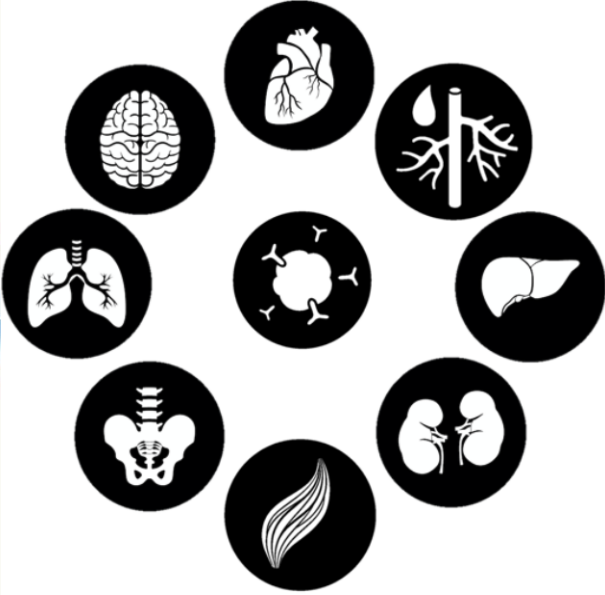
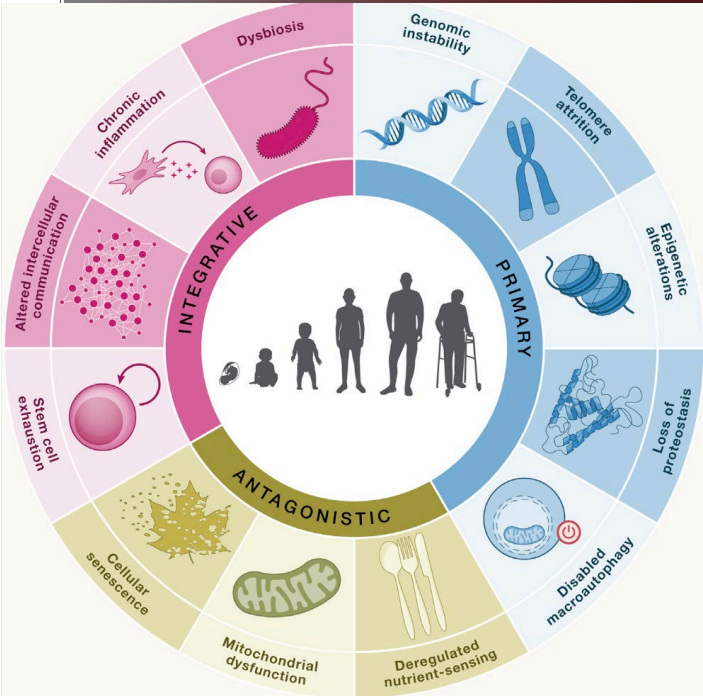


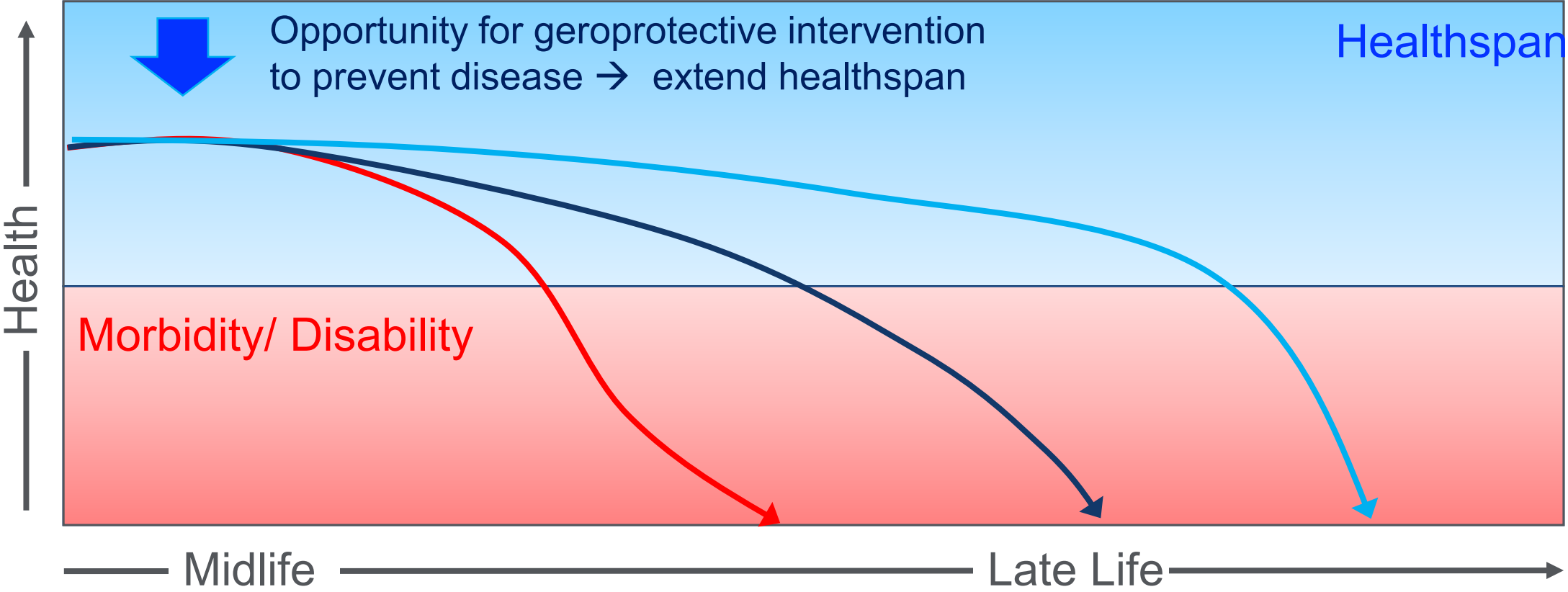
Pace of Aging and Timing of Disease Onset

