Temporal Changes and Regional Differences in Treatment Uptake of Hepatitis C Therapy in EuroSIDA

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Background

- Liver-related mortality has been assuming increasing importance in HIV-positive people since the introduction of ART[1]
- Co-infection with HCV occurs in up to 30% of HIV-positive people in Europe[2]
- Despite this, factors that influence starting treatment for HCV are not well understood, with uptake thought to be lower than 10% in some populations[3,4]
- The effect of HCV therapy on mortality has never been investigated in a RCT

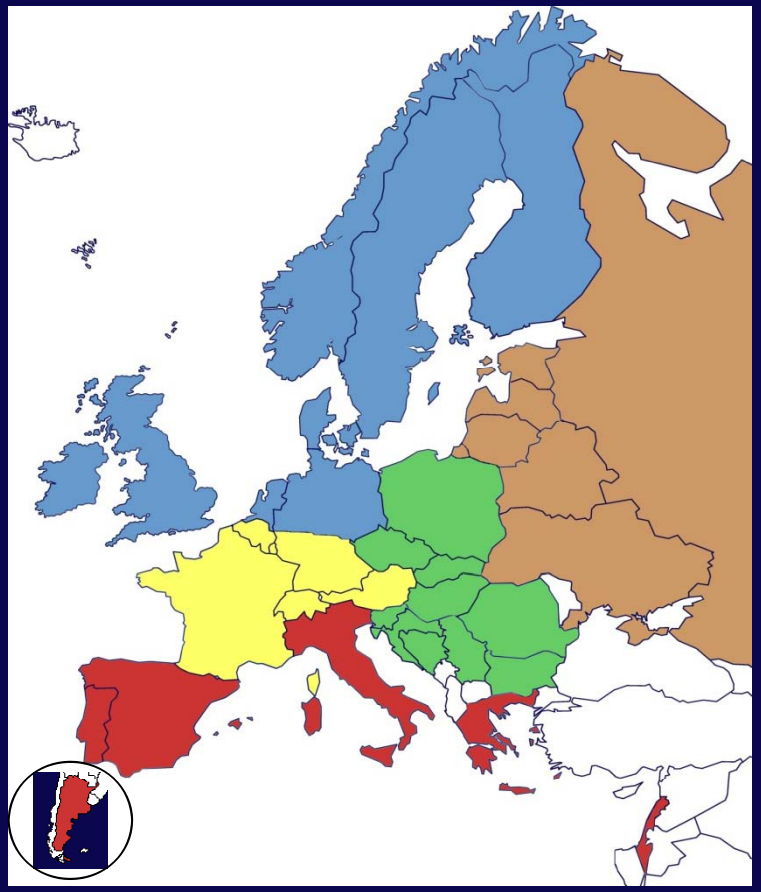
[1]Weber R, Arch Intern Med 2006
[2]Rockstroh JK, J Infect Dis 2005
[3]Kramer JR, J Hepatol 2012
[4]Smit C, Antiviral therapy 2012

Aims

- Describe temporal changes in the uptake of HCV treatment across Europe
- Identify factors associated with treatment uptake
- Estimate the effect of HCV treatment on all-cause mortality and liver-related death

EuroSIDA

EuroSIDA is a large prospective cohort with 16597 patients from 33 European countries, Israel and Argentina



- HCV antibody
- HCV-RNA and genotype
- CD4 counts, HIV viral loads
- All treatment start/stop dates
- CoDe forms for classification of deaths[1]

