Double Trouble:
The Surprising Connection Between Diabetes and Tuberculosis and Opportunities for Meaningful Collaboration

Sundari Mase, MD-MPH
Richard Brostrom, MD-MSPH
NDEP Webinar Series

Learning Objectives:

• Identify effective communication or education strategies that can be used in diabetes prevention or self-management programs.
• Identify evidence-based approaches to diabetes prevention or self-management that can be used in community or clinical settings.
• Describe strategies for reducing diabetes related health disparities.
• Describe tools and resources to support the implementation of best practices in improving diabetes education and communication and/or reducing diabetes related health disparities.
Objectives for Today

By the end of today’s webinar, you will be able to:

• Describe the interaction between TB and Diabetes.
• Identify at least 2 ways diabetes and TB impact outcomes for both conditions.
• Identify individuals with diabetes who may be at high-risk from TB, and the procedures to refer for TB testing.
• Identify at least 2 opportunities for program collaboration between TB and diabetes programs.
Today’s Presenters

Sundari Mase, MD, MPH
Team Lead for Medical Affairs
CDC, Division of Tuberculosis Elimination, Field Services and Evaluation Branch

Richard Brostrom, MD, MSPH
CDC Tuberculosis Medical Officer for the Pacific Region
Branch Chief, Hawaii State Tuberculosis Program
TB-DM: Opportunities for Collaboration

- TB 101: A few of the basics
- TB-DM Current Epidemiology
- TB-DM Literature Update
- TB-DM Current Collaborations
- TB-DM Opportunities for Partnership
What is Tuberculosis (TB)?

1. Tuberculosis (TB) is a disease caused by bacteria.
2. TB usually affects the lungs (85%), but it can also affect other parts of the body such as the brain, bones, kidneys, or the spine.
3. TB disease is curable, but it can be fatal if not treated properly.
There are Two Forms of TB

TB Disease

TB Infection
TB Disease

- Person has breathed in TB bacteria
- Immune system does not contain the TB bacteria
- TB is awake and multiplying
- Person sometimes feels sick
- Chest X-ray is abnormal
- If the TB is in the lungs, the person may be contagious
Symptoms of TB Disease

- Prolonged Cough (>2-3 weeks duration)
- Productive or Dry Cough
- Coughing Up Blood
- Feeling Weak or Constantly Tired
- Fever
- Night Sweats
- Loss of Appetite
- Weight Loss
- Chest Pain
How is TB Spread?

TB bacteria can be spread when a person with TB disease:

- Coughs
- Sings
- Sneezes
- Shouts
- Speaks
- Laughs

These actions send TB germs into the air.
TB is **NOT** Spread by Sharing

- Paper or pencils
- Books
- Desks
- Toilets
- Food
- Eating utensils
- Bedding
TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive
TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive
- Chest X-ray is normal
TB Infection

- Person has breathed in TB bacteria
- TB skin test is positive
- Chest X-ray is normal
- Immune system has contained the TB bacteria
- Bacteria becomes dormant (sleeping)
- Person is not sick
- Person is NOT contagious
- Medicine is available to treat the infection and prevent TB disease in the future
## TB Infection vs. TB Disease

<table>
<thead>
<tr>
<th></th>
<th>TB Infection</th>
<th>TB Disease (in the lungs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tubercle bacilli in the body</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tuberculin skin test reaction usually positive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest x-ray usually normal</td>
<td>Chest x-ray usually abnormal</td>
<td></td>
</tr>
<tr>
<td>Sputum smears and cultures negative</td>
<td>Sputum smears and/or cultures positive</td>
<td></td>
</tr>
<tr>
<td>No symptoms</td>
<td>Cough, fever, weight loss, night sweats, loss of appetite</td>
<td></td>
</tr>
<tr>
<td>Not infectious</td>
<td>Often infectious before treatment</td>
<td></td>
</tr>
<tr>
<td>Not a “case” of TB</td>
<td>A case of TB</td>
<td></td>
</tr>
</tbody>
</table>
TB Infection to TB Disease

• For healthy adults, if you have TB infection (positive TB skin test and normal chest X-ray), your highest risk (5%) of going from TB infection to TB disease is in the first two years after you have been infected.

• After the first two years, for the rest of your life there is a 5% risk of going from TB infection to TB disease.

• 10% total lifetime risk of developing TB disease.

• The risk of developing TB disease is higher for people with weak immune systems (e.g., children <5 years old and people with diabetes, cancer, HIV, or kidney disease).
TB Infection to TB Disease

Time of TB infection

Risk of developing TB disease during the first two years from the time of TB infection = 5%

Risk of developing TB disease after the first two years from the time of TB infection = 5%

Lifetime risk of developing TB disease = 10%
TB Pathogenesis
Progression to TB disease

TB infection
No risk factors

TB infection and diabetes

TB infection and HIV

TB Disease
(10% over a lifetime)

TB Disease
(30% over a lifetime)

TB Disease
(7-10% per year.)

TB infection
(no TB disease)

TB infection
(no TB disease)

TB infection
(no TB disease)
Poll 1:

How familiar are you with the risk of TB disease in your diabetes population?

• Never heard of the interaction
• Somewhat familiar
• Very familiar
How familiar are you with the risk of TB disease in your DM population?

