STANDARD of CARE for HIV and COINFECTIONS in EUROPE

Chairs: A. Antinori, A. d’Arminio Monforte, C. Mussini
HIV and Tuberculosis in Eastern Europe

Daria N. Podlekareva

Meeting "Standard of Care for HIV and Coinfections in Europe"
Rome, November 25-16 2014
TB notification rates (per 100,000) European region 2012

ECDC/WHO Regional Office for Europe. Tuberculosis Surveillance and Monitoring in Europe. 2014
Dynamics of TB incidence and mortality rates in Russia 1970 – 2000 (per 100.000)

Factors associated with TB increase in Eastern Europe

• Economic transition and decline
  – Increase in unemployment, impoverishment, crime
  – Malnutrition, crowded housing, alcohol, smoking

• Decline in public health infrastructure
  – Deterioration of TB control service
    • Severe drug shortages and interruptions in supply
    • Delays in diagnosis and treatment
    • Increased rates of progression to active disease
    • Increased mortality rates

• HIV Epidemic

Shilova et al. 2001
Arinaminpathy et al. 2010
MDR-TB in Russian Federation 1999-2010 (%)

Ministry of health Russia, 2010
### Multi-drug resistant TB and Extensively drug resistant TB (MDR-TB and XDR-TB)

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Minsk 2009-2010</th>
<th>Belarus 2010-2011</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>New (n=156)</td>
<td>Previously treated (n=68)</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>47.4</td>
<td>79.4</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>36.5</td>
<td>77.9</td>
</tr>
<tr>
<td><strong>MDR-TB</strong></td>
<td><strong>35.3</strong></td>
<td><strong>76.5</strong></td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>6.1</td>
<td>38.7</td>
</tr>
<tr>
<td>Injectable agents</td>
<td>7.5</td>
<td>32.3</td>
</tr>
<tr>
<td><strong>XDR-TB</strong></td>
<td><strong>2.0</strong></td>
<td><strong>32.3</strong></td>
</tr>
</tbody>
</table>

Skrahina *Eur Respir J* 2012; Skrahina *Bull World Health Organ* 2013
## Risk factors of MDR-TB in Eastern Europe

<table>
<thead>
<tr>
<th>General population:</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Previously treated cases</td>
<td>6.1 (4.8-7.7)</td>
</tr>
<tr>
<td>• Age &lt; 35 years</td>
<td>1.4 (1.0-1.8)</td>
</tr>
<tr>
<td>• History of imprisonment</td>
<td>1.5 (1.1-2.0)</td>
</tr>
<tr>
<td>• Excessive alcohol consumption</td>
<td>1.3 (1.0-1.8)</td>
</tr>
<tr>
<td>• Smoking</td>
<td>1.5 (1.1-2.0)</td>
</tr>
<tr>
<td>• Unemployed due to disability</td>
<td>1.9 (1.2-3.0)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>HIV-positive:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Previously treated cases</td>
<td>7.9 (2.4-6.5)</td>
</tr>
<tr>
<td>• Pulmonary (v. diss. disease)</td>
<td>2.5 (1.2-5.0)</td>
</tr>
<tr>
<td>• History of imprisonment</td>
<td>2.1 (1.0-4.4)</td>
</tr>
</tbody>
</table>

Skrahina *Bull World Health Organ* 2013; *Post J Infection* 2014
A patient with TB from Eastern Europe

• A “typical” TB patient:
  – Drug addict, alcoholic, and “marginalised” person who is also unwilling to be treated or resist treatment by all means
  – Former prisoners and homeless people – main sources of disease and the real breeders of TB

TB physicians, Samara Oblast, Russia
B. Dimitrova et al 2006
Management of Tuberculosis in Eastern Europe

- A large verticalized network of specialized institutes, dispensaries, hospitals, outpatient clinics, sanatoria and rural feldsher points
- In Russia, about 80,000 beds designated specifically for treating patients with TB
- Long hospitalisation period
  - poor infection control
  - high levels of TB transmission among patients and staff
- Long monitoring after successful clinical treatment and of patients with inactive TB
Management of Tuberculosis in Eastern Europe

• Case-finding and diagnostic are based on mass population screening, fluorography, X-rays, TST and to a lesser extent bacteriology

• Classification of TB allows a definition of “chronic TB”

• Limited availability of 2\textsuperscript{nd} – and 3\textsuperscript{rd} –line drugs

• In addition to the standard chemotherapy, other treatments are commonly used:
  – Surgical interventions
  – Artificial pneumothorax
  – Pathogenetic and immune-modulating therapy

K. Floyd et al. 2006
M. Mansfeld et al 2013
Personnal communication
HIV and HIV/TB epidemics in Eastern Europe
Dynamics of TB and HIV epidemics in Russia 1995 – 2012 per 100.000 population

HIV incidence
TB incidence in general population
TB among HIV patients in St.-Petersburg

Panteleev et al. 2011
Tuberculosis among HIV-positive patients: an international prospective observational study
The TB:HIV Study

