

Applicability of DNA methylation-based tools in a low-income, sub-Saharan African population: Malawi Longitudinal Study of Families and Health (MLSFH)

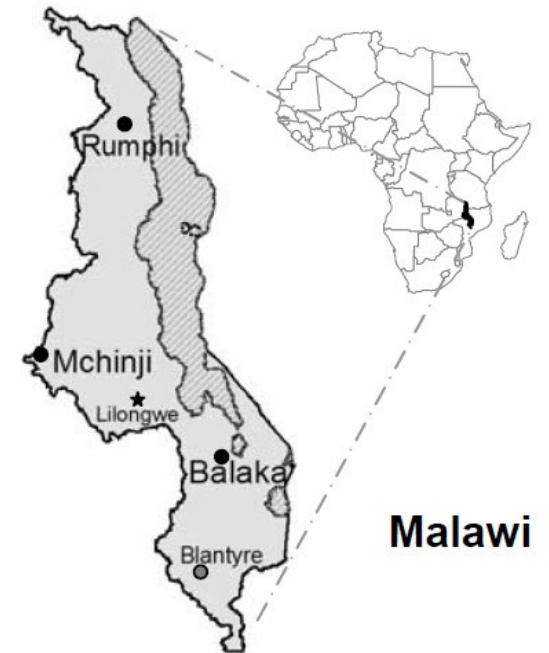
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April 9, 2025

Disclaimer:

The data presented herein are unpublished and part of ongoing research. This information is preliminary and subject to change as the research progresses. The associated manuscript is currently in preparation and has not yet undergone peer review. Any citation or use of this data should be done with caution and appropriate acknowledgment. Please contact the authors for permission before referencing or distributing this material.

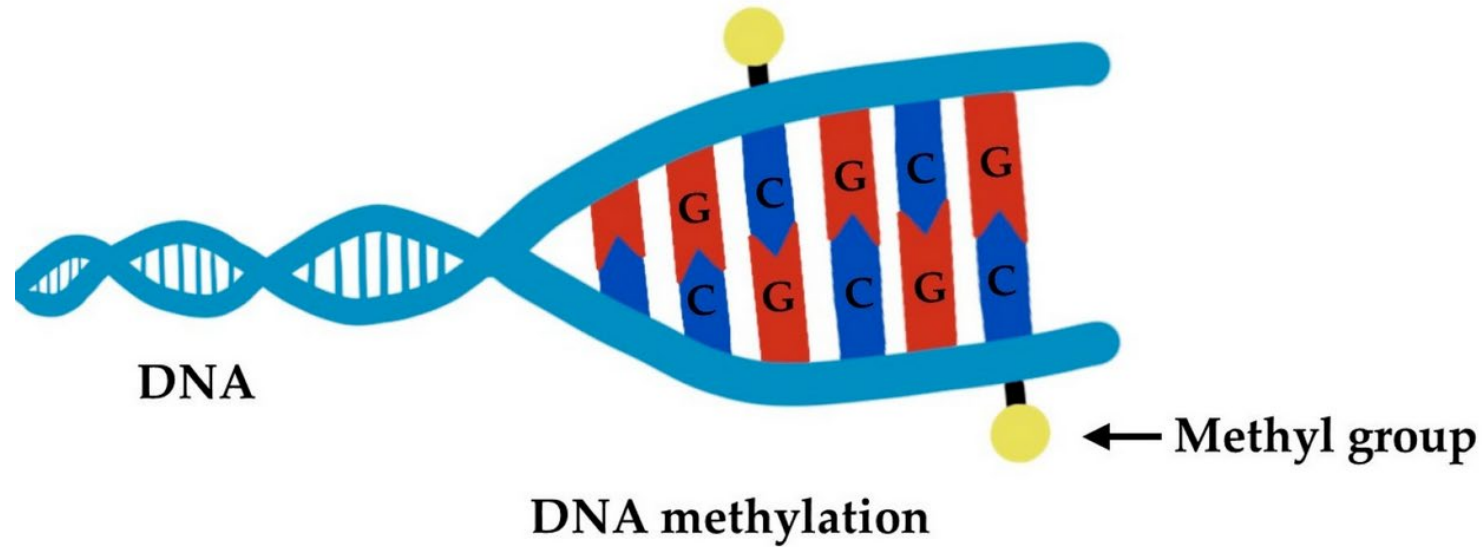
Cohort: Malawi Longitudinal Study of Families and Health

- Extensive longitudinal data
 - 1998 - current
 - socioeconomic context
 - physical and mental health
 - cognitive function and more.
- ~ 3500 dried blood spots (DBS) collected for DNA methylation profiling
- 49 pilot samples (46-90 years old)



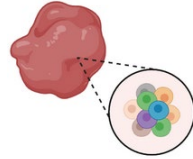
Refresher: DNA methylation

- Attachment of a methyl group at a cytosine
- Influenced by genetics, developmental stages, tissues, exposures, health conditions and etc.



