“The Cascade of care in LTBI
A shift in thinking about management of LTBI”

Dr Dick Menzies,
Montreal Chest Institute,
McGill International TB Centre
Potential impact of various control strategies on TB trends over next 35 years

(Dye, et al., Ann Rev Publ Health 2013)
What is the current impact of treatment on the Global burden of LTBI?
What has been done – to enhance uptake of LTBI treatment?

Adherence research
Randomized trials of shorter therapy


78 studies of LTBI adherence identified. In US and Canada in a 10 year period of time

- Adherence and completion rates of LTBI were suboptimal in all high-risk groups, regardless of regimen.
- Completion ranged from 20-80%. Median 50%
- Inconsistent associations between adherence and patient factors, clinic facilities or treatment characteristics.
- Several interventions to improve LTBI adherence tried, but no intervention consistently effective.
RCT of newer regimens

- Many RCT in past 20 years – of short regimens that enhance completion rates with adequate efficacy.

- **Essential** characteristics of new regimens:
  - **Less toxic** *(Safety is NUMBER 1)*
  - Better completion (so effectiveness better)
  - Efficacy same (not worse)

- Regimens meeting these criteria:
  - 3HP, 4R, 3-4HR
  - In other words – we have better regimens
“What is really the major limitation in LTBI treatment?”

(Getting people to start? Or to complete)
Cascade of care in LTBI – Example of contact investigation
The Cascade of Care in Latent TB (Alsdurf, Menzies Lancet ID 2016)

- Intended for Screening: 100%
- Initially Tested: 71.9% (71.8, 72.0)
- Received a Test Result: 66.7% (66.5, 66.9)
- Referred if Test positive: 56.0% (55.2, 56.8)
- Completed Medical Evaluation: 43.7% (42.5, 44.9)
- Recommended LTBI Treatment: 35.0% (33.8, 36.4)
- Accepted + Started Treatment: 30.7% (29.5, 32.1)
- Completed Treatment: 18.8% (17.9, 19.7)
Summary - Overall:

• Less than 20% of those estimated to have LTBI completed treatment

• Steps in the cascade with the greatest losses:
  – **28%** of those eligible for screening did not complete initial testing for LTBI
  – **34%** of those with positive LTBI test did not complete medical evaluation
  – **34%** of those who completed the medical evaluation were not recommended to take LTBI therapy
Risk factors/reasons associated with losses at specific cascade steps:

• Completing screening and testing:
  – Did not perceive TB to be a serious disease
  – Health systems issues:
  – Hard to access the clinic or long wait times, problem with insurance
  – Stigma, mistrust, or unwillingness to visit the TB centre
  – End of local health awareness campaigns
  – Social situations impeding screening completion.
  – Language or cultural barriers
Risk factors/reasons associated with losses at specific cascade steps:

• Completion of medical evaluation:
  – Older age (35 years of age or older)
  – Low perceived risk of tuberculosis infection

• Recommending treatment:
  – Low health-care worker knowledge about LTBI therapy
  – Medically contraindicated (previous treatment for LTBI/active TB)
  – Social situations impeding treatment - Substance abuse, recent release from jail/prison, no transportation
  – Fear of deportation/immigration status
Improving LTBI management in public health clinics

Our approach
- Using the Cascade analysis to identify and quantify problems
- Investigating the WHY through short questionnaires
- Feedback to find solutions – local decision making
- Ongoing monitoring - readjusting as needed
ACT4 - Enhancing LTBI management: A cluster randomized trial

- **6 countries**: Benin, Brazil, Canada, Ghana, Indonesia, Vietnam
- **Clusters**: Basic health units
- **Intervention**:
  1) Standardized public health evaluation;
  2) Local decision making
  3) Implementation of solutions and LTBI program strengthening
Evaluating the Current Cascade of care in Latent TB:

- Retrospective review – 3-9 months of Contact investigations, including the following information
  - Number of Contacts screened (symptoms, TST)
  - Number of TST positive contacts,
  - Number of TST positive contacts that completed medical evaluation & Chest Xray
  - Number of Contacts recommended to start, and that accept to start LTBI treatment
1: Tabulate number of contacts completing each step of cascade

