



ROME, November 25-26, 2014

AUDITORIUM, MINISTRY OF HEALTH



EACS European
AIDS Clinical Society

MEETING



STANDARD of CARE for **HIV**
and **COINFECTIONS** in **EUROPE**



Chairs: A. Antinori, A. d'Arminio Monforte, C. Mussini



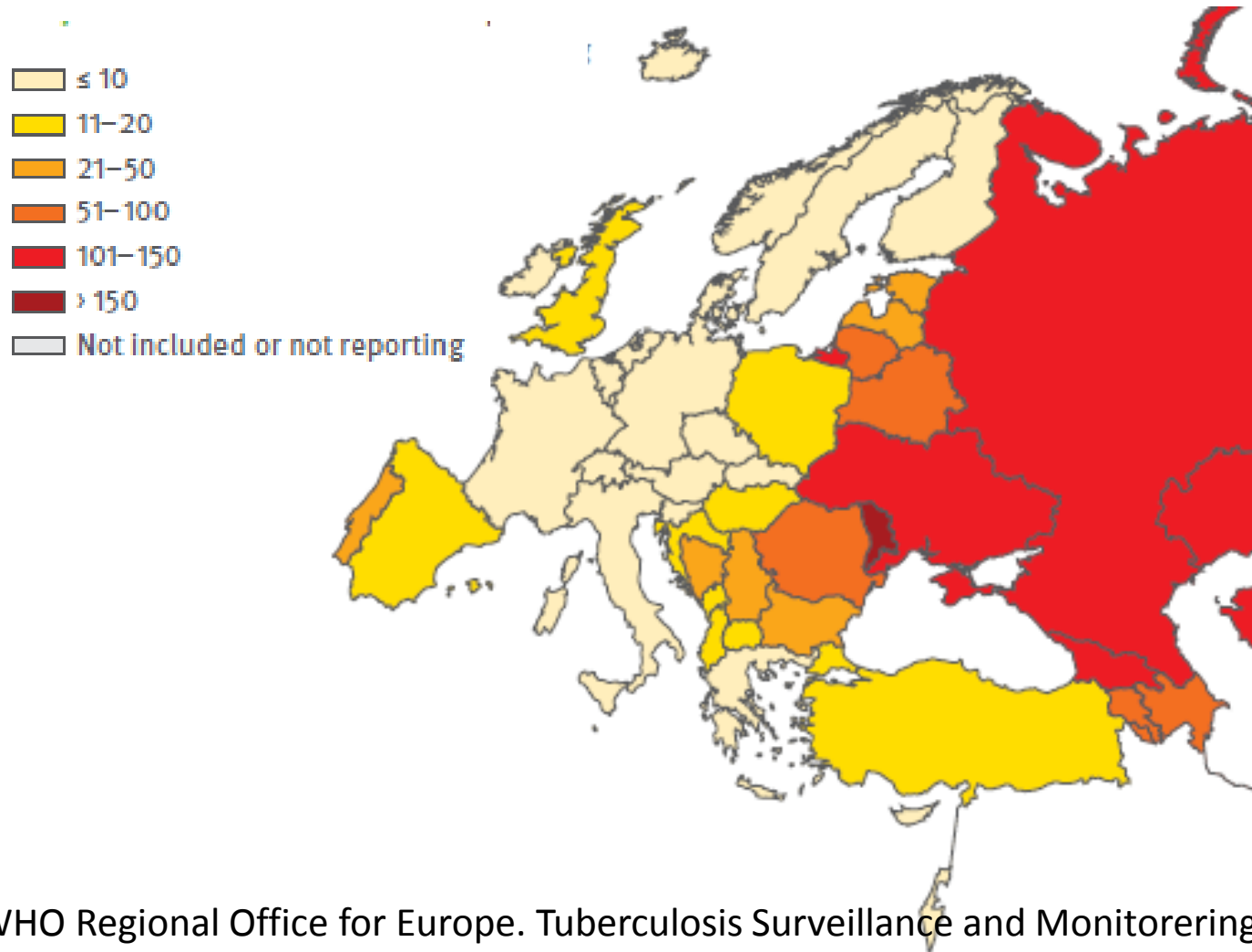
HIV and Tuberculosis in Eastern Europe

Daria N. Podlekareva

Meeting "Standard of Care for HIV and
Coinfections in Europe"
Rome, November 25-16 2014



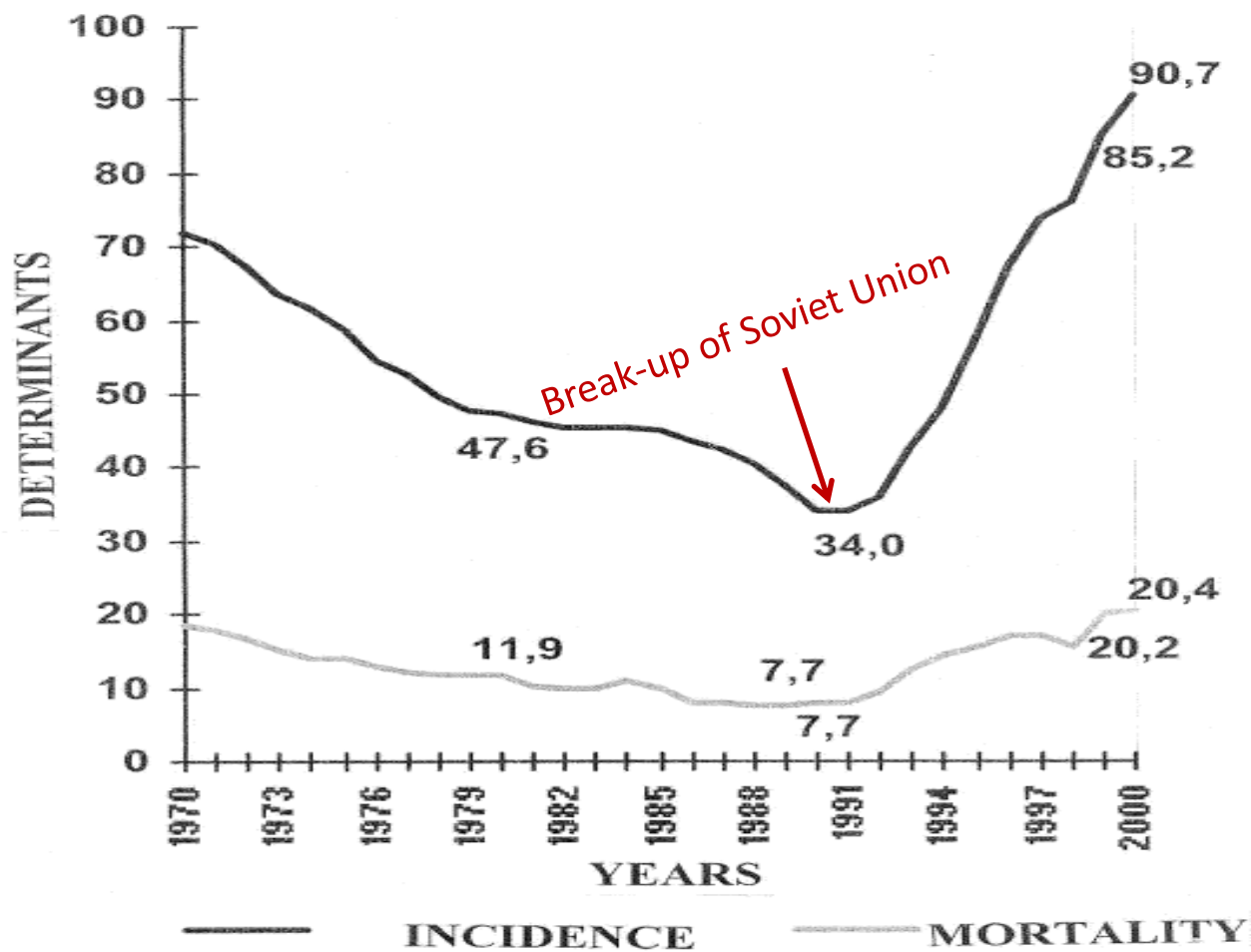
TB notification rates (per 100.000) European region 2012



