4th Global Laboratory Initiative partners Meeting

Progress Report – TB CARE II

Refiloe Matji
17-19th April, 2012
Outline

• Epidemiological status of TB in Malawi and Bangladesh
• Main challenges in TB control
• Progress on the implementation of new technologies including the Algorithms for the roll-out of Xpert MTB/RIF
• TB CARE II Support for diagnostics expansion
• Lessons learnt to date
• Way Forward
Malawi

- Population: 14M
- 21,092 cases notified in 2010
  - New Sm+ve PTB: 7,240
  - New Sm-ve PTB: 8,245
  - Retreatment cases: 2,194
- Treatment success 89%
  - Died 7%, Failed 1%, Default 2%
- HIV prevalence 12%
  - HIV testing: 88%
- TB/HIV co-infection: 63%
Progress to date – Malawi

• HTC uptake among TB patients has increased from 65% in 2006 to 86% in 2010.
• ART uptake among TB/HIV co-infected patients increased from 19% in 2006 to 54% in 2010.
• CPT uptake > 90%
• From 2004 to 2011, the number of microscopy centres has increased from 88 to 229 while treatment sites have increased from 50 to 108.
• Malawi intends to replace LM with LED microscopes from now onwards.
Major Diagnostic Challenges in Malawi

- Chronic laboratory personnel shortage
- High TB/HIV co-infection rates pose diagnostic challenges
  - mortality among TB/HIV co-infected patients estimated at 15%.
- Despite the increase in number of TB treatment sites (108), the number is greatly outpaced by ART sites currently at 417 sites throughout the country.
  - Disparity partly contributes to low ART uptake among TB patients.
- Long TAR for Culture & DST> 8 weeks resulting in a number of MDR-TB patients dying before treatment initiation due to:
  - Centralized C & DST at national level only;
  - Weak specimen referral system
  - C & DST predominantly LJ based
Highlights for 2011 – Malawi

• MGIT 960 liquid culture machine recently procured through Global Fund Grant

• National policy to phase in LED microscopes from 2011 onwards (replacing worn out LMs).
  – 54 LED microscopes installed in 2012 (CDC/HUTAP, TB CARE II)

• 12 health facilities currently have in place 4-module Xpert machines from (TB REACH, TB CARE II, PIH, COM)

• Skills update – laboratory assistants and over 80 microscopists trained (NTP, TB CARE II etc)
Case finding activities – Malawi

• **Facility-based**
  – Establish “Drop-in” TB corners
  – Routine screening of inpatients
  – Improve recording and reporting of TB suspects

• **Community-based**
  – Community sputum collection points
  – Active case finding (e.g. household contacts)
  – Adherence support and defaulter tracing
Xpert MTB/RIF implementation

• To optimize the use of Xpert MTB/RIF, Algorithm prioritizes PLHIV, Retreatment cases, MDR TB suspects & hospitalized TB suspects
• All patients diagnosed with Rif resistance are initiated on empirical MDR-TB treatment while awaiting conventional Culture & DST
Drug-resistant tuberculosis

- Program to support for increased diagnosis of RR TB at district level
- Designate MDR TB treatment sites in specific districts
- C-PMDT
  - Outpatient clinic visits
  - Home-based DOT
  - Social support
Challenges with Xpert Implementation

– Failure to adhere to the diagnostic algorithm
– High burden sites (urban facilities & central hospitals) still not yet equipped with GeneXpert machines
– MGIT liquid culture machine still not yet operational to support the rapid testing & diagnosis of MDR TB
– Ongoing severe economic crisis in the country may jeopardize the initiative
– Availability of funding for cartridges in the future
Xpert MTB/RIF

TB Suspect

MDR-TB Suspect?

Y

Xpert MTB/RIF

N

Submit 2 quality sputum samples

MDR-TB Suspect?

Y

SS +?

N

Treat for TB

Y

Treat for TB
Facility with Xpert – Central & District Hospital Level

Offer HIV Testing & Counseling to **ALL** Suspects

**Danger Sign**

- **No**
- **Yes**

**Hospitalize**

**Sputum Microscopy**

- **Yes**
- **No**

**Smear Positive**

- **Yes**
- **No**

**Treat for TB**

**Xpert MTB/RIF**

- **Yes** (continue to “acting on Xpert Results Algorithm”)
- **No**

**Culture & DST for Retreatment & MDR Suspects**

USAID TB CARE II PROJECT
Footnotes for “Facility with Xpert”

1. A **TB Suspect** is defined as a person who reports any one of the following current symptoms of any duration:
   - Cough, Fever, Weight Loss or Night Sweats

   If a person has a NEGATIVE HIV test documented within the last 3 months, the following alternative definition applies:

   - Productive cough OR fever for more than 2 weeks with or without respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss > 5%, night sweats).

