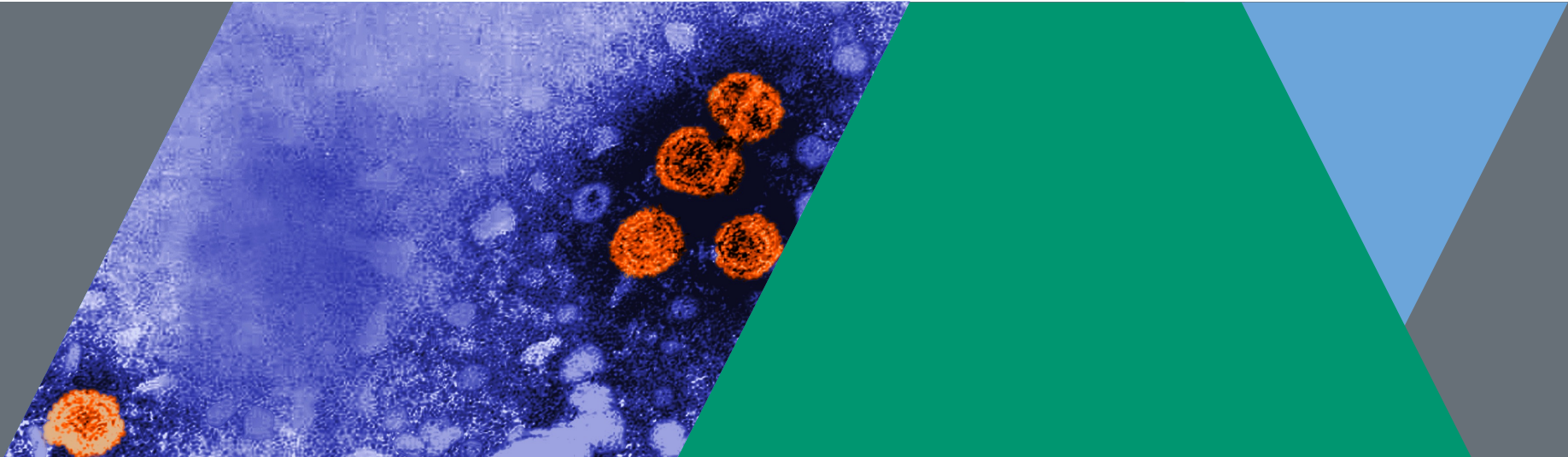


Serum HBV RNAs and HBcrAg in persons with HIV/HBV and HBsAg loss

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EuroSIDA Study Group

Lars Peters, Amanda Mocroft

French HIV/HBV cohort

Anders Boyd, Karine Lacome

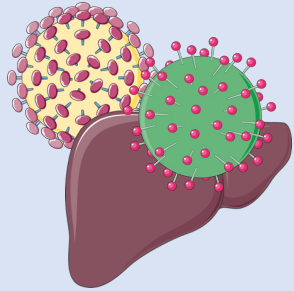
German HIV/HBV cohort

Jürgen K. Rockstroh, Kathrin van Bremen

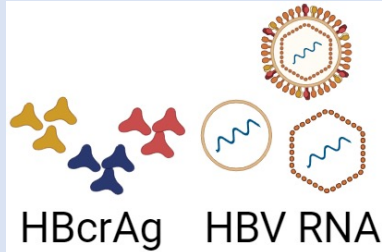
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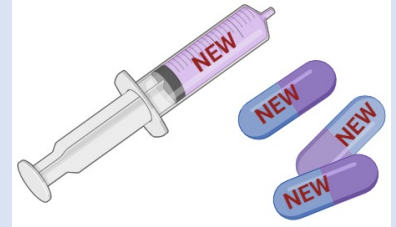
Background: HIV/HBV coinfection



