



# CLINICAL GUIDELINES PROGRAM

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

## *Mycoplasma genitalium* Management in Adults

### Updates, Authorship, and Related Guidelines

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**Committee:** [Medical Care Criteria Committee](#)

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## Purpose and Goals of This Guideline

This guideline on management of *Mycoplasma genitalium* infection was developed by the New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program. This update reflects changes included in the Centers for Disease Control and Prevention (CDC) [2021 STI Treatment Guidelines](#). By addressing the care of adults with and without HIV who have acquired sexually transmitted *M. genitalium*, the goals of this guideline are to:

- Assist clinicians in recognizing common clinical manifestations of *M. genitalium* infection.
- Provide clinicians with evidence-based recommendations on screening, diagnostic testing, and treatment of *M. genitalium* infection.
- Ensure that NYS recommendations for *M. genitalium* screening, diagnosis, and treatment reflect the rapidly evolving evidence regarding the organism, infection, potential complications, and implications of drug resistance.

The literature on this topic and the disease epidemiology are evolving rapidly. To prepare this guidance, the authors conducted a literature search through MEDLINE and published guidelines from multiple sources, including the [CDC](#), [International Union Against Sexually Transmitted Infections](#), [British Association for Sexual Health and HIV](#), [Australian Society for HIV, Viral Hepatitis and Sexual Health Medicine](#), and the [Public Health Agency of Canada](#).

Although previously considered an emerging sexually transmitted infection (STI), *M. genitalium* infection has now become a well-recognized cause of STIs worldwide, specifically linked to urethritis, cervicitis, and pelvic inflammatory disease, yet much is still unknown about the organism, infection, and potential complications. Treatment of *M. genitalium* infection is challenging in an era of increasing antimicrobial resistance across multiple drug classes. Emerging antimicrobial resistance worldwide has become a concern, and updates to treatment recommendations in the United States and elsewhere have been implemented to address this issue.

**Prevalence of *M. genitalium* infection:** The prevalence of *M. genitalium* infection varies depending on the clinical setting and population being tested. Prevalence rates in the general U.S. population are low, reported between 1% and 4%

[Torrone, et al. 2021; Manhart, et al. 2007], with higher rates (>4% to <40%) reported worldwide among individuals in STI clinic settings [Begniss, et al. 2021; Broad, et al. 2021; Calas, et al. 2021; Horseman, et al. 2021; Baumann, et al. 2018; Casin, et al. 2002]. Although these ranges are based on data from multiple countries and populations and include a mix of symptomatic and asymptomatic individuals, most reports suggest that asymptomatic infection is common [Calas, et al. 2021; Gesink, et al. 2016; Huppert, et al. 2008; Manhart, et al. 2007].

## Clinical Manifestations

Although asymptomatic infection is commonly reported, *M. genitalium* infection has been associated with the clinical syndromes of urethritis, cervicitis, and pelvic inflammatory disease (PID). The causative relationships between *M. genitalium* and cervicitis and urethritis have been established, with the strongest association seen with persistent or recurrent urethritis [CDC 2021; Dehon, et al. 2016; Lis, et al. 2015; Lusk, et al. 2011; Gaydos, et al. 2009; Wikström and Jensen 2006; Mena, et al. 2002; Totten, et al. 2001]. Symptoms are typically similar to those seen with chlamydial urethritis (non-purulent urethral discharge) as opposed to gonococcal urethritis (frankly purulent discharge).

