Supplements

Supplements 1, 2 and 3 are separate files.
Supplement 4. Violin plots of the imaging outcomes for the main analysis. AU, arbitrary units; GC, glucocorticoids
**Supplement 5.** Characteristics of included chronic glucocorticoid users and controls

<table>
<thead>
<tr>
<th></th>
<th>Patients using chronic systemic GC (n = 42)</th>
<th>Patients using chronic inhaled GC (n = 305)</th>
<th>Controls (n = 24106)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex: male, n (%)</strong></td>
<td>22 (52.4%)</td>
<td>137 (44.9%)</td>
<td>12154 (50.4%)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Age at time of scanning in years, mean (SD)</strong></td>
<td>65.2 (7.0)</td>
<td>63.0 (7.6)</td>
<td>63.5 (7.5)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Education level, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.81</td>
</tr>
<tr>
<td>College/University degree</td>
<td>24 (57.1)</td>
<td>171 (56.1)</td>
<td>12058 (50.0)</td>
<td></td>
</tr>
<tr>
<td>A levels or equivalent</td>
<td>6 (14.3)</td>
<td>38 (12.5)</td>
<td>2930 (12.2)</td>
<td></td>
</tr>
<tr>
<td>O levels/GCSE or equivalent</td>
<td>4 (9.5)</td>
<td>44 (14.4)</td>
<td>4155 (17.2)</td>
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</tr>
<tr>
<td>CSEs or equivalent</td>
<td>1 (2.4)</td>
<td>9 (3.0)</td>
<td>879 (3.6)</td>
<td></td>
</tr>
<tr>
<td>NVQ, HND, HNC, or equivalent</td>
<td>1 (2.4)</td>
<td>14 (4.6)</td>
<td>1396 (5.8)</td>
<td></td>
</tr>
<tr>
<td>Other professional qualifications</td>
<td>2 (4.8)</td>
<td>14 (4.6)</td>
<td>1150 (4.8)</td>
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</tr>
<tr>
<td>None of the above</td>
<td>1 (2.4)</td>
<td>14 (4.6)</td>
<td>1311 (5.4)</td>
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<tr>
<td>Missing</td>
<td>3 (7.1)</td>
<td>1 (0.3)</td>
<td>227 (0.9)</td>
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</tr>
<tr>
<td><strong>BMI in kg/m², mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>Number (%) missing</td>
<td>1 (2.4)</td>
<td>14 (4.6)</td>
<td>1325 (5.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Body fat percentage, mean (SD)</strong></td>
<td>30.0 (6.4)</td>
<td>32.0 (8.1)</td>
<td>30.2 (7.9)</td>
<td>4.6e-4</td>
</tr>
<tr>
<td>Number (%) missing</td>
<td>1 (2.4)</td>
<td>14 (4.6)</td>
<td>1331 (5.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>Current</td>
<td>1 (2.4)</td>
<td>6 (2.0)</td>
<td>647 (2.7)</td>
<td></td>
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<tr>
<td>Previous</td>
<td>8 (19.0)</td>
<td>112 (36.7)</td>
<td>7858 (32.6)</td>
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<tr>
<td>Never</td>
<td>31 (73.8)</td>
<td>206 (67.5)</td>
<td>15380 (63.8)</td>
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</tr>
<tr>
<td>Missing</td>
<td>2 (4.8)</td>
<td>2 (0.7)</td>
<td>221 (0.9)</td>
<td></td>
</tr>
</tbody>
</table>
BMI, body mass index; GC, glucocorticoids; n, number; SD, standard deviation.

P values were determined using analysis of variance (for continuous variables) and Fisher’s exact test (for categorical variables, because of the low number of patients using chronic glucocorticoids).
Supplement 6. Imaging parameters, presented as the adjusted mean difference of patients using chronic systemic glucocorticoids (n = 42) or chronic inhaled glucocorticoids (n = 305) compared to controls (n = 24106)

