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REGION H

15th European AIDS Conference
October 21-24, Barcelona, Spain

Outcome of TB in HIV Infected Patients in Eastern Europe

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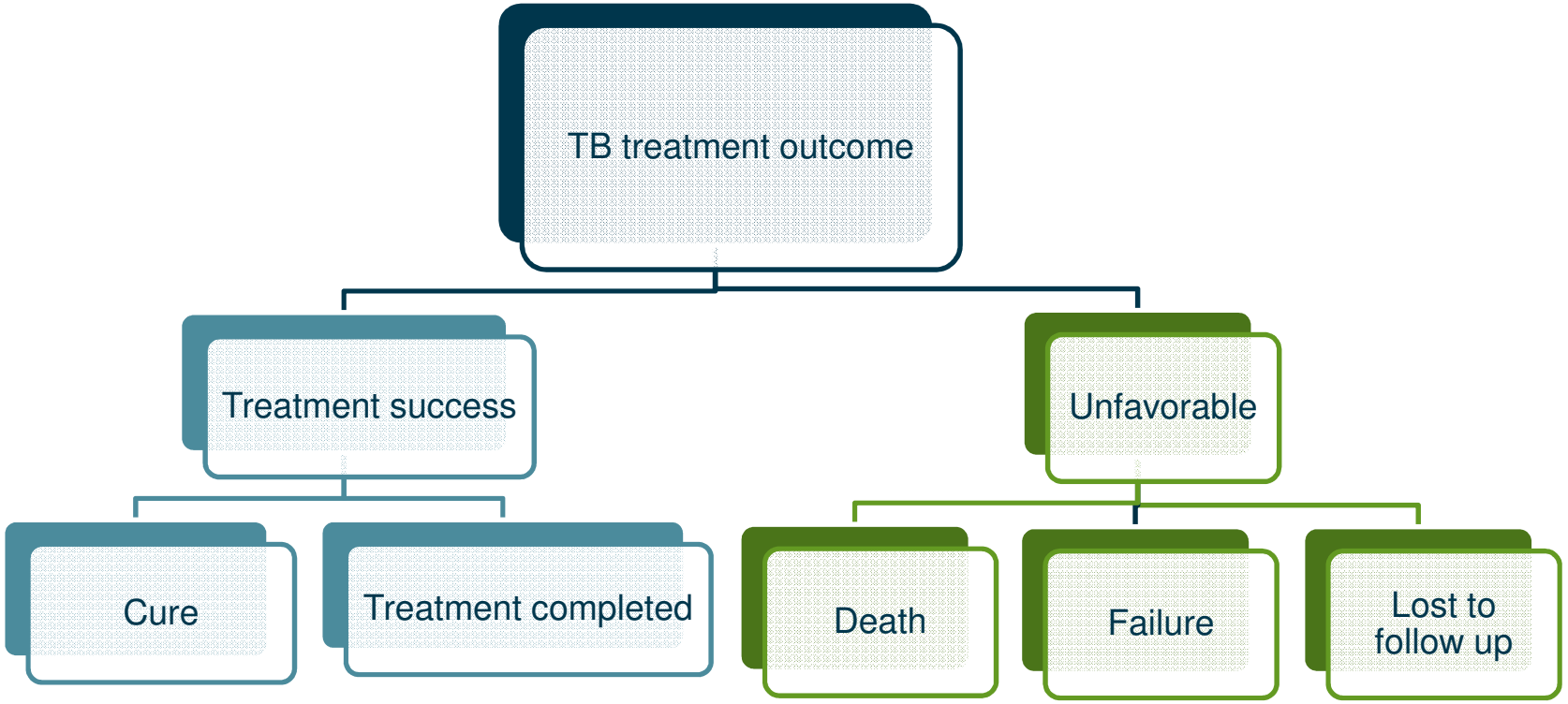
University of Copenhagen

GLOBAL EXCELLENCE IN HEALTH

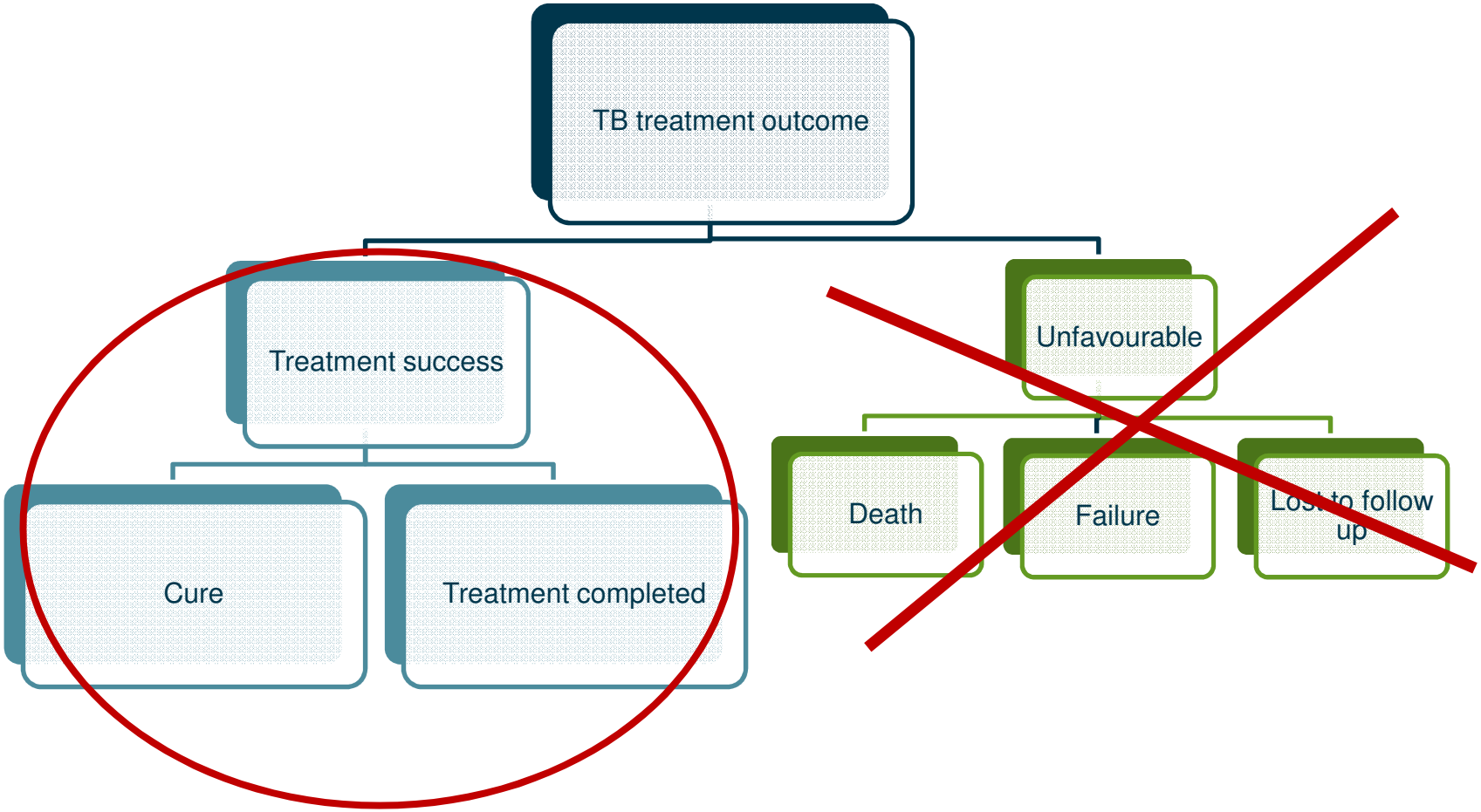
Disclosure

- I do not have any conflicts of interests

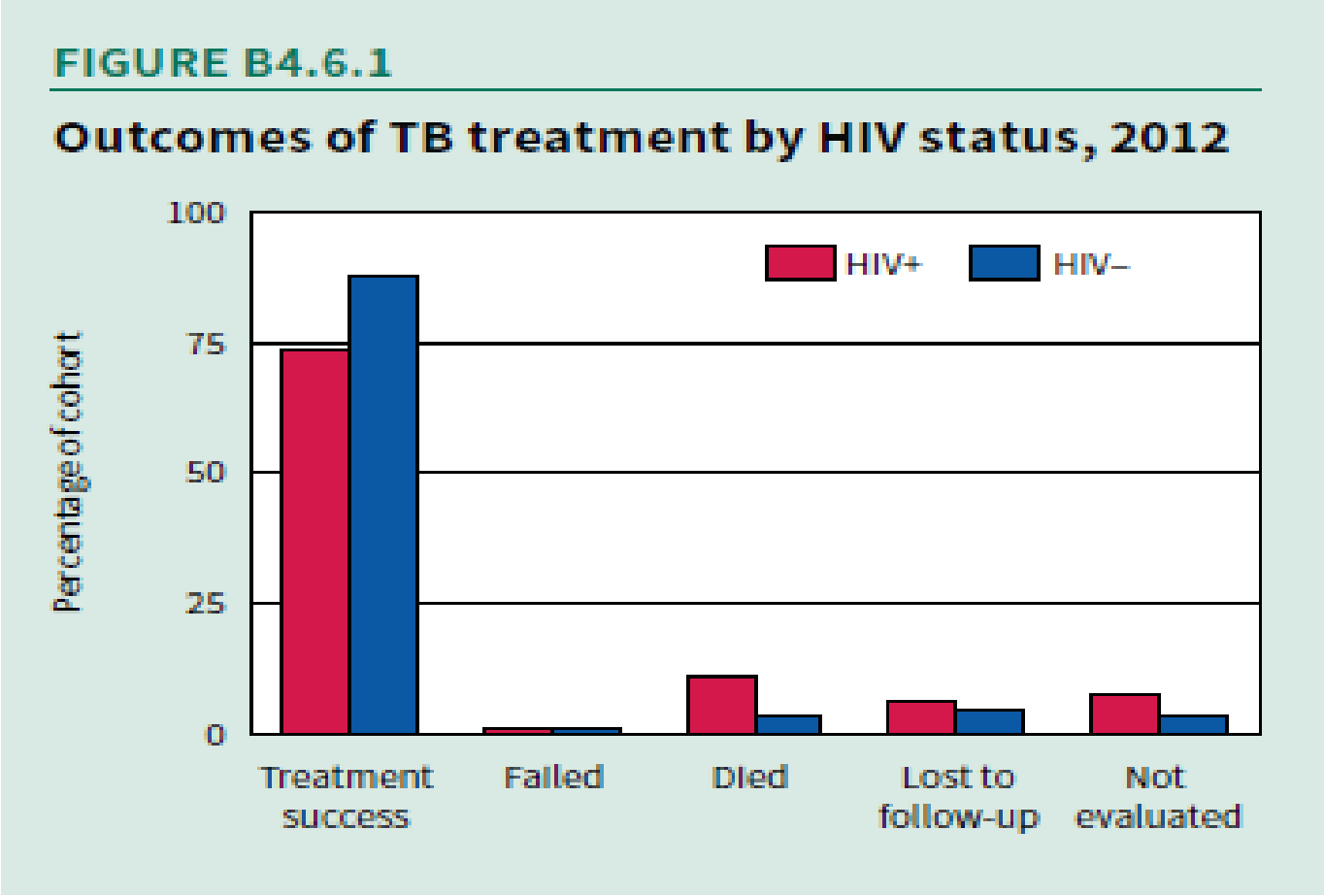
WHO definition of TB treatment outcome



WHO definition of TB treatment outcome



WHO TB report 2014



- TB treatment success 2012: African region 81% vs. European region 75%
- Treatment outcomes for patients treated on second-line regimens: 50% or less in most regions

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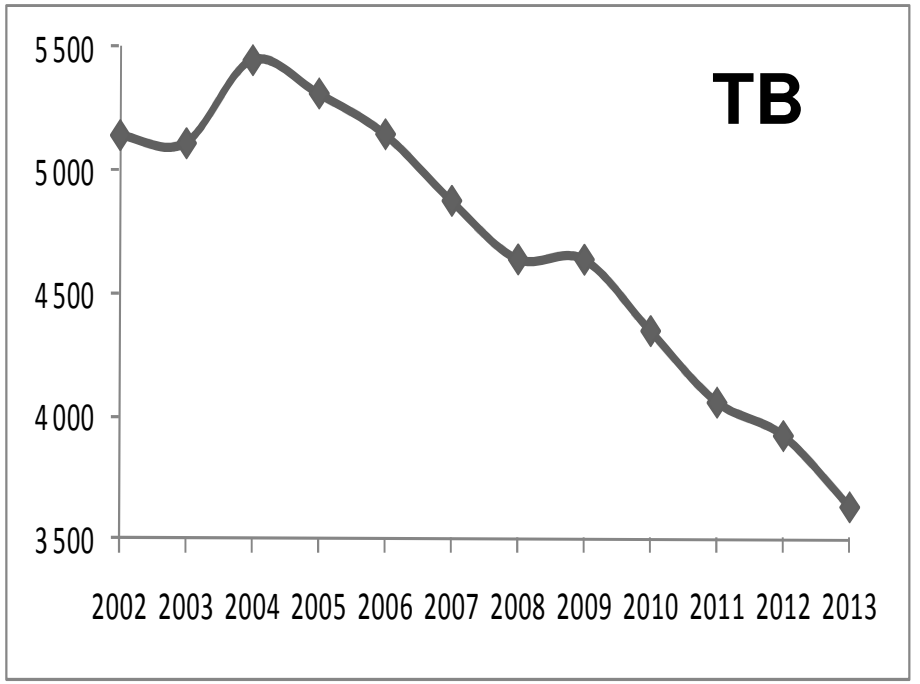
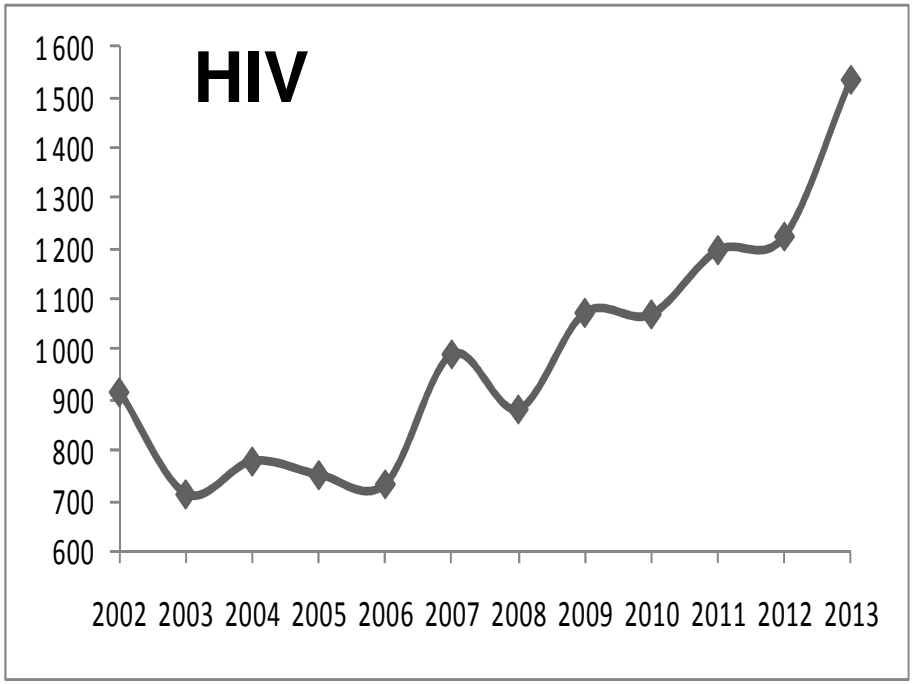
TB/HIV EPIDEMIC IN EASTERN EUROPE