Micah Savin (they/them), PhD
Postdoctoral Research Scientist
Mentors: Drs. Daniel Belsky & Stephanie Assuras

The Geroscience Hypothesis

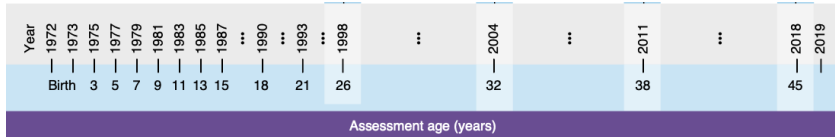


Geroprotection for Healthspan Extension

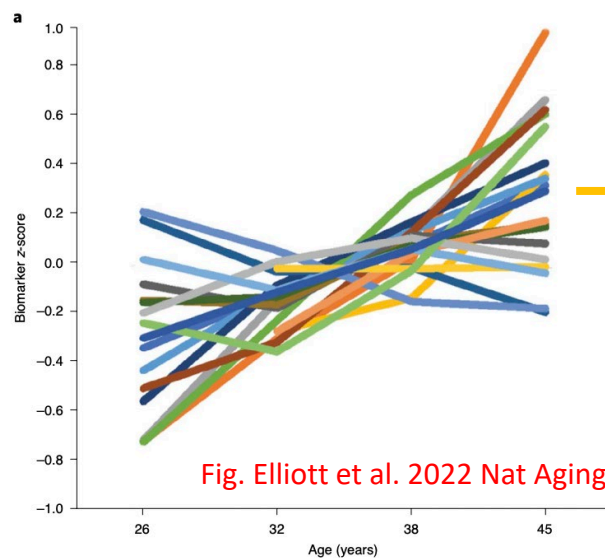


A DNAm biomarker of Pace of Aging: DunedinPACE

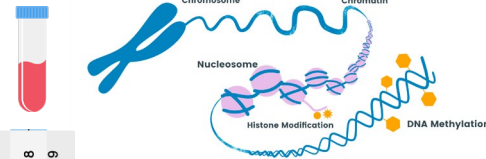
Dunedin Birth Cohort Follow-up



- BMI
- Waist-hip ratio
- Hemoglobin A1c
- Leptin
- Mean arterial pressure
- VO₂Max (rev)
- FEV₁/FVC (rev)
- FEV₁ (rev)
- Total cholesterol
- Triglycerides
- HDL cholesterol (rev)
- Lipoprotein(a)
- ApoB100/ApoA1
- eGFR (rev)
- Blood urea nitrogen
- hsCRP
- White blood cell count
- Mean periodontal attachmer
- Dental caries experience