*M. genitalium* has been associated with PID, though the evidence is inconclusive and conflicting. A 2015 meta-analysis found a statistically significant association between *M. genitalium* infection and an increased risk of both cervicitis and PID, even when accounting for coinfections with other sexually transmitted infections and limiting to those that used nucleic acid amplification testing [Lis, et al. 2015]. A later meta-analysis in 2019 included a sub-analysis of 2 prospective studies that demonstrated an increased risk for PID when *M. genitalium* was detected, though this was not statistically significant [Cina, et al. 2019]. A randomized trial comparing the addition of metronidazole or placebo to standard PID treatment (ceftriaxone plus doxycycline) noted a statistically significant reduction in detection of *M. genitalium* 30 days after treatment in the metronidazole arm, despite metronidazole's lack of activity against the organism [Wiesenfeld, et al. 2021]. Some experts suggest that these findings implicate the influence of the vaginal microbiome, which requires further investigation to determine whether *M. genitalium* is an independent contributor to development of PID [Mitchell, et al. 2021].

Though the organism has been discovered at multiple anatomic sites, at present there is insufficient evidence that *M. genitalium* is a primary cause of proctitis, and no evidence that it is a cause of pharyngitis or epididymo-orchitis. Similarly, there is insufficient evidence that *M. genitalium* is a cause of infertility or pregnancy complications; studies that are not serology-based are needed. The consequences of asymptomatic infections are unknown [CDC 2021].

## Laboratory Testing and Diagnosis

### RECOMMENDATIONS

#### Laboratory Testing and Diagnosis

- Clinicians should *not* routinely screen for *M. genitalium* in asymptomatic individuals. (A3)
- Clinicians should test for *M. genitalium* in individuals with persistent or recurrent urethritis or cervicitis. (B2)
- When testing is indicated, clinicians should use nucleic acid amplification testing (NAAT) to diagnose *M. genitalium* infection, with resistance testing if available. (A2)

*M. genitalium* bacteria have no cell wall and can take months to grow in culture; thus, traditional methods of diagnosis with gram stain or culture are not useful. Diagnosis was difficult until molecular tests, such as NAAT, became available. NAAT is the preferred U.S. Food and Drug Administration (FDA)-approved diagnostic method for *M. genitalium* infection. The FDA-approved tests currently cleared for use on urine, endocervical, urethra, and penile meatus specimens are the Aptima Mycoplasma genitalium Assay (Hologic Inc) and Cobas TV/MG Assay (Roche Diagnostics).

The specimen and site of optimal sensitivity for testing in transgender individuals with a neopenis or neovagina have not been evaluated.

**Screening:** Currently available evidence *does not* support routine screening for *M. genitalium* in asymptomatic individuals or in any specific population [Golden, et al. 2017; Horner and Martin 2017], and the Centers for Disease Control and

Prevention (CDC) recommends against routine screening of asymptomatic individuals [CDC 2021]. Prevalence estimates of *M. genitalium* in the general population are low, antimicrobial resistance is increasing, the implications of asymptomatic infection are unknown, and treatment options are limited [Fernández-Huerta, et al. 2020; Baumann, et al. 2018; Golden, et al. 2017; Horner and Martin 2017]. At present, there is insufficient evidence regarding pregnancy complications and treatment benefits to recommend for or against screening in asymptomatic pregnant individuals [Wiesenfeld and Manhart 2017].

**Diagnostic testing:** The recommended use of diagnostic testing for *M. genitalium* is largely limited to patients with persistent or recurrent symptoms. The CDC specifies that *M. genitalium* testing not be performed in the first round of testing for initial presenting sexually transmitted infection syndromes of cervicitis or urethritis [CDC 2021]. However, given the strong association of *M. genitalium* with persistent or recurrent urethritis and cervicitis, diagnostic testing is recommended in that clinical scenario.

The role of diagnostic testing for *M. genitalium* in the initial evaluation of pelvic inflammatory disease (PID) is unclear given the lack of robust evidence for *M. genitalium* as an independent cause of PID. This committee suggests limiting *M. genitalium* testing in those with PID when gonococcal and chlamydial tests are negative and symptoms persist despite empiric treatment.

Some international guidelines advise that diagnostic testing for *M. genitalium* be performed only in individuals with symptomatic urethritis, cervicitis, or PID [ASHM 2021; Soni, et al. 2019]; others advise that testing be performed only in those with negative gonorrhea and chlamydia test results or who do not respond to first-line empiric treatment [Public Health Agency of Canada 2017; Jensen, et al. 2016]. Non-response to first-line treatment increases the index of suspicion for *M. genitalium* as a causative agent.