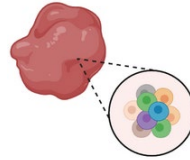
A rapidly growing area of research: DNA methylation-based tools/biomarkers

- Cell type deconvolution

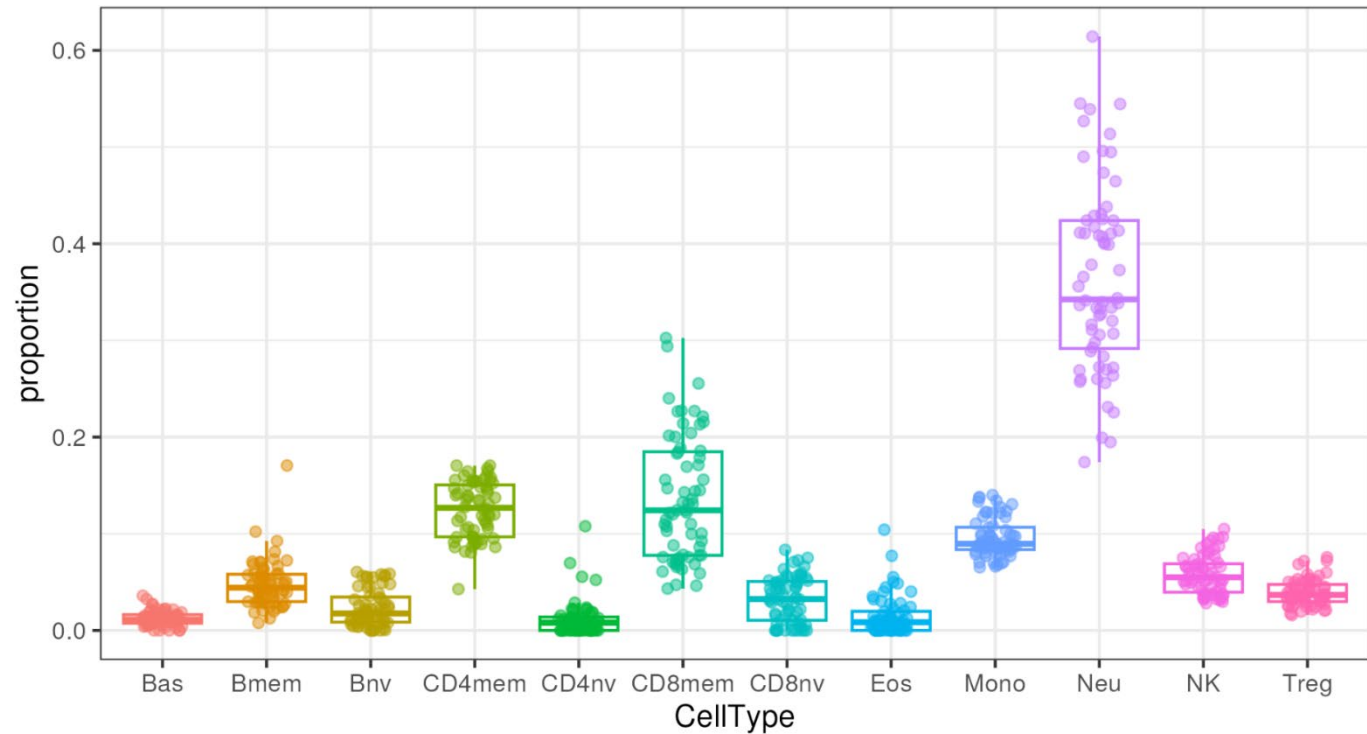


A rapidly growing area of research: DNA methylation-based tools/biomarkers

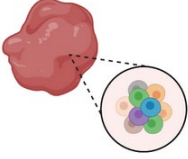
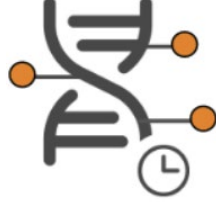
- Cell type deconvolution



