

Disseminated *Mycobacterium avium* Complex Disease

Updated: May 27, 2026

Reviewed: May 27, 2026

Epidemiology

Organisms of the *Mycobacterium avium* complex (MAC) are ubiquitous in the environment and are among the more common non-tuberculous mycobacteria (NTM), generally characterized as mycobacteria that cause infection and disease other than tuberculosis and leprosy.¹⁻⁶ In the era before effective antiretroviral therapy (ART) was available, *M. avium* was the etiologic agent in >95% of people with HIV with advanced immunosuppression who acquired disseminated MAC disease.^{4,7-13} Newer bacterial typing technology suggests organisms causing mycobacteremia in people with HIV represent a diversity of species, including the *M. avium* subspecies *hominissuis* and *M. colombiense* and other non-MAC species, including *M. genavense*, *M. kansasii*, *M. simiae*, *M. mycogenicum*, and others.¹⁴⁻¹⁷ These comprise what was historically referred to as disseminated MAC. An estimated 7% to 12% of adults with HIV have been previously infected with MAC, although rates of disease vary in different geographic locations.^{2,4,8,11,12} In particular, disseminated MAC in people with HIV has been described more frequently in the United States and Europe than in resource-limited settings.¹⁸

The mode of MAC infection is thought to be through repeated inhalation or ingestion of MAC bacteria via the respiratory or gastrointestinal (GI) tract, likely from environmental exposure.^{1,19} No singular environmental exposure or behavior has been consistently linked to subsequent increased risk of developing MAC disease, although one study suggested environmental water vapor exposure can increase risk in vulnerable populations.²⁰ Household or close contacts of those with MAC disease do not appear to be at increased risk of disease, and person-to-person transmission is unlikely.²¹⁻²³

MAC disease typically occurs in people with HIV with CD4 T lymphocyte (CD4) cell counts <50 cells/mm³. The previously reported incidence of disseminated MAC disease ranged from 20% to 40% in people with HIV with advanced immunosuppression in the absence of effective ART or chemoprophylaxis.^{24,25} However, the overall incidence of MAC disease among people with HIV has declined substantially in the modern ART era to current levels of <2 cases of MAC as the first opportunistic infection [OI] per 1,000 person-years for individuals in care, even among those not receiving effective ART.²⁶⁻³¹ In addition to a CD4 count <50 cells/mm³, factors associated with increased risk for MAC disease are ongoing HIV viral replication, previous or concurrent OIs, reduced *in vitro* lymphoproliferative immune responses to *M. avium* antigens (possibly reflecting defects in T-cell repertoire), and genetic predisposition in some populations.^{28-30,32,33}

While effective ART has clearly been associated with dramatic reductions in risk of developing MAC disease, MAC disease still can occur in people with HIV on suppressive ART (1) in the setting of recent initiation or reinitiation of ART; (2) in virologically suppressed people with HIV with immune reconstitution; or (3) in those who fail to have immune reconstitution despite viral suppression. The clinical presentation may differ from what is seen in people with untreated HIV. In a small retrospective case series of people with HIV most of whom were on ART, NTM disease occurred in nine who were virologically suppressed on ART at the time of their diagnosis—seven had pulmonary NTM only and two had extrapulmonary disease. MAC was the most common

pathogen, isolated in 19 of the 34 cases.¹⁴ Those with extrapulmonary disease were younger and had higher viral loads and lower CD4 counts at diagnosis.

Clinical Manifestations

In people with HIV and advanced immunosuppression who are not on ART, MAC disease generally presents as a disseminated, multi-organ infection, although localized disease may also be seen.³⁴⁻³⁸ Early symptoms may be minimal and can precede mycobacteremia or positive tissue cultures by several weeks. Systemic symptoms are nonspecific and include fever, night sweats, weight loss, fatigue, diarrhea, and abdominal pain; localized disease may cause only organ-specific symptoms.^{8,14-16}

Laboratory abnormalities particularly associated with disseminated MAC disease include anemia (often out of proportion to that expected for the stage of HIV disease) and elevated liver alkaline phosphatase levels.^{4,5,7-12,24,25,39,40} Hepatomegaly, splenomegaly, or lymphadenopathy (paratracheal, retroperitoneal, para-aortic, or less commonly peripheral) may be identified on physical examination or by radiographic or other imaging studies. Other focal physical findings or laboratory abnormalities may occur with localized disease.

Localized MAC disease occurs more often in people with HIV on suppressive ART with increased CD4 counts than in people with HIV not on ART, suggesting improved or preserved immune function is associated with control of disease. Localized disease may also be seen in the setting of “unmasking immune reconstitution inflammatory syndrome (IRIS)” (see discussion below) and might include cervical, intra-abdominal, or mediastinal lymphadenitis; lung lesions or pneumonia; pericarditis; osteomyelitis; skin or soft-tissue abscesses; bursitis; genital ulcers; and central nervous system infection, more often presenting with focal lesions and seizures in people with HIV.^{41,42} Localized syndromes may also be manifestations of IRIS, as discussed below.

Diagnosis

A confirmed diagnosis of disseminated MAC disease is based on compatible clinical signs and symptoms coupled with the isolation of MAC from cultures of blood, lymph fluid, bone marrow, or other normally sterile tissue or body fluids, although data suggest that bone marrow cultures have low yield for detection of MAC in this setting, particularly if blood cultures are negative.^{25,37,38,43-48} In a study among hospitalized people with HIV and CD4 counts <50 cells/mm³ in China, the prevalence of NTM bacteremia was 8.6%. The sensitivity of blood cultures in diagnosing culture-proven infection was 75% and was the only microbiological evidence in 25% of those diagnosed with MAC.⁴⁹ Species identification should be performed using molecular techniques (e.g., polymerase chain reaction-based assays, whole-genome sequencing), biochemical tests, high-performance liquid chromatography, or mass spectrometry, the details of which are discussed in further detail in a state-of-the-art review.⁵⁰ In addition to determining species or subspecies of MAC, molecular assays can also be used to identify mutations in the *rrs*, *rrl* or *erm* genes/sequevars that may be associated with constitutive or inducible macrolide resistance.⁵⁰ While phenotypic drug susceptibility testing is the preferred testing method and should be performed when cultures are positive to assist in selection of antimicrobial therapy, if available, molecular assays to identify mutations that confer inducible macrolide resistance would be an important adjunct to optimize treatment, particularly if disease occurs in the setting MAC prophylaxis with one of the macrolide drugs.

Other ancillary studies provide supportive diagnostic information, including acid-fast bacilli smear and culture of tissue, radiographic imaging, or other studies aimed at isolating organisms from focal infection sites.

Although isolated pulmonary MAC disease is not often observed in people with advanced HIV-associated immunosuppression, occasionally MAC disease may be limited to the lung in people with HIV who are virologically suppressed on ART and/or have other underlying conditions predisposing them to MAC pulmonary disease. Diagnostic criteria for disease limited to the lung in this setting should follow those established by the [American Thoracic Society \(ATS\), European Respiratory Society \(ERS\), European Society of Clinical Microbiology and Infectious Diseases \(ESCMID\), and the Infectious Disease Society of America \(IDSA\) joint guideline on Treatment of Nontuberculous Mycobacterial Pulmonary Disease](#) and the subsequently published consensus management recommendations for less common NTM pulmonary diseases,⁵¹ which include pulmonary clinical signs and symptoms, exclusion of other alternative diagnoses, nodular or cavitary disease on lung imaging, and a positive culture for MAC from at least two sputum specimens or at least one bronchoalveolar lavage or biopsy sample.⁵²

Detection of MAC organisms in the respiratory or GI tract in the absence of signs or symptoms of MAC disease may represent colonization of these sites and may be a harbinger of subsequent disseminated MAC disease. However, no data are available regarding efficacy of treatment for asymptomatic colonization with MAC organisms at these sites. Therefore, routine screening of respiratory or GI specimens and preemptive treatment for MAC **are not recommended**.

Preventing Exposure

MAC organisms commonly contaminate environmental sources, such as food, water, and soil. Available information does not support specific recommendations regarding avoidance of exposure.

Preventing Disease

Recommendations for Preventing First Episode of Disseminated <i>Mycobacterium avium</i> Complex Disease (Primary Prophylaxis)
<ul style="list-style-type: none">Primary prophylaxis is not recommended for people with HIV who immediately initiate ART, regardless of CD4 count (AII). <p>Indications for Primary Prophylaxis</p> <ul style="list-style-type: none">CD4 count <50 cells/mm³ and not receiving ART, remain viremic on ART, or have no options for a fully suppressive ART regimen (AI)Before primary prophylaxis is initiated, disseminated MAC disease should be ruled out by clinical assessment and, if appropriate, by obtaining a blood culture for MAC (AI). If blood culture is obtained, prophylaxis should be delayed until results are available to avoid exposing patients to monotherapy and the attendant risk of drug resistance (AI). <p>Preferred Therapy</p> <ul style="list-style-type: none">Azithromycin 1,200 mg PO once weekly (AI), orClarithromycin 500 mg PO twice daily (AI), orAzithromycin 600 mg PO twice weekly (BIII)

Alternative Therapy

- Rifabutin 300 mg PO daily (BI) for people who cannot tolerate azithromycin or clarithromycin
 - o Dose adjustment of rifabutin or concomitant ARVs may be necessary based on drug–drug interactions.
 - o Active TB should be ruled out before starting rifabutin to avoid monotherapy which could result in acquired rifamycin resistance.
- For information on drug–drug interactions between antimycobacterial agents (e.g. clarithromycin and rifabutin) and concomitant ARVs, refer to the [Liverpool HIV Drug Interaction Checker](#).

