Latent Tuberculosis Treatment in Health Care Personnel

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I have no conflicts of interest to report.
Latent Tuberculosis Infection (LTBI) is the leading cause of TB Disease in the US.

Treatment of LTBI is fundamental to TB elimination.
Tuberculosis in Healthcare Personnel

• HCP account for about 4% of active TB in the US.
• Incidence rates lower for HCP than non-HCP (2.5 vs 3.2 per 100K)
• Compared to non-HCP, HCP with TB were
  • More likely to be born outside US
  • Less likely to have recent infection

Tuberculosis in Health Care Personnel

TB Disease in HCP is disruptive, costly, and dangerous to others, including patients.

Fraser, et al, 2009. Active tuberculosis in a healthcare worker: are you ready?. Infection Control & Hospital Epidemiology, 30(1), pp.80-82.
Health care personnel are HALF as likely to accept treatment half as others.

(Gershon, 2004; Horsburgh, 2010; Colson, 2013; Sandgren, 2016)
HCP and LTBI treatment – what is known

- About 40% of HCP with LTBI accept treatment vs 70 – 80% of general patient population.
- Short course therapy improves adherence, but not acceptance.
- In general population:
  - treatment acceptance is lower in women.
  - immigrants are more likely to accept treatment.
  - higher educational attainment correlates to higher treatment acceptance.
HCP and LTBI treatment – gaps in knowledge

• Are some occupational subgroups of HCP more/less likely to accept treatment? (Doctors? Nurses? Techs?)

• Do trends seen in the general population also apply to HCP?
  • Age
  • Gender
  • Educational level
  • Immigration status

• Are foreign-born HCP are resistant to treatment – and if so is that independent of their occupational subgroup?

• Why are so few HCP willing to accept treatment?
Determinants of Latent Tuberculosis Treatment Acceptance and Completion Among Healthcare Personnel

Swift MD, Molella RG, Vaughn AIS, Breeher LE, Newcomb RD, Abdellatif S, and Murad MH. Clinical Infectious Diseases, 25 September 2019 (ePub online ahead of print) https://doi.org/10.1093/cid/ciz817
Research Questions

1. What occupational and demographic factors are associated with HCP acceptance of treatment for LTBI?
2. What factors are associated with successful completion of a full course of therapy among HCP?
Study Setting

- Mayo Clinic Rochester
- Approximately 35,000 employees
- TB screening required at hire/start
- For positive TB screening, clinical evaluation is required by employer
- Treatment is voluntary.
  - Individuals with infectious TB may not start work until deemed noninfectious.
  - Individuals with LTBI may start work regardless of treatment.
Inclusion Criteria

• Completed onboarding process to work or study at Mayo Clinic Rochester
• Start date 1/1/2006 – 12/31/2015
• Positive initial screen (usually with TST)
• Confirmed infection with second test (IGRA)
• Referred to Occupational Medicine Clinic to be counselled and offered treatment
Exclusion Criteria

• Active tuberculosis identified
• Previously completed treatment for LTBI
• Did not complete clinic visit
• LTBI treatment not recommended by evaluating provider
  • Medical contraindication.
  • Planning to leave US before treatment could be completed.
Data Sources

**Occupational record:**
- Hire date
- Occupation
- Birth date
- Gender
- TB Skin Test (TST) date and result
- IGRA date and result
- Prior treatment

**Medical record:**
- Country of origin
- BCG vaccine status
- Chest X-ray completion
- Clinic provider type
- Treatment recommendation
- Treatment acceptance
- Months of treatment completed and medication
- Nurse communications (treatment completion, side effects, discontinuation, loss to f/u)
Statistical Analysis

• Multivariate logistic regression to identify independent variables correlated with treatment acceptance and completion

• 80% power to detect OR of 1.55 for any independent variable
Outcomes

• Treatment acceptance (Y/N)
  • Identified by documentation of prescription issued
during or within a year of clinic visit

