TB:HIV an international prospective observational study

Major challenges in clinical management of TB/HIV coinfected patients in Eastern Europe compared with Western Europe and Latin America

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for the TB:HIV study group in EuroCoord

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REGION H Rigshospitalet

SEVENTH FRAMEWORK PROGRAMME

EuroCoord

Background

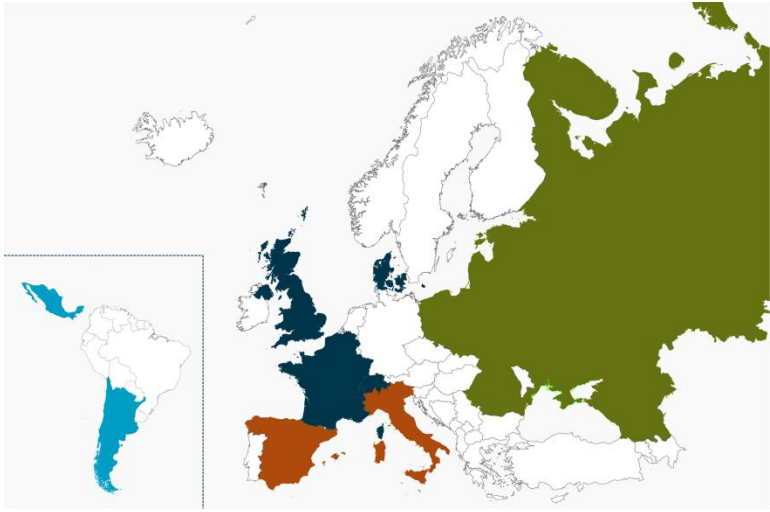
- Tuberculosis (TB) is the most common co-infection among HIV-positive patients and the most common cause of death

- Eastern Europe:
  - Rapidly increasing incidence of HIV[1]
  - Overlapping risk groups for HIV and TB (IDUs)[1,4]
  - The world's highest proportions of multi-drug resistant TB (MDR-TB*)[2]
  - Inadequate surveillance systems, data on TB/HIV patients remain scarce[3]

*MDR-TB = Resistance against Rifampicin and Isoniazid

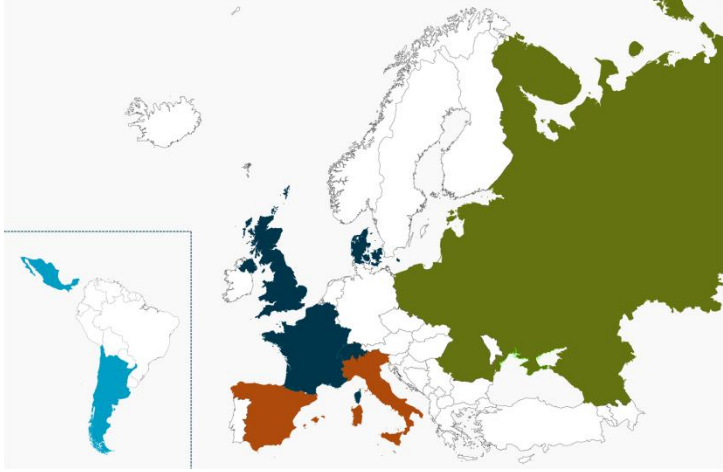
[1]UNAIDS Report, 2013
[2]WHO Global Tuberculosis Report, 2013
[3]Abubakar et al., Lancet, 2013
[4]Podlekareva et al., AIDS, 2009

Aims



- Compare clinical characteristics of TB/HIV coinfected patients in three European regions and Latin America at time of TB diagnosis
- Identify factors associated with having MDR-TB
- Assess the activity of empiric anti-TB therapy in relation to subsequent drug-susceptibility test (DST) results

TB:HIV Study



- TB:HIV Study: Prospective, observational cohort study of TB/HIV coinfected patients

- Inclusion criteria: Consecutively enrolled HIV-positive patients >16 years, diagnosed with TB between 2011 – 2013

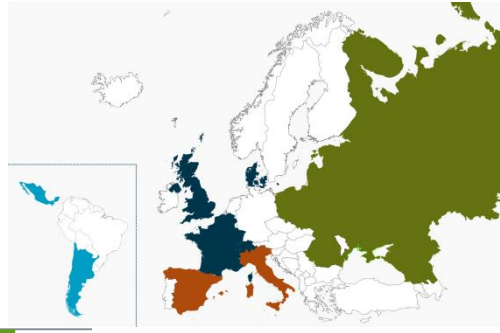
- Collaboration of 62 TB and HIV clinics:
  - **Eastern Europe**, (21 clinics in Belarus, Estonia, Georgia, Latvia, Lithuania, Poland, Romania, Ukraine, Russia),
  - **Western Europe** (19 clinics in Belgium, Denmark, France, Switzerland, United Kingdom)
  - **Southern Europe** (9 clinics in Italy and Spain)
  - **Latin America** (13 clinics in Argentina, Chile, and Mexico)

