

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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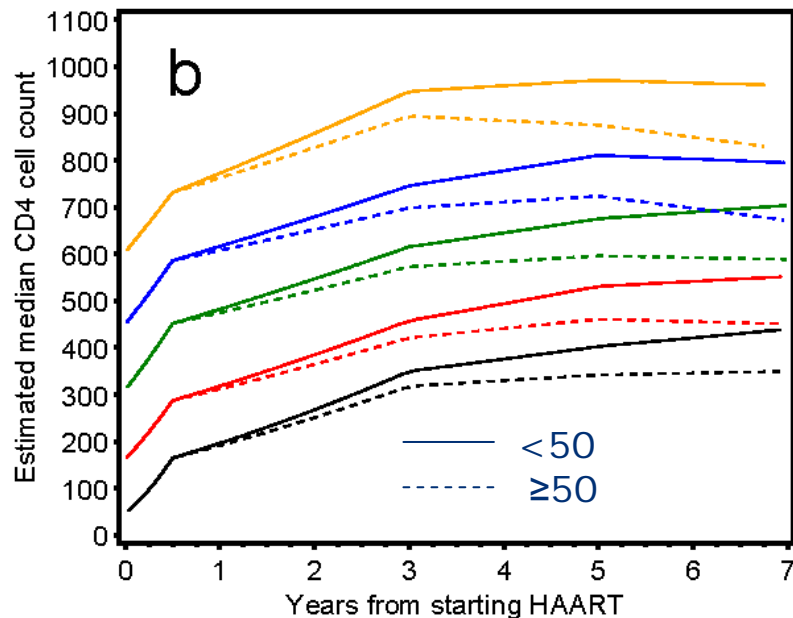


Background

- 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)
- No differences in CD4 cell count increases 5-12 years after first starting cART between <50 and ≥ 50 year. (Wright ST *et al.*, HIV Medicine 2013).

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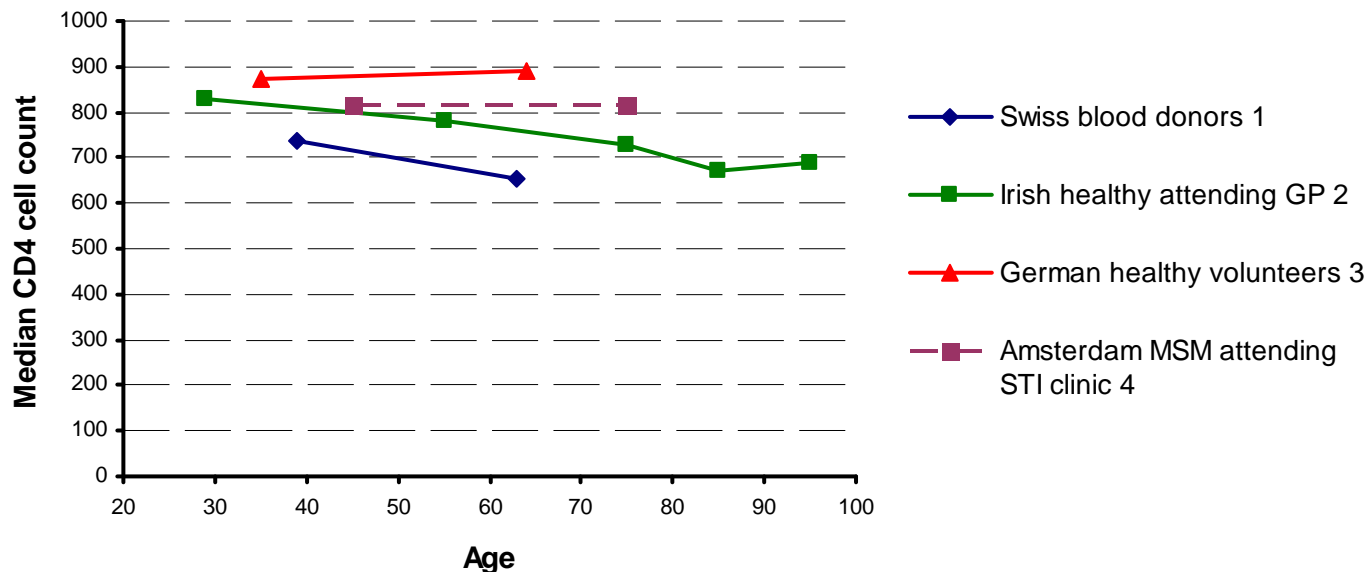
554 patients continuously on cART for 7 years or longer.

