**Supplementary Method 1. Code list for definitions**

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| **Variables** | **Vocabulary** | **OMOP Vocabulary Codes** |
| Bupropion | RxNorm | 750982 |
| Aripiprazole | RxNorm | 757688 |
| Antidepressants | ATC | 21604686 (ANTIDEPRESSANTS) |
| Subcategories ofantidepressants | RxNorm | 713109 (amoxapine),710062 (amitriptyline),750982 (bupropion),797617 (citalopram),798834 (clomipramine),717607 (desvenlafaxine),738156 (doxepin),715259 (duloxetine),715939 (escitalopram),755695 (fluoxetine),778268 (imipramine),725131 (mirtazapine)714684 (nefazodone),721724 (nortriptyline),722031 (paroxetine),739138 (sertraline),703547 (trazodone),19041910 (tianeptine),743670 (venlafaxine),44507700 (vortioxetine) |
| Depression | SNOMED | 440383 (Depressive disorder),442306 (Adjustment disorder with depressed mood),4175329 (Organic mood disorder of depressed type) |
| Schizophrenia spectrum and bipolar disorder | SNOMED | 435783 (Schizophrenia),4286201 (Schizoaffective disorder),4335169 (Acute transient psychotic disorder),35207135 (Shared psychotic disorder),37117049 (Substance induced psychotic disorder),434010 (Schizotypal personality disorder),432590 (Delusional disorder),436665 (Bipolar disorder) |
| Dementia | SNOMED | 4182210 (Dementia) |
| Delirium | SNOMED | 373995 (Delirium) |
| Seizure | SNOMED | 377091 (Seizure),380378 (Epilepsy) |
| Extrapyramidal and movement disorders | SNOMED | 381270 (Parkinson’s disease),4140090 (Parkinsonism),374013 (Secondary parkinsonism),378144 (Disorder of basal ganglia),443782 (Tremor),372604 (Movement disorder),375800 (Dystonia) |
| Substance use disorder | SNOMED | 4319165 (Therapeutic drug dependence),4217840 (Substance misuse behavior),4279309 (Substance abuse),443274 (Psychostimulant dependence),4004672 (Psychoactive substance use disorder),4219382 (Persistent substance misuse),37116660 (Marijuana user),440787 (Drug dependence in mother complicating pregnancy, childbirth AND/OR peurperium),440069 (Drug dependence),37116661 (Cocaine user) |
| Movement disorders | SNOMED | 374013 (Secondary parkinsonism),443782 (Tremor),372604 (Movement disorder),375800 (Dystonia) |



**Supplementary Figure 1. Empirical equipoise between the bupropion and aripiprazole groups**

**Supplementary Table 1. Comparisons of baseline characteristics, comorbidities, and concomitant drugs in adult patients with depression before propensity score matching**

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| --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **BPR(n=1525), n (%)** | **ARP(n=4001), n (%)** | **aSMD** | **BPR (≥60 years)(n=259), n (%)** | **ARP (≥60 years)(n=690), n (%)** | **aSMD** |
| **Socio-demographics** |
|  Male | 514 (33.7) | 1240 (31.0) | 0.06 | 92 (35.5) | 180 (26.1) | 0.21 |
|  Female | 1011 (66.3) | 2761 (69.0) | 0.06 | 167 (64.5) | 510 (73.9) | 0.21 |
|  18–39 years | 825 (54.1) | 2268 (56.7) | 0.10 | NA | NA | NA |
|  40–59 years | 442 (29.0) | 1044 (26.1) | 0.12 | NA | NA | NA |
|  ≥ 60 years | 258 (16.9) | 689 (17.2) | 0.04 | 259 (100.0) | 690 (100.0) | 0.00 |
|  Race, Korean | 1525 (100.0) | 4001 (100.0) | 0.00 | 259 (100.0) | 690 (100.0) | 0.00 |
| **Comorbid mental health disorders** |
|  Anxiety disorder | 880 (57.7) | 2372 (59.3) | 0.03 | 163 (63.3) | 447 (64.8) | 0.03 |
|  Sleep disorder | 727 (47.7) | 1912 (47.8) | 0.00 | 144 (55.9) | 372 (54.0) | 0.04 |
|  Obsessive-compulsive disorder | 37 (2.4) | 128 (3.2) | 0.05 | 4 (1.9) | 9 (1.3) | 0.10 |
|  Personality disorder | 41 (2.7) | 130 (3.2) | 0.03 | 7 (2.7) | 17 (2.5) | 0.02 |
| **Comorbid physical disorders** |
|  Hypertension | 242 (15.9) | 656 (16.4) | 0.01 | 146 (56.4) | 397 (57.6) | 0.02 |
|  Diabetes mellitus | 145 (9.5) | 356 (8.9) | 0.02 | 71 (27.4) | 195 (28.3) | 0.02 |
|  Ischemic heart disease | 56 (3.7) | 172 (4.3) | 0.03 | 32 (12.4) | 96 (13.9) | 0.04 |
|  Chronic kidney disease | 6 (0.4) | 16 (0.4) | 0.01 | 5 (1.9) | 15 (2.2) | 0.02 |
| **Medication use** |
|  Anticholinergics | 39 (2.6) | 116 (2.9) | 0.02 | 2 (0.7) | 3 (0.4) | 0.17 |
|  Antiepileptics | 64 (4.2) | 308 (7.7) | 0.15 | 1 (0.4) | 5 (0.8) | 0.17 |
|  Anxiolytics | 1372 (90.0) | 3677 (91.9) | 0.06 | 251 (96.9) | 659 (95.5) | 0.07 |
| BPR: bupropion; ARP: aripiprazole; aSMD: absolute standardized mean difference. |