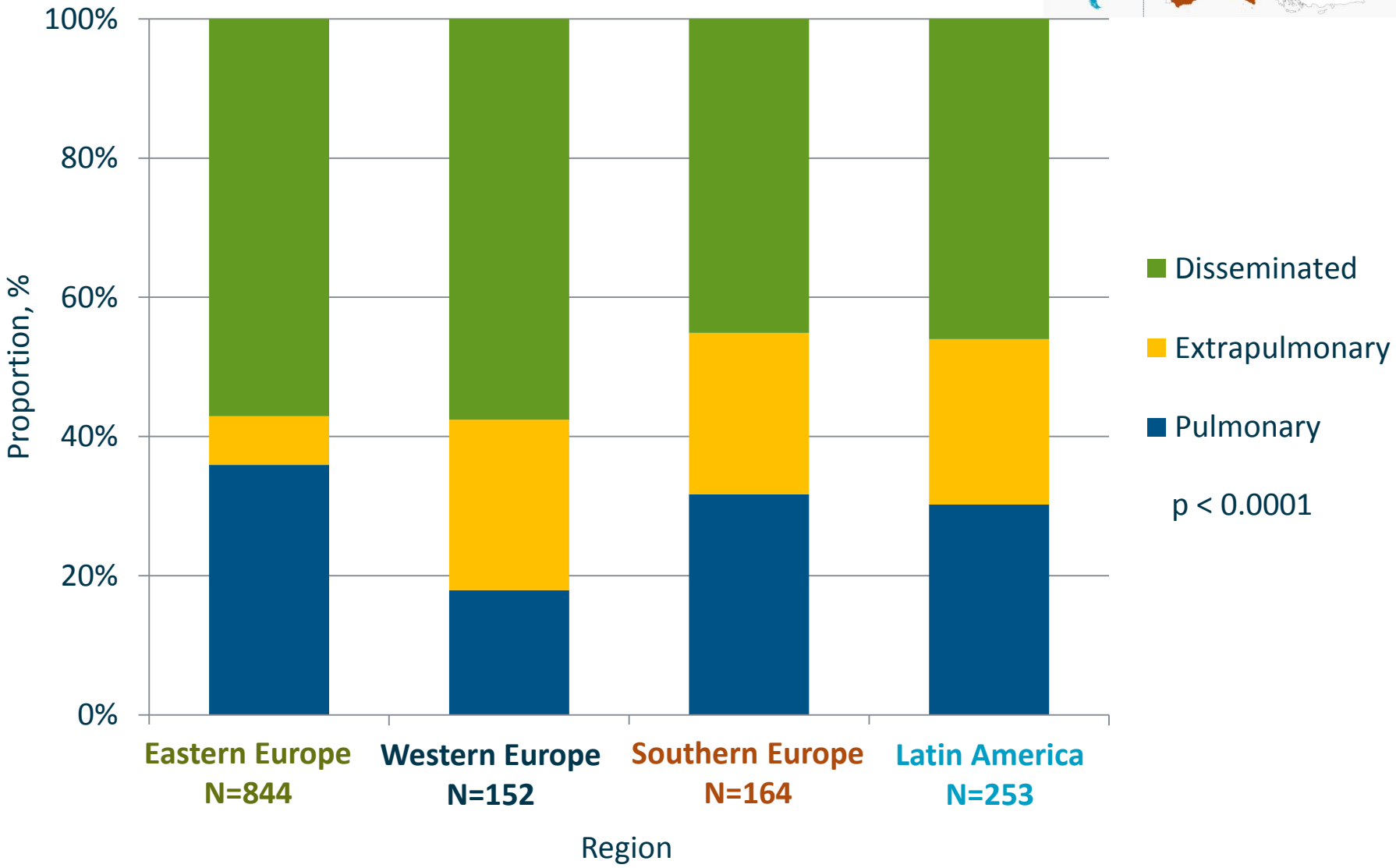
Clinical characteristics of 1413 TB/HIV patients at time of TB diagnosis

	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

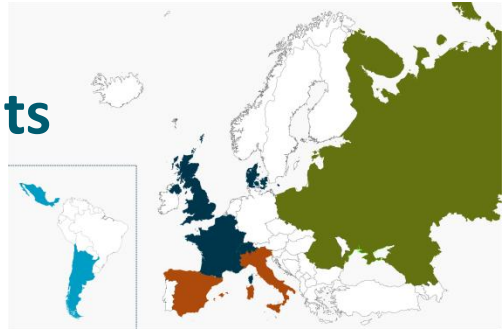
[1]OST = Opioid Substitution Therapy. The denominator is IDU (HIV) risk group.

