Almost at the Finish Line: Proposed Updates to Tuberculosis Screening and Testing of Healthcare Personnel

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Overview

- Background

- Systematic Review

- Proposed draft updates to guidelines
Background

- CDC guidelines on preventing TB transmission in healthcare settings published in 2005

- Concerns about the efficacy of serial TB testing with declining TB incidence were amplified by the PPD shortage in 2013 and multiple articles reporting on IGRA poor performance in low risk persons

- Joint NSTC-NTNC session at 2015 NTCA conference to discuss issue

- Working group created in Summer 2015

- Systematic review commenced in January 2017
Review Focused on TB Screening and Testing of Healthcare Workers

CONTENTS
Introduction .............................................................................................................. 1
Overview .................................................................................................................. 1
   HCWs Who Should Be Included in a TB Surveillance Program ......................... 3
   Risk for Health-Care–Associated Transmission of M. tuberculosis ................. 6
   Fundamentals of TB Infection Control ............................................................... 6
   Relevance to Biologic Terrorism Preparedness ................................................. 8
Recommendations for Preventing Transmission of M. tuberculosis in Health-Care Settings ............................................................... 8
TB Infection-Control Program ............................................................................ 8
TB Risk Assessment ............................................................................................... 9
Risk Classification Examples .............................................................................. 11

Systematic Review

- A process by which a body of literature is reviewed and assessed using systematic methods which are intended to reduce bias in the review process and improve understandability.
- Used to inform research, policy, and practice
- Evidence base for guideline development
Systematic Review Process

Meta-analysis

- A quantitative approach in which individual study findings addressing a common problem are statistically integrated and analyzed to determine the effectiveness of interventions.
Analytic Framework: Screening and Serial Testing of HCWs for LTBI

Key Effect Modifiers
- Guidelines/standards adopted by employer

Healthcare workers including, but not limited to: acute care hospitals, long-term care facilities, physician's offices, dental offices, rehabilitation centers, emergency care centers, adult surgical centers, dialysis centers, and outpatient clinics, home health care, and emergency medical services

**Serial Screening and Testing of HCWs for LTBI**

- Increased Number of HCWs Assessed for TB symptoms
- Enhanced TB Risk Factor Assessment of All HCW with Previous TST/IGRA Negative Results (occupational & Non-occupational related)
- Increased LTBI Testing (via TST or IGRA) for HCWs at High Risk
- Increased Detection of LTBI among HCWs
- Increased Number of HCWs Treated for LTBI
- Reduced Transmission of TB to Patients in HC Setting
- Reduced Transmission of TB to Colleagues in HC Setting
- Reduced Incidence of TB Disease among HCWs in Healthcare Setting
- Reduced TB-related Morbidity and Mortality

**Research Questions**

- What is the prevalence and incidence of LTBI among healthcare workers in the United States?
- What is the incidence of TB disease among healthcare workers in the United States?
- Does annual or serial testing (via TST or IGRA) of U.S. healthcare workers reduce the risk of TB transmission in U.S. healthcare settings?
- Does annual or serial testing (via TST or IGRA) of U.S. healthcare workers increase the detection of occult TB transmission in U.S. healthcare settings?
- Are certain individuals who work within healthcare facilities at higher risk of TB than others based on occupational and non-occupational factors?
**Methodology**

- Community Guide systematic review methods used to evaluate and summarize available evidence
- Two reviewers independently screened and abstracted data for each included study
- Disagreements were resolved by consensus
- Data analyzed using “metafor” and “meta” packages in R (v3.3.2)

**Search for Evidence**

- We conducted a search for studies that screened and/or tested healthcare personnel (HCP) for LTBI
- Electronic databases included:  
  - MEDLINE, EMBASE, and Scopus
- Search period:  
  - Original search: January 2006–February 2017  
  - Update search: February 2017–November 2017 (MEDLINE only)
- Language restriction:  
  - English only
**Inclusion/Exclusion Criteria**

- **Inclusion Criteria**
  - Study designs
    - Randomized controlled trial (RCT), quasi-experimental, observational studies, cross-sectional surveys, other designs with concurrent comparison groups
  - Target population
    - Paid or volunteer health care workers
  - Outcomes of interest
    - Prevalence, conversion, and reversion rates; TB transmission rates; TB disease
  - Setting
    - High-income, low TB-incidence countries

