Association between Age and Long-Term CD4 Cell Count Trajectory in HIV-1 Infected Individuals with Sustained Viral Suppression Depends on CD4 Cell Count at Start cART

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HIV Monitoring

Background

- Generally, CD4 cell count increases after starting cART have been reported to be smaller in older individuals. (Cohere Study Group, AIDS 2008; Moore, CID 2006; Khanna, CID 2008; Hunt, AIDS 2003)

- But no association between age and 'normal' CD4 cell counts in HIV negative MSM in the AGEhIV study. (unpublished data of AGEhIV study 2013, courtesy of Ferdinand Wit)

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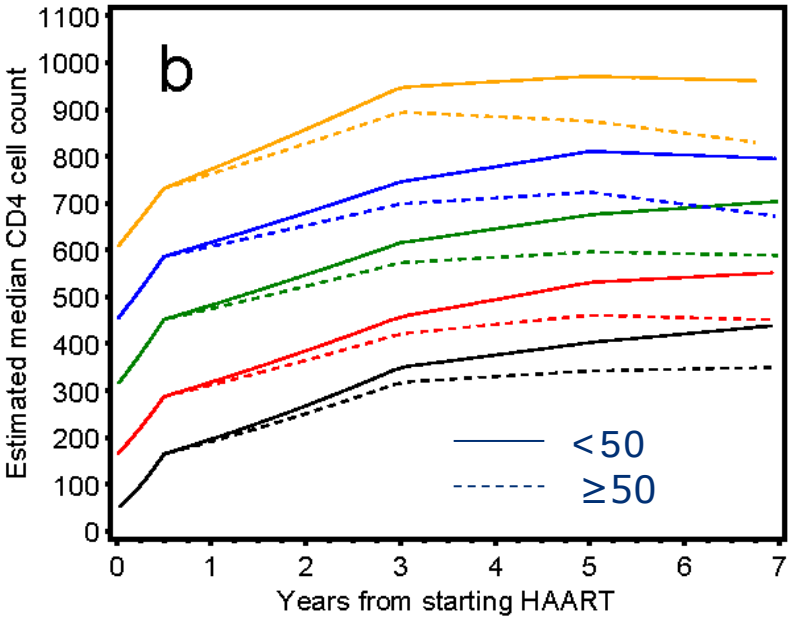
Background



554 patients continuously on virological suppressive cART for ≥7 years.

Same effect of age across all baseline CD4 strata.

Gras L *et al*, JAIDS 2007

Objective: Further explore association between age, CD4 cell count at start of cART and long term CD4 cell count in patients with sustained virological suppression on cART.

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Methods

Patients selected from the ATHENA cohort:

- ART-naïve when cART was started, ≥16 yr
- <500 copies/ml within 9 months of starting

- CD4 cell counts censored after
  - confirmed HIV RNA >500 copies/ml
  - therapy interruptions ≥2 weeks
  - start of chemo-, immunosuppressive, or PEGinterferon therapy.
  - 5 years.

Maximum capacity of cART to restore CD4 cell counts

- Mixed-effects models to estimate slopes of cubic root CD4 cell count changes (0-6, 6-24, and 24-60 months).

- Included covariates: CD4 cell count at cART initiation, age at the start (<50 and ≥50 year), gender, region of origin, transmission risk group, viral load, smoking status (ever/never) and HBV and HCV co-infection at the start of cART.

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Characteristics at the start of cART

N=10,012		Age (yrs)	
		<50, n=8359	≥50, n=1653
Age, years, median (IQR)		37 (31-42)	55 (52-59)
Gender, %	Male	78.7	88.7
Region of origin, %	W-Europe/N-America	62.5	84.2
	Sub Sahara Africa	18.2	3.8
Risk group, %	MSM	58.9	62.7
HCV +, % among known infection status		10.0	7.9
HBV +, % among known infection status		8.2	5.5
CD4 cell count, cells/mm^3, %	<50	12.8	13.4
	50-200	27.7	30.6
	200-350	37.7	38.2
	350-500	14.0	12.7
	≥500	7.8	5.1
HIV RNA, copies/ml, median (IQR)		4.9 (4.4-5.3)	5.0 (4.6-5.4)
Year of starting, median (IQR)		05 (01-09)	07 (03-09)
Ever smoker, %		48.2	54.3