<table>
<thead>
<tr>
<th></th>
<th>ANOVA</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>P&lt;sub&gt;FDR&lt;/sub&gt;</td>
</tr>
<tr>
<td>Volumetric measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Global volumes (in mm&lt;sup&gt;3&lt;/sup&gt;)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Total brain volume</td>
<td>17.0</td>
<td>4.1e-8</td>
<td>1.5e-6</td>
</tr>
<tr>
<td>Grey matter volume</td>
<td>12.2</td>
<td>5.0e-6</td>
<td>9.1e-5</td>
</tr>
<tr>
<td>White matter volume</td>
<td>10.8</td>
<td>2.0e-5</td>
<td>1.8e-4</td>
</tr>
<tr>
<td>Peripheral cortex</td>
<td>8.5</td>
<td>2.1e-4</td>
<td>9.4e-4</td>
</tr>
<tr>
<td>CSF volume</td>
<td>3.0</td>
<td>5.2e-2</td>
<td>7.4e-2</td>
</tr>
<tr>
<td><strong>Subcortical volumes (in mm&lt;sup&gt;3&lt;/sup&gt;)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>5.8</td>
<td>2.9e-3</td>
<td>8.2e-3</td>
</tr>
<tr>
<td>Caudate</td>
<td>7.2</td>
<td>7.6e-4</td>
<td>2.9e-3</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>4.9</td>
<td>7.8e-3</td>
<td>1.7e-2</td>
</tr>
<tr>
<td>Pallidum</td>
<td>7.1</td>
<td>7.9e-4</td>
<td>2.9e-3</td>
</tr>
<tr>
<td>Putamen</td>
<td>5.0</td>
<td>6.9e-3</td>
<td>1.6e-2</td>
</tr>
<tr>
<td>Thalamus</td>
<td>6.7</td>
<td>1.3e-3</td>
<td>4.1e-3</td>
</tr>
<tr>
<td><strong>Regional grey matter volumes (in mm&lt;sup&gt;3&lt;/sup&gt;)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>10.1</td>
<td>4.2e-5</td>
<td>3.0e-4</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>4.1</td>
<td>1.6e-2</td>
<td>2.9e-2</td>
</tr>
<tr>
<td>Cingulate gyrus, posterior</td>
<td>4.2</td>
<td>1.6e-2</td>
<td>2.9e-2</td>
</tr>
<tr>
<td>Region</td>
<td>Fractional anisotropy</td>
<td>Mean diffusivity</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------</td>
<td>------------------</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus</td>
<td>9.1</td>
<td>6.6e-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.1e-4</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td></td>
<td>63.5</td>
<td>-24.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-52.4; 179.5</td>
<td>-66.1; 17.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precuneal cortex</td>
<td>8.6</td>
<td>9.1e-4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.8e-4</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td></td>
<td>170.0</td>
<td>-59.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-201.0; 541.2</td>
<td>-194.0; 74.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DTI measures**

<table>
<thead>
<tr>
<th>DTI measures</th>
<th>Fractional anisotropy</th>
<th>Mean diffusivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td>5.4</td>
<td>4.4e-3</td>
</tr>
<tr>
<td></td>
<td>1.1e-2</td>
<td>-0.0066</td>
</tr>
<tr>
<td></td>
<td>-0.013; -3.2e-4</td>
<td>0.038</td>
</tr>
<tr>
<td></td>
<td>0.0025</td>
<td>-0.0048; -2.3e-4</td>
</tr>
<tr>
<td></td>
<td>0.027</td>
<td></td>
</tr>
<tr>
<td><strong>Genu of corpus callosum</strong></td>
<td>5.8</td>
<td>3.2e-3</td>
</tr>
<tr>
<td></td>
<td>8.2e-3</td>
<td>-0.014</td>
</tr>
<tr>
<td></td>
<td>-0.025; -0.0031</td>
<td>0.0087</td>
</tr>
<tr>
<td></td>
<td>-0.0020</td>
<td>-0.0060; 0.0020</td>
</tr>
<tr>
<td></td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td><strong>Cingulum hippocampus</strong></td>
<td>3.7</td>
<td>2.4e-2</td>
</tr>
<tr>
<td></td>
<td>3.9e-2</td>
<td>0.0032</td>
</tr>
<tr>
<td></td>
<td>-0.0078; 0.014</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>-0.0034</td>
<td>-0.0074; 6.4e-4</td>
</tr>
<tr>
<td></td>
<td>0.11</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted mean difference, calculated using linear models, adjusted for age, sex, education, X-, Y-, and Z-position of the head in the scanner, head size, assessment centre, and year of imaging acquisition.

CI, confidence interval; P_{FDR}, Benjamini-Hochberg false discovery rate corrected P values; SE, standard error. P values in bold are statistically significant (P < 0.05).
**Supplement 7.** Cognitive outcome measures of chronic systemic glucocorticoid users (n = 42) and chronic inhaled glucocorticoid users (n = 305) vs. controls

<table>
<thead>
<tr>
<th></th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
<th>Participants with available data, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>AMD*</td>
</tr>
<tr>
<td>Trail making A</td>
<td>0.41</td>
<td>0.66</td>
<td>0.84</td>
</tr>
<tr>
<td>Trail making B</td>
<td>0.28</td>
<td>0.75</td>
<td>0.84</td>
</tr>
<tr>
<td>Symbol substitution</td>
<td>0.35</td>
<td>0.70</td>
<td>0.84</td>
</tr>
</tbody>
</table>

* Adjusted mean difference between patients and controls, expressed in Z scores. Calculated using linear models, adjusting for age, sex, and education.

Trail making A, and trail making B were log transformed before generation of Z scores because they were non-normally distributed. Variables were transformed such that higher values indicate a better performance.

