

# Suboptimal immune recovery in HIV-1 infected individuals in Sub-Saharan Africa despite long-term suppressive antiretroviral therapy

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## Background

- Suboptimal immune recovery, despite suppressive antiretroviral therapy (ART), has been associated with an increased risk of HIV-related illnesses.

## Objectives

- To assess the occurrence of suboptimal immune recovery in sub-Saharan Africa, using clinical relevant CD4 cell count thresholds
- To identify factors associated with failure of immune recovery
- To assess the incidence of TB, AIDS and death and its association to Immune recovery during long term ART.

**Table 1. Clinically relevant CD4 cell count categories**

>500 cells/ $\mu$ L	No immunosuppression
350-499 cells/ $\mu$ L	Mild immunosuppression
200-349 cells/ $\mu$ L	Advanced immunosuppression
<200 cells/ $\mu$ L	Severe immunosuppression

## Study participants

1581 participants from Kenya, Nigeria, South Africa, Uganda, Zambia and Zimbabwe enrolled in the Pan-African Studies to Evaluate Resistance (PASER) adult cohort, were eligible for this analysis.

Inclusion criteria:

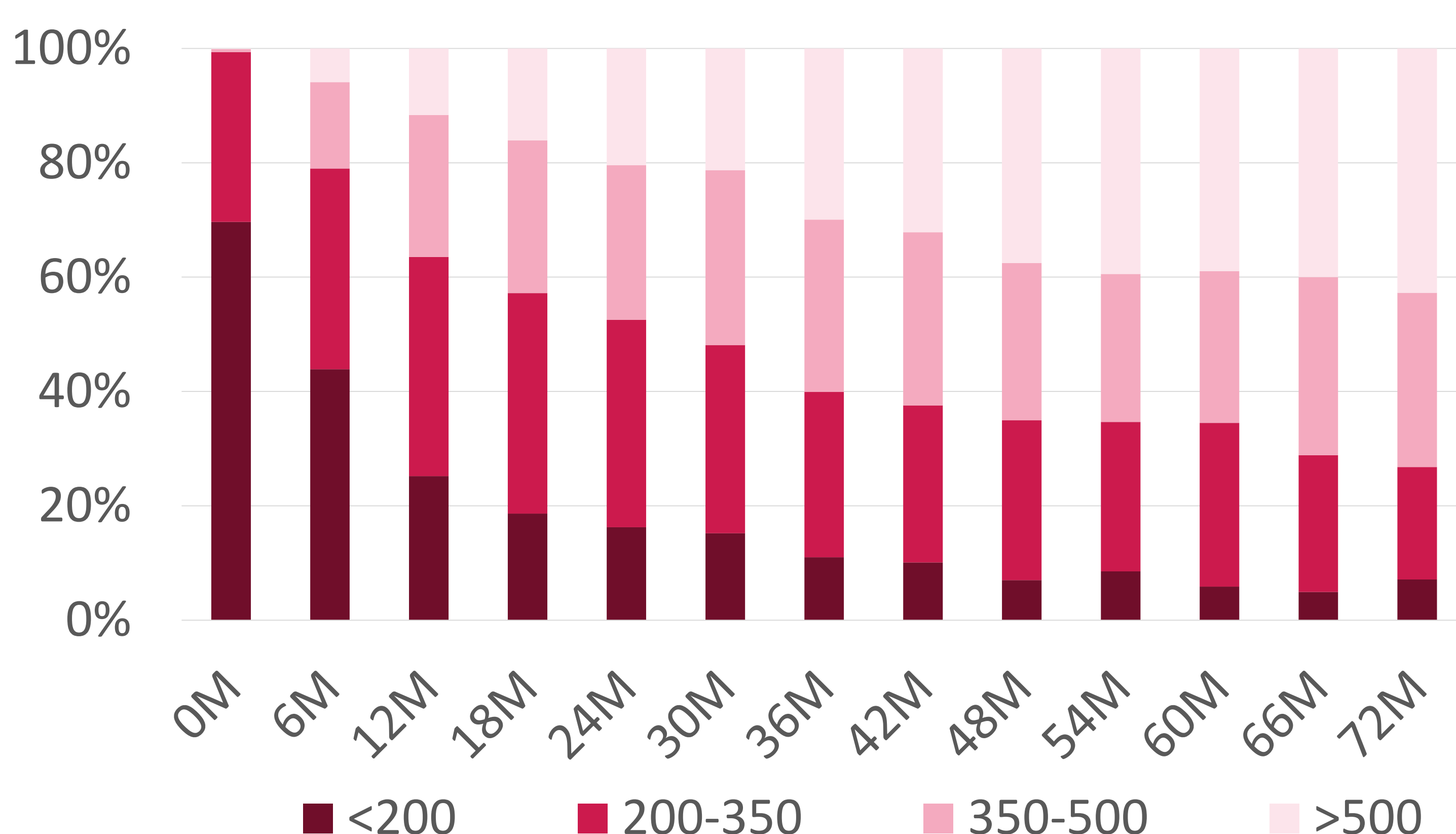
- Initiation of first-line non-nucleoside-reverse-transcriptase-inhibitor-based ART
- Undetectable plasma viral load (<50cps/mL) during follow up

## Data analysis

- Suboptimal immune recovery was defined by proportions of participants by CD4 cell count category
- Multivariate Cox regression analysis was done to identify factors associated with suboptimal immune recovery
- A time to event analysis was done to calculate incidence rates of TB, AIDS and death by CD4 categories <200, 200-350, 350-500 and >500 cells/ $\mu$ L.

