

# Supplementary Material

## Interaction of Alzheimer's Disease-Associated Genetic Risk with Indicators of Socioeconomic Position on Mild Cognitive Impairment in the Heinz Nixdorf Recall Study

**Supplementary Table 1.** Risk alleles of loci associated with Alzheimer's disease [1] used for calculating the genetic risk score (GRS<sub>AD</sub>) and their age- and sex-adjusted effects on mild cognitive impairment in the study population.

| Original SNP | Proxy SNP  | r <sup>2</sup> | Chr:Position Build 37 | Locus            | Risk Allele | Risk Allele Frequency | OR (95% CI)       | p    |
|--------------|------------|----------------|-----------------------|------------------|-------------|-----------------------|-------------------|------|
| rs4844610    | rs679515   | 0.92           | 1: 207802552          | <i>CR1</i>       | T           | 0.211                 | 0.95 (0.81; 1.11) | 0.50 |
| rs6733839    |            |                | 2:127892810           | <i>BINI</i>      | T           | 0.395                 | 0.92 (0.81; 1.05) | 0.20 |
| rs10933431   | rs7570061  | 0.75           | 2:233981912           | <i>INPP5D</i>    | G           | 0.166                 | 0.93 (0.79; 1.10) | 0.39 |
| rs9271058    | rs9271192  | 1.00           | 6:32575406            | <i>HLA -DRB1</i> | C           | 0.283                 | 1.14 (0.99; 1.31) | 0.07 |
| rs75932628   |            |                | 6:41129252            | <i>TREM2</i>     | T           | NA                    | NA                | NA   |
| rs9473117    | rs10948363 | 0.98           | 6: 47431284           | <i>CD2AP</i>     | G           | 0.264                 | 0.88 (0.76; 1.02) | 0.08 |
| rs12539172   |            |                | 7: 100091795          | <i>NYAPI</i>     | C           | 0.299                 | 0.92 (0.81; 1.06) | 0.24 |
| rs10808026   | rs11767557 | 1.00           | 7: 143099133          | <i>EPHA1</i>     | T           | 0.198                 | 0.98 (0.84; 1.15) | 0.85 |
| rs73223431   | rs28834970 | 0.98           | 8 27219987            | <i>PTK2B</i>     | C           | 0.334                 | 1.00 (0.87; 1.14) | 0.99 |
| rs9331896    |            |                | 8: 27467686           | <i>CLU</i>       | A           | 0.387                 | 1.08 (0.95; 1.23) | 0.24 |
| rs7920721    | rs11257240 | 0.87           | 10: 11720308          | <i>ECHDC3</i>    | G           | 0.372                 | 1.07 (0.94; 1.23) | 0.29 |
| rs3740688    | rs10769256 | 0.64           | 11: 47380340          | <i>SPI1</i>      | C           | 0.411                 | 1.00 (0.88; 1.14) | 0.99 |
| rs7933202    | rs12453    | 0.92           | 11: 59936926          | <i>MS4A2</i>     | A           | 0.389                 | 1.08 (0.95; 1.23) | 0.25 |
| rs3851179    |            |                | 11: 85868640          | <i>PICALM</i>    | G           | 0.360                 | 0.97 (0.85; 1.11) | 0.63 |
| rs11218343   |            |                | 11: 121435587         | <i>SORL1</i>     | T           | 0.040                 | 1.13 (0.81; 1.64) | 0.48 |
| rs17125924   | rs17125944 | 0.94           | 14: 53391680          | <i>FERMT2</i>    | C           | 0.097                 | 1.13 (0.91; 1.39) | 0.27 |
| rs12881735   | rs10498633 | 1.00           | 14: 92932828          | <i>SLC24A4</i>   | G           | 0.234                 | 0.95 (1.03; 1.05) | 0.52 |
| rs593742     | rs474875   | 0.78           | 15: 59045774          | <i>ADAM10</i>    | A           | 0.324                 | 0.89 (0.78; 1.01) | 0.08 |
| rs7185636    | rs1858973  | 0.94           | 16: 19808163          | <i>IQCK</i>      | A           | 0.171                 | 1.06 (0.89; 1.26) | 0.53 |
| rs138190086  | rs28369023 | 1.00           | 17: 61538148          | <i>ACE</i>       | A           | 0.019                 | 1.16 (0.73; 1.78) | 0.51 |
| rs6024870    | rs6064392  | 0.82           | 20: 54997568          | <i>CASS4</i>     | G           | 0.086                 | 1.15 (0.91; 1.47) | 0.26 |
| rs2830500    | rs7276338  | 0.85           | 21: 28156856          | <i>ADAMTS1</i>   | C           | 0.272                 | 1.04 (0.90; 1.21) | 0.57 |

[1] Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj AC, Boland A, Vronskaya M, van der Lee SJ, Amlie-Wolf A, et al. (2019) Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates A $\beta$ , tau, immunity and lipid processing. *Nat Genet* **51**, 414-430.