- Predicted 12 immune cell types proportions in blood

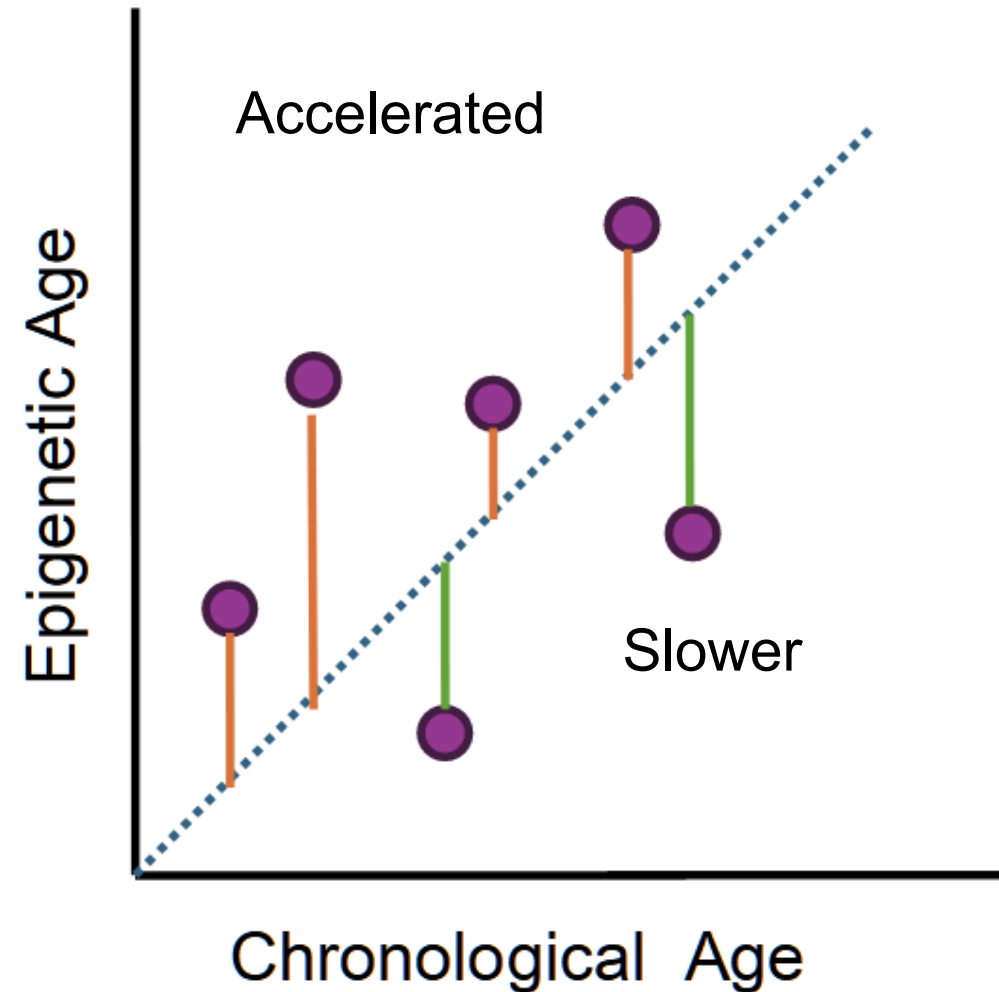


A rapidly growing area of research: DNA methylation-based tools/biomarkers

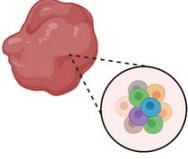
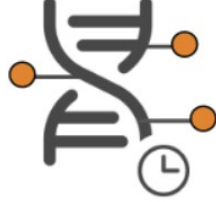

- Cell type deconvolution 
- Biomarkers of aging: Epigenetic clocks 

Epigenetic Clocks

- DNA Methylation at selected CpGs is used to make a prediction of epigenetic (biological) age
- Three generations of clocks
- Epigenetic Age Acceleration (EAA)



A rapidly growing area of research: DNA methylation-based tools/biomarkers

- Cell type deconvolution 
- Biomarkers of aging: Epigenetic clocks 
- Life style biomarker predictors 

Aims

Systematically test the applicability of DNAm-based tools on MLSFH pilot samples (n=49)

- for upcoming ~3500 samples

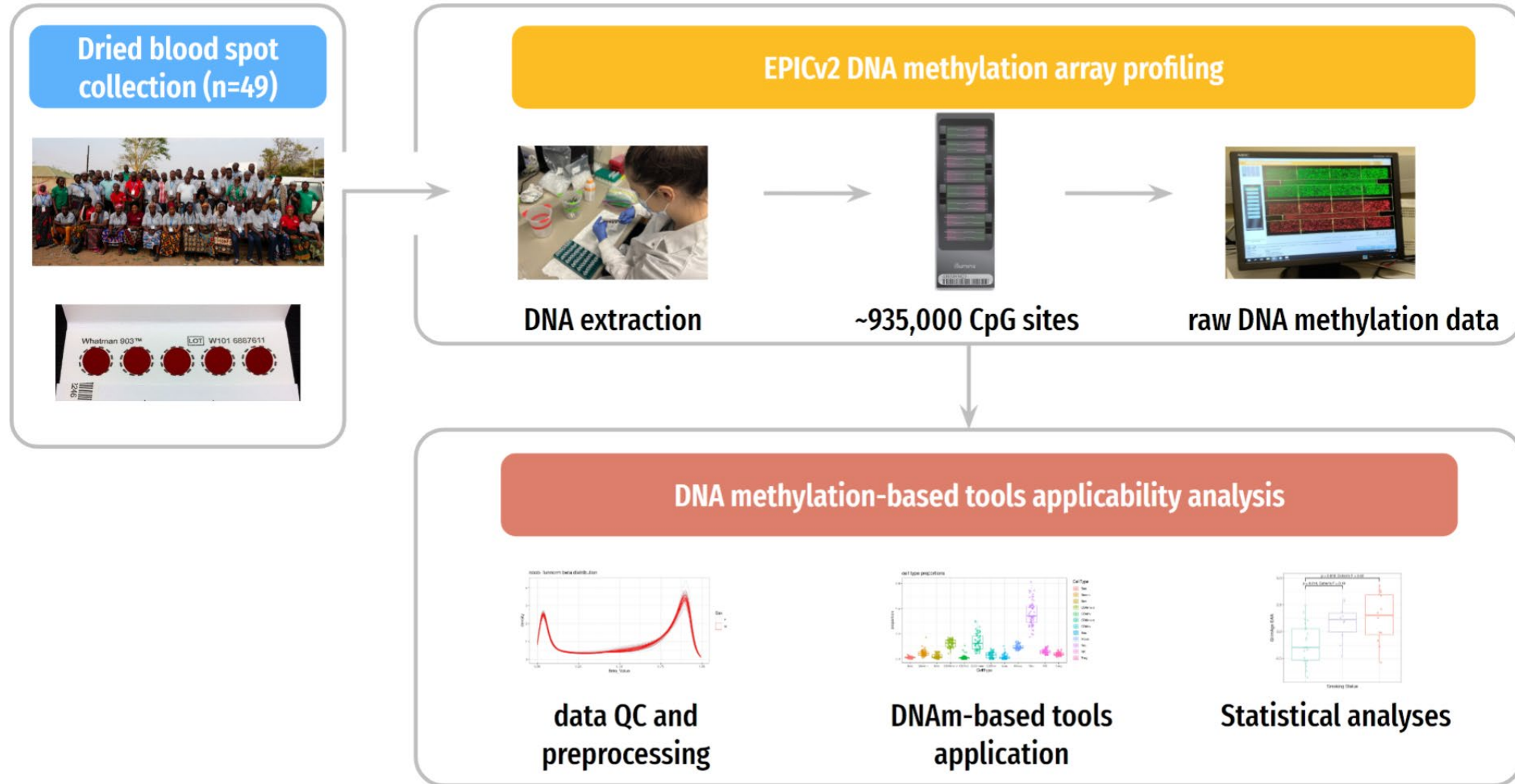
Aim 1: Collection conditions and DNAm variation

