During, and After, Tuberculosis: How can we make life better for TB survivors?

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Should we consider a ‘fourth 90’ for tuberculosis?

A. D. Harries,¹ ² R. A. Dlodlo,¹ G. Brigden,¹ K. Mortimer,¹ ³ P. Jensen,¹ P. I. Fujiwara,¹ J. L. Castro,¹ J. M. Chakaya¹ ⁴

Table 90-(90)-90 Stop TB partnership global targets for TB (adapted from⁴)

- Reach and treat at least 90% of all people with TB*
- As a part of this approach reach and treat at least (90%) of the key populations†
- Achieve at least 90% treatment success for all people diagnosed with TB‡

* Includes people with drug-susceptible and drug-resistant TB and people who require preventive therapy (for example, people living with HIV and those in contact with TB patients).
† Includes at-risk populations which can vary depending on country context.
‡ Includes achieving 90% treatment success among people diagnosed with drug-susceptible and drug-resistant TB and people who require TB preventive therapy.

TB = tuberculosis.
Should we consider a ‘fourth 90’ for tuberculosis?

A. D. Harries,1,2 R. A. Dlodlo,1 G. Brigden,1 K. Mortimer,1,3 P. Jensen,1 P. I. Fujiwara,1 J. L. Castro,1 J. M. Chakaya1,4

A Proposed 4th 90
‘Ensuring that 90% of all people successfully completing treatment for TB can have a good health related quality of life’.

• Diabetes
• HIV
• Smoking
• Alcohol
• Mental Health
• Pulmonary rehabilitation

Harries, IJTLID, 2019
Due to improvements in TB detection and treatment, we have a growing population of TB survivors.

<table>
<thead>
<tr>
<th>WHO REGION</th>
<th>HIV-NEGATIVE PEOPLE</th>
<th>HIV-POSITIVE PEOPLE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BEST ESTIMATE</td>
<td>UNCERTAINTY INTERVAL</td>
<td>BEST ESTIMATE</td>
</tr>
<tr>
<td>African Region</td>
<td>6.6</td>
<td>5.5–7.7</td>
<td>8.2</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>1.8</td>
<td>1.7–2.0</td>
<td>0.34</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>23</td>
<td>19–28</td>
<td>2.8</td>
</tr>
<tr>
<td>European Region</td>
<td>2.1</td>
<td>1.8–2.3</td>
<td>0.30</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>4.7</td>
<td>4.1–5.3</td>
<td>0.08</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>15</td>
<td>14–16</td>
<td>0.48</td>
</tr>
<tr>
<td>Global</td>
<td>54</td>
<td>47–60</td>
<td>12</td>
</tr>
</tbody>
</table>
**Quantifying the global number of tuberculosis survivors: a modelling study**  
Dodd, Lancet ID, 2020

<table>
<thead>
<tr>
<th>Region</th>
<th>African region</th>
<th>Region of the Americas</th>
<th>Eastern Mediterranean region</th>
<th>European region</th>
<th>South-East Asia region</th>
<th>Western Pacific region</th>
<th>Global</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total new tuberculosis cases, 1980-2019</td>
<td>77,400,000 (60,800,000-84,400,000)</td>
<td>11,500,000 (10,700,000-12,400,000)</td>
<td>25,600,000 (23,000,000-28,900,000)</td>
<td>14,300,000 (12,200,000-16,300,000)</td>
<td>161,000,000 (95,100,000-227,000,000)</td>
<td>77,800,000 (51,800,000-104,000,000)</td>
<td>363,000,000 (287,000,000-438,000,000)</td>
</tr>
<tr>
<td>New treated tuberculosis cases, 1980-2019</td>
<td>37,300,000 (31,900,000-41,700,000)</td>
<td>9,120,000 (6,000,000-12,400,000)</td>
<td>12,500,000 (11,800,000-13,200,000)</td>
<td>12,000,000 (6,600,000-16,400,000)</td>
<td>68,500,000 (56,400,000-80,600,000)</td>
<td>37,300,000 (16,900,000-72,100,000)</td>
<td>172,000,000 (126,000,000-228,000,000)</td>
</tr>
</tbody>
</table>

**Interpretation**  
The number of tuberculosis survivors alive in 2020 is more than ten times the estimated annual tuberculosis incidence. Interventions to alleviate respiratory morbidity, screen for and prevent recurrent tuberculosis, and reduce stigma should be immediately prioritised for recently treated tuberculosis survivors.