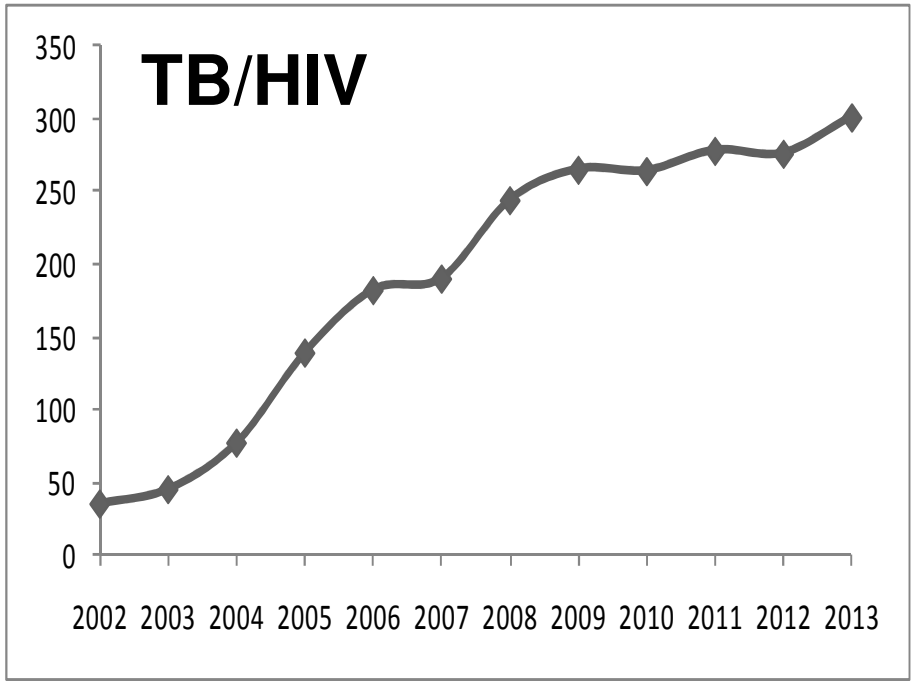
TB/HIV Epidemic in Eastern Europe

Example of Belarus

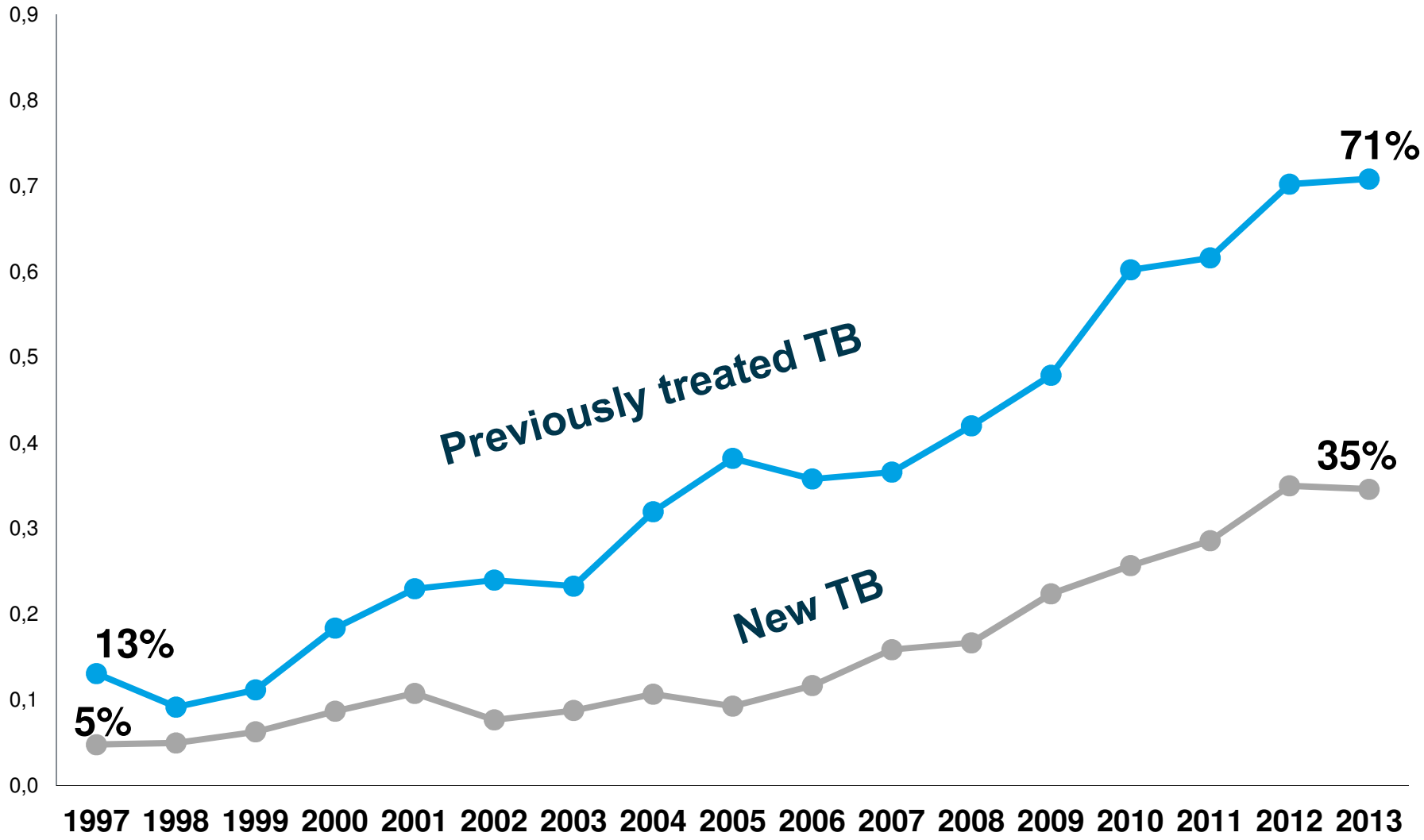
A. Skrahina. Personal communication





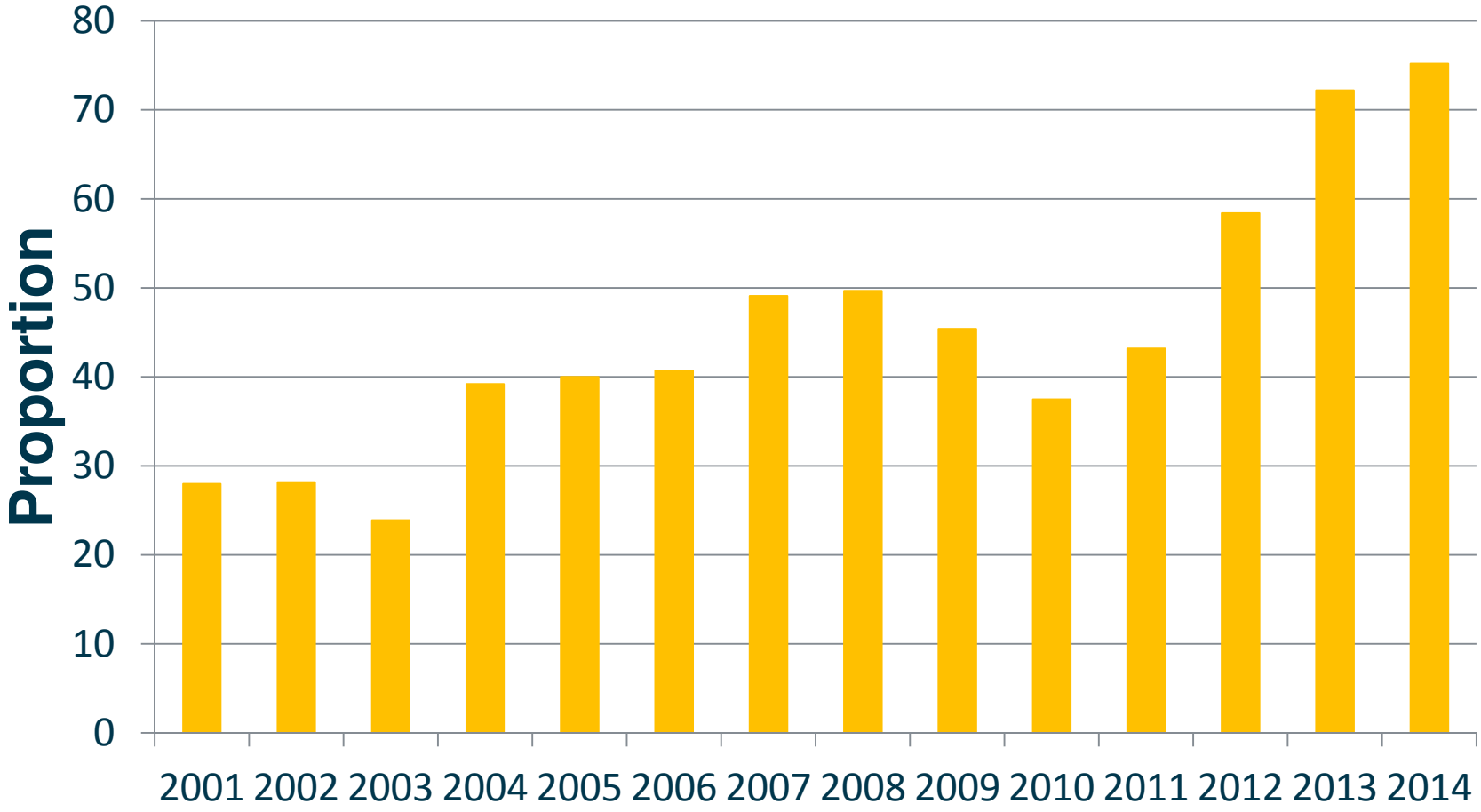


MDR-TB Epidemic - Example of Belarus



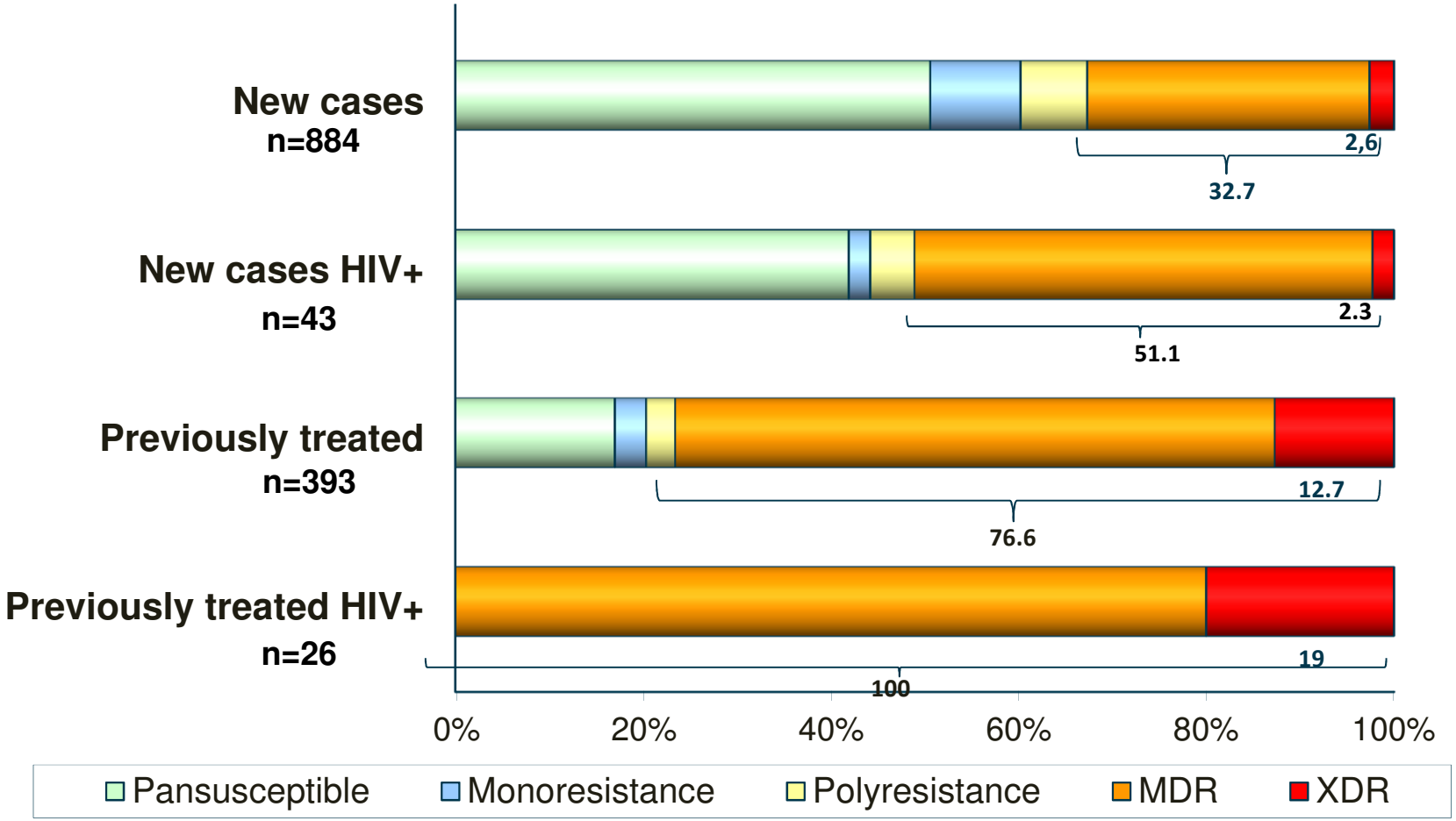
A. Skrahina. Personal communication

Primary MDR-TB in TB/HIV patients in St. Petersburg, Russia



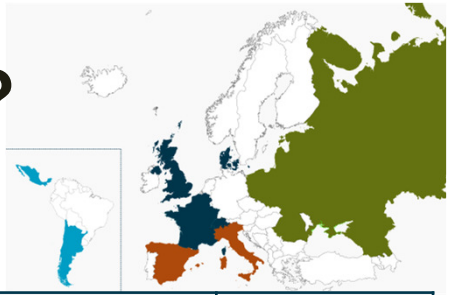
A Panteleev. Personal communication

MDR-TB and HIV co-infection
A study from Belarus



A Skrahina et al., Bull World Health Organ 2013;91:36–45

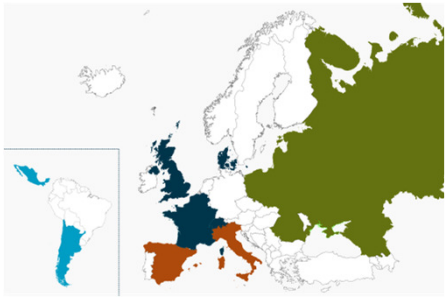
Who are TB/HIV patients in Eastern Europe? The TB:HIV Study



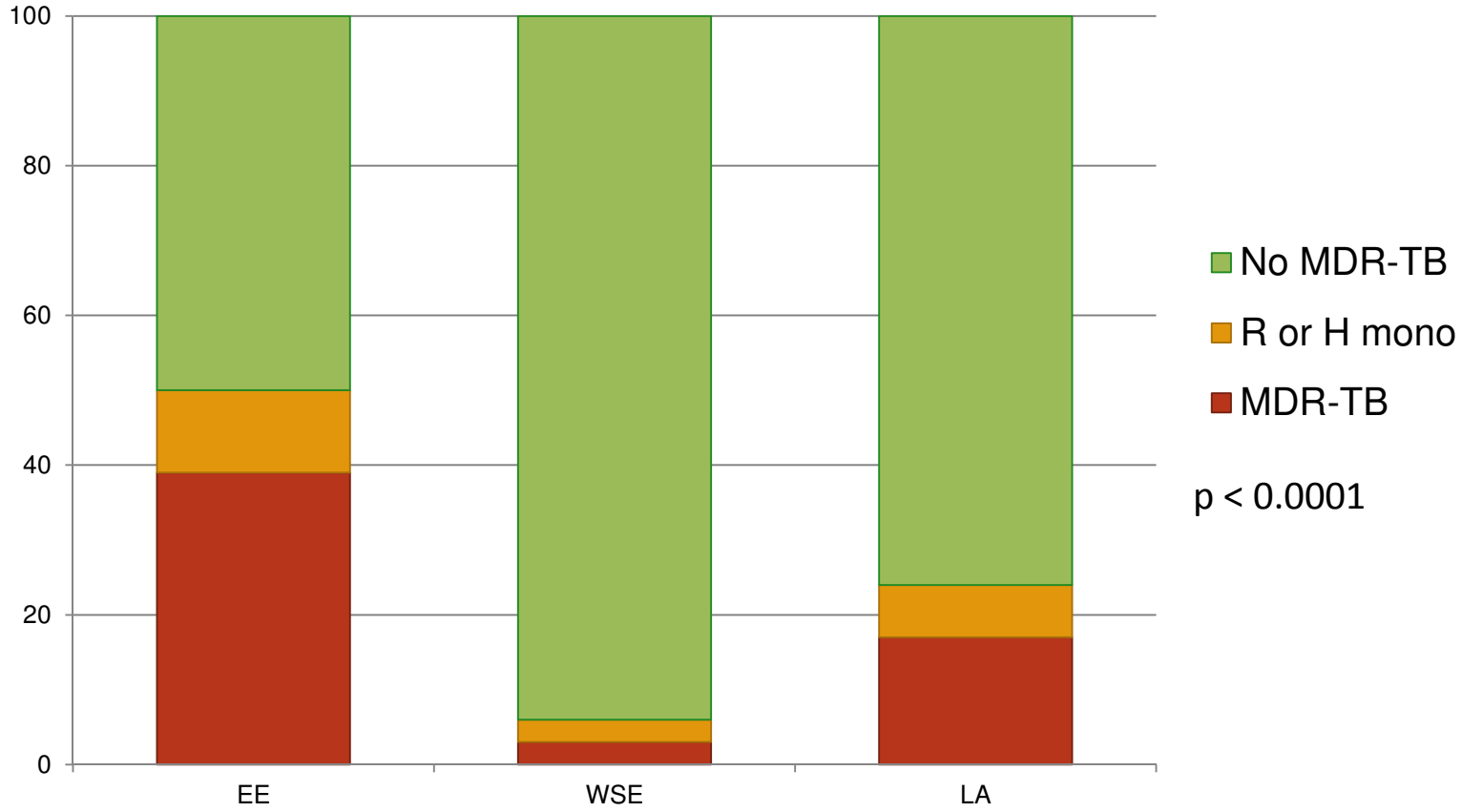
	Eastern Europe N = 844	Western Europe N = 152	Southern Europe N = 164	Latin America N = 253	P-value