Aim 2: Cell type deconvolution

Aim 3: Epigenetic clocks and EAA

Aim 4. Life style biomarker predictors

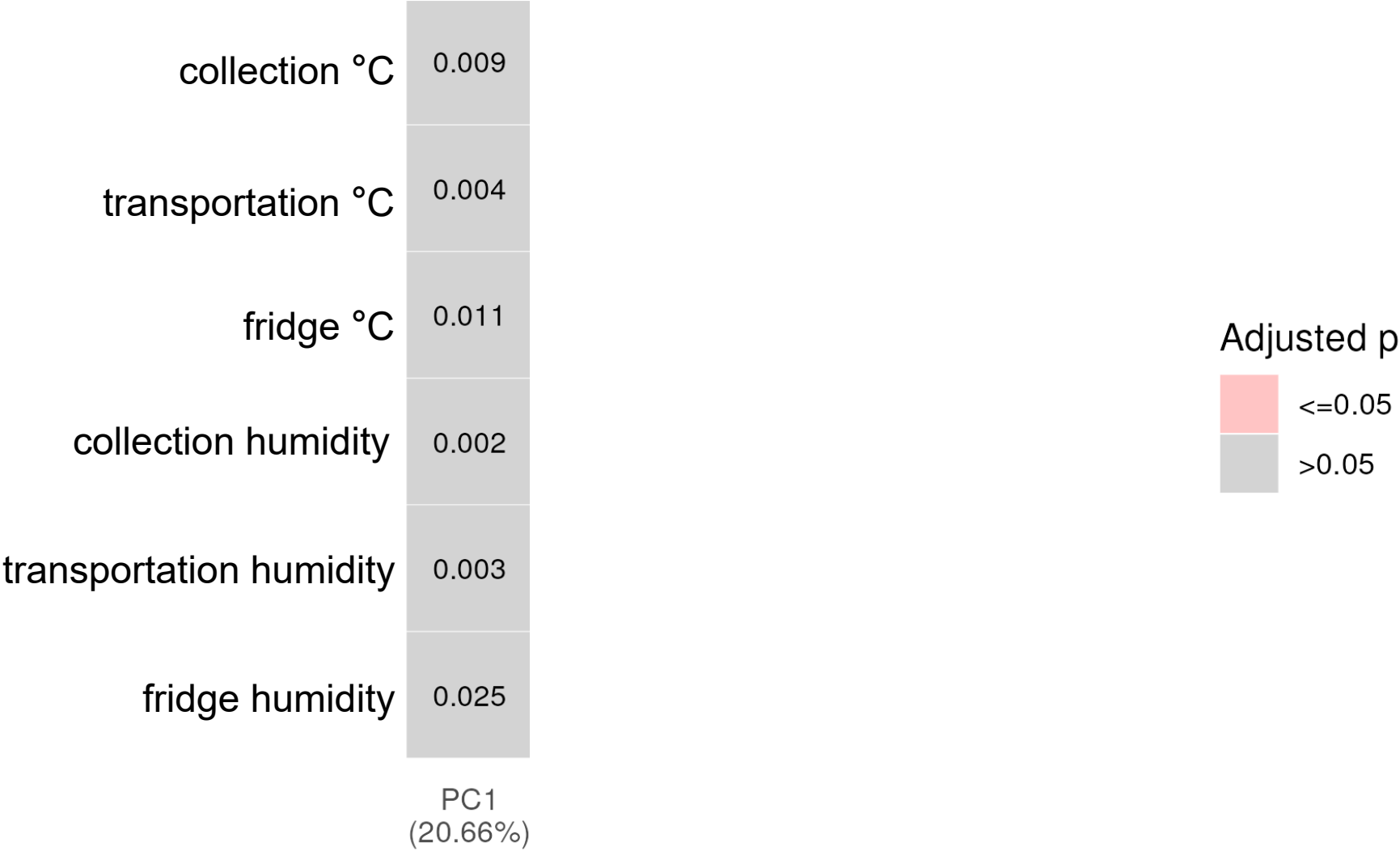
Pilot sample analysis pipeline



Aim 1

To determine whether sample collection and storage environmental conditions contribute to DNA methylation (DNAm) variation.

Principal component analysis with collection and storage conditions



Environmental differences in bio-sampling did not significantly contribute to the observed DNAm variation.

collection °C	0.009	0	0.004	0.001	0.046	0.028
transportation °C	0.004	0	0.036	0.019	0.005	0.034
fridge °C	0.011	0.015	0.03	0.016	0	0.04
collection humidity	0.002	0.01	0.016	0.001	0.028	0.035
transportation humidity	0.003	0	0.01	0.011	0.008	0.014
fridge humidity	0.025	0	0.049	0.019	0.002	0
	PC1 (20.66%)	PC2 (15.65%)	PC3 (5.16%)	PC4 (3.76%)	PC5 (2.53%)	PC6 (2.39%)

