Global estimates – 25% of world population have latent TB infection

Of these, about 10% will develop active TB

Meaning 1.7 billion infected and from these, 170 million will develop TB
IMPACT OF VARIOUS STRATEGIES ON TB TRENDS OVER NEXT 35 YEARS
(DYE, ET AL., ANN REV PUBL HEALTH 2013)
ASSESSING GAPS IN THE LTBI CASCADE OF CARE
What I often hear when I hear people talk about improving LTBI care…

50-60% of people complete LTBI treatment!

We need more people to complete treatment!!

Shorter regimens will solve our problems!!!
Cascade of care in LTBI management: TB contacts
CASCADE OF CARE IN LTBI – SYSTEMATIC REVIEW

373 articles identified from search

110 full-text articles selected for review

58 studies included, describing 70 cohorts
748,571 participants

270 excluded after review of title and abstract

52 full-text articles excluded
14 were reviews
4 were RCTs
14 initial numbers of patients identified or screened not specified
17 final numbers of patients treated not specified
1 no test positive specified
1 duplicate publication
1 could not obtain

7 added from references of reviews

*Alsdurf, et al., Lancet Infect Dis 2016
KEY LOSSES ALONG THE LTBI CASCADE OF CARE

Identify Contacts
Relative Loss: 28%

Complete MedEval
Relative Loss: 20%

Refer for Tx
Relative Loss: 20%

Complete Tx
Relative Loss: 40%

*Alsdurf, et al., Lancet Infect Dis 2016
KEY LOSSES ALONG THE LTBI CASCADE OF CARE

So relative losses highest in completing Tx – BUT 70% of patients don’t even start!!

Less than 20% of eligible contacts completed preventive therapy

28.1 lost at initial step of identification and screening

12.3 did not complete medical evaluation (of TST+)

8.7 were not recommended LTBI treatment

11.9 did not complete LTBI treatment (of those who started treatment)

*Alsdurf, et al., Lancet Infect Dis 2016
BARRIERS ASSOCIATED WITH LOSSES - EXAMPLES

- **Step 2 - Not completing screening and testing**
  - Social situations impeding completion of screening (i.e. language/cultural barriers, feels too ill)
  - Health-systems issues (i.e. hard to access clinic, long wait times, difficulties with insurance)

- **Step 4 – Not being referred or recommended for treatment**
  - Considered too old (older than 35 years)
  - Low healthcare worker (HCW) knowledge about need for preventive therapy
  - Social situations impeding treatment (i.e. substance abuse, fear of deportation or immigration status, recent release from jail/prison, no transportation)
Losses and drop-outs occur at every stage of care - initial identification to completion of therapy

70% of all persons who could benefit – never even start. They will derive no benefit from better / shorter treatment!

Latent TB care is a complex process!! A Cascade of care analysis can be helpful to pinpoint where the problems are occurring, and solutions needed

Research is needed to determine factors associated with these losses

But TB programs need to plan strategies to improve access to resources required for LTBI dx/tx, particularly among close household contacts of confirmed, pulmonary TB
EVALUATING AND (HOPEFULLY) FIXING THE LTBI CASCADE
ACT4 TRIAL

ACT4: Pragmatic, cluster randomized trial (2015-2019)
- **5 countries**: Benin, Canada, Ghana, Indonesia, Vietnam
- **Clusters**: 24 health facilities

**Objective**: To evaluate a process to strengthen the latent TB Cascade of Care
- Standard evaluation – Cascade analysis. Questionnaires to patients, contacts & HCWs
- Locally-selected solutions to address losses along the LTBI Cascade of Care
- Clinical in-service trainings were conducted with HCW at each site on a regular basis
- mTST: a mobile health approach for quality improvement and training of TST
Using a simple tool to assess the Cascade of Care in Latent TB

Cumulative proportion completing each cascade step

- Expected contacts
- Identified contacts (STEP1)
- Started Initial Assessment (STEP2)
- Completed Initial Assessment (STEP3)
- Started med eval (STEP4)
- Completed med eval (STEP5)
- Recommended LTBI Tx (STEP6)
- Started LTBI Tx (STEP7)
Percent of contacts completing each cascade step, as a percent of number completing previous step.
Percent of the total lost that is attributed to each step of the cascade.
Identifying and selecting solutions

