

# THE LANCET

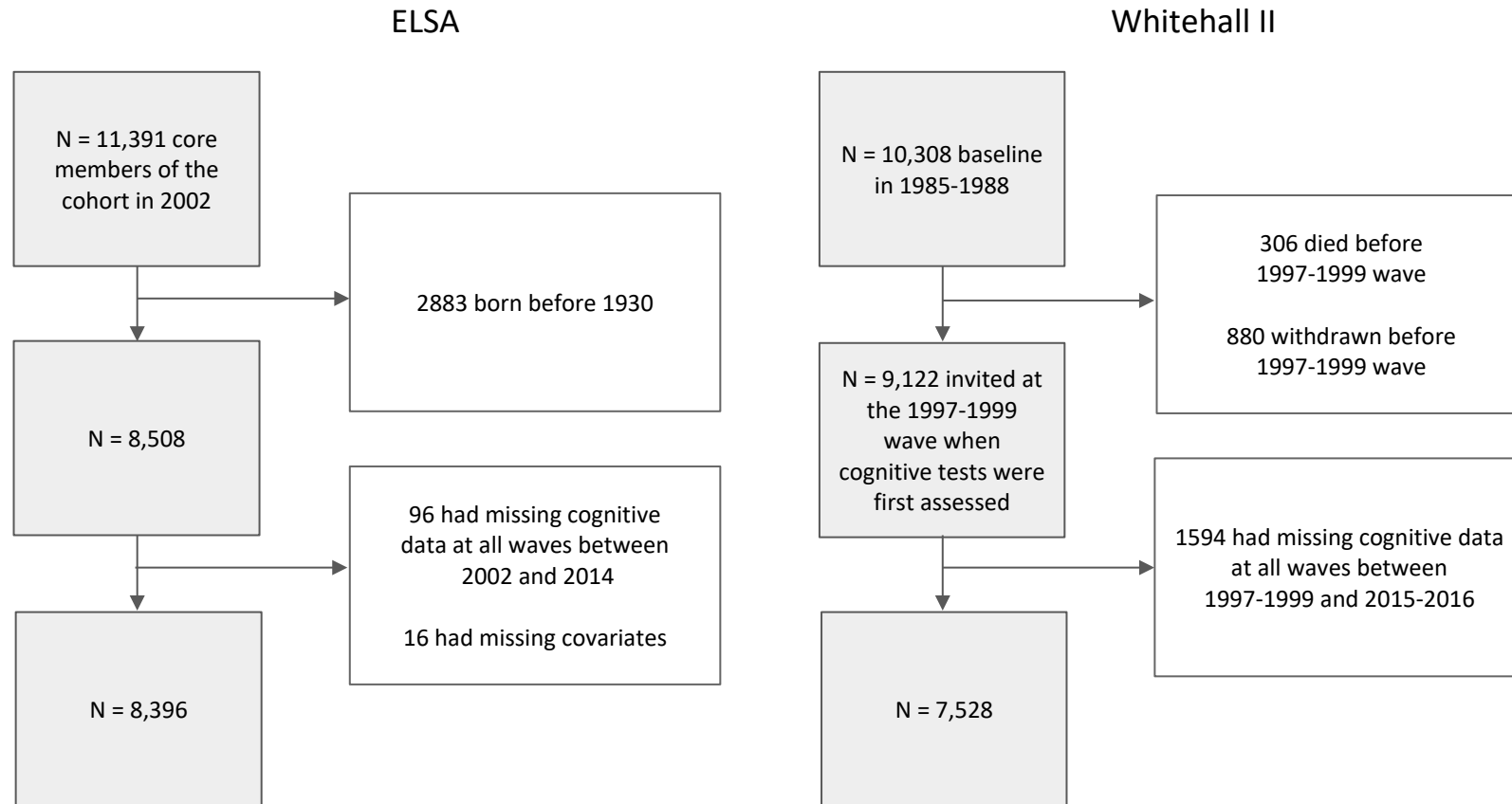
## Public Health

### **Supplementary appendix**

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Bloomberg M, Dugravot A, Dumurgier J, et al. Sex differences and the role of education in cognitive ageing: analysis of two UK-based prospective cohort studies. *Lancet Public Health* 2021; **6**: e106–15.

Figure S1. Flow chart.



**Table S1. Education categories available in Whitehall II and ELSA.**

| <b>Whitehall II</b> | <b>ELSA</b>                         | <b>Education-adjusted models<sup>a</sup></b> | <b>Education-stratified models<sup>b</sup></b> |
|---------------------|-------------------------------------|--|--|
| No qualification    | No qualification                    | Less than secondary                          | Low education                                  |
| O-level             | O-level                             | O-level                                      |  |
| A-level             | A-level                             | A-level                                      | High education                                 |
|                     | Higher education below degree level |  |  |
| BA/BSc              | University degree and above         | University degree and above                  |  |
| Higher degree       |                                     |  |  |

<sup>a</sup>Models adjusted for education include 4-class education variable as a categorical covariate. Models adjusted for education by sex interactions include education as a continuous variable to increase statistical power.

<sup>b</sup>Models stratified by education use this specification for high and low education categories.