Indication for Discontinuing Primary Prophylaxis

- If previously initiated, primary prophylaxis should be discontinued for those continuing on a fully suppressive ART regimen (AI).

Pregnancy Considerations

- During pregnancy, if ART is immediately initiated, then primary prophylaxis for MAC disease is **not recommended** (AIII).
- When primary prophylaxis is required because of the absence of effective ART, azithromycin is the preferred agent during pregnancy (BIII).
- Clarithromycin is **not recommended** as a first-line agent for prophylaxis of MAC during pregnancy (BIII).

Key: ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; MAC = *Mycobacterium avium* complex; PO = orally; TB = tuberculosis

Indication for Primary Prophylaxis

Primary prophylaxis against disseminated MAC disease **is not recommended** for people with HIV who immediately initiate ART, regardless of CD4 count (**AII**). People with HIV who have CD4 counts <50 cells/mm³ and who are not receiving ART, remain viremic on ART, or have no options for a fully suppressive ART regimen should receive chemoprophylaxis to prevent disseminated MAC (**AI**). Before prophylaxis is initiated, disseminated MAC disease should be ruled out by clinical assessment and, if appropriate based on that assessment, by obtaining a blood culture for MAC (**AI**). MAC prophylaxis should be delayed until results are available to avoid exposing patients to monotherapy and the attendant risk of drug resistance (**AI**).

Preferred and Alternative Drugs for Prophylaxis

While primary prophylaxis for MAC is not recommended for people on effective ART, for those meeting criteria for prophylaxis, azithromycin⁵³ and clarithromycin^{5,54} are the preferred prophylactic agents (**AI**).^{1,55} The combination of clarithromycin and rifabutin is no more effective than clarithromycin alone for chemoprophylaxis, is associated with a higher rate of adverse effects than either drug alone, and **should not be used (AI)**.⁵ The combination of azithromycin and rifabutin is more effective than azithromycin alone in preventing MAC disease.⁵³ However, based on the additional cost, increased occurrence of adverse effects, potential for drug interactions, and lack of greater survival benefit than with azithromycin alone, the combination regimen of azithromycin and rifabutin **is not recommended (AI)**. In people with HIV who cannot tolerate azithromycin or clarithromycin, rifabutin can be used as a prophylactic agent for MAC disease (**BI**), although drug interactions may complicate use of this agent. Moreover, if use of rifabutin is planned or anticipated, tuberculosis (TB) should be excluded to avoid monotherapy of active TB, which could result in acquired rifamycin resistance.

When to Stop Primary Prophylaxis

Primary MAC prophylaxis, if previously initiated, should be discontinued in those who are continuing on a fully suppressive ART regimen **(AI)**. Two randomized, placebo-controlled trials and several large observational cohort studies have demonstrated that people with HIV taking ART can discontinue primary prophylaxis with minimal risk of developing MAC disease, particularly if they are virologically suppressed.⁵⁶⁻⁶¹ Conclusions from these studies indicate that the overall incidence of disseminated MAC is very low within 6 to 12 months after stopping primary prophylaxis in these circumstances, regardless of CD4 count, at 0.6 to 0.8 cases per 100 person-years. In each of these studies, plasma HIV RNA level >1,000 copies/mL was the principal risk factor for developing MAC disease regardless of MAC prophylaxis. However, in a study from the TREAT Asia HIV Observational Database, which evaluated the impact of MAC prophylaxis on AIDS-defining conditions and HIV-associated mortality in people with HIV on ART; participants were enrolled beginning in September 2003 and data were collected both retroactively and prospectively until September 2015. Macrolide use within 3 months of starting ART for those with a CD4 count <50 cells/mm³ at ART initiation was associated with a decreased risk of HIV-associated mortality (hazard ratio 0.10; 95% confidence interval, 0.01–0.80; *P* = 0.031) but not with the combined outcome of developing an AIDS-defining condition or death.⁶² Despite this finding, only 10.6% of the 1,345 participants in the cohort eligible for MAC prophylaxis received it. The authors concluded that there may be an additive protective effect of macrolide prophylaxis in reducing overall HIV-related mortality among Asians with HIV and CD4 counts <50 cells/mm³ even though they received effective ART.

Thus, despite some nuances across published studies, for most individuals, particularly in higher resourced settings, the preponderance of current data suggests that primary MAC prophylaxis provides no additional benefit in people started on effective ART that results in viral suppression. Additional arguments against primary MAC prophylaxis while prioritizing effective ART to achieve viral suppression include (1) the potential for adding additional cost and adverse effects of the drugs used for prophylaxis; (2) the likelihood that only a small number of people with HIV will develop “unmasking MAC IRIS” (i.e., active MAC disease after starting ART); (3) the potential for acquired drug resistance if people fail monotherapy for MAC prophylaxis; and (4) limiting polypharmacy to assist with adherence to ART.⁶³⁻⁶⁵

Treating Disease

Recommendations for Treating Disseminated <i>Mycobacterium avium</i> Complex Disease
<p>Preferred Therapy</p> <ul style="list-style-type: none">• Use at least two drugs as initial therapy to prevent or delay emergence of resistance (AI)<ul style="list-style-type: none">○ Clarithromycin 500 mg PO twice daily (AI) plus ethambutol 15 mg/kg PO daily (AI), or○ Azithromycin 500–600 mg (AII) (when drug interactions, intolerance, or adherence issues preclude the use of clarithromycin [AI]) plus ethambutol 15 mg/kg PO daily (AI)○ Note: Testing of susceptibility to clarithromycin or azithromycin is recommended.• A third or fourth drug should be used if more severe disease is present, the risk of mortality is high, emergence of drug resistance is likely (e.g., after failure of MAC prophylaxis), if mycobacterial loads are high (>2 log₁₀ CFU/mL of blood), if the patient is not on ART, or if the patient is not virally suppressed on ART (CIII).

o Third Drug:

- Rifabutin 300 mg PO daily (CI). Dose adjustment of rifabutin or concomitant ARVs may be necessary based on drug–drug interactions.

o Fourth Drug:

- A fluoroquinolone (CIII) (levofloxacin 500 mg PO daily or moxifloxacin 400 mg PO daily), or
- An injectable aminoglycoside (CIII) (amikacin 10–15 mg/kg IV daily) (should generally be avoided unless in the setting of refractory disease when other alternatives are not available or tolerated)
- Bedaquiline, tedizolid, linezolid, omadacycline, and dual beta-lactams (meropenem + ceftaroline or cefdinir) have demonstrated *in vitro* activity against clinical isolates of MAC; these might also be considered in people with refractory MAC disease.

- For information on drug–drug interactions between antimycobacterial agents (e.g. clarithromycin, rifabutin, bedaquiline) and concomitant ARVs, refer to the [Liverpool HIV Drug Interaction Checker](#).
- See [Table 6](#) for renal dosing recommendations (e.g. clarithromycin, rifabutin, levofloxacin, and aminoglycosides).

Duration of Therapy

- At least 12 months (AII). Shorter duration may be considered depending on the degree of immunologic recovery following initiation of ART (CIII).
- CD4 count should be >100 cells/mm³ for ≥6 months before discontinuation of therapy (CIII).

Chronic Maintenance Therapy (Secondary Prophylaxis)

- If ART does not result in immune reconstitution, people with HIV and disseminated MAC disease should continue chronic maintenance therapy (AII).
- Use the same regimens as recommended for treatment (reduce to two-drug maintenance therapy for those completing treatment with three- or four-drug regimens)

Criteria for Discontinuing Chronic Maintenance Therapy (Secondary Prophylaxis) (AI)

- Completed at least 12 months of therapy, and
- No signs or symptoms of MAC disease, and
- Have sustained (≥6 months) CD4 count >100 cells/mm³ in response to ART

Indication for Restarting Chronic Maintenance Therapy (Secondary Prophylaxis)

- If a fully suppressive ART regimen is not possible and CD4 is consistently <100 cells/mm³ (BIII)

Pregnancy Considerations

- For chronic maintenance therapy (secondary prophylaxis), azithromycin plus ethambutol is the preferred drug combination (BIII).
- Clarithromycin is not recommended as a first-line agent for prophylaxis or treatment of MAC during pregnancy (BIII).
- As previously discussed, if MAC disease is more severe and a third drug is required for treatment, azithromycin plus ethambutol plus rifabutin is the preferred treatment combination (BIII).

Other Considerations

- NSAIDs may be used for people with HIV who experience mild or moderate symptoms attributed to IRIS (BIII).
- If IRIS symptoms are more severe or unremitting, a short-term course (4–8 weeks) of systemic corticosteroid therapy (equivalent to prednisone 20–40 mg/day) can be used (BII).