39 million persons with HIV worldwide, ~8% are HBsAg+



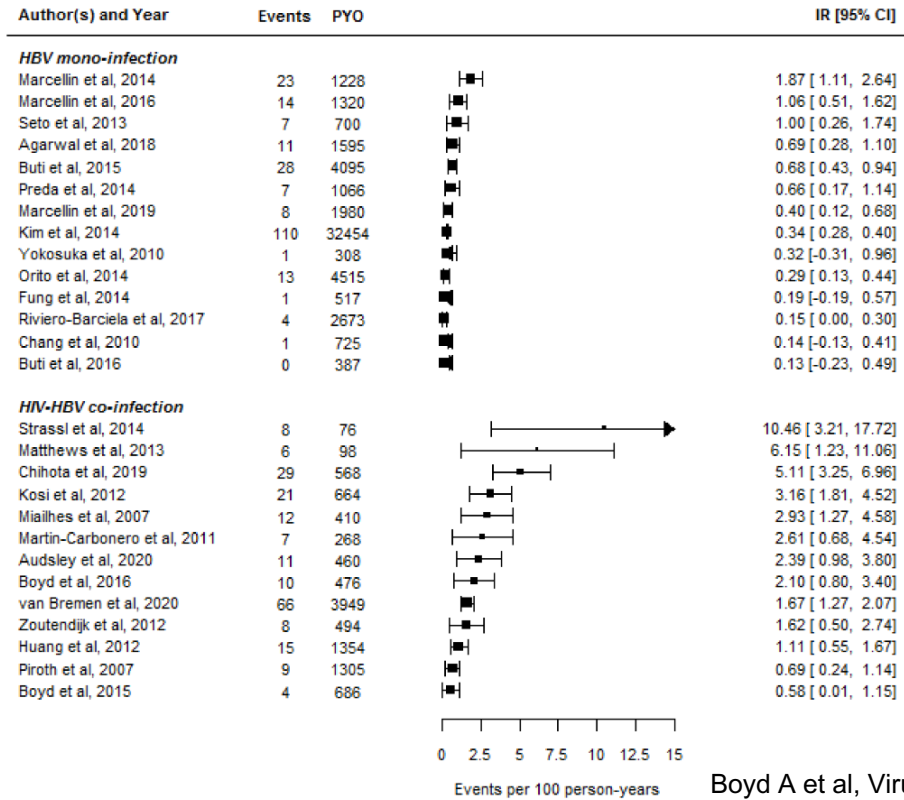
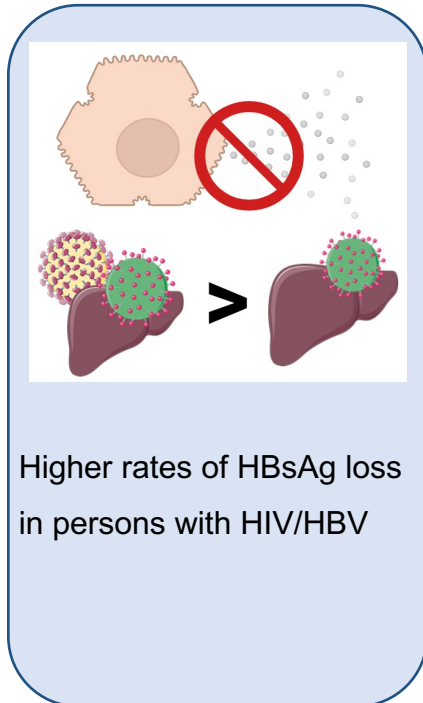
Novel biomarkers could improve the understanding of HBsAg loss during antiviral therapy



Relevance of biomarkers in the development of novel HBV drugs

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HBsAg seroclearance in persons with HIV

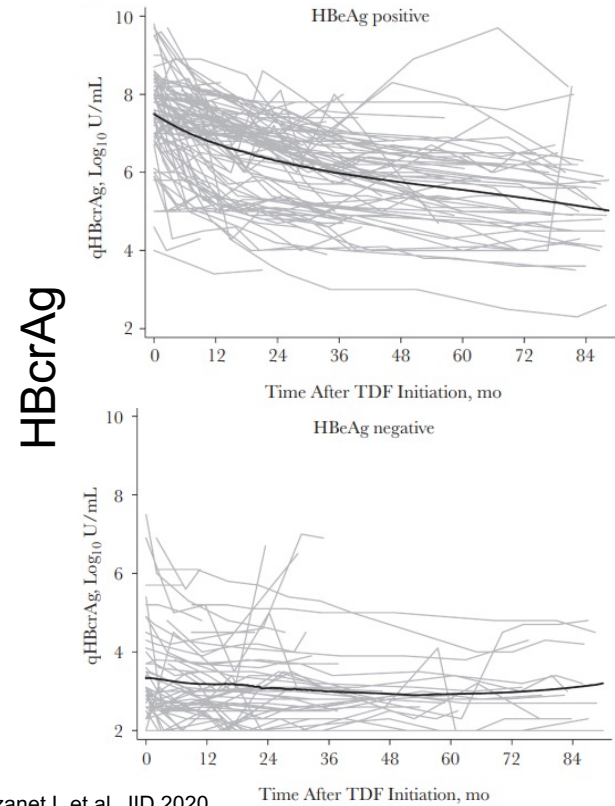


0.4/100 person-years
(range 0.0-1.1)