- Never heard of the interaction: 17.3%
- Somewhat familiar: 47.3%
- Very familiar: 35.4%
TB-DM: Opportunities for Collaboration

- TB 101: A few of the basics
- TB-DM Current Epidemiology
- TB-DM Brief Research Update
- TB-DM Current Collaborations
- TB-DM Opportunities for Partnership
Epidemiology
Worldwide Diabetes Burden

Estimated Burden (millions)

<table>
<thead>
<tr>
<th>Region</th>
<th>1995</th>
<th>2000</th>
<th>2025 (projected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Americas</td>
<td>15</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>10</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Europe</td>
<td>25</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>50</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>25</td>
<td>30</td>
<td>35</td>
</tr>
</tbody>
</table>

## The Global Burden of TB - 2012

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All forms of TB</strong></td>
<td>8.6 (8.3-9.0) million</td>
<td>1.3 (1.0-1.6) million*</td>
</tr>
<tr>
<td></td>
<td>- 0.5 m in children</td>
<td>- 74,000 in children</td>
</tr>
<tr>
<td></td>
<td>- 2.9 m in women</td>
<td>- 410,000 in women</td>
</tr>
<tr>
<td><strong>HIV-associated TB</strong></td>
<td>1.1 (1.0-1.2) million (13%)</td>
<td>320,000 (300k-340k)</td>
</tr>
<tr>
<td><strong>Multidrug-resistant TB</strong></td>
<td>450,000 (300k-600k)</td>
<td>170,000 (102k-242k)</td>
</tr>
</tbody>
</table>

* Including deaths attributed to HIV/TB

Source: WHO Global Tuberculosis Report 2013
Reported TB Cases
United States, 1982–2014*

*Updated as of June 5, 2015.
## TB Morbidity
### United States, 2009–2014

<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>11,523</td>
<td>3.8</td>
</tr>
<tr>
<td>2010</td>
<td>11,161</td>
<td>3.6</td>
</tr>
<tr>
<td>2011</td>
<td>10,510</td>
<td>3.4</td>
</tr>
<tr>
<td>2012</td>
<td>9,941</td>
<td>3.2</td>
</tr>
<tr>
<td>2013</td>
<td>9,565</td>
<td>3.0</td>
</tr>
<tr>
<td>2014</td>
<td>9,421</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*Cases per 100,000. Updated as of June 5, 2015.
TB Case Rates,* United States, 2014

*Cases per 100,000.
Map of U.S.-Affiliated Pacific Islands by TB Case Rates,* 2014

*Cases per 100,000

- United States overall: 3.0
- Hawaii: 9.6
- American Samoa: 1.8
- Palau: 66.1
- Guam: 34.8
- Northern Mariana Islands: 44.7
- Federated States of Micronesia: 156.1
- Marshall Islands: 212.7

*Cases per 100,000
TB Case Rates by Race/Ethnicity,*
United States, 2003–2014**

*All races are non-Hispanic.
**Updated as of June 5, 2015.
Number of TB Cases in U.S.-born vs. Foreign-born Persons, United States, 1993–2014*

*Updated as of June 5, 2015.
Trends in TB Cases in Foreign-born Persons, United States, 1993 – 2014*

*Updated as of June 5, 2015.
Percentage of TB Cases Among Foreign-born Persons, United States*

2004

2014

*Updated as of June 5, 2015.

*DC

>50%

25%–49%

<25%

No cases
TB Risk Factors in the US - 2012

- Diabetes Mellitus
- Contact of Infectious TB
- Immuno-suppression
- Incomplete LTBI Tx
- End-Stage Renal Disease
- Missed Contact
- Post-Transplant
- TNF-Alpha Antagonist Tx
- Contact of MDR TB
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958–2010

Percentage with Diabetes

Number with Diabetes

Year

Number with Diabetes (Millions)

Percentage with Diabetes

Adult TB Cases with DM

<table>
<thead>
<tr>
<th>Location</th>
<th>Percent with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>India*</td>
<td>20</td>
</tr>
<tr>
<td>Mexico**</td>
<td>40</td>
</tr>
<tr>
<td>United States***</td>
<td>30</td>
</tr>
<tr>
<td>Montgomery Co, MD**</td>
<td>20</td>
</tr>
<tr>
<td>South Texas</td>
<td>50</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>50</td>
</tr>
</tbody>
</table>

TB and Diabetes in Kiribati

- Setting: South Tarawa (capital of Kiribati)
- Participants: TB patients and community members without signs and symptoms of active TB
- Case control study: 275 TB patients and 499 controls from the community

**TB Rate:** 378/100,000  
(Source: WHO, 2013)

**DM Rate:** 29%  
Impact of Diabetes on TB in Kiribati:

Summary

• Additional burden of TB, attributable to diabetes was 25%.
• Additional burden of smear positive TB among people with diabetes was significant – impacting TB transmission in the community
• Treatment outcomes were not statistically significant – but very small sample.
• Undiagnosed diabetes (~50%)
TB and Diabetes in Kiribati

- 275 cases and 499 controls enrolled (774 in total)
- 195 (25%) people had diabetes (94 controls, 101 TB pts)
- Number of TB pts with diabetes: 101 (37%)
- Number of TB pts with known diabetes: 54 (53%)
- Number of TB pts newly diagnosed with diabetes: 47 (47%)
- Number of controls newly diagnosed with diabetes: 61 (64.8%)

Balakrishnan et al. PLoS One (2012). 552 TB patients screened; 243 (44%) had diabetes. Of these, 128 (53%) known diabetes, 115 (47%) newly diagnosed.
## TB Treatment Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Successful outcome N (%)</th>
<th>Poor outcome N (%)</th>
<th>Relative Risk (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with diabetes</td>
<td>93 (92)</td>
<td>8 (8)</td>
<td>0.99 (0.92 – 1.06)</td>
</tr>
<tr>
<td>Patients without diabetes</td>
<td>162 (93)</td>
<td>12 (7)</td>
<td>Referent</td>
</tr>
</tbody>
</table>

No differences in chest x-ray changes or sputum conversion at two months, however sample size was small
# Pacific Bi-Directional Screening for TB and DM

<table>
<thead>
<tr>
<th>Country</th>
<th>Proportion of TB patients with DM</th>
<th>Diabetes status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiribati</td>
<td>37%</td>
<td>Known and newly diagnosed DM</td>
</tr>
<tr>
<td>Fiji</td>
<td>13%</td>
<td>Known DM only. A further 21% had elevated random glucose, referred for fasting glucose</td>
</tr>
<tr>
<td>Marshall Islands</td>
<td>45%</td>
<td>Known and newly diagnosed DM</td>
</tr>
<tr>
<td>Federated States of Micronesia</td>
<td>24%</td>
<td>Known and newly diagnosed DM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country</th>
<th>Proportion of DM patients with TB</th>
<th>TB status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marshall Islands (Ebeye)</td>
<td>5%</td>
<td>Newly diagnosed only</td>
</tr>
<tr>
<td>Federated States of Micronesia</td>
<td>3%</td>
<td>Known and newly diagnosed. A further 25% had evidence of latent TB</td>
</tr>
</tbody>
</table>
Impacts of DM on TB Control

“Increases in diabetes prevalence in populations with high ongoing tuberculosis transmission rates.... counteract the positive effects of TB control efforts.

