatment was given, and the patient tested positive for either infection Overtreatment: Presumptive treatment followed by negative testing Missed treatment: No presumptive treatment but tested positive for either infection

ED = emergency department; MSM = men who have sex with men; NAAT = nucleic acid amplification test; NR = not reported; PPV = positive predictive value.

Note: We have retained the original terms that study authors used when describing sex, gender, and sexual orientation.

^aThis included individuals with positive and negative test results. Those tested positive received subsequent treatment.

^bAs reported in the study.

^cAs reported in the study, categories are not mutually exclusive.

^dPatients were not followed beyond the emergency department encounter to determine if those with missed treatment had subsequent follow-up for treatment.

Note that this table has not been copy-edited.

Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 3: Strengths and Limitations of Primary Clinical Studies Using the Downs and Black Checklist¹⁸

Strengths	Limitations
Shover (2018)²⁰	
<p>The study objectives and methods were clearly described. The inclusion criteria were clearly reported and was appropriate for the study objective. The characteristics of study participants in both treatment groups were reported in detail.</p> <p>The intervention given to both treatment groups were clearly described.</p> <p>The main outcomes of interests of the study were described in the methods section. Definitions of outcomes were reported.</p> <p>Patients in both intervention groups were recruited from the same population and over the same period of time. All eligible visits during the study period were included in the study.</p>	<p>This was cross-sectional chart review study. Therefore, there was no randomization or blinding in the study.</p> <p>The unit of analysis in the study was “visits” rather than individual patients. If an individual had multiple visits, they would be considered as separate visits and thus counted multiple times. There were 9,141 visits of 6,756 individuals included in the study. It was unclear if individuals who attended the clinic multiple times for the same episode of infection were counted separately.</p> <p>The comparator group consisted of visits in which same-day presumptive treatment was not given. It was unclear whether how many of those who tested positive in that group subsequently were lost to follow-up (no treatment given).</p> <p>While main study finds were reported (including simple outcome data), most of the results were descriptive. Effect estimate, or confidence intervals were not reported in the comparative result relevant to the current report. Potential confounding factors were not identified or adjusted.</p> <p>The accuracy of treatment was estimated based on NAAT results self-collected samples from the patients. The sensitivity, and specificity of NAAT were not factored in while measuring the ‘accuracy of treatment.’ It is possible that there were false positives and false negatives, lowering the validity of the results.</p> <p>It was unclear whether the staff, places, and facilities where the patients were treated was representative of the treatment most of patients receive. The study was conducted in a sexual clinic serving primarily gay, bisexual, and other MSM. Patients were treated based on the CDC treatment guidelines at the time.</p>
Wilson et al. (2017)¹⁹	
<p>The study objectives and methods were clearly described. The inclusion criteria were clearly reported and was appropriate for the study objective.</p> <p>The intervention given to both treatment groups were clearly described.</p> <p>The main outcomes of interests of the study were described in the methods section. Definitions of outcomes were reported.</p> <p>Patients in both intervention groups were recruited from the same population and over the same period of time. All eligible</p>	<p>This was observational study. Therefore, there was no randomization or blinding in the study</p> <p>The characteristics of participants included in the study were not reported in adequate detail.</p> <p>The comparator group consisted of visits in which presumptive treatment was not given during the initial encounter. It was unclear whether how many of those who tested positive in that group subsequently were lost to follow-up (no treatment given).</p> <p>The accuracy of treatment was estimated based on NAAT results. The sensitivity and specificity of NAAT were not</p>

Strengths	Limitations
<p>visits during the study period were included in the study. Actual P values were reported for the main outcomes.</p>	<p>described, and it is possible that there were false positives and false negatives, lowering the validity of the results.</p> <p>Characteristics of 2 patients lost to follow-up were not described and they were not included in the analysis.</p> <p>It was unclear whether patients were representative of the recruited population. The study was performed in parallel to a trial that required urine samples and therefore patients not providing a urine specimen were excluded.</p> <p>It was unclear whether the staff, places, and facilities where the patients were treated was representative of the treatment most of patients receive. The study was conducted in an urban emergency department.</p> <p>The study did not report whether sample size was calculated.</p>

CDC = Centers for Disease Control and Prevention; MSM = men who have sex with men, NAAT = nucleic acid amplification test.