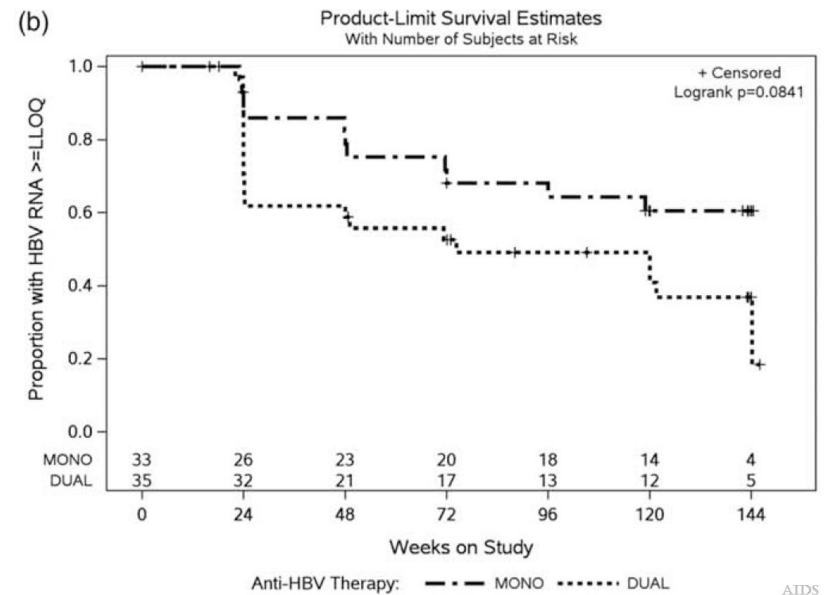
2.4/100 person-years
(range 0.6-10.5)

Boyd A et al, Viruses 2021;13:1341.

Background: HBcrAg and HBV RNA in persons with HIV



HBV RNA



Dezanet L et al, JID 2020.

Time After TDF Initiation, mo

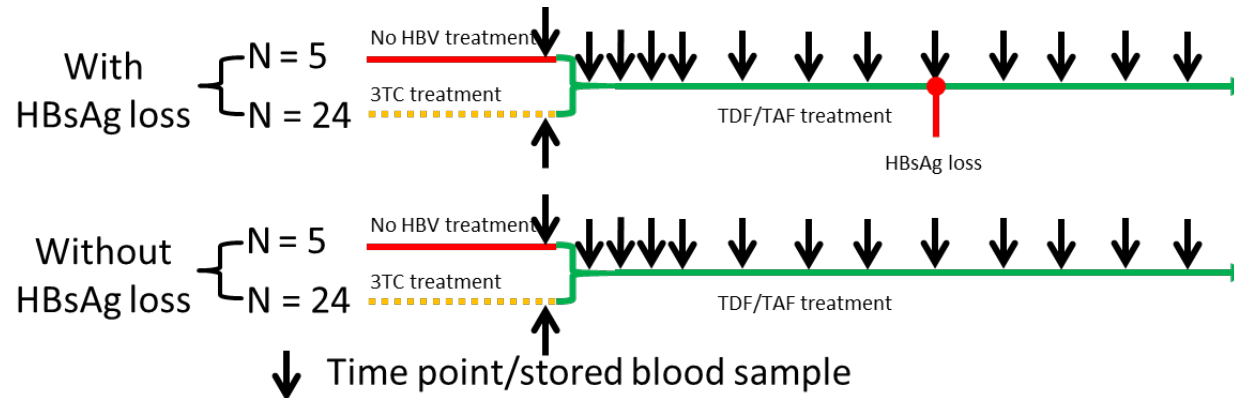
Hawkins C et al, AIDS 2022;36:975-984.

Study design

- Aim: Evaluate long-term trajectories of HBcrAg and circulating HBV RNA levels in persons with HIV with and without HBsAg loss
- Inclusion criteria
 - Participant in the Swiss HIV Cohort Study
 - 2x HBsAg+ ≥ 6 months apart
 - Starting tenofovir therapy (TDF or TAF)
 - HBsAg+ at tenofovir start
 - Stored plasma sample in the year before starting tenofovir

Study design

- 29 participants with and 29 participants without HBsAg loss starting tenofovir-containing ART
- Matched on age, sex, prior lamivudine treatment and CD4+ T-cell count
- Measurement of qHBsAg, HBV DNA, HBcrAg and HBV RNA



