Epidemiologic and virologic characteristics of chronic hepatitis C across Europe:

Results from EuroSIDA

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Objectives

- It is unknown which factors determine the rate of spontaneous clearance of hepatitis C virus (HCV) infection in HIV individuals.
- Moreover, the variables influencing serum HCV-RNA levels and HCV genotype distribution are not well defined in this population.

Patients & Methods

- HCV antibody positive (HCVAb+)
- Stored serum samples in the EuroSIDA sample repository

- Serum HCV-RNA testing by a reliable quantitative assay for distinct genotypes (Versant)
- HCV genotyping (LiPA) carried out in viremic subjects

Statistical Methods

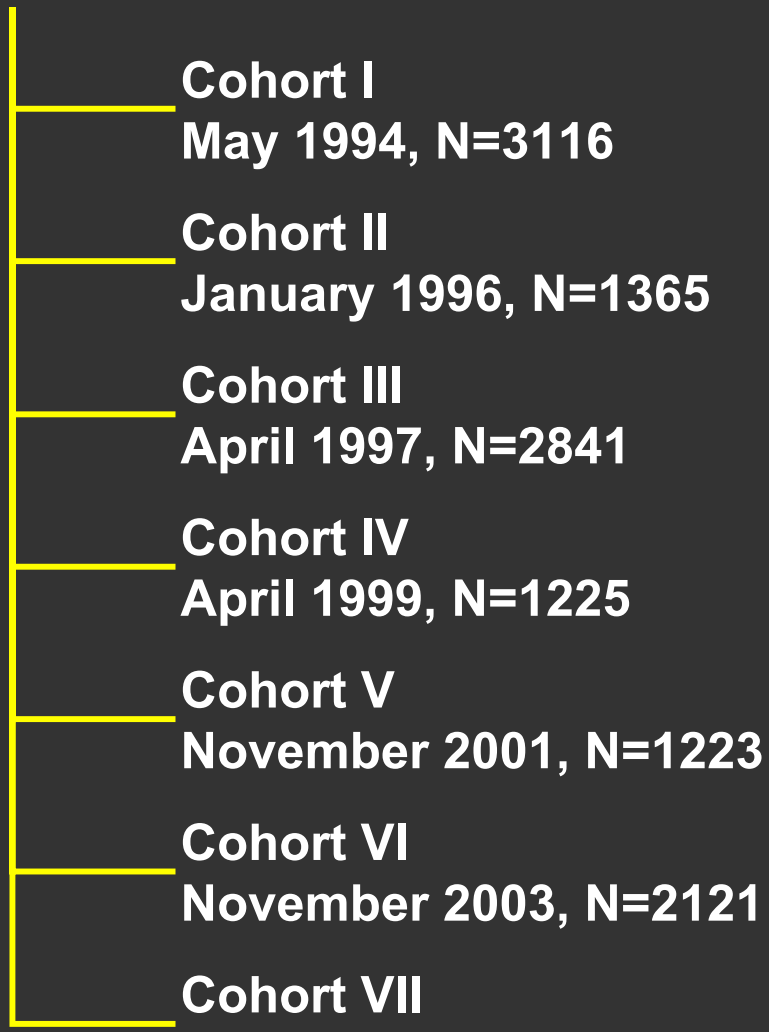
- Logistic regression was used to identify
  - variables associated with spontaneous HCV clearance
  - Variables associated with HCV genotype 1 (HCV-1) infection

Adjusting for demographic, clinical and therapeutic factors.

Recruitment in EuroSIDA

- Pre-defined number from each clinic for each cohort
- Pre-booked, routine outpatient appointment
- Aged over 16
- Cohorts I-III, CD4 < 500/mm^3 in 4 months before enrollment

EuroSIDA (n = 14,282)



Data collected in EuroSIDA

- Demographic data
- CD4 and viral loads
- Other markers
- HCV/HBV status
- Disease specific prophylaxis
- Antiretrovirals (start/stop dates)
- All AIDS defining illnesses
- Other severe opportunistic illnesses
- Non-AIDS malignancies
- Serious adverse events

Main characteristics of 2,263 HIV patients with positive HCV antibody in EuroSIDA.

	Total n = 2263	Positive serum HCV-RNA n = 1677 (74.1%)	Negative serum HCV-RNA n = 586 (25.9%)	p
Gender: Male	1577 (69.7%)	1173 (74.4%)	404 (25.6%)	0.88
Median age (years)	37.1	37.1	37.4	0.0025
Risk group: IDU	1586 (70.1%)	1233 (77.7%)	353 (22.3%)	<0.0001
Ethnicity: White	2027 (89.6%)	1504 (74.2%)	523 (25.8%)	0.10
Region: South/Argentina Central North East	773 (34.2%) 511 (22.6%) 442 (19.5%) 537 (23.7%)	603 (78.0%) 368 (72.0%) 301 (68.1%) 405 (75.4%)	170 (22.0%) 143 (28.0%) 141 (31.9%) 132 (24.6%)	<0.0001
Serum HBsAg: positive negative unknown	197 (8.7%) 1687 (74.5%) 379 (16.7%)	107 (54.4%) 1263 (74.9%) 307 (81.0%)	90 (45.6%) 424 (25.1%) 72 (19.0%)	<0.0001
Antiretroviral therapy: yes no	1915 (84.6%) 348 (15.4%)	1399 (73.1%) 278 (79.9%)	516 (26.9%) 70 (20.1%)	0.007
Prior interferon therapy	115 (5.1%)	69 (60.0%)	46 (40.0%)	0.0048