Note: We have retained the original terms that study authors used when describing sexual orientation.

Appendix 4: Main Study Findings

Note that this appendix has not been copy-edited.

Table 4: Summary of Findings by Outcome

Population	Shover et al. (2018) ²⁰		Wilson et al. (2017) ¹⁹	
	Presumptive treatment	No presumptive treatment	Presumptive treatment	No presumptive treatment
Total study population, n	1,677	7,464	512	650
Male	1,677	7,464	42	8
Female	NA	NA	470	640
Pregnant	NA	NA	58	280
Site of swab ^a				
Urethral swab	1,647	7,274	–	–
Rectal swab	569	7,183	–	–
Pharyngeal swab	1,590	7,228	–	–
<i>N. gonorrhoeae</i> test positive				
Total study population, n (%)	527 (31)	657 (9)	52 (4%)	
Presumptive treatment vs. no presumptive treatment	P < 0.01		–	
Male	527 (31)	657 (9)	4 (9%)	0
Female ^b	–	–	39 (8%)	9 (1%)
Pregnant	–	–	4 (7%)	0
Site of swab				
Urethral swab	266 (16)	74 (1)	–	–
Rectal swab	397 (25)	337 (5)	–	–
Pharyngeal swab	222 (14)	421 (6)	–	–
<i>N. gonorrhoeae</i> test negative				
Total study population, n (%)	1,150 (69)	6,807 (91)	NR	NR
Male	1,150 (69)	6,807 (91)	38 (91%)	8 (100)
Female ^b	NA	NA	431 (92%)	631 (99%)
Pregnant	NA	NA	54 (93%)	280 (100%)
Accurate presumptive treatment				
Total study population, n (%)	527 (31%)	–	NR	–
Male	–	–	4 (9%)	–
Female ^b	–	–	39 (8%)	–

Population	Shover et al. (2018) ²⁰		Wilson et al. (2017) ¹⁹	
	Presumptive treatment	No presumptive treatment	Presumptive treatment	No presumptive treatment
Pregnant	–	–	4 (7%)	–
Overtreatment or unnecessary presumptive treatment				
Total study population n (%)	–	–	NR	–
Male	–	–	38 (91%)	–
Female ^b	–	–	431 (92%)	–
Pregnant	–	–	54 (93%)	–
Missed treatment				
Total study population, n (%)	–	–	–	–
Male	–	–	–	0
Female ^b	–	–	–	9 (1%)
Pregnant	–	–	–	0

NA = not applicable; NR = not reported.

^aCategories are not mutually exclusive.

^bData of 2 patients (out of 1,110) were missing.

Table 5: Summary of Findings by Outcome – PPV of Signs, Symptoms, and Exposure

Study citation and study design	Population	Clinical assessment at visit ^a	Number of visits with indication	Number of visits with positive test result	PPV
Shover et al. (2018) ²⁰ Cross-sectional study	Presumptive treatment, n = 1,677 visits	Genitourinary symptoms	869	256	29%
		Genitourinary signs	240	134	56%
		Rectal symptoms	155	43	28%
		Rectal signs	11	2	18%
		Pharyngitis	49	3	6%
		Asymptomatic, exposed	591	154	26%

PPV = positive predictive value.

^aCategories are not mutually exclusive. All who had genitourinary signs also reported genitourinary symptoms.

Appendix 5: Summary of Single-Arm Studies

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Summary of Study Characteristics

We identified 5 noncomparative single-arm studies²¹⁻²⁵ describing the clinical effectiveness and potential harms of presumptive antibiotic treatment for gonorrhea. We have summarized characteristics in the subsequent sections. Additional details are provided in [Table 6](#).

