



HCV viremia increases the risk of chronic kidney disease in HIV-infected patients

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for EuroSIDA in EuroCoord

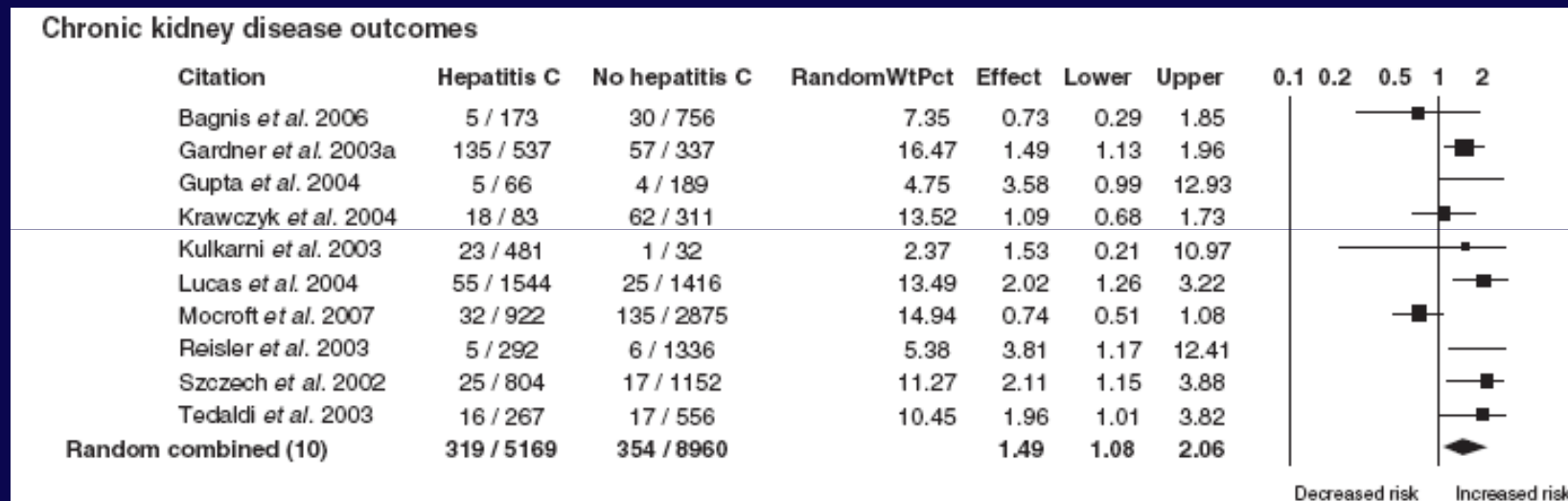
Background

- Although cART has resulted in a decrease in HIV-associated nephropathy, chronic kidney disease (CKD) is still an important cause of morbidity and mortality in HIV patients
- High prevalence of risk factors (hypertension, diabetes, smoking) for CKD in HIV patients
- In Europe around a third of all HIV patients are co-infected with hepatitis C virus (HCV)

Background (2)

- HCV can cause glomerulonephritis ($\pm$ cryoglobulinemia)
- HCV has been associated with higher risk of diabetes mellitus, which may contribute to the development of CKD
- HCV-related liver disease can cause CKD (hepatorenal syndrome)