155 Million Survivors

**Table 1:** Tuberculosis cases, life-years lived, and 2020 tuberculosis survivors globally and by WHO region

Data are number of cases (95% UI) or life-years (95% UI). Rounding means that the sums of treated and untreated might not equal the totals exactly. UI = uncertainty interval.
Long Term Mortality in People Treated for Tuberculosis

A systematic review and meta-analysis

Kamila Romanowski MSc, Brett Baumann MD, C Andrew Basham MSc, Faiz Ahmad Khan MD, Greg J Fox MD, James C Johnston MD
What do we know about the health of TB survivors?

- Often experience long-term disability after treatment completion
- Remain at-risk for recurrent TB disease
- Have high rates of socioeconomic marginalization and co-morbid disease

Do people treated for active TB have high mortality post-treatment?
The number of observed deaths for TB survivors was almost three times higher than the expected number of deaths.
Results remained consistent in sub-group analysis

Similar findings for both high and low income countries

Cardiovascular disease was the leading cause of post-treatment mortality followed by cancer and respiratory disease. Death due to TB or TB/HIV accounted for 9% of the causes of mortality.
The relationship between TB and mortality is complex. TB is likely associated with even greater morbidity and mortality than current estimates capture.
### TABLE 6.3.1 Global estimates of the number of TB cases attributable to selected risk factors, 2020

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative risk (uncertainty interval)</th>
<th>Exposed (millions)</th>
<th>Population attributable fraction (%)</th>
<th>Attributable TB cases (millions, uncertainty interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use disorders</td>
<td>3.3 (2.1–5.2)</td>
<td>291 000</td>
<td>8.1</td>
<td>0.74 (0.31–1.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.5 (1.3–1.8)</td>
<td>496 000</td>
<td>3.1</td>
<td>0.37 (0.15–0.68)</td>
</tr>
<tr>
<td>HIV infection</td>
<td>18 (15–21)</td>
<td>37 500</td>
<td>7.6</td>
<td>0.74 (0.65–0.83)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.6 (1.2–2.1)</td>
<td>1 050 000</td>
<td>7.1</td>
<td>0.73 (0.25–1.5)</td>
</tr>
<tr>
<td>Undernourishment</td>
<td>3.2 (3.1–3.3)</td>
<td>637 000</td>
<td>15</td>
<td>1.9 (1.3–2.6)</td>
</tr>
</tbody>
</table>
TB determinants

Estimates of TB cases attributable to 5 risk factors in 2020

Diabetes

Smoking

Alcohol use disorders

HIV infection

Undernourishment

0 0.5 1.0 1.5 2.0 2.5

Millions
EACH of these risk factors increases risk of bad outcomes (i.e. relapse, death) **DURING** treatment.

And, these **modifiable** risk factors increase risk of recurrent tuberculosis and death **AFTER** treatment.
Diabetes Mellitus and Tuberculosis Treatment Outcomes in Pune, India


Total screened (2577)

Diagnosed with TB (1780)

Provisionally enrolled in the cohort (832)

Excluded (12)
MDR TB at screening (8)
Consent withdrawn (4)

TB-DM (245)

TB (587)

Total enrolled in the cohort (807)

*Considered for analysis (799)

TB-DM (225)

TB (574)

Not enrolled (648)
Primary reasons
MDR TB: 87
HIV seropositive: 98
Refused: 224
Ineligible: 188
Not DM & controls fully enrolled: 283
Other: 68

*Completed 12 months of follow-up
Diabetes Mellitus and Tuberculosis Treatment Outcomes in Pune, India