Study Design

Of the 5 noncomparative single-arm studies, 4 were retrospective chart reviews,^{21,22,24,25} and 1 was a retrospective cohort study.²³

Study Settings and Country of Origin

One study was conducted in Canada²³ and the others were conducted in the US^{21,22,25} and Australia.²⁴

Study settings included STI testing and HIV or sexual health clinics,^{21,24,25} as well as emergency departments in urban areas.^{22,23} The study periods were from 2007 to 2017.²¹⁻²⁵

Patient Populations

One study only included individuals tested positive for *N. gonorrhoeae* or *C. trachomatis*,²² whereas the other 4 studies investigated those with unconfirmed *N. gonorrhoeae* infection at baseline.^{21,23-25} One study collected data from asymptomatic individuals with any STI contact,²⁴ whereas the other 4 studies included individuals with and without symptoms.^{21-23,25} The number of participants across the 5 studies ranged from 10,024 to 5,051.²⁵ Across studies, most participants were 25 years or older, with 3 studies^{21,22,24} reporting a mean age ranging from 24.8²² to 39 years.²⁴

Among the 3 studies that reported sex,²¹⁻²³ 1 study reported that 99% of participants identified as female,²³ and the other 2 studies reported that 55.2%²¹ and 49%²² of participants identified as male. In the Anker et al. study,²⁵ which included participants identifying as MSM, 99.6% identified as cisgender males and 0.4% identified as transgender (transwomen). One study with data from individuals identifying as MSM did not report sex.²⁴ We have retained the original terms that study authors used when describing sex, gender, and sexual orientation.

Intervention

The intervention of interest in all included single-arm studies was presumptive antibiotic treatment.²¹⁻²⁵ Details of presumptive antibiotic treatment therapy for gonorrhea were specified in 4 studies,^{21,23-25} while the remaining study reported that appropriate antibiotic therapy followed CDC guidelines.²²

Outcomes

All 5 studies conducted NAAT to confirm *N. gonorrhoeae* infection.²¹⁻²⁵

Clinical outcomes assessed across the studies included:

- accurate presumptive treatment,^{24,25} defined as the proportion of patients with presumptive antibiotic treatment who tested positive for *N. gonorrhoeae*
- overtreatment,^{23,25} defined as the proportion of patients with presumptive antibiotic treatment who tested negative for *N. gonorrhoeae*
- missed treatment,^{22,23} defined as the proportion of patients without presumptive antibiotic treatment who tested positive for *N. gonorrhoeae*.

Summary of Critical Appraisal

The 5 noncomparative single-arm studies clearly reported objectives of the study, patient characteristics, main outcomes to be measured, interventions of interest, and the main findings.²¹⁻²⁵ However, none of the studies reported adverse events experienced by individuals who received presumptive treatment but tested negative for *N. gonorrhoeae*, which is essential to assess potential consequences of overtreatment.²¹⁻²⁵

The 5 single-arm studies had methodological limitations due to the lack of a comparator group.²¹⁻²⁵ In general, inferring treatment effectiveness from single-arm studies is not possible since there is no alternative to compare it with. None of the studies reported the diagnostic accuracy (e.g., PPV) of NAATs used to confirm *N. gonorrhoeae* infection.²¹⁻²⁵ Potential false-positive and false-negative NAAT test results may increase measurement bias by misclassifying *N. gonorrhoeae* infection status, introducing a threat to internal validity.

Findings of all 5 studies may have limited external validity.²¹⁻²⁵ The representativeness of study populations was unclear. For example, 4 studies recruited participants from a single site,²¹⁻²⁴ and 3 of them had a small sample size ranging from 100 to 500,²²⁻²⁴ limiting the representativeness of the patients to the broader population. In addition, the representativeness of study settings was unknown for 2 studies^{22,23} conducted in emergency departments. While individuals may be screened for STI at emergency departments, STI testing is mostly conducted in sexual health clinics, local public health units, walk-in clinics, or by primary health care providers in Canada.²⁸ Moreover, none of the studies reported regional prevalence of *N. gonorrhoeae*,²¹⁻²⁵ which is critical to assess the generalizability of study findings to populations with various risk levels of *N. gonorrhoeae* infection.

Summary of Findings

We have summarized findings relevant to the current report in the subsequent sections. Additional details are provided in [Table 7](#).

