

## **Supplementary material**

### **Supplementary methods**

#### **Cognition**

For the purpose of the present study, we selected the fluid intelligence test, trail making task, symbol digit substitution task, and the numeric memory test from the cognitive function online follow-up as our tasks of interest because they were acquired at the same time-point (online follow-up) as the PHQ-ADS scale. The pairs matching task from the online follow-up was not used in this specific subsample due to floor effects. We also used the 'Snap' card-game task as a reaction time task that was acquired during the baseline assessment centre. The prospective memory task from the baseline assessment was not used for the present analysis because it is a binary outcome measure and therefore not suitable for linear structural equation modelling. The matrix pattern completion task, tower rearranging task, picture vocabulary test, and paired associate learning task were not used to assess cognitive function because these tasks were not introduced in the UK Biobank until 2016 at the imaging clinics, which is a considerable period of time later than the online follow-up questionnaire. The lights pattern memory task and the word production test were not used because they were only performed in the pilot phase of the study and are only available for a subset of participants.

From the Trial Making Test that measures executive functioning (Reitan, 1958), a ratio score was calculated by dividing the TMT Part B (TMTB) by the TMT Part A (TMTA) (Arbuthnott & Frank, 2000), with the TMTA measuring the time in seconds to correctly connect the numbers 1 to 25 in ascending order, and the TMTB measuring the time in seconds to correctly connect numbers and letters in ascending and alphabetic alternating between number and letter. This ratio serves as an indicator of the cognitive flexibility component of executive function (Arbuthnott & Frank, 2000). During the working memory task, the participant was shown a 2-digit number to remember, the number then disappeared

and after a short while, they were asked to enter the number onto the screen. The number became one digit longer each time they remembered correctly up to a maximum of 12 digits. The longest number correctly recalled serves as an indicator of numeric working memory. The fluid intelligence test measures the capacity to solve problems that require logic and reasoning ability, independent of acquired knowledge. It was a bespoke test only used for UK Biobank. During the symbol digit substitution test participants were presented with a series of symbols that they were asked to match to numbers according to a key. The number of correct symbol digit matches was used as the task score. The number of correct symbol digit matches is the number of times a participant correctly matched a symbol with a digit summed across all the rounds of the test, excluding the initial 8 items that correspond to the training round.

The mean reaction time and reaction time variability were derived from the snap card game. Rounds 5 to 11 were used thereby excluding the first four rounds that were used as training round and reaction times under 50ms were discarded because they were due to anticipation rather than reaction, and reaction times over 2000ms were discarded because the cards had disappeared by then. Participants with more than 3 missing rounds in the snap task were also excluded from the analysis. The intra-individual variability in reaction time was calculated following a procedure described by (Haynes et al., 2017) by dividing the intra-individual standard deviation in reaction time by the intra-individual mean reaction time.

Cognitive performance indicators were modelled using a two-step procedure: First, an exploratory factor analysis using an orthogonal varimax rotation was conducted to investigate the dimensionality of the cognitive data in the UK Biobank and to determine which cognitive scores measure the same latent construct. Second, using the factor dimensionality information from the exploratory factor analysis, cognitive performance was modelled as two latent variables that capture distinct aspects of cognitive functioning (Figures 1 and 2).

Only participants without any missing values in the variables and items used to create the variables of interest were included in the model. Such a complete-case analysis was suitable because the data were missing at random (Karahalios et al., 2012). Analyses were run listwise. Since the UK Biobank sample was large enough without missing values, power was not an issue, and the values were missing at random, listwise deletion was deemed to be a reasonable strategy (Kang, 2013). The structural equation model on childhood adversity included 64,051 participants. The structural equation model on adulthood adversity included 63,360 participants.

### **Covariates**

Age, gender (coded 0 for women and 1 for men), the Townsend deprivation index (Townsend et al., 1988) and the age at which subjects completed full-time education were included as covariates in the structural equation model. Missing data in the age when full-time education was completed were imputed using the Qualifications variable from the UK Biobank, using the following average ages corresponding to the qualifications: 21 years for College/University degree or other professional qualifications (e.g. nursing, teaching), 17 years for A-levels/AS-levels or NVQ/HND/HNC or equivalent, and 15 years for O-levels/GCSE and CSE or equivalent.