**Table S2. Characteristics of participants included in the analyses from ELSA and the Whitehall II study.**

|                                | 1930-1938       |                 |         | 1939-1945       |                 |         | 1946-1955       |                 |         | P trend Men | P trend Women |
|--------------------------------|-----------------|-----------------|---------|-----------------|-----------------|---------|-----------------|-----------------|---------|-------------|---------------|
|                                | Men             | Women           | P-value | Men             | Women           | P-value | Men             | Women           | P-value |             |               |
| <b>ELSA</b>                    | <b>N = 1377</b> | <b>N = 1525</b> |         | <b>N = 1153</b> | <b>N = 1338</b> |         | <b>N = 1376</b> | <b>N = 1627</b> |         |             |               |
| Baseline Age, M(SD)            | 67.9 (2.6)      | 68.1 (2.6)      | 0.16    | 60.1 (2.1)      | 60.0 (2.1)      | 0.18    | 53.5 (2.0)      | 53.4 (2.0)      | 0.40    | <0.0001     | <0.0001       |
| Ethnicity, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| White                          | 1322 (96.0)     | 1487 (97.5)     | 0.021   | 1116 (96.8)     | 1308 (97.8)     | 0.14    | 1325 (96.3)     | 1570 (96.5)     | 0.76    | 0.69        | 0.080         |
| Non-white                      | 55 (4.0)        | 38 (2.5)        |         | 37 (3.2)        | 30 (2.2)        |         | 51 (3.7)        | 57 (3.5)        |         |             |               |
| Education, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| Below A-level                  | 1133 (82.3)     | 1401 (91.9)     | <0.0001 | 863 (74.8)      | 1130 (84.5)     | <0.0001 | 928 (67.4)      | 1299 (79.8)     | <0.0001 | <0.0001     | <0.0001       |
| A-level and above              | 244 (17.7)      | 124 (8.1)       |         | 290 (25.2)      | 208 (15.5)      |         | 448 (32.6)      | 328 (20.2)      |         |             |               |
| <b>Whitehall II</b>            | <b>N = 1599</b> | <b>N = 793</b>  |         | <b>N = 1704</b> | <b>N = 722</b>  |         | <b>N = 1992</b> | <b>N = 718</b>  |         |             |               |
| Baseline Age, M(SD)            | 64.2 (3.6)      | 64.8 (4.3)      | 0.00030 | 56.9 (3.9)      | 57.2 (3.9)      | 0.12    | 51.0 (3.9)      | 50.9 (3.9)      | 0.49    | <0.0001     | <0.0001       |
| Ethnicity, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| White                          | 1455 (91.0)     | 693 (87.4)      | 0.0061  | 1587 (93.1)     | 590 (81.7)      | <0.0001 | 1912 (96.0)     | 638 (88.9)      | <0.0001 | <0.0001     | 0.48          |
| Non-white                      | 144 (9.0)       | 100 (12.6)      |         | 117 (6.9)       | 132 (18.3)      |         | 80 (4.0)        | 80 (11.1)       |         |             |               |
| Education, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| Below A-level                  | 777 (48.6)      | 588 (74.1)      | <0.0001 | 661 (38.8)      | 410 (56.8)      | <0.0001 | 610 (30.6)      | 281 (39.1)      | <0.0001 | <0.0001     | <0.0001       |
| A-level and above              | 822 (51.4)      | 205 (25.9)      |         | 1043 (61.2)     | 312 (43.2)      |         | 1382 (69.4)     | 437 (60.9)      |         |             |               |
| <b>ELSA &amp; Whitehall II</b> | <b>N = 2976</b> | <b>N = 2318</b> |         | <b>N = 2857</b> | <b>N = 2060</b> |         | <b>N = 3368</b> | <b>N = 2345</b> |         |             |               |
| Baseline Age, M(SD)            | 65.9 (3.7)      | 66.9 (3.6)      | <0.0001 | 58.2 (3.6)      | 59.0 (3.2)      | <0.0001 | 52.0 (3.5)      | 52.6 (2.9)      | <0.0001 | <0.0001     | <0.0001       |
| Ethnicity, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| White                          | 2777 (93.3)     | 2180 (94.0)     | 0.28    | 2703 (94.6)     | 1898 (92.1)     | 0.00050 | 3237 (96.1)     | 2208 (94.2)     | 0.00060 | <0.0001     | 0.87          |
| Non-white                      | 199 (6.7)       | 138 (6.0)       |         | 154 (5.4)       | 162 (7.9)       |         | 131 (3.9)       | 137 (5.8)       |         |             |               |
| Education, N (%)               |                 |                 |         |                 |                 |         |                 |                 |         |             |               |
| Below A-level                  | 1910 (64.2)     | 1989 (85.8)     | <0.0001 | 1524 (53.3)     | 1540 (74.8)     | <0.0001 | 1538 (45.7)     | 1580 (67.4)     | <0.0001 | <0.0001     | <0.0001       |
| A-level and above              | 1066 (35.8)     | 329 (14.2)      |         | 1333 (46.7)     | 520 (25.2)      |         | 1830 (54.3)     | 765 (32.6)      |         |             |               |

