What’s new in TB/HIV treatment?

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Chair, WHO HIV/TB Working Group
The landscape

- We know that EFV based ART regimen is compatible with TB treatment and works well
  - HIV integrase inhibitors can also be given with TB treatment and provide another option for those who cannot take EFV

- We know when ART should be started in TB cases 2-8 weeks to reduce morbidity and mortality

- We know that TB IRIS complicates management and requires clinician support

- We have one new drug for MDRTB that can be used with patients receiving ART, and many in the pipeline
  - We need to continue to advocate to have persons living with HIV included in new TB drug development
To succeed in reducing HIV/TB deaths... from a treatment perspective

- We need to have the capability to start ART promptly (2-8 weeks) in all patients with HIV/TB
  - Including those the MDRTB
  - Including children
  - Including special populations
To review – the key data on ART start

- Waiting beyond 8 weeks to start ART after TB treatment start is associated with increased DEATH.
- Those patients with less than 50 CD4 cells have increased DEATH for every day they delay ART starting from 2 weeks after TB therapy start.
- Starting ART at 2 weeks (compared to 8 weeks)
  - Does not jeopardize success of ART
  - Does not jeopardize success of TB treatment
  - Is not associated with more toxicity
  - Is associated with higher IRIS, but the protective effects of AIDS/Death outweigh this effect
- The one exception to early ART start is TB meningitis (and cryptococcal meningitis) when ART should be delayed to 8-10 weeks
WHO Policy– ART in setting of TB

- All HIV-positive TB patients eligible for ART, regardless of CD4+ count
- ART initiated as soon as possible after the start of TB treatment
- At 2 weeks when CD4<50 and no later than 8 weeks
  - Do not delay ART while waiting for CD4+ count
Its all about delivery now...
Those at risk for death: HIV/TB Care Cascade

- Acquire TB
- Diagnosed with TB
- Prescribed adequate TB treatment
- Begin ART (within 2 weeks of TB diagnosis)
- Complete TB regimen + ART Adherence
- Transition to long-term HIV care

UNDIAGNOSED + LOST TO FOLLOW UP = INADEQUATE CARE
What are the steps? Scenario 1: The hospitalized patient

- Patient severely ill
- Patient enters hospital
- TB is diagnosed
- TB therapy is started
- HIV and lab testing, counseling and ART prep education is performed
- CTX and ART are started within 2 weeks
- Patient leaves hospital
- Patient returns to TB clinic, HIV clinic or both
- Patient registered for HIV services/ lifelong care
- Patient provided support and management for HIV/TB care including IRIS
- Monitoring data are captured for HIV and TB reporting
- Household members screened for HIV and TB
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- Both TB and HIV diagnostics in hospital
- TB therapy is available and started (including second line for those with suspected multidrug resistance)
- ART is available in the hospital
- ART is provided to the patient upon discharge
- There is clear system of followup in HIV/TB with a safety net
- There are monitoring systems to capture this complex scenario
### What are the steps? Scenario 1: The hospitalized patient

<table>
<thead>
<tr>
<th>Brothers and Sisters</th>
<th>THE DOCTOR</th>
<th>THE SYSTEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>I don’t want to go to the hospital</td>
<td>Person severely ill</td>
<td>Both TB and HIV diagnostics in hospital</td>
</tr>
<tr>
<td>Who will care for my children?</td>
<td>Person enters hospital</td>
<td>TB therapy is available and started (including second line for those with suspected multidrug resistance)</td>
</tr>
<tr>
<td>Do I have to pay for Xray or lab tests?</td>
<td>TB is diagnosed</td>
<td>ART is available in the hospital</td>
</tr>
<tr>
<td>I am too tired to go to another clinic</td>
<td>TB therapy is started</td>
<td>ART is provided to the patient upon discharge</td>
</tr>
<tr>
<td>They are not welcoming in the clinic</td>
<td>HIV and lab tests performed</td>
<td>There is clear system of followup in HIV/TB with a safety net</td>
</tr>
<tr>
<td>Why do I have to go to 2 clinics? The wait is too long</td>
<td>CTX and ART is started</td>
<td>There are monitoring systems to capture this complex scenario</td>
</tr>
<tr>
<td>I don’t want to take all these pills. Is the this way it will always be?</td>
<td>Person leaves hospital</td>
<td></td>
</tr>
<tr>
<td>I don’t want to tell my husband</td>
<td>Person returns to TB clinic, HIV clinic or both</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Person registered for HIV services/ lifelong care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Monitoring data are captured for HIV and TB reporting</td>
<td></td>
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<tr>
<td></td>
<td>Household members screened for HIV and TB</td>
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**THE DOCTOR**
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- Monitoring data are captured for HIV and TB reporting
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**THE SYSTEM**
- Both TB and HIV diagnostics in hospital
- TB therapy is available and started (including second line for those with suspected multidrug resistance)
- ART is available in the hospital
- ART is provided to the patient upon discharge
- There is clear system of followup in HIV/TB with a safety net
- There are monitoring systems to capture this complex scenario
What are the steps? Scenario 2: The TB clinic patient