In 2013, an estimated 15% (nearly 1 out of every 6 cases) of TB in adults worldwide were attributed to diabetes, which corresponds to over 1 million cases of diabetes-associated TB per year.”

2010: WHO Collaborative Framework for Care and Control of TB and Diabetes
TB-DM: Opportunities for Collaboration

• TB 101: A few of the basics
• TB-DM Current Epidemiology
• TB-DM Brief Research Update
• TB-DM Current Collaborations
• TB-DM Opportunities for Partnership
REAL PEOPLE
Percentages and predictions can mask the enormity of the diabetes problem. Large numbers of people with diabetes are unaware they have the disease because they have not been diagnosed (shown as the shaded ridge in the country bubbles). The imperative for public-health professional is to diagnose and treat people as soon as possible.

AFRICA
Diabetes is relatively rare in sub-Saharan Africa, afflicting only 4.5% of adults. But prevalence is predicted to double over the next 20 years—the fastest rise of any region in the world.

MIDDLE EAST
Rapid economic development has led to soaring rates of diabetes, from around 6% in 1990 to over 20% in parts today.

INDIA
Nationwide prevalence now tops 9%, and is as high as 20% in the relatively prosperous southern cities. The resulting healthcare costs and depletion of productivity threaten to undo recent economic gains.

CHINA
Underestimated until only recently, the Chinese diabetes epidemic is the largest in the world.
### Table 2.3 Undiagnosed diabetes (20-79 years) by IDF Region and income group, 2013

<table>
<thead>
<tr>
<th>IDF REGION</th>
<th>PROPORTION UNDIAGNOSED %</th>
<th>CASES MILLIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td></td>
<td>12.4</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>75.1</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>46.0</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td></td>
<td>20.1</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>29.3</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>35.1</td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>36.6</td>
<td></td>
</tr>
<tr>
<td>North America and Caribbean</td>
<td></td>
<td>29.4</td>
</tr>
<tr>
<td>Low-income countries</td>
<td></td>
<td>25.0</td>
</tr>
<tr>
<td>Middle-income countries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>South and Central America</td>
<td></td>
<td>5.8</td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>24.1</td>
<td></td>
</tr>
<tr>
<td>South-East Asia</td>
<td></td>
<td>35.1</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>43.6</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>49.1</td>
<td></td>
</tr>
<tr>
<td>Western Pacific</td>
<td></td>
<td>74.7</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>63.0</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>54.1</td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>49.4</td>
<td></td>
</tr>
</tbody>
</table>
Double Trouble: TB-DM Lit Review

1. Does DM cause TB?
2. Does Diabetes affect TB treatment?
3. Can we make a difference?

Source: J. Flood, 2014
TB-DM: Diabetes Control

TB-DM: Diabetes Control

Hawaii Adult TB Cases with Diabetes

Begin A1c testing with TB intake

Brostrom, R and Young, B  Hawaii TB Control Program 2015
Adult TB Cases with DM in Hawaii: 2014

Percent Adult TB Patients with Diabetes

US-Born | JPN,KOR,THAI | Philippines | Pacific Islands

*Hawaii Case Reports for 2014
TB as the “Diabetes Defining Illness”

![Graph showing the percentage of new vs existing DM cases in different age groups.]

- **Old DM**:
  - < 50: 80%
  - 50+: 40%

- **New DM**:
  - < 50: 20%
  - 50+: 60%

*Hawaii Case Reports for 2014*
Double Trouble: TB-DM Lit Review

1. Does DM lead to TB? **Yes!**

2. Does diabetes affect TB treatment?

3. Can we make a difference?
TB and Diabetes: Case Management

People with DM and TB have....

- More atypical TB presentations
- A multitude of med interactions
- Longer periods of infectiousness
- Higher risk of hepatitis from TB meds
## TB-DM Outcomes: Relapse

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Population with DM Relapse/Total</th>
<th>Population without DM Relapse/Total</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wada, 2000 [54]</td>
<td>Japan</td>
<td>7/61 (11%)</td>
<td>4/284 (1%)</td>
<td>8.15 (2.46, 26.97)</td>
</tr>
<tr>
<td>Mboussa, 2003 [47]</td>
<td>Congo</td>
<td>6/17 (35%)</td>
<td>9/77 (12%)</td>
<td>3.02 (1.24, 7.35)</td>
</tr>
<tr>
<td>Singla, 2006 [50]</td>
<td>Saudi Arabia</td>
<td>2/130 (2%)</td>
<td>3/367 (1%)</td>
<td>1.88 (0.32, 11.14)</td>
</tr>
<tr>
<td>Maalej, 2009 [46]</td>
<td>Tunisia</td>
<td>4/55 (7%)</td>
<td>1/82 (1%)</td>
<td>6.96 (0.68, 51.95)</td>
</tr>
<tr>
<td>Zhang, 2009 [57]</td>
<td>China</td>
<td>33/165 (20%)</td>
<td>9/170 (5%)</td>
<td>(1.87, 7.65)</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td></td>
<td></td>
<td></td>
<td>3.89</td>
</tr>
</tbody>
</table>

Heterogeneity I-squared = 0% (0, 79)
Weights are from random effects analysis

*Baker et al. The impact of diabetes on TB treatment outcomes: A systematic review, BMC Medicine 2011, 9:81*
History of Prior TB*

OR 2.3  
(1.2 – 4.5)  
p = 0.016

<table>
<thead>
<tr>
<th>History of Prior TB</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB without DM</td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB with DM</td>
<td>12%</td>
<td>1.2 – 4.5</td>
<td>0.016</td>
</tr>
</tbody>
</table>

* Adult Pacific Islands TB Cases, 2010 – 2012, n = 511
### TB-DM Outcomes: Death during TB Tx

