a multicentre study

EuroSIDA

Tuberculosis among HIV-1 infected patients across Europe: change over time and risk factors

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Background

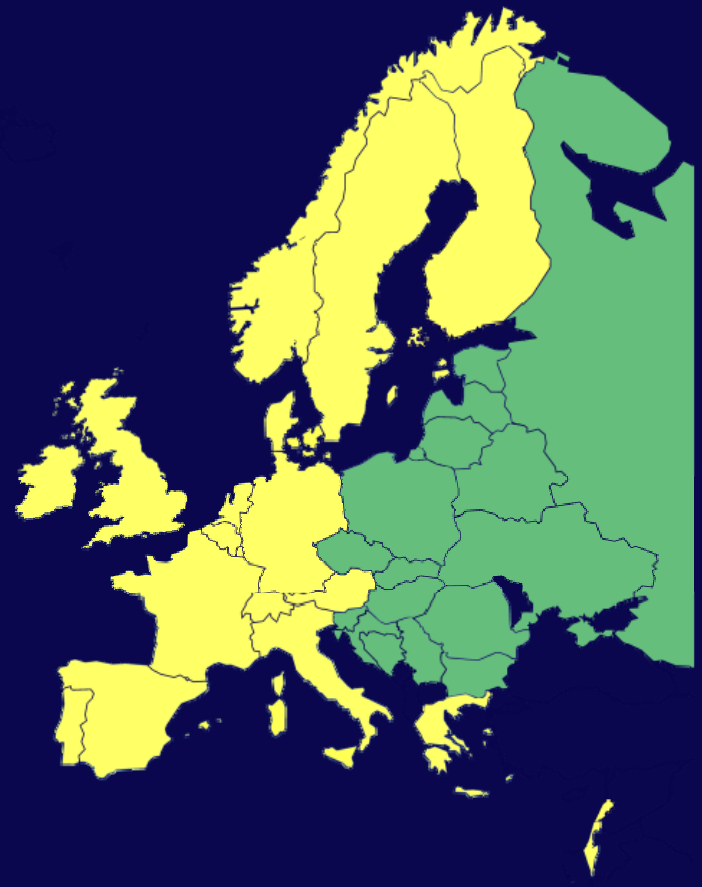
- Considerable decrease in the incidence of tuberculosis (TB) after the introduction of cART in Western Europe from 1994 to 1998 (*Kirk O. et al, AJRCCM 2000*)

- Limited data on TB incidence in HIV-infected patients in Western Europe afterwards (*Girardi E. et al, CID 2005*)

- Limited data on TB incidence in HIV-infected patients in Eastern Europe

EuroSIDA study

- EuroSIDA - prospective, observational cohort study of › 16.000 patients with HIV-1 infection in 103 centers across Europe.
- Unique opportunity to assess incidence of TB across Europe, including Eastern Europe



Western Europe: Austria, Belgium Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Luxembourg, Netherlands Norway, Portugal, Spain, Sweden Switzerland,United Kingdom

Eastern Europe: Belarus, Bosnia, Bulgaria, Croatia, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Russia, Serbia, Slovakia, Slovenia, Ukraine

