

# Early seroreversion after 2 doses of hepatitis A vaccination among HIV-positive patients who had achieved serologic response: incidence and associated factors

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## Background

Serologic responses (Seroresponse) and durability of hepatitis A virus (HAV) vaccination are reduced among HIV-positive patients. The incidence of and associated factors with early seroreversion (loss of seroresponse) among HIV-positive patients who have achieved seroresponses after 2 doses of HAV vaccination remains unclear during an outbreak setting.

## Methods

In this multicenter study, we followed HIV-positive adults who had mounted seroresponses after completing 2 doses of HAV vaccination during a recent outbreak of acute hepatitis A between 2015 and 2017. A 1:4 case-control study was conducted to identify factors associated with seroreversion. Case patients were those with seroreversion and controls were those with similar follow-up durations who were able to maintain seroresponses.

**Table 1. Characteristics of the 1256 included patients.**

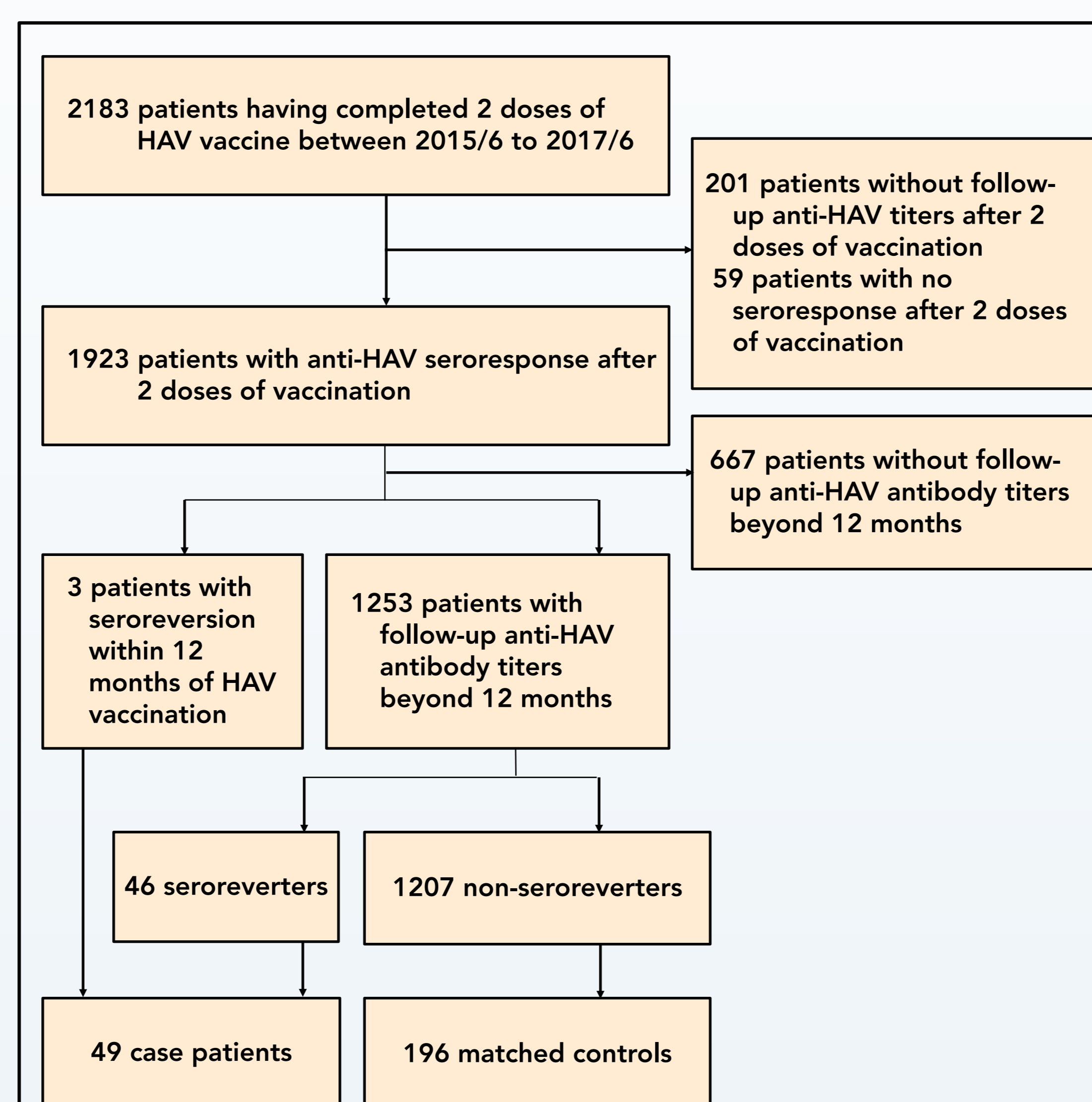
Age, median (IQR), years	32 (28, 38)
MSM, n (%) (N=1222)	1177 (96.3)
Weight, median (IQR), kg (N=1154)	66 (60,74)
BMI, median (IQR) (N=993)	22.4 (20.4, 24.7)