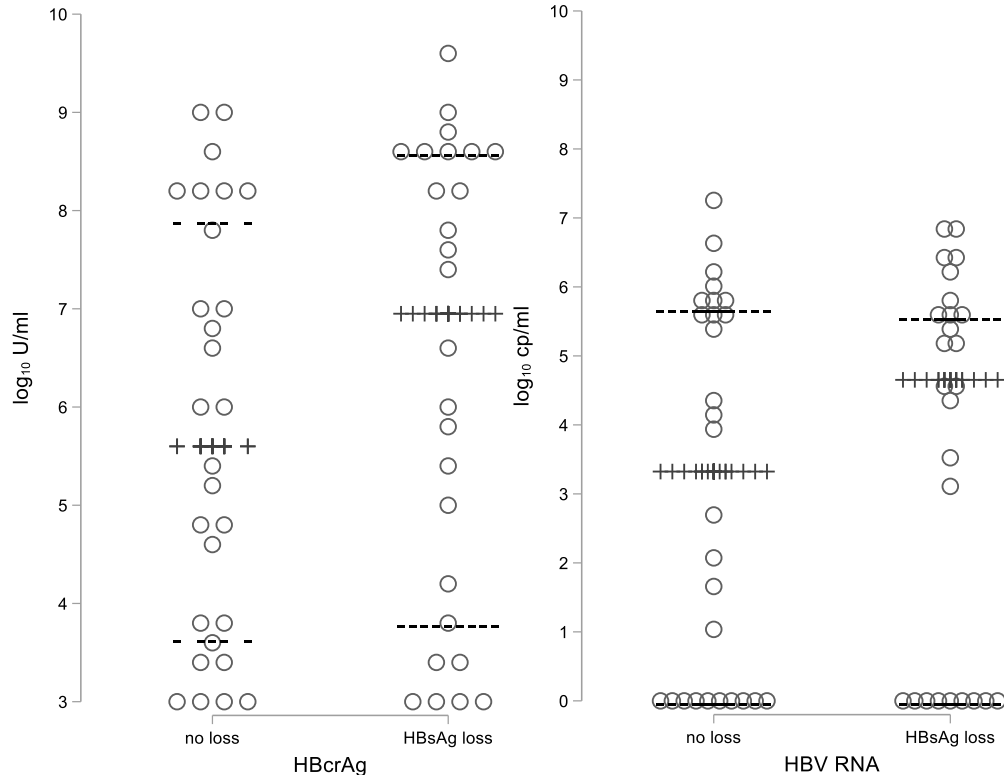
Outcomes and definitions

- Cumulative proportion of participants with negative HBV DNA, HBcrAg and HBV RNA levels during tenofovir therapy
- Proportions with a $\geq 1 \log_{10}$ decline in qHBsAg, HBcrAg and HBV RNA levels 1 and 2 years after starting tenofovir therapy
- Definitions:
 - HBsAg loss: 1st qHBsAg < 0.05 IU/ml
 - HBV DNA suppression: < 20 IU/ml
 - Negative HBcrAg: $\leq 3 \log_{10}$ U/ml
 - Undetectable HBV RNA: < 10 copies/ml

Study population

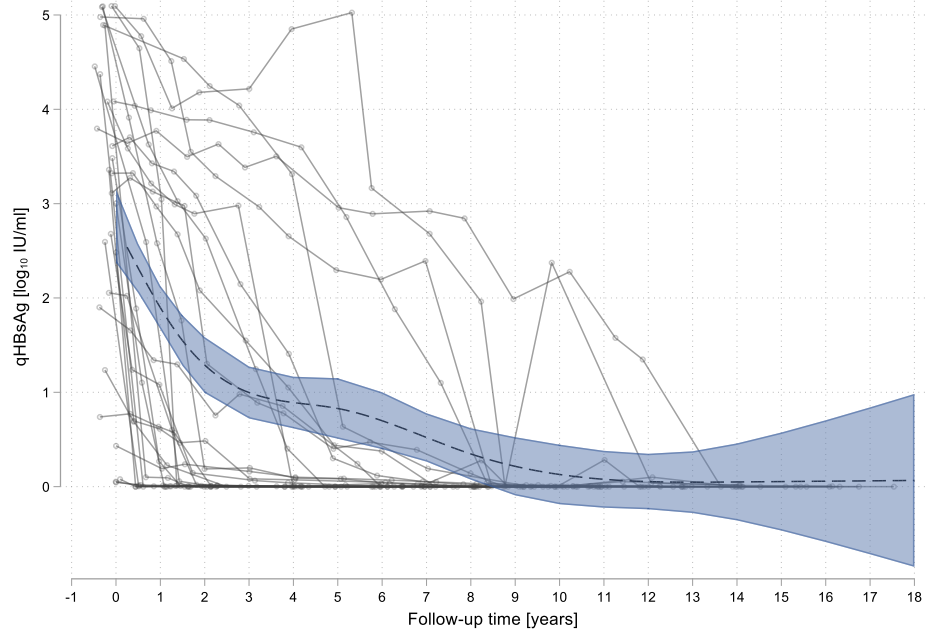
	Without HBsAg loss	With HBsAg loss
	<i>N</i> = 29	<i>N</i> = 29
Female sex	6/29 (21%)	6/29 (21%)
Median age [years]	39 (36 - 46)	42 (38 - 46)
Median follow-up duration [years]	11.1 (7.9 - 14.1)	12.3 (10.4 - 14.1)
European origin	14/29 (48%)	22/29 (76%)
Median BMI [kg/m ²]	22.7 (19.2 - 26.9)	22.9 (21.0 - 25.5)
Lamivudine pretreatment	24/29 (83%)	24/29 (83%)
Median duration [years]	6.3 (3.9 - 7.3)	6.2 (4.8 - 7.8)
CD4+ T-cell count <200 cells/μl	4/29 (14%)	4/29 (14%)
HIV viral load ≥50 copies/ml	15/29 (52%)	13/29 (45%)
HBeAg positive	10/24 (42%)	13/27 (48%)
Median HBV DNA [log ₁₀ IU/ml]	4.0 (1.5 - 7.9)	3.0 (1.2 - 7.5)
HBV DNA <20 IU/ml	7/29 (24%)	8/29 (28%)
Median qHBsAg, [log ₁₀ IU/ml]	4.0 (3.5 - 4.2)	3.4 (2.1 - 4.5)
qHBsAg <1 log ₁₀ IU/ml	1/29 (3%)	5/29 (17%)

