Connecting the DOTS: Clinical Complications and Behavioral Interventions for Tobacco and Tuberculosis

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Tobacco Use: the Leading Preventable Cause of Death

- Tobacco use is a risk factor for 6 of the 8 leading causes of death in the world
  - Ischemic heart disease
  - Cerebral vascular disease
  - COPD
  - Lower respiratory infections
  - Lung cancer
- Is tobacco causally related to Tuberculosis?

Tuberculosis: Major Global Burden of Disease

- Disease of poverty
- Global Incidence peaked in 2004 at 142/100,000 per year, now 137/100,000
- 9.4 million new cases in 2009
- 94% of global population lives in areas covered by DOTS
- 1/3 global population thought to be latently infected with M. tuberculosis
- DOTS not enough to meet Millennium Development Goal on TB (to cut prevalence and deaths in half by 2015)

Source: WHO (2010). Global Tuberculosis Control
The effects of tobacco use on TB outcomes are independent of the effects of alcohol use, SES, age, sex and other potential confounders.

<table>
<thead>
<tr>
<th>Exposure to tobacco</th>
<th>Outcome</th>
<th>Risk ratios</th>
<th>Strengthen of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active/passive</td>
<td>TB infection</td>
<td>1.03 to 3.2</td>
<td>Limited</td>
</tr>
<tr>
<td>Active</td>
<td>TB disease</td>
<td>1.01 to 6.3</td>
<td>Strong</td>
</tr>
<tr>
<td>Passive</td>
<td>TB disease</td>
<td>1.6 to 9.3</td>
<td>Strong</td>
</tr>
<tr>
<td>Active</td>
<td>Recurrent TB</td>
<td>2.5 to 3.1</td>
<td>Moderate</td>
</tr>
<tr>
<td>Active</td>
<td>Mortality</td>
<td>1.02 to 6.6</td>
<td>Limited</td>
</tr>
</tbody>
</table>


Population Attributable Risk (PAR) of Incident TB

- PAR = proportion of disease eliminated in absence of risk factor
- Assume smoking prevalence 30%
- RR of TB among smokers compared with nonsmokers is 2-3
- PAR is 22-36% of incident TB cases
- Second Hand Smoke (SHS) may increase PAR as well


<table>
<thead>
<tr>
<th>RR if factor present</th>
<th>Prevalence of factor</th>
<th>Population attributable risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition</td>
<td>3.0</td>
<td>17%</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.6</td>
<td>18%</td>
</tr>
<tr>
<td>Alcohol use (&gt; 40g/d)</td>
<td>2.9</td>
<td>7.9%</td>
</tr>
<tr>
<td>HIV</td>
<td>8.3</td>
<td>1%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.0</td>
<td>3.4%</td>
</tr>
</tbody>
</table>

* Proportion of disease eliminated in absence of risk factor
Questions

• About what proportion of the of new global TB cases might be eliminated if none of the TB patients smoked?
• How does tobacco rank in terms of a complicating risk factor for TB disease?

Active Smoking an Independent Risk for LTBI in US Adults (NHANES)

• Of 2,950 adult respondents with TST and cotinine levels (nicotine metabolite)
  – 813 (28%) active smoking
  – 991 (34%) passively exposed to smoke
  – 241 (8%) were LTBI
• Controlling for age, gender, race/ethnicity, SES, country of origin, household size, BCG vaccination, and having lived with someone with known TB--
• Active smokers had double the risk of LTBI compared with non-smokers (OR 2.1, 95%CI 1.1-4.0)

Source: Lindsay R, Shin SS, Novotny TE. The association between active and passive smoking and latent tuberculosis infection: results from NHANES
The Union North America Regional Meeting, Vancouver 2011

Smoking-TB Dynamics

• Causes structural damage to respiratory system: ciliary function and clearance mechanisms
• Impairs immune response:
  – Attenuates mycobactericidal activities
  – Nicotine turns off cytokine production by macrophages in lungs (reactivate LTBI)
• Associated with adverse treatment patterns (drop-outs, delayed smear conversion, longer infectivity)
• Influences spread of infectious disease among contact groups

Interaction of Smoking with TB and HIV

**TB Risks**
- Increase risk of activating latent TB
- Progression to active disease, MDR?
- Household spread
- Mortality

**HIV Risks**
- Increased susceptibility to HIV
- Increased bacterial pneumonia, lung cancer, PCP

**Overall Lung Health**
Post-TB airway disease, bronchitis, emphysema, lung CA, COPD

Social Determinants of TB-Smoking Interaction

- Poverty
- Crowding
- Urbanization
- Access to care
- Information asymmetry
- Solid fuel stoves in homes

