Partnerships for Care: Focus on Testing and Treatment of LTBI

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Objectives

• Explain targeted screening and why it is important in LTBI

• Describe how to diagnose LTBI and the most common treatment options

• Describe the major recommendations in the new USPSTF latent TB guidelines

• List most of the steps involved in implementing LTBI testing and treatment in primary care
Natural History of Tuberculosis

Reported TB Cases
United States, 1982–2016*
Molecular Clustering of *M. tuberculosis* by Date and Location

- New York City 1992 30%
- San Francisco 1993 40%
- Baltimore 1995 46%
- USA 2008 21%
- USA 2011-14 14%
- Cape Town 1993-8 72%
- Malawi 1995-2003 72%

Effect of Decreasing Transmission on TB Incidence

![Graph showing the effect of decreasing transmission on TB incidence.](Epidemiol Infect 2012;140:1868)
Prevalence of LTBI in the United States, 2011-2012

<table>
<thead>
<tr>
<th></th>
<th>US Born (%)</th>
<th>Foreign Born (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>1.5 (0.9-2.6)</td>
<td>20.5 (16.1-25.8)</td>
<td>4.7 (3.4-6.3)</td>
</tr>
<tr>
<td>IGRA</td>
<td>2.8 (2.0-3.8)</td>
<td>15.9 (13.5-18.7)</td>
<td>5.0 (4.2-5.8)</td>
</tr>
</tbody>
</table>

PLoS One 2015;0140881

Prevalence of LTBI in the United States, 2011-2012

• 4.7% (3.4%-6.3%) of U.S. population had LTBI; translates to roughly 13 million people
• 80% of these had had LTBI diagnosed previously
• Of those previously diagnosed, 44% had been prescribed treatment and 92% of those (40%) completed
• Reservoir of untreated LTBI of 8.8 million people

Efficacy of LTBI Treatment

FIVE YEAR INCIDENCE OF CULTURE-POSITIVE TUBERCULOSIS PER 100 PERSON-YEARS BY TREATMENT GROUP

- Placebo
- INH 12 WEEK
- INH 24 WEEK
- INH 52 WEEK

PERCENT REDUCTION
Prevent TB Study – Non-inferiority

Treatment of Latent Tuberculosis Infection

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Duration</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid 300 mg</td>
<td>6-9 months</td>
<td>Daily</td>
</tr>
<tr>
<td>Rifampin 600 mg</td>
<td>4 months</td>
<td>Daily</td>
</tr>
<tr>
<td>Isoniazid 300 mg + Rifampin 600 mg</td>
<td>3 months</td>
<td>Daily</td>
</tr>
<tr>
<td>Isoniazid 900 mg + Rifapentine 900 mg</td>
<td>12 weeks</td>
<td>Weekly</td>
</tr>
</tbody>
</table>
Completion of LTBI Treatment by Regimen

- Description: 3HP weekly by DOT vs Self-administration
- Regimens:
  - 3HP weekly for 12 weeks by DOT
  - 3HP weekly for 12 weeks by SAT
  - 3HP weekly for 12 weeks by eSAT
- Sponsor: TBTC
- Target population: TST+ adults
- Outcome: Completion of treatment
- Size: 998
- Sites: US, Spain, South Africa
- Expected Results: 2017

iAdhere Trial

- Description: 3HP weekly by DOT vs Self-administration
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- Expected Results: 2017
Targeting populations at highest risk
Estimate of Number of Persons Receiving LTBI Treatment per year

- 197,000 persons (133,000-262,000) initiated treatment in 2002 in U.S. in 2002
- 88,000 (59,000-117,000) completed treatment for LTBI in U.S. in 2002

AJRCCM 2006;173:927-31

Estimating Relative Effectiveness of a Screening/Treatment Program

\[
\text{Number Needed to Screen} = \frac{\text{Size of population screened}}{\text{Number of TB cases prevented}}
\]
### NNS for Adult Household Contact

NNS = \( \frac{53,000}{726} = 73 \)

### NNS to prevent a case of TB

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>NNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected</td>
<td>71</td>
</tr>
<tr>
<td>Close contact (adult)</td>
<td>73</td>
</tr>
<tr>
<td>Recent immigrant (adult)</td>
<td>110</td>
</tr>
<tr>
<td>Foreign-born (adult)</td>
<td>301</td>
</tr>
<tr>
<td>Homeless</td>
<td>436</td>
</tr>
<tr>
<td>Injection Drug User</td>
<td>557</td>
</tr>
<tr>
<td>Prisoner</td>
<td>655</td>
</tr>
<tr>
<td>TNF-alpha inhibitor therapy</td>
<td>1128</td>
</tr>
<tr>
<td>Underweight</td>
<td>2062</td>
</tr>
<tr>
<td>Silicosis</td>
<td>2962</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3631</td>
</tr>
<tr>
<td>End Stage Renal Disease</td>
<td>4904</td>
</tr>
</tbody>
</table>