Blood DNAm at age 45



$$\alpha + \sum_j^{173} \beta_j \times CpG_{ij}$$

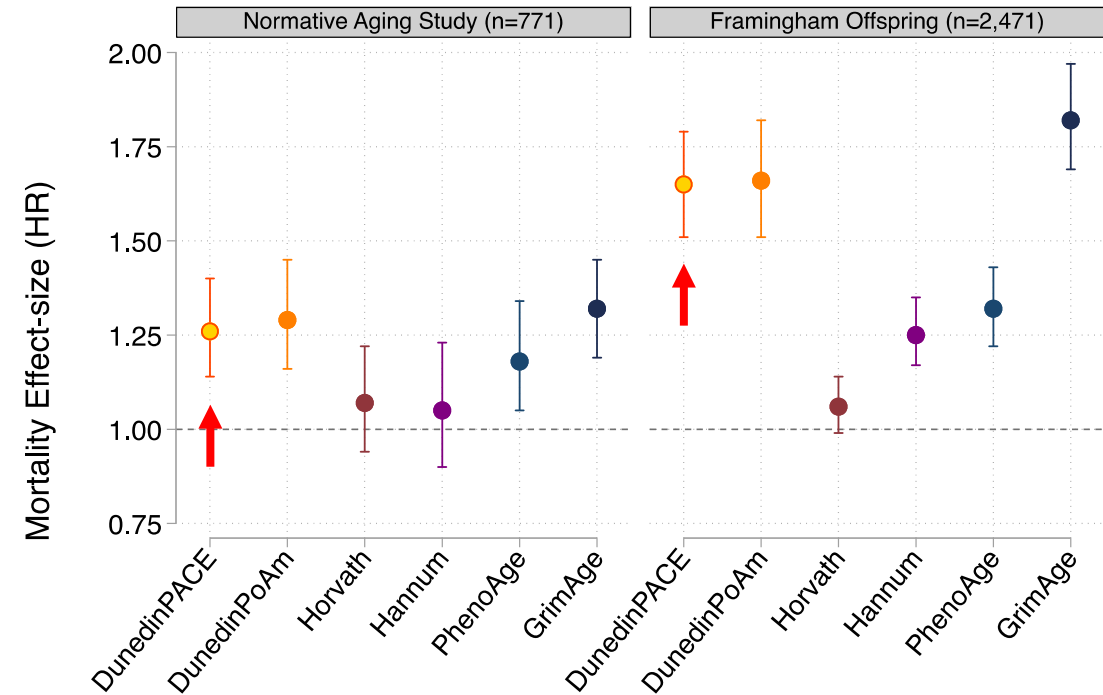
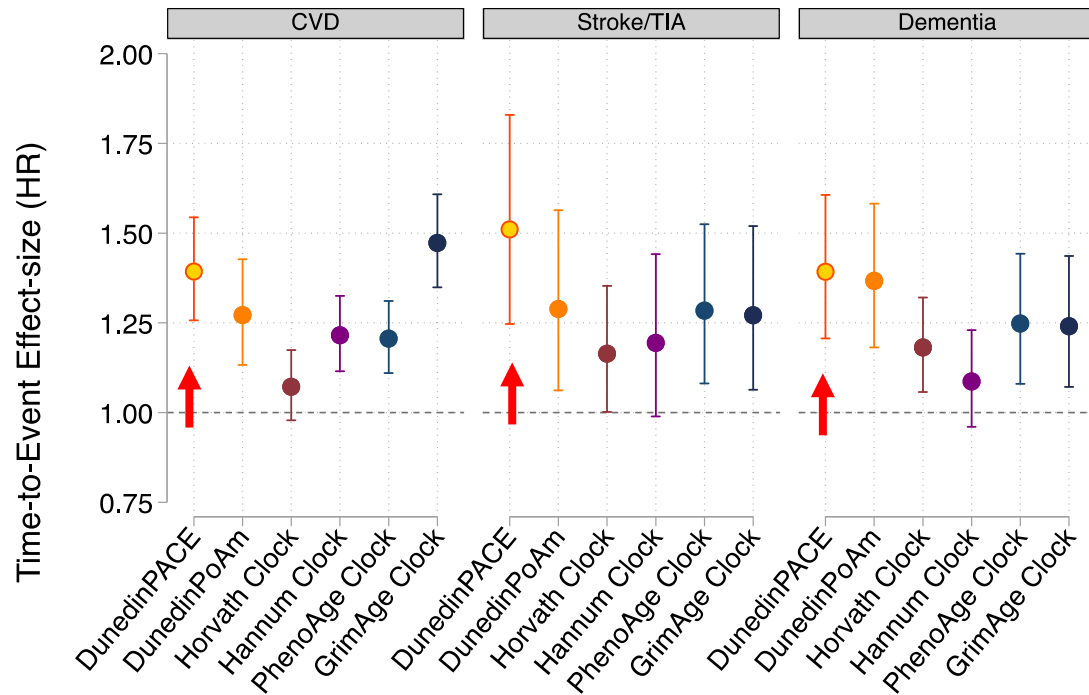
- Developed from analysis of Dunedin Study birth cohort
- Within-person change in 19 biomarkers
- Follow-up from age 26-45 across 4 measurements

AG032282 (Moffitt)