Age (median, IQR)	35 (31 - 40)	37 (32 - 48)	42 (33 - 48)	38 (30 - 45)	<.0001
Gender (female, %)	24.9	44.1	27.4	26.5	<.0001
Ethnicity (white, %)	95.2	26.2	72.3	19.0	<.0001
CD4 count (median, (IQR))	107 (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 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

AMW Efsen, HIV Drug Therapy, Glasgow 2014

MDR-TB prevalence among those tested for MDR. The TB:HIV Study

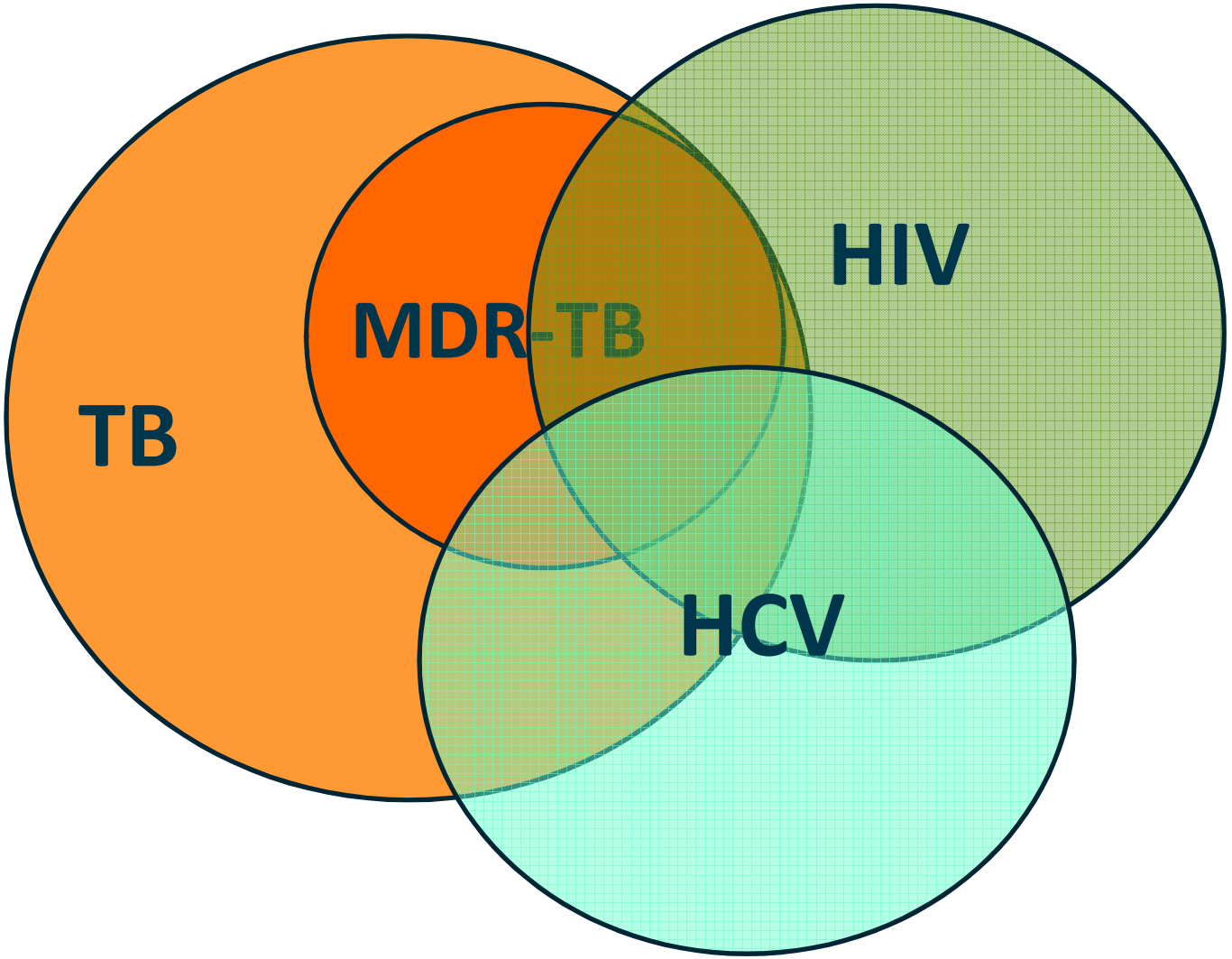


- **576** had baseline DST performed
  - **495** (86%) had data on both R and H resistance



A Schultze et al., IAS 2015, Vancouver, Canada

HIV and TB epidemics in Eastern Europe



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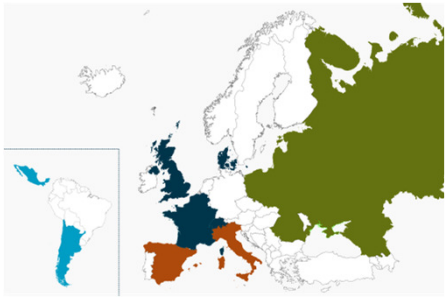
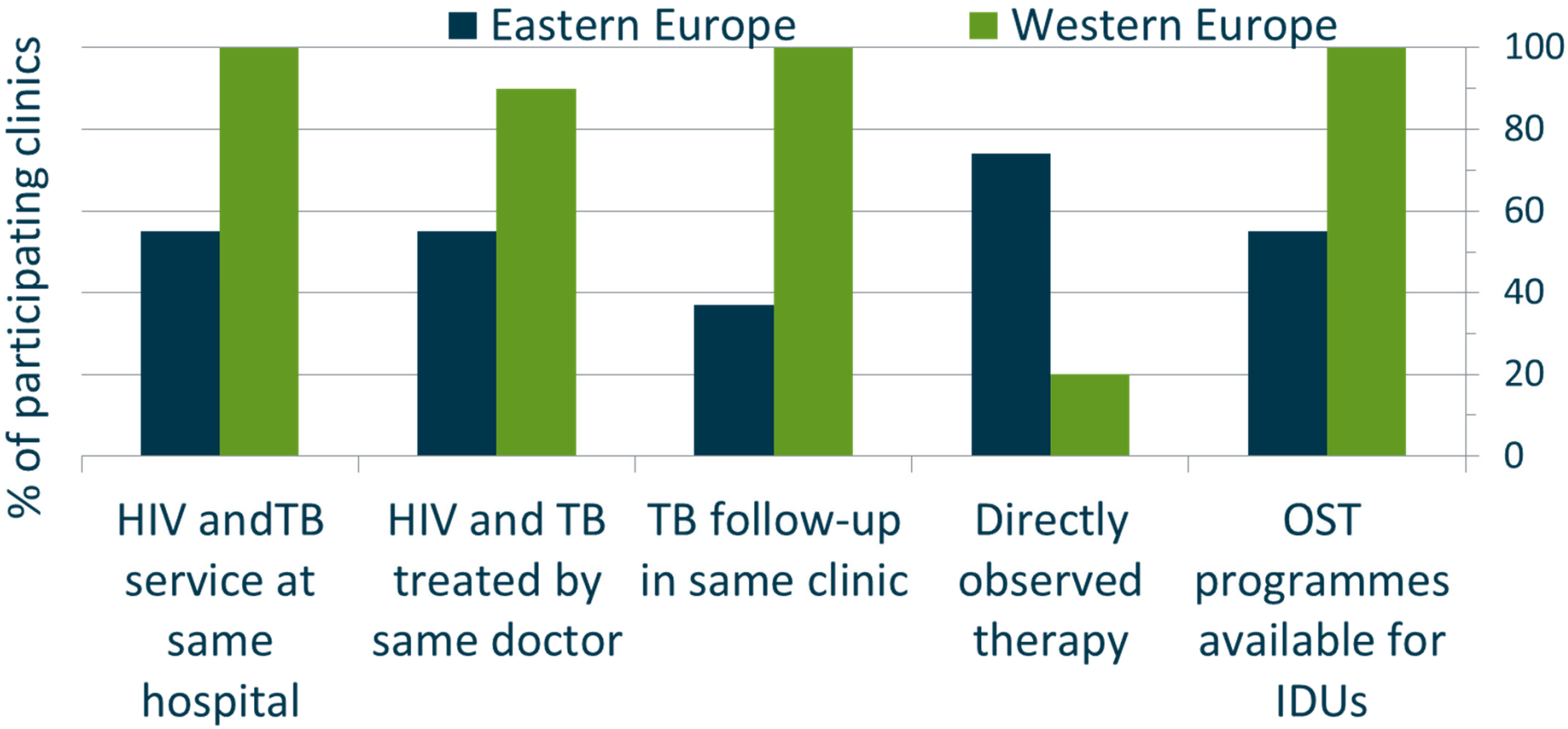
MANAGEMENT OF TB AND HIV IN EASTERN EUROPE