   Among children, a TB suspect is defined as a person who reports one of the following symptoms: poor weight gain, fever, current cough or history of contact with a known or suspected TB case.

2. A **Retreated TB Case** is defined as a person who has received TB treatment previously and starting CAT II treatment after failing treatment with first-line drugs, being diagnosed with TB relapse or returning after default.

   An **MDR suspect** is defined as a patient from one of the following risk groups:
   a. Persons who develop active TB after known exposure to a patient with documented MDR_TB or thought to have MDR_TB
   b. All patients who remain smear-positive after 2 months of therapy with first-line drugs
   c. New patients coming from areas with high prevalence of MDR (e.g. certain parts of South Africa, Lesotho etc.)
   d. Any patient in whom there is significant clinical concern for acquired resistance

3. **Danger signs** include: respiratory rate > 30 per min, temperature > 39°C, heart rate > 120 beats per minute, respiratory distress, systolic blood pressure <90mmHg, patient confused, agitated, inability to walk unassisted.

4. For seriously ill patients with danger signs, the key treatment is life-saving supportive therapy with oxygen, IV antibiotics and IV fluids (if the patient is in septic shock). The patient should be hospitalized immediately at the nearest facility that can provide this treatment. If such services are not available at the initial point of care, the patient should be transferred to the next highest-level facility, preferably one with GeneXpert to accelerate the TB diagnostic process.

5. SS = Sputum Smear examination

6. All retreatment suspects should submit sputum samples simultaneously for GeneXpert and for culture and first-line DST.

7. All retreatment cases & MDR suspects should submit sputum samples simultaneously for Xpert AND for culture and first-line drug susceptibility testing before starting treatment
Facility without Xpert –
But in an Xpert District

Offer HIV Testing & Counseling to **ALL** Suspects

Danger Sign\(^3\)?

- **No**
  - Sputum Microscopy
    - Smear Positive?\(^5\)
      - **Yes**
        - Treat for TB
          - TB unlikely but NOT ruled out\(^8\)
          - Assess for other diagnoses
          - CPT + ART Eval if HIV POS\(^9\)
          - Complete antibiotic course
      - **No**
    - **No**

- **Yes**
  - Hospitalize

- **Yes**
  - Xpert MTB/RIF\(^6\)
    - (continue to “acting on Xpert Results Algorithm”)
    - Culture & DST for Retreatment & MDR Suspects\(^10\)
    - Treat for bacterial infection &/or PCP\(^7\)
    - Detailed Follow-up Clinical Evaluation
    - **Still with symptoms?**
      - **Yes**
        - **Assess for other diagnoses - CPT + ART Eval if HIV POS**
        - **Complete antibiotic course**
      - **No**

- **No**
  - **Hospitalize**
  - **Still with symptoms?**
    - **Yes**
      - **Assess for other diagnoses - CPT + ART Eval if HIV POS**
      - **Complete antibiotic course**
    - **No**
Footnotes for “Microscopy Center without Xpert”

1. **TB Suspect** is defined as a person who reports any one of the following current symptoms of any duration:
   - Cough, Fever, Weight Loss or Night Sweats

   If a person has a NEGATIVE HIV test **DOCUMENTED** within the last 3 months, the following alternative definition applies:
   - Productive cough OR fever for more than 2 weeks with or without respiratory symptoms (shortness of breath, chest pains, hemoptysis) and/or constitutional symptoms (loss of appetite, weight loss > 5%, night sweats).

   Among children, a TB suspect is defined as a person who reports one of the following symptoms: poor weight gain, fever, current cough or history of contact with a known or suspected TB case.

2. **Retreated TB Case** is defined as a person who has received TB treatment previously and starting CAT II treatment after failing treatment with first line-line drugs, being diagnosed with TB relapse or returning after default.