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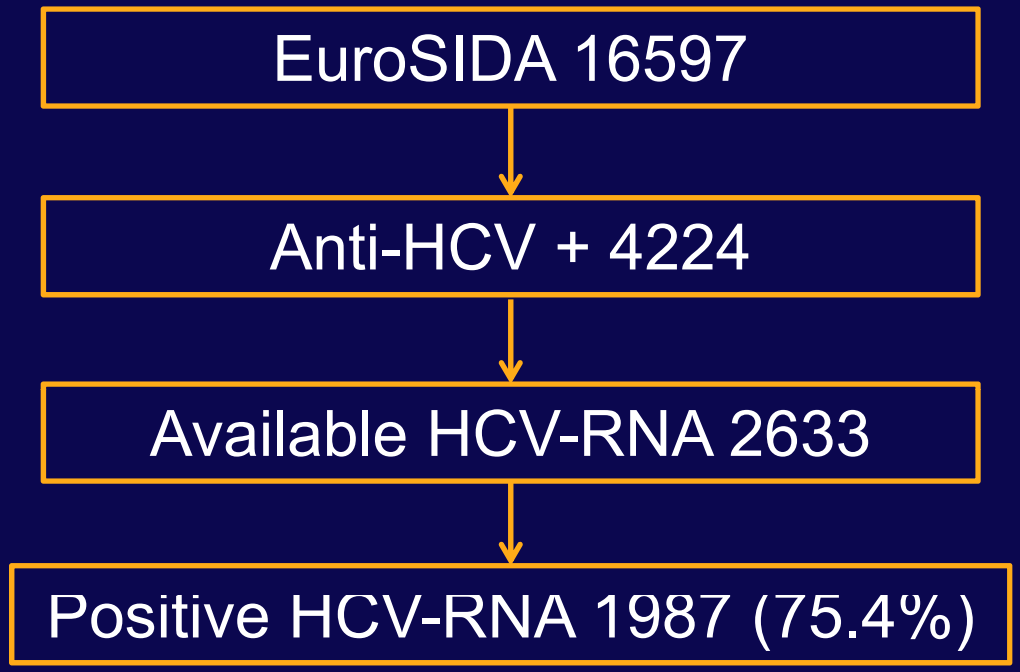
[1]Kowalska JD, Epidemiology 2011

Treatment and Baseline Definitions



- Baseline defined as first anti-HCV positive test result or entry into EuroSIDA, whichever occurred later
- HCV treatment defined as treatment with at least interferon

Statistical Methods

- Incidence rates and Poisson regression modelling for temporal trend in HCV treatment uptake
- CD4 cell count is a time dependant confounder of the association between treatment and mortality
    - Inverse probability weighting
    - Estimate the parameters of a marginal structural model

Baseline Characteristics

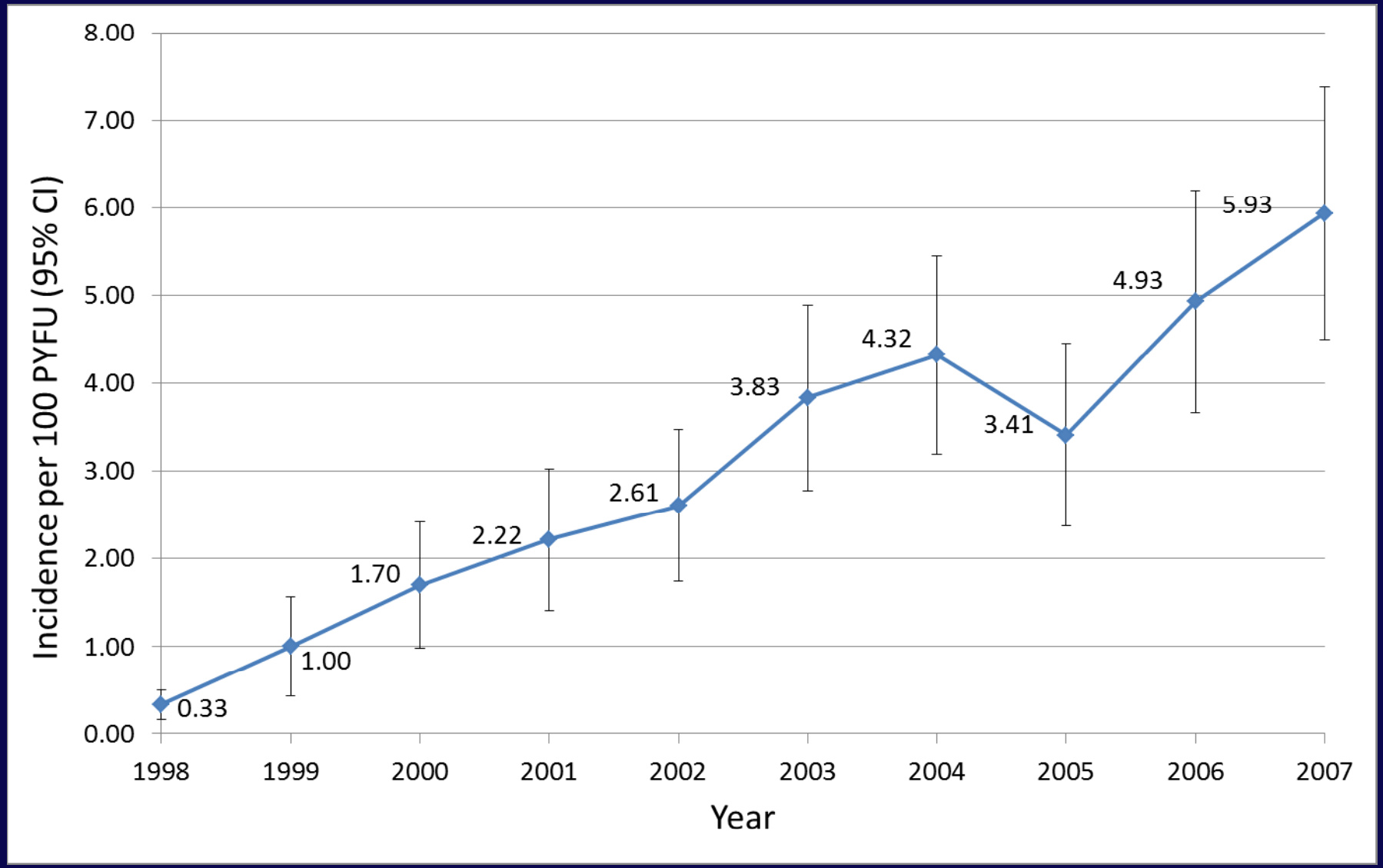
		No. Participants (%)
Total		1987 (100)
HCV Genotype	1	877 (44.1)
	2	52 (2.6)
	3	492 (24.8)
Genotype unknown for 321 (16.2%)	4	245 (12.3)
HIV Exposure Group	IDU	1452 (73.1)
	MSM	186 (9.4)
	Heterosexual	213 (10.7)
	Other	136 (6.8)
Region of Europe	North	329 (16.4)
	West Central	411 (20.7)
	South	696 (35.0)
	East Central	329 (16.6)
	East	226 (11.4)
Baseline HIV-RNA (Log_{10} cop/ml)	Median (IQR)	3.93 (2.70 – 4.82)
Baseline HCV-RNA (Log_{10} IU/ml)	Median (IQR)	5.75 (5.18 – 6.23)
CD4 cell count (/mm^3)	Median (IQR)	277 (147 – 408)

