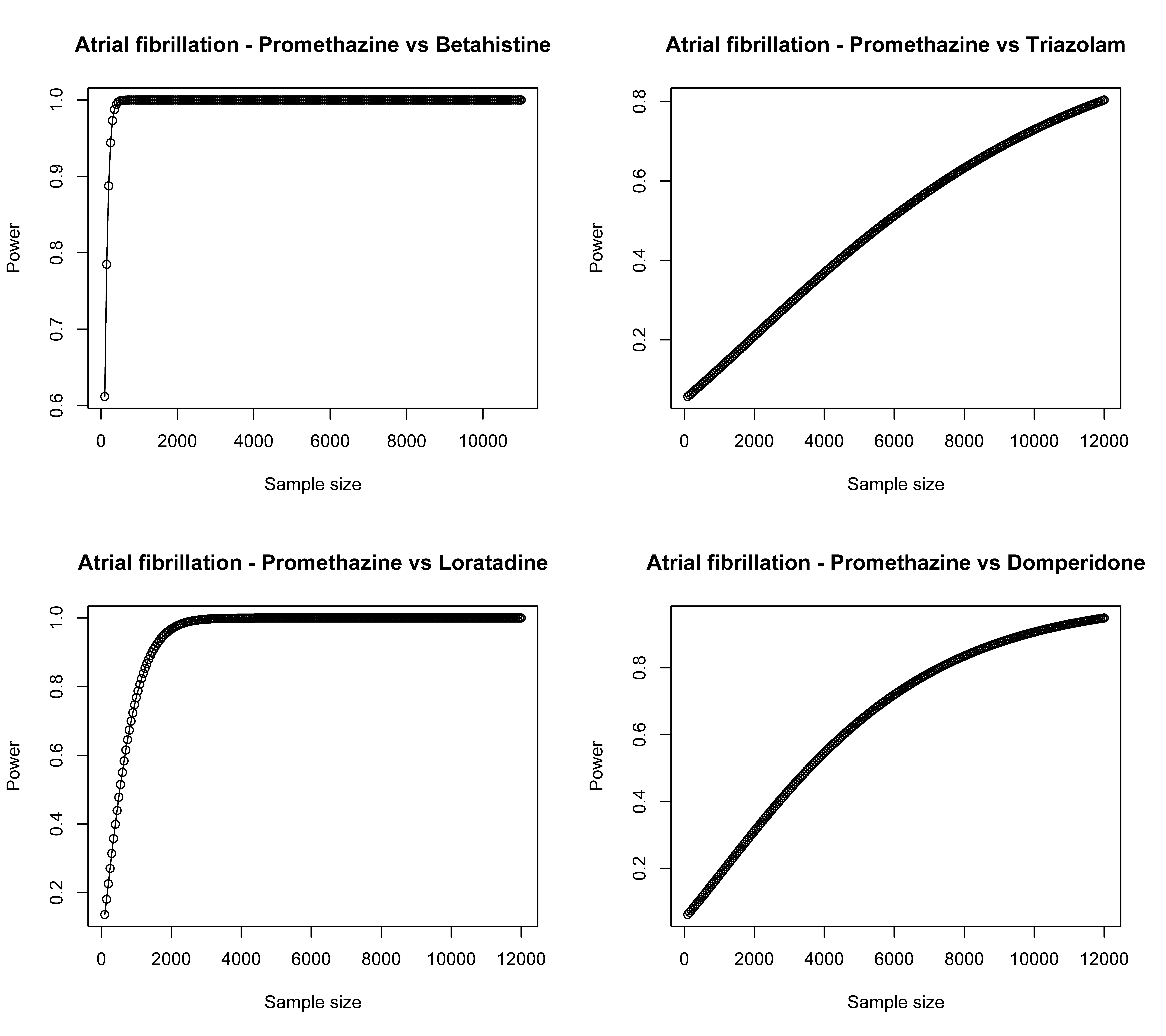
**Table S1.** Diagnoses and anatomical therapeutic classification codes used for defining outcomes, comorbidities, and drug exposure.