   **An MDR suspect** is defined as a patient from one of the following risk groups:
   a. Persons who develop active TB after known exposure to a patient with documented MDR_TB or thought to have MDR_TB
   b. All patients who remain smear-positive after 2 months of therapy with first line drugs
   c. New patients coming from areas with high prevalence of MDR (e.g certain parts of South Africa, Lesotho etc.)
   d. Any patient in whom there is significant clinical concern for acquired resistance

3. **Danger signs** include: respiratory rate > 30 per min, temperature > 39°C, heart rate > 120 beats per minute, respiratory distress, systolic blood pressure <90mmHg, patient confused, agitated, inability to walk unassisted.

4. For seriously ill patients with danger signs, the key treatment is life-saving supportive therapy with oxygen, IV antibiotics and IV fluids (if the patient is in septic shock). The patient should be hospitalized immediately at the nearest facility that can provide this treatment. If such services are not available at the initial point of care, the patient should be transferred to the next highest-level facility, preferably one with GeneXpert to accelerate the TB diagnostic process.

5. Depending on the local circumstances, the patient’s preference and the clinician’s judgment either the patient or a sputum sample may be referred to the nearest facility with GeneXpert.

6. **SS=Sputum smear microscopy**

7. Treat with antibiotics (except fluoroquinolones) to cover typical and atypical bacteria and/or high-dose trimethoprim-sulfamethoxazole to treat PCP according to the Malawi Standard Treatment Guidelines (MSTG). Clinical response to treatment for bacterial pneumonia or PCP does not automatically exclude a diagnosis of TB as both may occur in patients with underlying TB. Patients should be re-evaluated for TB, particularly if symptoms persist after treatment.

8. A TB diagnosis is NOT definitively ruled out by a negative sputum smear examination and negative chest x-ray. Advise the patient to return if
Acting on Xpert Results

**Xpert MTB/RIF**

1. **Xpert MTB+/RIF+**
   - Contact MDR-TB Focal Clinician
   - Start MDR-TB Treatment Immediately³
   - ART + CPT if HIV POS⁴
   - Submit additional sputum for C&DST⁵
   - Ensure TB IC Measures are in place

2. **Xpert MTB+/RIF-**
   - Treat for TB
   - ART + CPT if HIV POS⁴

3. **Xpert MTB-/RIF-**
   - ART + CPT if HIV POS⁴

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1. **Xpert MTB-/RIF-**
   - Detailed clinical assessment for EPTB AND other diagnoses
   - Treat for bacterial infection AND/OR PCP²
   - PTB still suspected?

   - Yes: Suggestive of PTB?
     - Yes: Treat for TB
       - ART + CPT if HIV POS⁴
     - No: No Improvement
       - TB unlikely but NOT ruled out
       - Reassess for other diagnoses
       - ART Assessment + CPT if HIV POS⁵
       - Complete Antibiotics Course
   - No: Treat underlying cause of symptoms
   - Chest X-Ray ⁶

2. **Condition on Repeat Clinical Evaluation**
   - Improvement
     - TB unlikely but NOT ruled out
     - Reassess for other diagnoses
     - ART Assessment + CPT if HIV POS⁵
     - Complete Antibiotics Course
   - Worse OR No Change
     - Hospitalize if danger sign⁸
     - Detailed clinical assessment for EPTB AND other diagnoses
     - Perform 2nd Xpert MTB/RIF
     - Consider Empiric TB Rx
     - Consider sending sample for C&DST
     - ART Assessment + CPT if HIV POS⁵
     - Complete Antibiotics Course
Footnotes for “Acting on Xpert Results”

1. Additional investigations for extra-pulmonary TB may include abdominal ultrasound, biopsy of lymph node or skin lesions for histopathology and culture of lymph node aspirate, sputum, CSF, pleural fluid, ascites and/or urine.

2. Treat with antibiotics (except fluoroquinolones) to cover typical and atypical bacteria and/or high-dose trimethoprim-sulfamethoxazole to treat PCP according to the Malawi Standard Treatment Guidelines (MSTG). Clinical response to treatment for bacterial pneumonia or PCP does not automatically exclude a diagnosis of TB as both may occur in patients with underlying TB. Patients should be re-evaluated for TB, particularly if symptoms persist after treatment.

3. While there is a risk of a false-positive test result for rifampicin resistance given the low background prevalence of MDR-TB in Malawi, immediate initiation of treatment is recommended due to benefit of preventing death, not delaying treatment in true positive cases and preventing transmission of MDR-TB. Health workers should request an additional sputum sample from patients for culture and DST against first-line drugs to confirm the diagnosis of MDR-TB. However, if a patient tests positive for Rifampicin resistance WITHOUT a prior history of TB treatment, discuss the case with the MDR-TB focal clinician before initiating treatment with second-line drugs.