Organisational set-up of TB services - results from a survey



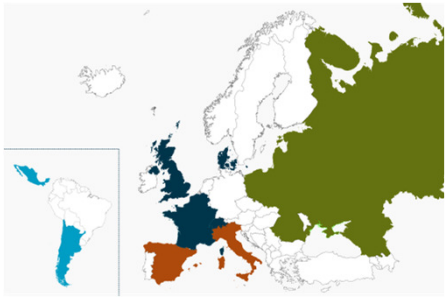


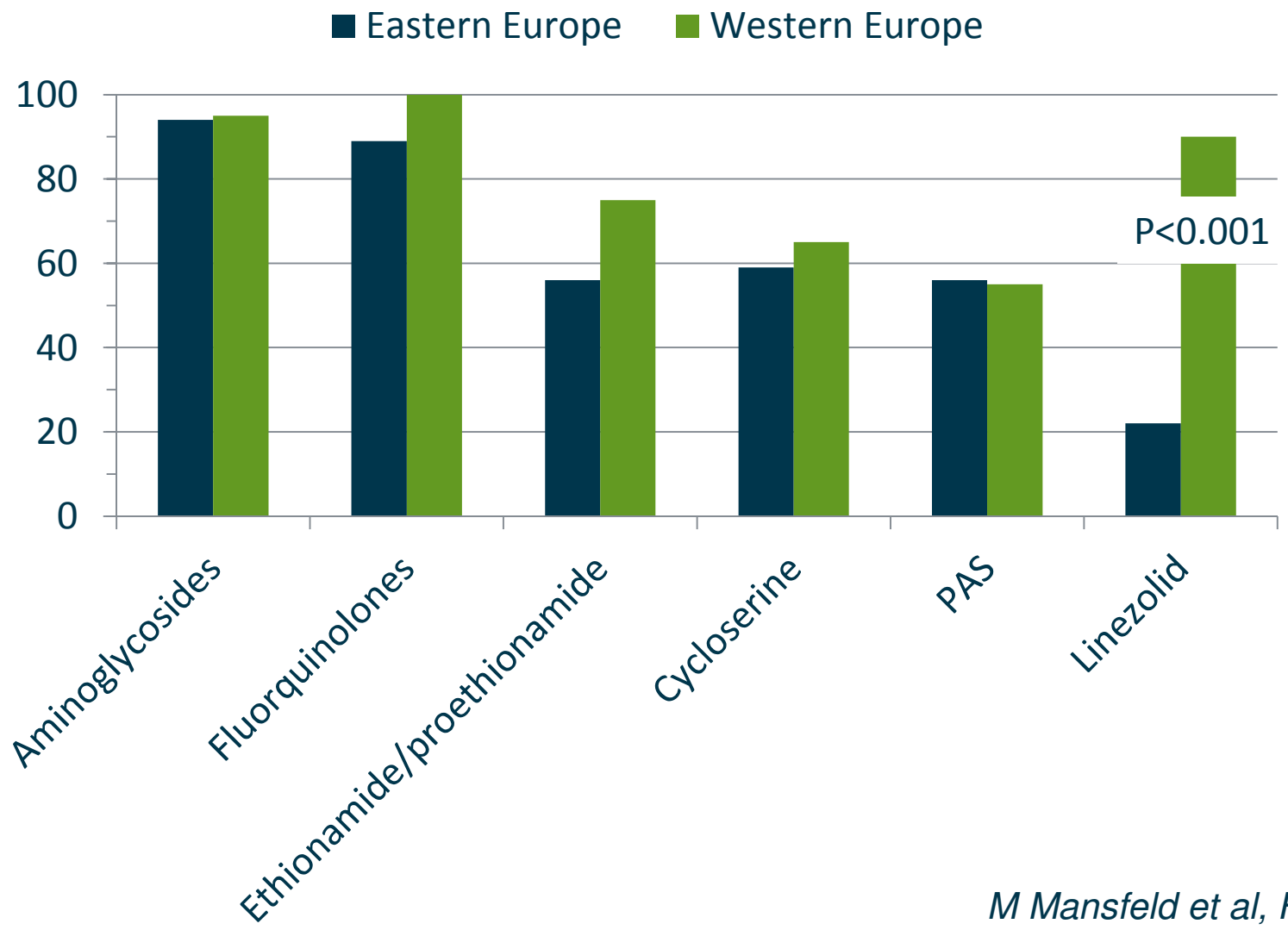
All, p<0.001; OST: opiate substitution therapy

M Mansfeld et al, HIV Med 2015

Availability of anti-TB drugs

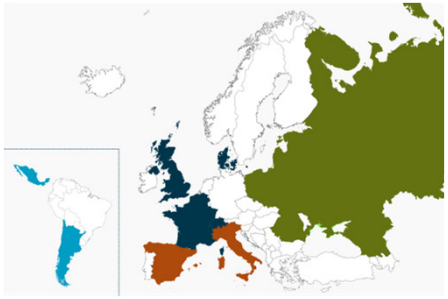
Reported ‘unlimited access’ to 2nd and 3rd line anti-TB drugs



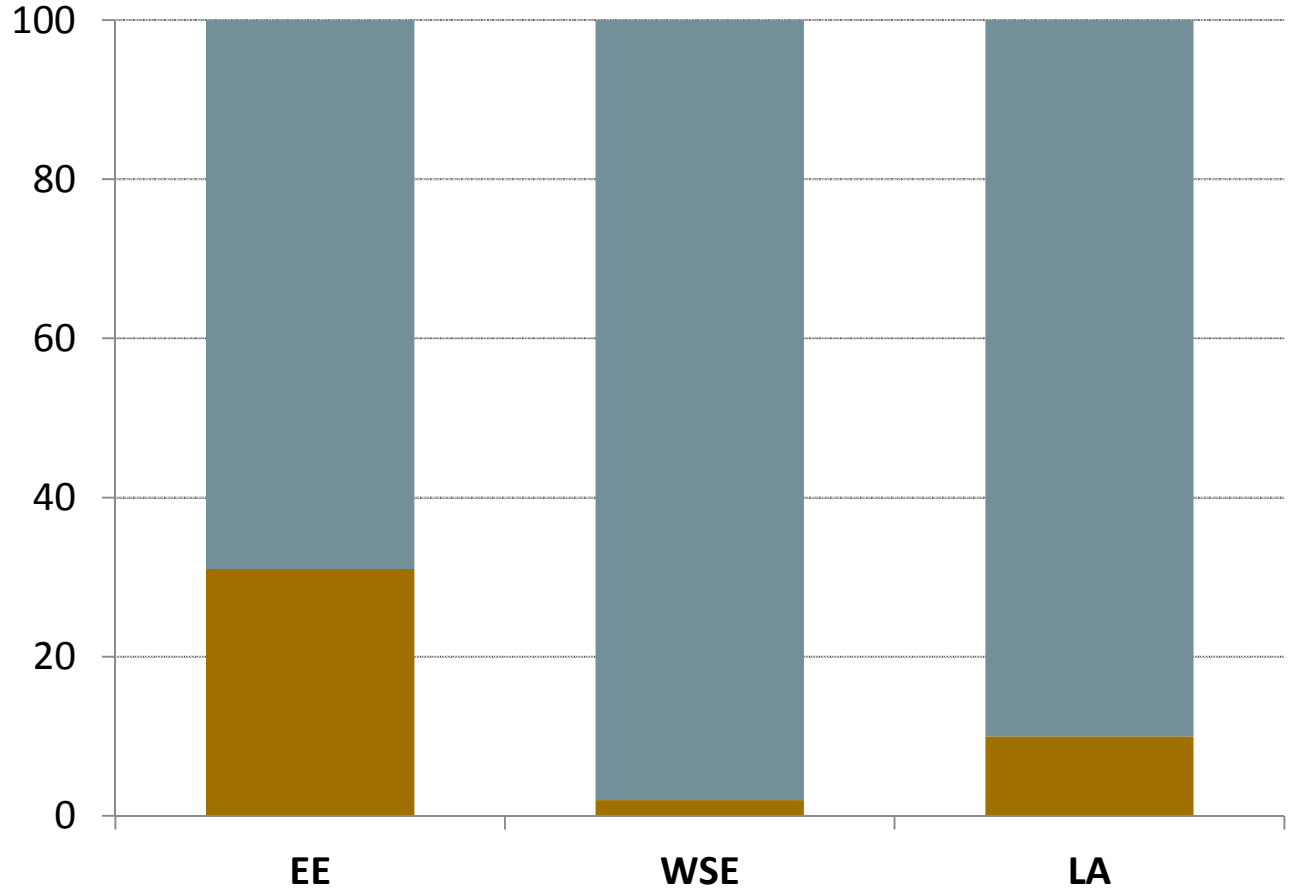


M Mansfeld et al, HIV Med 2015

Number of active drugs in the initial regimen. The TB:HIV Study



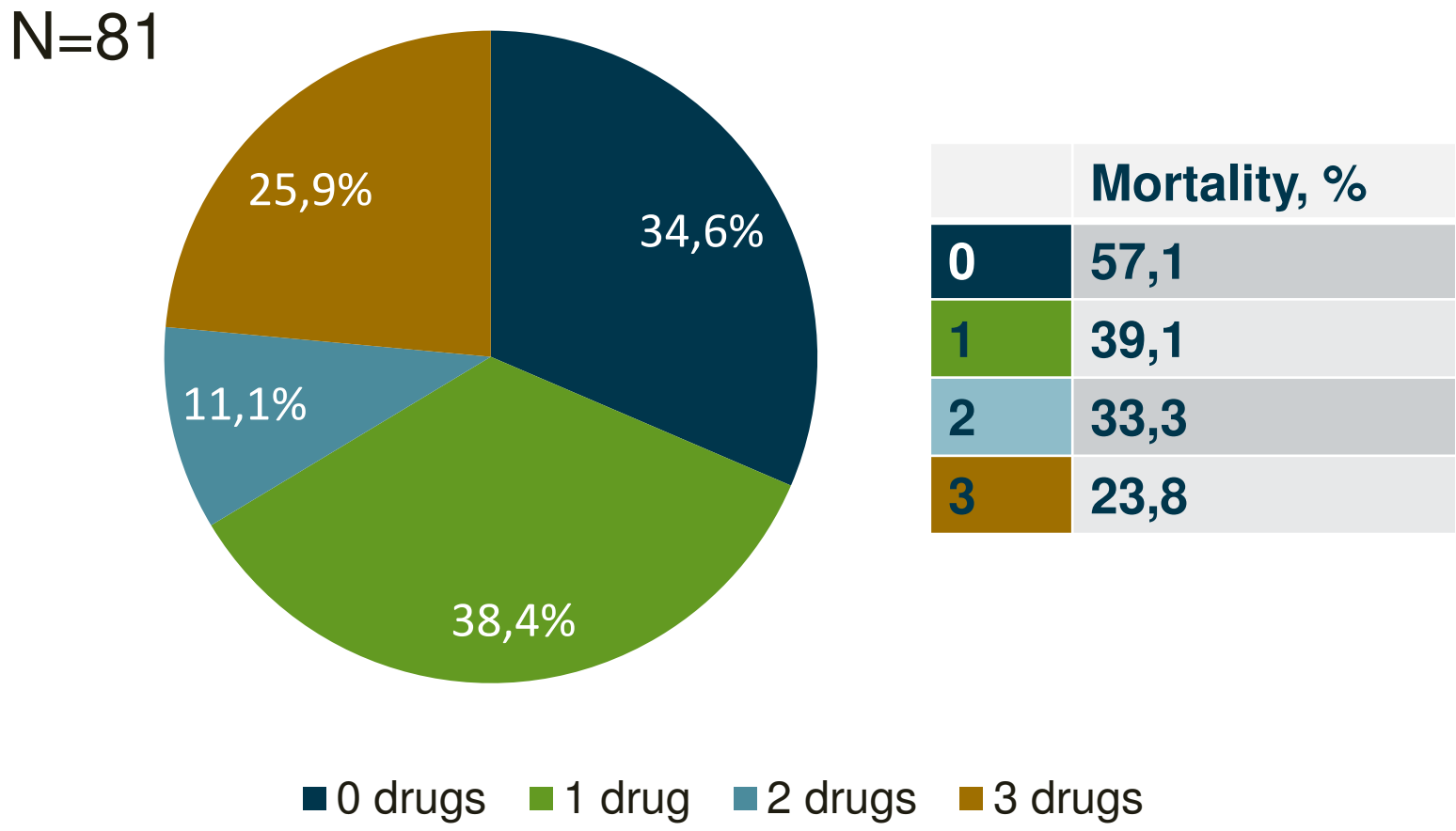
- **576** (41%) had baseline DST performed



	EE	WSE	LA
3 or more N(%)	201 (69)	197 (98)	90 (75)
2 or fewer N(%)	90 (31)	5 (2)	8 (10)