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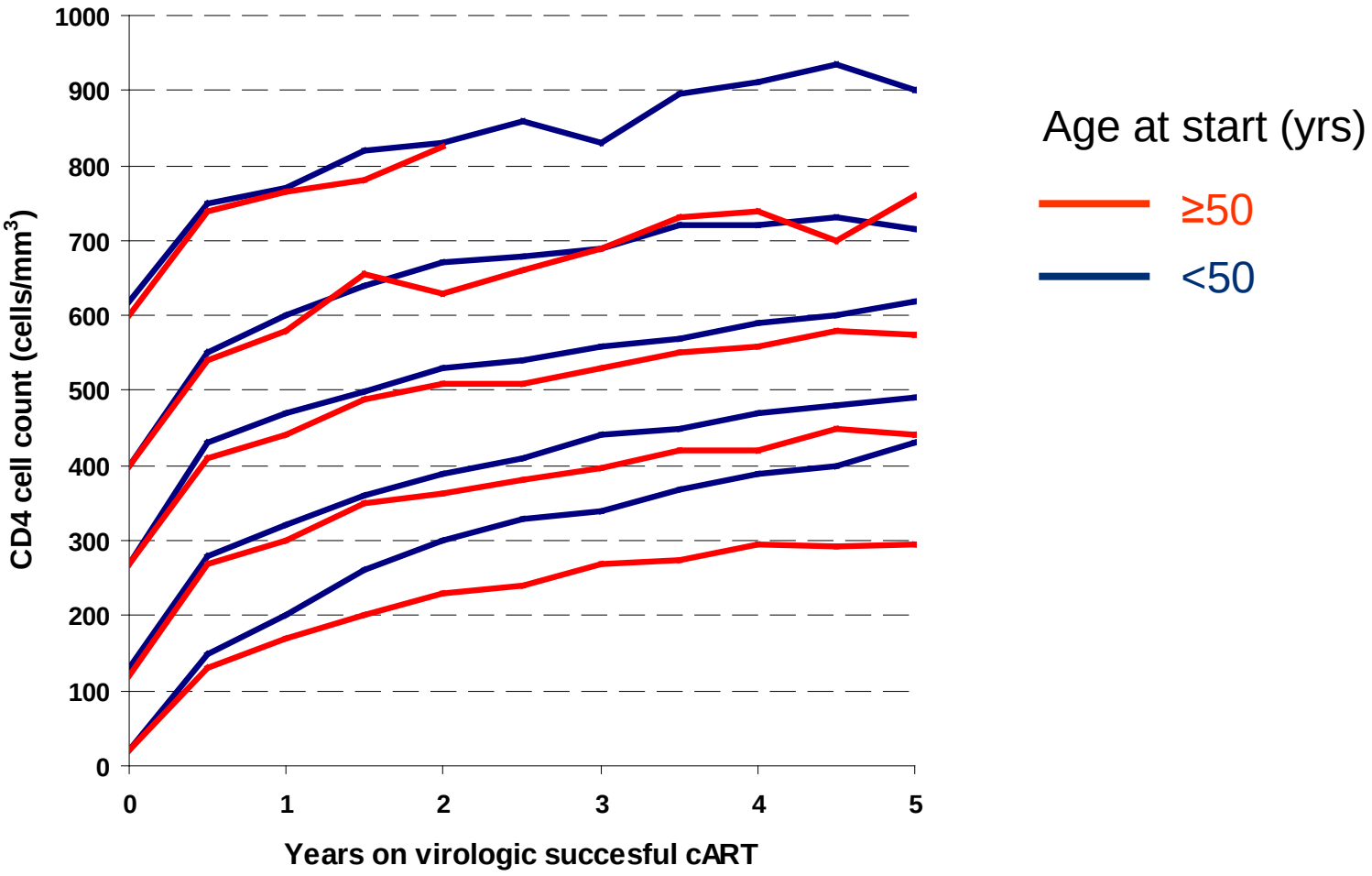
Median CD4 cell counts during virologic successful cART

