

# Real-World Concordance With the Framingham Stroke Risk Model in Atrial Fibrillation and Identification of Additional Significant Features

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**Objective: To quantify real-world stroke rates within four years of Atrial Fibrillation in patients with the most severe predicted risk and analyze the features associated with stroke vs remaining stroke-free**

## Background

The Framingham Heart Study (FHS) developed a well-known risk score for stroke (or death) following new-onset atrial fibrillation (AF), incorporating age, sex, systolic blood pressure, diabetes, and prior stroke its predictors<sup>1</sup>. However, real-world datasets often capture a broader array of diagnostic and comorbid features beyond classical risk factors. Evaluating which of these additional features are significantly associated with stroke may validate FHS-derived predictions and reveal novel risk signals.

## Methods

Using an administrative claims database, we conducted a retrospective cohort analysis of AF patients with a subsequent stroke event (N=1,365) and AF patients without stroke (N=4,399). Structured diagnosis and procedure or utilization features were summarized as binary indicators. Feature prevalence was calculated for each cohort and statistical significance assessed using p-values ( $p < 0.05$ ). To reduce outcome leakage, direct post-stroke sequelae and rehabilitation/testing artifacts were excluded from interpretation.

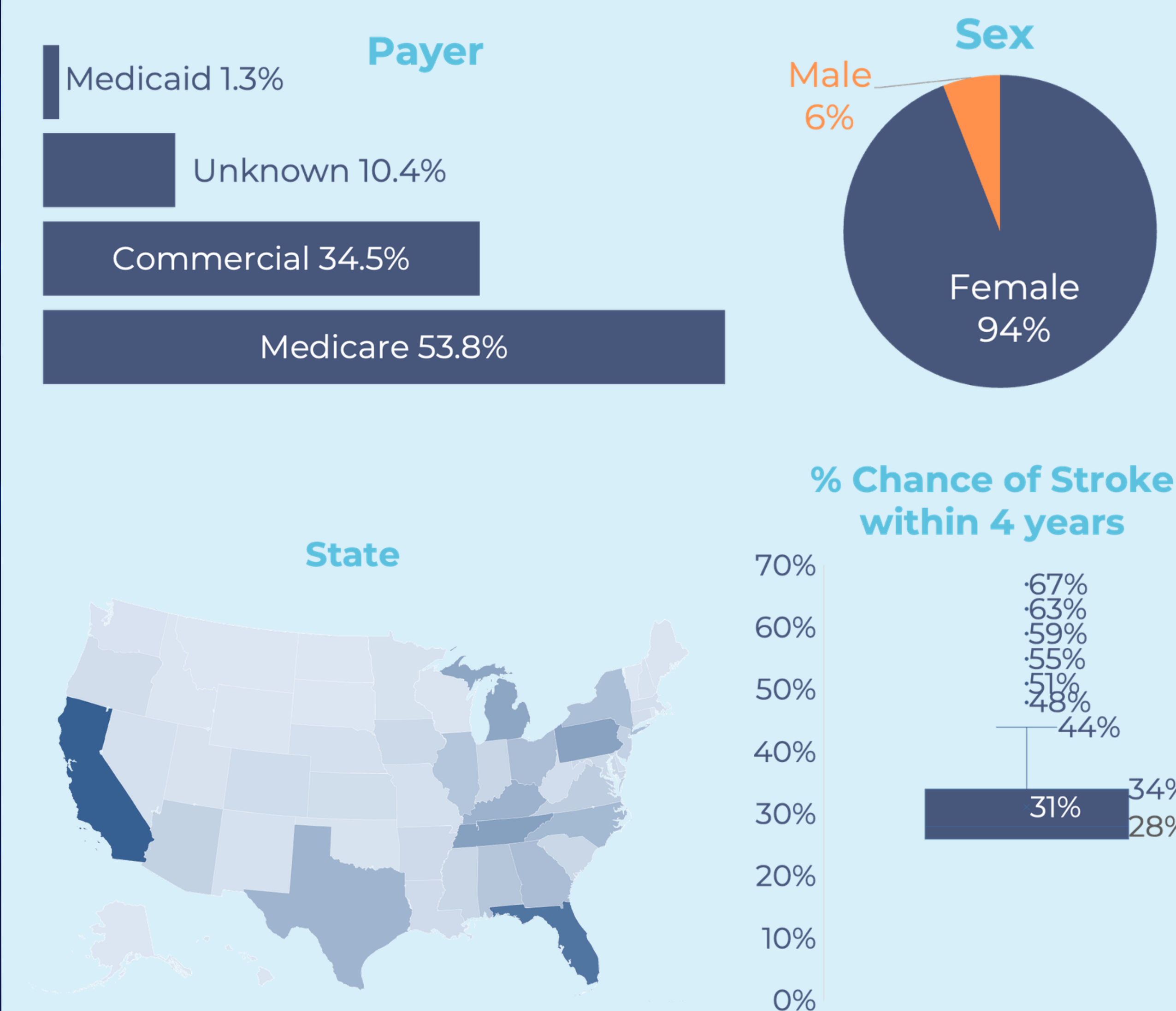