|  |  |  |
| --- | --- | --- |
| **Diagnosis** | **Definition** | **ICD codes** |
| Cancer | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: C00-97 |
| Heart failure | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I110, I42, I50, J819; *ICD8*b: 425, 4270, 4271 |
| Chronic kidney disease | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: E102, E112, E132, E142, I120, M3215, M300, M313, M319, N02-N08, N11-N12, N14, N158-N160, N162-N164, N168, N18-N19, N26, Q612-Q613, Q615, Q619, |
| Chronic obstructive pulmonary disease | Hospitalization/hospital contact ever prior to the index date | *ICD10*a J42-44 |
| Hypertension | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I10, I11, I12, I13, I15 |
| Hypertension, overall | Defined from combination treatment with a least two classes of antihypertensive drugs. This definition of hypertension has a positive predictive value of 80.0% and a specificity of 94.7%. | *Treatment:* Adrenergic α-antagonist, non-loop-diuretics, vasodilators, beta-blockers, calcium channel blockers, and renin-angiotensin system inhibitors. |
| Hyperthyroidism | Hospitalization/hospital contact ever prior to the index date or at least two dispensed prescriptions of anti-thyroid medications | *ICD10*a: *E05–E05.9 ATC=H03B* |
| Peripheral arterial disease | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I700, I702, I709 |
| Stroke | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I63, I64, G45.8, G45.9 |
| Pulmonary embolism | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I74 |
| Arterial embolism | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I63, I64, I26, I74, G458, G459 |
| Atrial fibrillation | *As comorbidity:* hospitalization/hospital contact ever prior to the index date  *As study outcome:* hospitalization/hospital contact ever within 90 days following the index date | *ICD10*a: I48 |
| Ventricular fibrillation | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I49 |
| Diabetes mellitus type 2 | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: E10, E11, E12, E13, E14 |
