



CLINICAL GUIDELINES PROGRAM

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Management of Periodontal Disease

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Introduction

In some patients with HIV, immunosuppression may allow the development of oral and periodontal lesions [Polvora, et al. 2018; Baccaglioni, et al. 2007]. Chronic periodontitis can influence systemic inflammation favoring viral replication, and periodontal pockets may serve as reservoirs for the virus [Polvora, et al. 2018]. Periodontal lesions associated with HIV include linear gingival erythema (LGE) and necrotizing periodontal diseases, which are subclassified as necrotizing ulcerative gingivitis (NUG), necrotizing ulcerative periodontitis (NUP), and necrotizing ulcerative stomatitis (NUS/NS). NUP and NUS/NS may represent different stages of the same pathologic process, with NUP being a more advanced stage of NUG [Ryder, et al. 2012; Kaplan, et al. 2009]. As the population with HIV ages, patients may develop chronic conditions that can contribute to an exacerbated or enhanced progression of chronic adult periodontitis [Stabholz, et al. 2010]. There is also a concern about oral hygiene care and the incidence of periodontal disease in youth with perinatally acquired HIV, who may be at higher risk for developing significant periodontal disease associated with tooth loss and HIV progression. Frequent dental care is needed to prevent potential periodontal progression in this population [Ryder, et al. 2020; Moscicki, et al. 2019]. Stricter periodontal recall and oral hygiene care within older/aging and perinatally infected youth are critical.

The identification of periodontal diseases may be critical even in patients taking antiretroviral therapy (ART). While the introduction of highly active ART has significantly reduced this incidence [Ntolou, et al. 2023; Mataftsi, et al. 2011], the occurrence of oral and periodontal infections despite ART may indicate the failure of ART or the development of viral resistance [Mataftsi, et al. 2011]. It has also been suggested that the oral microbiome of patients on ART may affect systemic and periodontal inflammation. A shift in the microbiome is most likely due to a complex relationship between HIV, ART, and

aging [Griffen, et al. 2019; Toljic, et al. 2018; Noguera-Julian, et al. 2017]. Studies describe a complex and multifactorial interplay between aging, HIV infection, and periodontal health and highlight their shared risk factors [DeVore, et al. 2025].

HIV-associated periodontal diseases, along with oral infections, are considered serious complications of HIV. The incidence of periodontal infections in patients with HIV is lower than the incidence of oral infections [Ryder, et al. 2012], but the increasing severity of periodontal diseases in the aging population of patients with HIV is a concern. Individuals with HIV, particularly older adults, have an elevated risk of moderate to severe periodontitis, necessitating close clinical monitoring [Ryder, et al. 2020; Groenewegen, et al. 2019].

Management of periodontal lesions in patients with HIV has changed little in the past 30 years [Goncalves, et al. 2013; Ryder, et al. 2012]. Basic periodontal therapy provided at regular periodic intervals can effectively reduce periodontal inflammation in HIV patients [Valentine, et al. 2016]. Removal of local irritants from the root surfaces, mechanical debridement of necrotic tissues, and appropriate use of local and systemic antibiotics remain essential components of the management of HIV-associated gingival and periodontal diseases. The interaction between bacteria and *Candida* may play a vital role in the etiology of periodontal lesions; therefore, the management of HIV-associated periodontal lesions involves treating both bacteria and fungi [Pihlstrom, et al. 2005]. Multiple factors affect response to treatment, including immune status and personal oral hygiene practices of keeping the mouth, gums, and teeth clean [Alpagot, et al. 2004].

→ KEY POINTS

- Routine dental care is needed to prevent periodontal progression in people with HIV, and stricter periodontal recall and oral hygiene care are critical in older patients.
- Chronic nonhealing lesions may indicate a more serious condition, and oral health care providers can use biopsies to identify any neoplastic changes [Ryder, et al. 2012].

Linear Gingival Erythema

✓ RECOMMENDATIONS

LGE Treatment

- Oral health care providers should treat LGE promptly before it evolves into a more severe form of periodontal disease. (A2)
- Oral health care providers should treat LGE with superficial debridement of affected tissue and antimicrobial rinse and schedule a follow-up appointment to determine if the patient is responding to treatment. (A2)

Abbreviation: LGE, linear gingival erythema.

Presentation and Diagnosis

LGE characteristically presents as a distinct 2- to 3-mm-wide linear erythematous band limited to the free gingival margin (see [Appendix: Photo- and Radiographs of Periodontal Disease Associated With HIV](#) for images).