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Objectives

I. Estimate the incidence of pulmonary or extrapulmonary TB in HIV-infected patients in Western Europe from 1994 to 2008

II. To compare the incidence of TB in Western and Eastern Europe after 2001

   – To identify risk factors for development of TB in both regions

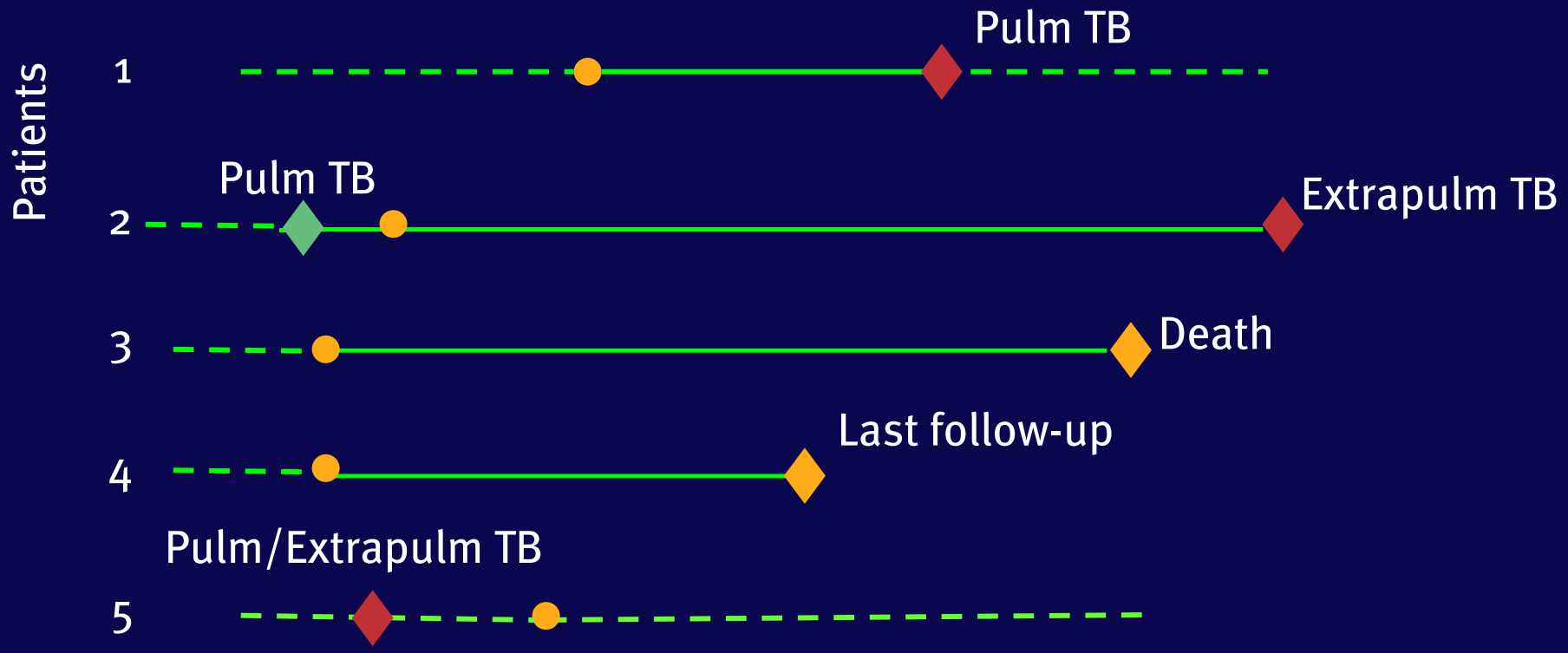
Methods

I. Patients only from Western Europe enrolled in EuroSIDA from May 1994 onwards were included to assess temporal trends in TB incidence

II. For regional comparison, patients from Western and Eastern Europe under EuroSIDA follow-up from 1st January 2001 onwards were included (time when Eastern Europe joined the study)

- Poisson regression analysis was used to identify risk factors for development of TB