## Results

**Figure 2. Proportions of participants by CD4 cell count category**



- At initiation of ART, 70% of the participants had CD4 cell counts of <200 cells/ $\mu$ L, and 99% <350cells/ $\mu$ L.
- After 6 years of suppressive ART, 57.6% had CD4 cell counts of <500cells/ $\mu$ L.

## Results continued

**Table 2. Patient characteristics associated with attaining clinically relevant thresholds**

Patient baseline factor	CD4 threshold 200 cells/ $\mu$ L		CD4 threshold 350 cells/ $\mu$ L		CD4 threshold 500 cells/ $\mu$ L	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Male sex	0.73 (0.61 – 0.86)	<0.001	0.72 (0.58 – 0.89)	0.003	0.57 (0.45 – 0.73)	<0.001
Age category						
18-29	1.00		1.00		1.00	
30-39	0.94 (0.69 – 1.26)	0.666	0.84 (0.65 – 1.09)	0.190	0.68 (0.51 – 0.89)	0.005
40-49	0.97 (0.79 – 1.19)	0.763	0.87 (0.68 – 1.12)	0.290	0.69 (0.59 – 0.81)	<0.001
50-older	0.74 (0.59 – 0.94)	0.013	0.64 (0.49 – 0.83)	0.001	0.38 (0.24 – 0.62)	<0.001
Baseline CD4 cell count (cells/ $\mu$ L)						
<100	1.00		1.00		1.00	
100-200	2.34 (0.93 – 2.86)	<0.001	1.94 (1.66 – 2.27)	<0.001	1.93 (1.53 – 2.44)	<0.001
>200	-		4.96 (4.43 – 5.56)	<0.001	4.89 (3.70 – 6.47)	<0.001
BMI (kg/m <sup>2</sup> )						
<18	1.00		1.00		1.00	
18-25	1.10 (0.96 – 1.25)	0.162	0.94 (0.76 – 1.17)	0.577	0.79 (0.56 – 1.13)	0.198
>25	1.36 (1.26 – 1.49)	<0.001	1.11 (0.92 – 1.34)	0.266	1.04 (0.76 – 1.48)	0.809
HIV subtype						
A	0.40 (0.32 – 0.49)	<0.001	0.60 (0.53 – 0.68)	<0.001	0.85 (0.70 – 1.02)	0.076
C	0.44 (0.29 – 0.67)	<0.001	0.72 (0.60 – 0.86)	<0.001	1.05 (0.92 – 1.19)	0.429
D	1.00		1.00		1.00	
other	0.47 (0.35 – 0.63)	<0.001	0.68 (0.54 – 0.85)	0.001	0.92 (0.73 – 1.16)	0.482

Patient characteristics associated with failure to attain CD4 $\geq$ 500 were increasing age, male sex, and pre-ART CD4<200 cells/ $\mu$ L; additionally, subtype A, C or other (compared to D) was associated with failure to attain CD4 $\geq$ 350 and CD4 $\geq$ 200, Higher BMI was associated with attaining CD4>200 cells/ $\mu$ L.

**Table 3. Incidence rates per 100person-years of TB, AIDS and death by CD4 category**

HIV related event	CD4 <200cells/ $\mu$ L Rate (95% CI)	CD4 200-350 cells/ $\mu$ L Rate (95% CI)	CD4 350-500 cells/ $\mu$ L Rate (95% CI)	CD4 >500cells/ $\mu$ L Rate (95% CI)
TB	3.32(2.40 - 4.58)	0.85(0.50 - 1.43)	0.40(0.17 - 0.95)	0.25(0.08 - 0.76)
AIDS	4.21(3.17 - 5.61)	1.33(0.88 - 2.02)	0.48(0.21 - 1.06)	0.41(0.17 - 0.99)
Death	0.72(0.36 - 1.43)	0.54(0.28 - 1.05)	0.08(0.01 - 0.56)	0.66(0.33 - 1.31)

Persons with CD4<500 cells/ $\mu$ L had an increased risk of TB and AIDS. Mortality rates were similar between CD4<200 and CD4>500 cells/ $\mu$ L.

## Conclusions

- Suboptimal immune recovery is frequent in African adults: 57,6% do not reach the CD4>500 cells/ $\mu$ L threshold after 6 years of ART.
- Persons with CD4<500 had an increased risk of TB and AIDS, but not death.
- Factors associated with suboptimal immune recovery were: Male sex, older age, low CD4 cell count at initiation of ART
- Close laboratory and clinical monitoring is required for those with CD4 cell counts of <500 cells/ $\mu$ L and those who have factors which are associated with not attaining the CD4 thresholds.
- This study highlights the importance of early ART initiation.

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