LGE typically presents at the anterior teeth initially [Cherry-Peppers, et al. 2003], with subsequent progression to the posterior dentition [Ryder, et al. 2012]. Clinically, it may be difficult to distinguish LGE from severe gingivitis in patients with poor plaque control. LGE lesions do not resolve or respond to conventional periodontal therapy, including plaque control, scaling, and root planing. Initial biopsy is not indicated for diagnosis unless the tissue does not heal after follow-up because no microscopic appearance specific to LGE exists. X-rays may be used to rule out alveolar bone involvement.

→ KEY POINT

- A lack of response to conventional periodontal therapy is a key diagnostic feature of LGE; LGE is refractory to standard plaque control.

LGE is classified as a gingival disease of fungal origin by the American Academy of Periodontology because *Candida* is the primary etiological factor [Armitage 1999]. LGE lesions are often resolved with topical and/or systemic antifungal treatment. Data are unavailable to establish whether LGE will evolve into a more severe form of periodontal disease; however, LGE may be a predecessor to the necrotizing ulcerative periodontal diseases that present in some patients with HIV [Goncalves, et al. 2013]. If LGE lesions do not resolve after 1 month of therapy, a biopsy may then help indicate a different diagnosis [Ryder, et al. 2012].

Treatment

Conventional periodontal therapy does not adequately treat LGE, likely because of the presence of yeast within the gingival tissues [Patton 2000]; *Candida* is the etiological factor. Treatment for LGE includes oral hygiene instructions and mechanical supragingival debridement using minimal pressure on soft tissue to remove plaque [Herrera, et al. 2014]. Oral antimicrobial rinses are effective in treating LGE. As a first-line treatment, patients should rinse twice daily with a 0.12% chlorhexidine gluconate suspension (a broad-spectrum oral antimicrobial) and be re-examined after 2 weeks. If lesions are persistent, topical antifungal medications can be used [Cherry-Peppers, et al. 2003].

Necrotizing Ulcerative Gingivitis and Necrotizing Ulcerative Periodontitis

RECOMMENDATIONS

NUG/NUP Treatment

- Oral health care providers should treat NUG and NUP to prevent the destruction of periodontal tissues. X-rays will determine the severity of the periodontal bone loss. (A2)
- Oral health care providers should treat the acute stage of NUG/NUP in the clinical setting as soon as possible after diagnosis; treatment should include superficial debridement of infected areas, scaling, and root planing, and lavage/irrigation with an antimicrobial rinse (see text for antimicrobial irrigation options). (A2)
- Oral health care providers should provide patients with a treatment plan for follow-up home care that includes daily antimicrobial rinses (see text for antimicrobial irrigation options) and instructions for and reinforcement of the importance of good oral hygiene and maintenance following treatment of acute disease and thereafter. (A2)
- For patients with severe or nonresponding NUG/NUP, oral health care providers should prescribe systemic antibiotics and concurrent treatment with an antifungal agent, as specified below. (A3)

NUG/NUP Follow-Up

- Oral health care providers should evaluate healing within 7 days of treatment and perform additional debridement if necessary. (A3)
- Clinicians should reevaluate the patient 2 months after treatment to determine the need for further intervention. (A3)

Abbreviations: NUG, necrotizing ulcerative gingivitis; NUP, necrotizing ulcerative periodontitis.

NUG and NUP are periodontal conditions that may be present in patients who do not have HIV, but both are more commonly associated with HIV and other systemic conditions [Bodhade, et al. 2011].

Because of their similar clinical appearance and treatment, most studies have tended to classify NUG and NUP together as necrotizing periodontal lesions. Additionally, *Candida* organisms may be present in the tissues of NUP sites among patients with HIV, which suggests that *Candida* may have a role in HIV-associated NUP. Because of the presence of *Candida* in both LGE and NUG/NUP lesions, the possibility exists that LGE is a precursor to the development of NUG/NUP lesions. NUG and NUP are considered to be on the spectrum of the same pathologic process [Ryder, et al. 2012; Bodhade, et al. 2011; Patton and McKaig 1998; Robinson, et al. 1998]; hence, early diagnosis and intervention will be effective in treating necrotizing periodontal diseases.

Presentation and Diagnosis

NUG, formerly referred to as acute necrotizing ulcerative gingivitis (ANUG), characteristically presents as a rapid onset of ulcerations of the interdental papilla with gingival bleeding and severe pain. Lesions are typically described as having a “punched out” appearance of the papilla, and the affected tissue appears to be covered with a fibrinous pseudomembrane (see [Appendix: Photo- and Radiographs of Periodontal Disease Associated With HIV](#) for images). Biopsy is not initially indicated for diagnosis unless the tissue does not show evidence of healing.