Key: ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CFU = colony-forming unit; IRIS = immune reconstitution inflammatory syndrome; IV = intravenous; MAC = *Mycobacterium avium* complex; NSAID = nonsteroidal anti-inflammatory drug; PO = orally

Initial treatment of MAC disease should consist of at least two antimycobacterial drugs to prevent or delay the emergence of resistance **(AI)**.^{1,6,11,12,19,66-74} Clarithromycin **(AI)** or azithromycin **(AII)** are preferred first-line agents; published data are more extensive for clarithromycin than for azithromycin in people with advanced HIV disease, and clarithromycin-containing regimens were nominally associated with more rapid and potentially higher rates of clearance of MAC from the blood.^{6,66,68,72,73,75,76} However, azithromycin has comparable treatment efficacy and is acceptable when drug interactions, intolerance, or adherence issues preclude the use of clarithromycin **(AII)**. Doses of clarithromycin >1 g/day for treatment of disseminated MAC disease have been associated with increased mortality and **should not be used (AI)**.⁷⁷ Testing MAC isolates for susceptibility to clarithromycin or azithromycin is recommended for all people with HIV, particularly those who developed MAC disease while receiving prophylaxis with one of these agents.^{78,79} In three randomized clinical trials, clarithromycin-resistant isolates were reported in 29% and 58% of people with HIV who developed MAC bacteremia during prophylaxis with clarithromycin, and azithromycin-resistant isolates were recovered from 11% of those who developed bacteremia while on azithromycin prophylaxis.^{5,53,54} More advanced immunosuppression at prophylaxis initiation and longer duration of MAC prophylaxis are associated with higher rates of clarithromycin resistance at the time of MAC prophylaxis failure.⁸⁰

Ethambutol is the recommended second drug for the initial treatment of MAC disease **(AI)** based on randomized trials of MAC therapy that indicate its use in the regimen is associated with lower rates of relapse.^{67,69,75,81} A third and possibly a fourth drug should be used for severe disease defined by high risk of mortality; in the likelihood of emergence of drug resistance (e.g., after failure of MAC prophylaxis); in the setting of high mycobacterial loads (>2 log₁₀ colony-forming units/mL of blood); or when the patient is not on ART or ART has not resulted in viral suppression **(CIII)**. Rifabutin is recommended as the third drug **(CI)**, and if a fourth drug is considered, a fluoroquinolone (levofloxacin or moxifloxacin) **(CIII)** or an injectable aminoglycoside (amikacin) **(CIII)** should be used.

Previous studies adding rifabutin to the combination of clarithromycin and ethambutol improved survival⁸² and reduced the emergence of drug resistance in individuals with advanced HIV and disseminated MAC disease.^{6,68} These studies were completed before the availability of effective ART. It has not been established whether similar results would be observed for people with HIV receiving effective ART.

The fluoroquinolones levofloxacin and moxifloxacin, as well as amikacin, have *in vitro* and animal model activity against MAC, although randomized trials evaluating the efficacy of adding a fluoroquinolone or injectable aminoglycoside as part of a multidrug regimen for treatment of MAC have not been done in people with HIV. Injectable aminoglycosides should generally be avoided, except in the setting of refractory disease when other alternative agents are not available or tolerated and when drug-level monitoring is available.^{78,83}

Additional drugs with *in vitro* activity against clinical isolates of MAC include bedaquiline, tedizolid, linezolid, and omadacycline; these might also be considered in people with refractory or drug-resistant MAC disease.⁸⁴⁻⁹⁰ Dual beta-lactams have been shown to increase MAC susceptibility to meropenem in *in vitro* studies (i.e., adding ceftaroline or cefdinir to meropenem).⁹¹ This approach may also be useful in the setting of refractory or drug-resistant disease, although not studied in clinical trials.

While not specifically applicable to people with HIV (who more often have disseminated MAC disease than isolated pulmonary disease), in 2020, the ATS/ERS/ESCMID/IDSA updated their jointly sponsored [clinical guideline for treatment of nontuberculous mycobacterial pulmonary disease](#), which includes pulmonary MAC.⁵² People with HIV who are fully suppressed on ART with higher CD4 counts may present with localized pulmonary or other local organ system MAC disease that may clinically resemble such disease in people without HIV. Following the ATS/ERS/ESCMID/IDSA guidelines would be reasonable in such settings. Although intermittent dosing (twice or thrice weekly) of antimycobacterial drugs as described in the ATS/ERS/ESCMID/IDSA guidelines is not recommended in people with HIV, it may also be reasonable in this setting (i.e., fully suppressed on ART, high CD4 counts, and localized disease).

People with HIV and disseminated MAC disease should be treated for a minimum duration of 12 months **(AII)**. Shorter duration of treatment may be considered depending on the degree of immunologic recovery following initiation of ART and viral suppression **(CIII)**. Viral suppression on ART and CD4 count >100 cells/mm³ should be maintained for at least 6 months before discontinuing MAC treatment **(CIII)**.⁹²⁻⁹⁴

Special Considerations Regarding Antiretroviral Therapy Initiation

People with HIV and disseminated MAC disease who are not receiving effective ART should initiate ART as soon as possible after receiving a MAC diagnosis, preferably at the same time as initiation of antimycobacterial therapy **(AIII)** to reduce the risk of further AIDS-defining OIs and to further improve the response to antimycobacterial therapy in the setting of advanced immunosuppression. If ART has already been initiated, it should be continued. The regimens should be modified when there is any potential for adverse drug–drug interaction(s) between the antiretroviral (ARV) and antimycobacterial drugs **(AIII)**. Refer to the [Liverpool HIV Drug Interaction Checker](#) for updated drug–drug interaction information.

Monitoring of Response to Therapy and Adverse Events

A repeat blood culture for MAC should be obtained 4 to 8 weeks after initiating antimycobacterial therapy in people with HIV who do not have a clinical response to their initial treatment regimens. Improvement in fever and other systemic symptoms and a decline in the quantity of mycobacteria in blood or tissue can be expected within 2 to 4 weeks after initiation of appropriate therapy; however, clinical response may be delayed in those with more extensive MAC disease or advanced immunosuppression. See [Table 5. Serious and/or Common Adverse Reactions Associated With Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections](#) for more information on antimycobacterial-related adverse drug reactions.

Adverse effects of clarithromycin and azithromycin include GI upset, metallic taste, elevations in liver transaminase levels, and hypersensitivity reactions. Clarithromycin's adverse effects may be exacerbated when drug levels are increased due to drug interactions associated with some ARV

drugs. Doses of clarithromycin >1 g/day for treatment of disseminated MAC disease have been associated with increased mortality and **should not be used (AI)**.⁷⁷ Protease inhibitors (PIs) and elvitegravir/cobicistat can increase clarithromycin levels; clarithromycin dose adjustment or switching clarithromycin to azithromycin may be necessary. Azithromycin metabolism is not affected by the cytochrome P450 (CYP) system; azithromycin can be used safely in the presence of PIs, non-nucleoside reverse transcriptase inhibitors, or integrase inhibitors without concerns about drug interactions.

Rifabutin is a CYP isoenzyme 3A4 (CYP3A4) inducer and substrate. Adverse effects are concentration related. When used with clarithromycin or other drugs that inhibit CYP3A4, rifabutin has been associated with a higher risk of adverse drug reactions, in particular sight-threatening uveitis and neutropenia.^{95,96} Rifabutin dose should be decreased in people with HIV receiving ritonavir-boosted PIs.^{97,98} It should not be coadministered with cobicistat-boosted PIs or elvitegravir/cobicistat.⁹⁹ Rifabutin dose should be increased in people with HIV receiving efavirenz. Due to rifabutin mediated CYP3A4 induction, rifabutin should not be coadministered with long-acting injectable cabotegravir/rilpivirine or lenacapavir as this may lead to loss of ARV effectiveness and ARV resistance.¹⁰⁰ Injectable cabotegravir alone may be coadministered, with adjustment of the initiation and continuation dosing schedules. Oral rilpivirine and doravirine doses should be increased if either is coadministered with rifabutin. No dose adjustment for rifabutin or the integrase inhibitors dolutegravir or raltegravir alone is currently recommended, although at least one study suggested that compared with people without TB or MAC, lower trough concentrations were observed when once daily dolutegravir was used together with rifabutin.¹⁰¹⁻¹⁰³ Little published information on the use of bictegravir with rifabutin is available, although a study of bictegravir used with rifampicin during treatment of TB suggests that bictegravir (coformulated with tenofovir alafenamide and emtricitabine) might be used with rifampin with dose adjustment to twice daily and close monitoring of viral load.¹⁰⁴ Refer to the [Liverpool HIV Drug Interaction Checker](#) for updated drug–drug interaction information.

Therapeutic drug monitoring may be considered to reduce the potential for adverse effects and to optimize drug dosing in the context of complex drug–drug interactions.¹⁰⁵

***Mycobacterium avium*-Associated Immune Reconstitution Inflammatory Syndrome**

IRIS associated with MAC disease is recognized as a systemic inflammatory syndrome, with signs and symptoms—such as fevers, fatigue, local or disseminated lymphadenopathy, abdominal pain, diarrhea, and weight loss—often clinically indistinguishable from active MAC infection. Bacteremia is generally absent except in the presence of “unmasking” IRIS. Similar to TB, MAC-associated IRIS can occur as either “unmasking” IRIS in people with HIV with subclinical (undiagnosed) MAC that emerges following initiation of ART or “paradoxical” IRIS in those with a previously established diagnosis of MAC disease that worsens after initiating either MAC treatment or ART.¹⁰⁶⁻¹¹⁰ Both variants occur primarily in persons with advanced immunosuppression who begin ART and have a rapid and marked reduction in plasma HIV RNA.^{110,111} Elevated alkaline phosphatase levels, low hemoglobin, and increased CD8 T lymphocyte cell activation markers may be predictors of MAC-associated IRIS.⁴² The syndrome may be benign and self-limited or may result in severe, unremitting symptoms that improve with the use of systemic anti-inflammatory therapy or corticosteroids.