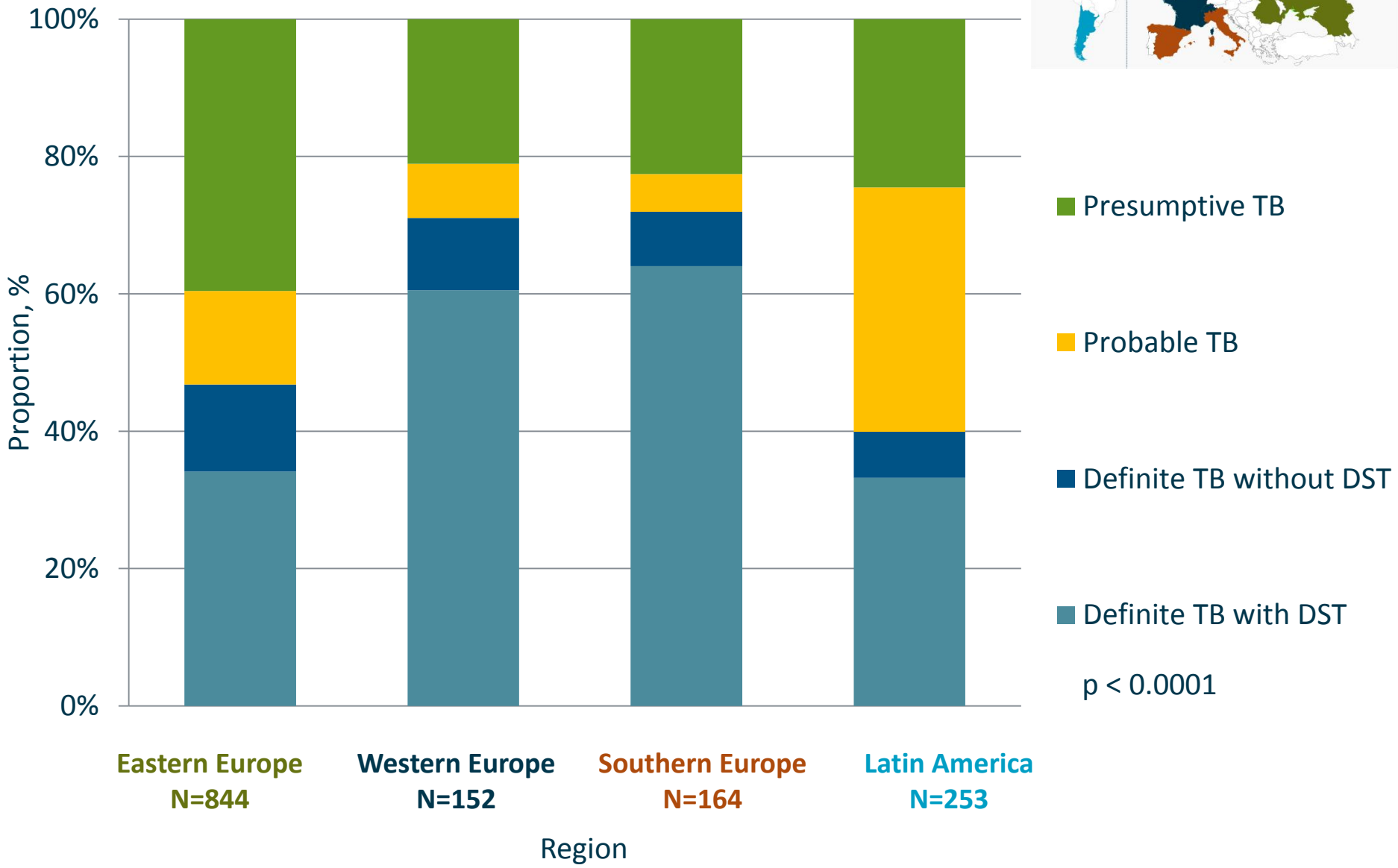
TB localisation



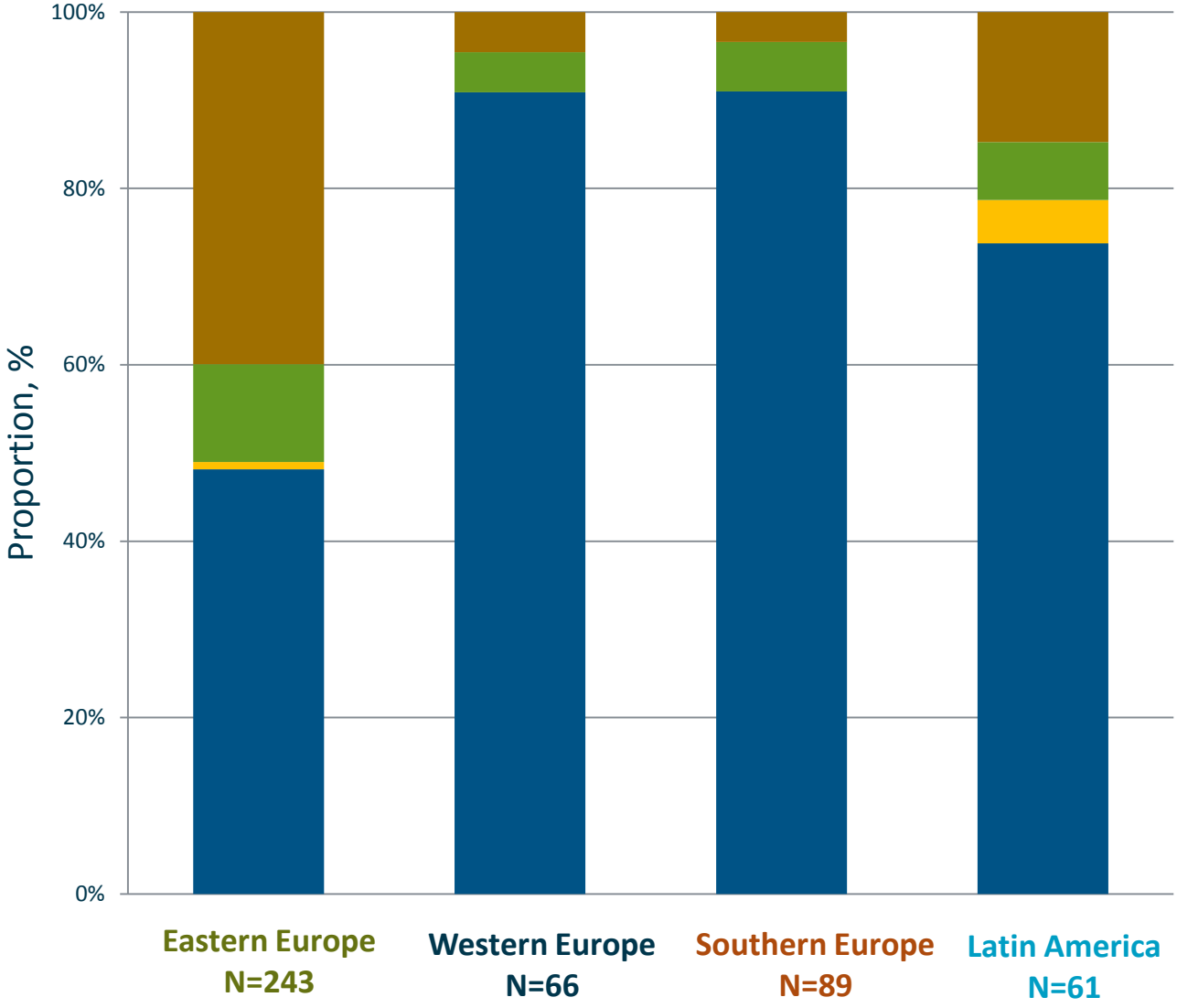


Diagnosis of TB and availability of DST results





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



Rifampicin resistant/ Isoniazid resistant (MDR-TB)