• **Impact of potential Solutions (*IJTL*... under revision):**
  – Scoping review of literature to identify potential “solutions”
  – What has been tried – In Latent TB, Active TB (or other diseases if nothing found)
  – Identified their impact – by step in Cascade.
  – *i.e. How much improvement* might be expected

• **Meetings:** with local TB programs, and the clinics
  – Review options for solutions, & evidence base for each
  – Select solutions: consider cost, feasibility, sustainability and potential impact (with help of modelling tool)
  – Approved by TB program, but finalized by clinic staff
To enhance initiation of LTBI therapy (Step 6-7):

- **Provider education**- regarding LTBI therapy. Prepare key messages. Study staff educate MDs and nurses (Brazil)
- **Evening clinics**- (for non-unionized new immigrants) (Calgary)
- **Payments to health workers**- for patients starting, and completing therapy. (Vietnam)
- **Incentives**- to patients who pick up prescriptions (Vancouver)
Brazil Cascade Experience
(The Pilot Site)

• Bottlenecks appear in sequence as problems in the earlier steps were solved…

• Slides courtesy of Dr. Anete Trajman
1st Trimester results

Problem Identified: no PPD and no TST training

Percentual acumulado (em relação aos que iniciaram a cascata)
de contatos que permanecem em cada etapa
1o trimestre

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Contatos esperados
Contatos identificados (Etapa 1)
Começaram avaliação inicial (Etapa 2)
Completaram avaliação inicial (Etapa 3)
Iniciaram avaliação clínica (Etapa 4)
Completaram avaliação clínica (Etapa 5)
Tratamento ILTB recomendado (Etapa 6)
Iniciaram tratamento ILTB (Etapa 7)
2nd Trimester results
Problem identified: Chest X-rays not available

![Graph showing cumulative percentage of contacts who initiated the cascade, per stage of the 2nd trimester.](Image)
3rd Trimester results

Problem discovered: MDs did not prescribe INH treatment
4th Trimester Results: All problems identified and resolved (at least partially)
MOBILE TST (mTST) – TRAINING TOOL

- Tuberculin Skin test (TST) is a relatively simple test, but requires careful training, as well as ongoing supervision.

- During ACT4 site visits in the fall 2017, our team found there were important errors in methods of TST administration.

- Objectives: 1) To establish the best technical method to capture a photo of TST injection and reading, and 2) to estimate the accuracy for the measurement of TST injection and reading - using photos taken with smartphone (mTST)

- Results: Tool was validated and resource is available online to help train HCW
  - [https://www.youtube.com/watch?v=S8gLalPqvho](https://www.youtube.com/watch?v=S8gLalPqvho)

The mTST – a tool for quality control for TST administration

The bleb is measured immediately following TST administration by TB nurse

Photos are taken using the protocol and transmitted by email

The independent reviewers, measure the bleb using software (i.e. Microsoft Paint). Reviewers do not know onsite measurement (blinded)

The measurements are dichotomized “Injection is correct or incorrect”
Photos are taken and transmitted by email.

TB nurse measures the induration using Ballpoint Pen Method. Reading in mm is transmitted to coordinator.

The reviewers, read and answer the question “Is there induration present” Yes or No. Reviewers do not know onsite measurement (blinded).

