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Comparative Risk Assessment of Severe Uterine Bleeding Following Exposure to Direct Oral Anticoagulants: A Network Study Across Four Observational Databases in the United States

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Online Resource 1. AF population: primary analysis diagnostics (preference score [PS] distribution, covariate balance, and empirical null distribution) for each pairwise comparison: a) rivaroxaban vs warfarin; b) apixaban vs warfarin; c) dabigatran vs warfarin; d) rivaroxaban vs apixaban; e) rivaroxaban vs dabigatran; and f) apixaban vs dabigatran.

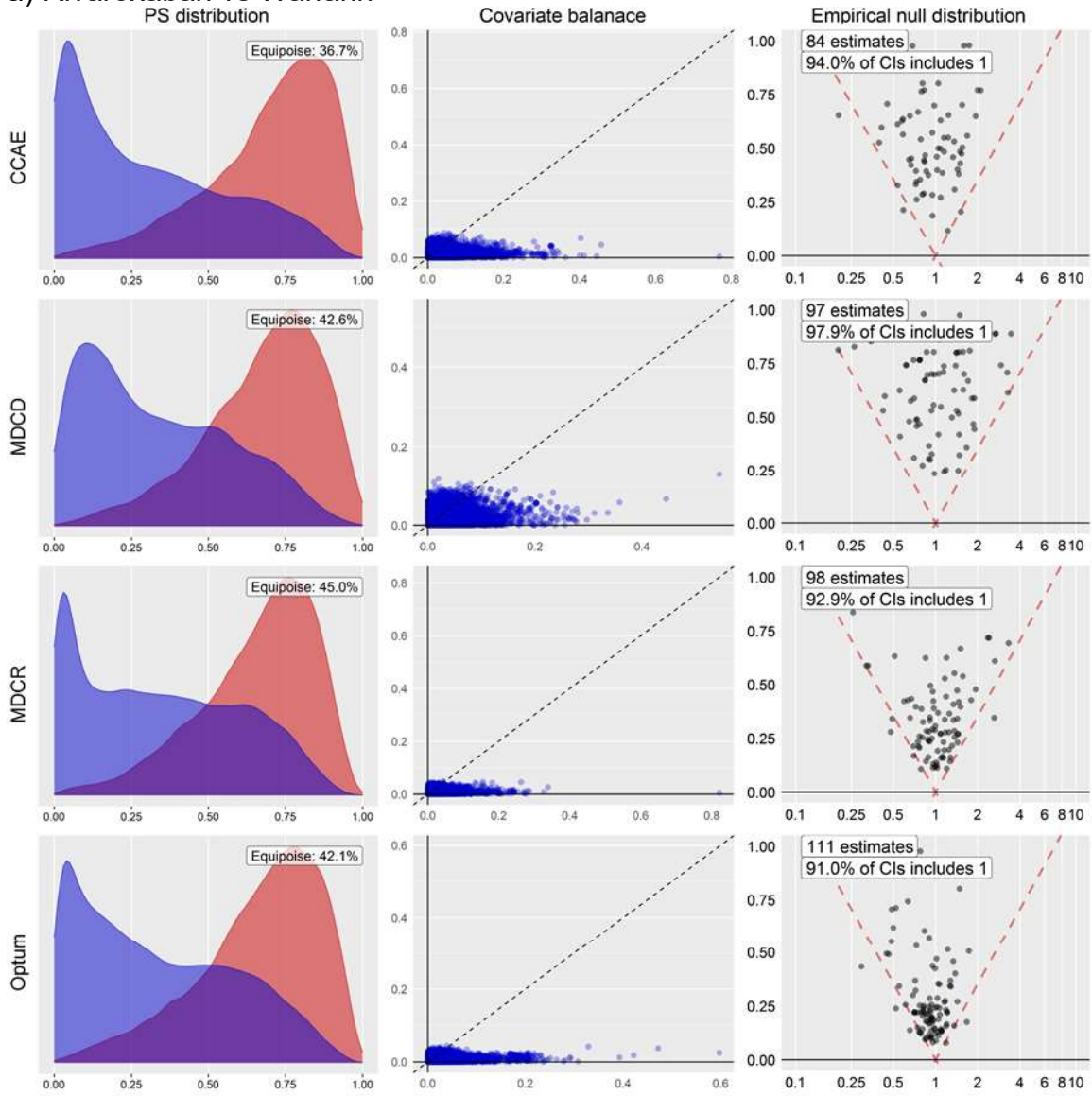
AF, atrial fibrillation; CCAE, IBM MarketScan® Commercial Database; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries.

The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two exposure cohorts in a pairwise comparison. A higher overlap indicates patients in the two cohorts were more similar in terms of their predicted probability of receiving one exposure relative to the other. In each preference score plot, the red curve represents the preference score for the first exposure in the comparison label and the blue curve represents the preference score for the second exposure in the comparison label. For example, in plot a) rivaroxaban vs warfarin, the red curve represents the preference score for patients exposed to rivaroxaban and the blue curve represents the preference score for patients exposed to warfarin.

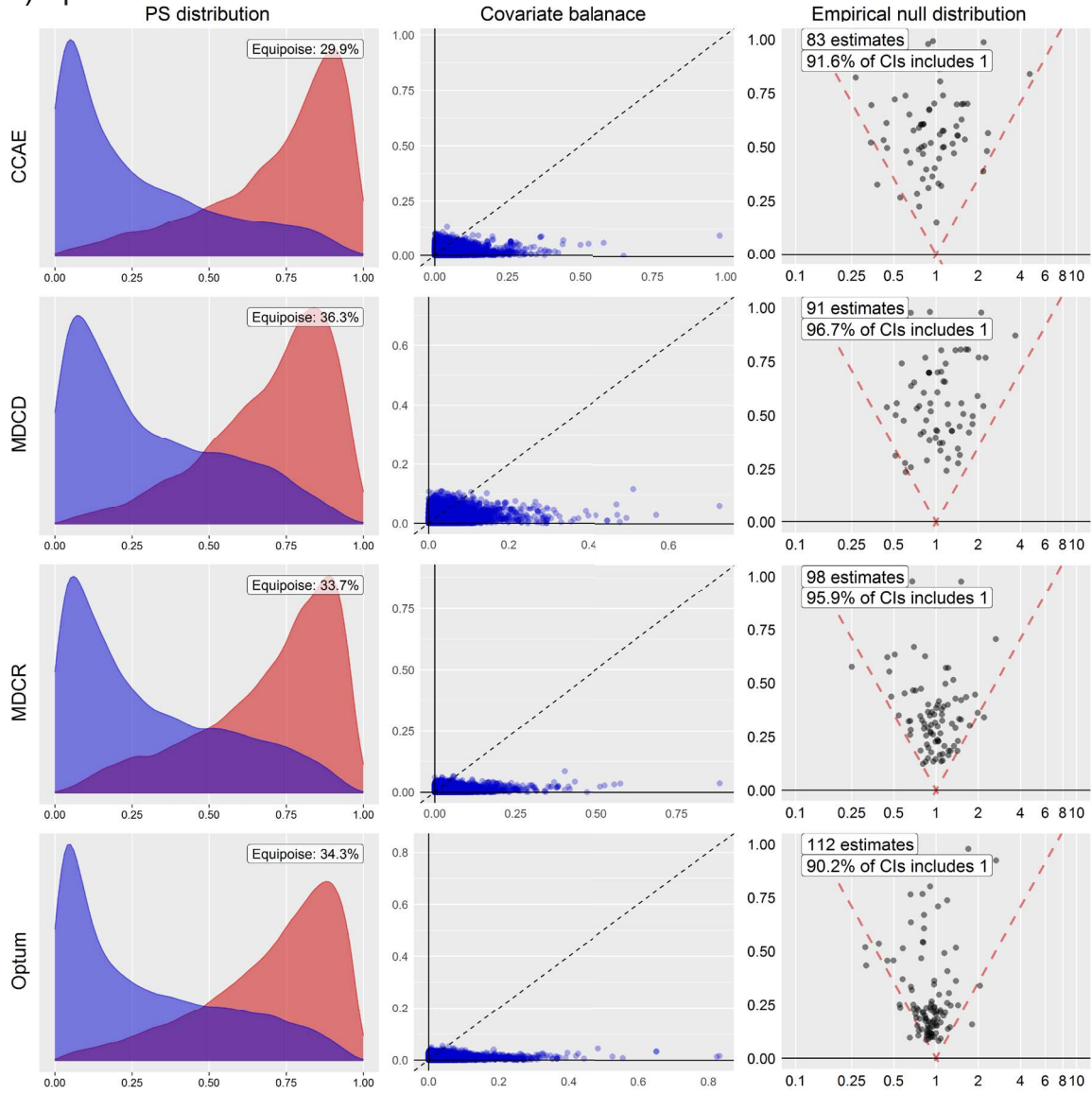
In the covariate balance plots, each data point represents the standardized difference of means for a single covariate before and after propensity score stratification. The x-axis measures the standardized difference of means before propensity score matching and the y-axis measures the standardized difference in means after propensity score matching. Plots where data points are of larger magnitude on the x-axis than on the y-axis represent covariate balance improvement after propensity score stratification.