NUP lesions are similar in appearance to NUG lesions; however, NUP lesions extend into and destroy the alveolar bone. Patients with NUP frequently present with exposed bone, gingival recession, and tooth mobility. These clinical signs and symptoms do not necessarily involve the entire periodontium; only localized areas of the tooth-bearing bone and associated soft tissues may be affected. NUP is characterized by rapid destruction of bone that often leads to tooth loss, severe deep jaw pain, widespread soft tissue necrosis, bleeding, and fetid mouth odor. Other signs and symptoms of NUG and NUP include swelling of the regional lymph nodes, fever, and malaise. These clinical findings do not present in all patients and are considered secondary presentations of disease. The presence of NUP may be indicative of severe or worsening immunosuppression [Ryder, et al. 2012; Bodhade, et al. 2011].

Treatment

Treatment initiation as soon as possible following the diagnosis of acute NUG/NUP is important to alleviate pain and tissue destruction. The well-established standard of care for NUG/NUP treatment by the oral health care provider includes debridement of infected areas; scaling and root planing of the teeth as needed; and intrasulcular lavage/irrigation with either 0.12% chlorhexidine gluconate or, as an alternative, 10% povidone-iodine [Herrera, et al. 2014]. This standard of care is based on the principle of eliminating or reducing the microbial load by mechanically removing debris and plaque [Hofer, et al. 2002]. Such practices have been rigorously used over many years in the management of periodontal diseases in patients with HIV [Ryder, et al. 2012; Mealey 1996; Holmstrup and Westergaard 1994; Winkler, et al. 1989]. In severe cases or nonresponding conditions, systemic antimicrobials should be used as an adjunct to standard treatment [Herrera, et al. 2014]. Because the use of prophylactic antibiotic therapy might risk candidiasis [Herrera, et al. 2014; Mealey 1996], the best option for antimicrobial therapy is metronidazole with an antifungal agent to prevent the development of a secondary manifestation of oral candidiasis. Once the acute disease is under control, definitive treatment, such as scaling and root planing as needed and therapy for pre-existing gingivitis or periodontitis, should be provided. These include adequate therapy for the pre-existing gingivitis or periodontitis, instructions on adequate oral hygiene practices at home, and supportive therapy such as periodontal recall maintenance [Herrera, et al. 2014; Hofer, et al. 2002].

Broad-spectrum antibiotics are effective for the treatment of periodontal diseases in patients with HIV [Murray 1994]. Follow-up treatment includes daily antimicrobial rinses and systemic antibiotics, specifically metronidazole 250 mg 3 times per day, for 7 to 14 days. Metronidazole is effective as an adjunct systemic antibiotic for treating periodontal diseases in patients with HIV [Winkler and Robertson 1992]. If the patient cannot tolerate metronidazole, clindamycin 150 mg 4 times per day or amoxicillin-clavulanate 875 mg twice per day for 7 to 10 days may be prescribed. Extraction of affected teeth may be necessary if the bone loss is severe. The use of systemic antibiotics increases the patient’s risk of developing candidiasis; therefore, concurrent, empiric administration of an antifungal agent should be considered to maintain the balance between treatment and potential negative side effects [Ryder 2000].

During the acute and healing stages of NUP, frequent recall visits are needed to administer the necessary periodontal therapies, assess tissue response, and monitor the patient’s oral hygiene performance. Periodontal maintenance is generally indicated every 3 months once the infection is controlled [Ryder, et al. 2012].

Favorable treatment responses to HIV-associated periodontal disease usually occur when the disease is addressed as early as possible [Ryder, et al. 2012]. Patients treated for NUP may develop repeated episodes, especially when oral hygiene practices are not good. NUP can be insidious, localized, and not necessarily related to plaque. Once clinical stabilization has occurred, visits every 3 months will allow for the detection and prevention of disease recurrence at an incipient stage [Ryder, et al. 2012].

Necrotizing Ulcerative Stomatitis and Necrotizing Stomatitis

RECOMMENDATIONS

NUS/NS Treatment

- Oral health care providers should perform a biopsy and refer patients to an oral surgeon, clinical pathologist, or oral medicine specialist when NUS/NS is diagnosed. (A2)
- Oral health care providers should treat NUS/NS with debridement of necrotic bone and soft tissue and concurrent antimicrobial therapy, as specified below. (A3)
- Clinicians should include the following as part of the treatment plan for patients with periodontal disease:
 - Use of a pre-procedural antimicrobial rinse. (A2)
 - Local debridement and disinfection using a 0.12% chlorhexidine gluconate or 10% povidone-iodine. (A2)
 - Removal of necrotic debris and sequestration, along with scaling and root planing, with local anesthesia to proceed as tolerated by the patient but no later than within 7 days of diagnosis. (A2)
 - Reinforcement of oral hygiene and home care instructions and prescriptions, including:
 - Daily use of an antimicrobial rinse for 30 days.
 - Antibacterial therapy.
 - Nutritional supplementation/advice.
 - Periodontal prescriptions. (B2)

Abbreviations: NS, necrotizing stomatitis; NUS, necrotizing ulcerative stomatitis.

