TB:HIV an international prospective observational study

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One-year Mortality of HIV-patients Treated for Susceptible TB is Higher in Eastern Europe than in Western/Southern Europe and Latin America

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on behalf of the TB:HIV study group in EuroCoord

EuroCoord

Disclosure

- I do not have any conflicts of interests

Background

- Prior results of the TB:HIV study documented increased mortality of TB/HIV patients in Eastern Europe[1]

- This was partly explained by the high prevalence of MDR-TB in the region and, as a consequence, the reduced number of active drugs in the initial TB treatment regimens

- It is unknown whether survival of patients with pan-susceptible TB differs across regions

[1]A Schultze et al., IAS Conference 2015, Vancouver, Canada

Aims

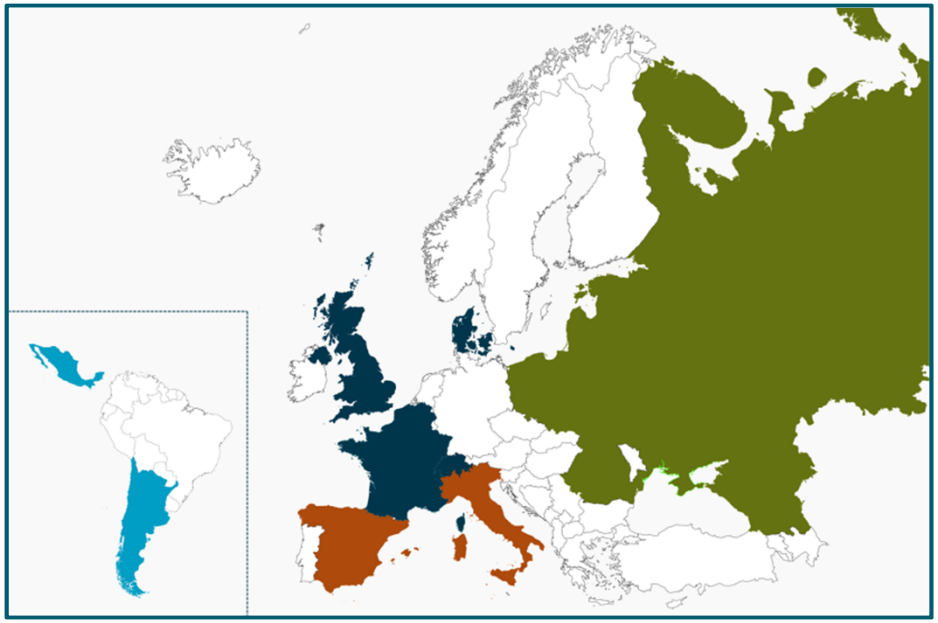
To compare mortality rates and risk factors of death in patients with pan-susceptible TB in Eastern Europe, Western/Southern Europe and Latin America

TB:HIV study

- Prospective cohort of TB/HIV co-infected patients

- Inclusion criteria:
  - HIV positive
  - Diagnosed with TB between 2011 – 2013
  - > 16 years of age

TB:HIV study



- **Eastern Europe**: 21 clinics in Belarus, Estonia, Georgia, Latvia, Lithuania, Poland, Romania, Ukraine and Russia — **EE**
- **Western Europe**: 19 clinics in Belgium, Denmark, France, Switzerland and the United Kingdom — **WSE**
- **Southern Europe**: 9 clinics in Italy and Spain — **WSE**
- **Latin America**: 13 clinics in Argentina, Chile and Mexico — **LA**

Methods I

Analysis limited to patients:

- Infected with Mycobacterium tuberculosis (Mtb) susceptible to both Rifamycin and Isoniazid (RH-susceptible)