The empirical calibration plots show effect estimates for the negative controls where the true hazard ratio is expected to equal 1. The x-axis measures the hazard ratio and the y-axis measures the standard error (which is related to the width of the confidence interval of the hazard ratio). Estimates below the diagonal dashed lines are statistically significantly different ($\alpha = 0.05$) from the true effect size. A well-calibrated estimator should produce the true effect sizes within the 95 percent confidence interval 95 percent of the time.

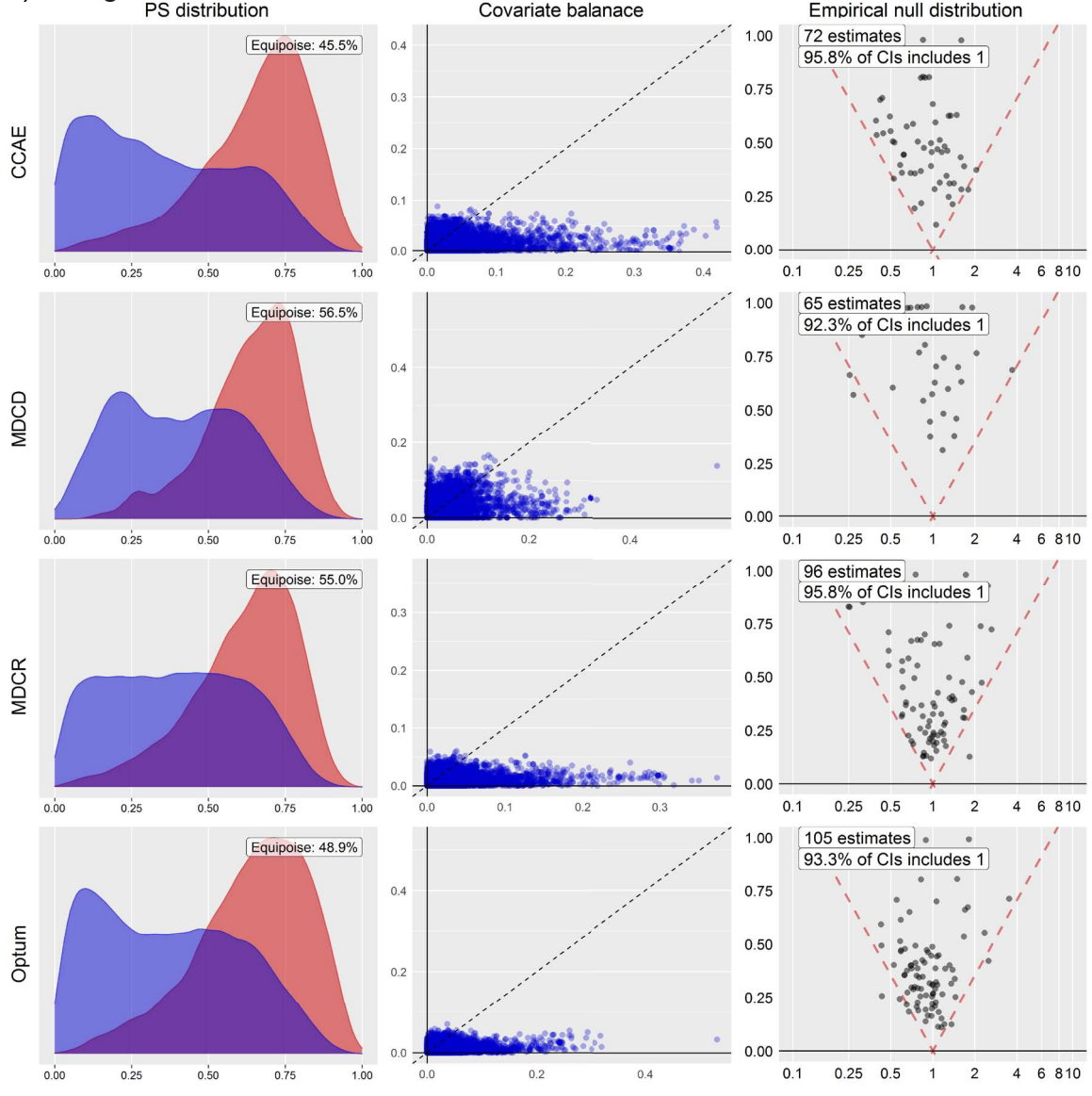
a) Rivaroxaban vs Warfarin