**Table S3. Role of education in sex differences in cognitive performance in the Whitehall II study.**

|   | Age 50 years               |                                      | Age 60 years               |                                      | Age 70 years               |                                      |
|---|----------------------------|--------------------------------------|----------------------------|--------------------------------------|----------------------------|--------------------------------------|
|   | Base Model <sup>a</sup>    | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education |
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Memory</b>                           |                            |                                      |                            |                                      |                            |                                      |
| Birth cohort                            |                            |                                      |                            |                                      |                            |                                      |
| 1930-1938                               | No data                    | No data                              | -0.06 (-0.16, 0.03)        | -0.20 (-0.30, -0.11)                 | -0.02 (-0.08, 0.05)        | -0.12 (-0.19, -0.06)                 |
| 1939-1945                               | No data                    | No data                              | -0.06 (-0.14, 0.01)        | -0.14 (-0.21, -0.07)                 | -0.06 (-0.13, 0.01)        | -0.13 (-0.20, -0.06)                 |
| 1946-1955                               | -0.17 (-0.26, -0.09)       | -0.21 (-0.29, -0.12)                 | -0.18 (-0.24, -0.11)       | -0.21 (-0.28, -0.15)                 | -0.18 (-0.27, -0.10)       | -0.22 (-0.30, -0.14)                 |
| <i>P sex difference by birth cohort</i> |                            |                                      | <i>0.031</i>               | <i>0.27</i>                          | <i>0.0078</i>              | <i>0.14</i>                          |
| <b>Fluency</b>                          |                            |                                      |                            |                                      |                            |                                      |
| Birth cohort                            |                            |                                      |                            |                                      |                            |                                      |
| 1930-1938                               | No data                    | No data                              | 0.38 (0.29, 0.47)          | 0.17 (0.09, 0.25)                    | 0.33 (0.27, 0.40)          | 0.14 (0.08, 0.21)                    |
| 1939-1945                               | No data                    | No data                              | 0.11 (0.03, 0.18)          | -0.02 (-0.09, 0.04)                  | 0.06 (-0.02, 0.13)         | -0.06 (-0.13, 0.01)                  |
| 1946-1955                               | -0.10 (-0.18, -0.01)       | -0.16 (-0.24, -0.09)                 | -0.11 (-0.17, -0.04)       | -0.17 (-0.23, -0.10)                 | -0.11 (-0.19, -0.03)       | -0.17 (-0.25, -0.10)                 |
| <i>P sex difference by birth cohort</i> |                            |                                      | <i>&lt;0.0001</i>          | <i>&lt;0.0001</i>                    | <i>&lt;0.0001</i>          | <i>&lt;0.0001</i>                    |

<sup>a</sup>Adjusted for ethnicity, practice effect, interactions with age.

Positive value indicates male advantage in performance.

**Table S4. Role of education in sex differences in cognitive performance in ELSA.**

|   | Age 50 years               |                                      | Age 60 years               |                                      | Age 70 years               |                                      |
|---|----------------------------|--------------------------------------|----------------------------|--------------------------------------|----------------------------|--------------------------------------|
|   | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education |
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Memory</b>                           |                            |                                      |                            |                                      |                            |                                      |
| Birth cohort                            |                            |                                      |                            |                                      |                            |                                      |
| 1930-1938                               | No data                    | No data                              | No data                    | No data                              | -0.22 (-0.29, -0.16)       | -0.35 (-0.41, -0.29)                 |
| 1939-1945                               | No data                    | No data                              | -0.18 (-0.25, -0.11)       | -0.27 (-0.34, -0.21)                 | -0.25 (-0.32, -0.17)       | -0.36 (-0.43, -0.28)                 |
| 1946-1955                               | -0.09 (-0.17, -0.01)       | -0.17 (-0.25, -0.09)                 | -0.16 (-0.21, -0.10)       | -0.25 (-0.30, -0.20)                 | No data                    | No data                              |
| <i>P sex difference by birth cohort</i> |                            |                                      | <i>0.69</i>                | <i>0.47</i>                          | <i>0.90</i>                | <i>0.83</i>                          |
| <b>Fluency</b>                          |                            |                                      |                            |                                      |                            |                                      |
| Birth cohort                            |                            |                                      |                            |                                      |                            |                                      |
| 1930-1938                               | No data                    | No data                              | No data                    | No data                              | 0.11 (0.04, 0.17)          | 0.00 (-0.07, 0.06)                   |
| 1939-1945                               | No data                    | No data                              | 0.07 (-0.00, 0.14)         | -0.02 (-0.09, 0.05)                  | 0.07 (-0.01, 0.15)         | -0.03 (-0.11, 0.05)                  |
| 1946-1955                               | 0.17 (0.09, 0.25)          | 0.08 (-0.00, 0.16)                   | 0.09 (0.03, 0.15)          | 0.00 (-0.06, 0.06)                   | No data                    | No data                              |
| <i>P sex difference by birth cohort</i> |                            |                                      | <i>0.57</i>                | <i>0.65</i>                          | <i>0.27</i>                | <i>0.47</i>                          |

<sup>a</sup>Adjusted for ethnicity, practice effect, interactions with age.

Positive value indicates male advantage in performance.