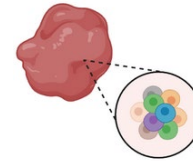
Adjusted p

≤0.05

>0.05

Aim 2

Cell type deconvolution



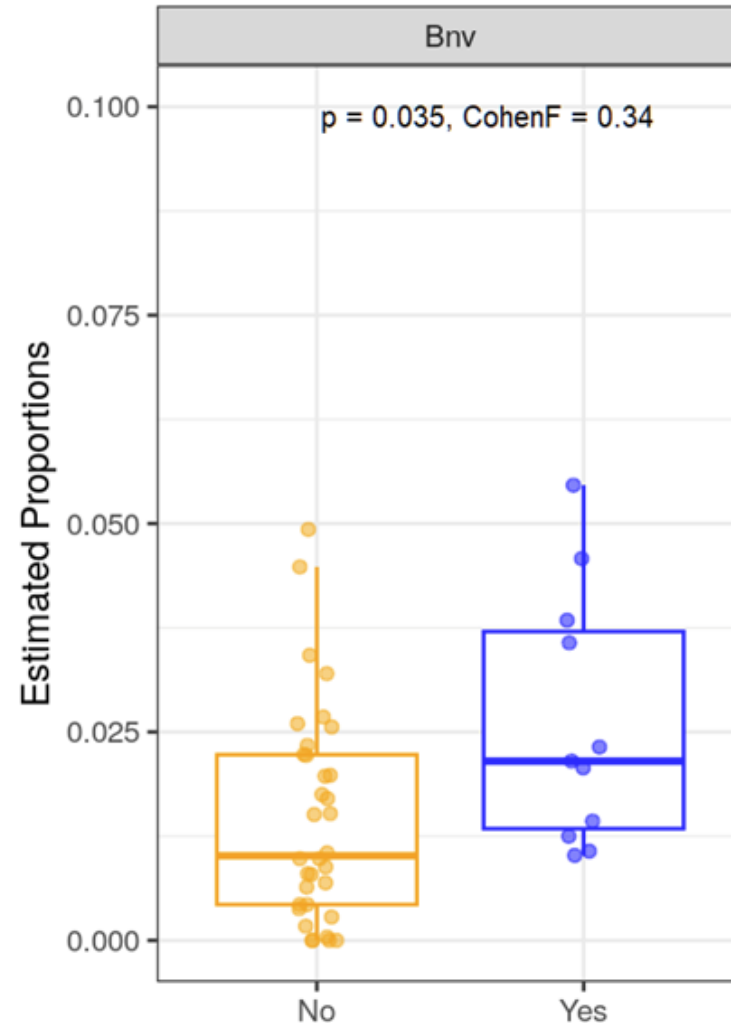
Main driver of DNAm variation is predicted cell type proportions as expected

Bas	0.121	0.017	0.293	0.104	0.004	0.009
Bmem	0.317	0.035	0.029	0.016	0.029	0.064
Bnv	0.033	0.049	0.308	0.013	0.06	0
CD4mem	0.311	0.001	0.078	0.004	0.008	0.011
CD4nv	0.026	0.007	0.205	0.116	0	0.001
CD8mem	0.73	0.025	0	0	0.001	0.002
CD8nv	0.178	0.009	0.373	0.19	0.009	0.013
Eos	0.008	0.074	0.013	0.028	0.062	0.048
Mono	0.099	0.002	0.015	0.007	0.022	0.051
Neu	0.52	0.112	0.188	0.003	0.005	0.001
NK	0.022	0.148	0.034	0.009	0	0.005
Treg	0.353	0.038	0.014	0.077	0.02	0.002
	PC1 (20.66%)	PC2 (15.65%)	PC3 (5.16%)	PC4 (3.76%)	PC5 (2.53%)	PC6 (2.39%)

Adjusted p

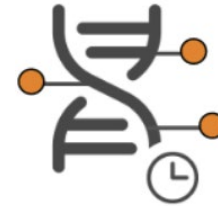
- ≤0.05
- >0.05

Increase in predicted naïve B cell in HIV undergoing ART compared to non-HIV



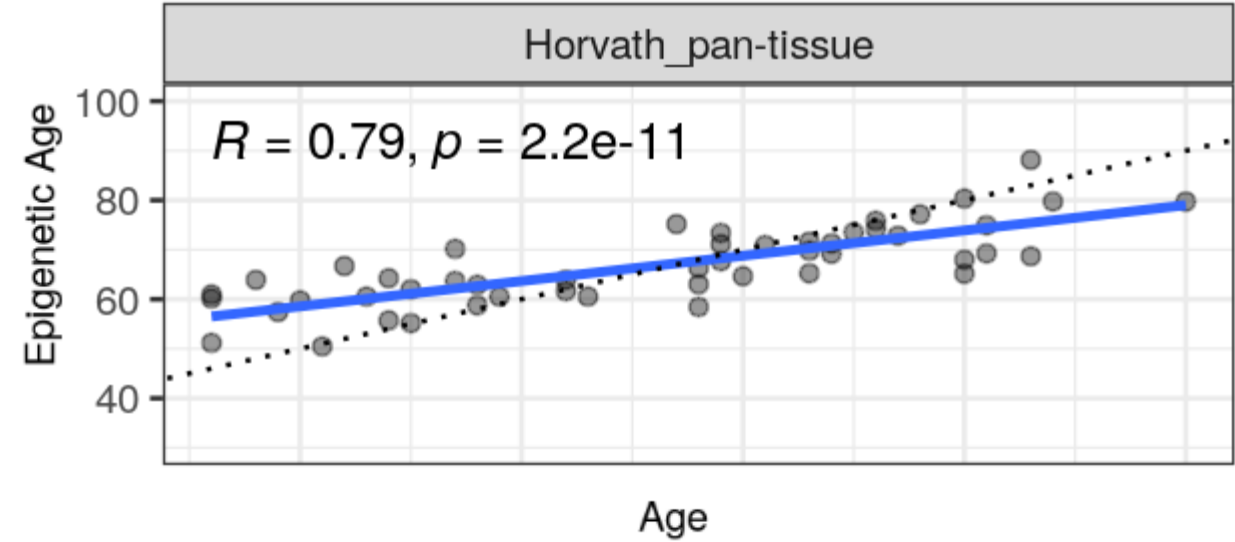
Aim 3

Epigenetic clocks and
Epigenetic age acceleration (EAA)