Same effect of age across all baseline CD4 strata.

Gras L *et al.*, JAIDS 2007

Background

- Conflicting results have been published on 'normal' CD4 cell counts by age among HIV negative individuals.



¹Bisset et al. Eur J Haematol, ²McNerlan *et al.*, Scand J Clin Lab Invest 1999, ³Jentsch-Ullrich *et al.*, Clin Immunol 2005, ⁴ unpublished data of AGEHIV study 2013, courtesy of Ferdinand Wit

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.

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.

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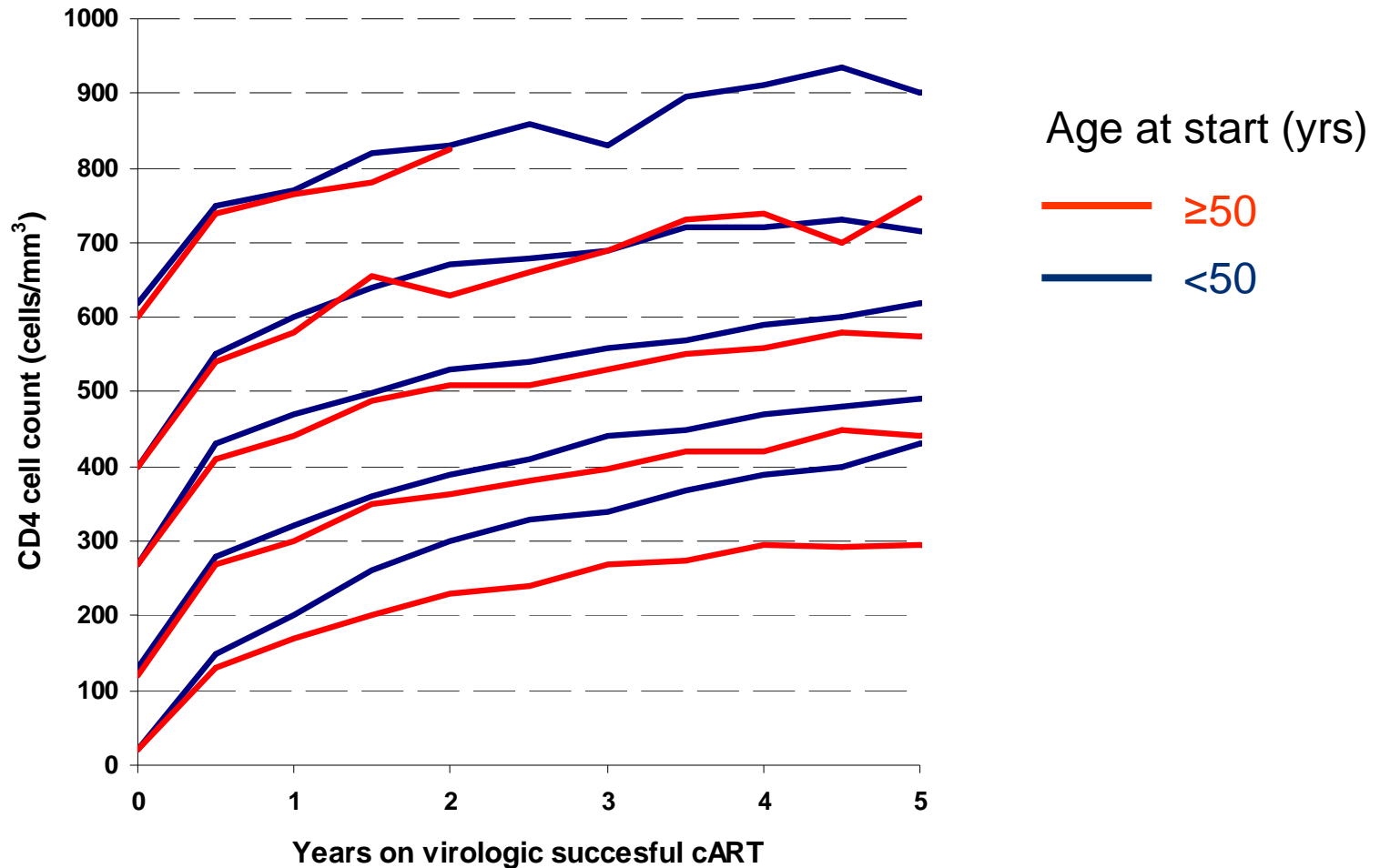
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- Maximum capacity of CD4 cell count restoration
- Mixed-effects models to estimate slopes of cubic root CD4 cell count changes (0-6, 6-24, and 24-60 months).
 - Included covariates: CD4 cell count at cART initiation, age at the start (< 50 and ≥ 50 year), gender, region of origin, transmission risk group, viral load and HBV and HCV co-infection at the start of cART.