CI, confidence interval; GC, glucocorticoids; n, number; P<sub>FDR</sub>, Benjamini-Hochberg false discovery rate corrected P values
**Supplement 8.** Self-reported frequency of mental health parameters in the past two weeks of patients using systemic glucocorticoids (n = 222) or inhaled glucocorticoids (n = 557) and controls, presented as number of participants (%) per category

<table>
<thead>
<tr>
<th></th>
<th>Systemic GC (n=222)</th>
<th>Inhaled GC (n=557)</th>
<th>Controls (n=24106)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depressed mood</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>170 (77)</td>
<td>455 (82)</td>
<td>19940 (83)</td>
</tr>
<tr>
<td>Several days</td>
<td>39 (18)</td>
<td>77 (14)</td>
<td>3017 (13)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>6 (2.7)</td>
<td>8 (1.4)</td>
<td>296 (1.2)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>1 (0.5)</td>
<td>3 (0.5)</td>
<td>150 (0.6)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (2.7)</td>
<td>14 (2.5)</td>
<td>703 (2.9)</td>
</tr>
<tr>
<td><strong>Disinterest</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>174 (78)</td>
<td>468 (84)</td>
<td>20536 (85)</td>
</tr>
<tr>
<td>Several days</td>
<td>34 (15)</td>
<td>61 (11)</td>
<td>2568 (11)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>3 (1.3)</td>
<td>7 (1.3)</td>
<td>292 (1.2)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>5 (2.3)</td>
<td>5 (0.9)</td>
<td>174 (0.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (2.7)</td>
<td>16 (2.9)</td>
<td>536 (2.2)</td>
</tr>
<tr>
<td><strong>Tenseness/restlessness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>162 (73)</td>
<td>437 (78)</td>
<td>19412 (81)</td>
</tr>
<tr>
<td>Several days</td>
<td>46 (21)</td>
<td>89 (16)</td>
<td>3630 (15)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>3 (1.3)</td>
<td>12 (2.2)</td>
<td>272 (1.1)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>5 (2.3)</td>
<td>5 (0.9)</td>
<td>126 (0.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (2.7)</td>
<td>14 (2.5)</td>
<td>666 (2.8)</td>
</tr>
<tr>
<td><strong>Tiredness/lethargy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>95 (43)</td>
<td>280 (50)</td>
<td>13792 (57)</td>
</tr>
<tr>
<td>Several days</td>
<td>91 (41)</td>
<td>221 (40)</td>
<td>8345 (35)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>9 (4.1)</td>
<td>32 (5.7)</td>
<td>815 (3.4)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>19 (8.6)</td>
<td>15 (2.7)</td>
<td>555 (2.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>8 (3.6)</td>
<td>9 (1.6)</td>
<td>599 (2.5)</td>
</tr>
</tbody>
</table>

GC, glucocorticoids; n, number.
Supplement 9. Self-reported frequency of mental health parameters in the past two weeks of chronic systemic glucocorticoid users (n = 42), chronic inhaled glucocorticoid users (n = 305) and controls, presented as number of participants (%) per category

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Systemic GC (n = 42)</th>
<th>Inhaled GC (n = 305)</th>
<th>Controls (n = 24106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>33 (79)</td>
<td>257 (84)</td>
<td>19940 (83)</td>
</tr>
<tr>
<td>Several days</td>
<td>6 (14)</td>
<td>35 (11)</td>
<td>3017 (13)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>0 (0)</td>
<td>3 (0.9)</td>
<td>296 (1.2)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>150 (0.6)</td>
</tr>
<tr>
<td>Missing</td>
<td>3 (7.1)</td>
<td>9 (3.0)</td>
<td>703 (2.9)</td>
</tr>
<tr>
<td>Disinterest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>34 (81)</td>
<td>267 (88)</td>
<td>20536 (85)</td>
</tr>
<tr>
<td>Several days</td>
<td>6 (14)</td>
<td>30 (9.8)</td>
<td>2568 (11)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>292 (1.2)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>174 (0.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (4.8)</td>
<td>7 (2.3)</td>
<td>536 (2.2)</td>
</tr>
<tr>
<td>Tenseness/restlessness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>30 (71)</td>
<td>245 (80)</td>
<td>19412 (81)</td>
</tr>
<tr>
<td>Several days</td>
<td>10 (24)</td>
<td>48 (16)</td>
<td>3630 (15)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>0 (0)</td>
<td>6 (2.0)</td>
<td>272 (1.1)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>126 (0.5)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (4.8)</td>
<td>5 (1.6)</td>
<td>666 (2.8)</td>
</tr>
<tr>
<td>Tiredness/lethargy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>24 (57)</td>
<td>156 (51)</td>
<td>13792 (57)</td>
</tr>
<tr>
<td>Several days</td>
<td>12 (29)</td>
<td>121 (40)</td>
<td>8345 (35)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>2 (4.8)</td>
<td>14 (4.6)</td>
<td>815 (3.4)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>2 (4.8)</td>
<td>8 (2.6)</td>
<td>555 (2.3)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (4.8)</td>
<td>6 (2.0)</td>
<td>599 (2.5)</td>
</tr>
</tbody>
</table>

