Implementation of Xpert MTB/RIF in Republic of Moldova

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Chisinau, Republic of Moldova
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• **Population**: 4.0 million
• **Surface**: 33.7 thousand sq. km
• **Population growth**: -0.08% (est.)
• **Life expectancy**: 70.8 years
• **Population below poverty line %**: 29.5
• **GDP (US$)**: 5.328 billion
• **GDP per capita (US$)**: 2.400
• **Migration**: 360,000–800,000 persons

TB incidence, abs
TB incidence - Rate/100000
Tb Mortality, abs
TB Mortality - Rate/100000

National health insurance
100% DOTS

Shortages in public health financing, including TB service

DOTS
DOTS Plus

NTP, 2001 - 2005
NTP, 2006 - 2010
NTP, 2011-2015
MDR TB, new cases and retreatment, R. Moldova, 2003 – 2011, %

- %MDR TB Primar
- %MDR TB Secundar
The rate of XDR TB among the patients with TB resistance. R. Moldova, 2006 - 2011

The number of patients with XDR TB. R. Moldova, 2006-2011

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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</thead>
<tbody>
<tr>
<td>MDR TB cases</td>
<td>605</td>
<td>822</td>
<td>1202</td>
<td>1141</td>
<td>1150</td>
<td>947</td>
</tr>
<tr>
<td>XDR TB cases</td>
<td>1</td>
<td>6</td>
<td>13</td>
<td>9</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>
Causes of TB epidemic in Moldova

1. Socio-economical crisis

2. Massive migration of population

3. Unemployment;

4. Shortages in public health financing, including TB service:
   a) deficiency of the cooperation between the TB service and both, Primary Health Care and Public Health Centers;
   b) insufficient support of implementation and inadequate financing of the programme;
   c) lack of antituberculosis drug supply during 1996-2001

5. Tuberculosis in prisons

6. High levels of MDR-TB
Reasons of TB Resistance in Moldova

1. Poor infection control in TB hospitals
2. Low compliance of treatment
3. The lack in surveillance of the treatment (~ 60% of DOT)
4. Very low treatment success rate of new and re-treatment TB (52,4%)
5. Increasing of number of patients with TB/HIV co-infection;
Our achievements in TB control
THE STRUCTURE OF THE TUBERCULOSIS CONTROL SERVICE

COUNTRY COORDINATION MISSION – CCM
Government of R. Moldova

Ministries

- Finances
- Justice
- Social Protection
- Education

Ministry of HEALTH

Technical Working Group of MoH in TB

NATIONAL TB PROGRAM
Director of Program - National TB Coordinator

Phthisiopneumology Institute

1 level

Teritorial TB Cabinets

National TB Reference Laboratory

2 level

TB Hospitals

Regional Reference Labs

3 level

Primary Health Care

Centers of Preventive Medicine
SIME TB

electronic system for notification of TB cases – clinicians&laboratory

Local level

- Case registration fill-in
- Unconditional automatic transfer
- Case evidence form transfer
- Synchronization of data (dictionaries, access levels, security)
- Case evidence for specific institution

Central level

- Case registration fill-in
- System maintenance

SIME TB database
## Task of TB laboratory services

### LEVEL 1
**Microscopy Centers**

1. TB Diagnosis, follow-up treatment SSM
   - Receipt of specimens
   - Preparation and staining SSM
   - ZN microscopy /recording
   - Reporting of results
   - Maintenance of lab register
   - Management reagen& supplies
   - Internal QC

2. Send samples for culture to RL or NRL

3. Participate in EQA for SSM

**Location:** TB cabinets municipaly/raionaly (59)
**Staff:** 1-2 persons
**Workload:** ~2000 SSM/year
**Coverage:** ~100,000 pop.

### LEVEL 2
**Reference laboratory**

1. All functions of level 1 for SSM + FA

2. Diagnosis of TB by culture (classic LJ+BACTEC)
   - Decontamination specimen
   - Isolation and identification *MTB*

3. DST for 1&2 line drugs

4. EQC for MC (EQC panel, monitoring visit)

5. EQA for culture & DST

6. GenoType® MTBDRplus

**Location:** Reg. TB Hospitals
**Staff:** 7-13 persons
**Workload:** ~10,000 SSM; ~10,000 culture; ~3000 DST/year
**Coverage:** ~1 mln population

### LEVEL 3
**National TB Reference Lab**

1-6. All functions of level 1&2 Laboratories

7. Identification of MOTT (Probe Tec system+ GenoType® Mycobacterium CM)

8. Develop protocol&guides

9. Organizing trainings

10. M&E visits to RL&MC (NTP)

11. Organize&conduct DRS

12. Conduct research

13. Lab equipment, supplies

**Location:** PPI - NTP
**Staff:** 25 persons
**Workload:** ~25,000 SSM; ~30,000 culture; ~10,000 DST.
**Total investigations:** ~100,000/year
**Coverage:** Countrywide
Implementation of TB rapid methods
R. Moldova