Methods



≥ 1 months of follow-up in EuroSIDA

● - EuroSIDA enrolment = Baseline ◆ / ◆ - Endpoint/ censoring

◆——◆ / - - - - - - Included/excluded from the analysis

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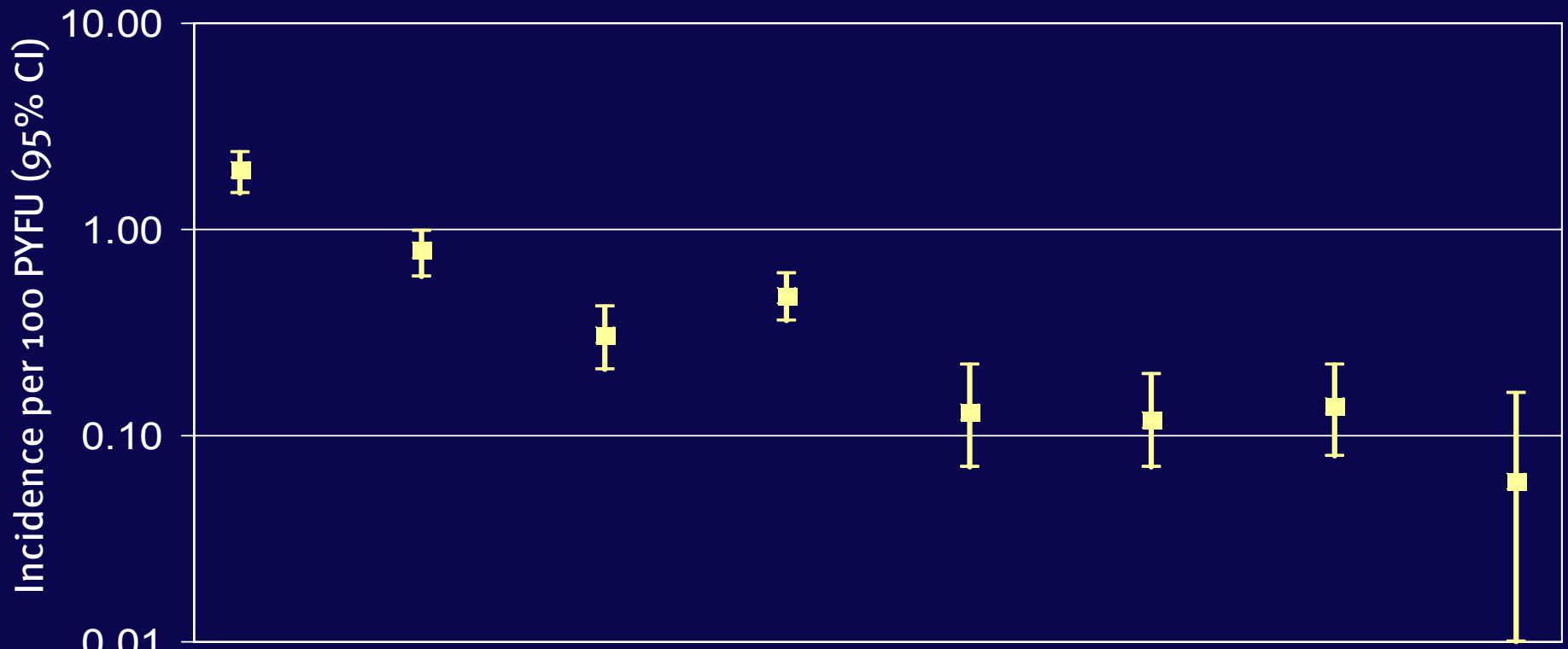
I. Baseline characteristics of patients from Western Europe 1994-2009

	N=11.706	%
Male		79
White		86
HIV exposure	MSM	46
	IDU	21
	Heterosexual	25
	Other	8
Origin	Same as clinical centre	73
	Other European country	7
	Africa, America, Asia	11
	Unknown	10
On cART		43
		median (IQR)
Baseline date		Apr '97 (Jul '94 – Nov '01)
Age (years),		38 (33-45)
CD_4 count (cells/mm^3)		278 (135-430)
HIV-RNA (log_{10}copies/ml)		2.7 (1.7-4.2)

I. Incidence of TB in Western Europe 1994 - 2009

N = 11.706 PYFU = 74.009 N TB events = 275 IR = 0.4/100 PYFU



	1994-95	1996-97	1998-99	2000-01	2002-03	2004-05	2006-07	2008-09
N events	78	60	34	55	15	14	16	3
Incidence	1.94	0.79	0.31	0.48	0.13	0.12	0.14	0.06