Agreement of reviewers reports with nurse onsite measurements estimated by coordinator.

mTST for Quality control of TST Reading

- All reviewers reported induration
- Onsite measurement: 70 mm
EXAMPLE OF LTBI CASCADE ANALYSIS – VIETNAM (courtesy Dr Buu)

Setting: 5 intervention districts in 2 Provinces in Central Vietnam (Da Nang and Quang Nam)

Most contacts likely to benefit from treatment not identified:

Gap 1: Identifying eligible contacts

100% 4.80% 1.70% 1.70% 0.80% 0.60%

% Among contacts estimated


48 17 17 8 6
Gap 1: Identifying eligible contacts

Solution: Health educational materials for community regarding LTBI

Rationale: With appropriate knowledge, the community will cooperate well with the health service in practice for LTBI management
## IMPROVEMENT IN CASCADE IN LTBI MANAGEMENT
### WITH ACT4 INTERVENTIONS - FROM 2/4/2018 – 30/9/2018 (courtesy Dr Buu)

<table>
<thead>
<tr>
<th></th>
<th>9 th đầu 2017</th>
<th>Can thiệp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Identified</td>
<td>5.0%</td>
<td>100%</td>
</tr>
<tr>
<td>Started</td>
<td>1.6%</td>
<td>91%</td>
</tr>
<tr>
<td>screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d Scr.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Med eva</td>
<td>1.3%</td>
<td>79%</td>
</tr>
<tr>
<td>Complet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>med eva</td>
<td>0.8%</td>
<td>56%</td>
</tr>
<tr>
<td>Indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx</td>
<td>0.6%</td>
<td>56%</td>
</tr>
<tr>
<td>Started</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tx</td>
<td></td>
<td>44%</td>
</tr>
</tbody>
</table>

HHCs corresponding to 240 index TB patients
Example from Denver: Improving the latent TB cascade: clinic dashboard (courtesy Dr B Burman)
Digging deeper – reasons for drop-offs in the clinic latent TB cascade (courtesy Dr B Burman)

Need to improve data systems – previously treated patients should be classified as not needing treatment

Need to work on patient/community education about TB risk

Need to decrease losses prior to treatment completion
HUMAN RESOURCE REQUIREMENTS TO IMPROVE QUALITY OF LTBI CARE
HUMAN RESOURCE REQUIREMENTS TO IMPROVE QUALITY OF LTBI CARE

- *Estimate the human resource requirements to improve the quality of LTBI care at study sites*
- To estimate the average HCW time spent on specific work tasks associated with each step in the LTBI Cascade of Care
- To calculate the change in personnel time spent on LTBI pre- and post-LTBI-strengthening activities
METHODS

- Used “Time and motion” (TAM) methods
- Follow HCW throughout a full, typical workday with continuous, direct observation
  - Write down every minute of work activity
  - Record time in pre-specified categories of activities
  - Break/pause time was removed from analysis – important that HCW know they aren’t being monitored for time spent on breaks
TIME SPENT ON PATIENT CARE – BY DIAGNOSIS

BEFORE LTBI Program Strengthening
- LTBI: 13%
- ATB: 46%
- Non-TB: 41%

AFTER LTBI Program Strengthening
- LTBI: 23%
- ATB: 36%
- Non-TB: 41%
<table>
<thead>
<tr>
<th>LTBI Cascade of Care Steps**</th>
<th>Number of HCW performing each Step on TAM day</th>
<th>Total number of patient encounters with HCW at each Step on TAM day</th>
<th>Mean time spent on each Step (Std. Dev.)</th>
<th>Median time spent on each Step (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Identification of contacts</td>
<td>33</td>
<td>73</td>
<td>10.5 (10.4)</td>
<td>6.0 (2-16)</td>
</tr>
<tr>
<td>High Income1</td>
<td>20</td>
<td>39</td>
<td>14.0 (11.2)</td>
<td>12.0 (5-21)</td>
</tr>
<tr>
<td>LMIC2</td>
<td>13</td>
<td>34</td>
<td>6.6 (8.0)</td>
<td>2.5 (2-7)</td>
</tr>
<tr>
<td>2. Place TST3</td>
<td>22</td>
<td>64</td>
<td>8.1 (7.5)</td>
<td>5.5 (2-12)</td>
</tr>
<tr>
<td>High Income</td>
<td>13</td>
<td>32</td>
<td><strong>13.1 (7.1)</strong></td>
<td><strong>11.0 (9-15)</strong></td>
</tr>
<tr>
<td>LMIC</td>
<td>9</td>
<td>32</td>
<td><strong>3.1 (3.4)</strong></td>
<td><strong>2.0 (2-4)</strong></td>
</tr>
<tr>
<td>3. Read TST3</td>
<td>17</td>
<td>59</td>
<td>6.4 (6.1)</td>
<td>4.0 (2-9)</td>
</tr>
<tr>
<td>High Income</td>
<td>11</td>
<td>22</td>
<td><strong>11.9 (6.9)</strong></td>
<td><strong>10.5 (8-14)</strong></td>
</tr>
<tr>
<td>LMIC</td>
<td>6</td>
<td>37</td>
<td><strong>3.2 (1.6)</strong></td>
<td><strong>3.0 (2-4)</strong></td>
</tr>
</tbody>
</table>
## HCW Time* Spent on Patient Encounters at Each Step of the LTBI Cascade of Care