**Testing of sex partners:** There is little evidence to date to guide the management for sex partners of those diagnosed with *M. genitalium* infection. The CDC and most international guidelines suggest limiting evaluation (i.e., testing and treatment) to ongoing sex partners of those individuals diagnosed and treated for a symptomatic *M. genitalium* infection (see guideline section [Treatment > Partner Management](#)).

#### → KEY POINT

- Asymptomatic *M. genitalium* infection is common and its implications unclear; therefore, routine screening is not recommended, and diagnostic testing is reserved for individuals who:
  - Have persistent or recurrent urethritis or cervicitis or PID in the absence of gonorrhea or chlamydia *and* with persistent symptoms despite therapy
  - Are current sex partners of individuals treated for symptomatic *M. genitalium* infection

**Resistance testing:** Molecular tests that detect both *M. genitalium* and antibiotic-associated resistance mutations are available in some countries. These combination tests are not commercially available in the United States but are anticipated to become available in the near future. At present, resistance assays are most useful in determining macrolide resistance. The association of certain resistance mutations with clinical treatment failure is inconsistent for quinolone antibiotics [Conway, et al. 2020]. However, resistance testing has been demonstrated to be a clinically useful tool to guide treatment, resulting in high cure rates, as evidenced by the resistance-guided antimicrobial therapy model (see guideline section [Treatment](#)) [Durukan, et al. 2020].

## Treatment

### ☑ RECOMMENDATIONS

#### Treatment

- Clinicians should treat patients with urethritis (A2), cervicitis (A2), and PID (B2) caused by *M. genitalium* infection as recommended in [Table 1: Recommended Antimicrobial Regimens for Mycoplasma genitalium Infection Treatment](#).
- When *M. genitalium* testing is unavailable, clinicians should treat patients when there is a high clinical index of suspicion for *M. genitalium* infection and other STIs have been reasonably excluded from the differential diagnosis. (B3)

**Abbreviations:** PID, pelvic inflammatory disease; STI, sexually transmitted infection.

Azithromycin, doxycycline, and moxifloxacin are the most frequently used antibacterial agents for *M. genitalium* infection treatment (see Table 1, below). Updates to treatment recommendations in the United States and elsewhere have been implemented to address the emerging concern of antimicrobial resistance across multiple drug classes. A 2015 literature review noted that treatment efficacy for both azithromycin and doxycycline has been declining [Manhart, et al. 2015]. With evidence of emerging macrolide resistance and treatment failure associated with azithromycin as a single 1-gram (g) oral dose, in 2021, the Centers for Disease Control and Prevention (CDC) recommended against use of this regimen in favor of 2-step antibiotic therapy (see discussion of 2-step treatment approach, below) [Horner, et al. 2018; Gesink, et al. 2016; Manhart, et al. 2013].

Though moxifloxacin once had documented cure rates approaching 100%, some studies report a rate <90% with monotherapy [Li, et al. 2017; Manhart, et al. 2015]. In the 2015 literature review noted above, levofloxacin and ofloxacin had lower cure rates than 4th-generation quinolones, including moxifloxacin, gatifloxacin, and sitafloxacin [Manhart, et al. 2015]. A meta-analysis of primarily observational studies compared the efficacy of 7- and 10-day treatment durations for moxifloxacin and found no significant difference [Li, et al. 2017]. For PID related to *M. genitalium* or the PID clinical syndrome in general, a 14-day course of moxifloxacin treatment was found to be effective [Ovens, et al. 2020; Latimer, et al. 2019; Judlin, et al. 2010; Ross, et al. 2006]. Because of emerging resistance overall and a lack of treatment alternatives, Australian, Canadian, and European STI guidelines do not recommend moxifloxacin for first-line empiric treatment of *M. genitalium* infection [ASHM 2021; Soni, et al. 2019; Public Health Agency of Canada 2017; Jensen, et al. 2016].