AJRCCM 2011;184:595
Public Health Impact of Screening

- ICER <$100,000, Highly recommended
- ICER <$100,000, Recommended
- ICER >$100,000, Not recommended

Cases of Active TB Prevented

- High risk
- Recent immigrants
- Foreign-born, up to 45 yrs.
- Vulnerable populations
- Chronic co-morbidities

JAMA 2016;316:962-9

Clinical Review & Education

Screening for Latent Tuberculosis Infection in Adults
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** Tuberculosis remains an important preventable disease in the United States. An effective strategy for reducing the transmission, morbidity, and mortality of active disease is the identification and treatment of latent tuberculosis infection (LTBI) to prevent progression to active disease.

**FINDINGS** The USPSTF found adequate evidence that accurate screening tests for LTBI are available, treatment of LTBI provides a moderate health benefit in preventing progression to active disease, and the harms of screening and treatment are small. The USPSTF has moderate certainty that screening for LTBI in persons at increased risk for infection provides a moderate net benefit.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends screening for LTBI in populations at increased risk. (B recommendation)
USPSTF Evidence Grading System

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Suggestions for Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td>B</td>
<td>The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.</td>
<td>Offer or provide this service.</td>
</tr>
<tr>
<td>C</td>
<td>The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.</td>
<td>Offer or provide this service for selected patients depending on individual circumstances.</td>
</tr>
<tr>
<td>D</td>
<td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td>
<td>Discourage the use of this service.</td>
</tr>
<tr>
<td>I statement</td>
<td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.</td>
<td>Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.</td>
</tr>
</tbody>
</table>

JAMA 2016;316:963

USPSTF LTBI Recommendations

Figure 2. Screening for Latent Tuberculosis Infection in Adults: Clinical Summary

<table>
<thead>
<tr>
<th>Population</th>
<th>Asymptomatic adults at increased risk for infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>Screen for latent tuberculosis infection (LTBI). Grade: B</td>
</tr>
</tbody>
</table>

JAMA 2016;316:964
USPSTF LTBI Recommendation Rationale

Risk Assessment: Populations at increased risk for LTBI include persons who were born in, or are former residents of, countries with increased tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (e.g., homeless shelters and correctional facilities). Local demographic patterns may vary across the United States, clinicians can consult their local or state health departments for more information about populations at risk in their community.

Screening Tests: Screening tests include the Mantoux tuberculin skin test and interferon-gamma release assays, both are moderately sensitive and highly specific for the detection of LTBI.


Balance of Benefits and Harms: The USPSTF concludes with moderate certainty that the net benefit of screening for LTBI in persons who are at increased risk for tuberculosis is moderate.

JAMA 2016;316:964

Check appropriate risk factor boxes below.

- Latent TB infection testing is recommended if any of the 3 boxes below is checked.
- If latent TB infection test result is positive and active TB disease is ruled out, latent TB infection treatment is recommended.

REPORT Latent TB Infection or Active/Suspected Active TB Disease
Go to www.imest.gov/philicdoh/tb for reporting forms

- Born or lived in a country with an elevated TB rate
  - Includes any country other than the United States, Canada, Australia, New Zealand, or a country in western or northern Europe.
  - If resources require prioritization within this group, prioritize patients with at least one medical risk for progression (see Fact Sheet for list).
  - Interferon Gamma Release Assay is preferred over Tuberculin Skin Test for non-US-born persons.

- Immunosuppression, current or planned
  - HIV infection, organ transplant recipient, treated with TNF-alpha antagonists (e.g., infliximab, adalimumab, etanercept), steroids (equivalent of prednisone ≥ 15 mg/day for ≥ 1 month) or other immunosuppressive medication

- Close contact to someone with infectious TB disease
From Policy to Practice – LTBI Testing and Treatment at an FQHC in MA

Family Health Center of Worcester

• In 2016, 27,243 unique patients

• 5,229 patients are foreign born (19%)
  – > 90% of these patients are from countries that warrant LTBI screening

• 1% are HIV-infected

• 2% have a LTBI diagnosis in their problem list
Family Health Center of Worcester

• Providers
  – 36 Family Physicians
  – 3 Internists
  – 25 Nurse Practitioners
  – 2 Physician Assistants
  – 11 Dentists
  – 51 nurses

Prior to USPSTF Guidelines...