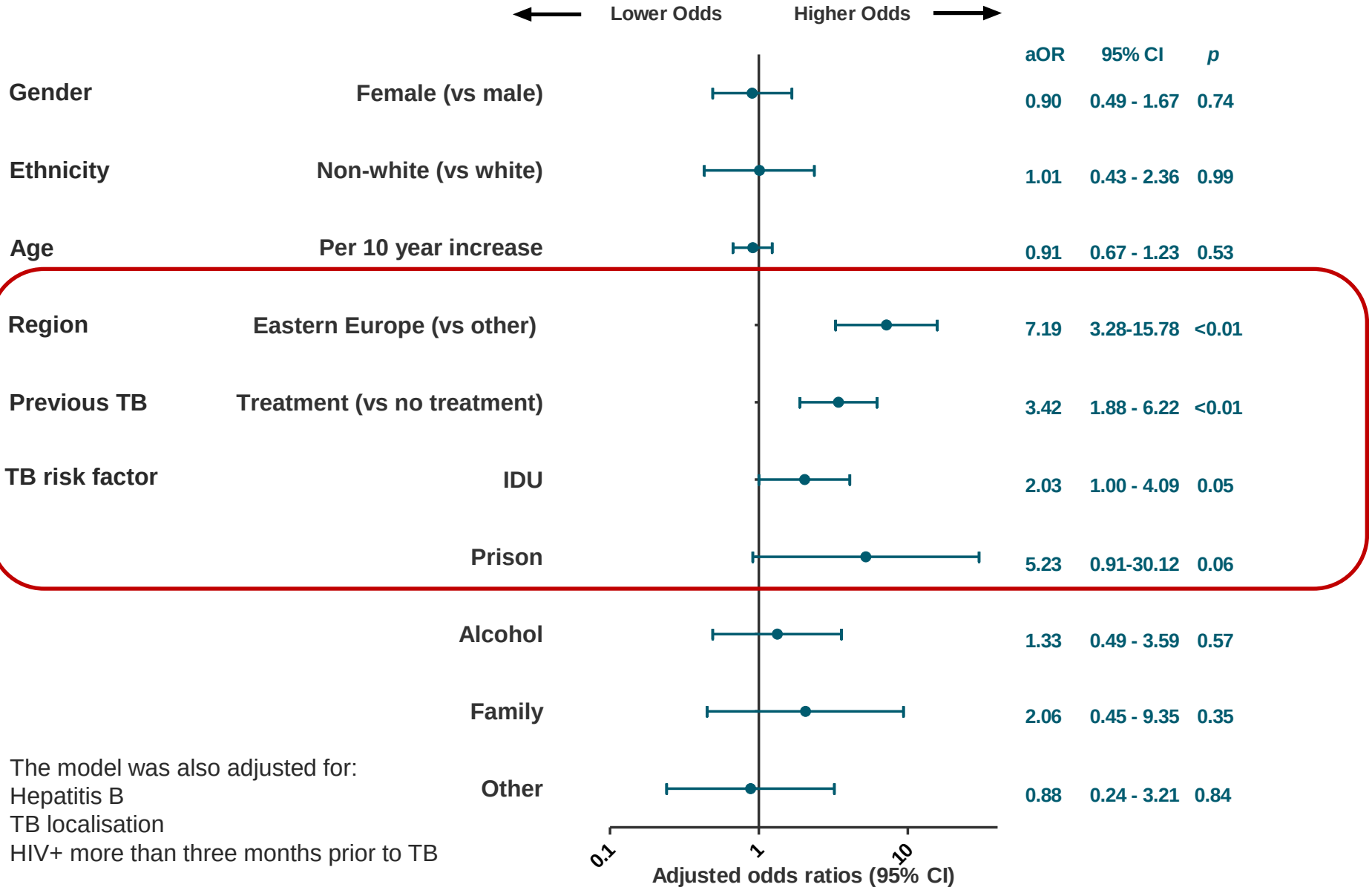
Rifampicin susceptible/ Isoniazid resistant