### **Supplementary results**

#### **Spearman correlations between all variables entered in the structural equation model**

Supplementary Table S2 shows the Spearman correlations with a Bonferroni correction between all variables entered in the structural equation model including covariates. Higher levels of childhood adversity were significantly correlated with higher levels of distress, higher levels of neuroticism, higher Townsend index, fewer years of education,

being younger, and lower performance in tasks requiring reasoning. Higher levels of adulthood adversity were significantly correlated with higher levels of distress, higher levels of neuroticism, higher Townsend index, fewer years of education, being younger, being female, lower performance in tasks requiring reasoning, and longer reaction times in processing speed tasks.

### **Effects of covariates in the childhood adversity model**

For the covariates, older individuals showed lower performance in cognitive tasks, lower levels of distress and neuroticism, and lower levels of childhood adversity. Being male was associated with higher performance in cognitive tasks, lower levels of distress and neuroticism, and lower levels of childhood adversity. Greater degrees of deprivation were associated with worse performance in cognitive tasks, higher levels of distress and neuroticism, and higher levels of childhood adversity. Finally, more years of full-time education were associated with better performance in cognitive tasks, lower levels of distress and neuroticism, and lower levels of childhood adversity. The path coefficients and test statistics for covariates are displayed in Supplementary Table S3.

### **Effects of covariates in the adulthood adversity model**

For the covariates, older individuals showed lower performance in cognitive tasks, lower levels of distress and neuroticism, and lower levels of adulthood adversity. Being male was associated with higher performance in the digit span task, the fluid intelligence task and the snap task, as well as lower levels of distress and neuroticism and lower levels of adulthood adversity. Greater degrees of deprivation were associated with worse performance in cognitive tasks, higher levels of neuroticism, and higher levels of adulthood adversity. Finally, more years of full-time education were associated with better performance in cognitive tasks, lower levels of distress and neuroticism, and lower levels of adulthood

adversity. The path coefficients and test statistics for covariates are displayed in Supplementary Table S4.

## Supplementary Tables

### Supplementary Table S1

*Frequency and percent of childhood adversity and adulthood adversity for each point of the adversity composite score*

| Adversity<br>composite<br>score | Child adversity |         | Adult adversity |         |
|---------------------------------|-----------------|---------|-----------------|---------|
|                                 | Frequency       | Percent | Frequency       | Percent |
| <b>0</b>                        | 27,644          | 43.16   | 25,807          | 40.73   |
| <b>1</b>                        | 14,806          | 23.12   | 10,604          | 16.74   |
| <b>2</b>                        | 8,818           | 13.77   | 10,202          | 16.1    |
| <b>3</b>                        | 4,483           | 7       | 4,918           | 7.76    |
| <b>4</b>                        | 3,112           | 4.86    | 6,711           | 10.59   |
| <b>5</b>                        | 1,753           | 2.74    | 1,687           | 2.66    |
| <b>6</b>                        | 1,230           | 1.92    | 1,369           | 2.16    |
| <b>7</b>                        | 792             | 1.24    | 666             | 1.05    |
| <b>8</b>                        | 551             | 0.86    | 528             | 0.83    |
| <b>9</b>                        | 315             | 0.49    | 290             | 0.46    |
| <b>10</b>                       | 217             | 0.34    | 200             | 0.32    |
| <b>11</b>                       | 145             | 0.23    | 112             | 0.18    |
| <b>12</b>                       | 80              | 0.12    | 141             | 0.22    |
| <b>13</b>                       | 46              | 0.07    | 62              | 0.1     |
| <b>14</b>                       | 34              | 0.05    | 39              | 0.06    |
| <b>15</b>                       | 10              | 0.02    | 14              | 0.02    |
| <b>16</b>                       | 15              | 0.02    | 10              | 0.02    |
| <b>Total</b>                    | 64,051          | 100     | 63,360          | 100     |

## Supplementary Table S2.

*Spearman correlations with a Bonferroni correction for all the variables in the structural equation models on childhood adversity and adult adversity including covariates.*