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Population with DM Deaths/Total</th>
<th>Population without DM Deaths/Total</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fielder, 2002 [38]</td>
<td>USA</td>
<td>13/22 (59%)</td>
<td>29/152 (19%)</td>
<td>3.80 (1.42, 10.16)</td>
</tr>
<tr>
<td>Oursler, 2002 [48]</td>
<td>USA</td>
<td>8/18 (44%)</td>
<td>14/108 (13%)</td>
<td>6.70 (1.57, 28.52)</td>
</tr>
<tr>
<td>Dooley, 2009 [12]</td>
<td>USA</td>
<td>6/42 (14%)</td>
<td>20/255 (8%)</td>
<td>6.50 (1.11, 38.20)</td>
</tr>
<tr>
<td>Wang, 2009 [56]</td>
<td>Taiwan</td>
<td>13/74 (18%)</td>
<td>11/143 (8%)</td>
<td>5.20 (1.77, 15.25)</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td></td>
<td></td>
<td></td>
<td>4.95 (2.69, 9.10)</td>
</tr>
</tbody>
</table>

Heterogeneity I-squared = 0% (0, 85)

Weights are from random effects analysis
All-Cause Mortality During TB Treatment*

OR 5.2  (1.2 – 24.0)
\[ p = 0.037 \]

TB without DM: 4%

TB with DM: 19%

* Pacific Islands TB Cases, 40 – 60 years old, 2010–2012, n=129
Data excludes “lost”, “discontinued”, “moved”, “unknown”
# More DM Complications: More TB Risk

Table 4. Multivariate Associations for Tuberculosis Disease, by Complications of Diabetes Mellitus

<table>
<thead>
<tr>
<th>Variable</th>
<th>Tuberculosis Cases</th>
<th>Total Population</th>
<th>Adjusted Hazard Ratio (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications of DM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No DM</td>
<td>44</td>
<td>16,557</td>
<td>1.00</td>
<td>.0016</td>
</tr>
<tr>
<td>Treated DM and ( \leq 1 ) complication</td>
<td>4</td>
<td>609</td>
<td>1.73 (1.61–4.89)</td>
<td></td>
</tr>
<tr>
<td>Treated DM and ( \geq 2 ) complications</td>
<td>9</td>
<td>549</td>
<td>3.45 (1.59–7.50)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Complications Severity Index</td>
<td></td>
<td></td>
<td></td>
<td>.0002</td>
</tr>
<tr>
<td>No DM</td>
<td>44</td>
<td>16,557</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Treated DM and severity score ( \leq 3 )</td>
<td>6</td>
<td>881</td>
<td>1.72 (1.72–4.13)</td>
<td></td>
</tr>
<tr>
<td>Treated DM and severity score ( \geq 4 )</td>
<td>7</td>
<td>277</td>
<td>5.05 (2.11–12.04)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; DM, diabetes mellitus.

---

## Higher A1C: Worsening TB Presentation

<table>
<thead>
<tr>
<th></th>
<th>A1C&lt;7%</th>
<th></th>
<th>A1C 7%-9%</th>
<th></th>
<th>A1C&gt;9%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AdjRRR</td>
<td>(95% CI)</td>
<td>AdjRRR</td>
<td>(95% CI)</td>
<td>AdjRRR</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Any Cavity</td>
<td>0.79</td>
<td>(0.42–1.49)</td>
<td>2.00</td>
<td>(1.30–3.09)</td>
<td>3.59</td>
<td>(2.53–5.11)</td>
</tr>
<tr>
<td>Location (field)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>0.89</td>
<td>(0.46–1.62)</td>
<td>1.86</td>
<td>(1.20–2.88)</td>
<td>2.71</td>
<td>(1.92–3.83)</td>
</tr>
<tr>
<td>Lower</td>
<td>1.02</td>
<td>0.30–3.51)</td>
<td>2.28</td>
<td>(1.10–4.71)</td>
<td>4.47</td>
<td>(2.62–7.62)</td>
</tr>
<tr>
<td>Number of cavities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>0.97</td>
<td>(0.41–2.29)</td>
<td>2.46</td>
<td>(1.40–4.32)</td>
<td>3.97</td>
<td>(2.53–6.25)</td>
</tr>
<tr>
<td>Multiple</td>
<td>0.68</td>
<td>0.30–1.53)</td>
<td>1.71</td>
<td>(1.02–2.88)</td>
<td>3.37</td>
<td>(2.26–5.03)</td>
</tr>
<tr>
<td>Size of cavity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>0.80</td>
<td>(0.36–1.77)</td>
<td>2.20</td>
<td>(1.32–3.67)</td>
<td>3.34</td>
<td>(2.19–5.08)</td>
</tr>
<tr>
<td>Large</td>
<td>0.79</td>
<td>(0.34–1.88)</td>
<td>1.77</td>
<td>(1.01–3.12)</td>
<td>3.87</td>
<td>(2.54–5.90)</td>
</tr>
</tbody>
</table>

TB and Diabetes Summary: 2-3-4-5

People with DM and TB have....

- 2x risk of remaining culture positive
- 3x risk of progression to TB disease
- 4x risk of relapse after standard tx
- 5x risk of death during TB treatment
Double Trouble: TB-DM Lit Review

1. Does DM cause TB? Yes!
2. Does diabetes affect TB treatment? Yes!
3. Can we make a difference?
TB-DM: Opportunities for Collaboration

- TB 101: A few of the basics
- TB-DM Current Epidemiology
- TB-DM Brief Research Update
- TB-DM Current Collaborations
- TB-DM Opportunities for Partnership
### Screening for DM in persons with TB

**Standard 1** Every person with tuberculosis (TB) over the age of 18 should be screened for diabetes mellitus (DM)

1. The diagnosis of DM may be made using one of the following criteria:
   - Fasting plasma glucose \( \geq 126 \text{ mg/dl} \) (7.0 mmol/l)
   - Random plasma glucose \( \geq 200 \text{ mg/dl} \) (11.1 mmol/l)
   - Hemoglobin A1c \( \geq 6.5 \% \) (48 mmol/mol)

1.2 Abnormal glucose values should be verified in patients who have no symptoms of DM.

1.3 Rifampin can elevate blood glucose in TB patients. Glucose testing may be repeated after 2-4 weeks of TB treatment, or if symptoms of hyperglycemia develop during TB treatment.