A Schultze et al, IAS 2015

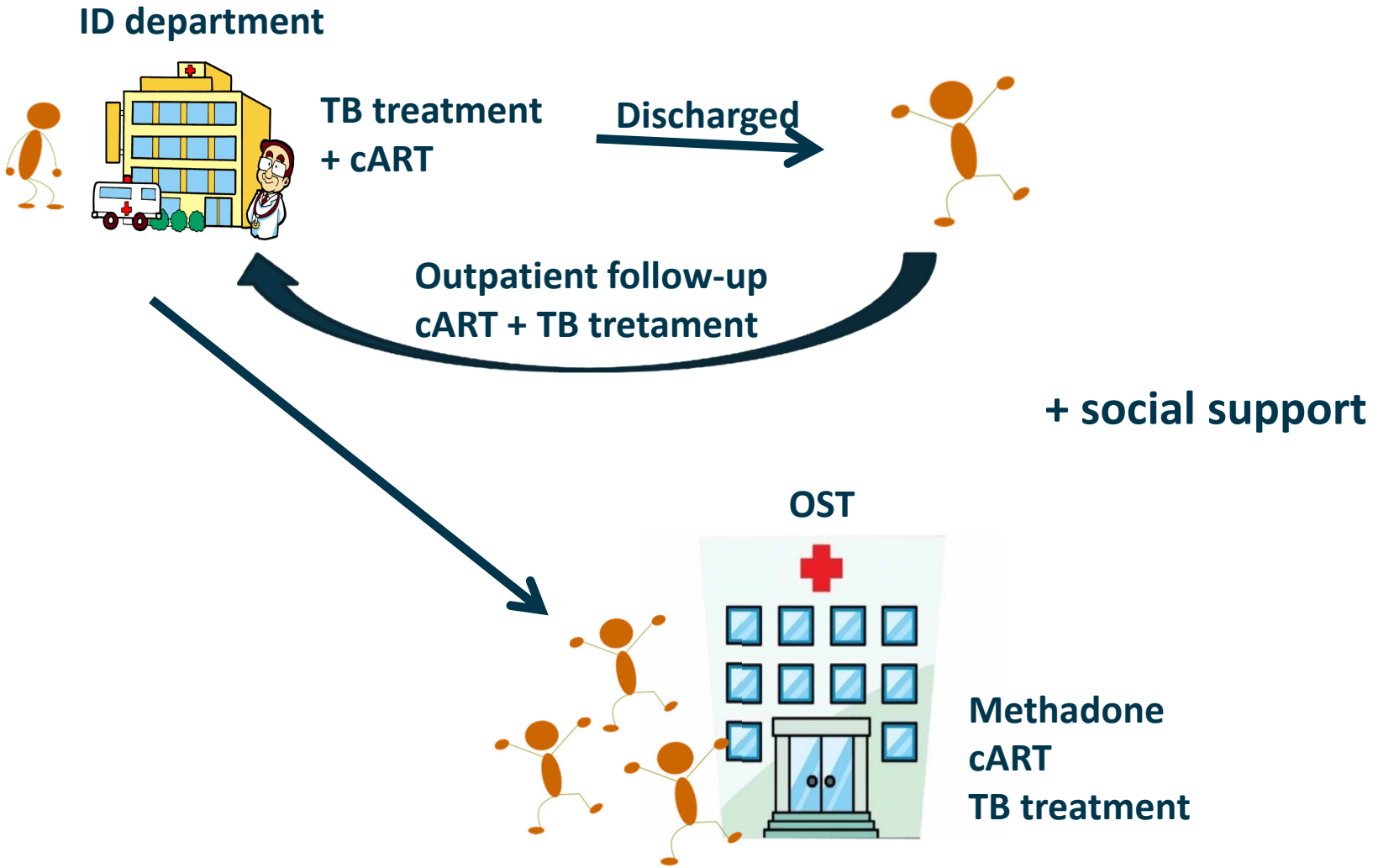
Number of active drugs in the initial regimen TB/HIV cohort from St. Petersburg, 2013



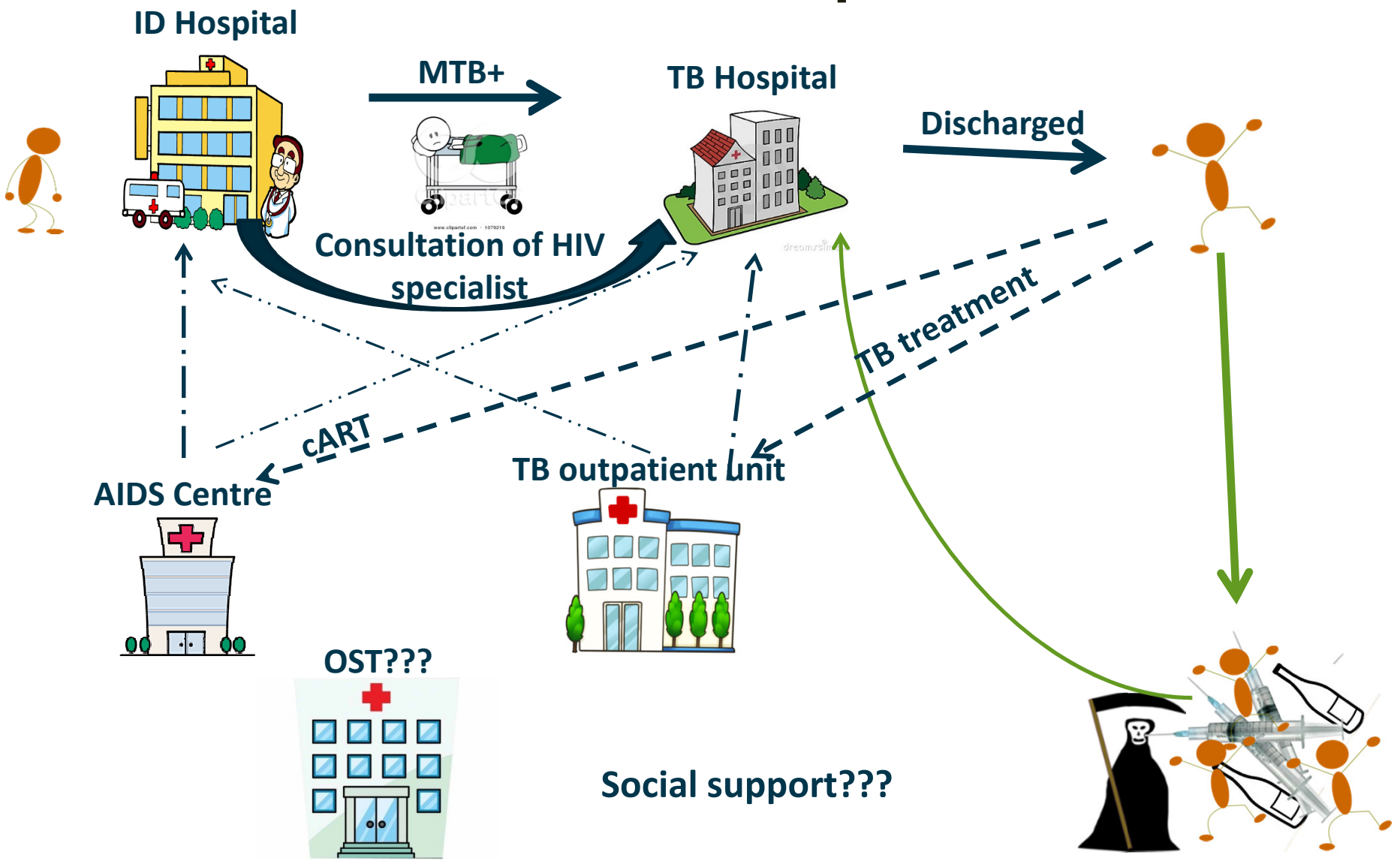
	Mortality, %
0	57,1
1	39,1
2	33,3
3	23,8

A. Panteleev. Personal communication

Management of TB/HIV patient in Western Europe



Management of TB/HIV patient in Eastern Europe



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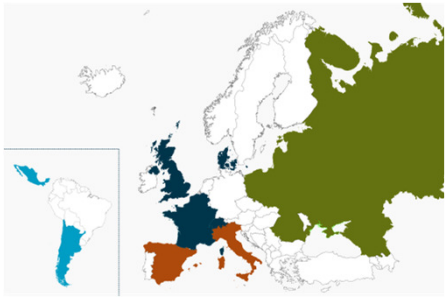
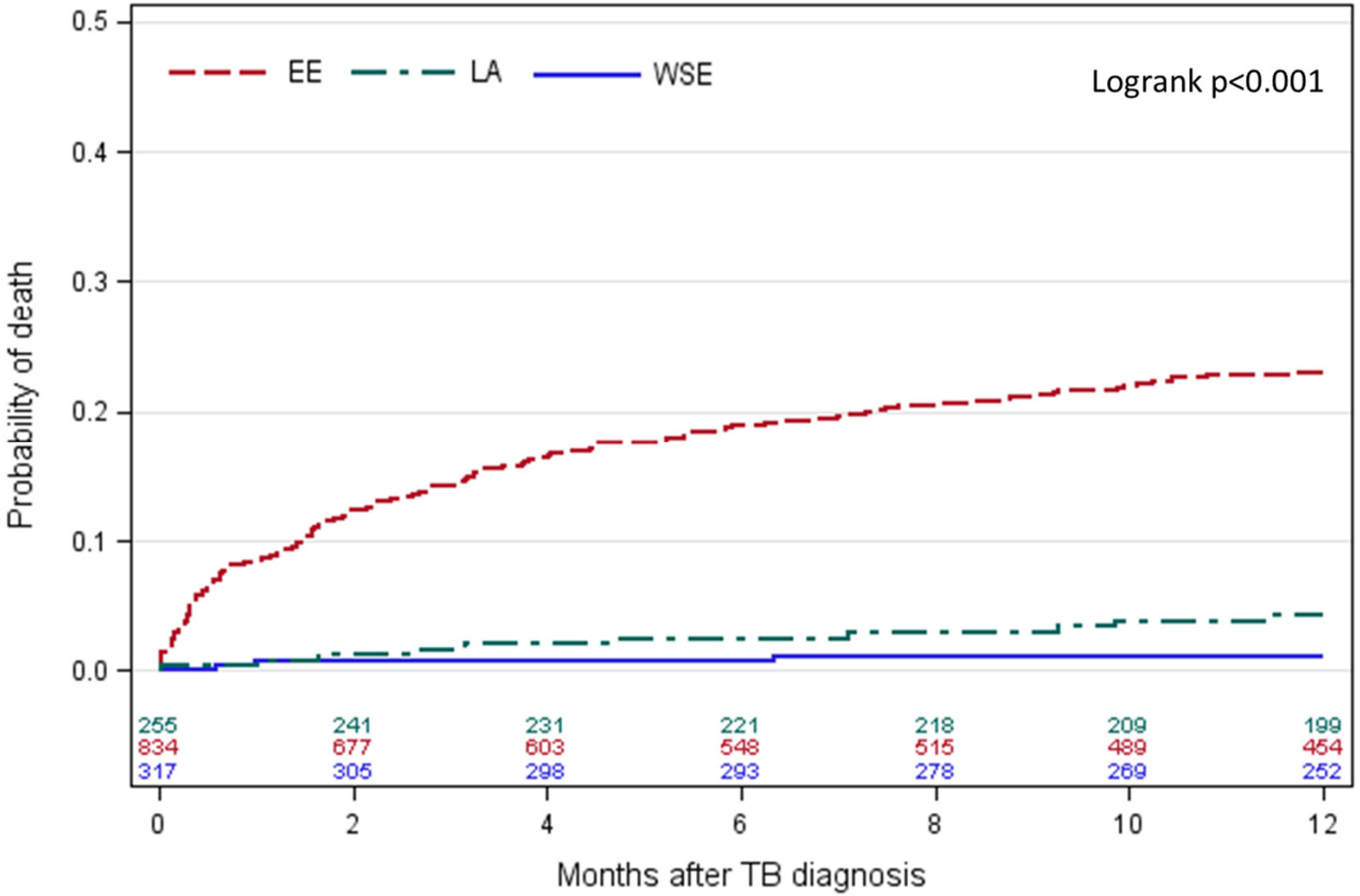
TB OUTCOMES IN TB AND TB/HIV PATIENTS IN EASTERN EUROPE

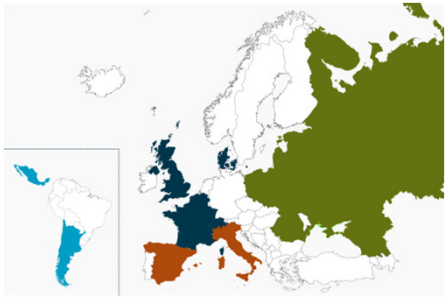
Probability of TB death, according to geographical region. The TB:HIV Study