Rifampicin resistant/ Isoniazid susceptible

Rifampicin susceptible/ Isoniazid susceptible

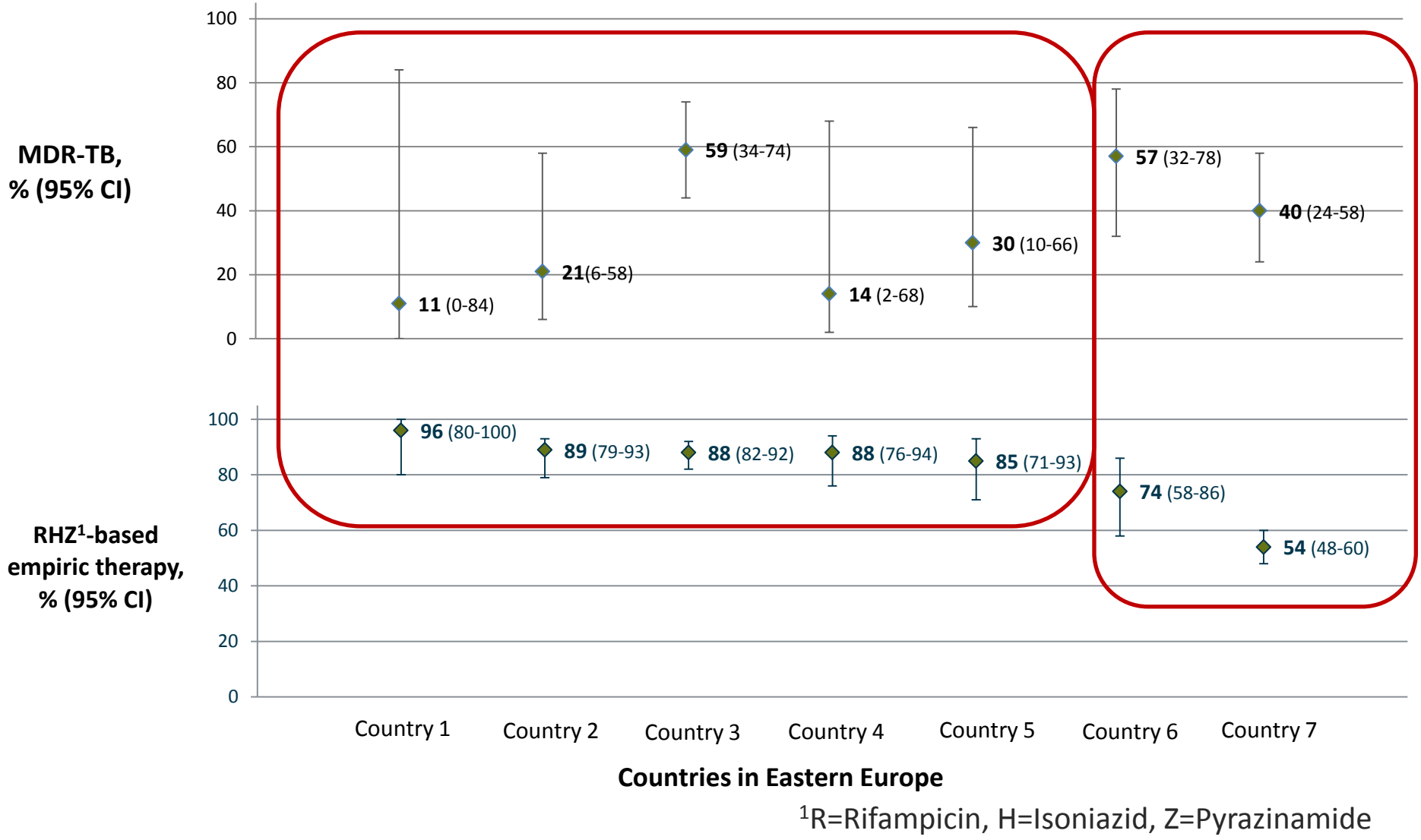
459/569 DSTs were tested for both Rifampicin and Isoniazid

Factors associated with MDR-TB in multivariable logistic regression analysis



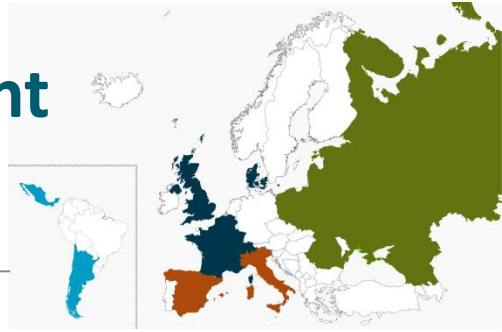
The model was also adjusted for:
Hepatitis B
TB localisation
HIV+ more than three months prior to TB