GC, glucocorticoids; n, number.
**Supplement 10.** Likelihood of experiencing mental health complaints in the past two weeks of chronic systemic glucocorticoid users (n = 42) and chronic inhaled glucocorticoid users (n = 305) compared to controls

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Likelihood ratio test</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$X^2$</td>
<td>P value</td>
<td>$P_{FDR}$</td>
</tr>
<tr>
<td>Depression</td>
<td>1.1</td>
<td>0.57</td>
<td>0.57</td>
</tr>
<tr>
<td>Disinterest</td>
<td>2.2</td>
<td>0.33</td>
<td>0.44</td>
</tr>
<tr>
<td>Tensionness</td>
<td>2.5</td>
<td>0.28</td>
<td>0.44</td>
</tr>
<tr>
<td>Tiredness</td>
<td>4.4</td>
<td>0.11</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Calculated using logistic regression analysis, adjusting for age, sex, and education. P values in bold are statistically significant after Bonferroni correction for family-wise error rate of two tests ($P < 0.025$).

CI, confidence interval; GC, glucocorticoids; OR, odds ratio; $P_{FDR}$, Benjamini-Hochberg false discovery rate corrected P values.
**Supplement 11.** Sensitivity analysis: Characteristics of included glucocorticoid users and controls (without exclusion of participants based on psychiatric, neurological, or endocrine history or medication use)

<table>
<thead>
<tr>
<th></th>
<th>Patients using systemic GC (n = 312)</th>
<th>Patients using inhaled GC (n = 806)</th>
<th>Controls (n = 36310)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex: male, n (%)</strong></td>
<td>145 (46.5)</td>
<td>344 (42.7)</td>
<td>17041 (46.9)</td>
<td>0.057</td>
</tr>
<tr>
<td><strong>Age at time of scanning in years, mean (SD)</strong></td>
<td>66.1 (6.9)</td>
<td>62.8 (7.5)</td>
<td>63.7 (7.5)</td>
<td>3.6e-10</td>
</tr>
<tr>
<td><strong>Education level, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>College/University degree</td>
<td>143 (45.8)</td>
<td>407 (50.5)</td>
<td>17637 (48.6)</td>
<td></td>
</tr>
<tr>
<td>A levels or equivalent</td>
<td>39 (12.5)</td>
<td>98 (12.2)</td>
<td>4392 (12.1)</td>
<td></td>
</tr>
<tr>
<td>O levels/GCSE or equivalent</td>
<td>53 (17.0)</td>
<td>136 (16.9)</td>
<td>6400 (17.6)</td>
<td></td>
</tr>
<tr>
<td>CSEs or equivalent</td>
<td>13 (4.2)</td>
<td>26 (3.2)</td>
<td>1372 (3.8)</td>
<td></td>
</tr>
<tr>
<td>NVQ, HND, HNC, or equivalent</td>
<td>11 (3.5)</td>
<td>50 (6.2)</td>
<td>2142 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Other professional qualifications</td>
<td>21 (6.7)</td>
<td>45 (5.6)</td>
<td>1795 (4.9)</td>
<td></td>
</tr>
<tr>
<td>None of the above</td>
<td>27 (8.7)</td>
<td>40 (5.0)</td>
<td>2208 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>5 (1.6)</td>
<td>4 (0.5)</td>
<td>364 (1.0)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI in kg/m², mean (SD)</strong></td>
<td>26.7 (4.4)</td>
<td>27.1 (4.7)</td>
<td>26.5 (4.4)</td>
<td>2.2e-4</td>
</tr>
<tr>
<td>Number (%) missing</td>
<td>11 (3.5)</td>
<td>31 (3.8)</td>
<td>1932 (5.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Body fat percentage, mean (SD)</strong></td>
<td>31.9 (8.2)</td>
<td>32.6 (8.4)</td>
<td>31.1 (8.1)</td>
<td>5.5e-7</td>
</tr>
<tr>
<td>Number (%) missing</td>
<td>11 (3.5)</td>
<td>31 (3.8)</td>
<td>1942 (5.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.096</td>
</tr>
<tr>
<td>Current</td>
<td>10 (3.2)</td>
<td>25 (3.1)</td>
<td>1231 (3.3)</td>
<td></td>
</tr>
<tr>
<td>Previous</td>
<td>118 (37.8)</td>
<td>299 (37.1)</td>
<td>12063 (33.2)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>181 (58.0)</td>
<td>477 (59.2)</td>
<td>22661 (62.4)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>3 (1.0)</td>
<td>5 (0.6)</td>
<td>355 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>
BMI, body mass index; GC, glucocorticoids; n, number; SD, standard deviation.

