NON-INTERVENTIONAL (NI) STUDY PROTOCOL

Study Information

Title	Effectiveness and Safety of Oral Anticoagulants Among Obese Patients with Non-Valvular Atrial Fibrillation in the Veterans Affairs Population with Medicare
Protocol number	B0661162
Protocol version identifier	1.0
Date	September 14, 2020
Active substance	N/A
Medicinal product	Apixaban
Research question and objectives	The primary analysis will compare apixaban vs warfarin only. **Primary Objectives:** **Aim 1:** Evaluate the demographics and clinical characteristics of obese and severely obese NVAF patients initiating OACs (all patients, standard dose, and low dose). **Aim 2:** Determine if there is a difference in OAC treatment effect between obese and non-obese and severely obese and non-severely obese patients for stroke/systolic embolism (SE), MB, and net clinical benefit. **Aim 3:** Compare the risk of stroke/SE, major bleeding, net clinical benefit among obese and severely obese NVAF patients initiating OACs.

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2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
AF	atrial fibrillation
ARIC	Atherosclerosis Risk in Communities
BMI	body mass index
CCI	[redacted]
$CHADS_2$	Acronym: congestive heart failure, hypertension, age 75 years or older, diabetes mellitus
CMS	Center of Medicare Services
CPI	Consumer Price Index
CPT	Current Procedural Terminology
CrCl	creatinine clearance rate
DME	durable medical equipment
DOAC	direct aral anticoagulant
DSS	Decision Support System
EDB	enrollment database
ER	emergency room
GHP	group health plan
GLM	generalized linear models
GPP	Good Pharmacoepidemiology Practices
HAS-BLED	Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding, Labile INR, Elderly (Age >65 years), Drugs or Alcohol
HCFA	Health Care Financing Agency
HCPCS	Healthcare Common Procedure Coding System
HCRU	Healthcare resource utilization
HHA	Home Health Agency
HR	hazard ratios
ICD-9-CM	International Classification of Disease, Nineth Revision, Clinical Modification
ICD-10-CM	International Classification of Disease, Tenth Revision, Clinical Modification
ICH	intracranial hemorrhage
IPTW	inverse probability treatment weightings
INR	international normalized ratio
LAB	laboratory
LAR	labartory results
LOS	length of stay
MB	major bleeding
NDE	non-destructive examinations
NVAF	non-valvular atrial fibrillation
OAC	oral anticoagulant

Abbreviation	Definition
PHA	pharmacy
PPPM	per patient per month
RAD	radiology
RIF	research identifiable file
RWD	real world data
SE	systolic embolism
SNF	skilled nursking facility
SSN	social security number
TTR	time in therapeutic range
USD	United States dollar
VA	Veterans' Affairs
VHA	Veterans' Health Affairs
VKA	Vitamin K antagonist

3. RESPONSIBLE PARTIES

Principal Investigator(s) of the Protocol

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4. ABSTRACT

Title: Effectiveness and Safety of Oral Anticoagulants Among Obese Patients with Non Valvular Atrial Fibrillation in the Veterans Affairs Population with Medicare

Rationale and Background: Prior RWD studies have evaluated the use of oral anticoagulants (OAC) in obese patients with atrial fibrillation (AF), but they are limited by sample size or by using ICD-9 diagnosis codes to define obesity. Conducting analyses of different datasets and addressing some of these limitations could add important information about the use of OACs in this population.

Research Question and Objectives: The overall objective of this analysis is to understand patient characteristics, use of treatment, and clinical outcomes among obese and severely obese patients with non-valvular atrial fibrillation (NVAF) who initiate therapy with OACs. The aim of this study is to compare all DOACs to warfarin; however, the primary analysis will be conducted among apixaban vs warfarin patients only. If sample size permits, we will also conduct other DOAC vs warfarin and DOAC vs DOAC analysis.

Study Design: This retrospective observational study will be conducted using linked national patient-level data from the Veterans Affairs (VA) Population and Center for Medicare and Medicare Services (CMS) fee-for-service database. The study period will be from January 1, 2013 through December 31, 2017. The study allows for a 6-month baseline period prior to the index date in the identification period. The index date will be defined as the date of first prescription for an OAC from July 1, 2013 – December 31, 2017; the first direct oral anticoagulant (DOAC) pharmacy claim date during the identification period will be designated as the index date. The first warfarin prescription date will be designated as the index date for patients without any DOAC claim. Patients will be required to have ≥1 AF medical claim in any position in the inpatient or outpatient setting before or on the index therapy date. Patients will be followed from the day after the index date until the earliest of 30 days after the date of discontinuation, switch, death, end of study period, or end of continuous medical enrollment (Parts A and B).

Population: Obese or severely obese AF patients in the CMS Medicare and Veterans' Health Affairs (VHA) databases who were newly prescribed OACs between January 1, 2013 and December 31, 2017.

Variables: Demographic and clinical characteristics and clinical outcomes including stroke/systolic embolism (SE), major bleeding (MB), and net clinical benefit.

Data Sources: The study will be conducted using linked CMS Medicare fee-for-service databases and Veterans Health Affairs Database.

Study Size: All eligible patients available for analysis will be included.

Data Analysis: Means, medians, and standard deviations will be provided for continuous variables. Numbers and percentages will be provided for dichotomous and polychotomous variables. Bivariate comparisons of baseline characteristics and outcomes measures will be provided. The primary analysis will be conducted among apixaban vs warfarin patients only. Inverse probability treatment weighting (IPTW) will be used to balance patient characteristics when comparing outcomes among different cohorts (for primary and secondary analyses). Appropriate tests (eg, t-test, chi-square test) will be used based on the distribution of the measure. Kaplan-Meier survival curves will be generated to illustrate the time to first Stroke/SE, MB Event, and Net Clinical Benefit. The cumulative incidence rate for clinical outcomes will be calculated. Cox proportional hazard ratio models will be used to evaluate the risk of clinical outcomes. Time to therapeutic range (TTR) will be calculated using the Rosendaal method and will be computed using INR values among warfarin patients during the follow-up. TTR will be calculated based on the percentage of time a patient remained in therapeutic range evaluated during the entire follow-up period. Data analysis will be executed using statistical software SAS version 9.4 (Cary, NC).

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

Milestone	Planned Date
Completion of protocol development	Draft 1: 1 July 2020
Protocol revisions	Final: 14 August 2020
Start of data collection	10 June 2020
End of data collection	December 2020
Completion of Descriptive Tables	October 2020
Completion of Multivariate Analysis	November 2020
Completion of Dose Subgroup Analysis	December 2020
Final Study Report	December 2020

7. RATIONALE AND BACKGROUND

Atrial fibrillation (AF) is recognized as the most common sustained cardiac arrhythmia in the United States and is associated with a near five-fold excess of stroke.[1] The prevalence of AF was estimated at 5.1 million in 2010 and projected to be 9.3 million in 2030 in the United States with an annual increase of 3.6%.[2] AF also bears substantial economic burden. The direct health care costs associated with AF were estimated at approximately $6 billion annually.[3]

Vitamin K antagonists (VKAs; ie, warfarin) have been the mainstay treatment for stroke prevention among AF patients, reducing stroke by approximately 60%.[4] Over the past 25 years, VKA use has been expanded from preventing stroke in valvular disease-associated AF patients to patients with non-valvular AF (NVAF).[4]

Warfarin therapy requires close monitoring of the international normalized ratio (INR). The INR range from 2.0 to 3.0 (therapeutic range) was proven to be efficient in stroke prevention among AF patients, and is recommended in the treatment of AF.[5,6] However, due to its limited therapeutic index and possible drug and food interactions, only about half of AF patients in the United States receive warfarin therapy as recommended.[7]

Over the last several years, direct oral anticoagulants (DOACs), including apixaban, dabigatran, edoxaban, and rivaroxaban, were approved in the United States for stroke prevention among NVAF patients. Clinical trials demonstrated that DOAC use has shown stroke risk reduction similar or superior to warfarin, and lower or similar rates of bleeding.[8-11] In the years since their approval, DOACs have been increasingly preferred over warfarin due to

the convenience of fewer routine monitoring visits, no requirements for dose adjustment, and limited dietary interactions.

Obesity, another prevalent health condition in the United States, had an age-adjusted prevalence of 39.8% in 2015-2016.[12] In the Atherosclerosis Risk in Communities (ARIC) study, obese and overweight individuals accounted for 17.9% of all AF cases;[13] Additionally, obese patients have a 49% increased risk of AF compared with non-obese patients.[14] Obese patients have been included in RCTs of DOACs and these studies did not show different results by weight.[15-20] However, the severely obese population (BMI 40) has a more limited representation in RCTs.[19,20] With the current fixed-dose DOAC prescriptions, the clinical impact of anticoagulation on NVAF patients with obesity is expected to be similar, provided patients have optimum peak and trough levels of DOACs.[21]

Real world data (RWD) examining the use of oral anticoagulants (OACs) in obese and severely obese patients is limited by sample size or by using ICD-9 diagnosis codes to define obesity, with most literature focusing on outcomes of AF regardless of intervention.[22] ARISTOPHANES obesity subgroup analysis found that in obese patients, apixaban was associated with lower risk of stroke/systemic embolism (SE) and major bleeding (MB) compared to warfarin. Rivaroxaban was associated with lower risk of stroke/SE but similar risk of MB, whereas dabigatran was associated with lower risk of MB, but similar risk of stroke/SE compared to warfarin.[23] The goal of this study is to evaluate the risk of stroke/SE, MB, and net clinical benefit among obese and severely obese OAC treated patients using VA linked Medicare databases. The results of this linked, retrospective claims analysis will provide unique insight into outcomes of OAC use in obese and severely obese patients as the VA database includes vital measures (BMI, body weight, height) and laboratory results (INR, TTR) in addition to typical health outcomes from Medicare claims data.

8. RESEARCH QUESTION AND OBJECTIVES

8.1. Study Obectives

The overall objective of this analysis is to understand patient characteristics, treatment effect, and clinical outcomes among obese and severely obese patients with NVAF who initiate therapy with OACs (all patients, standard dose, and low dose). The primary analysis will be conducted among apixaban vs warfarin patients only.

8.1.1. Primary Objectives

Aim 1: Evaluate the demographics and clinical characteristics of obese and severely obese NVAF patients initiating OACs (all patients, standard dose, and low dose; primary analysis will compare apixaban vs warfarin).

Aim 2: Determine if there is a difference in OAC treatment effect between obese and non-obese and severely obese and non-severely obese patients for stroke/SE, MB, and net clinical benefit.

Aim 3: Compare the risk of stroke/SE, MB, net clinical benefit among obese and severely obese NVAF patients initiating OACs (primary analysis will compare apixaban vs warfarin).

8.1.2. Secondary Objectives

Aim 4: A secondary analysis will also evaluate the following among warfarin treated obese and severely obese patients:

- Distribution of international normalized ratio (INR; <2, 2-3, >3).
- Distribution of time in therapeutic range (TTR ≥65% [good] and TTR <65% [poor]).
- Compare the baseline characteristics of patients with good vs poor TTR.

CCI [redacted]

9. RESEARCH METHODS

9.1. Study Design

9.1.1. Key Index Period Definitions

- **Study Period:** The study period will range from January 1, 2013 through December 31, 2017.
- **Patient Identification Period:** The identification period will range from July 1, 2013 until December 31, 2017, allowing for a 6-month baseline period prior to the index date.
- **Baseline Period:** The baseline period will be 6 months prior to, and on, the index date.
- **Follow-up Period:** The follow-up period will be defined as the time period between the day after the index date and end of study period (December 31, 2017). Patients will be followed from the day after the index date to 30 days after the date of discontinuation, switch, death, end of study period, or end of continuous medical enrollment (Parts A & B), whichever is earlier.

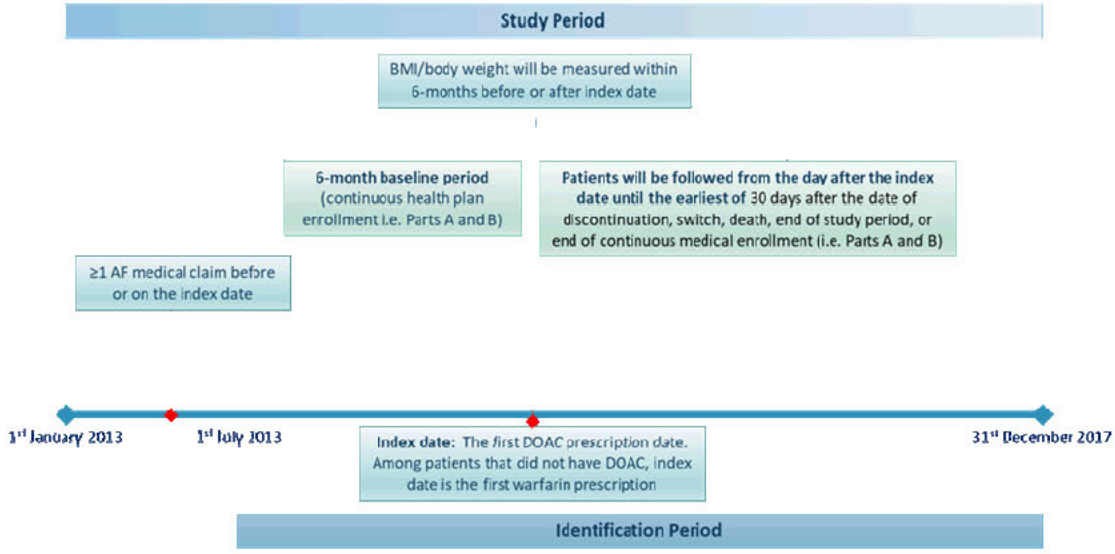
9.1.2. Key Index Point Definitions

- **Index Therapy Date:** The index date will be defined as the date of first prescription for an OAC from July 1, 2013 – December 31, 2017; the first DOAC pharmacy claim date during the identification period (July 1, 2013-December 31, 2017) will be designated as the index date. The first warfarin prescription date will be designated as the index date for patients without any DOAC claim.

- **AF Diagnosis:** Evidence of AF diagnosis must be present, as evidenced from 1 or more claims for AF in any position in the inpatient or outpatient setting, before or on the index therapy date.

Study Design Figure (for Illustration Purposes, May Not Be Proportionate):

Figure 1. Study Design



9.2. Setting

Adult patients prescribed a DOAC or warfarin will be selected between July 1, 2013 and December 31, 2017. Patients will be required to have one or more AF diagnosis claim in any position before or on index date. Patients will be required to have health plan enrollment (Parts A and B) for 6 months prior to the index date to ensure availability of complete patient medical history.

Follow-up Period:

The follow-up period will be defined as the time period between the day after the index date and end of study period (December 31, 2017). Patients will be followed from the day after the index date to 30 days after the date of discontinuation, switch, death, end of study period, or end of continuous medical enrollment (Parts A & B), whichever is earlier.

To assess first stroke/SE event, patients will be censored at first stroke/SE occurring anytime during period on the drug or within 30 days from the last day of days' supply of treatment prescription, 30 days after date of discontinuation, switch, death, end of study or end of continuous medical enrollment (Parts A and B), whichever is earlier.

To assess first MB event, patients will be censored at first major bleeding occurring anytime during period on the drug or within 30 days from the last day of days' supply of treatment prescription, 30 days after date of discontinuation, switch, death, end of study or end of continuous medical enrollment (Parts A and B), whichever is earlier.

For patients with stroke/SE or MB event, net clinical benefit will be assessed by evaluating the first hospital claim for a stroke/SE or MB. The hospital claim can occur anytime during the period of drug use or within 30 days from the last day of supply of treatment prescription.

Other Factors Affecting Censoring During Follow-up

Discontinuation

Discontinuation will be defined as no evidence of index OAC prescription for 30 days from the last day of days' supply of last filled prescription. The date of discontinuation will be the last day of days' supply of last filled prescription. The follow-up will be censored at 30 days after the index drug discontinuation date.

