TB & LTBI Guidelines: What’s New?

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GRADE METHODOLOGY (Grading of Recommendations Assessment, Development, and Evaluation)

Recommendations based on the certainty in the evidence assessed according to the GRADE methodology to address PICO questions, incorporating patient values and costs as well as judgments about tradeoffs between benefits and harms.

PICO = Population, Intervention, Comparison, Outcome

New CDC/IDSA TB Guidelines: 2016-2017

- Diagnosis of TB in Children and Adults, *Clinical Infectious Disease* 2017
- Treatment of Drug-Susceptible TB, *Clinical Infectious Disease* 2016

Diagnosis of TB in Children and Adults, 2017

ATS/CDC/IDSA Clinical Practice Guideline
Previous CDC TB Diagnosis Guidelines

- Diagnostic Standards/Classification of TB in Adults and Children, 2000
- Targeted Tuberculin Testing and Treatment of LTBI, 2000
- Tuberculosis Associated with Blocking Agents Against Tumor Necrosis Factor Alpha, 2004
- Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC, 2005
- Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005
- Guidelines for Using the QuantiFERON-TB Gold Test for Detecting Mycobacterium tuberculosis Infection, United States, 2005
- Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis, 2009
- Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents, 2009
- Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis Infection — United States, 2010

https://www.cdc.gov/tb/publications/guidelines/testing.htm

Guideline Contents

- TB: Epidemiology, Transmission, and Pathogenesis
- Diagnostic Tests for LTBI
- Testing for LTBI
- Testing for Pulmonary TB Disease
- Testing for Extrapulmonary TB Disease
- Genotyping of M. TB
- Research Needs

Example: Diagnostics for Extrapulmonary TB

Guidelines 2000

- “[AFB] smears of urine are usually negative and therefore may not be cost-effective to perform.”

Guidelines 2017

- “Even though a positive AFB smear result is infrequent, the committee judged the benefits of early diagnosis (early initiation of treatment, potential to reduce transmission) to outweigh the cost and burden of AFB smear microscopy.”

2000 ATS/CDC/IDSA TB Diagnosis Guidelines

Testing for LTBI

Step 1. Determine Risk of Infection: Likely or Unlikely

Step 2. Determine Risk of Disease Progression: Low, Intermediate, High

2017 ATS/CDC/IDSA TB Diagnosis Guidelines
LTBI Testing

- We recommend performing an interferon-γ release assay (IGRA) rather than a tuberculin skin test (TST) in individuals 5 years or older who meet the following criteria:

  1. are likely to be infected with *Mtb*,
  2. have a low or intermediate risk of disease progression,
  3. it has been decided that testing for LTBI is warranted, and
  4. either have a history of BCG vaccination or are unlikely to return to have their TST read

  * Strong recommendation, moderate-quality evidence

LTBI Testing

- There are insufficient data to recommend a preference for either a TST or IGRA in individuals 5 years or older who meet the following criteria:

  1. are likely to be infected with *Mtb*,
  2. have a high risk of disease progression,
  3. it has been decided that testing for LTBI is warranted

  * Conditional recommendation, moderate-quality evidence

LTBI Testing

- If LTBI testing is performed in individuals who are unlikely to be infected with *Mtb* (not recommended), we suggest

  - Performing an IGRA instead of a TST

  * Conditional recommendation, low-quality evidence

  - Second diagnostic test if the initial test is positive; person considered positive if both tests are positive*

  * Conditional recommendation, very low-quality evidence

  * Note: Person may also be determined to be a “false positive” and not treated
Serial IGRAs for Healthcare Workers

- IGRAS are not a solution to false-positive results associated with serial testing in low-risk individuals
- “At present there is insufficient information available to guide the establishment of definitive criteria for the conversion and possible reversion of IGRAS..[especially] in the context of serial testing.”
- In serial LTBI testing of U.S. healthcare workers, IGRA conversions noted be 6-8%, 6-9x higher than for TST and thought to be false conversions
- For further guidance on healthcare worker LTBI testing, refer to 2005 CDC Guidelines for Preventing the Transmission of M. TB in Health-Care Settings