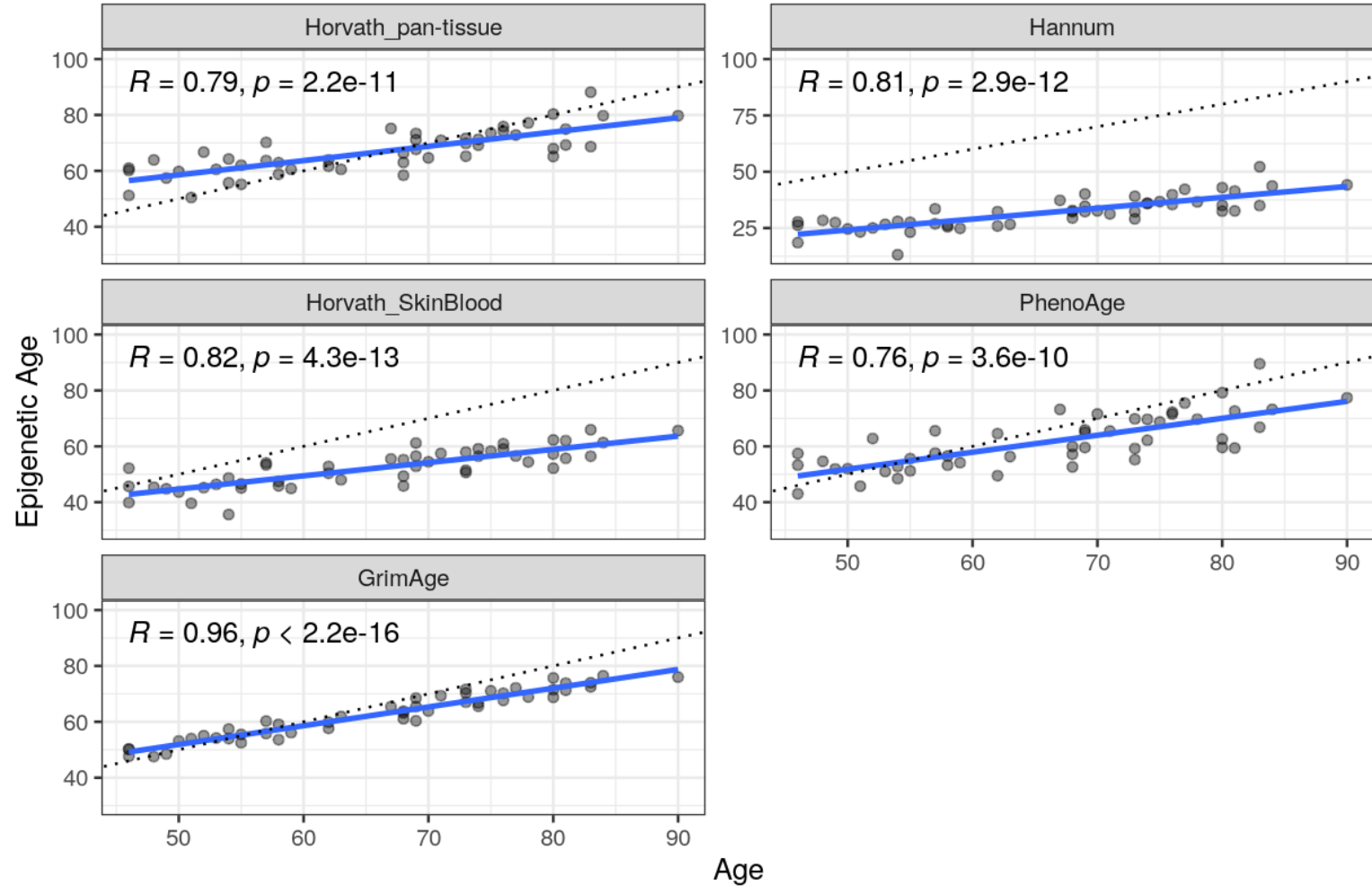
Epigenetic clocks showed high correlation with chronological age

	Pearson correlation (r)	Median Absolute Error (MdAE)
Horvath pan-tissue	0.79	4.92

