**Supplementary Table 1**: Overview of cognitive data in LASA 1992-2016\*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Birth cohort:** | | | | | | | | | |
| **Year of measurement:** | **1908-1917** |  | **1918-1927** |  | **1928-1937** |  | **1938-1947** |  | **1948-1957** |  |
| **1992/93** | 74-85 y  n=1151 | t0 | 64-75 y  n=963 | t0 | 54-65 y  n=987 | t0 |  |  |  |  |
| **1995/96** | 77-88 y  n=709 | t3 | 67-78 y  n=746 | t3 | 57-68 y  n=841 | t3 |  |  |  |  |
| **1998/99** | 80-91 y  n=453 | t6 | 70-81 y  n=640 | t6 | 60-71 y  n=779 | t6 |  |  |  |  |
| **2001/02**  **2002/03** | 83-94 y  n=267 | t9 | 73-84 y  n=503 | t9 | 63-74 y  n=702 | t9 | 54-65 y  n=998 | t0 |  |  |
| **2005/06** | 88-97 y  n=97 | t13 | 77-88 y  n=348 | t13 | 67-78 y  n=599 | t13 | 57-68 y  n=861 | t3 |  |  |
| **2008/09** | 91-100 y  n=52 | t16 | 81-91 y  n=264 | t16 | 70-81 y  n=518 | t16 | 60-71 y  n=766 | t6 |  |  |
| **2011/12**  **2012/13** | 94-102 y  n=21 | t19 | 84-94 y  n=158 | t19 | 73-84 y  n=433 | t19 | 63-74 y  n=694 | t9 | 54-65 y  n=1023 | t0 |
| **2015/16** | 98-102 y  n=4 | t23 | 88-98 y  n=75 | t23 | 77-88 y  n=314 | t23 | 67-78 y  n=612 | t13 | 57-68 y  n=765 | t3 |

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\* 5 birth cohorts are included and repeatedly measured at 3-4 year intervals. t0 represents the first cognitive measurement of the participants.

**Supplementary Table 2**: Overview of cognitive data in DCS 1995-2018\*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Birth cohort:** | | | | | | | | |
| **Year of measurement:** | **1928-1937** |  | **1938-1947** |  | **1948-1957** |  |  | **1958-1967** |  |
| **1995-2018** | 57-82 y  n=872 | t0 | 48-74 y  n=1404 | t0 | 45-66 y  n=1769 | t0 |  |  |  |
| **2000-2018** | 62-82 y  n=634 | t5 | 52-77 y  n=1118 | t5 | 49-68 y  n=1450 | t5 | **2003-2018** | 45-60 y  n=724 | t0 |
| **2005-2018** | 67-85 y  n=484 | t10 | 57-78 y  n=978 | t10 | 54-69 y  n=1101 | t10 | **2008-2018** | 50-60 y  n=228 | t5 |
| **2010-2018** | 72-85 y  n=316 | t15 | 62-80 y  n=780 | t15 | 59-69 y  n=875 | t15 | **2012-2013** | 54-55 y  n=6 | t10 |
| **2015-2018** | 77-85 y  n=21 | t20 | 67-79 y  n=96 | t20 | 65-69 y  n=78 | t20 |  |  |  |

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\* Since 1995, participants aged 45 y and over, were invited to participate in cognitive testing. t0 represents the first cognitive measurement of the participants.

**Supplementary Table 3**: Overview of level of education by birth cohorts in LASA and DCS

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Level of education | | | | | | |
| Birth cohort | Men | | | | Women | | |
| **LASA** | Low | Medium | High | Low | | Medium | High |
| 1908-1917 | 42.2 % | 30.3 % | 27.5 % | 63.4 % | | 20.2 % | 16.4 % |
| 1918-1927 | 29.7 % | 37.9 % | 32.4 % | 53.7 % | | 28.6 % | 17.7 % |
| 1928-1937 | 20.7 % | 32.0 % | 47.3 % | 40.7 % | | 37.6 % | 21.8 % |
| 1938-1947 | 17.9 % | 28.6 % | 53.6 % | 22.6 % | | 47.6 % | 29.8 % |
| 1948-1957 | 9.4 % | 29.5 % | 61.2 % | 10.0 % | | 35.0 % | 54.9 % |
| **DCS** |  |  |  |  | |  |  |
| 1928-1937 | 11.7 % | 36.3 % | 52.0 % | 20.2 % | | 56.4 % | 23.4 % |
| 1938-1947 | 7.7 % | 33.8 % | 58.5 % | 5.9 % | | 54.2 % | 39.9 % |
| 1948-1957 | 2.7 % | 30.8 % | 66.6 % | 2.8 % | | 47.7 % | 49.5 % |
| 1958-1967 | 0.8 % | 25.3 % | 73.9 % | 2.8 % | | 31.8 % | 65.4 % |

