The 2023 NIA Biomarker Network Annual Meeting

Using Epigenetic Clocks in Analysis

Eileen Crimmins, Jessica Faul, Bharat Thyagarajan, Colter Mitchell,
Cathal McCrory, Aisling O'Halloran, Albert Higgins-Chen, Giovanni Fiorito

Epigenetic Clocks

Three Generations of Clocks

Gen 1
Trained on Age

E.g.,
Horvath Clock
Hannum Clock

Gen 2
Trained on Mortality and Health

E.g.,
GrimAge
PhenoAge

Gen 3
Trained on Change in Health Indicators
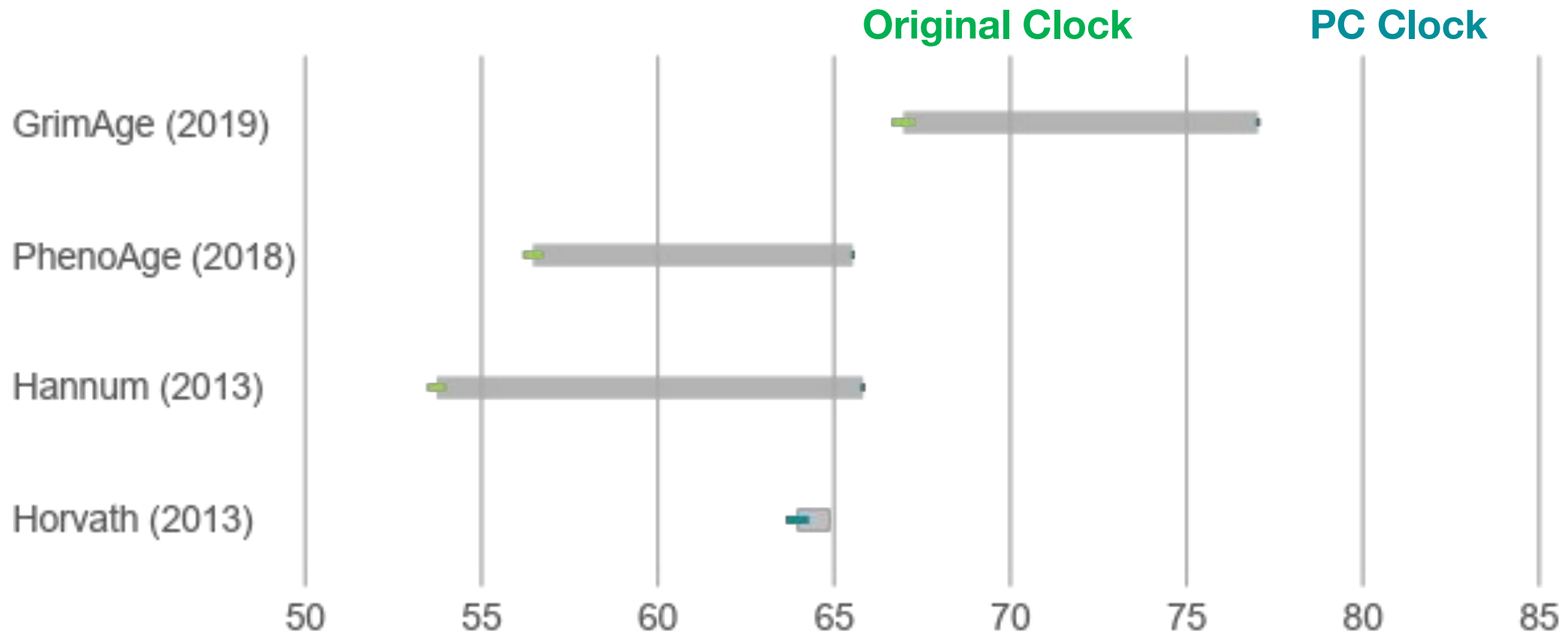
E.g.,
Dunedin

