

Supplementary Table 2. Survival analysis for DNA methylation clocks and clinical biomarkers on all-cause mortality, controlled by gender, age, age², and nativity, NHANES 1999-2002 (n=2,402). Bold indicates statistical significance (p-value<0.05).

	All-cause mortality		Cardiovascular-specific mortality			Cancer-specific mortality		
	HR	(95% CI)	HR	(95% CI)		HR	(95% CI)	
Chronological age clocks								
Hannum	1.04	(1.02 1.05)	1.01	(0.97	1.05)	1.05	(1.02	1.07)
Hovarth	1.03	(1.01 1.04)	1.00	(0.98	1.03)	1.04	(1.02	1.07)
Weidner	1.01	(1.00 1.02)	1.00	(0.98	1.02)	1.01	(0.99	1.03)
Lin	1.01	(1.00 1.02)	1.00	(0.98	1.02)	1.01	(0.99	1.03)
Vidal-Bralo	1.02	(1.01 1.04)	1.00	(0.97	1.04)	1.04	(1.02	1.07)
SkinBlood	1.02	(1.00 1.04)	1.01	(0.97	1.06)	1.01	(0.98	1.04)
Zhang	1.06	(1.01 1.11)	1.03	(0.93	1.14)	1.02	(0.95	1.09)
Physiological functioning clocks								
PhenoAge	1.04	(1.03 1.05)	0.99	(0.96	1.02)	1.04	(1.01	1.07)
GrimAge	1.11	(1.09 1.13)	1.10	(1.06	1.14)	1.12	(1.07	1.16)
GrimAge2	1.10	(1.09 1.12)	1.09	(1.05	1.13)	1.10	(1.06	1.14)
Pace of aging clock								
DunedinPoAm	43.7	(16.9 113)	17.9	(2.37	136)	30.1	(5.52	164)
Clocks trained on other aging biomarkers								
Yang	21.6	(0.23 2.03E+03)	120	(0.00	2.61E+08)	1.44	(0.00	1.14E+04)
Telomere	0.39	(0.29 0.51)	0.69	(0.28	1.67)	0.34	(0.18	0.66)
Behavioral/Lifestyle measures								
Sedentary behavior	1.71	(1.45 2.01)	2.43	(1.67	3.52)	1.31	(0.85	2.03)
Healthy eating index	0.99	(0.98 1.00)	1.00	(0.99	1.02)	0.97	(0.96	0.99)
Smoking pack years	1.01	(1.01 1.01)	1.01	(1.00	1.01)	1.01	(1.01	1.02)
Alcohol drinker	0.75	(0.63 0.88)	0.60	(0.38	0.94)	1.19	(0.78	1.83)
Anthropometric measures								
Waist to thigh ratio	3.54	(2.18 5.76)	4.73	(1.26	17.8)	1.79	(0.60	5.37)
BMI	1.01	(0.99 1.03)	1.00	(0.95	1.07)	1.00	(0.98	1.03)
Clinical used blood Biomarkers								
Total cholesterol	1.01	(0.94 1.08)	0.97	(0.75	1.25)	1.12	(0.93	1.34)
HDL	1.00	(0.99 1.00)	1.00	(0.99	1.02)	1.00	(0.99	1.01)
LDL	1.00	(1.00 1.00)	1.00	(0.99	1.00)	1.00	(1.00	1.01)
Glucose	1.00	(1.00 1.01)	1.01	(1.00	1.01)	1.00	(0.99	1.00)
C-reactive protein	1.12	(1.06 1.17)	1.04	(0.93	1.17)	1.09	(1.01	1.18)

Supplementary Table 3. Average mediated proportions for DNA methylation and clinical mediators on the relationship between race and ethnicity and all-cause mortality, NHANES 1999-2002 (n=2,402). Bold indicates statistical significance (p-value<0.05), and bold with two asterisks indicates significance passed Bonferroni adjustment (p-value<0.0021).