Switch

Atrial fibrillation patients that receive a prescription for an OAC (warfarin, apixaban, dabigatran, edoxaban, or rivaroxaban) other than the index drug prescription during the follow-up period will be considered switchers if this OAC prescription is within ±30 days of last days' supply. The follow-up will be censored at the switching of the index drug.

9.2.1. Inclusion Criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in the study:

- Obese or severely obese.
- Initiated an OAC from July 1, 2013 - December 31, 2017; the first DOAC pharmacy claim date during the identification period will be designated as the index date. The first warfarin prescription date will be designated as the index date for patients without any DOAC claim.
- Individuals ≥18 years old as of the index date.
- Had 6 months continuous health plan enrollment with medical benefits (Parts A & B) for at least 6 months pre-index date (baseline period).

- At least 1 diagnosis of AF prior to or on index date, identified by any medical claim associated with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 427.31 or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code of I480-I482, and I4891.

- Had body weight or BMI value reported within ±6 months of the index date.

9.2.2. Exclusion Criteria

Patients meeting any of the following criteria will not be included in the study:

- Had medical claims indicating a diagnosis or procedure of rheumatic mitral valvular heart disease, heart valve replacement/transplant, venous thromboembolism, or transient AF 6 months prior to or on the index date.

- Had hip/knee replacement surgery within 6 weeks prior to or on the index date.

- Were pregnant during the study period.

- Had an OAC prescription during the 6 months pre-index date.

- Had follow-up time equal to 0 days.

- Had more than one OAC on the index date.

Flag: A flag will be created to evaluate the mechanical heart valve/mitral stenosis during the 6 months prior to or on the index date using narrow definition.

All codes for the selection criteria are detailed in Appendix Table 4.

9.2.3. Cohorts

After applying the selection criteria, patients will be assigned to the following subgroups based on body weight and BMI measures:

1. Obese Patients: Patients with body mass index (BMI) ≥30 or body weight ≥100 kg within ±6 months from the index date.

2. Non-Obese Patients: Patients not categorized as obese patients i.e. BMI <30 or body weight <100 kg patients within ±6 months from the index date will be designated as non-obese patients.

3. Severely Obese Patients: Patients with BMI >40 or body weight >120 kg within ±6 months from the index date.

4. Non-Severely Obese Patients: Patients not categorized as Severely Obese ie, BMI ≤40 or body weight ≤120 kg patients within ±6 months from the index date will be designated as non-severely obese patients.[24]

For patients that have multiple body weights during ±6 months from the index date, the body weight closest to the index date will be used. Also, BMI will be given a preference over body weight in identifying patients into the above categories.

For each of the proceeding subgroup, patients will be categorized into the following cohorts based on their index OAC:

a. Apixaban Cohort;

b. Dabigatran Cohort;

c. Edoxaban Cohort;

d. Rivaroxaban Cohort;

e. Warfarin Cohort.

The descriptive analysis will also be conducted separately among patients with low and standard dose OACs, defined below in Section 9.3 Variables.

9.3. Variables

Baseline variables during the 6 months prior to, and on, the index date will be measured. Baseline variables will be evaluated using codes in any position unless noted otherwise.

Table 1. Baseline Demographic and Clinical Characteristic Variables

Variable	Data Source(s)	Operational Definition
Age	Both VA and Medicare	Age will be defined as of the index date and used to assign patients to age groups (eg, 18-54, 55-64, 65-74, 75-79, ≥80 years).
Sex	Both VA and Medicare	A flag will be created for female beneficiaries and reported as a percentage.
US Geographic Region	Both VA and Medicare	The United States will be divided into 5 regions: Northeast, South, Midwest, West, and Other.
Race	Both VA and Medicare	Race will be identified and will be categorized as: White, Black, Other, and unknown.
Year of index OAC	Both VA and Medicare	A flag will be created for proportion of unique patients with index OAC identified in 2013, 2014, 2015, 2016, and 2017.

Variable	Data Source(s)	Operational Definition
Dose of Index DOAC	Both VA and Medicare	-Standard dose (apixaban 5 mg, dabigatran 150 mg, and rivaroxaban 20 mg) based on dose of the initial prescription of DOAC; -lower dose (apixaban 2.5 mg, dabigatran 75 mg, rivaroxaban 15 mg/10 mg) based on dose of the initial prescription of DOAC.
Body Weight	VA	Body weight will be obtained as continuous and categorical variables. The categories will be: ≤60 kg, 61-99 kg, 100-119 kg, and ≥120 kg. If a patient has multiple values, the value closest to the index date will be used.
BMI	VA	Body Mass Index: Body mass index will be calculated as weight in kilograms divided by the square of height in meters. Mean, median, and standard deviation will be provided for the continuous variable. The categories will be <18.5, 18.5-24.9, 25-29.9, 30-39, and ≥40. If a patient has multiple values, the value closest to the index date will be used.
Creatinine Clearance	VA	Creatinine Clearance: Creatinine clearance will be identified using LOINC codes (2160-0, 33914-3, 48642-3, 48643-1, 62238-1, 2164-2, 14682-9). A categorical variable for the glomerular filtration rate (GFR) will be created with the following cutoff points: <15 ml/min, 15-29 ml/min, 30-59 ml/min, 60-89 ml/min, and ≥90 ml/min. If a patient has multiple values, the value closest to the index date will be used. The creatinine clearance rate (CrCl) will be calculated based on serum creatinine for patients who only had serum creatinine information.[25]
INR	VA	International Normalized Ratio Test Results will be identified using Logical Observation Identifiers Names and Codes (LOINC; 34714-6, 38875-1, 46418-0, 52129-4, 5895-7, 5896-5, 61189-7, 6301-6, 72281-9) occurring anytime during the baseline period will be evaluated.
$CHADS_2$ Score	Both VA and Medicare	$CHADS_2$ Score will be calculated according to the points algorithm outlined in Appendix Table 5.

Variable	Data Source(s)	Operational Definition
$CHA2DS_2$-VASc Score	Both VA and Medicare	CHA2DS2-VASc score will be calculated according to the points algorithm outlined in Appendix Table 6.
HAS-BLED Score	Both VA and Medicare	HAS-BLED score will be calculated according to the points algorithm outlined in Appendix Table 7.
Baseline Medication Use	Both VA and Medicare	A flag will be created for the following medications prescribed during the baseline period: angiotensin-converting enzyme inhibitors/ angiotensin-receptor blockers, aspirin, beta blockers, statins, proton pump inhibitors, H2-receptor antagonists, antiplatelets, nonsteroidal anti-inflammatory drugs, inhibitors of warfarin, inducers of warfarin, dronedarone, digoxin, calcium channel blockers, renin angiotensin system antagonists, glucocorticoids, diuretics, metformin, sulfonylureas, thiazolidinedione, insulin, other diabetes drugs, antiulcer agents, and antidepressants (See Appendix Table 8 for codes).
Bariatric Surgery	Both VA and Medicare	A flag will be created for patients with claims for bariatric surgery (See Appendix Table 9 for codes).
CCI	Both VA and Medicare	Charlson Comorbidity index will be calculated as a continuous variable (See Appendix Table 10 for calculation and codes).
Comorbid Conditions	Both VA and Medicare	The following comorbid conditions will be flagged in baseline: History of stroke/SE, history of bleeding, myocardial infarction, renal disease, liver disease, dyspepsia or stomach discomfort, diabetes, hypertension, congestive heart failure, non-stroke/SE peripheral vascular disease, anemia and coagulation defects , transient ischemic attack, coronary artery disease, peripheral artery disease (See Appendix Table 11 for codes).

Table 2. Clinical and Outcome Variables

Variable	Data Source(s)	Operational Definition
Major Bleeding Event	Both VA and Medicare	Major bleeding event(s) observed during follow-up will be identified using hospital claims which had a MB diagnosis as the primary diagnosis code and occurring anytime during the follow-up period of drug use or within 30 days from the last day of supply of treatment prescription. A major bleeding event will be a dichotomous variable that equals 1 if there is ≥1 bleeding event during the follow-up period. Time to the first major bleeding event will be calculated. The first major bleeding event will be stratified by gastrointestinal (GI), intracranial hemorrhage (ICH), and other MB. (See Appendix Table 12 for codes).
Stroke/SE Event	Both VA and Medicare	Stroke/SE will be identified using hospital claims which had a stroke/SE diagnosis code as the primary diagnosis code and occurring anytime during the period of drug use or within 30 days from the last day of supply of treatment prescription. Stroke/SE will be a dichotomous variable that equals 1 if there is ≥1 stroke event during the follow-up period. Time to the first stroke/SE event will be calculated. The first stroke/SE event will be stratified by ischemic stroke, hemorrhagic stroke, and SE. (See Appendix Table 12 for codes).
Net Clinical Benefit	Both VA and Medicare	For patients with stroke/SE OR MB event, net clinical benefit will be assessed by evaluating the first hospital claim for a stroke/SE or MB event. The hospital claim can occur anytime during the period of drug use or within 30 days from the last day of supply of treatment prescription.
INR	VA	International Normalized Ratio Test Results will be identified using Logical Observation Identifiers Names and Codes (LOINC; 34714-6, 38875-1, 46418-0, 52129-4, 5895-7, 5896-5, 61189-7, 6301-6, 72281-9) occurring anytime during the period of drug use or within 30 days from the last day of supply of treatment prescription. The mean

Variable	Data Source(s)	Operational Definition
		and median number of INR tests for warfarin patients will be calculated. The distribution of INR values (mean, median, maximum, minimum, Q1, Q3) will be evaluated descriptively and flags will be created for INR <2, 2-3, and >3.
Time in Therapeutic Range (TTR)	VA	TTR will be calculated using the Rosendaal method[26] and will be computed using INR values among warfarin patients during the follow-up. This method calculates INR-specific person-time by incorporating the frequency of INR measurements and their actual values, and assuming that changes between consecutive INR measurements are linear over time. TTR will be calculated based on the percentage of time a patient remained in therapeutic range evaluated during the entire follow-up period. Flags will be created for TTR ≥65% [good] and TTR <65% [poor].
CCI [redacted]	[redacted]	[redacted]
CCI [redacted]	[redacted]	[redacted]

Variable	Data Source(s)	Operational Definition
CCI [redacted]	[redacted]	[redacted]

9.4. Data Sources

This retrospective observational study will be conducted using linked national patient-level data from the VA and Center for Medicare and Medicare Services (CMS) fee-for-service database and Veterans' Health Affairs database. The study period will be from January 1, 2013 through December 31, 2017. Patients with NVAF diagnosis will first be identified in VA dataset and then linked to Medicare data using social security number (SSN) as a unique patient identifier. Linked patient records will be deidentified before analysis. There will be no duplicate records and all outcomes will be counted only once in the linked database. Once the linked database is created, demographic, clinical, HRU, and cost outcomes will be available from the linked patient records using both Medicare and VA database. There will not be any overlapping HCRU or costs claims since VA is a closed system. If patient uses VA system then we will see a claim from VA database, if they use Medicare, they we will see a claim from Medicare database. So, all the claims will be unique with no overlapping.

In addition, VA data includes vital measures (BMI, body weight, height) and laboratory results (INR, TTR) that are not available in Medicare claims data. Using linked VA and Medicare data provides a more robust patient history as vital measures and laboratory results can be evaluated. BMI, body weight, and height are of importance when stratifying patients in obese and severely obese cohorts and INR and TTR allow evaluation of warfarin management. This study will add to an existing body of literature that evaluates various populations across different disease states the use linked VA and Medicare data to provide a more robust study population.[27,28]

Veterans' Health Affairs (VHA) Data

9.4.1. VA Database

The VHA is the largest integrated health care system in the United States, providing care for veterans across the country. According to U.S. Department of Veterans Affairs (VA) estimates, there were approximately 24 million living veterans of the U.S. military in 2006. That year, the department provided medical services to more than five million of those veterans and to more than 400,000 other patients (ie, employees, eligible dependents and survivors of disabled veterans, and patients seen through sharing agreements with other providers such as the Department of Defense's TRICARE program). An additional 2.9 million veterans were enrolled in the system but did not seek services from the department that year, and the VA estimates that 5.8 million eligible veterans were never enrolled.[29]

The size and structure of the VHA system is quite different from most private care organizations. The system includes:

- 162 VA hospitals;
- 137 nursing homes;
- 43 domiciliaries;
- 850+ community and facility-based clinics;
- 14,800 doctors;
- 61,000 nurses; and
- 5 million patients.[30]

The system began as a network of hospitals and grew to include more aspects of care including clinics and nursing homes. Twenty-two regional networks, called the Veterans Integrated Service Networks (VISNs) have been created since 1995. Most VISNs consist of 7 to 10 hospitals, 25 to 30 ambulatory care clinics, 4 to 7 nursing homes, and 1 to 2 domiciliaries.[31]

The VHA Medical SAS® datasets are national administrative data for VHA-provided health care utilized primarily by veterans, but also by some non-veterans (eg, employees, research participants). The datasets are provided in SAS® format by fiscal year (FY) (October 1-September 30). These data are extracted from the National Patient Care Database (NPCD) as maintained by the VHA Office of Information at the Austin Information Technology Center (AITC), the central repository for VA data.

VHA Medical SAS® datasets include four inpatient datasets and two outpatient datasets. Variables common to both inpatient and outpatient data files include demographics (age, sex, race, birth date, marital status, city, county, and state of residence); period of military service; and selected special characteristics, including the patient's spinal cord injury status, prisoner of war history, and radiation or Agent Orange exposure. Also included are the patient's category of eligibility for VHA medical care, and the extent of a service-connected disability.

VHA Medical SAS® Inpatient Datasets

The Medical SAS® Inpatient datasets cover four main categories of care: acute, extended, observation, and non-VA. Within each of these categories there are four datasets:

- **Main:** A patient's inpatient stay (episode of care);
- **Bed Section:** A patient's inpatient stay under a specified physician treating for a specialty service;
- **Procedure:** One day's procedure during an inpatient stay; and
- **Surgery:** One day's surgeries during an inpatient stay.

Inpatient variables describing each hospital admission include date, time, facility, and the primary diagnosis at admission. Discharge data include date, time, destination (eg, home, hospice, community nursing home), type of discharge (eg, regular, transfer to another hospital, death), and length of stay (LOS).

VHA Medical SAS® Outpatient Datasets

Each outpatient data record represents one date of service for one outpatient, and includes a facility identifier, date and time of visit, and the type of clinic location where care was provided. Visits on a single day to multiple clinics, laboratories, and treatment programs are captured.

Outpatient care is reported in terms of diagnoses (International Classification of Diseases, 9th and 10th Revision, Clinical Modification [ICD-9-CM and ICD-10-CM] codes) and procedure (Current Procedural Terminology [CPT] codes), including dates and times. The type of provider for each service is reported using a VHA list of more than 500 categories (these may be changed in the future to agree with provider-type codes used by the Centers for Medicare and Medicaid Services [CMS]).

There currently are two Medical SAS® Datasets for outpatient care, visit and event.

- **Visit:** One day's occasions of service; and
- **Event:** One ambulatory encounter (coded as DSS Identifier/Clinic Stop).

VHA Decision Support System

The VHA Decision Support System (DSS) is a managerial cost accounting system based on a commercial software named Eclipsys©. VHA modified Eclipsys© to interact with VistA and other VA national databases to populate the data elements required to allocate VHA costs to VHA products (goods and services provided during patient care). Introduced in 1994, full implementation of the VHA DSS in all facilities was completed in 1999.

The VHA DSS data files comprise a longitudinal, secondary relational database combining selected clinical data and fiscal (cost) data. The DSS provides a mechanism for integrating expenses, workload, and patient utilization. DSS information supports process and performance improvements by measuring quality of care, clinical outcomes, and financial impact. Within a fiscal year, periodic rollups of production data are performed to produce year-to-date non-destructive examinations (NDEs).