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)

STANDARD of CARE for HIV
and COINFECTIONS in EUROPE



Shilova et al *Ann.N Y.Acad.Sci.* 2001



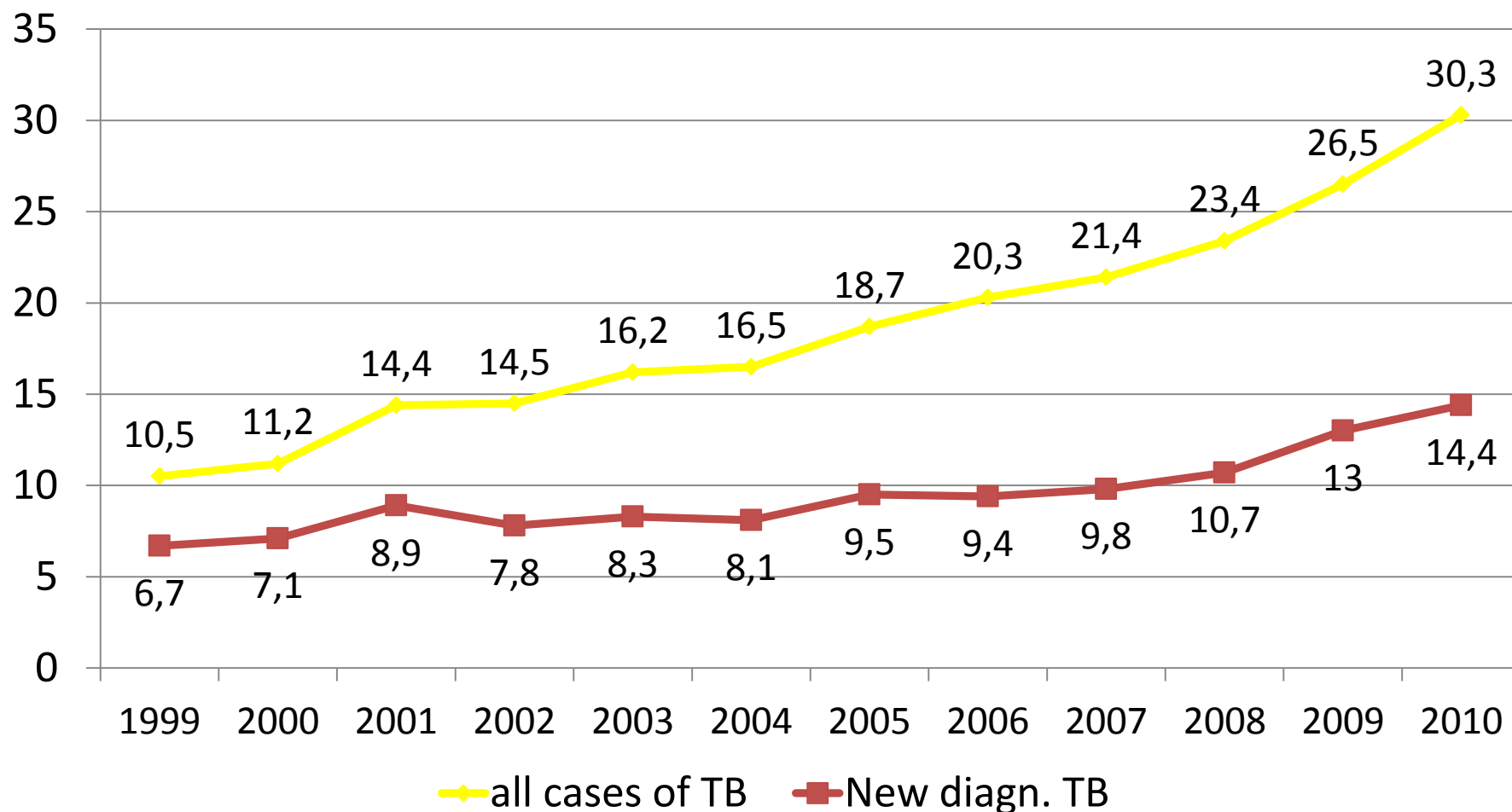
Factors associated with TB increase in Eastern Europe

- 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)

| | Minsk 2009-2010 | | Belarus 2010-2011 | |
|-------------------|--------------------|---------------------------------|----------------------|----------------------------------|
| Resistance | New (n=156) | Previously treated (n=68) | New (n=934) | Previously treated (n=410) |
| Isoniazid | 47.4 | 79.4 | 40.4 | 77.8 |
| Rifampicin | 36.5 | 77.9 | 32.9 | 77.1 |
| MDR-TB | 35.3 | 76.5 | 32.3 | 75.6 |
| Ofloxacin | 6.1 | 38.7 | | |
| Injectable agents | 7.5 | 32.3 | | |
| XDR-TB | 2.0 | 32.3 | | |

Skrahina *Eur Respir J* 2012; Skrahina *Bull World Health Organ* 2013



Risk factors of MDR-TB in Eastern Europe

General population:

- **Previously treated cases**
- Age < 35 years
- **History of imprisonment**
- Excessive alcohol consumption
- Smoking
- Unemployed due to disability

Adjusted odds ratio (95% CI)

6.1 (4.8-7.7)

1.4 (1.0-1.8)

1.5 (1.1-2.0)

1.3 (1.0-1.8)

1.5 (1.1-2.0)

1.9 (1.2-3.0)

HIV-positive:

- **Previously treated cases**
- Pulmonary (v. diss. disease)
- **History of imprisonment**

7.9 (2.4-6.5)

2.5 (1.2-5.0)

2.1 (1.0-4.4)

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 2nd – and 3rd –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