• Treatment completion (Y/N)
  • Identified by nursing note indicating treatment protocol
  completion confirmed by patient (phone or email
  response)
Baseline Characteristics

• $N = 470$
• Median age 35.3 (range 18.1 - 74.0)
• 60% male
• 67% BCG-vaccinated (by self-report)
• >70 countries of origin
  • India - 108
  • China - 91
  • Republic of Korea - 36
  • US - 31
Occupational Subgroups

Researchers, 146
Nonclinical Staff, 123
Doctors, 118
Clinical Staff, 43
Nurses, 25
Students, 15
TB Burden in Country of Origin

- High: 296
- Medium: 111
- Low: 43
Outcomes

470
Treatment offered

193 (41.1%)
Accepted treatment

277 declined treatment

56 Did not complete treatment (Includes 9 lost to follow-up.)

137 (29.1%) Completed treatment
Factors Associated with Treatment Acceptance

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio for Starting Treatment (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.97 (0.94, 0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.90 (1.21, 2.99)</td>
<td>0.01</td>
</tr>
<tr>
<td>BCG vaccination</td>
<td>0.75 (0.25, 2.28)</td>
<td>0.62</td>
</tr>
<tr>
<td>Job Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonclinical Staff</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td>0.47 (0.26, 0.85)</td>
<td>0.01</td>
</tr>
<tr>
<td>Researcher</td>
<td>0.34 (0.19, 0.64)</td>
<td>0</td>
</tr>
<tr>
<td>Nurse</td>
<td>0.62 (0.23, 1.68)</td>
<td>0.35</td>
</tr>
<tr>
<td>Clinical Staff</td>
<td>0.67 (0.28, 1.53)</td>
<td>0.34</td>
</tr>
<tr>
<td>Student</td>
<td>0.41 (0.12, 1.41)</td>
<td>0.16</td>
</tr>
<tr>
<td>Clinic provider</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>NP/PA</td>
<td>0.94 (0.42, 2.11)</td>
<td>0.87</td>
</tr>
</tbody>
</table>

1 Multilevel mixed-effects logistic regression, controlling for individual provider practice patterns.

2 Including IGRA level, dichotomizing age (at 35), and immediate vs delayed treatment acceptance do not change the conclusions.
## Factors Associated with Treatment Acceptance

<table>
<thead>
<tr>
<th>Country of Origin</th>
<th>Odds Ratio for Starting Treatment (95% CI)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>US</td>
<td>1.00 (ref)</td>
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</tr>
<tr>
<td>China</td>
<td>0.52 (0.08, 3.39)</td>
<td>0.5</td>
</tr>
<tr>
<td>India</td>
<td>1.27 (0.17, 9.77)</td>
<td>0.82</td>
</tr>
<tr>
<td>Korea</td>
<td>0.75 (0.10, 5.68)</td>
<td>0.78</td>
</tr>
<tr>
<td>Other</td>
<td>1.22 (0.25, 6.10)</td>
<td>0.81</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Geographic Region (GBD)</th>
<th>Odds Ratio for Starting Treatment (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High income (US, W. Eur, Japan, Aus/NZ, Chile)</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Central &amp; Eastern Europe, Central Asia</td>
<td>1.09 (0.21, 5.81)</td>
<td>0.92</td>
</tr>
<tr>
<td>East and Southeast Asia</td>
<td>1.35 (0.31, 5.88)</td>
<td>0.69</td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>0.85 (0.19, 3.81)</td>
<td>0.83</td>
</tr>
<tr>
<td>North Africa and Middle East</td>
<td>0.95 (0.22, 4.03)</td>
<td>0.95</td>
</tr>
<tr>
<td>South Asia</td>
<td>0.72 (0.14, 3.67)</td>
<td>0.69</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>1.59 (0.37, 6.86)</td>
<td>0.54</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.51 (0.27, 8.34)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TB Burden Category for Country of Origin</th>
<th>Odds Ratio for Starting Treatment (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>1.39 (0.56, 3.47)</td>
<td>0.48</td>
</tr>
<tr>
<td>Low</td>
<td>2.1 (0.33, 13.32)</td>
<td>0.43</td>
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</table>
Factors Associated with Treatment Completion