**Supplementary Table 2.** Age- adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) on mild cognitive impairment in logistic regression models including main effects of income and education as indicators of socioeconomic position, *APOE*  $\epsilon$ 4 status and an AD-associated genetic risk score (GRS<sub>AD</sub>), stratified by sex.

|                          | Male  |                    |                       | Female |                    |                       |
|--------------------------|-------|--------------------|-----------------------|--------|--------------------|-----------------------|
|                          | n     | OR (95%-CI)        | <i>p</i>              | n      | OR (95%-CI)        | <i>p</i>              |
| Intercept                |       | 0.01 (0.005; 0.04) | 4.6*10 <sup>-15</sup> |        | 0.02 (0.01; 0.06)  | 7.2*10 <sup>-13</sup> |
| Income low               | 1,837 | 1.52 (1.15; 2.01)  | 0.003                 | 1,772  | 1.26 (0.96; 1.66)  | 0.10                  |
| Age                      |       | 1.04 (1.02; 1.06)  | 2.9*10 <sup>-5</sup>  |        | 1.03 (1.01; 1.05)  | 0.0003                |
| Intercept                |       | 0.01 (0.004; 0.03) | 5.4*10 <sup>-16</sup> |        | 0.02 (0.01; 0.06)  | 9.0*10 <sup>-14</sup> |
| Education low            | 1,901 | 1.28 (0.99; 1.67)  | 0.06                  | 1,928  | 1.58 (1.10; 2.33)  | 0.02                  |
| Age                      |       | 1.04 (1.02; 1.06)  | 2.7*10 <sup>-6</sup>  |        | 1.03 (1.01; 1.05)  | 0.001                 |
| Intercept                |       | 0.01 (0.004- 0.04) | 5.7*10 <sup>-16</sup> |        | 0.02 (0.01- 0.06)  | 9.5*10 <sup>-14</sup> |
| <i>APOE</i> $\epsilon$ 4 | 1,905 | 1.14 (0.85- 1.52)  | 0.36                  | 1,929  | 1.40 (1.06- 1.84)  | 0.01                  |
| Age                      |       | 1.04 (1.02- 1.06)  | 1.3*10 <sup>-6</sup>  |        | 1.03 (1.02- 1.05)  | 9.1*10 <sup>-5</sup>  |
| Intercept                |       | 0.02 (0.004- 0.07) | 8.9*10 <sup>-8</sup>  |        | 0.02 (0.004- 0.09) | 3.3*10 <sup>-7</sup>  |
| GRS <sub>AD</sub>        | 1,905 | 0.99 (0.94- 1.04)  | 0.63                  | 1,929  | 1.01 (0.96- 1.06)  | 0.75                  |
| Age                      |       | 1.04 (1.03- 1.06)  | 1.2*10 <sup>-6</sup>  |        | 1.03 (1.02- 1.05)  | 8.3*10 <sup>-5</sup>  |

**Supplementary Table 3.** Age- adjusted effects and corresponding 95% confidence intervals (95% CI) on mild cognitive impairment in logistic regression models including main effects and interaction terms of the *APOE* ε4 status and an AD-associated genetic risk score (GRS<sub>AD</sub>) with indicators of socioeconomic status (years of education and income/month), stratified by sex.

|                                  | Male  |                    |                       | Female |                      |                       |
|----------------------------------|-------|--------------------|-----------------------|--------|----------------------|-----------------------|
|                                  | n     | OR (95%-CI)        | p                     | n      | OR (95%-CI)          | p                     |
| Intercept                        |       | 0.01 (0.004- 0.04) | 4.4*10 <sup>-15</sup> |        | 0.02 (0.01- 0.06)    | 6.9*10 <sup>-13</sup> |
| Income low                       |       | 1.57 (1.13- 2.19)  | 0.01                  |        | 1.17 (0.84- 1.62)    | 0.35                  |
| <i>APOE</i> ε4                   | 1,837 | 1.25 (0.75- 2.02)  | 0.38                  | 1,772  | 1.18 (0.75- 1.83)    | 0.47                  |
| Age                              |       | 1.04 (1.02- 1.06)  | 3.5*10 <sup>-5</sup>  |        | 1.03 (1.01- 1.05)    | 0.0003                |
| <i>APOE</i> ε4 *Income low       |       | 0.90 (0.49- 1.69)  | 0.75                  |        | 1.32 (0.74- 2.38)    | 0.35                  |
| Intercept                        |       | 0.01 (0.004- 0.03) | 7.1*10 <sup>-16</sup> |        | 0.02 (0.01- 0.06)    | 7.1*10 <sup>-13</sup> |
| Education low                    |       | 1.26 (0.92- 1.71)  | 0.14                  |        | 1.28 (0.85- 1.99)    | 0.25                  |
| <i>APOE</i> ε4                   | 1,901 | 1.10 (0.71- 1.69)  | 0.65                  | 1,928  | 0.72 (0.30- 1.56)    | 0.43                  |
| Age                              |       | 1.04 (1.02- 1.06)  | 3.1*10 <sup>-6</sup>  |        | 1.03 (1.01- 1.05)    | 0.001                 |
| <i>APOE</i> ε4 *Education low    |       | 1.08 (0.60- 1.94)  | 0.80                  |        | 2.17 (0.94- 5.48)    | 0.08                  |
| Intercept                        |       | 0.03 (0.003- 0.22) | 0.001                 |        | 0.02 (0.002- 0.14)   | 0.0002                |
| Income low                       |       | 0.53 (0.05- 5.68)  | 0.60                  |        | 1.63 (0.16- 16.52)   | 0.68                  |
| GRS <sub>AD</sub>                | 1,837 | 0.97 (0.90- 1.05)  | 0.48                  | 1,772  | 1.01 (0.94- 1.09)    | 0.78                  |
| Age                              |       | 1.04 (1.02- 1.06)  | 2.8*10 <sup>-5</sup>  |        | 1.03 (1.01- 1.05)    | 0.0003                |
| GRS <sub>AD</sub> *Income low    |       | 1.05 (0.95; 1.16)  | 0.38                  |        | 0.99 (0.90; 1.09)    | 0.82                  |
| Intercept                        |       | 0.01 (0.001; 0.06) | 1.74*10 <sup>-6</sup> |        | 0.003 (0.001; 0.07)  | 0.0003                |
| Education low                    |       | 3.46 (0.38; 31.80) | 0.27                  |        | 13.25 (0.54; 366.34) | 0.12                  |
| GRS <sub>AD</sub>                | 1,901 | 1.01 (0.95; 1.09)  | 0.71                  | 1,928  | 1.09 (0.96; 1.24)    | 0.19                  |
| Age                              |       | 1.04 (1.02; 1.06)  | 2.6*10 <sup>-6</sup>  |        | 1.03 (1.01; 1.05)    | 0.001                 |
| GRS <sub>AD</sub> *Education low |       | 0.96 (0.87; 1.05)  | 0.38                  |        | 0.91 (0.80; 1.05)    | 0.19                  |