Number Treated

- In total 504/1987 people were treated for HCV (25.4%)

Characteristics at Treatment Initiation		
HIV-RNA (Log_{10} cop/ml)	Median (IQR)	1.69 (1.59 – 2.54)
HCV-RNA (Log_{10} IU/ml)	Median (IQR)	5.80 (5.30 – 6.29)
CD4 cell count (/mm^3)	Median (IQR)	479 (349 – 650)
	CD4 < 200 cells/mm^3	25 (5.0%)
	CD4 ≥ 350 cells/mm^3	368 (72.9%)

Incidence of Treatment Uptake 1998-2007



Crude Incidence Rate Ratio (IRR): 1.27 (95% C.I. 1.23 – 1.31; p<0.0001)

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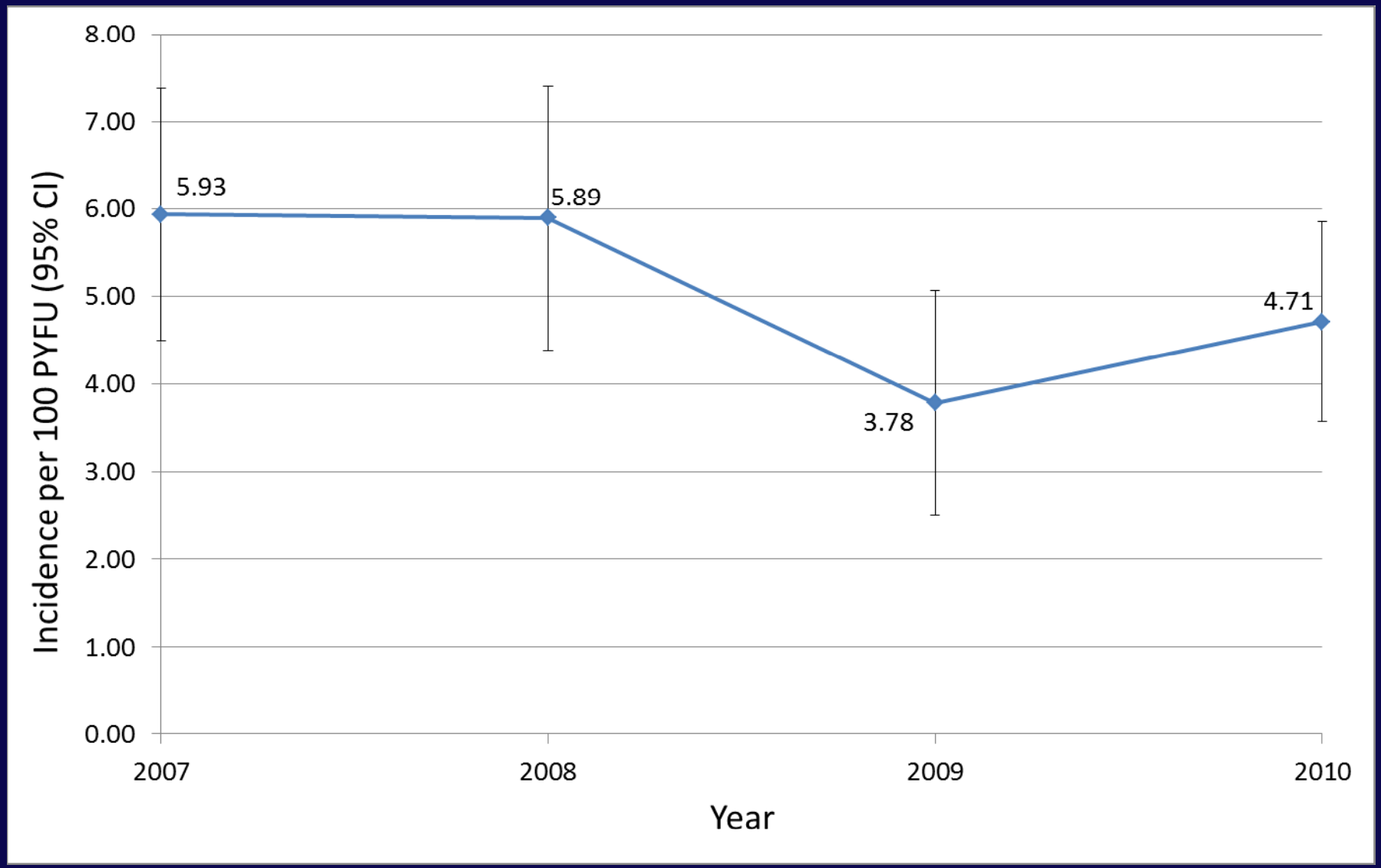
Incidence of Treatment Uptake Since 2007