Vidya Mave,1,2 Sanjay Gaikwad,1 Madhusudan Barthwal,4 Ajay Chandanwale,1,2 Rahul Lokhanda,1,2 Dileep Kadam,1,2 Sujata Dharmsale,1,2 Renu Bharadwaj,1,2 Anju Kagal,1 Neeta Pradhan,1 Sona Deshmukh,1 Sachin Atre,4 Tushar Sahasrabudhe,4 Shailesh Meshram,4 Arjun Kakrani,4 Vandana Kulkarni,1 Swapnil Raskar,1 Nishi Suryavanshi,1 Hardy Kornfeld,4,6 Kelly E. Dooley,2 Sandy Chon,2 Akshay Gupta,5 Amita Gupta,1,2,5 Nikhil Gupta,2,5 and Jonathan E. Golub2,5

Figure 2. A, Kaplan-Meier curve showing time to early mortality (death during the period of tuberculosis treatment) among patients with tuberculosis (TB) by diabetes mellitus (DM) status. The red line represents patients with DM, and the blue line represents patients without DM. B, Kaplan-Meier curve showing time to early mortality by newly diagnosed diabetes mellitus (DM) and known DM among patients with tuberculosis (TB). The blue line represents patients with TB without DM, the green line represents newly diagnosed DM, and the red line represents known DM.
Diabetes is associated with early mortality

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Yes</th>
<th>No</th>
<th>Unadjusted Risk Ratio (RR) (95% CI%)</th>
<th>#Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unfavourable outcomes, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No DM (n=574)</td>
<td>119 (21%)</td>
<td>455 (79%)</td>
<td>1</td>
<td>1.07 (0.66 – 1.72)</td>
</tr>
<tr>
<td>DM (n=225)</td>
<td>44 (20%)</td>
<td>181 (80%)</td>
<td>1.01 (0.71 – 1.42)</td>
<td></td>
</tr>
<tr>
<td><strong>All-cause mortality (HR)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No DM (n=574)</td>
<td>42 (7%)</td>
<td>532 (93%)</td>
<td>1</td>
<td>1.52 (0.75 – 3.08)</td>
</tr>
<tr>
<td>DM (n=225)</td>
<td>23 (10%)</td>
<td>202 (90%)</td>
<td>1.55 (0.93 – 2.59)</td>
<td></td>
</tr>
<tr>
<td><strong>Early Mortality (HR)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No DM (n = 574)</td>
<td>9 (2%)</td>
<td>565 (98%)</td>
<td>1</td>
<td>R1ef</td>
</tr>
<tr>
<td>DM (n = 225)</td>
<td>17 (8%)</td>
<td>208 (92%)</td>
<td><strong>5.06 (2.26 – 11.35)</strong></td>
<td><strong>4.77 (1.41 – 16.11)</strong></td>
</tr>
</tbody>
</table>

#adjusted for sex, age, household income, alcohol, body mass index, smear grade, cavitary disease and daily vs. intermittent regimen

Mave, OFID, 2021
Estimated risk of TB outcomes by DM status among a prospective TB cohort in Pune, India.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (95% CI)</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ratio$^b$ (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Composite unfavorable outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB-only (n=574)</td>
<td>20.0 (16.6–24.0)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>TB-DM (n=225)</td>
<td>20.1 (14.6–27.0)</td>
<td>1.01 (0.71–1.42)</td>
<td>&gt;0.95</td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB-only (n=424)</td>
<td>12.2 (8.7–16.5)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>TB-DM (n=159)</td>
<td>7.5 (3.4–14.2)</td>
<td>0.62 (0.30–1.27)</td>
<td>0.19</td>
</tr>
<tr>
<td>Recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB-only (n=574)</td>
<td>6.5 (4.7–8.8)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>TB-DM (n=225)</td>
<td>9.9 (6.3–14.9)</td>
<td>1.55 (0.93–2.59)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