|                    | Child<br>adversity | Adult<br>adversity | Gender   | Age      | TDI     | Education | Neuro-<br>ticism | Distress | Reasoning | Processing<br>speed | Digit<br>span | Fluid<br>intelli-<br>gence | Symbol<br>matches | TMT     | Snap<br>RT | RT<br>variability |
|--------------------|--------------------|--------------------|----------|----------|---------|-----------|------------------|----------|-----------|---------------------|---------------|----------------------------|-------------------|---------|------------|-------------------|
| Child adversity    | —                  |                    |          |          |         |           |                  |          |           |                     |               |                            |                   |         |            |                   |
| Adult adversity    | 0.2774*            | —                  |          |          |         |           |                  |          |           |                     |               |                            |                   |         |            |                   |
| Gender             | -0.0048            | -0.1152*           | —        |          |         |           |                  |          |           |                     |               |                            |                   |         |            |                   |
| Age                | -0.0518*           | -0.0577*           | 0.1041*  | —        |         |           |                  |          |           |                     |               |                            |                   |         |            |                   |
| TDI                | 0.0770*            | 0.1316*            | -0.0371* | -0.0970* | —       |           |                  |          |           |                     |               |                            |                   |         |            |                   |
| Education          | -0.0510*           | -0.0684*           | 0.0215*  | -0.1145* | 0.0013  | —         |                  |          |           |                     |               |                            |                   |         |            |                   |
| Neuroticism        | 0.1569*            | 0.1574*            | -0.1177* | -0.1457* | 0.0432* | -0.0531*  | —                |          |           |                     |               |                            |                   |         |            |                   |
| Distress           | 0.1682*            | 0.1932*            | -0.1284* | -0.1541* | 0.0582* | 0.0013    | 0.4373*          | —        |           |                     |               |                            |                   |         |            |                   |
| Reasoning          | -0.0516*           | -0.0805*           | 0.0107   | 0.0114   | -0.0007 | 0.0208*   | -0.0653*         | -0.0706* | —         |                     |               |                            |                   |         |            |                   |
| Processing speed   | 0.0119             | 0.0390*            | -0.002   | -0.0325* | -0.0019 | 0.0049    | 0.0389*          | 0.0415*  | -0.2463*  | —                   |               |                            |                   |         |            |                   |
| Digit span         | -0.0095            | -0.0340*           | 0.0641*  | -0.1057* | 0.0025  | 0.1384*   | -0.0308*         | -0.0145  | 0.5005*   | -0.0585*            | —             |                            |                   |         |            |                   |
| Fluid intelligence | -0.0322*           | -0.0782*           | 0.0468*  | -0.1020* | -0.0159 | 0.3141*   | -0.0231*         | -0.01    | 0.8359*   | -0.1228*            | 0.2977*       | —                          |                   |         |            |                   |
| Symbol matches     | -0.0136            | -0.0354*           | -0.0461* | -0.4432* | -0.0099 | 0.1548*   | 0.0167           | 0.0247*  | 0.4485*   | -0.1427*            | 0.1865*       | 0.2981*                    | —                 |         |            |                   |
| TMT                | 0.0206*            | 0.0262*            | 0.0360*  | 0.1022*  | 0.013   | -0.0954*  | 0.0112           | 0.0154   | -0.3305*  | 0.0562*             | -0.1435*      | -0.2066*                   | -0.0981*          | —       |            |                   |
| Snap RT            | -0.0031            | 0.0341*            | -0.0895* | 0.2958*  | -0.0014 | -0.0792*  | -0.0061          | -0.0097  | -0.1598*  | 0.8962*             | -0.0680*      | -0.1109*                   | -0.2599*          | 0.0634* | —          |                   |
| RT variability     | -0.0061            | 0.0052             | -0.0219* | 0.0737*  | -0.0082 | -0.0327*  | -0.0007          | -0.0033  | -0.0841*  | 0.4314*             | -0.0335*      | -0.0558*                   | -0.0725*          | 0.0316* | 0.2606*    | —                 |

*Note.* TDI: Townsend Deprivation Index, TMT: Trail Making Test, RT: Reaction Time. \*  $p \leq .001$ .

**Supplementary Table S3**

*Standardized path coefficients and test statistics for covariates in the childhood adversity structural equation model*