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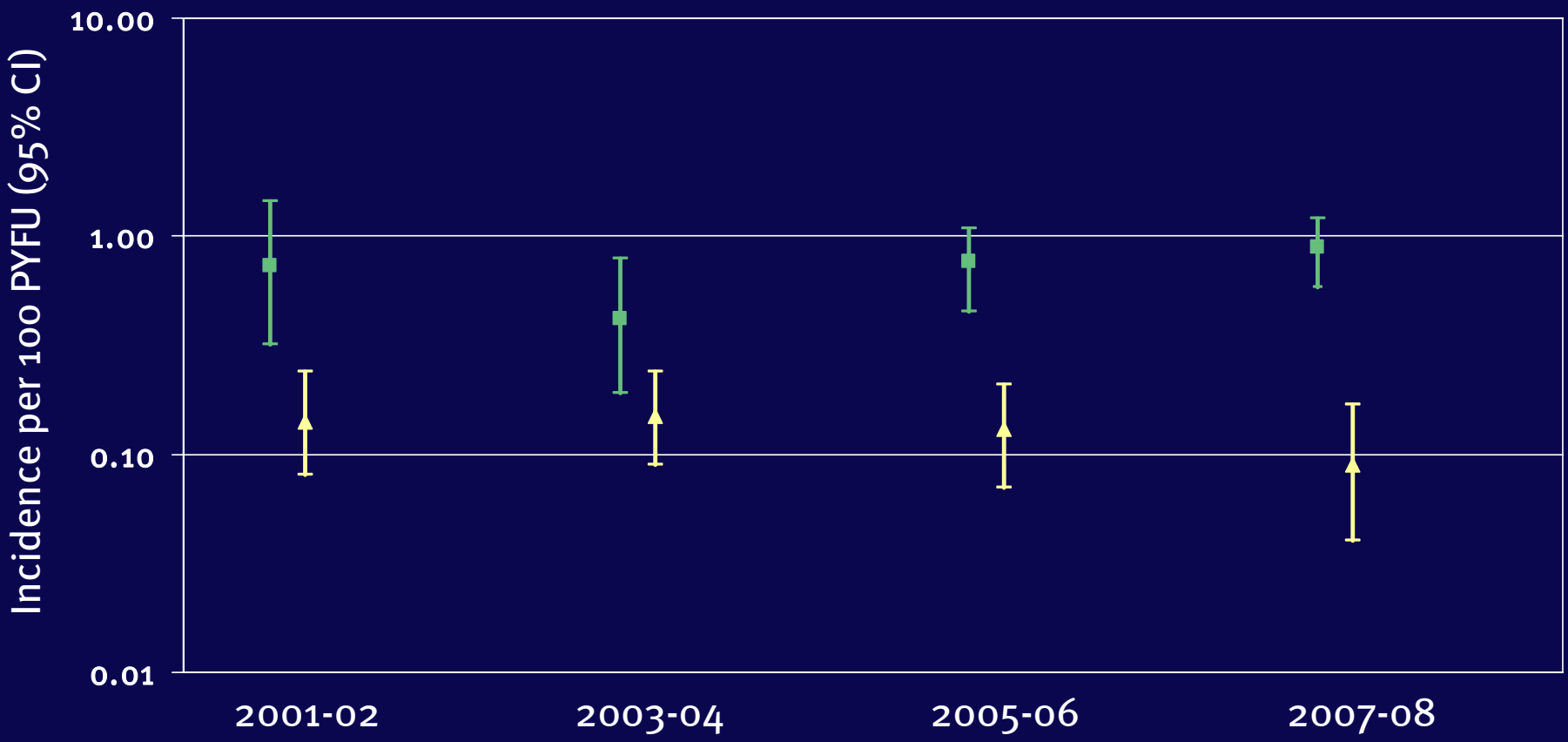
II. Baseline characteristics of patients from Western and Eastern Europe 2001 - 2009

$p < 0.001$ for all variables		%	West N = 8.890	East N = 3.210
Male			77	64
White			86	100
HIV exposure	MSM		45	22
	IDU		19	38
	Heterosexual		28	34
Origin	Same as clinical centre		69	95
HCV	Positive		19	40
	Unknown		23	14
Prior AIDS			70	79
On cART			78	50
		Median (IQR)		
Age (years)			41 (36-48)	33 (28-40)
CD4 count (cells/mm^3)			422 (276-604)	387 (253-545)
HIV-RNA (log_{10}copies/ml)			2 (1.7-3.5)	2.7 (1.7-4.2)

