Implementation of Xpert MTB/RIF®:
Experience of Republic of Moldova

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Antalia, Turkey
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# TB Epidemic Breakdown

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Value</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case notification rate, per 100,000 inhabitants</td>
<td>114.3</td>
<td>2012</td>
</tr>
<tr>
<td>TB mortality, per 100,000 inhabitants</td>
<td>14.4</td>
<td>2012</td>
</tr>
<tr>
<td>Case detection rate, %</td>
<td>64.6</td>
<td>2012</td>
</tr>
<tr>
<td>DOTS treatment success rate, %</td>
<td>62.2</td>
<td>2011</td>
</tr>
<tr>
<td>DOTS treatment default rate, %</td>
<td>8.5</td>
<td>2011</td>
</tr>
<tr>
<td>MDR rate among new TB cases, %</td>
<td>24.2</td>
<td>2012</td>
</tr>
<tr>
<td>MDR rate among retreatment TB cases, %</td>
<td>62.0</td>
<td>2012</td>
</tr>
<tr>
<td>DOTS+ treatment, success rate, %</td>
<td>51.5</td>
<td>2009</td>
</tr>
<tr>
<td>DOTS+ treatment, default rate, %</td>
<td>23.2</td>
<td>2009</td>
</tr>
</tbody>
</table>
TB Incidence and Mortality, 1991-2012

- **Tb incidence - Rate/100000**
- **TB Mortality - Rate/100000**
Resistance Profile among All TB Cases 2012, %

- MDR TB: 43%
- Sensitive all FLD: 40%
- Mono DR: 7%
- Poli DR: 10%

98.6% of cases with resistance to RIF (913 / 926) are MDR
Achievements in TB Diagnosis

• Well developed TB laboratory network
• 4 level III laboratories, 59 microscopy centers, sputum collection points
• DSM, culture (LJ, MGIT), DST to FLD and SLD; LPA, genotyping
• Specimen transportation system
• Internal and external quality assurance
• Universal coverage with culturing and DST ensured
Challenges in TB diagnosis

• Delays in full diagnosis were common
• Delays in initiation of correct treatment according to resistance profile
• These all contribute to—
  – Further spread of drug resistance
  – Amplification of drug resistance
Moldova TB REACH Project (1)

• **Scope of laboratory strengthening**
  • Maintain full and universal coverage with TB and DR-TB diagnosis
  • Increase the speed of diagnosis of resistance
  • Improve the link between diagnosis and treatment

• **Objectives**
  • Rapidly roll out Xpert MTB/RIF to peripheral (district) level
  • Address the needs of populations at risk and with limited access to services: prisoners, PLHIV, transient population
  • Cover 70% of population
Moldova TB REACH Project (2)

Thirty Gene Xpert instruments—28,000 tests for 1.5 years

- 25 in the civilian TB services
- 3 in penitentiary institutions
- 2 in AIDS centers
Moldova TB REACH Project—Step One: Distributed and Installed Equipment
Step Two—Trained Staff
Step Three—Approved the New Algorithm and Define Target Group for Testing

EXAMINATION OF DIFFERENT GROUPS OF PATIENTS FOR TB DIAGNOSIS (SS Microscopy - Xpert MTB/RIF)

1. PATIENTS with TB clinical symptom (all who are nor include in p.2)

   Sputum Smear MICROSCOPY
   
   RESULTS
   
   SSM Negative*
   SSM repeated
   SSM Negative, Rn=Norma.
   Other diseases
   
   SSM Positive
   Culture method LJ
   M SSM Negative, Clinical&Rn - TB??
   Culture -negative; Clinical&Rn – NonTB

2. Rapid Diagnostic of TB, including MDR TB, of patients with high risk of TB developed*

   Xpert MTB/RIF
   
   RESULTS
   
   TB
   Xpert negative
   Xpert +RIF-Sens
   Xpert+RIF=Rez
   BACTEC
   Xpert- negative BACTEC- neg
   MDR TB?
   MTBDRsL

2. Rapid Diagnostic of TB, including MDR TB, of patients with high risk of TB developed

   A. Patients with TB symptoms, who had contact with TB MDR;
   B. Children with TB symptoms, in special from contact with TB MDR;
   C. HIV positive patients, with TB symptoms;
   D. Patients from prison, with high risk to be infected with MDR TB;
   E. Vulnerable groups: homeless, drug users, immunosuppressive, memorializes;
   F. Groups of enhanced risk that have suggestive TB symptoms, -medical workers from labs, or the ones who take care of the MDR TB patients;
   G. Patients with suspected of relapse of TB, but with repeated SSM results negative;
   H. Patients with clinical symptoms of extrapulmonary TB
Step Four—Changed Request Form, Registers, and Recording Forms

**SOLICITANT**: unitatea medicală / secția ......................................................... / .............................................Tel..................
- Medic ................................................................. Nr. de expediere secție............................................................