Rapid molecular DST

- Should rapid molecular drug susceptibility testing for isoniazid and rifampin be performed as part of the initial diagnostic evaluation?
- Recommended for persons who are either AFB smear or MTD positive and who meet one of the following criteria:
  (1) Treated for TB in the past
  (2) Born in or lived at least 1 year in a foreign country with at least a moderate tuberculosis incidence (≥20 per 100,000) or a high primary multidrug-resistant tuberculosis prevalence (≥2%)
  (3) Contacts of patients with multidrug-resistant tuberculosis
  (4) HIV-infected

TB Disease Testing: Pulmonary TB

Recommended Tests on Initial Respiratory Specimens

- Both liquid and solid mycobacterial cultures
- Culture-based Direct Susceptibility Testing (DST)
- Nucleic Acid Amplification Test (NAAT)
- Rapid molecular DST for rifampin using specimen that is either AFB smear positive or M.TB Direct (MTD) positive, if patient meets specific criteria
- For culture-positive patients, one isolate to regional genotyping laboratory for genotyping

TB Disease Testing: Extrapulmonary TB

Recommended Tests for Specimens from Extrapulmonary Sites

- Cells counts and chemistries
- AFB smear microscopy
- Mycobacterial cultures
- NAAT
- Adenosine Deaminase (ADA) levels for suspected pleural TB, TB meningitis, peritoneal TB, or pericardial TB
- IFN-γ level for suspected pleural/peritoneal TB

Conditional recommendation, low-quality evidence
Guideline Contents

Supervision of treatment
- Patient-Centered Care and Case Management
- Ensuring adherence and treatment success

Recommended treatment
- Preferred regimens
- Alternative regimens
- Patient at increased risk of relapse
- Interruptions of therapy

Recurrent tuberculosis, treatment failure and drug resistance

Treatment in special situations
- HIV infection
- Children
- Pregnancy/Breastfeeding
- Renal disease
- Hepatic disease
- Diabetes
- Advance age
- Extrapulmonary disease

Management of adverse effects, drug-drug interactions

2016 ATS/CDC/IDSA TB Guidelines

Key Changes/Updates from 2003 edition

- Evidence base for case management (patient education, incentives, enablers, DOT) reviewed
- Evidence base for intermittent therapy reviewed
- Early initiation of ART in most HIV/TB patients
- Duration of TB treatment in HIV w/o ART extended
- Steroids not routinely recommended for TB pericarditis

Tables Providing Practical Support for TB Treatment

- Table 3. Doses of Antituberculosis Drugs for Adults and Children
- Table 7. Other causes of abnormal liver function tests that should be excluded
- Table 8. Clinically significant drug-drug interactions involving the rifamycins
- Table 9. Conditions or situations in which therapeutic drug monitoring may be helpful
DOT remains the standard of practice

- Evidence in support of this practice guideline showed that DOT was significantly associated with improved treatment outcomes in terms of patients cured and patients completing treatment.
- However, the evidence did not find significant differences between SAT and DOT in terms of mortality, treatment completion and relapses.
- We suggest using DOT rather than SAT for routine treatment of all forms of tuberculosis.

_Dot recommendation, low certainty in the evidence_

2016 ATS/CDC/IDSA TB Treatment Guidelines

Dosing schedules of 6-month regimens and relapse

- Systematic review of 17 studies with 5,208 patients, and 200 relapse events.
  - Daily throughout: RR= 1.0
  - Daily then 3X weekly: RR = 1.6
  - Daily then 2X weekly: RR = 2.8
  - 3X weekly throughout: RR = 5.0
- Greatest risk if cavitation or 2nd month culture was positive.


Intermittent therapy for drug-susceptible TB

- Should tuberculosis medications be dosed daily or intermittently in the intensive phase of treatment?
  - Recommendation: We recommend the use of daily rather than intermittent dosing in the intensive phase of therapy for drug-susceptible pulmonary tuberculosis.
    _Strong recommendation, moderate certainty in the evidence_
  - Should tuberculosis medications be dosed daily or intermittently in the continuation phase of treatment?
  - Recommendation: We recommend the use of daily or three times weekly dosing in the continuation phase of therapy for drug-susceptible pulmonary tuberculosis.
    _Strong recommendation, moderate certainty in the evidence_