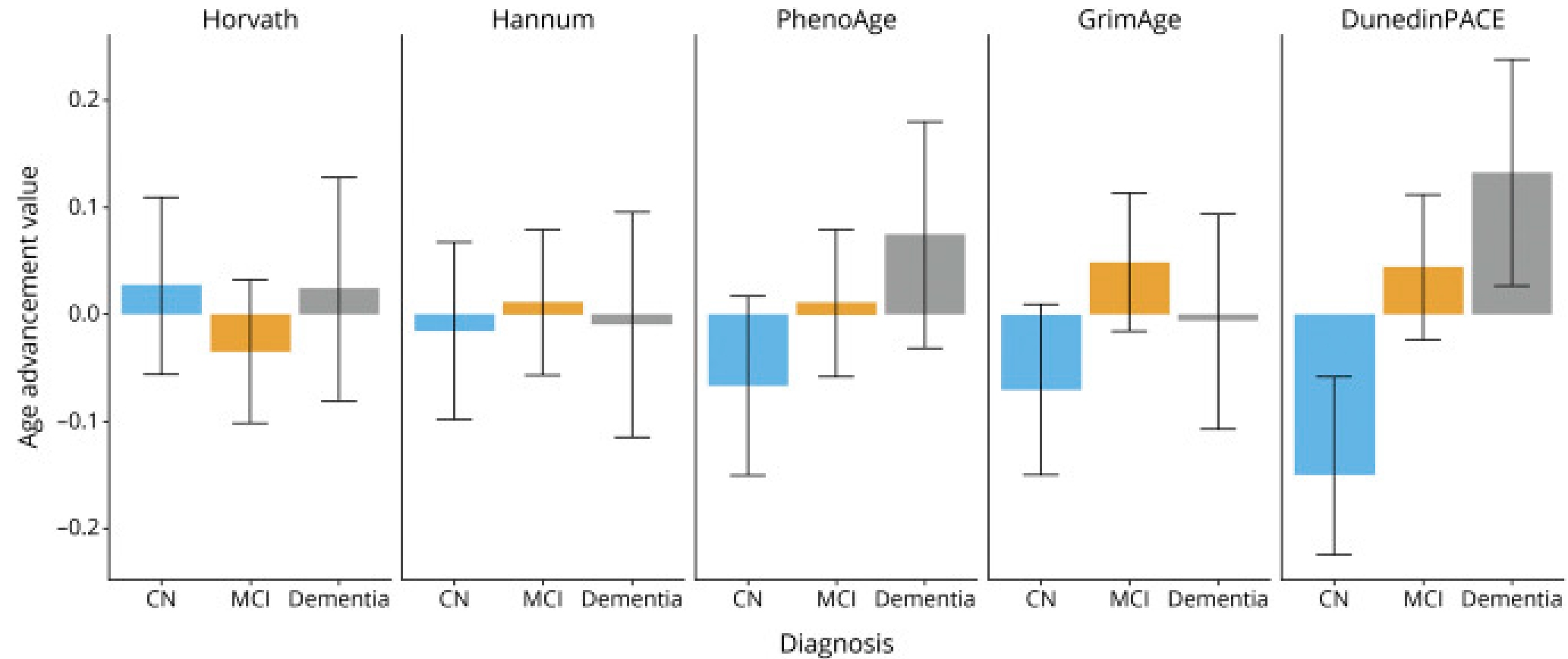
A DNAm biomarker of Pace of Aging: DunedinPACE

Consistent prediction of disease, disability, and mortality



[Belsky et al. 2022 eLife](#)
[Sugden et al. 2022 Neurology](#)

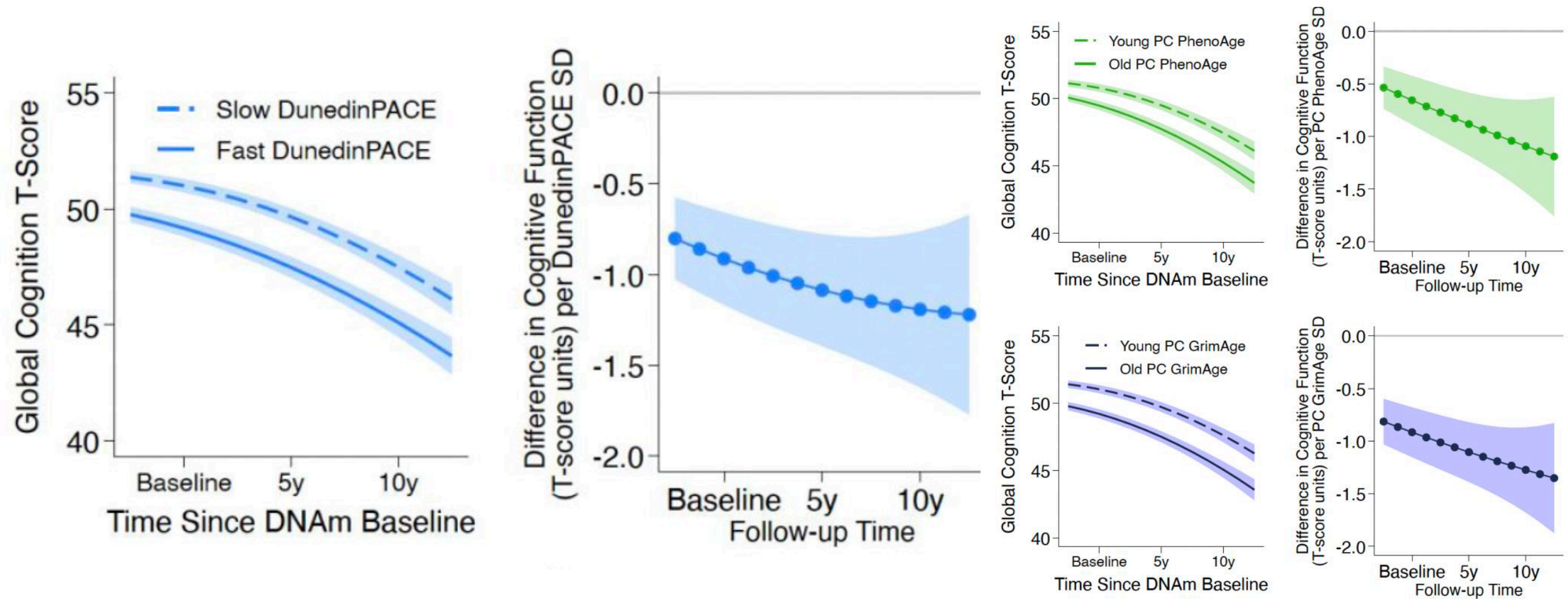
What is the role of biological aging in ADRD?