- Person ill
- Person goes to health care center, TB suspected*
- TB is diagnosed (TB clinic*)
- TB therapy is started*
- HIV testing is performed (HIV+) *
- ART is started at TB clinic* OR
- Person sent to HIV clinic*
- Registration at HIV clinic*
- ART counseling and baseline labs*
- Person starts ART within 2-8 week time frame*
- Person completes TB therapy at TB clinic*
- Monitoring data are captured for HIV and TB reporting*
- Household members screened for HIV and TB *
What are the steps? Scenario 2: The TB clinic patient

- Patient ill
- Patient goes to health care center, TB suspected
- TB is diagnosed (TB clinic)
- TB therapy is started
- HIV testing is performed (HIV+)
- ART is started at TB clinic OR Patient sent to HIV clinic
- Registration at HIV clinic
- ART counseling
- Patient starts ART
- Patient completes TB therapy at TB clinic
- Monitoring data are captured for HIV and TB reporting
- Household members screened for HIV and TB

- TB diagnostics that detect cases in HIV+ population/HIV testing
- TB therapy is available and started (including second line for those with suspected multidrug resistance)
- TB clinic trained to deliver ART/CTX
- ART can be started within 8 weeks is provided to the patient upon discharge
- There is clear system of followup in HIV/TB with a safety net
- There are monitoring systems to capture this complex scenario
What are the steps? Scenario 3: The HIV or PMTCT clinic

- Patient goes to initial or routine clinic
- TB screenin performed, TB suspected*
- TB is diagnosed
- Patient is sent to TB clinic
- TB therapy is started*
- Patient continues HIV care at primary clinic*
- ART counseling and baseline labs* if not done
- Patient starts ART within 2-8 week time frame*
- Patient completes TB therapy at TB clinic*
- Monitoring data are captured for HIV and TB reporting*
- Household members screened for HIV and TB *
What are the steps? Scenario 3:
The HIV or PMTCT clinic

- Patient goes to initial or routine clinic
- TB screening performed, TB suspected*
- TB is diagnosed
- Patient is sent to TB clinic
- TB therapy is started*
- Patient continues care at primary clinic*
- ART counseling/labs* if not done
- Patient starts ART within 2-8 weeks*
- Patient complete TB therapy at TB clinic*
- Monitoring data are captured for HIV and TB reporting*
- Household members screened for HIV and TB *

- TB diagnostics that detect cases in HIV+ population/HIV
- TB therapy is available and started (including second line for those with suspected multidrug resistance)
- ART can be started within 8 weeks or revised as needed
- There is clear system of followup in HIV/TB with a safety net
- There are monitoring systems to capture this complex scenario
Why is it important to discuss these scenarios?

- Our goal is to improve things for the patient -- reduce morbidity and mortality. Achieving this goal dependent on a FUNCTIONAL HIV/TB care cascade
  - Examining the cascade highlights the complexity for the patient that should simplified when possible
  - Examining the cascade highlights the bottlenecks
  - Monitoring the cascade predicts the likelihood we can achieve our goal

- The architecture, challenges and solutions for bottlenecks will depend on the setting
What do we know about the HIV/TB treatment Cascade?

- Countries are beginning to examine performance for all of HIV, for MTCT, for TB/HIV
- These strategies do not examine the time to start of ART which is CRITICAL in HIV/TB
  - Time to start ART not standard data collection metric
  - Measurement of lost to followup suspect unless rigorous methods utilized
- Some research groups are now beginning to evaluate time to ART start and barriers

ART in TB treatment can be delivered at either HIV or TB clinics
We should support both models
Cascade of TB/HIV services (by end of 2012)

- Number of registered TB patients (all types): 103,578
- TB patients receiving HIV test: 68,259
- TB patients diagnosed HIV-positive: 4,775
- Number received treatment for both TB and HIV: 2,232
- No. still receiving ART: n.a
- No. receiving VL: n.a
- VL suppressed: n.a

Testing coverage still limited

Do not receive ART although active TB/HIV diagnosed

Associate Professor Dr. Bui Duc Duong,
Deputy Director of Vietnam Authority of HIV/AIDS Control, Ministry of Health
Cascade of TB/HIV (2012): Cambodia

- No. newly registered TB (incl. known HIV): 40,214
- No. HIV test results recorded (incl. known HIV): 32,557
- No. HIV+ TB cases: 1,657
- No. ART during TB treatment: 1,267
- Retention (12 months): No. receiving VL: No. VL suppressed: 0

National HIV/AIDS and STI Programme Managers Meeting for Asian Countries in the Western Pacific Region 25-28 February 2013, Kunming
South Africa: Uptake and Barriers to starting ART in TB patients

