

Epigenetic Age Advancement Is Associated With Cognition, Frailty, and Mortality in Older PWH

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BACKGROUND

People with HIV (PWH) are more likely to experience medical comorbidities and geriatric syndromes including frailty as they m

- Epigenetic changes to DNA by different patterns of methylation have been associated with aging
- People with HIV have been demonstrated to have advancement of epigenetic-based age calculation compared to chronologic age¹
- Early and/or untreated HIV advances epigenetic age, and ART attenuates age advancement²

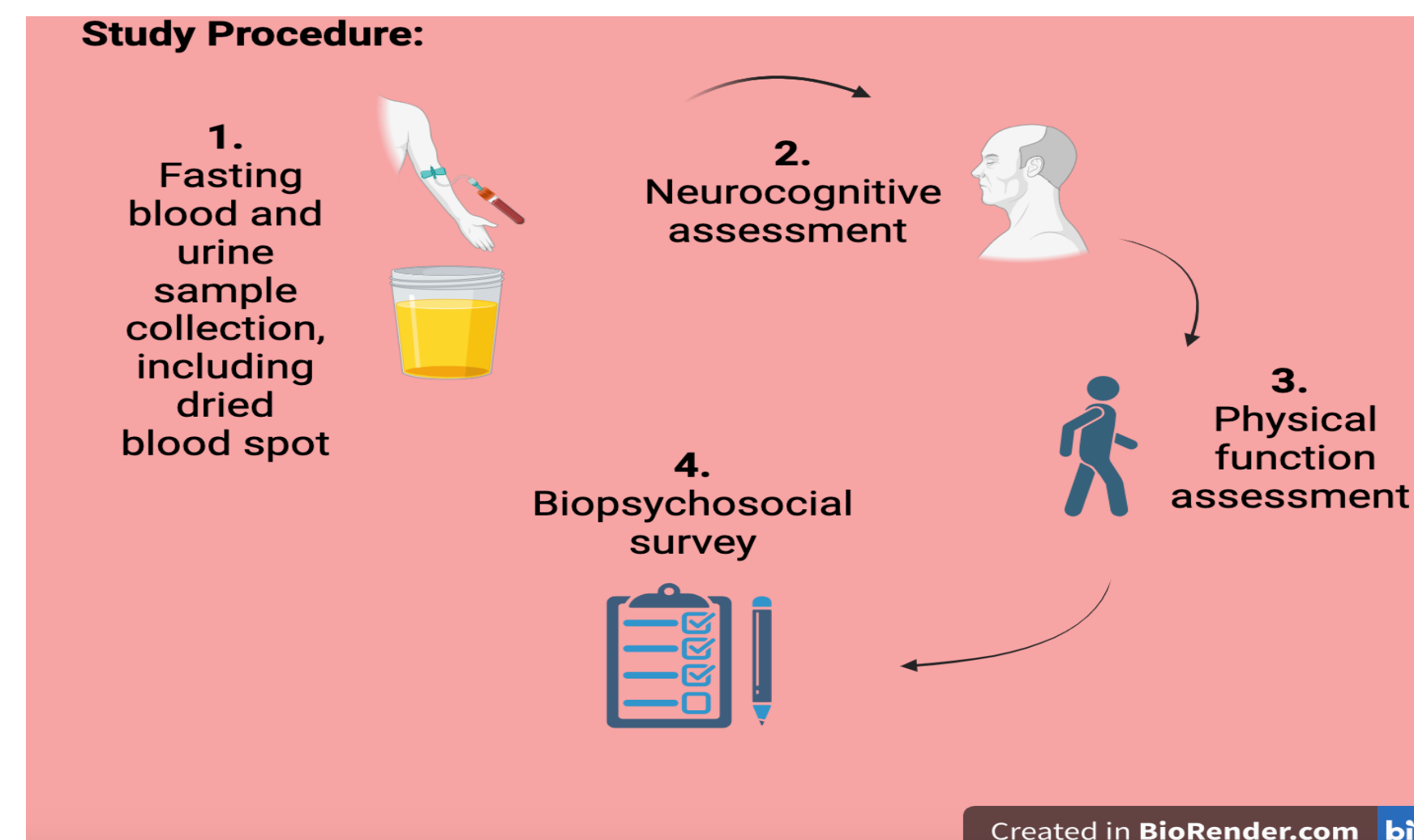
We investigated associations between phenotypic measures of cognition, frailty, and 7-year survival with epigenetic age estimates derived from the modification of DNA methylation (DNAm).