DSS Clinical NDEs

- **Laboratory (LAB):** Laboratory test utilization and costs (inpatient and outpatient);
- **Laboratory Results (LAR):** Laboratory test results for a specific list of tests (inpatient and outpatient);
- **Pharmacy (PHA):** Pharmacy prescription utilization and costs (inpatient and outpatient); and
- **Radiology (RAD):** Radiological procedure utilization and costs.

The stability of VHA data sources allows for superior analysis of the continuity of care of patients over multiple years.

US Centers for Medicare & Medicaid Services (CMS) Data

Medicare Inpatient Data

The inpatient claim file contains final action claims data submitted by inpatient hospital providers for reimbursement of facility costs. Some information contained in this file includes diagnosis (International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification [ICD-9-CM and ICD-10-CM] diagnosis code, procedure (ICD-9 and ICD-10 procedure code), diagnosis-related group (DRG), dates of service, reimbursement amount, hospital provider, and beneficiary demographic information. Each observation in this file is at the claim level.

Medicare Outpatient Data

The outpatient claim file contains final action claims data submitted by institutional outpatient providers. Examples of institutional outpatient providers include hospital outpatient departments, rural health clinics, renal dialysis facilities, outpatient rehabilitation facilities, comprehensive outpatient rehabilitation facilities, and community mental health centers. Some information contained in this file includes diagnosis and procedure (ICD-9-CM diagnosis, ICD-9 procedure, ICD-10 diagnosis, ICD-10 procedure, Centers for Medicare and Medicaid Service [CMS] Healthcare Common Procedure Coding System [HCPCS] codes), dates of service, reimbursement amount, outpatient provider number, revenue center codes, and beneficiary demographic information. Each observation in this file is at the claim level.

Medicare Part D Drug Events (PDE) Data

The PDE data contains prescription drug costs and payment data (including out-of-pocket costs [co-payments and deductibles]) that enable CMS to make payments to the plans and otherwise administer Part D benefits. When a beneficiary fills a prescription under Medicare Part D, a prescription drug plan sponsor must submit a summary record to CMS. The PDE data are not the same as individual drug claim transactions but are summary extracts using CMS-defined standard fields.

Skilled Nursing Facility (SNF) Research Identifiable File (RIF)

The SNF file contains final action, fee-for-service (FFS) claims data submitted by SNF providers. This file includes ICD-9-CM and ICD-10-CM diagnosis and procedure codes, dates of service, reimbursement amount, SNF provider number, and beneficiary demographic information.

Home Health Agency (HHA) RIF

The HHA file contains final action, FFS claims submitted by HHA providers. This file includes: number of visits, type of visit (skilled nursing care, home health aides, physical therapy, speech therapy, occupational therapy, and medical social services), diagnosis (ICD-9-CM and ICD-10-CM diagnosis), date of visit, reimbursement amount, HHA provider number, and beneficiary demographic information.

Hospice RIF

The Hospice file contains final action claims submitted by hospice providers. Once a beneficiary elects hospice care, all hospice-related claims will be found in this file, regardless of if the beneficiary is in Medicare FFS or in a Medicare managed care plan. This file includes level of hospice care received (eg, routine home care, inpatient respite care), terminal diagnosis (ICD-9-CM and ICD-10-CM diagnosis), dates of service, reimbursement amounts, hospice provider number, and beneficiary demographic information.

Durable Medical Equipment (DME) RIF

The DME file contains final action, FFS claims submitted by DME suppliers. This file includes diagnosis (ICD-9-CM and ICD-10-CM diagnosis), services provided (CMS Common Procedure Coding System [HCPCS] codes), dates of service, reimbursement amounts, DME provider number, and beneficiary demographic information.

Medicare Carrier File

The Carrier file (also known as the Physician/Supplier Part B claims file) contains final action, FFS claims submitted on a CMS-1500 claim form. Most of the claims are from non-institutional providers, such as physicians, physician assistants, clinical social workers, and nurse practitioners. Claims for other providers, such as free-standing facilities, are also found in the Carrier file. Examples include independent clinical laboratories, ambulance providers and free-standing ambulatory surgical centers. This file includes diagnosis and procedure codes, dates of service, reimbursement amounts, provider numbers, and patient demographic information.

Medicare Denominator File

The denominator file contains demographic and enrollment information of Medicare beneficiaries enrolled or entitled in a given year. It combines Medicare beneficiary entitlement status information from administrative enrollment records with third-party payer information and group health plan (GHP) enrollment information. It is an abbreviated version of the enrollment database (EDB) (selected data elements).

Some information contained in this file includes the beneficiary's unique identifiers, state and county codes, ZIP codes, dates of birth, dates of death, sex, race, age, monthly entitlement indicators (A/B/both), reasons for entitlement, state buy-in indicators, and monthly managed care indicators (yes/no). However, all Medicare files described above can be linked by de-identified patient ID and will be included in the same CMS access request.

Data are collected on an ongoing basis with files constructed annually. It does not contain data on all beneficiaries ever entitled to Medicare. The file contains data only for beneficiaries who were entitled during the year of the data. These data are available annually in May of the current year for the previous year.

9.5. Study Size

All elibgile patients available for analysis will be included.

A feasibility analysis was conducted to examine the sample size of patients available in the linked VA and Medicare dataset with diagnosis of NVAF and BMI or body weight reported within ±6 months of index diagnosis. Enrollment in Medicare Part D was removed as an inclusion criterion during the feasibility analysis as 50% of the study population would be excluded. Many patients in this study population use VA prescription drug benefits due to

cost savings over Medicare Part D. However, we will identify OAC use from Medicare Part D in patients who have this coverage along with VA pharmacy benefits. Approximately 56,000 patients would be included in this study population, with 20,000 included in the apixaban cohort. The VA feasibility study results and hazard ratios (HR) were used to calculate the needed sample size below.

A power calculation was completed for effectiveness outcomes comparing the difference between stroke rates using an alpha of 0.05, power of 80%, an accrual period of 4.5 years (identification period where patients are selected into the study), and a loss of follow-up of 55% for the warfarin cohort and 40% for the apixaban cohort. Using the stroke hazard ratio of 0.63 (from ARISTOPHANES Obesity subgroup[23] and an incidence rate of 1.10 per 100 person-years (from VA-Medicare feasibility analysis conducted in Q1-Q2 2020) in the warfarin group, a Cox proportional hazards analysis of stroke would need 7,945 patients per cohort (1:1 matching).

- **Accrual Period:** 4.5 years (identification period).
- **Loss of follow-up:** 55% for the warfarin cohort and 40% for the apixaban cohort.
- **Alpha**: 0.05.
- **Power**: 80%.

Table 3. Power Calculation

Hazard Ratio (HR) Apixaban vs Warfarin		Incidence Rates for Stroke/SE (per 100 person-years)		Stroke/SE Sample Size		
HR	**Source**	**Rate (warfarin)**	**Source**	**Apixaban**	**Warfarin**	**Total**
OBESITY						
0.63	ARISTOPHANES-Obesity subgroup[23]	1.80	ARISTOPHANES-Obesity subgroup	4,882	4,882	9,764
0.63	ARISTOPHANES-Obesity subgroup	1.10	VA Feasibility	7,945	7,945	15,890
0.76	Sandhu et al[19]	1.28	Sandhu et al	17,769	17,769	35,538
0.76	Sandhu et al	1.10	VA Feasibility	20,646	20,646	41,292
SEVERE OBESITY						
0.72	ARISTOPHANES-Obesity subgroup	1.60	ARISTOPHANES-Obesity subgroup	10,195	10,195	20,390
0.72	ARISTOPHANES-Obesity subgroup	0.87	VA Feasibility	18,640	18,640	37,280
0.39	Hohnloser et al[32]	1.13	Hohnloser et al	2,356	2,356	4,712
0.39	Hohnloser et al	0.87	VA Feasibility	3,055	3,055	6,110

Sandhu et al used BMI ≥30 kg/m^2; Hohnloser et al used weight >120 kg

9.6. Data Management

N/A.

9.7. Data Analysis

All variables will be analyzed descriptively. Cohorts will be compared; however, the main analysis will be between apixaban vs warfarin. Other comparisons (DOAC vs warfarin and DOAC vs DOAC) will be optional depending on the sample size. Means, medians, and standard deviations will be provided for continuous variables when performing descriptive analysis of continuous data. Numbers and percentages will be provided for dichotomous and polychotomous variables when performing descriptive analysis of categorical data. Bivariate comparisons of baseline characteristics and outcomes measures will be provided. Appropriate tests (eg, t-test, chi-square test) will be used based on the distribution of the measure. The incidence rate of stroke/SE, MB, and net clinical benefit will be calculated. The incidence rate will be calculated as the number of patients who experience the event divided by the observed time at risk. Kaplan-Meier survival curves will be generated to illustrate time-to-first stroke/SE, MB, and net clinical benefit. Statistical tests of significance will be conducted to determine differences between the cohorts. Baseline and outcome tables will be stratified by obese, severely obese, and index dose of DOAC.

All data analysis will be executed using statistical software SAS version 9.4 (Cary, NC).

9.7.1. Analysis Plan for Primary Objective

Baseline demographic and clinical factors such as age, sex, geographic region, baseline medications, and co-morbidities among NVAF patients initiating OAC will be summarized. Descriptive statistics, (ie, mean, standard deviation, median, and inter-quartile range for continuous variables and differences across treatments) will be compared using the Student's t-test or Wilcoxon rank sum test. Percentages for categorical and binary variables will be presented for all baseline patient characteristics and will be compared using the chi-square test or Fisher's Exact test.

The cumulative incidence rate for clinical outcomes (stroke/SE, MB, net clinical benefit) will be calculated. MB will be stratified by GI bleeding, ICH, and other bleeding; Stroke/SE will be stratified by hemorrhagic, ischemic, and systemic embolism. The incidence rate will be calculated as the number of patients who experience the event divided by the observed time at risk. The incidence rate will be calculated per 100 person-years.

Inverse Probability Treatment Weighting (IPTW)

Inverse probability treatment weighting (IPTW) will be used to balance patient characteristics when comparing outcomes among different cohorts. Three sets of IPTW will be conducted (all patients, obese patients, and severely obese patients). Depending on sample size, IPTW will also be conducted for the standard dose patients separately. In addition, the primary analysis will be conducted for apixaban vs warfarin and depending on the sample size, other OAC comparisons will be conducted.

IPTW uses propensity scores to obtain estimates of the average treatment effect. The propensity score will be calculated using a logistic model with treatment cohorts included in the model, using warfarin patients as the reference (ie, control cohort). The propensity score is defined as the probability of a patient receiving a certain treatment or not conditional on their observed baseline covariates (eg, age, gender, comorbidities, medications, etc.). The list of variables included in the logistic model will be based on clinical rationale. The propensity score acts as a balancing score between the cohorts. After calculating the propensity score, the distribution of the propensity scores will be reviewed. Each patient will be weighted by the inverse of the probability of their treatment option (weight=1/propensity score).

If a treated patient has a very low propensity score, a very large weight will be generated. Large weights can increase the variability of estimated treatment effect. In order to address this, the weights will be stabilized. In order to stabilize the weights, the treatment option and control weights will be multiplied by a constant, equal to the expected value of being in the treatment or comparison cohorts, respectively (see below). This reduces the variability of the weights and reduces the variance of the treatment effect estimates.

$$\frac{\sum_{i=1}^{N_T} PS_i}{N_T} * \frac{1}{PS_i}$$

The distribution of the stabilized weight will be reviewed. If no extreme outliers are observed, the stabilized weights will be applied to the sample. In cases of extreme outliers, the large weights could be set to a less extreme value (eg, recoding all weights that are outside 5th and 95th percentile to the 5th and 95th value, respectively). If needed, truncation can be done after stabilizing the weights.

After the weights are applied, the balance of the baseline covariates will be assessed. First, the means and proportions of baseline variables will be compared. The standardized difference compares the difference in means in units of the standard deviation. If the standardized difference is less than 10%, the covariates will be considered balanced. For continuous variables, the balance of the distribution will also be assessed. The high-order movements and interactions between variables should be similar between cohorts. The standardized difference will be used to compare the mean of the square of continuous variables. Graphical comparisons of the distribution of continuous variables will be completed. Side-by-side boxplots and empirical cumulative distribution functions will be used to the compare the distribution of continuous covariates in the unweighted and weighted samples. Since the graphical approach can be subjective, a numerical method for comparing the distribution of continuous baseline covariates will also be completed. Kolmogorov-Smirnov test allows a comparison of the distribution of a continuous variable between two independent groups.[33-36]

Cox Proportional Hazards Model

Cox models will be used to compare the risk of stroke/SE, MB, and net clinical benefit between cohorts. Variables that are not balanced in the weighted population will be included in the models in addition to treatment variables. For the secondary objective, an interaction term for treatment and obesity status will be included in the models. The proportional hazards assumption will be evaluated by visually inspecting the Kaplan-Meier plot. It the proportional hazards assumption appears to be violated, it will be confirmed by testing the significance of interactions between treatment and log of time.

9.7.2. Analysis Plan for Secondary[redacted]

Any further comparisons or sub-group analysis will be assessed and conducted based on feasibility analysis to ensure adequate sample size through power calculation.

[redacted]

Sensitivity Analysis: Propensity Score Matching

The propensity score matching (PSM) technique will be used to control for potential confounders when comparing the cohorts.[37] Covariates to be included in the logistic regression model may include the following variables: age, geographic region, Charlson comorbidity index score, comorbidities, and other clinical characteristics. The final list of

variables to be used in the model will be discussed and determined during analysis development, after reviewing the pre-matched descriptive tables. Each subject in the reference cohort will be matched to a subject in the comparator cohort with the closest propensity score. The nearest neighbor method without replacement and with a caliper of 0.01 will be used to select the matched samples. The balance of covariates between treatment groups will be determined using the absolute standardized difference of the mean ≤0.10.

After PSM, no significant differences are expected among all pre-index measures between the patient cohorts. PSM with a different ratio (1:2 or 1:3) can also be considered if the matched sample size using a ratio of 1:1 is too small.

9.8. Quality Control

STATinMED Research's approach combines scientific rigor with accurate results. The company focuses on quality at each step of the process, including, but not limited to the following:

- Sound scientific design and clinically rigorous review.
- Detailed study protocol, that includes definitions, codes, analyses, and table shells. A member of the STATinMED clinical team will review the appropriateness and validity of the coding strategy and identify relevant issues. The protocol further provides STATinMED Research and Pfizer the opportunity to solidify research questions and to address any potential gaps in information.
- Rigorous quality assurance checks will be performed during the construction of the dataset. Several checks are used, including record-level verification of all data elements, double programming of certain portions of the dataset, programming data edit checks, visual review of raw data against the constructed data elements, and review of analysis to assess validity of results.
- STATinMED Research's analysis will be performed by an analyst under the supervision of the project manager, lead analyst, and/or vice president. These team members review programs and output for consistency with the analysis plan, quality, and accuracy. Further, results will be reviewed with Pfizer to establish that the results meet Pfizer's expectations.

Additional quality control procedures are enlisted below.