2016 ATS/CDC/IDSA TB Treatment Guidelines

Intermittent therapy for drug-susceptible TB: Review of RCTs

Primary analysis: Jan 1965-March 2016: 64 trials

- Population with DS-TB or no DST with at least 6 months Rifampin
  - Analysis of treatment failure, relapse, ADR with the following treatment schedules:
    - Daily (≥5 days per week) throughout
    - Thrice weekly throughout
    - Daily intensive phase then twice weekly
    - Daily intensive phase then thrice weekly

- Numbers of patients with outcomes of interest:
  - Failure: 13,401 patients
  - Relapse: 12,184 patients
  - ADR: 7,443 patients

### Initial Phase: Daily vs Intermittent

<table>
<thead>
<tr>
<th>Initial Phase Schedule</th>
<th>Arms (N)</th>
<th>Failure Events/Participants (N)</th>
<th>Point Estimate 95% CI</th>
<th>Failure Rate 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily 62</td>
<td>112/8223</td>
<td></td>
<td>0.2% (0 - 0.4)</td>
<td></td>
</tr>
<tr>
<td>3x per week 19</td>
<td>28/2310</td>
<td></td>
<td>0.6% (0 - 1.4)</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily 59</td>
<td>254/7475</td>
<td></td>
<td>2.5% (1.8 - 3.2)</td>
<td></td>
</tr>
<tr>
<td>3x per week 19</td>
<td>128/2130</td>
<td></td>
<td>6.8% (3.8 - 9.9)</td>
<td></td>
</tr>
</tbody>
</table>

**Risk of Failure**

| Daily throughout 62 | 112/8223 | 0.2% (0.1 - 0.4) |
| Daily then 3x per week 18 | 19/2075 | 0.4% (0 - 1.1) |
| Daily then 2x per week 9 | 21/793 | 1.3% (0.2 - 2.9) |

**Risk of Relapse**

| Daily throughout 59 | 254/7475 | 2.5% (1.8 - 3.2) |
| Daily then 3x per week 18 | 72/2007 | 3.0% (1.0 - 5.1) |
| Daily then 2x per week 9 | 49/572 | 7.3% (3.5 - 11.1) |

**Risk of Acquired Drug Resistance**

| Daily throughout 43 | 11/4700 | 0.1% (0 - 0.2) |
| Daily then 3x per week 9 | 1/588 | 0.1% (0 - 0.3) |
| Daily then 2x per week 5 | 2/377 | 0.2% (0.1 - 0.6) |

**Note:** No trials found with Twice weekly through-out (Initial & Continuation phase – the “Denver regimen”)

### Intermittency and treatment outcomes, 2012: 34 studies of HIV-TB patients included

<table>
<thead>
<tr>
<th>Failure Rate (95%CI)</th>
<th>Risk of Relapse (95%CI)</th>
<th>Risk of Death (95%CI)</th>
<th>Risk of ADR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily throughout 62</td>
<td>2.7% (1.6, 3.7)</td>
<td>6.3% (1.2, 11.4)</td>
<td>11.8% (8.5, 15.0)</td>
</tr>
<tr>
<td>3x per week 19</td>
<td>5.2% (1.5, 8.8)</td>
<td>18.2% (0, 39)</td>
<td>10.1% (4.3, 16)</td>
</tr>
</tbody>
</table>

**Khan FA, et al. Treatment of active TB in HIV co-infected patients. CID, 2012**

### Continuation Phase: Daily vs Intermittent

<table>
<thead>
<tr>
<th>Factor</th>
<th>Arms (N)</th>
<th>Failure Events/Participants (N)</th>
<th>Point Estimate</th>
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### Intermittent Regimens

- **Thrice-Weekly dosing Throughout**
  - Associated with higher rates of treatment failure, relapse, and ADR
  - Risk of poor outcomes of treatment higher in HIV-infected patients, cavitary disease and baseline DR

- **This regimen may be considered when daily is not feasible or poorly tolerated in patients who are not HIV-infected, non-cavitary, smear negative, DS organisms.**

  **Conditional recommendation, low certainty in the evidence**
**Intermittent Regimens**

- Twice-Weekly Dosing Throughout or Twice-Weekly Dosing after 2-3 Weeks of Daily dosing
  - Not generally recommended because of lack of high quality evidence to support its use
- Some tuberculosis programs have reported long standing programmatic treatment success with the “Denver Regimen”
- In situations where daily or thrice-weekly DOT can not be used this regimen may be consider in patients who are not HIV-infected, non-cavitary, smear negative, DS organisms
  