Overweight or obesity <sup>a</sup> , n (%)	312 (31.4)
Obesity <sup>a</sup> , n (%)	112 (11.3)
Use of cART, n (%)	
At the first dose of HAV vaccination	1194 (95.1)
At month 6 of vaccination	1236 (98.4)
Viral hepatitis coinfection, n (%)	
HBsAg-positive	123 (9.8)
Anti-HCV-positive (N=1255)	65 (5.2)
Recent syphilis, n (%)	288 (22.9)
Current smoker, n (%) (N=1128)	305 (27.0)
Plasma HIV RNA load >50 cp/ml at vaccination, n (%)	180 (14.3)
Plasma HIV RNA load >50 cp/ml at month 12, n (%) (N=1249)	47 (3.8)
Nadir CD4 count, median (IQR), cells/mm <sup>3</sup> (N=1194)	292 (154, 413)
Nadir CD4 <200 cells/mm <sup>3</sup> , n (%)	395 (33.1)
CD4 count at vaccination, median (IQR), cells/mm <sup>3</sup> (N=1255)	575 (433, 748)
CD4 count at month 12, median (IQR), cells/mm <sup>3</sup> (N=1248)	636 (496, 815)
Brand of the 1 <sup>st</sup> dose of HAV vaccine, n (%)	
Havrix®	306 (24.4)
Vaqta®	950 (75.6)
Brand of the 2 <sup>nd</sup> dose of HAV vaccine, n (%)	
Havrix®	15 (1.2)
Vaqta®	1241 (98.8)
Positive anti-HAV IgG at month 6, n (%) (N=910)	587 (64.5)
Peak anti-HAV IgG titer, median (IQR)	
By chemiluminescent immunoassay, S/CO (N=799)	10.35 (8.35, 12.03)
By ELISA, IU/L (N=395)	>60 (>60, >60)
Follow-up duration, median (IQR), days after the 1 <sup>st</sup> dose of HAV vaccination	611 (526, 721)

