Liver-Related Events in the Treated HIV Population in the Netherlands observational ATHENA cohort

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Objective

Might HIV increase the risk of liver related events and death?

- To investigate the effect of HIV- and HIV treatment related factors, such as immunodefiency, viremia and cART regimens, on the occurrence of liver related events.
- In the setting of a treated HIV population, while adjusting for traditional risk factors.

Characteristics of HIV patients starting at the start of cART (after 1 Jan 1996).

N		11208	
Gender, N (%)	Male	8743	(78 %)
Region of origin, N (%)	W-Europe	7116	(64 %)
Age, Median (IQR)		38	(32-45)
Prior ART, N (%)		1906	(17 %)
Prior AIDS, N (%)		2836	(25 %)
Exposure Group, N (%)	MSM	6074	(54 %)
	Hetero	3743	(34 %)
	IDU	502	(5 %)
HBV, N (%)	Surface antigen	531	(5 %)
HCV, N (%)	RNA	399	(4 %)
Alcohol abuse, N (%)		756	(7 %)
Smoking status, N (%)	Ever	5374	(48 %)

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Case finding

- New cases after the start of cART, n=341.
- Definition of cases: liver fibrosis, cirrosis, or hepatocellular carcinoma (HCC). Also death due to cirrosis was taken into account.
- Exclude cases prior to cART n=96.
- Histology reports of first events available in 150 (47%) of patients. Diagnosis based on radiological reports in 108 (34 %) of patients. Based on communication in hospital records, n= 13 (4%) . Ongoing source data verification in 15% of patients.
- 92 (61%) of available histologic rapports in patients with HBV or HCV coinfection.
- Incidence of liver-related events in co-infected patients 22 per 1000 pyrs versus 2 per 1000 pyrs in mono-infected patients.

Liver related events (LRE)

	n	Time till event, median (IQR)	CD4 at event
*Any LRE (first events)	341	5.8 (2.7–8.6)	360 (200-570)
Fibrosis	319	5.7 (2.7- 8.6)	350 (210-550)
Cirrosis	168	6.1 (3.9 - 9.1)	299 (160-420)
HCC	15	8.1 (6.1 - 10.1)	410 (280-510)
Deaths due to cirrosis	46	4.9 (3.2-8.0)	270 (110-380)

*Multiple events per patient possible

- 92% were on cART at time of diagnosis
- 80% had an undetectable viral load at time of diagnosis.

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Potential risk factors investigated