$^a$adjusted for sex, age, household income, alcohol, BMI, smear grade and cavitary disease and daily vs. intermittent regimen

TB with and without DM did NOT differ in composite outcome BUT, mortality MAY be increased among people with DM
Estimated risk of **EARLY mortality** by DM subtype (new or known) among a prospective TB cohort in Pune, India

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (95% CI)</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td></td>
<td>aHR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>TB-only (n=574)</td>
<td>3.4 (1.6–6.5)</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>TB-DM (n=225)</td>
<td>17.5 (10.2–28.0)</td>
<td>5.06 (2.26–11.35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.36 (1.62–11.76)</td>
<td>0.004</td>
</tr>
<tr>
<td>New DM (n=70)</td>
<td>24.7 (10.0–51.0)</td>
<td>7.17 (2.67–19.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.56 (2.18–19.71)</td>
<td>0.001</td>
</tr>
<tr>
<td>Known DM (n=155)</td>
<td>14.5 (6.9–26.7)</td>
<td>4.20 (1.70–10.33)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.14 (1.03–9.61)</td>
<td>0.045</td>
</tr>
<tr>
<td>DM on metformin (n=117)</td>
<td>11.4 (4.2–24.8)</td>
<td>3.30 (1.18–9.28)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.32 (0.67–8.08)</td>
<td>0.20</td>
</tr>
<tr>
<td>DM no metformin (n=108)</td>
<td>24.8 (12.4–44.4)</td>
<td>7.13 (2.06–17.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.17 (2.24–17.04)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<sup>a</sup>adjusted for sex, age, household income, alcohol, BMI, smear grade and cavitary disease and daily vs. intermittent regimen

TB patients with DM at greater risk of death **DURING** TB treatment. True for NEW DM and KNOWN DM.

DM on metformin had increased risk of early mortality.

DM NOT on metformin had a 6-fold increased risk of mortality!
Estimated risk of POST-TREATMENT mortality by DM subtype (new or known) among a prospective TB cohort in Pune, India

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (95% CI)</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>TB-only (n = 487)</td>
<td>8.6 (5.9 – 12.1)</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>TB-DM (n = 176)</td>
<td>4.5 (1.6 – 9.7)</td>
<td>0.54 (0.22 – 1.28)</td>
<td>0.16</td>
</tr>
<tr>
<td>New DM (n = 49)</td>
<td>5.3 (0.6 – 19.1)</td>
<td>0.64 (0.15 – 2.69)</td>
<td>0.55</td>
</tr>
<tr>
<td>Known DM (n = 126)</td>
<td>4.2 (1.1 – 10.7)</td>
<td>0.50 (0.18 – 1.41)</td>
<td>0.19</td>
</tr>
<tr>
<td>DM on Metformin (n = 98)</td>
<td>2.6 (0.3 – 9.5)</td>
<td>0.31 (0.07 – 1.29)</td>
<td>0.11</td>
</tr>
<tr>
<td>DM no Metformin (n = 78)</td>
<td>6.8 (1.9 – 17.5)</td>
<td>0.84 (0.30 – 2.39)</td>
<td>0.75</td>
</tr>
</tbody>
</table>

TB patients with DM are NOT at greater risk of death AFTER TB treatment.

\(^a\)adjusted for sex, age, household income, alcohol, BMI, smear grade and cavitary disease and daily vs. intermittent regimen.
Higher risk of death following TB treatment

- Treated TB patients have higher risk of death
- SMR ~ 3 to 4
- Excess of 7.6 deaths /1000 p-yrs
- Multifactorial
- *Chronic lung diseases* thought to play an important role in excess mortality

Higher prevalence of airflow obstruction in individuals with a history of TB

- Higher prevalence of chronic obstructive pulmonary disease (COPD) from global surveys
- Pooled OR = 3.05 (95%CI 2.42-3.82) adjusting for smoking and self-report bio-mass fuel use
- Association stronger in high-burden settings

Byrne et al 2015
Lung function improves with treatment but may not normalize despite microbiologic cure

- 50% with lung function impairment at treatment initiation
- 25% with residual lung function impairment by treatment completion
- Greatest improvement in first 2 months

Maguire et al 2009
Respiratory impairment (RI) is common in treated PTB cases

- 20-70% of treated PTB cases have lung function impairment
- Degree of impairment may correlate with extent of disease

PTB-associated RI persists beyond treatment completion

- 65% of PTB patients had abnormal lung function 14-18 years after successful treatment.