Epigenetic Clocks

New Cohort of Clocks

Reduce effects of unreliability of CpG probes

E.g., Principal Component Clocks (Higgins-Chen,…, Levine); DunedinPACE
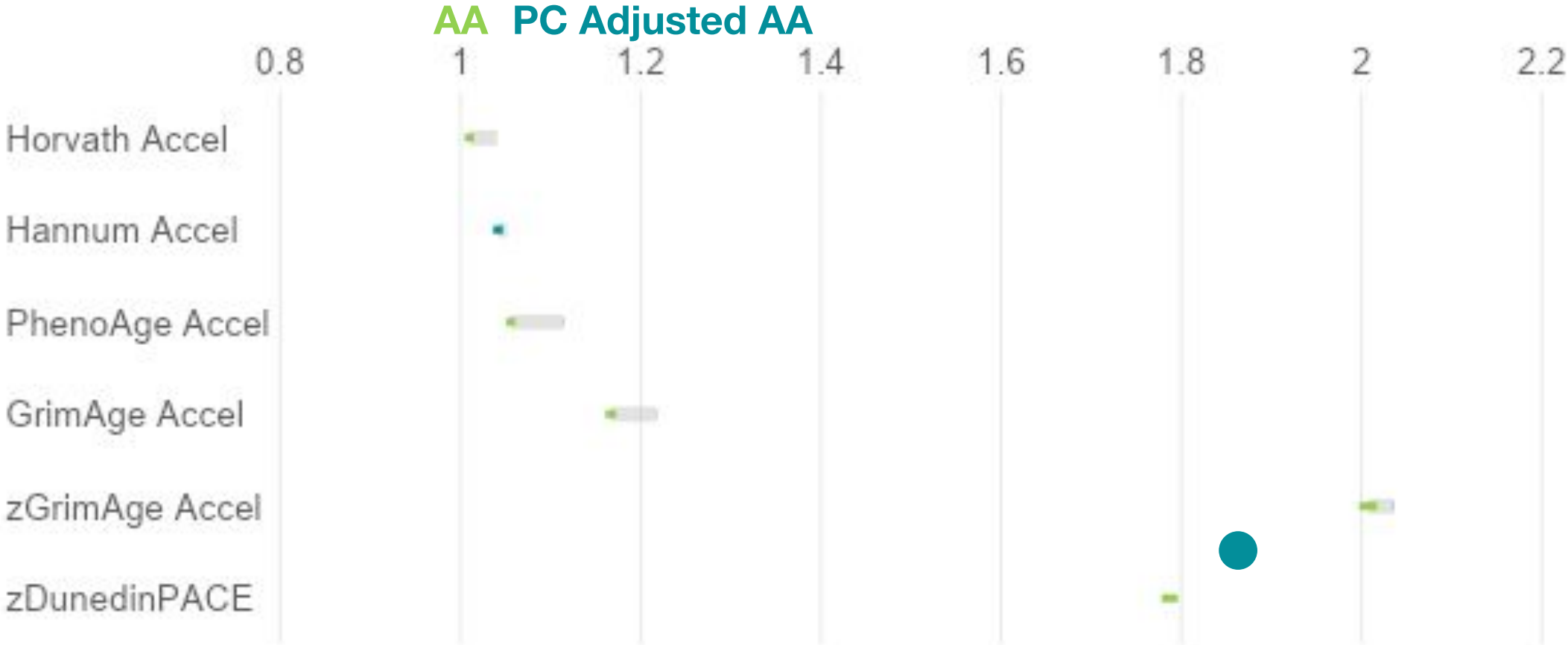
Do PC Clocks Change the Estimates of Epigenetic Age?
Mean Epigenetic Age for HRS Sample with 4 Original Clocks and Principal Component Clocks

Does the Relationship of Epigenetic Age to MORTALITY Change with the Original Acceleration (AA) vs PC Adjusted Age Acceleration?
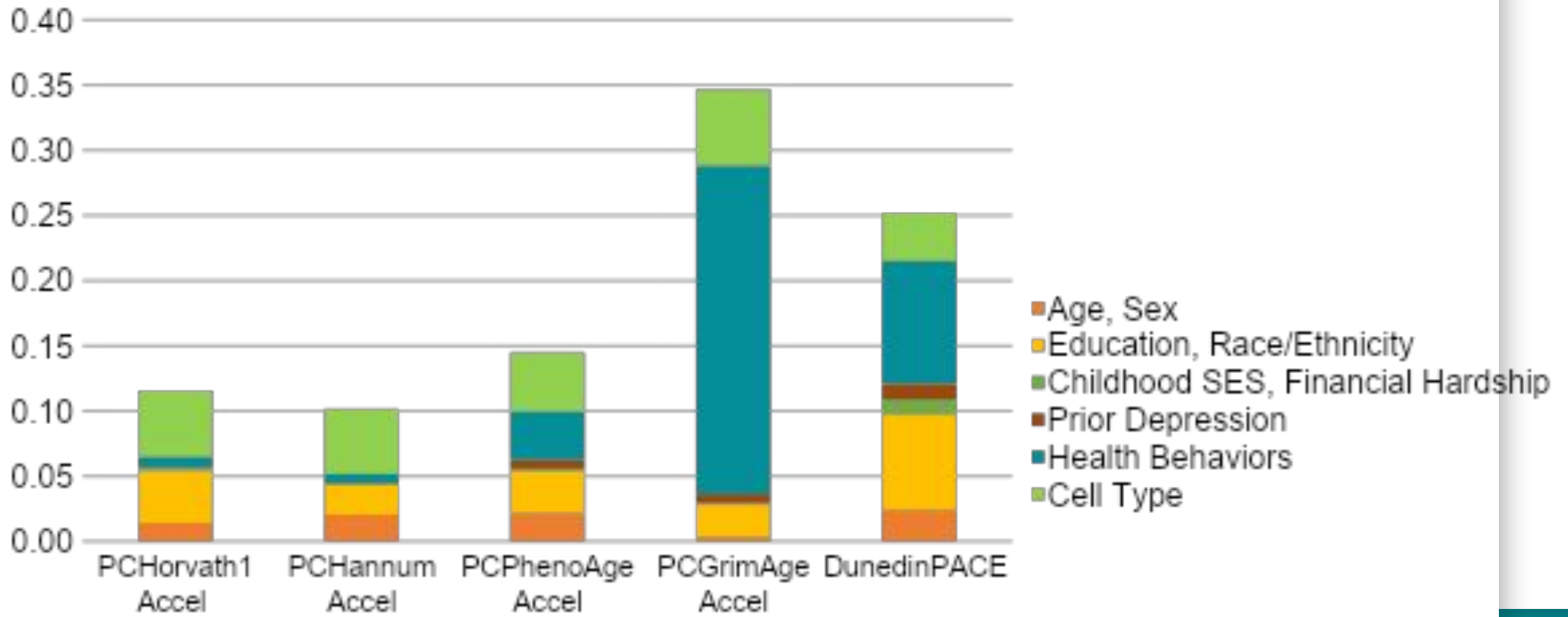
Odds Ratios when Predicting Mortality