	Model 1. Black (N= 516) vs. White (N= 943)		Model 2. Hispanic (N=860) vs. White (N= 943)		Model 3. Other races (N=83) vs. White (N= 943)	
	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)
Chronological age clocks						
Hannum	-19.1%**	(-37.8%- 10.5%)	5.7%	(-4.9% 22.4%)	4.5%	(-100.1% 99.9%)
Hovarth	-5.2%	(-14.6%- 0.7%)	-5.0%	(-28.6% 1.1%)	-1.3%	(-93.6% 56.7%)
Weidner	-2.5%	(-8.2%- 0.3%)	-3.7%	(-16.4% 0.5%)	-4.9%	(-98.1% 82.1%)
Lin	-2.9%	(-10.6% 0.3%)	-3.4%	(-18.0% 1.6%)	-3.8%	(-62.5% 73.0%)
Vidal-Bralo	-14.6%**	(-35.9%- 4.9%)	-10.5%	(-43.9%- 2.3%)	-13.5%	(-251.5% 159.5%)
SkinBlood	-4.9%	(-15.5%- 0.5%)	0.1%	(-5.2% 4.3%)	1.0%	(-38.1% 47.3%)
Zhang	-9.9%	(-27.0%- 2.8%)	-1.2%	(-8.3% 2.3%)	-2.4%	(-59.4% 50.6%)
Physiological functioning clocks						
PhenoAge	-6.8%	(-22.8% 0.6%)	8.9%	(-1.9% 37.8%)	5.7%	(-119.3% 161.6%)
GrimAge	34.4%**	(18.7% 66.8%)	15.3%	(-9.8% 53.8%)	12.0%	(-193.5% 234.7%)
GrimAge2	46.0%**	(26.6% 88.7%)	39.3%**	(18.2% 100.9%)	24.8%	(-206.7% 288.7%)
Pace of aging clock						
DunedinPoAm	23.6%**	(10.0% 48.9%)	28.3%**	(12.6% 70.4%)	27.2%	(-211.4% 340.7%)
Clocks trained on other aging biomarkers						
Yang	7.4%	(-6.8% 20.9%)	3.6%	(-10.9% 21.1%)	1.3%	(-98.4% 124.6%)
Telomere	-44.4%**	(-79.1%- 27.2%)	2.8%	(-21.6% 20.4%)	9.1%	(-177.4% 157.2%)
Behavioral/Lifestyle measures						
Sedentary behavior	27.8%**	(13.4% 54.0%)	23.4%**	(6.7% 63.6%)	18.5%	(-217.7% 298.3%)
Healthy eating index	6.9%	(0.6% 19.6%)	2.9%	(-2.8% 15.3%)	0.0%	(-43.2% 62.5%)
Smoking pack years	-15.4%**	(-34.8%- 6.9%)	-14.1%	(-37.1%- 4.6%)	-9.1%	(-125.4% 170.8%)
Alcohol drinker	11.9%	(4.6% 25.7%)	8.2%	(0.3% 27.8%)	19.6%	(-309.1% 358.3%)
Anthropometric measures						
Waist to thigh ratio	-25.8%	(-54.2%- 12.6%)	15.9%	(4.7% 46.3%)	11.1%	(-150.4% 251.1%)
BMI	2.3%	(-6.6% 15.3%)	0.3%	(-8.3% 13.5%)	-0.1%	(-26.1% 27.6%)
Clinical used blood Biomarkers						
Total cholesterol	-0.5%	(-4.7% 1.4%)	0.0%	(-4.1% 3.7%)	-0.2%	(-27.5% 21.8%)
HDL	-0.8%	(-7.7% 3.1%)	6.2%	(-3.2% 19.6%)	1.6%	(-46.2% 47.4%)
LDL	0.0%	(-2.6% 1.5%)	0.0%	(-3.7% 3.8%)	0.0%	(-17.3% 16.4%)
Glucose	8.1%**	(2.2% 19.0%)	5.5%	(0.7% 18.2%)	7.4%	(-82.9% 127.0%)
C-reactive protein	9.5%**	(3.2% 24.3%)	1.7%	(-2.2% 7.7%)	-0.8%	(-37.7% 35.0%)

Supplementary Table 4. Average mediated proportions for DNA methylation and clinical mediators on the relationship between education attainment and all-cause mortality, NHANES 1999-2002 (n=2,402). Bold indicates statistical significance (p-value<0.05), and bold with two asterisks indicates significance passed Bonferroni adjustment (p-value<0.0021).