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/mm³, %	<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)

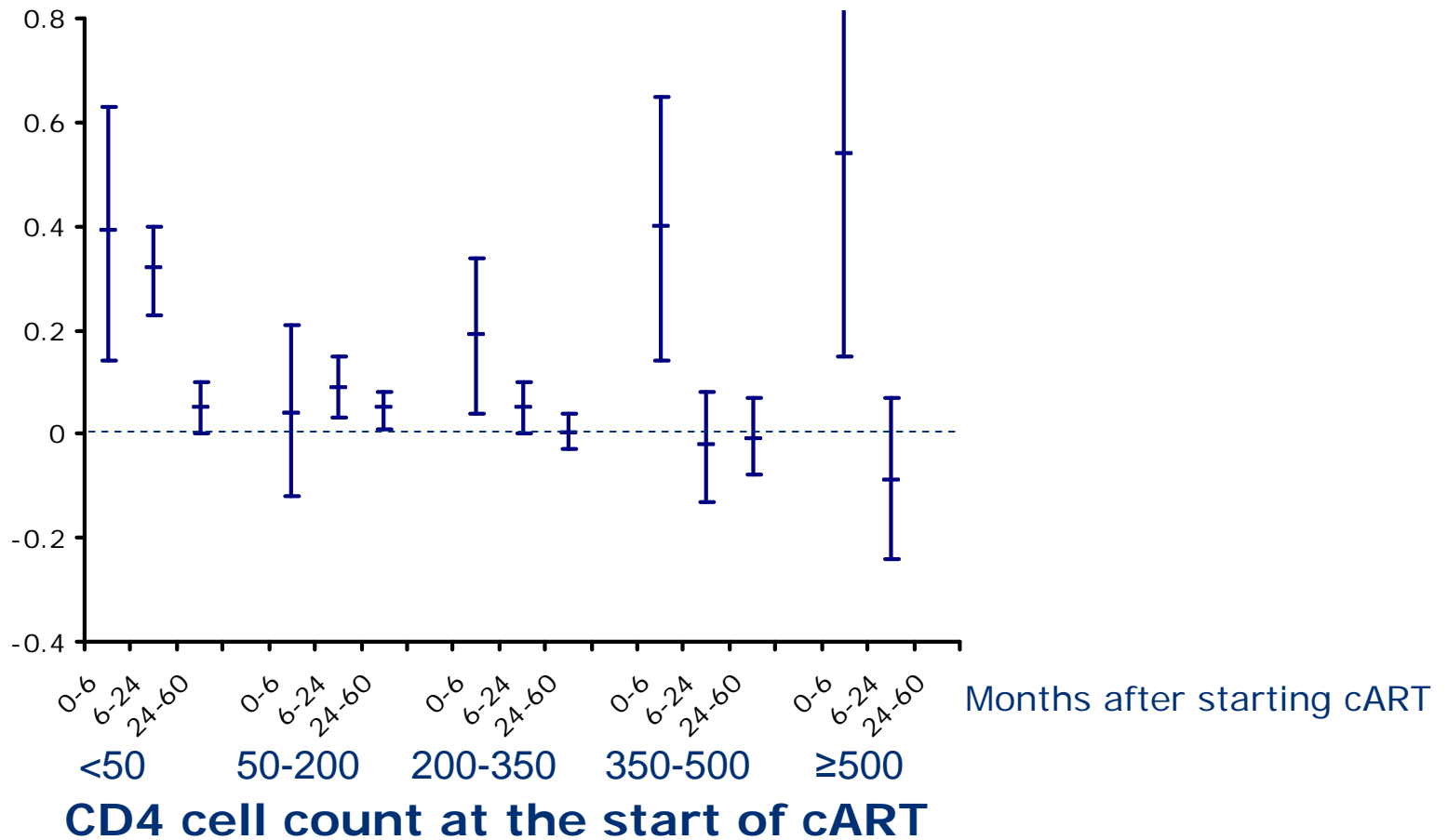
Median CD4 cell counts during virologic successful cART