People with HIV on ART who develop mild or moderate symptoms typical of IRIS should continue ART and receive initial treatment with nonsteroidal anti-inflammatory drugs (or NSAIDs) **(BIII)**. If IRIS symptoms are more severe and unremitting, short-term (4–8 weeks) systemic corticosteroid

therapy, in doses equivalent to 20 to 40 mg of oral prednisone daily, may be used to reduce symptoms and morbidity **(BII)**.^{107,112} Severe forms of MAC IRIS with a hemophagocytic lymphohistiocytosis phenotype may occur; low hemoglobin prior to ART may predict this more severe form of IRIS.^{42,113} Patients with this more severe form of IRIS may have a genetic predisposition. Persistent severe MAC IRIS may require more prolonged corticosteroid therapy or additional immunosuppression.^{113,114}

Managing Treatment Failure

MAC treatment failure is defined by the absence of a clinical response and the persistence of mycobacteremia (or persistently positive tissue cultures from other sites) after 4 to 8 weeks of treatment. Repeat testing of MAC isolates for antimycobacterial drug susceptibility is recommended for people with HIV whose disease relapses after an initial response to treatment. Because the number of drugs with demonstrated clinical activity against MAC is limited, results of susceptibility testing should be used to construct a new multidrug regimen. The regimen should consist of at least two new drugs (i.e., not previously used) to which the isolate is fully susceptible. Similar to the discussion above, additional drugs if not previously used include rifabutin, fluoroquinolones (levofloxacin or moxifloxacin), an injectable aminoglycoside (amikacin or streptomycin), or possibly bedaquiline, tedizolid, linezolid, omadacycline, or dual beta-lactams (meropenem and ceftaroline or cefdinir), although data supporting a survival or microbiologic benefit when these latter agents are added are limited.^{11,12,52,67-71,75,81,85-88,91,115-118} Continuing clarithromycin or azithromycin despite resistance **is not recommended (AIII)**, as there is likely to be no additional benefit but added toxicity. Clofazimine **should generally not be used** because randomized trials have demonstrated lack of efficacy and an association with increased mortality **(AI)**.^{67,69,81} Optimization of ART is an important adjunct to second-line or salvage therapy for MAC disease in people with HIV for whom initial treatment is unsuccessful or who have disease that is resistant to antimycobacterial drugs **(AIII)**.

Although anecdotal data and individual case reports suggest potential benefit, adjunctive treatment of MAC disease with immunomodulators has not been thoroughly studied. Therefore, data are insufficient to support a recommendation for routine use, except in the setting of familial immunodeficiencies associated with increased risk of MAC disease.¹¹⁹ An investigational approach reported the addition of a cyclic peptide (R4W4) to a THP-1 monocyte cell line infected with MAC enhanced macrophage killing when combined with antibiotics; this may be an approach for further investigation of future treatments for refractory MAC or NTM disease.¹²⁰

Preventing Recurrence

As indicated above, people with HIV and disseminated MAC disease should be treated for a minimum duration of 12 months **(AII)**. Shorter duration of treatment may be considered depending on the degree of immunologic recovery following initiation of ART **(CIII)**. The CD4 count should be maintained >100 cells/mm³ and viral suppression maintained on ART for at least 6 months before discontinuing MAC treatment **(CIII)**. If ART initiation does not result in immune reconstitution, people with HIV and disseminated MAC disease should continue chronic maintenance therapy (secondary prophylaxis) as previously indicated **(AII)**,⁹²⁻⁹⁴ using the same regimens as recommended for treatment (reduce to two-drug maintenance therapy for those completing treatment with three- or four-drug regimens).

When to Stop Chronic Maintenance Therapy (Secondary Prophylaxis)

The risk of MAC recurrence is low in people with HIV who have completed at least a 12-month MAC treatment course, remain asymptomatic with respect to MAC signs and symptoms, and sustain an increase in CD4 count to >100 cells/mm³ and viral suppression for ≥ 6 months after initiation of ART. In this setting, it is reasonable to discontinue maintenance therapy based on data from studies in people with HIV and inferences from more extensive observational study data that indicate the safety of discontinuing secondary prophylaxis for other OIs **(AI)**.^{58,71,92-94,121-123} Reintroducing chronic maintenance therapy or secondary prophylaxis may be indicated for people with HIV for whom a fully suppressive ART regimen is not possible and who have a decline in their CD4 count to levels consistently <100 cells/mm³ **(BIII)**.

Special Considerations During Pregnancy

During pregnancy, if ART is initiated immediately, primary prophylaxis for MAC disease **is not recommended (AIII)**. When primary prophylaxis is required because of the absence of effective ART, azithromycin is the preferred agent **(BIII)**. For treatment of MAC disease and for secondary prophylaxis (chronic maintenance therapy), azithromycin plus ethambutol is the preferred drug combination **(BIII)**. As previously discussed, if MAC disease is more severe and a third drug is required for treatment, azithromycin plus ethambutol plus rifabutin is the preferred treatment combination **(BIII)**. Because clarithromycin is associated with an increased risk of birth defects based on evidence from certain animal studies, it **is not recommended** as the first-line agent for prophylaxis or treatment of MAC in pregnancy **(BIII)**. Two studies, each with slightly more than 100 women with first-trimester exposure to clarithromycin, did not demonstrate an increase in or specific pattern of defects, although an increased risk of spontaneous abortion was noted in one study.^{124,125}

Azithromycin did not produce defects in animal studies, but experience with its use in humans during the first trimester is limited. A nested case-control study conducted within the large Quebec Pregnancy cohort found an association between azithromycin use and spontaneous miscarriage¹²⁶; however, the authors were not able to adjust for severity of infection, an important confounder. Multiple studies, including large cohort studies, have found no association between the use of azithromycin in the first trimester and major congenital malformations, including heart defects.¹²⁷⁻¹²⁹ A systematic review of pregnancy outcomes following macrolide use found no significant increased risks for major congenital malformations or congenital heart defects following all macrolide use in the first trimester, but a small but significant increased rate of major congenital malformations with azithromycin though maternal confounders could not be excluded. In a Cochrane systematic review of *Chlamydia trachomatis* infection treatment in pregnancy efficacy and pregnancy complications did not differ in persons treated with azithromycin versus other agents.¹³⁰

References

1. Karakousis PC, Moore RD, Chaisson RE. *Mycobacterium avium* complex in patients with HIV infection in the era of highly active antiretroviral therapy. *Lancet Infect Dis*. 2004;4(9):557-565. Available at: <https://pubmed.ncbi.nlm.nih.gov/15336223>.
2. Hoefsloot W, van Ingen J, Andrejak C, et al. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: an NTM-NET collaborative study. *Eur Respir J*. 2013;42(6):1604-1613. Available at: <https://pubmed.ncbi.nlm.nih.gov/23598956>.
3. Reed C, von Reyn CF, Chamblee S, et al. Environmental risk factors for infection with *Mycobacterium avium* complex. *Am J Epidemiol*. 2006;164(1):32-40. Available at: <https://pubmed.ncbi.nlm.nih.gov/16675537>.
4. Inderlied C B. Microbiology and minimum inhibitory concentration testing for *Mycobacterium avium* complex prophylaxis. *Am J Med*. 1997;102(5):2-10. Available at: <https://www.sciencedirect.com/science/article/pii/S0002934397000375>.
5. Benson CA, Williams PL, Cohn DL, et al. Clarithromycin or rifabutin alone or in combination for primary prophylaxis of *Mycobacterium avium* complex disease in patients with AIDS: a randomized, double-blind, placebo-controlled trial. The AIDS Clinical Trials Group 196/Terry Bein Community Programs for Clinical Research on AIDS 009 Protocol Team. *J Infect Dis*. 2000;181(4):1289-1297. Available at: <https://pubmed.ncbi.nlm.nih.gov/10762562/>.
6. Benson CA, Williams PL, Currier JS, et al. A prospective, randomized trial examining the efficacy and safety of clarithromycin in combination with ethambutol, rifabutin, or both for the treatment of disseminated *Mycobacterium avium* complex disease in persons with acquired immunodeficiency syndrome. *Clin Infect Dis*. 2003;37(9):1234-1243. Available at: <https://pubmed.ncbi.nlm.nih.gov/14557969/>.
7. Kemper CA, Havlir D, Bartok AE, et al. Transient bacteremia due to *Mycobacterium avium* complex in patients with AIDS. *J Infect Dis*. 1994;170(2):488-493. Available at: <https://pubmed.ncbi.nlm.nih.gov/8035044/>.
8. Gordin FM, Cohn DL, Sullam PM, Schoenfelder JR, Wynne BA, Horsburgh CR, Jr. Early manifestations of disseminated *Mycobacterium avium* complex disease: a prospective evaluation. *J Infect Dis*. 1997;176(1):126-132. Available at: <https://pubmed.ncbi.nlm.nih.gov/9207358/>.
9. Benson CA, Ellner JJ. *Mycobacterium avium* complex infection and AIDS: advances in theory and practice. *Clin Infect Dis*. 1993;17(1):7-20. Available at: <https://pubmed.ncbi.nlm.nih.gov/8353249/>.