**Supplementary Table 4.** Age-adjusted relative excess risk due to interaction (RERI) and corresponding 95% CI as a measure of interaction between *APOE*  $\epsilon$ 4xSES (socioeconomic status) and the  $GRS_{AD}$ xSES on additive scale, stratified by sex.

|                        | Male  |                     | Female |                     |
|------------------------|-------|---------------------|--------|---------------------|
|                        | n     | RERI (95% CI)       | n      | RERI (95% CI)       |
| <i>APOE</i> *Income    | 1,837 | -0.04 (-0.91; 0.82) | 1,772  | 0.05 (-0.23; 1.24)  |
| <i>APOE</i> *Education | 1,901 | 0.14 (-0.58; 0.86)  | 1,928  | 1.00 (0.26; 1.75)*  |
| $GRS_{AD}$ *Income     | 1,837 | 0.06 (-0.66; 0.78)  | 1,772  | -0.42 (-1.23; 0.38) |
| $GRS_{AD}$ *Education  | 1,901 | -0.18 (-0.86; 0.50) | 1,928  | -1.17 (-3.02; 0.68) |

\*p < 0.05

**Supplementary Table 5.** Age- and sex-adjusted effects and corresponding 95% confidence interval (95% CI) for the interaction between each Alzheimer’s disease associated single nucleotide polymorphism (SNP) and income (per 1000€/month) in separate linear regression models, sorted by descending interaction effect size estimates.

| <b>Chr:Position<br/>Build 37</b> | <b>Locus</b>     | <b>SNP</b> | <b>Risk<br/>Allele</b> | <b>OR<sub>SNP×inc</sub>(95%CI)</b> | <b>RERI<sub>SNP×inc</sub>(95%CI)</b> |
|----------------------------------|------------------|------------|------------------------|------------------------------------|--------------------------------------|
| 17: 61538148                     | <i>ACE</i>       | rs28369023 | A                      | 1.53 (0.57; 4.56)                  | 0.62 (-0.66; 1.90)                   |
| 11: 59936926                     | <i>MS4A2</i>     | rs12453    | T                      | 1.19 (0.90; 1.57)                  | 0.20 (-0.04; 0.45)                   |
| 2:127892810                      | <i>BIN1</i>      | rs6733839  | T                      | 1.16 (0.88; 1.54)                  | 0.13 (-0.15; 0.42)                   |
| 20: 54997568                     | <i>CASS4</i>     | rs6064392  | G                      | 1.14 (0.67; 1.90)                  | 0.18 (-0.18; 0.54)                   |
| 15: 59045774                     | <i>ADAM10</i>    | rs474875   | A                      | 1.13 (0.85; 1.49)                  | 0.09 (-0.21; 0.39)                   |
| 2:233981912                      | <i>INPP5D</i>    | rs7570061  | G                      | 1.12 (0.78; 1.60)                  | 0.10 (-0.26; 0.47)                   |
| 14: 53391680                     | <i>FERMT2</i>    | rs17125944 | C                      | 1.12 (0.71; 1.76)                  | 0.21 (-0.37; 0.79)                   |
| 8:27219987                       | <i>PTK2B</i>     | rs28834970 | C                      | 1.08 (0.81; 1.45)                  | 0.08 (-0.24; 0.39)                   |
| 21: 28156856                     | <i>ADAMTS1</i>   | rs7276338  | C                      | 1.03 (0.76; 1.40)                  | 0.05 (-0.29; 0.38)                   |
| 6:32575406                       | <i>HLA -DRB1</i> | rs9271192  | C                      | 1.02 (0.76; 1.37)                  | 0.09 (-0.27; 0.45)                   |
| 11: 85868640                     | <i>PICALM</i>    | rs3851179  | G                      | 1.00 (0.75; 1.34)                  | 0.003 (-0.33; 0.33)                  |
| 14: 92932828                     | <i>SLC24A4</i>   | rs10498633 | G                      | 0.99 (0.72; 1.36)                  | -0.05 (-0.45; 0.35)                  |
| 1: 207802552                     | <i>CRI</i>       | rs679515   | T                      | 0.99 (0.71; 1.39)                  | -0.03 (-0.41; 0.36)                  |
| 8: 27467686                      | <i>CLU</i>       | rs9331896  | A                      | 0.97 (0.73; 1.29)                  | 0.0004 (-0.32; 0.33)                 |
| 11: 47380340                     | <i>SPI1</i>      | rs10769256 | C                      | 0.96 (0.73; 1.27)                  | -0.04 (-0.38; 0.29)                  |
| 16: 19808163                     | <i>IQCK</i>      | rs1858973  | A                      | 0.96 (0.66; 1.40)                  | -0.02 (-0.26; 0.42)                  |
| 6: 47431284                      | <i>CD2AP</i>     | rs10948363 | G                      | 0.95 (0.69; 1.30)                  | -0.10 (-0.46; 0.26)                  |
| 7: 143099133                     | <i>EPHA1</i>     | rs11767557 | T                      | 0.89 (0.64; 1.25)                  | -0.14 (-0.61; 0.33)                  |
| 10: 11720308                     | <i>ECHDC3</i>    | rs11257240 | G                      | 0.86 (0.65; 1.14)                  | -0.17 (-0.54; 0.21)                  |
| 7: 100091795                     | <i>NYAPI</i>     | rs12539172 | C                      | 0.82 (0.61; 1.10)                  | -0.30 (-0.79; 0.18)                  |
| 6:41129252                       | <i>TREM2</i>     | rs75932628 | T                      | NA                                 | NA                                   |