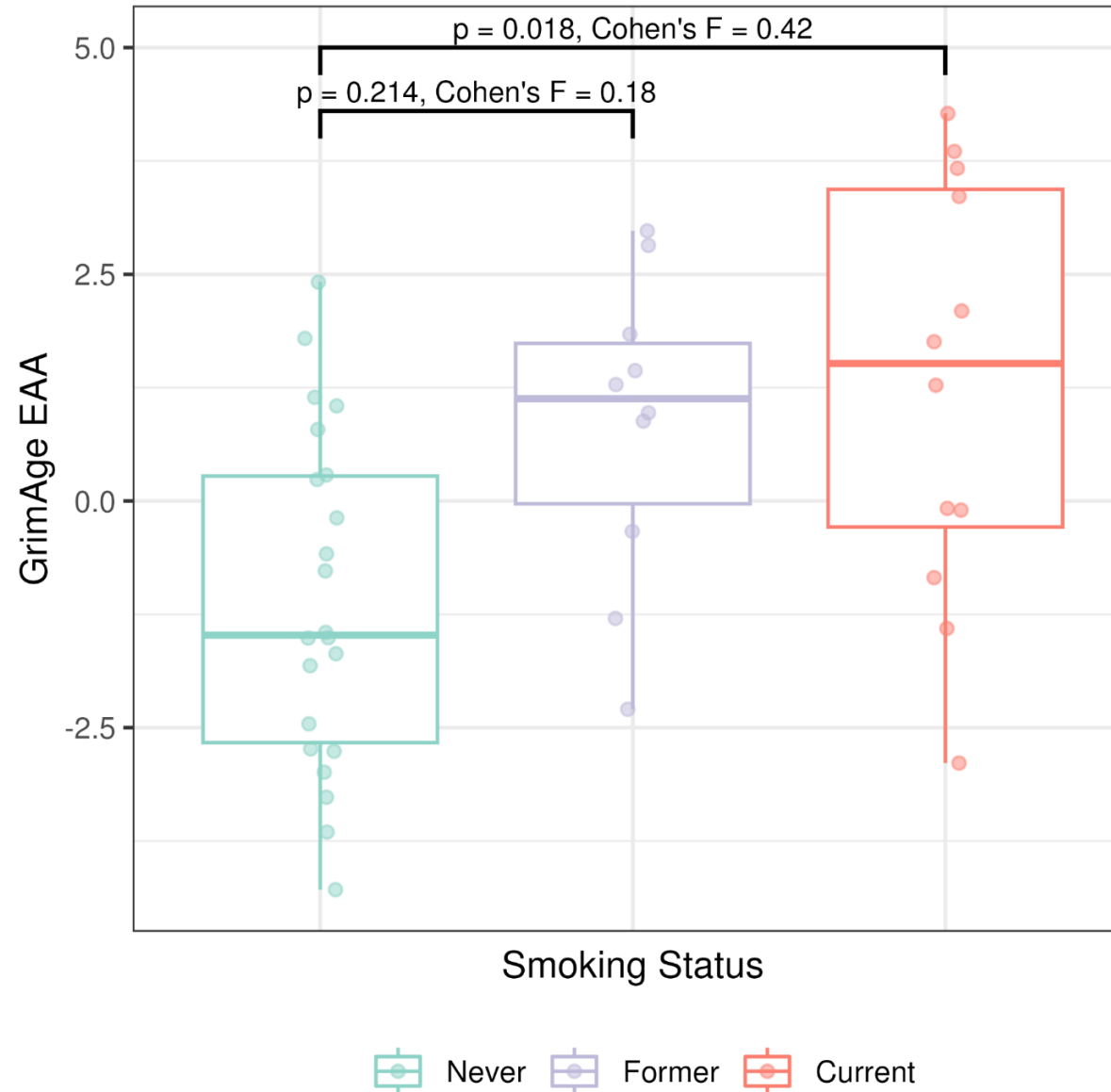


Epigenetic clocks showed high correlation with chronological age

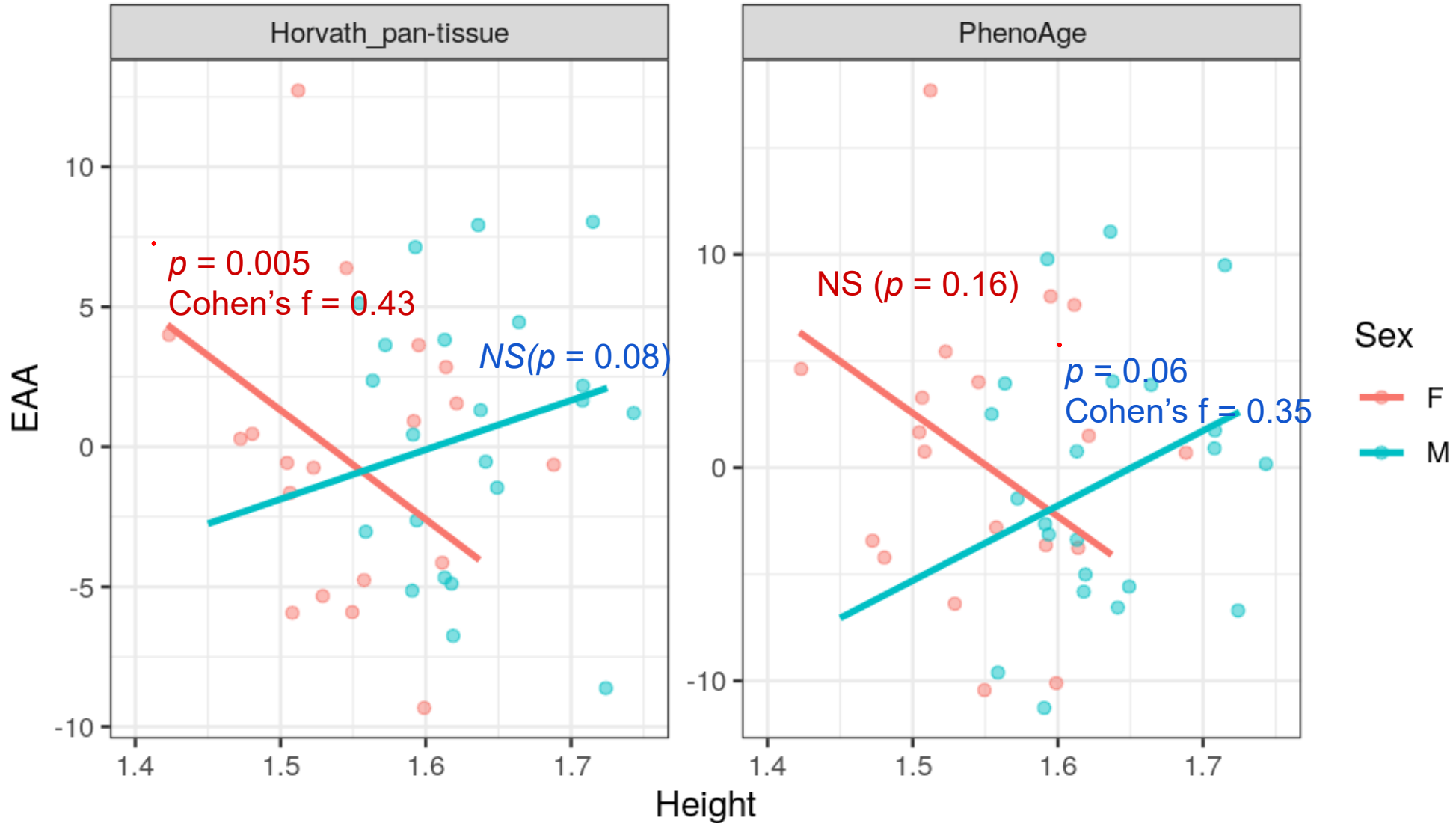
	r	MdAE
Horvath pan-tissue	0.79	4.92
Hannum	0.81	35.19
Horvath Skin and Blood	0.82	14.89
PhenoAge	0.76	6.2
GrimAge	0.96	4.17