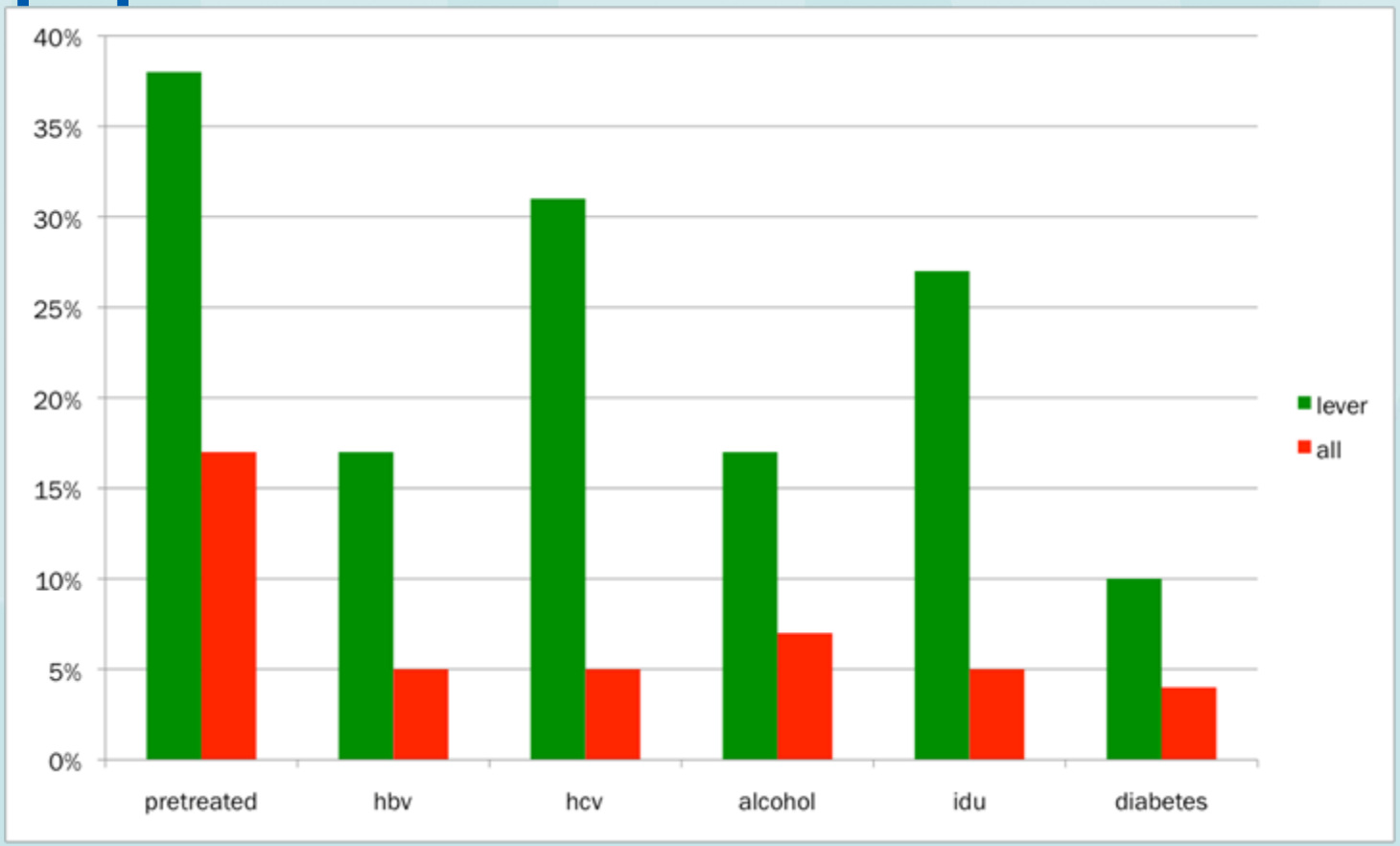
HIV related

- Nadir CD4
- Prior AIDS
- Duration of HIV infection
- Exposure to ART/cART
- Latest CD4
- Cumulative exposure to CD4 <200/350/500 cells/mm^3
- Latest VL
- Cumulative exposure to VL>400 cps/ml

