Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
eFigure. Flow Chart of the Analytic Sample

- Baseline survey (2006, 499,309 participants)
- Online mental health questionnaire survey (2016, 156,749 participants)
- Participated in both (156,749 participants)
- Excluded 3,728 with missing data on childhood adversity
- Excluded 25,526 with missing data on clinical biomarkers used to calculate phenotypic age acceleration
- 127,495 participants
| Childhood adversity questions     | Responses/description                                                                 | Cut off |
|-----------------------------------|---------------------------------------------------------------------------------------|---------|
| Physical neglect                   | Someone to take to doctor when needed as a child.                                     | ≤3      |
| Emotional neglect                  | Felt loved as a child.                                                                 | ≤2      |
| Sexual abuse                       | Sexually molested as a child.                                                          | ≥1      |
| Physical abuse                     | Physically abused by family as a child.                                               | ≥1      |
| Emotional abuse                    | Felt hated by family member as a child.                                                | ≥1      |
| Cumulative childhood adversity risk| Summary score of childhood adversity.                                                 | —       |

Summary: Summary score of five childhood adversity items. (0-5)
eTable 2. Associations of Unhealthy Lifestyle With Phenotypic Age Acceleration

|                          | Model 1        | Model 2        |
|--------------------------|----------------|----------------|
|                          | β (95% CI)     | β (95% CI)     |
| Unhealthy lifestyle score| 0.68 (0.66, 0.70) | 0.62 (0.60, 0.65) |

Abbreviations: CI, confidence interval.

Notes:
Model 1: adjusted for sex.
Model 2: further adjusted for race and ethnicity, educational level, occupation, Townsend deprivation index, maternal smoking around birth, and history of cardiovascular disease and cancer based on Model 1.
## eTable 3. Associations Between Childhood Adversity and Phenotypic Age Acceleration by Chronological Age

| Childhood adversity | Model 1 | Model 2 | Model 3 | P for interaction |
|---------------------|---------|---------|---------|-------------------|
|                     | $\beta$ (95% CI) | $\beta$ (95% CI) | $\beta$ (95% CI) |                     |
| Physical neglect    |         |         |         |                   |
| 40-59 years         | 0.529 (0.422, 0.635) | 0.323 (0.216, 0.430) | 0.281 (0.176, 0.387) | 0.12               |
| 60-69 years         | 0.266 (0.160, 0.372) | 0.159 (0.053, 0.266) | 0.163 (0.057, 0.268) |                   |
| Emotional neglect   |         |         |         |                   |
| 40-59 years         | 0.260 (0.173, 0.347) | 0.146 (0.059, 0.233) | 0.049 (-0.004, 0.135) | 0.22               |
| 60-69 years         | 0.137 (0.034, 0.240) | 0.084 (-0.019, 0.187) | 0.015 (-0.087, 0.117) |                   |
| Sexual abuse        |         |         |         |                   |
| 40-59 years         | 0.400 (0.274, 0.526) | 0.316 (0.190, 0.442) | 0.184 (0.060, 0.309) | 0.04               |
| 60-69 years         | 0.277 (0.121, 0.434) | 0.255 (0.100, 0.411) | 0.164 (0.010, 0.319) |                   |
| Physical abuse      |         |         |         |                   |
| 40-59 years         | 0.436 (0.346, 0.526) | 0.310 (0.220, 0.400) | 0.196 (0.011, 0.285) | 0.42               |
| 60-69 years         | 0.382 (0.266, 0.498) | 0.319 (0.203, 0.434) | 0.216 (0.101, 0.330) |                   |
| Emotional abuse     |         |         |         |                   |
| 40-59 years         | 0.393 (0.297, 0.489) | 0.290 (0.194, 0.386) | 0.170 (0.074, 0.265) | 0.004              |
| 60-69 years         | 0.241 (0.112, 0.369) | 0.196 (0.068, 0.324) | 0.100 (-0.026, 0.227) |                   |
| Cumulative childhood adversity score (0-5) |         |         |         |                   |
| 40-59 years         | 0.204 (0.172, 0.236) | 0.141 (0.109, 0.173) | 0.088 (0.056, 0.120) | 0.06               |
| 60-69 years         | 0.145 (0.105, 0.185) | 0.109 (0.069, 0.149) | 0.072 (0.032, 0.112) |                   |

Abbreviations: CI, confidence interval.