Predictions of 3 other Health Outcomes using Epigenetic Age Acceleration (AA) vs PC Adjusted Age Acceleration

Coefficients when Predicting 3 Health Outcomes
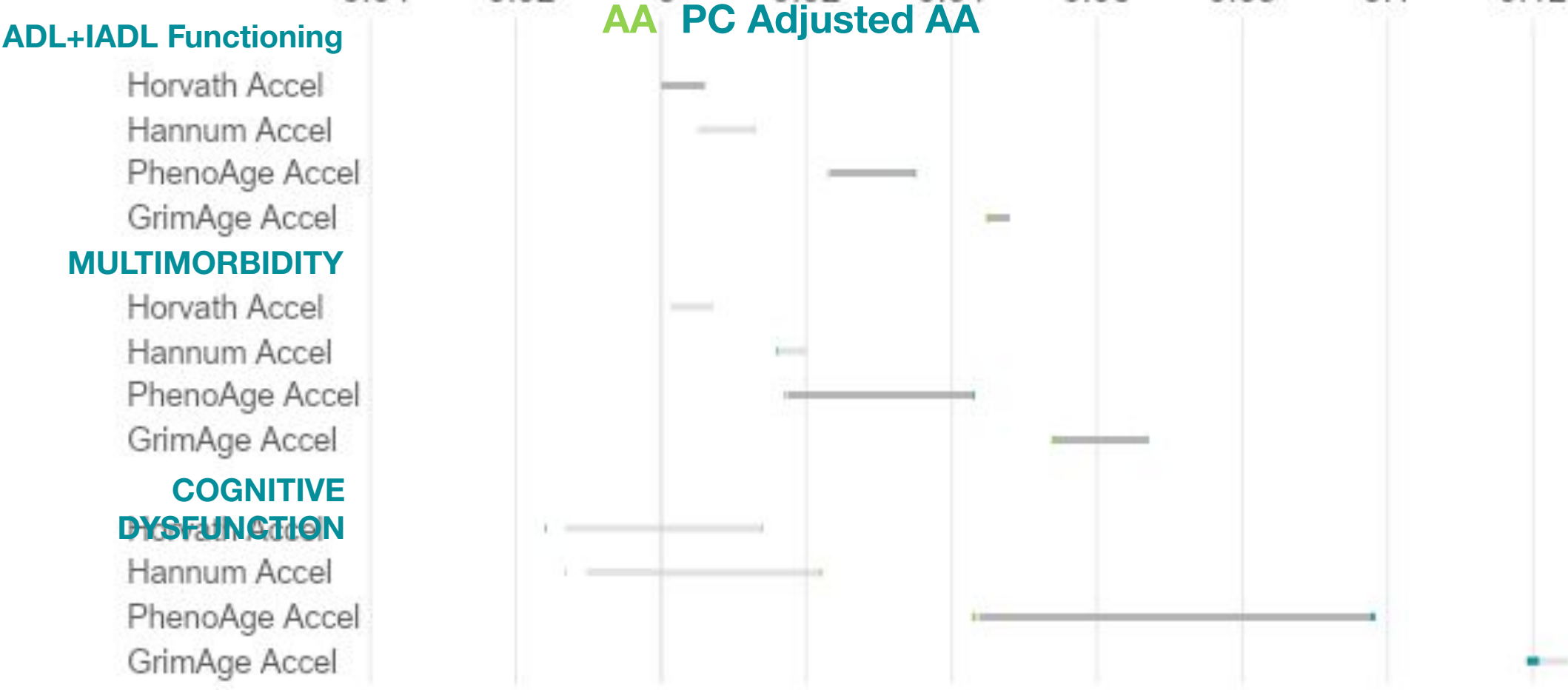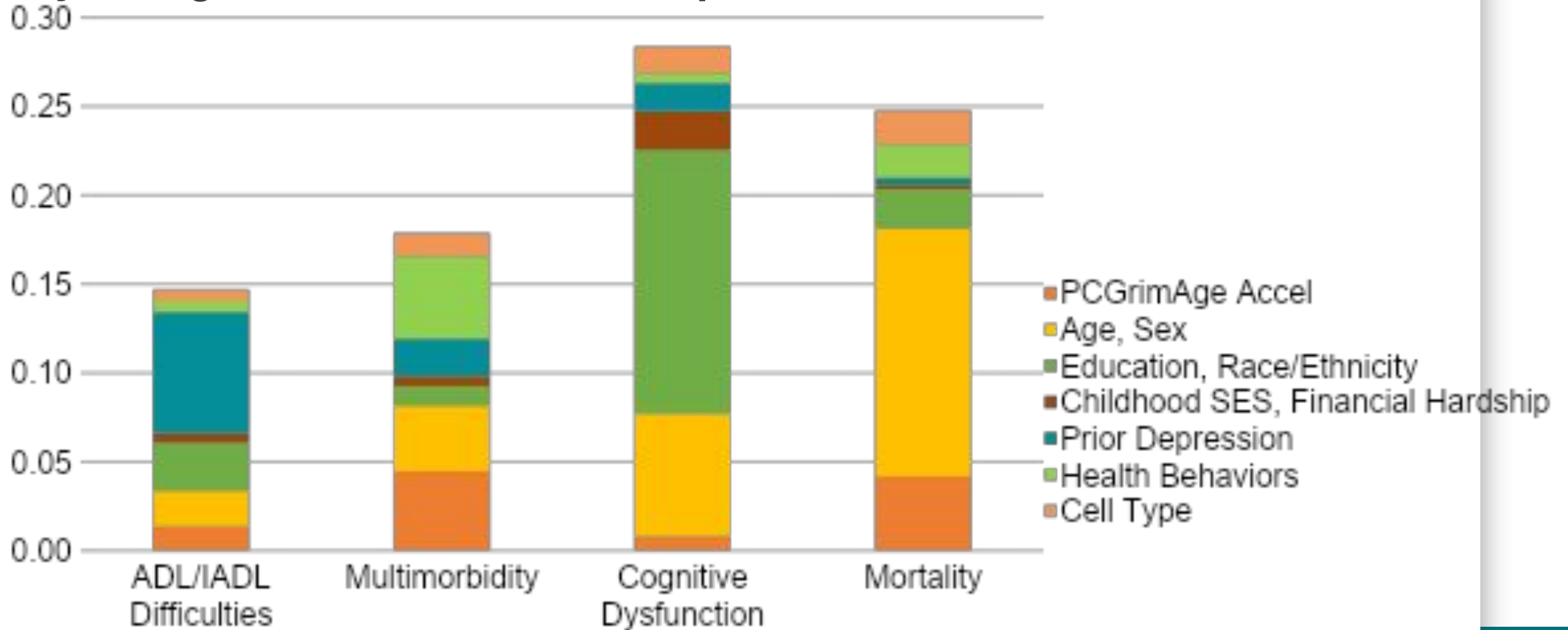
Predictors of Epigenetic Age Differ by Epigenetic Measure: R^2 Decomposition for 5 Measures of Epigenetic Age Acceleration