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**Supplementary Table 4**: Differences in level of cognitive functioning and cognitive decline with ageing between men and women in LASA, from middle into old age (range 55-104 years) – *adjusted for birth cohort and level of education.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Memory function**  **(z-score)** | | **Information processing speed**  **(z-score)** | | **Fluid intelligence**  **(z-score)** | | **Global cognitive function**  **(MMSE score)** | |
|  | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) |
|  | (n=4626, 14403 observations) | | (n=4575, 14231 observations) | | (n=3857, 12035 observations) | | (n=5115, 17306 observations) | |
| **sex (female)** | **0.517**  [0.471 0.563] | **0.568**  [0.497 0.639] | **0.229**  [0.184 0.274] | **0.302**  [0.242 0.363] | 0.004  [-0.044 0.052] | -0.071  [-0.147 0.005] | **0.242**  [0.136 0.349] | 0.062  [-0.175 0.299] |
| **sex (female)\*age (y)** |  | -0.004  [-0.007 0.000] |  | **-0.005**  [-0.008 -0.002] |  | **0.005**  [0.001 0.009] |  | 0.030  [-0.000 0.061] |
| **sex (female)\*age2 (y)** |  |  |  |  |  |  |  | **-0.001**  [-0.002 -0.000] |

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Cognitive function was modelled as a function of sex, adjusting for age, age2, birth cohort (10-year groups) and educational level (3 levels), with age centered at age 55 years. Sex differences are presented as average [95% CL] and represents the average difference in cognitive function between men and women, regardless of age (Model 1) or at age 55 years (Model 2). Positive values represent better scores (sex) or less decline for every year of ageing (sex\*age and sex\*age2) for women compared to men. Estimates in bold are statistically significant at p<0.05.

**Supplementary Table 5**: Differences in level of cognitive functioning and cognitive decline with ageing between men and women in DCS, from middle into old age (range 45-85 years) – *adjusted for birth cohort and level of education.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Memory function**  **(z-score)** | | **Information processing speed**  **(z-score)** | | **Cognitive flexibility**  **(z-score)** | | **Global cognitive function**  **(z-score)** | |
|  | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) |
|  | (n=4761, 12881 observations) | | (n=4749, 12832 observations) | | (n=4752, 12836 observations) | | (n=4740, 12754 observations) | |
| **sex (female)** | **0.515**  [0.467 0.562] | **0.527**  [0.477 0.577] | **0.278**  [0.229 0.328] | **0.291**  [0.241 0.341] | **0.223**  [0.175 0.272] | **0.210**  [0.160 0.259] | **0.400**  [0.353 0.447] | **0.420**  [0.372 0.468] |
| **sex (female)\*age (y)** |  | -0.003  [-0.007 0.001] |  | **-0.005**  [-0.008 -0.001] |  | -0.001  [-0.006 0.003] |  | **-0.006**  [-0.009 -0.003] |
| **sex (female)\*age (y2)** |  |  |  |  |  | **0.000**  [0.000 0.001] |  |  |

DCS Doetinchem Cohort Study

Cognitive function was modelled as a function of sex, adjusting for age, age2, birth cohort (10-year groups) and educational level (3 levels), with age centered at age 55 years. Sex differences are presented as average [95% CL] and represents the average difference in cognitive function between men and women, regardless of age (Model 1) or at age 55 years (Model 2). Positive values represent better scores (sex) or less decline for every year of ageing (sex\*age and sex\*age2) for women compared to men. Estimates in bold are statistically significant at p<0.05.