10. Havlik JA, Jr., Horsburgh CR, Jr., Metchock B, Williams PP, Fann SA, Thompson SE, 3rd. Disseminated *Mycobacterium avium* complex infection: clinical identification and epidemiologic trends. *J Infect Dis*. 1992;165(3):577-580. Available at: <https://pubmed.ncbi.nlm.nih.gov/1347060/>.
11. Benson CA. Treatment of disseminated disease due to the *Mycobacterium avium* complex in patients with AIDS. *Clin Infect Dis*. 1994;18 Suppl 3:S237-242. Available at: <https://pubmed.ncbi.nlm.nih.gov/8204776/>.
12. Benson CA. Disease due to the *Mycobacterium avium* complex in patients with AIDS: epidemiology and clinical syndrome. *Clin Infect Dis*. 1994;18 Suppl 3:S218-222. Available at: <https://pubmed.ncbi.nlm.nih.gov/8204773/>.
13. Horsburgh CR, Jr., Selik RM. The epidemiology of disseminated nontuberculous mycobacterial infection in the acquired immunodeficiency syndrome (AIDS). *Am Rev Respir Dis*. 1989;139(1):4-7. Available at: <https://pubmed.ncbi.nlm.nih.gov/2912355/>.
14. Lee EH, Chin B, Kim YK, et al. Clinical characteristics of nontuberculous mycobacterial disease in people living with HIV/AIDS in South Korea: A multi-center, retrospective study. *PLoS One*. 2022;17(11):e0276484. Available at: <https://pubmed.ncbi.nlm.nih.gov/36355915/>.
15. Ricotta EE, Adjemian J, Blakney RA, Lai YL, Kadri SS, Prevots DR. Extrapulmonary nontuberculous mycobacteria infections in hospitalized patients, United States, 2009-2014. *Emerg Infect Dis*. 2021;27(3):845-852. Available at: <https://pubmed.ncbi.nlm.nih.gov/33622461/>.
16. Wetzstein N, Geil A, Kann G, et al. Disseminated disease due to non-tuberculous mycobacteria in HIV positive patients: a retrospective case control study. *PLoS One*. 2021;16(7):e0254607. Available at: <https://pubmed.ncbi.nlm.nih.gov/34255788/>.
17. Lee MR, Chien JY, Huang YT, et al. Clinical features of patients with bacteraemia caused by *Mycobacterium avium* complex species and antimicrobial susceptibility of the isolates at a medical centre in Taiwan, 2008-2014. *Int J Antimicrob Agents*. 2017;50(1):35-40. Available at: <https://pubmed.ncbi.nlm.nih.gov/28478210/>.
18. Heidary M, Nasiri MJ, Mirsaeidi M, et al. *Mycobacterium avium* complex infection in patients with human immunodeficiency virus: a systematic review and meta-analysis. *J Cell Physiol*. 2019;234(7):9994-10001. Available at: <https://pubmed.ncbi.nlm.nih.gov/30548598/>.
19. Corti M, Palmero D. *Mycobacterium avium* complex infection in HIV/AIDS patients. *Expert Rev Anti Infect Ther*. 2008;6(3):351-363. Available at: <https://pubmed.ncbi.nlm.nih.gov/18588499/>.

20. Mullen B, Hout ER, Colston J, et al. Geographic variation and environmental predictors of nontuberculous mycobacteria in laboratory surveillance, Virginia, USA, 2021–2023. *Emerg Infect Dis*. 2024;30(3):548-554. Available at: <https://pubmed.ncbi.nlm.nih.gov/38407146>.
21. Carbonne A, Lemaitre N, Bochet M, et al. *Mycobacterium avium* complex common-source or cross-infection in AIDS patients attending the same day-care facility. *Infect Control Hosp Epidemiol*. 1998;19(10):784-786. Available at: <https://pubmed.ncbi.nlm.nih.gov/9801289/>.
22. Reed C, von Reyn CF, Chamblee S, et al. Environmental risk factors for infection with *Mycobacterium avium* complex. *American journal of epidemiology*. 2006;164(1):32-40. Available at: <https://europepmc.org/article/MED/16675537>.
23. O'Brien RJ. The epidemiology of nontuberculous mycobacterial disease. *Clin Chest Med*. 1989;10(3):407-418. Available at: <https://pubmed.ncbi.nlm.nih.gov/2673649>.
24. Nightingale SD, Byrd LT, Southern PM, Jockusch JD, Cal SX, Wynne BA. Incidence of *Mycobacterium avium-intracellulare* complex bacteremia in human immunodeficiency virus-positive patients. *J Infect Dis*. 1992;165(6):1082-1085. Available at: <https://pubmed.ncbi.nlm.nih.gov/1349906/>.
25. Chaisson RE, Moore RD, Richman DD, Keruly J, Creagh T. Incidence and natural history of *Mycobacterium avium*-complex infections in patients with advanced human immunodeficiency virus disease treated with zidovudine. The Zidovudine Epidemiology Study Group. *Am Rev Respir Dis*. 1992;146(2):285-289. Available at: <https://pubmed.ncbi.nlm.nih.gov/1362634/>.
26. Marochi-Telles JP, Muniz R, Jr., Sztajnbok J, Cosme-de Oliveira A. Disseminated *mycobacterium avium* on HIV/AIDS: historical and current literature review. *AIDS Rev*. 2020;22(1):9-15. Available at: <https://pubmed.ncbi.nlm.nih.gov/32167509/>.
27. Buchacz K, Baker RK, Palella FJ, Jr., et al. AIDS-defining opportunistic illnesses in US patients, 1994–2007: a cohort study. *AIDS*. 2010;24(10):1549-1559. Available at: <https://pubmed.ncbi.nlm.nih.gov/20502317/>.
28. Buchacz K, Lau B, Jing Y, et al. Incidence of AIDS-defining opportunistic infections in a multicohort analysis of HIV-infected persons in the United States and Canada, 2000-2010. *J Infect Dis*. 2016;214(6):862-872. Available at: <https://pubmed.ncbi.nlm.nih.gov/27559122/>.
29. Collins LF, Clement ME, Stout JE. Incidence, long-term outcomes, and healthcare utilization of patients with human immunodeficiency virus/acquired immune deficiency syndrome and disseminated *Mycobacterium avium* complex from 1992-2015. *Open Forum Infect Dis*. 2017;4(3):ofx120. Available at: <https://pubmed.ncbi.nlm.nih.gov/28748197/>.

30. Jung Y, Song KH, Choe PG, et al. Incidence of disseminated *Mycobacterium avium*-complex infection in HIV patients receiving antiretroviral therapy with use of *Mycobacterium avium*-complex prophylaxis. *Int J STD AIDS*. 2017;28(14):1426-1432. Available at: <https://pubmed.ncbi.nlm.nih.gov/28592210/>.
31. Bielick C, Strumpf A, Ghosal S, McMurry T, McManus KA. National hospitalization rates and in-hospital mortality rates of HIV-related opportunistic infections in the United States, 2011–2018. *Clin Infect Dis*. 2024;79(2):487-497. Available at: <https://pubmed.ncbi.nlm.nih.gov/38306316/>.
32. Hsu DC, Breglio KF, Pei L, et al. Emergence of polyfunctional cytotoxic CD4+ T cells in mycobacterium avium immune reconstitution inflammatory syndrome in human immunodeficiency virus-infected patients. *Clin Infect Dis*. 2018;67(3):437-446. Available at: <https://pubmed.ncbi.nlm.nih.gov/29538651/>.
33. Fernández-Díaz MDR, Faro-Miguez N, Aguilera-Franco M, et al. Mycobacterium avium complex (MAC) infection in severely immunocompromised people living with HIV: findings from a five-year cohort. *Int J STD AIDS*. 2025;36(2):126-131. Available at: <https://pubmed.ncbi.nlm.nih.gov/39499859>.
34. Barbaro DJ, Orcutt VL, Coldiron BM. *Mycobacterium avium*-*Mycobacterium intracellulare* infection limited to the skin and lymph nodes in patients with AIDS. *Rev Infect Dis*. 1989;11(4):625-628. Available at: <https://pubmed.ncbi.nlm.nih.gov/2772468/>.
35. Hellyer TJ, Brown IN, Taylor MB, Allen BW, Easmon CS. Gastro-intestinal involvement in *Mycobacterium avium*-*intracellulare* infection of patients with HIV. *J Infect*. 1993;26(1):55-66. Available at: <https://pubmed.ncbi.nlm.nih.gov/8454889/>.
36. Torriani FJ, McCutchan JA, Bozzette SA, Grafe MR, Havlir DV. Autopsy findings in AIDS patients with *Mycobacterium avium* complex bacteremia. *J Infect Dis*. 1994;170(6):1601-1605. Available at: <https://pubmed.ncbi.nlm.nih.gov/7996004>.
37. Roth RI, Owen RL, Keren DF, Volberding PA. Intestinal infection with *Mycobacterium avium* in acquired immune deficiency syndrome (AIDS): histological and clinical comparison with Whipple's disease. *Dig Dis Sci*. 1985;30(5):497-504. Available at: <https://pubmed.ncbi.nlm.nih.gov/2580679>.
38. Gillin JS, Urmacher C, West R, Shike M. Disseminated *Mycobacterium avium*-*intracellulare* infection in acquired immunodeficiency syndrome mimicking Whipple's disease. *Gastroenterology*. 1983;85(5):1187-1191. Available at: <https://pubmed.ncbi.nlm.nih.gov/6194041/>.
39. Inderlied CB, Kemper CA, Bermudez LE. The *Mycobacterium avium* complex. *Clin Microbiol Rev*. 1993;6(3):266-310. Available at: <https://pubmed.ncbi.nlm.nih.gov/8358707/>.