Legend:
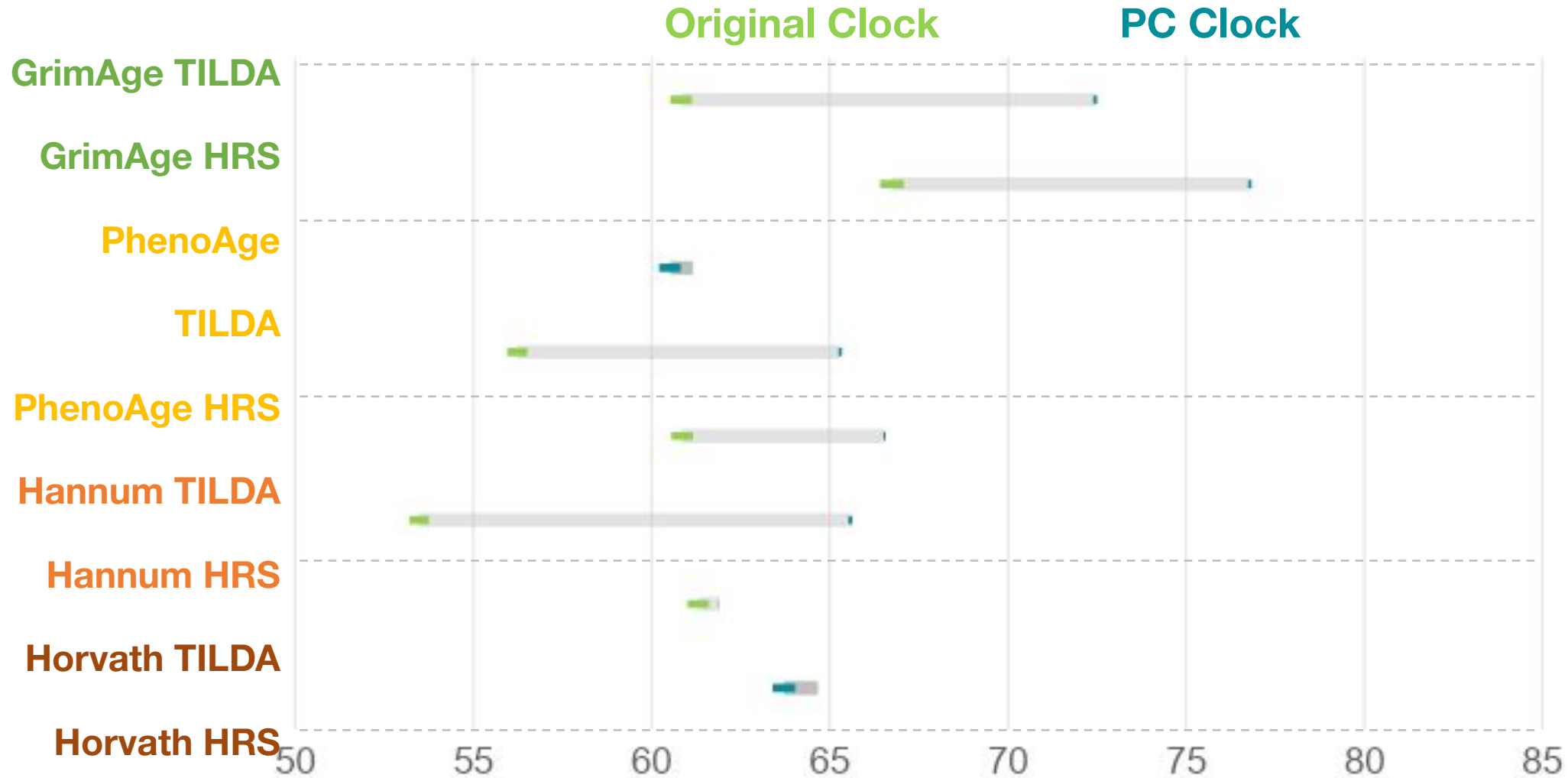- Age, Sex
- Education, Race/Ethnicity
- Childhood SES, Financial Hardship
- Prior Depression
- Health Behaviors
- Cell Type

