MELODEM Workshop Paper Results

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## Table 1: Participant characteristics

| **Characteristic** | **Overall** | **Apolipoprotein E** | |
| --- | --- | --- | --- |
| **Non-carrier** | **Carrier** |
| ACT | | | |
| No. of participants | 3,742 | 2,712 | 1,030 |
| Age | 71.0 (68.0, 75.0) | 72.0 (68.0, 75.0) | 71.0 (68.0, 75.0) |
| Sex |  |  |  |
| male | 1,651 (44%) | 1,241 (46%) | 410 (40%) |
| female | 2,091 (56%) | 1,471 (54%) | 620 (60%) |
| Stroke | 93 (2.5%) | 72 (2.7%) | 21 (2.0%) |
| Heart conditions | 572 (15%) | 408 (15%) | 164 (16%) |
| Hypertension | 1,477 (40%) | 1,073 (40%) | 404 (39%) |
| Race/Ethnicity |  |  |  |
| White | 3,336 (96%) | 2,414 (97%) | 922 (96%) |
| Black | 123 (3.6%) | 83 (3.3%) | 40 (4.2%) |
| Asian | 0 (0%) | 0 (0%) | 0 (0%) |
| Other | 0 (0%) | 0 (0%) | 0 (0%) |
| Body mass index | 26.9 (24.1, 30.3) | 27.0 (24.3, 30.3) | 26.7 (23.9, 30.4) |
| Physical activity | 2,736 (73%) | 1,982 (73%) | 754 (73%) |
| Education |  |  |  |
| bachelor's | 905 (24%) | 660 (24%) | 245 (24%) |
| doctorate | 225 (6.0%) | 162 (6.0%) | 63 (6.1%) |
| GED or HS | 1,380 (37%) | 994 (37%) | 386 (37%) |
| master's | 631 (17%) | 442 (16%) | 189 (18%) |
| none | 252 (6.7%) | 181 (6.7%) | 71 (6.9%) |
| other | 349 (9.3%) | 273 (10%) | 76 (7.4%) |
| Myocardial infarction | 253 (6.8%) | 184 (6.8%) | 69 (6.7%) |
| ARIC | | | |
| No. of participants | 8,650 | 5,933 | 2,717 |
| Age | 74.4 (68.5, 77.7) | 74.5 (68.5, 77.8) | 74.3 (68.5, 77.6) |
| Sex |  |  |  |
| male | 4,113 (48%) | 2,824 (48%) | 1,289 (47%) |
| female | 4,537 (52%) | 3,109 (52%) | 1,428 (53%) |
| Heart conditions | 504 (5.9%) | 335 (5.8%) | 169 (6.3%) |
| Hypertension | 3,252 (38%) | 2,197 (37%) | 1,055 (39%) |
| Diabetes | 1,306 (15%) | 922 (16%) | 384 (14%) |
| Race/Ethnicity |  |  |  |
| White | 5,891 (68%) | 4,264 (72%) | 1,627 (60%) |
| Black | 2,759 (32%) | 1,669 (28%) | 1,090 (40%) |
| Asian | 0 (0%) | 0 (0%) | 0 (0%) |
| Other | 0 (0%) | 0 (0%) | 0 (0%) |
| Body mass index | 27.2 (24.2, 30.9) | 27.2 (24.2, 30.9) | 27.1 (24.1, 30.9) |
| Smoking status | 2,871 (33%) | 1,925 (32%) | 946 (35%) |
| Education |  |  |  |
| 1 | 2,293 (27%) | 1,522 (26%) | 771 (28%) |
| 2 | 3,446 (40%) | 2,419 (41%) | 1,027 (38%) |
| 3 | 2,896 (34%) | 1,977 (33%) | 919 (34%) |
| HRS | | | |
| No. of participants | 8,704 | 6,367 | 2,337 |
| Age | 64 (60, 70) | 64 (60, 70) | 64 (60, 69) |
| Sex |  |  |  |
| male | 3,706 (43%) | 2,718 (43%) | 988 (42%) |
| female | 4,998 (57%) | 3,649 (57%) | 1,349 (58%) |
| Stroke | 327 (3.8%) | 240 (3.8%) | 87 (3.7%) |
| Heart conditions | 1,580 (18%) | 1,122 (18%) | 458 (20%) |
| Hypertension | 4,084 (47%) | 2,951 (46%) | 1,133 (48%) |
| Diabetes | 1,144 (13%) | 825 (13%) | 319 (14%) |
| Smoking status |  |  |  |
