**Supplementary Tables 1-3**

**Supplementary Table 1. ICD-10 diagnostic codes used for outcomes, exclusions, and propensity score matching of cohorts**

|  |  |  |
| --- | --- | --- |
| **Category** | **ICD-10 code(s)** | **Main sub-categories** |
| ***Outcomes of interest*** | | |
| Dementia | F01-F03, G30, G31.0, G31.2, G31.83 | F01 (vascular dementia), G30 (Alzheimer’s disease) |
| Movement disorders | G20-G26 | G20 (Parkinson’s disease) |
| Mild cognitive impairment | G31.84 |  |
| Cerebrovascular disease | I60-I69 | I63 (stroke), I60-I62 (cerebral haemorrhage) |
|  |  |  |
| ***Additional diagnoses excluded at baseline*** | | |
| REM sleep behaviour disorder | G7.52, F51.8 |  |
| Transient ischaemic attacks | G45 |  |
| Delirium | F05 |  |
|  |  |  |
| ***Propensity score matched diagnoses*** | | |
| Ischaemic heart disease | I20-I25 |  |
| Other forms of heart disease | I30-I52 | I48 (Atrial fibrillation and flutter), I50 (heart failure) |
| Diabetes mellitus | E08-E13 |  |
| Mood disorder | F30-F39 |  |
| Psychotic disorders | F20-F29 |  |
| Nicotine dependence | F17 |  |
| Alcohol use disorder | F10 |  |
| Epilepsy | G40 |  |
| Migraine | G43 |  |
| Intracranial injury with loss of consciousness | S06 |  |
|  |  |  |
| ***Negative control outcomes*** | | |
| Benign colonic polyp | D12.0 |  |
| Cutaneous abscess | L02 |  |
| Ganglion | M67.4 |  |
| Hallux valgus (acquired) | M20.1 |  |
| Hernia | K40-K46 |  |
| Ingrowing nail | L60.0 |  |
| Onycholysis | L60.1 |  |
| Otalgia | H92.09 |  |
| Sebaceous cyst | L72.3 |  |
| Senile keratosis | L82.1 |  |
| Trigger finger | M65.3 |  |
| Viral warts | B07 |  |

**Supplementary Table 2. Unmatched cohorts: baseline characteristics**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **CCBs vs diuretics** | | | **CCBs vs RAS agents** | | | **CCBs vs beta-blockers** | | |
| ***Baseline characteristics*** | | | | | | | | |  |
|  | *CCBs* | *Diuretics* | *SD* | *CCBs* | *RAS agents* | *SD* | *CCBs* | *Beta-blockers* | *SD* |
| Cohort size | 233,860 | 604,411 |  | 183,721 | 768,950 |  | 276,939 | 573,303 |  |
| Age at index (y) | 63.4 (10.9) | 61.7 (11.0) | 0.15 | 64.0 (11.5) | 61.2 (10.5) | 0.26 | 62.6 (10.8) | 63.0 (11.1) | 0.04 |
| Sex (M:F) | 50%: 50% | 39%:61% | 0.22 | 41%: 59% | 50%: 50% | 0.17 | 45%:55% | 50%:50% | 0.09 |
| Race (W, B/AA, O/NK)a | 64%, 20%, 16% | 74%, 15%, 11% | 0.21 | 63%, 24%, 13% | 76%, 11%, 13% | 0.28 | 62%, 25%, 13% | 78%, 9%, 13% | 0.42 |
| Systolic BPb | 137 (21) | 132 (20) | 0.24 | 135 (22) | 134 (20) | 0.09 | 139 (20) | 128 (21) | 0.52 |
| Diastolic BPb | 79 (13) | 77 (13) | 0.13 | 78 (14) | 78 (13) | 0.05 | 80 (13) | 74 (13) | 0.46 |
| BMIb | 29 (6) | 32 (8) | 0.43 | 29 (7) | 31 (7) | 0.29 | 30.4 (7.0) | 30.3 (7.1) | 0.02 |
| Diabetes mellitus | 15% | 17% | 0.06 | 10% | 21% | 0.31 | 16% | 17% | 0.01 |
| Previous exposure to AHTsc | 29% ACEI, 15% ARB, 30% BB | 34% ACEI, 19% ARB, 32% BB | 0.11, 0.12, 0.06 | 33% BB, 29% D | 30% BB, 40% D | 0.08 0.23 | 36% D, 32% ACEI, 20% ARB | 33% D, 27% ACEI, 12% ARB | 0.06, 0.10, 0.21 |
| Data density (average facts per patient)d | 8,188 | 10,375 |  | 9,478 | 8,955 |  | 9,942 | 9,345 |  |

SD: standard difference.

aW: white. B/AA: black or African American. O/NK: other or not known.

bMost recent value before exposure period. BP: blood pressure.

cACEI: angiotensin converting enzyme inhibitors. ARB: angiotensin II inhibitors. BB: beta-blockers. D: diuretics.

dComprising diagnoses, procedures, medications, lab results, and vital signs.