- **Exclusion Criteria**
  - Study designs: case reports, editorials, commentaries, descriptive articles on nosocomial outbreaks

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**Search Results**

Original Search Period
Jan. 2006-Feb. 2017
(n = 1129)

- Duplicates (n=2)
- Not relevant (n=1047)

Ordered Full Text (n=80)

- Did not meet inclusion criteria (n=37)
- Unable to retrieve full text (n=8)

TB Screening & Testing in HCP Articles (n=35)

- Limited quality of execution (n=1)

Included in Analysis (n=34)

- Not relevant (n=14)

Total Included in Meta-analysis (n=36)

Update Search Period
Feb. 2017-Nov. 2017
(n = 18)

Ordered Full Text (n=4)

- Modelling study (n=1)
- Type of QFT test used (n=1)

TB Screening & Testing in HCP Articles (n=2)

- Limited quality of execution (n=0)

Included in Analysis (n=2)
Quality of Execution Assessment

- Description
- Sampling Frame
- Data Analysis
- Measurement
- Interpretation of Results

Percent of Studies Reporting Assigned Limitation

Study Characteristics (n=36)

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th># of Studies Reporting (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>16 (44.4%)</td>
</tr>
<tr>
<td>Europe</td>
<td>17 (47.2%)</td>
</tr>
<tr>
<td>Israel</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Australia/New Zealand</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>Setting</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>34 (94.4%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5.6%)</td>
</tr>
<tr>
<td>Study Design</td>
<td></td>
</tr>
<tr>
<td>Randomized controlled trial</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Prospective design</td>
<td>8 (22.2%)</td>
</tr>
<tr>
<td>Retrospective design</td>
<td>14 (38.9%)</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>14 (38.9%)</td>
</tr>
<tr>
<td>Study Focus</td>
<td></td>
</tr>
<tr>
<td>Testing</td>
<td>15 (41.7%)</td>
</tr>
<tr>
<td>Screening and Testing</td>
<td>21 (58.3%)</td>
</tr>
<tr>
<td>Type of Test Used at Baseline</td>
<td></td>
</tr>
<tr>
<td>TST</td>
<td>12 (33.3%)</td>
</tr>
<tr>
<td>IGRA</td>
<td>11 (30.6%)</td>
</tr>
<tr>
<td>TST &amp; IGRA</td>
<td>13 (36.1%)</td>
</tr>
</tbody>
</table>
Healthcare Personnel Characteristics (n=36)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th># of Studies Reporting (%)</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20 (55.6%)</td>
<td>38.7 yrs. old (37.0 yrs.–42.3 yrs.)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27 (79.4%)</td>
<td>75.2% (68.2%–79.6%)</td>
</tr>
<tr>
<td>Male</td>
<td>27 (79.4%)</td>
<td>24.8% (20.5%–31.9%)</td>
</tr>
<tr>
<td>BCG Vaccinated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24 (70.6%)</td>
<td>45.5% (14.0%–76.5%)</td>
</tr>
<tr>
<td>No</td>
<td>24 (70.6%)</td>
<td>54.5% (23.5%–86.1%)</td>
</tr>
<tr>
<td>Non-U.S.–Born (U.S. studies)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (11.8%)</td>
<td>10.6% (3.3%–36.7%)</td>
</tr>
<tr>
<td>No</td>
<td>4 (11.8%)</td>
<td>89.4% (63.4%–96.8%)</td>
</tr>
</tbody>
</table>

Definitions

- **Baseline Testing**: TST or IGRA test conducted during the pre-employment onboarding process or upon hire

- **Conversion**: a positive TST or IGRA test result after a documented prior negative test result