| Cuurent | 1,213 (14%) | 882 (14%) | 331 (14%) |
| Former | 3,815 (44%) | 2,792 (44%) | 1,023 (44%) |
| Never | 3,609 (42%) | 2,648 (42%) | 961 (42%) |
| Physical activity (Vigorous vs. other) | 4,395 (50%) | 3,216 (51%) | 1,179 (50%) |
| Education |  |  |  |
| <12 | 1,994 (23%) | 1,458 (23%) | 536 (23%) |
| 12 | 3,134 (36%) | 2,309 (36%) | 825 (35%) |
| 13-15 | 1,746 (20%) | 1,273 (20%) | 473 (20%) |
| 16+ | 1,830 (21%) | 1,327 (21%) | 503 (22%) |
| REGARDS | | | |
| No. of participants | 5,381 |  |  |
| Age | 64 (59, 70) |  |  |
| Sex |  |  |  |
| male | 2,121 (39%) |  |  |
| female | 3,260 (61%) |  |  |
| simulated | | | |
| No. of participants | 974 | 503 | 471 |
| Age | 65.0 (61.5, 68.4) | 65.1 (61.9, 68.4) | 64.9 (61.4, 68.3) |
| Sex |  |  |  |
| male | 463 (48%) | 236 (47%) | 227 (48%) |
| female | 511 (52%) | 267 (53%) | 244 (52%) |
| UKBB | | | |
| No. of participants | 3,060 | 2,211 | 849 |
| Age | 62.5 (59.2, 65.8) | 62.5 (59.2, 65.9) | 62.5 (59.2, 65.6) |
| Sex |  |  |  |
| male | 1,387 (45%) | 996 (45%) | 391 (46%) |
| female | 1,673 (55%) | 1,215 (55%) | 458 (54%) |
| Race/Ethnicity |  |  |  |
| White | 2,970 (97%) | 2,142 (97%) | 828 (98%) |
| Black | 20 (0.7%) | 16 (0.7%) | 4 (0.5%) |
| Asian | 38 (1.2%) | 31 (1.4%) | 7 (0.8%) |
| Other | 32 (1.0%) | 22 (1.0%) | 10 (1.2%) |
| Body mass index | 27.0 (24.5, 30.0) | 27.0 (24.5, 30.0) | 26.9 (24.4, 29.9) |
| Smoking status | 1,448 (47%) | 1,029 (47%) | 419 (49%) |
| Physical activity | 2,335 (78%) | 1,683 (78%) | 652 (79%) |
| Education |  |  |  |
| High school | 1,829 (60%) | 1,328 (60%) | 501 (59%) |
| Less than high school | 1,231 (40%) | 883 (40%) | 348 (41%) |
| WHICAP | | | |
| No. of participants | 3,819 | 2,756 | 1,063 |
| Age | 72.3 (69.7, 75.7) | 72.3 (69.7, 75.7) | 72.3 (69.5, 75.5) |
| Sex |  |  |  |
| female | 2,489 (65%) | 1,791 (65%) | 698 (66%) |
| male | 1,330 (35%) | 965 (35%) | 365 (34%) |
| Hypertension | 2,338 (62%) | 1,668 (62%) | 670 (64%) |
| Diabetes | 975 (26%) | 734 (27%) | 241 (23%) |
| Race/Ethnicity |  |  |  |
| Black | 1,133 (30%) | 732 (27%) | 401 (38%) |
| Hisp | 1,683 (44%) | 1,262 (46%) | 421 (40%) |
| White | 1,003 (26%) | 762 (28%) | 241 (23%) |
| Body mass index | 27.0 (25.0, 30.0) | 27.0 (25.0, 30.0) | 27.0 (24.0, 30.0) |
| Smoking status | 1,862 (51%) | 1,346 (51%) | 516 (51%) |
| Education | 12.0 (7.0, 14.0) | 12.0 (7.0, 14.0) | 12.0 (7.0, 14.0) |
| Occupation |  |  |  |
| 1 | 163 (4.4%) | 127 (4.8%) | 36 (3.5%) |
| 2 | 37 (1.0%) | 29 (1.1%) | 8 (0.8%) |
| 3 | 1,575 (42%) | 1,137 (43%) | 438 (42%) |
| 4 | 378 (10%) | 268 (10%) | 110 (11%) |
| 5 | 458 (12%) | 320 (12%) | 138 (13%) |
| 6 | 157 (4.2%) | 115 (4.3%) | 42 (4.0%) |
| 7 | 879 (24%) | 627 (23%) | 252 (24%) |
| 8 | 62 (1.7%) | 48 (1.8%) | 14 (1.3%) |
| income | 5.0 (4.0, 9.0) | 5.0 (4.0, 9.0) | 5.0 (3.0, 9.0) |