Presentation and Diagnosis

Necrotizing ulcerative stomatitis and necrotizing stomatitis (NUS/NS) may be an extension of NUP into the adjacent supporting bone, leading to osteonecrosis and subsequent sequestration of the surrounding bone.

Patients may present with pronounced residual soft tissue and bony defects in the affected areas following treatment and healing of the necrotic tissues [Ryder, et al. 2012; Armitage 1999; Horning and Cohen 1995]. If the tissue does not heal, a soft tissue biopsy is indicated to exclude other potential diagnoses, such as the increased risk of cancer in patients with HIV [Chen, et al. 2015].

When the soft tissue destruction is no longer contained to the soft tissue and bone of the oral cavity, this condition can be clinically consistent with Noma disease (also referred to as cancrum oris), which is more often seen in the pediatric population and is associated with severe or life-threatening malnourishment [Feller, et al. 2014].

Treatment

Box 1: Periodontal Disease Prescription Dosing

- Preferred: Metronidazole, 250 mg 3 times per day for 7 days
- Alternative: Augmentin, 500 mg 2 times per day for 7 days
- For patients allergic to penicillin: Clindamycin, 300 mg 3 times per day for 7 days
- As needed for pain: Rinse with 2 teaspoons of xylocaine 2% viscous solution

Broad-spectrum antibiotics are effective for the treatment of periodontal diseases in patients with HIV (see Box 1, above) [Patton and McKaig 1998; Murray 1994]. Metronidazole is very effective as an adjunct systemic antibiotic for treating periodontal diseases in patients with HIV [Winkler and Robertson 1992]. Metronidazole is effective against gram-negative bacteria that are typically involved in periodontal diseases. Augmentin can be used as an alternative if a patient has gastrointestinal problems with metronidazole. Both 0.12% chlorhexidine gluconate and 10% povidone-iodine are effective treatment modalities and either may be used in office and at home as an antimicrobial rinse [Hofer, et al. 2002]. A local anesthetic may be indicated for pain management during the removal of necrotic debris, scaling, and root planing.

Chronic Pre-Existing Periodontal Disease

RECOMMENDATIONS

Chronic Pre-Existing Periodontal Disease Treatment

- For treatment of pre-existing periodontitis, clinicians should follow the current [standard guidelines](#). (A3)
- Clinicians should perform additional diagnostic procedures (biopsy, cytologic smear, or culture) for lesions that show no healing within 10 days or refer the patient to a periodontist as indicated. (A3)

Presentation and Diagnosis

About half of the U.S. population >30 years of age is affected by chronic periodontal disease, and the prevalence of periodontal disease increases with age [Eke, et al. 2015]. No data currently exist to indicate the extent to which HIV infection may accelerate the destruction of periodontal tissues in the population with HIV. However, the occurrence of rapid attachment loss may indicate severe immunosuppression [Ryder, et al. 2012; Mealey 1996]. Pre-existing periodontal disease can be diagnosed by clinical characteristics and radiographic examination for bone loss as recommended by the American Academy of Periodontology [American Academy of Periodontology 2000; Armitage 1999]. The clinical characteristics for chronic periodontitis include the presence of periodontal pockets, clinical attachment loss, and bleeding on probing. Radiographic analysis can reveal the presence of periodontal bone loss with horizontal or vertical bony defects. Increased mobility of teeth may also be observed in association with clinical attachment loss and bone loss.

Treatment

Scaling and root planing is recommended for nonsurgical treatment of periodontal disease [American Academy of Periodontology 2000]. A recent case-control study further reinforced that nonsurgical periodontal therapy has a beneficial effect on clinical and immunological parameters of chronic periodontitis, reduction of oral *Candida* counts, and improvement of HIV infection status. Patients with chronic periodontitis treated with nonsurgical periodontal therapy had an increase in CD4+ T-lymphocytes and a reduction in viral load [Nobre, et al. 2019].