### Screening for TB in persons with DM

**Standard 2** Every high-risk person with DM should be periodically screened for TB disease and TB infection

1. Program may choose to screen all patients with DM for TB, or may choose to screen highest risk patients only:
   - People with DM under age 50.
   - People with poorly controlled DM (A1C \( \geq 8.0 \% \))

2.2 Persons with TB symptoms or TB disease should be referred to the local TB Program for TB management.

2.3 A test for TB infection should be done at the time of DM diagnosis.

2.4 Screening should be repeated as often as the local TB epidemiology may warrant. Annual symptom screening for TB disease is reasonable. Screening for TB infection every 2 - 5 years is reasonable.

**Standard 3** Persons with DM and TB infection should be encouraged to take preventive therapy

3.1 Persons with DM are at increased risk of peripheral neuropathy. If INH is used for prevention, give B6 to prevent neuropathy (10 – 25 mg/day).

3.2 Monitor for adherence and side effects of preventive treatment.

---

### Treating TB in persons with DM

**Standard 4** Clinicians may need to adjust TB treatment in persons with DM

4.1 Make sure that TB medications are properly dosed.
- Check creatinine for diabetic nephropathy, and if present, adjust the frequency of PZA and EMB according to ATS-CDC guidelines.*
- Administer B6 to prevent INH-induced neuropathy (10 – 25 mg/day).

4.2 Observe closely for TB treatment failure in persons with DM.
- Be aware of poor absorption of some TB meds in DM.
- Manage the many interactions between TB and DM meds.
- Some programs follow INH or RIF levels in persons with DM.

4.3 “Assure the Cure”
- Consider extending treatment to 9 months for persons with DM, especially persons with cavitary disease or delayed sputum clearance.*
- Upon completion of therapy, obtain sputum for AFB smear and culture.
- Evaluate at one year after treatment for evidence of relapse.

*Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52

### Managing DM in persons with TB

**Standard 5** Use TB clinic visits to help persons manage their DM

5.1 There should be a glucometer in every TB clinic for monitoring glucose.

5.2 TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if diabetes is controlled.
- Monthly glucose testing during treatment is recommended.

5.3 All clinic staff should reinforce lifestyle changes at TB clinic visits.

5.4 If available, refer persons with DM to the Diabetes Clinic for diabetes care.
- Ensure DM clinician is aware of TB diagnosis and TB medications.

**Standard 6** Use DOT visits to help persons manage their DM

6.1 DOT workers should encourage lifestyle changes at every encounter.
- DOT workers should use structured and culturally-appropriate diabetes educational materials.*
- Dietary changes and physical activity are the most important in this effort.

2. Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have non-adherence to diabetic medications.

Best Practices: RMI Diabetes Clinic

Program Collaboration

In 2010, the KAHCBS adopted and started implementing the USAPI Standards for the Management of Tuberculosis and Diabetes. In this guideline – standards were set for DM screening in persons with active TB; screening for TB in persons with DM; treating TB in persons with DM; and managing DM in persons with active TB.

To improve implementation of the USAPI clinical guidelines – KAHCBS have set the following measures to accomplish the collaborative initiatives:

- Tuberculosis screening in the DM Clinic
- Strengthening DM-TB co-morbid clinical management
- DM Screening and Glucose Monitoring for TB Cases
TB Screening in Diabetes Clinic: Finding TB

- Ebeye Diabetes Clinic Rate
- Ebeye Island
- RMI NTP Rate
- Global TB Rate
- US TB Rate

Rate of TB per 100,000

0 1000 2000 3000 4000 5000
Death During TB Treatment in Ebeye
(2010 – 2012, n=23)
What Happens After Bidirectional Screening?

"Geez, I had no idea there was a Nobel Prize for accounting."
Diabetes For Dummies
2nd Edition

Dr Alan L. Rubin
Diabetes specialist
Dr Sarah Jarvis, GP
Fellow of the Royal College of General Practitioners

A Reference for the Rest of Us!
Battle Creek Sanitarium: Exercises, 1911
### Basic DM Management for TB Clinic

#### Treating TB in persons with DM

<table>
<thead>
<tr>
<th>Standard 4</th>
<th>Clinicians may need to adjust TB treatment in persons with DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1</td>
<td>Make sure that TB medications are properly dosed. Check creatinine for diabetic nephropathy, and if present, adjust the frequency of PZA and EMB according to ATS-CDC guidelines.* Administer B6 to prevent INH-induced neuropathy (10 – 25 mg/day).</td>
</tr>
<tr>
<td>4.2</td>
<td>Observe closely for TB treatment failure in persons with DM. Be aware of poor absorption of some TB meds in DM. Manage the many interactions between TB and DM meds. Some programs follow INH or RIF levels in persons with DM.</td>
</tr>
<tr>
<td>4.3</td>
<td>“Assure the Cure” Consider extending treatment to 9 months for persons with DM, especially persons with cavitary disease or delayed sputum clearance.* Upon completion of therapy, obtain sputum for AFB smear and culture. Evaluate at one year after treatment for evidence of relapse.</td>
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*Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52
## Enhanced DM Management for TB Clinic

### Managing DM in persons with TB

<table>
<thead>
<tr>
<th>Standard 5</th>
<th>Use TB clinic visits to help persons manage their DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1</td>
<td>There should be a glucometer in every TB clinic for monitoring glucose.</td>
</tr>
<tr>
<td>5.2</td>
<td>TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if diabetes is controlled. Monthly glucose testing during treatment is recommended.</td>
</tr>
<tr>
<td>5.3</td>
<td>All clinic staff should reinforce lifestyle changes at TB clinic visits.</td>
</tr>
<tr>
<td>5.4</td>
<td>If available, refer persons with DM to the Diabetes Clinic for diabetes care. Ensure DM clinician is aware of TB diagnosis and TB medications.</td>
</tr>
</tbody>
</table>

### Standard 6 | Use DOT visits to help persons manage their DM

| 6.1        | DOT workers should encourage lifestyle changes at every encounter. DOT workers should use structured and culturally-appropriate diabetes educational materials.* |
|            | Dietary changes and physical activity are the most important in this effort. |
| 6.2        | Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have non-adherence to diabetic medications. |

* NDEP, US Dept of Health and Human Services: http://www.yourdianetesinfo.org/
Key Messages for TB & Diabetes
Week 2 (Day 1)
DOT helps cure TB!

