**Supplementary figure 1.** Flowchart illustrating the participant selection process for the final study sample.

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**Supplementary table 1.** Demographic characteristics of CN participants across NPS groups

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | No-NPS (N=5078) | NPS-not-MBI (N=5625) | MBI (N=1408) | p-value  NPS-not-MBI vs No-NPS | p-value  MBI vs No-NPS |
| Age |  |  |  |  |  |
| Mean (SD) | 71.2 (8.99) | 71.6 (8.83) | 75.2 (9.48) | 0.0106 | <0.001 |
| Median [Min, Max] | 71.0 [50.0, 101] | 71.0 [50.0, 104] | 75.0 [50.0, 102] |  |  |
| Sex |  |  |  |  |  |
| Female | 3435 (67.6%) | 3682 (65.5%) | 764 (54.3%) | 0.0176 | <0.001 |
| Male | 1643 (32.4%) | 1943 (34.5%) | 644 (45.7%) |  |  |
| Years of education |  |  |  |  |  |
| Mean (SD) | 15.9 (2.86) | 15.8 (2.99) | 15.5 (3.20) | 0.0272 | <0.001 |
| Median [Min, Max] | 16.0 [1.00, 29.0] | 16.0 [0, 28.0] | 16.0 [0, 26.0] |  |  |
| Race |  |  |  |  |  |
| White | 3914 (77.1%) | 4685 (83.3%) | 1188 (84.4%) | <0.001 | <0.001 |
| Black | 969 (19.1%) | 750 (13.3%) | 157 (11.2%) |  |  |
| Other | 195 (3.8%) | 190 (3.4%) | 63 (4.5%) |  |  |
| ApoeE-e4 status |  |  |  |  |  |
| Carrier | 1584 (31.2%) | 1750 (31.1%) | 447 (31.7%) | 0.943 | 0.716 |
| Noncarrier | 3494 (68.8%) | 3875 (68.9%) | 961 (68.3%) |  |  |
| SCD |  |  |  |  |  |
| Absent | 4023 (79.2%) | 3719 (66.1%) | 884 (62.8%) | <0.001 | <0.001 |
| Present | 1055 (20.8%) | 1906 (33.9%) | 524 (37.2%) |  |  |

**Supplementary table 2.** Demographic characteristics of CN participants with SCD across NPS groups.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | No-NPS (N=1055) | NPS-not-MBI (N=1906) | MBI (N=524) | p-value  NPS-not-MBI vs No-NPS | p-value  MBI vs No-NPS |
| Age |  |  |  |  |  |
| Mean (SD) | 71.2 (8.99) | 71.1 (8.71) | 74.5 (9.20) | 0.731 | **<0.001** |
| Median [Min, Max] | 71.0 [50.0, 97.0] | 71.0 [50.0, 99.0] | 75.0 [50.0, 102] |  |  |
| Sex |  |  |  |  |  |
| Female | 723 (68.5%) | 1234 (64.7%) | 278 (53.1%) | **0.041** | **<0.001** |
| Male | 332 (31.5%) | 672 (35.3%) | 246 (46.9%) |  |  |
| Years of education |  |  |  |  |  |
| Mean (SD) | 16.0 (2.88) | 15.7 (3.14) | 15.5 (3.38) | **0.039** | **0.0065** |
| Median [Min, Max] | 16.0 [1.00, 23.0] | 16.0 [0, 28.0] | 16.0 [2.00, 25.0] |  |  |
| Race |  |  |  |  |  |
| White | 806 (76.4%) | 1540 (80.8%) | 432 (82.4%) | **0.0024** | **0.0026** |
| Black | 199 (18.9%) | 267 (14.0%) | 63 (12.0%) |  |  |
| Other | 50 (4.7%) | 99 (5.2%) | 29 (5.5%) |  |  |
| ApoeE-e4 status |  |  |  |  |  |
| Carrier | 348 (33.0%) | 649 (34.1%) | 177 (33.8%) | 0.585 | 0.796 |
| Noncarrier | 707 (67.0%) | 1257 (65.9%) | 347 (66.2%) |  |  |

**Supplementary table 3.** Hazard ratios for incident dementia associated with the interaction between NPS group and SCD status in CN older adults.

| **Group** | **No-NPS** | **NPS-not-MBI** | **MBI** | **Effect of NPS-not-MBI**  **on strata of SCD status** | | **Effect of MBI on**  **strata of SCD status** |
| --- | --- | --- | --- | --- | --- | --- |
|  | **HR [95% CI]**  **p-value** | **HR [95% CI]**  **p-value** | **HR [95% CI]**  **p-value** | **HR [95% CI]**  **p-value** | | **HR [95% CI]**  **p-value** |
| **SCD-** | 1 [Reference] | 0.99 [0.80-1.23]  p=0.911 | 3.53 [2.77-4.51]  **p<0.001** | 0.99 [0.80-1.23]  p=0.911 | | 3.53 [2.77-4.51]  **p<0.001** |
| **SCD+** | 2.60 [1.97-3.44]  **p<0.001** | 2.30 [1.85-2.86]  **p<0.001** | 5.10 [3.90-6.66]  **p<0.001** | 0.88 [0.68-1.15]  p=0.365 | | 1.96 [1.44-2.66]  **p<0.001** |
| **Multiplicative interaction test** | | **NPS-not-MBI (ref: No-NPS): SCD+ vs SCD-** | | | HR=0.89, CI:0.64-1.26, p=0.530 | |
| **MBI (ref: No-NPS):** **SCD+ vs SCD-** | | | HR=0.56, CI:0.38-0.82, **p=0.003** | |