Accurate Presumptive Treatment

Three studies reported data on accurate presumptive treatment by evaluating the proportion of presumptively treated patients who tested positive for *N. gonorrhoeae* in various patient populations.²³⁻²⁵

Accurate presumptive treatment ranged from 0%²³ to 46.1%,²⁵ which means that less than half of individuals receiving presumptive treatment for *N. gonorrhoeae* were followed with positive laboratory test results.

One study with patients identifying as MSM and transgender women found:²⁵

- 2,329 of 5,051 (46.1%) individuals received accurate presumptive treatment for *N. gonorrhoeae*.

One study focusing on asymptomatic MSM participants found:²⁴

- 10 of 38 (26.3%) individuals with *N. gonorrhoeae* contact alone received accurate presumptive treatment
- 0 of 16 (0%) individuals with *N. gonorrhoeae* and *C. trachomatis* contacts received accurate presumptive treatment for *N. gonorrhoeae*.

One study including male and female participants found:²³

- 0 of 19 (0%) individuals receiving presumptive treatment for *N. gonorrhoeae* tested positive.

Overtreatment

Two studies reported overtreatment between 68%²¹ to 100%,²³ indicating that a large proportion of presumptive treatment for *N. gonorrhoeae* was unnecessary (i.e., followed with negative laboratory test results).

One of the studies reported a total of 822 of 1,209 (68%) individuals receiving presumptive treatment for *N. gonorrhoeae* tested negative,²¹ including:

- 26 of 30 (86.6%) individuals with presumptive treatment for *N. gonorrhoeae* infection alone
- 402 of 623 (65.2%) individuals with presumptive treatment for both *N. gonorrhoeae* and *C. trachomatis* infection.

The other study²³ found 19 of 19 (100%) individuals with presumptive treatment for *N. gonorrhoeae* tested negative. However, the authors acknowledged that overtreatment was high due to the low proportion of positive *N. gonorrhoeae* results.²³

Missed Treatment

One study found that 13 of 31 (41.9%) of individuals without presumptive treatment who tested positive for *N. gonorrhoeae* did not receive subsequent treatment.²²

One study that reported that none of the 19 individuals (0%) without presumptive antibiotics tested positive for *N. gonorrhoeae*,²³ meaning no missed gonorrhea treatment at the initial clinic visit.

Table 6: Characteristics of Relevant Single-Arm Studies

Study citation, country, funding source	Study design, settings	Population characteristics	Intervention, testing method	Clinical outcomes
Anker et al. (2021) ²⁵ Country: US Funding source: NR	Retrospective chart review study Setting: STI testing clinics in California and Florida between January 2013 and December 31, 2017.	MSM and transgender women receiving presumptive treatment for <i>N. gonorrhoeae</i> . The units of analysis were patient encounters. <i>N. gonorrhoeae</i> testing and CDC guideline-based presumptive <i>N. gonorrhoeae</i> treatment, n = 5,051 Age in years, n (%): <ul style="list-style-type: none"> • 18 to 24: 13,584 (32.3) • 25 to 29: 4,780 (11.4) • 30 to 34: 6,965 (16.6) • 35 to 39: 9,817 (23.4) • 40 or order: 6,904 (16.4) Gender, n (%): <ul style="list-style-type: none"> • Male: 41,894 (99.6) • Transgender male to female: 156 (0.4) Sexual orientation, n (%): <ul style="list-style-type: none"> • Gay male: 35,242 (83.8) • Bisexual: 6,334 (15.1) • Other: 474 (1.1) 	Presumptive antibiotic treatment (intramuscular ceftriaxone and either oral azithromycin or oral doxycycline per 2010 and 2015 CDC guidelines) Testing method: Pharyngeal, rectal, and/or urine site-specific NAATs for <i>N. gonorrhoeae</i> .	Accurate presumptive treatment (same-day <i>N. gonorrhoeae</i> testing and presumptive <i>N. gonorrhoeae</i> treatment plus a positive <i>N. gonorrhoeae</i> laboratory test result) Inaccurate treatment (same-day <i>N. gonorrhoeae</i> testing and presumptive <i>N. gonorrhoeae</i> treatment plus a negative <i>N. gonorrhoeae</i> laboratory test result) Number of patients who received “inaccurate treatment” but tested positive for <i>C. trachomatis</i>
Pearce et al. (2019) ²⁴ Country: Australia Funding source: No funding received	Retrospective chart review study Setting: HIV Sexual Health clinic in Sydney, between January to November 2017.	Asymptomatic MSM patients with any STI contact Relevant population: Asymptomatic MSM with <i>N. gonorrhoeae</i> contact Number of participants, n = 100 (All patients received empiric antimicrobial therapy for the named STI) Age in years: mean (range): 39 (17 to 78)	Empiric antimicrobial therapy on the day of presentation: ceftriaxone 500 mg IM plus azithromycin 1 g PO stat for patients with <i>N. gonorrhoeae</i> contacts <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> testing method: NAAT performed using Cobas 4800 C.	Positive test result proportions: confirmed <i>N. gonorrhoeae</i> diagnosis in patients with <i>N. gonorrhoeae</i> contacts receiving empiric antimicrobial therapy