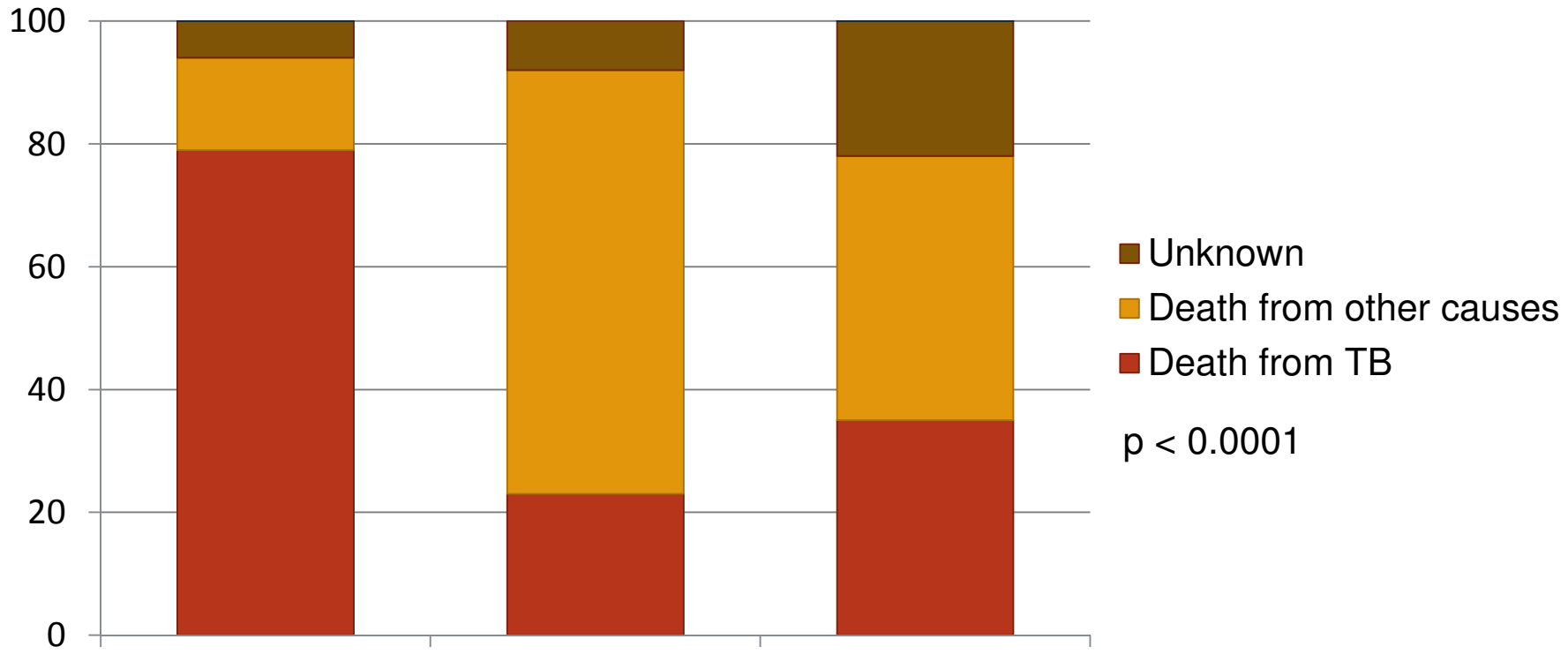


A Schultze et al, IAS 2015

Overall Mortality and Causes of Death The TB:HIV Study



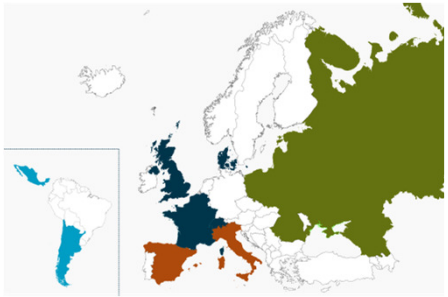
- **265** individuals (19%) died within 12 months
  - **188** (71%) of these deaths could be classified as TB-related

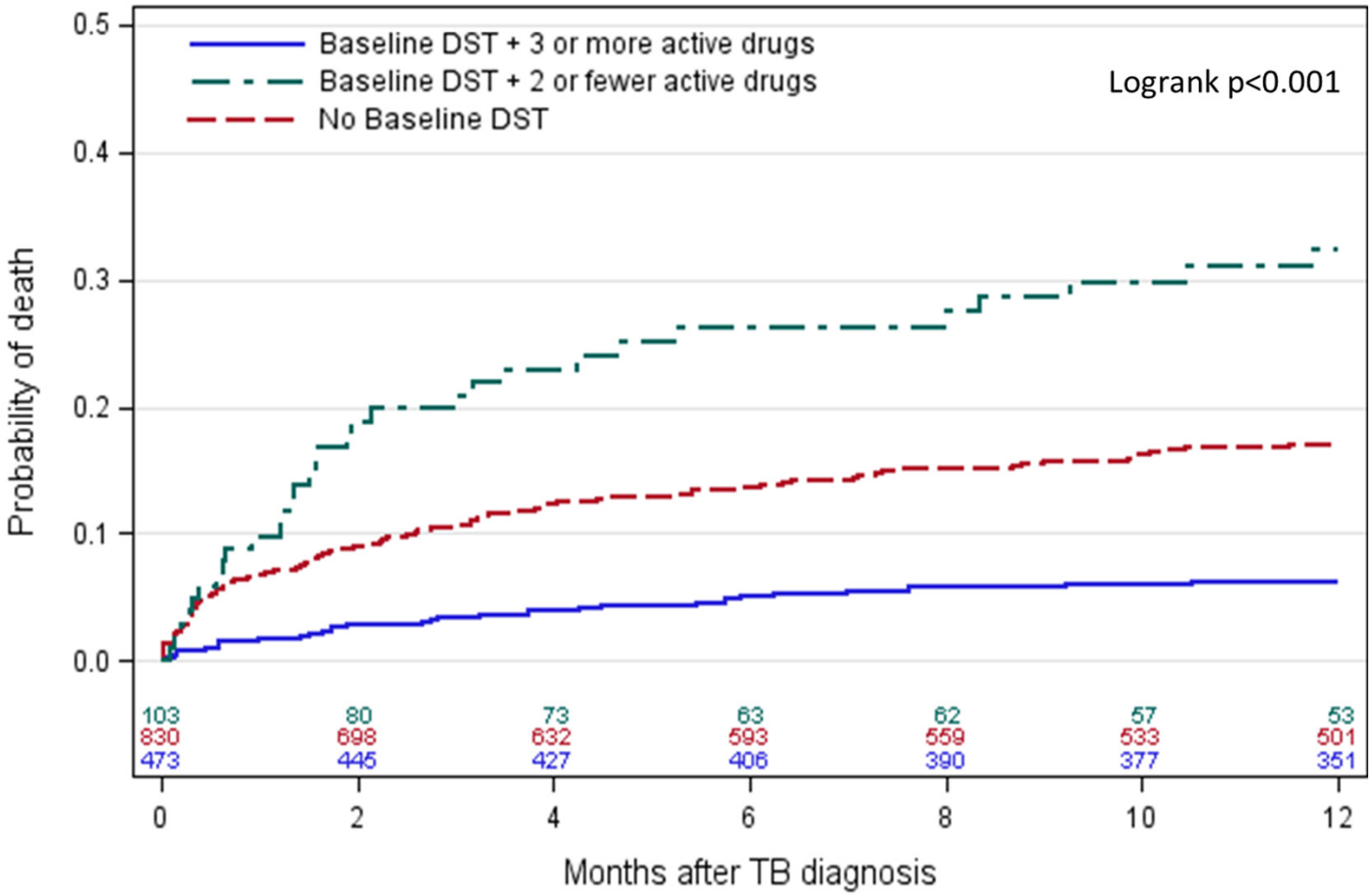


	EE	WSE	LA
TB N(%)	175 (79)	3 (23)	10 (36)
Other N(%)	34 (15)	9 (69)	12 (43)
Unknown N(%)	14 (6)	1 (8)	6 (21)

A Schultze et al, IAS 2015

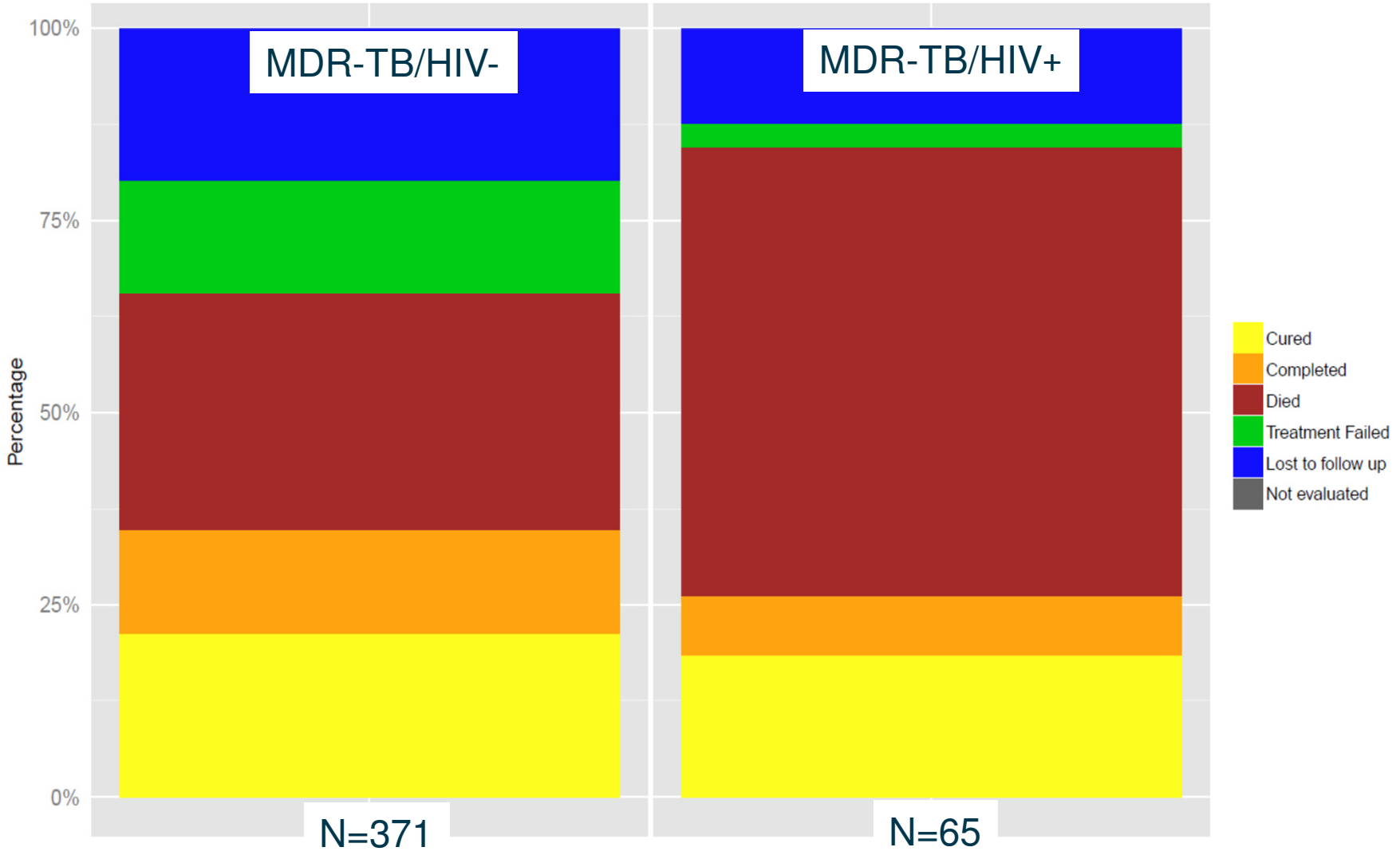
Probability of TB death, according to number of active drugs in the initial regimen. The TB:HIV Study





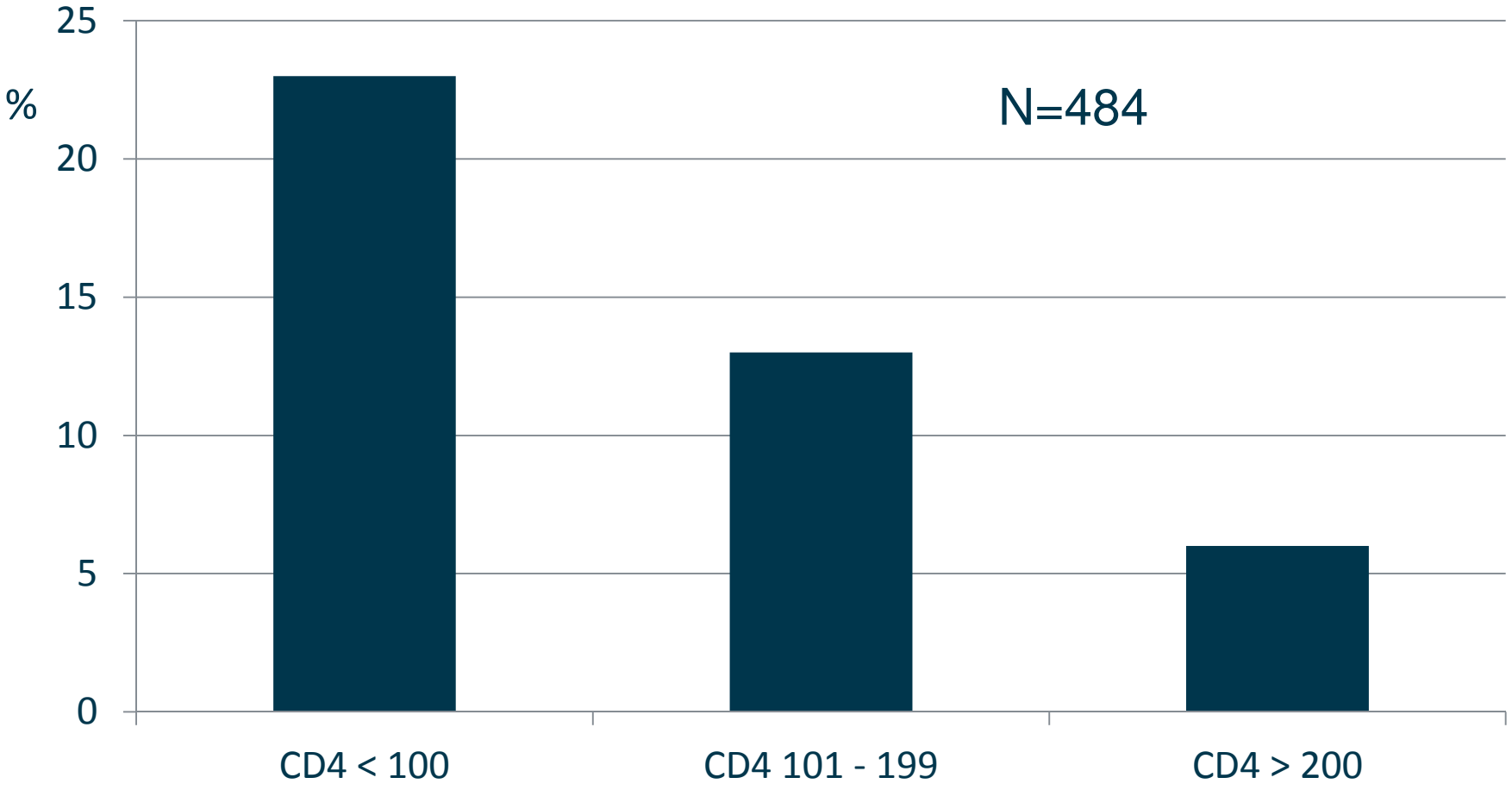
A Schultze et al, IAS 2015

Treatment outcomes for MDR-TB patients without and with HIV. A study from Belarus