**Supplementary Table 6**: Differences in level of cognitive functioning and cognitive decline with ageing between men and women, from middle into old age (range **55**-85 years) in DCS – *adjusted for birth cohort and level of education.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Memory function  (z-score) | | Information processing speed  (z-score) | | Cognitive flexibility  (z-score) | | Global cognitive function  (z-score) | |
|  | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) |
|  | (n=3920, 9060 observations) | | (n=3902, 9013 observations) | | (n=3906, 9015 observations) | | (n=3893, 8955 observations) | |
| sex (female) | **0.506**  [0.451 0.561] | **0.565**  [0.495 0.635] | **0.251**  [0.195 0.306] | **0.288**  [0.225 0.351] | **0.213**  [0.159 0.266] | **0.171**  [0.108 0.234] | **0.369**  [0.316 0.422] | **0.429**  [0.367 0.490] |
| sex (female)\*age (y) |  | **-0.007**  [-0.013 -0.002] |  | **-0.006**  [-0.010 -0.001] |  | **0.006**  [0.001 0.011] |  | **-0.008**  [-0.012 -0.004] |

DCS Doetinchem Cohort Study

Cognitive function was modelled as a function of sex, adjusting for age, age2, birth cohort (10-year groups) and educational level (3 levels), with age centered at age 55 years. Sex differences are presented as average [95% CL] and represents the average difference in cognitive function between men and women, regardless of age (Model 1) or at age 55 years (Model 2). Positive values represent better scores (sex) or less decline for every year of ageing (sex\*age) for women compared to men. Estimates in bold are statistically significant at p<0.05.

**Supplementary Table 7a**: Differences in level of cognitive functioning and cognitive decline with ageing between men and women, from middle into old age among persons *up to age 80 years* in LASA – *adjusted for birth cohort and level of education.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Memory function  (z-score) | | Information processing speed  (z-score) | | Fluid intelligence  (z-score) | | Global cognitive function  (MMSE score) | |
|  | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) |
|  | (n=4118, 11597 observations) | | (n=4092, 11575 observations) | | (n=3341, 9755 observations) | | (n=4523, 13795 observations) | |
| sex (female) | **0.529**  [0.481 0.578] | **0.553**  [0.478 0.629] | **0.240**  [0.192 0.288] | **0.302**  [0.241 0.363] | 0.007  [-0.044 0.058] | **-0.086**  [-0.167 -0.006] | **0.224**  [0.115 0.334] | **0.205**  [0.038 0.372] |
| sex (female)\*age (y) |  | -0.002  [-0.007 0.003] |  | **-0.005**  [-0.009 -0.002] |  | **0.007**  [0.002 0.012] |  | 0.002  [-0.011 0.015] |

LASA Longitudinal Aging Study Amsterdam

Cognitive function was modelled as a function of sex, adjusting for age, age2, birth cohort (10-year groups) and educational level (3 levels), with age centered at age 55 years. Sex differences are presented as average [95% CL] and represents the average difference in cognitive function between men and women, regardless of age (Model 1) or at age 55 years (Model 2). Positive values represent better scores (sex) or less decline for every year of ageing (sex\*age) for women compared to men. Estimates in bold are statistically significant at p<0.05.

**Supplementary Table 7b**: Differences in level of cognitive functioning and cognitive decline with ageing between men and women, from middle into old age among persons *up to age 80 years* in DCS – *adjusted for birth cohort and level of education.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Memory function  (z-score) | | Information processing speed  (z-score) | | Cognitive flexibility  (z-score) | | Global cognitive function  (z-score) | |
|  | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) | Model 1  (Level of  cognitive functioning) | Model 2  (Cognitive decline) |
|  | (n=4760, 12719 observations) | | (n=4748, 12670 observations) | | (n=4753, 12678 observations) | | (n=4739, 12595 observations) | |
| sex (female) | **0.515**  [0.467 0.563] | **0.537**  [0.486 0.587] | **0.280**  [0.231 0.330] | **0.294**  [0.243 0.344] | **0.224**  [0.176 0.273] | **0.211**  [0.161 0.261] | **0.401**  [0.354 0.448] | **0.422**  [0.374 0.469] |
| sex (female)\*age (y) |  | 0.001  [-0.004 0.007] |  | **-0.005**  [-0.008 -0.002] |  | -0.001  [-0.006 0.004] |  | **-0.007**  [-0.010 -0.004] |
| sex (female)\*age (y2) |  | **-0.000**  [-0.001 -0.000] |  |  |  | **0.000**  [0.000 0.001] |  |  |

DCS Doetinchem Cohort Study

Cognitive function was modelled as a function of sex, adjusting for age, age2, birth cohort (10-year groups) and educational level (3 levels), with age centered at age 55 years. Sex differences are presented as average [95% CL] and represents the average difference in cognitive function between men and women, regardless of age (Model 1) or at age 55 years (Model 2). Positive values represent better scores (sex) or less decline for every year of ageing (sex\*age and sex\*age2) for women compared to men. Estimates in bold are statistically significant at p<0.05.