II. Incidence of TB in Western and Eastern Europe 2001 - 2008

	N	PYFU	N TB events	IR/100PYFU
East	3.210	9.907	71	0.7
West	8.890	45.786	59	0.1



	2001-02	2003-04	2005-06	2007-08
N events	8	9	23	31
N events	16	18	15	10

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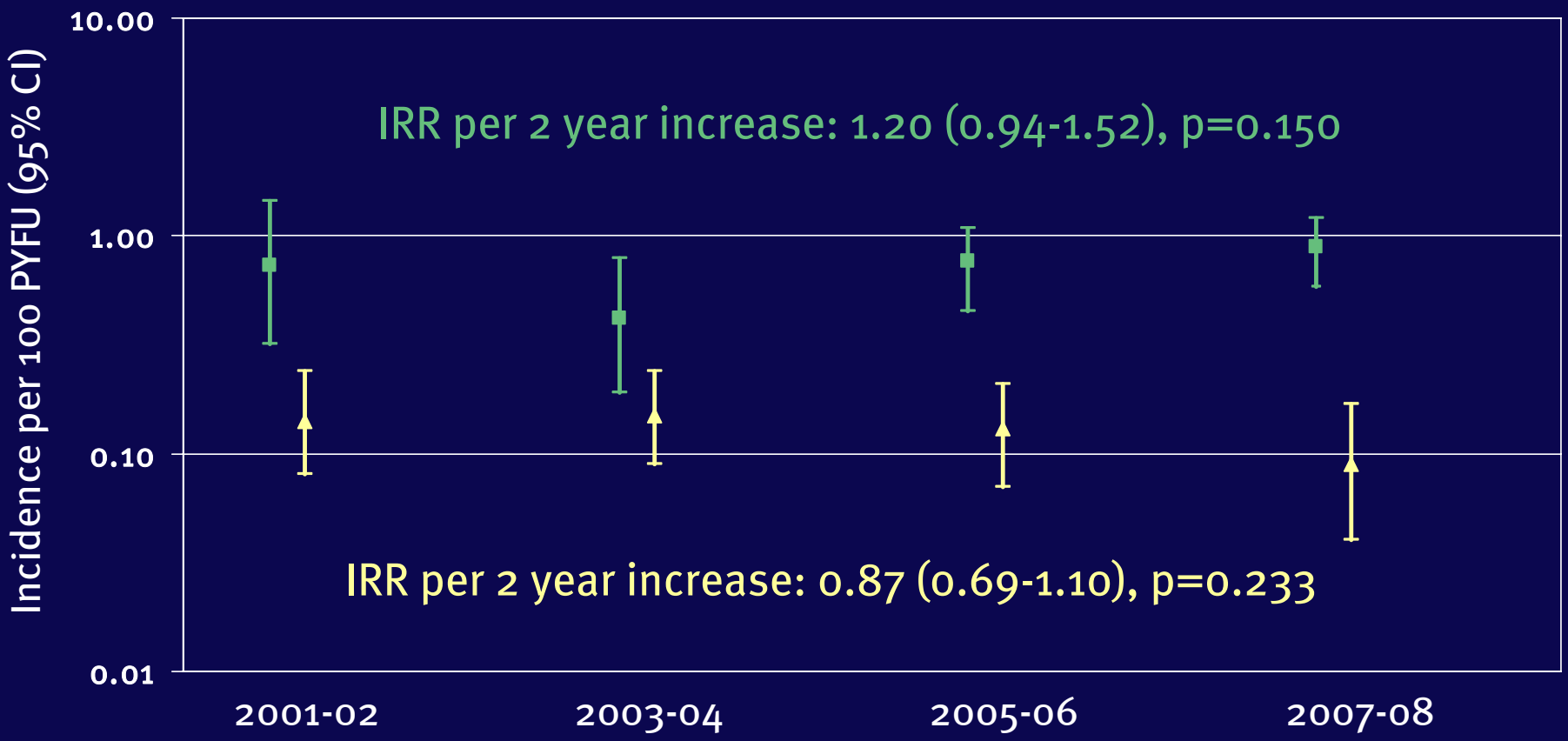