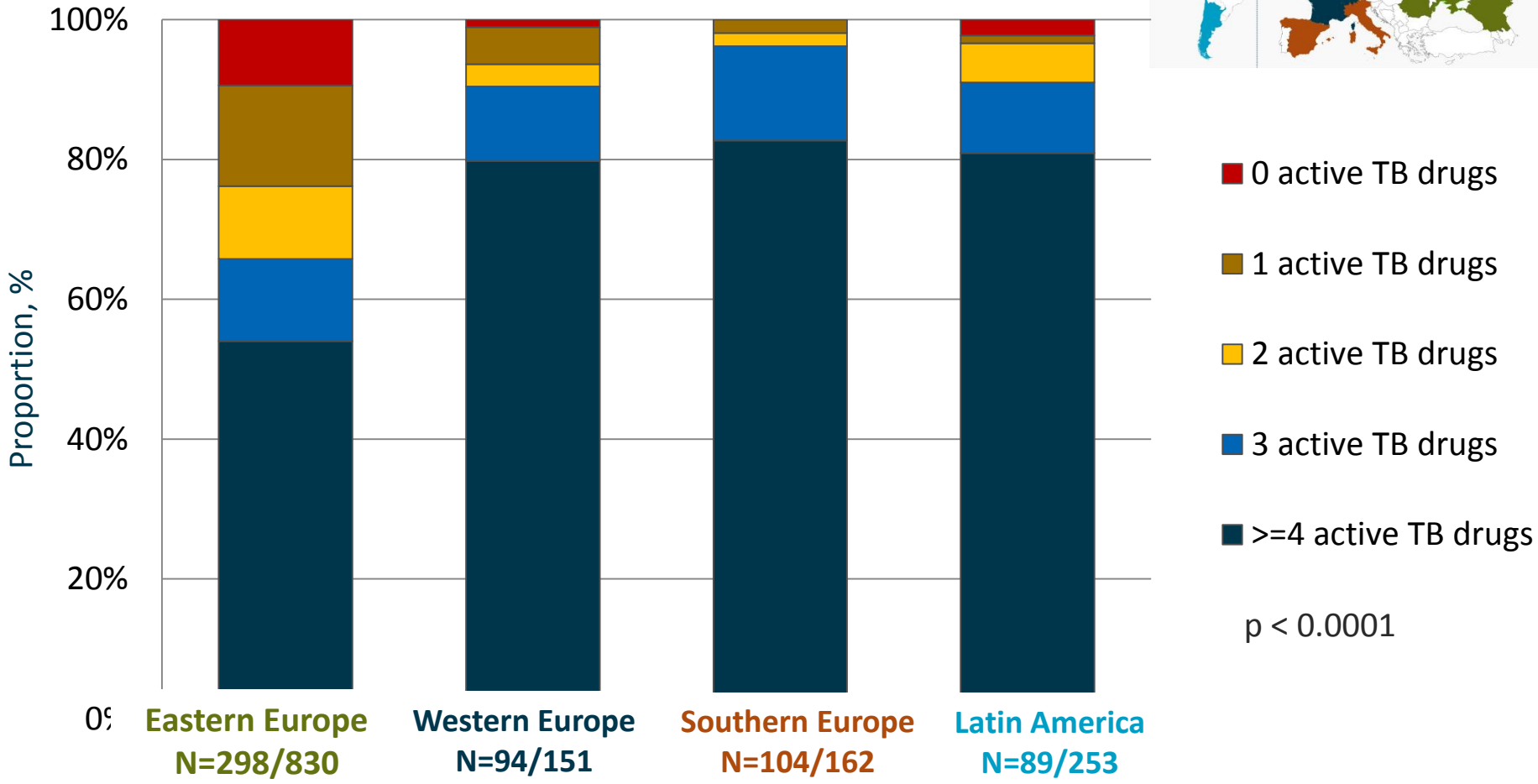
Proportion with MDR-TB and RHZ-based empiric therapy in countries in Eastern Europe



[1]R=Rifampicin, H=Isoniazid, Z=Pyrazinamide

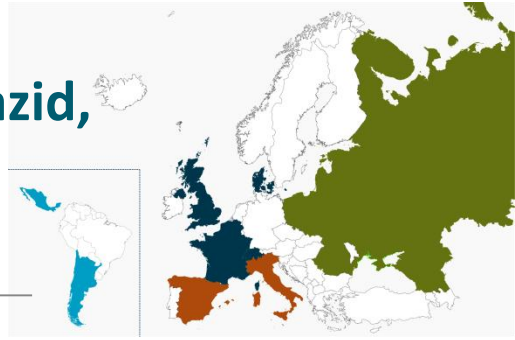
Susceptibility of empiric anti-TB treatment in relation to subsequent DST results