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

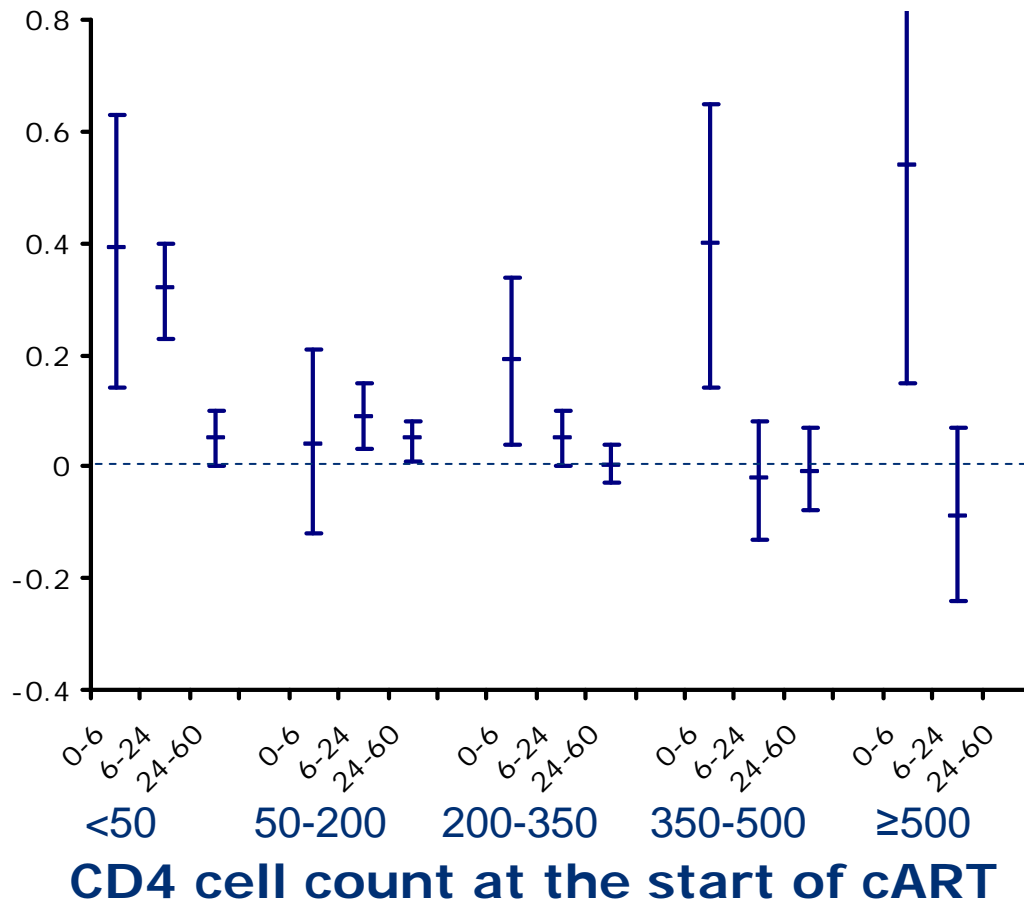
Adjusted estimates

Difference in slope $\sqrt[3]{\text{cells}/\text{mm}^3/\text{year}}$
between <50 and ≥ 50 year