[Sugden et al. 2022 Neurology](#)



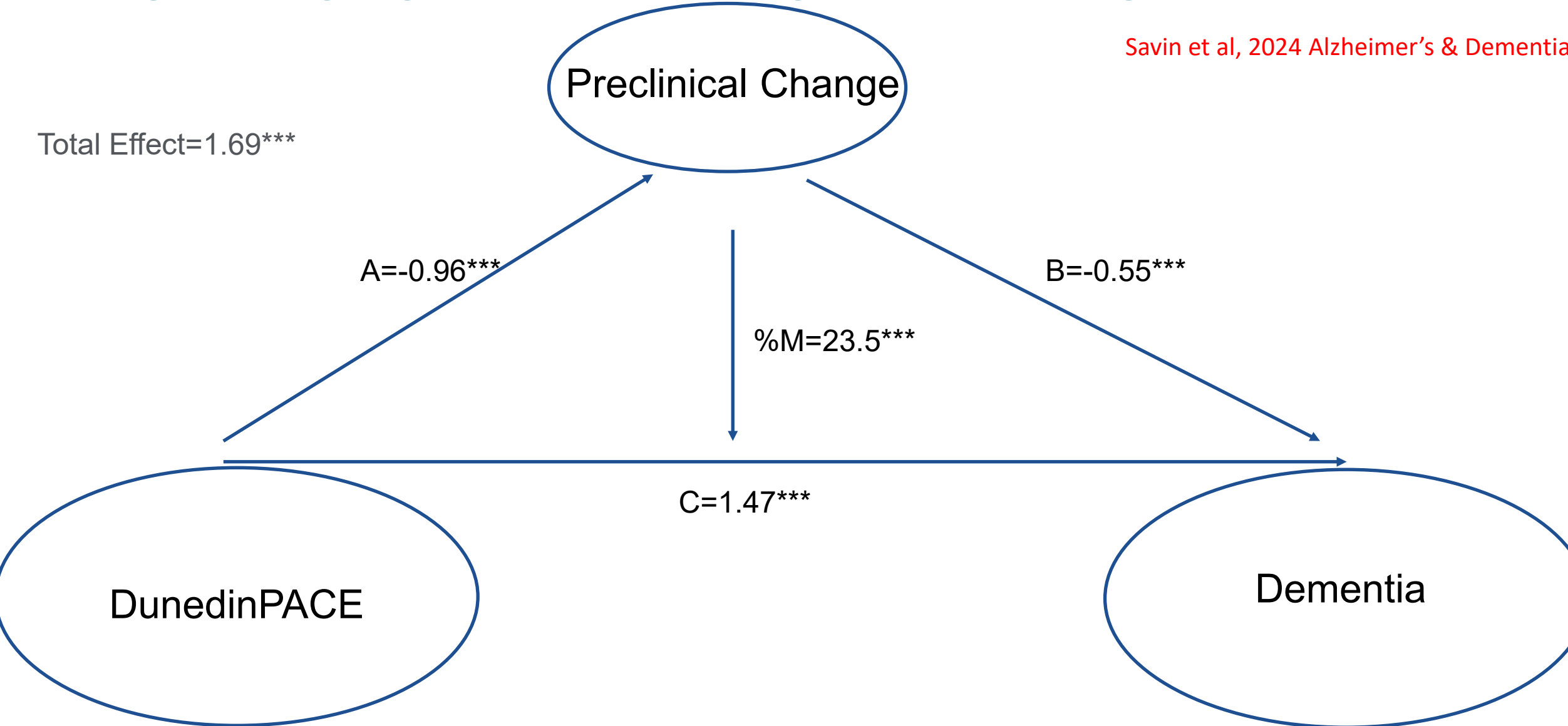
Biological aging predicts preclinical cognitive changes in ADRD