**Table S5. Role of education in sex differences in 13-year cognitive decline: Analyses stratified by birth cohort and undertaken separately in Whitehall II and ELSA.**

|   | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education |
|---|----------------------------|--------------------------------------|
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Whitehall II</b>                     |                            |                                      |
| <b>Memory</b>                           |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | 0.06 (-0.02, 0.14)         | 0.10 (0.02, 0.19)                    |
| 1939-1945                               | 0.00 (-0.07, 0.08)         | 0.01 (-0.06, 0.09)                   |
| 1946-1955                               | -0.01 (-0.08, 0.06)        | -0.01 (-0.08, 0.06)                  |
| <i>P sex difference by birth cohort</i> | <i>0.43</i>                | <i>0.10</i>                          |
| <b>Fluency</b>                          |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.06 (-0.13, 0.00)        | -0.04 (-0.10, 0.03)                  |
| 1939-1945                               | -0.06 (-0.12, -0.00)       | -0.05 (-0.11, 0.01)                  |
| 1946-1955                               | -0.01 (-0.07, 0.05)        | -0.01 (-0.06, 0.05)                  |
| <i>P sex difference by birth cohort</i> | <i>0.37</i>                | <i>0.53</i>                          |
| <b>ELSA</b>                             |                            |                                      |
| <b>Memory</b>                           |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.02 (-0.12, 0.08)        | -0.04 (-0.14, 0.07)                  |
| 1939-1945                               | -0.09 (-0.19, 0.02)        | -0.11 (-0.22, -0.01)                 |
| 1946-1955                               | -0.09 (-0.18, 0.00)        | -0.10 (-0.19, -0.00)                 |
| <i>P sex difference by birth cohort</i> | <i>0.54</i>                | <i>0.57</i>                          |
| <b>Fluency</b>                          |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.04 (-0.14, 0.06)        | -0.05 (-0.15, 0.05)                  |
| 1939-1945                               | 0.00 (-0.10, 0.10)         | -0.01 (-0.11, 0.09)                  |
| 1946-1955                               | -0.10 (-0.19, -0.01)       | -0.10 (-0.19, -0.01)                 |
| <i>P sex difference by birth cohort</i> | <i>0.32</i>                | <i>0.42</i>                          |

<sup>a</sup>Adjusted for ethnicity, practice effect, interactions with age. Results are shown for the reference category: participants aged 60 years.

Positive value indicates slower cognitive decline in men.

**Table S6. Role of education in sex differences in cognitive performance: Analyses stratified by birth cohort and excluding participants with dementia.<sup>a</sup>**

|   | Age 50 years             |                                      | Age 60 years             |                                      | Age 70 years             |                                      |
|---|--------------------------|--------------------------------------|--------------------------|--------------------------------------|--------------------------|--------------------------------------|
|   | Basic Model <sup>b</sup> | Basic Model <sup>b</sup> + Education | Basic Model <sup>b</sup> | Basic Model <sup>b</sup> + Education | Basic Model <sup>b</sup> | Basic Model <sup>b</sup> + Education |
| ELSA & Whitehall II                     | Sex difference (95% CI)  | Sex difference (95% CI)              | Sex difference (95% CI)  | Sex difference (95% CI)              | Sex difference (95% CI)  | Sex difference (95% CI)              |
| <b>Memory</b>                           |                          |                                      |                          |                                      |                          |                                      |
| Birth cohort                            |                          |                                      |                          |                                      |                          |                                      |
| 1930-1938                               | No data                  | No data                              | -0.12 (-0.20, -0.04)     | -0.27 (-0.34, -0.19)                 | -0.14 (-0.19, -0.09)     | -0.26 (-0.30, -0.21)                 |
| 1939-1945                               | No data                  | No data                              | -0.13 (-0.18, -0.07)     | -0.22 (-0.27, -0.17)                 | -0.22 (-0.27, -0.16)     | -0.30 (-0.35, -0.25)                 |
| 1946-1955                               | -0.07 (-0.13, -0.01)     | -0.14 (-0.20, -0.09)                 | -0.18 (-0.22, -0.14)     | -0.25 (-0.29, -0.21)                 | -0.29 (-0.35, -0.22)     | -0.36 (-0.42, -0.29)                 |
| <i>P sex difference by birth cohort</i> |                          |                                      | <i>0.22</i>              | <i>0.46</i>                          | <i>0.0019</i>            | <i>0.028</i>                         |
| <b>Fluency</b>                          |                          |                                      |                          |                                      |                          |                                      |
| Birth cohort                            |                          |                                      |                          |                                      |                          |                                      |
| 1930-1938                               | No data                  | No data                              | 0.19 (0.07, 0.31)        | 0.03 (-0.09, 0.15)                   | 0.18 (0.13, 0.24)        | 0.05 (-0.00, 0.10)                   |
| 1939-1945                               | No data                  | No data                              | 0.09 (0.03, 0.14)        | -0.02 (-0.08, 0.03)                  | 0.02 (-0.04, 0.07)       | -0.08 (-0.14, -0.03)                 |
| 1946-1955                               | 0.06 (-0.01, 0.13)       | -0.04 (-0.11, 0.03)                  | 0.00 (-0.05, 0.04)       | -0.10 (-0.14, -0.05)                 | -0.02 (-0.11, 0.08)      | -0.09 (-0.18, 0.01)                  |
| <i>P sex difference by birth cohort</i> |                          |                                      | <i>0.0023</i>            | <i>0.038</i>                         | <i>&lt;0.0001</i>        | <i>0.00030</i>                       |

<sup>a</sup>This analysis is conducted on 15,372 participants free of dementia during the follow-up period (N dementia cases excluded: 434 in Whitehall II and 118 in ELSA).