The Impact of HCV coinfection of HIV-related CKD: a meta-analysis



Limitation: Hepatitis C diagnosis based on antibody status

Objectives

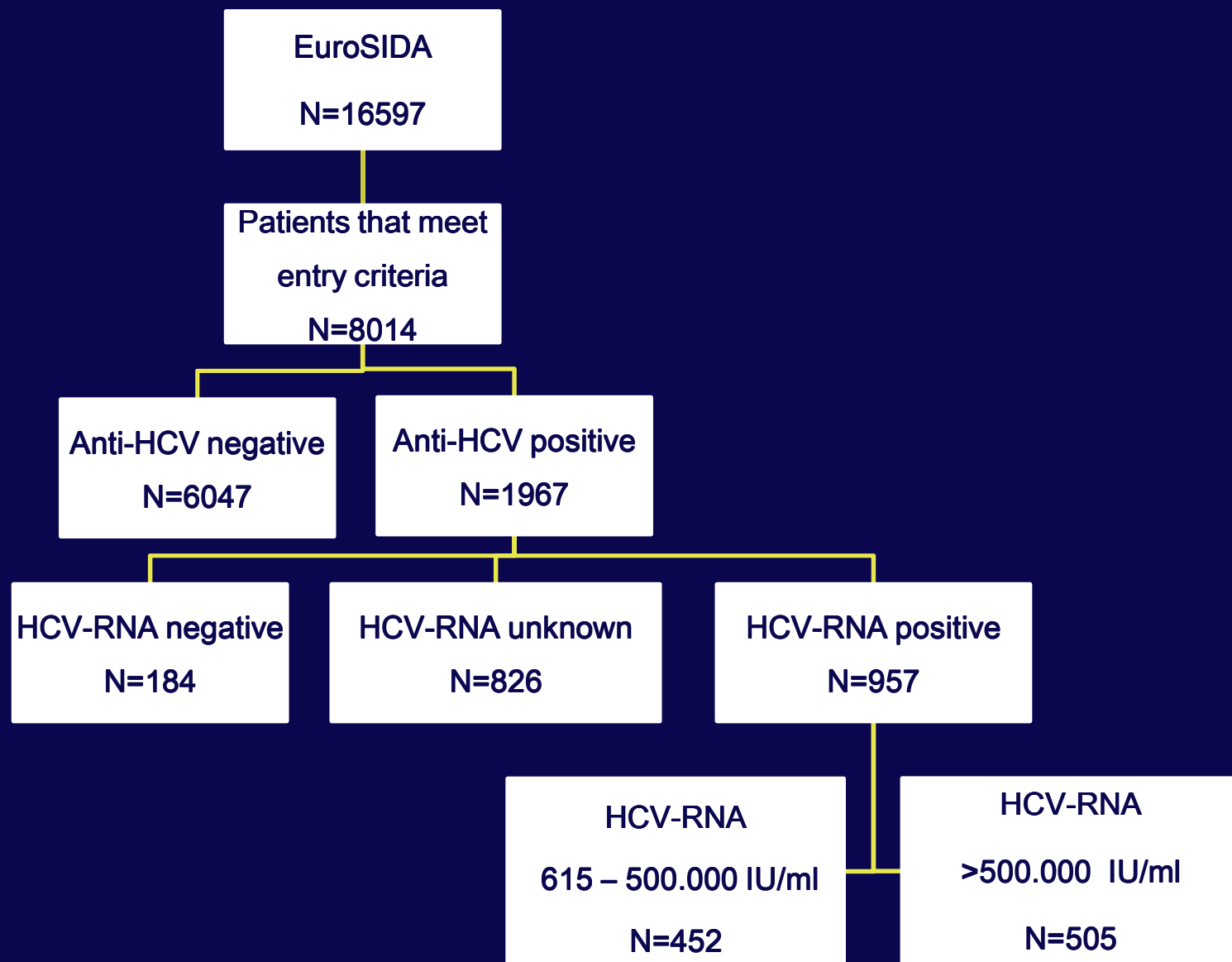
- To investigate the association of HCV viremia and genotype with incidence of CKD in the EuroSIDA observational cohort

Methods (1)

- Eligible patients:
 - ≥ 3 serum creatinine measurements after 01.01.04,
 - body weight measured within ≤ 12 months of each creatinine measurement
 - known HCVA status
- Baseline was the first available estimated glomerular filtration rate (eGFR) (Cockcroft-Gault equation)
- $$\text{eGFR} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine} \times 72} \times 0.85 \text{ (if female)}$$
- eGFR standardised for body surface area