Why does a health worker need to see you every day for TB medication?

- "DOT" means Directly Observed Therapy. DOT makes it easy to take your pills. DOT is when a nurse or health care worker sees you every day to give you TB medicine. A health worker can meet with you every day or a few times a week to watch you take your TB pills. He or she will bring you your pills at the place and time that is most easy for you. This is the best way to make sure you get all the medicine you need and your treatment is working. If there is a problem with your medication it can be fixed right away.

- Our goal is to ensure that everyone completes their treatment and is cured.

- Note for the healthworker: if your local policy requires, you may need to obtain agreement from the patient to complete DOT and to record their signature on each day they take their medication.
Week 5 (Day 1)

You have also been diagnosed with diabetes

What do you know about diabetes?
Hawaii TB Nurses Training
# Hawaii TB Nurses Documentation

## Hawaii TB-Diabetes Patient Care Worksheet

<table>
<thead>
<tr>
<th>Date and Initials</th>
<th>/ /</th>
<th>/ /</th>
<th>/ /</th>
<th>/ /</th>
<th>/ /</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DM education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-10 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-30 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **DM test results** |     |     |     |     |     |
| Gluc: ___ mg/dL    |     |     |     |     |     |
| A1c: ___ %         |     |     |     |     |     |

| **Seeing DM provider?** |     |     |     |     |     |
| Yes | No |     |     |     |     |

| **Taking DM medications?** |     |     |     |     |     |
| Yes | No |     |     |     |     |
| None needed             |     |     |     |     |     |

| **Comments:** |     |     |     |     |     |

Patient Name: ________________________  CC#: ____
Can the TB Clinic Help with Glucose Control?

• A1c data collection (586 tests)
• Initial A1C on intake
• For follow-up, standing order for every 3 months (ADA standard)
• 55 patients with 2 or more results
  • 154 A1c tests in this cohort
Average A1C during TB treatment in Hawaii
(at least 2 measurements, 2011 - 2013, Cases=55, A1C's=154)
Mean hemoglobin A1c during TB treatment: 2013 - 2014
(by initial HbA1c category, Hawaii TB-DM cases, n=50)

Source: Alexandra Pyan, CSTE Fellow, Hawaii TB Program, 2015
Can Our TB Program Take Credit for This?

What is the natural change in A1c during TB treatment?

<table>
<thead>
<tr>
<th>A1c should drop during treatment</th>
<th>A1c should rise during treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections usually elevate blood glucose. Glucose is an “acute phase reactant”.</td>
<td>Rifampin (and INH) will elevate blood glucose throughout treatment and can interfere with some DM medications.</td>
</tr>
<tr>
<td>Patients may use this as an opportunity to address multiple health problems.</td>
<td>Almost all patients gain weight during TB treatment</td>
</tr>
</tbody>
</table>
1% A1c Change and Retinopathy

Risk of sustained retinopathy progression at assumed fixed levels of A1c over time within the intensive and conventional treatment groups.

- Conventional
- Intensive

50% decrease in rate of retinopathy progression

1% A1c decrease

1% A1c Change and Nephropathy

### Table 4. Baseline predictors of time to death (all-cause mortality) in 227 type 2 diabetic patients with nephropathy followed for 6.5 years (Cox proportional hazard model)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per 10 years</td>
<td>1.82 (1.32 to 2.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albuminuria log(_{10})</td>
<td>2.56 (1.34 to 4.88)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>1.14 (1.00 to 1.29)</td>
<td>0.049</td>
</tr>
<tr>
<td>per 10 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c per 1%</td>
<td>1.24 (1.05 to 1.47)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
"For every 1% reduction in A1c (e.g., from 8.0% to 7.0%), the risk of developing eye, kidney, and nerve disease is reduced by....."
Double Trouble: TB-DM Lit Review

1. Does DM cause TB? Yes!

2. Does diabetes affect TB treatment? Yes!

3. Can we make a difference?
   - We can diagnose TB with active case-finding for early diagnosis to improve outcomes
   - We can identify high-risk individuals in DM clinics for TB prevention
TB-DM: Opportunities for Collaboration

• TB 101: A few of the basics
• TB-DM Current Epidemiology
• TB-DM Brief Research Update
• TB-DM Current Collaborations
• TB-DM Opportunities for Partnership
TB-DM: Evolution of Man
TB Screening in DM Clinic

1. Where was my patient born?

2. What is the current level of glucose control?

3. What is the age of my patient?

4. What test should I use?
TB Screening in DM Clinic

Percentage of TB Cases Among Foreign-born Persons, United States*

2000

2010

≥50%  25%–49%  <25%

*Updated as of July 21, 2011.
Poll 2:

Approximately what percent of your DM patients are foreign born?

• 0-25%
• 26-50%
• 51-75%
• 76%+
Approximately what percent of your DM patients are foreign born?

- 0-25%: 32.2%
- 26-50%: 28.4%
- 51-75%: 20.7%
- 76%+: 18.6%
TB Screening in DM Clinic

1. Where was my patient born?

2. What is the current level of glucose control?

3. What is the age of my patient?

4. What test should I use?
TB-DM: Diabetes Control

Percentage of DM with A1c < 8% by Race/Ethnicity, United States, 1988 - 2006

Source: CDC DDT
Poll 3:

Approximately what percent of your DM patients currently have an A1C < 8.5?

- No data
- 20%
- 50%
- 80%
- More than 90%
Approximately what percent of your DM patients currently have an A1C < 8.5?