## Macrolide Resistance

The prevalence of macrolide-associated resistance mutations is >50% in many areas and was >62% in an STI clinic population in the United States [Bachmann, et al. 2020]. Risk factors for macrolide-associated resistance mutations include male-to-male sexual contact, recent STI, STI coinfection, and use of antibiotics within the previous 30 days [Bercot, et al. 2021; Broad, et al. 2021; De Baetselier, et al. 2021; de Salazar, et al. 2021; Latimer, et al. 2020; Li, et al. 2020; Anagrus, et al. 2013].

In cases of treatment failure with macrolides and moxifloxacin, pristinamycin 1 g 4 times per day for 10 days has been found effective in European and Australian studies [Read, et al. 2018; Bissessor, et al. 2015]; however, this treatment is not commercially available in the United States.

**2-step treatment approach:** With evidence of emerging macrolide resistance and treatment failure associated with azithromycin as a single 1 g oral dose [Horner, et al. 2018; Gesink, et al. 2016; Manhart, et al. 2013], the CDC recommends against using this regimen in favor of 2-step antibiotic therapy [CDC 2021]. The premise of the 2-step treatment approach is that pretreatment with doxycycline has been shown to decrease the overall bacterial burden, making treatment with a second follow-up drug more efficacious [Durukan, et al. 2020; Anagrus, et al. 2013; Björnelius, et al. 2008].

Published reports have shown improved antimicrobial treatment success with a 2-step approach, leading to recommendations for 2-step treatment in Australian and British treatment guidelines [ASHM 2021; Soni, et al. 2019]. In Australia, cure rates have risen to >90% with the implementation of resistance-guided therapy (RGT) [Durukan, et al. 2020]: Individuals with an STI syndrome received 7 days of oral doxycycline 100 mg twice daily empirically and then, if found to have *M. genitalium* infection without macrolide resistance, received 2.5 g oral azithromycin over 4 days (1 g on day 1 and 500 mg once daily on days 2 through 4). After initial treatment with doxycycline, individuals with macrolide-resistant *M. genitalium* infection received oral moxifloxacin 400 mg once daily for 7 days. A test of cure was performed 2 to 4 weeks after treatment. The cure rate with the RGT approach was 92%, even in regions with reported quinolone resistance of 15% to 20% [Durukan, et al. 2020].

The CDC [2021 STI Treatment Guidelines](#) include updated treatment recommendations for uncomplicated chlamydial infections, nongonococcal urethritis, and cervicitis. First-line therapy of oral doxycycline 100 mg twice daily for 7 days replaced single-dose 1 g oral azithromycin [CDC 2021]. This change is consistent with other international guideline recommendations and facilitates use of a 2-step doxycycline-containing regimen for individuals with persistent or recurrent urethritis or cervicitis who return for follow-up. Standard empiric therapy for PID also includes doxycycline as a component. The CDC recommends that when testing results become available after treatment initiation in cases of PID attributed to *M. genitalium*, moxifloxacin should be added to the empiric PID regimen rather than given sequentially [CDC 2021].

## Antimicrobial Treatment

Table 1, below, summarizes currently recommended treatment options.