HBcrAg and HBV RNA levels at baseline

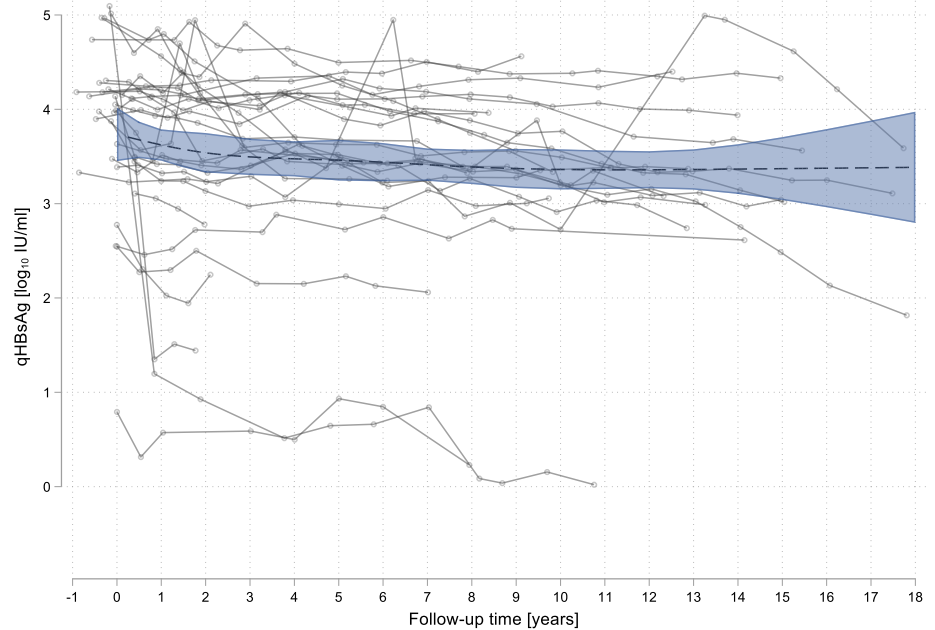


- Negative HBcrAg
 - 15% with HBsAg loss
 - 14% without HBsAg loss
- Undetectable HBV RNA
 - 35% with HBsAg loss
 - 36% without HBsAg loss