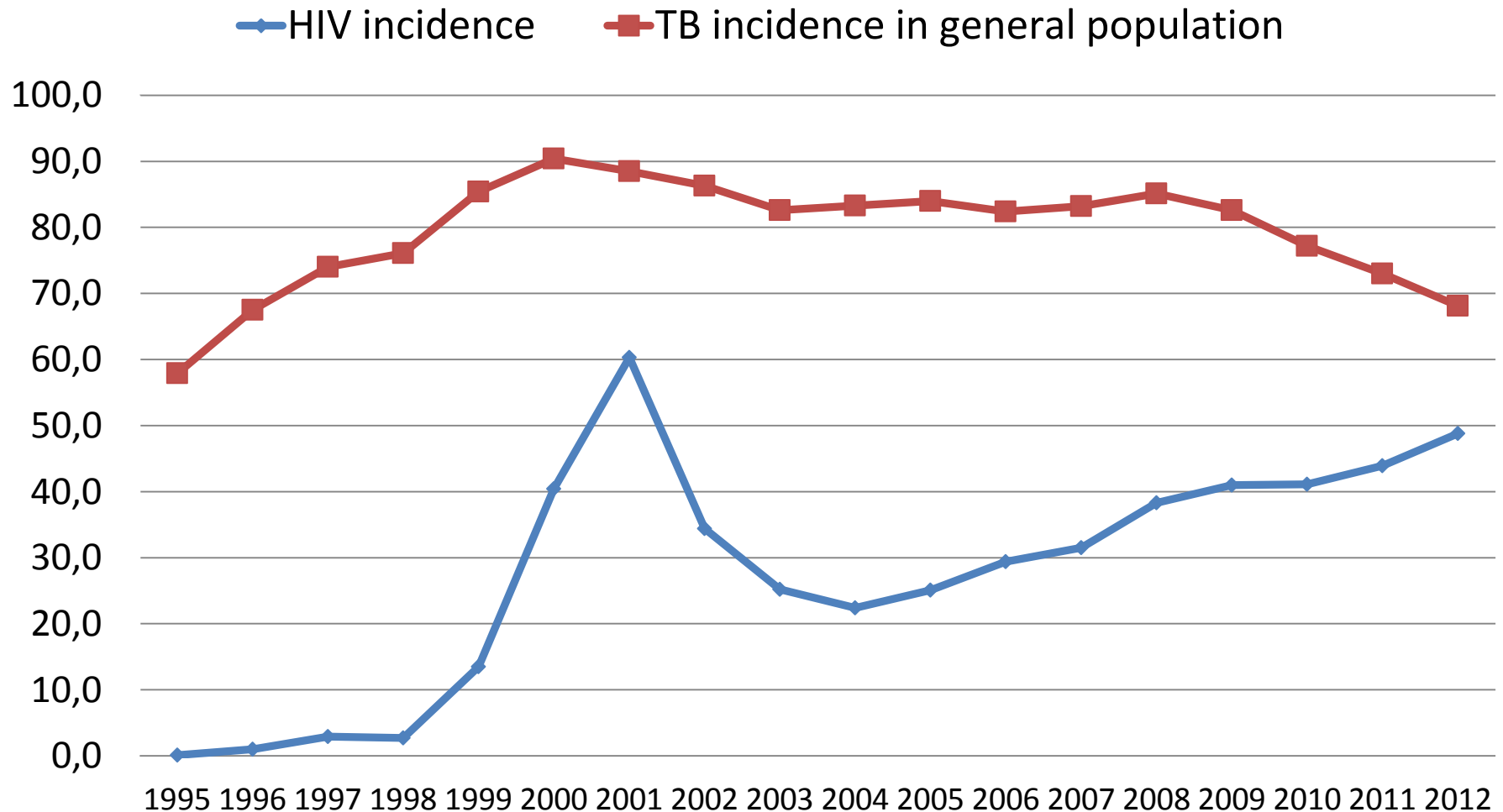


HIV and HIV/TB epidemics in Eastern Europe

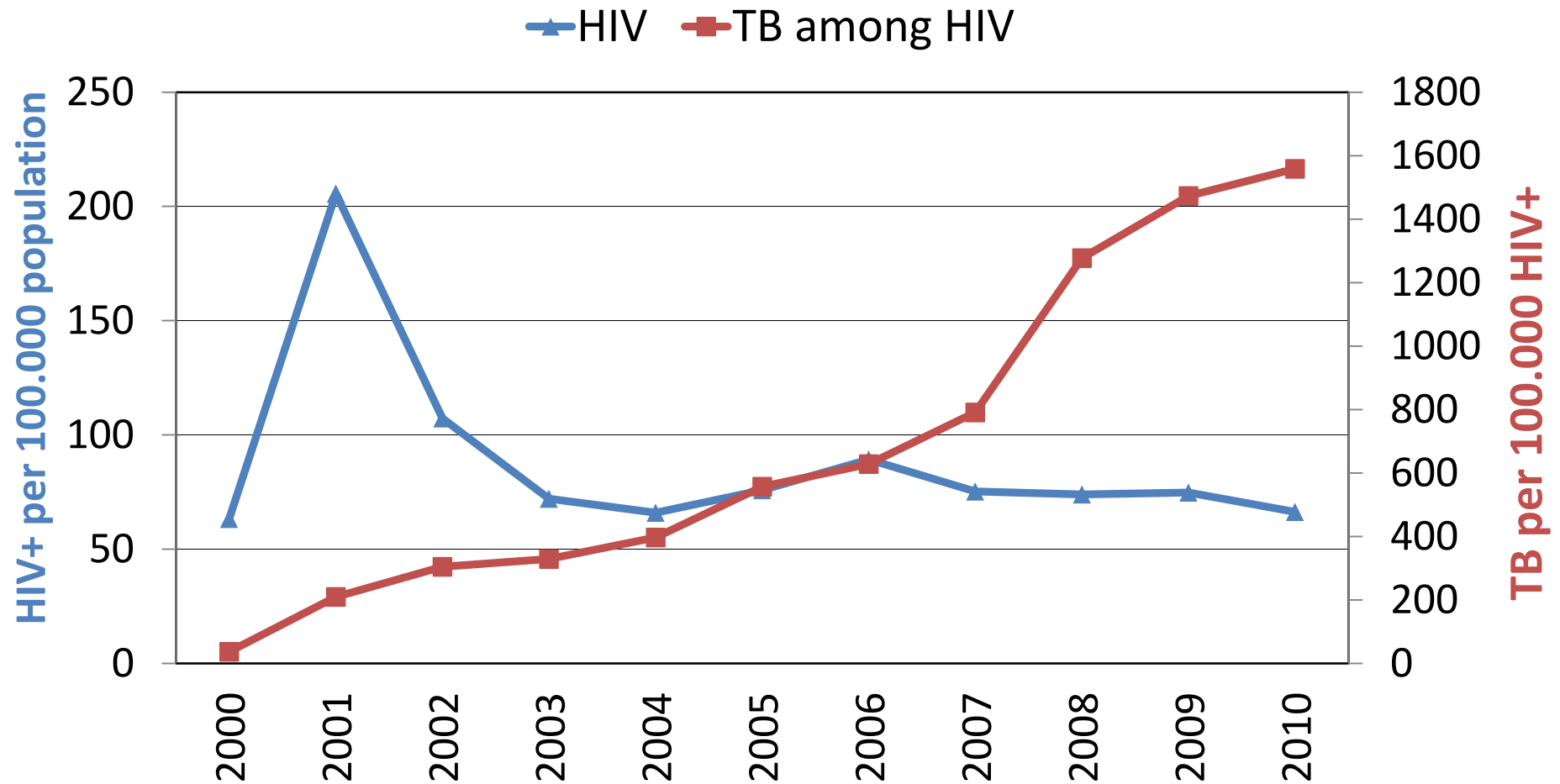


Dynamics of TB and HIV epidemics in Russia

1995 – 2012 per 100.000 population



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



Rigshospitalet



Clinical characteristics of 1413 TB/HIV patients at time of TB diagnosis



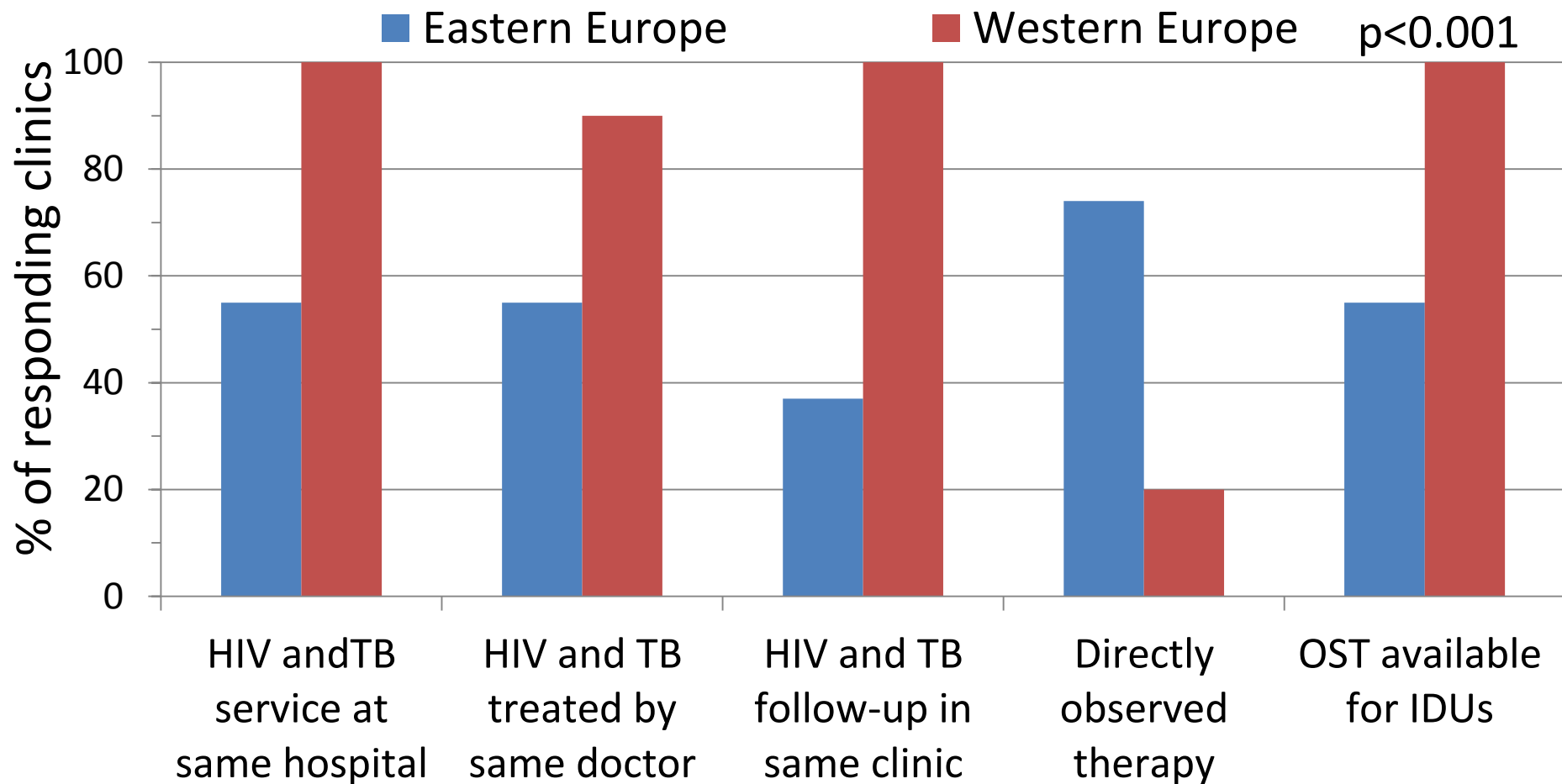
| | Eastern Europe N = 844 | Western Europe N = 152 | Southern Europe N = 164 | Latin America N = 253 | P-value |
|--|------------------------------|------------------------------|-------------------------------|-----------------------------|---------|
| Age (median, IQR) | 35 (31 - 40) | 37 (32 - 48) | 42 (33 - 48) | 38 (30 - 45) | <.0001 |
| Gender (female, %) | 24.9 | 44.1 | 27.4 | 26.5 | <.0001 |
