Association of Type of Antidepressant Initiation with Bleeding Risk in Atrial Fibrillation Patients taking Oral Anticoagulants

Running title: Association of Antidepressant Initiation with Bleeding

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| Antidepressant Category | Antidepressant Detail and Therapeutic Detail Codes |
|-------------------------|--------------------------------------------------|
| SSRI                    | 2816040040 (Citalopram) 2816040050 (Escitalopram) 2816040120 (Fluoxetine) 2816040130 (Fluvoxamine Maleate) 2816040140 (Sertraline) 2816040847 (Paroxetine) 2816049300 (Vilazodone) |
| SNRI                    | 2816040043 (Desvenlafaxine) 2816040045 (Duloxetine HCl) 2816040134 (Levomilnacipran) 2816040155 (Venlafaxine HCl) |
| SRI                     | 2816040135 (Nefazodone HCl) 2816040855 (Trazodone) |
| TCA                     | 2816040805 (Amitriptyline) 2816040810 (Amoxapine) 2816040812 (Clomipramine) 2816040815 (Desipramine) 2816040820 (Doxepin) 2816040830 (Imipramine) 2816040845 (Nortriptyline) 2816040860 (Trimipramine) |
| Other                   | 2816040139 (Selegiline) 2816040420 (Isocarboxazid) 2816040450 (Phenelzine) 2816040465 (Tranylcypromine) 2816040840 (Maprotiline) 2816040843 (Mirtazapine) 2816040850 (Protriptyline) 2816040910 (Bupropion) 2816049200 (Other Psychotherapeutic Agents) |
Table S2. ICD 9-CM Definition for Comorbid Conditions

| Comorbid Condition       | ICD 9-CM Codes                                                                 |
|--------------------------|-------------------------------------------------------------------------------|
| Anemia                   | 280, 281, 282, 283, 284, 285                                                  |
| Bleeding                 | 430, 431, 432, 852, 455.2, 455.5, 455.8, 456.0, 456.20, 530.7, 530.82, 531.0,  |
|                          | 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6,  |
|                          | 534.0, 534.2, 534.4, 534.6, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51,  |
|                          | 535.61, 537.83, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 578.0, |
|                          | 578.1, 578.9, 423.0, 459.0, 568.81, 593.81, 599.7, 623.8, 626.6, 719.1, 784.7,  |
|                          | 784.8, 786.3                                                                  |
| Cancer                   | 140 - 172, 174 - 195, 200-208, 238.6                                          |
| Coagulopathy             | 286, 287.1, 287.3, 287.4, 287.5                                               |
| Cognitive Impairment     | 331.1 - 331.9                                                                 |
| Heart Failure            | 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93,  |
|                          | 425.4, 425.9, 428                                                             |
| Hypertension             | 401, 402, 403, 404, 405                                                       |
| Prevalent Ischemic Stroke| 433, 434, 435, 436, 437, 438                                                  |
| Incident Ischemic Stroke | 434, 436                                                                      |
| Kidney Disease           | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582,  |
|                          | 583.0, 583.1, 583.2, 583.3, 583.4, 583.5, 583.6, 583.7, 585, 586, 588.0, V42.0,  |
|                          | V45.1, V56                                                                    |
| Myocardial Infarction    | 410, 412                                                                      |
| Mood Disorders           | 293.83, 296, 311                                                               |
| Peripheral Artery Disease| 440.0, 440.2, 440.9, 443.9                                                    |

*Presence of Comorbid Conditions is determined by the presence of ICD 9-CM codes on any position in an inpatient or outpatient claim, except for incident ischemic stroke, which was defined by presence of ICD 9-CM code on primary position in the inpatient claims database.*
Table S3. Risk of Bleeding Associated with Type of Antidepressant in Atrial Fibrillation Patients Taking Oral Anticoagulants, Unmatched Sample Excluding Those without New Oral Anticoagulant Prescription 90 Days Prior to Antidepressant Initiation, MarketScan®, 2007-2015

|                | TCA† | SSRI‡ | SNRI‡ | SRI† | Other |
|----------------|------|-------|-------|------|-------|
| N. events      | 26   | 247   | 38    | 45   | 66    |

|               | Hazard Ratio (95% Confidence Interval) |
|---------------|----------------------------------------|
| Model 1 ‡     | 1.16 (0.78, 1.74) 1.27 (0.77, 2.09) 1.12 (0.69, 1.82) 1.23 (0.78, 1.94) |
| Model 2 §     | 1.13 (0.75, 1.70) 1.20 (0.73, 2.00) 1.08 (0.66, 1.75) 1.19 (0.75, 1.88) |

† SSRI: Selective Serotonin Reuptake Inhibitors; SNRI: Serotonin/Norepinephrine Reuptake Inhibitors; SRI: Serotonin Reuptake Inhibitors; TCA: Tricyclic Antidepressants; Other: other antidepressants
‡ Model 1 was adjusted for age and sex.
§ Model 2 was adjusted for age, sex, HAS-BLED score, CHA2DS2-VASc score, alcohol use, comorbid conditions (heart failure, hypertension, diabetes, myocardial infarction, peripheral artery disease, kidney failure, stroke, bleeding, anemia, coagulopathy, cancer, mood disorder, cognitive impairment, chronic obstructive pulmonary disease, liver disease) and other medications (antiplatelet, diuretic drugs, antiarrhythmic drugs, digoxin, angiotensin-converting-enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, and lipid lowering medications).