<table>
<thead>
<tr>
<th>Step</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected contacts</td>
<td>180</td>
</tr>
<tr>
<td>Identified contacts (STEP1)</td>
<td>140</td>
</tr>
<tr>
<td>Started initial assessment (STEP2)</td>
<td>120</td>
</tr>
<tr>
<td>Completed initial assessment (STEP3)</td>
<td>100</td>
</tr>
<tr>
<td>Needing med eval</td>
<td>80</td>
</tr>
<tr>
<td>Started med eval (STEP4)</td>
<td>60</td>
</tr>
<tr>
<td>Completed med eval (STEP5)</td>
<td>40</td>
</tr>
<tr>
<td>Recommended LTBI Tx (STEP6)</td>
<td>20</td>
</tr>
<tr>
<td>Started LTBI Tx (STEP7)</td>
<td>10</td>
</tr>
</tbody>
</table>
2: Calculate 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)
3: Estimate proportion of the total losses – that occur at each step of the cascade
Open-ended interviewer administered Questionnaires:

• Ask about experience in care, attitudes, usual practices, knowledge. Last 5-10 minutes each

• Interviews at each clinic for 4 types of persons:
  – **Index TB patients (active pulmonary TB)**
  – **Contacts (adults)**
  – **Parents of child contacts**
  – **Health care workers (TB care providers)**
ACT4: Cluster randomized RCT

Transition - analysis

• **Analysis** of Cascade
  – *Where* are the problems, and **how big** are the problems?

• **Analysis** of Questionnaires
  – *Why* do these problems occur?

• Putting these together
  – Picking steps in the Cascade to focus efforts
  – Using questionnaires to help identify specific barriers
  – Guide thinking for potential solutions to recognized barriers
Transition – discussing problems & selecting solutions

- **Meetings:** with local TB programs, and the clinics
  - Review Cascade of care – WHERE are the problems
  - Review questionnaire results – WHY
  - Present options for solutions, & evidence base for each
  - Select solutions: consider evidence, cost, feasibility, sustainability and potential impact
  - May require more than one meeting
  - Approved by TB program, but finalized by clinic staff
ACT4: Cluster randomized RCT

Training & Implementation

• **Initial training** of TB care providers:
  – TST administration and reading
  – Medical evaluation (rule out active TB)
  – LTBI treatment (INH, or other).

• **Implementation of solutions**: specific to each site

• **In-service training** *(formerly known as monitoring & supervision)*
  – Every week 1st month, then every 2 weeks for 2 months, then monthly for rest of study
  – Discuss problems, answer questions, reinforce training
  – Train new workers (turnover)
ACT4: Cluster randomized RCT

Monitoring progress – through Repeat Cascade analyses

• Experience in a clinic in Manaus, Brazil
• Bottlenecks appeared in sequence as problems in the earlier steps were solved.
1st Trimester results: Contacts Identified, but nothing further

Problem Identified - no PPD and no TST training
2\textsuperscript{nd} Trimester results: Contacts tested but not evaluated

Problem identified - Chest X-rays not available
3rd Trimester results: No contacts starting treatment

Problem discovered - MDs did not prescribe INH treatment
4\textsuperscript{th} Trimester Results: All problems identified and resolved (at least partially)
Conclusions and Implications

• Losses before starting LTBI therapy result in much greater reduction in public health benefit than patient non-adherence to therapy

• Improving the cascade of care requires systematic investigation of the HOW and WHY of losses at each step

• We are evaluating a method to improve Latent TB management in low income and high income countries:
  – Identifying the local barriers
  – Selecting solutions to overcome those barriers
  – Training and ongoing support
  – Repeated evaluation to monitor progress, and identify persistent, or new problems
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**McGill Coordinating Team:**
Olivia Oxlade  
Chantal Valiquette  
Federica Fregonese  
Saeedeh Moayedi Nia  
Hannah Alsdurf  
Mei Xin Li  

**Benin:**
Menonli Adjobimey & Severin Anagonou  

**Brazil:**
Anete Trajman & Mayara Bastos  

**Ghana:**
Joseph Obeng  

**Vietnam:**
Greg Fox,  
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