| Ethnicity (white, %) | 95.2 | 26.2 | 72.3 | 19.0 | <.0001 |
| CD4 count (median, (IQR)) | 107 (35 - 254) | 149 (35 - 360) | 129 (38 - 315) | 96 (35 - 289) | 0.12 |
| HIV+ more than 3 months before TB diagnosis | 75.2 | 54.0 | 60.4 | 62.1 | <.0001 |
| HIV treatment, cART (%) | 16.6 | 39.5 | 43.9 | 35.2 | <.0001 |
| TB Risk Group | | | | | |
| - IDU (%) | 61.1 | 9.2 | 29.3 | 15.0 | <.0001 |
| - In prison in last 2 years (%) | 18.6 | 2.6 | 4.9 | 6.7 | <.0001 |
| TB in the past, yes (%) | 13.4 | 10.1 | 14.5 | 16.5 | 0.36 |
| Current OST, yes ¹ (%) | 3.7 | 66.7 | 48.8 | 0 | <.0001 |



Management of HIV/TB in Eastern Europe



Organisational set-up of TB services: results from survey



M. Mansfeld. EACS 2013

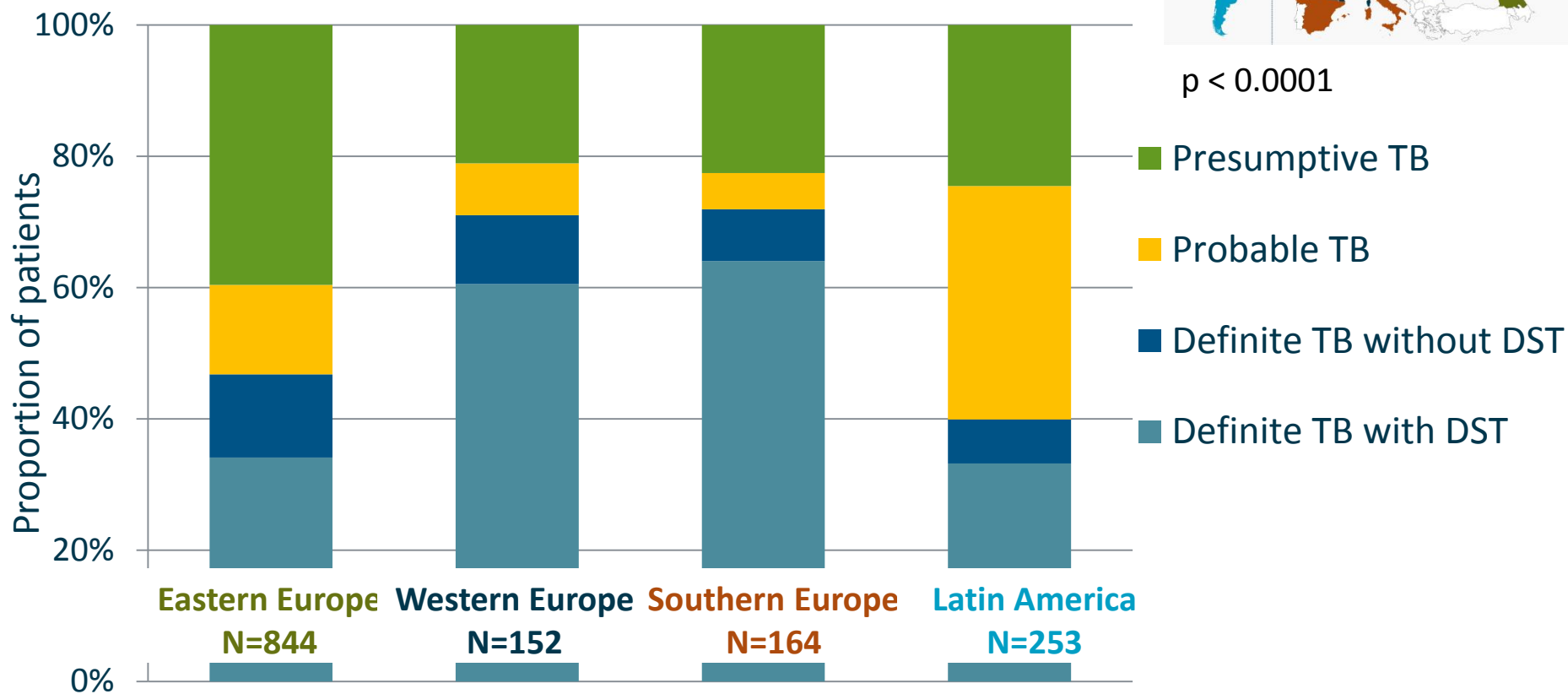
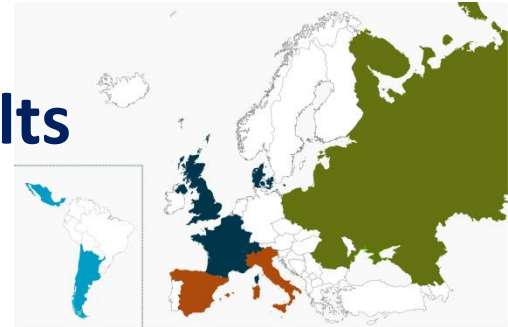
Role of opiate substitution therapy: results from Ukraine