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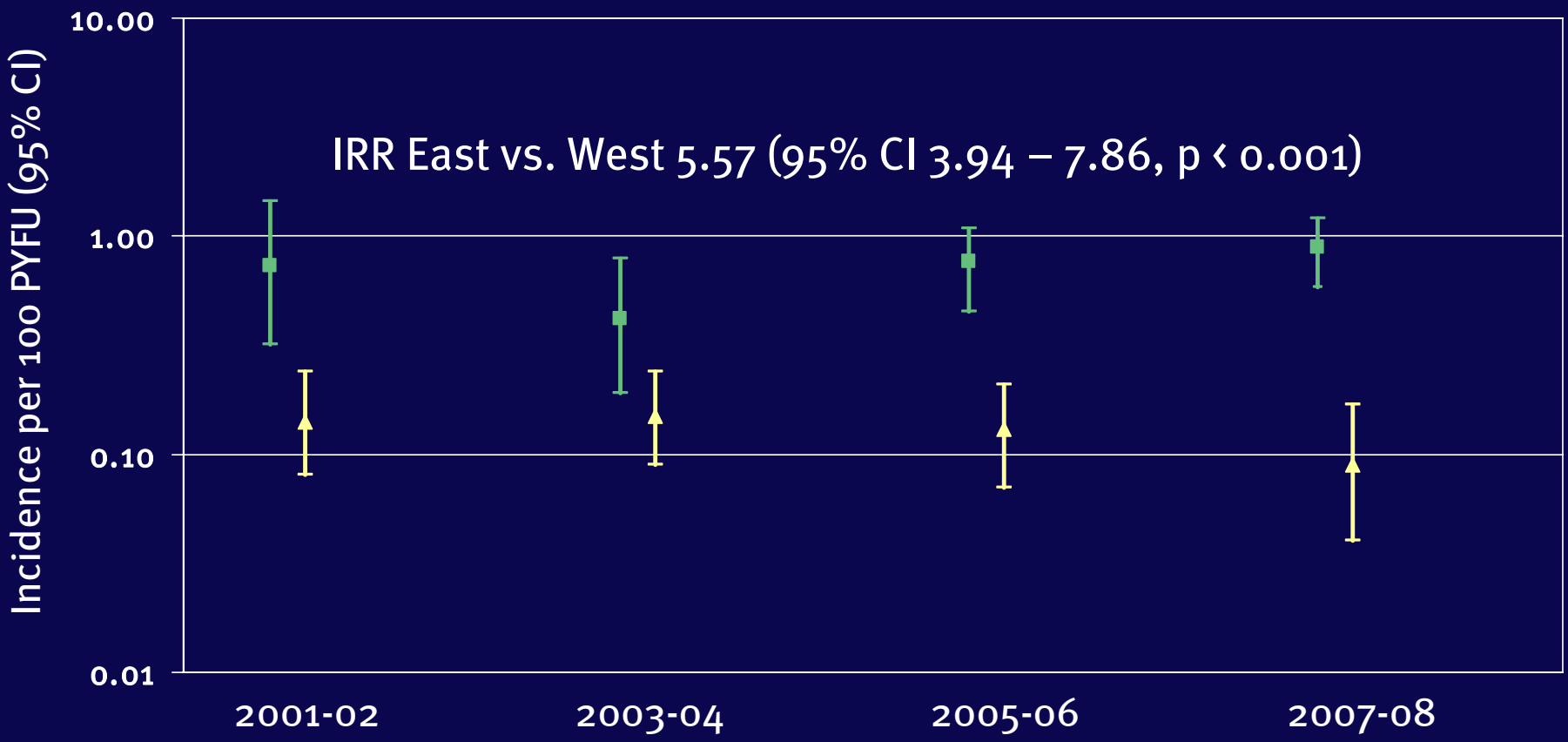