Study citation, country, funding source	Study design, settings	Population characteristics	Intervention, testing method	Clinical outcomes
		Sexual orientation, n: <ul style="list-style-type: none"> • MSM: 94 • Bisexual: 3 • Heterosexual: 1 • Unknown: 2 Contacts with STI, n: <ul style="list-style-type: none"> • <i>C. trachomatis</i> alone: 42 • <i>N. gonorrhoeae</i> alone: 38 • <i>C. trachomatis</i> and <i>N. gonorrhoeae</i>: 16 • <i>C. trachomatis</i> and <i>M. genitalium</i>: 1 • Syphilis: 3 	<i>trachomatis</i> or <i>N. gonorrhoeae</i> assay Results for <i>C. trachomatis</i> , <i>N. gonorrhoeae</i> , <i>Mycoplasma genitalium</i> syphilis and HIV were recorded.	
Friedland et al. (2017) ²³ Country: Canada Funding source: No funding received	Retrospective cohort study Setting: ED of an academic urban medical centre, between January and June 2015.	All patients tested for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> All samples from any site (e.g., endocervical, vaginal, rectal, or urinary) during the study period were included. Conditions other than uncomplicated <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> were excluded. All patient cases observed in the study, N = 209 Patients received presumptive treatment for <i>N. gonorrhoeae</i> , n = 19 Age in years, n (%): <ul style="list-style-type: none"> • 18 to 24: 44 of 209 (21) • > 25: 165 of 209 (79) Sex, n (%): <ul style="list-style-type: none"> • Female: 206 (99) Sample site, n (%): <ul style="list-style-type: none"> • Endocervical: 175 (84) • Vagina: 24 (11) 	Presumptive treatment for uncomplicated <i>N. gonorrhoeae</i> infection (ceftriaxone 250 mg intramuscularly administered in a single dose or cefixime 800 mg orally administered in a single dose, with cotreatment with azithromycin) Testing method: NAAT for <i>N. gonorrhoeae</i> using Cobas 4800. Single swab (e.g., endocervical, vaginal, rectal, urethral, or urinary).	Prevalence of presumptive treatment Overtreatment (the proportion of patients given antibiotics, but who ultimately tested negative) Undertreatment (the proportion of patients not given antibiotics, but who ultimately tested positive) Positive test result proportions