Savin et al, 2024 Alzheimer's & Dementia

Biological aging acts upon cognition through multiple paths

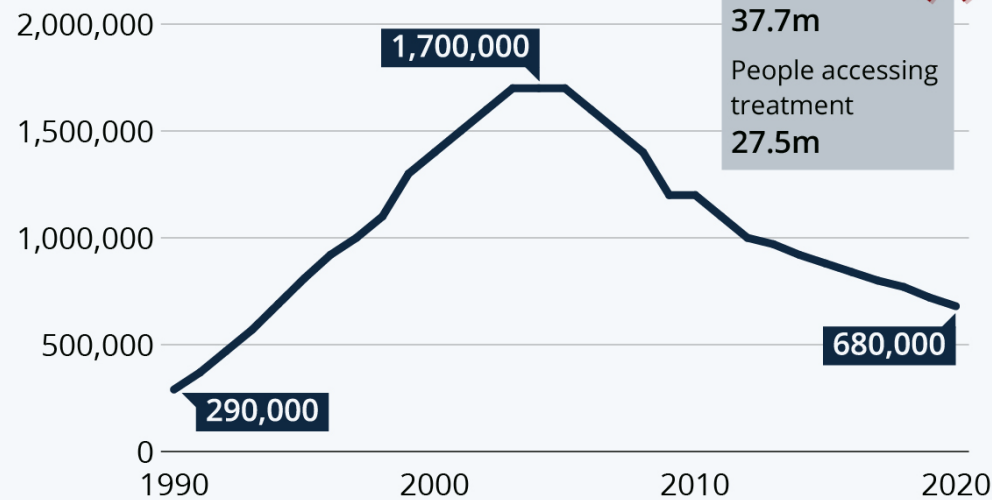
Savin et al, 2024 Alzheimer's & Dementia



The Greying of HIV

Almost 700,000 Still Die of AIDS/HIV Per Year

Estimated number of AIDS-related deaths worldwide from 1990 to 2020



Source: UNAIDS



statista

BY 2030, UP TO 70% OF PEOPLE WITH HIV WILL BE OVER THE AGE OF 50.