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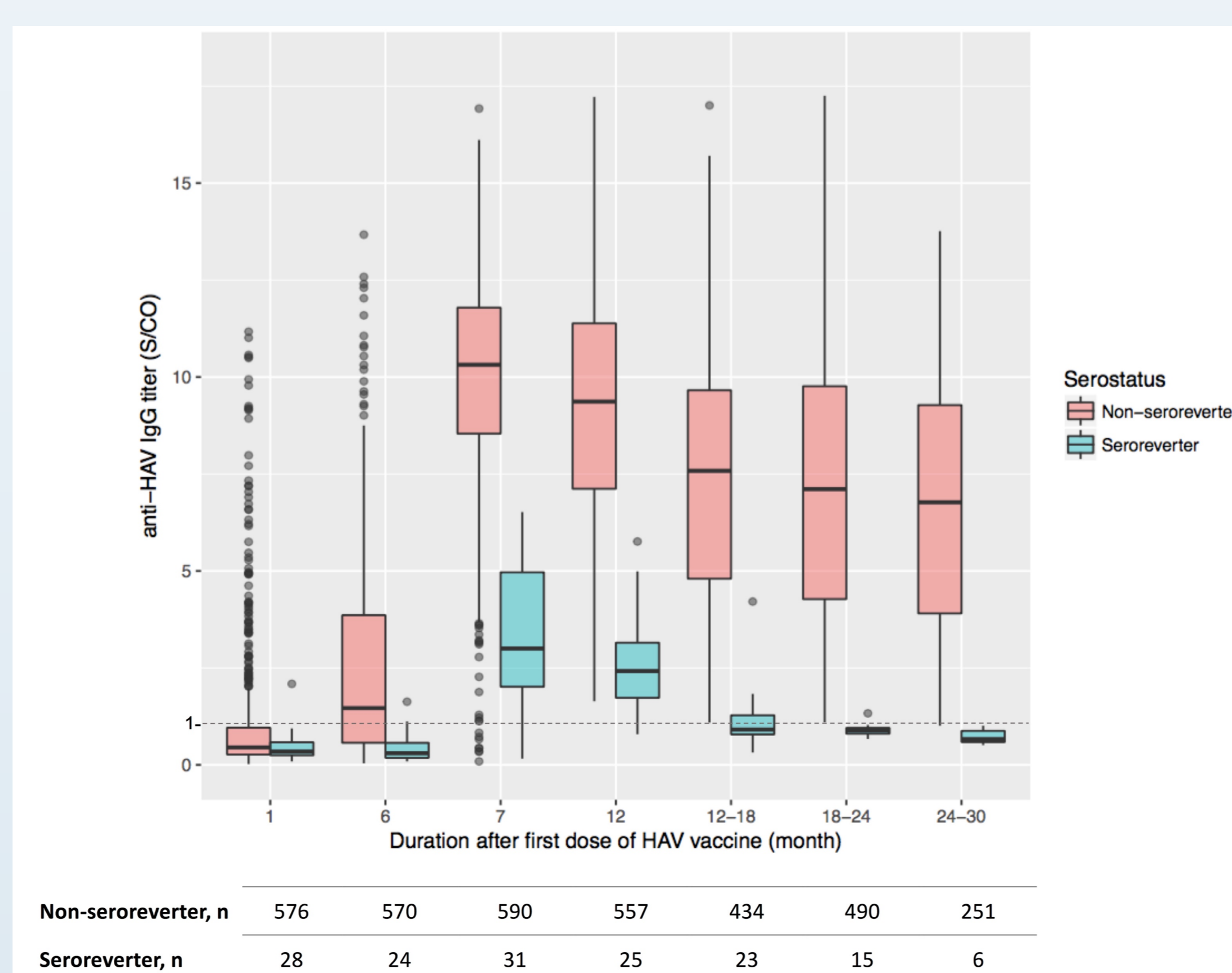
## Results