Study citation, country, funding source	Study design, settings	Population characteristics	Intervention, testing method	Clinical outcomes
		<ul style="list-style-type: none"> • Urine: 2 (1) • Urethra: 1 (0.5) • Unknown: 7 (3) 		
Schechter-Perkins et al. (2015) ²² Country: US Funding source: NR	Retrospective chart review, as part of a larger case-control study Setting: Urban academic ED, between January 2010 and June 2011.	Patients (aged 15 years or older) who tested positive for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> infection. The units of analysis were positive cases. All patient cases observed in the study, N = 500 (for 484 unique patients) Age in years, mean (SD): 24.8 (8.6) Sex, n (%): Female: 247 (51) Male: 237 (49)	Appropriate presumptive antibiotics treatment for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> , ^a delayed antibiotic treatment for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> Testing method: GenProbe Aptima Combo TMA Assay test result for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i>	The proportion of patients treated appropriately, both presumptively in the ED (presumptive treatment followed by positive testing), and at follow-up (treatment followed by positive testing), among those patients who ultimately tested positive for <i>N. gonorrhoeae</i> Proportion of patients without presumptive treatment who tested positive but did not receive follow-up treatment
Andric et al. (2013) ²¹ Country: US Funding source: NR	Retrospective chart review Setting: STI clinic in Florida, between November 2007 to October 2008.	Adult patients who received presumptive <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> treatment and provided pre-treatment urogenital swabs. Relevant Population: Adult patients who received presumptive <i>N. gonorrhoeae</i> treatment and provided pre-treatment urogenital swabs Pregnant women were excluded. Total number of patients: N = 1,209 Mean age (range), years: <ul style="list-style-type: none"> • 27.6 (18 to 67 years) • Sex: male, n (%): 667 (55.2%) Ethnicity, n (%):	Presumptive antibiotic treatment as for <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> (1 g azithromycin orally for chlamydia and/or 125 mg ceftriaxone intramuscularly for gonorrhea.) Testing method: NAAT by COBAS Amplicor	Overtreatment (presumptive treatment followed by negative testing)

Study citation, country, funding source	Study design, settings	Population characteristics	Intervention, testing method	Clinical outcomes
		<ul style="list-style-type: none"> • African American: 773 (63.9%) • Non-Hispanic white: 184 (15.2%) • Hispanic: 212 (17.5%) • Other/unknown: 40 (3.3%) • Number of patients who received treatment for <i>N. gonorrhoeae</i>, n = 30 • Number of patients who received treatment for <i>N. gonorrhoeae</i> and <i>C. trachomatis</i>, n = 623 		

CDC = Centers for Disease Control and Prevention; ED = emergency department; IM = intramuscular; MSM = men who have sex with men; NA = not applicable; NAAT = nucleic acid amplification test; NR = not reported; PO = orally; STI = sexually transmitted infection.

Note: We have retained the original terms that study authors used when describing sex, gender, sexual orientation, and ethnicity.

^aAntibiotics were considered appropriate for *N. gonorrhoeae* or *C. trachomatis* if they were listed as appropriate therapy in the CDC publication, 2010 STD Treatment Guidelines.

Table 7: Summary of Findings of Relevant Single-Arm Studies

Study citation and study design	Population	Main study findings
Anker et al. (2021) ²⁵ Cross-sectional study	CDC guideline-based presumptive treatment for <i>N. gonorrhoeae</i> , n = 5,051	<i>N. gonorrhoeae</i> test result positive, n = 2,329 <i>N. gonorrhoeae</i> test result negative, n = 2,722 Accurate presumptive treatment = 2,329 of 5,051 (46.1%) Inaccurate treatment = 2,722 of 5,051 (53.9%) Number of patients who received “inaccurate treatment” but tested positive for <i>C. trachomatis</i> = 404 of 2,722 (14.8%)
Pearce et al. (2019) ²⁴ Cross-sectional study	Empiric antimicrobial therapy for <i>N. gonorrhoeae</i> , n: Total: 54 <i>N. gonorrhoeae</i> alone: 38 <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> : 16	<i>N. gonorrhoeae</i> test result positive, n (%): Contacts with <i>N. gonorrhoeae</i> alone receiving empiric therapy: 10 of 38 (26.3%) Contacts with <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> receiving empiric therapy: 0 of 16 (0%)
Friedland et al. (2017) ²³ Retrospective cohort study	Total number of patients, N = 209 Patients received presumptive treatment for <i>N. gonorrhoeae</i> , n = 19 Patients not received presumptive treatment for <i>N. gonorrhoeae</i> , n = 190	<i>N. gonorrhoeae</i> test positive, n = 0 Overtreatment: Treated presumptively but tested negatively for <i>N. gonorrhoeae</i> , n = 19 Overtreatment proportion (%): 19 of 19 (100%) Undertreatment: No presumptive treatment but tested positively for <i>N. gonorrhoeae</i> , n = 0 Undertreatment proportion (%): 0 of 19 (0%)
Schechter-Perkins et al. (2015) ²² Cross-sectional study	Total number of test positive cases (<i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i>), N = 500 <i>N. gonorrhoeae</i> positive cases, n = 93 <i>C. trachomatis</i> and <i>N. gonorrhoeae</i> positive, n = 33	No presumptive treatment but tested positively for <i>N. gonorrhoeae</i>, n (%): Total: 31 Follow-up treatment: 18 of 31 (58.1%) No treatment: 13 of 31 (41.9%)
Andric et al. (2013) ²¹ Retrospective cohort	Presumptive antimicrobial therapy for <i>N. gonorrhoeae</i> , n: Total: 1,209 <i>N. gonorrhoeae</i> alone: 30 <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> : 623	Overtreatment (<i>N. gonorrhoeae</i> test negative), n (%): Total (<i>C. trachomatis</i> and/or <i>N. gonorrhoeae</i>) = 822 of 1,209 (68%) Treated presumptively for <i>N. gonorrhoeae</i> alone, n = 26 of 30 (86.6%) Treated presumptively for <i>N. gonorrhoeae</i> and <i>C. trachomatis</i> , n = 402 of 623 (65.2%) Authors added that: “If the 205 patients who were dually treated for chlamydia and gonorrhea but tested positive for only one organism are added to the 822 patients who had no positive test for the organisms for which they were tested and treated [...], the total percentage of patients who received any

