CHIP COPENHAGEN HIV PROGRAMME

Causes of death in HIV-infected patients with active TB disease

D.N. Podlekareva, D. Grint, A. Panteleev, A. Rakhmanova, R. Miller, M. Bruyand, H. Furrer, F. Post, I. Zeltina, A. Skrahin, J.M. Miro, N. Obel, E. Girardi, M.H. Losso, J. Toibaro, J. Caylá, A. Mocroft, J.D. Lundgren, O. Kirk and the HIV / TB Collaborative Study Group

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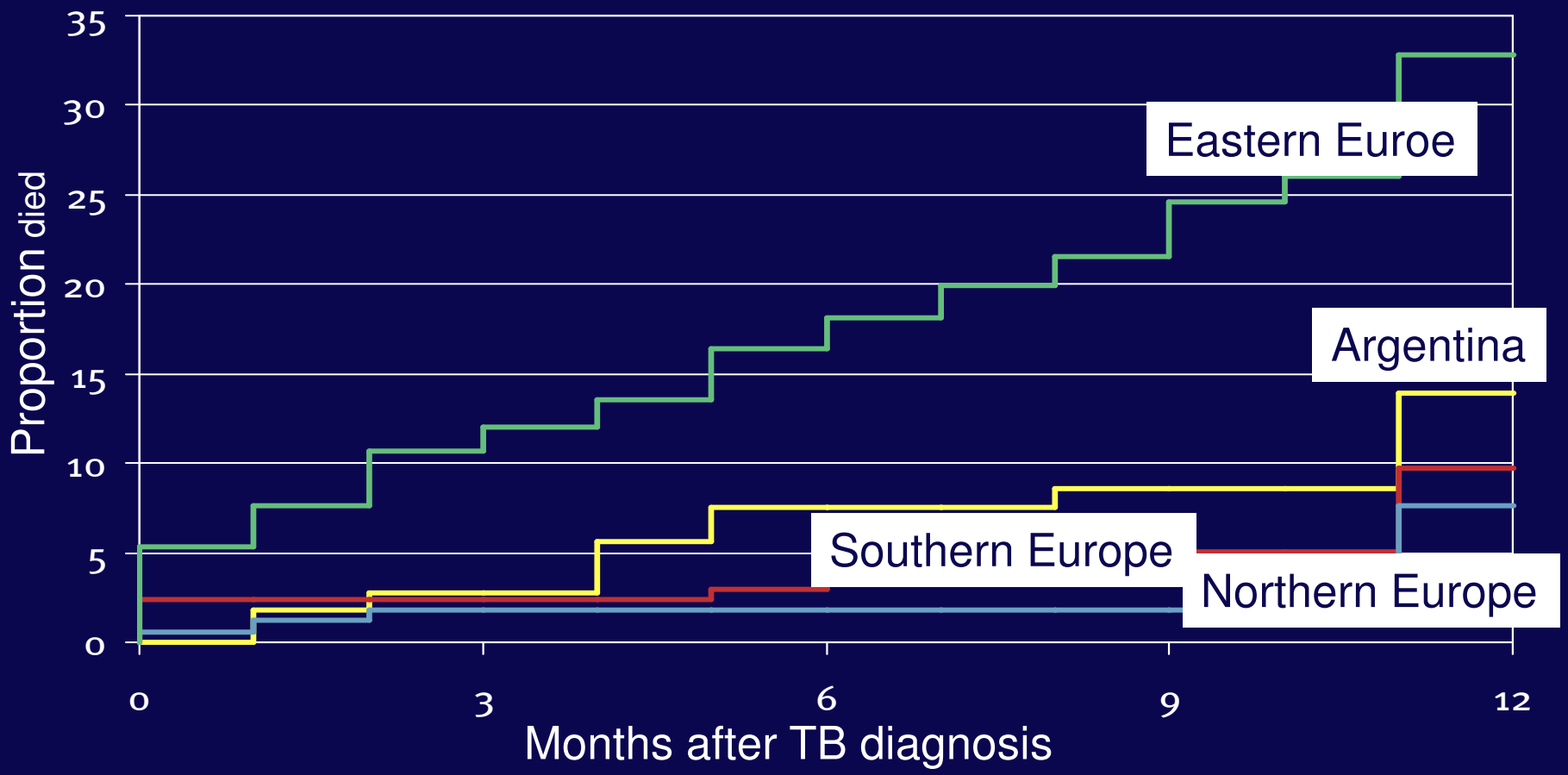
HIV/TB collaborative project

- Consecutive HIV-patients with tuberculosis (TB) between 1/2004 and 12/2006 (N=1078)
- Laboratory confirmed and presumptive TB diagnosis
- Recurrence of TB - either relapse of the same TB case or re-infection with *mycobacterium tuberculosis* after treatment for original TB case has been completed