40. Packer SJ, Cesario T, Williams JH, Jr. *Mycobacterium avium* complex infection presenting as endobronchial lesions in immunosuppressed patients. *Ann Intern Med.* 1988;109(5):389-393. Available at: <https://pubmed.ncbi.nlm.nih.gov/3165608/>.
41. Mina Y, Kline A, Manion M, et al. Neurological manifestations of nontuberculous mycobacteria in adults: case series and review of the literature. *Front Neurol.* 2024;15:1360128. Available at: <https://pubmed.ncbi.nlm.nih.gov/38742044>.
42. Breglio KF, Vinhaes CL, Arriaga MB, et al. Clinical and immunologic predictors of *Mycobacterium avium* complex immune reconstitution inflammatory syndrome in a contemporary cohort of patients with human immunodeficiency virus. *J Infect Dis.* 2021;223(12):2124-2135. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8205640/>.
43. Shanson DC, Dryden MS. Comparison of methods for isolating *Mycobacterium avium-intracellulare* from blood of patients with AIDS. *J Clin Pathol.* 1988;41(6):687-690. Available at: <https://pubmed.ncbi.nlm.nih.gov/3385000/>.
44. Hafner R, Inderlied CB, Peterson DM, et al. Correlation of quantitative bone marrow and blood cultures in AIDS patients with disseminated *Mycobacterium avium* complex infection. *J Infect Dis.* 1999;180(2):438-447. Available at: <https://pubmed.ncbi.nlm.nih.gov/10395860/>.
45. Cornejo-Juárez P, Islas-Muñoz B, Ramírez-Ibarguen AF, et al. Bone marrow culture yield for the diagnosis of opportunistic diseases in patients with AIDS and disseminated Kaposi sarcoma. *Curr HIV Res.* 2020;18(4):277-282. Available at: <https://pubmed.ncbi.nlm.nih.gov/32493198>.
46. Prabhu V, Coelho S, Achappa B, Baliga S, Sharon L, Shah J. Role of fluorescence in situ hybridization in detecting mycobacterium avium complex presenting as fever in treatment failure HIV. *J Clin Tuberc Other Mycobact Dis.* 2020;21:100188. Available at: <https://pubmed.ncbi.nlm.nih.gov/32995570>.
47. Sharma S, Latawa R, Wanchu A, Verma I. Differential diagnosis of disseminated *mycobacterium avium* and *mycobacterium tuberculosis* infection in HIV patients using duplex PCR. *Future Microbiol.* 2021;16(3):159-173. Available at: <https://pubmed.ncbi.nlm.nih.gov/33528278>.
48. Sharvit G, Schwartz D, Heering G, et al. Evaluation of the clinical impact of bone marrow cultures in current medical practice. *Sci Rep.* 2022;12(1):9664. Available at: <https://pubmed.ncbi.nlm.nih.gov/35690634>.
49. Miao M, Zhu H, Liu Z, et al. The role of mycobacteremia screening in enhancing non-tuberculous mycobacteria detection in hospitalized persons with HIV. *Front Microbiol.* 2025;16:1517418. Available at: <https://pubmed.ncbi.nlm.nih.gov/39959163>.

50. Nguyen MH, Haas MK, Kasperbauer SH, et al. Nontuberculous mycobacterial pulmonary disease: patients, principles, and prospects. *Clin Infect Dis*. 2024;79(4):e27-e47. Available at: <https://pubmed.ncbi.nlm.nih.gov/39405483>.
51. Lange C, Böttger EC, Cambau E, et al. Consensus management recommendations for less common non-tuberculous mycobacterial pulmonary diseases. *Lancet Infect Dis*. 2022;22(7):e178-e190. Available at: <https://pubmed.ncbi.nlm.nih.gov/35090639>.
52. Daley CL, Iaccarino JM, Lange C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. *Clin Infect Dis*. 2020;71(4):e1-e36. Available at: <https://pubmed.ncbi.nlm.nih.gov/32628747>.
53. Havlir DV, Dube MP, Sattler FR, et al. Prophylaxis against disseminated *Mycobacterium avium* complex with weekly azithromycin, daily rifabutin, or both. California Collaborative Treatment Group. *N Engl J Med*. 1996;335(6):392-398. Available at: <https://pubmed.ncbi.nlm.nih.gov/8676932/>.
54. Pierce M, Crampton S, Henry D, et al. A randomized trial of clarithromycin as prophylaxis against disseminated *Mycobacterium avium* complex infection in patients with advanced acquired immunodeficiency syndrome. *N Engl J Med*. 1996;335(6):384-391. Available at: <https://pubmed.ncbi.nlm.nih.gov/8663871>.
55. Uthman MM, Uthman OA, Yahaya I. Interventions for the prevention of *Mycobacterium avium* complex in adults and children with HIV. *Cochrane Database Syst Rev*. 2013(4):CD007191. Available at: <https://pubmed.ncbi.nlm.nih.gov/23633339>.
56. Dworkin MS, Hanson DL, Kaplan JE, Jones JL, Ward JW. Risk for preventable opportunistic infections in persons with AIDS after antiretroviral therapy increases CD4+ T lymphocyte counts above prophylaxis thresholds. *J Infect Dis*. 2000;182(2):611-615. Available at: <https://pubmed.ncbi.nlm.nih.gov/10915098/>.
57. El-Sadr WM, Burman WJ, Grant LB, et al. Discontinuation of prophylaxis for *Mycobacterium avium* complex disease in HIV-infected patients who have a response to antiretroviral therapy. Terry Bein Community Programs for Clinical Research on AIDS. *N Engl J Med*. 2000;342(15):1085-1092. Available at: <https://pubmed.ncbi.nlm.nih.gov/10766581/>.
58. Currier JS, Williams PL, Koletar SL, et al. Discontinuation of *Mycobacterium avium* complex prophylaxis in patients with antiretroviral therapy-induced increases in CD4+ cell count: a randomized, double-blind, placebo-controlled trial. AIDS Clinical Trials Group 362 Study Team. *Ann Intern Med*. 2000;133(7):493-503. Available at: <https://pubmed.ncbi.nlm.nih.gov/11015162/>.
59. Furrer H, Telenti A, Rossi M, Ledergerber B. Discontinuing or withholding primary prophylaxis against *Mycobacterium avium* in patients on successful antiretroviral combination therapy. The Swiss HIV Cohort Study. *AIDS*. 2000;14(10):1409-1412. Available at: <https://pubmed.ncbi.nlm.nih.gov/10930156/>.

60. Brooks JT, Song R, Hanson DL, et al. Discontinuation of primary prophylaxis against *Mycobacterium avium* complex infection in HIV-infected persons receiving antiretroviral therapy: observations from a large national cohort in the United States, 1992-2002. *Clin Infect Dis*. 2005;41(4):549-553. Available at: <https://pubmed.ncbi.nlm.nih.gov/16028167/>.
61. Chene G, Phillips A, Costagliola D, et al. Cohort profile: Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord. *Int J Epidemiol*. 2017;46(3):797-797n. Available at: <https://pubmed.ncbi.nlm.nih.gov/27864413/>.
62. Pasayan MKU, ML SM, Boettiger D, et al. Effect of macrolide prophylactic therapy on AIDS-defining conditions and HIV-associated mortality. *J Acquir Immune Defic Syndr*. 2019;80(4):436-443. Available at: <https://pubmed.ncbi.nlm.nih.gov/30550488>.
63. Lange CG, Woolley IJ, Brodt RH. Disseminated *Mycobacterium avium-intracellulare* complex (MAC) infection in the era of effective antiretroviral therapy: is prophylaxis still indicated? *Drugs*. 2004;64(7):679-692. Available at: <https://pubmed.ncbi.nlm.nih.gov/15025543/>.
64. Sax PE. "Choosing wisely" in HIV medicine — should we stop giving MAC prophylaxis? *HIV and ID Observations*. 2016;2018. Available at: <https://blogs.jwatch.org/hiv-id-observations/index.php/choosing-wisely-in-hiv-medicine-should-we-stop-giving-mac-prophylaxis/2016/03/20>.
65. Vervoort SC, Borleffs JC, Hoepelman AI, Grypdonck MH. Adherence in antiretroviral therapy: a review of qualitative studies. *AIDS*. 2007;21(3):271-281. Available at: <https://pubmed.ncbi.nlm.nih.gov/17255734/>.
66. Chaisson RE, Benson CA, Dube MP, et al. Clarithromycin therapy for bacteremic *Mycobacterium avium* complex disease. A randomized, double-blind, dose-ranging study in patients with AIDS. AIDS Clinical Trials Group Protocol 157 Study Team. *Ann Intern Med*. 1994;121(12):905-911. Available at: <https://pubmed.ncbi.nlm.nih.gov/7978715/>.
67. May T, Brel F, Beuscart C, et al. Comparison of combination therapy regimens for treatment of human immunodeficiency virus-infected patients with disseminated bacteremia due to *Mycobacterium avium*. ANRS Trial 033 Curavium Group. Agence Nationale de Recherche sur le Sida. *Clin Infect Dis*. 1997;25(3):621-629. Available at: <https://pubmed.ncbi.nlm.nih.gov/9314450/>.
68. Gordin FM, Sullam PM, Shafran SD, et al. A randomized, placebo-controlled study of rifabutin added to a regimen of clarithromycin and ethambutol for treatment of disseminated infection with *Mycobacterium avium* complex. *Clin Infect Dis*. 1999;28(5):1080-1085. Available at: <https://pubmed.ncbi.nlm.nih.gov/10452638/>.