## Table 2: Hazard ratios for dementia overall and in subgroups based on Apolipoprotein E.

| **Characteristic** | **Hazard ratio (95% CI)** | | |
| --- | --- | --- | --- |
| **Overall** | **Non-carrier** | **Carrier** |
| simulated | | | |
| Age | 0.95 (0.86, 1.0) | 0.97 (0.58, 1.6) | 0.95 (0.87, 1.0) |
| Women versus men | 1.0 (0.85, 1.2) | 1.3 (0.44, 3.7) | 1.0 (0.84, 1.2) |
| Apolipoprotein E | 175 (100, 308) |  |  |

## Table 3: Heterogeneity in the effect of APOE-4 on dementia risk using time since birth

| **Age, years** | **Estimated effect of APOE-4 on dementia-free survival time, years** | **P-value for heterogeneity in effect** | **Best linear projection of effect** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Women versus men** | **Black versus White** | **Other versus White** | **Asian versus White** | **Men versus women** | **Hispanic versus White** | **White versus black** |
| ACT | | | | | | | | | |
| 70 | -0.07 (-0.38, 0.24) | 0.998 | -0.57 (-1.2, 0.09) | -2.2 (-4.2, -0.18) | 0.70 (-0.43, 1.8) |  |  |  |  |
| 75 | -0.52 (-0.78, -0.25) | 0.69 | -0.35 (-0.90, 0.20) | -2.2 (-4.0, -0.43) | 0.22 (-0.73, 1.2) |  |  |  |  |
| ARIC | | | | | | | | | |
| 65 | 0.05 (-0.22, 0.31) | 0.52 | 0.10 (-0.45, 0.64) | -2.8 (-3.4, -2.2) |  |  |  |  |  |
| 70 | -0.04 (-0.24, 0.16) | 0.84 | 0.03 (-0.38, 0.44) | -1.8 (-2.3, -1.3) |  |  |  |  |  |
| 75 | -0.16 (-0.31, -0.02) | 0.13 | -0.02 (-0.31, 0.28) | -0.78 (-1.1, -0.43) |  |  |  |  |  |
| HRS | | | | | | | | | |
| 60 | -0.05 (-0.44, 0.33) | 0.40 | -0.24 (-1.1, 0.57) |  |  |  |  |  |  |
| 65 | -0.28 (-0.61, 0.05) | 0.43 | -0.50 (-1.2, 0.21) |  |  |  |  |  |  |
| 70 | -0.89 (-1.2, -0.58) | 0.71 | -1.0 (-1.7, -0.34) |  |  |  |  |  |  |
| 75 | -1.6 (-1.9, -1.2) | 0.05 | -1.0 (-1.8, -0.27) |  |  |  |  |  |  |
| REGARDS | | | | | | | | | |
| 60 | 0.45 (-0.04, 0.93) | 0.05 | -1.6 (-2.6, -0.66) |  |  |  |  |  |  |
| 65 | 0.43 (0.00, 0.87) | 0.31 | -1.6 (-2.5, -0.67) |  |  |  |  |  |  |
| 70 | 0.31 (-0.08, 0.70) | 0.47 | -1.1 (-1.9, -0.25) |  |  |  |  |  |  |
| 75 | -0.50 (-0.84, -0.16) | 0.049 | -0.66 (-1.4, 0.04) |  |  |  |  |  |  |
| simulated | | | | | | | | | |
| 60 | -1.7 (-2.5, -0.88) | 0.22 | 0.14 (-1.5, 1.8) |  |  |  |  |  |  |
| 65 | -4.3 (-4.9, -3.7) | 0.96 | -0.08 (-1.2, 1.1) |  |  |  |  |  |  |
| 70 | -7.3 (-7.7, -6.8) | 0.88 | 0.05 (-0.92, 1.0) |  |  |  |  |  |  |
| UKBB | | | | | | | | | |
| 60 | 0.01 (-0.36, 0.39) | 0.996 | 0.02 (-0.75, 0.79) | 1.3 (-2.2, 4.7) | -2.2 (-6.2, 1.9) | -0.69 (-4.5, 3.1) |  |  |  |
| 65 | -0.03 (-0.30, 0.23) | 0.97 | 0.31 (-0.23, 0.85) | 1.7 (-0.69, 4.0) | -0.09 (-2.3, 2.1) | 0.31 (-2.6, 3.2) |  |  |  |
| WHICAP | | | | | | | | | |
| 70 | 0.02 (-0.31, 0.36) | 0.21 |  |  |  |  | -0.08 (-0.99, 0.83) | -2.1 (-3.3, -0.99) | -3.1 (-4.3, -1.9) |
| 75 | 0.14 (-0.11, 0.40) | 0.09 |  |  |  |  | -0.05 (-0.74, 0.64) | -0.63 (-1.6, 0.30) | -1.9 (-2.8, -0.91) |