  *Conditional recommendation, low certainty in the evidence*
- We recommend against use of once-weekly therapy with INH 900 mg + RPT 600 mg
  
  *Strong recommendation, high certainty in the evidence*

**TB Patients with HIV: ART Initiation**

We recommend initiating ART during TB treatment:

- **Within the first 2 weeks** of tuberculosis treatment for patients with CD4 cell counts <50/mm³
- By 8-12 weeks of tuberculosis treatment initiation for patients with CD4 cell counts ≥50/mm³
- Exception: Do not initiate ART in the first 8 weeks in patients with **TB meningitis**

*Strong recommendation, high certainty in the evidence*

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**TB patients with HIV: Treatment Duration**

- For HIV-infected patients receiving antiretroviral therapy, we suggest using the standard 6-month daily regimen
- In uncommon situations in which HIV-infected patients do NOT receive antiretroviral therapy during tuberculosis treatment, we suggest extending the continuation phase to 7 months in duration, corresponding to a total of 9 months of therapy

*Conditional recommendation, very low certainty in the evidence*

**Initiation of ART During TB Treatment**

- **SAPit trial**: patients with TB and HIV (CD4 <500) initiating ART within 8 weeks (integrated) vs after 6 months of TB treatment (sequential) demonstrated 56% reduction relative risk of death (2010)
- **CAMELIA trial**: patients with TB and HIV (CD4 <200) initiating ART within 2 weeks of starting TB treatment had 34% reduced mortality compared to starting treatment after 8 weeks (2011)
- **STRIDE trial**: patients with TB and HIV (CD4 <50) initiating ART within 2 weeks had lower rates of new AIDS defining illness and death with immediate therapy compared to those starting ART at 8-12 weeks (2011)
- **Ethiopia trial**: patients with TB and HIV (CD4 <200) initiating ART at 1, 2, 8 weeks of starting TB treatment; no significant difference mortality (2015)

In all these studies immediate ART associated with more IRIS

USPSTF

- Every USPSTF recommendation is assigned a letter grade
- These grades are based on the strength of the evidence on a specific preventive service

USPSTF: U.S. Preventive Services Task Force

- The USPSTF is an independent panel of national experts in prevention and evidence-based medicine.
- The primary goal of the USPSTF is to develop and disseminate evidence-based recommendations about clinical preventive services
- Recommendations address only services offered in the primary care setting or services referred by a primary care clinician.
- Recommendations apply only to people who have no signs or symptoms of the specific disease or condition that the screening, counseling, or preventive medication targets.

USPSTF Recommendation

Screening for LTBI in Adults, 2016

History of USPSTF LTBI recommendations

- 1996: USPSTF recommended (Grade A) LTBI screening of high-risk persons.
- 2002: USPSTF deferred to CDC LTBI testing recommendations to avoid duplication of other Federal Agency efforts (no USPSTF Grade issued).

For current recommendation*

- 2013: CDC and the Agency for Healthcare Research and Quality signed an interagency agreement to initiate a review.
- 2014: USPSTF posted LTBI Research Plan for 30-day public comment period.
- 2016: USPSTF posted Recommendation and Evidence Review for 30-day public comment period.
- 2016: USPSTF published final Recommendation

* USPSTF Grade of A or B are covered without cost-sharing (e.g., copayment or deductible) by many health insurance plans or policies

http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm
2016 Recommendation

The USPSTF recommends screening for LTBI in populations that are at increased risk (B recommendation).

*B Recommendation = USPSTF recommends this service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults who are at increased risk for tuberculosis</td>
<td>The USPSTF recommends screening for latent tuberculosis infection (LTBI) in populations that are at increased risk.</td>
<td>B</td>
</tr>
</tbody>
</table>

Additional Populations at Risk for LTBI

- The recommendation does not address the additional need for LTBI testing in other high-risk populations.
- CDC recommends the following populations continue to be tested for LTBI as part of other screening efforts:
  - Persons with immunosuppression (e.g. HIV/AIDS, immunosuppressive medications, silicosis): TB testing is conducted by specialists.
  - Persons who are contacts of persons with active TB disease: TB testing is conducted as part of public health programs.
  - Health care workers and workers in high-risk congregate settings: TB testing is conducted as part of employee health programs.