P values determined using analysis of variance (for continuous variables) and Pearson’s Chi squared test (for categorical variables).
**Supplement 12.** Sensitivity analysis: Imaging parameters, presented as the adjusted mean difference of patients using systemic glucocorticoids (n = 312) or inhaled glucocorticoids (n = 806) compared to controls (n = 36310) (without exclusion of participants based on psychiatric, neurological, or endocrine history or medication use)

<table>
<thead>
<tr>
<th>Volumetric measures</th>
<th>ANOVA</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>P_{FDR}</td>
</tr>
<tr>
<td><strong>Global volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total brain volume</td>
<td>17.7</td>
<td>2.2e-8</td>
<td><strong>1.3e-7</strong></td>
</tr>
<tr>
<td>Grey matter volume</td>
<td>22.3</td>
<td>2.0e-10</td>
<td><strong>2.4e-9</strong></td>
</tr>
<tr>
<td>White matter volume</td>
<td>5.5</td>
<td>4.1e-3</td>
<td><strong>6.7e-3</strong></td>
</tr>
<tr>
<td>Peripheral cortex</td>
<td>24.6</td>
<td>2.0e-11</td>
<td><strong>4.4e-10</strong></td>
</tr>
<tr>
<td>CSF volume</td>
<td>14.2</td>
<td>7.1e-7</td>
<td><strong>2.3e-6</strong></td>
</tr>
<tr>
<td><strong>Subcortical volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accumbens</td>
<td>10.2</td>
<td>3.8e-5</td>
<td><strong>1.0e-4</strong></td>
</tr>
<tr>
<td>Caudate</td>
<td>4.5</td>
<td>1.1e-2</td>
<td><strong>1.7e-2</strong></td>
</tr>
<tr>
<td>Pallidum</td>
<td>6.9</td>
<td>1.0e-3</td>
<td><strong>1.9e-3</strong></td>
</tr>
<tr>
<td>Putamen</td>
<td>9.8</td>
<td>5.6e-5</td>
<td><strong>1.5e-4</strong></td>
</tr>
<tr>
<td>Thalamus</td>
<td>9.3</td>
<td>9.4e-5</td>
<td><strong>2.3e-4</strong></td>
</tr>
<tr>
<td><strong>Regional grey matter volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>21.0</td>
<td>7.8e-10</td>
<td><strong>7.0e-9</strong></td>
</tr>
<tr>
<td>Caudate</td>
<td>12.3</td>
<td>4.7e-6</td>
<td><strong>1.4e-5</strong></td>
</tr>
<tr>
<td>Cerebellum</td>
<td>5.8</td>
<td>3.1e-3</td>
<td><strong>5.2e-3</strong></td>
</tr>
<tr>
<td>Structure</td>
<td>FA</td>
<td>p-value</td>
<td>MDD</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------------</td>
<td>-----------------------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>Insular cortex</strong></td>
<td>8.7</td>
<td>1.7e-4</td>
<td><strong>3.5e-4</strong></td>
</tr>
<tr>
<td><strong>Precuneal cortex</strong></td>
<td>4.0</td>
<td>1.9e-2</td>
<td><strong>2.7e-2</strong></td>
</tr>
<tr>
<td><strong>DTI measures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fractional anisotropy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>15.5</td>
<td>1.8e-7</td>
<td><strong>9.4e-7</strong></td>
</tr>
<tr>
<td>Body of corpus callosum</td>
<td>8.9</td>
<td>1.4e-4</td>
<td><strong>3.1e-4</strong></td>
</tr>
<tr>
<td>Genu of corpus callosum</td>
<td>15.2</td>
<td>2.5e-7</td>
<td><strong>1.1e-6</strong></td>
</tr>
<tr>
<td>Cingulum cingulate</td>
<td>3.8</td>
<td>2.3e-2</td>
<td><strong>3.1e-2</strong></td>
</tr>
<tr>
<td><strong>Mean diffusivity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>24.5</td>
<td>2.4e-11</td>
<td><strong>4.4e-10</strong></td>
</tr>
<tr>
<td>Body of corpus callosum</td>
<td>14.2</td>
<td>6.7e-7</td>
<td><strong>2.3e-6</strong></td>
</tr>
<tr>
<td>Genu of corpus callosum</td>
<td>17.9</td>
<td>1.7e-8</td>
<td><strong>1.2e-7</strong></td>
</tr>
<tr>
<td>Splenium of corpus callosum</td>
<td>6.7</td>
<td>1.2e-3</td>
<td><strong>2.2e-3</strong></td>
</tr>
<tr>
<td>Cingulum cingulate</td>
<td>4.9</td>
<td>7.6e-3</td>
<td><strong>1.2e-2</strong></td>
</tr>
<tr>
<td>Cingulum hippocampus</td>
<td>14.5</td>
<td>4.9e-7</td>
<td><strong>2.0e-6</strong></td>
</tr>
<tr>
<td>Uncinate fasciculus</td>
<td>7.3</td>
<td>6.6e-4</td>
<td><strong>1.3e-3</strong></td>
</tr>
</tbody>
</table>

* Adjusted mean difference, calculated using linear models, adjusted for age, sex, education, X-, Y-, and Z-position of the head in the scanner, head size, assessment centre, and year of imaging acquisition.