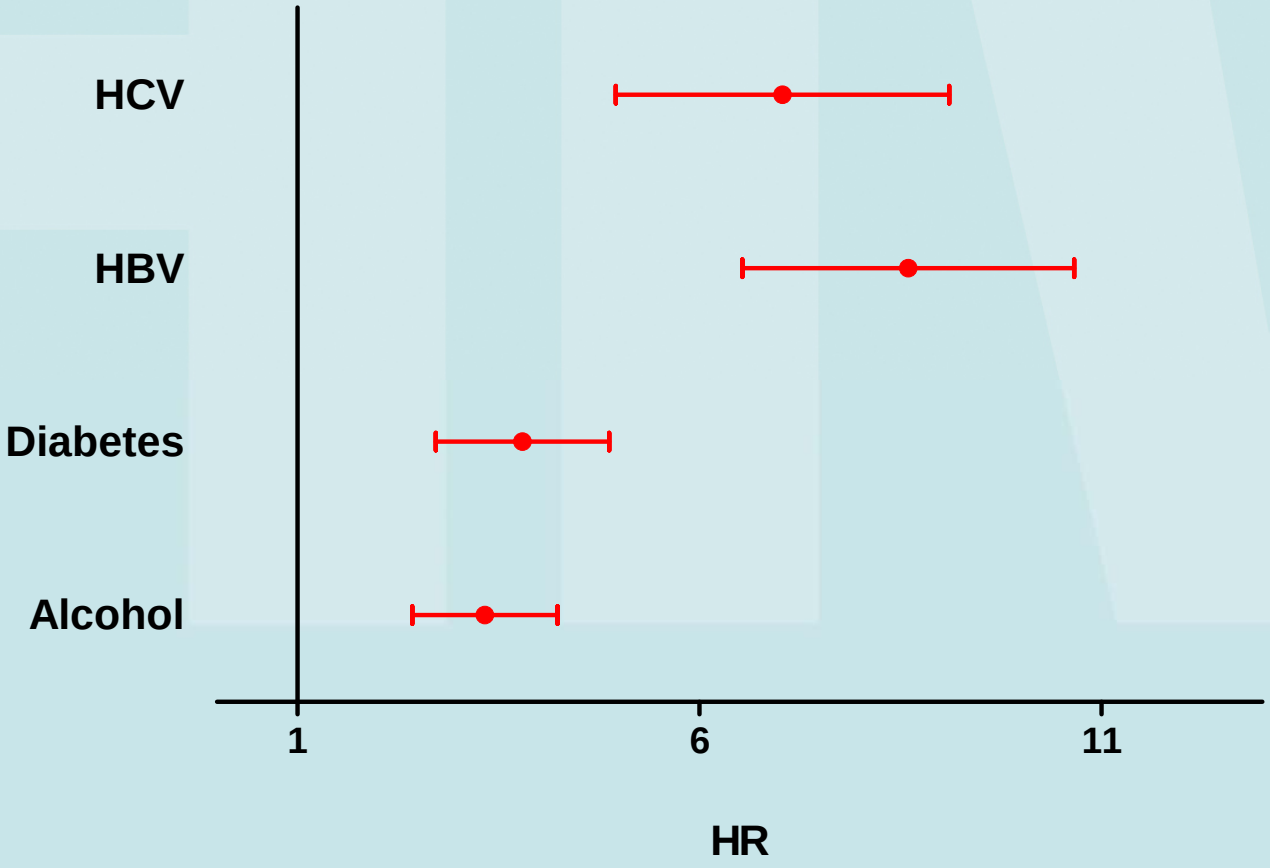
Traditional risk factors

- HBV / HCV coinfections
- Mode of transmission
- Alcohol abuse
- Smoking, ever
- BMI
- Diabetes Mellitus
- Age
- Gender
- Region of origin

Characteristics of patients with liver fibrosis compared to overall HIV population



Traditional risk factors for liver cirrosis



Adjusted for latest CD4 count, cumulative exposure to immunodeficiency and cART, estimated duration of HIV infection prior to start cART.