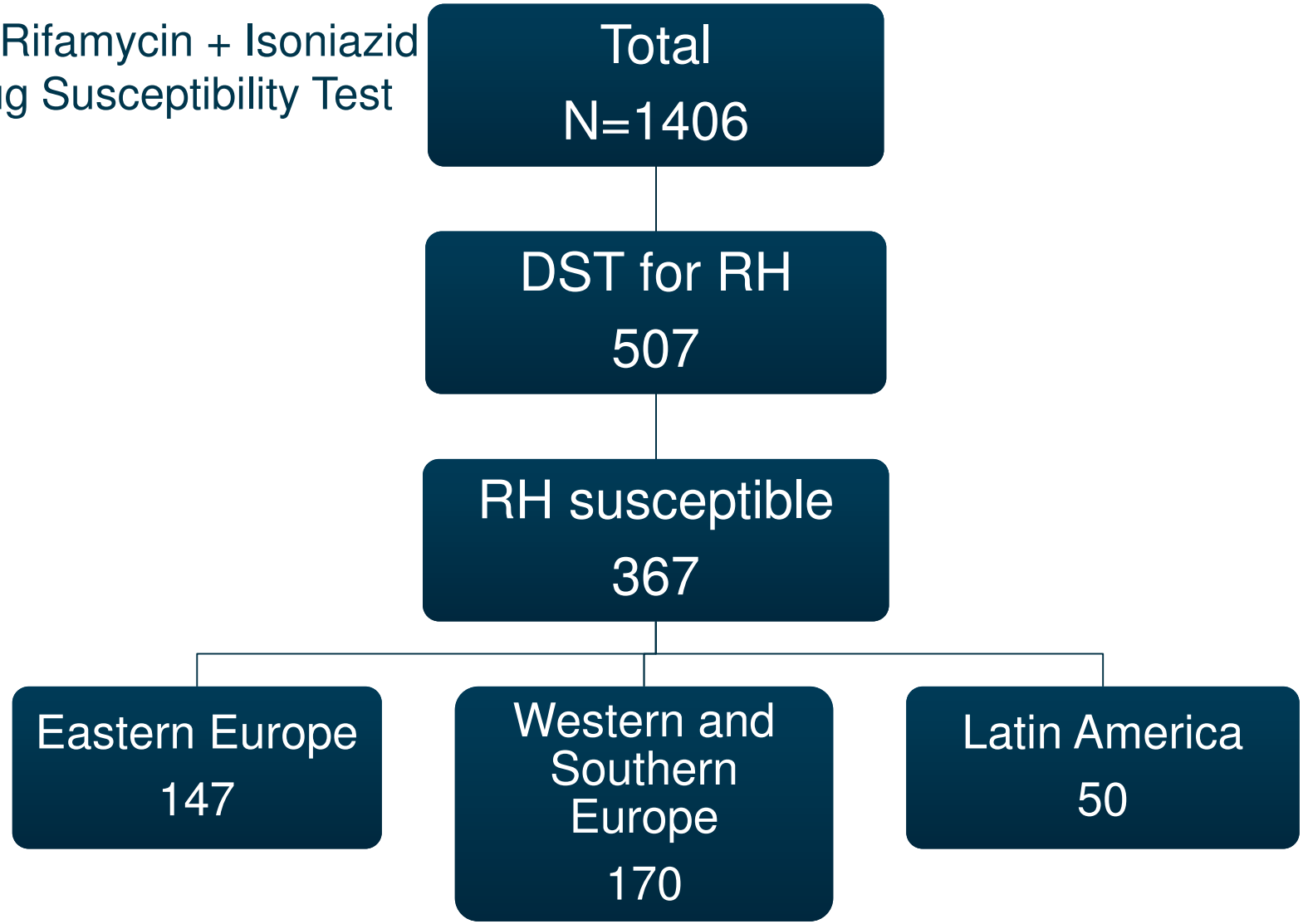
- Drug Susceptibility Testing (DST) performed on Mtb isolates from samples taken +/- 4 weeks of starting TB treatment

Methods II

- Patients were stratified by region of residence (EE, WSE, LA)
- One-year mortality from the start of TB treatment (baseline) was assessed by Kaplan-Meier analysis
- Risk factors of death were identified by Cox proportional hazard models
- Individuals censored at their last clinic visit, date of death or 12 months from baseline, whichever occured first

TB:HIV Study

RH: Any Rifamycin + Isoniazid
DST: Drug Susceptibility Test



Baseline Characteristics (n=367)

		EE N=147 (40%)	WSE N=170 (46%)	LA N=50 (14%)	
			N (%)		*P*
Gender	Male	113 (77)	114 (67)	36 (72)	0.15
IDU	ever	86 (59)	34 (30)	8 (16)	<0.0001
Hepatitis C	HCV Ab+	64 (44)	28 (16)	6 (12)	<0.0001
TB Type	Disseminated[1]	67 (46)	71 (42)	21 (42)	0.78
TB Treatment	RHZ based[2]	134 (91)	158 (93)	47 (94)	0.75
HIV treatment	On cART[3]	22 (15)	66 (39)	20 (40)	<0.0001
HIV-RNA	(<500 cp/ml)	11 (14)	36 (22)	12 (29)	0.10
			Median [IQR]		*P*
Age	years	35 (30-42)	38 (33-46)	38 (29-45)	0.006
CD4 count	cells/mm^3	107 (33-263)	121 (34-280)	85 (26-231)	0.60