- 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

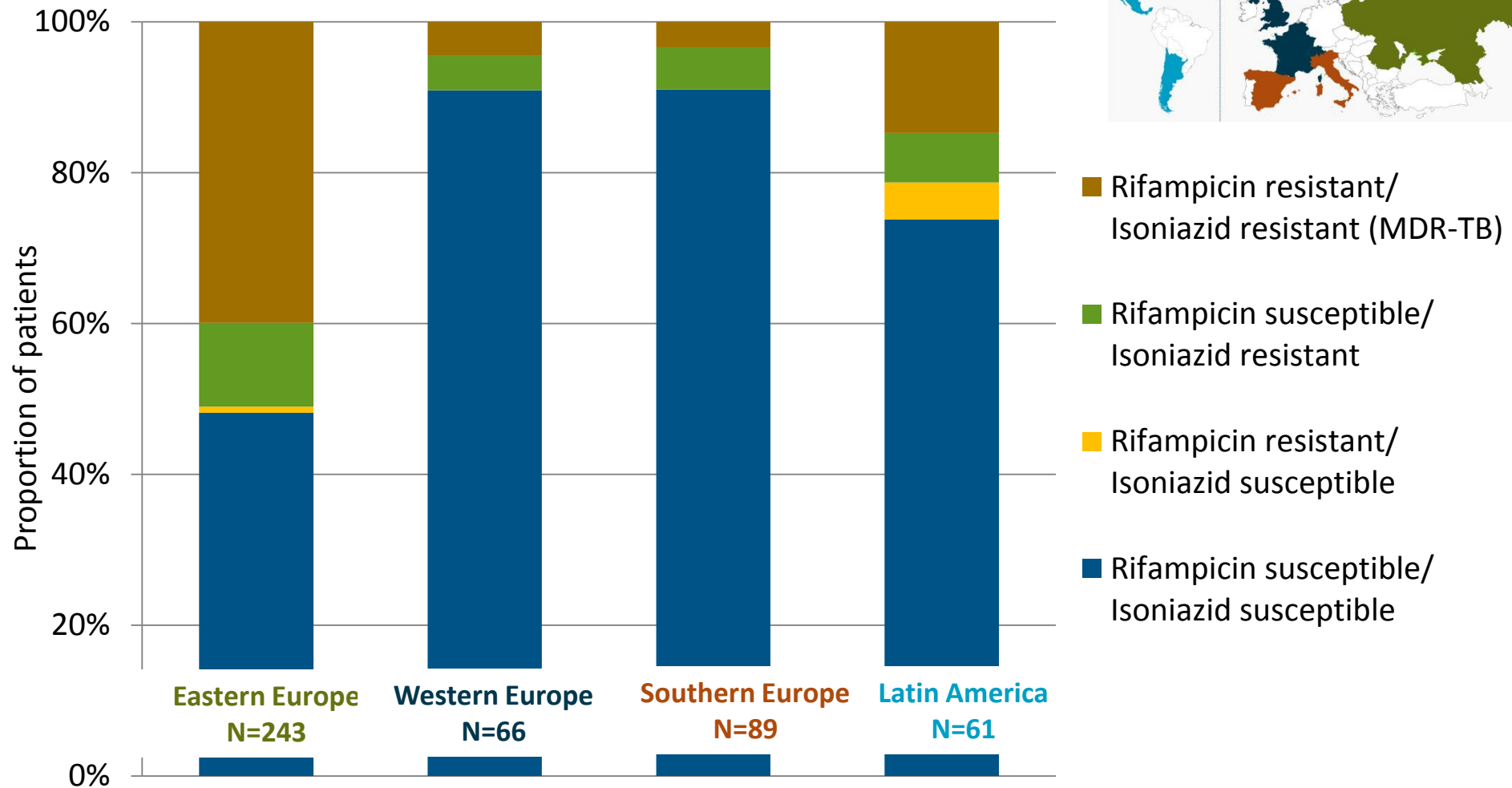


Diagnosis of TB and availability of DST results



A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014

Anti-TB drug-resistance among patients with DST results within one month of TB diagnosis



A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014

Choice of empiric therapy in relation to prevailing resistance pattern

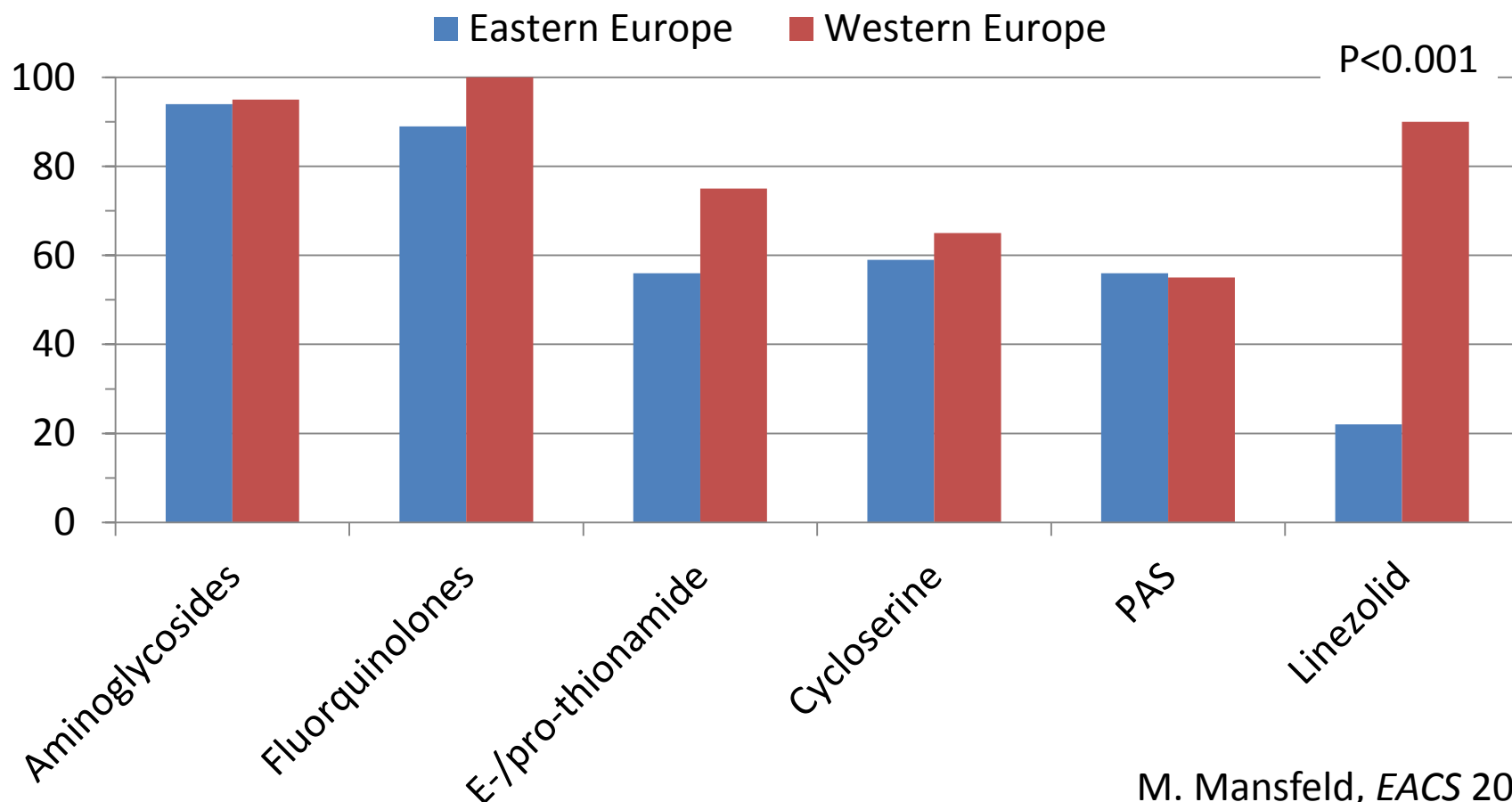
- In treatment of MDR-TB, WHO advises
 - ≥ 4 drugs known/likely to be effective + pyrazinamide
 - If possible amikacin, capreomycin or kanamycin plus a fluorquinolone should be core drugs