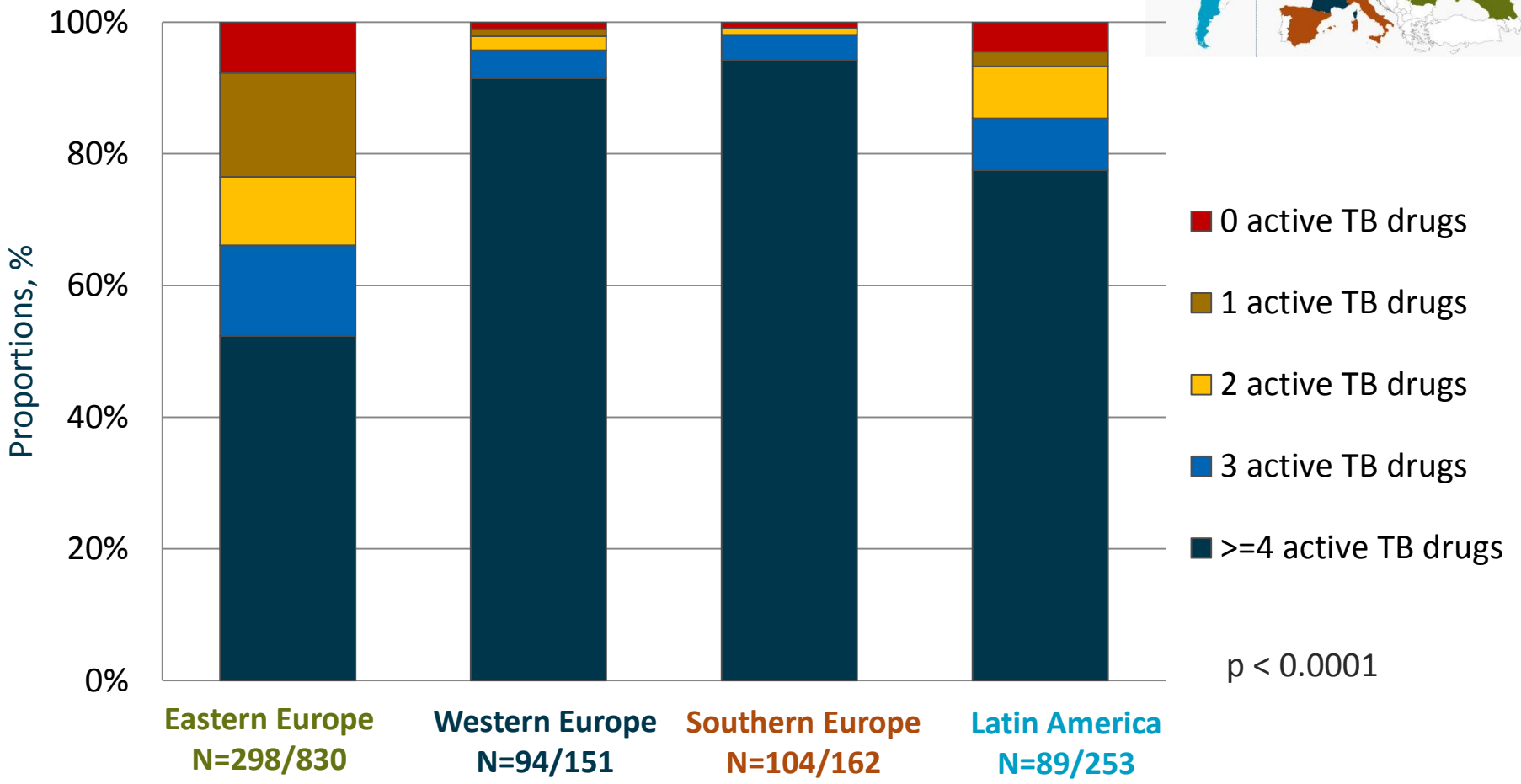




Active drugs calculated from comparing empiric anti-TB therapy and subsequently known DST results within the first month of TB therapy. MTB isolates were assumed to be susceptible to all drugs for which no DST results were available.

Would empiric anti-TB treatment with rifampicin, isoniazid, pyrazinamide and ethambuthol have been better?





Hypothetically assuming empiric anti-TB treatment had been initiated with rifampicin, isoniazid, pyrazinamide and ethambutol

Limitations

- Observational study; selection bias
- Hospitals/clinics were not necessarily representative of their country/region
- Full anti-TB DST results were not available for all patients

Summary

- Large differences in clinical characteristics of TB/HIV coinfected patients across Europe and Latin America
- The situation in Eastern Europe was characterised by:
  - Lower proportion of definite TB diagnosis and DST results
  - High levels of MDR-TB and no correlation between proportion of MDR-TB and RHZ-based empiric therapy
  - Fewer active drugs in empiric therapy
- Pronounced variation between countries within Eastern Europe in levels of MDR-TB and in the empiric anti-TB regimens prescribed

Perspectives

- Given the very low CD4 cell counts observed, important to maintain patients under follow-up and initiate cART when appropriate
- Clear need for improving and implementing more accurate and rapidly available diagnostics
- Improve empiric anti-TB therapy, particularly in high resistance settings such as Eastern Europe
- The long-term clinical consequences will be further analysed as FU data accumulates (www.chip.dk under TB:HIV study)

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The TB:HIV Study Group

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