**Supplementary Table 6.** Age- and sex-adjusted effects and corresponding 95% confidence interval (95% CI) for the interaction between each Alzheimer’s disease associated single nucleotide polymorphism (SNP) and education (per year) in separate linear regression models, sorted by descending interaction effect size estimates.

| <b>Chr:Position<br/>Build 37</b> | <b>Locus</b>     | <b>SNP</b> | <b>Risk<br/>Allele</b> | <b>OR<sub>SNP<sub>x</sub>edu</sub>(95%CI)</b> | <b>RERI<sub>SNP<sub>x</sub>edu</sub>(95%CI)</b> |
|----------------------------------|------------------|------------|------------------------|---|---|
| 11: 47380340                     | <i>SPI1</i>      | rs10769256 | C                      | 1.31 (0.99; 1.73)                             | 0.25 (0.02; 0.48)*                              |
| 11: 59936926                     | <i>MS4A2</i>     | rs12453    | T                      | 1.22 (0.91; 1.63)                             | 0.22 (-0.03; 0.46)                              |
| 17: 61538148                     | <i>ACE</i>       | rs28369023 | A                      | 1.18 (0.46; 3.31)                             | 0.27 (-0.96; 1.50)                              |
| 11: 121435587                    | <i>SORL1</i>     | rs11218343 | T                      | 1.09 (0.44; 2.48)                             | 0.14 (-0.47; 0.75)                              |
| 11: 85868640                     | <i>PICALM</i>    | rs3851179  | G                      | 1.06 (0.79; 1.42)                             | 0.05 (-0.26; 0.36)                              |
| 10: 11720308                     | <i>ECHDC3</i>    | rs11257240 | G                      | 1.02 (0.76; 1.37)                             | 0.04 (-0.28; 0.37)                              |
| 14: 92932828                     | <i>SLC24A4</i>   | rs10498633 | G                      | 1.02 (0.73; 1.42)                             | 0.009 (-0.37; 0.38)                             |
| 2:127892810                      | <i>BINI</i>      | rs6733839  | T                      | 0.98 (0.74; 1.32)                             | -0.05 (-0.38; 0.28)                             |
| 6: 47431284                      | <i>CD2AP</i>     | rs10948363 | G                      | 0.97 (0.70; 1.35)                             | -0.07 (-0.43; 0.28)                             |
| 21: 28156856                     | <i>ADAMTS1</i>   | rs7276338  | C                      | 0.97 (0.70; 1.33)                             | -0.02 (-0.38; 0.34)                             |
| 15: 59045774                     | <i>ADAM10</i>    | rs474875   | A                      | 0.95 (0.71; 1.28)                             | -0.10 (-0.48; 0.28)                             |
| 16: 19808163                     | <i>IQCK</i>      | rs1858973  | A                      | 0.92 (0.61; 1.36)                             | -0.07 (-0.54; 0.40)                             |
| 8:27219987                       | <i>PTK2B</i>     | rs28834970 | C                      | 0.91 (0.68; 1.22)                             | -0.11 (-0.47; 0.24)                             |
| 6:32575406                       | <i>HLA -DRB1</i> | rs9271192  | C                      | 0.91 (0.67; 1.24)                             | -0.05 (-0.44; 0.33)                             |
| 2:233981912                      | <i>INPP5D</i>    | rs7570061  | G                      | 0.90 (0.61; 1.31)                             | -0.16 (-0.7; 0.37)                              |
| 14: 53391680                     | <i>FERMT2</i>    | rs17125944 | C                      | 0.89 (0.57; 1.41)                             | -0.09 (-0.69; 0.50)                             |
| 20: 54997568                     | <i>CASS4</i>     | rs6064392  | G                      | 0.86 (0.49; 1.47)                             | -0.09 (-0.73; 0.54)                             |
| 7: 143099133                     | <i>EPHA1</i>     | rs11767557 | T                      | 0.81 (0.56; 1.15)                             | -0.29 (-0.85; 0.27)                             |
| 7: 100091795                     | <i>NYAPI</i>     | rs12539172 | C                      | 0.79 (0.57; 1.08)                             | -0.35 (-0.87; 0.16)                             |
| 8: 27467686                      | <i>CLU</i>       | rs9331896  | A                      | 0.78 (0.58; 1.04)                             | -0.28 (-0.71; 0.15)                             |
| 1: 207802552                     | <i>CRI</i>       | rs679515   | T                      | 0.73 (0.52; 1.03)                             | -0.40 (-0.85; 0.05)                             |
| 6:41129252                       | <i>TREM2</i>     | rs75932628 | T                      | NA  | NA  |

\*p < 0.05

**Supplementary Table 7.** Sex- and age- adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) for the association of income, education, *APOE*  $\epsilon$ 4 genotype and the AD-associated genetic risk score (GRS<sub>AD</sub>) with mild cognitive impairment (MCI) using a more rigorously defined non-MCI group by including only those participants who did not report a cognitive complaint and did not show any impairment in the applied cognitive tests calculated using separate logistic regression models.