- Collaboration of HIV and TB clinicians from:
  - Western Europe and Argentina (WEA) Denmark, France, Italy, Spain, Switzerland and the United Kingdom
  - Eastern Europe (EE): Belarus, Latvia, Romania, Russia and Ukraine

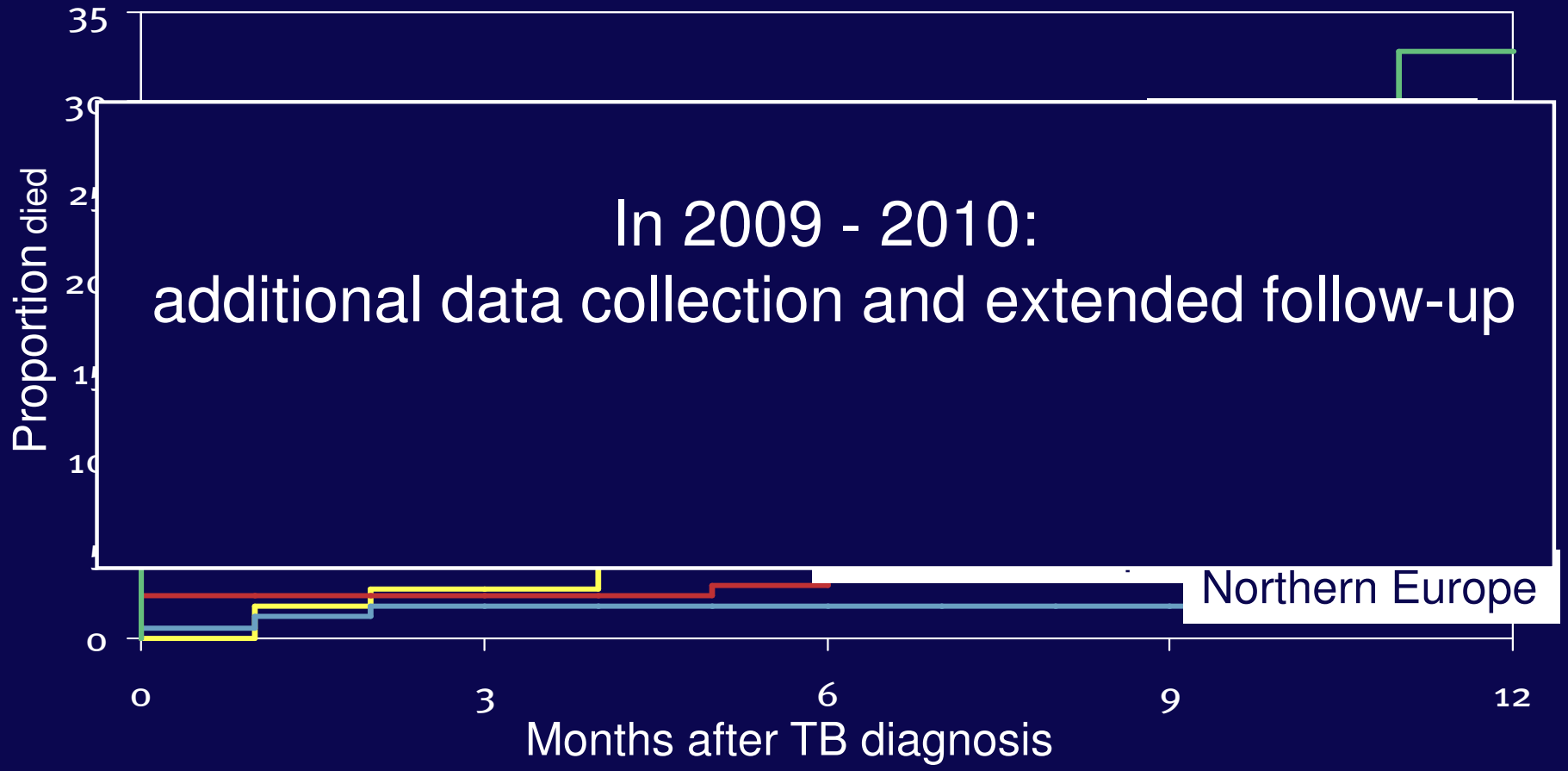
Background



A 3-fold higher one-year mortality risk in patients from Eastern Europe (EE) compared with patients from Western Europe and Argentina (WEA)[1]

[1]AIDS 2009, 23:*2485–2495*

Background



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Objectives

- To assess and compare:
  - Mortality rates and causes of death
  - Risk factors for TB-related death

in HIV/TB patients across EE and WEA in order to identify targets for improved patient management