- **Reversion**: a negative TST or IGRA test result after a documented prior positive test result
Baseline Testing for U.S. HCP: TST (n=6)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Positive</th>
<th>Total</th>
<th>Proportion</th>
<th>95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frenzel,2006</td>
<td>114</td>
<td>4059</td>
<td>0.03</td>
<td>[0.02; 0.03]</td>
<td>17.1%</td>
</tr>
<tr>
<td>Gillenwater,2006</td>
<td>246</td>
<td>1852</td>
<td>0.13</td>
<td>[0.12; 0.15]</td>
<td>16.9%</td>
</tr>
<tr>
<td>Cummings,2009</td>
<td>4</td>
<td>182</td>
<td>0.02</td>
<td>[0.01; 0.06]</td>
<td>14.7%</td>
</tr>
<tr>
<td>Gandr,2010</td>
<td>6</td>
<td>6530</td>
<td>0.00</td>
<td>[0.00; 0.00]</td>
<td>17.1%</td>
</tr>
<tr>
<td>Dorman,2014</td>
<td>125</td>
<td>2418</td>
<td>0.05</td>
<td>[0.04; 0.06]</td>
<td>17.0%</td>
</tr>
<tr>
<td>Dobler,2017</td>
<td>862</td>
<td>40142</td>
<td>0.02</td>
<td>[0.02; 0.02]</td>
<td>17.2%</td>
</tr>
</tbody>
</table>

Random effects model: 55183
Proportion: 0.03
95% CI: [0.01; 0.06]
100.0%

Baseline Testing for U.S. HCP: IGRA (n=11)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Positive</th>
<th>Total</th>
<th>Proportion</th>
<th>95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock,2008</td>
<td>26</td>
<td>143</td>
<td>0.18</td>
<td>[0.12; 0.25]</td>
<td>6.9%</td>
</tr>
<tr>
<td>Pollock,2008</td>
<td>5</td>
<td>36</td>
<td>0.14</td>
<td>[0.05; 0.29]</td>
<td>3.9%</td>
</tr>
<tr>
<td>Miranda,2009</td>
<td>68</td>
<td>1528</td>
<td>0.04</td>
<td>[0.03; 0.06]</td>
<td>9.0%</td>
</tr>
<tr>
<td>Cummings,2009</td>
<td>2</td>
<td>182</td>
<td>0.01</td>
<td>[0.00; 0.04]</td>
<td>7.3%</td>
</tr>
<tr>
<td>Fong,2012</td>
<td>486</td>
<td>7374</td>
<td>0.07</td>
<td>[0.06; 0.07]</td>
<td>9.2%</td>
</tr>
<tr>
<td>Joshi,2012</td>
<td>129</td>
<td>3290</td>
<td>0.04</td>
<td>[0.03; 0.05]</td>
<td>9.2%</td>
</tr>
<tr>
<td>Slater,2013</td>
<td>828</td>
<td>9153</td>
<td>0.09</td>
<td>[0.08; 0.10]</td>
<td>9.3%</td>
</tr>
<tr>
<td>Dorman,2014</td>
<td>118</td>
<td>2418</td>
<td>0.05</td>
<td>[0.04; 0.06]</td>
<td>9.1%</td>
</tr>
<tr>
<td>Joshi,2014</td>
<td>69</td>
<td>2303</td>
<td>0.03</td>
<td>[0.02; 0.04]</td>
<td>9.1%</td>
</tr>
<tr>
<td>Dorman,2014</td>
<td>144</td>
<td>2418</td>
<td>0.06</td>
<td>[0.05; 0.07]</td>
<td>9.1%</td>
</tr>
<tr>
<td>Weddle,2015</td>
<td>22</td>
<td>758</td>
<td>0.03</td>
<td>[0.02; 0.04]</td>
<td>8.7%</td>
</tr>
<tr>
<td>King,2015</td>
<td>443</td>
<td>19630</td>
<td>0.02</td>
<td>[0.02; 0.02]</td>
<td>9.3%</td>
</tr>
</tbody>
</table>

Random effects model: 49233
Proportion: 0.05
95% CI: [0.03; 0.07]
100.0%
U.S. HCP Conversions: TST (n=5)

Of note, only 1 study from Europe used TST for serial testing and reported a conversion rate of 6.8%.