Crude Incidence Rate Ratio (IRR): 0.88 (95% C.I. 0.79 – 0.98; p=0.020)

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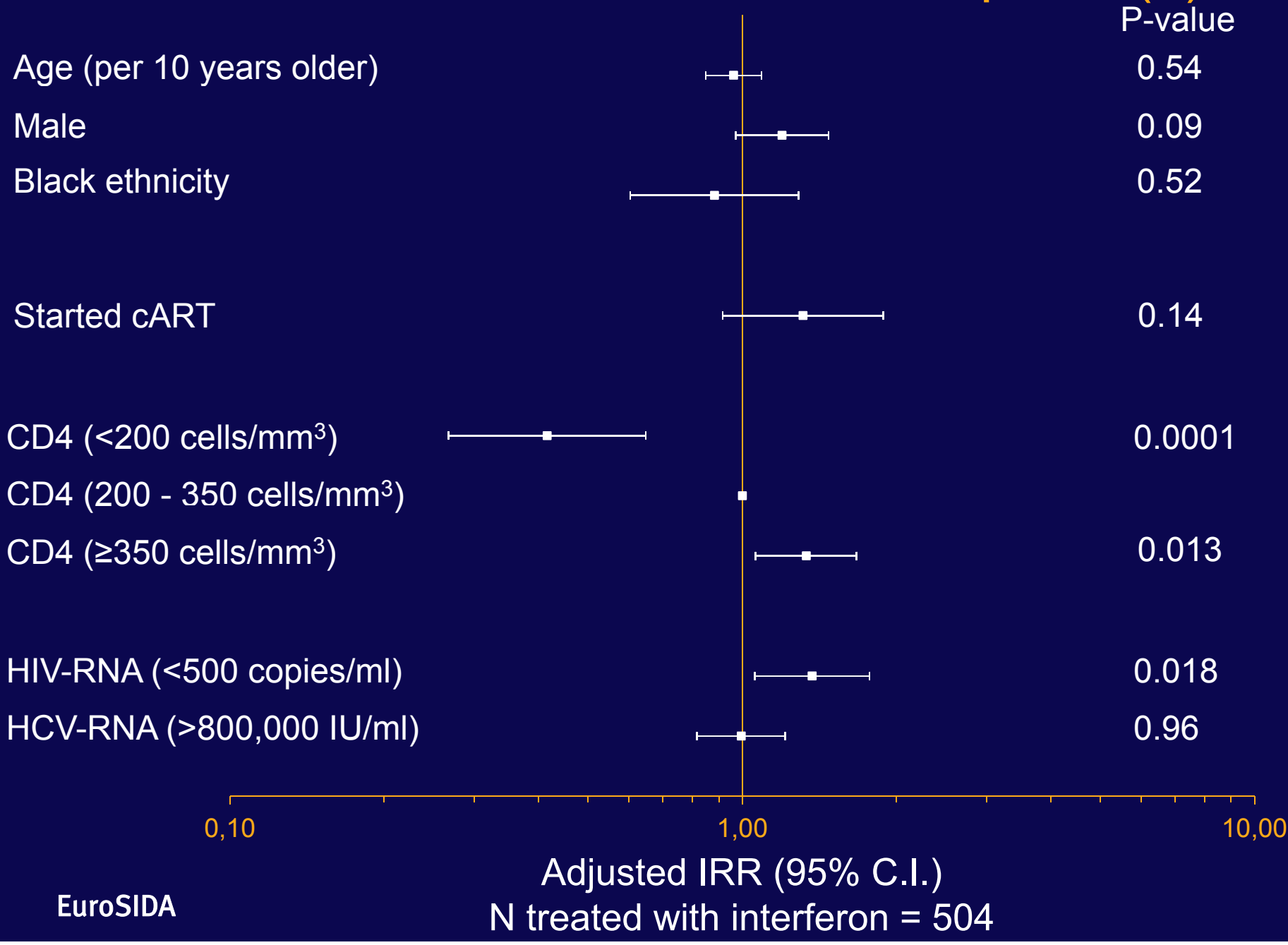
Factors Associated with Treatment Uptake (1)