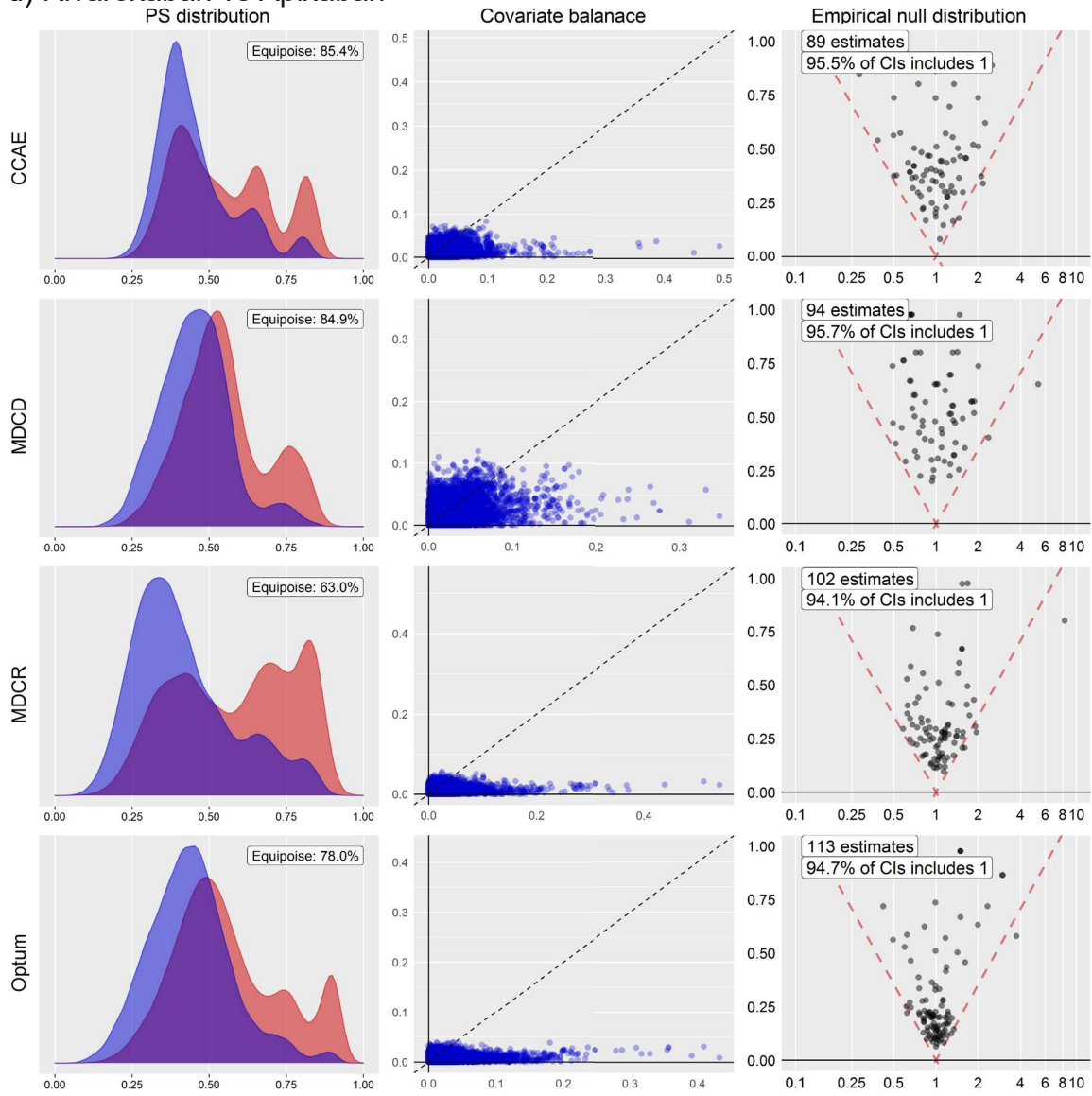
b) Apixaban vs Warfarin
PS distribution



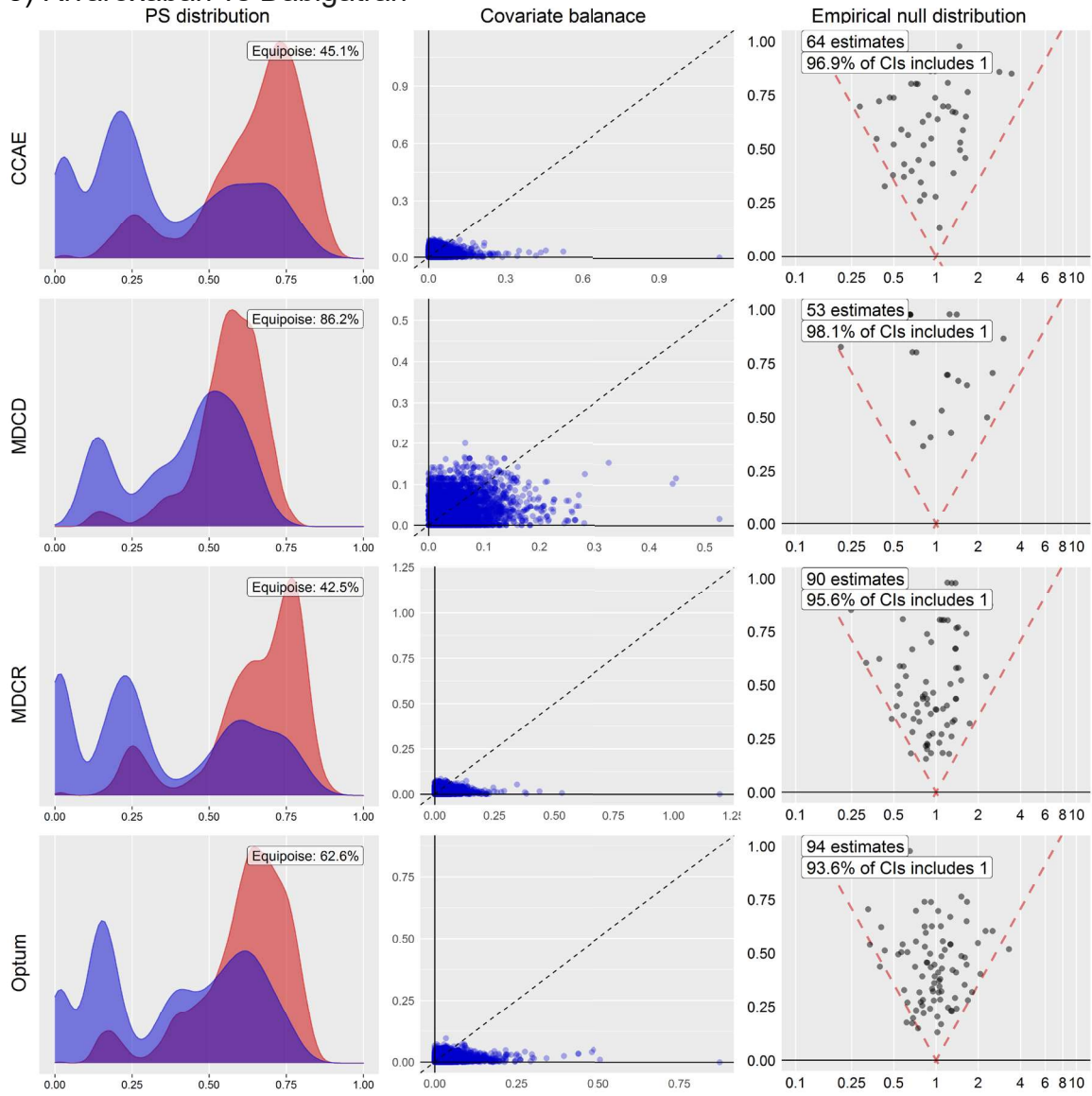
c) Dabigatran vs Warfarin



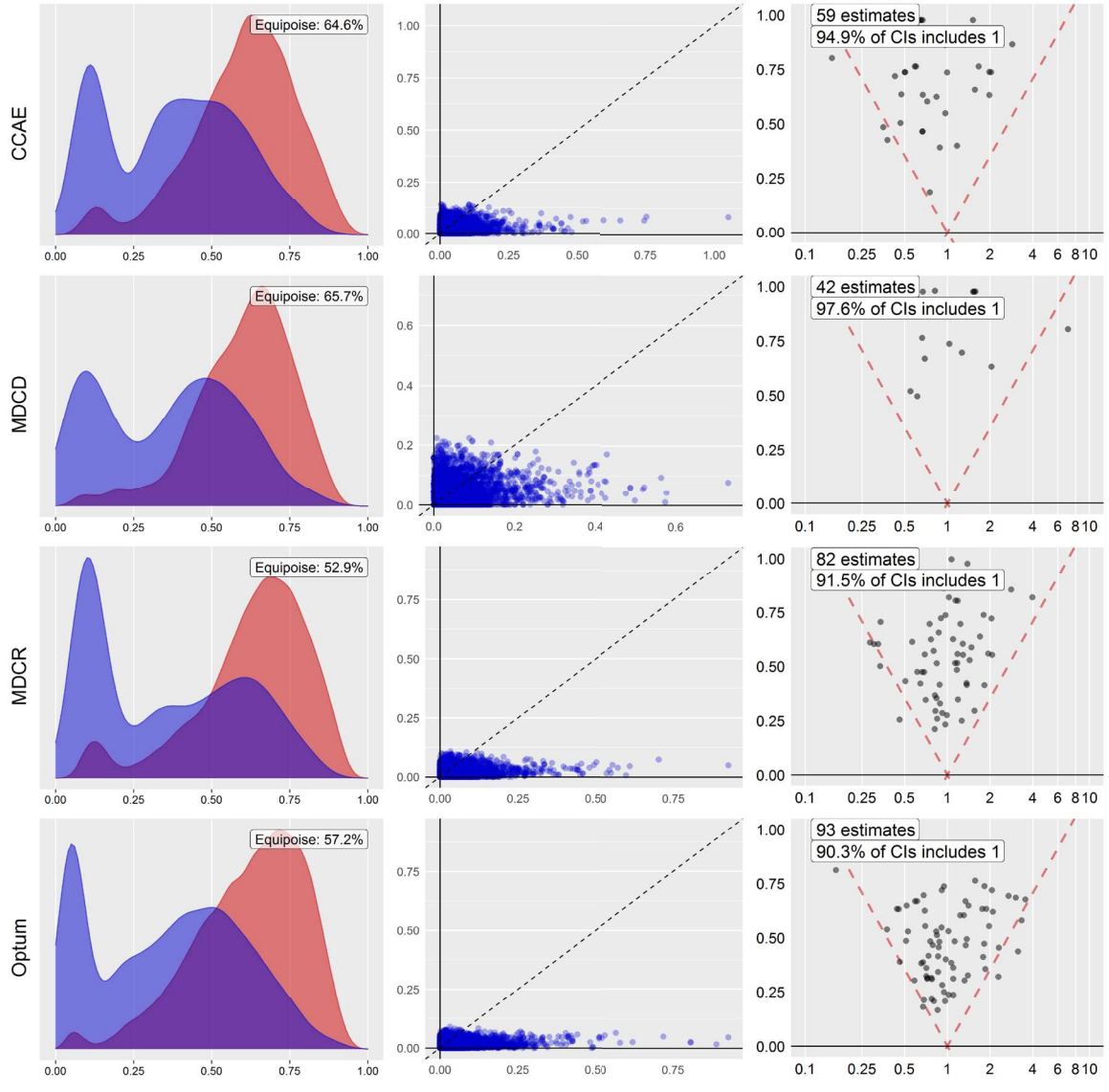
d) Rivaroxaban vs Apixaban



e) Rivaroxaban vs Dabigatran



f) Apixaban vs Dabigatran
PS distribution



Online Resource 2. VTE population: primary analysis diagnostics (preference score [PS] distribution, covariate balance, empirical null distribution) for each pairwise comparison: a) rivaroxaban vs warfarin; b) apixaban vs warfarin; c) dabigatran vs warfarin; d) rivaroxaban vs apixaban; e) rivaroxaban vs dabigatran; and f) apixaban vs dabigatran.