Lange, for TBNET; *Eur Respir J* 2014; Falzon, *Eur Respir J* 2011



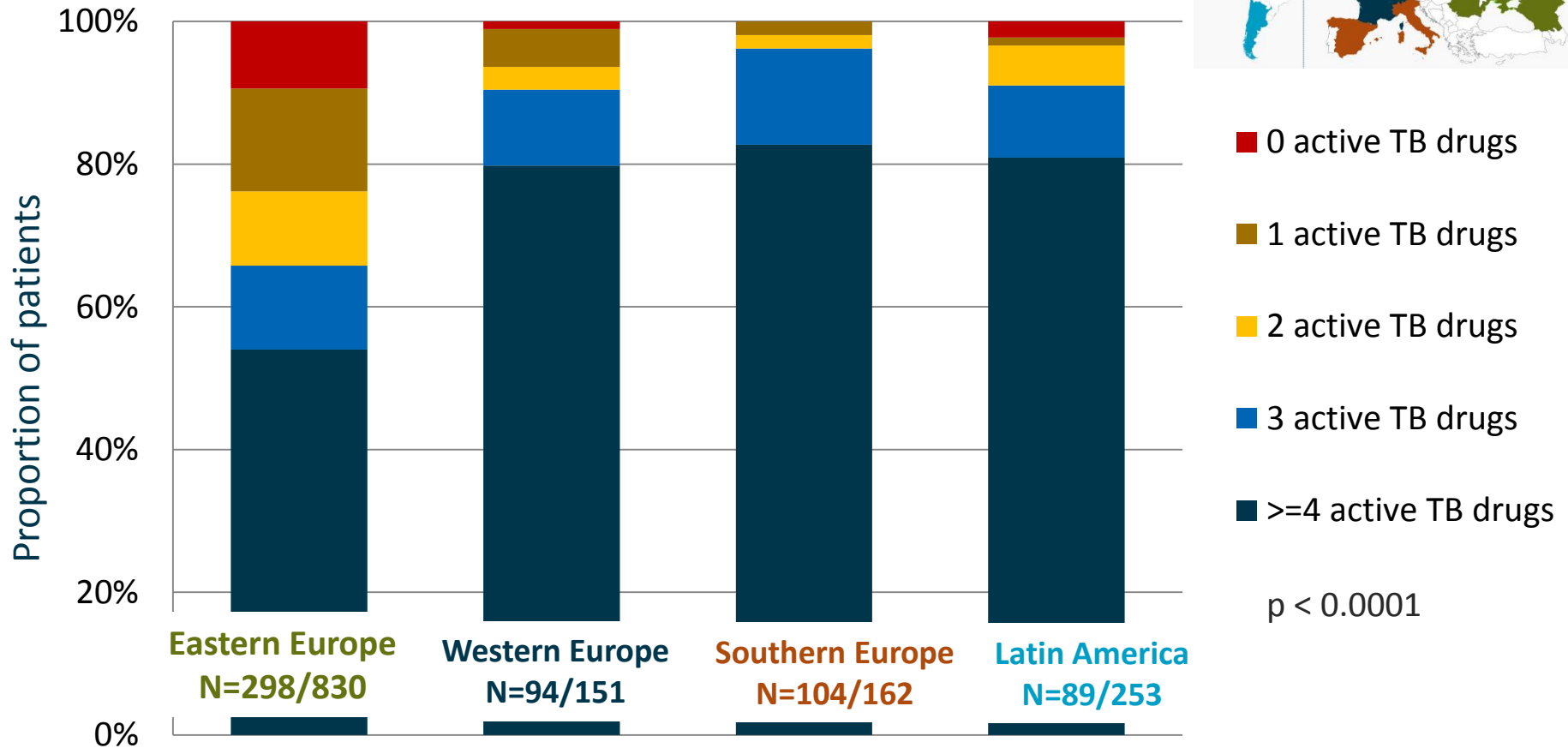
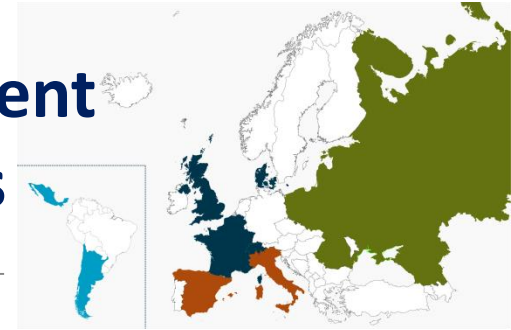
Availability of anti-TB drugs

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

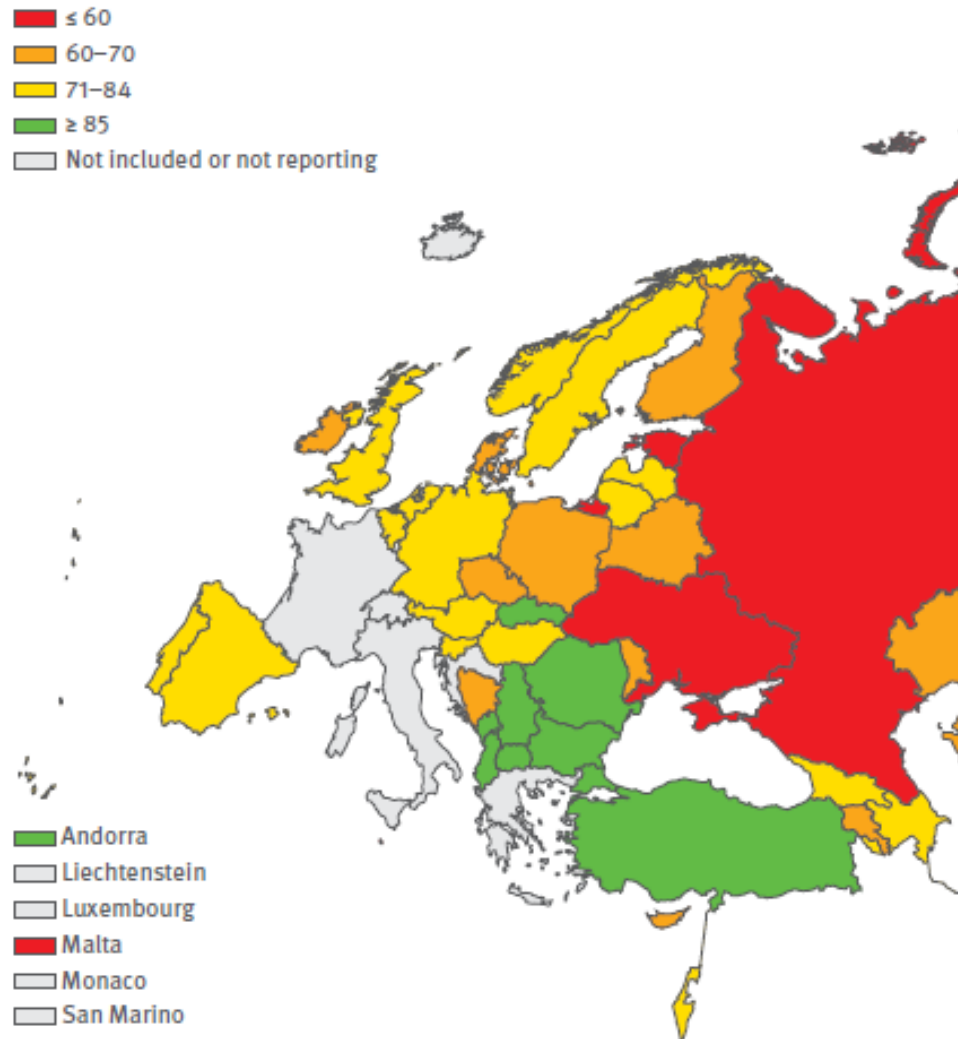


Active drugs calculated from comparing empiric anti-TB therapy and subsequently known DST results