| Cerebrovascular disorders | Hospitalization/hospital contact ever prior to the index date | *ICD10*a: I60, I62, I69 |
| Acute myocardial infarction | *As comorbidity:* hospitalization/hospital contact ever prior to the index date  *As study outcome:* hospitalization/hospital contact ever within 90 days following the index date | *ICD10*a: I21, I22 |
| Fractures | *As comorbidity:* hospitalization/hospital contact ever prior to the index date  *As study outcome:* hospitalization/hospital contact ever within 90 days following the index date | *ICD10*a: S42, S52, S62, S72 |
| Ventricular arrhythmia | *As study outcome:* hospitalization/hospital contact ever within 90 days following the index date | *ICD10*a: I472, I490 |
| **Drug class/active ingredient** | **Definition** | **ATCb codes** |
| Lipid modifying agents | Redemption of a prescription within 90 days prior to the index date | C10 |
| Glucose-lowering agents | Redemption of a prescription within 90 days prior to the index date | A10 |
| Opioids | Redemption of a prescription within 90 days prior to the index date | N02A |
| Benzodiazepines | Redemption of a prescription within 90 days prior to the index date | N05BA |
| Steroids | Redemption of a prescription within 90 days prior to the index date | H02A. H02B |
| Antidepressants | Redemption of a prescription within 90 days prior to the index date | N06A |
| Antipsychotics | Redemption of a prescription within 90 days prior to the index date | N05A |
| Barbiturates | Redemption of a prescription within 90 days prior to the index date | N05CA, N05CB |
| Pro-arrhythmic drugs | Time-dependent covariate | Defined according to 20 |
| Promethazine | First redeemed prescription during the study period | R06AD02,R06AD52 |
| Loratadine | First redeemed prescription during the study period | R06AX13 |
| Domperidone | First redeemed prescription during the study period | A03FA03 |
| Betahistine | First redeemed prescription during the study period | N07CA01 |
| Triazolam | First redeemed prescription during the study period | A03FA01 |