Results

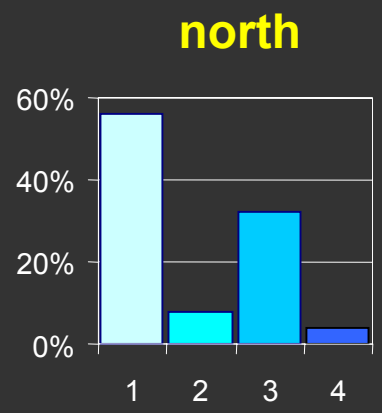
- Of 2263 HCVAb+ patients, 1677 (74%) were serum HCV-RNA+ (95% CI: 71-78%).

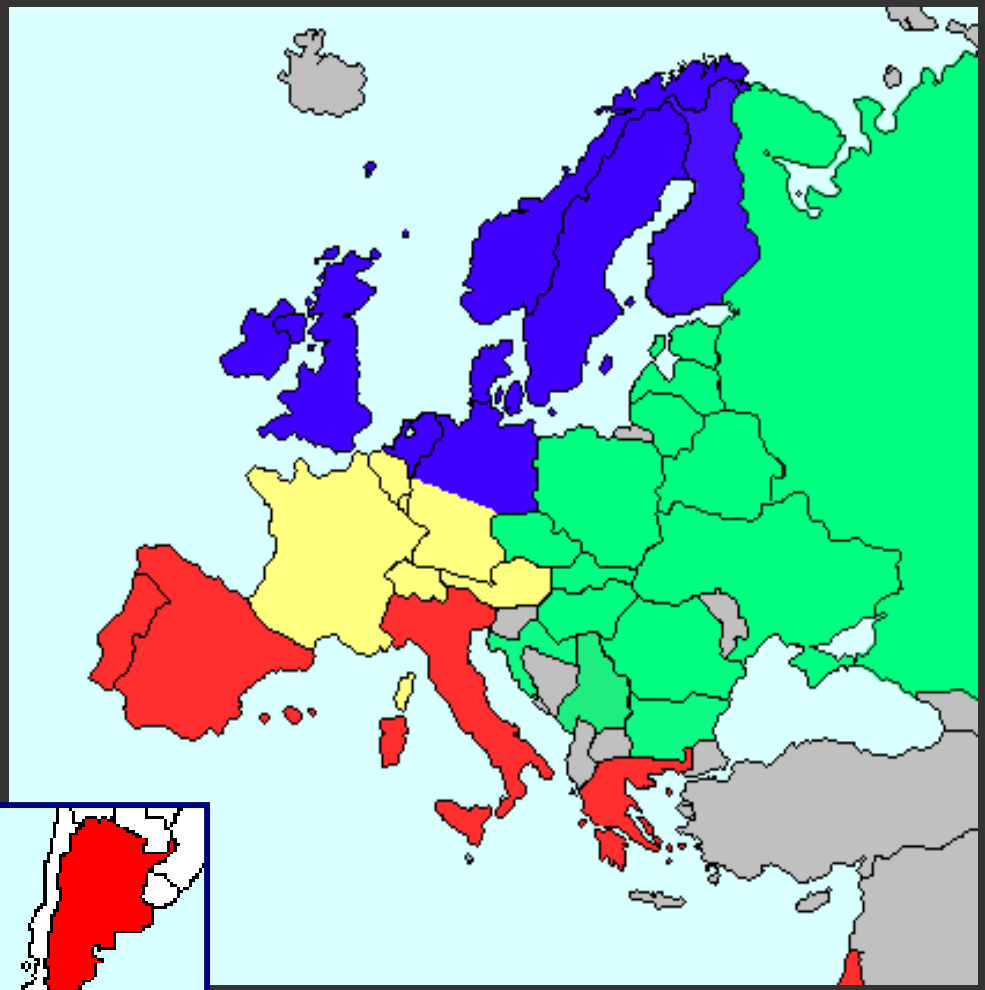
Variables associated with spontaneous HCV clearance