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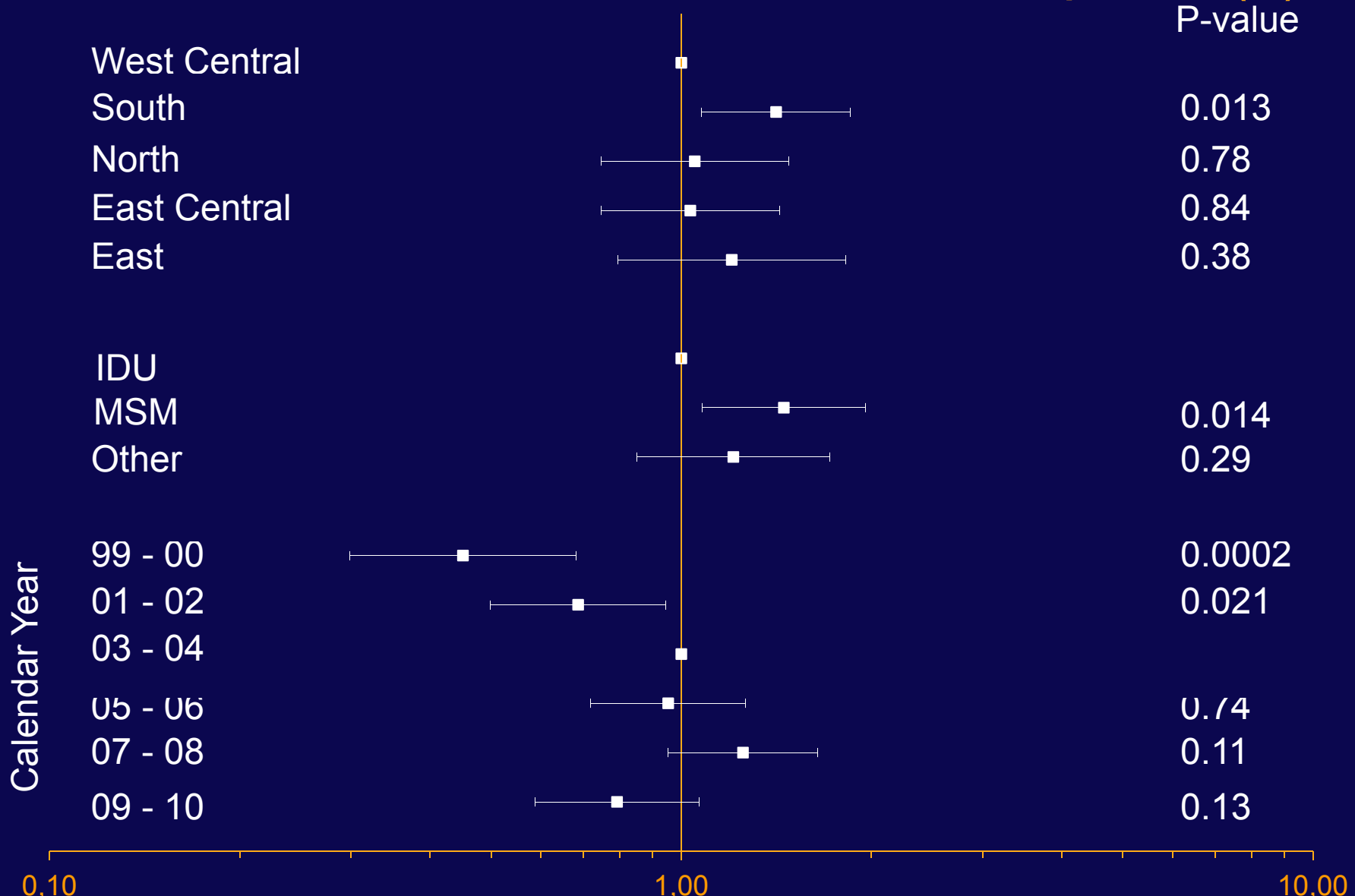
Factors Associated with Treatment Uptake (2)