Surgical therapy, including flap debridement and extraction of teeth, can be performed without postoperative complications. Before surgical treatment, consultation with the patient's physician may be indicated to obtain information regarding hematological levels of immune cells. Low neutrophil counts may indicate the adjunct use of systemic antimicrobial therapy.

Appendix: Photo- and Radiographs of Periodontal Disease Associated With HIV

Photographs courtesy of Dr. Gwen Cohen Brown and the Dental Hygiene Department of New York City College of Technology

Figure 1: Patient with linear gingival erythema (LGE)



Figure 2: Patient with necrotizing ulcerative periodontitis (NUP)



Figure 3: Patient with linear gingival erythema (LGE) and necrotizing ulcerative periodontitis (NUP)



Figure 4: Patient with necrotizing ulcerative gingivitis (NUG)



Figure 5: Patient with localized bone loss



All Recommendations

✓ ALL RECOMMENDATIONS: MANAGEMENT OF PERIODONTAL DISEASE

LGE Treatment

- Oral health care providers should treat LGE promptly before it evolves into a more severe form of periodontal disease. (A2)
- Oral health care providers should treat LGE with superficial debridement of affected tissue and antimicrobial rinse and schedule a follow-up appointment to determine if the patient is responding to treatment. (A2)

NUG/NUP Treatment

- Oral health care providers should treat NUG and NUP to prevent the destruction of periodontal tissues. X-rays will determine the severity of the periodontal bone loss. (A2)
- Oral health care providers should treat the acute stage of NUG/NUP in the clinical setting as soon as possible after diagnosis; treatment should include superficial debridement of infected areas, scaling, and root planing, and lavage/irrigation with an antimicrobial rinse (see text for antimicrobial irrigation options). (A2)
- Oral health care providers should provide patients with a treatment plan for follow-up home care that includes daily antimicrobial rinses (see text for antimicrobial irrigation options) and instructions for and reinforcement of the importance of good oral hygiene and maintenance following treatment of acute disease and thereafter. (A2)
- For patients with severe or nonresponding NUG/NUP, oral health care providers should prescribe systemic antibiotics and concurrent treatment with an antifungal agent, as specified below. (A3)

NUG/NUP Follow-Up

- Oral health care providers should evaluate healing within 7 days of treatment and perform additional debridement if necessary. (A3)
- Clinicians should reevaluate the patient 2 months after treatment to determine the need for further intervention. (A3)

NUS/NS Treatment

- Oral health care providers should perform a biopsy and refer patients to an oral surgeon, clinical pathologist, or oral medicine specialist when NUS/NS is diagnosed. (A2)
- Oral health care providers should treat NUS/NS with debridement of necrotic bone and soft tissue and concurrent antimicrobial therapy, as specified below. (A3)
- Clinicians should include the following as part of the treatment plan for patients with periodontal disease:
 - Use of a pre-procedural antimicrobial rinse. (A2)
 - Local debridement and disinfection using a 0.12% chlorhexidine gluconate or 10% povidone-iodine. (A2)
 - Removal of necrotic debris and sequestration, along with scaling and root planing, with local anesthesia to proceed as tolerated by the patient but no later than within 7 days of diagnosis. (A2)
 - Reinforcement of oral hygiene and home care instructions and prescriptions, including:
 - Daily use of an antimicrobial rinse for 30 days.
 - Antibacterial therapy.
 - Nutritional supplementation/advice.
 - Periodontal prescriptions. (B2)

Chronic Pre-Existing Periodontal Disease Treatment

- For treatment of pre-existing periodontitis, clinicians should follow the current [standard guidelines](#). (A3)
- Clinicians should perform additional diagnostic procedures (biopsy, cytologic smear, or culture) for lesions that show no healing within 10 days or refer the patient to a periodontist as indicated. (A3)

Abbreviation: LGE, linear gingival erythema; NS, necrotizing stomatitis; NUG, necrotizing ulcerative gingivitis; NUS, necrotizing ulcerative stomatitis; NUP, necrotizing ulcerative periodontitis.

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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

Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff .
Mission	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.
Expert committees	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.
Committee structure	<ul style="list-style-type: none"> • 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 • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	<ul style="list-style-type: none"> • 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. • 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.
Evidence collection and review	<ul style="list-style-type: none"> • Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • 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. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • 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.
Recommendation development	<ul style="list-style-type: none"> • The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee’s expert opinion. • 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.

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

Review and approval process	<ul style="list-style-type: none"> Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. 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. Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	<ul style="list-style-type: none"> External review of each guideline is invited at the developer’s discretion. External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	<ul style="list-style-type: none"> 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. 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.

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 [†] 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.