4. CPT= Cotrimoxazole preventive therapy. ART = antiretroviral therapy. An ART assessment includes WHO clinical staging and/or CD4 count to assess ART eligibility. All TB patients living with HIV are eligible for ART irrespective of CD4 count. Start TB treatment first, followed by ART as soon as possible within the first 2 weeks of TB treatment. See National ART guidelines.

5. All patients testing positive for rifampicin resistance by GeneXpert should submit an additional sputum specimen for conventional culture and DST against first-line drugs to confirm the diagnosis of MDR-TB. However, if a patient tests positive for Rifampicin resistance WITHOUT a prior history of TB treatment, discuss the case with the MDR-TB focal clinician before initiating treatment with second-line drugs.

6. A chest x-ray can assist with the diagnosis of pulmonary and extrapulmonary TB and help with evaluation for other causes of respiratory symptoms.

7. A TB diagnosis is NOT definitively ruled out by a negative sputum smear examination and negative chest x-ray. Advise the patient to return if symptoms recur.

8. Danger signs include: respiratory rate > 30 per min, temperature > 39°C, heart rate > 120 beats per minute and inability to walk unassisted.
# XPERT MTB/RIF

<table>
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<th>No.</th>
<th>XPERT MTB/RIF SITE</th>
<th>No of samples tested (Dec 2011 to January 2012)</th>
<th>MTB +</th>
<th>RIF+</th>
<th>Staff Trained on XPERT MTB/RIF Operation</th>
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Way forward

- Evaluation of Xpert scale up & impact planned
- Strengthening of specimen transportation network
- In-service microscopists need to undergo further skills development in line with evolving technologies (LED & Xpert MTB/RIF scale up)
- Need for technical & financial support Malawi to maintain EQA with SNRL
Bangladesh: Epidemiology

(Estimates from WHO)

- Population: 148 million
- Incidence rate (all cases: 225/100K/yr)
- Prevalence rate (all cases: 411/100k/yr)
- Mortality rate: 43/100k/yr
- Ranks 6th among the 22 HBC
- Ranks 10th among 27 HB MDR TB countries
- Estimated % of MDR TB among new cases: 2.1%
- Retreatment cases: 28%
Epidemiology (Cont.2)

• New cases:
  • Sm+ve PTB: 98948
  • Sm-ve PTB: 21920
  • EP TB: 27335

• All categories of retreatment cases:
  – Relapses: 2702
  – Failures: 886
  – Defaulters: 320

• Others: 3460

• Total case finding: 155571
Treatment outcome: 2010

New Smear positive cases: 105659

- Cured: 90.45%
- Treatment completed: 1.18%
- Treatment success: 91.62%
- Died: 3.84%
- Failure: 0.83%
- Defaulter: 1.75%
- Transfer out: 1.87%
- Non evaluated: 0.09%
HIV: Bangladesh situation

- First HIV case in the country was detected in 1989.
- Bangladesh still a low HIV prevalent country in the region with prevalence < 1% among MARP.
- Estimated number of HIV infected is 7,500

- Total number of reported cases until Dec 2011: 2533 (cumulative)
- Total number of HIV infected people develop AIDS until 2011: 1101
- Total AIDS death: 325
- Total number of new infection in 2011: 445
- Total number of HIV infected people develop AIDS in 2011: 251
- Total number of AIDS death in 2011: 84

*Source: NASP*
Major challenges in TB control

- Sustaining the hard earned gain and maintaining quality
- Management of drug resistant TB
- Diagnosis of EP TB/Smear negative/Child TB
- TB/HIV co-infection
- Urban TB control
- Health system strengthening including MIS
- Continuation of funding (GF, USAID etc.)
Challenges (Cont.2)

– High burden sites (division level & some district level hospitals) still not yet equipped with GeneXpert machines
– LPA & MGIT liquid culture machine still not yet operational to support the rapid testing & diagnosis of MDR TB
– Availability of funding for cartridges in the future
Technological platforms

NTRL (National)
RTRL (Regional)
Intermediate (EQA)
Peripheral (MC)
Progress on Diagnostic issues

LED microscope: 22 placed and functional. 70 (50 TBCARE II and 20 GF) more will be placed in 2012.