METHODS

Recruitment:

- Older adults (55 years and older) with HIV were recruited from the outpatient HIV clinical practice at Weill Cornell using an age-stratified random selection strategy.

Procedures:



Analysis:

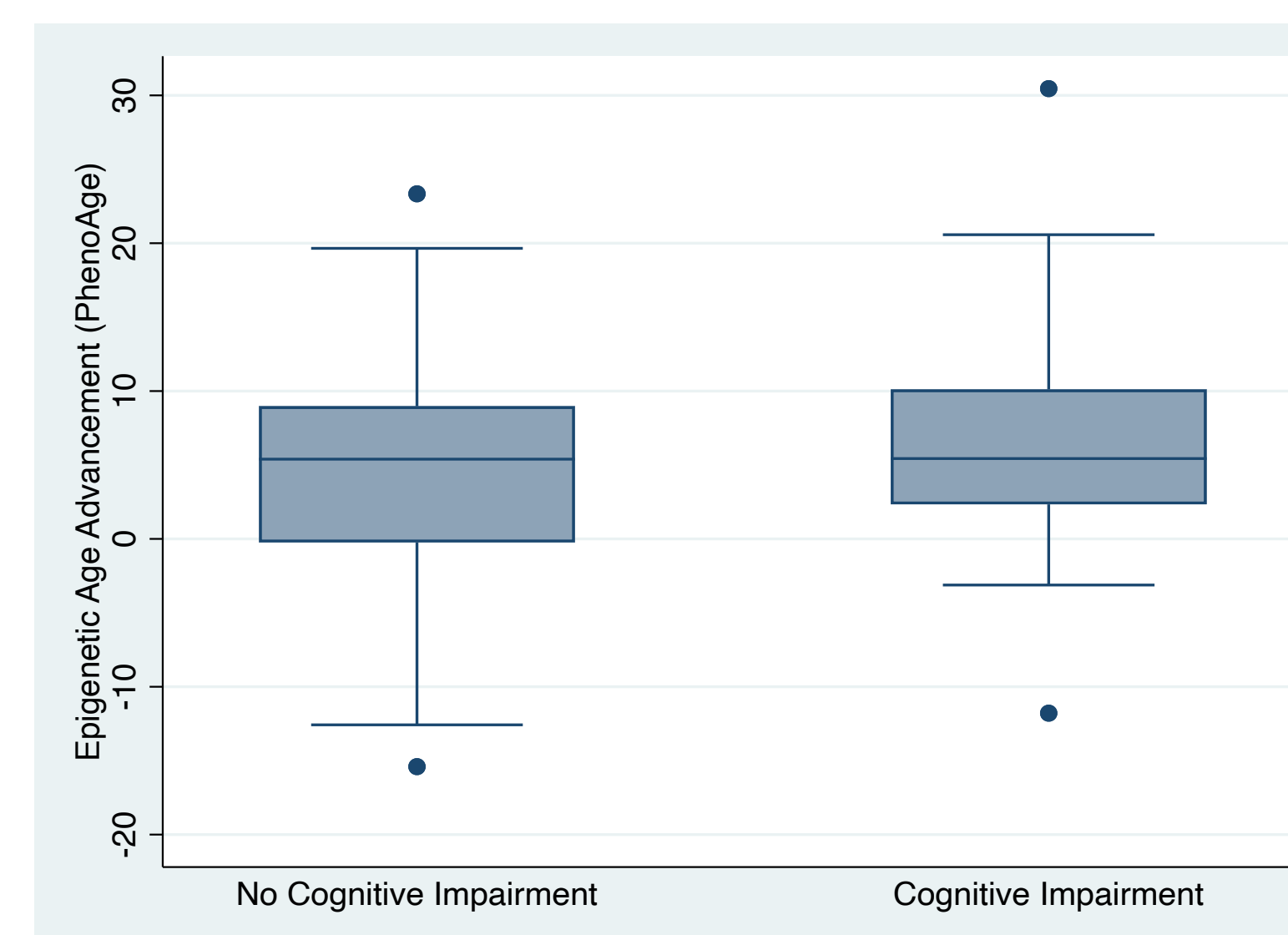
- Genome-wide DNA methylation was measured from dried blood spots using the Illumina MethylationEPIC platform and analyzed using 6 established epigenetic age algorithms including DNAm