qHBsAg trajectories on tenofovir

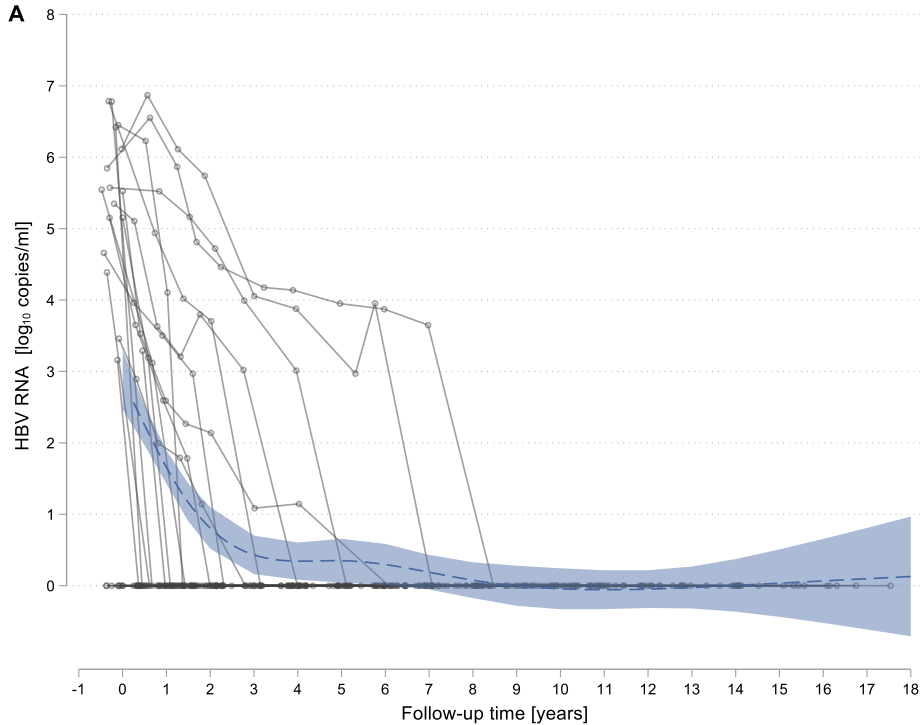


Participants with HBsAg loss

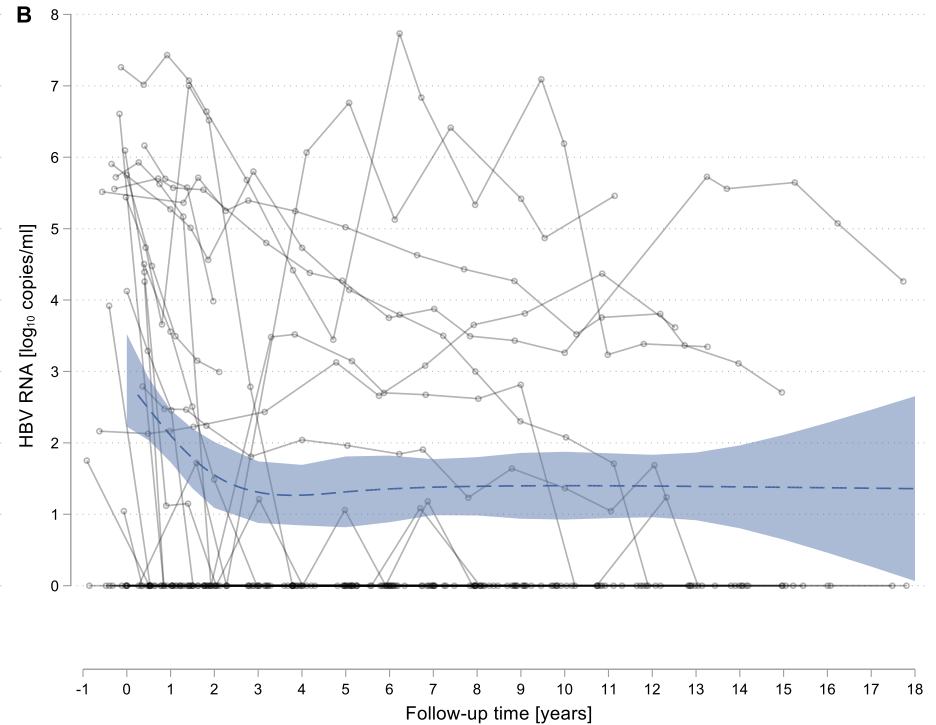


Participants without HBsAg loss

Circulating HBV RNA trajectories on tenofovir



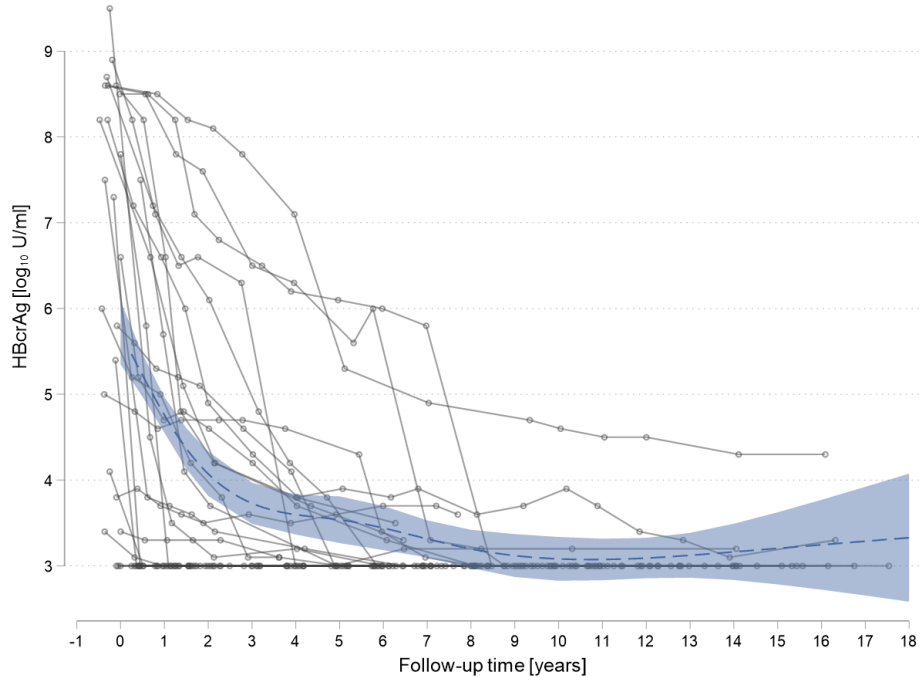