HIVAGE

GILEAD

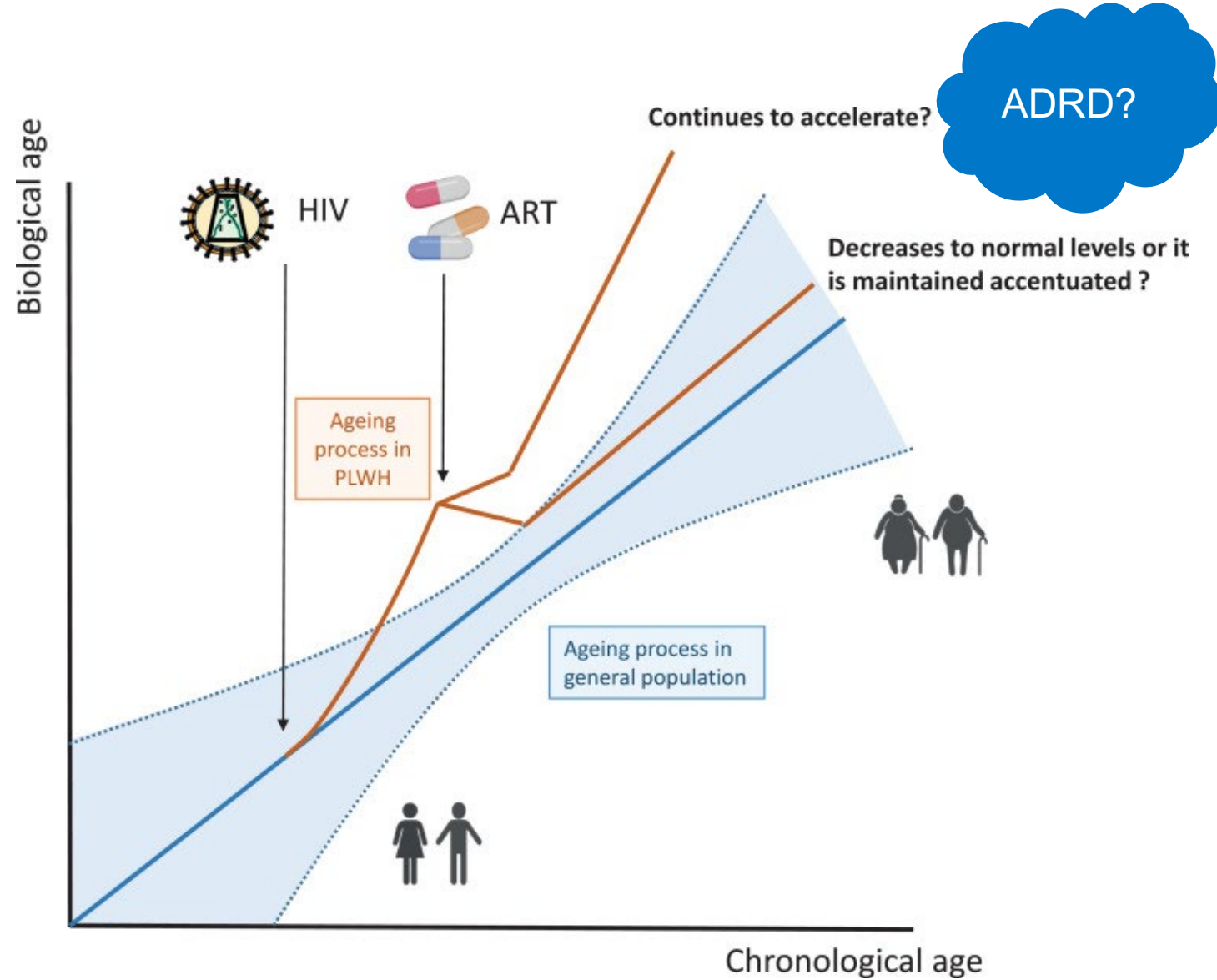
Stories from an Aging Pandemic





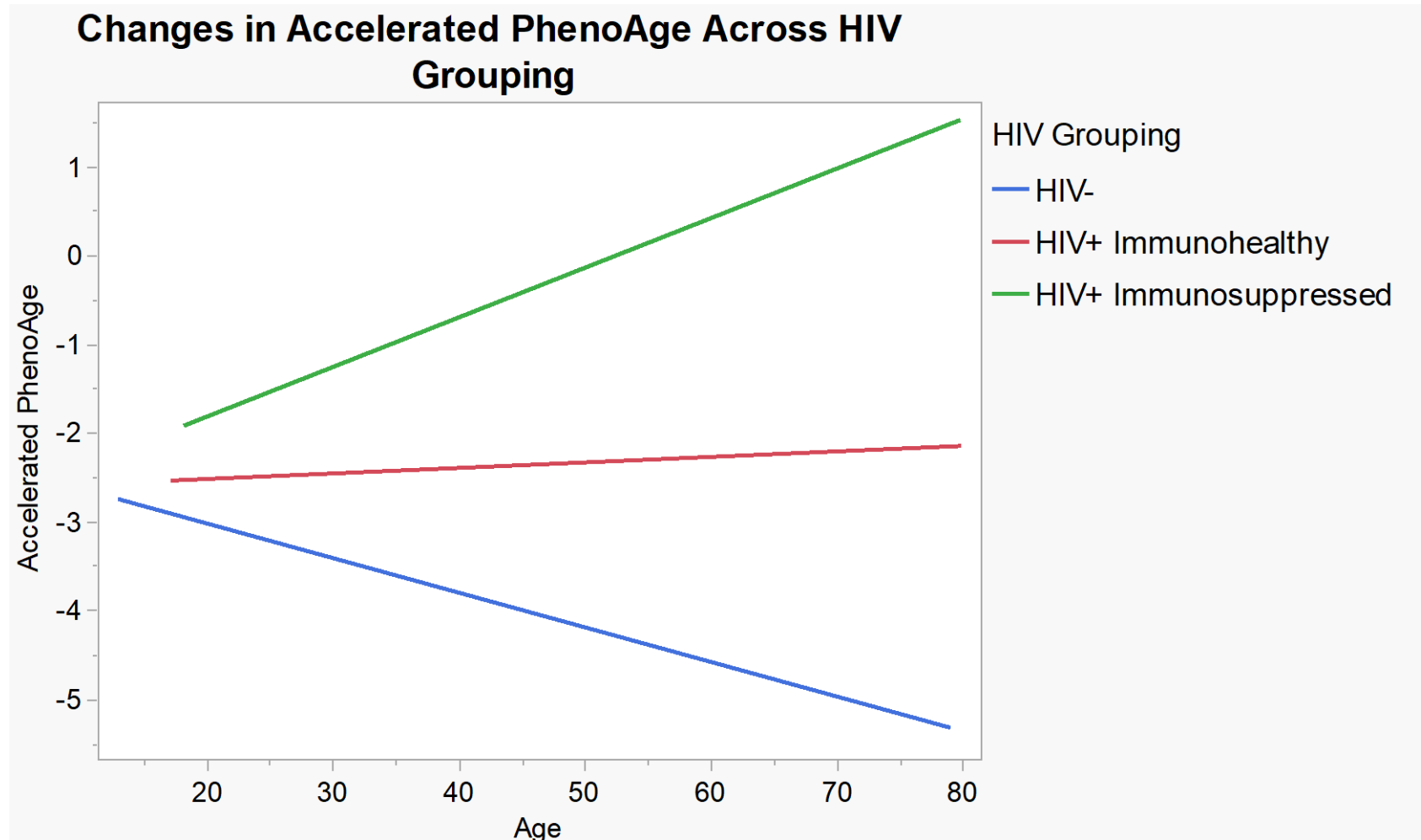
Postulated cause of ADRD in HIV

One possible explanation for the co-occurring nature of ADRD in HIV is accelerated biological aging, wherein molecular changes contribute to the progressive loss of system integrity and resilience capacity that in turn cause aging-associated conditions and multimorbidity (e.g., AD in HIV)