Methods (2)

- CKD:
 - i) a confirmed $\text{eGFR} \leq 60 \text{ mL/min/1.73m}^2$ for patients with $\text{eGFR} > 60 \text{ mL/min/1.73m}^2$ at baseline, or
 - ii) a confirmed 25% decline in eGFR for patients with $\text{eGFR} \leq 60 \text{ mL/min/1.73m}^2$ at baseline
- HCV viremic defined as $\text{HCV-RNA} > 615 \text{ IU/mL}$
 - Low viremia: $615 - 500.000 \text{ IU/mL}$
 - High viremia: $> 500.000 \text{ IU/mL}$
- Follow-up was from baseline to either CKD or the last eGFR measurement
- Incidence rates of CKD were compared between groups using Poisson regression



Baseline Characteristics of 8014 HIV patients according to HCV serostatus

	Anti-HCV+ N=1967 (24.5%)	Anti-HCV– N=6047 (75.5%)
Age, median (IQR) years	39 (33 – 44)	42 (36 – 50)
Gender (male)	68.0%	75.9%
Caucasian ethnicity	91.8%	85.7%
Risk group (IDU)	71.2%	2.5%
HBsAg+	6.7%	5.9%
CD4 nadir, median (IQR) cells/μl	131 (49 – 223)	146 (51 – 245)
cART at baseline	82.8%	86.6%
Arterial hypertension	4.4%	8.8%
Smoking (current)	51.5%	28.2%
ACE inhibitor use	2.2%	4.6%
eGFR median (IQR) ml/min per 1.73m ²	100 (86.6 – 116.1)	96.6 (82.8 – 112.0)

Baseline Characteristics of anti-HCV+ patients according to HCV-RNA status

	HCV-RNA+ N=957	HCV-RNA- N=184	P-value
Age, median (IQR) years	40 (36 – 45)	41 (38 – 45)	0.12
Gender (male)	68.1%	64.1%	0.29
Risk group (IDU)	74.0%	64.1%	0.0001
HBsAg+	5.4%	14.7%	<0.0001
cART at baseline	90.5%	90.2%	0.64
CD4+ nadir median (IQR) cells/ μ l	124 (41 – 211)	92 (23.5 – 176)	0.013
Diabetes	3.8%	5.4%	0.29
Arterial hypertension	5.0%	4.4%	0.70
Smoking (current)	56.3%	54.4%	0.21
ACE inhibitor use	2.2%	4.4%	0.94
eGFR median (IQR) ml/min per 1.73m ²	99.9 (86.8 – 115.2)	102.0 (86.7 – 114.6)	0.76