|                          | <b>n</b> | <b>OR (95% CI)</b> | <b><i>p</i></b> |
|--------------------------|----------|--------------------|-----------------|
| Intercept                | 1,819    | 0.02(0.01; 0.05)   | $<2*10^{-16}$   |
| Low income               |          | 1.65 (1.33; 2.04)  | $5.1*10^{-6}$   |
| Sex                      |          | 1.07 (0.87; 1.31)  | 0.53            |
| Age                      |          | 1.04 (1.03; 1.06)  | $4.6*10^{-10}$  |
| Intercept                | 1,939    | 0.02 (0.01; 0.05)  | $<2*10^{-16}$   |
| Low education            |          | 1.51 (1.20; 1.90)  | 0.0005          |
| Sex                      |          | 0.91 (0.74; 1.13)  | 0.40            |
| Age                      |          | 1.05 (1.03; 1.06)  | $1*10^{-11}$    |
| Intercept                | 1,940    | 0.02 (0.01; 0.04)  | $<2*10^{-16}$   |
| <i>APOE</i> $\epsilon$ 4 |          | 1.31 (1.04; 1.63)  | 0.02            |
| Sex                      |          | 1.03 (0.84; 1.25)  | 0.79            |
| Age                      |          | 1.05 (1.04; 1.06)  | $1.6*10^{-13}$  |
| Intercept                | 1,940    | 0.03 (0.01; 0.10)  | $2.4*10^{-9}$   |
| GRS <sub>AD</sub>        |          | 0.99 (0.95; 1.02)  | 0.43            |
| Sex                      |          | 1.03 (0.85; 1.26)  | 0.75            |
| Age                      |          | 1.05 (1.04; 1.06)  | $1.2*10^{-13}$  |

**Supplementary Table 8.** Sex- and age- adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) in logistic regression models including main effects and interaction terms for the interaction of *APOE*  $\epsilon$ 4 status and AD-associated genetic risk score ( $GRS_{AD}$ ) with education and income on mild cognitive impairment (MCI) using a more rigorously defined non-MCI group by including only those participants who did not report a cognitive complaint and did not show any impairment in the applied cognitive tests.

|  | <b>n</b> | <b>OR (95% CI)</b> | <b>p</b>       |
|--|----------|--------------------|----------------|
| Intercept                              | 1,819    | 0.02 (0.01; 0.05)  | $<2*10^{-16}$  |
| Income low                             |          | 1.64 (1.27; 2.11)  | 0.0001         |
| <i>APOE</i> $\epsilon$ 4               |          | 1.30 (0.90; 1.85)  | 0.15           |
| Sex                                    |          | 1.06 (0.86; 1.31)  | 0.55           |
| Age                                    |          | 1.04 (1.03; 1.06)  | $7.3*10^{-10}$ |
| <i>APOE</i> $\epsilon$ 4*Income low    |          | 1.04 (0.65; 1.67)  | 0.87           |
| <hr/>                                  |          |                    |                |
| Intercept                              | 1,939    | 0.02 (0.01; 0.05)  | $<2*10^{-16}$  |
| Education low                          |          | 1.37 (1.05; 1.80)  | 0.02           |
| <i>APOE</i> $\epsilon$ 4               |          | 1.03 (0.68; 1.55)  | 0.88           |
| Sex                                    |          | 0.91 (0.74; 1.13)  | 0.39           |
| Age                                    |          | 1.05 (1.03; 1.06)  | $1.5*10^{-11}$ |
| <i>APOE</i> $\epsilon$ 4*Education low |          | 1.41 (0.87; 2.32)  | 0.17           |
| <hr/>                                  |          |                    |                |
| Intercept                              | 1,819    | 0.03 (0.01; 0.14)  | $1.6*10^{-5}$  |
| Income low                             |          | 1.39 (0.23; 8.37)  | 0.72           |
| $GRS_{AD}$                             |          | 0.99 (0.93; 1.05)  | 0.70           |
| Sex                                    |          | 1.07 (0.87; 1.32)  | 0.53           |
| Age                                    |          | 1.04 (1.03; 1.06)  | $4.8*10^{-10}$ |
| $GRS_{AD}$ *Income low                 |          | 1.01 (0.93; 1.09)  | 0.85           |
| <hr/>                                  |          |                    |                |
| Intercept                              | 1,939    | 0.01 (0.001; 0.05) | $1.0*10^{-7}$  |
| Education low                          |          | 8.22 (1.29; 53.35) | 0.03           |
| $GRS_{AD}$                             |          | 1.04 (0.97; 1.11)  | 0.26           |
| Sex                                    |          | 0.92 (0.74; 1.14)  | 0.44           |
| Age                                    |          | 1.05 (1.03; 1.06)  | $9.4*10^{-12}$ |
| $GRS_{AD}$ *Education low              |          | 0.93 (0.86; 1.01)  | 0.07           |



**Supplementary Table 9.** Age- and sex-adjusted relative excess risk due to interaction (RERI) and corresponding 95% confidence intervals as a measure of interaction between *APOE*  $\epsilon 4$  x SEP and the GRS<sub>AD</sub> x SEP on the additive scale using a more rigorously defined non-MCI group by including only those participants who did not report a cognitive complaint and did not show any impairment in the applied cognitive tests.

|                                     | <b>n</b> | <b>RERI (95% CI)</b> |
|-------------------------------------|----------|----------------------|
| <i>APOE</i> $\epsilon 4$ *Income    | 1819     | 0.24 (-0.12; 0.61)   |
| <i>APOE</i> $\epsilon 4$ *Education | 1939     | 0.31 (0.12; 0.51)*   |
| GRS <sub>AD</sub> *Income           | 1819     | 0.006 (-0.09; 0.11)  |
| GRS <sub>AD</sub> *Education        | 1939     | -0.32 (-1.14; 0.49)  |

\*p < 0.05

**Supplementary Table 10.** Sex- and age- adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) for the association of income, education, *APOE*  $\epsilon$ 4 genotype and the AD-associated genetic risk score (GRS<sub>AD</sub>) with amnesic mild cognitive impairment calculated using separate logistic regression models.