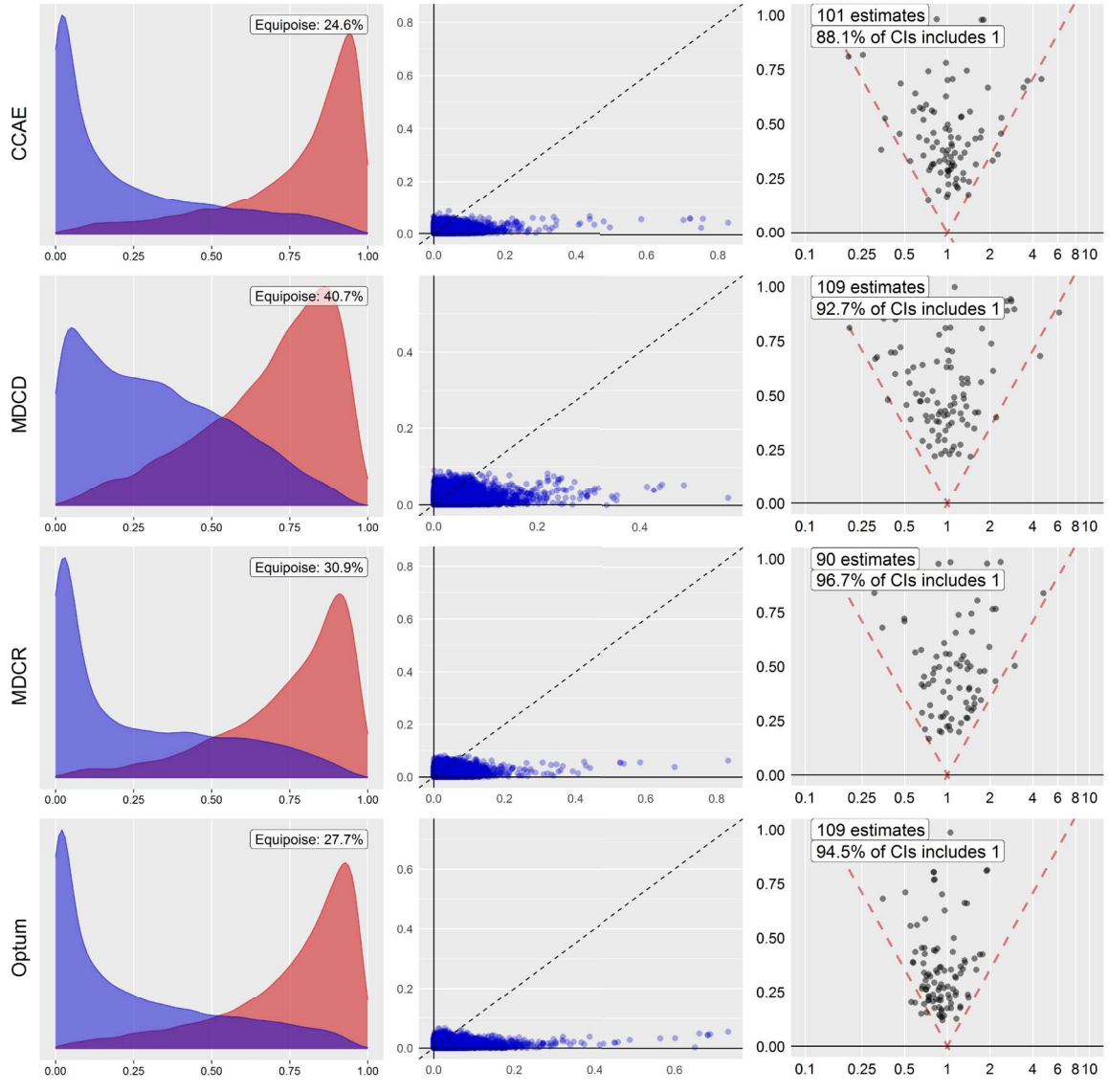
CCAE, IBM MarketScan® Commercial Database; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; VTE, venous thromboembolism.

The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two exposure cohorts in a pairwise comparison. A higher overlap indicates patients in the two cohorts were more similar in terms of their predicted probability of receiving one exposure relative to the other. In each preference score plot, the red curve represents the preference score for the first exposure in the comparison label and the blue curve represents the preference score for the second exposure in the comparison label. For example, in plot a) rivaroxaban vs warfarin, the red curve represents the preference score for patients exposed to rivaroxaban and the blue curve represents the preference score for patients exposed to warfarin. Note that a propensity score model was unable to be fit for rivaroxaban vs dabigatran in the MDCD database.

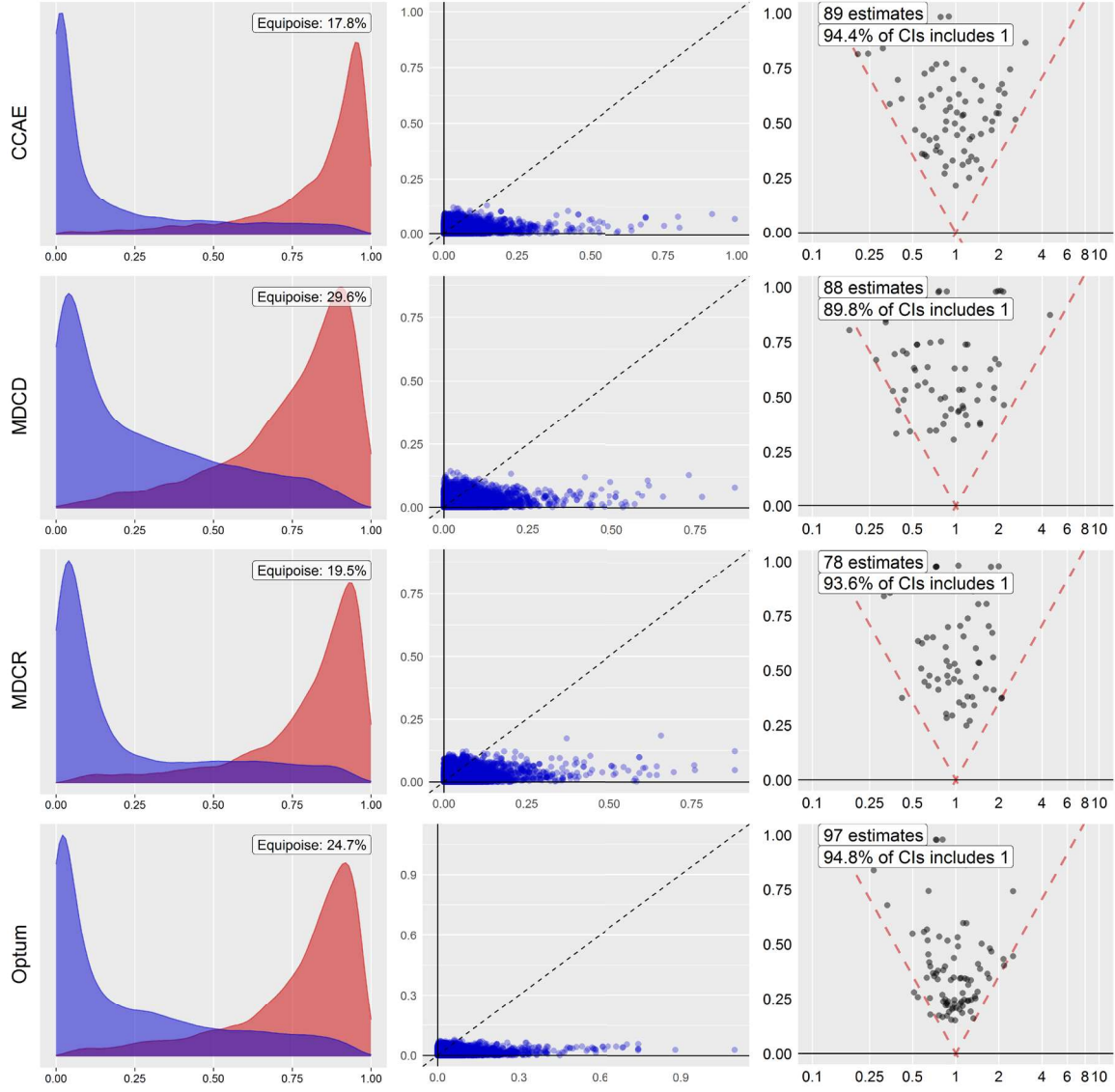
In the covariate balance plots, each data point represents the standardized difference of means for a single covariate before and after propensity score stratification. The x-axis measures the standardized difference of means before propensity score matching and the y-axis measures the standardized difference in means after propensity score matching. Plots where data points are of larger magnitude on the x-axis than on the y-axis represent covariate balance improvement after propensity score stratification.

The empirical calibration plots show effect estimates for the negative controls where the true hazard ratio is expected to equal 1. The x-axis measures the hazard ratio and the y-axis measures the standard error (which is related to the width of the confidence interval of the hazard ratio). Estimates below the diagonal dashed lines are statistically significantly different ($\alpha = 0.05$) from the true effect size. A well-calibrated estimator should produce the true effect sizes within the 95 percent confidence interval 95 percent of the time.