- Every episode of PTB was associated with approx. 200ml (5-10%) permanent and irreversible loss of lung function.

Hnizdo et al 2006, Rekha et al 2009
Assessment of persistent depression among TB patients

Authors: Suryavanshi, N. ¹; Sane, M. ¹; Gaikwad, S. ²; Paradkar, M. ¹; Mave, V. ³; Chandrasekaran, P. ⁴; Shivakumar, S. V. B. Y. ⁵; Gupta, A. ⁶; Gupte, N. ³; Thomas, B. ⁴; for TRIUMPH RePORT India study

Source: The International Journal of Tuberculosis and Lung Disease, Volume 24, Number 11, 1 November 2020, pp. 1208-1211(4)

Publisher: International Union Against Tuberculosis and Lung Disease

DOI: https://doi.org/10.5588/ijtld.20.0231
Objective and study design

Prospective observational cohort study to assess the prevalence and risk factors of PDS among adult (>18 years) pulmonary TB patients enrolled in the Cohort for Tuberculosis Research by the Indo-US Medical Partnership (CTRIUMPh) study in India.

Depression was assessed using a validated Centre for Epidemiological Scale-Depression-10 scale (CESD-10) at ATT initiation and at the EOT.

Participants having cut off score of >9 were considered depressed.
Results

• Of 464 adult TB patients enrolled, 40 were lost to follow-up, and 3 did not have baseline depression data.
• Among the remaining 421 participants, 200 (47.5%) had BDS but depression symptoms disappeared for 145 patients at the end of treatment.
• Of 254 participants included, 55 (22%) had PDS
Assessment of persistent depression symptoms among Tuberculosis patients in India

- Prevalence of baseline depression symptoms was 47.5% (200/421)
- Prevalence of persistent depression symptoms (PDS: Depressed at ATT initiation and at EOT) among those depressed at baseline was 27.5% (55/200).
- PD symptoms were correlated with more disadvantage and vulnerable group
  - Female tuberculosis (TB) patients with stigma are at increased risk PDS symptoms.
  - AUDIT ≥ 8 is risk factor for PDS
- Integrating screening for depression and TB stigma into routine TB care would facilitate early identification and timely intervention with the potential to enhance TB care.
Conclusions:

Our study identified a high prevalence of PDS among adult TB patients and particularly among women reporting TB stigma.

Recommendations

Integrating screening for depression and TB stigma into routine TB care along with counseling support would facilitate early identification and timely intervention.

This has the potential to enhance treatment adherence and overall TB care.
Unhealthy alcohol use independently associated with unfavorable TB treatment outcomes among Indian men

S. R. Cox,¹ A. N. Gupte,¹ B. Thomas,² S. Gaikwad,³ V. Mave,¹,⁴ C. Padmapriyadarsini,² T. R. Sahasrabudhe,⁵ D. Kadam,³ N. Gupte,¹,⁴ L. E. Hanna,² A. Kagal,³ M. Paradkar,¹,⁴,⁶ K. Thiruvengadam,² D. Jain,⁴ S. Atre,¹,⁵,⁶ K. Sekar,² S. Raskar,¹,⁴,⁶ S. V. B. Y. Shivakumar,¹,⁶ R. Santhappan,² S. Deshmukh,¹,⁴,⁶ N. Pradhan,¹,⁴,⁶ V. Kulkarni,¹,⁴,⁶ A. Kakrani,⁵ M. S. Barthwal,⁵ T. Sawant,⁵ A. DeLuca,¹ N. Suryavanshi,¹,⁴,⁶ G. Chander,¹ R. Bollinger,¹ J. E. Golub,¹ A. Gupta¹

