**Parity is not associated with multiple measures of biological age:**

**Evidence from NHANES 1999-2010**

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**ESM Text I. Regression equations for primary and sensitivity analyses**

**Primary model**

Predicted biological aging measure = b0 + b1(live births) + b2(live births2) + b3(menopause) + b4(age) + b5(BMI) + b6(BMI2) + b7(FIPR) +b8(smoking) +b9(education) + b10(ethnicity) + b11(live births)(menopause) + b12(live births2)(menopause)

**Sensitivity analysis 1**

Predicted biological aging measure = b0 + b1(live births) + b2(live births2) + b3(menopause) + b4(age) + b5(live births)(menopause) + b6(live births2)(menopause)

**Sensitivity analysis 2**

Predicted biological aging measure = b0 + b1(live births) + b2(live births2) + b3(menopause) + b4(age) + b5(BMI) + b6(BMI2) + b7(FIPR) +b8(smoking) +b9(education) + b10(ethnicity) + b11(live births)(menopause) + b12(live births2)(menopause) +b13(years since last live birth) + b14(years since last live birth)(live births) + b15(years since last live birth)(live births2)

**Sensitivity analysis 3**

Predicted biological aging measure = b0 + b1(live births) + b2(live births2) + b3(months since last live birth) + b4(age) + b5(BMI) + b6(BMI2) + b7(FIPR) +b8(smoking) +b9(education) + b10(ethnicity) + b11(live births)(months since last live birth) + b12(live births2)(months since last live birth)

**ESM Table I.** Ranges of biomarker values used to restrict the reference population for Homeostatic Dysregulation (HD) algorithm. *Note*: values from https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/

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| --- | --- | --- |
|  | **Units of Measure** | **Range** |
| Albumin | g/L | 35 - 50 |
| Creatinine | mg/dL | 0.59 - 1.04 |
| Glucose | mg/dL | <126 |
| CRP | mg/L | <3 |
| Lymphocyte Percent | % | 28 - 55 |
| Mean (red) cell volume | fL | 78.2 - 97.9 |
| Red Cell Distribution Width | % | 12.2 - 16.1 |
| Alkaline Phosphatase | U/L | 35 - 104 |
| White Cell Count | 1000 cell/uL | 3.4 - 9.6 |

**ESM Table II.** Descriptive statistics for the reference population (n = 482 women) used to define the Homeostatic Dysregulation (HD) algorithm.

|  |  |  |  |
| --- | --- | --- | --- |
|  | UNITS | **𝜇** | **𝜎** |
| Age | Yrs | 24.97 | 3.10 |
| Albumin | g/L | 41.58 | 3.24 |
| Creatinine | umol/L | 65.95 | 6.70 |
| Glucose | mmol/L | 4.81 | 0.38 |
| CRP | ln(mg/dL) | -1.36 | 0.47 |
| Lymphocyte Percent | % | 38.19 | 6.35 |
| Mean cell volume | fL | 88.55 | 3.98 |
| Red cell width | % | 12.98 | 0.68 |
| Alkaline Phosphatase | U/L | 66.90 | 15.38 |
| White Cell Count | 1000 cell/uL | 6.29 | 1.42 |

**ESM Table III.** Biomarker variance covariance matrix for the reference population used to define the Homeostatic Dysregulation (HD) algorithm. *Note:* Biomarkers were standardized to mean=0, standard deviation=1 prior to computing the variance covariance matrix.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Albumin | Creatinine | Glucose | Ln(CRP) | Lymphocyte Percent | Mean Cell Volume | Red Cell Width | Alkaline Phosphatase | White Cell Count |
| Albumin | 1.00 | 0.06 | -0.06 | -0.22 | -0.04 | 0.20 | 0.00 | -0.02 | 0.12 |
| Creatinine | 0.06 | 1.00 | -0.05 | -0.04 | 0.07 | 0.02 | -0.03 | -0.02 | -0.03 |
| Glucose | -0.06 | -0.05 | 1.00 | 0.02 | -0.07 | 0.00 | -0.03 | 0.05 | -0.07 |
| Ln(CRP) | -0.22 | -0.04 | 0.02 | 1.00 | -0.05 | -0.05 | 0.02 | 0.10 | 0.09 |
| Lymphocyte Percent | -0.04 | 0.07 | -0.07 | -0.05 | 1.00 | 0.00 | 0.09 | -0.15 | -0.28 |
| Mean Cell Volume | 0.20 | 0.02 | 0.00 | -0.05 | 0.00 | 1.00 | -0.38 | -0.05 | 0.02 |
| Red Cell Width | 0.00 | -0.03 | -0.03 | 0.02 | 0.09 | -0.38 | 1.00 | 0.08 | -0.05 |
| Alkaline Phosphatase | -0.02 | -0.02 | 0.05 | 0.10 | -0.15 | -0.05 | 0.08 | 1.00 | 0.15 |
| White Cell Count | 0.12 | -0.03 | -0.07 | 0.09 | -0.28 | 0.02 | -0.05 | 0.15 | 1.00 |

**ESM Table IV.** Biomarker descriptive statistics for the reference population used to build the Klemera-Doubal Method (KDM) biological age algorithm (n = 5,995). *Note:* The reference sample consisted of non-pregnant women aged 30-75 participating in NHANES III.