U.S. HCP Conversions: IGRA (n=7)
U.S. HCP Reversions: TST (n=2)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Reversions Total</th>
<th>Proportion</th>
<th>95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gillenwater, 2006</td>
<td>17 23</td>
<td>0.74</td>
<td>[0.52; 0.90]</td>
<td>42.6%</td>
</tr>
<tr>
<td>Dorman, 2014</td>
<td>29 54</td>
<td>0.54</td>
<td>[0.40; 0.67]</td>
<td>57.4%</td>
</tr>
</tbody>
</table>

Random effects model: 77 0.62 [0.42; 0.81] 100.0%

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U.S. HCP Reversions: IGRA (n=9)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Reversions Total</th>
<th>Proportion</th>
<th>95% CI</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gandra, 2010</td>
<td>66 135</td>
<td>0.49</td>
<td>[0.40; 0.58]</td>
<td>11.7%</td>
</tr>
<tr>
<td>Fong, 2012</td>
<td>8 10</td>
<td>0.80</td>
<td>[0.44; 0.97]</td>
<td>7.2%</td>
</tr>
<tr>
<td>Joshi, 2012</td>
<td>18 45</td>
<td>0.40</td>
<td>[0.26; 0.56]</td>
<td>10.6%</td>
</tr>
<tr>
<td>Slater, 2013</td>
<td>395 1223</td>
<td>0.32</td>
<td>[0.30; 0.35]</td>
<td>12.3%</td>
</tr>
<tr>
<td>Dorman, 2014</td>
<td>67 118</td>
<td>0.57</td>
<td>[0.47; 0.66]</td>
<td>11.6%</td>
</tr>
<tr>
<td>Joshi, 2014</td>
<td>31 69</td>
<td>0.45</td>
<td>[0.33; 0.57]</td>
<td>11.2%</td>
</tr>
<tr>
<td>Dobier, 2017</td>
<td>60 91</td>
<td>0.66</td>
<td>[0.55; 0.76]</td>
<td>11.4%</td>
</tr>
<tr>
<td>Dorman, 2014</td>
<td>92 144</td>
<td>0.64</td>
<td>[0.55; 0.72]</td>
<td>11.8%</td>
</tr>
<tr>
<td>King, 2015</td>
<td>76 443</td>
<td>0.18</td>
<td>[0.14; 0.21]</td>
<td>12.2%</td>
</tr>
</tbody>
</table>

Random effects model: 2278 0.48 [0.36; 0.61] 100.0%
Tuberculosis Disease

- From 8 U.S. studies reporting—with nearly 64,000 participants—no U.S.-based HCP developed active tuberculosis disease.

Review Limitations

- Included studies were highly heterogeneous in population, study design, and type of test used
- Most of the included studies were of moderate or least design suitability—only 7 were of good design suitability
- Few studies used T-SPOT.TB for testing—most of the included evidence focused on TST and QFT
- Few studies reported demographic data, making it difficult to know whether included studies are representative of U.S. healthcare worker population
- Evidence is mostly limited to hospital setting
Summary of Findings

- Relatively low proportion (3%–5%) of U.S. HCP test positive for *M. tuberculosis* at baseline
- <1% of U.S. HCP previously testing negative convert to a positive test result during serial testing
- Nearly 50% of U.S. HCP previously testing positive revert to a negative test result during serial testing
- Insufficient evidence to assess incidence and transmission of TB disease among HCP

So what does this all mean?

- Updated recommendations are based primarily on expert opinion.
Updated *DRAFT* Recommendations

Definitions

- **Healthcare Personnel (HCP)**
  - Replaces Healthcare Worker (HCW) to be consistent with current HHS and CDC preferred language
  - Definition unchanged from 2005

- **TB screening**
  - Broad process that includes a risk assessment, symptom evaluation, a test for LTBI (either a TST or IGRA), and additional work-up for TB disease as needed

- **TB Testing**
  - TST or IGRA
Baseline (Pre-Employment) Screening and Testing

- Baseline screening on hire should include:
  - TB risk assessment
  - Symptom evaluation
  - TST or IGRA (not both)

- Low risk HCP testing positive should have second test
  - Consistent with TB Diagnostic Guidelines (Lewinsohn CID 1/15/2017)

Postexposure Screening and Testing

- Known exposure without adequate personal protection
- No history of positive TB test
  - Symptom assessment and TB test
  - Retest 8–10 weeks after last exposure
- History of positive TB test regardless of treatment
  - Symptom assessment, no test
Serial Screening and Testing Based on Occupational Risk

- No routine testing of HCP at any interval in the absence of known exposure or ongoing transmission.

- Healthcare facilities can choose to conduct routine testing of specific HCP (e.g. pulmonologists, respiratory therapists) or staff in specific settings based on historic risk (e.g. emergency departments).
  - This decision should be individualized to each facility and may be made in consultation with state/local health department.