QC Checklist	Initials
QC of Excel File	
• Evaluate each step of attrition table (eg, check percentage drop at each step, compare to prior studies (rerun, other internal, external (if applicable)).	
• 5 separate database equal total pooled population (pre-match and post-match).	
• Check percentage drop after PSM (expect ~10% drop but dependent on database/original sample size; add PSM sample size to attrition table).	
• Baseline table → ensure all categorical variables equal 100% and total sample size, make sure all three dose variables are complete (Auto-check using formulas).	
• Outcome table → components of MB or stroke/SE should be equal or larger than overall MB or stroke/SE (N and incidence rates; auto check using formula), all other categorical variables equal 100% and total sample size, minimum follow-up should be at least 1 day and check distribution.	
• Outcome table → ensure incidence rates can be calculated using number of events and person time	
• Check conditional formatting for p-values and standardized difference (red for p-values <0.05 (unless interaction p-value where the cutoff is <0.10), green for standardized difference ≥10.00).	
• (Rerun) Compare percent difference between original and new results (10% cutoff) in baseline and outcome tables (using formula).	
• Compare incidence rates, KM curves, and Cox model results to ensure alignment (eg, compare log rank test to Cox model, visually inspect KM curve, can calculate IRR to see similarity to HR).	
• Ensure pooled dose pre-match table has the same sample size as indicated in baseline table.	
• Sample size in subgroup matches the sample size in baseline table (eg, CHF subgroup tables match CHF baseline row in pooled baseline table). For each analysis, will be customized for the subgroups.	
• Sample size of combined subgroup equals total population (for interaction).	
• If lower CI is >1 or upper CI is <1, then p-value should be <0.05 (using formula).	
• Check duplicates within a sheet for Cox models (using formula).	
Data Integrity Review Tasks for Publications (will be customized for each manuscript; each figure and table will be listed) – Completion by medical writer and data check against excel file by non-project team member	
Check whether all data sources are annotated and traceable for future retrieval.	
Check the following data by comparing it against the appropriate source documentation (including, but not limited to):	

QC Checklist	Initials
QC of Excel File	
• Numbers, units, and symbols (for example, >, <, ≥, *) in text.	
• Numbers, units, and symbols in all tables.	
• Numbers and units (including those on axes) and symbols in all figures, including flow charts and diagrams.	
• Measurement units.	
• Data-driven statements.	
Check that all data values are consistent throughout the document sections, tables, figures, legends, and footnotes (for example, data in the abstract match data in the body of document, and results section match figure).	
Check that values from other sources match reference.	
For any items not completed and marked N/A, provide rationale below. Additional comments. Click here to enter text.	

9.9. Limitations of the Research Methods

A key strength of this study design is that retrospective observational analyses provide a better understanding about the study population in real-world clinical practice and offer complimentary information to controlled clinical trials. Retrospective observational studies also allow the evaluation of patients who are often under-represented in clinical trials, such as those with comorbidities and older adults. Since prescribing patterns in the real world can be complex, retrospective analysis provides a more comprehensive picture of how medications are used by clinicians in routine practice. In addition, the claims databases include all medical and pharmacy claims of patients and allow for longitudinal analysis of a nationally representative sample.

A second key strength of this study design is the linked VA and Medicare databases, which allow us to see a comprehensive patient journey and health resource utilization across two databases. The VHA database includes lab values that will be used to identify obese and severely obese patients as opposed to ICD codes only. Additionally, INR values are available in the VHA data, which will also be evaluated to provide insights into warfarin management.

While claims data are extremely valuable for the efficient and effective examination of health care outcomes, treatment patterns, HCRU, and costs, all claims databases have certain inherent limitations because the claims are collected for administrative purposes and not research. For instance, the presence of a claim for a filled prescription does not indicate that the medication was taken as prescribed or at all. Medications filled over the counter or provided as samples by the physician cannot be observed in the claims data. And the presence of a diagnosis code on a medical claim does not indicate the positive presence of

disease, as the diagnosis code may be incorrectly coded or included as rule-out criteria rather than actual disease.

9.10. Other Aspects

Not Applicable.

10. PROTECTION OF HUMAN SUBJECTS

10.1. Patient Information

This study involves data that exist in anonymized structured format and contain no patient personal information.

10.2. Patient Consent

As this study involves anonymized structured data, which according to applicable legal requirements do not contain data subject to privacy laws, obtaining informed consent from patients by Pfizer is not required.

10.3. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

N/A.

10.4. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE).

11. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

This study involves data that exist as structured data by the time of study start. In these data sources, individual patient data are not retrieved or validated, and it is not possible to link (ie, identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (ie, identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

In these data sources, individual patient data are not retrieved or validated, and it is not possible to link (ie, identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an adverse event (AE) (ie, identifiable patient, identifiable reporter, a suspect product, and event) cannot be met.

12. PLANS FOR DISSEMINATING AND COMMUNICATING STUDY RESULTS

In the event of any prohibition or restriction imposed (eg, clinical hold) by an applicable competent authority in any area of the world, or if the investigator is aware of any new information which might influence the evaluation of the benefits and risks of a Pfizer product, Pfizer should be informed immediately.

An Excel file will be provided with all the descriptive and multivariate analysis tables. A final study report detailing the final study protocol and the analysis results will be provided when the study is complete.

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16. ANNEX 1. LIST OF STAND ALONE DOCUMENTS

None.

17. ANNEX 2. ADDITIONAL INFORMATION

17.1. Appendix

Table 4. Exclusion Criteria

Diagnosis	ICD-9 Code	ICD-10 Code
Valvular Heart Disease	394.0, 394.1, 394.2, 394.9, 396.0, 396.1, 396.8, 396.9, 424.0, 745.xx	I050, I051, I052, I058, I059, I080, I088, I089, I340, I341, I342, I348, I349, Q213, Z952, Z953, Z954
Mechanical Heart Valve/ Mitral Stenosis (narrow definition)	**ICD-9-CM:** 996.02, 996.71, 394.0, 394.2, 396.0, 396.1, 746.5 **ICD-9 procedure:** 35.20, 35.22, 35.24, 36.23, 35.97 **CPT:** 33405, 92987, 33427, 33426, 33425, 33422, 33420, 33430	**ICD- 10 diagnosis codes:** T82.01XA, T82.02XA, T82.03XA, T82.09XA, T82.817A- T82.897A, T82.9XXA, I05.0, I05.2, I08.0, Q23.2 **ICD-10 Procedure Codes:**02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ, 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ, 02RF47Z, 02RF48Z, 02RF4JZ, 02RF4KZ, 02RG07Z, 02RG08Z, 02RG0JZ, 02RG0KZ, 02RG37H, 02RG37Z, 02RG38H, 02RG38Z, 02RG3JH, 02RG3JZ, 02RG3KH, 02RG3KZ, 02RG47Z, 02RG48Z, 02RG4JZ, 02RG4KZ, 02RH07Z, 02RH08Z, 02RH0JZ, 02RH0KZ, 02RH37H, 02RH37Z, 02RH38H, 02RH38Z, 02RH3JH, 02RH3JZ, 02RH3KH, 02RH3KZ, 02RH47Z, 02RH48Z, 02RH4JZ, 02RH4KZ, 02RJ07Z, 02RJ08Z, 02RJ0JZ, 02RJ0KZ, 02RJ47Z, 02RJ48Z, 02RJ4JZ, 02RJ4KZ, 02UG3JZ, X2RF032, X2RF332, X2RF432
VTE	DVT: 451-453, 671.3, 671.4, 671.9; or PE: 415.1, 673.2, 673.8	I2601, I2602, I2609, I2690, I2692, I2699, I8010, I8011, I8012, I8013, I80201, I80202, I80203, I80209, I80211, I80212, I80213, I80219, I80221, I80222, I80223, I80229, I80231, I80232, I80233, I80239, I80291, I80292, I80293, I80299, I803, I808, I809, I81, I820, I821, I82210, I82211, I82220, I82221, I82290, I82291, I823, I82401, I82402, I82403, I82409, I82411, I82412, I82413, I82419, I82421, I82422, I82423, I82429, I82431, I82432, I82433, I82439, I82441, I82442, I82443, I82449, I82491, I82492, I82493, I82499, I824Y1, I824Y2, I824Y3, I824Y9, I824Z1, I824Z2, I824Z3, I824Z9, I82501, I82502, I82503, I82509, I82511, I82512, I82513, I82519, I82521, I82522, I82523, I82529, I82531, I82532, I82533, I82539, I82541, I82542, I82543, I82549, I82591, I82592, I82593, I82599, I825Y1, I825Y2, I825Y3, I825Y9, I825Z1, I825Z2, I825Z3, I825Z9, I82601, I82602, I82603, I82609, I82621, I82622, I82623, I82629, I82701, I82702, I82703, I82709, I82711, I82712, I82713, I82719, I82721, I82722, I82723, I82729, I82890, I82891, I8290, I8291, I82A11, I82A12, I82A13, I82A19, I82A21, I82A22, I82A23, I82A29, I82B11, I82B12, I82B13, I82B19, I82B21, I82B22, I82B23, I82B29, I82C11, I82C12, I82C13, I82C19, I82C21, I82C22, I82C23, I82C29, O871, O88211, O88212, O88213, O88219, O8822,

Diagnosis	ICD-9 Code	ICD-10 Code
		O8823, T82817A, T82818A
Transient AF	Pericarditis: 006.8, 017.9, 036.41, 074.21, 093.81, 098.83, 115.93, 390, 391, 392.0, 393, 411.0, 420.90, 420.91, 420.99, 423.0, 423.1, 423.2, 423.8, 423.9; Hyperthyroidism and Thyrotoxicity: 242.0, 242.1, 242.2, 242.3, 242.4, 242.8, 242.9	A1884, A3953, A5206, A5483, B3323, E0500, E0501, E0510, E0511, E0520, E0521, E0530, E0531, E0540, E0541, E0580, E0581, E0590, E0591, I010, I011, I012, I018, I019, I020, I092, I241, I300, I301, I308, I309, I310, I311, I312, I313, I318, I319, I32, Z952, Z953, Z954, I300, I301, I308, I309
Valve Replacement Procedure	**ICD-9-PCS/HCPCS Codes:** 35.05-35.09, 35.20-35.28, 35.97	**ICD-10-PCS Codes:** 02RF07Z, 02RF08Z, 02RF0JZ, 02RF0KZ, 02RF37H, 02RF37Z, 02RF38H, 02RF38Z, 02RF3JH, 02RF3JZ, 02RF3KH, 02RF3KZ, 02RF47Z, 02RF48Z, 02RF4JZ, 02RF4KZ, 02RG07Z, 02RG08Z, 02RG0JZ, 02RG0KZ, 02RG37H, 02RG37Z, 02RG38H, 02RG38Z, 02RG3JH, 02RG3JZ, 02RG3KH, 02RG3KZ, 02RG47Z, 02RG48Z, 02RG4JZ, 02RG4KZ, 02RH07Z, 02RH08Z, 02RH0JZ, 02RH0KZ, 02RH37H, 02RH37Z, 02RH38H, 02RH38Z, 02RH3JH, 02RH3JZ, 02RH3KH, 02RH3KZ, 02RH47Z, 02RH48Z, 02RH4JZ, 02RH4KZ, 02RJ07Z, 02RJ08Z, 02RJ0JZ, 02RJ0KZ, 02RJ47Z, 02RJ48Z, 02RJ4JZ, 02RJ4KZ, 02UG3JZ, X2RF032, X2RF332, X2RF432
Hip/knee replacement surgery	**ICD-9-PCS/HCPCS Codes:** 81.40, 81.51, 81.52, 81.53, 81.54, 81.55	**ICD-10-PCS Codes:** 0SQ90ZZ, 0SQ93ZZ, 0SQ94ZZ, 0SQ9XZZ, 0SQB0ZZ, 0SQB3ZZ, 0SQB4ZZ, 0SQBXZZ, 0SR90J9, 0SR90JA, 0SR90JZ, 0SRB0J9, 0SRB0JA, 0SRB0JZ, 0SRA009, 0SRA00A, 0SRA00Z, 0SRA019, 0SRA01A, 0SRA01Z, 0SRA039, 0SRA03A, 0SRA03Z, 0SRA07Z, 0SRA0J9, 0SRA0JA, 0SRA0JZ, 0SRA0KZ, 0SRE009, 0SRE00A, 0SRE00Z, 0SRE019, 0SRE01A, 0SRE01Z, 0SRE039, 0SRE03A, 0SRE03Z, 0SRE07Z, 0SRE0J9, 0SRE0JA, 0SRE0JZ, 0SRE0KZ, 0SRR019, 0SRR01A, 0SRR01Z, 0SRR039, 0SRR03A, 0SRR03Z, 0SRR07Z, 0SRR0J9, 0SRR0JA, 0SRR0JZ, 0SRR0KZ, 0SRS019, 0SRS01A, 0SRS01Z, 0SRS039, 0SRS03A, 0SRS03Z, 0SRS07Z, 0SRS0J9, 0SRS0JA, 0SRS0JZ, 0SRS0KZ, 0SW90JZ, 0SW93JZ, 0SW94JZ, 0SWA0JZ, 0SWA3JZ, 0SWA4JZ, 0SWB0JZ, 0SWB3JZ, 0SWB4JZ, 0SWE0JZ, 0SWE3JZ, 0SWE4JZ, 0SWR0JZ, 0SWR3JZ, 0SWR4JZ, 0SWS0JZ, 0SWS3JZ, 0SWS4JZ, 0SRC07Z, 0SRC0JZ, 0SRC0KZ, 0SRC0LZ, 0SRD07Z, 0SRD0JZ, 0SRD0KZ, 0SRD0LZ, 0SRT07Z, 0SRT0JZ, 0SRT0KZ, 0SRU07Z, 0SRU0JZ, 0SRU0KZ, 0SRV07Z, 0SRV0JZ, 0SRV0KZ, 0SRW07Z, 0SRW0JZ, 0SRW0KZ, 0SWC0JC, 0SWC0JZ, 0SWC3JC, 0SWC3JZ, 0SWC4JC, 0SWC4JZ, 0SWD0JC, 0SWD0JZ, 0SWD3JC, 0SWD3JZ, 0SWD4JC, 0SWD4JZ, 0SWT0JZ, 0SWT3JZ, 0SWT4JZ, 0SWU0JZ,

Diagnosis	ICD-9 Code	ICD-10 Code
		0SWU3JZ, 0SWU4JZ, 0SWV0JZ, 0SWV3JZ, 0SWV4JZ, 0SWW0JZ, 0SWW3JZ, 0SWW4JZ
Pregnancy	**ICD-9 diagnosis codes:** 630-679, V22, V23, V24, V27, V28, V61.6, V61.7, 792.3, 796.5 **ICD-9 procedure codes:** 72.00-75.99 **HCPCS:** 59000-59350, 59400-59430, 59510-59866, 59870-59899, 76801-76828, 83661-8366	**ICD- 10 Diagnosis codes:** O00-O16, O20-O48, O60-O77, O80-O82, O85-O92, O94-O9A, Z370, Z371, Z372, Z373, Z374, Z3750, Z3751, Z3752, Z3753, Z3754, Z3759, Z3760, Z3761, Z3762, Z3763, Z3764, Z3769, Z377, Z379, Z36, Z36, Z36, Z36, Z36, Z36, Z36, Z36, Z36, Z36, Z640, Z640 **ICD-10 procedure codes:** 102, 109, 10A, 10D, 10E, 10H. 10J, 10P, 10Q, 10S,10T, 10Y, 2Y44X5Z, 30273H1, 30273J1, 30273K1, 30273L1, 30273M1, 30273N1, 30273P1, 30273Q1, 30273R1, 30273S1, 30273T1, 30273V1, 30273W1, 30277H1, 30277J1, 30277K1, 30277L1, 30277M1, 30277N1, 30277P1, 30277Q1, 30277R1, 30277S1, 30277T1, 30277V1, 30277W1, 3E0DXGC, 3E0E305, 3E0E329, 3E0E33Z, 3E0E36Z, 3E0E37Z, 3E0E3BZ, 3E0E3GC, 3E0E3HZ, 3E0E3KZ, 3E0E3NZ, 3E0E3SF, 3E0E3TZ, 3E0E705, 3E0E729, 3E0E73Z, 3E0E76Z, 3E0E77Z, 3E0E7BZ, 3E0E7GC, 3E0E7HZ, 3E0E7KZ, 3E0E7NZ, 3E0E7SF, 3E0E7TZ, 3E0E805, 3E0E829, 3E0E83Z, 3E0E86Z, 3E0E87Z, 3E0E8BZ, 3E0E8GC, 3E0E8HZ, 3E0E8KZ, 3E0E8NZ, 3E0E8SF, 3E0E8TZ, 3E0P3VZ, 3E0P7VZ , 4A0H74Z, 4A0H7CZ, 4A0H7FZ, 4A0H7HZ, 4A0H84Z, 4A0H8CZ, 4A0H8FZ, 4A0H8HZ, 4A0HX4Z, 4A0HXCZ, 4A0HXFZ, 4A0HXHZ, 4A0J72Z, 4A0J74Z, 4A0J7BZ, 4A0J82Z, 4A0J84Z, 4A0J8BZ, 4A0JX2Z, 4A0JX4Z, 4A0JXBZ, 4A1H74Z, 4A1H7CZ, 4A1H7FZ, 4A1H7HZ, 4A1H84Z, 4A1H8CZ, 4A1H8FZ, 4A1H8HZ, 4A1HX4Z, 4A1HXCZ, 4A1HXFZ, 4A1HXHZ, 4A1J72Z, 4A1J74Z, 4A1J7BZ, 4A1J82Z, 4A1J84Z, 4A1J8BZ, 4A1JX2Z, 4A1JX4Z, 4A1JXBZ