Participants with HBsAg loss



Participants without HBsAg loss

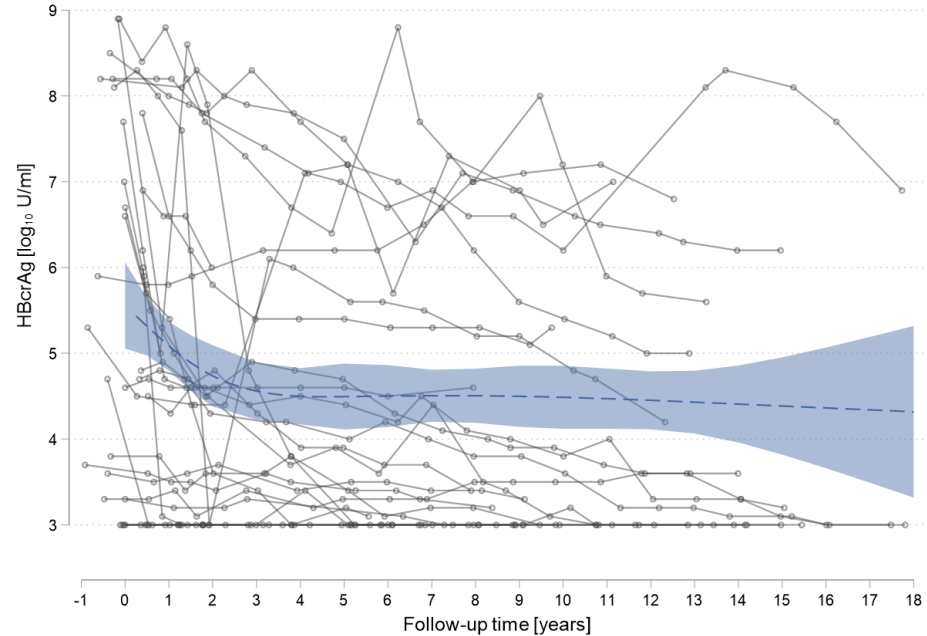
HBcrAg trajectories on tenofovir

A



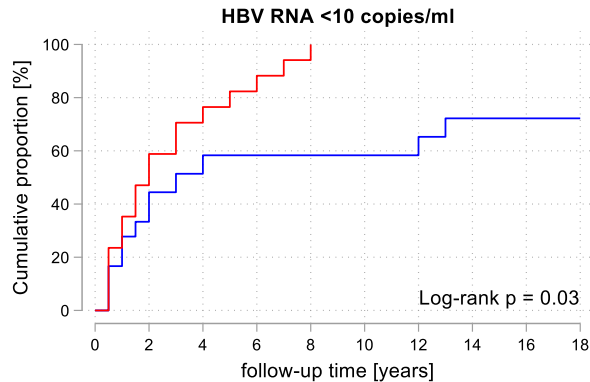
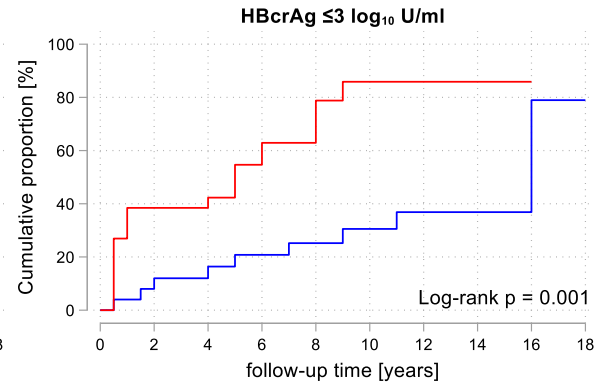
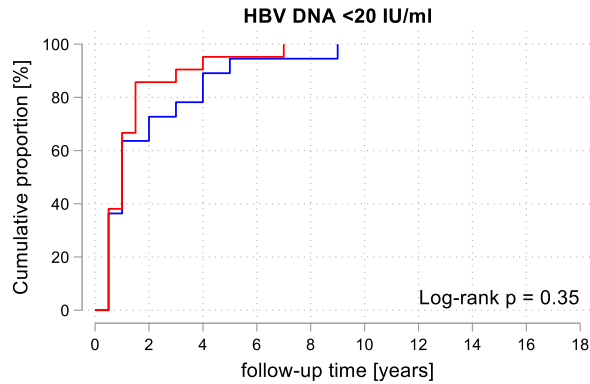
Participants with HBsAg loss