• Overall objective

To prospectively study long-term clinical prognosis of HIV-positive patients with active TB disease across Europe, and temporal changes and regional differences
Clinical characteristics of 1413 TB/HIV patients at time of TB diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Eastern Europe N = 844</th>
<th>Western Europe N = 152</th>
<th>Southern Europe N = 164</th>
<th>Latin America N = 253</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (median, IQR)</strong></td>
<td>35 (31 - 40)</td>
<td>37 (32 - 48)</td>
<td>42 (33 - 48)</td>
<td>38 (30 - 45)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Gender (female, %)</strong></td>
<td>24.9</td>
<td>44.1</td>
<td>27.4</td>
<td>26.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Ethnicity (white, %)</strong></td>
<td>95.2</td>
<td>26.2</td>
<td>72.3</td>
<td>19.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>CD4 count (median, (IQR))</strong></td>
<td>107 (35 - 254)</td>
<td>149 (35 - 360)</td>
<td>129 (38 - 315)</td>
<td>96 (35 - 289)</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>HIV+ more than 3 months before TB diagnosis</strong></td>
<td>75.2</td>
<td>54.0</td>
<td>60.4</td>
<td>62.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>HIV treatment, cART (%)</strong></td>
<td>16.6</td>
<td>39.5</td>
<td>43.9</td>
<td>35.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>TB Risk Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- IDU (%)</td>
<td>61.1</td>
<td>9.2</td>
<td>29.3</td>
<td>15.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>- In prison in last 2 years (%)</td>
<td>18.6</td>
<td>2.6</td>
<td>4.9</td>
<td>6.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>TB in the past, yes (%)</strong></td>
<td>13.4</td>
<td>10.1</td>
<td>14.5</td>
<td>16.5</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>Current OST, yes (%)</strong></td>
<td>3.7</td>
<td>66.7</td>
<td>48.8</td>
<td>0</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
Management of HIV/TB in Eastern Europe
Organisational set-up of TB services: results from survey

- HIV and TB service at same hospital
- HIV and TB treated by same doctor
- HIV and TB follow-up in same clinic
- Directly observed therapy
- OST available for IDUs

Eastern Europe vs. Western Europe

% of responding clinics

Eastern Europe
Western Europe
p<0.001

M. Mansfeld. EACS 2013
Role of opiate substitution therapy: results from Ukraine

• Methadone maintenance therapy (MMT) was associated with 3-fold higher odds of 90-day retention on TB treatment compared with control group (adjusted OR: 3.05 (95%-CI 1.08-8.66))

• Out of 109 in-patient TB clinics in Ukraine, only 11 provide MMT

Morozova , Int J of Drug Policy 2013
Diagnosis of TB and availability of DST results

- Presumptive TB
- Probable TB
- Definite TB without DST
- Definite TB with DST

Eastern Europe: N=844
Western Europe: N=152
Southern Europe: N=164
Latin America: N=253

p < 0.0001

A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014
Anti-TB drug-resistance among patients with DST results within one month of TB diagnosis

- **Eastern Europe**: N=243
- **Western Europe**: N=66
- **Southern Europe**: N=89
- **Latin America**: N=61

- **Rifampicin resistant/Isoniazid resistant (MDR-TB)**
- **Rifampicin susceptible/Isoniazid resistant**
- **Rifampicin resistant/Isoniazid susceptible**
- **Rifampicin susceptible/Isoniazid susceptible**

A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014
In treatment of MDR-TB, WHO advises

- >4 drugs known/likely to be effective + pyrazinamide
- If possible amikacin, capreomycin or kanmycin plus a fluorquinolone should be core drugs

Lange, for TBNET; *Eur Respir J* 2014; Falzon, *Eur Respir J* 2011
Availability of anti-TB drugs
Reported ‘unlimited access’ to 2nd and 3rd line anti-TB drugs

M. Mansfeld, EACS 2013
Susceptibility of empiric anti-TB treatment in relation to subsequent DST results

Active drugs calculated from comparing empiric anti-TB therapy and subsequently known DST results

A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014
Treatment success among new lab-confirmed pulmonary TB cases in 2011

ECDC/WHO Regional Office for Europe. Tuberculosis Surveillance and Monitoring in Europe. 2014
Mortality among HIV+ patients with a TB diagnosis

Eastern Europe: 33%
Argentina, Southern and Central Europe: 8-14%

Podlekareva, AIDS 2009
Mortality among HIV+ patients with a TB diagnosis in Eastern Europe – influence of MDR-TB

F. Post, J Infection 2014
Mortality among HIV+ patients with a TB diagnosis in Eastern Europe – influence of MDR-TB

Adjusted Cox models:

- MDR: RH: 2.28 (95%-CI 1.00-5.20)
- Disseminated disease: RH: 1.99 (95%-CI 1.10-3.59)

F. Post, *J Infection* 2014
Management of TB and HIV in Eastern Europe

- Treatment for TB and HIV is under different services of Health Ministry and carried out in different hospitals by different specialists
  - TB: Tuberculosis (Phthisiology) service
  - HIV: Infectious disease hospitals
- IDU managed by Narcology service
  - Opiate substitution therapy only limited or unavailable
- Prisons are under Ministry of Internal Affairs
- Limited level of collaboration and data exchange
- Poor outcomes
- Serious surveillance problems

personal communication
A patient with HIV/TB from Eastern Europe
Management history

ID hospital → Specialised TB hospital → Discharged

Consultation of ID doctor on HIV-status and cART

MTB+

TB dispensary for outpatient treatment
AIDS Centre

LOST TO FOLLOW-UP

Other challenges include (but not limited to):
- limited availability of Opiate Substitution Therapy and harm reduction programmes
- Limited social support
There is a need for concerted actions to improve the situation including:

– Strong infection control to stop spread of TB/MDR-TB and HIV infections, intensified case finding

– Availability of rapid TB diagnostic and drug susceptibility tests for TB

– Adequate empiric TB-treatment and subsequent TB-treatment guided by results of drug susceptibility testing
  • unlimited availability of all TB drugs

– Adequate treatment of HIV infection
  • Unlimited cART coverage

– Treatment of concomitant conditions (IDU and HCV)
  • Accounting for local conditions

• Political will and commitment
Acknowledgement

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  – Jens D. Lundgren
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  – Anne Marie W. Efsen
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