## Table 3: Heterogeneity in the effect of APOE-4 on dementia risk using time since baseline

| **Time since baseline visit, years** | **Estimated effect of APOE-4 on dementia-free survival time, years** | **P-value for heterogeneity in effect** | **Best linear projection of effect** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Age, per year** | **Women versus men** | **Black versus White** | **Other versus White** | **Asian versus White** | **Men versus women** | **Hispanic versus White** | **White versus black** |
| ACT | | | | | | | | | | |
| 5.0 | -0.17 (-0.68, 0.34) | 0.09 | 0.34 (-0.19, 0.88) | -1.7 (-2.8, -0.61) | -1.3 (-4.5, 1.9) | 1.0 (-0.91, 3.0) |  |  |  |  |
| 10 | -0.52 (-1.1, 0.01) | 0.21 | 0.35 (-0.22, 0.93) | -0.97 (-2.1, 0.17) | -0.52 (-4.0, 3.0) | 0.13 (-2.0, 2.2) |  |  |  |  |
| 15 | -0.44 (-1.0, 0.11) | 0.72 | -0.27 (-0.85, 0.30) | -0.31 (-1.5, 0.85) | -0.67 (-4.4, 3.1) | 1.4 (-0.71, 3.5) |  |  |  |  |
| ARIC | | | | | | | | | | |
| 25 | -0.24 (-0.49, 0.00) | 0.30 | 0.34 (-0.02, 0.71) | -0.01 (-0.51, 0.49) | -1.8 (-2.3, -1.2) |  |  |  |  |  |
| 30 | -0.39 (-0.60, -0.19) | <0.001 | 0.30 (-0.01, 0.61) | -0.12 (-0.54, 0.29) | -0.85 (-1.3, -0.36) |  |  |  |  |  |
| HRS | | | | | | | | | | |
| 5.0 | -0.01 (-0.27, 0.25) | 0.60 | 0.29 (0.03, 0.56) | -0.24 (-0.78, 0.31) |  |  |  |  |  |  |
| 10 | -0.16 (-0.33, 0.02) | 0.88 | 0.13 (-0.05, 0.31) | -0.31 (-0.68, 0.07) |  |  |  |  |  |  |
| 15 | -0.51 (-0.67, -0.34) | 0.03 | -0.18 (-0.35, 0.00) | -0.30 (-0.65, 0.04) |  |  |  |  |  |  |
| REGARDS | | | | | | | | | | |
| 5.0 | 0.10 (-0.13, 0.33) | 0.28 | 0.36 (0.14, 0.59) | -0.76 (-1.2, -0.30) |  |  |  |  |  |  |
| 10 | -0.24 (-0.46, -0.03) | 0.71 | -0.02 (-0.25, 0.21) | -0.09 (-0.54, 0.35) |  |  |  |  |  |  |
| simulated | | | | | | | | | | |
| 0.70 | -0.47 (-0.58, -0.35) | 0.67 | 0.04 (-0.08, 0.15) | 0.10 (-0.14, 0.33) |  |  |  |  |  |  |
| UKBB | | | | | | | | | | |
| 5.0 | -0.01 (-0.30, 0.27) | 0.08 | 0.14 (-0.16, 0.43) | 0.15 (-0.44, 0.74) | 1.4 (-2.1, 4.8) | -0.85 (-4.0, 2.3) | 1.7 (-0.88, 4.3) |  |  |  |
| 10 | -0.09 (-0.25, 0.06) | 0.28 | -0.03 (-0.19, 0.12) | 0.15 (-0.17, 0.47) | -0.52 (-3.7, 2.7) | -0.30 (-1.8, 1.2) | 0.94 (-0.29, 2.2) |  |  |  |
| WHICAP | | | | | | | | | | |
| 5.0 | -0.49 (-1.4, 0.43) | 0.24 | -0.47 (-1.5, 0.60) |  |  |  |  | -1.1 (-3.5, 1.3) | -4.4 (-7.4, -1.3) | -6.6 (-9.8, -3.3) |
| 10 | 0.08 (-1.1, 1.2) | 0.46 | -0.68 (-2.0, 0.60) |  |  |  |  | -2.5 (-5.2, 0.27) | -3.0 (-6.5, 0.57) | -5.6 (-9.5, -1.6) |
| 15 | 0.81 (-0.38, 2.0) | 0.85 | 0.49 (-0.74, 1.7) |  |  |  |  | -1.3 (-3.8, 1.2) | -0.79 (-4.0, 2.4) | -3.5 (-7.2, 0.12) |

## Cumulative incidence of dementia stratified by study