Notes:
Model 1: adjusted for sex.
Model 2: further adjusted for race and ethnicity, educational level, occupation, Townsend deprivation index, maternal smoking around birth, and history of cardiovascular disease and cancer based on Model 1.
Model 3: further adjusted for unhealthy lifestyle score based on Model 2.
**eTable 4. Associations Between Childhood Adversity and Phenotypic Age Acceleration by Sex**

| Childhood adversity | Model 1 | Model 2 | Model 3 | P for interaction |
|---------------------|---------|---------|---------|-------------------|
|                     | β (95% CI) | β (95% CI) | β (95% CI) |         |
| Physical neglect    |         |         |         |       |
| Women               | 0.382 (0.283, 0.482) | 0.225 (0.125, 0.324) | 0.206 (0.108, 0.305) | 0.002 |
| Men                 | 0.479 (365, 0.594) | 0.256 (0.141, 0.370) | 0.254 (0.140, 0.368) |         |
| Emotional neglect   |         |         |         | 0.40   |
| Women               | 0.200 (0.111, 0.289) | 0.110 (0.021, 0.199) | 0.023 (-0.065, 0.111) |         |
| Men                 | 0.220 (0.120, 0.320) | 0.618 (-0.038, 0.161) | 0.007 (-0.091, 0.106) |         |
| Sexual abuse        |         |         |         | 0.95   |
| Women               | 0.339 (0.220, 0.459) | 0.241 (0.122, 0.360) | 0.132 (0.014, 0.250) |         |
| Men                 | 0.324 (0.150, 0.498) | 0.230 (0.057, 0.403) | 0.146 (-0.026, 0.317) |         |
| Physical abuse      |         |         |         | 0.003  |
| Women               | 0.420 (0.321, 0.520) | 0.319 (0.219, 0.419) | 0.206 (0.107, 0.305) |         |
| Men                 | 0.389 (0.288, 0.489) | 0.257 (0.157, 0.357) | 0.171 (0.072, 0.270) |         |
| Emotional abuse     |         |         |         | 0.10   |
| Women               | 0.300 (0.201, 0.398) | 0.200 (0.102, 0.299) | 0.096 (-0.001, 0.194) |         |
| Men                 | 0.394 (0.270, 0.517) | 0.220 (0.098, 0.344) | 0.140 (0.018, 0.262) |         |
| Cumulative childhood adversity score (0-5) |         |         |         | <0.001 |
| Women               | 0.164 (0.132, 0.196) | 0.110 (0.078, 0.142) | 0.066 (0.034, 0.098) |         |
| Men                 | 0.208 (1.066, 1.077) | 0.116 (0.076, 0.156) | 0.081 (0.041, 0.120) |         |

**Abbreviations:** CI, confidence interval.

**Notes:**
- Model 1: no adjustment.
- Model 2: adjusted for race and ethnicity, educational level, occupation, Townsend deprivation index, maternal smoking around birth, and history of cardiovascular disease and cancer based on Model 1.
- Model 3: further adjusted for unhealthy lifestyle score based on Model 2.
### eTable 5. Baseline Characteristics of Participants Excluded Because of Missing Data on Clinical Biomarkers (Used to Calculate Phenotypic Age Acceleration) and the Total Population Who Participated in Both the Baseline Survey and Online Mental Health Survey