TB Treatment and Smoking Cessation

- Standard TB treatment (DOTS) involves regular provider-patient contact for at least 6 months
- High prevalence of smoking among TB patients
- Smoking adversely affects TB infection, progression, mortality
- Smoking adversely affects smear conversion, adherence, and spread
- Treatment programs for TB = “teachable moment” on smoking and other risk factors
Guide to Clinical Preventive Services (USPHS)

• Take a complete history of tobacco use
• Offer smoking cessation counseling to all patients who use tobacco
• Provide direct, face-to-face brief, unambiguous, and informative statement on the need to stop using tobacco
• Set a quit date
• Provide scheduled reinforcement: “support visits” or follow-up telephone calls
• Provide self-help materials available from voluntary organizations
• Refer to community programs
• Prescribe drug therapy as needed for three months but not beyond six months

Chemotherapeutics for Cessation (Assist)

• Nicotine patches, gums, lozenges OTC
• Inhaler and spray (Nicotrol) by prescription
• Harm reduction with new tobacco products?
• Varenicline (Chantix): Blocks effects of nicotine in brain (agonist)
• Bupropion (Wellbutrin, Zyban): Antidepressant

Is Treatment of Tobacco Dependence Effective?

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparator</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-help</td>
<td>No intervention</td>
<td>1.24</td>
</tr>
<tr>
<td>MD advice</td>
<td>No advice</td>
<td>1.74</td>
</tr>
<tr>
<td>MD intensive advice</td>
<td>Minimal advice</td>
<td>1.44</td>
</tr>
<tr>
<td>Group counseling</td>
<td>No intervention</td>
<td>2.17</td>
</tr>
<tr>
<td>Nicotine Replacement Tx</td>
<td>Placebo or non-NRT</td>
<td>1.58</td>
</tr>
<tr>
<td>Telephone counseling</td>
<td>No telephone counseling</td>
<td>1.41</td>
</tr>
</tbody>
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Basic Research Needed

• Among new patients in TB treatment programs, does inclusion of a smoking cessation program improve cessation rates (compared with standard programs)?
• Does smoking cessation improve TB treatment outcomes (smear conversion time, relapse rate) in TB patients?
• Does smoking cessation decrease TB spread among household members and the community?
• Does NRT/Bupropion/Varenicline treatment impact TB therapy?

WHO Recommendation:
Incorporate brief advice on smoking cessation in TB treatment programs

Clinical Intervention: WHO Recommendations

Five A’s
• Ask if TB patients smoke
• Advise the patient to quit
• Assess willingness to quit
• Assist the patient in making a quit attempt
• Arrange for follow-up

Five R’s
• Relevance why quitting is personally relevant
• Risks identify potential negative consequences including TB relapses
• Rewards identify potential benefits of stopping
• Roadblocks identify barriers to quitting
• Repetition repeated every time for TB patients
Does Stopping Smoking Decrease TB Mortality Risk?

- Taipei (Taiwan) cohort of 486,431 adults followed from 1994-2007
- 15,268 deaths, 77 from TB
- Hazard ratio=8.56 for smokers vs. non-smokers without prior history of TB
- After quitting, risk of death from TB reduced by 65%
- (37.7% of TB mortality in Taiwan accounted for by smoking [PAR])

Source: Wen, C-P. Reduction of tuberculosis risks by smoking cessation, BMC Infect Dis, 2010

Can an Intervention Work?

- Pakistan, 2010, trial will use WHO "5 A's" model for TB patients
- Goals:
  - Design evidence-based cessation package for TB programs
  - Assess cost-effectiveness compared with usual care
  - Determine barriers and drivers to provision of treatment of tobacco dependence in TB programs
  - Support long term implementation


Feasibility of Cessation Interventions, Brazil

- Trained TB providers in brief counseling over 1.5 days
- Implemented counseling in two Rio de Janeiro clinics with DOTS programs
- Good results of training, but poor implementation:
  - Lack of 'ownership' by TB providers
  - Lack of assurance and follow up
  - Referred patients but did not implement counseling as part of TB program

**Biological Confirmation**

* Urine dipstick, semi-quantitative cotinine test

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**Will Smoking Cessation Make a Difference?**

- Is there evidence of effectiveness for brief counseling/education for smoking cessation among TB patients?
- What will it take to get TB providers to provide such integrated treatment?

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**Conclusions**

- Smoking may increase risk for TB mortality, morbidity, and household spread
- 5 A’s will likely increase cessation success in all smokers: specific training needed for TB program providers
- Clinical trials of cessation are needed in various populations
- TB treatment programs should incorporate smoking cessation as standard of care
Next Steps

- Surgeon General’s Report will address TB and smoking risks (2011)
- Randomized, controlled clinical trials in multiple cultural settings (Brazil, India, Pakistan, Mexico, China)
- Interaction between NRT and TB drugs needs research
- Tailored programs needed for specific populations

Questions and Comments