**Supplementary Figure 2. Scatter plots between before and after the propensity score adjustment between the bupropion and aripiprazole groups**

**Supplementary Table 2. Results of sensitivity analyses between the bupropion and aripiprazole groups**

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| --- | --- | --- | --- | --- |
| **Analysis description** | **Hospitalization** | **Movement disorder** | **Seizure** | **NC** |
| **Main setting** | 0.51 [0.29–0.86] | 0.56 [0.36–0.85] | 0.65[0.30–1.31] | 1.11[0.64–1.92] |
| **AT PS matched (1: n)** | 0.55 [0.32–0.87] | 0.67 [0.45–0.97] | 0.71[0.35–1.31] | 1.10 [0.69–1.71] |
| **AT PS stratified** | 0.58 [0.34–0.94] | 0.66 [0.44–0.97] | 0.79 [0.38–1.48] | 1.13 [0.70–1.80] |
| **ITT PS matched (1: 1)** | 0.66 [0.45–0.96] | 1.03 [0.80–1.35] | 1.33 [0.86–2.07] | 1.31 [0.94–1.83] |
| **ITT PS matched (1: n)** | 0.58 [0.42–0.79] | 0.99 [0.79–1.22] | 0.97 [0.69–1.36] | 1.15 [0.88–1.49] |
| **ITT PS stratified** | 0.59 [0.42–0.82] | 0.93 [0.75–1.16] | 1.03 [0.72–1.44] | 1.11 [0.84–1.45] |

**Supplementary Table 3. Results of sensitivity analyses between the bupropion and aripiprazole groups in the subgroup**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Analysis description** | **Hospitalization** | **Movement disorder** | **Seizure** | **NC** |
| **Main setting** | 0.76 [0.23–2.31] | 0.96 [0.35–2.47] | 0.46[0.02–3.59] | 1.14[0.38–3.40] |
| **AT PS matched (1: n)** | 0.58 [0.20–1.39] | 1.00 [0.40–2.20] | 0.36[0.02–1.90] | 0.92 [0.39–1.95] |
| **AT PS stratified** | 0.58 [0.20–1.39] | 1.00 [0.40–2.20] | 0.36 [0.02–1.90] | 0.92 [0.39–1.95] |
| **ITT PS matched (1: 1)** | 0.96 [0.51–1.77] | 0.88 [0.54–1.43] | 0.84 [0.34–2.04] | 1.14 [0.67–1.95] |
| **ITT PS matched (1: n)** | 0.87 [0.51–1.45] | 1.01 [0.65–1.52] | 0.99 [0.44–2.07] | 1.15 [0.73–1.76] |
| **ITT PS stratified** | 0.87 [0.51–1.45] | 1.01 [0.65–1.52] | 0.99 [0.44–2.07] | 1.15 [0.73–1.76] |