- No data: 52.6%
- 20%: 18.3%
- 50%: 22.2%
- 80%: 6.2%
- More than 90%: 0.7%
TB Screening in DM Clinic

1. Where was my patient born?

2. What is the current level of glucose control?

3. What is the age of my patient?

4. What test should I use?
TB-DM: Younger DM Cases at Highest Risk

Age Specific TB Rates and Cases in Southern Mexico*

Ponce De-Leon, A. Tuberculosis and Diabetes in Southern Mexico, Diabetes Care 27:1584–1590, 2004
Summary: TB Infection for DM Cases

1) Younger DM cases seem to be at a higher relative risk of TB.
   - Younger DM cases may be closer to their initial TB exposure

2) Younger DM cases tolerate preventive treatment better

3) Younger DM cases will realize more long-term benefit from preventive treatment
Possible Risk Profile for TB Screening in Persons with DM

- **Higher Risk**
- **Moderate Risk**
- **Lower Risk**

- **Age of Person with DM at time of TB Screening**

- **Most Recent HA1C (%)**

R. Brostrom
1. Where was my patient born?

2. What is the current level of glucose control?

3. What is the age of my patient?

4. What TB screening test should I use?
TB Screening Cornucopia

- TB skin test: TST
- TB blood test: IGRA
- TB Symptom Screen
- Chest X-ray (CXR)
- Sputum AFB Smear
- GeneXpert MTB-Rif
TST and IGRA

**TST**
- Skin test
- 2 patient visits
- **BCG falsely positive**
- Less expensive
- Reader variability
- Results in 2 to 3 days

**IGRA**
- Blood test
- 1 patient visit
- Specific antigens
- More expensive
- Lab variability
- Results in 1 or 2 days
IGRA or TST? Diabetes

• For DM cases with good control
  – TST seems to work fairly well
  – Test placement and reading requires

• For younger individuals with DM
  – TST has more false positives (ex. BCG vaccination) and IGRA should reduce the number of TB-infections you will need to treat.

• For older individuals with DM (ex. ESRD)
  – TST has many false negatives and can miss 30% to 50% of TB-infected individuals. IGRA seems to perform better in this population.

Rogerson, T Chen, S, Tests for Latent Tuberculosis in People With ESRD: A Systematic Review. AJKD 2013, V61-1 pg 33
Winthrop, K. Nyenday, M, IGRA for Diagnosing TB Infection in Renal Dialysis Patients. CJASN 2008 V3-5 pg 1357-1363
TB-DM for DM Clinics: Where to Start?

**Screening in DM Clinic for TB Disease**

**WHO?** All persons with diabetes, especially foreign born individuals from high-risk countries

**HOW?** Use a routine periodic TB-symptom screen to find TB cases

**WHEN?** Annual symptom screening

**THEN?** Refer all positives to TB Clinic for chest x-ray and further workup
**TB-DM for DM Clinics: Where to Start?**

*Screening in DM Clinic for TB Infection*

**WHO?** Focus on those with A1C > 8%
Focus on those under age 50 y.o.

**HOW?** Use TST or IGRA to dx TB infection

**WHEN?** Test for TB infection *every 2 to 5 years*

**THEN?** Refer all positives to TB Clinic for treatment. 3HP ideal for short course treatment
Poll 4:

Tuberculosis screening in your DM clinic—

- I will advocate for TB screening for DM cases from countries with high TB rates.
- I will advocate for TB screening for all DM cases.
- I need to think about this. I am still not sure the data supports routine TB screening.
- Sorry Dr B, but we have enough problems with DM control. Right now, there’s no room for TB screening in my DM program.
Tuberculosis screening in DM clinic:

- Will advocate/TB screen/countries: 45.5%
- Will advocate/All TB cases: 43.4%
- Unsure data supports TB screening: 9%
- Sorry. No room for TB screening: 2.2%
Enhanced TB-DM Program Collaboration
Enhanced TB-DM Program Collaboration

• Seek out and meet with your TB program
  • Choose a pilot DM clinic serving high-risk cases.
  • Decide together which DM cases need to be screened for TB?
• Who is going to perform the TB screening?
• Who is going to pay for the TB screening?
• How are the screening results going to be recorded and communicated?
How Else Can DM Programs Help?

- Provide culturally appropriate patient education materials to TB clinic
- Provide feedback on TB materials
- Offer to teach basic DM principles to TB nurses and DOT workers
  - Teach RBG, A1C, DM education
- Consider TB-only DM classes
Metformin could be used to treat tuberculosis


*Sci Transl Med 19 November 2014:
Vol. 6, Issue 263, p. 263ra159
Sci. Transl. Med. DOI: 10.1126/scitranslmed.3009885

RESEARCH ARTICLE

TUBERCULOSIS

Metformin as adjunct antituberculosis therapy

Amit Singhal¹,*, Liu Jie¹,*, Pavanish Kumar¹,†, Gan Suay Hong2, Melvin Khee-Shing Leow³,⁴, Bhairav Paleja¹, Liana Tsenova⁵,⁶, Natalia Kurepina⁵, Jinmiao Chen¹, Francesca Zolezzi¹, Barry Kreiswirth⁵, Michael Poidinger¹,⁷, Cynthia Chee², Gilla Kaplan⁵,⁸, Yee Tang Wang² and Gennaro De Libero¹,⁹,*
TB-DM – Framework Summary

- **Diabetes Education:** Clinic/DOT
- **Refer TB-DM Cases to DM Center**
- **Frequent Glucose and A1c Testing**
- **Diabetes Meds with DOT**

**Control Glucose During TB Tx**
TB-DM – Framework Summary

Control Glucose During TB Tx

- Frequent Glucose and A1c Testing
- Diabetes Education: Clinic/DOT
- Refer TB-DM Cases to DM Center
- Diabetes Meds with DOT
- Improved TB Outcomes
TB-DM – Framework Summary

- Diabetes Education: Clinic/DOT
- Refer TB-DM Cases to DM Center
- Frequent Glucose and A1c Testing
- DiabeticsMed with DOT

Control Glucose During TB Tx

Improved Life-Long Diabetes Control

Improved TB Outcomes
Collaborative framework for care and control of tuberculosis and diabetes:  

Pacific Standards for Management of TB and DM:  
http://www.spc.int/tb/component/content/article/75-pacific-standards-for-management-of-tb-and-diabetes