$P_{FDR}$, Benjamini-Hochberg false discovery rate corrected P values; SE, standard error. P values in bold are statistically significant (P < 0.05).
Supplement 13. Sensitivity analysis: Cognitive outcome measures of systemic glucocorticoid users (n = 312) and inhaled glucocorticoid users (n = 806) vs. controls (n = 36310) (without exclusion of participants based on psychiatric, neurological, or endocrine history or medication use)

<table>
<thead>
<tr>
<th></th>
<th>ANOVA</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
<th>Participants with available data, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>P_{FDR}</td>
<td>AMD*</td>
</tr>
<tr>
<td>Trail making A</td>
<td>6.6</td>
<td>0.0014</td>
<td>0.0028</td>
<td>-0.11</td>
</tr>
<tr>
<td>Trail making B</td>
<td>6.7</td>
<td>0.0013</td>
<td>0.0028</td>
<td>-0.12</td>
</tr>
<tr>
<td>Symbol substitution</td>
<td>9.7</td>
<td>6.2e-5</td>
<td>0.00037</td>
<td>-0.15</td>
</tr>
</tbody>
</table>

* Adjusted mean difference between patients and controls, expressed in Z scores. Calculated using linear models, adjusted for age, sex, and education. Trail making A, and trail making B were log transformed before generation of Z scores because they were non-normally distributed. Variables were transformed such that higher values indicate a better performance.

GC, glucocorticoids; P_{FDR}, Benjamini-Hochberg false discovery rate corrected P values.
**Supplement 14.** Sensitivity analysis: Self-reported frequency of mental health parameters in the past two weeks of patients using systemic glucocorticoids (n = 312) or inhaled glucocorticoids (n = 806) and controls, presented as number of participants (%) per category (without exclusion of participants based on psychiatric, neurological, or endocrine history or medication use)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Systemic GC (n = 312)</th>
<th>Inhaled GC (n = 806)</th>
<th>Controls (n = 36310)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depressed mood</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>240 (76.9)</td>
<td>620 (76.9)</td>
<td>29014 (80.0)</td>
</tr>
<tr>
<td>Several days</td>
<td>55 (17.6)</td>
<td>139 (17.2)</td>
<td>5197 (14.3)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>8 (2.6)</td>
<td>14 (1.7)</td>
<td>593 (1.6)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>2 (0.6)</td>
<td>14 (1.7)</td>
<td>360 (1.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>7 (2.2)</td>
<td>19 (2.4)</td>
<td>1146 (3.2)</td>
</tr>
<tr>
<td><strong>Disinterest</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>237 (76.0)</td>
<td>639 (79.3)</td>
<td>29916 (82.4)</td>
</tr>
<tr>
<td>Several days</td>
<td>55 (17.6)</td>
<td>118 (14.6)</td>
<td>4583 (12.6)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>8 (2.6)</td>
<td>17 (2.1)</td>
<td>604 (1.7)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>5 (1.6)</td>
<td>12 (1.5)</td>
<td>357 (1.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>7 (2.2)</td>
<td>20 (2.5)</td>
<td>850 (2.3)</td>
</tr>
<tr>
<td><strong>Tenseness/restlessness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>221 (70.8)</td>
<td>588 (73.0)</td>
<td>28266 (77.8)</td>
</tr>
<tr>
<td>Several days</td>
<td>71 (22.8)</td>
<td>157 (19.5)</td>
<td>6113 (16.8)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>6 (1.9)</td>
<td>23 (2.9)</td>
<td>565 (1.6)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>6 (1.9)</td>
<td>16 (2.0)</td>
<td>313 (0.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>8 (2.6)</td>
<td>22 (2.7)</td>
<td>1053 (2.9)</td>
</tr>
<tr>
<td><strong>Tiredness/lethargy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>125 (40.0)</td>
<td>366 (45.4)</td>
<td>19107 (52.6)</td>
</tr>
<tr>
<td>Several days</td>
<td>130 (41.7)</td>
<td>321 (39.8)</td>
<td>13373 (36.8)</td>
</tr>
<tr>
<td>More than half of the days</td>
<td>22 (7.1)</td>
<td>53 (6.6)</td>
<td>1533 (4.2)</td>
</tr>
<tr>
<td>Nearly every day</td>
<td>26 (8.3)</td>
<td>51 (6.3)</td>
<td>1358 (3.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>9 (2.9)</td>
<td>15 (1.9)</td>
<td>939 (2.6)</td>
</tr>
</tbody>
</table>