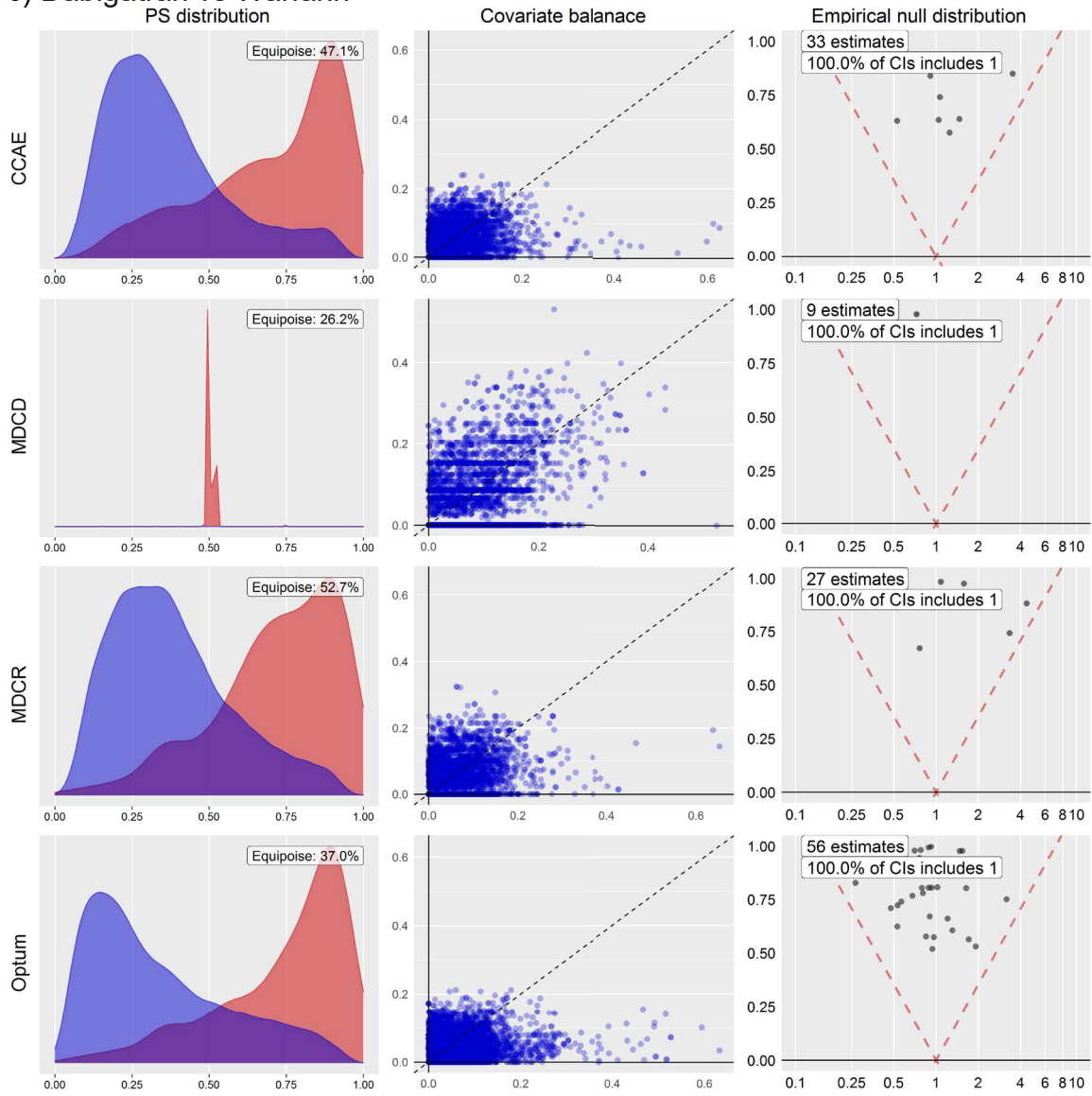
a) Rivaroxaban vs Warfarin
PS distribution