Methods

- Crude mortality rates stratified by time after TB diagnosis: <3 months, 3-12 months, >12 months (per 100 person years of follow-up (PYFU))
- Deaths were categorised as being directly related or unrelated to TB
- Poisson regression was used to identify factors associated with TB related death
- The Coding of Death in HIV (CoDe) procedure used to ascertain immediate and underlying COD[1]
  - Information on COD collected on CoDe Case Report Forms
- Immediate COD - endpoint for the present analysis (disease/condition directly leading to death)

[1]Kowalska et al Epidemiology 2011

HIV/TB study cohort

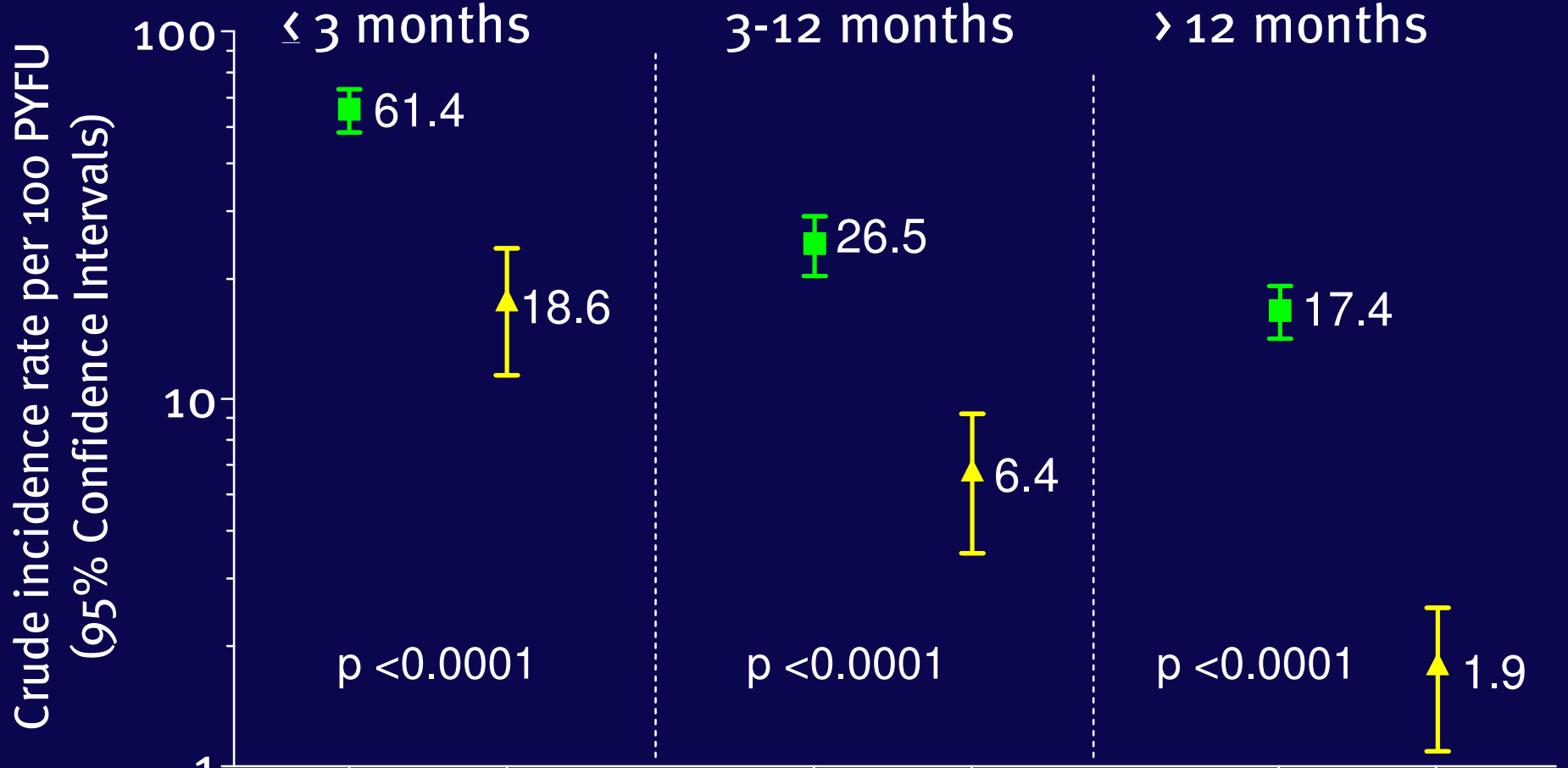
	EE	WEA	P
Total	585	493	
TB culture confirmed, %	55	67	<0.0001
TB recurrence, %	14	4	<0.0001
Death %	49	13	<0.0001
- TB-related death % of deaths	76	37	<0.0001
Median time to death (IQR) [Months]	8.7 (2.5 - 19.5)	5.1 (1.6 - 13.5)	0.11
No data beyond 1 year	222 (38.0%)	81 (16.4%)	<0.0001