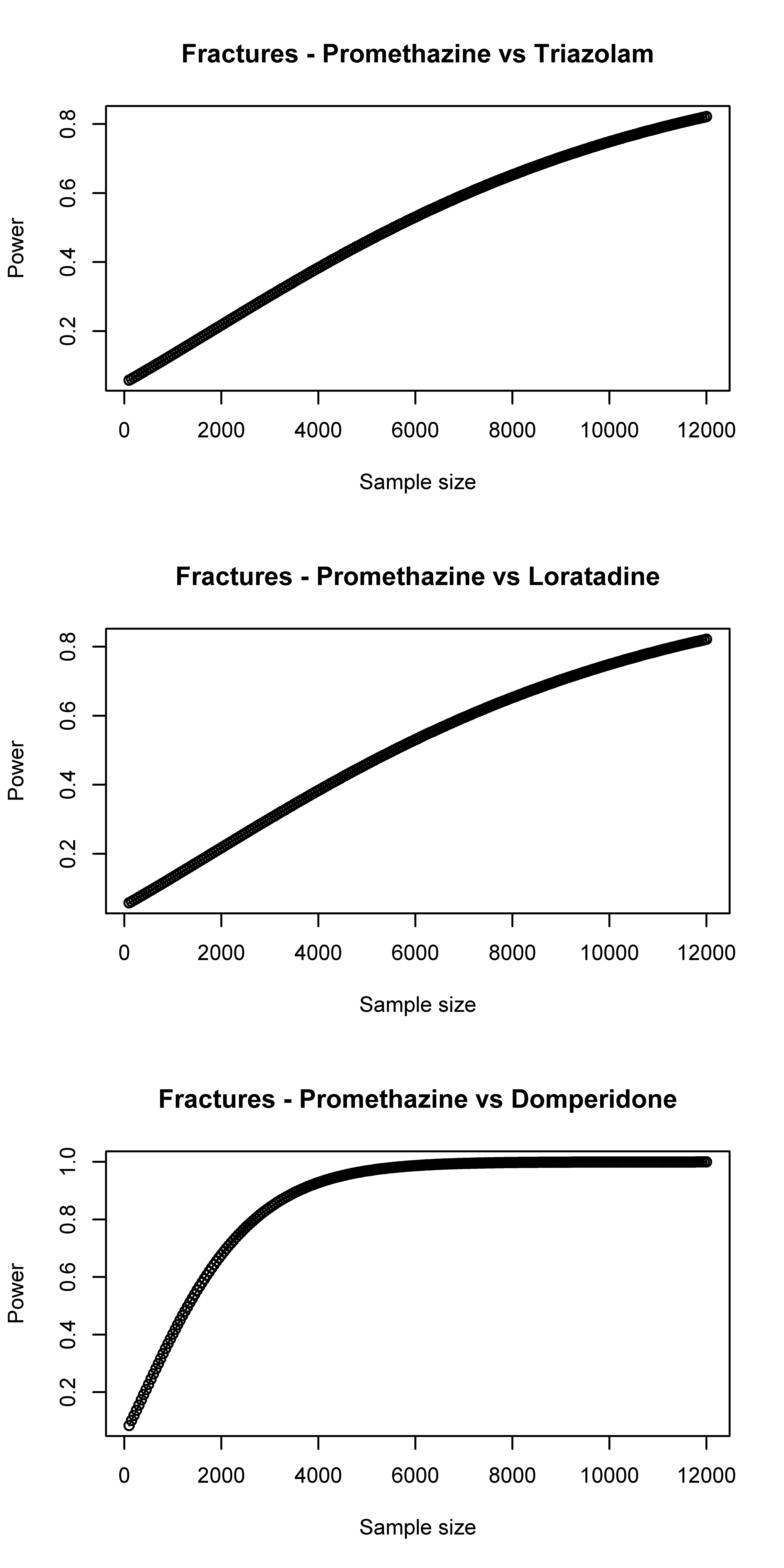
aICD10: 10th revision of the International Classification of Diseases system; bATC: Anatomical Therapeutic Classification



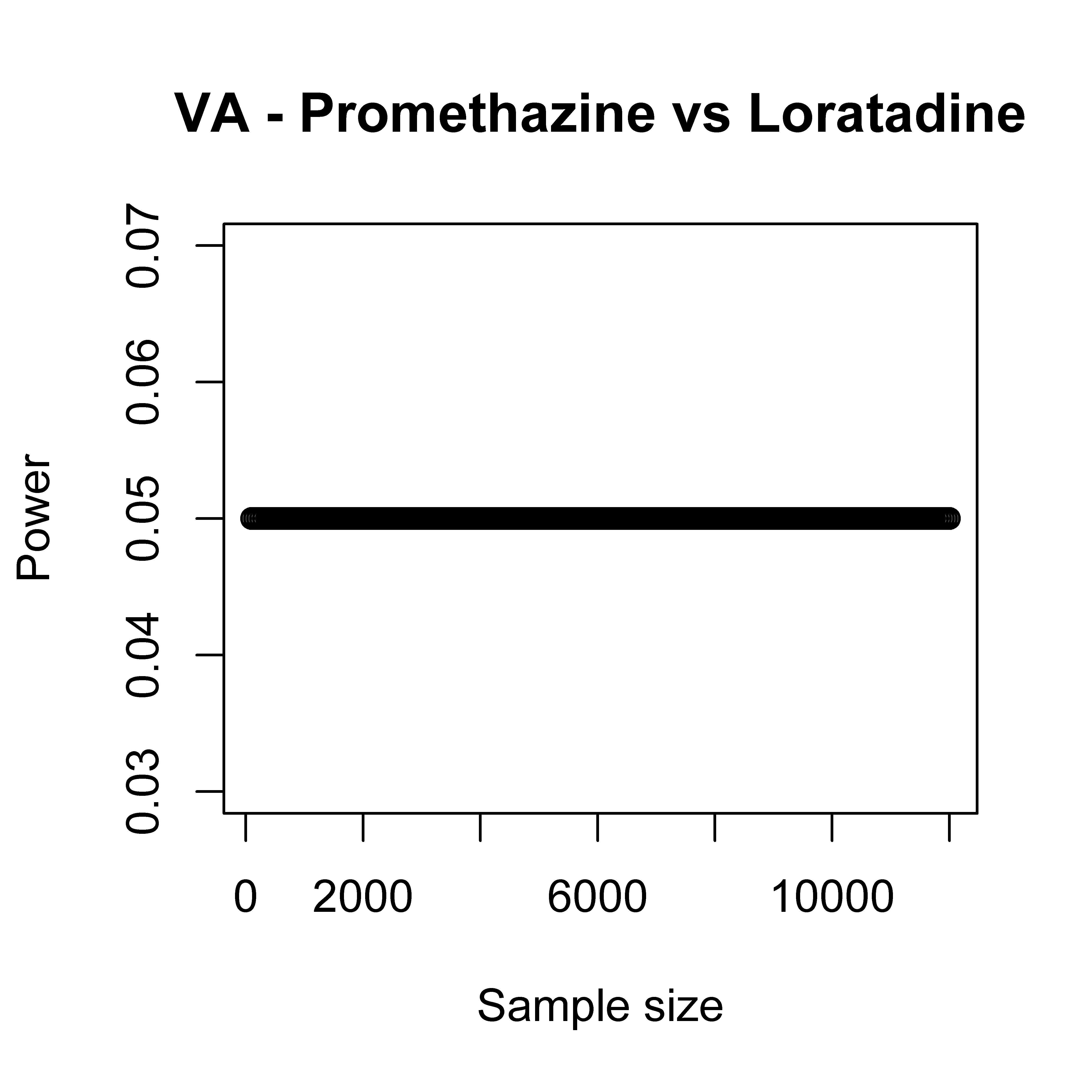
**Figure S1.** Power calculation – atrial fibrillation hospitalizations.

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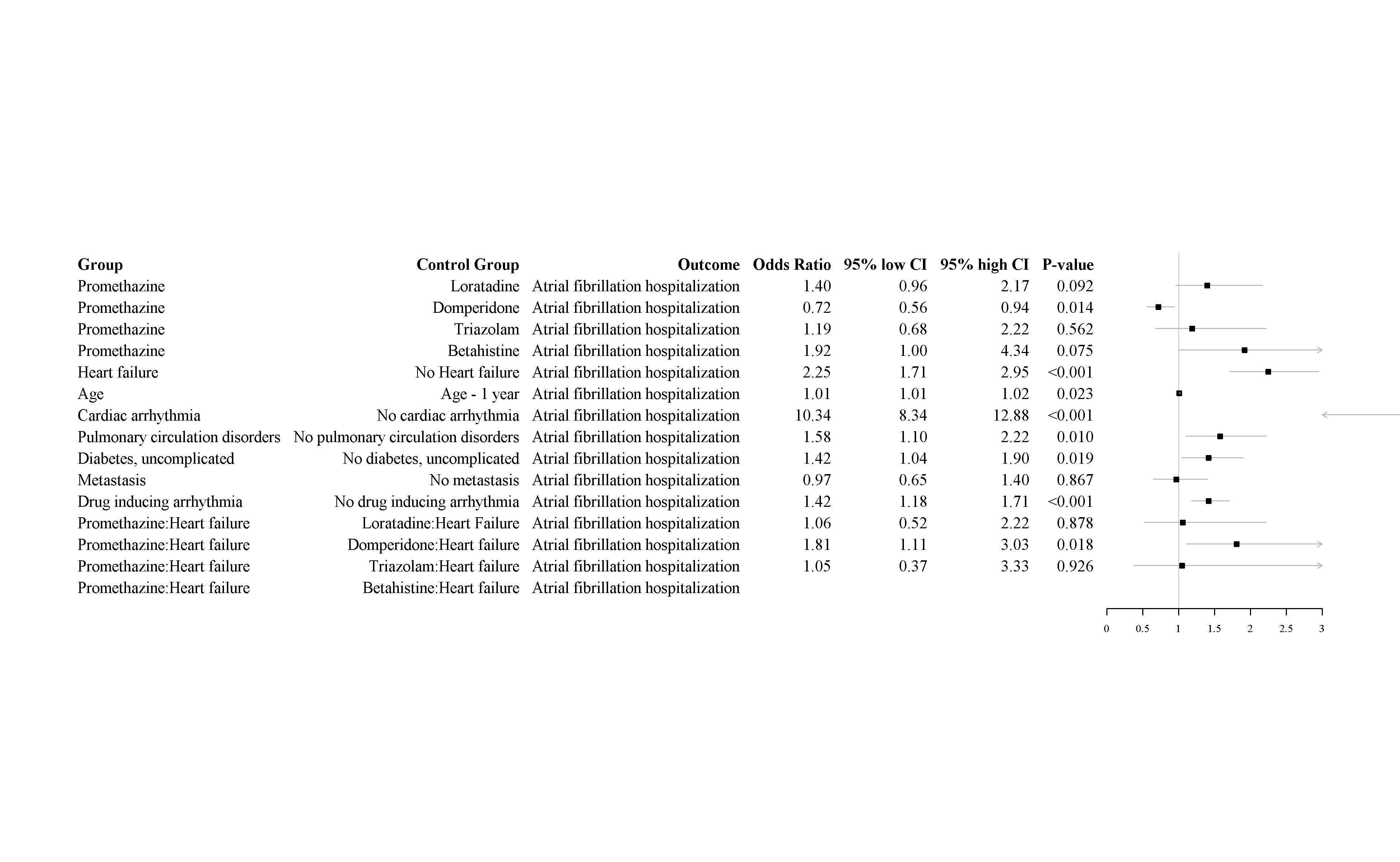
**Figure S2.** Power calculation – acute myocardial infarction (AMI) hospitalizations.



**Figure S3.** Power calculation – fractures hospitalizations.



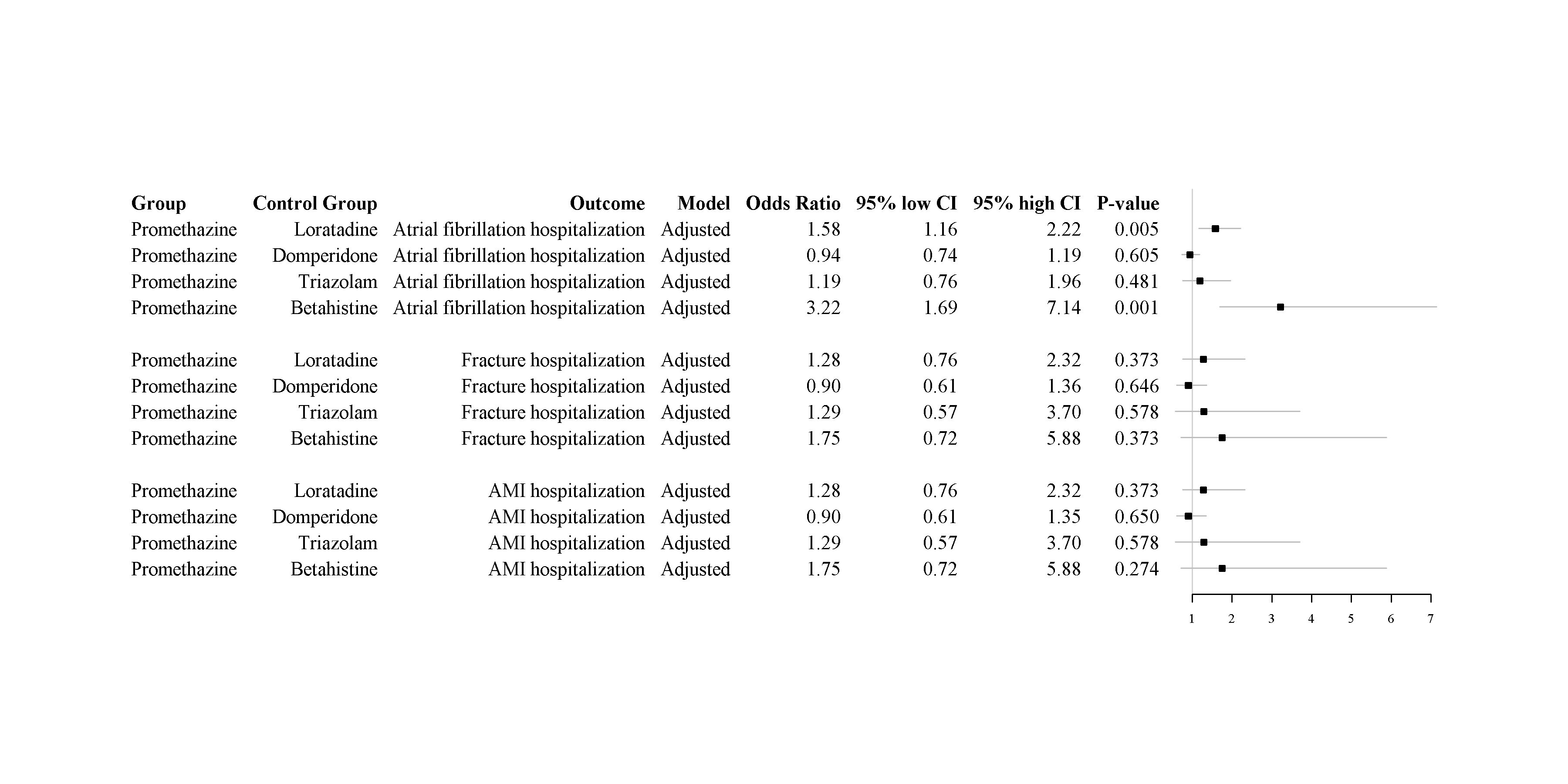
**Figure S4.** Power calculation – ventricular arrhythmia (VA) hospitalizations.



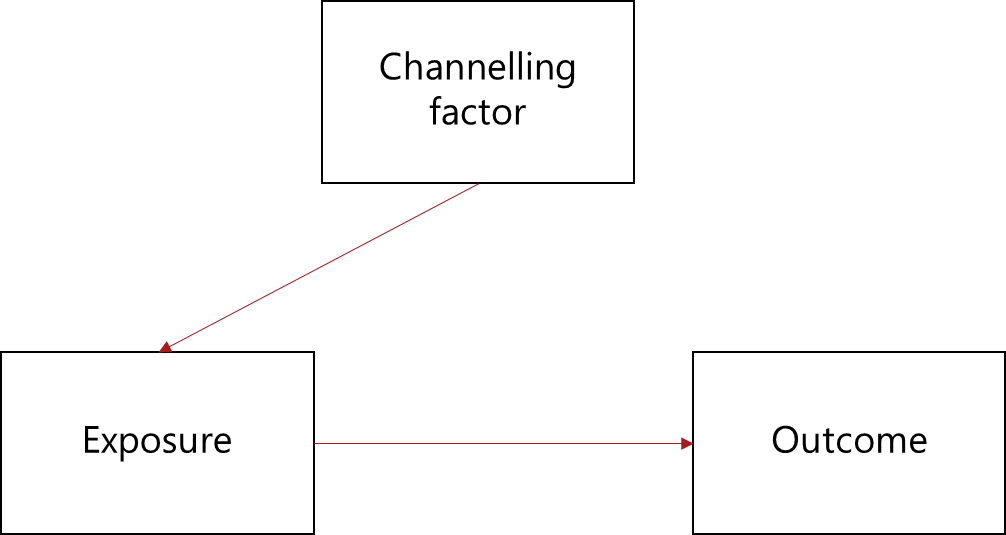
**Figure S5.** Results of the second sensitivity analysis.

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**Figure S6.** Results of the third sensitivity analysis.



**Figure S7.** Results of the fourth sensitivity analysis.



**Figure S8**. Channeling bias in the interpretation of drug effects.