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio for Completing Treatment (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.05 (0.89, 1.23)</td>
<td>0.57</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.51 (0.05, 4.97)</td>
<td>0.56</td>
</tr>
<tr>
<td>BCG vaccination</td>
<td>0.10 (0.01, 1.01)</td>
<td>0.05</td>
</tr>
<tr>
<td>Job Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonclinical Staff</td>
<td>1.00 (ref)</td>
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</tr>
<tr>
<td>Physician</td>
<td>1.10 (0.35, 3.41)</td>
<td>0.87</td>
</tr>
<tr>
<td>Researcher</td>
<td>2.65 (0.25, 28.53)</td>
<td>0.42</td>
</tr>
<tr>
<td>Nurse</td>
<td>***</td>
<td>***</td>
</tr>
<tr>
<td>Clinical Staff</td>
<td>0.99 (0.08, 12.03)</td>
<td>0.99</td>
</tr>
<tr>
<td>Student</td>
<td>***</td>
<td>***</td>
</tr>
<tr>
<td>TB Burden Category for Country of Origin</td>
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<td></td>
</tr>
<tr>
<td>High</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>8.510 (3.928, 18.438)</td>
<td>0.000</td>
</tr>
<tr>
<td>Low</td>
<td>9.493 (2.060, 43.734)</td>
<td>0.004</td>
</tr>
<tr>
<td>Clinic provider</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>NP/PA</td>
<td>1.339 (0.338, 5.306)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*Multilevel mixed-effects logistic regression, controlling for individual provider practice patterns.

*Including IGRA results, dichotomizing age (at 35), and immediate vs delayed treatment acceptance do not change the conclusions.
Adherence Better on Short Course Regimen

- Isoniazid x 9 months: 67% Completed, P = 0.005
- Rifampin x 4 months: 95% Completed

Completed vs. Discontinued
Most Dropouts Occurred Early

![Bar chart showing the number of patients who dropped out at different stages of medication use.](chart.png)
Things to Ponder

• Phenomenon of deferred decision-making
  • Late acceptance in 8% of treated
  • No clear declination in 1/3 of untreated

• Is the one-visit model adequate for LBTI treatment education, counseling, and decision-making?
Takeaways

• Health care personnel are a heterogeneous population.
• Older age and female gender were associated with less treatment acceptance.
• Dropouts occurred early.
• Physicians* and researchers were less likely to accept treatment.
• Individuals from high TB burden countries were less likely to complete treatment.
• Short course adherence was superior.

Recommendations

1. Measure treatment completion, not just acceptance.
2. Highly educated HCP (MD/PhD) may need a more sophisticated and scientific approach to LTBI education.
   - Scientific underpinnings of recommendations
   - Public health strategy
   - Impact of HCP exposure events
   - Explore medication concerns and promote shorter course therapy
Recommendations

3. Clinic interventions may improve treatment rates.
   • Follow-up with HCP who do not accept treatment initially.
   • Early follow-up with those who do accept treatment*.
   • Use short course therapy as first line regimen.

*4 or more visits associated with higher adherence
Recommendations

4. Further research is needed to identify the knowledge, attitudes and beliefs of HCPs who decline treatment.
   - Keep occupation and country of origin in mind.
Recommendations

5. Partner with local public health

**Occupational Health**
- ✓ Diagnose
- ✓ Educate
- ✓ Counsel
- +/- Prescribe
- +/- Monitor

**Primary Care Provider**
- ✓ Diagnose
- ✓ Educate
- ✓ Counsel
- +/- Prescribe
- ✓ Monitor

**Public Health**
- ✓ Diagnose
- ✓ Educate
- ✓ Counsel
- ✓ Prescribe
- ✓ Monitor
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Bibliography


Q & A

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