¹Johns Hopkins University (JHU), School of Medicine, Baltimore, USA; ²National Institute of Research in Tuberculosis (NIRT), Chennai, ³Byramjee Jeejeebhoy Government Medical College (BJGMC) and Sassoon General Hospital, Pune, ⁴BJGMC Clinical Research Site, Pune, ⁵Dr DY Patil Medical College Hospital and Research Centre, Dr DY Patil Vidyapeeth, Pune, ⁶Johns Hopkins India Private Limited, Pune, India
Study Overview

We used the validated Alcohol Use Disorders Identification Test-Concise (AUDIT-C) scale to determine whether unhealthy alcohol use was independently associated with unfavorable TB treatment outcomes among men with drug-susceptible pulmonary TB (PTB) in well-defined longitudinal cohorts in India.

- Restricted to men given very low prevalence of alcohol use among women (<1%).
- Unhealthy alcohol use = AUDIT-C ≥4 at entry.
- Why study alcohol & TB in India?
  - India has the world’s largest burden of TB.
  - Alcohol use is on the rise in India.
  - Unhealthy alcohol use is a challenge for many TB patients (22-55% of TB patients in India).
Association of alcohol use with poor TB treatment outcomes

**A**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exposed</th>
<th></th>
<th>Unexposed</th>
<th></th>
<th>Model</th>
<th>IRR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Event</td>
<td>py</td>
<td>Total</td>
<td>Event</td>
<td>py</td>
<td></td>
</tr>
<tr>
<td>Ever had a drink containing alcohol</td>
<td>407</td>
<td>131</td>
<td>473</td>
<td>344</td>
<td>67</td>
<td>393</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unadjusted</td>
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Adjusted for location, age, BMI, education, smoking, smear grade. Tx=Treatment; IRR=incidence rate ratio; OR=Odds Ratio; BMI=body mass index.
Key findings

1. Unhealthy alcohol use was common - identified in 40% of men with active TB in our study (302 of 751 men).

2. Unhealthy alcohol use is independently associated with higher risk of unfavorable TB treatment outcomes and specifically with death.
   - About 50% increased risk of unfavorable TB treatment outcomes.
   - Nearly two-fold increased risk of death within 2 years of TB diagnosis.

3. Majority of deaths occurred prior to TB treatment completion and among men with unhealthy alcohol use.

4. Malnutrition and unhealthy alcohol use had a combined adverse effect.
   - Checking AUDIT-C, height and weight may be a simple screening tool at TB treatment initiation to identify high-risk patients in need of additional services, such as alcohol reduction counseling.
Thus, a TB diagnosis is an opportunity…

• To provide/improve health care linkage:
  – Diabetes treatment
  – Smoking cessation counseling/treatment
  – Alcohol reduction
  – Mental health
  – HIV treatment
  – Physical rehabilitation therapy for lung impairment
  – Financial improvement
Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, Annie Oravec, Madison Billingsley, Kate Shearer, Akshay Gupte, Moises A. Huaman, Greg J. Fox, Jonathan E. Golub, and James C. Johnston
Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence
Kamila Romanowski, UBC-BCCDC
What is the existing evidence on interventions that address common non-communicable diseases among people with TB?
Smoking cessation works in people with TB

A systematic review of the effectiveness of smoking cessation interventions among patients with tuberculosis