| Characteristics                              | Total population N=153,021 | Participants excluded N=25,526 | P value |
|----------------------------------------------|-----------------------------|--------------------------------|---------|
| Chronological age, years, mean (SD)          | 56.4 (7.7)                  | 56.2 (7.7)                     | 0.01    |
| Sex, No. (%)                                 |                             |                                | <0.01   |
| Women                                        | 86,204 (56.3)               | 15,225 (59.6)                  |         |
| Men                                          | 66,817 (43.7)               | 10,301 (40.4)                  |         |
| Race and ethnicity, No. (%)                  |                             |                                | 0.02    |
| Black                                        | 1,065 (0.7)                 | 215 (0.8)                      |         |
| Chinese                                      | 349 (0.2)                   | 61 (0.2)                       |         |
| Multiple                                     | 794 (0.5)                   | 143 (0.6)                      |         |
| South Asian                                  | 1,259 (0.8)                 | 247 (1.0)                      |         |
| White                                        | 148,242 (97.2)              | 24,627 (96.8)                  |         |
| Othera                                       | 837 (0.5)                   | 144 (0.6)                      |         |
| Educational level, No. (%)                   |                             |                                | 0.77    |
| High                                         | 70,591 (46.4)               | 11,697 (46.5)                  |         |
| Intermediate                                 | 50,068 (32.9)               | 8,207 (32.7)                   |         |
| Low                                          | 31,600 (20.8)               | 5,231 (20.8)                   |         |
| Occupation, No. (%)                          |                             |                                | 0.24    |
| Working                                      | 97,503 (63.9)               | 16,308 (64.1)                  |         |
| Retired                                      | 45,077 (29.5)               | 7,404 (29.1)                   |         |
| Other                                        | 10,122 (6.6)                | 1,739 (6.8)                    |         |
| Townsend deprivation index, mean (SD)c       | -1.7 (2.8)                  | -1.7 (2.9)                     | 0.01    |

Abbreviations: SD: Standard Deviation

Notes:
*Other includes any races or ethnicities not otherwise specified.

1High educational level: college or university degree; Intermediate educational level: A/AS levels or equivalent, O levels/GCSEs or equivalent; Low educational level: none of the aforementioned.

Intermediate educational levels were equivalent to grades 6-12 (O-level equals middle school/junior high, grade 6-8; A-level equals high school, grade 9-12) in the US school system.

2For the Townsend Deprivation Index, 0 indicates the mean value for an area, positive numbers indicate lower socioeconomic status, and negative numbers indicate higher socioeconomic status.
### eTable 6. Associations of Childhood Adversity (as a Continuous Variable, Range 0-20) With Phenotypic Age Acceleration and Mediation Proportion of Childhood Adversity in Phenotypic Age Acceleration Attributed to Unhealthy Lifestyle

| Childhood adversity                        | Model 1 β (95% CI) | Model 2 β (95% CI) | Model 3 β (95% CI) | Mediation proportion (%) (95% CI)* | P value |
|-------------------------------------------|--------------------|--------------------|--------------------|-----------------------------------|---------|
| Physical neglect                          | 0.207 (0.170, 0.245) | 0.116 (0.079, 0.154) | 0.107 (0.070, 0.144) | 13.6 (10.4, 18.0) | <0.001 |
| Emotional neglect                         | 0.108 (0.080, 0.137) | 0.046 (0.018, 0.075) | 0.015 (-0.014, 0.043) | 44.0 (35.2, 59.0) | <0.001 |
| Sexual abuse                              | 0.269 (0.215, 0.323) | 0.189 (0.136, 0.243) | 0.129 (0.076, 0.182) | 30.3 (24.5, 38.0) | <0.001 |
| Physical abuse                            | 0.300 (0.259, 0.341) | 0.209 (0.168, 0.251) | 0.147 (0.106, 0.188) | 28.0 (24.2, 33.0) | <0.001 |
| Emotional abuse                           | 0.212 (0.175, 0.249) | 0.137 (0.101, 0.174) | 0.089 (0.052, 0.125) | 31.3 (26.5, 38.0) | <0.001 |
| Cumulative childhood adversity score (0-20) | 0.095 (0.083, 0.106) | 0.059 (0.047, 0.070) | 0.040 (0.028, 0.051) | 28.8 (25.5, 33.0) | <0.001 |

Abbreviations: CI, confidence interval.