<sup>b</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions.

Positive value indicates male advantage in performance.



**Table S7. Sex differences in cognitive performance: Analyses stratified by birth cohort and education and excluding participants with dementia.<sup>a</sup>**

| ELSA & Whitehall II                     | Age 50 years            | Age 60 years            | Age 70 years            |
|---|-------------------------|-------------------------|-------------------------|
|   | Sex difference (95% CI) | Sex difference (95% CI) | Sex difference (95% CI) |
| <b>Memory</b>                           |                         |                         |                         |
| <b>Education: Below A-level</b>         |                         |                         |                         |
| 1930-1938                               | No data                 | -0.18 (-0.27, -0.10)    | -0.19 (-0.24, -0.14)    |
| 1939-1945                               | No data                 | -0.18 (-0.24, -0.12)    | -0.29 (-0.35, -0.23)    |
| 1946-1955                               | -0.09 (-0.16, -0.02)    | -0.22 (-0.27, -0.16)    | -0.34 (-0.43, -0.26)    |
| <i>P sex difference by birth cohort</i> |                         | 0.68                    | 0.0042                  |
| <b>Education: A-level and above</b>     |                         |                         |                         |
| 1930-1938                               | No data                 | -0.23 (-0.38, -0.09)    | -0.24 (-0.33, -0.14)    |
| 1939-1945                               | No data                 | -0.15 (-0.23, -0.06)    | -0.20 (-0.28, -0.11)    |
| 1946-1955                               | -0.18 (-0.26, -0.10)    | -0.24 (-0.30, -0.18)    | -0.30 (-0.39, -0.21)    |
| <i>P sex difference by birth cohort</i> |                         | 0.19                    | 0.25                    |
| <b>Fluency</b>                          |                         |                         |                         |
| <b>Education: Below A-level</b>         |                         |                         |                         |
| 1930-1938                               | No data                 | 0.23 (0.07, 0.38)       | 0.13 (0.07, 0.19)       |
| 1939-1945                               | No data                 | 0.08 (0.01, 0.15)       | 0.03 (-0.03, 0.10)      |
| 1946-1955                               | 0.16 (0.06, 0.25)       | 0.00 (-0.06, 0.06)      | 0.01 (-0.12, 0.15)      |
| <i>P sex difference by birth cohort</i> |                         | 0.016                   | 0.036                   |
| <b>Education: A-level and above</b>     |                         |                         |                         |
| 1930-1938                               | No data                 | -0.07 (-0.28, 0.14)     | -0.01 (-0.12, 0.11)     |
| 1939-1945                               | No data                 | -0.10 (-0.19, -0.00)    | -0.20 (-0.29, -0.11)    |
| 1946-1955                               | -0.20 (-0.30, -0.09)    | -0.18 (-0.25, -0.10)    | -0.13 (-0.27, 0.01)     |
| <i>P sex difference by birth cohort</i> |                         | 0.34                    | 0.028                   |

<sup>a</sup>This analysis is conducted on 15,372 participants free of dementia during the follow-up period (N dementia cases excluded: 434 in Whitehall II and 118 in ELSA).

Models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions.

Positive value indicates male advantage in performance.

**Table S8. Role of education in sex differences in 13-year cognitive decline: Analyses stratified by birth cohort and excluding participants with dementia.<sup>a</sup>**

| ELSA & Whitehall II                     | Basic Model <sup>b</sup>   | Basic Model <sup>b</sup> + Education |
|---|----------------------------|--------------------------------------|
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Memory</b>                           |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.02 (-0.09, 0.05)        | 0.01 (-0.05, 0.08)                   |
| 1939-1945                               | -0.12 (-0.18, -0.05)       | -0.11 (-0.17, -0.05)                 |
| 1946-1955                               | -0.14 (-0.20, -0.08)       | -0.14 (-0.19, -0.08)                 |
| <i>P sex difference by birth cohort</i> | <i>0.019</i>               | <i>0.0017</i>                        |
| <b>Fluency</b>                          |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.04 (-0.16, 0.09)        | -0.01 (-0.13, 0.11)                  |
| 1939-1945                               | -0.06 (-0.13, 0.00)        | -0.05 (-0.11, 0.02)                  |
| 1946-1955                               | 0.06 (-0.11, 0.23)         | 0.09 (-0.09, 0.26)                   |
| <i>P sex difference by birth cohort</i> | <i>0.46</i>                | <i>0.38</i>                          |

<sup>a</sup>This analysis is conducted on 15,372 participants free of dementia during the follow-up period (N dementia cases excluded: 434 in Whitehall II and 118 in ELSA).

<sup>b</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions. Results are shown for the reference category: participants aged 60 years. Positive value indicates slower cognitive decline in men.