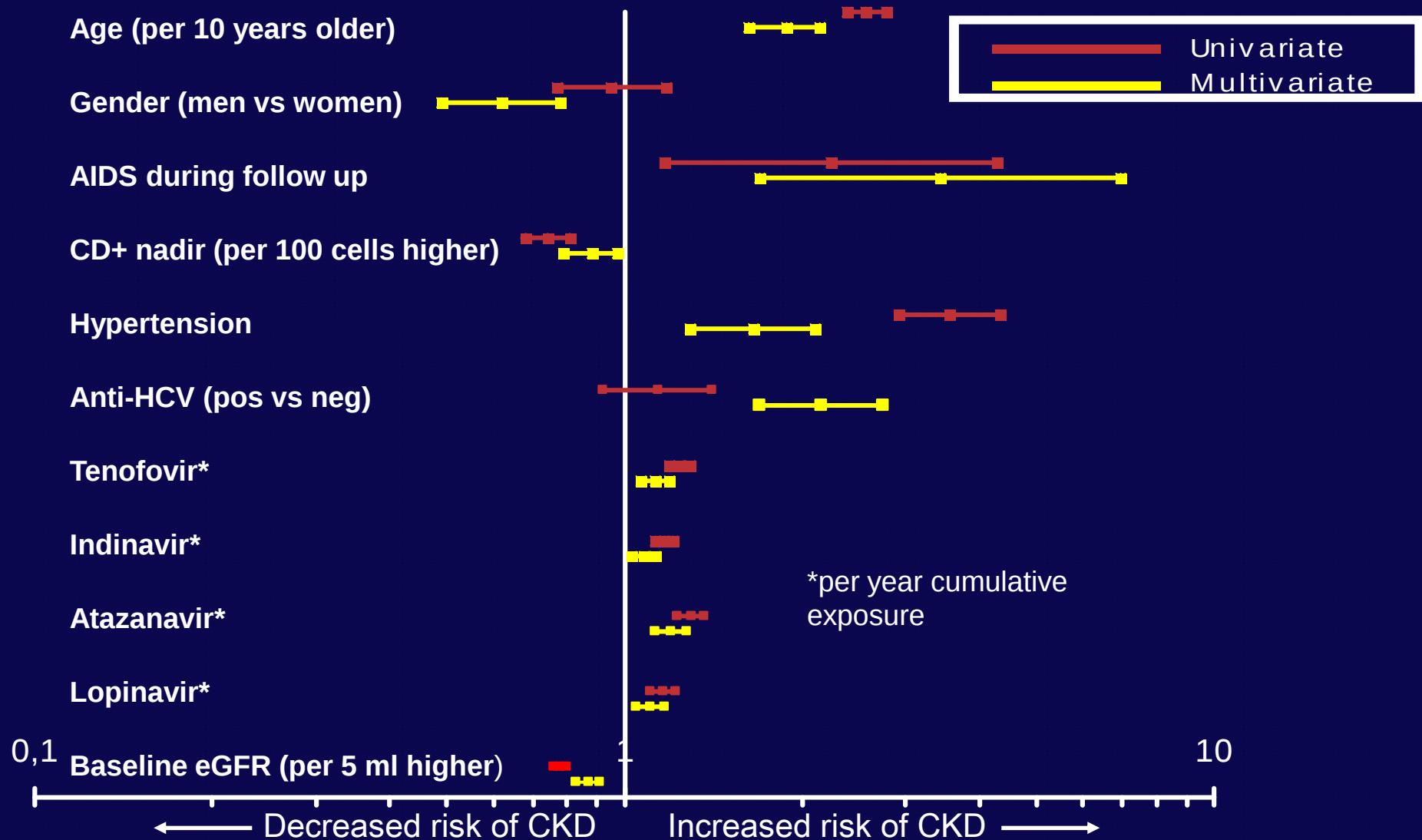
Results

- Median number of eGFR measurements/patient was 11 (IQR 7-16)
- A total of 419 patients (5.5%) progressed to CKD during 30164 PYFU
- Incidence of CKD 13.9/1000 PYFU (95% CI 12.6–15.2)

Progression to CKD

(All patients; 419 events)