X-axis categories: PCHorvath1 Accel, PCHannum Accel, PCPhenoAge Accel, PCGrimAge Accel, DunedinPACE

Y-axis: 0.00 to 0.40

Importance of Epigenetic Age Varies with Health Outcome: Prediction of 4 Health Outcomes by GrimAge and Demographic, Social, Psychological Variables: R^2 Decomposition for 4 Health Outcomes

Legend:
- PCGrimAge Accel
- Age, Sex
- Education, Race/Ethnicity
- Childhood SES, Financial Hardship
- Prior Depression
- Health Behaviors
- Cell Type

Categories: ADL/IADL Difficulties, Multimorbidity, Cognitive Dysfunction, Mortality
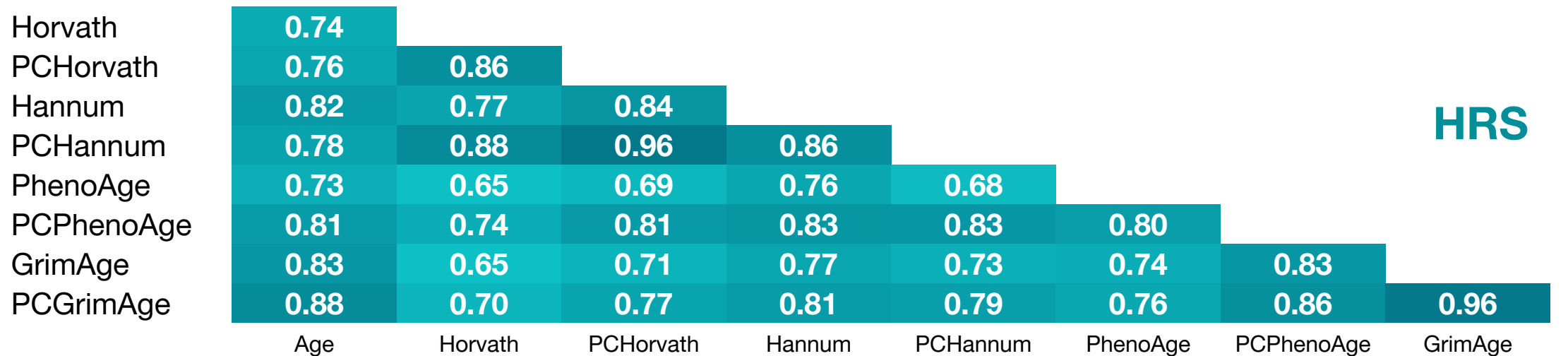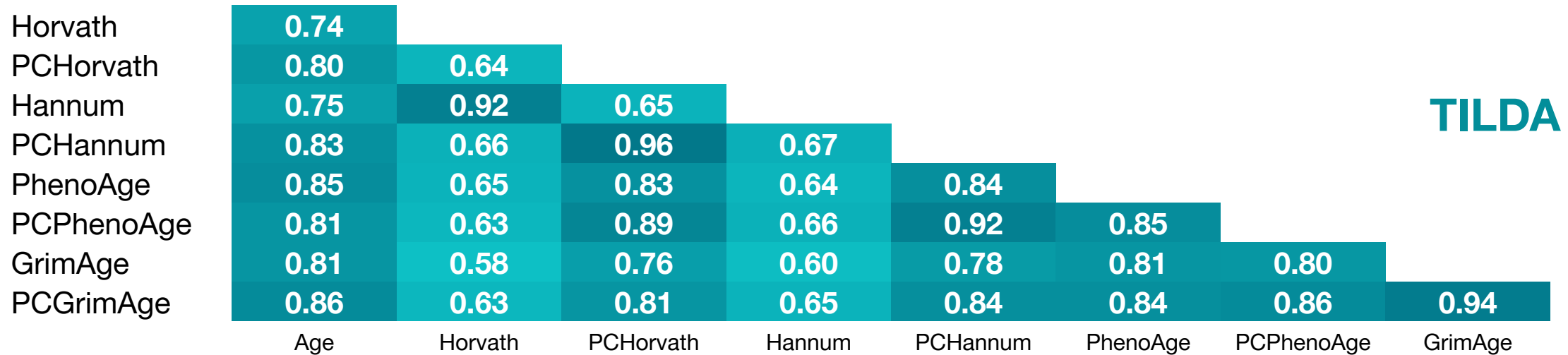
Are the Findings Similar in Two Settings – HRS and TILDA? Epigenetic Age from Original and Principal Components Clocks