Table 5. $CHADS_2$ Score

$CHADS_2$	Point	ICD-9 Codes	ICD-10 Codes
Congestive Heart Failure	1	402.x1, 404.x1, 404.x3, 428.xx	I0981, I110, I132, I501, I5020, I5021, I5022, I5023, I5030, I5031, I5032, I5033, I5040, I5041, I5042, I5043, I509
Hypertension	1	401.xx-405.xx	I10, I110, I119, I120, I129, I130, I1310, I1311, I132, I150, I151, I152, I158, I159, I160, I161, I169, N262
Age ≥75 years	1	-	-
Diabetes mellitus	1	250.xx 357.2, 362.0, 366.41	E08311, E08319, E083211, E083212, E083213, E083219, E083291, E083292, E083293, E083299, E083311, E083312, E083313, E083319, E083391, E083392, E083393, E083399, E083411, E083412, E083413, E083419, E083491, E083492, E083493, E083499, E083511, E083512, E083513, E083519, E083521, E083522, E083523, E083529, E083531, E083532, E083533, E083539, E083541, E083542, E083543, E083549, E083551, E083552, E083553, E083559, E083591, E083592, E083593, E083599, E0836, E0840, E0842, E09311, E09319, E093211, E093212, E093213, E093219, E093291, E093292, E093293, E093299, E093311, E093312, E093313, E093319, E093391, E093392, E093393, E093399, E093411, E093412, E093413, E093419, E093491, E093492, E093493, E093499, E093511, E093512, E093513, E093519, E093521, E093522, E093523, E093529, E093531, E093532, E093533, E093539, E093541, E093542, E093543, E093549, E093551, E093552, E093553, E093559, E093591, E093592, E093593, E093599, E0936, E0940, E0942, E1010, E1011, E1021, E1022, E1029, E10311, E10319, E103211, E103212, E103213, E103219, E103291, E103292, E103293, E103299, E103311, E103312, E103313, E103319, E103391, E103392, E103393, E103399, E103411,

$CHADS_2$	Point	ICD-9 Codes	ICD-10 Codes
			E103412, E103413, E103419, E103491, E103492, E103493, E103499, E103511, E103512, E103513, E103519, E103521, E103522, E103523, E103529, E103531, E103532, E103533, E103539, E103541, E103542, E103543, E103549, E103551, E103552, E103553, E103559, E103591, E103592, E103593, E103599, E1036, E1037X1, E1037X2, E1037X3, E1037X9, E1039, E1040, E1041, E1042, E1043, E1044, E1049, E1051, E1052, E1059, E10610, E10618, E10620, E10621, E10622, E10628, E10630, E10638, E10641, E10649, E1065, E1069, E108, E109, E1100, E1101, E1121, E1122, E1129, E11311, E11319, E113211, E113212, E113213, E113219, E113291, E113292, E113293, E113299, E113311, E113312, E113313, E113319, E113391, E113392, E113393, E113399, E113411, E113412, E113413, E113419, E113491, E113492, E113493, E113499, E113511, E113512, E113513, E113519, E113521, E113522, E113523, E113529, E113531, E113532, E113533, E113539, E113541, E113542, E113543, E113549, E113551, E113552, E113553, E113559, E113591, E113592, E113593, E113599, E1136, E1137X1, E1137X2, E1137X3, E1137X9, E1139, E1140, E1141, E1142, E1143, E1144, E1149, E1151, E1152, E1159, E11610, E11618, E11620, E11621, E11622, E11628, E11630, E11638, E11641, E11649, E1165, E1169, E118, E119, E1300, E1301, E1310, E1311, E1321, E1322, E1329, E13311, E13319, E133211, E133212, E133213, E133219, E133291, E133292, E133293, E133299, E133311, E133312, E133313, E133319, E133391, E133392, E133393, E133399, E133411, E133412, E133413, E133419, E133491, E133492, E133493, E133499,

$CHADS_2$	Point	ICD-9 Codes	ICD-10 Codes
			E133511, E133512, E133513, E133519, E133521, E133522, E133523, E133529, E133531, E133532, E133533, E133539, E133541, E133542, E133543, E133549, E133551, E133552, E133553, E133559, E133591, E133592, E133593, E133599, E1336, E1337X1, E1337X2, E1337X3, E1337X9, E1339, E1340, E1341, E1342, E1343, E1344, E1349, E1351, E1352, E1359, E13610, E13618, E13620, E13621, E13622, E13628, E13630, E13638, E13641, E13649, E1365, E1369, E138, E139, E0851, E0852, E0951, E0952, E1051, E1052, E1151, E1152, E1351, E1352
Stroke	2	V12.54, 433-436	I6300, I63011, I63012, I63013, I63019, I6302, I63031, I63032, I63033, I63039, I6309, I6310, I63111, I63112, I63113, I63119, I6312, I63131, I63132, I63133, I63139, I6319, I6320, I63211, I63212, I63213, I63219, I6322, I63231, I63232, I63233, I63239, I6329, I6330, I63311, I63312, I63313, I63319, I63321, I63322, I63323, I63329, I63331, I63332, I63333, I63339, I63341, I63342, I63343, I63349, I6339, I6340, I63411, I63412, I63413, I63419, I63421, I63422, I63423, I63429, I63431, I63432, I63433, I63439, I63441, I63442, I63443, I63449, I6349, I6350, I63511, I63512, I63513, I63519, I63521, I63522, I63523, I63529, I63531, I63532, I63533, I63539, I63541, I63542, I63543, I63549, I6359, I636, I638, I639, I6501, I6502, I6503, I6509, I651, I6521, I6522, I6523, I6529, I658, I659, I6601, I6602, I6603, I6609, I6611, I6612, I6613, I6619, I6621, I6622, I6623, I6629, I663, I668, I669

Table 6. $CHADS_2$-VASc Score

$CHA2DS_2$ –VASc	Point	ICD-9 Codes	ICD-10 Codes
Congestive Heart Failure	1	402.x1, 404.x1, 404.x3, 428.xx	I0981, I110, I132, I501, I5020, I5021, I5022, I5023, I5030, I5031, I5032, I5033, I5040, I5041, I5042, I5043, I509
Hypertension	1	401.xx-405.xx	I10, I110, I119, I120, I129, I130, I1310, I1311, I132, I150, I151, I152, I158, I159, I160, I161, I169, N262
Age ≥75 years	2	-	-
Diabetes mellitus	1	250, 357.2, 362.0, 366.41	E08311, E08319, E083211, E083212, E083213, E083219, E083291, E083292, E083293, E083299, E083311, E083312, E083313, E083319, E083391, E083392, E083393, E083399, E083411, E083412, E083413, E083419, E083491, E083492, E083493, E083499, E083511, E083512, E083513, E083519, E083521, E083522, E083523, E083529, E083531, E083532, E083533, E083539, E083541, E083542, E083543, E083549, E083551, E083552, E083553, E083559, E083591, E083592, E083593, E083599, E0836, E0840, E0842, E09311, E09319, E093211, E093212, E093213, E093219, E093291, E093292, E093293, E093299, E093311, E093312, E093313, E093319, E093391, E093392, E093393, E093399, E093411, E093412, E093413, E093419, E093491, E093492, E093493, E093499, E093511, E093512, E093513, E093519, E093521, E093522, E093523, E093529, E093531, E093532, E093533, E093539, E093541, E093542, E093543, E093549, E093551, E093552, E093553, E093559, E093591, E093592, E093593, E093599, E0936, E0940, E0942, E1010, E1011, E1021, E1022, E1029, E10311, E10319, E103211, E103212, E103213, E103219, E103291, E103292, E103293, E103299, E103311, E103312, E103313, E103319, E103391, E103392,

$CHA2DS_2$ –VASc	Point	ICD-9 Codes	ICD-10 Codes
			E103393, E103399, E103411, E103412, E103413, E103419, E103491, E103492, E103493, E103499, E103511, E103512, E103513, E103519, E103521, E103522, E103523, E103529, E103531, E103532, E103533, E103539, E103541, E103542, E103543, E103549, E103551, E103552, E103553, E103559, E103591, E103592, E103593, E103599, E1036, E1037X1, E1037X2, E1037X3, E1037X9, E1039, E1040, E1041, E1042, E1043, E1044, E1049, E1051, E1052, E1059, E10610, E10618, E10620, E10621, E10622, E10628, E10630, E10638, E10641, E10649, E1065, E1069, E108, E109, E1100, E1101, E1121, E1122, E1129, E11311, E11319, E113211, E113212, E113213, E113219, E113291, E113292, E113293, E113299, E113311, E113312, E113313, E113319, E113391, E113392, E113393, E113399, E113411, E113412, E113413, E113419, E113491, E113492, E113493, E113499, E113511, E113512, E113513, E113519, E113521, E113522, E113523, E113529, E113531, E113532, E113533, E113539, E113541, E113542, E113543, E113549, E113551, E113552, E113553, E113559, E113591, E113592, E113593, E113599, E1136, E1137X1, E1137X2, E1137X3, E1137X9, E1139, E1140, E1141, E1142, E1143, E1144, E1149, E1151, E1152, E1159, E11610, E11618, E11620, E11621, E11622, E11628, E11630, E11638, E11641, E11649, E1165, E1169, E118, E119, E1300, E1301, E1310, E1311, E1321, E1322, E1329, E13311, E13319, E133211, E133212, E133213, E133219, E133291, E133292, E133293, E133299, E133311, E133312, E133313, E133319, E133391, E133392, E133393, E133399, E133411, E133412, E133413,

$CHA2DS_2$ –VASc	Point	ICD-9 Codes	ICD-10 Codes
			E133419, E133491, E133492, E133493, E133499, E133511, E133512, E133513, E133519, E133521, E133522, E133523, E133529, E133531, E133532, E133533, E133539, E133541, E133542, E133543, E133549, E133551, E133552, E133553, E133559, E133591, E133592, E133593, E133599, E1336, E1337X1, E1337X2, E1337X3, E1337X9, E1339, E1340, E1341, E1342, E1343, E1344, E1349, E1351, E1352, E1359, E13610, E13618, E13620, E13621, E13622, E13628, E13630, E13638, E13641, E13649, E1365, E1369, E138, E139, E0851, E0852, E0951, E0952, E1051, E1052, E1151, E1152, E1351, E1352
Stroke (non-hemorrhagic only & transient ischemic attack)	2	V12.54, 433.xx-436.xx	I6300, I63011, I63012, I63013, I63019, I6302, I63031, I63032, I63033, I63039, I6309, I6310, I63111, I63112, I63113, I63119, I6312, I63131, I63132, I63133, I63139, I6319, I6320, I63211, I63212, I63213, I63219, I6322, I63231, I63232, I63233, I63239, I6329, I6330, I63311, I63312, I63313, I63319, I63321, I63322, I63323, I63329, I63331, I63332, I63333, I63339, I63341, I63342, I63343, I63349, I6339, I6340, I63411, I63412, I63413, I63419, I63421, I63422, I63423, I63429, I63431, I63432, I63433, I63439, I63441, I63442, I63443, I63449, I6349, I6350, I63511, I63512, I63513, I63519, I63521, I63522, I63523, I63529, I63531, I63532, I63533, I63539, I63541, I63542, I63543, I63549, I6359, I636, I638, I639, I6501, I6502, I6503, I6509, I651, I6521, I6522, I6523, I6529, I658, I659, I6601, I6602, I6603, I6609, I6611, I6612, I6613, I6619, I6621, I6622, I6623, I6629, I663, I668, I669
Vascular Disease (myocardial infarction, peripheral arterial disease, aortic	1	410.xx, 412, 440.xx, 441.xx, 442.xx, 443.xx, 444.2x, 445.0x	I200, I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I214, I220, I221, I222, I228, I229, I240, I241, I248, I249, I25110, I252, I25700, I25710, I25720, I25730, I25750,

$CHA2DS_2$ –VASc	Point	ICD-9 Codes	ICD-10 Codes
plaque)			I25760, I25790, I670, I700, I701, I70201, I70202, I70203, I70208, I70209, I70211, I70212, I70213, I70218, I70219, I70221, I70222, I70223, I70228, I70229, I70231, I70232, I70233, I70234, I70235, I70238, I70239, I70241, I70242, I70243, I70244, I70245, I70248, I70249, I7025, I70261, I70262, I70263, I70268, I70269, I70291, I70292, I70293, I70298, I70299, I70301, I70302, I70303, I70308, I70309, I70311, I70312, I70313, I70318, I70319, I70321, I70322, I70323, I70328, I70329, I70331, I70332, I70333, I70334, I70335, I70338, I70339, I70341, I70342, I70343, I70344, I70345, I70348, I70349, I7035, I70361, I70362, I70363, I70368, I70369, I70391, I70392, I70393, I70398, I70399, I70401, I70402, I70403, I70408, I70409, I70411, I70412, I70413, I70418, I70419, I70421, I70422, I70423, I70428, I70429, I70431, I70432, I70433, I70434, I70435, I70438, I70439, I70441, I70442, I70443, I70444, I70445, I70448, I70449, I7045, I70461, I70462, I70463, I70468, I70469, I70491, I70492, I70493, I70498, I70499, I70501, I70502, I70503, I70508, I70509, I70511, I70512, I70513, I70518, I70519, I70521, I70522, I70523, I70528, I70529, I70531, I70532, I70533, I70534, I70535, I70538, I70539, I70541, I70542, I70543, I70544, I70545, I70548, I70549, I7055, I70561, I70562, I70563, I70568, I70569, I70591, I70592, I70593, I70598, I70599, I70601, I70602, I70603, I70608, I70609, I70611, I70612, I70613, I70618, I70619, I70621, I70622, I70623, I70628, I70629, I70631, I70632, I70633, I70634, I70635, I70638, I70639, I70641, I70642, I70643, I70644, I70645, I70648, I70649, I7065, I70661, I70662, I70663, I70668, I70669, I70691, I70692, I70693, I70698, I70699,

$CHA2DS_2$ –VASc	Point	ICD-9 Codes	ICD-10 Codes
			I70701, I70702, I70703, I70708, I70709, I70711, I70712, I70713, I70718, I70719, I70721, I70722, I70723, I70728, I70729, I70731, I70732, I70733, I70734, I70735, I70738, I70739, I70741, I70742, I70743, I70744, I70745, I70748, I70749, I7075, I70761, I70762, I70763, I70768, I70769, I70791, I70792, I70793, I70798, I70799, I708, I7090, I7091, I7092, I7100, I7101, I7102, I7103, I711, I712, I713, I714, I715, I716, I718, I719, I720, I721, I722, I723, I724, I725, I726, I728, I729, I7300, I7301, I731, I7381, I7389, I739, I742, I743, I744, I75011, I75012, I75013, I75019, I75021, I75022, I75023, I75029, I7770, I7771, I7772, I7773, I7774, I7775, I7776, I7777, I7779, I790, I791, I798
Age	1	Age 65-75 years	-
Sex Category	1 (Female)	-	-