**Table S9. Sex differences in 13-year cognitive decline: Analyses stratified by birth cohort and education, and excluding participants with dementia.<sup>a</sup>**

| ELSA & Whitehall II                     | Sex difference (95% CI) |
|---|-------------------------|
| <b>Memory</b>                           |                         |
| <b>Education: Below A-level</b>         |                         |
| 1930-1938                               | -0.01 (-0.09, 0.07)     |
| 1939-1945                               | -0.14 (-0.22, -0.06)    |
| 1946-1955                               | -0.16 (-0.24, -0.09)    |
| <i>P sex difference by birth cohort</i> | <i>0.012</i>            |
| <b>Education: A-level and above</b>     |                         |
| 1930-1938                               | -0.01 (-0.14, 0.12)     |
| 1939-1945                               | -0.07 (-0.16, 0.03)     |
| 1946-1955                               | -0.08 (-0.16, -0.00)    |
| <i>P sex difference by birth cohort</i> | <i>0.64</i>             |
| <b>Fluency</b>                          |                         |
| <b>Education: Below A-level</b>         |                         |
| 1930-1938                               | -0.11 (-0.28, 0.05)     |
| 1939-1945                               | -0.02 (-0.10, 0.06)     |
| 1946-1955                               | 0.07 (-0.17, 0.31)      |
| <i>P sex difference by birth cohort</i> | <i>0.30</i>             |
| <b>Education: A-level and above</b>     |                         |
| 1930-1938                               | 0.05 (-0.16, 0.27)      |
| 1939-1945                               | -0.13 (-0.23, -0.02)    |
| 1946-1955                               | 0.16 (-0.11, 0.43)      |
| <i>P sex difference by birth cohort</i> | <i>0.10</i>             |

<sup>a</sup>This analysis is conducted on 15,372 participants free of dementia during the follow-up period (N dementia cases excluded: 434 in Whitehall II and 118 in ELSA).

Models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions. Results are shown for the reference category: participants aged 60 years. Positive value indicates slower cognitive decline in men.

**Table S10. Role of education in sex differences in cognitive performance: Analyses stratified by birth cohort and restricted to follow-up period 2002 to 2015.<sup>a</sup>**

|   | Age 50 years                   |                                      | Age 60 years                   |                                      | Age 70 years                   |                                      |
|---|--------------------------------|--------------------------------------|--------------------------------|--------------------------------------|--------------------------------|--------------------------------------|
|   | Basic Model <sup>b</sup>       | Basic Model <sup>b</sup> + Education | Basic Model <sup>b</sup>       | Basic Model <sup>b</sup> + Education | Basic Model <sup>b</sup>       | Basic Model <sup>b</sup> + Education |
| <b>ELSA &amp; Whitehall II</b>          | <b>Sex difference (95% CI)</b> | <b>Sex difference (95% CI)</b>       | <b>Sex difference (95% CI)</b> | <b>Sex difference (95% CI)</b>       | <b>Sex difference (95% CI)</b> | <b>Sex difference (95% CI)</b>       |
| <b>Memory</b>                           |                                |                                      |                                |                                      |                                |                                      |
| Birth cohort                            |                                |                                      |                                |                                      |                                |                                      |
| 1930-1938                               | No data                        | No data                              | No data                        | No data                              | -0.14 (-0.20, -0.09)           | -0.26 (-0.30, -0.21)                 |
| 1939-1945                               | No data                        | No data                              | -0.14 (-0.19, -0.08)           | -0.23 (-0.28, -0.18)                 | -0.21 (-0.27, -0.16)           | -0.30 (-0.35, -0.25)                 |
| 1946-1955                               | -0.06 (-0.13, 0.01)            | -0.14 (-0.20, -0.07)                 | -0.17 (-0.22, -0.13)           | -0.25 (-0.29, -0.21)                 | No data                        | No data                              |
| <i>P sex difference by birth cohort</i> |                                |                                      | <i>0.31</i>                    | <i>0.58</i>                          | <i>0.080</i>                   | <i>0.21</i>                          |
| <b>Fluency</b>                          |                                |                                      |                                |                                      |                                |                                      |
| Birth cohort                            |                                |                                      |                                |                                      |                                |                                      |
| 1930-1938                               | No data                        | No data                              | No data                        | No data                              | 0.18 (0.13, 0.23)              | 0.05 (-0.00, 0.10)                   |
| 1939-1945                               | No data                        | No data                              | 0.10 (0.04, 0.16)              | 0.00 (-0.06, 0.05)                   | 0.04 (-0.02, 0.10)             | -0.06 (-0.11, -0.01)                 |
| 1946-1955                               | 0.12 (0.01, 0.23)              | 0.03 (-0.08, 0.14)                   | -0.01 (-0.06, 0.04)            | -0.10 (-0.14, -0.05)                 | No data                        | No data                              |
| <i>P sex difference by birth cohort</i> |                                |                                      | <i>0.0031</i>                  | <i>0.011</i>                         | <i>0.00040</i>                 | <i>0.0041</i>                        |

<sup>a</sup>N = 15,368.

<sup>b</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions.

Positive value indicates male advantage in performance.