**PACIENT**: NPP ................................................................. Sex........... data nașterii (z/l/a) .........../......./........
- Raionul.................................. Localitatea................................. Strada................................. Nr........................
- IDNP .................................................................
- Motiv examinare: □ Diagnostic*............. □ Urmărire tratament/luni tratament ............ □ Altele (se indică) ................
- Tip pacient: □ Caz nou □ Recidivă □ Abandon □ Eșec □ Altele (se indică) ................
- Clasificarea afecțiunii: □ Pulmonară □ Extrapulmonară □ Altele (se indică) 

**PROBA**: Data colectării sputei (z/l/lun/an) ........... / ........ / .......
- Tip produs patologic: □ Sputa □ Altele (se indică) .................................................................

**LABORATOR**: Primit: data......................................................... ora.................. de către ...........
- Conformitate la recepție: DA NU Detalii................................. Aspectul vizual al sputei: □ Salivar □
- Mucopurulent □ Purulent □ Hemoptic

**REZULTATUL ANALIZEI**
1. Microscopia Zeihl-Neelson
2. Microscopia Fluorescentă
3. Xpert MTB/RIF

<table>
<thead>
<tr>
<th>Data</th>
<th>Proba</th>
<th><strong>Microscopia</strong></th>
<th><strong>Xpert MTB/RIF</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Zeihl-Neelson</strong></td>
<td><strong>Fluorescentă</strong></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Step Five—Made Changes in National TB Database
Number of Tests by Quarter, All Sites, abs

Q1: 1526
Q2: 2682
Q3: 4065
Q4: 5160
Q5: 3366
Q6: 2426
Xpert MTB/RIF positive rate

MTB+ results as percentage of total valid results

- MTB+: 82%
- MTB-: 18%
Xpert MTB/RIF Investigations

- MTB+ / RIF S: 2%
- MTB+ / RIF R: 63%
- MTB+ / RIF Indeterminate: 35%
Xpert MTB/RIF Added Value to Smear Microscopy

Sputum samples results as percentage of MTB+ GX results with valid microscopy results

- SS+ 56%
- SS- 44%
Share of HIV+ Results

Percentage of HIV + results among MTB+ GX results with Valid HIV Test Results

84% HIV+
12% HIV-
4% Not done / unknown
Pulmonary vs. Extrapulmonary

<table>
<thead>
<tr>
<th></th>
<th>Positive results</th>
</tr>
</thead>
<tbody>
<tr>
<td>extarpulmonare</td>
<td>9.5</td>
</tr>
<tr>
<td>pulmonare</td>
<td>22.4</td>
</tr>
</tbody>
</table>

- 327 samples (extarpulmonare)
- 2012 samples (pulmonare)
Share of Invalid Tests, Percentage of Total Tests

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.6%</td>
<td>Invalid Results</td>
</tr>
<tr>
<td>94.4%</td>
<td>Valid Results</td>
</tr>
</tbody>
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Challenges Based on Early Implementation

• Substantial lead time was required to start (logistics), taking into account the number and specifics of project sites

• A key problem at the initial stages had been slow uptake of the new technology by clinical staff (at all levels)

• Universal access to diagnosis (rapid method) contributed to high number of patients enrolled, but treatment coverage is limited
Planned vs. Enrolled

<table>
<thead>
<tr>
<th>Year</th>
<th>Planned</th>
<th>Enrolled</th>
</tr>
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<tbody>
<tr>
<td>2010</td>
<td>586</td>
<td>791</td>
</tr>
<tr>
<td>2011</td>
<td>555</td>
<td>763</td>
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<tr>
<td>2012</td>
<td>535</td>
<td>853</td>
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<td>2013</td>
<td>660</td>
<td>740</td>
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<tr>
<td>2014</td>
<td>630</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td>180</td>
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Conclusions based on early implementation of Xpert MTB/RIF

is sensitive and specific for detection of TB
- increased case detection of TB
- improved the quality of rapid TB diagnosis
- facilitated earlier diagnosis
- usefulness in the diagnosis of extrapulmonary TB
- reduced time-to-initiation TB treatment
- contributed to enroll the high number of patient in treatment and
- increased procurement of drugs
- fortified the infection control measures and
- decreased the transmission infection in hospitals
Thank you!