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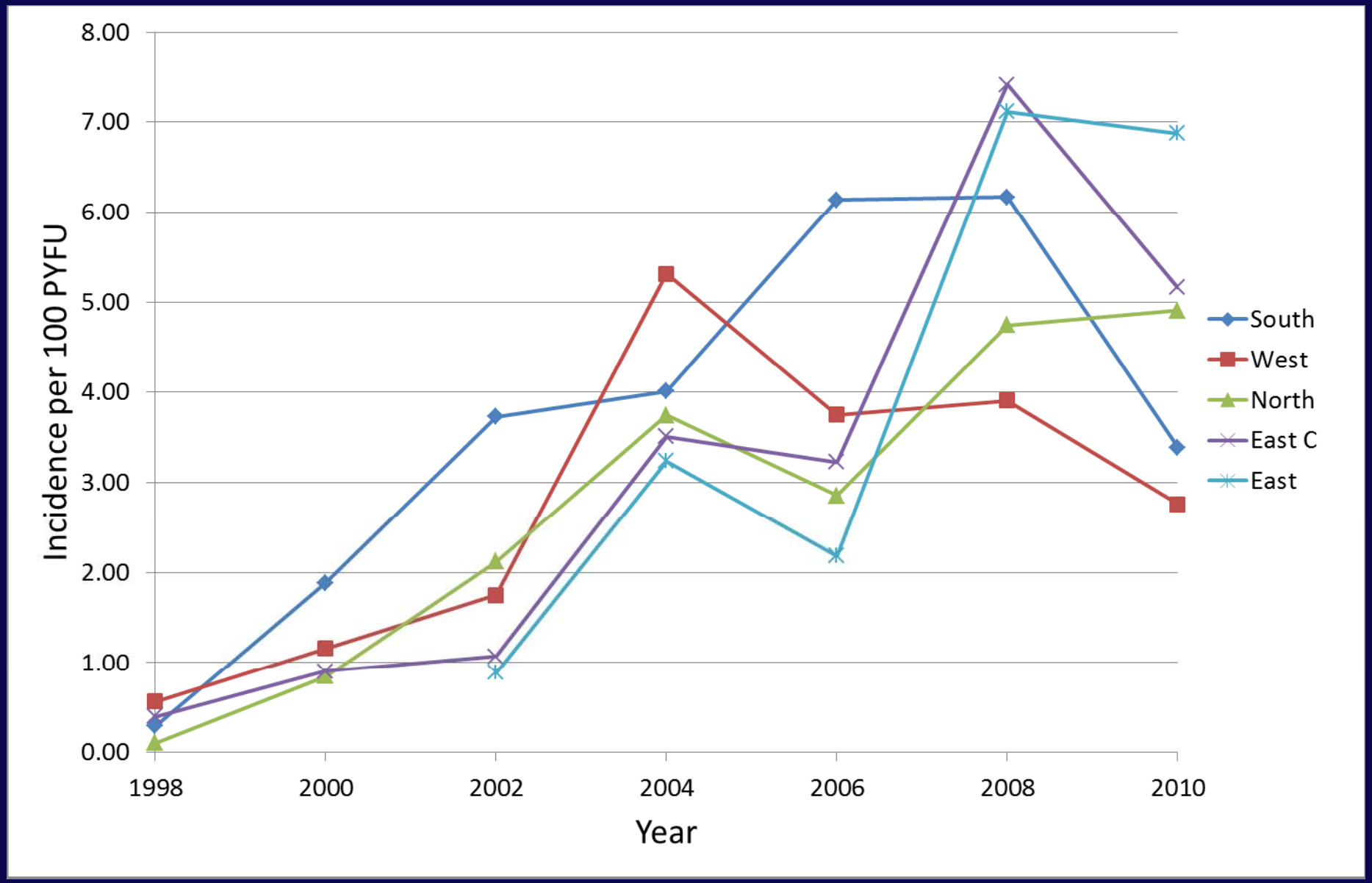
Treatment Uptake by Region