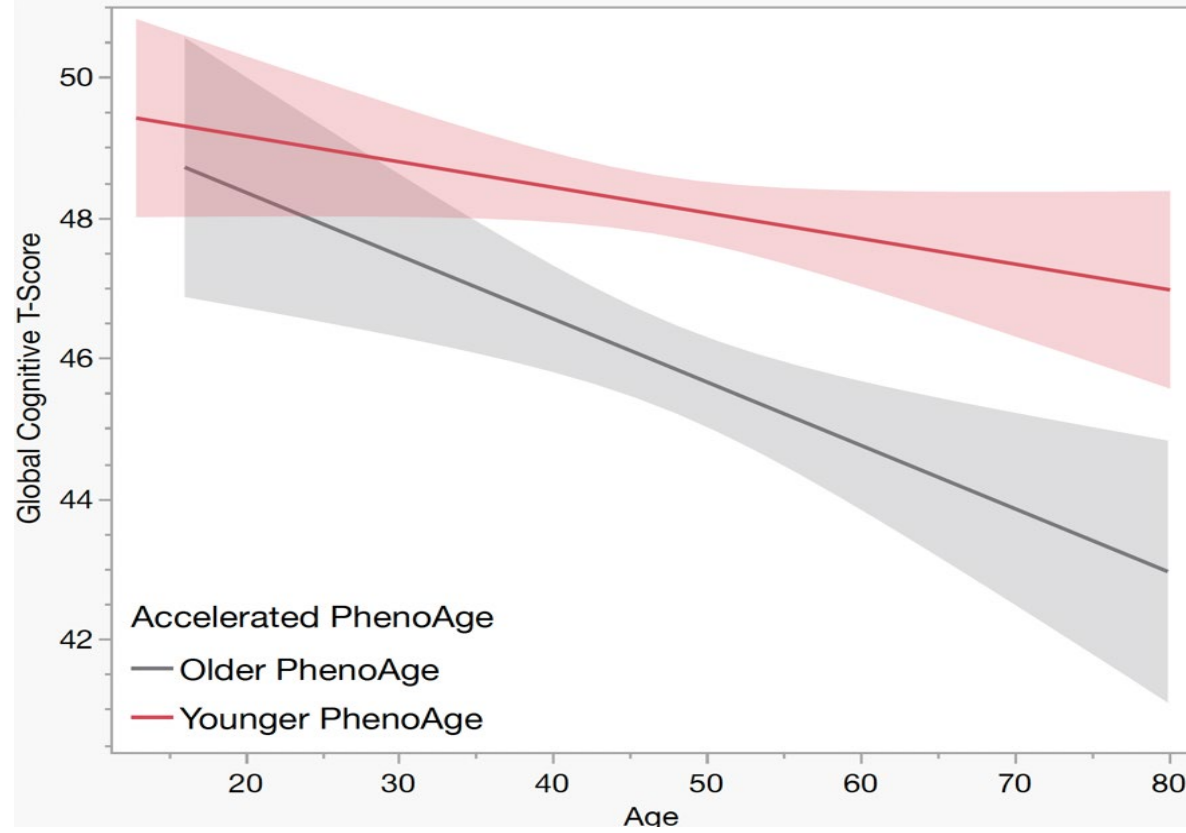
HIV Status Informs Pace of Biological Aging



Changes in Pace of Aging Coincides with Cognitive Decline



Figure 3: Older biological age coincides with faster cognitive decline



Acknowledgements – Questions?



Mentors

- Richard Armenta
- Daniel Belsky
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- Tedd Judd
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- CNS HIV Antiretroviral Therapy Effects Research (CHARTER)
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- SALUD Lab
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Supporters

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- West LA VA Medical Center

Biological aging acts upon cognition through multiple paths

	DunedinPACE			PhenoAge			GrimAge		
	HR	CI	p	HR	CI	p	HR	CI	p
<i>Base Model</i>									
Total Effect	1.69	1.29, 2.03	<0.001	1.30	1.07, 1.57	0.007	1.36	1.09, 1.70	<0.001
Direct Effect	1.47	1.81, 1.84	<0.001	1.20	0.99, 1.44	0.056	1.24	1.00, 1.54	0.049
Indirect Effect	1.10	1.05, 1.15	<0.001	1.08	1.04, 1.12	<0.001	1.10	1.05, 1.41	<0.001
% Mediated	23.5	11.8, 35.3	<0.001	33.2	10.1, 56.3	0.005	32.7	10.8, 54.6	0.003
<i>Adjusted for baseline cognition</i>									
Total Effect	1.42	1.21, 1.80	0.003	1.20	0.98, 1.47	0.066	1.18	0.93, 1.49	0.153
Direct Effect	1.35	1.07, 1.71	0.011	1.14	0.93, 1.39	0.195	1.13	0.89, 1.42	0.300
Indirect Effect	1.05	1.01, 1.09	0.010	1.05	1.02, 1.09	0.001	1.05	1.01, 1.08	0.008
% Mediated	16.1	2.3, 29.9	0.022	32.5	-1.1, 66.0	0.058	30.2	-10.6, 70.9	0.147