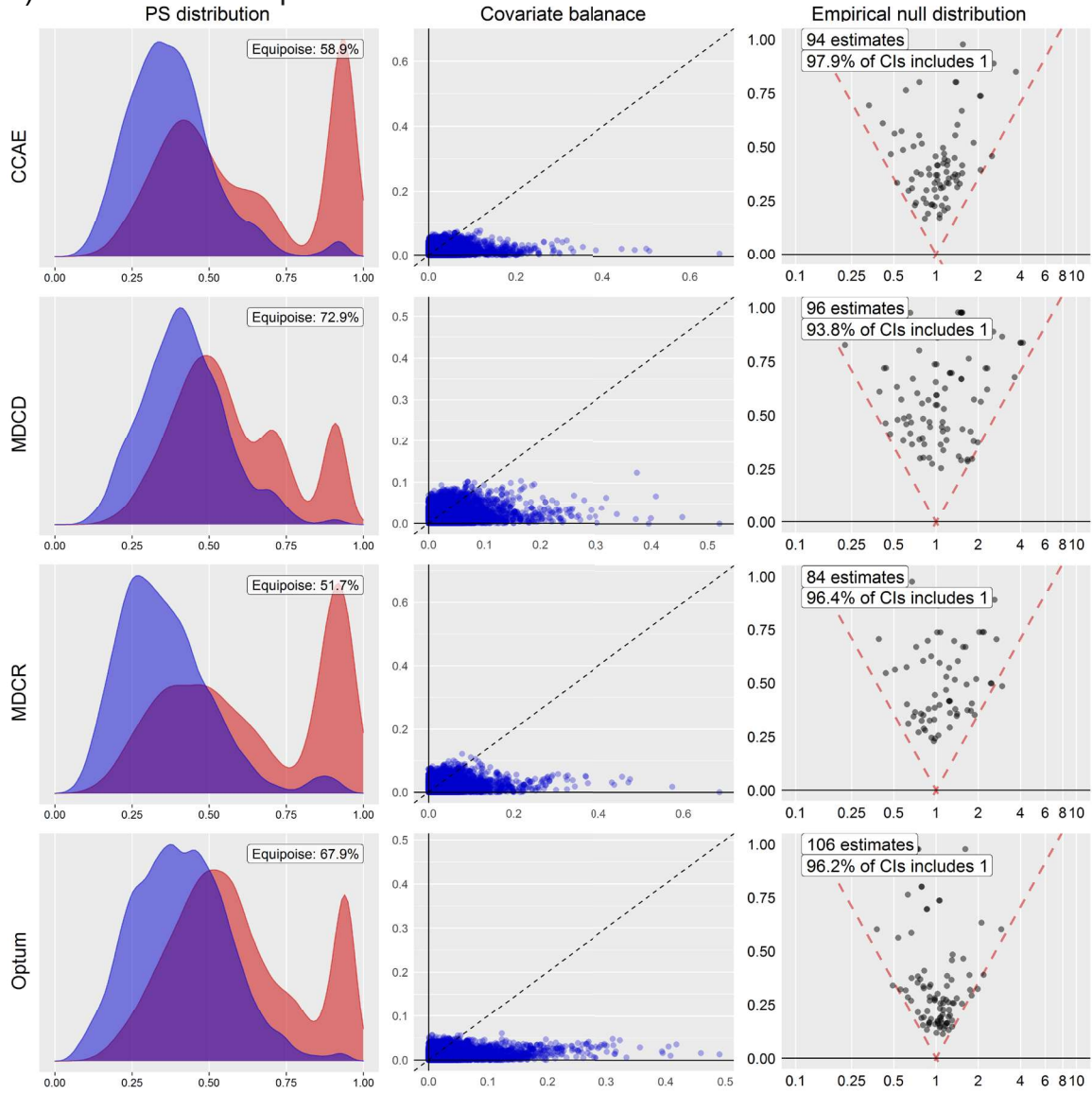
b) Apixaban vs Warfarin
PS distribution



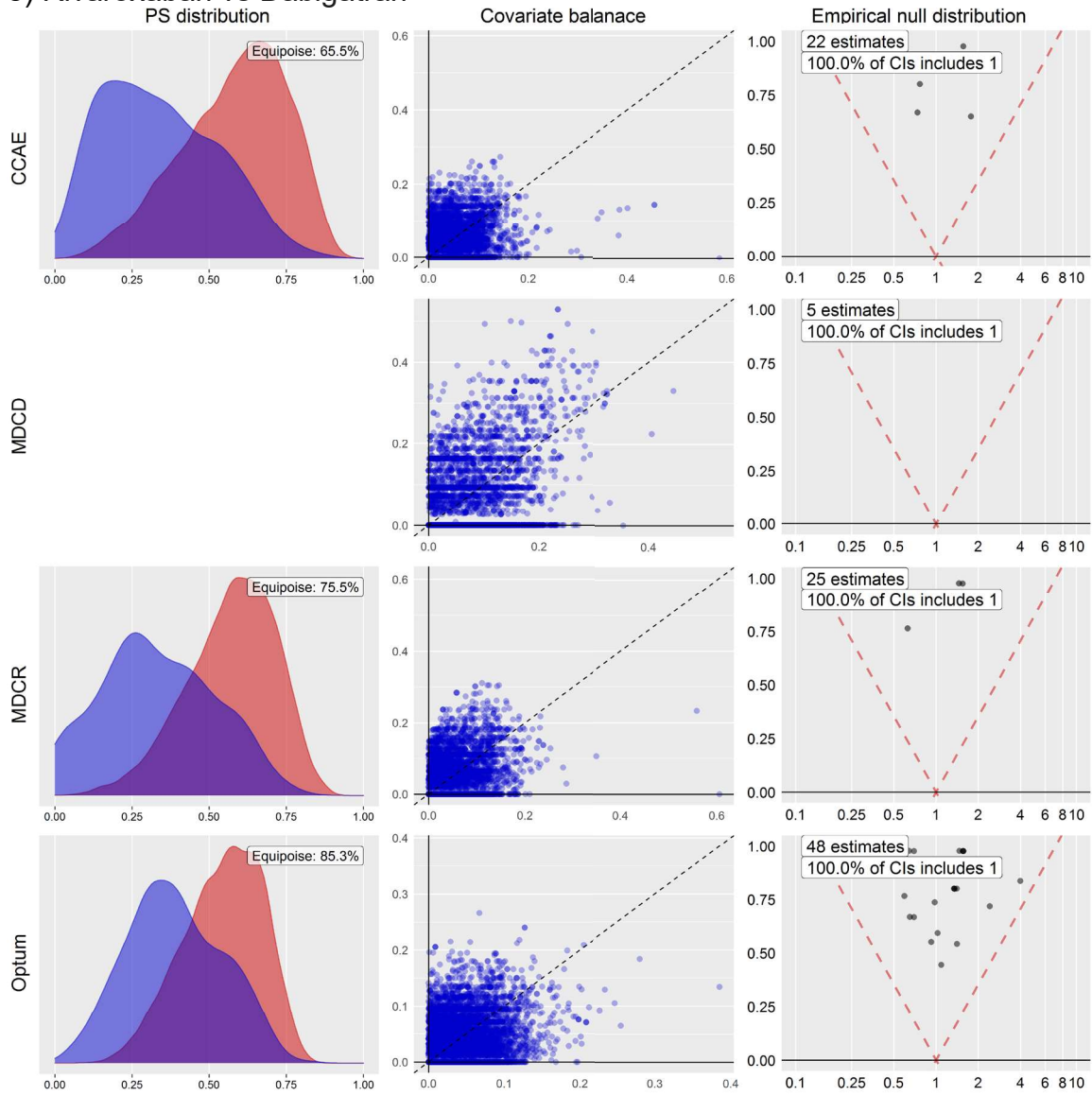
c) Dabigatran vs Warfarin



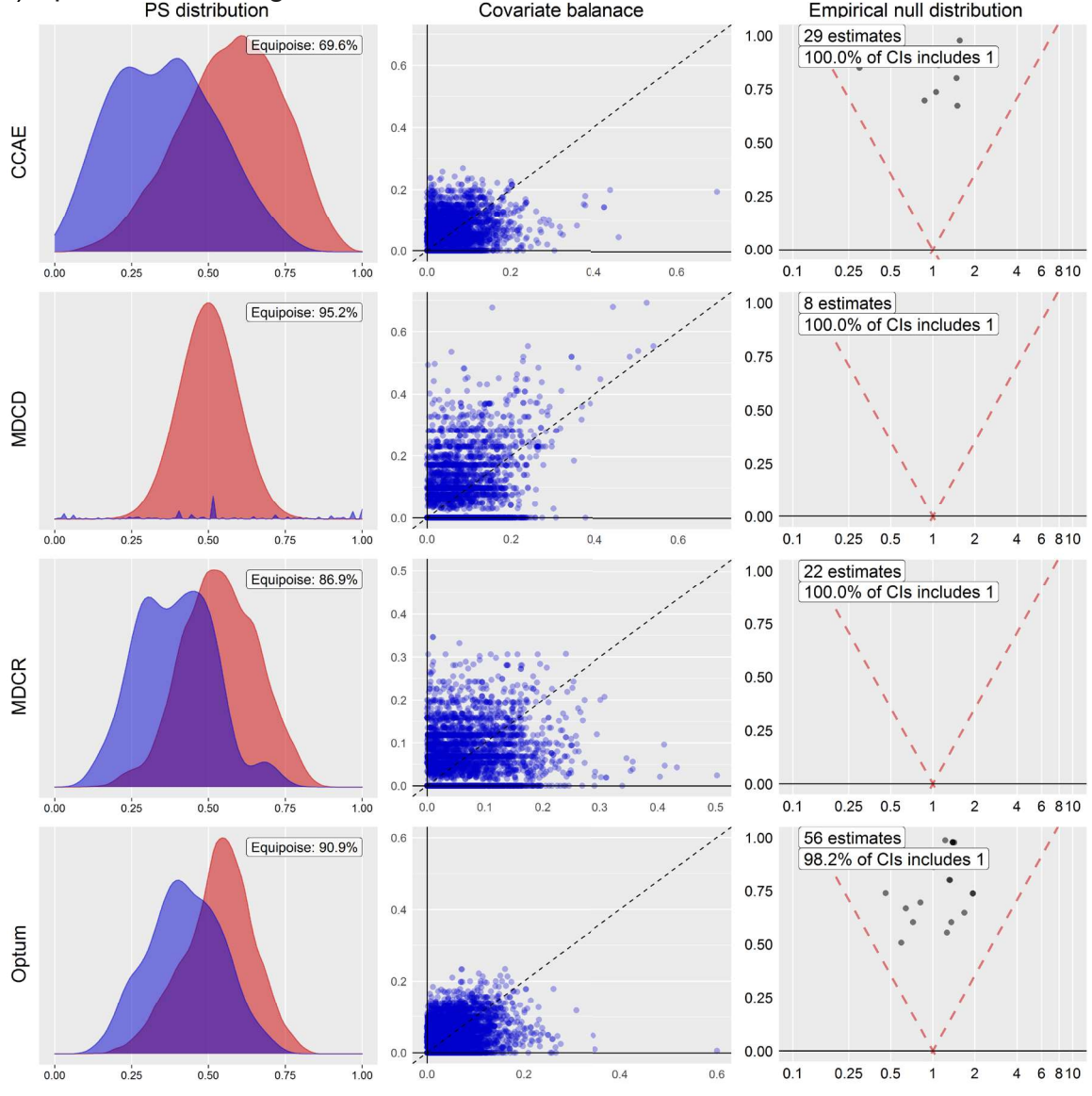
d) Rivaroxaban vs Apixaban



e) Rivaroxaban vs Dabigatran



f) Apixaban vs Dabigatran



Online Resource 3. Negative control outcomes used for empirical calibration.

Abnormal posture	Functional urinary incontinence	Paranoid schizophrenia
Abscess of abdominal wall	Generalized hyperhidrosis	Paresthesia
Acute bronchospasm	Herpes zoster without complication	Patient dependence on care provider
Acute mycoplasma bronchitis	Hyperglycemia due to type 2 diabetes mellitus	Postoperative hypothyroidism
Acute upper respiratory infection	Hyperparathyroidism	Posttraumatic stress disorder
Acute vaginitis	Idiopathic sleep related non-obstructive alveolar hypoventilation	Pseudobulbar affect
Adjustment disorder with depressed mood	Imaging of abdomen abnormal	Psychoactive substance dependence
Alcohol dependence	Imaging of gastrointestinal tract abnormal	Psychologic conversion disorder
Altered sensation of skin	Impacted cerumen	Pure hyperglyceridemia
Anesthesia of skin	Impaired fasting glycaemia	Restless legs
Anhedonia	Impingement syndrome of shoulder region	Retrograde amnesia
Asymptomatic human immunodeficiency virus infection	Incontinence of feces	Schizoaffective disorder
Attention deficit hyperactivity disorder	Incoordination	Schizophreniform disorder
Bacteremia	Increased frequency of urination	Sepsis due to methicillin resistant Staphylococcus aureus
Bacterial infection due to Klebsiella pneumoniae	Infection by methicillin sensitive Staphylococcus aureus	Severe mixed bipolar I disorder without psychotic features
Bipolar I disorder	Infection due to Escherichia coli	Severe protein-calorie malnutrition
Bipolar II disorder	Ingrowing nail	Shoulder stiff
Blood glucose abnormal	Intra-abdominal and pelvic swelling, mass and lump	Sickle cell trait
Borderline personality disorder	Ketoacidosis in type 1 diabetes mellitus	Simple goiter
Candida infection of genital region	Ketoacidosis in type 2 diabetes mellitus	Skin sensation disturbance
Cannabis abuse	Knee stiff	Slurred speech
Cervical somatic dysfunction	Lichenification and lichen simplex chronicus	Snoring
Chronic fatigue syndrome	Localized enlarged lymph nodes	Solitary nodule of lung
Chronic hepatitis C	Localized infection of skin and/or subcutaneous tissue	Spinal stenosis of lumbar region
Chronic pain syndrome	Localized swelling, mass and lump, trunk	Stimulant dependence
Chronic post-traumatic stress disorder	Malnutrition of moderate degree	Suicidal thoughts
Chronic schizoaffective schizophrenia	Mammography abnormal	Tension-type headache
Cocaine abuse	Methicillin resistant Staphylococcus aureus infection	Thyroid function tests abnormal
Continuous opioid dependence	Mild protein-calorie malnutrition	Thyrotoxicosis without goiter or other cause

Coordination problem	Mixed urinary incontinence	Tobacco dependence syndrome
Cramp in limb	Moderate intellectual disability	Toxic diffuse goiter with no crisis
Crohn's disease	Moderate protein-calorie malnutrition	Type 1 diabetes mellitus uncontrolled
Dependence on supplemental oxygen	Nasal congestion	Type II diabetes mellitus uncontrolled
Diabetic ketoacidosis without coma	Neurogenic bladder	Uncomplicated umbilical hernia
Difficulty speaking	Nicotine dependence	Unsteady when standing
Disorientated	Non-toxic unimodular goiter	Urinary incontinence
Dysphagia	Obsessive-compulsive disorder	Viral hepatitis B without hepatic coma
Eating disorder	Obstructive sleep apnea syndrome	Viral hepatitis C
Eosinophilic asthma	Onychomycosis due to dermatophyte	Vitamin B deficiency
Falls	Open wound of anterior abdominal wall without complication	Vitamin D deficiency
Female stress incontinence	Opioid dependence	Wheezing

Online Resource 4. Study cohort counts by a) indication and exposure and b) database and indication.

a)