B



Participants without HBsAg loss

Cumulative proportions with undetectable levels

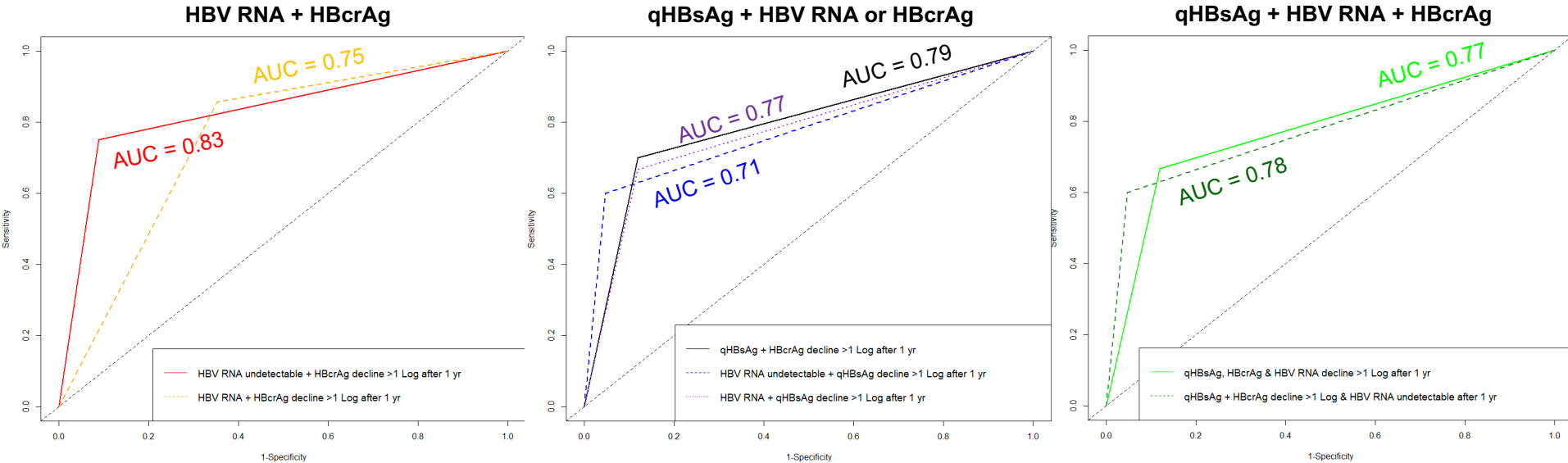


— with HBsAg loss
— without HBsAg loss

HBV RNA and HBcrAg as predicting markers for HBsAg loss

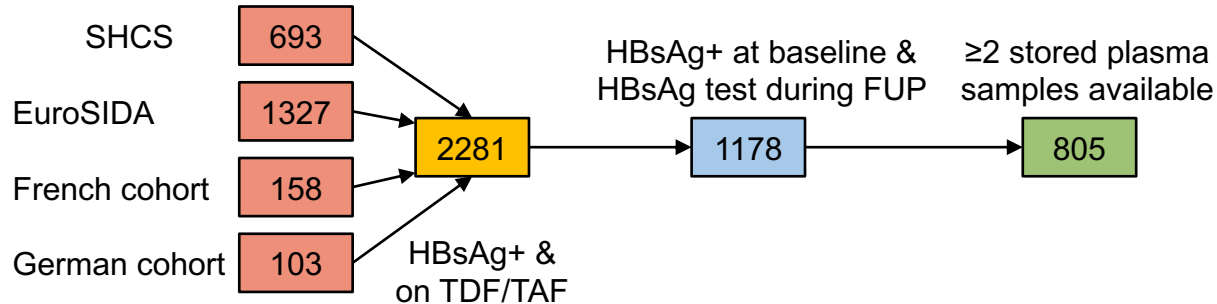
Decline after 1 year of tenofovir-containing ART	HBsAg loss within two years		
	Sensitivity (%)	Specificity (%)	AUROC
qHBsAg decline $\geq 1 \log_{10}$ IU/ml	70.0	88.1	0.791
HBcrAg decline $\geq 1 \log_{10}$ U/ml	87.5	64.7	0.761
HBV RNA decline $\geq 1 \log_{10}$ copies/ml	100.0	40.0	0.700
HBV RNA [cp/ml] and HBcrAg [U/ml] decline $\geq 1 \log_{10}$	85.7	64.7	0.752
HBcrAg [U/ml] and qHBsAg [IU/ml] decline $\geq 1 \log_{10}$	70.0	88.1	0.791
HBV RNA [cp/ml] and qHBsAg [IU/ml] decline $\geq 1 \log_{10}$	66.7	88.1	0.774

HBV RNA and HBcrAg as predicting markers for HBsAg loss



Euro-B: an international multi-cohort collaboration

- Aim: Collate data of persons with HIV/HBV from Europe to improve the understanding of the determinants of treatment outcomes
 - HBV virological suppression, HBsAg loss
 - Changes in liver fibrosis stage and transaminases levels
 - Predictors of HBsAg loss and its correlation with HBcrAg and HBV RNA levels



Conclusions

- HBV RNA suppression precedes HBsAg loss, but also ~80% without HBsAg loss become HBV RNA undetectable
- HBcrAg detectable at end of FUP in ~20% with HBsAg loss and >50% without HBsAg loss
- A $\geq 1 \log_{10}$ decline in HBV RNA or HBcrAg levels within one year had high sensitivity but low specificity for HBsAg loss

→ Potential to identify individuals who will not experience HBsAg loss

→ Could improve predictions of HBsAg loss in clinical trials of HBV drugs