- MGIT 960 - 2005
- ProbeTec - 2008
- MTBDRPlus - 2009
- MTBDRsl - 2011
- MODS - 2011
- Xpert - 2012
- PyroMark - 2012
Country’s eligibility for Xpert MTB/RIF

- The country has extremely **high burden of drug resistance** and increase of TB/HIV co-infection;
- The network of **laboratory services** is well developed and processes the full range of investigations;
- Universal **access to treatment of MDR-TB** and ARV treatment;
- Appropriate **infrastructure** (including power supply, storage space, waste management, etc. as required for the technology)
- Qualified medical **staff**
- Small territory, reliable **transportation**, etc.
Timeline of project Implementation

**Xpert is part of the new NTP 2011-2015**

- **January 2012** - received in country, investigations in NRL
- **February 2012** – in-country staff training
- **February 2012** - TB Reach evaluation visit
- **March 2012** – distributed to all territories (order by MofH)
- **March – April 2012** – installed in place by designated company
- **April 2012** – UPS procurement, should be distributed
- **April 2012** – received QC specimens, tested in NRL, should be distributed in the territories
Equipment distribution

Xpert - 25 equipments (G4 – 9, G2 – 16)
Cartridges - 12000

Civilian TB services – 21 (84%):
- NRL – 2
- Chisinau city – 5
- Regional RL city Balti – 2
- Regional Bender RL Transnistria – 3
- 9 district TB institutions

Penitentiary TB services – 2 (8%):
- Central Prison Hospital Pruncul – 1
- Pre-trial isolators in Chisinau and Balti – 1
- NB: Other penitentiary institutions ‘assigned’ to civilian services in respective areas

AIDS services – 2 (8%):
- Regional AIDS Centre Chisinau ans Balti (Northern part) – 2
**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**

       - Xpert negative
       - Xpert +RIF-Sens
       - Xpert+RIF=Rez

       - **BACTEC**

         - Xpert- negative
         - BACTEC- neg

       - **MDR TB?**

         - **MTBDRsl**

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*If SSM is negative, but other symptoms persist (clinical&Rn) - SSM repeated

**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
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 Localizare

-----------------------------------------------

PROBA: Data colectării sputei (zi/luna/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>Microscopia</th>
<th>Xpert MTB/RIF</th>
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<tr>
<td></td>
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<td>Zeihl-Neelson</td>
<td>Fluorescentă</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
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</table>
## Preliminary results

<table>
<thead>
<tr>
<th>Total</th>
<th>MTB Not detect</th>
<th>MTB RIF –</th>
<th>MTBRIF+</th>
<th>Invalid</th>
<th>No result</th>
</tr>
</thead>
<tbody>
<tr>
<td>184*</td>
<td>118 (63,6%)</td>
<td>35 (19%)</td>
<td>25 (13,6%)</td>
<td>6 (3,3%)</td>
<td>1 (0,5%)</td>
</tr>
</tbody>
</table>

* including 16 extra-pulm.- all neg.  
** main errors 5011, 5007, 5006
## Preliminary results

<table>
<thead>
<tr>
<th></th>
<th>SSM+</th>
<th>SSM-</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB detect</td>
<td>39</td>
<td>7</td>
</tr>
<tr>
<td>MTB Not detect</td>
<td>1</td>
<td>105</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>MGIT+</th>
<th>MGIT-</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB detect</td>
<td>31</td>
<td>4</td>
</tr>
<tr>
<td>MTB Not detect</td>
<td>4</td>
<td>47</td>
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<table>
<thead>
<tr>
<th></th>
<th>LPA MTBDRplus+</th>
<th>LPA MTBDRplus-</th>
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</thead>
<tbody>
<tr>
<td>MTB RIF+</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>MTB RIF-</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>
Some problems

- Lack of the initial training for national trainers
- 1 equipment-damaged
- Lack of tubes for sputum processing in the territories
- Not graduated pipettes in the package – for 0.5 ml, 1 ml.
- Lack of Internet connection in the regions to include all in the networking system

Not resolved Questions

- Errors, invalid tests - should be repeated?
- 1 or 2 sputum per patients?
Challengers and Issues

**MDR-TB treatment**

Challenge to manage the potentially increased number of diagnosed MDR patients

**Funding**

Concerns about funding for next years- project duration

**Equipment maintenance**

After expiration of warranty
Expected outcomes

Implementation of rapid methods for detection TB and tested drug resistance have to improve

- the early diagnostic and decrease the time of appreciate the correct treatment
- the early diagnostic of children
- the infection control and decrease the transmission infection in hospitals
- the treatment success rate
Thank you!