A.M.W. Efsen. HIV Drug Therapy, Glasgow 2014

Treatment success among new lab-confirmed pulmonary TB cases in 2011

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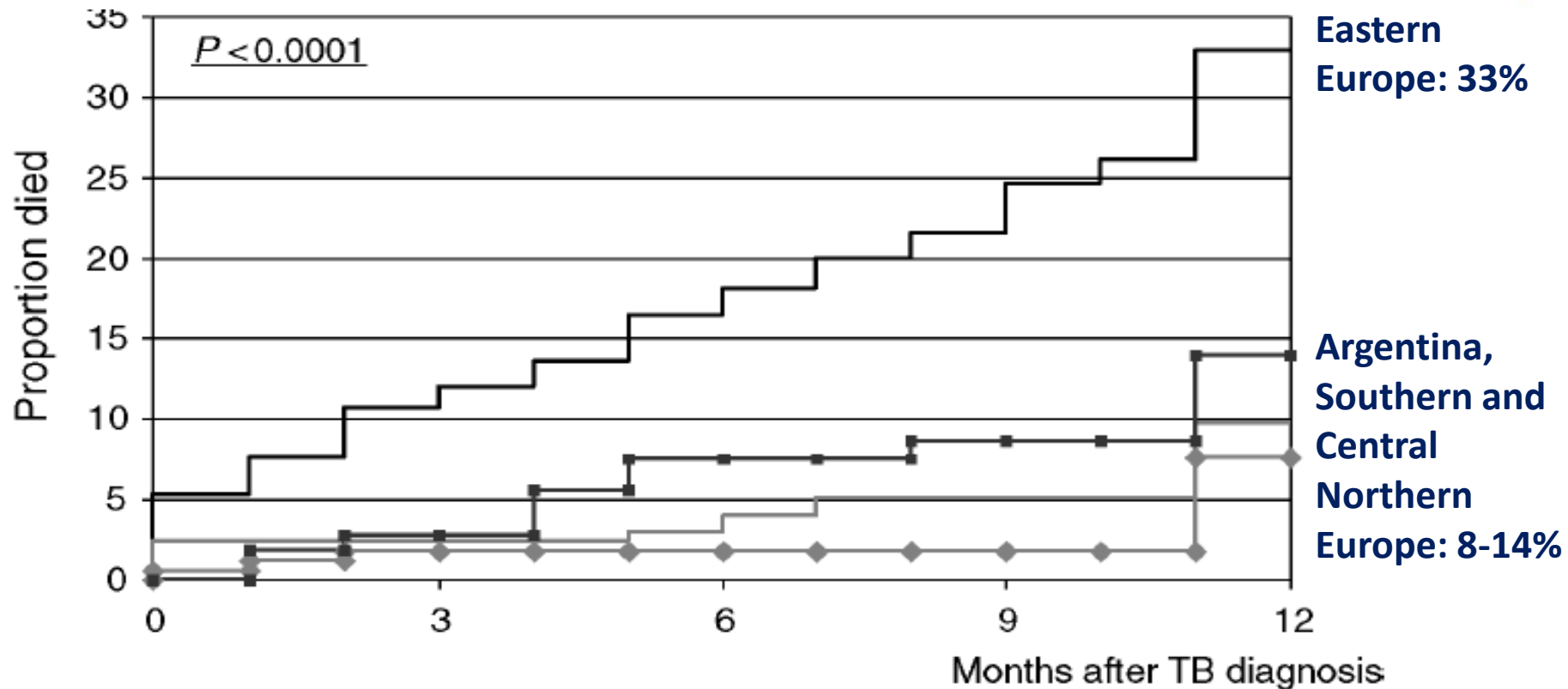


ECDC/WHO Regional Office for Europe. Tuberculosis Surveillance and Monitoring in Europe. 2014



Mortality among HIV+ patients with a TB diagnosis

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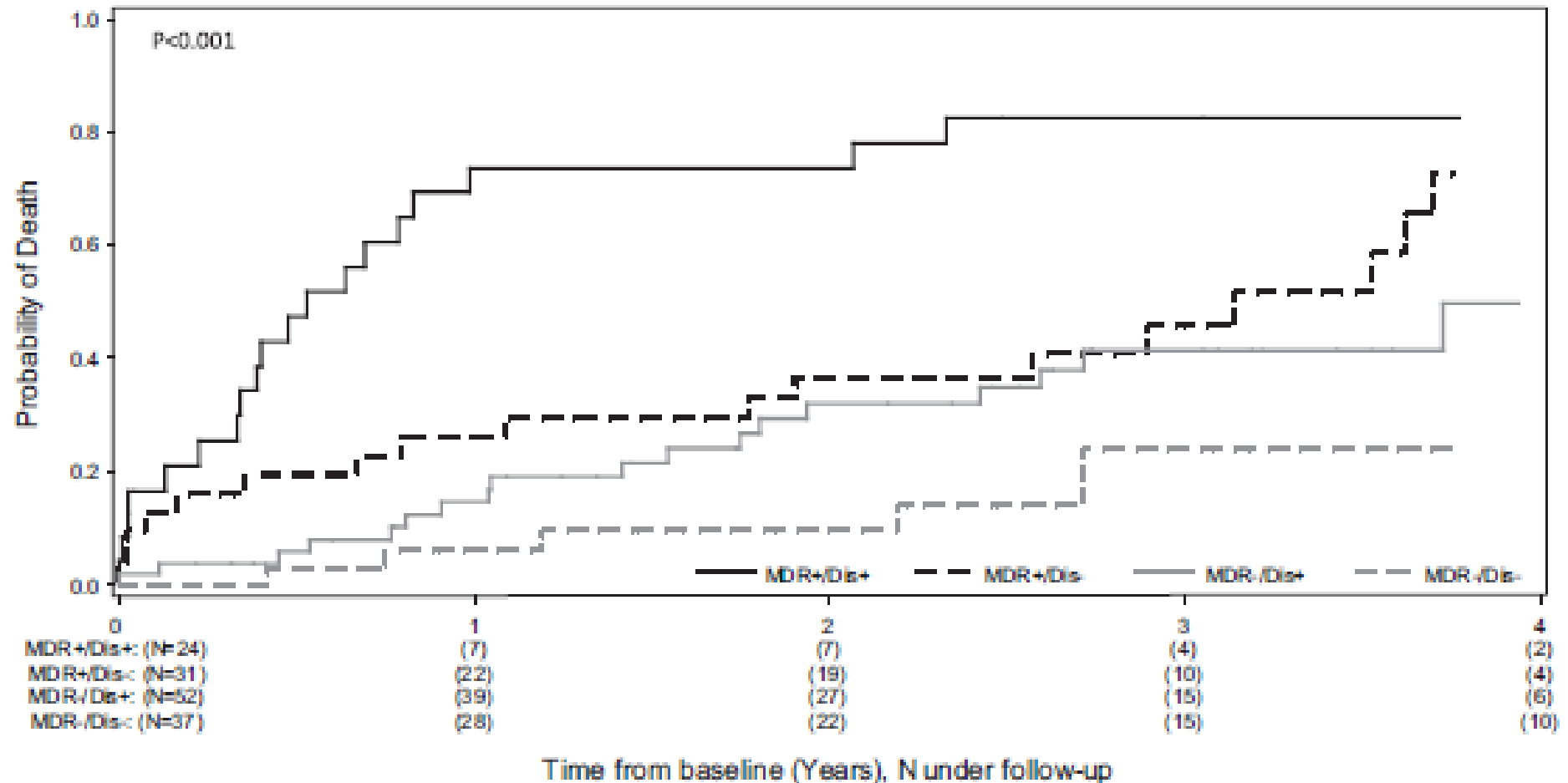
| | | | | | |
|-----|-----|-----|-----|-----|-----|
| EE | 582 | 485 | 395 | 339 | 281 |
| CNE | 168 | 163 | 161 | 157 | 151 |
| SE | 210 | 193 | 183 | 171 | 162 |
| AR | 115 | 104 | 96 | 83 | 69 |