Table 7. HAS-BLED Score

HAS-BLED	Point	ICD-9 Codes	ICD-10 Codes
Hypertension	1 point	401.xx-405.xx	I10, I110, I119, I120, I129, I130, I1310, I1311, I132, I150, I151, I152, I158, I159, I160, I161, I169, N262
Abnormal kidney and/or liver function:	1 point each	Kidney: 580.xx-589.xx	B520, E0821, E0822, E0829, E0921, E0922, E0929, M3214, M3215, M3504, N000, N001, N002, N003, N004, N005, N006, N007, N008, N009, N010, N011, N012, N013, N014, N015, N016, N017, N018, N019, N020, N021, N022, N023, N024, N025, N026, N027, N030, N031, N032, N033, N034, N035, N036, N037, N038, N039, N040, N041, N042, N043, N044, N045, N046, N047, N048, N049, N050, N051, N052, N053, N054, N055, N056, N057, N058, N059, N060, N061, N062, N063, N064, N065, N066, N067, N068, N069, N070, N071, N072, N073, N074, N075, N076, N077, N078, N079, N08, N140, N141, N142, N143, N144, N150, N158, N159, N16, N170, N171, N172, N178, N179, N181, N182, N183, N184, N185, N186, N189, N19, N250, N251, N2581, N2589, N259, N261, N269, N270, N271, N279
Age ≥75 years	2	Liver: 570.xx-573.xx	B251, K700, K7010, K7011, K702, K7030, K7031, K7040, K7041, K709, K710, K7110, K7111, K712, K713, K714, K7150, K7151, K716, K717, K718, K719, K7200, K7201, K7210, K7211, K7290, K7291, K730, K731, K732, K738, K739, K740, K741, K742, K743, K744, K745, K7460, K7469, K750, K751, K752, K753, K754, K7581, K7589, K759, K760, K761, K762, K763, K764, K765, K766, K767, K7681, K7689, K769, K77
Stroke	1 point	History of stroke V12.54, 433.xx-436.xx	G450, G451, G452, G458, G459, G460, G461, G462, I6300, I63011, I63012, I63013, I63019, I6302, I63031, I63032, I63033, I63039, I6309, I6310, I63111, I63112,

HAS-BLED	Point	ICD-9 Codes	ICD-10 Codes
			I63113, I63119, I6312, I63131, I63132, I63133, I63139, I6319, I6320, I63211, I63212, I63213, I63219, I6322, I63231, I63232, I63233, I63239, I6329, I6330, I63311, I63312, I63313, I63319, I63321, I63322, I63323, I63329, I63331, I63332, I63333, I63339, I63341, I63342, I63343, I63349, I6339, I6340, I63411, I63412, I63413, I63419, I63421, I63422, I63423, I63429, I63431, I63432, I63433, I63439, I63441, I63442, I63443, I63449, I6349, I6350, I63511, I63512, I63513, I63519, I63521, I63522, I63523, I63529, I63531, I63532, I63533, I63539, I63541, I63542, I63543, I63549, I6359, I636, I638, I639, I6501, I6502, I6503, I6509, I651, I6521, I6522, I6523, I6529, I658, I659, I6601, I6602, I6603, I6609, I6611, I6612, I6613, I6619, I6621, I6622, I6623, I6629, I663, I668, I669, I67841, I67848, Z8673
Bleeding	1 point	Baseline bleeding (Table 12) and 280.xx-286.xx	A985, D500, D508, D509, D510, D511, D512, D513, D518, D519, D520, D521, D528, D529, D530, D531, D532, D538, D539, D550, D551, D552, D553, D558, D559, D560, D561, D562, D563, D565, D568, D569, D5700, D5701, D5702, D571, D5720, D57211, D57212, D57219, D573, D5740, D57411, D57412, D57419, D5780, D57811, D57812, D57819, D580, D581, D582, D588, D589, D590, D591, D592, D593, D594, D595, D596, D598, D599, D600, D601, D608, D609, D6101, D6109, D611, D612, D613, D61810, D61811, D61818, D6182, D6189, D619, D62, D62, D630, D631, D638, D640, D641, D642, D643, D644, D6481, D6489, D649, D65, D66, D67, D680, D681, D682, D68311, D68312, D68318, D6832, D684, D688, D689, D7801, D7802, D7821, D7822, E3601, E3602, E89810, E89811, G9731, G9732,

HAS-BLED	Point	ICD-9 Codes	ICD-10 Codes
			G9751, G9752, H05231, H05232, H05233, H05239, H1130, H1131, H1132, H1133, H2100, H2101, H2102, H2103, H31301, H31302, H31303, H31309, H31311, H31312, H31313, H31319, H31411, H31412, H31413, H31419, H3560, H3561, H3562, H3563, H35731, H35732, H35733, H35739, H4310, H4311, H4312, H4313, H44811, H44812, H44813, H44819, H47021, H47022, H47023, H47029, H59111, H59112, H59113, H59119, H59121, H59122, H59123, H59129, H59311, H59312, H59313, H59319, H59321, H59322, H59323, H59329, H61121, H61122, H61123, H61129, H9521, H9522, H9541, H9542, I312, I6000, I6001, I6002, I6010, I6011, I6012, I602, I6030, I6031, I6032, I604, I6050, I6051, I6052, I606, I607, I608, I609, I610, I611, I612, I613, I614, I615, I616, I618, I619, I6200, I6201, I6202, I6203, I621, I629, I8501, I8511, I97410, I97411, I97418, I9742, I97610, I97611, I97618, I97620, J9561, J9562, J95830, J95831, K2211, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K2901, K2921, K2931, K2941, K2951, K2961, K2971, K2981, K2991, K31811, K3182, K5521, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K625, K6381, K640, K641, K642, K643, K648, K661, K9161, K9162, K91840, K91841, K920, K921, K922, L7601, L7602, L7621, L7622, M2500, M25011, M25012, M25019, M25021, M25022, M25029, M25031, M25032, M25039, M25041, M25042, M25049, M25051, M25052, M25059, M25061, M25062,

HAS-BLED	Point	ICD-9 Codes	ICD-10 Codes
			M25069, M25071, M25072, M25073, M25074, M25075, M25076, M2508, M96810, M96811, M96830, M96831, N421, N837, N857, N920, N9961, N9962, N99820, N99821, R040, R041, R042, R0489, R049, R310, R319, R58, R710, S0190XA, S062X0A, S062X1A, S062X2A, S062X3A, S062X4A, S062X5A, S062X6A, S062X7A, S062X8A, S062X9A, S06300A, S06301A, S06302A, S06303A, S06304A, S06305A, S06306A, S06307A, S06308A, S06309A, S06340A, S06341A, S06342A, S06343A, S06344A, S06345A, S06346A, S06347A, S06348A, S06349A, S06350A, S06351A, S06352A, S06353A, S06354A, S06355A, S06356A, S06357A, S06358A, S06359A, S06360A, S06361A, S06362A, S06363A, S06364A, S06365A, S06366A, S06367A, S06368A, S06369A, S064X0A, S064X1A, S064X2A, S064X3A, S064X4A, S064X5A, S064X6A, S064X7A, S064X8A, S064X9A, S065X0A, S065X1A, S065X2A, S065X3A, S065X4A, S065X5A, S065X6A, S065X7A, S065X8A, S065X9A, S066X0A, S066X1A, S066X2A, S066X3A, S066X4A, S066X5A, S066X6A, S066X7A, S066X8A, S066X9A, S06890A, S06891A, S06892A, S06893A, S06894A, S06895A, S06896A, S06897A, S06898A, S06899A, S069X0A, S069X1A, S069X2A, S069X3A, S069X4A, S069X5A, S069X6A, S069X7A, S069X8A, S069X9A, S36112A, S37021A, S37022A, S37029A, T792XXA
Labile INR	Not applicable	Not measurable.	Not applicable
Elderly	1 point for age 65 or older	65+ years	65+ years
Alcohol/ Drug Therapy	1 point	303.xx, 305.0x, V11.3x Antiplatelets administered (abciximab, anagrelide HCL, aspirin, aspirin/dipyridamole,	F1010, F10120, F10129, F1020, F1021, F10220, F10229

HAS-BLED	Point	ICD-9 Codes	ICD-10 Codes
		cilostazol, clopidogrel, dipyridamole, eptifibatide, prasugrel, ticagrelor, ticlopidine, tirofiban) NSAIDs administered (bromfenac, celecoxib, diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, lansoprazole/naproxen, meclofenamate, mefenamic acid, meloxicam, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin)	

Table 8. Baseline Medication List

Mechanism of Action	Drug	
Angiotensin converting enzyme inhibitor	Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Ramipril, Trandolapril	
Amiodarone	Amiodarone	
Angiotensin receptor blocker	Azilsartan, Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan	
Beta blockers	Acebutolol, Atenolol, Betaxolol, Bisoprolol, Esmolol, Carteolol, Carvedeolol, Labetalol, Levobunolol, Metipranolol, Metoprolol, Nebivolol, Nadolol, Penbutolol, Pinodolol, Propranolol, Sotalal, Timolol,	
H2-receptor antagonist	Burimamide, Cimetidine, Ebrotidine, Famotidine, Metiamide, Nizatidine, Ranitidine	
Proton pump inhibitor	Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole, Dexlansoprazole, Esomeprazole	
Statins	Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin.	
Anti-platelets	Aspirin, Clopidogrel, Prasugrel, Ticlopidine, Cilostazol, Abciximab, Epifibatide, Tirofiban, Dipyridamole, Ticagrelor	
Inhibitors of Warfarin	CYP2C9 inhibitors	amiodarone, capecitabine, cotrimoxazole, etravirine, fluconazole, fluvastatin, fluvoxamine, metronidazole, miconazole, oxandrolone, sulfinpyrazone, tigecycline, voriconazole, zafirlukast
	CYP1A2 inhibitors	acyclovir, allopurinol, caffeine, cimetidine, ciprofloxacin, disulfiram, enoxacin, famotidine, fluvoxamine, methoxsalen, mexiletine, norfloxacin, oral contraceptives (ethinyl estradiol, levonorgestrel, desogestrel, norethindrone, norgestrel, mestranol,

Mechanism of Action	Drug	
		drospirenone), phenylpropanolamine, propafenone, propranolol, terbinafine, thiabendazole, ticlopidine, verapamil, zileuton
	CYP3A4 inhibitors	alprazolam, amiodarone, amlodipine, amprenavir, aprepitant, atorvastatin, atazanavir, bicalutamide, cilostazol, cimetidine, ciprofloxacin, clarithromycin, conivaptan, cyclosporine, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fluoxetine, fluvoxamine, fosamprenavir, imatinib, indinavir, isoniazid, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, nilotinib, oral contraceptives (ethinyl estradiol, levonorgestrel, desogestrel, norethindrone, norgestrel, mestranol, drospirenone), posaconazole, ranitidine, ranolazine, ritonavir, saquinavir, telithromycin, tipranavir, voriconazole, zileuton
Inducers of Warfarin	CYP2C9 inducers	aprepitant, bosentan, carbamazepine, phenobarbital, rifampin
	CYP1A2 inducers	montelukast, moricizine, omeprazole, phenobarbital, phenytoin
	CYP3A4 inducers	armodafinil, amprenavir, aprepitant, bosentan, carbamazepine, efavirenz, etravirine, modafinil, nafcillin, phenytoin, prednisone, rifampin, rufinamide
Dronedarone	dronedarone	
Digoxin	digoxin; J1160; J1162	
Calcium Channel Blockers	diltiazem, felodipine, Isradipine, nicardipine, nisoldipine, verapamil, amlodipine, bepridil, clevidipine, mibefradil, nifedipine and nimodipine	
Renin Angiotensin System Antagonists	benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan, azilsartan, candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan, eplerenone, spironolactone	
Glucocorticoids [oral and injectable]	beclomethasone, betamethasone, budesonide, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone	
Diuretics	acetazolamide, methazolamide, bumetanide, ethacrynic acid, torsemide, furosemide, pamabrom, eplerenone, triamterene, spironolactone, amiloride, indapamide, hydrochlorothiazide, chlorthalidone, metolazone, methyclothiazide, bendroflumethiazide, polythiazide	
Metformin	Metformin	
Sulfonylureas	acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, tolazamide, tolbutamide	
Thiazolidinedione	pioglitazone, rosiglitazone	
Insulin	insulin	

Mechanism of Action	Drug
Other Diabetes Drugs	exenatide, liraglutide, dulaglutide, repaglinide, sitagliptin, saxagliptin, linagliptin, alogliptin, nateglinide, acarbose, miglitol, canagliflozin, dapagliflozin, empagliflozin, pramlintide
Antiulcer Agents	nitzatidine, sucralfate, misoprostol, famotidine, omeprazole, cimetidine, ranitidine hydrochloride, Dexlansoprazole, Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole, Burimamide, Ebrotidine, Metiamide, Cisapride, Pirenzepine, Propantheline, Roxatidine acetate
Antidepressant	citalopram, escitalopram, paroxetine, fluoxetine, fluvoxamine, sertraline, desvenlafaxine, duloxetine, levomilnacipran, milnacipran, venlafaxine, vilazodone, vortioxetine, nefazodone, trazodone, reboxetine, teniloxazine, viloxazine, bupropion, amitriptyline, amitriptylinoxide, clomipramine, desipramine, dibenzepin, dimetacrine, dosulepin, doxepin, imipramine, lofepramine, melitracen, nitroxazepine, nortriptyline, noxiptiline, opipramol, pipofezine, protriptyline, trimipramine, amoxapine, maprotiline, mianserin, mirtazapine, setiptiline, isocarboxazid, phenelzine, tranylcypromine, selegiline, caroxazone, metralindole, moclobemide, pirlindole, toloxatone, bifemelane, amisulpride, lurasidone, quetiapine, aripiprazole, brexpiprazole, lurasidone, olanzapine, quetiapine, risperidone, lithium

Table 9. Bariatric Surgery Codes

Type	Codes	Description
CPT	43842	Gastric restrictive procedure without gastric bypass for morbid obesity; vertical-banded gastroplasty
	43843	Gastric restrictive procedure without gastric bypass for morbid obesity; other than vertical-banded gastroplasty
	43846	Gastric restrictive procedure with gastric bypass for morbid obesity with short limb Roux-en-y gastroenterostomy
	43847	Gastric restrictive procedure with gastric bypass for morbid obesity with small intestine reconstruction to limit absorption
	43848	Revision of gastric restrictive procedure for morbid obesity
	43659	Unlisted laparoscopic procedure, stomach
	43644	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and Roux-en-Y gastroenterostomy
	43844	Laparoscopic gastric restrictive procedure with gastric bypass and Roux- en-Y gastroenterostomy
	S2085	laparoscopic gastric bypass
	43645	Laparoscopy, surgical, gastric restrictive procedure; with gastric bypass and small intestine reconstruction to limit absorption
	43770	Laparoscopy, surgical, gastric restrictive procedure; placement of adjustable gastric band