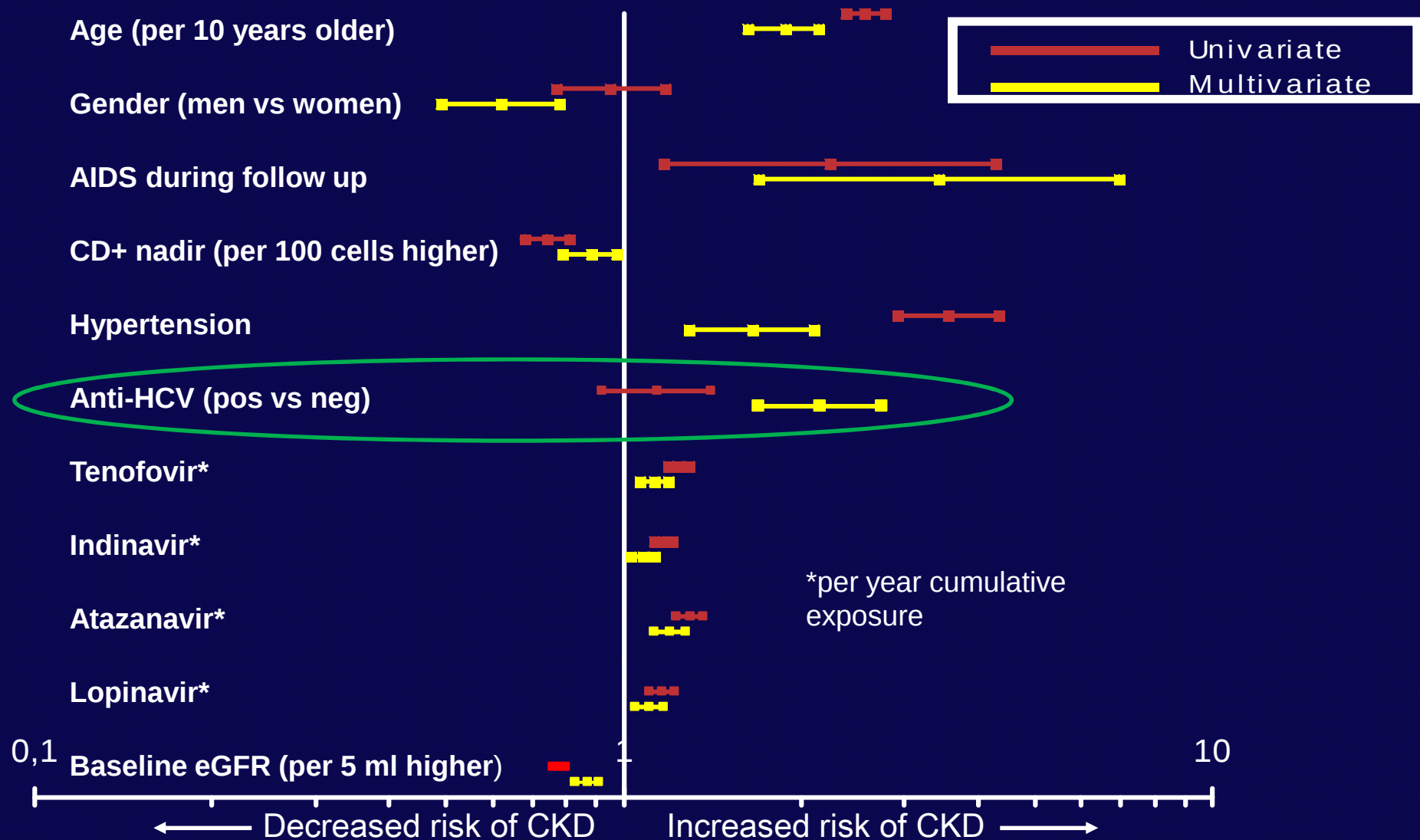
Incidence Rate Ratio (95% CI)