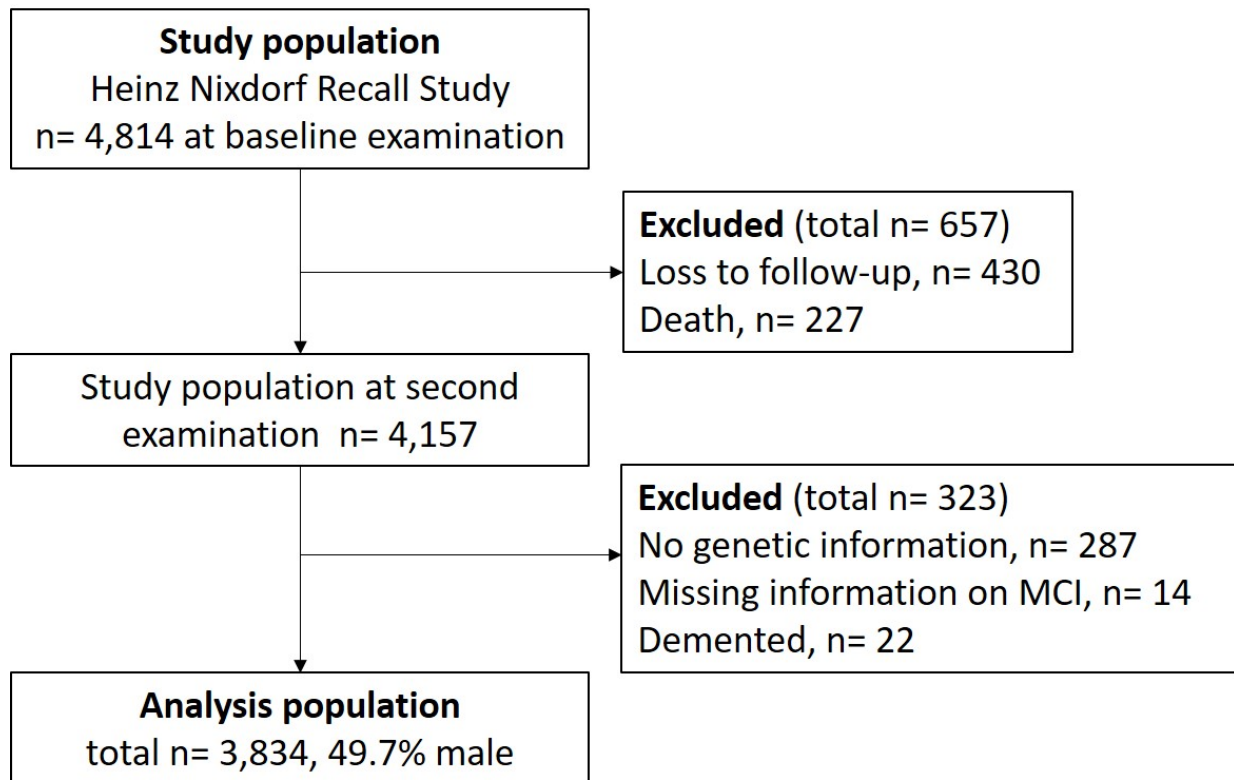
|                          | <b>n</b> | <b>OR (95% CI)</b> | <b><i>p</i></b> |
|--------------------------|----------|--------------------|-----------------|
| Intercept                | 3,361    | 0.01 (0.005; 0.04) | $<2*10^{-16}$   |
| Low income               |          | 1.65 (1.27; 2.16)  | 0.0002          |
| Sex                      |          | 0.85 (0.66; 1.09)  | 0.20            |
| Age                      |          | 1.03 (1.01; 1.05)  | 0.001           |
| Intercept                | 3,562    | 0.01 (0.005; 0.03) | $<2*10^{-16}$   |
| Low education            |          | 1.53 (1.16; 2.03)  | 0.003           |
| Sex                      |          | 0.72 (0.56; 0.93)  | 0.01            |
| Age                      |          | 1.03 (1.01; 1.05)  | 0.0002          |
| Intercept                | 3,567    | 0.01 (0.05; 0.03)  | $<2*10^{-16}$   |
| <i>APOE</i> $\epsilon$ 4 |          | 1.36 (1.04; 1.76)  | 0.02            |
| Sex                      |          | 0.81 (0.64; 1.03)  | 0.09            |
| Age                      |          | 1.03 (1.02; 1.05)  | $3.0*10^{-5}$   |
| Intercept                | 3,567    | 0.01 (0.002; 0.04) | $3.9*10^{-11}$  |
| GRS <sub>AD</sub>        |          | 1.02 (0.97; 1.06)  | 0.48            |
| Sex                      |          | 0.81 (0.64; 1.03)  | 0.09            |
| Age                      |          | 1.03 (1.02; 1.05)  | $2.6*10^{-5}$   |

**Supplementary Table 11.** Sex- and age- adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) in logistic regression models including main effects and interaction terms for the interaction of *APOE*  $\epsilon 4$  status and AD-associated genetic risk score ( $GRS_{AD}$ ) with education and income on amnesic mild cognitive impairment.