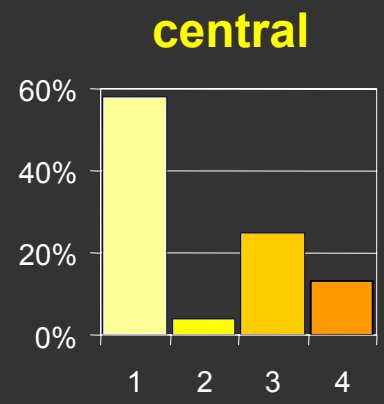
Variables	Univariate		Multivariate	
	aOD (95% CI)	p	aOD (95% CI)	p
Female gender (vs male)	1.05 (0.86-1.29)	0.65	1.22 (0.99-1.51)	0.069
Older age (per 10 years)	1.24 (1.12-1.39)	<0.0001	1.10 (0.97-1.25)	0.14
Exposure group				
MSM	1.00	-	1.00	-
IDU	0.36 (0.27-0.47)	<0.0001	**0.43** (0.32-0.58)	**<0.0001**
Heterosexual	0.55 (0.39-0.79)	0.0012	0.59 (0.40-0.87)	0.0082
Other	0.43 (0.28-0.66)	0.0002	0.47 (0.30-0.73)	0.0007
Serum HBsAg+ status				
Negative	1.00	-	1.00	-
Positive	2.51 (1.85-3.39)	<0.0001	**2.48** (1.82-3.38)	**<0.0001**
Unknown	0.70 (1.53-0.92)	0.012	0.62 (0.47-0.83)	0.0014
Region of Europe				
South/Argentina	1.00	-	1.00	-
Central	1.38 (1.07-1.78)	0.015	1.49 (1.13-1.98)	0.0052
North	1.66 (1.28-2.16)	0.0002	1.38 (1.05-1.82)	0.019
East	1.16 (0.89-1.50)	0.27	2.10 (1.50-2.92)	<0.0001

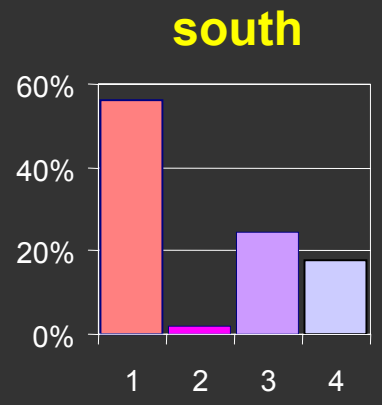
Model additionally adjusted for data source, ethnic origin, exposure group, serum HBsAg serostatus, date of HCV genotyping, date recruited to EuroSIDA, and CD4 count at date of HCV testing.

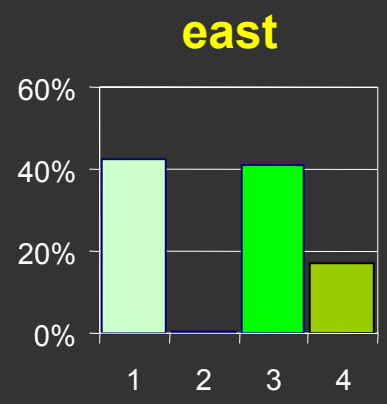
Distribution of HCV genotypes by regions











Variables associated with HCV genotype 1 infection

Variables	Univariate		Multivariate	
	aOD (95% CI)	p	aOD (95% CI)	P
Female gender (vs male)	0.81 (0.66-1.00)	0.049	0.72 (0.56-0.92)	0.0082
Older age (per 10 years)	1.00 (0.89-1.12)	0.99	0.78 (0.67-0.92)	0.0035
Region of Europe				
South/Argentina	1.00		1.00	
Central	1.07 (0.82-1.39)	0.61	0.89 (0.65-1.23)	0.49
North	0.97 (0.74-1.28)	0.83	0.88 (0.63-1.22)	0.45
East	0.57 (0.44-0.73)	<0.0001	**0.38** (0.26-0.56)	**<0.0001**
Higher HCV-RNA (per 1 log higher)	1.27 (1.13-1.44)	<0.0001	**1.29** (1.14-1.47)	**<0.0001**
Prior AIDS (yes vs no)	1.23 (0.99-1.54)	0.067	1.35 (1.03-1.76)	0.015

Model additionally adjusted for data source, ethnic origin, exposure group, serum HBsAg serostatus, date of HCV genotyping, date recruited to EuroSIDA, and CD4 count at date of HCV testing.

HCV load by genotypes

- Median serum HCV-RNA (IU/mL):

• G1	n=890 (53.1%)	758,578	p <0.0001
• G2	n=51 (3%)	691,831	
• G3	n=500 (29.8%)	398,107	
• G4	n=236 (14.1%)	436,516	

Conclusion

- Nearly three quarters of HIV+/HCVAb+ patients in EuroSIDA show active HCV replication.
- HCV viremia is more frequent in IDUs and conversely less common in the presence of chronic hepatitis B.
- Up to 53% of HCV viremic patients are infected by HCV-1; and this genotype is associated with higher serum HCV-RNA levels and male gender, whereas it is less prevalent in Eastern Europe.

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