During the study period, 1256 HIV-positive patients with documented seroconversion after HAV vaccination had anti-HAV IgG measured 12 months or longer after vaccination. After a median follow-up of 611 days, 49 (3.9%) seroreverted.

In case-control study, seroreversion was more likely to occur in patients with a higher weight (adjusted odds ratio (aOR), 1.703; 95% CI, 1.292–2.323, per 10-kg increment) and HIV viremia at the time of vaccination (aOR, 2.922; 95% CI, 1.067–7.924), while positive seroresponse at 6 months of HAV vaccination and higher CD4 lymphocyte counts at vaccination were inversely associated with early seroreversion with an aOR of 0.059 (95% CI, 0.020–0.154) and 0.837 (95% CI, 0.704–0.979, per 100-cell/mm<sup>3</sup> increment), respectively, in multivariable analyses.



**Figure 1. Study flow.**



**Figure 2. Evolution of serologic responses after HAV vaccination in HIV-positive patients according to their status of seroreversion. Seroreverters were less likely to mount anti-HAV IgG responses before the second dose of HAV vaccination (month 6) had lower peak anti-HAV IgG titers after completion of 2 doses of vaccination.**

**Table 2. Case-control analysis of factors associated with early seroreversion after HAV vaccination.**

	Seroreverters N=49	Non-seroreverters N=196	p-value
Age, median (IQR), years	34 (29, 39)	33 (28, 39)	0.331
MSM, n (%) (N=241)	48/49 (98.0)	185/192 (96.4)	>0.999
Weight, median (IQR), kg (N=225)	72 (62, 85)	66 (58, 73)	0.001
BMI, median (IQR), (N=215)	23.7 (21.2, 27.0)	22.3 (20.1, 24.5)	0.003
Overweight or obesity <sup>a</sup> , n (%)	21/44 (47.7)	51/171 (29.8)	0.032
Obesity <sup>a</sup> , n (%)	11/44 (25.0)	14/171 (8.2)	0.006
Use of cART, n (%)			
At the first dose of HAV vaccination	43 (87.8)	185 (94.4)	0.117
At month 6 of vaccination	49 (100)	195 (99.5)	>0.999
Viral hepatitis coinfection, n (%)			
HBsAg-positive	4 (8.2)	18 (9.2)	>0.999
Anti-HCV-positive	3 (6.1)	11 (5.6)	>0.999
Recent syphilis <sup>b</sup> , n (%)	14 (28.6)	47 (24.0)	0.580
Current smoker, n (%) (N=230)	16/47 (34.0)	54/183 (29.5)	0.595
Plasma HIV RNA load >50 cp/ml at vaccination	14 (28.6)	29 (14.8)	0.034
HIV RNA load >200 copies/ml, n (%)	11 (22.4)	18 (9.2)	0.023
Plasma HIV RNA load >50 cp/ml at month 12	4 (8.2)	7 (3.6)	
HIV RNA load >200 copies/ml, n (%)	1 (2.0)	3 (1.5)	>0.999
Nadir CD4 count, median (IQR), cells/mm <sup>3</sup> (N=234)	264 (153, 431)	304 (145, 453)	0.615
Nadir CD4 <200 cells/mm <sup>3</sup> , n (%)	16/49 (32.7)	67/185 (36.2)	0.738
CD4 count at vaccination, median (IQR), cells/mm <sup>3</sup>	486 (394, 662)	576 (452, 760)	0.024
Brand of the 1 <sup>st</sup> dose of HAV vaccine, n (%)			0.325
Havrix®	21 (42.9)	69 (35.2)	
Vaqta®	28 (57.1)	127 (64.8)	
Positive anti-HAV IgG at month 6, n (%) (N=185)	2/36 (5.5)	100/149 (67.1)	<0.001
Peak anti-HAV IgG titer, median (IQR)			
By chemiluminescent immunoassay, S/CO (N=166)	3.15 (2.50, 5.06)	10.89 (8.60, 11.99)	<0.001
By ELISA, IU/L (N=79)	38.44 (32.94, 57.28)	>60 (>60, >60)	<0.001
Duration of follow-up, median (IQR), days after 1 <sup>st</sup> dose of HAV vaccination	549 (450, 648)	566 (489, 665)	0.291

**Table 3. Multivariable analysis of factors associated with early seroreversion after HAV vaccination.**

	aOR	p-value
Weight, per 10-kg increment	1.703 (1.292-2.323)	<0.001
HIV RNA load >200 copies/ml at vaccination	2.922 (1.067-7.924)	0.035
CD4 count at vaccination, per 100-cell/mm <sup>3</sup> increment	0.837 (0.704-0.979)	0.034
Positive anti-HAV IgG at month 6	0.059 (0.020-0.154)	<0.001

## Conclusions

During an outbreak setting, early seroreversion following 2-dose HAV vaccination occurred in 3.9% of HIV-positive patients. Lower and delayed seroresponses to HAV vaccination, and a higher weight, and HIV viremia and lower CD4 lymphocyte counts at the time of HAV vaccination were associated with early seroreversion.