Notes:
Model 1: adjusted for sex.
Model 2: further adjusted for race and ethnicity, educational level, occupation, Townsend deprivation index, maternal smoking around birth, and history of cardiovascular disease and cancer based on Model 1.
Model 3: further adjusted for unhealthy lifestyle score based on Model 2.
*The model included sex and unhealthy lifestyle score.
# eTable 7. Associations of Childhood Adversity With Phenotypic Age Acceleration and Mediation Proportion of Childhood Adversity in Phenotypic Age Acceleration Attributed to Unhealthy Lifestyle in a Complete-Case Sample (N=95,273)

| Childhood adversity          | Model 1     | Model 2     | Model 3     | Mediation proportion (%) (95% CI)* | P value |
|-----------------------------|-------------|-------------|-------------|-----------------------------------|---------|
|                             | β (95% CI)  | β (95% CI)  | β (95% CI)  |                                  |         |
| Physical neglect            | 0.388 (0.301, 0.476) | 0.220 (0.132, 0.307) | 0.215 (0.128, 0.302) | 15.7 (12.0, 20.0) | <0.001 |
| Emotional neglect           | 0.203 (0.126, 0.279) | 0.096 (0.019, 0.173) | 0.029 (-0.047, 0.105) | 50.3 (38.6, 70.0)  | <0.001 |
| Sexual abuse                | 0.329 (0.216, 0.442) | 0.254 (0.141, 0.367) | 0.157 (0.045, 0.269) | 34.5 (27.8, 45.0)  | <0.001 |
| Physical abuse              | 0.402 (0.321, 0.483) | 0.294 (0.214, 0.375) | 0.197 (0.117, 0.277) | 32.8 (27.4, 40.0)  | <0.001 |
| Emotional abuse             | 0.321 (0.232, 0.410) | 0.213 (0.125, 0.302) | 0.123 (0.035, 0.211) | 31.7 (26.4, 39.0)  | <0.001 |
| Cumulative childhood adversity score (0-5) | 0.177 (0.149, 0.206) | 0.116 (0.087, 0.145) | 0.077 (0.048, 0.106) | 31.0 (26.9, 35.0)  | <0.001 |
| 0                           | Ref.        | Ref.        | Ref.        |                                  |         |
| 1                           | 0.135 (0.060, 0.210) | 0.076 (0.001, 0.151) | 0.043 (-0.031, 0.117) | 35.8 (21.2, 79.0)  | <0.001 |
| 2                           | 0.273 (0.170, 0.376) | 0.158 (0.055, 0.261) | 0.076 (-0.025, 0.178) | 41.4 (29.5, 66.0)  | <0.001 |
| 3                           | 0.550 (0.410, 0.690) | 0.369 (0.229, 0.509) | 0.256 (0.118, 0.395) | 28.6 (22.5, 38.0)  | <0.001 |
| 4                           | 0.701 (0.505, 0.897) | 0.464 (0.269, 0.660) | 0.310 (0.116, 0.504) | 29.7 (23.1, 41.0)  | <0.001 |
| 5                           | 1.293 (0.920, 1.667) | 0.903 (0.530, 1.276) | 0.697 (0.328, 1.067) | 22.4 (16.5, 32.0)  | <0.001 |

Abbreviations: CI, confidence interval.
Notes:
Model 1: adjusted for sex.
Model 2: further adjusted for race and ethnicity, educational level, occupation, Townsend deprivation index, maternal smoking around birth, and history of cardiovascular disease and cancer based on Model 1.
Model 3: further adjusted for unhealthy lifestyle score based on Model 2.
*The model included sex and unhealthy lifestyle score.