69. Dube MP, Sattler FR, Torriani FJ, et al. A randomized evaluation of ethambutol for prevention of relapse and drug resistance during treatment of *Mycobacterium avium* complex bacteremia with clarithromycin-based combination therapy. California Collaborative Treatment Group. *J Infect Dis*. 1997;176(5):1225-1232. Available at: <https://pubmed.ncbi.nlm.nih.gov/9359722/>.
70. Cohn DL, Fisher EJ, Peng GT, et al. A prospective randomized trial of four three-drug regimens in the treatment of disseminated *Mycobacterium avium* complex disease in AIDS patients: excess mortality associated with high-dose clarithromycin. Terry Bein Community Programs for Clinical Research on AIDS. *Clin Infect Dis*. 1999;29(1):125-133. Available at: <https://pubmed.ncbi.nlm.nih.gov/10433575/>.
71. Aberg JA, Yajko DM, Jacobson MA. Eradication of AIDS-related disseminated *Mycobacterium avium* complex infection after 12 months of antimycobacterial therapy combined with highly active antiretroviral therapy. *J Infect Dis*. 1998;178(5):1446-1449. Available at: <https://pubmed.ncbi.nlm.nih.gov/9780266/>.
72. Ward TT, Rimland D, Kauffman C, Huycke M, Evans TG, Heifets L. Randomized, open-label trial of azithromycin plus ethambutol vs. clarithromycin plus ethambutol as therapy for *Mycobacterium avium* complex bacteremia in patients with human immunodeficiency virus infection. Veterans Affairs HIV Research Consortium. *Clin Infect Dis*. 1998;27(5):1278-1285. Available at: <https://pubmed.ncbi.nlm.nih.gov/9827282/>.
73. Dunne M, Fessel J, Kumar P, et al. A randomized, double-blind trial comparing azithromycin and clarithromycin in the treatment of disseminated *Mycobacterium avium* infection in patients with human immunodeficiency virus. *Clin Infect Dis*. 2000;31(5):1245-1252. Available at: <https://pubmed.ncbi.nlm.nih.gov/11073759/>.
74. Xu HB, Jiang RH, Li L. Treatment outcomes for *Mycobacterium avium* complex: a systematic review and meta-analysis. *Eur J Clin Microbiol Infect Dis*. 2014;33(3):347-358. Available at: <https://pubmed.ncbi.nlm.nih.gov/23979729/>.
75. Shafran SD, Singer J, Zarowny DP, et al. A comparison of two regimens for the treatment of *Mycobacterium avium* complex bacteremia in AIDS: rifabutin, ethambutol, and clarithromycin versus rifampin, ethambutol, clofazimine, and ciprofloxacin. Canadian HIV Trials Network Protocol 010 Study Group. *N Engl J Med*. 1996;335(6):377-383. Available at: <https://pubmed.ncbi.nlm.nih.gov/8676931/>.
76. Asuphon O, Boonpatharatthiti K, Rattanachaisit N, Wangteeraprasert A, Dhippayom T. Comparing clinical outcomes of antibiotics for treating *Mycobacterium avium* complex infection in adults with HIV: a systematic review and network meta-analysis. *AIDS*. 2026;40(1):16-23. Available at: https://journals.lww.com/aidsonline/fulltext/2026/01000/comparing_clinical_outcomes_of_antibiotics_for.3.aspx.
77. Food and Drug Administration. Clarithromycin [package insert]. 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/050662s061,050698s041,050775s029lbl.pdf

78. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med*. 2007;175(4):367-416. Available at: <https://pubmed.ncbi.nlm.nih.gov/17277290/>.
79. Gardner EM, Burman WJ, DeGroot MA, Hildred G, Pace NR. Conventional and molecular epidemiology of macrolide resistance among new *Mycobacterium avium* complex isolates recovered from HIV-infected patients. *Clin Infect Dis*. 2005;41(7):1041-1044. Available at: <https://pubmed.ncbi.nlm.nih.gov/16142672/>.
80. Craft JC, Notario GF, Grosset JH, Heifets LB. Clarithromycin resistance and susceptibility patterns of *Mycobacterium avium* strains isolated during prophylaxis for disseminated infection in patients with AIDS. *Clin Infect Dis*. 1998;27(4):807-812. Available at: <https://pubmed.ncbi.nlm.nih.gov/9798037/>.
81. Chaisson RE, Keiser P, Pierce M, et al. Clarithromycin and ethambutol with or without clofazimine for the treatment of bacteremic *Mycobacterium avium* complex disease in patients with HIV infection. *AIDS*. 1997;11(3):311-317. Available at: <https://pubmed.ncbi.nlm.nih.gov/9147422/>.
82. Benson CA, Williams PL, Currier JS, et al. A prospective, randomized trial examining the efficacy and safety of clarithromycin in combination with ethambutol, rifabutin, or both for the treatment of disseminated *Mycobacterium avium* complex disease in persons with acquired immunodeficiency syndrome. *Clin Infect Dis*. 2003;37(9):1234-1243. Available at: <https://pubmed.ncbi.nlm.nih.gov/14557969/>.
83. Koh WJ, Hong G, Kim SY, et al. Treatment of refractory *Mycobacterium avium* complex lung disease with a moxifloxacin-containing regimen. *Antimicrob Agents Chemother*. 2013;57(5):2281-2285. Available at: <https://pubmed.ncbi.nlm.nih.gov/23478956/>.
84. Chapagain M, Pasipanodya JG, Athale S, et al. Omadacycline efficacy in the hollow fibre system model of pulmonary *Mycobacterium avium* complex and potency at clinically attainable doses. *Journal of Antimicrobial Chemotherapy*. 2022;77(6):1694-1705. Available at: <https://pubmed.ncbi.nlm.nih.gov/35257162/>.
85. Litvinov V, Makarova M, Kudlay D, Nikolenko N, Mikhailova J. In vitro activity of bedaquiline against *Mycobacterium avium* complex. *J Med Microbiol*. 2021;70(10). Available at: <https://pubmed.ncbi.nlm.nih.gov/34668850/>.
86. Lin S, Hua W, Wang S, et al. In vitro assessment of 17 antimicrobial agents against clinical *Mycobacterium avium* complex isolates. *BMC Microbiol*. 2022;22(1):175. Available at: <https://pubmed.ncbi.nlm.nih.gov/35804298/>.
87. Gil E, Sweeney N, Barrett V, et al. Bedaquiline as treatment for disseminated nontuberculous mycobacteria infection in 2 patients co-infected with HIV. *Emerg Infect Dis*. 2021;27(3):944-948. Available at: <https://pubmed.ncbi.nlm.nih.gov/33622490/>.

88. Philley JV, Wallace RJ, Jr., Benwill JL, et al. Preliminary results of bedaquiline as salvage therapy for patients with nontuberculous mycobacterial lung disease. *Chest*. 2015;148(2):499-506. Available at: <https://pubmed.ncbi.nlm.nih.gov/25675393>.
89. Deshpande D, Srivastava S, Gumbo T. Pharmacodynamic evidence for tedizolid use in *Mycobacterium avium* lung disease. *IJTL D Open*. 2026;3(1):17-23. Available at: <https://pubmed.ncbi.nlm.nih.gov/41552671/>.
90. Yuste JR, Bertó J, Del Pozo JL, Leiva J. Prolonged use of tedizolid in a pulmonary non-tuberculous mycobacterial infection after linezolid-induced toxicity. *J Antimicrob Chemother*. 2017;72(2):625-628. Available at: <https://pubmed.ncbi.nlm.nih.gov/27999019>.
91. Al-Jabri MY, Dousa KM, Wilson BM, Bonomo RA. The use of dual β -lactams to restore susceptibility of *Mycobacterium avium* complex. *JAC Antimicrob Resist*. 2024;6(5):dlae142. Available at: <https://pubmed.ncbi.nlm.nih.gov/39281290>.
92. Aberg JA, Williams PL, Liu T, et al. A study of discontinuing maintenance therapy in human immunodeficiency virus-infected subjects with disseminated *Mycobacterium avium* complex: AIDS Clinical Trial Group 393 Study Team. *J Infect Dis*. 2003;187(7):1046-1052. Available at: <https://pubmed.ncbi.nlm.nih.gov/12660918/>.
93. Shafran SD, Mashinter LD, Phillips P, et al. Successful discontinuation of therapy for disseminated *Mycobacterium avium* complex infection after effective antiretroviral therapy. *Ann Intern Med*. 2002;137(9):734-737. Available at: <https://pubmed.ncbi.nlm.nih.gov/12416943>.
94. Kirk O, Reiss P, Uberti-Foppa C, et al. Safe interruption of maintenance therapy against previous infection with four common HIV-associated opportunistic pathogens during potent antiretroviral therapy. *Ann Intern Med*. 2002;137(4):239-250. Available at: <https://pubmed.ncbi.nlm.nih.gov/12186514>.
95. Shafran SD, Deschenes J, Miller M, Phillips P, Toma E. Uveitis and pseudojaundice during a regimen of clarithromycin, rifabutin, and ethambutol. MAC Study Group of the Canadian HIV Trials Network. *N Engl J Med*. 1994;330(6):438-439. Available at: <https://pubmed.ncbi.nlm.nih.gov/8284019>.
96. Hafner R, Bethel J, Power M, et al. Tolerance and pharmacokinetic interactions of rifabutin and clarithromycin in human immunodeficiency virus-infected volunteers. *Antimicrob Agents Chemother*. 1998;42(3):631-639. Available at: <https://pubmed.ncbi.nlm.nih.gov/9517944/>.
97. Hennig S, Svensson EM, Niebecker R, et al. Population pharmacokinetic drug-drug interaction pooled analysis of existing data for rifabutin and HIV PIs. *J Antimicrob Chemother*. 2016;71(5):1330-1340. Available at: <https://pubmed.ncbi.nlm.nih.gov/26832753/>.

