



Hepatitis delta in HIV patients in Europe

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Hepatitis D

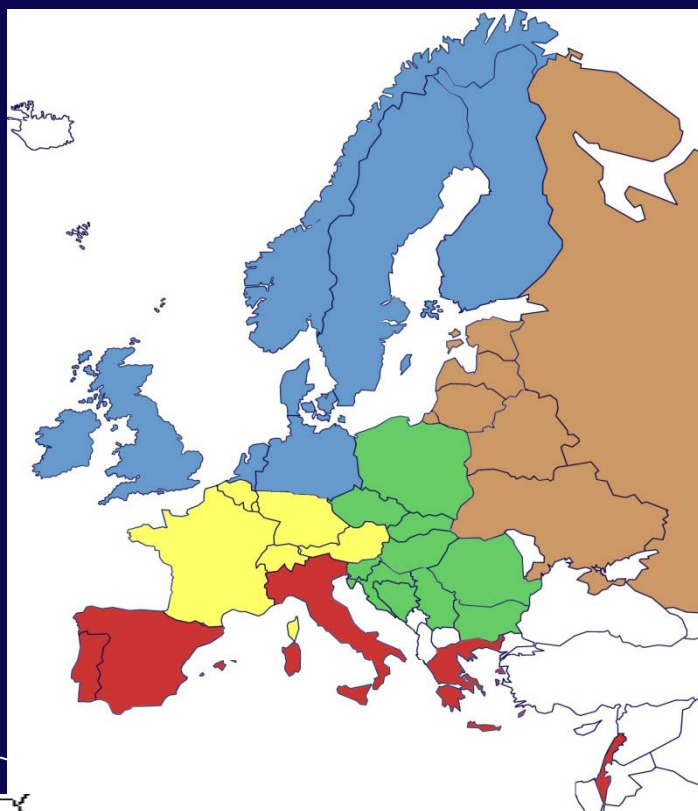
- HDV is a small RNA (1.7 Kb) defective agent that only replicates in the presence of HBsAg.
- Two clinical forms: co-infection and super-infection.
- Hepatitis delta is the most aggressive viral hepatitis.
- 15-20 million people infected worldwide (~5% of chronic HBV).
- Endemic in the Middle East, Amazonian region, Central Asia, Central Africa & Mediterranean basin
- Transmitted mainly parenterally (IDU outbreaks) and sexually.
- Given that HDV use human host enzymes for replication, no specific antivirals have been developed so far. Interferon provides benefit in less than a quarter of patients.

Objectives

- Investigation of delta hepatitis in EuroSIDA:
 - Prevalence and correlates of HDV infection
 - Impact on survival

EuroSIDA

Large prospective cohort with over 16,597 patients from 33 European countries, Israel and Argentina.



- Demographics
- CD4 counts & viral loads
- Start/stop dates of all drugs
- AIDS defining illnesses & deaths
- Non-AIDS malignancies



EuroSIDA

Study population

- All individuals with available plasma samples recruited in EuroSIDA until 2006.
- Clinical follow-up extended up to March 2011.

Soriano et al. JAC 2010; 65: 548-55.

Delta virologic sub-study in EuroSIDA

Virus	Markers	Method
HBV	HBsAg	EIA
	HBV-DNA	bDNA (LLD 600 IU/ml)
	HBV genotypes	LiPA
HDV	HBV Ab	EIA
	HDV-RNA	q-PCR (LLD 10 IU/ml)*
HCV	HCV Ab	EIA
	HCV-RNA	real time-PCR (Roche)

* Le Gal et al. JCM 2005

Statistical analysis

- Chi square tests and Wilcoxon (or Kruskal-Wallis) for comparisons.
- Logistic regression for identification of factors associated with anti-HDV+.
- Multivariate Poisson regression modelling for assessing predictors of progression to clinical end points (AIDS, LRD, death).