Baseline characteristics of HIV/TB patients

	EE		WEA	
	Dead N=284	Alive N=301	Dead N=63	Alive N=430
Gender: male, %	77	66	63	64
Origin: same as centre, %	94	97	60	50
HCV positive, %	49	43	17	17
TB risk factor: IDU, %	79	65	30	22
R-resistance, %	52	18	5	4
RHZ-based therapy, %	37	53	76	84
Expulm/diss TB, %	72	56	68	66
On cART at TB, % of HIV+	11	23	63	52
CD4 count, median (IQR)	148 (59-322)	311 (143-514)	86 (28-200)	140 (55-289)

R-rifamycin, H – isoniazid, Z- pyrazinamide

The crude mortality rate in HIV/TB patients stratified by time from TB diagnosis



	≤ 3 months		3-12 months		> 12 months	
	EE	WEA	EE	WEA	EE	WEA
N under FU	585	493	493	461	363	412
N deaths	81	22	83	21	120	20

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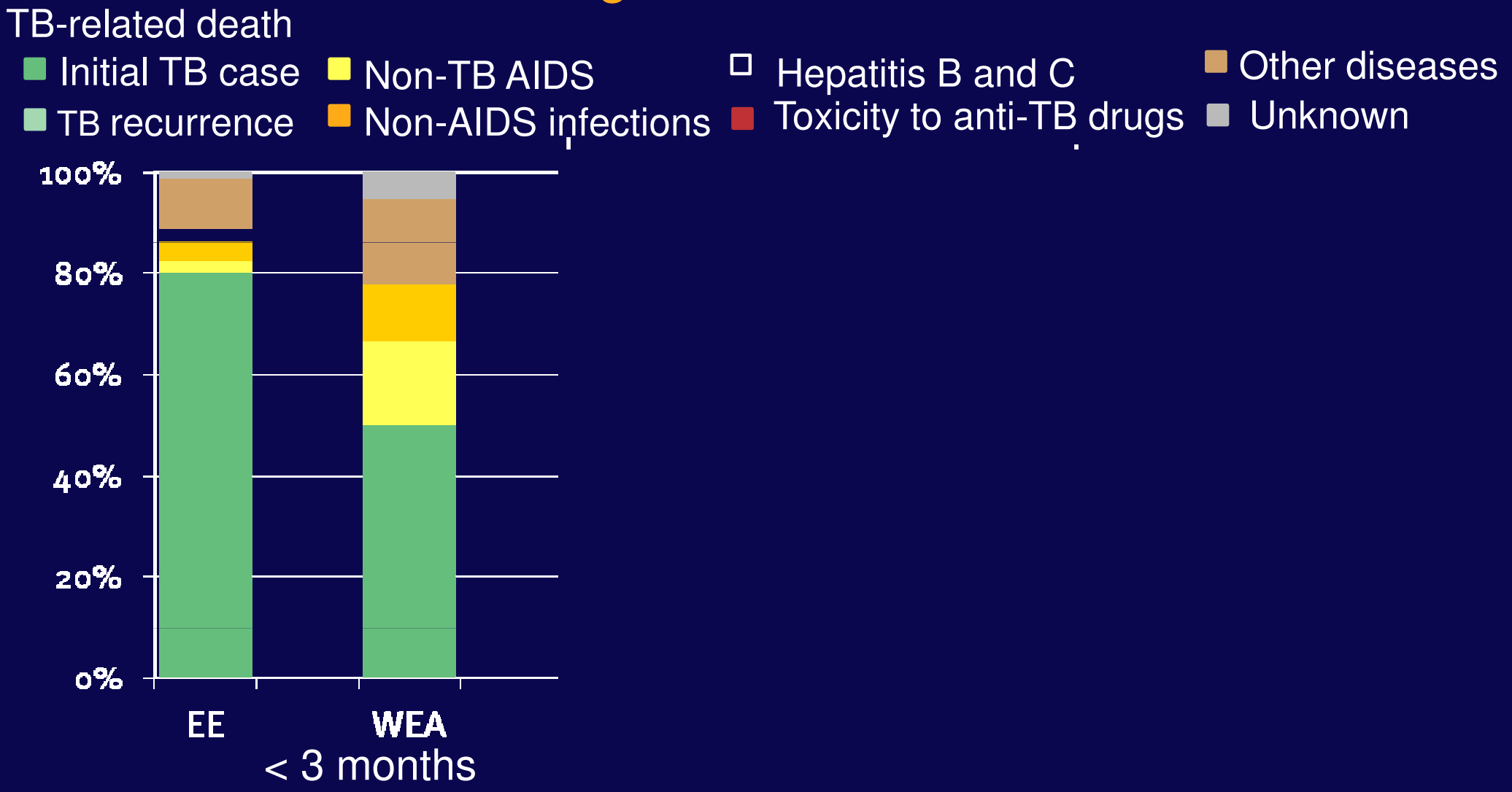
Causes of death among HIV/TB patients according to the time of death