E. Whitehouse,1 J. Lai,2 J. E. Golub,2,3 J. E. Farley1,4

Smoking is a significant risk factor for morbidity and mortality, particularly among patients with tuberculosis (TB). Although smoking cessation is recommended by the World Health Organization and the International Union Against Tuberculosis and Lung Disease, there has been no published evaluation of smoking cessation interventions among people with TB. The purpose of this review was to synthesize the evidence on interventions and suggest practice, research and policy implications. A systematic re-view of the literature identified 14 peer-reviewed studies describing 13 smoking cessation interventions between 2007 and 2017. There were five randomized controlled trials, three non-randomized interventions, and five prospective cohort studies. The primary types of interventions were brief advice (n = 9), behavioral counseling (n = 4), medication (n = 3), and community-based care (n = 3). A variety of health care workers (HCWs) implemented interventions, from physicians, nurses, clinic staff, community health workers (CHWs), as did family members. There was significant heterogeneity of design, definition of smoking and smoking abstinence, and implementation, making comparison across studies difficult. Although all smoking interventions increased smoking cessation between 15% and 82%, many studies had a high risk for bias, including six without a control group.
Inclusion:

- **Population:** people enrolled or completed treatment for active TB
- **Intervention:** structured program of care, implemented within a TB program to prevent or manage common NCDs
- **Common NCDs:** respiratory disease, cardiovascular disease, substance use disorder, and mental health disorders
- Assessed implementation and effectiveness outcomes

Exclusion:

- Screened but resulted in no further intervention.
- Only used TB treatment adherence or treatment completion as an outcome.
- Evaluated interventions for infectious disease comorbidities, smoking cessation interventions, or surgical or pharmacological interventions
Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

20 studies

- 17 conducted in LMICs
- 16 interventions during TB treatment
- 12 published after 2011
Common NCDs among people who experience TB

- Respiratory disease
  - Pulmonary rehabilitation: 5 studies
- Cardiovascular disease
  - Referral for diabetes and hypertension care: 6 studies
- Substance and alcohol use disorder
  - Care programs for alcohol use disorder: 4 studies
- Mental health disorder
  - Individual counselling and psychosocial support: 5 studies

Interventions identified
Is the decision to screen, a decision to treat?
Interventions to Mitigate Common Non-Communicable Diseases Among People Who Experience Tuberculosis: A Scoping Review of the Evidence

Kamila Romanowski, UBC-BCCDC

Category: Implementation
E-poster #: Oral Abstract
Further evidence demonstrating the feasibility and effectiveness of interventions is needed before scale up to ensure resources are well invested, and the cascade of chronic disease care is addressed.
NEW study: Assess TB patients with drug-sensitive TB at three time points:

a) as they start anti-TB treatment;

b) as they complete anti-TB treatment; and

c) one month after completion of anti-TB treatment.

Assessment will comprise smoking, alcohol use, malnutrition and exposure to silica through mining work, diabetes mellitus, hypertension, COVID-19 and measuring disability using the 6MWT.
Overview of HATHI study

- **Aim 1.** To examine the effectiveness of CAP (Counseling for alcohol problem) alcohol reduction intervention, integrated into TB and HIV/TB care compared to usual care on alcohol reduction.
  - CAP has 4-session combined Cognitive Behavioral Therapy (CBT) + 3 booster Motivational Enhancement Therapy (MET).
  - Aim 1 will occur in two phases, the intervention tailoring phase and the RCT phase.

- **Aim 2.** To examine the effectiveness of CAP (CBT/MET) integrated into TB and HIV/TB care compared to usual care on TB and HIV treatment outcomes.

- **Aim 3:** To understand multi-level factors that influence alcohol reduction intervention integration into these clinical settings.
  3a) evaluate patient, provider and organizational barriers and facilitators to integrated alcohol treatment in TB and HIV/TB settings, and
  3b) measure incremental costs from health system and societal perspectives, and to estimate their incremental cost-effectiveness, compared to treatment as usual.
Study Sites

BJGMC and Sassoon General Hospital, Pune, India

Dr. D.Y. Medical College, Pune, India

Policy and program level stakeholders (n=10-15). Ministry of health officials, key informants in the HIV/TB health system and community advisors to the India ART and TB program will be interviewed using in-depth interviews.
TB PuRe: Pulmonary Rehabilitation to Reduce Post-Tuberculosis Morbidity (NIH; NIAID; Golub, Gupte, Mave)

Overall objective:
To measure the effectiveness, feasibility and cost-effectiveness of a pulmonary rehabilitation (PR) program to prevent post-tuberculosis (TB) respiratory morbidity in India