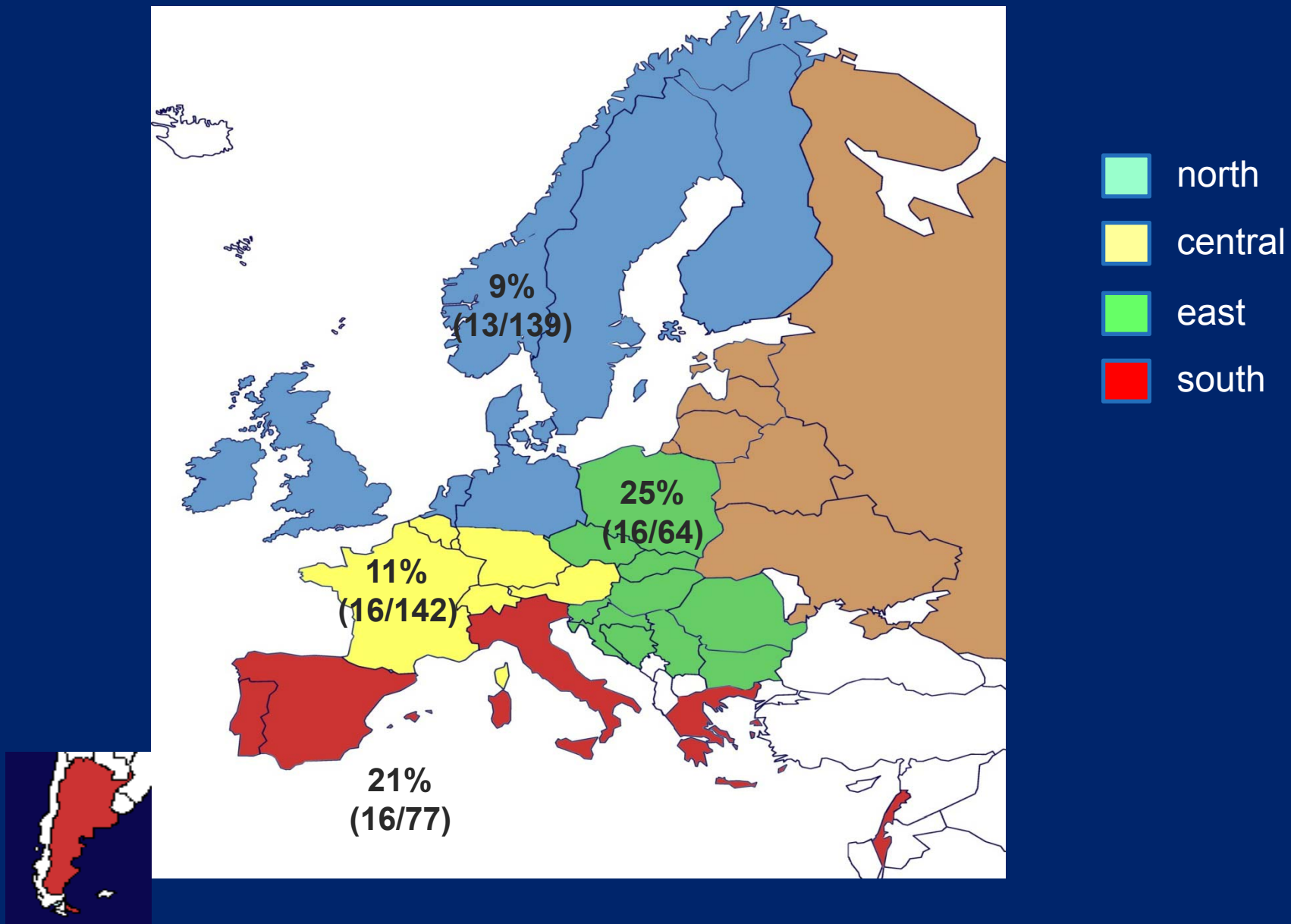
Results

Total no. patients	16,597
HBsAg+	1,319 (7.9%)
Anti-HDV Ab+	61/422 (14.5%) (95% CI: 11.1-17.8)
HDV-RNA+	31/38 (81.6%) (95% CI: 69.3-93.9%)

Median follow-up HBsAg+ patients

90.2 months (IQR 51.1 – 135.2).