**Supplementary Table 3: Matched cohort characteristics and outcomes over a 2 year period associated with CCBs compared to diuretics, RAS agents, and beta-blockers**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **CCBs vs diuretics** | | **CCBs vs RAS agents** | | **CCBs vs beta-blockers** | |
| ***Baseline characteristics*** | | | | | | |
|  | *CCBs* | *Diuretics* | *CCBs* | *RAS agents* | *CCBs* | *Beta-blockers* |
| Cohort size | 231,764 | 231,764 | 181,495 | 181,495 | 234,015 | 234,015 |
| Age at index (y) | 63.3 (10.9) | 63.5 (11.1) | 63.9 (11.4) | 64.0 (11.4) | 62.9 (10.8) | 63.1 (11.0) |
| Sex (M:F) | 50%:50% | 49%:51% | 41%:59% | 41%:59% | 44%:56% | 45%:55% |
| Race (W, B/AA, O/NK)a | 65%, 20%, 15% | 66%, 18%, 16% | 64%, 23%, 13% | 64%, 23%, 13% | 69%, 17%, 14% | 70%, 17%, 13% |
| Systolic BPb | 137 (21) | 135 (21) | 135 (21.7) | 134 (20.7) | 137 (20)d | 134 (20)d |
| Diastolic BPb | 79 (13) | 78 (13) | 78 (14) | 78 (13) | 79 (13)e | 78 (13)e |
| BMIb | 29 (6) | 30 (7) | 29 (7) | 29 (7) | 30 (7) | 31 (7) |
| Diabetes mellitus | 15% | 16% | 10% | 10% | 16% | 16% |
| Previous exposure to AHTsc | 29% ACEI, 15% ARB, 30% BB | 30% ACEI, 14% ARB, 30% BB | 33% BB, 29% D | 34% BB, 29% D | 35% D, 30%, 18% ARB | 35% D, 30% ACEI, 18% ARB |
|  |  |  |  |  |  |  |
| ***Outcomes*** |  |  |  |  |  |  |
|  | *CCBs vs diuretics* | *Odds ratio (95% CI)* | *CCBs vs RAS agents* | *Odds ratio (95% CI)* | *CCBs vs beta-blockers* | *Odds ratio (95% CI)* |
| Dementia | 1.2% vs 1.0% | **1.19 (1.13-1.26)** | 1.4% vs 1.1% | **1.24 (1.17-1.32)** | 1.0% vs 1.1% | 0.96 (0.90-1.01) |
| Alzheimer’s disease | 0.40% vs 0.29% | **1.39 (1.26-1.53)** | 0.43% vs 0.40% | 1.08 (0.91-1.20) | 0.36% vs 0.35% | 1.05 (0.96-1.16) |
| Vascular dementia | 0.18% vs 0.11% | **1.54 (1.32-1.79)** | 0.19% vs 0.15% | **1.26 (1.08-1.48)** | 0.15% vs 0.14% | 1.04 (0.90-1.21) |
| Other dementias | 1.0% vs 0.89% | **1.14 (1.08-1.21)** | 1.2% vs 1.0% | **1.26 (1.19-1.34)** | 0.87% vs 0.91% | 0.96 (0.90-1.02) |
| MCI | 0.48% vs 0.38% | **1.26 (1.15-1.38)** | 0.52% vs 0.43% | **1.21 (1.10-1.33)** | 0.44% vs 0.40% | **1.11 (1.02-1.22)** |
| Movement disorders | 1.8% vs 1.9% | **0.92 (0.88-0.96)** | 2.0% vs 1.6% | **1.21 (1.16-1.28)** | 1.6% vs 2.2% | **0.73 (0.70-0.76)** |
| Parkinson’s disease | 0.34% vs 0.34% | 1.01 (0.91-1.13) | 0.35% vs 0.33% | 1.06 (0.95-1.19) | 0.28% vs 0.39% | **0.73 (0.66-0.81)** |
| Cerebrovascular disease | 4.5% vs 3.9% | **1.17 (1.14-1.21)** | 4.9% vs 3.7% | **1.34 (1.29-1.38)** | 3.7% vs 4.3% | **0.86 (0.84-0.89)** |
| Stroke | 1.6% vs 1.3% | **1.25 (1.19-1.31)** | 1.6% vs 1.2% | **1.40 (1.33-1.48)** | 1.2% vs 1.4% | **0.87 (0.82-0.91)** |
| Cerebral haemorrhage | 0.33% vs 0.27% | **1.25 (1.13-1.39)** | 0.40% vs 0.23% | **1.77 (1.56-1.99)** | 0.25% vs 0.33% | **0.77 (0.69-0.86)** |
| Any of the above | 7.6% vs 6.8% | **1.12 (1.10-1.15)** | 8.3% vs 6.5% | **1.29 (1.26-1.32)** | 6.6% vs 7.6% | **0.85 (0.83-0.87)** |
| Negative control outcomesf |  | **0.89 (0.84-0.93)** |  | 1.04 (0.97-1.11) |  | 1.06 (1.00-1.13) |
|  |  |  |  |  |  |  |
| Most recent systolic BP | 133 (17) vs 130 (18) | | 132 (18) vs 131 (18) | | 133 (17) vs 131 (18.2) | |
| Most recent diastolic BP | 76 (11) vs 75 (11) | | 76 (11) vs 76 (11) | | 77 (11) vs 76 (11) | |

aW: white. B/AA: black or African American. O/NK: other or not known.

bMost recent value before exposure period.

cACEI: angiotensin converting enzyme inhibitors. ARB: angiotensin II inhibitors. BB: beta-blockers. D: diuretics.

dStandard difference = 0.16.

eStandard difference = 0.12.

fMean of 12 negative control outcomes.