Podlekareva, AIDS 2009



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

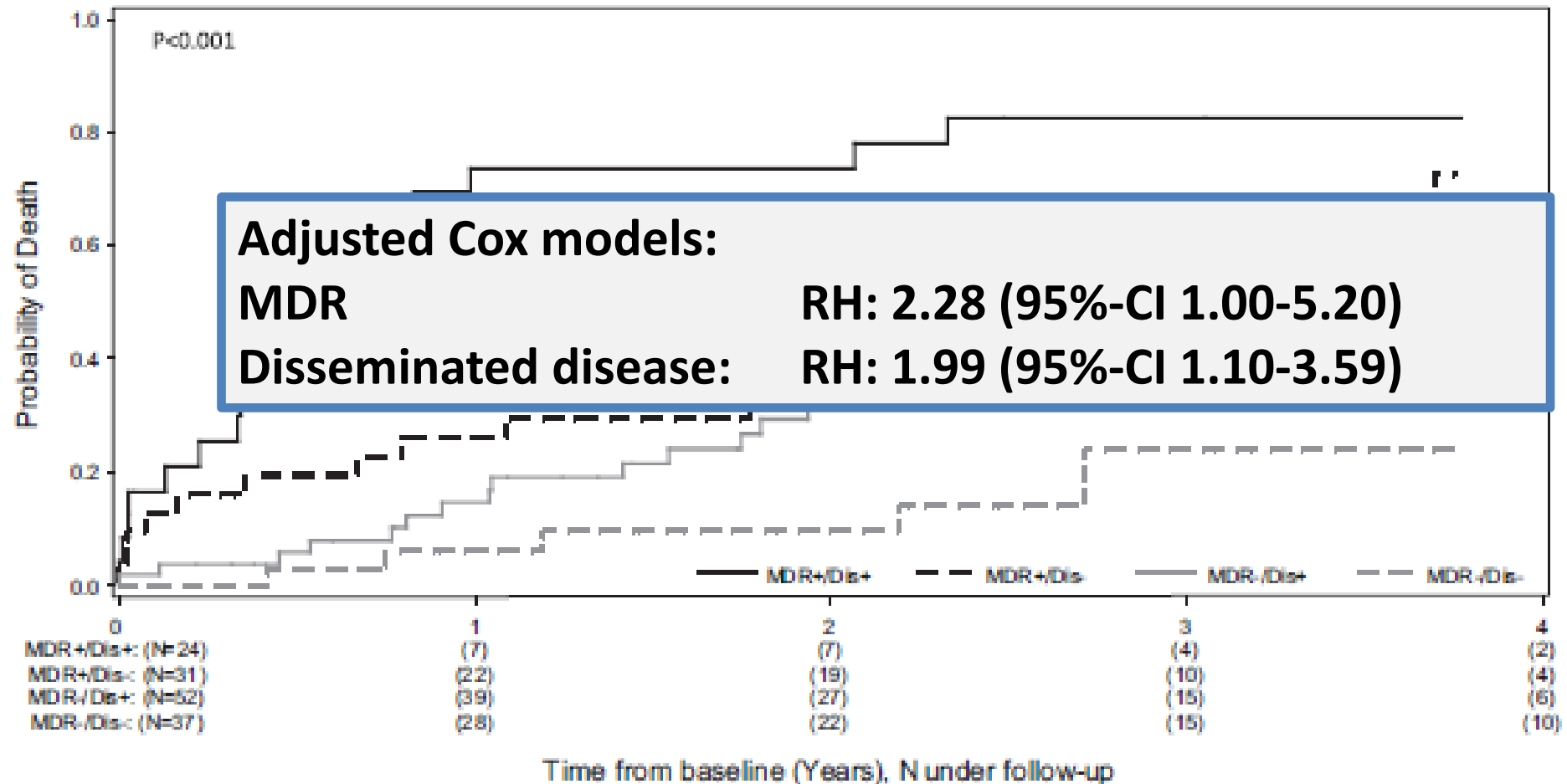
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F. Post, *J Infection* 2014



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



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

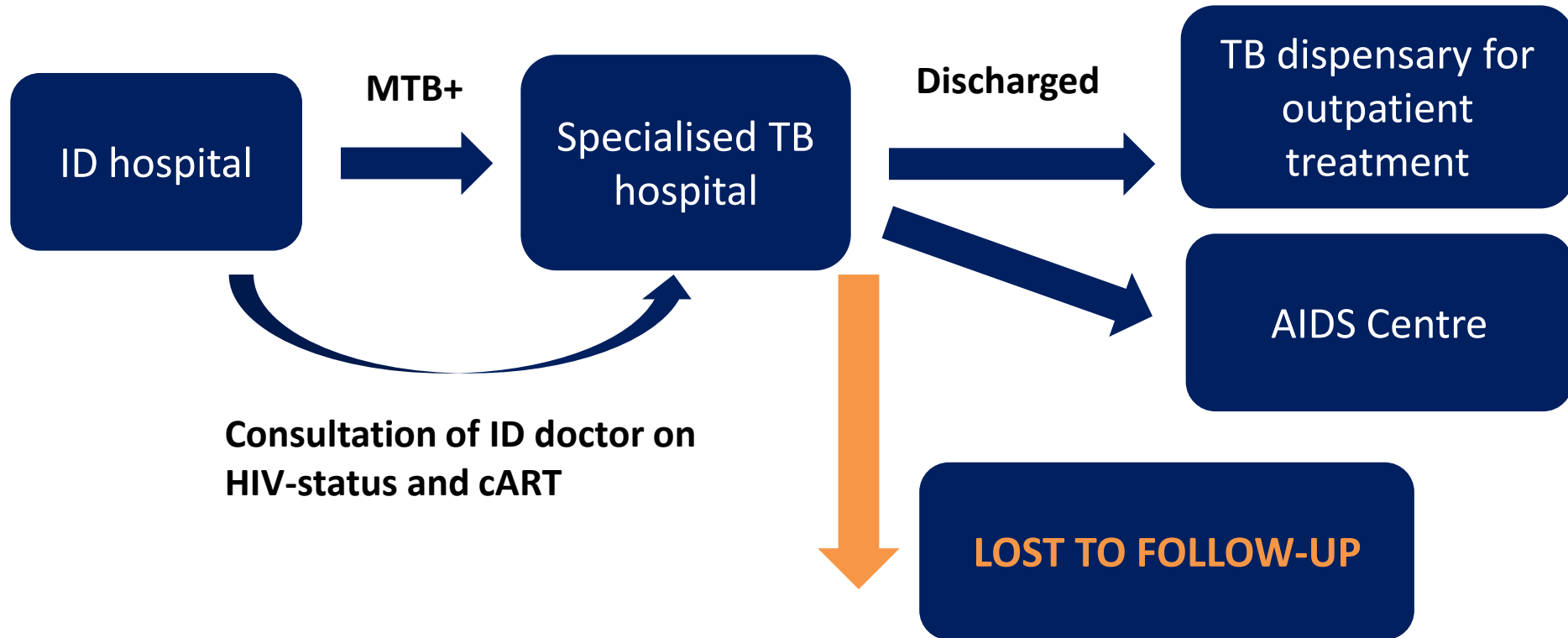
personal communication



A patient with HIV/TB from Eastern Europe

Management history

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Other challenges include (but not limited to):

- limited availability of Opiate Substitution Therapy and harm reduction programmes
- Limited social support



Actions to improve the situation with TB and HIV/TB in Eastern Europe

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**

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