**Supplementary Material: Detailed information on the cognitive tests**

*Cognitive tests in LASA:*

The 15-word learning test consists of 15 words, which have to be learned during three trials, with immediate recall after every trial and a delayed recall after 20 minutes. In the present analyses, we included three measures: the total number of words during the immediate recalls, which ranged from 0-45, the highest score of one of the 3 trials, ranging from 0-15, and the number of words at the delayed recall, ranging from 0-15. Higher scores indicate better memory functioning.

In the letter substitution task, two rows of characters are shown, each character in the upper row belongs to a character in the bottom row and in addition two rows, one with characters and one empty. Respondents had to complete as many character combinations as possible, by naming the corresponding character (verbal response). This was done in three cycles of one minute. The mean score for the three trials was used in the analyses (range in LASA: 1.0 to 42.7).

The Raven Colored Progressive Matrices consisted of two subsets, A and B, each containing 12 items. Each item consisted of a drawing (matrix) of a pattern from which a section was missing. The respondent had to choose the pattern that fitted best out of six alternatives. Each correctly chosen pattern counted for one point, resulting in a total scale score ranging from 0 to 24. The items increased in difficulty, and so did the sections.

The Mini-Mental State Examination (MMSE) consisted of 20 items and scores ranged from 0-30. The questions represent different cognitive domains of functioning: Orientation in time (5 questions; 5 points), orientation in place (5 questions, 5 points), registration of 3 words (3 points), attention and calculation (5 points) recall of three words (3 points), language (8 points) and visual construction (1 point).

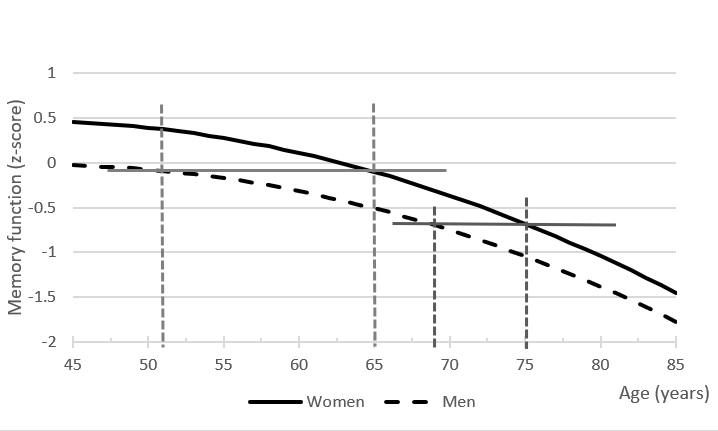
*Cognitive tests in DCS:*

In the 15 Words Verbal Learning Test, fifteen monosyllabic words printed on paper were displayed, one by one, in three subsequent trials, with a free recall procedure immediately following each presentation (immediate recall). After a delay of about fifteen minutes, there was an additional free recall trial (delayed recall, range 0-15). Next to the delayed recall score, the total number of words on the immediate recalls, which ranges from 0-45, and the highest score of one of the 3 trials, ranging from 0-15, were calculated.

In the Stroop Color-Word Test, time needed to complete three skills were recorded: 1) to read 40 written color names, 2) to name the color of 40 colored patches, and 3) to name the color of the ink in which 40 incongruously named color words are printed (so, for example, the word ‘blue’ is printed in red).

In the Fluency Testthe participant is asked to name as many animals as possible within one minute.

In the Letter Digit Substitution Test, nine letters of the alphabet are given a unique digit-code (1 to 9) in a key displayed on top of the paper. The test on the same paper contains two rows, the upper one containing letters and the bottom row empty. Participants are asked to fill in as many correct digits corresponding to the letters as possible within one minute.



**Supplementary Figure 1:** Example of difference in cognitive age between men and women for memory function in the DCS Doetinchem Cohort Study. Difference in cognitive age was calculated based on the regression model as the difference in calendar age at which the cognitive function of men is at the same level as the cognitive function of women. For instance, at what calendar age do men have the same memory function as women at calendar age 65 years? This was at age 52 years (as illustrated in graph). So, in this instance, men are about 13 years cognitively older than women. Women at age 75 years have the same cognitive function as men at age 68-69 years, so a difference in cognitive age of 6-7 years.