Serial Screening and Testing Based on Non-Occupational Risk

- Important to recognize non-occupational exposures to TB and risk factors for TB progression.

- Facilities should educate HCP annually about TB.
  - Include risk factors.
  - Signs and symptoms.
  - Encourage HCP to discuss any new exposures both occupational and non-occupational.

- Decision to test HCP based on individual risk identified.
Follow-Up of Positive Test Results

- HCP with positive TB test result:
  - Chest imaging
  - Symptom assessment
  - Further evaluation for TB disease if warranted

- All HCP with LTBI should be offered and encouraged to complete LTBI treatment unless a contraindication exists

### Summary of (Draft) Updated Recommendations

<table>
<thead>
<tr>
<th>Category</th>
<th>2005 Recommendation</th>
<th>2018 Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (on hire) Screening</td>
<td>TB screening of all HCP including a symptom evaluation and test (IGRA or TST) for those without documented prior TB or LTBI</td>
<td>TB screening of all HCP including a symptom evaluation and test (IGRA or TST) for those without documented prior TB or LTBI (unchanged); individual TB risk assessment (new)</td>
</tr>
<tr>
<td>and Testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postexposure Screening and</td>
<td>Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure</td>
<td>Symptom evaluation for all HCP when an exposure is recognized. For HCP with a baseline negative TB test and no prior TB or LTBI, perform a test (IGRA or TST) when the exposure is identified. If that test is negative, do another test 8–10 weeks after the last exposure (unchanged)</td>
</tr>
<tr>
<td>Testing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serial Screening and Testing</td>
<td>Based on a healthcare facility and setting risk assessment. Not recommended for HCP working in low-risk healthcare settings. Recommended for HCP working in medium-risk healthcare settings and settings with potential ongoing transmission.</td>
<td>Not routinely recommended (new); can consider for select HCP groups (unchanged); Recommend annual TB education of all HCP (unchanged), including information on TB exposure risks for all HCP (new emphasis)</td>
</tr>
<tr>
<td>Follow-Up of Positive Test</td>
<td>Referral to determine whether LTBI treatment is indicated.</td>
<td>LTBI treatment is strongly recommended for all HCP diagnosed with LTBI unless contraindications exist (new)</td>
</tr>
<tr>
<td>Results</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HCP, healthcare personnel; IGRA, Interferon-Gamma Release Assay; LTBI, latent tuberculosis infection; TB, tuberculosis; TST, tuberculin skin test
Initial Feedback

- Positive overall
  - Informal review by TB, Infection Control and Occupational Health SMEs
  - Formally presented to ACET and HICPAC
  - Informally presented to occupational health professionals
- Most feedback had been on potential recommendation to consider an annual risk assessment of HCP (now removed)
  - Logistics of implementation
  - Sharing of private medical information
  - Stigmatization of HCP

Important Clarification

- The 2005 CDC Guidelines document is not dead!

- Recommendations about infection control including environmental and respiratory precautions still apply and are key to preventing TB transmission in healthcare settings
Current Status

- Document submitted to CDC clearance 8/2/2018
  - Currently winding it’s way through CDC
- Hoping for a possible spring publication in the MMWR

- Parallel work on companion document (led by Wendy Thanassi, VA)
  - Focus on implementation of recommendations
  - Include practical guidance, examples
  - Hope to be available around the time the MMWR article is published

Workgroup Members

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- Gibril Njie
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- Neela Goswani
- Jerry Mazurek

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- David Lewinsohn, Oregon Health Sciences University
- Trini Mathew, Beaumont Hospital
- Randall Reves, NSTC/Denver Public Health
- Annie Wiest, AOHP
- Silvia Quevedo, APIC
Thank you!

TB Risk Assessment Questions

• Being born in or living for > 1 month in a country with an elevated TB rate
  Any country other than the United States, Canada, Australia, New Zealand, or a country in Western or Northern Europe
  OR
• Current or planned immunosuppression including:
  HIV infection, organ transplant recipient, treatment with a TNF-alpha antagonist (e.g., infliximab, etanercept, others), chronic steroids (equivalent of prednisone ≥15 mg/day for ≥1 month) or other immunosuppressive medication
  OR
• Close contact to someone with infectious TB disease since last TB test

Adapted from California Tuberculosis Adult Risk Assessment