Key Messages for TB and DM:  
TB-DM: Opportunities for Collaboration

TB DM Cases

• Screening for TB Disease (Active TB)

• Screening for TB Infection (Latent TB)
Mr. Hernandez is a 43 year old male from Mexico, living and working in Houston TX

Complains of blurry vision and nocturia

Primary care clinician ordered a RBG (276 mg/dl)

Referral made to DM clinic for care

He is admitted to DM clinic, initial A1C is 9.2%

He is very compliant and attends a total of 6 weekly group sessions (2 hours each) for DM education

After 3 months, his A1C is down to 8.7%
TB-DM for DM Clinics: Case

• After 4 months, another patient noted that Mr. Hernandez had been coughing in the waiting area over the past three weeks
• DM clinic told him to see his primary care doc to manage his “cold”
• 4 weeks later, he sees his primary care clinician who tries to manage him with some outpatient antibiotics (levofloxacin 500mg x 1 week). It helped some, but the cough persisted
• CXR was ordered:
TB-DM for DM Clinics: Case
Sputum was ordered for AFB and was 4+
Referral made to public health for TB treatment
Started on 4 medications (R-I-P-E)
Initial RBG after treatment initiated was 340 mg/dl
After 2 weeks, public health inquired about other patients seen at DM clinic
Contact investigation was initiated for 23 other people with DM who had significant contact to this case
  16 other patients, 7 DM clinic staff
TB-DM for DM Clinics: Case

- After 6 weeks, TB culture was confirmed and was sensitive to all 4 TB medications.
- From the workplace contact investigation, a total of 8 contacts (7 patients, 1 staff) were found to have a positive IGRA test:
  - 5 of these had no prior TB test.
  - 3 had positive TSTs in the past.
  - All 8 individuals are placed on preventive treatment with 3HP.
TB-DM for DM Clinics: Case

- After 2 months, he continued to have positive AFB. In response, TB treatment was extended to 9 months.
- TB and DM clinic met to optimize his treatment. Sulfonylureas were discontinued and metformin was increased. Patient returned to DM clinic after he was deemed non-infectious by the TB program.
- DM lifestyle changes were reinforced by both programs, and patient received DM education and monitoring as part of his DOT for TB.
- After 9 months, patient completed treatment.
TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Disease

WHO? All persons with diabetes, especially foreign born individuals from high-risk countries

HOW? Use a routine periodic TB-symptom screen to find TB cases

WHEN? Annual symptom screening

THEN? Refer all positives to TB Clinic for chest x-ray and further workup
Symptoms of TB Disease

- Prolonged Cough (>2-3 weeks duration)
- Productive or Dry Cough
- Coughing Up Blood
- Feeling Weak or Constantly Tired
- Fever
- Night Sweats
- Loss of Appetite
- Weight Loss
- Chest Pain
Who is at Highest Risk of TB?

A. 32 y.o. born in the Cambodia
   A1c = 7.5   Loss of appetite

B. 57 y.o. Caucasian from New York
   A1c = 8.7   Homeless   Cough 2 weeks
TB-DM for DM Clinics: Where to Start?

Screening in DM Clinic for TB Infection

WHO? Focus on those with A1C > 8%
Focus on those under age 50 y.o.

HOW? Use TST or IGRA to dx TB infection

WHEN? Test for TB infection every 2 to 5 years

THEN? Refer all positives to TB Clinic for treatment. 3HP ideal for short course treatment
Who Needs Latent TB Screening?

A. 32 y.o. born in the Philippines
   A1c = 9.3

B. 67 y.o. Caucasian from Iowa
   A1c = 7.3
Case Study

• 36 yr old Latino woman with close exposure to an infectious individual with drug susceptible pulmonary TB

• She has a long history of poorly controlled diabetes
Compared to other contacts to the source case is she more at risk of developing LTBI?

A. Yes
B. * No
Linkage Between Tuberculosis and Diabetes

Patient diagnosed with diabetes

Immune Response is weakened

Exposure to M. Tuberculosis

No increased risk of LTBI
Compared to other contacts, is she more at risk of progressing to active TB disease if she develops LTBI?

A. *Yes  
B. No
People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB.

WHO 2009

People with diabetes have a 2-3 times higher risk of TB compared to people without diabetes.

About 10% of TB cases globally are linked to diabetes.
What Additional Evaluation or Treatment Should This Patient Have?

A. Medical History
B. TST or IGRA
C. CXR
D. Hb A1C
E. Start INH for LTBI
F. A and B
Case Study

- TST 20 mm
- Patient notes several weeks of dry cough but is otherwise well
  - Incidentally her HB A1C is > 8.9%
- Now what?
Case Study

- CXR was read as normal by radiologist
- Exam was normal
- Patient reported frequent allergies
- One sputum specimen was submitted
  - Smear negative for AFB
What Else Should Be Done?

A. Sputum for smear & culture x 3
B. Bronchoscopy with BAL?
C. Start treatment for LTBI
D. Start treatment for active TB disease (RIPE)
E. A and C
F. *A and D
Case Study

• 3 months later:
  o Fever
  o Productive cough
  o Hemoptysis
Case Study

Smear + for AFB

CXR notes bilateral upper lobe opacifications and cavitation
What Now?

A. *Start RIPE
B. Stop INH continue RPE
C. Stop INH, start RPE and add a fluoroquinolone
Case Study

• Culture grows M TB

Later found resistant to INH
Are Outcomes Different Than For Other TB Patients?

A. Slower sputum conversion
B. Increased risk of failure
C. Increased risk of death
D. Increased risk of relapse
E. * All of above

20% 20% 20% 20% 20%
Case Study

- Slow conversion of cultures and smears after > 2 ½ months of therapy
- Slow radiographic improvement
- HB A1C remains > 9%
- Nausea and some vomiting after TB meds
- Rifampin level (900 mg qd) - trace - (nl 8 – 24)
Case Study

• Improved diabetic control with diet modification, exercise and medication
• Increase in rifampin dosage due to low serum level
• Clinically improved
• Radiographically improved
Month 5 of treatment
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