Type	Codes	Description
	43771	Revision of adjustable gastric band component only
	43773	Laparoscopy, surgical, gastric restrictive procedure; removal and replacement of adjustable gastric restrictive device component only
	S2082	Laparoscopy, surgical; gastric restrictive procedure, adjustable gastric band includes placement of subcutaneous port
ICD-9 diagnosis	V45.86	Bariatric surgery status
ICD-10 diagnosis	Z98.84	Bariatric surgery status
ICD-9 procedure	43.89	Open and other partial gastrectomy
	44.31	High gastric bypass
	44.38	Laparoscopic gastroenterostomy
	44.39	Other gastroenterostomy without gastrectomy
	44.68	Laparoscopic gastroplasty
	44.95	Laparoscopic gastric restrictive procedure
	44.96	Laparoscopic Revision of Gastric Restrictive Procedure
	44.97	Laparoscopic Removal of Gastric Restrictive Device(s)
	44.99	Other Operations on Stomach
	44.5	Revision of Gastric Anastomosis
	45.51	Isolation of Segment of Small Intestine
	45.9	Intestinal Anastomosis
ICD-10 procedure	0D16079	Bypass Stomach to Duodenum with Autologous Tissue Substitute, Open Approach
	0D1607A	Bypass Stomach to Jejunum with Autologous Tissue Substitute, Open Approach
	0D160J9	Bypass Stomach to Duodenum with Synthetic Substitute, Open Approach
	0D160JA	Bypass Stomach to Jejunum with Synthetic Substitute, Open Approach
	0D160K9	Bypass Stomach to Duodenum with Nonautologous Tissue Substitute, Open Approach
	0D160KA	Bypass Stomach to Jejunum with Nonautologous Tissue Substitute, Open Approach
	0D160Z9	Bypass Stomach to Duodenum, Open Approach
	0D160ZA	Bypass Stomach to Jejunum, Open Approach
	0D160ZB	Bypass Stomach to Ileum, Open Approach
	0D16479	Bypass Stomach to Duodenum with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0D1647A	Bypass Stomach to Jejunum with Autologous Tissue Substitute,

Type	Codes	Description
		Percutaneous Endoscopic Approach
	0D164J9	Bypass Stomach to Duodenum with Synthetic Substitute, Percutaneous Endoscopic Approach
	0D164JA	Bypass Stomach to Jejunum with Synthetic Substitute, Percutaneous Endoscopic Approach
	0D164K9	Bypass Stomach to Duodenum with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0D164KA	Bypass Stomach to Jejunum with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0D164Z9	Bypass Stomach to Duodenum, Percutaneous Endoscopic Approach
	0D164ZA	Bypass Stomach to Jejunum, Percutaneous Endoscopic Approach
	0D16879	Bypass Stomach to Duodenum with Autologous Tissue Substitute, Via Natural or Artificial Opening Endoscopic
	0D1687A	Bypass Stomach to Jejunum with Autologous Tissue Substitute, Via Natural or Artificial Opening Endoscopic
	0D168J9	Bypass Stomach to Duodenum with Synthetic Substitute, Via Natural or Artificial Opening Endoscopic
	0D168JA	Bypass Stomach to Jejunum with Synthetic Substitute, Via Natural or Artificial Opening Endoscopic
	0D168K9	Bypass Stomach to Duodenum with Nonautologous Tissue Substitute, Via Natural or Artificial Opening Endoscopic
	0D168KA	Bypass Stomach to Jejunum with Nonautologous Tissue Substitute, Via Natural or Artificial Opening Endoscopic
	0D168Z9	Bypass Stomach to Duodenum, Via Natural or Artificial Opening Endoscopic
	0D168ZA	Bypass Stomach to Jejunum, Via Natural or Artificial Opening Endoscopic
	0DB60ZZ	Excision of Stomach, Open Approach
	0DB63ZZ	Excision of Stomach, Percutaneous Approach
	0DB67ZZ	Excision of Stomach, Via Natural or Artificial Opening
	0DB80ZZ	Excision of Small Intestine, Open Approach
	0DB90ZZ	Excision of Duodenum, Open Approach
	0DBB0ZZ	Excision of Ileum, Open Approach
	0DP643Z	Removal of Infusion Device from Stomach, Percutaneous Endoscopic Approach
	0DP64CZ	Removal of Extraluminal Device from Stomach, Percutaneous Endoscopic Approach
	0DQ60ZZ	Repair Stomach, Open Approach

Type	Codes	Description
	0DQ63ZZ	Repair Stomach, Percutaneous Approach
	0DQ64ZZ	Repair Stomach, Percutaneous Endoscopic Approach
	0DQ67ZZ	Repair Stomach, Via Natural or Artificial Opening
	0DQ68ZZ	Repair Stomach, Via Natural or Artificial Opening Endoscopic
	0DV64CZ	Restriction of Stomach with Extraluminal Device, Percutaneous Endoscopic Approach
	0DW643Z	Revision of Infusion Device in Stomach, Percutaneous Endoscopic Approach
	0DW64CZ	Revision of Extraluminal Device in Stomach, Percutaneous Endoscopic Approach
	0D190Z9	Bypass Duodenum to Duodenum, Open Approach
	0D190ZA	Bypass Duodenum to Jejunum, Open Approach
	0D190ZB	Bypass Duodenum to Ileum, Open Approach
	0D190ZL	Bypass Duodenum to Transverse Colon, Open Approach
	0D194Z9	Bypass Duodenum to Duodenum, Percutaneous Endoscopic Approach
	0D194ZA	Bypass Duodenum to Jejunum, Percutaneous Endoscopic Approach
	0D194ZB	Bypass Duodenum to Ileum, Percutaneous Endoscopic Approach
	0D194ZL	Bypass Duodenum to Transverse Colon, Percutaneous Endoscopic Approach
	0D198Z9	Bypass Duodenum to Duodenum, Via Natural or Artificial Opening Endoscopic
	0D198ZA	Bypass Duodenum to Jejunum, Via Natural or Artificial Opening Endoscopic
	0D198ZB	Bypass Duodenum to Ileum, Via Natural or Artificial Opening Endoscopic
	0D198ZL	Bypass Duodenum to Transverse Colon, Via Natural or Artificial Opening Endoscopic
	0D1A0ZA	Bypass Jejunum to Jejunum, Open Approach
	0D1A0ZB	Bypass Jejunum to Ileum, Open Approach
	0D1A0ZH	Bypass Jejunum to Cecum, Open Approach
	0D1A0ZK	Bypass Jejunum to Ascending Colon, Open Approach
	0D1A0ZL	Bypass Jejunum to Transverse Colon, Open Approach
	0D1A0ZM	Bypass Jejunum to Descending Colon, Open Approach
	0D1A0ZN	Bypass Jejunum to Sigmoid Colon, Open Approach
	0D1A0ZP	Bypass Jejunum to Rectum, Open Approach
	0D1A4ZA	Bypass Jejunum to Jejunum, Percutaneous Endoscopic Approach

Type	Codes	Description
	0D1A4ZB	Bypass Jejunum to Ileum, Per cutaneous Endoscopic Approach
	0D1A4ZH	Bypass Jejunum to Cecum, Per cutaneous Endoscopic Approach
	0D1A4ZK	Bypass Jejunum to Ascending Colon, Percutaneous Endoscopic Approach
	0D1A4ZL	Bypass Jejunum to Transverse Colon, Percutaneous Endoscopic Approach
	0D1A4ZM	Bypass Jejunum to Descending Colon, Percutaneous Endoscopic Approach
	0D1A4ZN	Bypass Jejunum to Sigmoid Colon, Percutaneous Endoscopic Approach
	0D1A4ZP	Bypass Jejunum to Rectum, Percutaneous Endoscopic Approach
	0D1A8ZA	Bypass Jejunum to Jejunum, Via Natural or Artificial Opening Endoscopic
	0D1A8ZB	Bypass Jejunum to Ileum, Via Natural or Artificial Opening Endoscopic
	0D1A8ZH	Bypass Jejunum to Cecum, Via Natural or Artificial Opening Endoscopic
	0D1A8ZK	Bypass Jejunum to Ascending Colon, Via Natural or Artificial Opening Endoscopic
	0D1A8ZL	Bypass Jejunum to Transverse Colon, Via Natural or Artificial Opening Endoscopic
	0D1A8ZM	Bypass Jejunum to Descending Colon, Via Natural or Artificial Opening Endoscopic
	0D1A8ZN	Bypass Jejunum to Sigmoid Colon, Via Natural or Artificial Opening Endoscopic
	0D1A8ZP	Bypass Jejunum to Rectum, Via Natural or Artificial Opening Endoscopic
	0D1B0ZB	Bypass Ileum to Ileum, Open Approach
	0D1B0ZH	Bypass Ileum to Cecum, Open Approach
	0D1B0ZK	Bypass Ileum to Ascending Colon, Open Approach
	0D1B0ZL	Bypass Ileum to Transvers e Colon, Open Approach
	0D1B0ZM	Bypass Ileum to Descending Colon, Open Approach
	0D1B4ZN	Bypass Ileum to Sigmoid Colon, Percutaneous Endoscopic Approach
	0D1B4ZP	Bypass Ileum to Rectum, Percutaneous Endoscopic Approach
	0D1B4ZQ	Bypass Ileum to Anus, Percutaneous Endoscopic Approach
	0D1B8ZB	Bypass Ileum to Ileum, Via Natural or Artificial Opening Endoscopic
	0D1B8ZH	Bypass Ileum to Cecum, Vi a Natural or Artificial Opening Endoscopic

Type	Codes	Description
	0D1B8ZK	Bypass Ileum to Ascending Colon, Via Natural or Artificial Opening Endoscopic
	0D1B8ZL	Bypass Ileum to Transvers e Colon, Via Natural or Artificial Opening Endoscopic
	0D1B8ZM	Bypass Ileum to Descending Colon, Via Natural or Artificial Opening Endoscopic
	0D1B8ZN	Bypass Ileum to Sigmoid Colon, Via Natural or Artificial Opening Endoscopic
	0D1B8ZP	Bypass Ileum to Rectum, Via Natural or Artificial Opening Endoscopic
	0D1B8ZQ	Bypass Ileum to Anus, Via Natural or Artificial Opening Endoscopic

Table 10. Charlson Comorbidity Index Score Calculation

Condition	ICD-9 Code(s)	ICD-10 Code(s)	Point
Myocardial Infarction	410.xx; 412.xx	I21, I22, I252	1
Congestive Heart Failure	428.xx	I43, I50, I099, I110, I130, I132, I255, I420, I425, I426, I427, I428, I429, P290	1
Peripheral vascular disease	441.xx; 443.9x; 785.4x; v43.4x, procedure: 38.48	I70, I71, I731, I738, I739, I771, I790, I792, K551, K558, K559, Z958, Z959	1
Cerebrovascular disease	430.xx-438.99 Modified to remove 430.xx-432.xx	G45, G46, I60, I61, I62, I63, I64, I65, I66, I67, I68, I69, H340	1
Dementia	290.xx	F00, F01, F02, F03, G30, F051, G311	1
Chronic obstructive pulmonary disease	490.xx-496.99; 500.xx-505.99; 506.4x	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, I278, I279, J684, J701, J703	1
Rheumatologic disease	710.0x-710.19; 710.4x-; 714.0x-714.29; 714.81; 725.xx	M05, M32, M33, M34, M06, M315, M351, M353, M360	1
Peptic ulcer disease	531.0x-531.79; 532.4x-532.79; 533.4x-533.79; 534.0x-534.79; 531.9x; 532.9x; 533.9x; 534.9x Modified to remove: 531.00, 531.01, 531.20, 531.21, 531.40, 531.41, 531.60, 531.61 532.40, 532.41, 532.60, 532.61 533.40, 533.41, 533.60, 533.61, 534.00, 534.01, 534.20, 534.21, 534.40, 534.41, 534.60, 534.61	K25, K26, K27, K28	1

Condition	ICD-9 Code(s)	ICD-10 Code(s)	Point
Mild liver disease	571.2x; 571.4x-571.69	B18, K73, K74, K700, K701, K702, K703, K709, K717, K713, K714, K715, K760, K762, K763, K764, K768, K769, Z944	1
Diabetes (mild to moderate)	250.0x-250.39, 250.7x	E100, E101, E106, E108, E109, E110, E111, E116, E118, E119, E120, E121, E126, E128, E129, E130, E131, E136, E138, E139, E140, E141, E146, E148, E149	1
Diabetes + complications	250.4x-250.69	E102, E103, E104, E105, E107, E112, E113, E114, E115, E117, E122, E123, E124, E125, E127, E132, E133, E134, E135, E137, E142, E143, E144, E145, E147	2
Hemiplegia or paraplegia	342.xx; 344.1x	G81, G82, G041, G114, G801, G802, G830, G831, G832, G833, G834, G839	2
Renal disease	582.xx; 583.0x-583.79; 585.xx-586.99; 588.xx	N18, N19, N052, N053, N054, N055, N056, N057, N250, I120, I131, N032, N033, N034, N035, N036, N037, Z490, Z491, Z492, Z940, Z992	2
Any malignancy, including lymphoma and leukemia	140.xx-172.99; 174.xx-195.99; 200.xx-208.99	C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C81, C82, C83, C84, C85, C88, C90, C91, C92, C93, C94, C95, C96, C97	2
Moderate/severe liver disease	456.0x-456.29; 572.2x-572.89 Modified to remove: 456.0x, 456.20	K704, K711, K721, K729, K765, K766, K767, I850, I859, I864, I982	3
Metastatic solid tumor	196.xx-199.99	C77, C78, C79, C80	6
AIDS	042.xx-044.99	B20, B21, B22, B24	6

Table 11. Baseline Comorbidities

Covariates	ICD-9-CM/CPT/HCPCS Codes	ICD-10-CM Codes
History Stroke/SE	Same as the outcome stroke/SE (Table 12)	Same as the outcome stroke/SE (Table 12)
History of Bleeding	Same as the outcome major bleeding (Table 12)	Same as the outcome major bleeding (Table 12)
Congestive Heart Failure (CHF)	398.91, 402.x1, 404.x3, 428.xx	I0981, I110, I132, I501, I5020, I5021, I5022, I5023, I5030, I5031, I5032, I5033, I5040, I5041, I5042, I5043, I509
Diabetes	250.xx, 357.2, 362.0, 366.41	E08311, E08319, E083211, E083212, E083213, E083219, E083291, E083292, E083293, E083299, E083311, E083312, E083313, E083319, E083391, E083392, E083393, E083399, E083411, E083412, E083413, E083419, E083491, E083492, E083493, E083499, E083511, E083512, E083513, E083519, E083521, E083522, E083523, E083529, E083531, E083532, E083533, E083539, E083541, E083542, E083543, E083549, E083551, E083552, E083553, E083559, E083591, E083592, E083593, E083599, E0836, E0840, E0842, E09311, E09319, E093211, E093212, E093213, E093219, E093291, E093292, E093293, E093299, E093311, E093312, E093313, E093319, E093391, E093392, E093393, E093399, E093411, E093412, E093413, E093419, E093491, E093492, E093493, E093499, E093511, E093512, E093513, E093519, E093521, E093522, E093523, E093529, E093531, E093532, E093533, E093539, E093541, E093542, E093543, E093549, E093551, E093552, E093553, E093559, E093591, E093592, E093593, E093599, E0936, E0940, E0942, E1010, E1011, E1021, E1022, E1029, E10311, E10319, E103211, E103212, E103213, E103219, E103291, E103292, E103293, E103299, E103311, E103312, E103313, E103319, E103391, E103392, E103393, E103399, E103411, E103412, E103413, E103419, E103491, E103492, E103493, E103499, E103511, E103512, E103513, E103519, E103521, E103522, E103523, E103529, E103531, E103532, E103533, E103539, E103541, E103542, E103543, E103549, E103551, E103552, E103553, E103559, E103591, E103592, E103593, E103599, E1036, E1037X1, E1037X2, E1037X3, E1037X9, E1039, E1040, E1041, E1042, E1043, E1044, E1049, E1051, E1052, E1059, E10610, E10618, E10620, E10621, E10622, E10628, E10630, E10638, E10641, E10649, E1065, E1069, E108, E109, E1100, E1101, E1121, E1122, E1129, E11311, E11319, E113211, E113212, E113213, E113219, E113291, E113292, E113293, E113299, E113311, E113312,