Prevalence of anti-HDV Ab in HBsAg+ patients in EuroSIDA

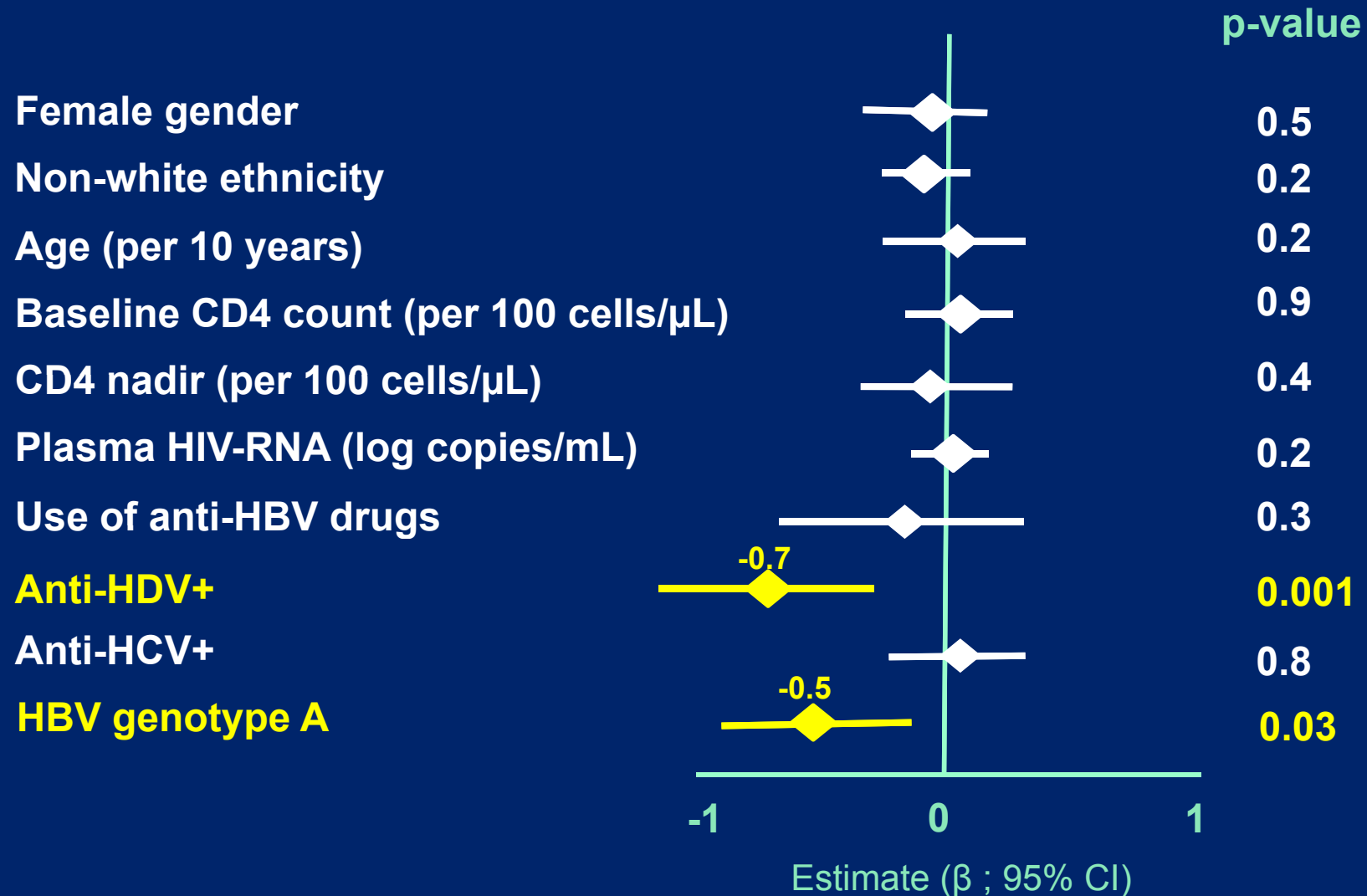


Main characteristics of the study population

Variable	All HBsAg+ patients	HDV Ab-positive	HDV Ab-negative	p
No. (%)	422	61 (14.5)	361 (85.5)	
Median age (years)	37	34	38	0.0007
Male gender (%)	84.1	72.1	86.1	0.0056
White ethnicity (%)	357 (84.6)	54 (88.5)	303 (83.9)	0.36
Risk group (%)				<0.0001
MSM	213 (50.5)	7 (11.5)	206 (57.1)	
IDU	104 (24.6)	44 (72.1)	60 (16.6)	
Heterosexual	67 (15.9)	6 (9.8)	61 (16.9)	
Others	38 (9.0)	4 (6.5)	34 (9.4)	
Median CD4 count (cells/ μ L)	285	281	294	0.53
Median nadir CD4 count (cells/ μ L)	142	143	141	0.90
Median plasma HIV-RNA (log cop/mL)	2.7	2.7	2.7	0.77
Patients on HAART (%)	310 (73.5)	41 (67.2)	269 (74.5)	0.23
Patients on 3TC, TDF or FTC (%)	299 (70.9)	41 (67.2)	258 (71.5)	0.50
HCV-Ab positive (%)	119 (28.2)	43 (70.5)	76 (21.1)	<0.0001
Serum HBV-DNA positive (%)	61	59	63	0.54
Median HBV-DNA (IU/mL)	19,346	949	24,522	0.003
Serum HBV-DNA >10 ⁷ IU/ml (%)	17	11	20	0.11
HBV genotypes (%)				<0.0001
D	39	50	12	<0.01
A	56	27	78	<0.01