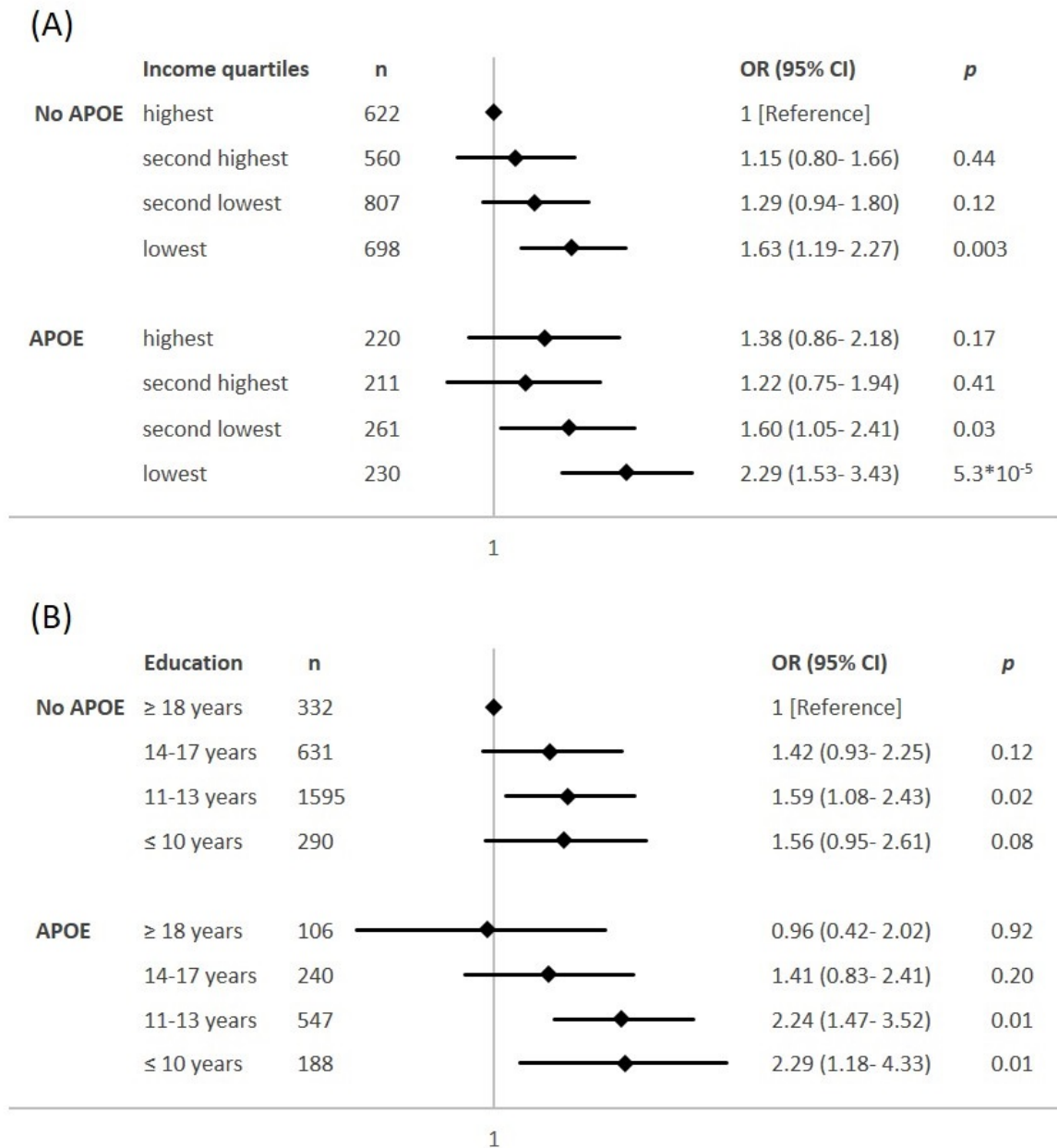
|   | <b>n</b> | <b>OR (95% CI)</b>   | <b>p</b>      |
|---|----------|----------------------|---------------|
| Intercept                               | 3,361    | 0.01 (0.004; 0.03)   | $<2*10^{-16}$ |
| Income low                              |          | 1.86 (1.35; 2.59)    | 0.0002        |
| <i>APOE</i> $\epsilon 4$                |          | 1.69 (1.08; 2.62)    | 0.02          |
| Sex                                     |          | 0.85 (0.66; 1.08)    | 0.19          |
| Age                                     |          | 1.03 (1.01; 1.04)    | 0.001         |
| <i>APOE</i> $\epsilon 4$ *Income low    |          | 0.71 (0.41; 1.25)    | 0.23          |
| Intercept                               | 3,562    | 0.01 (0.004; 0.03)   | $<2*10^{-16}$ |
| Education low                           |          | 1.52 (1.10; 2.14)    | 0.01          |
| <i>APOE</i> $\epsilon 4$                |          | 1.34 (0.81; 2.16)    | 0.24          |
| Sex                                     |          | 0.72 (0.56; 0.92)    | 0.01          |
| Age                                     |          | 1.03 (1.01; 1.05)    | 0.0002        |
| <i>APOE</i> $\epsilon 4$ *Education low |          | 1.04 (0.59; 1.87)    | 0.89          |
| Intercept                               | 3,361    | 0.01 (0.001; 0.05)   | $1.6*10^{-6}$ |
| Income low                              |          | 1.91 (0.21; 17.49)   | 0.56          |
| $GRS_{AD}$                              |          | 1.03 (0.96; 1.11)    | 0.41          |
| Sex                                     |          | 0.85 (0.66; 1.09)    | 0.19          |
| Age                                     |          | 1.03 (1.01; 1.05)    | 0.001         |
| $GRS_{AD}$ *Income low                  |          | 0.99 (0.90; 1.09)    | 0.90          |
| Intercept                               | 3,562    | 0.002 (0.0002; 0.02) | $2.7*10^{-8}$ |
| Education low                           |          | 10.15 (1.07; 100.57) | 0.05          |
| $GRS_{AD}$                              |          | 1.08 (0.99; 1.17)    | 0.07          |
| Sex                                     |          | 0.72 (0.56; 0.93)    | 0.01          |
| Age                                     |          | 1.03 (1.01; 1.05)    | 0.0002        |
| $GRS_{AD}$ *Education low               |          | 0.92 (0.84; 1.02)    | 0.10          |

**Supplementary Table 12.** Age- and sex-adjusted relative excess risk due to interaction (RERI) and corresponding 95% confidence intervals as a measure of interaction between *APOE*  $\epsilon 4$ xSEP and the GRS<sub>AD</sub>xSEP on the additive scale (amnesic mild cognitive impairment).