34% eligible for ART did not start

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0019484

Pepper, PLOS One, 2011
## Risk Factors for Not Starting ART in TB patients

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No ART (n = 34)</th>
<th>ART (n = 66)</th>
<th>P-value</th>
<th>aOR</th>
<th>(95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>24 (71)</td>
<td>30 (45)</td>
<td>0.017*</td>
<td>3.7</td>
<td>(1.25–10.95)</td>
<td>0.018*</td>
</tr>
<tr>
<td>Age &lt;36 years, n (%)</td>
<td>24 (71)</td>
<td>31 (47)</td>
<td>0.025*</td>
<td>3.3</td>
<td>(1.12–9.69)</td>
<td>0.031*</td>
</tr>
<tr>
<td>CD4+ count &gt;100 cells/μL, n (%)</td>
<td>14 (41)</td>
<td>16 (24)</td>
<td>0.080</td>
<td>1.6</td>
<td>(0.54–4.87)</td>
<td>0.384</td>
</tr>
<tr>
<td>No TMP-SMX chemoprophylaxis, n (%)</td>
<td>3 (9)</td>
<td>2 (3)</td>
<td>0.208</td>
<td>2.4</td>
<td>(0.84–7.08)</td>
<td>0.102</td>
</tr>
<tr>
<td>Previous tuberculosis, n (%)</td>
<td>16 (47)</td>
<td>14 (21)</td>
<td>0.008*</td>
<td>3.2</td>
<td>(0.33–31.68)</td>
<td>0.311</td>
</tr>
<tr>
<td>Diagnosis of TB at clinic, n (%)</td>
<td>21 (62)</td>
<td>33 (50)</td>
<td>0.264</td>
<td>1.9</td>
<td>(0.47–7.32)</td>
<td>0.378</td>
</tr>
<tr>
<td>No extra-pulmonary tuberculosis, n (%)</td>
<td>24 (71)</td>
<td>32 (48)</td>
<td>0.035*</td>
<td>2.3</td>
<td>(0.73–7.53)</td>
<td>0.151</td>
</tr>
<tr>
<td>Drug susceptibility test results known at TB diagnosis, n (%)</td>
<td>13 (38)</td>
<td>13 (20)</td>
<td>0.045*</td>
<td>2.1</td>
<td>(0.67–6.39)</td>
<td>0.209</td>
</tr>
<tr>
<td>Weight less than 50 kilograms</td>
<td>13 (38)</td>
<td>17 (26)</td>
<td>0.214</td>
<td>1.1</td>
<td>(0.35–3.61)</td>
<td>0.851</td>
</tr>
<tr>
<td>No clinical deterioration, n (%)</td>
<td>14 (41)</td>
<td>20 (30)</td>
<td>0.277</td>
<td>2.2</td>
<td>(0.73–6.86)</td>
<td>0.158</td>
</tr>
<tr>
<td>Admission to hospital, n (%)</td>
<td>18 (53)</td>
<td>32 (48)</td>
<td>0.673</td>
<td>2.6</td>
<td>(0.70–9.50)</td>
<td>0.155</td>
</tr>
</tbody>
</table>

*P<0.05 considered statistically significant, Model likelihood ratio: P = 0.003, R² = 0.2235.

aOR: adjusted odds ratio, 95% CI: 95% confidence interval. ART: antiretroviral treatment. TB: tuberculosis. TMP-SMX chemoprophylaxis: daily trimethoprim-sulfamethoxazole chemoprophylaxis 160/800 mg.

doi:10.1371/journal.pone.0019484.t002

Male gender and age <36 years risk for not starting ART

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0019484.t002
What about timing of starting ART? ... South Africa

- 2010 in Capetown
- 497 with HIV/TB
- 274 “eligible” for ART
- 220 start ART – 54 did not

- Time to start 51 days (IQR 29-77)
- Only 58% started ART within 8 weeks of TB treatment
- Only 12.7% with CD4<50 started within 2 weeks

ART initiation in TB patients in Uganda

ART initiation - by year of TB

N=886

Preliminary data, courtesy of Geng, et al
Obstacles/Gaps to address

- **Structural**
  - Inpatient/outpatient gaps
  - Access to ART dispensing systems (i.e., in TB clinics)

- **Patient barriers**
  - Knowledge
  - Structural barriers (transport, wait time)
  - Psychosocial issues
  - Relationship with provider

- **Provider barriers**
  - Knowledge
  - Attitudes
  - IRIS management

- **No “official” measurement system for time to ART start**
Summary

- There is a major gap between knowledge and practice for ART uptake (especially need to rapidly start ART) in patients with HIV and TB.
- We are not measuring a key outcome in country monitoring plans (time to ART start).
- There is increasing recognition at country level that attention needs to be put into HIV/TB ART start.
- This area is a potential high impact area for the HIV/TB working group to address.
- Implementation science research can be very informative to guide practices.