Covariates	ICD-9-CM/CPT/HCPCS Codes	ICD-10-CM Codes
		E113313, E113319, E113391, E113392, E113393, E113399, E113411, E113412, E113413, E113419, E113491, E113492, E113493, E113499, E113511, E113512, E113513, E113519, E113521, E113522, E113523, E113529, E113531, E113532, E113533, E113539, E113541, E113542, E113543, E113549, E113551, E113552, E113553, E113559, E113591, E113592, E113593, E113599, E1136, E1137X1, E1137X2, E1137X3, E1137X9, E1139, E1140, E1141, E1142, E1143, E1144, E1149, E1151, E1152, E1159, E11610, E11618, E11620, E11621, E11622, E11628, E11630, E11638, E11641, E11649, E1165, E1169, E118, E119, E1300, E1301, E1310, E1311, E1321, E1322, E1329, E13311, E13319, E133211, E133212, E133213, E133219, E133291, E133292, E133293, E133299, E133311, E133312, E133313, E133319, E133391, E133392, E133393, E133399, E133411, E133412, E133413, E133419, E133491, E133492, E133493, E133499, E133511, E133512, E133513, E133519, E133521, E133522, E133523, E133529, E133531, E133532, E133533, E133539, E133541, E133542, E133543, E133549, E133551, E133552, E133553, E133559, E133591, E133592, E133593, E133599, E1336, E1337X1, E1337X2, E1337X3, E1337X9, E1339, E1340, E1341, E1342, E1343, E1344, E1349, E1351, E1352, E1359, E13610, E13618, E13620, E13621, E13622, E13628, E13630, E13638, E13641, E13649, E1365, E1369, E138, E139, E0851, E0852, E0951, E0952, E1051, E1052, E1151, E1152, E1351, E1352, E1359, E13610, E13618, E13620, E13621, E13622, E13628, E13630, E13638, E13641, E13649, E1365, E1369, E138, E139
Hypertension	401.xx -405.xx	I10, I110, I119, I120, I129, I130, I1310, I1311, I132, I150, I151, I152, I158, I159, I160, I161, I169, N262
Renal Disease	582.xx; 583.0x-583.79; 585.xx-586.99; 588.xx	B520, E0821, E0822, E0829, E0921, E0922, E0929, I120, I129, I130, I1310, I1311, I132, M3214, M3215, M3504, N000, N001, N002, N003, N004, N005, N006, N007, N008, N009, N010, N011, N012, N013, N014, N015, N016, N017, N018, N019, N020, N021, N022, N023, N024, N025, N026, N027, N028, N029, N030, N031, N032, N033, N034, N035, N036, N037, N038, N039, N040, N041, N042, N043, N044, N045, N046, N047, N048, N049, N050, N051, N052, N053, N054, N055, N056, N057, N058, N059, N060, N061, N062, N063, N064, N065, N066,

Covariates	ICD-9-CM/CPT/HCPCS Codes	ICD-10-CM Codes
		N067, N068, N069, N070, N071, N072, N073, N074, N075, N076, N077, N078, N079, N08, N140, N141, N142, N143, N144, N150, N158, N159, N16, N170, N171, N172, N178, N179, N181, N182, N183, N184, N185, N186, N189, N19, Z992, Z9115, Z4931, Z4901, Z4902, Z4931, Z4932, Z4932 Procedure codes: 5A1D00Z, 5A1D60Z, 05HY33Z, 06HY33Z, 03130ZD, 03140ZD, 03150ZD, 03160ZD, 03170ZD, 03180ZD, 03190ZF, 031A0ZF, 031B0ZF, 031C0ZF, 031209D, 031209F, 03120AD, 03120AF, 03120JD, 03120JF, 03120KD, 03120KF, 03120ZD, 03120ZF, 031309D, 031309F, 03130AD, 03130AF, 03130JD, 03130JF, 03130KD, 03130KF, 03130ZD, 03130ZF, 031409D, 031409F, 03140AD, 03140AF, 03140JD, 03140JF, 03140KD, 03140KF, 03140ZD, 03140ZF, 031509D, 031509F, 03150AD, 03150AF, 03150JD, 03150JF, 03150KD, 03150KF, 03150ZD, 03150ZF, 031609D, 031609F, 03160AD, 03160AF, 03160JD, 03160JF, 03160KD, 03160KF, 03160ZD, 03160ZF, 031709D, 031709F, 03170AD, 03170AF, 03170JD, 03170JF, 03170KD, 03170KF, 03170ZD, 03170ZF, 031809D, 031809F, 03180AD, 03180AF, 03180JD, 03180JF, 03180KD, 03180KF, 03180ZD, 03180ZF, 031909F, 03190AF, 03190JF, 03190KF, 03190ZF, 031A09F, 031A0AF, 031A0JF, 031A0KF, 031A0ZF, 031B09F, 031B0AF, 031B0JF, 031B0KF, 031B0ZF, 031C09F, 031C0AF, 031C0JF, 031C0KF, 031C0ZF, 03PY07Z, 03PY0JZ, 03PY0KZ, 03PY37Z, 03PY3JZ, 03PY3KZ, 03PY47Z, 03PY4JZ, 03PY4KZ, 03130JD, 03140JD, 03150JD, 03160JD, 03170JD, 03180JD, 03190JF, 031A0JF, 031B0JF, 031C0JF, 3E1M39Z
Liver Disease	570-573	K70-K77
Myocardial Infarction	410.xx, 412.xx	I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I214, I220, I221, I222, I228, I229, I252
Dyspepsia or Stomach Discomfort	787.1: Heartburn	
	789.0: Abdominal Pain	R100, R1010-R1012
	789.4: Abdominal Rigidity	
	789.6: Abdominal Tenderness	
	536.8: Dyspepsia	K30, R1013, R102, R10811, R10812, R10813, R10814, R10816, R10817, R10819, R10821, R10822, R10826, R10827, R10829, R1084, R109, R12, R1930, R1931, R1932, R1936, R1937

Covariates	ICD-9-CM/CPT/HCPCS Codes	ICD-10-CM Codes
Peripheral artery disease	440.xx-445.xx	I700, I701, I70201, I70202, I70203, I70208, I70209, I70211, I70212, I70213, I70218, I70219, I70221, I70222, I70223, I70228, I70229, I70231, I70232, I70233, I70234, I70235, I70238, I70239, I70241, I70242, I70243, I70244, I70245, I70248, I70249, I7025, I70261, I70262, I70263, I70268, I70269, I70291, I70292, I70293, I70298, I70299, I70301, I70302, I70303, I70308, I70309, I70311, I70312, I70313, I70318, I70319, I70321, I70322, I70323, I70328, I70329, I70331, I70332, I70333, I70334, I70335, I70338, I70339, I70341, I70342, I70343, I70344, I70345, I70348, I70349, I7035, I70361, I70362, I70363, I70368, I70369, I70391, I70392, I70393, I70398, I70399, I70401, I70402, I70403, I70408, I70409, I70411, I70412, I70413, I70418, I70419, I70421, I70422, I70423, I70428, I70429, I70431, I70432, I70433, I70434, I70435, I70438, I70439, I70441, I70442, I70443, I70444, I70445, I70448, I70449, I7045, I70461, I70462, I70463, I70468, I70469, I70491, I70492, I70493, I70498, I70499, I70501, I70502, I70503, I70508, I70509, I70511, I70512, I70513, I70518, I70519, I70521, I70522, I70523, I70528, I70529, I70531, I70532, I70533, I70534, I70535, I70538, I70539, I70541, I70542, I70543, I70544, I70545, I70548, I70549, I7055, I70561, I70562, I70563, I70568, I70569, I70591, I70592, I70593, I70598, I70599, I70601, I70602, I70603, I70608, I70609, I70611, I70612, I70613, I70618, I70619, I70621, I70622, I70623, I70628, I70629, I70631, I70632, I70633, I70634, I70635, I70638, I70639, I70641, I70642, I70643, I70644, I70645, I70648, I70649, I7065, I70661, I70662, I70663, I70668, I70669, I70691, I70692, I70693, I70698, I70699, I70701, I70702, I70703, I70708, I70709, I70711, I70712, I70713, I70718, I70719, I70721, I70722, I70723, I70728, I70729, I70731, I70732, I70733, I70734, I70735, I70738, I70739, I70741, I70742, I70743, I70744, I70745, I70748, I70749, I7075, I70761, I70762, I70763, I70768, I70769, I70791, I70792, I70793, I70798, I70799, I708, I7090, I7091, I7092, I7100, I7101, I7102, I7103, I711, I712, I713, I714, I715, I716, I718, I719, I720, I721, I722, I723, I724, I725, I726, I728, I729, I7300, I7301, I731, I7381, I7389, I739, I742, I743, I744, I75011, I75012, I75013, I75019, I75021, I75022, I75023, I75029, I7770, I7771, I7772, I7773, I7774, I7775, I7776, I7777, I7779, I790, I791, I798

Covariates	ICD-9-CM/CPT/HCPCS Codes	ICD-10-CM Codes
Non-stroke/SE peripheral vascular disease	440, 441, 442, 443	I70-I73, I77-I79
Transient ischemic attack (TIA)	435.x	G458, G459, Z8673
Coronary artery disease	410.xx-414.xx	I200, I201, I208, I209, I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I214, I220, I221, I222, I228, I229, I240, I241, I248, I249, I2510, I25110, I25111, I25118, I25119, I252, I253, I2541, I2542, I255, I256, I25700, I25701, I25708, I25709, I25710, I25711, I25718, I25719, I25720, I25721, I25728, I25729, I25730, I25731, I25738, I25739, I25750, I25751, I25758, I25759, I25760, I25761, I25768, I25769, I25790, I25791, I25798, I25799, I25810, I25811, I25812, I2582, I2583, I2584, I2589, I259
Anemia and coagulation defects	280.xx-286.xx	D50-D53, D55-D59, D60-D69,

Table 12. Clinical Outcomes

Outcome Variables		ICD-9-CM/Procedure Codes	ICD-10-CM Codes/Procedure Codes
Stoke/ SE	Hemorrhagic Stroke	430.xx-432.xx Cases will be excluded if traumatic brain injury (ICD-9: 800-804, 850-854) was present during hospitalization.	I6000, I6001, I6002, I6010, I6011, I6012, I602, I6030, I6031, I6032, I604, I6050, I6051, I6052, I606, I607, I608, I609, I610, I611, I612, I613, I614, I615, I616, I618, I619; Cases will be excluded according to Table 12.
	Ischemic Stroke	433.x1, 434.x1, 436	I6300, I63011, I63012, I63013, I63019, I6302, I63031, I63032, I63033, I63039, I6309, I6310, I63111, I63112, I63113, I63119, I6312, I63131, I63132, I63133, I63139, I6319, I6320, I63211, I63212, I63213, I63219, I6322, I63231, I63232, I63233, I63239, I6329, I6330, I63311, I63312, I63313, I63319, I63321, I63322, I63323, I63329, I63331, I63332, I63333, I63339, I63341, I63342, I63343, I63349, I6339, I6340, I63411, I63412, I63413, I63419, I63421, I63422, I63423, I63429, I63431, I63432, I63433, I63439, I63441, I63442, I63443, I63449, I6349, I6350, I63511, I63512, I63513, I63519, I63521, I63522, I63523, I63529, I63531, I63532, I63533, I63539, I63541, I63542, I63543, I63549, I6359, I636, I638, I639, I6789
	Systemic	444.x, 445.x	I7401, I7409, I7410, I7411, I7419, I742, I743,

Outcome Variables		ICD-9-CM/Procedure Codes	ICD-10-CM Codes/Procedure Codes
	Embolism		I744, I745, I748, I749, I75011, I75012, I75013, I75019, I75021, I75022, I75023, I75029, I7581, I7589
Major Bleeding	Major Gastrointestinal bleeding event	456.0, 456.20, 530.82, 531.0x, 531.2x, 531.4x, 531.6x, 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 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.x; Procedure Code: 44.43	I8501, I8511, K2211, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K2901, K2921, K2931, K2941, K2951, K2961, K2971, K2981, K2991, K31811, K3182, K5521, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K625, K6381, K661, K920, K921, K922, K9161, K9162, K91840, K91841
	Major Intracranial Hemorrhage (ICH)	430, 431, 432.0, 432.1, 432.9, 852.0x, 852.2x, 852.4x, 853.0x	I6000, I6001, I6002, I6010, I6011, I6012, I602, I6030, I6031, I6032, I604, I6050, I6051, I6052, I606, I607, I608, I609, I610, I611, I612, I613, I614, I615, I616, I618, I619, I6200, I6201, I6202, I6203, I621, I629, S06340A, S06341A, S06342A, S06343A, S06344A, S06345A, S06346A, S06347A, S06348A, S06349A, S06350A, S06351A, S06352A, S06353A, S06354A, S06355A, S06356A, S06357A, S06358A, S06359A, S06360A, S06361A, S06362A, S06363A, S06364A, S06365A, S06366A, S06367A, S06368A, S06369A, S064X0A, S064X1A, S064X2A, S064X3A, S064X4A, S064X5A, S064X6A, S064X7A, S064X8A, S064X9A, S065X0A, S065X1A, S065X2A, S065X3A, S065X4A, S065X5A, S065X6A, S065X7A, S065X8A, S065X9A, S066X0A, S066X1A, S066X2A, S066X3A, S066X4A, S066X5A, S066X6A, S066X7A, S066X8A, S066X9A
	Major Other hemorrhage	285.1, 360.43, 362.43, 362.81, 363.61, 363.62, 363.72, 364.41, 372.72, 374.81, 376.32, 377.42, 379.23, 423.0x, 596.7x, 599.7x, 602.1x, 620.1, 621.4, 626.2, 626.5, 626.7, 626.8, 626.9, 719.1x, 782.7, 784.7, 784.8, 786.3x, 958.2, 997.02, 998.11; Procedure codes: 99.04	D62, D7801, D7802, D7821, D7822, E3601, E3602, E89810, E89811, G9731, G9732, G9751, G9752, H05231, H05232, H05233, H05239, H1130, H1131, H1132, H1133, H2100, H2101, H2102, H2103, H31301, H31302, H31303, H31309, H31311, H31312, H31313, H31319, H31411, H31412, H31413, H31419, H3560, H3561, H3562, H3563, H35731, H35732, H35733, H35739, H4310, H4311, H4312, H4313, H44811, H44812, H44813, H44819, H47021, H47022, H47023, H47029, H59111, H59112, H59113, H59119, H59121, H59122, H59123, H59129, H59311, H59312, H59313, H59319,

Outcome Variables		ICD-9-CM/Procedure Codes	ICD-10-CM Codes/Procedure Codes
			H59321, H59322, H59323, H59329, H9521, H9522, H9541, H9542, I312, I97410, I97411, I97418, I9742, I97610, I97611, I97618, I97620, J9561, J9562, J95830, J95831, L7601, L7602, L7621, L7622, M2500, M25011, M25012, M25019, M25021, M25022, M25029, M25031, M25032, M25039, M25041, M25042, M25049, M25051, M25052, M25059, M25061, M25062, M25069, M25071, M25072, M25073, M25074, M25075, M25076, M2508, M96810, M96811, M96830, M96831, N421, N857, N897, N920, N923, N930, N938, N939, N9961, N9962, N99820, N99821, R040, R041, R042, R0489, R049, R233, R310, R319, R58, T792XXA; Procedure codes: 30230N1, 30230P1, 30233N1, 30233P1, 30240N1, 30240P1, 30243N1, 30243P1, 30250N1, 30250P1, 30253N1, 30253P1, 30260N1, 30260P1, 30263N1, 30263P1