| Dependent variable        | Covariate | $\beta$ | SE    | z        | p     | 95% CI |        |
|---------------------------|-----------|---------|-------|----------|-------|--------|--------|
|                           |           |         |       |          |       | LL     | UL     |
| <b>Child adversity</b>    | TDI       | 0.098   | 0.004 | 25.130   | 0.000 | 0.091  | 0.106  |
|                           | Education | -0.061  | 0.004 | -15.510  | 0.000 | -0.069 | -0.053 |
|                           | Age       | -0.070  | 0.004 | -17.770  | 0.000 | -0.078 | -0.063 |
|                           | Gender    | -0.034  | 0.004 | -8.740   | 0.000 | -0.042 | -0.027 |
| <b>Neuroticism</b>        | TDI       | 0.016   | 0.004 | 4.140    | 0.000 | 0.008  | 0.024  |
|                           | Education | -0.056  | 0.004 | -14.610  | 0.000 | -0.064 | -0.049 |
|                           | Age       | -0.124  | 0.004 | -31.950  | 0.000 | -0.131 | -0.116 |
|                           | Gender    | -0.095  | 0.004 | -24.700  | 0.000 | -0.102 | -0.087 |
| <b>Distress</b>           | TDI       | 0.029   | 0.004 | 7.550    | 0.000 | 0.022  | 0.037  |
|                           | Education | -0.009  | 0.004 | -2.320   | 0.020 | -0.016 | -0.001 |
|                           | Age       | -0.129  | 0.004 | -33.710  | 0.000 | -0.137 | -0.122 |
|                           | Gender    | -0.104  | 0.004 | -27.440  | 0.000 | -0.112 | -0.097 |
| <b>Digit span</b>         | TDI       | -0.008  | 0.004 | -1.970   | 0.049 | -0.015 | 0.000  |
|                           | Education | 0.118   | 0.004 | 30.450   | 0.000 | 0.110  | 0.126  |
|                           | Age       | -0.108  | 0.004 | -27.370  | 0.000 | -0.116 | -0.100 |
|                           | Gender    | 0.066   | 0.004 | 16.990   | 0.000 | 0.059  | 0.074  |
| <b>Fluid intelligence</b> | TDI       | -0.026  | 0.004 | -6.900   | 0.000 | -0.033 | -0.019 |
|                           | Education | 0.294   | 0.004 | 82.980   | 0.000 | 0.287  | 0.301  |
|                           | Age       | -0.083  | 0.004 | -21.750  | 0.000 | -0.091 | -0.076 |
|                           | Gender    | 0.047   | 0.004 | 12.450   | 0.000 | 0.040  | 0.054  |
| <b>Symbol matches</b>     | TDI       | -0.056  | 0.004 | -15.750  | 0.000 | -0.063 | -0.049 |
|                           | Education | 0.106   | 0.004 | 29.940   | 0.000 | 0.099  | 0.113  |
|                           | Age       | -0.423  | 0.003 | -134.110 | 0.000 | -0.429 | -0.417 |
|                           | Gender    | -0.003  | 0.004 | -0.760   | 0.446 | -0.010 | 0.004  |
| <b>TMT</b>                | TDI       | 0.028   | 0.004 | 7.050    | 0.000 | 0.020  | 0.035  |
|                           | Education | -0.083  | 0.004 | -21.210  | 0.000 | -0.091 | -0.076 |
|                           | Age       | 0.092   | 0.004 | 23.270   | 0.000 | 0.085  | 0.100  |
|                           | Gender    | 0.031   | 0.004 | 7.850    | 0.000 | 0.023  | 0.039  |
| <b>Snap RT</b>            | TDI       | 0.030   | 0.004 | 7.830    | 0.000 | 0.022  | 0.037  |
|                           | Education | -0.042  | 0.004 | -11.090  | 0.000 | -0.050 | -0.035 |
|                           | Age       | 0.287   | 0.004 | 78.490   | 0.000 | 0.280  | 0.294  |
|                           | Gender    | -0.103  | 0.004 | -27.200  | 0.000 | -0.111 | -0.096 |
| <b>RT variability</b>     | TDI       | -0.003  | 0.004 | -0.830   | 0.408 | -0.011 | 0.004  |
|                           | Education | -0.019  | 0.004 | -4.760   | 0.000 | -0.027 | -0.011 |
|                           | Age       | 0.077   | 0.004 | 19.290   | 0.000 | 0.069  | 0.085  |
|                           | Gender    | -0.028  | 0.004 | -6.960   | 0.000 | -0.035 | -0.020 |



*Note.*  $\beta$ : Standardized path coefficient, SE: standard error, CI: confidence Interval, LL: lower limit, UL: upper limit, TDI: Townsend Deprivation Index, TMT: Trail Making Test, RT: Reaction Time.