<table>
<thead>
<tr>
<th>LTBI Cascade of Care Steps**</th>
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<th>Mean time spent on each Step (Std. Dev.)</th>
<th>Median time spent on each Step (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Conduct Medical Evaluation</td>
<td>43</td>
<td>116</td>
<td>12.1 (7.8)</td>
<td>11.0 (6-16)</td>
</tr>
<tr>
<td>High Income</td>
<td>33</td>
<td>90</td>
<td>13.0 (7.9)</td>
<td>12.0 (7-17)</td>
</tr>
<tr>
<td>LMIC</td>
<td>10</td>
<td>26</td>
<td>9.0 (6.6)</td>
<td>7.5 (2-15)</td>
</tr>
<tr>
<td>5. Recommend and discuss LTBI treatment</td>
<td>42</td>
<td>143</td>
<td>10.8 (8.5)</td>
<td>9.0 (4-13)</td>
</tr>
<tr>
<td>High Income</td>
<td>34</td>
<td>92</td>
<td>13.9 (8.9)</td>
<td>11.0 (8-18)</td>
</tr>
<tr>
<td>LMIC</td>
<td>8</td>
<td>51</td>
<td>5.3 (3.5)</td>
<td>4.0 (4-5)</td>
</tr>
<tr>
<td>6. LTBI treatment follow-up</td>
<td>56</td>
<td>276</td>
<td>9.3 (9.5)</td>
<td>6.0 (2-12)</td>
</tr>
<tr>
<td>High Income</td>
<td>44</td>
<td>191</td>
<td>12.0 (9.9)</td>
<td>9.0 (5-16)</td>
</tr>
<tr>
<td>LMIC</td>
<td>12</td>
<td>85</td>
<td>3.4 (4.4)</td>
<td>2.0 (1-5)</td>
</tr>
</tbody>
</table>
CONCLUSIONS

- **10% increase** in proportion of HCW time spent on **LTBI-related activities** as a result of LTBI programme strengthening

- **BUT --- Time is taken away from active TB patient care activities** (10% decrease in time on care for these type of patients)
  - HCW’s in the same program had to shift work tasks as no staff were added

- TAMs provide a quantification of the **ADDITIONAL HCW time required to expand LTBI services**
  - To expand LTBI services – need added staffing to perform these work tasks
ACT4 addressed multiple components of the Lancet Global Health Commission’s Framework including:

- **Workforce requirements:**
  - Evaluated through the use of TAM studies

- **Tools:**
  - Site evaluation of the LTBI Cascade of Care
  - Questionnaires used to identify barriers to LTBI care
  - Trainings for HCW using a mobile health technology (mTST) for placing and reading TST

My special thanks to Hannah Alsdurf for this impressive body of work.

Special THANKS! to the ACT4 teams involved in data collection:

**Coordinating Center:** Dr. Dick Menzies, Dr. Olivia Oxlade, Dr. Federica Fregonese, Chantal Valiquette

**Benin:** Dr. Menonli Adjobimey, Lydia Yaha

**Canada:** Nancy Bedingfield, Catherine Paulsen, Kamila Romanowski, Leslie Chiang, Saeedeh Moayedi Nia

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**Vietnam:** Dr. Thu Anh Nguyen, Dr. Tran Buu

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