2016 USPSTF Recommendation

- This recommendation applies to asymptomatic adults ≥18 years of age who are at increased risk for TB and are seen in primary care settings.
  - Born in, or former residents of, countries with increased tuberculosis prevalence (e.g., Mexico, Philippines, Vietnam, India, China, Haiti, Guatemala)
  - Currently live in, or have lived in, high-risk congregate settings (e.g., homeless shelters, long-term care facilities, correctional facilities)
- It does not apply to adults with symptoms of TB disease or children and adolescents.

Implications for Clinical Practice

- TB control and prevention has traditionally been a function of state and local public health departments.
- However, many people at high risk for TB who need to be screened receive care from local community health clinics.
- The USPSTF recommendation expands opportunities for additional public and private health care providers to prevent and control TB.
- Providers should consult with their local or state health departments for populations at risk in their communities based on local demographic patterns.
Acknowledgements

TB Diagnosis Guidelines


USPSTF Recommendation


Acknowledgements: TB Treatment Guidelines


• ATS Documents Editor Kevin Wilson and GRADE Methodologist Jan Brozek

• Reviewers: ATS, IDSA, CDC, NTCA, ERS, ACET

• Community Research Advisors Group of the CDC-TBTC and Treatment Action Group

• Susan Dorman (IDSA), GB Migliori (ERS), Andrew Vernon (CDC)
Relation to the Patient Protection and Affordable Care Act (ACA) and Medicare/Medicaid

- Under the law, preventive services with a USPSTF Grade of A or B are covered without cost-sharing (e.g., copayment or deductible) by many health insurance plans or policies.
- For LTBI screening without cost-sharing to be available to Medicare beneficiaries, the Centers for Medicare and Medicaid Services must first complete a Medicare National Coverage Determination.
- LTBI screening may not be available without cost-sharing to traditional Medicaid beneficiaries.
- LTBI screening may be available to Medicaid beneficiaries enrolled in alternative benefit plans.

USPSTF Recommendation: Implications for Clinical Practice (2)

- In the near future, many health plans should cover LTBI screening without cost-sharing for at-risk asymptomatic adults age ≥18 years in the following groups when using a provider within the health plan’s network:
  - Persons born in, or former residents of, countries with increased TB prevalence
  - Persons who currently live in, or have lived in, high-risk congregate settings
- Other adults assumed to be at risk for LTBI may incur cost of co-pays, co-insurance, or deductibles for LTBI screening (depending on type of health coverage and setting in which screening is provided).

FAQS (Frequently asked questions)

- How many studies used DOT
  - Used DOT throughout therapy: 57% (most of intermittent)
  - Used DOT in part of therapy: 14%
  - Did not use DOT: 29% (mostly daily)
- How many studies had <10% total of loss to follow-up & default & transfer & unknown?
  - <10% loss: 66% of studies
  - >10% loss: 33% of studies
**FAQS (Frequently asked questions)**

- **How many HIV infected patients were included in these studies?**
  - 1509 Patients were HIV positive (11% of all patients)
  - In 67% of the studies 0 (zero) patients had HIV

- **How many studies were published since 1990 and how many since 2000?**
  - Prior to 1990: 69%,
  - 1990 – 2000: 19%
  - Post 2000: 12%

**Evidence review for Intermittent therapy**

**Discussion - Limitations**

- Very few large scale randomized trials with direct comparison of Intermittent vs Daily. Could not pool data from Head-to-Head comparisons
- Most studies conducted in Low and Middle income countries. But drop-out rates and non-adherence low in most studies. Quality of care could be considered similar to US programme standards
- Some studies/regimens did not use PZA
  - But sensitivity analyses – Arms with PZA only = same findings
- Even though differences are significant, and odds ratios are high, the absolute effect size is small – difference in relapse rates of 4%, and of acquired drug resistance of 1%

**Evidence review for Intermittent therapy**

**Discussion - Strengths**

- Large number of trials identified. Only studies with bacteriologically confirmed diagnoses & outcomes (fail and relapse were confirmed) were included.
- Consistent results from multiple reviews in different populations (adults, children, HIV infected). Even if not always significant, consistent trends seen.
- In 3 reviews multivariate analysis used – to adjust for confounding factors (eg use of PZA). Findings stronger
- Studies from many countries, including resource-poor, “real-life” settings - more applicable/generalizable