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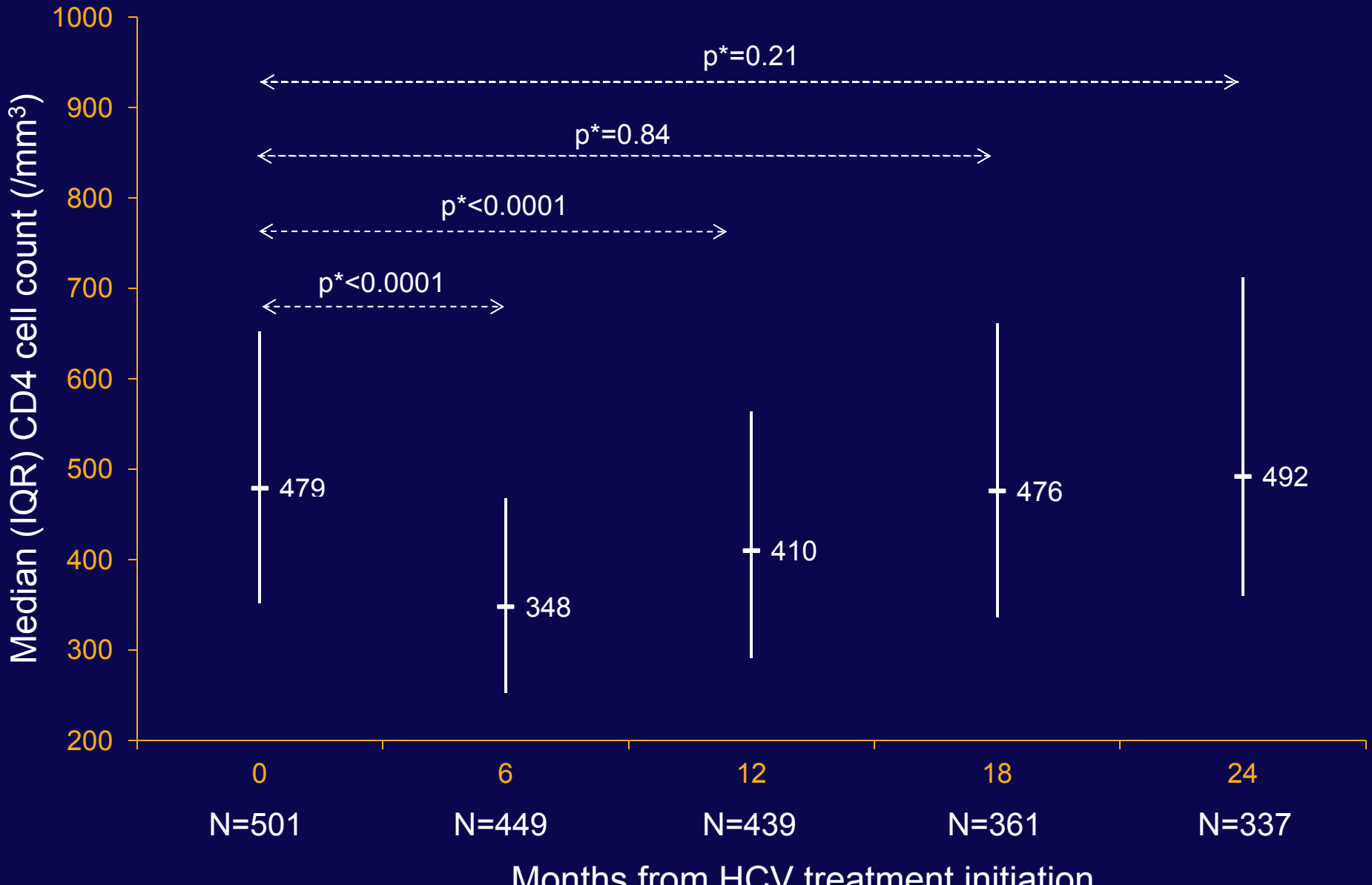
Global Interaction p-value=0.44