## Results

Among a broad set of candidate features, the most significant and clinically plausible predictors of stroke in AF patients were TIA ( $p < 0.001$ ) and prior stroke history ( $p < 0.001$ ), both core predictors in the FHS study. Additional significant associations included cerebrovascular disease and related vascular diagnoses ( $p < 0.05$ ). Neurologic vulnerability features, including altered brain structure or lesion history, brain injury, encephalopathy, dementia or impaired cognition, obtundation, and seizures, were modestly enriched (all  $p < 0.05$ ). Diabetes and hypertension diagnosis codes were statistically significant but more prevalent in the non-stroke cohort. Several preventative care or utilization features (e.g., vaccination codes, infections, inflammatory diagnoses, and outpatient visit frequency) reached statistical significance; they were more prevalent in the non-stroke cohort, likely reflecting differential healthcare utilization or preventive care rather than increased stroke risk.

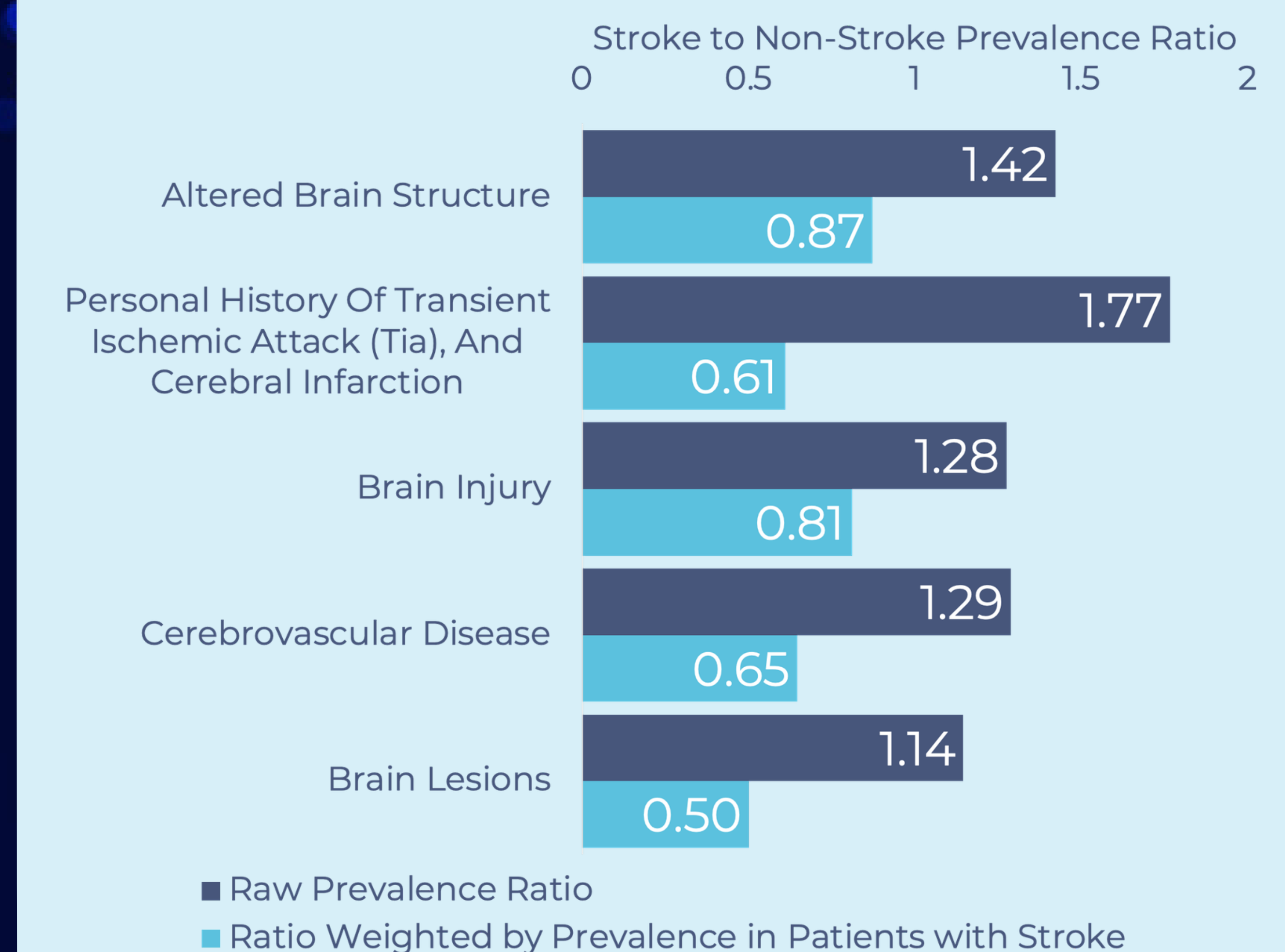
## Conclusions

While females dominate the severe risk category, the severe risk males are much more likely to eventually have a stroke within 4 years. The features which are most associated with Stroke are Cerebrovascular Diseases, Altered Brain Structure, Brain Lesions, and personal history of TIA/Stroke. The patients who remained stroke free were more likely to have used preventative medications and visited various specialties.