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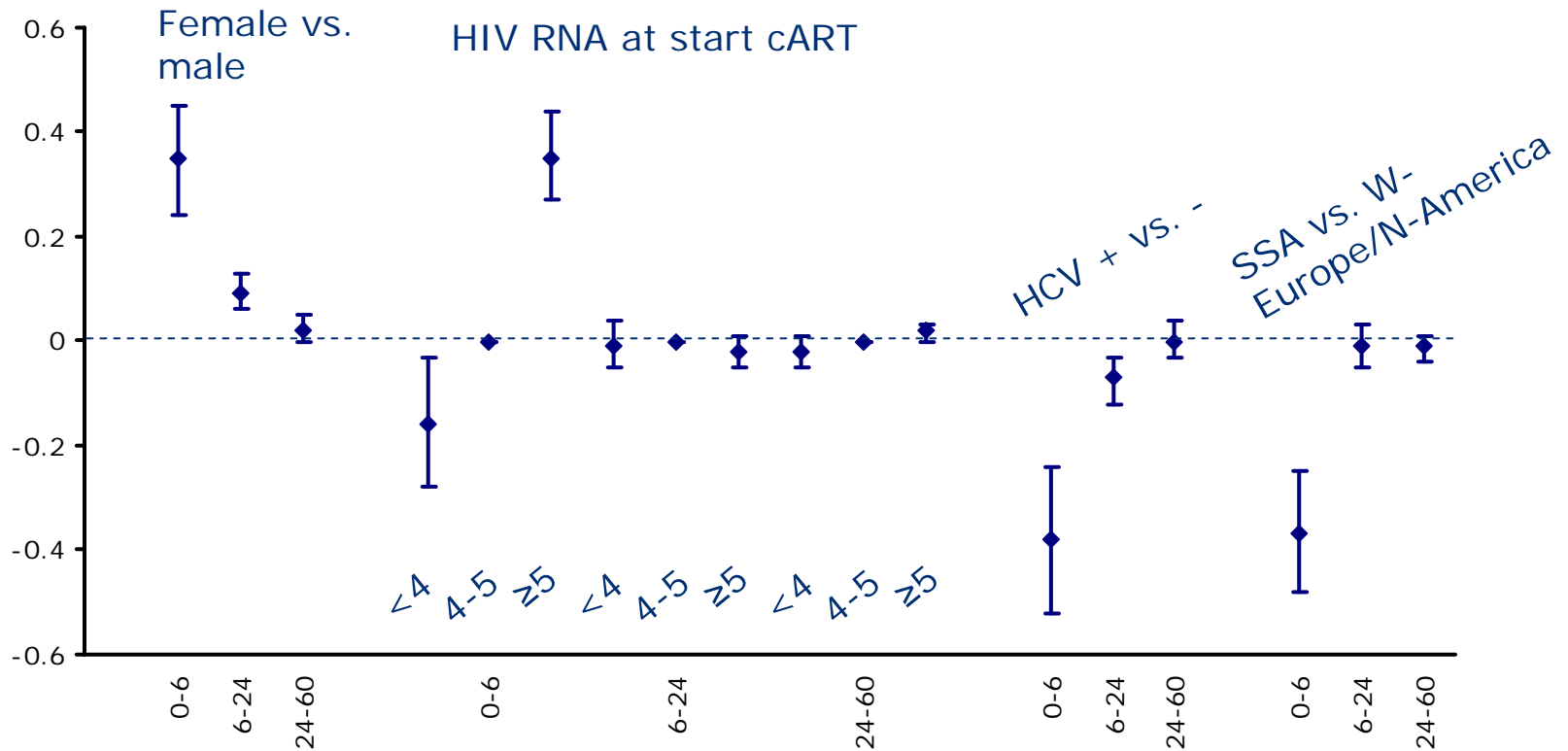


Test for interaction
CD4 cell count
and age at start:

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

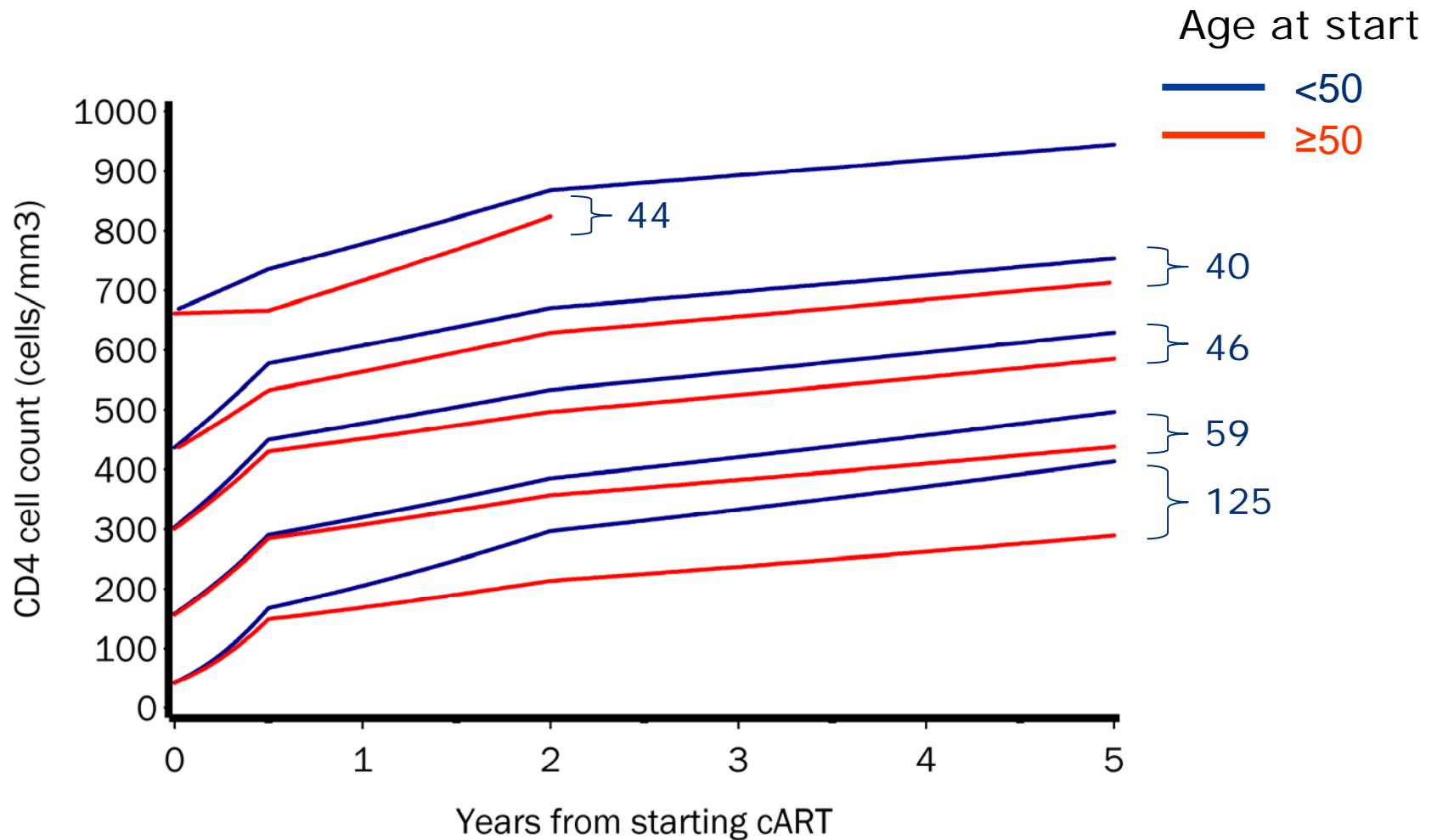
Other covariates

Difference in slope $\sqrt[3]{\text{cells}/\text{mm}^3/\text{year}}$
between <50 and ≥ 50 year



Months after starting cART

Adjusted estimates



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.

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/mm³, 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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