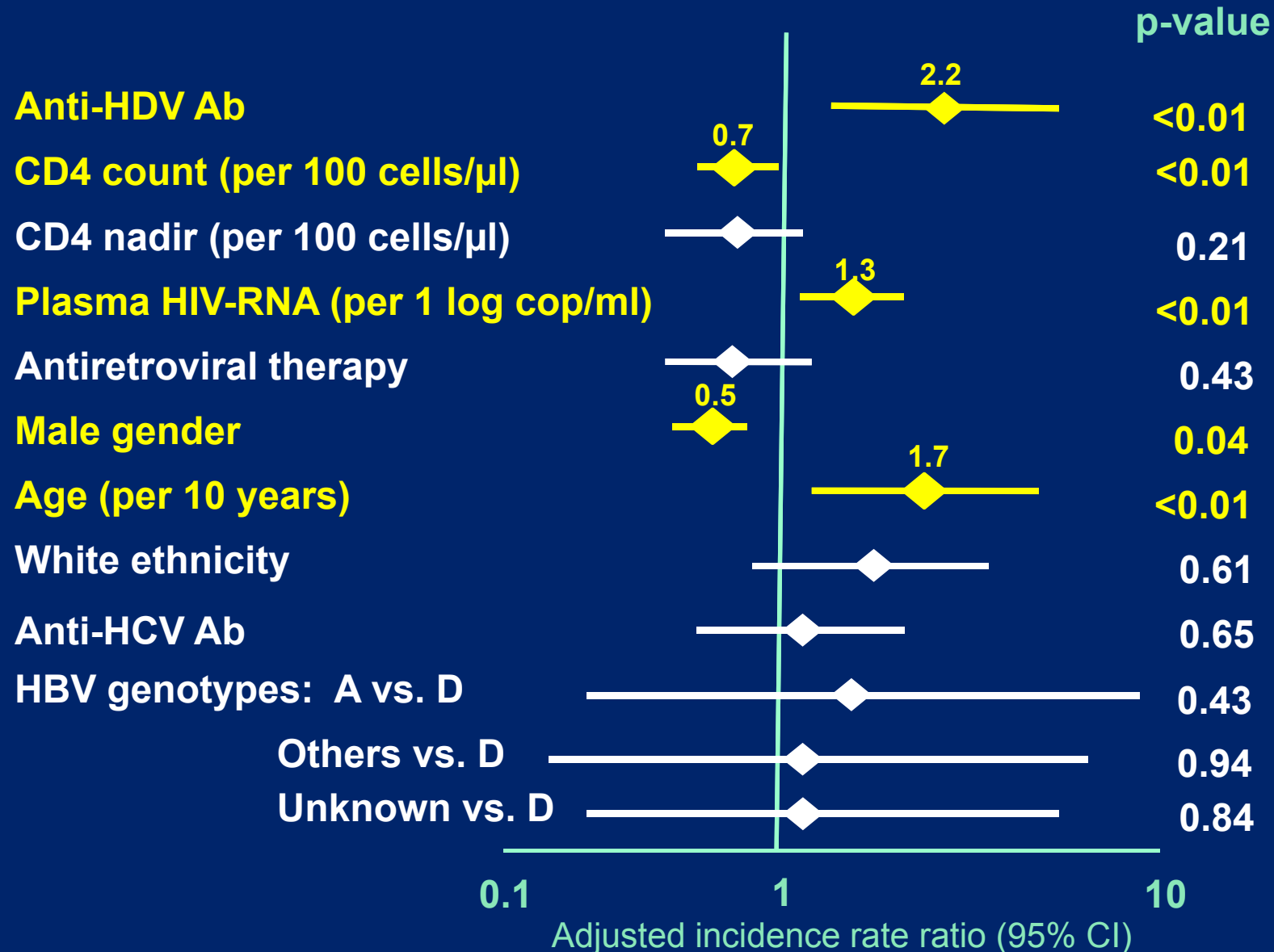
Predictors of serum HBV-DNA levels

Multivariate regression model