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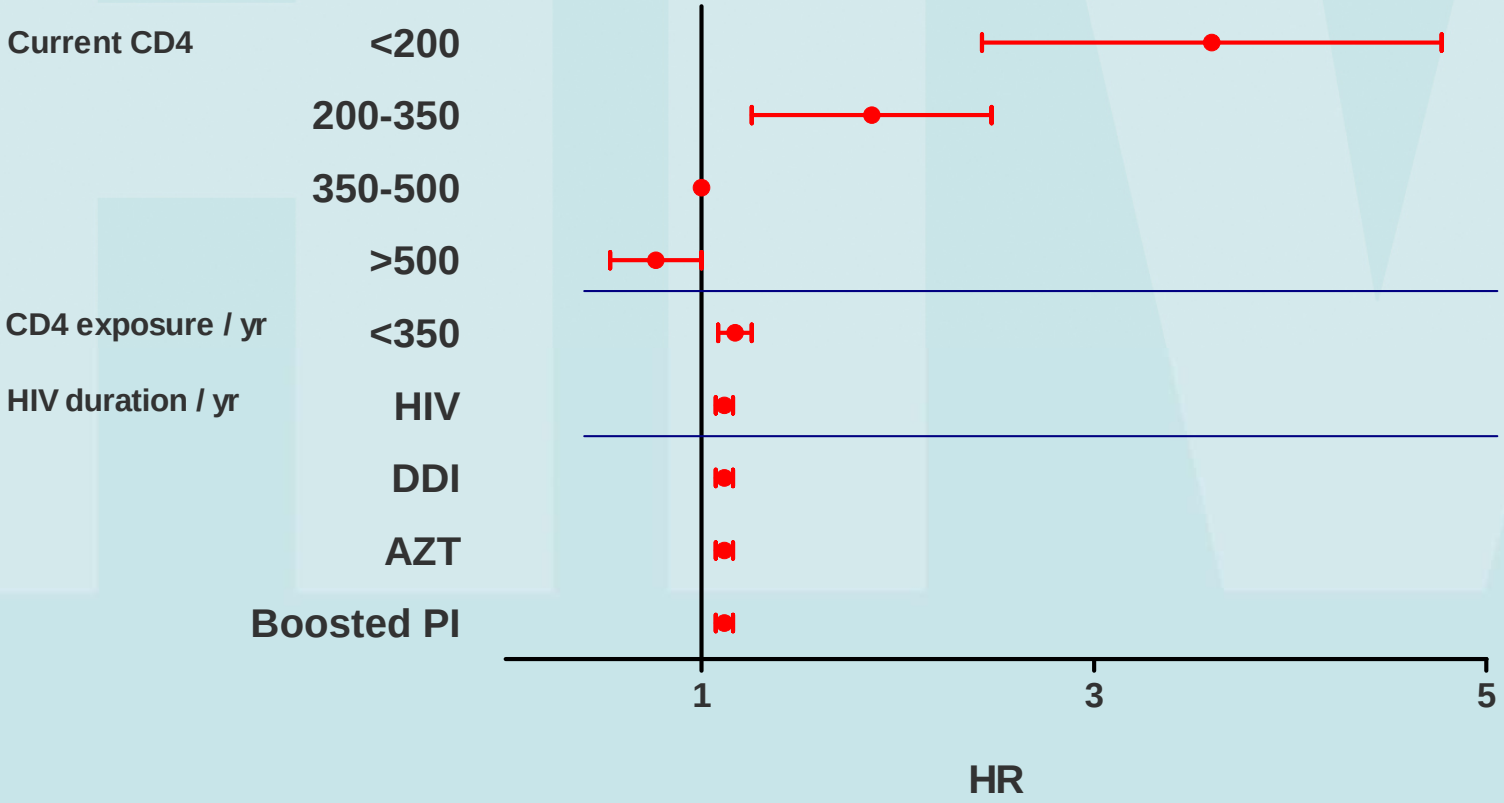
HIV related risk factors for liver cirrosis



Adjusted for age, prior AIDS, gender, region of origin, coinfections, diabetes, smoking, alcohol abuse.

