

Supplementary Tables

Epigenetic Age Estimates in Blood Shift by Decades with Cell Population: A Within-Donor Variance Partition Across Two Platforms and Two Study Designs
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Supplementary Table S1. Normalisation sensitivity

Every reported quantity under both pipelines. P3 = arrays as deposited (primary analysis); P1 = per-sample beta-mixture quantile normalisation (BMIQ) via waterRmelon 2.16.0. Across the four-clock panel BMIQ moved individual estimates by a mean of 3.13 years (maximum 10.52) on the 60 HumanMethylation450 arrays and a mean of 2.65 years (maximum 12.60) on the 37 EPIC arrays.

S1a. GSE35069, HumanMethylation450, within-donor variance partition. Percentages are shares of total sum of squares. Ranges in years.

Pipeline	Clock	Donor (%)	Preparation (%)	Residual (%)	Median range	Maximum range
P3 as deposited	Horvath skin-and-blood	89.48	8.050	2.475	15.01	17.32
P3 as deposited	Horvath	86.53	9.377	4.094	15.57	21.56
P3 as deposited	Hannum	62.94	32.293	4.767	36.71	45.22
P3 as deposited	PhenoAge	59.62	33.838	6.537	36.75	54.05
P1 BMIQ	Horvath skin-and-blood	89.11	8.354	2.541	17.58	19.75
P1 BMIQ	Horvath	86.90	9.345	3.754	17.68	25.34
P1 BMIQ	Hannum	63.59	31.648	4.759	40.82	48.81
P1 BMIQ	PhenoAge	62.40	31.374	6.225	40.11	60.82

S1b. GSE110554, EPIC, age-adjusted between-donor analysis. Shares are upper bounds on the cell-type effect, donor and cell type being structurally confounded (\$2.3). p-values are from 10,000-fold permutation of the cell-type label and floor at 1×10^{-4} . Ranges in years.

Pipeline	Clock	Cell-type share, upper bound (%)	Permutation p	Acceleration range	Youngest	Oldest
P3 as deposited	Horvath	43.40	2.9×10^{-3}	8.50	B cells	Monocytes
P3 as deposited	Horvath skin-and-blood	75.84	$< 1 \times 10^{-4}$	15.21	B cells	Monocytes
P3 as deposited	Hannum	85.76	$< 1 \times 10^{-4}$	26.49	CD8+ T	Monocytes
P3 as deposited	PhenoAge	89.51	$< 1 \times 10^{-4}$	51.21	CD8+ T	Monocytes
P1 BMIQ	Horvath	46.11	1.3×10^{-3}	10.43	B cells	Monocytes
P1 BMIQ	Horvath skin-and-blood	77.09	$< 1 \times 10^{-4}$	17.22	B cells	Monocytes
P1 BMIQ	Hannum	85.38	$< 1 \times 10^{-4}$	29.06	CD8+ T	Monocytes
P1 BMIQ	PhenoAge	90.40	$< 1 \times 10^{-4}$	59.59	CD8+ T	Monocytes

S1c. Leave-one-donor-out resampling, GSE35069. Range of each variance component across the six refits, each omitting one donor.

Clock	Preparation share, min (%)	Preparation share, max (%)	Donor share, min (%)	Donor share, max (%)
Horvath skin-and-blood	6.47	17.46	79.54	91.24
Horvath	7.78	17.20	76.75	88.25
Hannum	28.42	56.65	37.39	67.18
PhenoAge	30.21	56.39	36.21	63.33

Supplementary Table S2. Offsets relative to whole blood

Paired within-donor offset for every preparation against whole blood from the same donor, GSE35069, arrays as deposited. Each value is the median across the six donors of $\text{estimate}(\text{preparation}) - \text{estimate}(\text{whole blood})$; the range across donors is given in brackets. Positive values indicate the preparation reads older than whole blood from the same person. Table 3 in the main text gives the subset of substitutions that occur most often in published cohorts.

Preparation	Horvath skin-and-blood	Horvath	Hannum	PhenoAge
PBMC	-0.8 [-5.3, 2.1]	-1.5 [-4.3, 1.5]	-5.6 [-7.4, -0.4]	-4.5 [-9.1, 2.2]
Granulocytes	-0.7 [-2.6, 1.8]	-0.1 [-1.1, 1.1]	+4.1 [2.2, 5.5]	+3.7 [-4.2, 7.5]
Neutrophils	-6.1 [-9.4, 2.2]	-3.9 [-9.8, 5.2]	+0.4 [-4.8, 12.7]	-0.6 [-8.3, 7.8]
Eosinophils	-0.9 [-3.9, 0.2]	+7.8 [2.5, 10.2]	+14.4 [9.4, 19.0]	+1.8 [-0.6, 5.0]
CD14+ monocytes	+0.1 [-1.3, 2.6]	-1.3 [-3.5, 0.2]	+3.3 [0.9, 5.5]	+11.0 [10.1, 15.2]
CD19+ B cells	-10.9 [-13.9, -7.6]	-3.3 [-10.3, 0.1]	+5.8 [0.8, 13.3]	+1.0 [-11.8, 8.1]
CD4+ T cells	+2.7 [-1.0, 5.4]	-6.8 [-9.6, 1.7]	-5.3 [-7.2, -0.04]	-16.4 [-19.6, -3.3]
CD8+ T cells	-3.0 [-7.2, 4.5]	+1.3 [-6.6, 7.4]	-21.6 [-32.2, -10.5]	-26.6 [-39.7, -8.0]
CD56+ NK cells	+3.3 [1.2, 4.2]	+8.2 [1.5, 11.5]	+6.1 [-3.7, 12.6]	-2.0 [-5.9, 5.8]

Offsets are computed within donor and are therefore not attributable to between-person variation. They are characteristic of this calibrator — six healthy male donors from a single study — and should not be applied as universal correction factors. The largest single value, -26.6 years for PhenoAge in CD8+ T cells, arises where the estimator is evaluated outside the domain on which it was fitted.