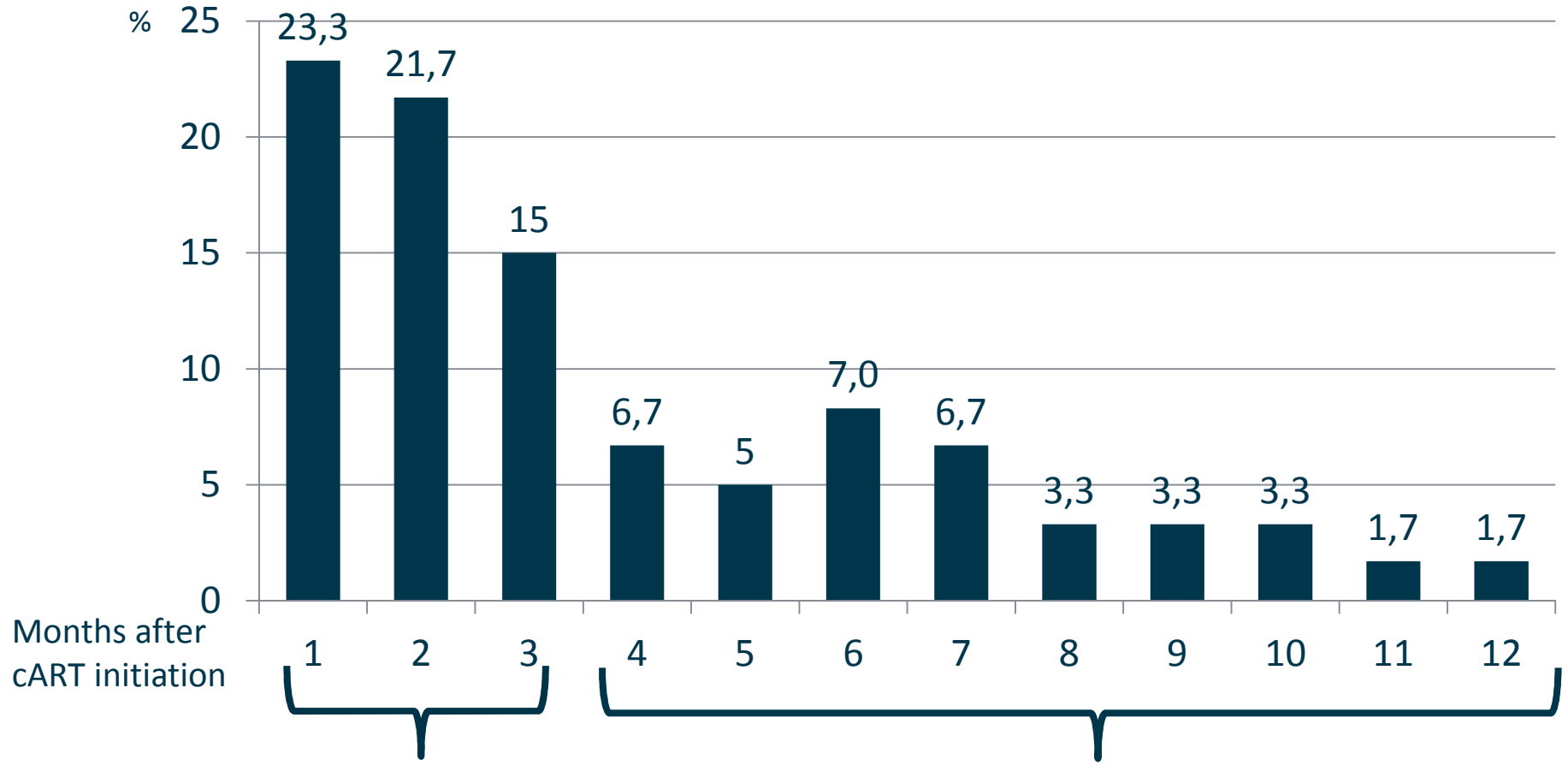
A Skrahina. Personal communication

Mortality of TB/HIV patients depending on CD4 cell count
A study from St. Petersburg



A Panteleev. Personal communication

Mortality of TB/HIV patients after cART initiation
A study from St. Petersburg



MDR-TB **82.1%** p<0.05 **57.5%**

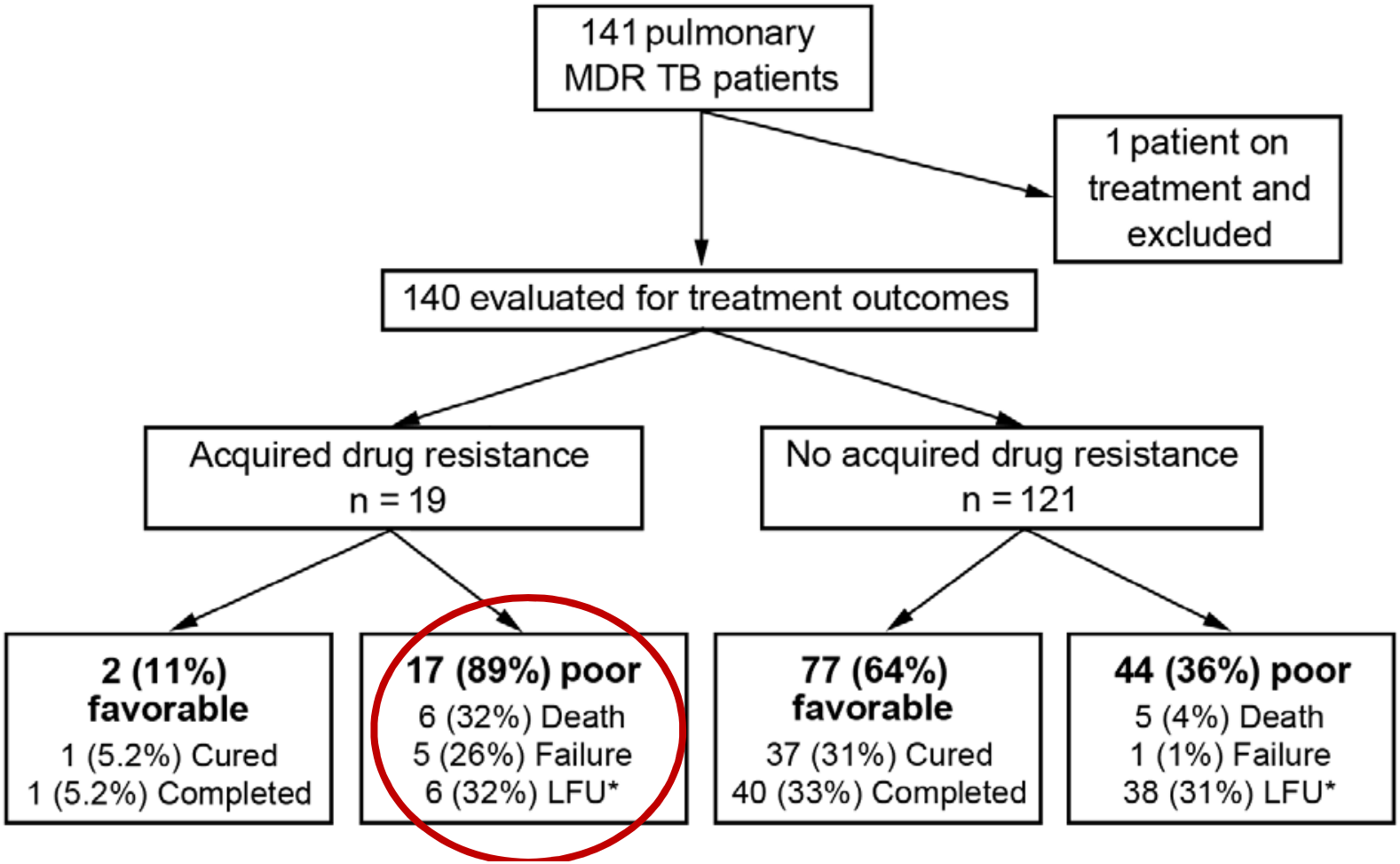
Disseminated TB **84,3%** p<0.05 **51.5%**

A Panteleev. Personal communication

MDR-TB treatment outcomes
A study from Georgia

RR Kempker et al., Emerging Infectious Diseases. Vol. 21, No. 6

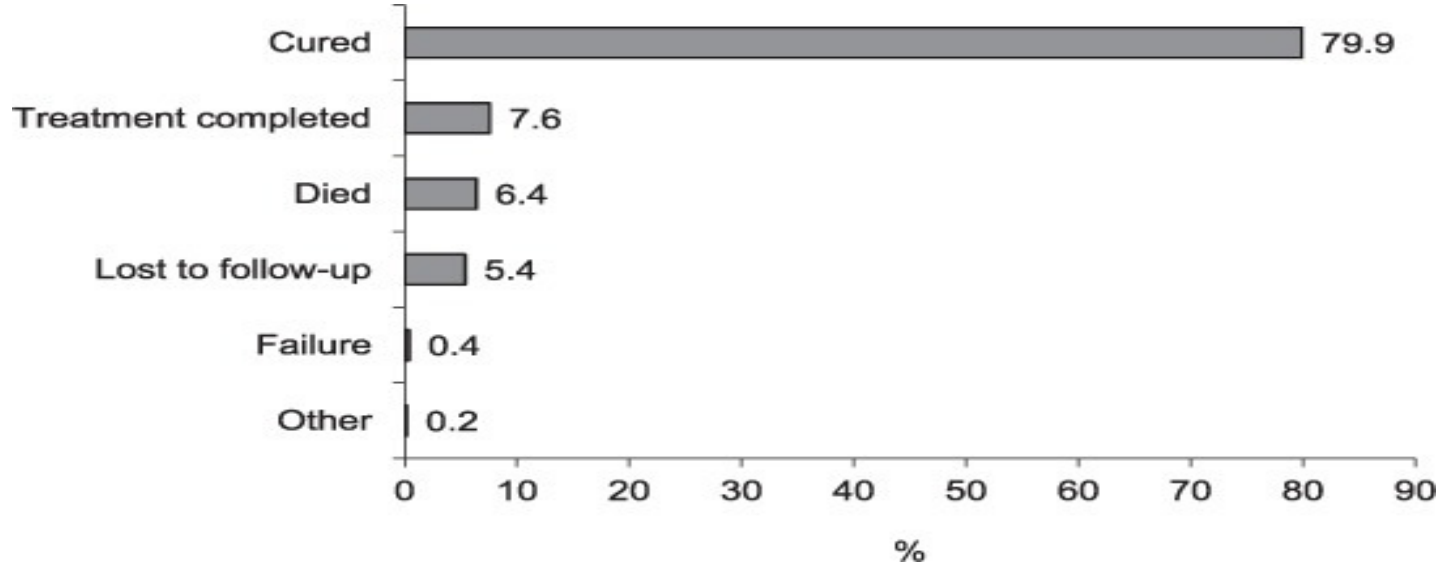
Final treatment outcomes for patients with multidrug-resistant tuberculosis (MDR TB), Georgia, March 2009–October 2012



Treatment outcomes among drug-susceptible tuberculosis patients in Latvia, 2006–2010

I. Lucenko,[1] V. Riekstina,[2] J. Perevoscikovs,[1] D. Mozgis,[1,3] M. Khogali,[4] J. Gadoev,[5] P. de Colombani,[6] A. M. V. Kumar[7]

Public Health Action. 2014 Oct 21;4(Suppl 2)



Factors, significantly associated with unsuccessful treatment	Adjusted RR (95% CI)
HIV+	2.0 (1.4–2.8)
Unemployment	3.4 (2.3–5.0)
Alcohol use	1.5 (1.2–1.9)

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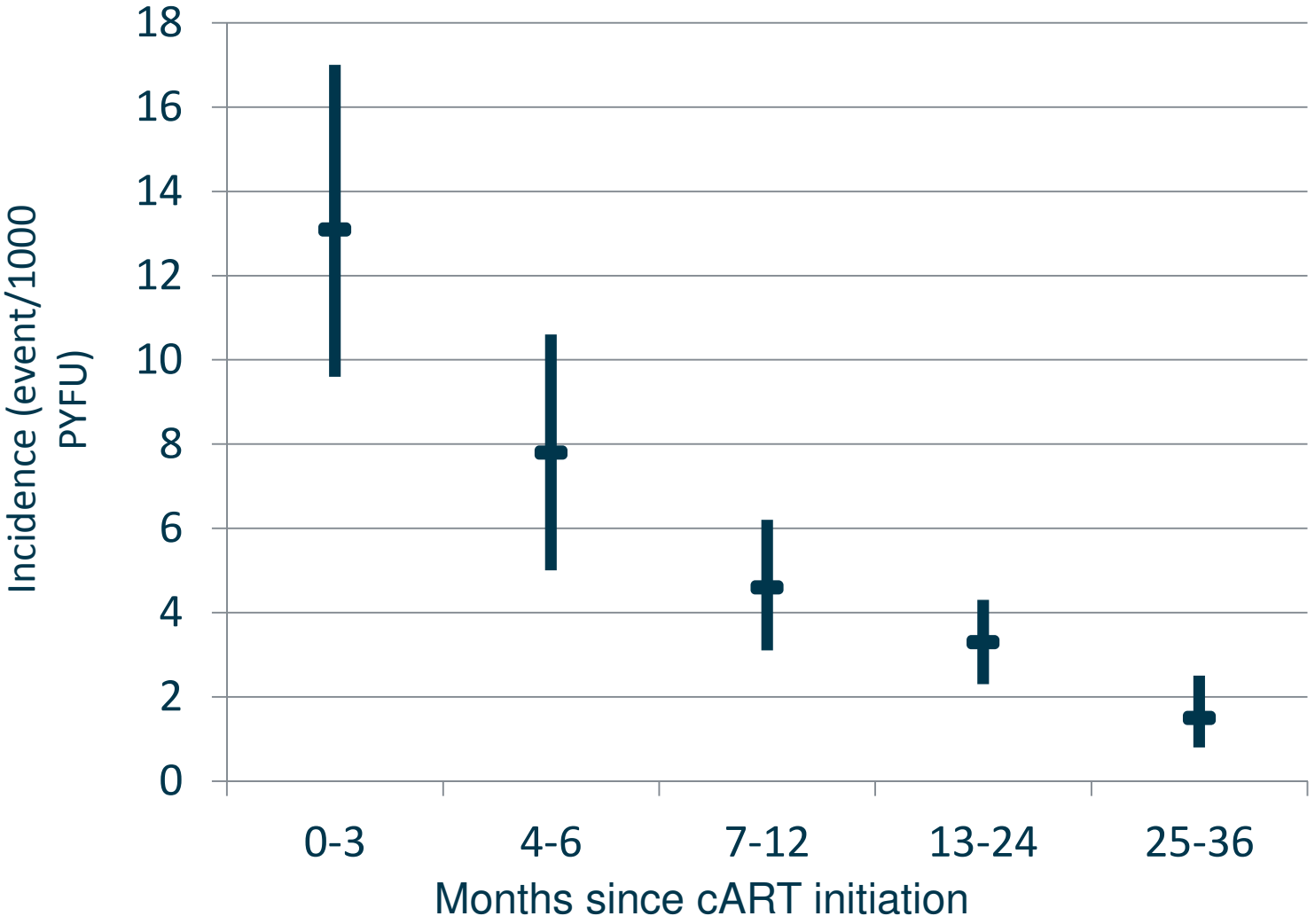
WHAT CAN BE DONE TO IMPROVE TB OUTCOMES IN EASTERN EUROPE