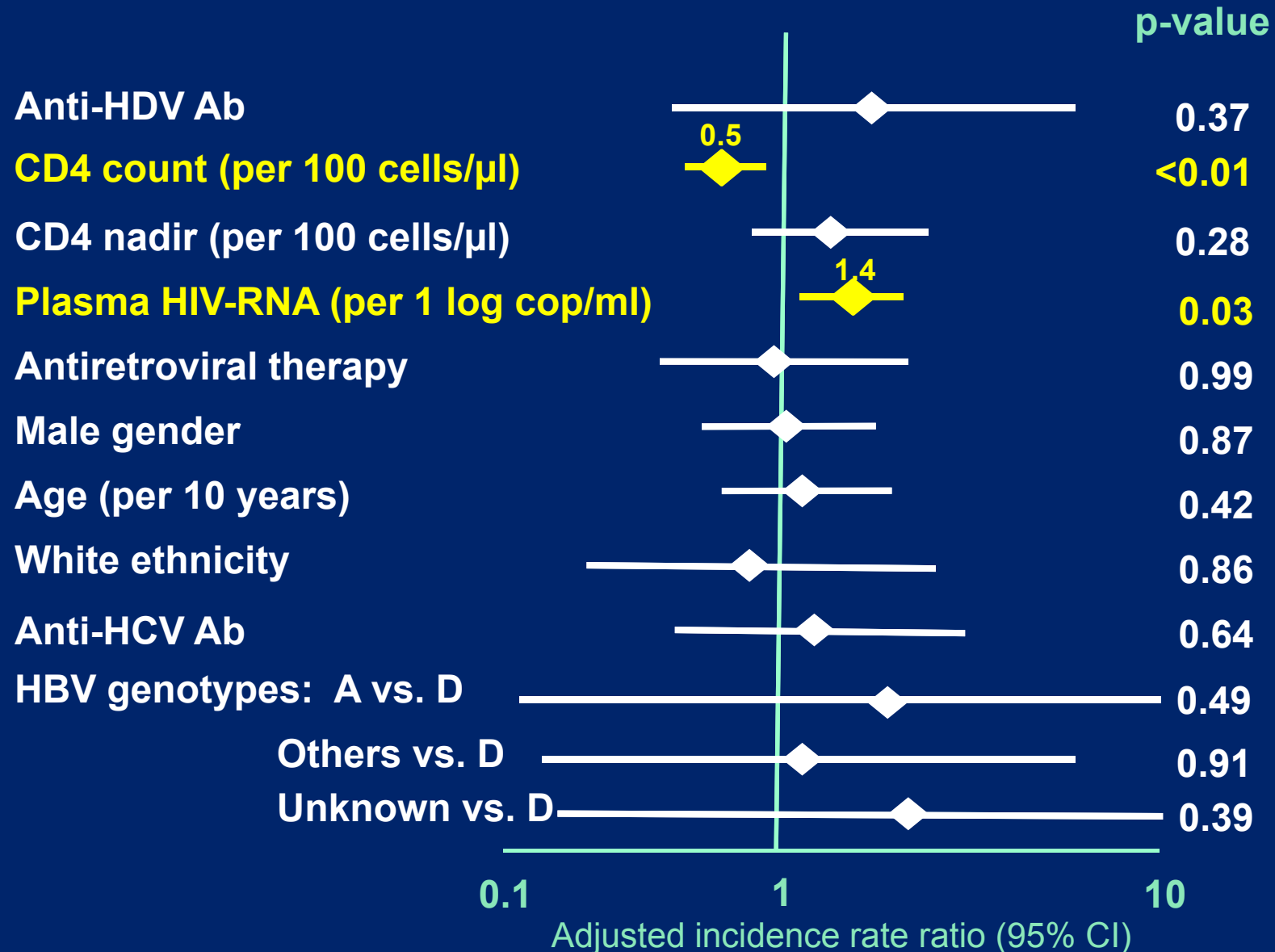
Progression to AIDS or death

(91 events; 3233 PYFU)