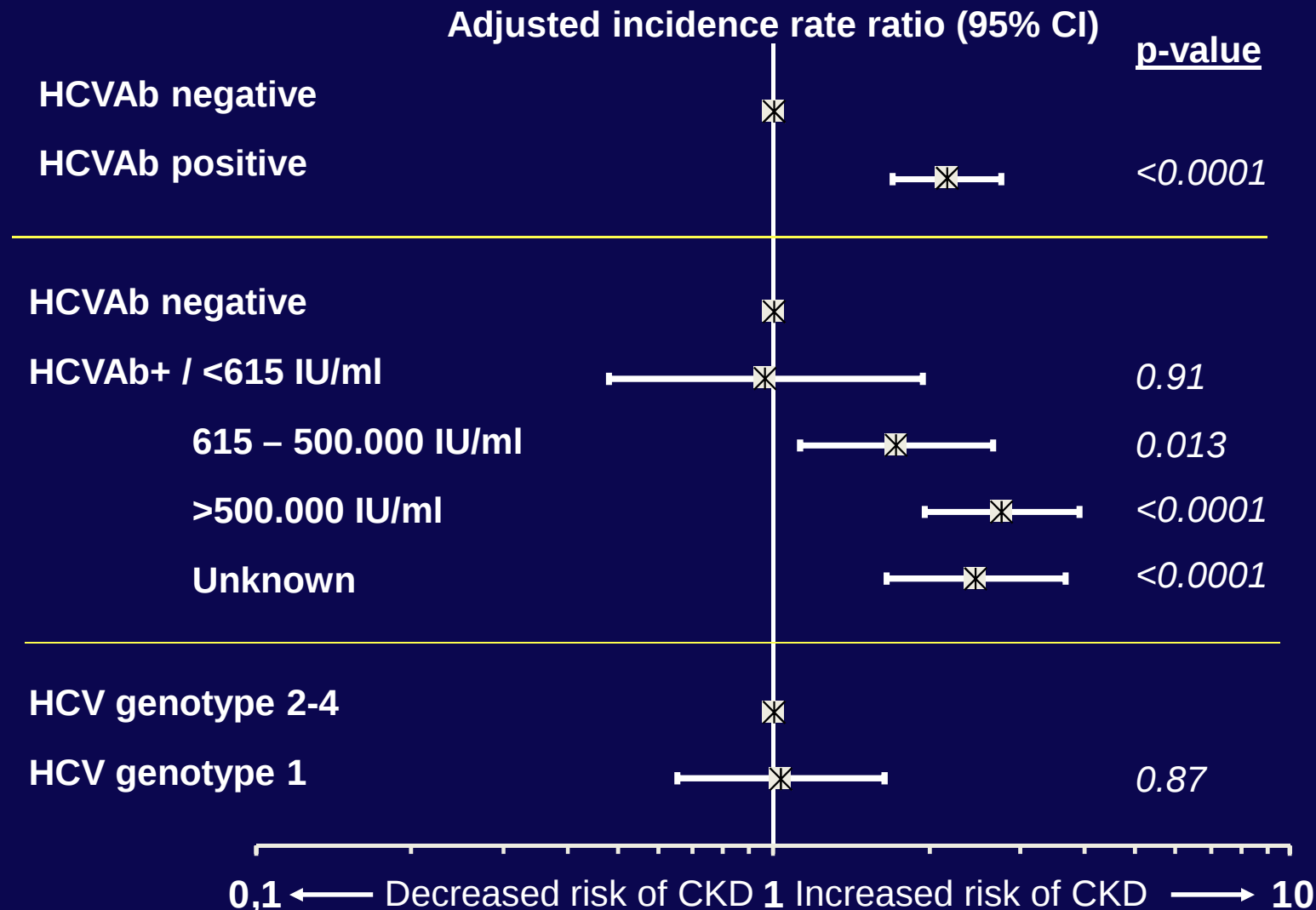
Progression to CKD

(All patients; 419 events)

Incidence Rate Ratio (95% CI)



Role of HCV Viremia and Genotype in Progression to CKD



Sensitivity analysis

- Adjustment for intravenous drug use did not change the results, and was not included in the final model due to collinearity between this variable and HCV status

Summary

- Patients with chronic HCV infection were at higher risk of CKD
- Higher HCV-RNA levels were associated with an increased risk of CKD
- The risk of CKD was similar in anti-HCV negative patients and anti-HCV+ patients with resolved infection
- HCV genotype was not significantly associated with risk of CKD

Perspectives

- The mechanisms by which HCV may affect renal function are unclear and warrant further study
 - Direct effect of the virus?
 - Marker of severe liver disease?
- Should HIV/HCV coinfecting patients avoid ARVs associated with risk of CKD?
- Does anti-HCV treatment reverse the decline in renal function in HCV patients with CKD?

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The multi-centre study group of EuroSIDA (national coordinators in parenthesis).

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