**Table S11. Sex differences in cognitive performance: Analyses stratified by birth cohort and education, and restricted to follow-up period 2002 to 2015.<sup>a</sup>**

| ELSA & Whitehall II                     | Age 50 years            | Age 60 years            | Age 70 years            |
|---|-------------------------|-------------------------|-------------------------|
|   | Sex difference (95% CI) | Sex difference (95% CI) | Sex difference (95% CI) |
| <b>Memory</b>                           |                         |                         |                         |
| <b>Education: Below A-level</b>         |                         |                         |                         |
| 1930-1938                               | No data                 | No data                 | -0.20 (-0.26, -0.15)    |
| 1939-1945                               | No data                 | -0.18 (-0.25, -0.12)    | -0.28 (-0.35, -0.21)    |
| 1946-1955                               | -0.10 (-0.18, -0.02)    | -0.21 (-0.27, -0.16)    | No data                 |
| <i>P sex difference by birth cohort</i> |                         | 0.47                    | 0.079                   |
| <b>Education: A-level and above</b>     |                         |                         |                         |
| 1930-1938                               | No data                 | No data                 | -0.24 (-0.34, -0.13)    |
| 1939-1945                               | No data                 | -0.18 (-0.28, -0.09)    | -0.22 (-0.31, -0.13)    |
| 1946-1955                               | -0.14 (-0.24, -0.04)    | -0.24 (-0.30, -0.18)    | No data                 |
| <i>P sex difference by birth cohort</i> |                         | 0.31                    | 0.83                    |
| <b>Fluency</b>                          |                         |                         |                         |
| <b>Education: Below A-level</b>         |                         |                         |                         |
| 1930-1938                               | No data                 | No data                 | 0.12 (0.07, 0.18)       |
| 1939-1945                               | No data                 | 0.09 (0.02, 0.16)       | 0.06 (-0.01, 0.13)      |
| 1946-1955                               | 0.17 (0.02, 0.31)       | 0.00 (-0.06, 0.06)      | No data                 |
| <i>P sex difference by birth cohort</i> |                         | 0.051                   | 0.18                    |
| <b>Education: A-level and above</b>     |                         |                         |                         |
| 1930-1938                               | No data                 | No data                 | 0.03 (-0.08, 0.14)      |
| 1939-1945                               | No data                 | -0.08 (-0.18, 0.02)     | -0.20 (-0.29, -0.10)    |
| 1946-1955                               | -0.18 (-0.36, 0.00)     | -0.17 (-0.24, -0.09)    | No data                 |
| <i>P sex difference by birth cohort</i> |                         | 0.18                    | 0.0028                  |

<sup>a</sup>N = 15,368.

Models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions.

Positive value indicates male advantage in performance.

**Table S12. Role of education in sex differences in 13-year cognitive decline: Analyses stratified by birth cohort and restricted to follow-up period 2002 to 2015.<sup>a</sup>**

| ELSA & Whitehall II                     | Basic Model <sup>b</sup>   | Basic Model <sup>b</sup> + Education |
|---|----------------------------|--------------------------------------|
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Memory</b>                           |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | No data                    | No data                              |
| 1939-1945                               | -0.09 (-0.18, -0.01)       | -0.09 (-0.17, -0.02)                 |
| 1946-1955                               | -0.15 (-0.23, -0.08)       | -0.14 (-0.21, -0.07)                 |
| <i>P sex difference by birth cohort</i> | <i>0.28</i>                | <i>0.33</i>                          |
| <b>Fluency</b>                          |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | No data                    | No data                              |
| 1939-1945                               | -0.03 (-0.11, 0.04)        | -0.02 (-0.10, 0.05)                  |
| 1946-1955                               | 0.14 (-0.11, 0.39)         | 0.16 (-0.09, 0.41)                   |
| <i>P sex difference by birth cohort</i> | <i>0.20</i>                | <i>0.17</i>                          |

<sup>a</sup>N = 15,368.

<sup>b</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions. Results are shown for the reference category: participants aged 60 years. Positive value indicates slower cognitive decline in men.

**Table S13. Sex differences in 13-year cognitive decline: Analyses stratified by birth cohort and education, and restricted to follow-up period 2002 to 2015.<sup>a</sup>**

| ELSA & Whitehall II                     | Sex difference (95% CI) |
|---|-------------------------|
| <b>Memory</b>                           |                         |
| <b>Education: Below A-level</b>         |                         |
| 1930-1938                               | No data                 |
| 1939-1945                               | -0.13 (-0.23, -0.03)    |
| 1946-1955                               | -0.14 (-0.24, -0.05)    |
| <i>P sex difference by birth cohort</i> | <i>0.84</i>             |
| <b>Education: A-level and above</b>     |                         |
| 1930-1938                               | No data                 |
| 1939-1945                               | -0.05 (-0.18, 0.08)     |
| 1946-1955                               | -0.13 (-0.24, -0.02)    |
| <i>P sex difference by birth cohort</i> | <i>0.37</i>             |
| <b>Fluency</b>                          |                         |
| <b>Education: Below A-level</b>         |                         |
| 1930-1938                               | No data                 |
| 1939-1945                               | 0.02 (-0.07, 0.11)      |
| 1946-1955                               | 0.09 (-0.23, 0.42)      |
| <i>P sex difference by birth cohort</i> | <i>0.68</i>             |
| <b>Education: A-level and above</b>     |                         |
| 1930-1938                               | No data                 |
| 1939-1945                               | -0.12 (-0.25, 0.00)     |
| 1946-1955                               | 0.23 (-0.20, 0.66)      |
| <i>P sex difference by birth cohort</i> | <i>0.12</i>             |

<sup>a</sup>N = 15,368.

Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions. Results are shown for the reference category: participants aged 60 years.

Positive value indicates slower cognitive decline in men.

**Table S14. Role of education in sex differences in cognitive performance: Analyses stratified by birth cohort using multiple imputation to account for missing education data.**

|   | At age 50 years          |                                      | At age 60 years          |                                      | At age 70 years          |                                      |
|---|--------------------------|--------------------------------------|--------------------------|--------------------------------------|--------------------------|--------------------------------------|
|   | Basic Model <sup>a</sup> | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup> | Basic Model <sup>a</sup> + Education | Basic Model <sup>a</sup> | Basic Model <sup>a</sup> + Education |
| ELSA & Whitehall II                     | Sex difference (95% CI)  | Sex difference (95% CI)              | Sex difference (95% CI)  | Sex difference (95% CI)              | Sex difference (95% CI)  | Sex difference (95% CI)              |
| <b>Memory</b>                           |                          |                                      |                          |                                      |                          |                                      |
| Birth cohort                            |                          |                                      |                          |                                      |                          |                                      |
| 1930-1938                               | No data                  | No data                              | -0.10 (-0.16, -0.03)     | -0.24 (-0.31, -0.17)                 | -0.13 (-0.18, -0.09)     | -0.25 (-0.29, -0.20)                 |
| 1939-1945                               | No data                  | No data                              | -0.12 (-0.16, -0.07)     | -0.21 (-0.26, -0.17)                 | -0.20 (-0.26, -0.15)     | -0.29 (-0.34, -0.24)                 |
| 1946-1955                               | -0.06 (-0.12, -0.01)     | -0.14 (-0.19, -0.08)                 | -0.17 (-0.22, -0.13)     | -0.25 (-0.28, -0.21)                 | -0.29 (-0.35, -0.23)     | -0.35 (-0.41, -0.29)                 |
| <i>P sex difference by birth cohort</i> |                          |                                      | <i>0.070</i>             | <i>0.57</i>                          | <i>0.00040</i>           | <i>0.014</i>                         |
| <b>Fluency</b>                          |                          |                                      |                          |                                      |                          |                                      |
| Birth cohort                            |                          |                                      |                          |                                      |                          |                                      |
| 1930-1938                               | No data                  | No data                              | 0.19 (0.08, 0.31)        | 0.04 (-0.08, 0.16)                   | 0.18 (0.13, 0.23)        | 0.06 (0.01, 0.10)                    |
| 1939-1945                               | No data                  | No data                              | 0.10 (0.04, 0.15)        | -0.02 (-0.07, 0.04)                  | 0.03 (-0.02, 0.08)       | -0.07 (-0.12, -0.02)                 |
| 1946-1955                               | 0.06 (-0.01, 0.13)       | -0.03 (-0.10, 0.04)                  | 0.00 (-0.05, 0.05)       | -0.09 (-0.13, -0.04)                 | -0.01 (-0.11, 0.08)      | -0.08 (-0.17, 0.02)                  |
| <i>P sex difference by birth cohort</i> |                          |                                      | <i>0.0018</i>            | <i>0.034</i>                         | <i>&lt;0.0001</i>        | <i>0.00040</i>                       |

<sup>a</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions.

Positive value indicates male advantage in performance.



**Table S15. Role of education in sex differences in 13-year cognitive decline: Analyses stratified by birth cohort using multiple imputation to account for missing education data.**

| ELSA & Whitehall II                     | Basic Model <sup>a</sup>   | Basic Model <sup>a</sup> + Education |
|---|----------------------------|--------------------------------------|
|   | Sex difference<br>(95% CI) | Sex difference<br>(95% CI)           |
| <b>Memory</b>                           |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.05 (-0.11, 0.01)        | -0.01 (-0.07, 0.06)                  |
| 1939-1945                               | -0.12 (-0.18, -0.05)       | -0.10 (-0.17, -0.04)                 |
| 1946-1955                               | -0.15 (-0.20, -0.09)       | -0.14 (-0.20, -0.09)                 |
| <i>P sex difference by birth cohort</i> | <i>0.068</i>               | <i>0.0074</i>                        |
| <b>Fluency</b>                          |                            |                                      |
| Birth cohort                            |                            |                                      |
| 1930-1938                               | -0.05 (-0.17, 0.08)        | -0.01 (-0.13, 0.11)                  |
| 1939-1945                               | -0.05 (-0.12, 0.01)        | -0.04 (-0.10, 0.03)                  |
| 1946-1955                               | 0.06 (-0.11, 0.24)         | 0.09 (-0.08, 0.27)                   |
| <i>P sex difference by birth cohort</i> | <i>0.48</i>                | <i>0.41</i>                          |

<sup>a</sup>Basic models include sex, sex by age, age<sup>2</sup>, age<sup>3</sup>, birth cohort, sex by birth cohort, birth cohort by age, sex by birth cohort by age, ethnicity, and practice effect. Memory models additionally include birth cohort by age<sup>3</sup> and lower-order interactions. Fluency models additionally include practice effect by sex and birth cohort by sex by age<sup>2</sup> and lower-order interactions. Results are shown for the reference category: participants aged 60 years. Positive value indicates slower cognitive decline in men.