Transient Effect of Treatment on CD4 cell counts



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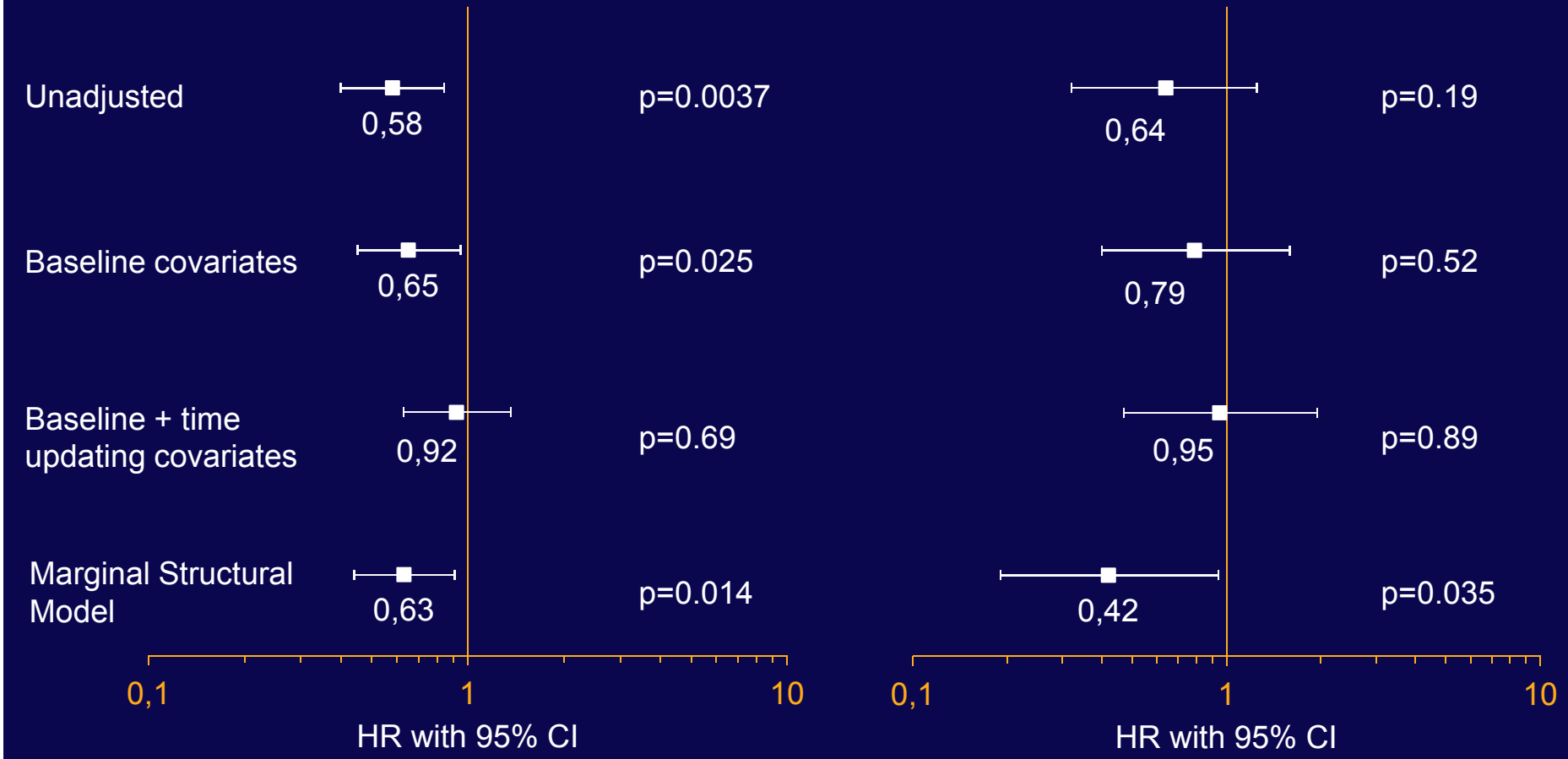
*P-value from Kruskal-Wallis test

Effect of Treatment on Mortality
Hazard Ratio Estimates



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Covariates: age, CD4, HIV-RNA, HCV-RNA, cART use, HCV genotype, AIDS, region of Europe, HIV transmission route, ALT levels, baseline calendar year

Limitations

- Currently lacking some follow-up HCV-RNA data meaning we are unable to determine the rate of sustained virological response in all of those treated
- Data on the level of fibrosis or the amount of alcohol consumed starting to be collected

Conclusions

- The incidence of HCV treatment uptake increased 27% per year until 2007 in EuroSIDA, stabilising thereafter
- Individuals with CD4 cell counts >350 cells/mm^3 and HIV-RNA <500 copies/ml are being selected for treatment, in line with current guidelines
- Significant benefit of HCV treatment on all-cause and liver-related mortality in a guideline adherent population

  Future work to study the association between SVR and mortality

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