GC, glucocorticoids; n, number.
Supplement 15. Sensitivity analysis: Likelihood of experiencing mental health complaints in the past two weeks of systemic glucocorticoid users (n = 312) and inhaled glucocorticoid users (n = 806) compared to controls (without exclusion of participants based on psychiatric, neurological, or endocrine history or medication use)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Likelihood ratio test</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X²</td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Depression</td>
<td>11.1</td>
<td>0.0039</td>
<td>0.0039</td>
</tr>
<tr>
<td>Disinterest</td>
<td>17.8</td>
<td>1.4e-04</td>
<td>1.9e-04</td>
</tr>
<tr>
<td>Tenseness</td>
<td>24.0</td>
<td>6.1e-06</td>
<td>1.2e-05</td>
</tr>
<tr>
<td>Tiredness</td>
<td>39.2</td>
<td>3.1e-09</td>
<td>1.2e-08</td>
</tr>
</tbody>
</table>

Calculated using logistic regression analysis, adjusting for age, sex, and education. P values in bold are statistically significant after Bonferroni correction for family-wise error rate of two tests (P < 0.025). CI, confidence interval; GC, glucocorticoids; OR, odds ratio; P_FDR, Benjamini-Hochberg false discovery rate corrected P values.
**Supplement 16.** Sensitivity analysis: Imaging parameters, presented as the adjusted mean difference of patients using systemic glucocorticoids (n = 222) or inhaled glucocorticoids (n = 557) compared to controls (n = 24106) (after exclusion of outlier values per group per variable)

<table>
<thead>
<tr>
<th>Volumetric measures</th>
<th>ANOVA</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>P_FDR</td>
</tr>
<tr>
<td><strong>Global volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total brain volume</td>
<td>16.0</td>
<td>1.1e-7</td>
<td><strong>4.6e-7</strong></td>
</tr>
<tr>
<td>Grey matter volume</td>
<td>28.8</td>
<td>3.4e-13</td>
<td><strong>6.1e-12</strong></td>
</tr>
<tr>
<td>White matter volume</td>
<td>5.4</td>
<td>4.6e-3</td>
<td><strong>7.1e-3</strong></td>
</tr>
<tr>
<td>Peripheral cortex</td>
<td>27.0</td>
<td>2.0e-12</td>
<td><strong>1.8e-11</strong></td>
</tr>
<tr>
<td>CSF volume</td>
<td>16.8</td>
<td>5.0e-8</td>
<td><strong>2.3e-7</strong></td>
</tr>
<tr>
<td><strong>Subcortical volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accumbens</td>
<td>13.0</td>
<td>2.3e-6</td>
<td><strong>5.8e-6</strong></td>
</tr>
<tr>
<td>Caudate</td>
<td>4.7</td>
<td>8.8e-3</td>
<td><strong>1.1e-2</strong></td>
</tr>
<tr>
<td>Hippocampus</td>
<td>5.4</td>
<td>4.7e-3</td>
<td><strong>7.1e-3</strong></td>
</tr>
<tr>
<td>Pallidum</td>
<td>4.9</td>
<td>7.4e-3</td>
<td><strong>9.8e-3</strong></td>
</tr>
<tr>
<td>Putamen</td>
<td>13.7</td>
<td>1.1e-6</td>
<td><strong>3.4e-6</strong></td>
</tr>
<tr>
<td>Thalamus</td>
<td>10.0</td>
<td>4.6e-5</td>
<td><strong>8.7e-5</strong></td>
</tr>
<tr>
<td><strong>Regional grey matter volumes (in mm$^3$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amygdala</td>
<td>28.3</td>
<td>5.1e-13</td>
<td><strong>6.1e-12</strong></td>
</tr>
<tr>
<td>Caudate</td>
<td>12.6</td>
<td>3.5e-6</td>
<td><strong>8.4e-6</strong></td>
</tr>
<tr>
<td>Cerebellum</td>
<td>10.3</td>
<td>3.3e-5</td>
<td><strong>6.6e-5</strong></td>
</tr>
<tr>
<td>Region</td>
<td>Fractional anisotropy</td>
<td>Mean diffusivity</td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------</td>
<td>------------------</td>
<td></td>
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<tr>
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<td>Global</td>
<td>Body of corpus callosum</td>
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<td></td>
<td>22.7 1.4e-10</td>
<td>11.4 1.1e-5</td>
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<td>1.0e-9</td>
<td>2.5e-5</td>
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<td>-0.0043</td>
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<td>-0.0067; -0.0018</td>
<td>-0.0086; -0.0010</td>
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<td>-0.0045; 3.4e-4</td>
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<td>0.11</td>
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<td>-0.0065; 0.0021</td>
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<td>-0.0053; 9.7e-5</td>
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<td>Cingulum cingulate</td>
<td>6.5 1.5e-3</td>
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<td>-0.0065; 0.0021</td>
<td>0.42</td>
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<tr>
<td></td>
<td>-0.0026</td>
<td>-0.0053; 9.7e-5</td>
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<td>0.061</td>
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<td></td>
<td>Cingulum hippocampus</td>
<td>7.5 5.7e-4</td>
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<td>-0.00012</td>
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<td>0.010</td>
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</table>

* Adjusted mean difference, calculated using linear models, adjusted for age, sex, education, X-, Y-, and Z-position of the head in the scanner, head size, assessment centre, and year of imaging acquisition.