# Correlations of the clocks in TILDA and HRS: Original and PC Versions

TILDA

	Age	Horvath	PCHorvath	Hannum	PCHannum	PhenoAge	PCPhenoAge	GrimAge
Horvath	0.74							
PCHorvath	0.80	0.64						
Hannum	0.75	0.92	0.65					
PCHannum	0.83	0.66	0.96	0.67				
PhenoAge	0.85	0.65	0.83	0.64	0.84			
PCPhenoAge	0.81	0.63	0.89	0.66	0.92	0.85		
GrimAge	0.81	0.58	0.76	0.60	0.78	0.81	0.80	
PCGrimAge	0.86	0.63	0.81	0.65	0.84	0.84	0.86	0.94

HRS

	Age	Horvath	PCHorvath	Hannum	PCHannum	PhenoAge	PCPhenoAge	GrimAge
Horvath	0.74							
PCHorvath	0.76	0.86						
Hannum	0.82	0.77	0.84					
PCHannum	0.78	0.88	0.96	0.86				
PhenoAge	0.73	0.65	0.69	0.76	0.68			
PCPhenoAge	0.81	0.74	0.81	0.83	0.83	0.80		
GrimAge	0.83	0.65	0.71	0.77	0.73	0.74	0.83	
PCGrimAge	0.88	0.70	0.77	0.81	0.79	0.76	0.86	0.96