Line Probe Assay: LPA will be placed at NTRL supported by Expand TB Project. TBCARE II Project supported renovation work. Tentative timeline is May 2012.

Liquid culture: LC supported by Expand TB Project and will be placed in NTRL. Tentative timeline is July 2012.

GeneXpert: Two machines installed at NTRL and RTRL Chittagong. 10 more will be installed by July 2012 and will be placed in all divisional level and some big district Chest disease clinics.
Available Xpert MTB/RIF in Bangladesh

Private diagnostic Centers-2011
   03

TB REACH-ICDDRdB (2011)
   4

NTP Bangladesh (TB CARE II project support)
Functional: 2 (2012)
Pipeline: 10 (2012)
NTP plan for distribution of GeneXpert MTB/RIF

Lab name:
- NTRL: 01
- Shamoly: 01
- Sylhet CDC: 01
- RTRL Ctg: 01
- Khulna: CDH: 01
- Netrokona DF: 01
- Tangail Jalsatro DF: 01
- RTRL Rajshahi: 01
- Rangpur CDC: 01
- Barisal CDC: 01
- Jessore CDC: 01
- Pabna CDC: 01
Diagnostics algorithms for MDR TB

MDR TB SUSPECTS

- **GXP positive**
  - Rifampicin susceptible: **Treat as TB**
    - As per NTP guidelines
    - Collect one sputum specimen for a repeat GXP/LPA
  - Rifampicin resistant: **Line probe assay (LPA)**
    - **Treat as MDR-TB**
      - Refer to MDR-TB Unit
    - Follow up with microscopy
  - Rifampicin unsuccessful: **Repeat GXP**
    - **GXP positive**
      - Rifampicin unsuccessful: **Treat as TB**
        - as per National guidelines
        - Collect one specimen for microscopy Culture & DST / LPA
      - Rifampicin unsuccessful: **Treat as TB**
        - as per National guidelines
        - Collect one specimen for microscopy Culture & DST / LPA
  - GXP unsuccessful: **Collect one specimen for culture and LPA or culture and DST (for R and H)**
    - **LPA/ DST results Resistant to R only**
    - **LPA/ DST results Resistant to R and H**
      - **Treat as MDR TB**
        - As per NTP guidelines
        - Review culture results

HIV positive: Collect one sputum specimen for a repeat GXP/LPA

- **GXP negative**
  - **Collect one specimen for culture and LPA or culture and DST (for R and H)**

USAID TB CARE II PROJECT
# Xpert MTB/RIF experience in NTP, Bangladesh

### Laboratory name: NTRL
Installation date: 23.03.12

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<th>Drug history</th>
<th>suspects</th>
<th>MTB/RIF resistant</th>
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### Laboratory name: RTRL
Installation date: 08.04.12

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<td>06</td>
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For validation: 10 tests done with known results
Total suspects tested: 59
MTB/RIF detected: 25
Future needs for laboratory as a priority

- Switch over from light to LED fluorescence microscope
- Equipment maintenance and calibration
- EQA strengthening
- Biosafety level 3 laboratory (National level)
- Quality Management System for laboratory
- Accreditation of NTRL and RTRLs (ISO certification)
- Capacity building
Support from TB CARE II Globally

- Development of training materials
- Development of job aids
- Purchase of machines, installation & renovation
- Analysis of data
- Ensuring that patients are initiated on treatment
- Identifying future needs
- Ensuring sustainability, especially drugs
General Lessons learnt Globally

- Acceptance of new technologies
- Fear of additional cases diagnosed
- Advocacy to support new technology
- Commitment for funding (additional machines, cartridges and Drugs)
- A need to develop a pamphlet on FAQs (Lab related and facility related questions)
- Use of the Technology in 2 different settings
  - High HIV burden
  - High MDR TB burden

Question:
- Identify what proportion of patients who were found to be RR and true MDR TB cases?
Susceptible & Resistant TB
Susceptible and Resistant TB suspects
Susceptible and Resistant TB suspects

Availability of drugs (1\textsuperscript{st} & 2\textsuperscript{nd} line drugs)
Prompt Initiation of treatment
Cure the patients & reduce TB transmission

Susceptible and Resistant TB suspects

Availability of drugs (1st & 2nd line drugs) Prompt Initiation of treatment
Happy and Healthy children
“Stop TB in my life Time”
Acknowledgements

- USAID & WHO
- GLI team
- Bangladesh and Malawi NTP staff
- TB CARE II staff
- The Health Care Workers