P<sub>FDR</sub>, Benjamini-Hochberg false discovery rate corrected P values; SE, standard error. P values in bold are statistically significant (P < 0.05).
**Supplement 17.** Cognitive outcome measures of systemic glucocorticoid users (n = 222) and inhaled glucocorticoid users (n = 557) vs. controls (after exclusion of outlier values per group per variable)

<table>
<thead>
<tr>
<th>ANOVA</th>
<th>Systemic GC vs. controls</th>
<th>Inhaled GC vs. controls</th>
<th>Participants with available data, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F value</td>
<td>P value</td>
<td>P_FDR</td>
</tr>
<tr>
<td>Trail making A</td>
<td>5.2</td>
<td>0.0057</td>
<td>0.011</td>
</tr>
<tr>
<td>Trail making B</td>
<td>9.6</td>
<td>6.8e-5</td>
<td>2.0e-4</td>
</tr>
<tr>
<td>Symbol substitution</td>
<td>11.6</td>
<td>8.9e-6</td>
<td>5.3e-5</td>
</tr>
</tbody>
</table>

* Adjusted mean difference between patients and controls, expressed in Z scores. Calculated using linear models, adjusted for age, sex, and education. Trail making A, and trail making B were log transformed before generation of Z scores because they were non-normally distributed. Variables were transformed such that higher values indicate a better performance.

GC, glucocorticoids; P_FDR, Benjamini-Hochberg false discovery rate corrected P values.
**Supplement 18. STROBE Statement – Checklist of items that should be included in reports of cohort studies**

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
<th>Where to be found</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
<td>Abstract: Design (p.2)</td>
</tr>
<tr>
<td>1</td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>Abstract: Main outcome measures, Results (p.2)</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>Introduction (p.4)</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
<td>Introduction (p.4)</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>Study design (p.5)</td>
</tr>
<tr>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>Study design, Data collection (p.5)</td>
</tr>
<tr>
<td>6</td>
<td>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
<td>Participants (pp.5-6)</td>
</tr>
<tr>
<td>6</td>
<td>(b) For matched studies, give matching criteria and number of exposed and unexposed</td>
<td>Not applicable</td>
</tr>
<tr>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>Data collection, Imaging data, Cognitive and Emotional data, Statistical analysis (pp.5-9)</td>
</tr>
<tr>
<td>8</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
<td>Data collection, Imaging data, Cognitive and Emotional data (pp.5-7)</td>
</tr>
<tr>
<td><strong>Bias</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>Statistical analysis (pp.7-9)</td>
</tr>
<tr>
<td><strong>Study size</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Explain how the study size was arrived at</td>
<td>Participants (pp.5-6)</td>
</tr>
<tr>
<td><strong>Quantitative variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
<td>Statistical analysis (pp.7-9)</td>
</tr>
<tr>
<td><strong>Statistical methods</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
<td>Statistical analysis (pp.7-9)</td>
</tr>
<tr>
<td>12</td>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>(c) Explain how missing data were addressed</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>(d) If applicable, explain how loss to follow-up was addressed</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>(e) Describe any sensitivity analyses</td>
<td></td>
</tr>
</tbody>
</table>
### Results

<table>
<thead>
<tr>
<th>Participants</th>
<th>13</th>
<th>(a) Report numbers of individuals at each stage of study – e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed</th>
<th>Demographic characteristics (p.10) and Figure 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(b) Give reasons for non-participation at each stage</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) Consider use of a flow diagram</td>
<td></td>
</tr>
<tr>
<td>Descriptive data</td>
<td>14</td>
<td>(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders</td>
<td>Demographic characteristics (p.10) and Table 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Indicate number of participants with missing data for each variable of interest</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) Summarize follow-up time (e.g., average and total amount)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Outcome data</td>
<td>15*</td>
<td>Report numbers of outcome events or summary measures over time</td>
<td>Results (pp.12-19)</td>
</tr>
<tr>
<td>Main results</td>
<td>16</td>
<td>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included</td>
<td>Results (pp.12-19), Tables 2-4, Supplements</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Report category boundaries when continuous variables were categorized</td>
<td>Statistical analysis (p.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Other analyses</td>
<td>17</td>
<td>Report other analyses done – e.g. analyses of subgroups and interactions, and sensitivity analyses</td>
<td>Results (p.20), Supplements</td>
</tr>
</tbody>
</table>

### Discussion

| Key results | 18 | Summarize key results with reference to study objectives | Discussion (pp.21-22) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Strengths and limitations (pp.23-25) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Findings in context, Potential consequences and implications (pp.21-23) |
| Generalizability | 21 | Discuss the generalizability (external validity) of the study results | Strengths and limitations (pp.23-25) |

### Other information

| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Funding (p.26) |