*1. **Disseminated TB** = TB in > 1 organ system; 2. **R**=any Rifamycin; **H**=Isoniazid; **Z**=Pyrazinamide; 3. **cART**=on at least 3 HIV drugs at diagnosis*

***N with missing data:** **HCV**: 49, 46, 14; **HIV-RNA:** 66, 9, 9; **CD4 cell count**: 30, 4, 6 in EE, WSE and LA respectively*

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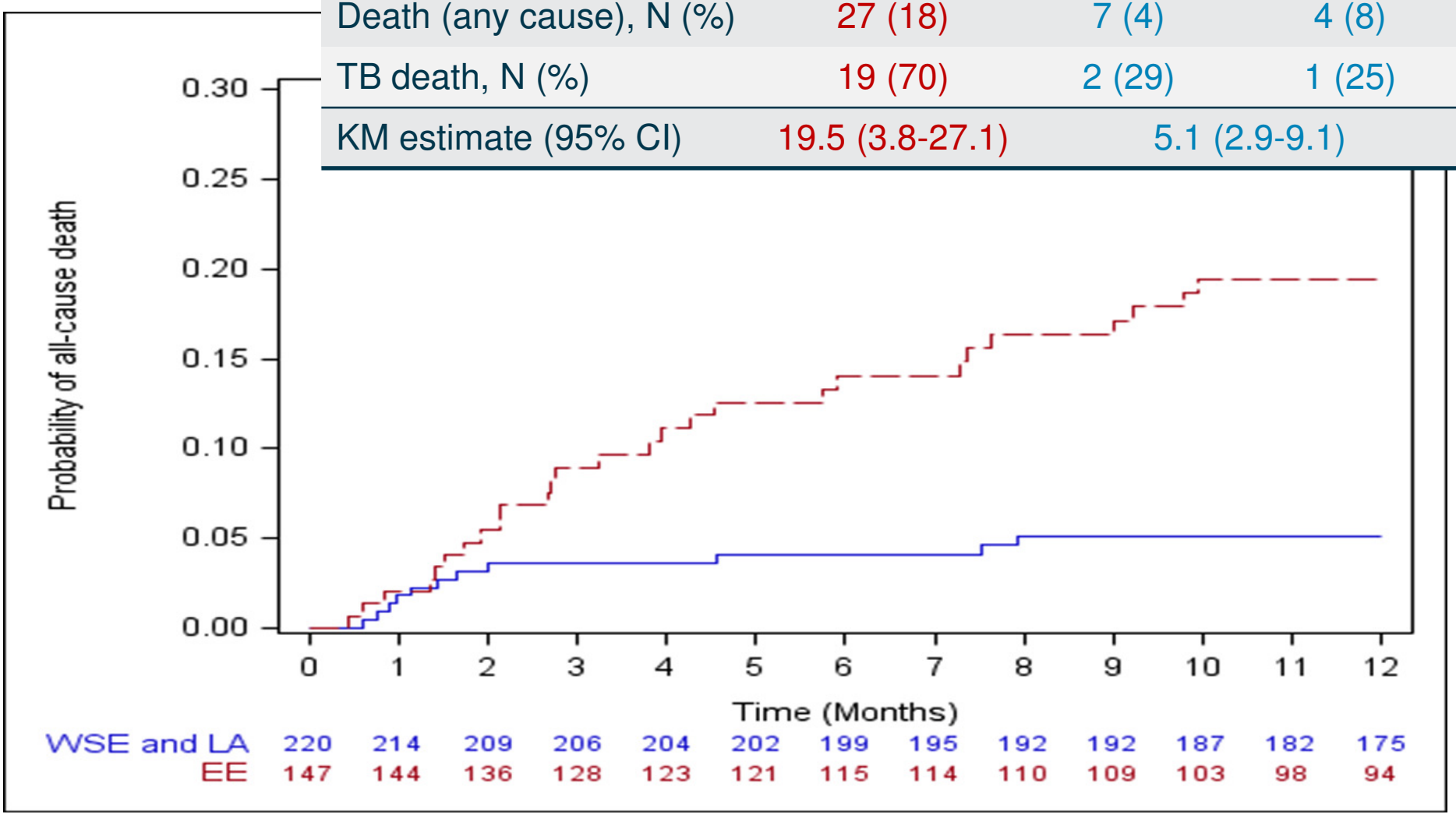
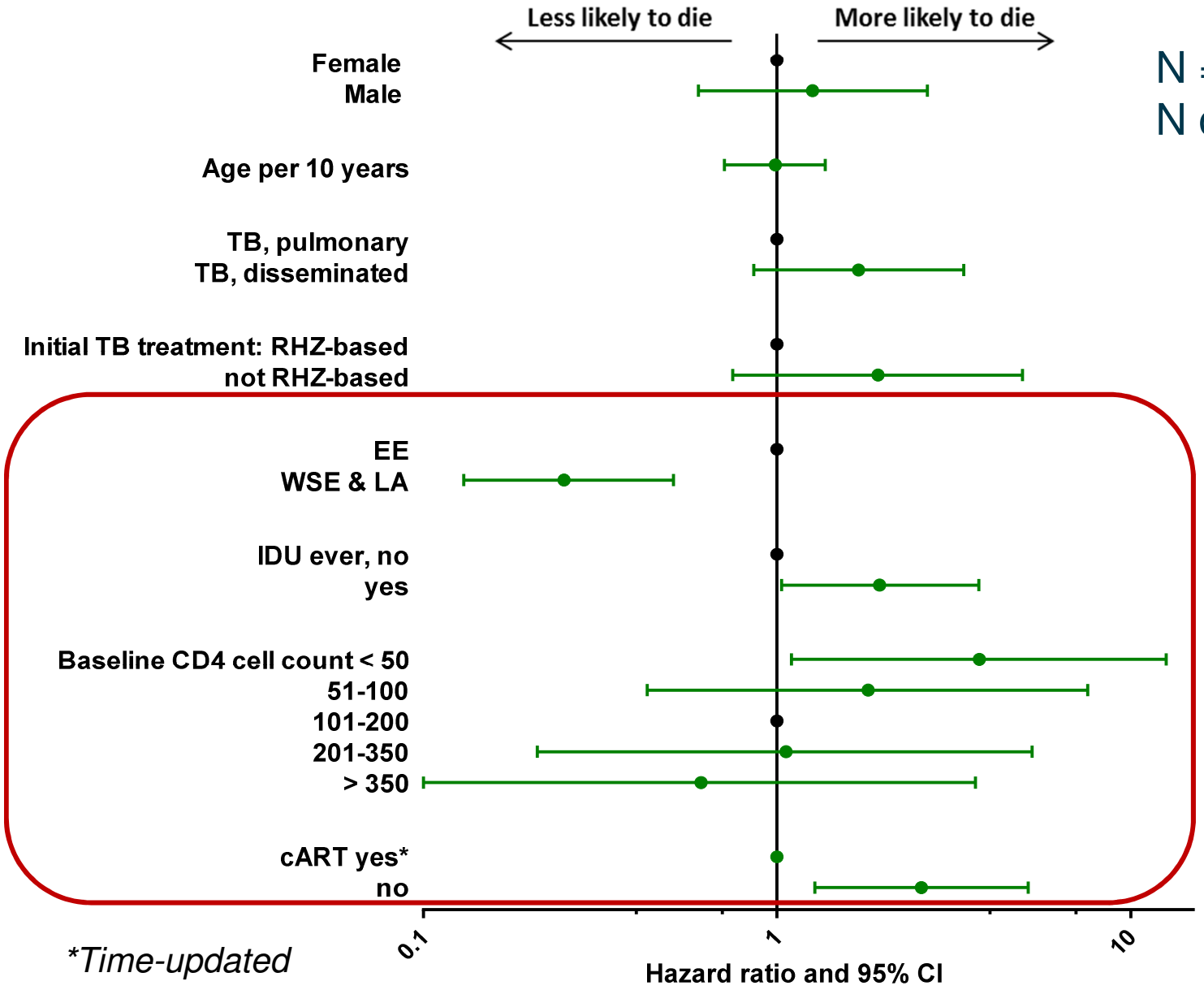
Probability of death, according to the geographical region