• < 5 providers reported ever treating LTBI

• LTBI testing occurred in refugees, pregnant women, HIV patients, and those who required testing for work
  – Only HIV patients were being treated at FHCW by HIV team

• Providers felt most comfortable with PPD – difficult in our patient population

• Majority of patients with LTBI were referred to local TB clinic (Getchell) for treatment
Common Barriers to LTBI Testing and Tx

- Time

- Misperception that LTBI must be treated in a TB clinic or by a specialist

- Lack of knowledge – not incorporated into primary care residency training

- Fear – “I won’t fill out the necessary forms correctly” “Isoniazid is a scary drug”

USPSTF Recommendation

Latent Tuberculosis Infection: Screening
Release Date: September 2016

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What’s This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic adults at increased risk for infection</td>
<td>The USPSTF recommends screening for latent tuberculosis infection (LTBI) in populations at increased risk.</td>
<td>B</td>
</tr>
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</table>
USPSTF Rec – The Highlights

• Screen all asymptomatic individuals > 18 years at increased risk for TB infection

• IGRA is preferred screening test for BCG vaccinated or those who will not come back for TST reading

How to implement LTBI testing and treatment in your primary care practice

• Step 1: Identify a LTBI champion(s)
• Step 2: Develop Partnerships
• Step 3: Train Providers and Staff
• Step 4: Ensure follow up capacity
• Step 5: Monitor and evaluate your progress
Step 1: Identify a LTBI champion(s)

- FHCW – Refugee Health and HIV/Hepatitis Teams
- Individual(s) who are willing to lead the effort will...
  - Develop partnerships with DPH and TB clinic
  - Organize training for providers and staff
  - Create infrastructure for treatment and strengthen monitoring and evaluation for LTBI

Step 2: Develop Partnerships

- Department of Public Health – Local and State
  - Meet the TB team in person (if possible) or by phone
  - Understand reporting and surveillance forms
  - Ask for help!
Develop Partnerships

• Local TB clinic (Getchell)
  – Meet with TB specialist to get buy in
  – Ensure specialist willingness to answer questions via email and decrease referrals
  – Confirm that appropriate information from primary care clinic is reaching specialists

Develop Partnerships

• Within your organization
  – LTBI testing and treatment will require support from other staff – nursing, referral department, pharmacy
  – As your program grows, you may need additional administrative time -> Track number of visits generated from LTBI follow up visits
Step 3: Train Providers and Staff

- Training Sept 2016
  - Providers
  - Nursing

Consider treating LTBI at FHCW!

- If you can answer yes to ALL of these questions, consider treating!
  - Can you see the patient MONTHLY and ensure tracking those who are lost to follow up?
  - Is your patient healthy without any of the following: history of liver disease, not on immunosuppressive agents including steroids or TNF-alpha antagonists, and does not have a history of TB treatment or radiographic evidence of TB?
  - Is your patient older than 18 years of age?

- If you answered no to one of the questions above, order chest x-ray and refer to Getchell

Step 4: Ensure follow up capacity

- Providers are responsible for follow up visits
  - No additional staff available so this worked best for FHCW

- HIV team nurse will alternate monthly follow up visits with clinicians for their patients

LTBI My Phrases for Providers

- Patient reports taking INH and Rif/ethambutol as prescribed. Denies missing any doses.
- -Practitioner treats in XX.
- -Denies any complaints (see below).

- No additional staff available so this worked best for FHCW

- HIV team nurse will alternate monthly follow up visits with clinicians for their patients
Step 5: Monitor and Evaluate Progress

- Implemented e-referral
- Created new TB clinic referral work flow

FHCW LTBI Progress Report

- In 2017, 517 IGRAs ordered compared to only 454 in 2016
- Since the workshop, 12 providers have reported successfully treating or are currently treating 17 patients with LTBI
- 6 patients were treated with rifampin and 11 with isoniazid
- Diagnosed and referred 87 other patients to Getchell TB clinic for LTBI treatment
Challenges

• Visit availability
  – Providers do not have space in schedules
  – Possible solution: Working on training a nurse who can see follow ups

• Surveillance is difficult
  – Tests ordered
  – Treatment initiated and completed
  – Possible solution: EMR, Bi-annual meeting with LTBI champion, TB clinic, and DPH to review

Conclusions

• Screening for LTBI and treatment to prevent reactivation disease could substantially reduce TB disease in the US

• New USPSTF recommendations put LTBI screening and treatment into the mainstream of primary care practice

• Screening and treatment should target groups where screening and treatment will be most efficient: foreign-born, immunosuppressed, contacts
Conclusions

• Screening with IGRA is more cost-effective than screening with Tuberculin Skin Test
• Shorter treatment regimens could increase adherence and augment program effectiveness
• Implementing LTBI screening and treatment into primary care is possible through partnerships

Questions?