Effect of cART duration on TB incidence



Girardi, CID 2005

Timing of ART Initiation in patients initiating TB treatment

- SAPiT study: higher incidence of death in patients deferring ART therapy to end of TB treatment (sequential) vs initiation during TB therapy (integrated)[1]
- CAMELIA study: significant reduction in mortality with ART initiation at Wk 2 vs Wk 8 of TB therapy in pts with CD4+ counts ≤ 200 cells/mm3 [2]
- SAPiT and ACTG5221 studies: suggest all pts with CD4+ counts < 50 cells/mm3 should begin ART within 2-4 wks of TB therapy initiation[3,4]

[1]A Karim SS, et al. N Engl J Med. 2010;362:697-706.
[2]Blanc FX, et al. N Engl J Med. 2011;365:1471-81
[3]Abdool Karim SS, et al. N Engl J Med. 2011;365:1492-501
[4]Havlir D, et al. N Engl J Med. 2011;365:1482-91

Improving Outcomes for Multidrug-Resistant Tuberculosis: Aggressive Regimens Prevent Treatment Failure and Death

CID 2014:59 (1 July)

Gustavo E. Velásquez,[1] Mercedes C. Becerra,[2,3,4,5] Irina Y. Gelmanova,[3,4] Alexander D. Pasechnikov,[3,4] Askar Yedilbayev,[3,4] Sonya S. Shin,[3,4,5] Yevgeny G. Andreev,[6] Galina Yanova,[7] Sidney S. Atwood,[5] Carole D. Mitnick,[2,3,4,5] Molly F. Franke,[2,3,4] Michael L. Rich,[2,3,4,5] and Salmaan Keshavjee[2,3,4,5]

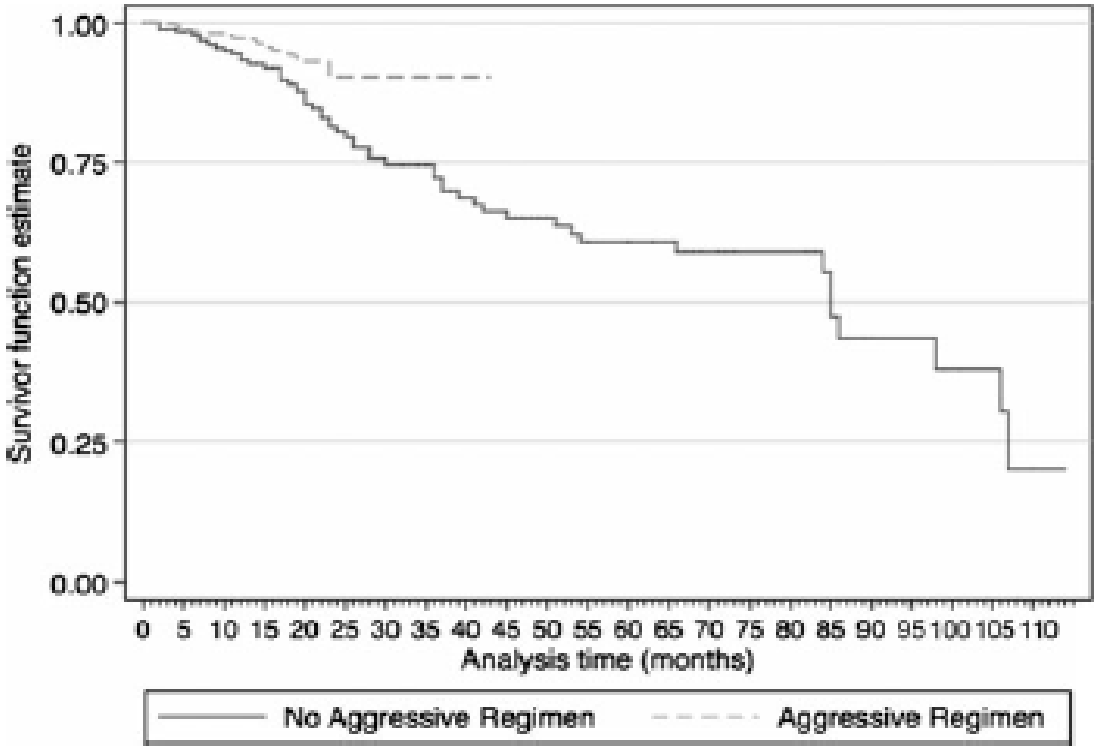


Figure 1. Death or treatment failure among patients treated for multidrug-resistant tuberculosis by time-varying monthly exposure to an aggressive regimen.

Cohort of 614 MDR-TB patients in Tomsk, Russia

Aggressive MDR-TB regimen:

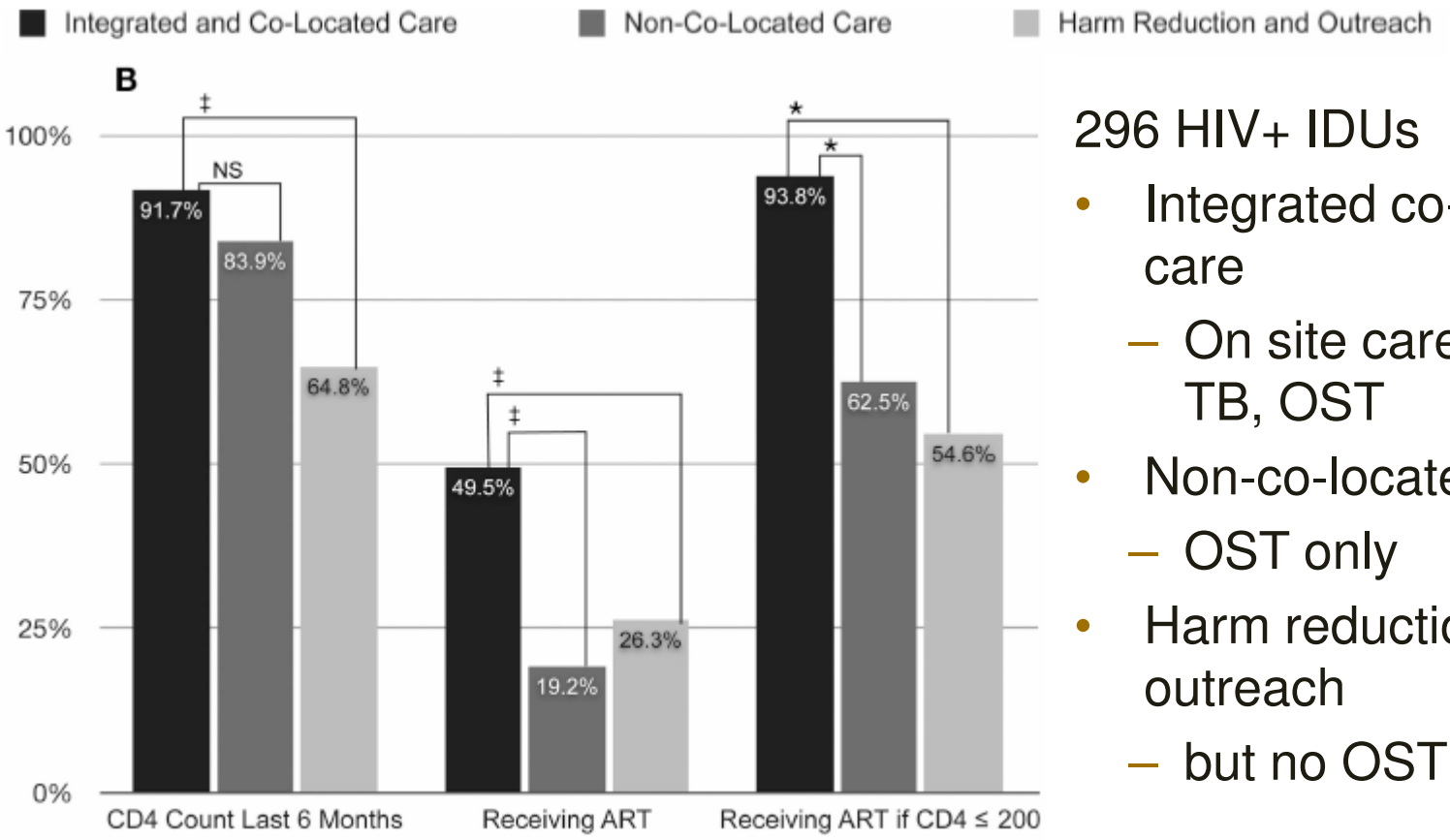
- Intensive phase: ≥5 likely effective drugs
- Cont. phase: ≥4 likely effective drugs

Adjusted hazard ratio 0.52 [95% CI 0.29–0.94]

Integrated health care works
A study from Ukraine

Quality Healthcare Indicators (QHI) based on service delivery setting:

HIV-Related Quality Healthcare Indicators



296 HIV+ IDUs

- Integrated co-located care
  - On site care for HIV, TB, OST
- Non-co-located care
  - OST only
- Harm reduction and outreach
  - but no OST

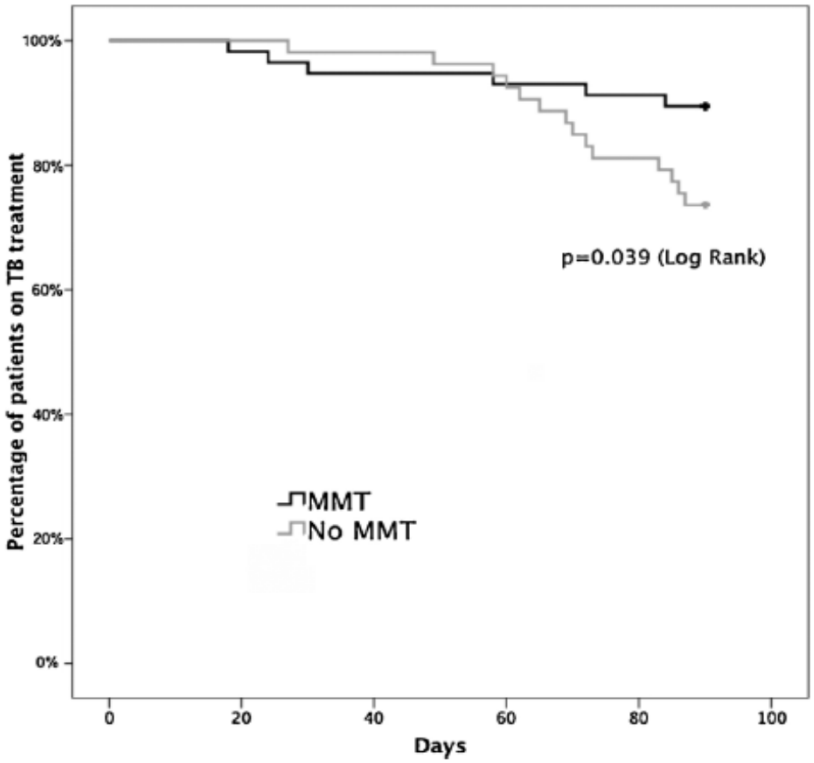
C Bachireddy et al., Drug Alcohol Depend. 2014

Opiate substitution therapy works
A study from Ukraine

O Morozova et al., International Journal of Drug Policy 24 (2013)

Observational study of 110 TB patients (68% HIV+)
MMT (methadone maintenance): N=57 / non-MMT N = 53

Time to discontinuation of TB treatment over 90-day observation period



90-day retention on tuberculosis treatment was significantly associated with MMT:

- adjusted OR (95% CI) 3.05 (1.08–8.66)

Summary:
Actions to improve TB outcomes in HIV+ people in Eastern Europe

- Integration of health care systems (HIV/TB/OST)
- Strong infection control to stop spread of TB/MDR-TB and HIV infections
  - Early case detection
- Adequate treatment of TB based on the results of the Drug Susceptibility Testing
  - Rapid DST
- Adequate treatment of HIV infection
  - Early initiation of ART
- Treatment of concominent conditions (IDU/HCV)
- **Political will and commitment**

Acknowledgement

- CHIP, Copenhagen
  - Jens D. Lundgren
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  - Anne Marie W. Efsen
  - Maiken Mansfeld
- Royal Free Hospital, London
  - Amanda Mocroft
  - Anna Schultze
- Colleagues from Eastern Europe
  - Alena Skrahina
  - Aza Rakhmanova
  - Alexander Panteleev

Thank you very much for your attention!