Total, N	EE: 147	WSE: 170	LA: 50
Death (any cause), N (%)	27 (18)	7 (4)	4 (8)
TB death, N (%)	19 (70)	2 (29)	1 (25)
KM estimate (95% CI)	19.5 (3.8-27.1)	5.1 (2.9-9.1)	



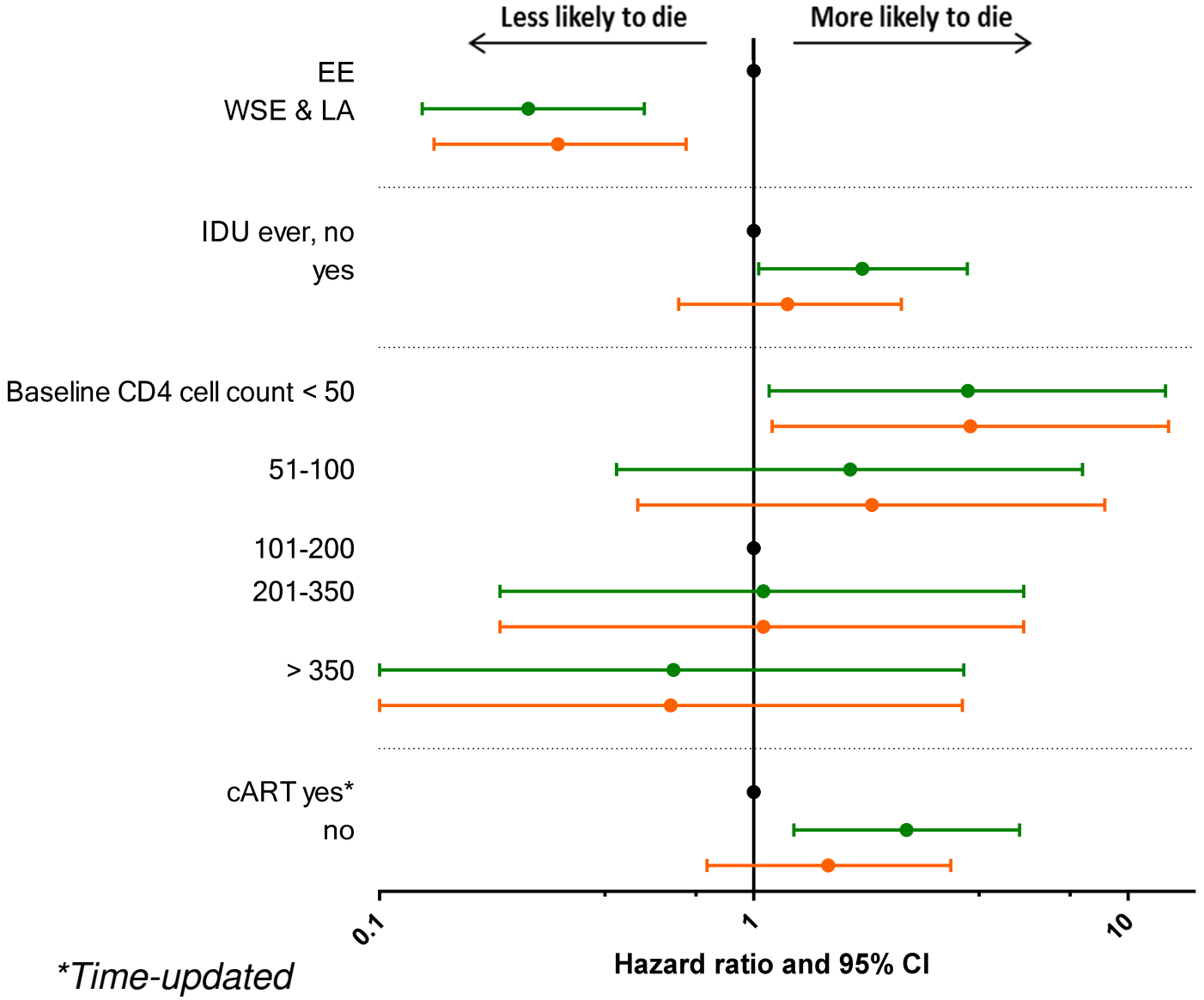
Factors Associated with death: unadjusted results



N = 367
N death = 38

*Time-updated

Factors Associated with death: unadjusted and adjusted results



N = 367
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*Time-updated

Limitations

- Intraregional and intra-country variations may limit the generalisability of our findings
- Limited power to study individual countries
- Limited power to study risk factors of death

Summary and Conclusions

- Mortality in HIV+ people with drug-susceptible TB in EE is approximately 4-fold higher compared with WSE and LA
- This is despite:
  - Comparable usage of RHZ
  - Similar TB characteristics
- Thus, the observed differences in mortality are unlikely to be explained by the high prevalence of MDR-TB or the TB treatment regimens
- Injecting drug use, hepatitis C co-infection, and limited cART use may contribute to the poor outcome in EE

Summary and Conclusions

- Previous results showed that management of TB/HIV in EE differs from other regions by[1]
  - Non-integrated TB and HIV care
  - Limited availability of TB-drugs and ARVs
  - Lack of opiate substitution therapy
- Further research is needed to identify the reasons for the high mortality in EE
- National level health care system research will help to identify the specific problems and points of interaction in each particular country

[1]*M Mansfeld et al., HIV Med. 2015 Oct;16(9):544-52*

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