	Model 1. Less than high school (N=1,096) vs. College degree or higher (N= 370)		Model 2. High school graduate/GED (N=496) vs. College degree or higher (N= 370)		Model 3. Some college or associates degree (N=440) vs. College degree or higher (N= 370)	
	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)
Chronological age clocks						
Hannum	1.6%	(-0.0% 4.5%)	4.4%	(0.3% 13.4%)	0.5%	(-6.9% 7.7%)
Hovarth	-0.1%	(-1.7% 1.3%)	-1.7%	(-8.9% 1.3%)	-4.1%	(-14.0%- 0.2%)
Weidner	-0.3%	(-3.1% 1.3%)	0.1%	(-3.0% 3.7%)	-0.9%	(-7.8% 1.6%)
Lin	-0.2%	(-2.1% 1.2%)	-1.2%	(-5.5% 1.0%)	-0.5%	(-5.4% 3.1%)
Vidal-Bralo	-0.7%	(-3.4% 0.5%)	-0.3%	(-5.0% 1.6%)	-0.7%	(-5.8% 2.6%)
SkinBlood	0.3%	(-1.0% 2.2%)	0.9%	(-1.2% 5.7%)	0.0%	(-3.4% 2.7%)
Zhang	0.5%	(-0.7% 2.6%)	0.2%	(-1.7% 3.1%)	-0.1%	(-5.5% 3.2%)
Physiological functioning clocks						
PhenoAge	6.5%**	(2.4% 13.7%)	2.9%	(-1.3% 12.2%)	3.1%	(-5.0% 12.4%)
GrimAge	23.3%**	(14.2% 36.6%)	18.7%**	(8.1% 41.7%)	31.8%**	(17.8% 57.5%)
GrimAge2	27.6%**	(16.4% 44.9%)	21.4%**	(9.9% 48.5%)	32.4%**	(17.2% 64.2%)
Pace of aging clock						
DunedinPoAm	13.6%**	(6.7% 23.6%)	11.4%**	(2.8% 27.6%)	22.0%**	(11.0% 38.0%)
Clocks trained on other aging biomarkers						
Yang	-1.0%	(-4.4% 1.9%)	1.2%	(-1.5% 6.0%)	0.3%	(-3.9% 4.5%)
Telomere	5.3%	(1.7% 10.1%)	5.7%**	(1.9% 13.1%)	3.5%	(-0.9% 10.9%)
Behavioral/Lifestyle measures						
Sedentary behavior	12.9%**	(5.9% 23.2%)	21.2%	(9.4% 44.9%)	6.2%	(-0.4% 17.7%)
Healthy eating index	1.8%	(-6.5% 14.1%)	1.3%	(-15.4% 14.5%)	3.7%	(-6.3% 14.6%)
Smoking pack years	10.6%**	(4.8% 18.3%)	10.4%	(2.6% 27.3%)	16.2%**	(7.3% 35.2%)
Alcohol drinker	1.9%	(-2.5% 7.1%)	6.6%	(1.0% 19.2%)	2.4%	(-1.7% 10.6%)
Anthropometric measures						
Waist to thigh ratio	5.6%	(1.6% 12.6%)	3.0%	(-4.1% 12.0%)	4.0%	(-3.4% 14.6%)
BMI	0.4%	(-3.8% 6.3%)	3.0%	(-2.7% 13.0%)	4.5%	(-7.5% 23.6%)
Clinical used blood Biomarkers						
Total cholesterol	0.0%	(-1.4% 1.6%)	-0.4%	(-15.5% 8.9%)	-3.4%	(-16.2% 2.8%)
HDL	0.1%	(-5.8% 5.9%)	0.3%	(-4.7% 5.4%)	0.0%	(-3.9% 3.9%)
LDL	-0.1%	(-2.3% 1.2%)	0.4%	(-13.7% 11.5%)	-3.9%	(-15.4% 0.7%)
Glucose	2.3%	(-0.2% 6.5%)	1.3%	(-2.0% 6.4%)	-1.8%	(-12.1% 3.7%)
C-reactive protein	2.0%	(0.5% 4.5%)	0.6%	(-2.7% 4.4%)	0.7%	(-3.7% 5.9%)

Supplementary Table 5. Average mediated proportions for DNA methylation and clinical mediators on the relationship between household income and all-cause mortality, NHANES 1999-2002 (n=2,402). Bold indicates statistical significance (p-value<0.05), and bold with two asterisks indicates significance passed Bonferroni adjustment (p-value<0.0021).