Prediction of Walking Speed with Original and PC versions of 4 Clocks in 2 Countries (z scored IEAA)
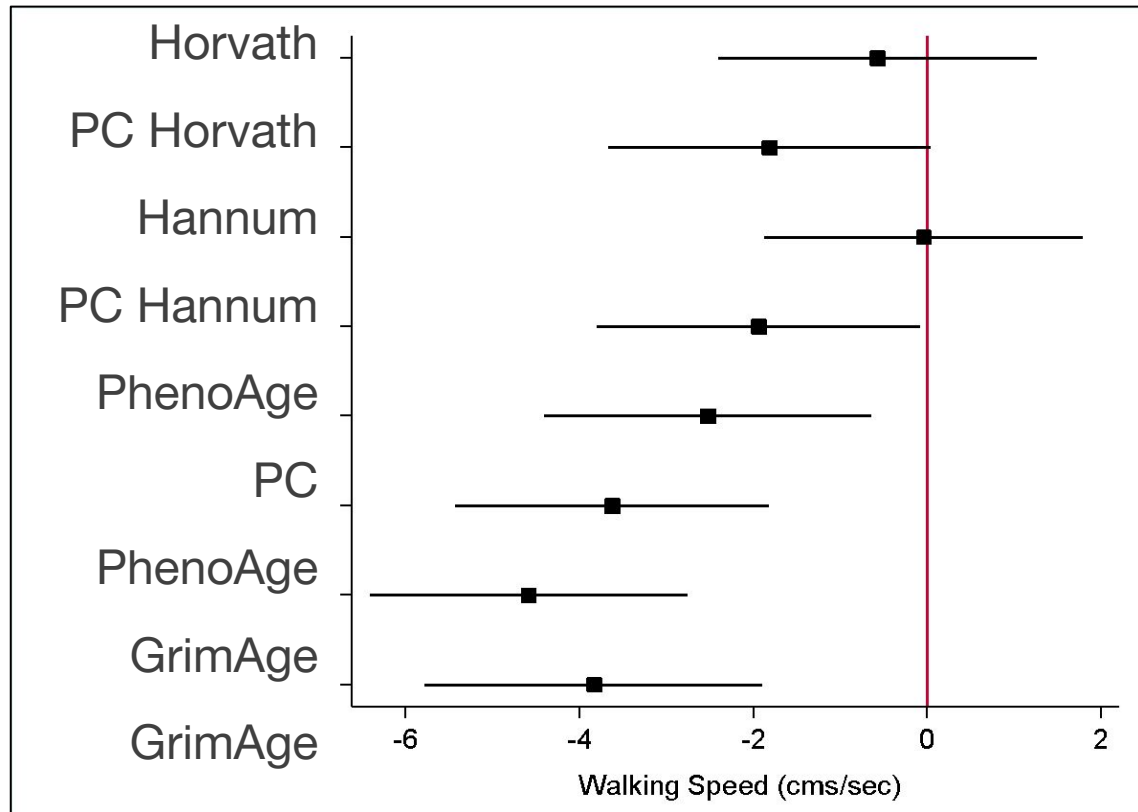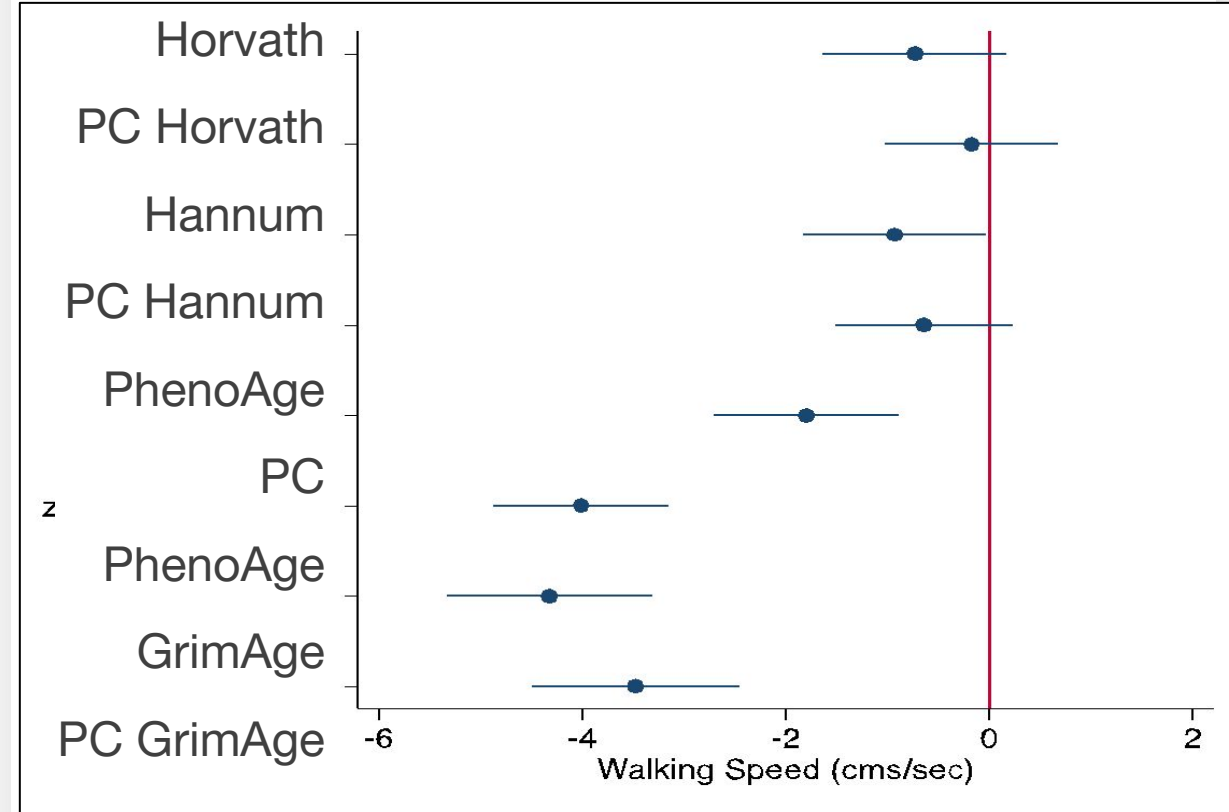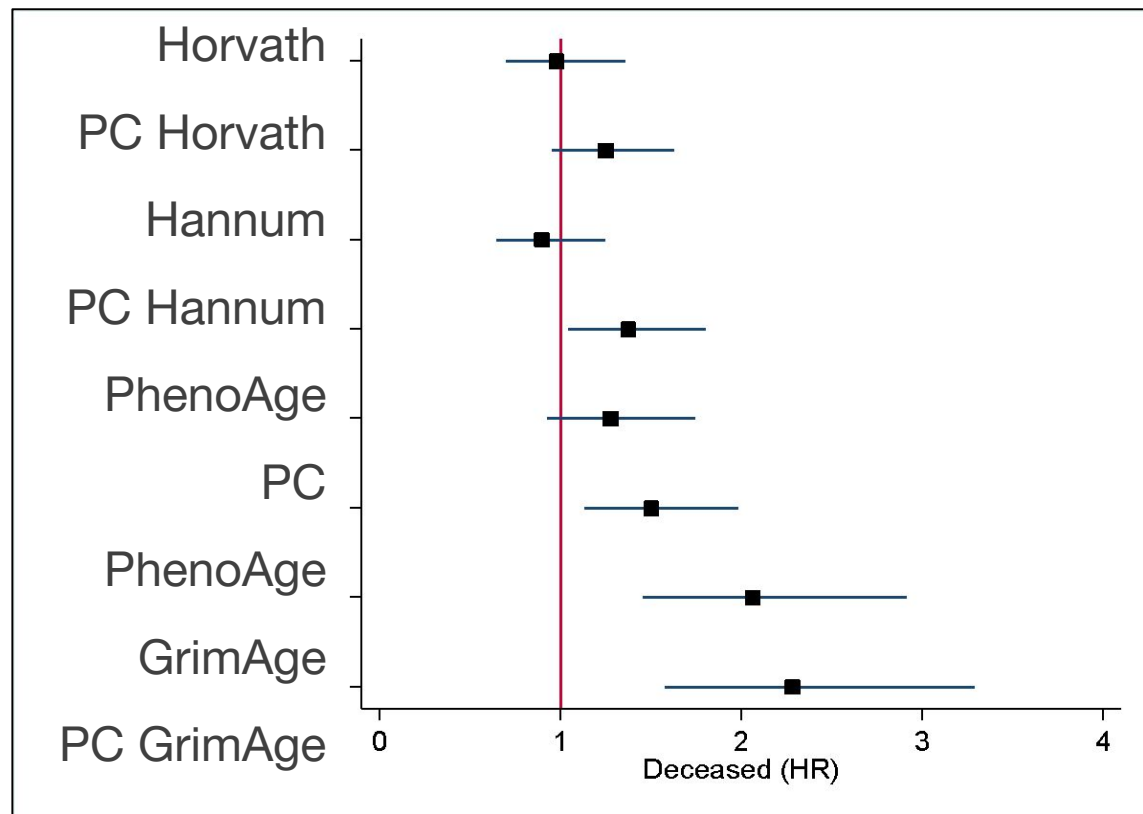