Study citation and study design	Population	Main study findings
		treatment for which they subsequently had a negative test was 84.9% (1027/1209). ²¹ p. 323

Appendix 6: References of Potential Interest

Note that this appendix has not been copy-edited.

Previous CADTH Reports

Screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* during pregnancy: a health technology assessment. Ottawa: CADTH; 2018 Oct. (CADTH health technology assessment report; no. 148) [Screening for Chlamydia Trachomatis and Neisseria Gonorrhoeae During Pregnancy: A Health Technology Assessment \(cadth.ca\)](#)

Scoping Review

Allen KS, Hinrichs R, Heumann CL, et al. Findings From a Scoping Review: Presumptive Treatment for Chlamydia trachomatis and Neisseria gonorrhoeae in the United States, 2006-2021. *Sex Transm Dis*. 2023 04 01;50(4):209-214. [PubMed](#)

Nonrandomized Studies

Single-Arm Studies – Mixed Population

Llata E, Braxton J, Asbel L, et al. Presumptive and Follow-Up Treatment Associated With Gonorrhea and Chlamydia Testing Episodes in Sexually Transmitted Disease Clinics: Impact of Changing Treatment Guidelines for Gonorrhea, Sexually Transmitted Disease Surveillance Network, 2015-2018. *Sex Transm Dis*. 2023 01 01;50(1):5-10. [PubMed](#)

Rasul R, McIver R, Patel P, Foster R, McNulty A. Non-empirical management of asymptomatic chlamydia and gonorrhoea reduces unnecessary antibiotic use fivefold: a before and after study. *Sex Transm Infect*. 2023 02;99(1):30-34. [PubMed](#)

Garlock J, Lee L, Cucci M, Frazee LA, Mullen C. Suspected gonorrhea and chlamydia: Incidence and utilization of empiric antibiotics in a health system emergency department. *American Journal of Emergency Medicine*. 2019 05;37(5):884-889. [PubMed](#)

Pugsley RA, Peterman TA. Presumptive and Follow-up Treatment for Gonorrhea and Chlamydia Among Patients Attending Public Health Department Clinics in Virginia, 2016. *Sex Transm Dis*. 2019 03;46(3):199-205. [PubMed](#)

Breslin K, Tuchman L, Hayes KL, Badolato G, Goyal MK. Sensitivity and Specificity of Empiric Treatment for Sexually Transmitted Infections in a Pediatric Emergency Department. *J Pediatr*. 2017 10;189:48-53. [PubMed](#)

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McIver R, Low S, Varma R, Vickers T, McNulty A. Empirical treatment of asymptomatic contacts of gonorrhoea: patient views. *Sexual Health*. 2020 11;17(5):462-466. [PubMed](#)

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