Indication	Exposure	Database	Patients	Exposure %
AF (n = 221,368)	Rivaroxaban (n = 46,827)	CCAIE	7,525	16.07
		MDCD	2,622	5.6
		MDCR	14,817	31.64
		Optum	21,863	46.69
	Apixaban (n = 69,727)	CCAIE	8,247	11.83
		MDCD	3,363	4.82
		MDCR	18,499	26.53
		Optum	39,618	56.82
	Dabigatran (n = 21,025)	CCAIE	4,193	19.94
		MDCD	743	3.53
		MDCR	8,571	40.77
		Optum	7,518	35.76
Warfarin (n = 83,789)	CCAIE	8,800	10.5	
	MDCD	5,530	6.6	
	MDCR	28,240	33.7	
	Optum	41,219	49.19	
VTE (n = 142,551)	Rivaroxaban (n = 37,401)	CCAIE	12,270	32.81
		MDCD	4,808	12.86
		MDCR	5,834	15.6
		Optum	14,489	38.74
	Apixaban (n = 20,568)	CCAIE	5,203	25.3
		MDCD	2,414	11.74
		MDCR	2,931	14.25
		Optum	10,020	48.72
	Dabigatran (n = 1,055)	CCAIE	326	30.9
		MDCD	89	8.44
		MDCR	206	19.53
		Optum	434	41.14
	Warfarin (n = 83,527)	CCAIE	25,955	31.07
		MDCD	9,284	11.11
		MDCR	17,892	21.42
		Optum	30,396	36.39

b)

Database	Indication	Exposure	Patients	Database %
CCAIE (n = 115,410)	AF (n = 28,765)	Rivaroxaban	7,525	6.52
		Apixaban	8,247	7.15
		Dabigatran	4,193	3.63
		Warfarin	8,800	7.62
	VTE (n = 43,754)	Rivaroxaban	12,270	10.63
		Apixaban	5,203	4.51
		Dabigatran	326	0.28
		Warfarin	25,955	22.49
MDCD (n = 33,678)	AF (n = 12,258)	Rivaroxaban	2,622	7.79
		Apixaban	3,363	9.99
		Dabigatran	743	2.21
		Warfarin	5,530	16.42
	VTE (n = 16,595)	Rivaroxaban	4,808	14.28
		Apixaban	2,414	7.17
		Dabigatran	89	0.26
		Warfarin	9,284	27.57
MDCR (n = 118,536)	AF (n = 70,127)	Rivaroxaban	14,817	12.5
		Apixaban	18,499	15.61
		Dabigatran	8,571	7.23
		Warfarin	28,240	23.82
	VTE (n = 26,863)	Rivaroxaban	5,834	4.92
		Apixaban	2,931	2.47
		Dabigatran	206	0.17
		Warfarin	17,892	15.09
Optum (n = 201,590)	AF (n = 110,218)	Rivaroxaban	21,863	10.85
		Apixaban	39,618	19.65

		Dabigatran	7,518	3.73
		Warfarin	41,219	20.45
	VTE (n = 55,339)	Rivaroxaban	14,489	7.19
		Apixaban	10,020	4.97
		Dabigatran	434	0.22
		Warfarin	30,396	15.08

AF, atrial fibrillation; CCAE, IBM MarketScan® Commercial Database; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; VTE, venous thromboembolism.

Online Resource 5. Age distribution of study cohorts by indication, exposure, and data source

Indication	Exposure	Database	n	Mean (years)	SD	Min	25%ile	Median	75%ile	Max
AF	Rivaroxaban	CCAIE	7,525	58.03	6.32	19	55	60	63	65
		MDCD	2,622	63.84	13.08	21	56	63	74	90
		MDCR	14,817	78.2	7.62	52	72	78	84	109
		Optum	21,863	74.37	9.53	22	68	75	82	89
	Apixaban	CCAIE	8,247	58.43	5.98	18	56	60	63	65
		MDCD	3,363	65.92	12.75	19	58	64	76	90
		MDCR	18,499	79.69	7.9	54	73	80	86	103
		Optum	39,618	76.25	9.06	23	70	77	84	89
	Dabigatran	CCAIE	4,193	58.22	6.17	20	56	60	63	65
		MDCD	743	66.42	12.51	21	58	66	76	90
		MDCR	8,571	78.05	7.36	54	72	78	84	105
		Optum	7,518	73.42	9.38	25	68	74	82	89
	Warfarin	CCAIE	8,800	57.91	6.59	18	55	60	63	65
		MDCD	5,530	65.98	13.27	18	57	64	77	90
		MDCR	28,240	79.47	7.49	50	74	80	85	106
		Optum	41,219	76.12	8.58	19	71	78	83	89
VTE	Rivaroxaban	CCAIE	12,270	51.76	10.39	18	46	54	60	65
		MDCD	4,808	47.75	14.69	18	36	48	58	90
		MDCR	5,834	76.65	8.08	46	70	76	83	105
		Optum	14,489	66.1	14.65	18	57	68	77	89
	Apixaban	CCAIE	5,203	52.67	10.24	18	47	55	61	65
		MDCD	2,414	50.19	15.11	18	39	51	60	90
		MDCR	2,931	78.25	8.53	43	71	78	85	104
		Optum	10,020	70.59	13.25	18	64	72	80.25	89
	Dabigatran	CCAIE	326	51.76	10.58	18	46	54	60	65
		MDCD	89	49.89	15	22	41	50	58	88
		MDCR	206	78.05	8.69	53	71	78	85	96
		Optum	434	66.64	14.14	21	57	69	77	89
	Warfarin	CCAIE	25,955	51.45	10.73	18	45	54	60	65
		MDCD	9,284	49.29	15.58	18	37	50	60	90
		MDCR	17,892	77.79	8.39	44	71	77	84	103
		Optum	30,396	68.06	14.3	18	60	70	80	89

AF, atrial fibrillation; CCAIE, IBM MarketScan® Commercial Database; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; SD, standard deviation; VTE, venous thromboembolism.

Selected baseline characteristics in the AF population (Online Resources 6-10) and VTE population (Online Resources 11-15) before and after 1:1 PS matching for each pairwise comparison are reported. A reader can review the full set of baseline characteristics by using the online application (<https://data.ohdsi.org/DoacsWarfarinSub/>). The online application is searchable for the baseline prevalence of any covariate by navigating to the “population characteristics” tab and selecting the “raw” view and searching for a covariate of interest.

Online Resource 6. Baseline characteristics before and after 1:1 PS matching in the AF population in the Optum database: Apixaban vs Warfarin

Characteristic	Before matching			After matching		
	Apixaban %	Warfarin %	Std. diff	Apixaban %	Warfarin %	Std. diff
Age group, years						
25-29	0.0	0.0	-0.01	0.0	0.0	0.00
30-34	0.0	0.1	-0.01	0.0	0.1	-0.01
35-39	0.1	0.1	-0.02	0.1	0.1	-0.02
40-44	0.2	0.2	0.00	0.2	0.2	0.02
45-49	0.5	0.4	0.01	0.5	0.4	0.01
50-54	1.1	1.1	0.00	1.1	1.0	0.01
55-59	2.6	2.5	0.01	2.2	2.1	0.00
60-64	4.9	4.7	0.01	4.4	4.5	-0.01
65-69	12.5	11.7	0.02	11.8	11.8	0.00
70-74	18.4	17.1	0.04	18.3	18.7	-0.01
75-79	18.8	19.5	-0.02	19.3	19.4	0.00
80-84	18.0	27.6	-0.23	19.4	19.2	0.00
85-89	22.8	14.9	0.20	22.8	22.5	0.01
Medical history: General						
Acute respiratory disease	27.8	27.0	0.02	26.8	27.1	-0.01
Attention-deficit/hyperactivity disorder	0.2	0.1	0.02	0.1	0.2	-0.03
Chronic liver disease	1.4	1.9	-0.04	1.8	1.7	0.01
Chronic obstructive lung disease	22.2	21.7	0.01	21.7	22.1	-0.01
Crohn's disease	0.4	0.4	0.00	0.3	0.5	-0.03
Dementia	7.8	6.9	0.04	7.9	7.5	0.02
Depressive disorder	19.1	16.2	0.08	18.5	18.5	0.00
Diabetes mellitus	33.0	35.1	-0.04	34.9	35.0	0.00
Gastroesophageal reflux disease	26.4	20.5	0.14	23.9	24.8	-0.02
Gastrointestinal hemorrhage	3.3	3.8	-0.03	3.6	3.7	0.00
Human immunodeficiency virus infection	0.0	0.0	0.01	0.0	0.0	0.00
Hyperlipidemia	69.1	64.1	0.11	67.1	67.1	0.00
Hypertensive disorder	85.5	83.6	0.05	84.3	84.9	-0.02
Lesion of liver	1.2	1.2	0.00	1.4	1.1	0.03
Obesity	20.4	15.2	0.14	19.2	18.9	0.01
Osteoarthritis	37.3	30.9	0.14	34.6	35.2	-0.01
Pneumonia	12.7	13.4	-0.02	13.0	12.9	0.00
Psoriasis	1.2	0.8	0.04	1.2	1.0	0.02
Renal impairment	28.7	29.2	-0.01	30.8	30.4	0.01
Rheumatoid arthritis	3.1	3.2	0.00	2.9	3.1	-0.01
Schizophrenia	0.3	0.2	0.02	0.2	0.2	0.00
Ulcerative colitis	0.5	0.4	0.01	0.6	0.5	0.00
Urinary tract infectious disease	20.6	21.4	-0.02	20.5	20.4	0.00
Viral hepatitis C	0.5	0.4	0.01	0.5	0.5	0.00
Visual system disorder	39.7	37.8	0.04	38.7	38.7	0.00
Medical history: Cardiovascular disease						
Atrial fibrillation	96.0	94.7	0.06	95.0	95.1	-0.01
Cerebrovascular disease	19.5	22.2	-0.06	20.3	20.4	0.00
Coronary atherosclerosis	30.1	32.0	-0.04	31.9	31.6	0.00
Heart disease	99.3	98.7	0.07	98.7	99.0	-0.03
Heart failure	33.6	37.8	-0.09	36.4	36.4	0.00
Ischemic heart disease	20.5	21.4	-0.02	21.9	21.5	0.01