Characteristic (N=158)	N(%), Median (IQR)
Age (years)	60 (56-64)
Female sex	52 (33%)
CD4 T-cell Count (cells/ml)	588 (323-811)
Montreal Cognitive Assessment (MoCA)	24 (21-27)
PhenoAge (years)	66 (62-71)
Epigenetic Age Advancement [†]	5.4 (SD 6.6)
eFRS Frailty Score	0.09 (0.06-0.12)
Fried Frailty Category [‡]	
- Nonfrail	49 (33%)
- Prefrail	84 (56%)
- Frail	16 (11%)

Epigenetic age advancement was common in older PWH, and greater epigenetic advancement was associated with cognitive dysfunction, more advanced frailty state, and mortality over the course of 7 years.

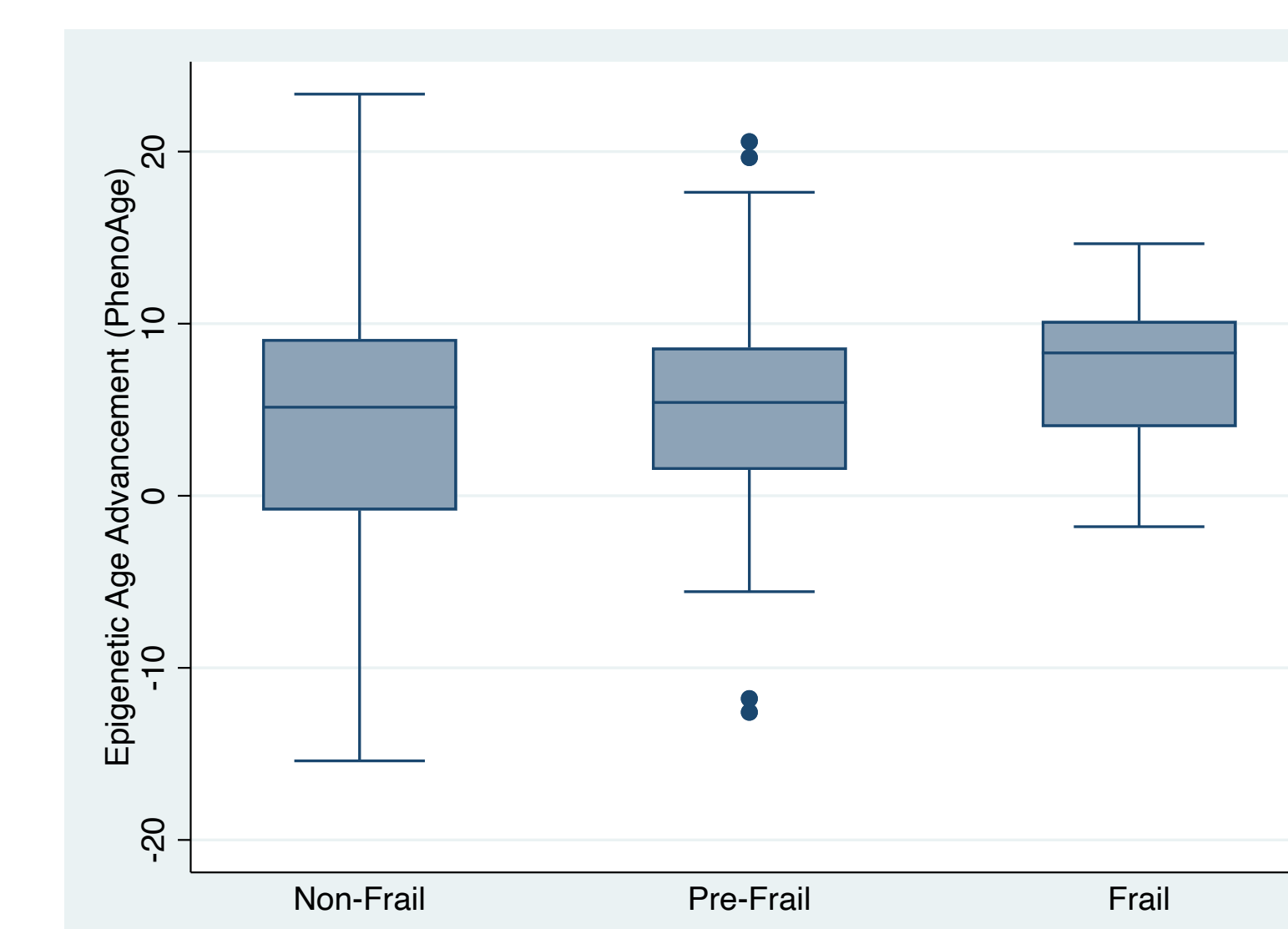
RESULTS

Epigenetic Age Advancement Related to Cognitive Dysfunction (MoCA <23)



Multivariable Linear Regression Model: Cognitive Dysfunction as Outcome			
Variable.	Beta Coefficient	95% CI	P-Value
EAA (years)	-0.12	(-0.21, -0.04)	<0.01
Age (years)	-0.11	(-0.02, -0.01)	0.03
Female Sex	-0.29	(-1.47, 0.90)	0.63
Race			
White (ref)			
Black	-1.57	(-2.86, -0.28)	0.02
Other	-2.50	(-4.03, -1.00)	<0.01