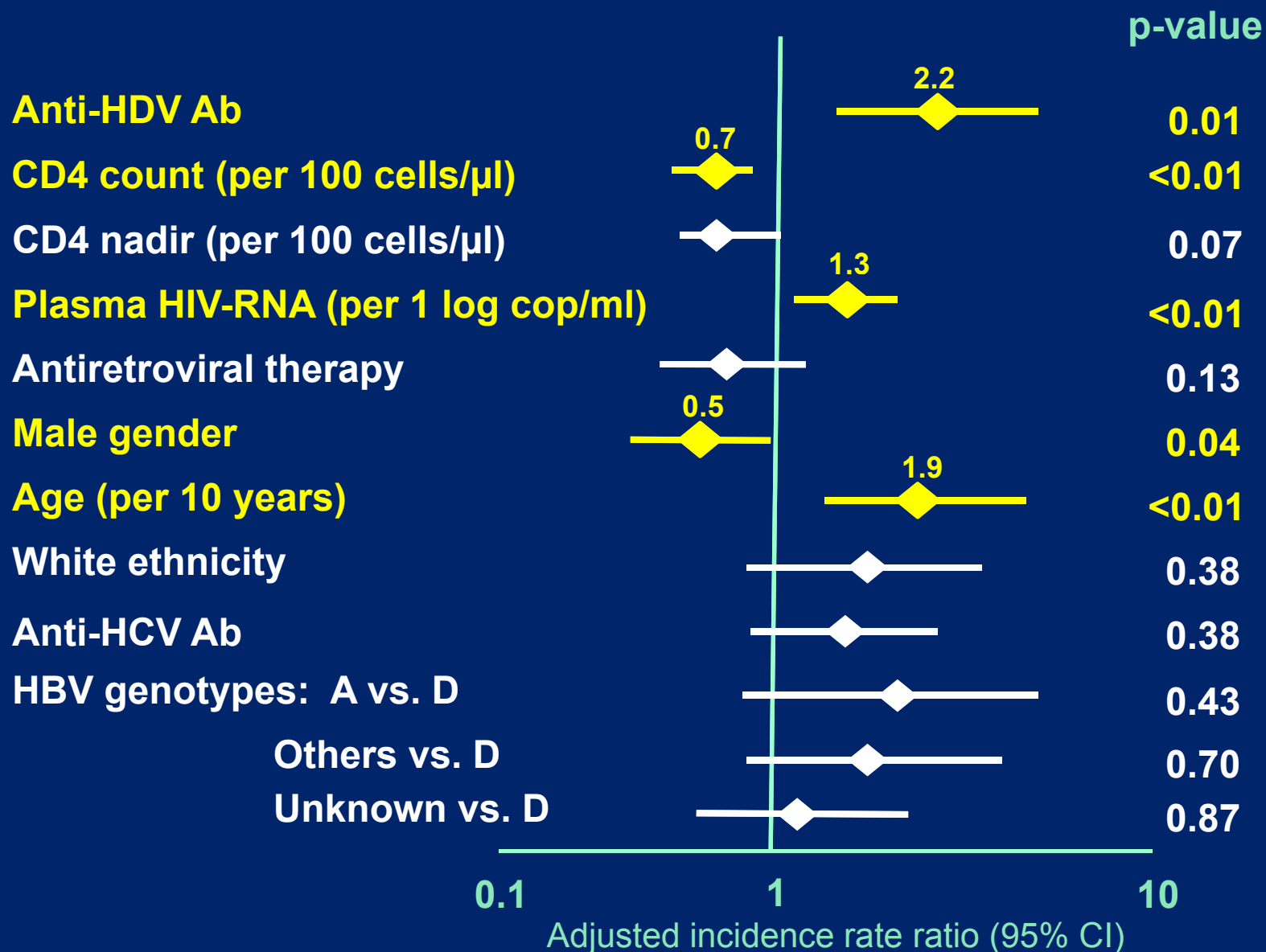
Progression to AIDS

(31 events; 3069 PYFU)