GrimAge EAA is associated with reported smoking status



Sex specific EAA associations in anthropometric measurements (sex stratified analysis)

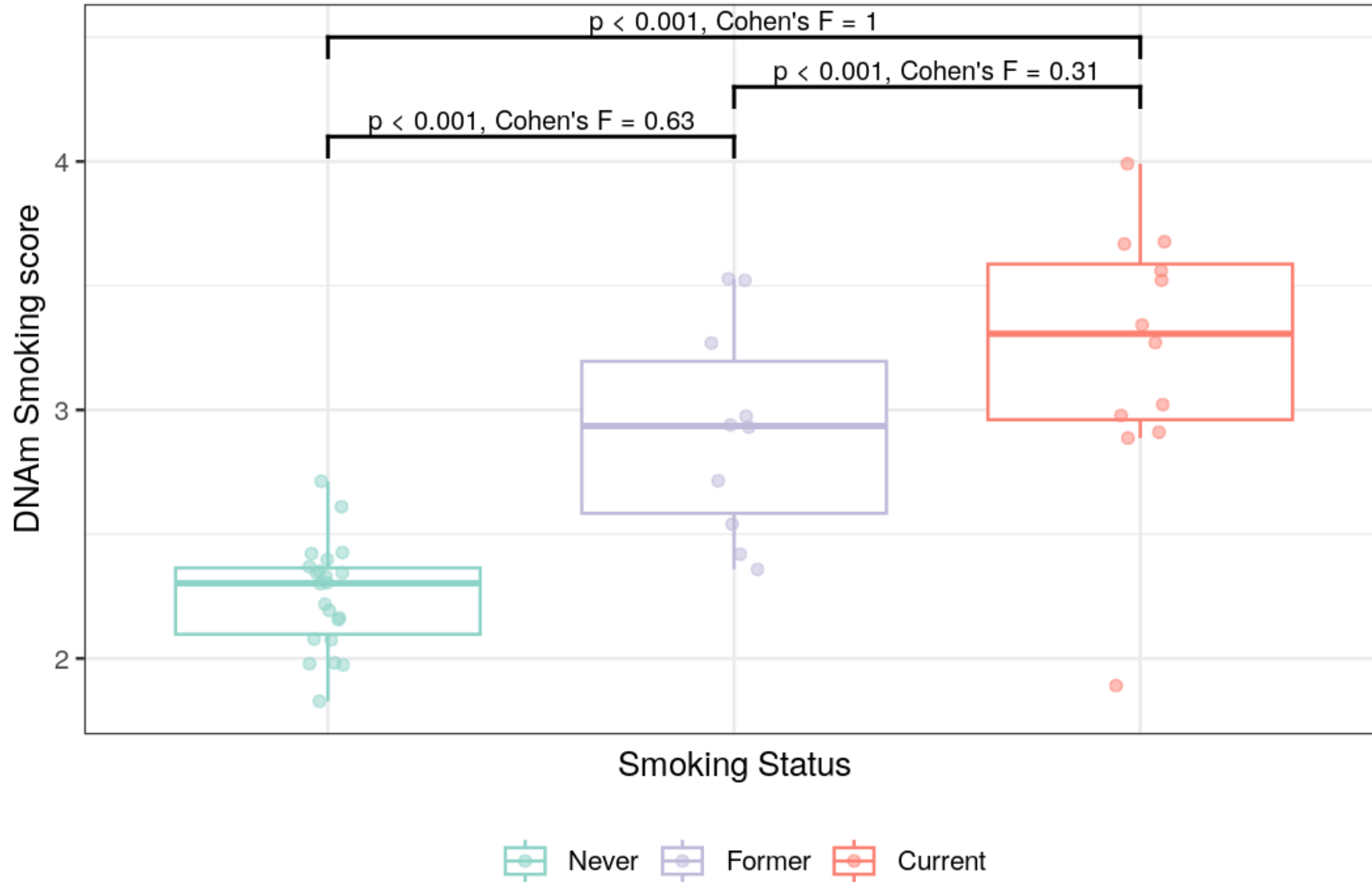


Aim 4

Life style biomarker predictors



Predicted smoking scores is highly correlated with reported status



Conclusion

DNAm-based tools (epigenetic clocks, cell type deconvolution, and biomarker predictors), are applicable to this understudied low-income population.

- able to detect previously established association between DNAm predicted biomarkers and biological variables



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**MLSFH: A GLOBAL
COLLABORATION**

Thank you!

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