N with CoDe form

80 18 79 16 114 13

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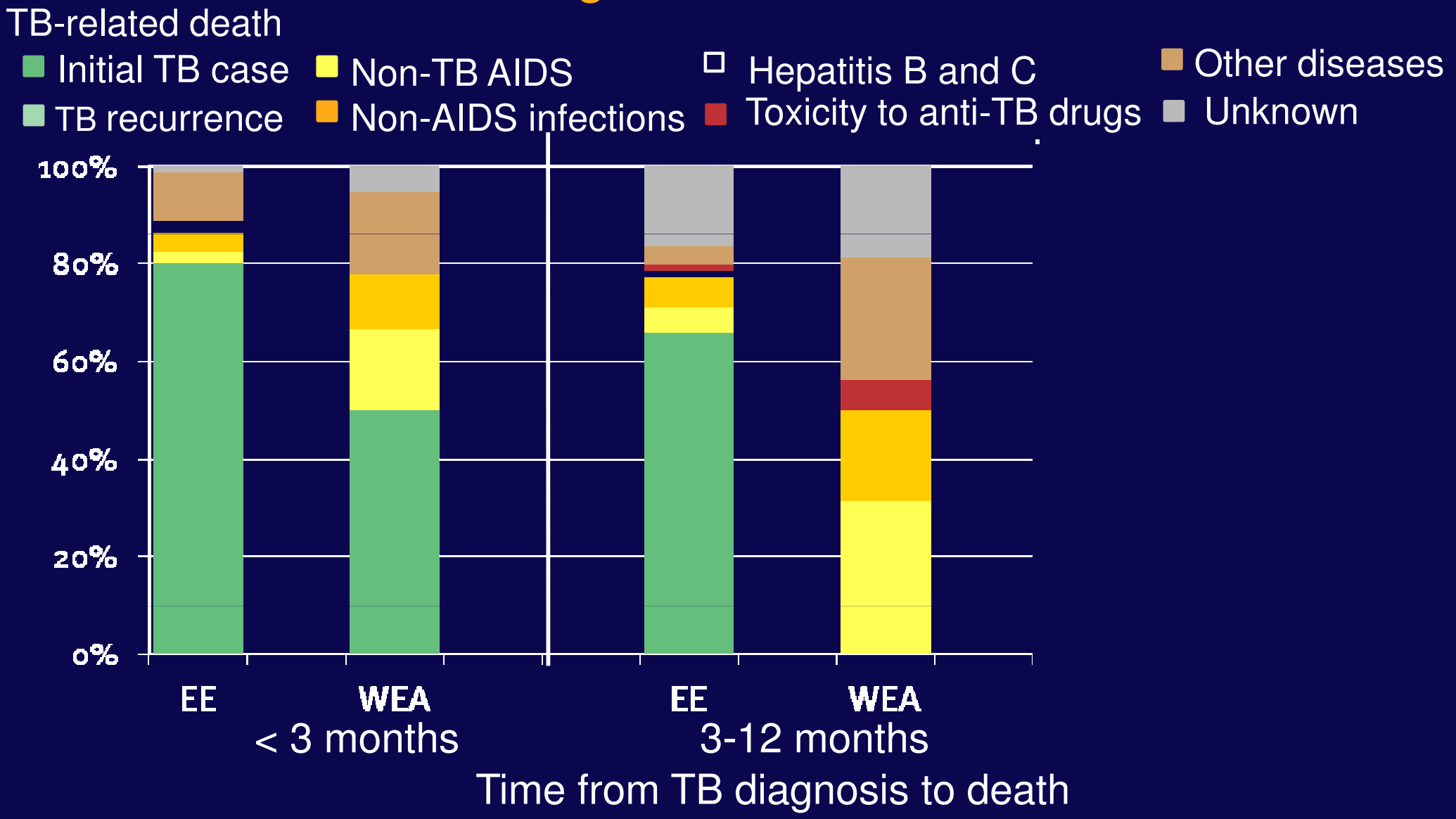