**Figure 1. Severe Stroke Risk Study Population**



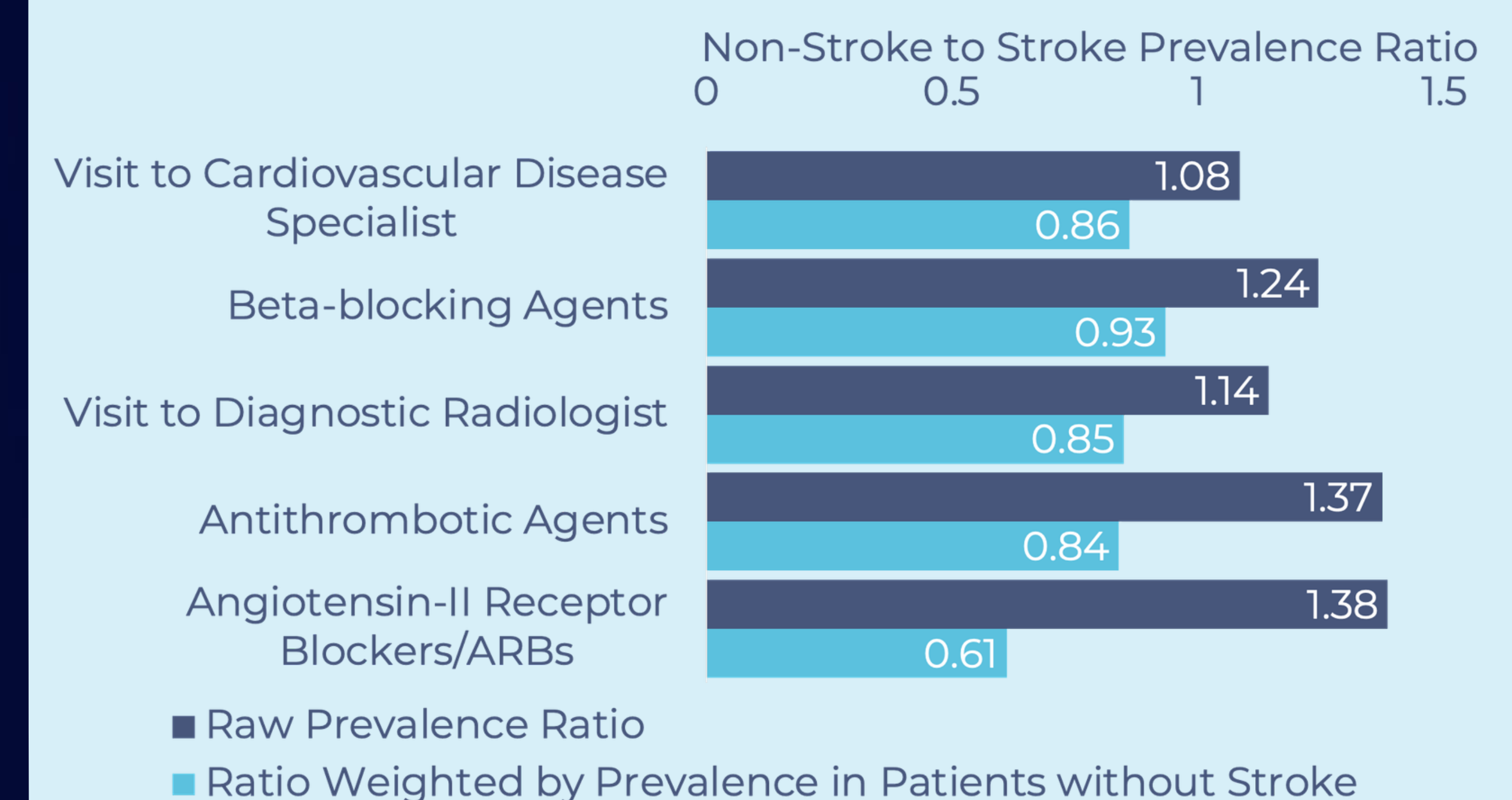
**Figure 2. Neurological Diagnoses More Common in Stroke Patients**



**Figure 3. Stroke Outcomes Within Four Years of Atrial Fibrillation Stratified by Patient Sex and Payer**

| Payer Type           | % Males with Stroke | % Females with Stroke |
|----------------------|---------------------|-----------------------|
| Commercial (n=1,977) | 48%                 | 23%                   |
| Medicare (n=3,085)   | 33%                 | 21%                   |
| Medicaid (n=73)      | 25%                 | 26%                   |

**Figure 4. Preventative Medications and Specialist Care More Common in Patients Who Remained Stroke Free**



## Citations

1. Wang TJ, Massaro JM, Levy D, et al. A Risk Score for Predicting Stroke or Death in Individuals With New-Onset Atrial Fibrillation in the Community: The Framingham Heart Study. JAMA. 2003;290(8):1049-1056. doi:10.1001/jama.290.8.1049 (<https://jamanetwork.com/journals/jama/fullarticle/197176>)