Table 1: Recommended Antimicrobial Regimens for <i>Mycoplasma genitalium</i> Infection Treatment		
Selected Conditions	Oral Regimens	Considerations
<i>M. genitalium</i> Detected by FDA-Approved NAAT		
Resistance testing unavailable <i>or</i> macrolide resistant	Doxycycline 100 mg twice daily for 7 days <i>followed by</i> moxifloxacin 400 mg once daily for 7 days	<ul style="list-style-type: none"> <li>• <b>Pregnancy:</b> Doxycycline and moxifloxacin are generally not recommended [a].</li> <li>• <b>Preferred for PID:</b> 14-day moxifloxacin-containing regimen [b]</li> </ul>
Macrolide susceptible <i>or</i> moxifloxacin unavailable	Doxycycline 100 mg twice daily for 7 days <i>followed by</i> azithromycin 1 g on day 1 <i>followed by</i> azithromycin 500 mg once daily for 3 days	<ul style="list-style-type: none"> <li>• <b>Persistent symptoms:</b> If regimen is used in the absence of macrolide-susceptibility testing, perform test of cure at 21 days after treatment completion [CDC 2021].</li> <li>• <b>Pregnancy:</b> Doxycycline is generally not recommended [a].</li> </ul>
<i>M. genitalium</i> NAAT Unavailable		
High clinical index of suspicion (other STIs should be reasonably excluded before initiating treatment)	Doxycycline 100 mg twice daily for 7 days <i>followed by</i> moxifloxacin 400 mg once daily for 7 days	<ul style="list-style-type: none"> <li>• <b>Pregnancy:</b> Doxycycline and moxifloxacin are generally not recommended [a].</li> <li>• <b>Preferred for PID:</b> 14-day moxifloxacin-containing regimen [b]</li> </ul>
<p><b>Abbreviations:</b> FDA, U.S. Food and Drug Administration; NAAT, nucleic acid amplification testing; PID, pelvic inflammatory disease; STI, sexually transmitted infection.</p> <p><b>Notes:</b></p> <p>a. See guideline section Treatment &gt; Treatment in Pregnancy, below.</p> <p>b. A 14-day regimen containing moxifloxacin (400 mg per day) is effective for PID treatment [Ovens, et al. 2020; Latimer, et al. 2019; Judlin, et al. 2010; Ross, et al. 2006], in addition to an empiric 14-day regimen for PID that contains doxycycline [CDC 2021]. The evaluation and treatment of PID are not limited to the management discussed here.</p>		

**Testing unavailable:** Some clinical settings and care providers may not have access to *M. genitalium* nucleic acid amplification testing (NAAT) to guide diagnosis in the cases of persistent or recurrent urethritis or cervicitis. In these cases, empiric therapy can be prescribed when a high clinical index of suspicion for *M. genitalium* infection exists and other common STIs in the differential have been reasonably excluded (e.g., *C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, and herpes simplex virus). Doxycycline remains the recommended first step in the treatment regimen at time of diagnosis, followed by moxifloxacin.

**Test of cure:** The timeframe used for test of cure in the published literature is highly variable. Existing international guidelines include recommendations ranging from  $\geq 2$  to  $\geq 5$  weeks following treatment [ASHM 2021; Soni, et al. 2019; Jensen, et al. 2016]. Testing too soon after treatment carries the risk of detecting residual noninfectious particles. The CDC recommends a test of cure at 21 days for those treated with the 2-step doxycycline plus azithromycin regimen (see Table 1, above) who did not complete macrolide-resistance testing [CDC 2021]. This committee prefers that test of cure be reserved for patients who remain symptomatic and obtained no sooner than 21 days after treatment.

**STI coinfection:** When coinfection with another STI is present, it remains unclear based on available evidence whether *M. genitalium* is a true pathogen requiring treatment. If *M. genitalium* is detected in a patient with another STI, this

committee recommends reserving treatment for *M. genitalium* for those with persistent symptoms despite appropriate treatment of the other infection (e.g., gonorrhea, chlamydia, trichomoniasis).

## Treatment in Pregnancy

Moxifloxacin and doxycycline are generally *not recommended* for pregnant individuals. An azithromycin-only course of treatment (e.g., azithromycin 1 g on day 1 followed by 500 mg once daily on days 2, 3, and 4) can be considered with acknowledgment of the risk of treatment failure (see guideline section Treatment > Macrolide Resistance, above). Given the high rates of azithromycin resistance, shared decision-making is warranted after considering the risks of untreated *M. genitalium* infection during pregnancy and possible adverse drug events associated with antibiotics not generally used during pregnancy.