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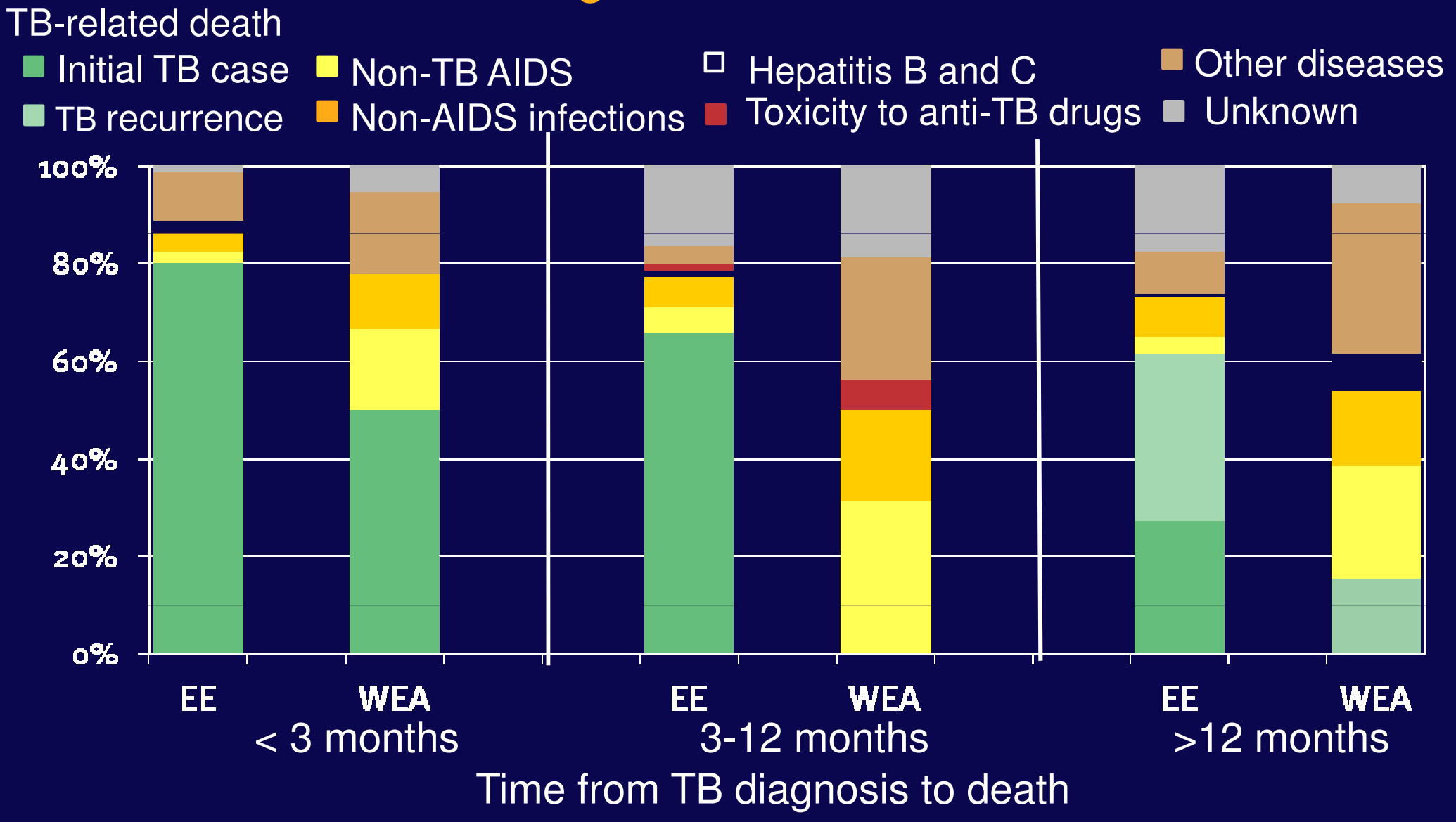
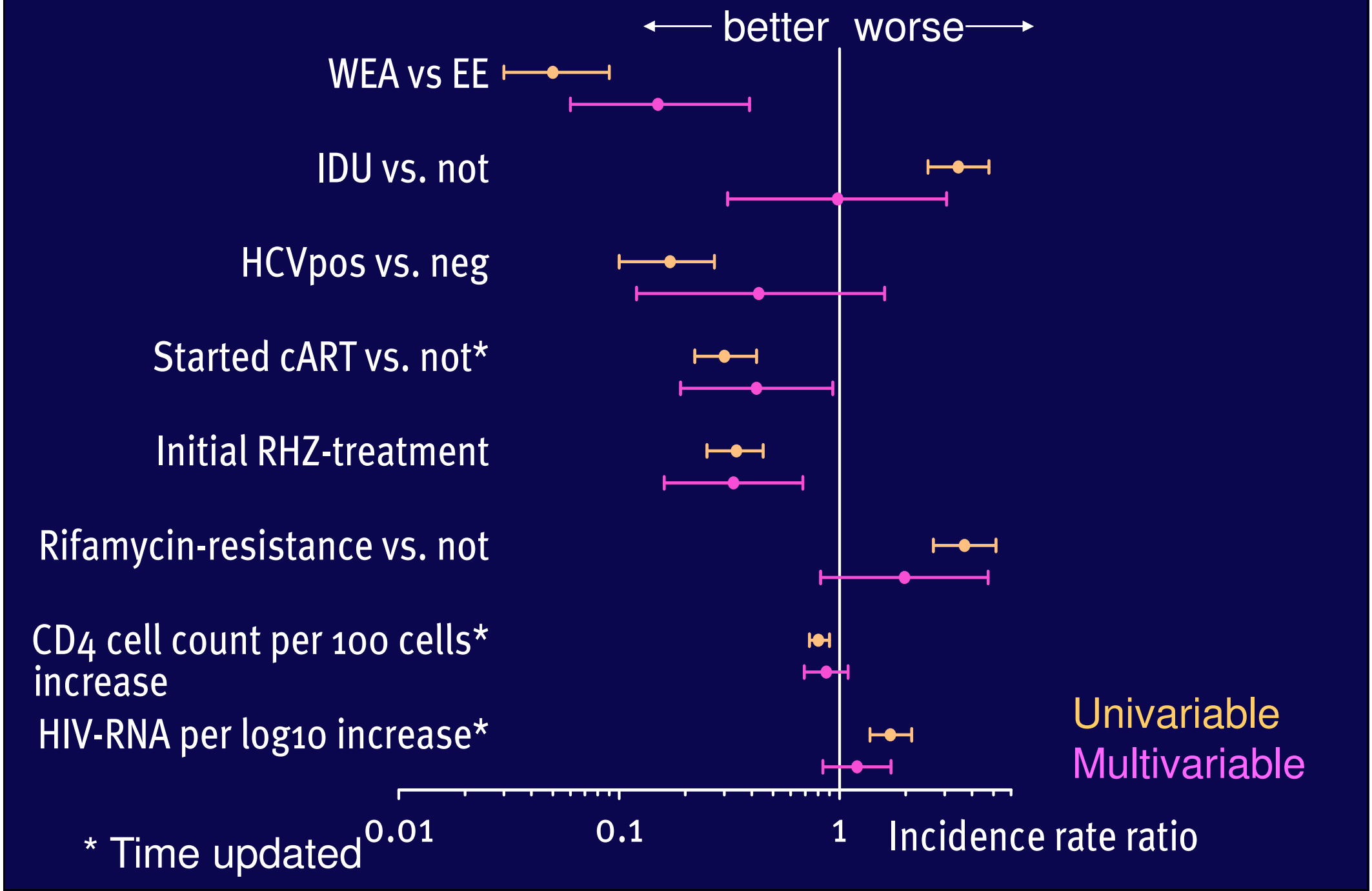