**Supplementary Table S4**

*Standardized path coefficients and test-statistics for covariates in the adulthood adversity structural equation model*

| Dependent variable        | Covariate | $\beta$ | SE    | z        | p     | 95% CI |        |
|---------------------------|-----------|---------|-------|----------|-------|--------|--------|
|                           |           |         |       |          |       | LL     | UL     |
| <b>Adult adversity</b>    | TDI       | 0.133   | 0.004 | 34.530   | 0.000 | 0.125  | 0.140  |
|                           | Education | -0.083  | 0.004 | -21.360  | 0.000 | -0.090 | -0.075 |
|                           | Age       | -0.050  | 0.004 | -12.680  | 0.000 | -0.058 | -0.042 |
|                           | Gender    | -0.143  | 0.004 | -37.250  | 0.000 | -0.150 | -0.135 |
| <b>Neuroticism</b>        | TDI       | 0.014   | 0.004 | 3.470    | 0.001 | 0.006  | 0.021  |
|                           | Education | -0.055  | 0.004 | -14.070  | 0.000 | -0.062 | -0.047 |
|                           | Age       | -0.128  | 0.004 | -32.890  | 0.000 | -0.136 | -0.120 |
|                           | Gender    | -0.081  | 0.004 | -20.810  | 0.000 | -0.089 | -0.074 |
| <b>Distress</b>           | TDI       | 0.022   | 0.004 | 5.650    | 0.000 | 0.014  | 0.030  |
|                           | Education | -0.004  | 0.004 | -0.960   | 0.339 | -0.011 | 0.004  |
|                           | Age       | -0.133  | 0.004 | -34.540  | 0.000 | -0.140 | -0.125 |
|                           | Gender    | -0.085  | 0.004 | -21.860  | 0.000 | -0.092 | -0.077 |
| <b>Digit span</b>         | TDI       | -0.004  | 0.004 | -1.030   | 0.305 | -0.012 | 0.004  |
|                           | Education | 0.118   | 0.004 | 30.240   | 0.000 | 0.110  | 0.126  |
|                           | Age       | -0.108  | 0.004 | -27.340  | 0.000 | -0.116 | -0.100 |
|                           | Gender    | 0.063   | 0.004 | 16.050   | 0.000 | 0.055  | 0.071  |
| <b>Fluid intelligence</b> | TDI       | -0.021  | 0.004 | -5.570   | 0.000 | -0.029 | -0.014 |
|                           | Education | 0.290   | 0.004 | 81.440   | 0.000 | 0.283  | 0.297  |
|                           | Age       | -0.083  | 0.004 | -21.650  | 0.000 | -0.091 | -0.076 |
|                           | Gender    | 0.041   | 0.004 | 10.620   | 0.000 | 0.033  | 0.048  |
| <b>Symbol matches</b>     | TDI       | -0.054  | 0.004 | -15.100  | 0.000 | -0.061 | -0.047 |
|                           | Education | 0.105   | 0.004 | 29.350   | 0.000 | 0.098  | 0.112  |
|                           | Age       | -0.422  | 0.003 | -132.750 | 0.000 | -0.428 | -0.415 |
|                           | Gender    | -0.006  | 0.004 | -1.730   | 0.084 | -0.013 | 0.001  |
| <b>TMT</b>                | TDI       | 0.025   | 0.004 | 6.440    | 0.000 | 0.018  | 0.033  |
|                           | Education | -0.081  | 0.004 | -20.550  | 0.000 | -0.089 | -0.073 |
|                           | Age       | 0.092   | 0.004 | 23.160   | 0.000 | 0.084  | 0.100  |
|                           | Gender    | 0.033   | 0.004 | 8.350    | 0.000 | 0.025  | 0.041  |
| <b>Snap RT</b>            | TDI       | 0.027   | 0.004 | 7.050    | 0.000 | 0.020  | 0.035  |
|                           | Education | -0.039  | 0.004 | -10.180  | 0.000 | -0.046 | -0.031 |
|                           | Age       | 0.287   | 0.004 | 78.140   | 0.000 | 0.280  | 0.295  |
|                           | Gender    | -0.099  | 0.004 | -25.810  | 0.000 | -0.107 | -0.092 |
| <b>RT variability</b>     | TDI       | -0.004  | 0.004 | -0.950   | 0.340 | -0.012 | 0.004  |
|                           | Education | -0.017  | 0.004 | -4.350   | 0.000 | -0.025 | -0.010 |
|                           | Age       | 0.077   | 0.004 | 19.040   | 0.000 | 0.069  | 0.085  |
|                           | Gender    | -0.026  | 0.004 | -6.440   | 0.000 | -0.034 | -0.018 |

*Note.*  $\beta$ : Standardized path coefficient, SE: standard error, CI: confidence Interval, LL: lower limit, UL: upper limit, TDI: Townsend Deprivation Index, TMT: Trail Making Test, RT: Reaction Time.