Sites: a) Bharati Vidhyapeeth Medical College and Hospital (BVMC), Pune; b) Kashibai Navle Medical College and General Hospital (KNMC), Pune; c) Yenepoya Medical College (YMC), Mangalore
Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: a modelling study

Fiorlan M Marx¹, Reza Yaeoubi², Nicolas A Menzies, Joshua A Salomon, Alyssa Billinski, Nulda Beyers, and Ted Cohen

Figure 4. Projected epidemiological effect of interventions targeted to individuals with a history of previous complete tuberculosis treatment in a high-incidence setting in suburban Cape Town, 2016–2025
TB Aftermath
A hybrid type I effectiveness-implementation non-inferiority randomized trial in India comparing two active case finding (ACF) strategies among individuals treated for TB and their household contacts

Principal Investigators:
Vidya Mave, MD, TM, MPH
Madhusudan Barthwal, MBBS, MD, DM
Jonathan E. Golub, PhD, MPH
Background & Evidence Gap

- Optimized active case finding (ACF) strategies targeting high-risk population are needed.

- **Individuals recently treated for TB are a high-risk group**
  - 7% of reported TB cases worldwide are recurrent
  - 10-13% of treatment-completed individuals develop TB again

- **Standard of Care** per India’s National TB Elimination Program (NTEP):
  - Follow-up of index patients at 6, 12, 18, and 24 months after TB treatment completion.
  - No defined approach for detecting TB among treated patients and their household contacts.

- **Evidence gap:**
  - No published ACF trials targeting treated TB patients
  - Only conditional recommendation by WHO

Aims

1. To conduct a non-inferiority randomized trial to measure the comparative effectiveness of two potentially implementable ACF strategies within the NTEP, conducted by existing NTEP healthcare workers (HCWs): (i) Home-based ACF (HACF) and (ii) Telephonic ACF (TACF).

2. To characterize implementation processes of the ACF strategies using the RE-AIM framework to inform their future scale-up and sustainability.

3. To model the impact and cost-effectiveness of the ACF strategies evaluated in the trial, and of potential alternative strategies for the targeting and timing of those strategies.

4. To measure the association of the severity, chronicity, and progression of post-TB lung impairment with recurrent TB disease.
Design & Setting

- **Hybrid Type I effectiveness-implementation non-inferiority trial with individual randomization**

- **Setting:** Six public TB units in Pune district, India

- **Index Case Eligibility Criteria**
  - Adults (≥18 years)
  - Completed TB treatment within 60 days of enrolment
  - Informed consent

- **All household contacts (HHC) eligible**
TB Aftermath

Study Schema

**INDEX PATIENT SCREENING:**
Assess individuals who completed TB treatment for eligibility

**INFORMED CONSENT & ENROLMENT**

**RANDOMIZATION (1:1)**

**HOME-BASED ACTIVE CASE FINDING (HACF)**
- Index patient: n=538
- HHCC: n=1076

**TELEPHONIC ACTIVE CASE FINDING (TACF)**
- Index patient: n=538
- HHCC: n=1076

**INDEX PATIENT BASELINE EVALUATIONS**

**HOME VISIT AT MONTH 6 AND MONTH 12:**
- Informed consent & enrolment of HHCCs; symptom screen; follow-up evaluations; outcome ascertainment

**PHONE CALL AT MONTH 6 AND MONTH 12:**
- Symptom screen; follow-up evaluations; outcome ascertainment

**IDENTIFY SYMPTOMATIC INDIVIDUALS:**
- Collect sputum samples; send to TU for microbiologic testing; refer individuals to TU for care

**HOME VISIT AT MONTH 18 ("MOP-UP"):**
- Informed consent & enrolment of remaining HHCCs; symptom screen; "mop-up" evaluations; outcome ascertainment
Acknowledgements

- TB Aftermath study team and PIs
- TB Aftermath participants and their families
- National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) under award number R01AI143748