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| --- | --- | --- | --- |
|  | **Units** | **Mean** | **SD** |
| Age | Yrs | 50.04 | 13.69 |
| Albumin | g/L | 40.46 | 3.37 |
| Creatinine | umol/L | 66.04 | 14.35 |
| Glucose | mmol/L | 5.76 | 2.16 |
| Ln(CRP) | ln(mg/dL) | -1.02 | 0.77 |
| Lymphocyte Percent | % | 33.92 | 8.43 |
| Mean cell volume | fL | 88.83 | 5.66 |
| Red cell width | % | 13.26 | 1.14 |
| Alkaline Phosphatase | U/L | 86.57 | 28.70 |
| White Cell Count | 1000 cell/uL | 7.16 | 2.10 |

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**ESM Table V.** KDM biological age model parameters estimated from NHANES III reference sample. We report the intercept (Q), slope (K), and root mean squared error (S) for the regressions of biomarkers onto chronological age in the NHANES III reference sample. Rchar refers to a ‘characteristic correlation’ describing a summary relationship between the biomarker panel and chronological age. SBA2 corresponds to the squared variance in chronological age explained by the biomarker panel in the reference sample.

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| --- | --- | --- | --- |
|  | **Intercept** | **Slope** | **RMSE** |
| Albumin | 41.545 | -0.022 | 3.361 |
| Creatinine | 52.070 | 0.279 | 13.836 |
| Glucose | 4.094 | 0.033 | 2.114 |
| Ln(CRP) | -1.228 | 0.004 | 0.766 |
| Lymphocyte Percent | 34.673 | -0.015 | 8.426 |
| Mean cell volume | 86.302 | 0.050 | 5.615 |
| Red cell width | 13.077 | 0.004 | 1.135 |
| Alkaline Phosphatase | 55.182 | 0.628 | 27.385 |
| White Cell Count | 7.528 | -0.007 | 2.101 |
|  |  |  |  |
| rchar | 0.277 | | |
| SBA2 | 870.150 | | |

**ESM Table VI.** Biomarker summary statistics for the final analytical sample (n = 2,669).

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|  | **Units** | **Mean** | **SD** |
| Age | Yrs | 37.52 | 10.57 |
| Albumin | g/L | 41.56 | 3.15 |
| Creatinine | umol/L | 64.77 | 11.64 |
| Glucose | mmol/L | 5.50 | 1.25 |
| Ln(CRP) | ln(mg/dL) | -1.39 | 1.26 |
| Lymphocyte Percent | % | 31.11 | 7.95 |
| Mean cell volume | fL | 88.42 | 5.85 |
| Red cell width | % | 12.83 | 1.22 |
| Alkaline Phosphatase | U/L | 67.46 | 21.86 |
| White Cell Count | 1000 cell/uL | 6.86 | 1.95 |

**ESM Table VII.** Nationally-representative coefficient estimates (and standard errors) from sensitivity models on the effects of number of live births on biological age when including chronological age as the only covariate (*n* = 3,235), National Health and Nutrition Examination Survey 1999-2010. *Note*: \* *p* < 0.05,  \*\* *p* < 0.01, \*\*\* *p* < 0.001

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| --- | --- | --- | --- |
|  | **LM** | **HD (log)** | **KDM** |
| Live births (linear) | -0.03 (0.26) | 0.002 (0.02) | -0.33 (0.56) |
| Live births (quadratic) | 0.08 (0.06) | -0.001 (0.004) | 0.07 (0.12) |
| Menopause status | 0.85 (0.83) | 0.15 (0.07) \* | 5.80 (2.22) \* |
| Live births (linear) x menopause status | -0.93 (0.67) | -0.09 (0.05) | -1.21 (1.45) |
| Live births (quadratic) x menopause status | 0.14 (0.14) | 0.01 (0.01) | 0.24 (0.28) |
| Age | 1.00 (0.02) \*\*\* | 0.002 (0.001) | 0.71 (0.03) \*\*\* |

**ESM Table VIII.** Coefficient estimates (and standard errors) from sensitivity analyses on the effect of number of live births and years since last live birth on biological age (*n* = 2,056), National Health and Nutrition Examination Survey 1999-2010. *Note*: \* *p* < 0.05,  \*\* *p* < 0.01, \*\*\* *p* < 0.001

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| --- | --- | --- | --- |
|  | **LM** | **HD (log)** | **KDM** |
| Live births (linear) | -0.36 (0.77) | 0.06 (0.07) | -2.93 (1.63) |
| Live births (quadratic) | 0.07 (0.13) | -0.02 (0.01) | 0.34 (0.28) |
| Years since last live birth | -0.003 (0.07) | -0.007 (0.007) | -0.16 (0.19) |
| Live births (linear) x years since last live birth | 0.03 (0.06) | -0.007 (0.005) | 0.15 (0.14) |
| Live births (quadratic) x years since last live birth | -0.006 (0.01) | 0.001 (0.001) | -0.02 (0.03) |

**ESM Table IX.** Coefficient estimates (and standard errors) from sensitivity analyses on the effect of number of live births and months since last live birth on biological age (*n* = 107),, National Health and Nutrition Examination Survey 2007-2010. *Note*: \* *p* < 0.05,  \*\* *p* < 0.01, \*\*\* *p* < 0.001

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|  | **LM** | **HD (log)** | **KDM** |
| Live births (linear) | -6.63 (2.36) \*\* | 0.25 (0.23) | -3.87 (5.27) |
| Live births (quadratic) | 1.15 (0.36) \*\* | -0.02 (0.04) | 0.87 (0.93) |
| Months since last live birth | -1.07 (0.27) \*\*\* | 0.05 (0.03) | -0.95 (0.59) |
| Live births (linear) x months since last live birth | 0.60 (0.16) \*\* | -0.04 (0.02) | 0.33 (0.41) |
| Live births (quadratic) x months since last live birth | -0.09 (0.02) \*\* | 0.005 (0.003) | -0.05 (0.06) |