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**Intermittent therapy stratified by ART use: Updated 2012, 34 studies included**

<table>
<thead>
<tr>
<th>Dosing Schedule</th>
<th>Failure: aOR (95% CI)</th>
<th>Relapse: aOR (95% CI)</th>
<th>Death: aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ART</td>
<td>ART</td>
<td>ART</td>
</tr>
<tr>
<td>Daily (reference)</td>
<td>None / NR</td>
<td>All / Some</td>
<td>None / NR</td>
</tr>
<tr>
<td>Thrice weekly</td>
<td>4.1 (1.9, 9.1)</td>
<td>0.4 (0.1, 2.7)</td>
<td>2.1 (0.6, 6.9)</td>
</tr>
</tbody>
</table>

aOR, adjusted odds ratio; ART, antiretroviral therapy; CI, confidence interval; NR, not reported

Sensitivity Analysis

- Examined the following:
  1. Drug sensitive TB only (No DST dropped)
  2. All studies (i.e., like Menzies *PLOS Med.* 2009)
  3. Streptomycin-based regimens removed
  4. Streptomycin resistant strains included
  5. Drug resistant strains only
  6. Regimen of 2HRZ(E), 4HR(E) only
  7. Removed arms with only HIV infected patients

Findings essentially unchanged with all these


### Duration of treatment and adjusted odds of outcomes stratified by ART use

<table>
<thead>
<tr>
<th>Duration</th>
<th>Rifampin</th>
<th>Failure: OR (95% CI)</th>
<th>Relapse: OR (95% CI)</th>
<th>Death: OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ART</td>
<td>ART</td>
<td>ART</td>
<td>ART</td>
</tr>
<tr>
<td></td>
<td>None / NR</td>
<td>All / Some</td>
<td>None / NR</td>
<td>All / Some</td>
</tr>
<tr>
<td>6 Months</td>
<td>0.7 (0.4, 1.4)</td>
<td>1.8 (0.3, 12.2)</td>
<td>3.1 (14, 6.7)</td>
<td>0.2 (0.01, 2.2)</td>
</tr>
<tr>
<td>8 Months</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>p value</td>
<td>0.63</td>
<td>0.30</td>
<td>0.001</td>
<td>0.40</td>
</tr>
</tbody>
</table>

αOR, adjusted odds ratio; ART, antiretroviral therapy; CI, confidence interval; NR, not reported.


### Does the use of adjuvant corticosteroids in tuberculosis pericarditis provide mortality and morbidity benefits?

Recommendation: We suggest initial adjunctive corticosteroid therapy not be routinely used in patients with tuberculous pericarditis (Conditional recommendation / Very low certainty in the evidence).

Pericardial Tuberculosis

- Corticosteroids have previously been universally recommended as adjunctive therapy for tuberculosis pericarditis
- A RCT of 1400 patients did not find differences in mortality, cardiac tamponade, or constrictive pericarditis in patients that received corticosteroids versus placebo
- A systematic review for the guidelines did not find a benefit in using corticosteroids
- Patients at higher risk of inflammatory complications such as large pericardial effusions, high levels of inflammatory markers or those with early signs of constriction can be given corticosteroids

Among HIV-negative patients with paucibacillary TB (i.e., confirmed to be smear negative, culture negative), does a shorter duration of treatment have similar outcomes compared to the standard 6-month treatment duration?

Recommendation: We suggest that a 4-month treatment regimen is adequate for treatment of HIV-negative adult patients with AFB smear- and culture-negative pulmonary tuberculosis (Conditional recommendation / Very low certainty in the evidence).

2016 ATS/CDC/IDSA TB treatment Guidelines

**TB Disease Testing: Bronchoscopy**

- Flexible bronchoscopic testing sampling should be performed in TB suspects who cannot produce an induced sputum sample
- Bronchoscopic sampling in patients with suspected military TB should include bronchial brushings and/or transbronchial biopsy, yield from washings/BAL is less/unknown

2017 ATS/CDC/IDSA TB Diagnosis Guidelines