Xpert MTB/RIF use for TB diagnosis in TB suspects with no significant risk of drug resistance or HIV infection

Results of Group Work

DOTS expansion and enhancement
Objective

• This group deals with the majority of TB suspects and patients
• Most patients needing immediate and more specialized/ additional care are excluded into HIV and DR-TB algorithms
• Primary objective is for early and increased case detection
  – Smear negatives are difficult to diagnose and current algorithm not being practiced
• Global level broad guidance but decisions at country level
  – Promote countries to develop models
Consensus...1

1. Introduction of Xpert should include district level, or sub-district level facilities, preferably, but not limited to, facilities with quality CXR / (public and private)

   - Discussion points for the agreement:
     • Epidemiological situation / individual patient risk factors / level of health system
     • Public health goals versus individual patient care
     • PAL and health system links
     • NTPs and Partners will buy machines – guidance required on where and how to use them given the cost of cartridges
Consensus…2

2. For all health facilities develop country level models and test them (public and private)

   Consider:
   - Local context of flow patterns for patient, specimen and result
   - Balance between decentralization, local needs, hardware feasibility
   - Prioritization is a country level decision
     - Consider SS- suspects, abnormal CXR
     - Amongst SS- decide which risk groups require Xpert on a priority
     - Do not exclude pediatric, private sector, etc.
Consensus…..3

3. Diagnostic algorithms
People with suspected TB

1. HIV status
2. DR-TB risk

Risk of DR-TB (e.g., TB Rx history >1m, DR-TB suspect) irrespective of HIV status

1. HIV- or unknown HIV status in low HIV setting
2. Not significant risk for DR-TB
3. Not seriously ill

Follow TB/HIV algorithm

1. HIV+
2. Unknown HIV in high HIV setting

Follow DR-TB algorithm

Quality CXR available and accessible (e.g., district level)

Microscopy center

CXR

CXR Normal

Further Clinical Management**

CXR abnormal

XPERT MTB/RIF

No TB

Resul

TB+ No Rif Res

Follow DR algorithm / repeat Xpert

TB+ Rif Res

Resul

SS-

SS+

Treat with FLD

**TB diagnosis can not be totally ruled out, particularly for the TB suspects who have normal CXR and did not undergo any bacteriological examination. For this specific category of patients, a sputum smear examination may be needed.
Absolute Increases in bacteriologically identified Case Detection Assuming 15% C+ in a Population of 10,000 TB Suspects

- **Absolute TB Cases detected**
  - Standard (SS only): 1070
  - Xpert: 1550
  - SS Xpert: 1687
  - CXR, Xpert: 1403

- **Absolute True Positives**
  - Standard (SS only): 900
  - Xpert: 1380
  - SS Xpert: 1350
  - CXR, Xpert: 1352

- **Number of Xpert tests done**
  - Standard (SS only): 10000
  - Xpert: 8930
  - SS Xpert: 4020
  - CXR, Xpert: 4020

- **PPV = Positive Predictive Value**
  - Standard (SS only): PPV = 84%
  - Xpert: PPV = 89%
  - SS Xpert: PPV = 80%
  - CXR, Xpert: PPV = 96%
People with suspected TB

1. HIV status
2. DR-TB risk

Risk of DR-TB (e.g. TB Rx history >1m, DR-TB suspect) irrespective of HIV status

Facility with Xpert as well as quality CXR (result) available and accessible

CXR

CXR Normal

CXR abnormal

XPERT MTB/RIF

TB+
Rif Res

TB+
No Rif Res

No TB

Treat with FLD

Follow DR algorithm
repeat Xpert

Follow TB/HIV algorithm

Follow DR-TB algorithm

1. HIV+
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Footnotes to algorithms

• Algorithm is for adults
• Seriously ill patients are not included
  – Likely to be a very small proportion – will require quick and appropriate clinical management, including referral for hospitalization.
• Process of diagnosis to be completed on a single day
Opportunities

• For reemphasising policy
  – On front loaded microscopy; HIV testing for TB suspects; PAL

• Health system related
  – Investing on CXR
  – Use of Xpert for other diseases
  – Human resource benefit from Xpert
  – Engaging private sector

• CXR
  – QA, new X-ray technology, automated reading technology
  – Collecting evidence on CXR containing algorithm as a whole

• Strengthening specimen referral system
• Improving quality assurance of smear microscopy
• Improving availability of drugs for additional patients
• Electronic notification, data storage, inventory
Unresolved issues

- Diagnostic algorithm for pediatric TB
- Case definitions and treatment outcome definitions
- Treatment monitoring tool
  - Need to preserve smear in monitoring of TB treatment
- Scaling up availability of quality Xray – Health system issue
- Xpert in low burden setting / active case finding
  - Role of screening tests, or repeat Xpert to increase PPV
- Regulatory issues related to Xpert
Operational research questions

- Reassess the definition of TB suspect
- Proportion of TB suspects with CXR already available & quality of CXRs
- Cost and CE of different algorithms and definitions of TB suspect
- Impact of the whole algorithm in different settings and risk groups
  - Additional yield, sensitivity, specificity and predictive values
  - Impact on treatment and patient management
  - Impact on access to care by different socio-economic groups
- Performance of Xpert in remote and peripheral settings
- Performance of Xpert in pediatric TB suspects
- Use and results of screening tests in the FIND demonstration studies
- Impact of automated, electronic notification from Xpert machines for improving patient care and engaging all care providers using Xpert

- In addition, basic minimum data to be collected within programatic M&E
- OR questions should not impede scaling up
Private sector and Xpert

- PPM subgroup to work on this and form a global task force
- In addition, include in the discussion with the manufacturer:
  - Creating inventory of Xpert machines supplied to private sector
  - Use the incentive of negotiated pricing of cartridges/machines for linking private providers to NTP
Key next steps

• Finalize algorithm and guidance
• Announce WHO policy
• Disseminate policy and guidance to countries and donors
• Provide technical assistance
Thanks
CXR considerations

• CXR is a good screening test, not a diagnostic test
• In many settings a large proportion of TB suspects already have a CXR done
  – Because of clinical practice for management of patients with respiratory symptoms, both in public hospitals and private sector
• Benefits of using CXR to screen TB suspects prior to Xpert:
  – increases pre-test probability and therefore PPV for Xpert;
  – reduces the number of Xpert test (cost) by screening out TB suspects with normal CXRs
Assumptions and principles

Beyond the current algorithm for improved early case detection

• Intensified early case detection of **all TB cases** is essential for TB control
• **Delays and patient costs** need to be substantially decreased
• Beyond finding the appropriate place of Xpert in the current algorithms, we also need to **re-consider the whole algorithm**, including potentially changed role of microscopy and X-ray for screening, diagnosis and case categorization.
• X-ray is already widely used. It is a poor tool for diagnosis of TB, but a good TB screening tool, if used correctly.
• There are other new tools in the pipeline that may be more relevant in low MDR settings

Principles in the ISTC and patient charter

• "To prove a diagnosis of tuberculosis, every effort must be made to identify the causative agent of the disease." (ISTC-2)
• "All persons with chest radiographic abnormalities should have sputum specimens submitted for TB laboratory examination." (ISTC-4)
• The diagnosis of TB should be provided free of cost to the patient (Patient Charter), this includes the cost of microscopy, CXR, Xpert MTB/RIF and culture.
• Prompt notification of all definite TB cases, including those diagnosed by Xpert, should be done by all care providers (ISTC-17)