Incidence rate ratios (IRR) for TB related death



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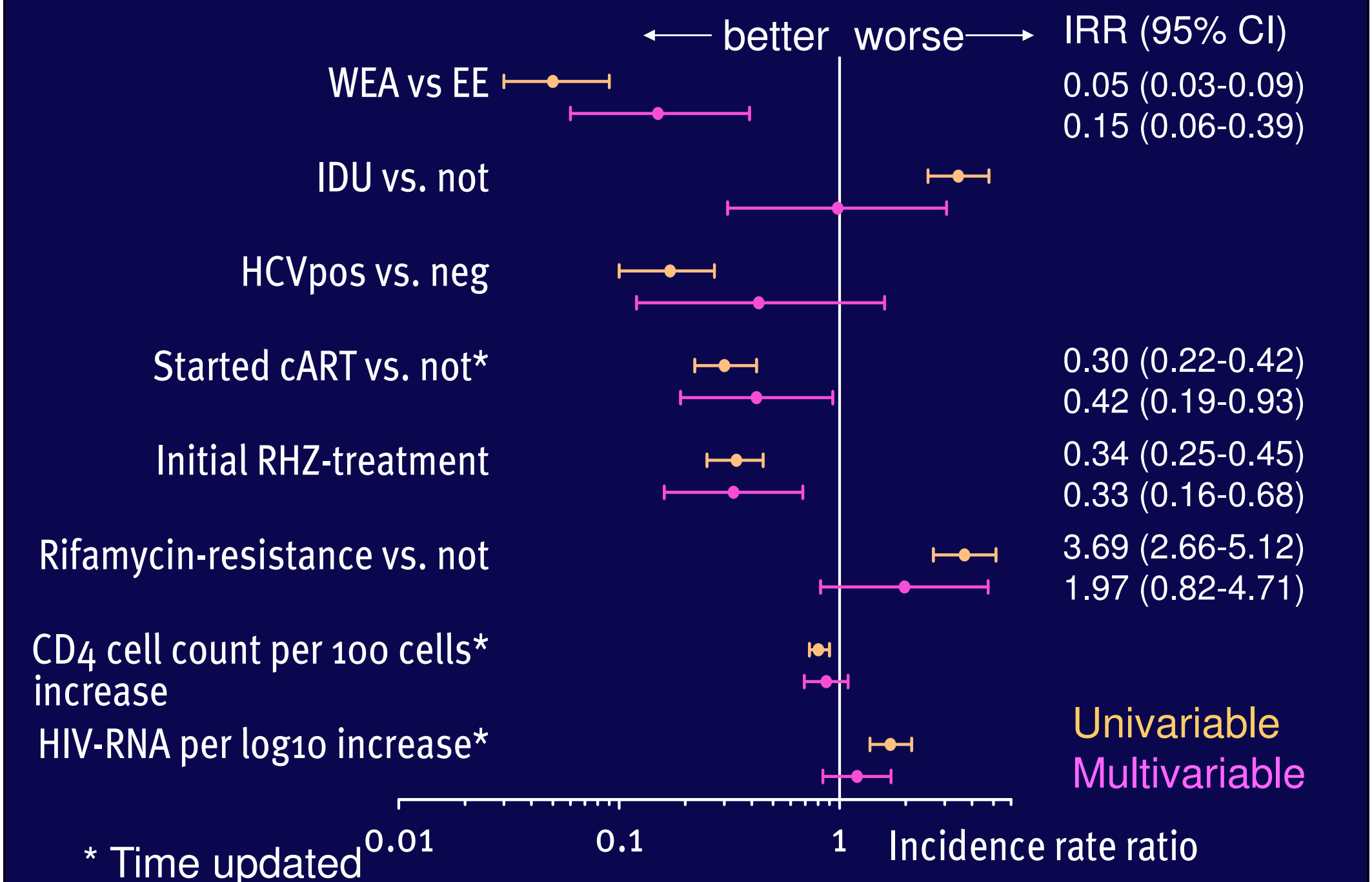

Strengths and limitations

- Large cohort of HIV/TB patients from across Europe and Argentina
- Follow-up at least 2 years after TB diagnosis
- Detailed information on causes of death (including autopsy reports)
- CoDe procedure applied

- Higher rate of LTFU in Eastern Europe compared to Western Europe and Argentina
- Retrospective data collection

Summary

- Persistently higher mortality rates observed in HIV/TB patients in Eastern Europe
  - Low proportion with culture confirmed TB
- TB remained the dominant cause of death in Eastern Europe - even after 12 months of TB diagnosis
  - Low usage of RHZ-based anti-TB treatment and cART
- Initiation of a standard anti-TB treatment and cART were significantly associated with reduced incidence of TB-related death

Implications

- Target interventions to optimise management of HIV/TB patients and limit TB-mortality in Eastern Europe should include:
  - Improved diagnostic procedures for TB and resistance testing
  - Adequate treatment regimens
    - RHZ-based initial treatment subsequently adjusted according to the resistance patterns
  - Widespread use of cART
- Prospective TB:HIV study is currently recruiting patients and aims to address issues outlined above

TB:HIV an international prospective observational study

The HIV/TB Collaboration Study Group

(principal investigator/ representing person):

Argentina (MH Losso) Buenos Aires; Belarus Minsk (I Karpov), Gomel (V Mitsura), Svetlogorsk (O Suetnov); Denmark (N Obel) Danish HIV Cohort; France (M Bruyand) Aquitaine Cohort; Italy Brescia (A Matteeli); Bergamo (F Maggiolo); Modena (C Mussini); Rome (E Girardi); ICONA cohort (E Girardi); Latvia (V Riekstina) Riga; Romania (D Duiculescu) Bucharest; Russia St Petersburg (A Panteleev & A Rakhmanova); Novgorod the Great (S Buzunova); Spain (JM Miro) Barcelona; Switzerland (H Furrer) Swiss HIV Cohort; United Kingdom London (F Post & R Miller); Ukraine (N Chentsova) Kiev ; EuroSIDA cohort (JD Lundgren)

Coordinating centre (CHIP) D Podlekareva, AM Werlinrud, D Grint, A Mocroft, J Kjær, M Ellefson, O Kirk

Steering Committee: N Chentsova, D Duiculescu, H Furrer, E Girardi, M Bruyand, MH Losso, JD Lundgren, A Panteleev, R Miller, JM Miro, N Obel, F Post, V Riekstina, A Skrahin, JJ Toibaro