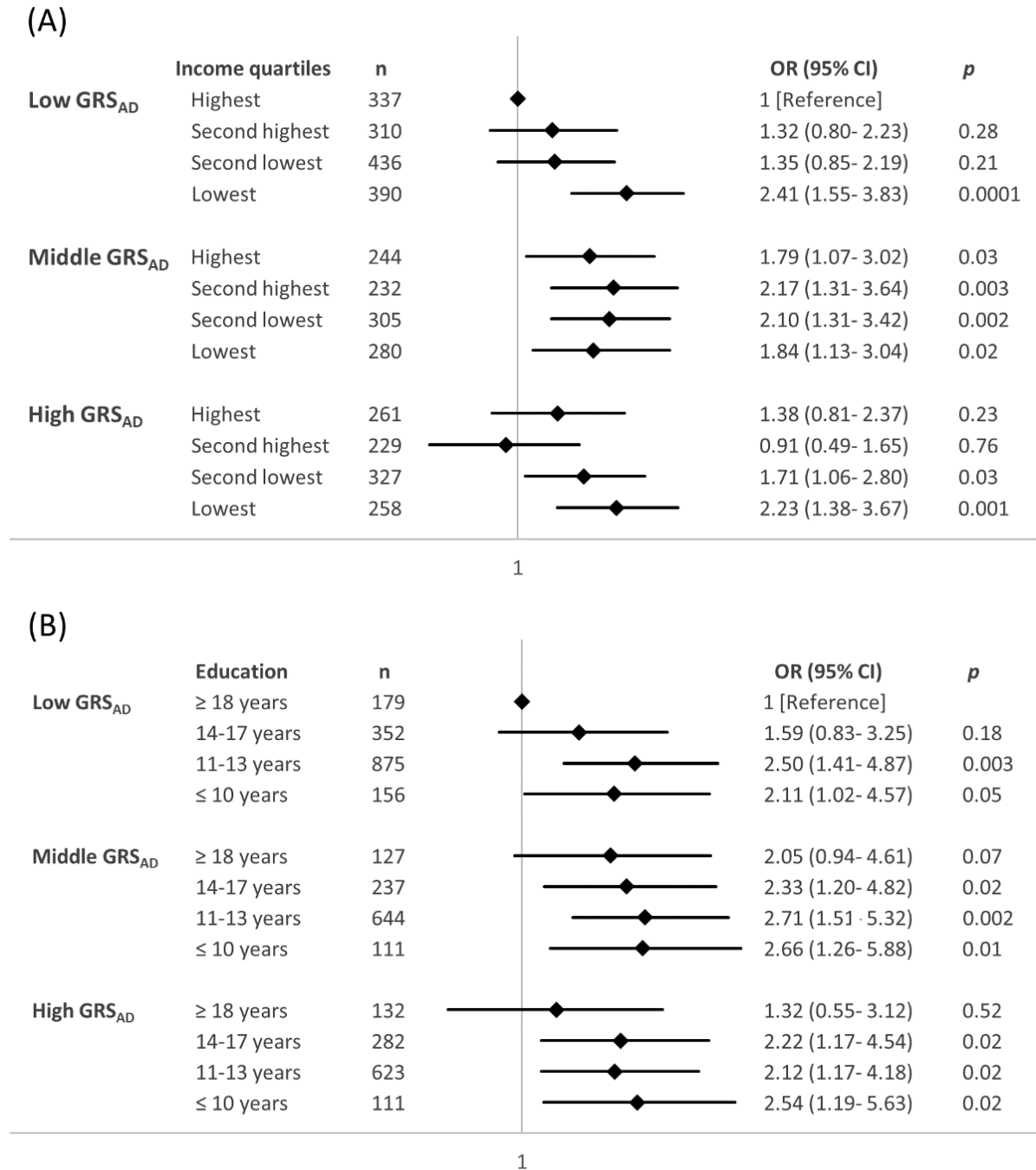
|                                     | <b>n</b> | <b>RERI (95% CI)</b> |
|-------------------------------------|----------|----------------------|
| <i>APOE</i> $\epsilon 4$ *Income    | 3,361    | -0.09 (-1.01; 0.84)  |
| <i>APOE</i> $\epsilon 4$ *Education | 3,562    | 0.23 (-0.19; 0.65)   |
| GRS <sub>AD</sub> *Income           | 3,361    | 0.02 (-0.03; 0.06)   |
| GRS <sub>AD</sub> *Education        | 3,562    | -0.14 (-0.75; 0.47)  |



**Supplementary Figure 1.** Flow-chart of participants of the Heinz Nixdorf Recall Study cohort included in the analysis.



**Supplementary Figure 2.** Sex- and age-adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) for single reference joint effects of *APOE*  $\epsilon 4$  genotype and socioeconomic position indicators on mild cognitive impairment calculated in separate logistic regression models for (A) income quartiles and (B) education categories, with the group of a negative *APOE*  $\epsilon 4$  status and a high socioeconomic position as reference.



**Supplementary Figure 3.** Sex- and age-adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CI) for single reference joint effects of tertiles of an AD-associated genetic risk score (GRS<sub>AD</sub>) and socioeconomic position indicators on mild cognitive impairment calculated in separate logistic regression models for (A) income quartiles and (B) education categories, with the group of a low GRS and a high socioeconomic position as reference.