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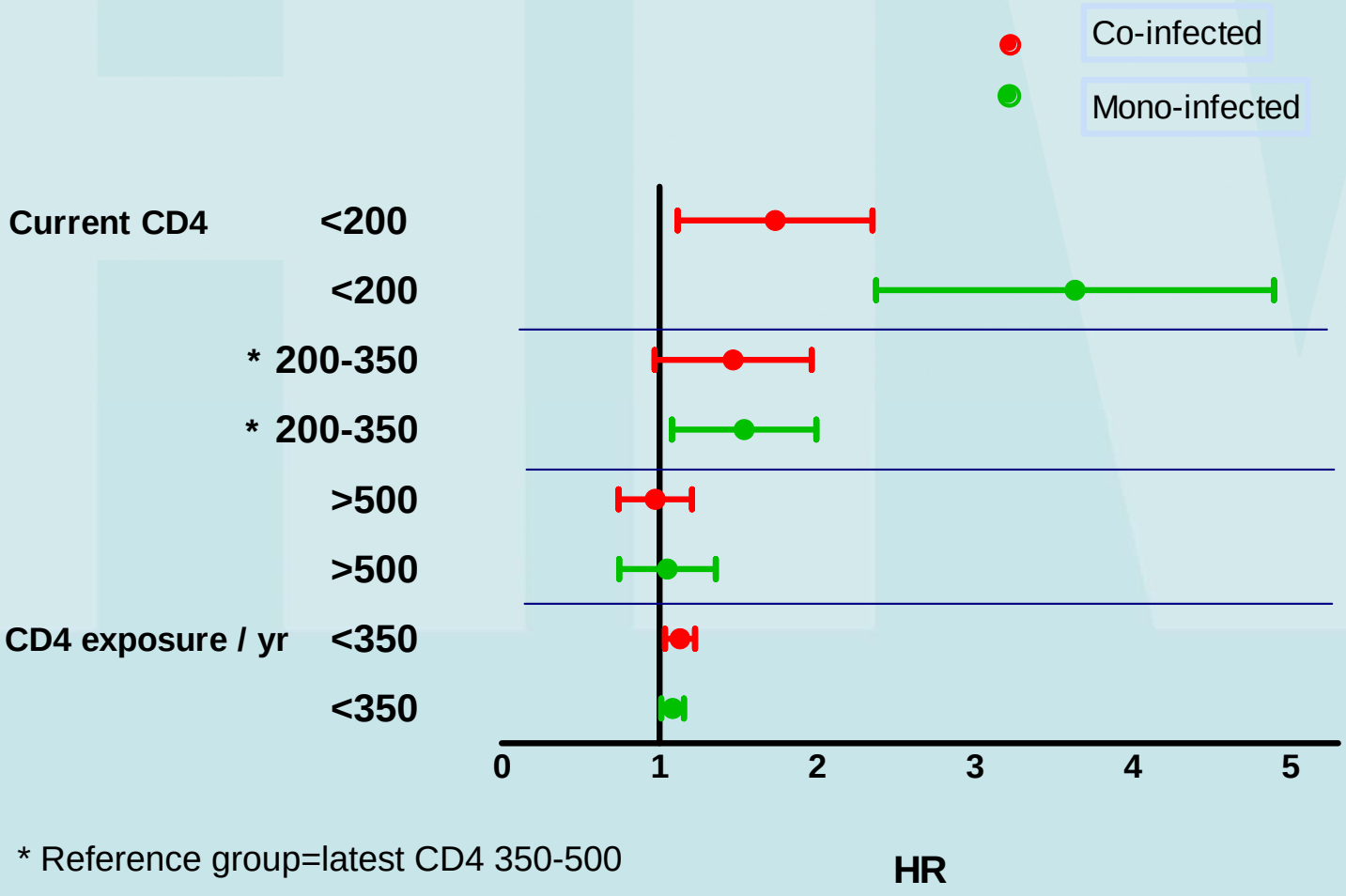
Immunodeficiency and liver cirrosis according to chronic hepatitis status.



* Reference group=latest CD4 350-500

Adjusted for age, prior AIDS, gender, region of origin, cumulative exposure to cART, estimated duration of HIV infection prior to start cART, diabetes, smoking, alcohol abuse.

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Conclusions

In the setting of a treated HIV population:

- Independent from traditional risk factors, immunodeficiency seems to be related to onset of liver-related events.
- No effect of viremia on liver-related events, however this is difficult to observe in the treated population. An association with duration of HIV infection prior to starting cART was found.
- Exposure to boosted PI, didanosine and zidovudine containing regimens is related to onset of liver-related events. No effect of other cART regimens was found.
- Policy: Test and treat HCV, HBV vaccination, address traditional risk factors (alcohol, smoking, BMI).

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