	Model 1. PIR<1 (N=372) vs. PIR 5+ (N= 399)		Model 2. PIR 1-2 (N=707) vs. PIR 5+ (N= 399)		Model 3. PIR 2-5 (N=923) vs. PIR 5+ (N= 399)	
	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)	Average mediated proportion	(95% CI)
Chronological age clocks						
Hannum	3.0%	(-0.5% 8.2%)	2.6%	(-0.8% 6.5%)	0.3%	(-7.1% 6.6%)
Hovarth	-0.1%	(-2.6% 1.6%)	-0.1%	(-3.7% 2.9%)	-0.6%	(-5.5% 2.5%)
Weidner	0.2%	(-1.5% 3.1%)	0.5%	(-1.6% 2.9%)	0.0%	(-1.8% 1.7%)
Lin	0.2%	(-1.5% 2.7%)	-0.7%	(-3.0% 0.6%)	-1.1%	(-6.0% 1.5%)
Vidal-Bralo	-0.3%	(-3.1% 0.9%)	0.6%	(-1.9% 3.4%)	-0.3%	(-3.6% 1.9%)
SkinBlood	-0.2%	(-3.7% 1.7%)	0.0%	(-1.1% 1.2%)	-1.2%	(-5.1% 1.7%)
Zhang	-0.4%	(-2.9% 1.0%)	-0.5%	(-2.2% 0.7%)	-1.0%	(-5.3% 1.1%)
Physiological functioning clocks						
PhenoAge	5.1%	(0.3% 13.4%)	8.3%	(2.5% 16.5%)	4.0%	(-0.8% 15.3%)
GrimAge	32.1%**	(20.1% 50.0%)	24.7%**	(14.5% 41.4%)	22.6%**	(9.6% 53.5%)
GrimAge2	36.6%**	(22.2% 57.8%)	29.2%**	(17.4% 50.8%)	24.9%**	(10.6% 59.5%)
Pace of aging clock						
DunedinPoAm	19.5%**	(9.8% 35.7%)	14.1%**	(6.6% 29.0%)	15.0%	(4.1% 40.5%)
Clocks trained on other aging biomarkers						
Yang	0.1%	(-4.4% 5.1%)	1.0%	(-1.1% 4.8%)	0.0%	(-4.0% 1.9%)
Telomere	1.8%	(-1.2% 7.5%)	5.4%**	(1.9% 10.3%)	3.7%	(0.3% 11.4%)
Behavioral/Lifestyle measures						
Sedentary behavior	21.0%	(5.2% 39.7%)	12.9%	(4.2% 31.0%)	14.0%	(1.4% 48.4%)
Healthy eating index	4.0%	(-10.9% 16.8%)	1.9%	(-3.7% 9.5%)	2.9%	(-3.5% 18.1%)
Smoking pack years	11.5%**	(5.1% 19.8%)	10.9%**	(3.6% 27.9%)	12.7%**	(3.8% 31.0%)
Alcohol drinker	-3.7%	(-17.5% 7.4%)	2.1%	(-8.5% 13.6%)	6.0%	(0.3% 16.6%)
Anthropometric measures						
Waist to thigh ratio	5.1%	(-1.1% 12.5%)	5.8%	(-1.7% 15.3%)	8.1%	(-0.0% 21.3%)
BMI	-0.5%	(-11.2% 8.2%)	-0.4%	(-11.5% 6.0%)	2.6%	(-10.4% 17.1%)
Clinical used blood Biomarkers						
Total cholesterol	0.0%	(-3.6% 3.0%)	0.3%	(-1.3% 3.5%)	-0.4%	(-5.8% 4.5%)
HDL	-4.0%	(-16.7% 5.2%)	0.6%	(-7.1% 7.4%)	0.1%	(-6.9% 7.6%)
LDL	-1.7%	(-7.9% 1.9%)	0.2%	(-2.0% 3.7%)	-1.6%	(-9.7% 4.3%)
Glucose	6.2%	(1.1% 14.8%)	1.2%	(-2.5% 6.8%)	4.5%	(-0.1% 12.9%)
C-reactive protein	2.0%	(0.3% 5.1%)	4.9%	(1.3% 10.0%)	2.1%	(-0.3% 8.0%)