Epigenetic Age Advancement Related to Frailty Status

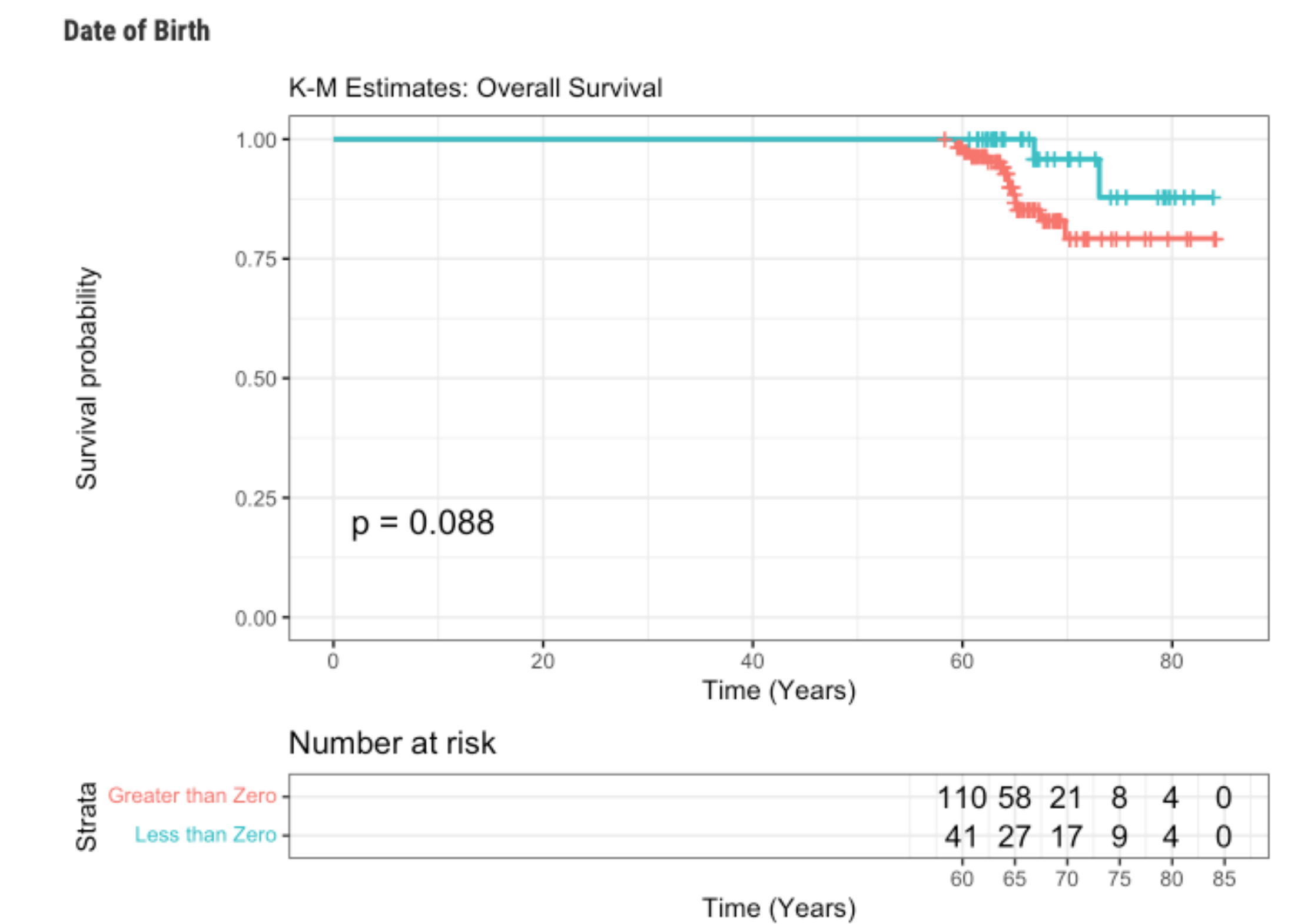


Multivariable Ordinal Logistic Regression Model: Frailty State as Outcome			
Variable	Beta Coefficient	95% CI	P-Value
EAA (years)	1.05	(1.00, 1.12)	0.07
Age (years)	1.11	(1.05, 1.19)	<0.01
Female Sex	1.09	(0.51, 2.32)	0.83
Race			
White (ref)			
Black	1.20	(0.55, 2.62)	0.65
Other	2.11	(0.79, 5.59)	0.13

Results:

PhenoAge Advancement Associated with Decreased Survival

PhenoAge and Survival



Cox Proportional Hazards Regression - Adjusted for Age

Characteristic	HR [†]	95% CI [†]	p-value
Difference between PhenoAge Epigenetic Age and Current Age (years)	1.10	1.02, 1.18	0.011
Age (years)	0.79	0.65, 0.95	0.013

[†]HR = Hazard Ratio, CI = Confidence Interval

CONCLUSIONS

In this study of older adults with HIV, the average epigenetic age advancement (EAA) was 5.4 years, as calculated by PhenoAge.

- EAA was associated with lower MoCA score in a linear regression model adjusted for age, sex and race (p<0.01).
- There was trend towards EAA association with more advanced frailty state adjusted for age, sex and race (p=0.07).
- EAA was associated with greater mortality after adjusting for chronologic age in a Cox Proportional hazards model (p=0.02).

These results suggest epigenetic clocks are a valuable biomarker of aging-related pathologies including cognitive dysfunction, frailty and mortality in older PWH and warrant further study.

ADDITIONAL KEY INFORMATION

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2. Schoepf IC et al. 2023. Lancet Healthy Longev. Ay 4(5)211-218

[†] Epigenetic Age Advancement defined as PhenoAge – Chronologic Age

[‡] Frailty data missing/incomplete for 8 participants