

## The complexities of HIV infection

### OC 27 Burden of advanced HIV disease (AHD) among antiretroviral therapy (ART)-experienced persons with HIV (PWH) in Italy over the past 20 years

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#### ABSTRACT

**Introduction:** Recent data from low- and middle-income countries indicates that AHD has become increasingly common among PWH already enrolled in care, raising an emerging issue in the HIV continuum of care. Estimates of the incidence of AHD after ART initiation in high-income countries are sparse, and risk factors for AHD are poorly investigated.

**Methods:** All PWH enrolled in the Icona Cohort who started ART with CD4 $\geq$ 200 cells/mm<sup>3</sup> and without history of AIDS-defining-event (ADE) between January 1st, 2004, and December 31st, 2023, were included. The cumulative probability of developing for the first time AHD (CD4<200 cells/mm<sup>3</sup> or an ADE) >3 months after ART initiation was estimated using Kaplan-Meier curves. A case-control study nested in the Icona cohort was conducted after matching PWH with incident AHD (cases) with 2 AHD-free controls by CD4 count nadir, age and time from ART start. The total effect of pre-specified potential predictors of AHD was estimated by fitting separate conditional logistic regression models.

**Results:** Among the 9,433 PWH free from AHD who started ART over the observation, 405 (4.3%) had a diagnosis of AHD >3 months after treatment initiation, of which 107 were due to an ADE. The probability of developing AHD was higher in the first few years after starting ART (4.2% 95% CI: 3.7-4.7 by 5 years) and flattened over time (6.6% 95% CI: 5.9-7.3 by 10 years, Figure 1). In the case-control study, 401 PWH with AHD were matched to 801 PWH without AHD (4 cases did not match). Compared to controls, cases were more likely to be female (25% vs 20%, p=0.026), to have acquired HIV through injecting drug use (IDU, 17% vs 9%, p<0.001), and to have a lower educational level (university 8% vs 14%, p<0.001). Additionally, at the time of AHD diagnosis, cases had higher HIV-RNA (median 1.60 vs 1.48 log<sub>10</sub>cp/mL, p<0.001, 6 months before AHD, p<0.001) and were more likely to have a history of discharge from care (DFC) for >18 months (11% vs 2%, p<0.001) and virological failure (12% vs 3%, p<0.001). After blocking potential confounding pathways, subjects with previous DFC but also those in care with HIV-RNA>1,000 cp/mL showed a significantly higher risk of AHD compared to PWH in care and virologically suppressed. Similarly, female sex, IDU as the modality for HIV infection, a lower educational level, being unemployed, and having started ART in less recent years (2004-2013) were all associated with a higher risk of developing AHD (Table 1).

**Conclusions:** Our data suggests that the actual risk of developing AHD among ART-experienced PWH in Italy is not negligible, although it appears to have decreased over the last decade. Prevention of AHD after charge in care is crucial and should focus on women and individuals with signs of social deprivation (low education, unemployment or use of injecting drugs). Discharge from care should be carefully monitored to ensure rapid re-engagement, as long gaps can significantly increase the risk of incident AHD.

Figure 1: Kaplan-Meier estimates of cumulative incidence of AHD with 95% confidence interval

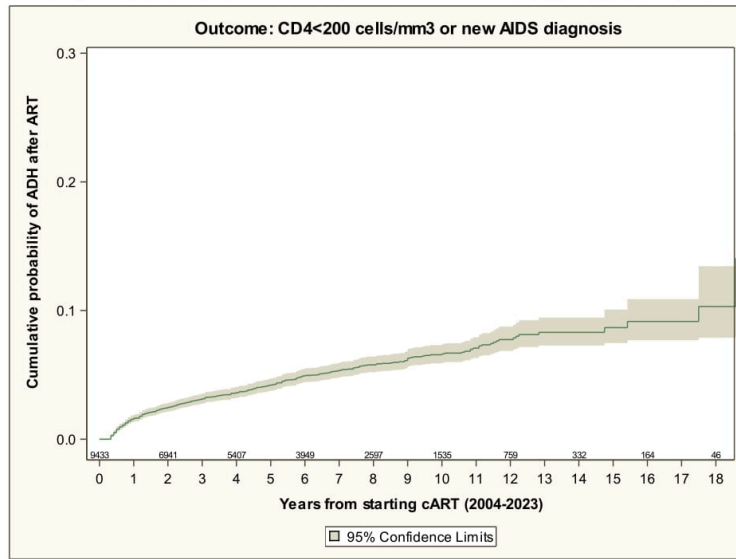


Table 1: Unadjusted and adjusted odds ratios of AHD from fitting a number of separate conditional logistic regression models

Exposure	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
<b>Model 1</b>				
<b>Gaps in care and viral load<sup>a</sup> composite exposure</b>		<b>&lt;0.001</b>		<b>&lt;0.001</b>
- No gap in care/HIVRNA≤1000 cp/mL	1		1	
- No gap in care/HIVRNA>1000 cp/mL	2.86 (2.24, 5.53)		3.23 <sup>1</sup> (1.95, 5.34)	
- Gap in care/ HIV-RNA≤1000 cp/mL	12.49 (5.39, 44.48)		18.61 <sup>1</sup> (5.37, 64.51)	
- Gap in care/ HIV-RNA>1000 cp/mL	9.42 (3.00, 22.36)		4.38 <sup>1</sup> (1.29, 14.80)	
<b>Model 2</b>				
<b>Sex at birth</b>				
- Male	1	<b>0.029</b>		
- Female	1.37 (1.03-1.81)			
<b>Year of ART initiation</b>				
- 2004-2013	1	<b>&lt;0.001</b>		
- 2014-2023	0.55 (0.42-0.71)			
<b>Model 3</b>				
<b>Maximum level of Education</b>		<b>&lt;0.001</b>		<b>&lt;0.001</b>
- University or higher	1		1	
- Primary/secondary School	1.80 (1.327, 2.56)		1.60 <sup>2</sup> (1.11, 2.30)	
<b>Model 4</b>				
<b>Mode of HIV transmission</b>		<b>&lt;0.001</b>		<b>&lt;0.001</b>
- Heterosexual contacts	1		1	
- IDU	1.81 (1.22, 2.71)		1.40 <sup>3</sup> (0.86, 2.27)	
- Homosexual contacts	0.73 (0.56, 0.96)		0.82 <sup>3</sup> (0.47, 1.38)	
<b>Model 5</b>				
<b>Employment</b>		<b>0.022</b>		<b>&lt;0.001</b>
- Unemployed	1		1	
- Employed	0.64 (0.45, 0.93)		0.73 <sup>4</sup> (0.48, 1.12)	
- Student	0.38 (0.16, 0.88)		0.51 <sup>4</sup> (0.18, 1.41)	
- Occasional work/retired	1.66 (0.86, 3.20)		2.01 <sup>4</sup> (0.94, 4.27)	
- Other jobs	0.59 (0.38, 0.92)		0.72 <sup>4</sup> (0.44, 1.20)	

<sup>1</sup>adjusted for nationality, mode of HIV transmission, year of ART initiation, alcohol use, level of education, employment status.  
<sup>2</sup>adjusted for nationality and year of ART initiation  
<sup>3</sup>adjusted for sex, alcohol use, level of education, nationality and year of ART initiation  
<sup>4</sup>adjusted for sex, alcohol use, mode of HIV transmission, nationality, and year of ART initiation  
<sup>a</sup>HIVRNA 6 months before AHD diagnosis