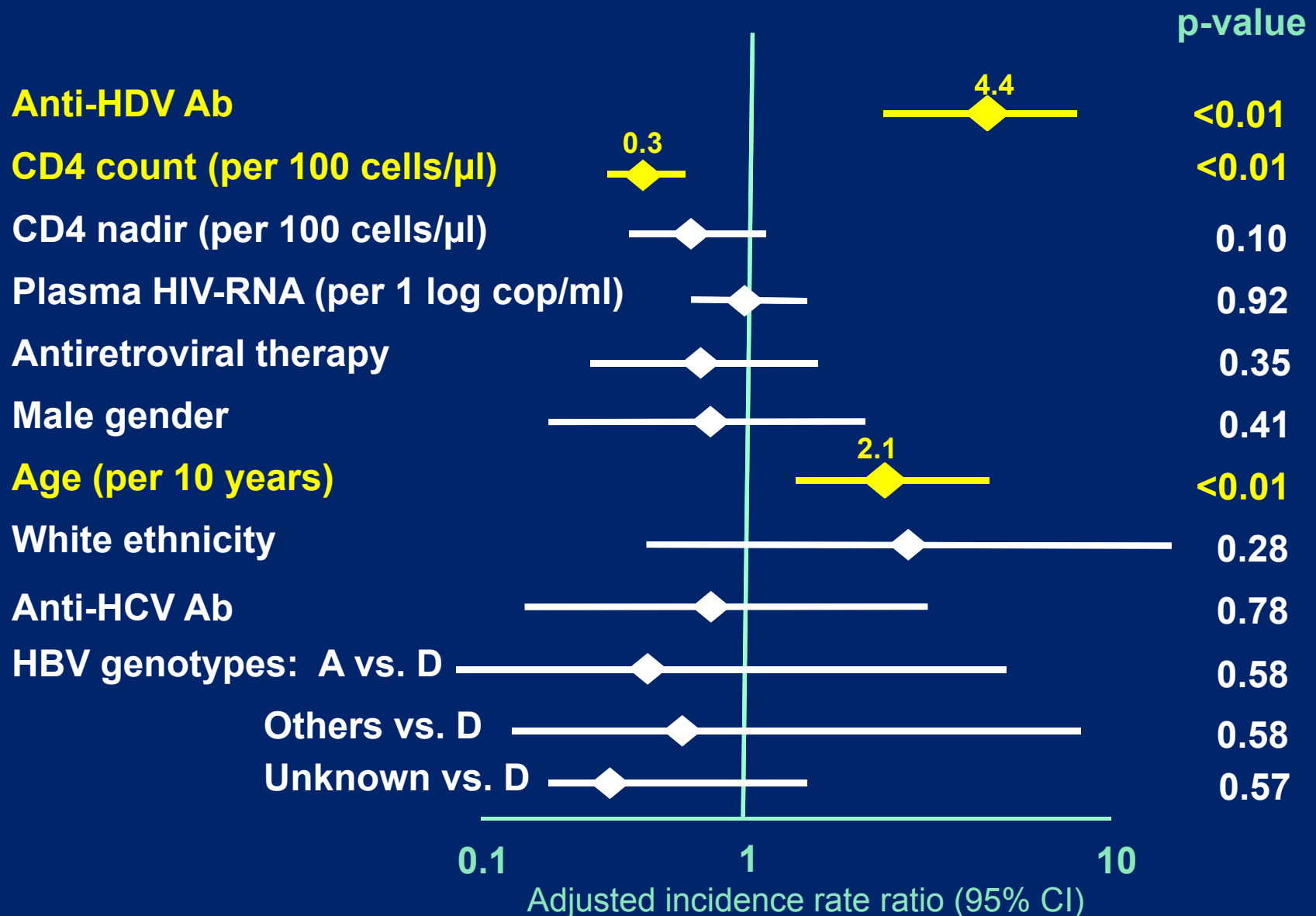
Progression to death

(76 events; 3355 PYFU)



Progression to LRD

(21 events; 3382 PYFU)



Limitations

- Assessment of HDV markers in only a fraction of HBsAg+ patients (422/1319; 32%). However, the delta population (n=61) is the largest characterized virologically so far in HIV patients.
- Lack information on HBeAg status. It was not recorded and could have driven the association found between HBV genotypes and serum HDV-RNA.

Conclusions

- The overall prevalence of anti-HDV in chronic HBsAg+/HIV carriers in EuroSIDA is **14.5%**.
- Most anti-HDV patients exhibit detectable HDV viremia.
- Viral interference between HBV and HDV is manifested in all but HBV genotype D carriers, in whom overt co-replication of both viruses occurs, which might result in enhanced liver damage.
- We report for the first time that Delta hepatitis increases the risk of liver-related deaths and overall mortality in HIV patients.

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