TILDA
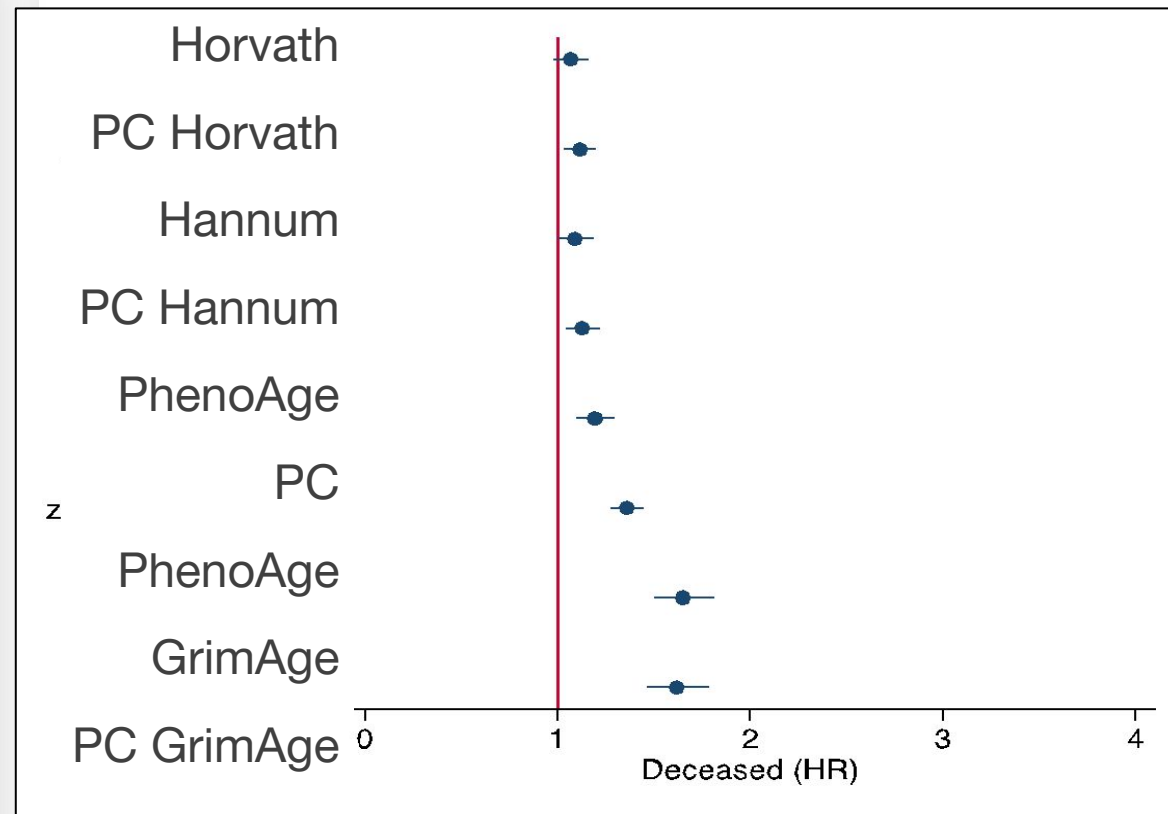
HRS

HRS and Tilda: Prediction of Mortality using 4 Clocks in 2 Countries: (z scored IEAA)

TILDA

HRS

Summary

More reliable clocks more strongly related to each other

More reliable clocks have different means but rarely change associations with other variables

Correlations among clocks quite similar across countries

Associations of clocks with health variables are quite similar across countries

Conclusion

Epigenetic clocks add to our explanation of health outcomes

They do not eliminate the importance of the social variables

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