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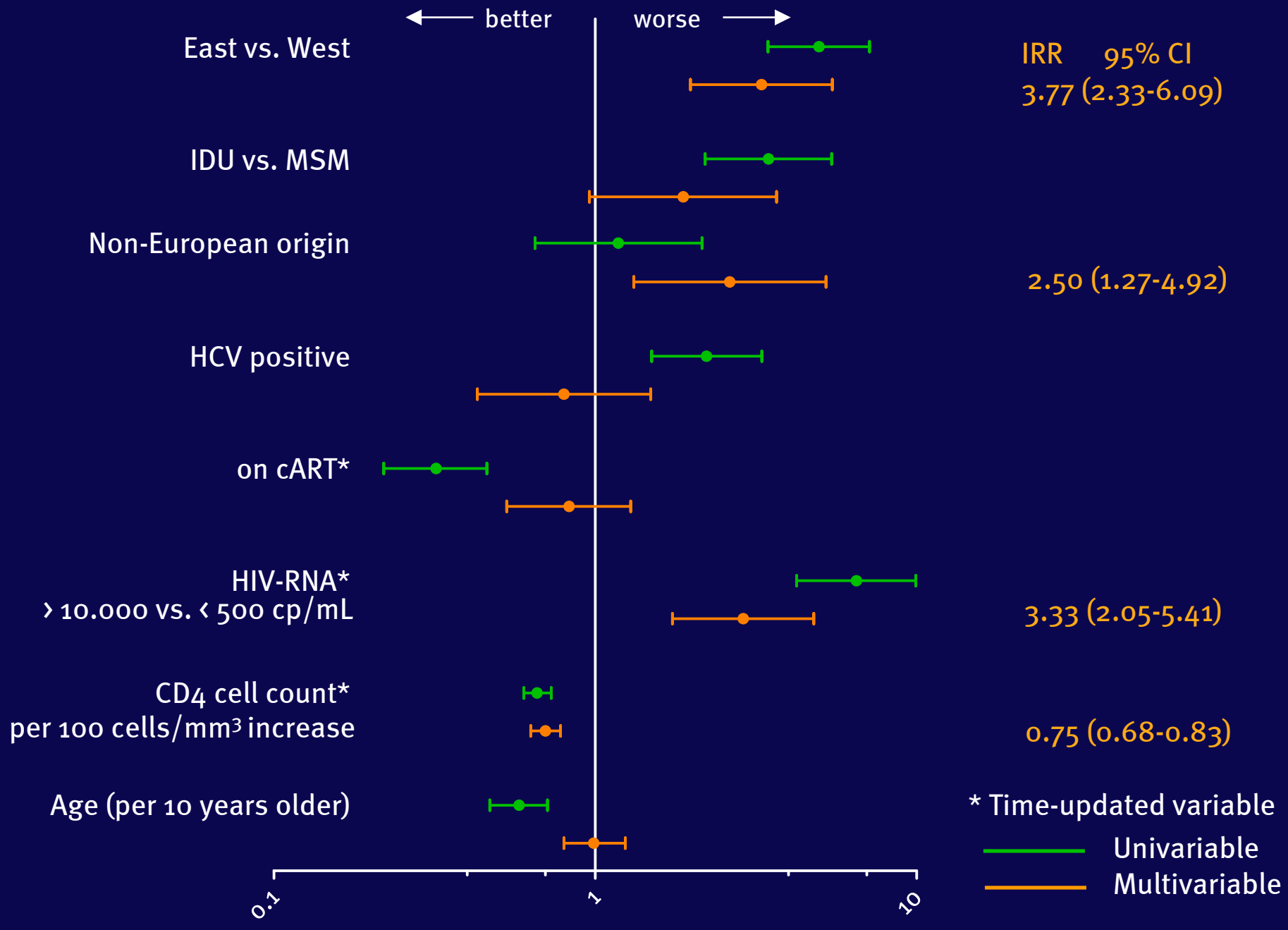
II. Incidence rate ratios (IRR) of TB in Europe 2001-2008