Some studies have raised concerns about associations between *M. genitalium* infection and infertility and pregnancy complications, though the evidence is limited and insufficient to demonstrate causation. A meta-analysis of available studies has suggested significant associations with preterm birth and spontaneous abortion [Lis, et al. 2015]. In this same analysis, the risk of infertility was described as elevated but was not statistically significant [Lis, et al. 2015]. Existing data are from observational studies and are further limited by use of serology, which is not an appropriate diagnostic tool [CDC 2021].

## Partner Management

There is insufficient evidence to clarify whether sex partners of individuals with symptomatic *M. genitalium* infection should receive treatment without testing or be treated only if infection is detected through a laboratory test [ASHM 2021; Soni, et al. 2019; Public Health Agency of Canada 2017; Jensen, et al. 2016]. This committee considers it reasonable to limit treatment to ongoing sex partners with positive test results, which is also supported by current CDC guidelines. The CDC recommends treating the partner with the same regimen that was provided to the patient if testing is unavailable [CDC 2021].

## All Recommendations

### ☑ ALL RECOMMENDATIONS: *MYCOPLASMA GENITALIUM* MANAGEMENT IN ADULTS

#### Laboratory Testing and Diagnosis

- Clinicians should *not* routinely screen for *M. genitalium* in asymptomatic individuals. (A3)
- Clinicians should test for *M. genitalium* in individuals with persistent or recurrent urethritis or cervicitis. (B2)
- When testing is indicated, clinicians should use NAAT to diagnose *M. genitalium* infection, with resistance testing if available. (A2)

#### Treatment

- Clinicians should treat patients with urethritis (A2), cervicitis (A2), and PID (B2) caused by *M. genitalium* infection as recommended in [Table 1: Recommended Antimicrobial Regimens for Mycoplasma genitalium Infection Treatment](#).
- When *M. genitalium* testing is unavailable, clinicians should treat patients when there is a high clinical index of suspicion for *M. genitalium* infection and other STIs have been reasonably excluded from the differential diagnosis. (B3)

**Abbreviations:** NAAT, nucleic acid amplification testing; PID, pelvic inflammatory disease; STI, sexually transmitted infection.

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# Supplement: Guideline Development and Recommendation Ratings

**Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program**

<b>Developer</b>	<a href="#">New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program</a>
<b>Funding source</b>	NYSDOH AI
<b>Program manager</b>	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See <a href="#">Program Leadership and Staff</a> .
<b>Mission</b>	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
<b>Expert committees</b>	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
<b>Committee structure</b>	<ul style="list-style-type: none"> <li>• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor</li> <li>• Contributing members</li> <li>• Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders</li> </ul>
<b>Disclosure and management of conflicts of interest</b>	<ul style="list-style-type: none"> <li>• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation.</li> <li>• The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.</li> </ul>
<b>Evidence collection and review</b>	<ul style="list-style-type: none"> <li>• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update.</li> <li>• A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations.</li> <li>• A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years.</li> <li>• Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.</li> </ul>

**Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program**

<b>Recommendation development</b>	<ul style="list-style-type: none"> <li>• The lead author drafts recommendations to address the defined scope of the guideline based on available published data.</li> <li>• Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations.</li> <li>• When published data are not available, support for a recommendation may be based on the committee’s expert opinion.</li> <li>• The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.</li> </ul>
<b>Review and approval process</b>	<ul style="list-style-type: none"> <li>• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee.</li> <li>• Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations.</li> <li>• Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.</li> </ul>
<b>External reviews</b>	<ul style="list-style-type: none"> <li>• External review of each guideline is invited at the developer’s discretion.</li> <li>• External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.</li> </ul>
<b>Update process</b>	<ul style="list-style-type: none"> <li>• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations.</li> <li>• If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.</li> </ul>

**Table S2: Recommendation Ratings and Definitions**

Strength	Quality of Evidence	
A: Strong B. Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2 <sup>†</sup>	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.