98. Naiker S, Connolly C, Wiesner L, et al. Randomized pharmacokinetic evaluation of different rifabutin doses in African HIV- infected tuberculosis patients on lopinavir/ritonavir-based antiretroviral therapy. *BMC Pharmacol Toxicol*. 2014;15:61. Available at: <https://pubmed.ncbi.nlm.nih.gov/25406657/>.
99. Ramanathan S, Mathias AA, German P, Kearney BP. Clinical pharmacokinetic and pharmacodynamic profile of the HIV integrase inhibitor elvitegravir. *Clin Pharmacokinet*. 2011;50(4):229-244. Available at: <https://pubmed.ncbi.nlm.nih.gov/21348537>.
100. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. 2026. Available at: <https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/coinfections-tuberculosis-hiv#:~:text=Drug%20Interaction%20Considerations>
101. Dooley KE, Sayre P, Borland J, et al. Safety, tolerability, and pharmacokinetics of the HIV integrase inhibitor dolutegravir given twice daily with rifampin or once daily with rifabutin: results of a phase 1 study among healthy subjects. *J Acquir Immune Defic Syndr*. 2013;62(1):21-27. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23075918>.
102. Brainard DM, Kassahun K, Wenning LA, et al. Lack of a clinically meaningful pharmacokinetic effect of rifabutin on raltegravir: *in vitro/in vivo* correlation. *J Clin Pharmacol*. 2011;51(6):943-950. Available at: <https://pubmed.ncbi.nlm.nih.gov/20852006/>.
103. Le X, Guo X, Sun J, et al. Pharmacokinetic features of dolutegravir with rifampicin and rifabutin among patients coinfectd with human immunodeficiency virus and tuberculosis/*Mycobacterium avium* complex. *Int J Infect Dis*. 2022;116:147-150. Available at: <https://pubmed.ncbi.nlm.nih.gov/34999246>.
104. Naidoo A, Naidoo K, Letsoalo MP, et al. Fixed-dose combination bictegravir-emtricitabine-tenofovir alafenamide twice-daily for treatment of HIV during rifampicin-based tuberculosis treatment (INSIGHT Study): a phase 2b, open-label, randomised non-comparative trial. *Lancet HIV*. 2026;13(1):e9-e20. Available at: <https://pubmed.ncbi.nlm.nih.gov/41344350>.
105. Alffenaar JW, Martson AG, Heysell SK, et al. Therapeutic drug monitoring in non-tuberculosis mycobacteria infections. *Clin Pharmacokinet*. 2021;60(6):711-725. Available at: <https://pubmed.ncbi.nlm.nih.gov/33751415/>.
106. Phillips P, Kwiatkowski MB, Copland M, Craib K, Montaner J. Mycobacterial lymphadenitis associated with the initiation of combination antiretroviral therapy. *J Acquir Immune Defic Syndr*. 1999;20(2):122-128. Available at: <https://pubmed.ncbi.nlm.nih.gov/10048898>.

107. Phillips P, Bonner S, Gataric N, et al. Nontuberculous mycobacterial immune reconstitution syndrome in HIV-infected patients: spectrum of disease and long-term follow-up. *Clin Infect Dis*. 2005;41(10):1483-1497. Available at: <https://pubmed.ncbi.nlm.nih.gov/16231262/>.
108. Race EM, Adelson-Mitty J, Kriegel GR, et al. Focal mycobacterial lymphadenitis following initiation of protease-inhibitor therapy in patients with advanced HIV-1 disease. *Lancet*. 1998;351(9098):252-255. Available at: <https://pubmed.ncbi.nlm.nih.gov/9457095>.
109. Cabie A, Abel S, Brebion A, Desbois N, Sobesky G. Mycobacterial lymphadenitis after initiation of highly active antiretroviral therapy. *Eur J Clin Microbiol Infect Dis*. 1998;17(11):812-813. Available at: <https://pubmed.ncbi.nlm.nih.gov/9923530/>.
110. Smibert OC, Trubiano JA, Cross GB, Hoy JF. Short communication: *Mycobacterium avium* complex infection and immune reconstitution inflammatory syndrome remain a challenge in the era of effective antiretroviral therapy. *AIDS Res Hum Retroviruses*. 2017;33(12):1202-1204. Available at: <https://pubmed.ncbi.nlm.nih.gov/28791872>.
111. Barber DL, Andrade BB, McBerry C, Sereti I, Sher A. Role of IL-6 in *Mycobacterium avium*—associated immune reconstitution inflammatory syndrome. *J Immunol*. 2014;192(2):676-682. Available at: <https://pubmed.ncbi.nlm.nih.gov/24337386/>.
112. Wormser GP, Horowitz H, Dworkin B. Low-dose dexamethasone as adjunctive therapy for disseminated *Mycobacterium avium* complex infections in AIDS patients. *Antimicrob Agents Chemother*. 1994;38(9):2215-2217. Available at: <https://pubmed.ncbi.nlm.nih.gov/7811052>.
113. Rocco JM, Laidlaw E, Galindo F, et al. Severe mycobacterial immune reconstitution inflammatory syndrome (IRIS) in advanced human immunodeficiency virus (HIV) has features of hemophagocytic lymphohistiocytosis and requires prolonged immune suppression. *Clin Infect Dis*. 2023;76(3):e561-e570. Available at: <https://pubmed.ncbi.nlm.nih.gov/36048425/>.
114. Rocco JM, Laidlaw E, Galindo F, et al. Mycobacterial immune reconstitution inflammatory syndrome in HIV is associated with protein-altering variants in hemophagocytic lymphohistiocytosis-related genes. *J Infect Dis*. 2023;228(2):111-115. Available at: <https://pubmed.ncbi.nlm.nih.gov/37040388/>.
115. Masur H. Recommendations on prophylaxis and therapy for disseminated *Mycobacterium avium* complex disease in patients infected with the human immunodeficiency virus. Public Health Service Task Force on Prophylaxis and Therapy for *Mycobacterium avium* Complex. *N Engl J Med*. 1993;329(12):898-904. Available at: <https://pubmed.ncbi.nlm.nih.gov/8395019/>.

116. Kemper CA, Meng TC, Nussbaum J, et al. Treatment of *Mycobacterium avium* complex bacteremia in AIDS with a four-drug oral regimen: rifampin, ethambutol, clofazimine, and ciprofloxacin. The California Collaborative Treatment Group. *Ann Intern Med*. 1992;116(6):466-472. Available at: <https://pubmed.ncbi.nlm.nih.gov/1739237/>.
117. Chiu J, Nussbaum J, Bozzette S, et al. Treatment of disseminated *Mycobacterium avium* complex infection in AIDS with amikacin, ethambutol, rifampin, and ciprofloxacin. California Collaborative Treatment Group. *Ann Intern Med*. 1990;113(5):358-361. Available at: <https://pubmed.ncbi.nlm.nih.gov/2382918/>.
118. Rodriguez Diaz JC, Lopez M, Ruiz M, Royo G. *In vitro* activity of new fluoroquinolones and linezolid against non-tuberculous mycobacteria. *Int J Antimicrob Agents*. 2003;21(6):585-588. Available at: <https://pubmed.ncbi.nlm.nih.gov/12791475/>.
119. Liu L, Song Z, Xun J, et al. PD-1 inhibitor for disseminated mycobacterium avium infection in a person with HIV. *Open Forum Infect Dis*. 2023;10(1):ofac700. Available at: <https://pubmed.ncbi.nlm.nih.gov/36686637/>.
120. Kelley M, Sasaninia K, Badaoui A, et al. The effects of cyclic peptide [R4W4] in combination with first-line therapy on the survival of *Mycobacterium avium*. *Front Cell Infect Microbiol*. 2025;15:1547376. Available at: <https://pubmed.ncbi.nlm.nih.gov/40308965/>.
121. Aberg J, Powderly W. HIV: primary and secondary prophylaxis for opportunistic infections. *BMJ Clin Evid*. 2010. Available at: <https://pubmed.ncbi.nlm.nih.gov/21418688/>.
122. Green H, Hay P, Dunn DT, McCormack S, Investigators S. A prospective multicentre study of discontinuing prophylaxis for opportunistic infections after effective antiretroviral therapy. *HIV Med*. 2004;5(4):278-283. Available at: <https://pubmed.ncbi.nlm.nih.gov/15236617/>.
123. El-Sadr WM, Murphy RL, Yurik TM, et al. Atovaquone compared with dapsone for the prevention of *Pneumocystis carinii* pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. Community Program for Clinical Research on AIDS and the AIDS Clinical Trials Group. *N Engl J Med*. 1998;339(26):1889-1895. Available at: <https://pubmed.ncbi.nlm.nih.gov/9862944/>.
124. Einarson A, Phillips E, Mawji F, et al. A prospective controlled multicentre study of clarithromycin in pregnancy. *Am J Perinatol*. 1998;15(9):523-525. Available at: <https://pubmed.ncbi.nlm.nih.gov/9890248/>.
125. Drinkard CR, Shatin D, Clouse J. Postmarketing surveillance of medications and pregnancy outcomes: clarithromycin and birth malformations. *Pharmacoepidemiol Drug Saf*. 2000;9(7):549-556. Available at: <https://pubmed.ncbi.nlm.nih.gov/11338912/>.

126. Muanda FT, Sheehy O, Berard A. Use of antibiotics during pregnancy and risk of spontaneous abortion. *CMAJ*. 2017;189(17):E625-E633. Available at: <https://pubmed.ncbi.nlm.nih.gov/28461374/>.
127. Berard A, Sheehy O, Zhao JP, Nordeng H. Use of macrolides during pregnancy and the risk of birth defects: a population-based study. *Pharmacoepidemiol Drug Saf*. 2015;24(12):1241-1248. Available at: <https://pubmed.ncbi.nlm.nih.gov/26513406/>.
128. Lin KJ, Mitchell AA, Yau WP, Louik C, Hernandez-Diaz S. Safety of macrolides during pregnancy. *Am J Obstet Gynecol*. 2013;208(3):221 e221-228. Available at: <https://pubmed.ncbi.nlm.nih.gov/23254249/>.
129. Bahat Dinur A, Koren G, Matok I, et al. Fetal safety of macrolides. *Antimicrob Agents Chemother*. 2013;57(7):3307-3311. Available at: <https://pubmed.ncbi.nlm.nih.gov/23650169/>.
130. Cluver C, Novikova N, Eriksson DO, Bengtsson K, Lingman GK. Interventions for treating genital Chlamydia trachomatis infection in pregnancy. *Cochrane Database Syst Rev*. 2017;9(9):CD010485. Available at: <https://pubmed.ncbi.nlm.nih.gov/28937705/>.

mycobacterium-avium-complex-adult-adolescent-oi