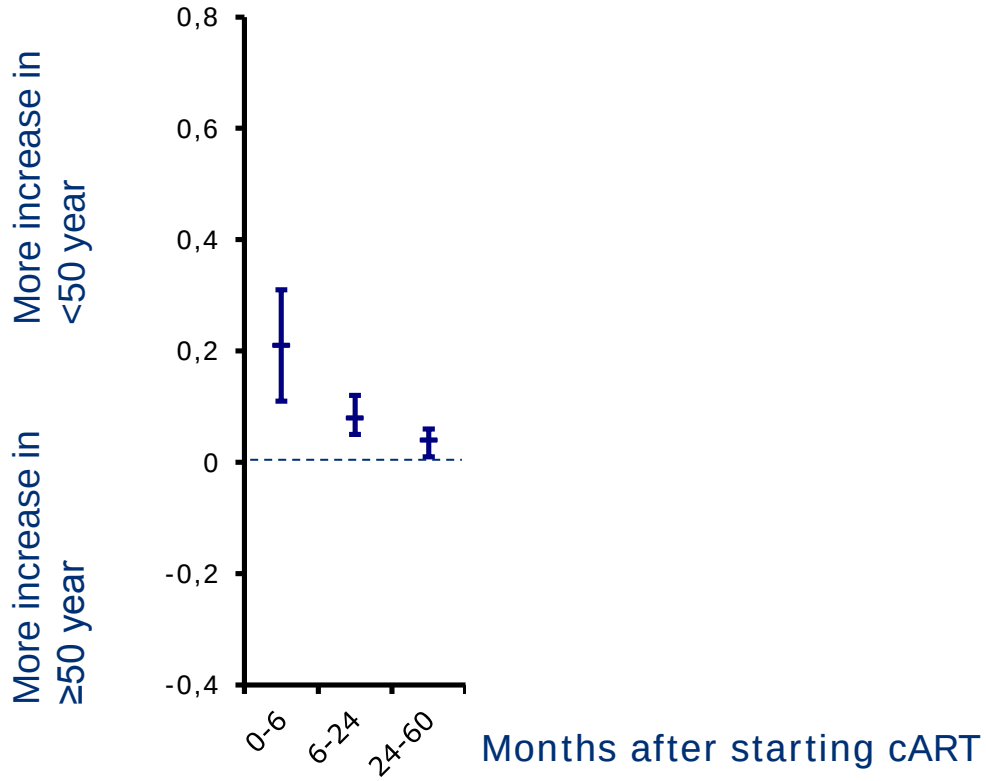


6-monthly median counts, shown only if ≥40 patients remained in follow-up.

Adjusted estimates

10,012 patients, 120,051 CD4 cell counts, median 10 (IQR 6-16)

Mean difference in slope $\sqrt[3]{\text{cells}}/\text{mm}^3/\text{year}$
between <50 and ≥50 year (95% CI)



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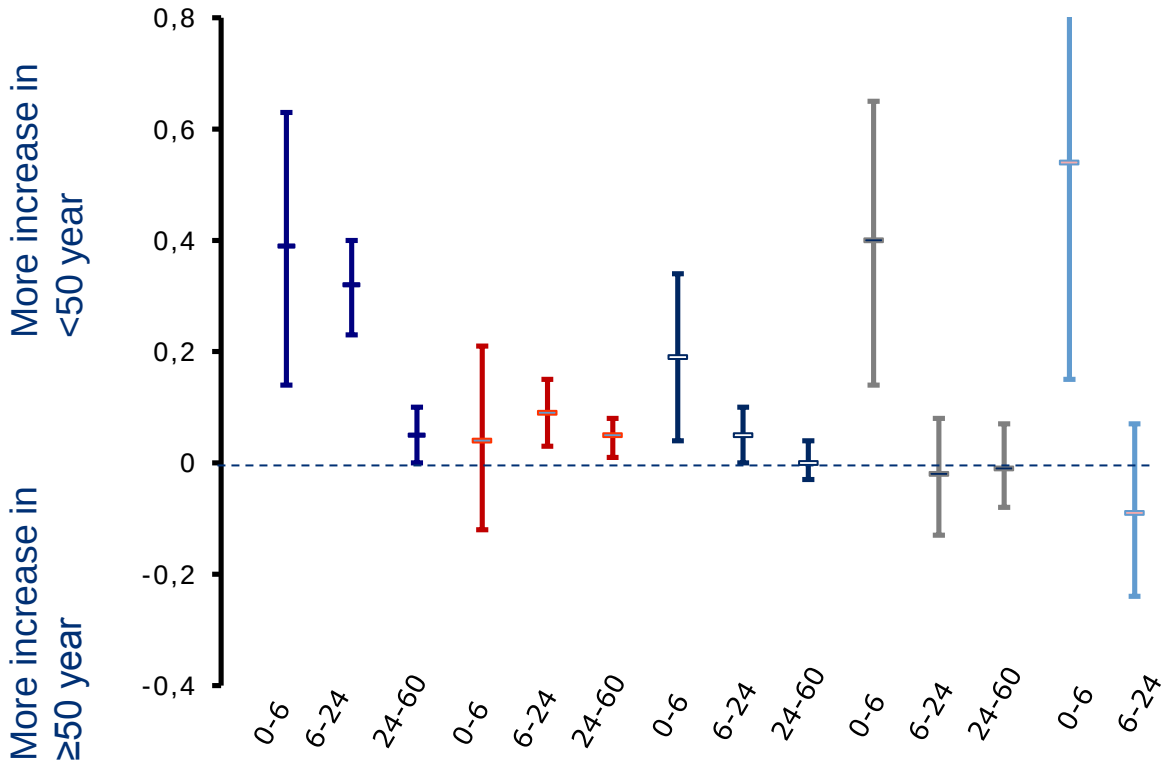

Test for interaction CD4 cell count and age at start:

Months	P-value
0- 6	0.02
6-24	<0.0001
24-60	0.004

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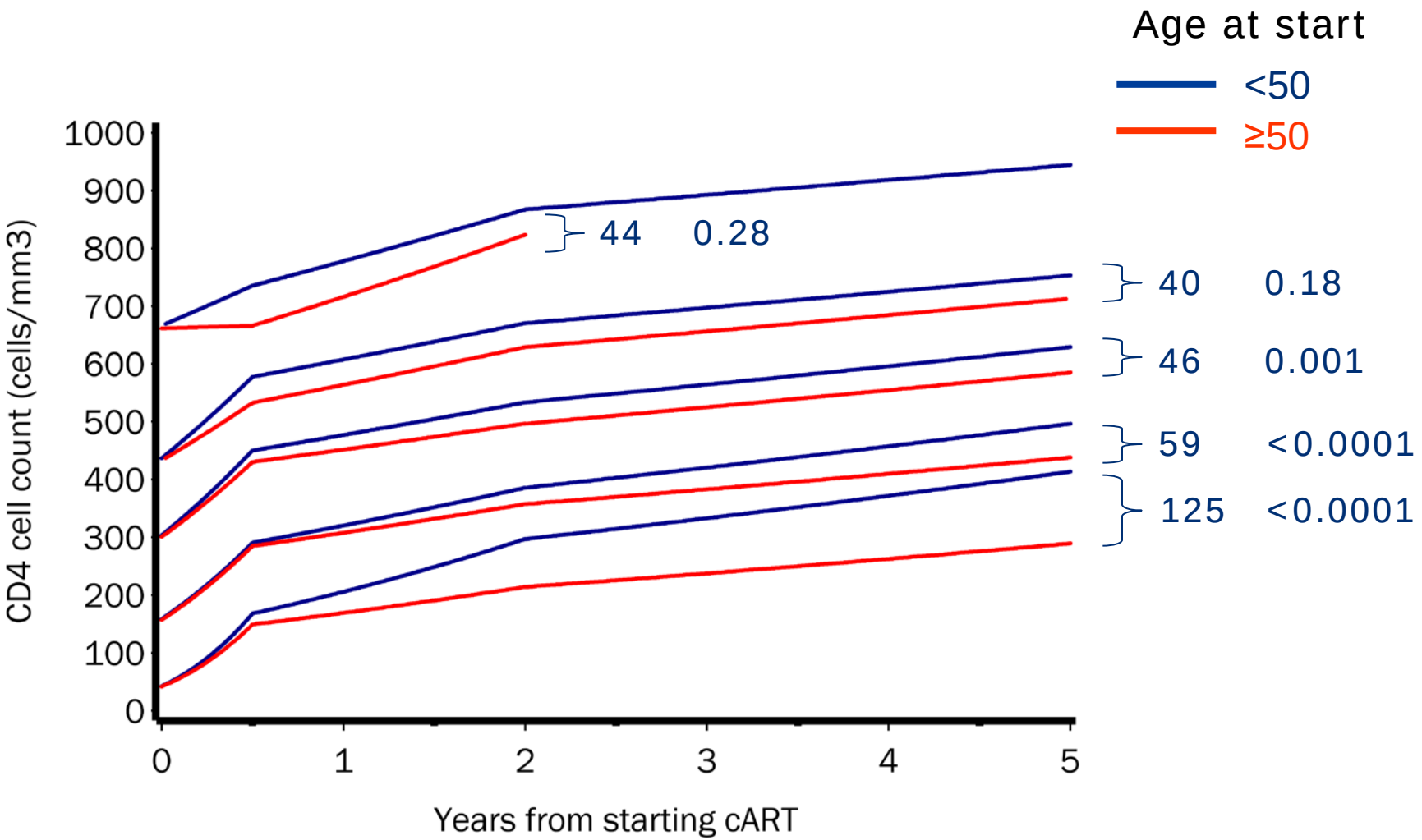
Adjusted estimates



For a male reference patient from W-Europe/N-America with between 4 and 5 $\log_{10}$ HIV RNA copies/ml at start cART.

Limitations

- Small subgroups, especially older patients starting at high CD4 cell counts.
- Cut-off used of 500 to define virological successful therapy rather than 50 copies/ml.
- Analyses on longitudinal CD8 cell counts and CD4/CD8 ratio are ongoing.
- Arbitrary cut-off of 50 years of age used.

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Conclusion

- Lesser CD4 count increases *in the first 6 months* after starting cART were generally observed in those over 50 years.

- *Over the longer-term* however, difference in CD4 gain became less pronounced, and only remained significant for those starting cART at <200 CD4 cells/mm^3, which stresses the continued importance of earlier identification and linkage to care.

- According to our results, patients over 50 years starting cART above CD4 levels recommended by current guidelines, and maintain viral suppression, can be expected to have a long-term CD4 cell recovery similar to younger patients.

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