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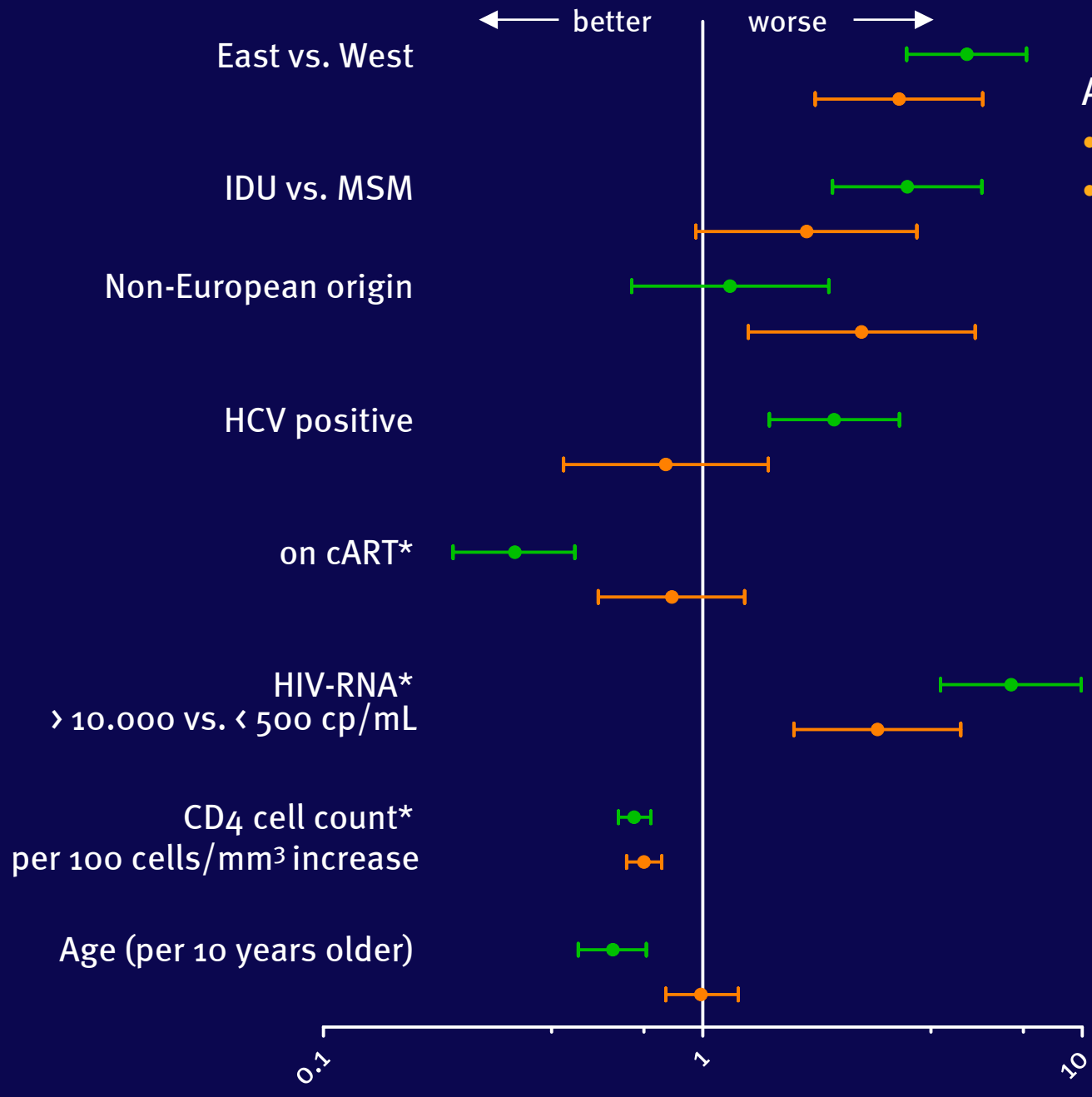

Also adjusted for:

- Calendar time, p = 0.394
- Diabetes status, p = 0.095

* Time-updated variable

Univariable

Multivariable

Conclusions

- After a pronounced decline in the 1990's, the incidence rate of TB in Western Europe remained at a very low and stable level since 2001
- After 2001, patients in Eastern Europe were at substantially higher risk of TB compared to patients in Western Europe
- cART is important component in decreasing risk of TB development
- TB is still of concern in HIV-infected patients, especially in areas with high TB prevalence, with high levels of immigration from TB-endemic regions, and in areas with suboptimal access to cART

Perspectives

- Implementation of strategies to reduce burden of TB among HIV-infected patients in Eastern Europe is urgently required and may include:
  - Wide use and timely initiation of cART
  - Regular screening for TB among HIV-infected population
  - Universal HIV-testing among TB-patients
  - Implementation of DOTs strategies
  - Adequate anti-TB treatment
  - Integration of HIV and TB health care systems

- Further research should be aimed on improvement of:
  - TB diagnostic tools
  - Anti-TB treatment, in particular MDR- and XDR-TB

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