Peripheral vascular disease	10.5	10.1	0.01	10.8	10.5	0.01
Venous thrombosis	0.9	0.9	0.00	1.0	1.0	0.00
Medical history: Neoplasms						
Hematologic neoplasm	2.0	1.9	0.01	1.9	2.0	0.00
Malignant lymphoma	1.1	0.8	0.02	1.0	0.9	0.00
Malignant neoplasm of anorectum	0.2	0.2	0.00	0.2	0.2	0.01
Malignant neoplastic disease	13.0	12.0	0.03	12.6	12.4	0.01
Malignant tumor of breast	4.2	3.8	0.02	4.1	4.0	0.00
Malignant tumor of colon	0.8	0.8	-0.01	0.8	0.8	0.01
Malignant tumor of lung	1.1	0.9	0.02	1.0	1.0	0.00
Malignant tumor of urinary bladder	0.4	0.3	0.00	0.3	0.4	-0.01
Medication use						
Agents acting on the renin-angiotensin system	58.0	56.1	0.04	57.3	57.6	-0.01
Antibacterials for systemic use	52.0	47.9	0.08	50.0	50.5	-0.01
Antidepressants	30.9	27.7	0.07	30.5	30.1	0.01
Anti-epileptics	18.9	15.7	0.08	18.6	18.9	-0.01
Anti-inflammatory and antirheumatic products	18.6	15.4	0.08	16.6	16.7	0.00
Antineoplastic agents	4.3	3.8	0.03	3.8	4.1	-0.02
Antipsoriatics	1.0	1.3	-0.03	1.3	1.2	0.00
Antithrombotic agents	20.9	23.1	-0.05	23.0	22.4	0.01
Beta-blocking agents	73.6	70.9	0.06	72.9	72.8	0.00
Calcium channel blockers	47.5	44.6	0.06	46.1	46.1	0.00
Diuretics	55.3	57.4	-0.04	56.6	56.6	0.00
Drugs for acid related disorders	36.0	33.4	0.05	35.1	35.7	-0.01
Drugs for obstructive airway diseases	30.1	25.9	0.09	27.2	28.3	-0.02
Drugs used in diabetes	23.1	23.7	-0.02	24.0	24.0	0.00
Immunosuppressants	3.8	3.0	0.05	3.4	3.4	0.00
Lipid-modifying agents	58.7	56.4	0.05	58.1	58.6	-0.01
Opioids	24.2	24.1	0.00	25.1	24.9	0.00
Psycholeptics	27.2	23.8	0.08	26.8	26.9	0.00
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	1.0	0.7	0.03	0.9	1.0	-0.01

AF, atrial fibrillation; PS, propensity score.

Online Resource 7. Baseline characteristics before and after 1:1 PS matching in the AF population in the Optum database: Dabigatran vs Warfarin

Characteristic	Before matching			After matching		
	Dabigatran %	Warfarin %	Std. diff	Dabigatran %	Warfarin %	Std. diff
Age group, years						
25-29	<0.1	0.0	0.00	<0.1	0.0	0.00
30-34	<0.1	0.1	0.00	<0.1	<0.1	0.01
35-39	0.2	0.1	0.02	0.2	0.1	0.01
40-44	0.3	0.2	0.02	0.3	0.3	0.01
45-49	0.9	0.4	0.06	0.8	0.6	0.03
50-54	2.3	1.1	0.10	2.0	1.9	0.01
55-59	4.7	2.5	0.12	4.0	4.2	-0.01
60-64	8.5	4.7	0.15	7.5	7.6	0.00
65-69	14.7	11.7	0.09	14.5	14.3	0.00
70-74	18.6	17.1	0.04	18.8	18.2	0.01
75-79	17.5	19.5	-0.05	18.2	18.0	0.00
80-84	23.8	27.6	-0.09	24.8	26.2	-0.03
85-89	8.4	14.9	-0.20	8.9	8.6	0.01
Medical history: General						
Acute respiratory disease	23.5	27.0	-0.08	23.6	23.7	0.00
Attention-deficit/hyperactivity disorder	0.2	0.1	0.02	0.2	0.2	0.01
Chronic liver disease	1.7	1.9	-0.01	1.7	1.6	0.01
Chronic obstructive lung disease	16.9	21.7	-0.12	17.4	16.7	0.02
Crohn's disease	0.3	0.4	-0.01	0.3	0.3	-0.01
Dementia	4.6	6.9	-0.10	4.8	4.5	0.01
Depressive disorder	13.5	16.2	-0.07	13.6	13.7	0.00
Diabetes mellitus	29.8	35.1	-0.11	30.1	29.6	0.01
Gastroesophageal reflux disease	18.4	20.5	-0.05	18.5	19.0	-0.01
Gastrointestinal hemorrhage	3.0	3.8	-0.04	3.1	3.1	0.00
Human immunodeficiency virus infection	<0.1	0.0	0.00	<0.1	<0.1	0.00
Hyperlipidemia	66.0	64.1	0.04	65.8	66.3	-0.01
Hypertensive disorder	82.7	83.6	-0.02	83.0	82.9	0.00
Lesion of liver	1.0	1.2	-0.02	1.0	0.7	0.04
Obesity	14.4	15.2	-0.02	14.3	14.1	0.00
Osteoarthritis	28.5	30.9	-0.05	28.7	29.3	-0.01
Pneumonia	9.1	13.4	-0.14	9.3	9.2	0.00
Psoriasis	0.9	0.8	0.01	1.0	0.8	0.02
Renal impairment	17.0	29.2	-0.29	17.8	15.9	0.05
Rheumatoid arthritis	3.0	3.2	-0.01	3.1	3.0	0.00
Schizophrenia	0.2	0.2	0.00	0.2	0.3	0.00
Ulcerative colitis	0.4	0.4	0.00	0.4	0.5	-0.01
Urinary tract infectious disease	16.5	21.4	-0.13	16.8	16.8	0.00
Viral hepatitis C	0.3	0.4	-0.03	0.3	0.3	0.00
Visual system disorder	37.4	37.8	-0.01	37.6	37.6	0.00
Medical history: Cardiovascular disease						
Atrial fibrillation	96.0	94.7	0.06	95.9	95.4	0.03
Cerebrovascular disease	18.8	22.2	-0.08	19.2	18.6	0.02
Coronary arteriosclerosis	26.1	32.0	-0.13	26.6	26.4	0.00
Heart disease	98.9	98.7	0.03	98.9	99.0	-0.01
Heart failure	25.5	37.8	-0.27	26.3	25.8	0.01
Ischemic heart disease	16.3	21.4	-0.13	16.6	16.7	0.00
Peripheral vascular disease	6.8	10.1	-0.12	7.0	6.7	0.01
Venous thrombosis	0.8	0.9	-0.01	0.8	0.8	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.3	1.9	-0.04	1.4	1.4	0.00
Malignant lymphoma	0.6	0.8	-0.03	0.6	0.6	0.00
Malignant neoplasm of anorectum	0.2	0.2	-0.01	0.2	0.2	0.01
Malignant neoplastic disease	11.6	12.0	-0.02	11.6	11.1	0.02
Malignant tumor of breast	4.1	3.8	0.02	4.1	3.8	0.02
Malignant tumor of colon	0.6	0.8	-0.03	0.6	0.8	-0.02
Malignant tumor of lung	0.7	0.9	-0.02	0.7	0.8	0.00
Malignant tumor of urinary bladder	0.2	0.3	-0.03	0.2	0.3	-0.02
Medication use						
Agents acting on the renin-angiotensin system	55.6	56.1	-0.01	56.1	55.8	0.01
Antibacterials for systemic use	48.1	47.9	0.00	48.1	49.7	-0.03

Antidepressants	26.7	27.7	-0.02	26.6	26.2	0.01
Anti-epileptics	13.4	15.7	-0.06	13.5	13.6	0.00
Anti-inflammatory and antirheumatic products	18.1	15.4	0.07	18.0	17.8	0.00
Antineoplastic agents	3.6	3.8	-0.01	3.6	3.5	0.01
Antipsoriatics	0.6	1.3	-0.07	0.6	0.5	0.02
Antithrombotic agents	15.8	23.1	-0.19	16.1	15.9	0.00
Beta-blocking agents	70.8	70.9	0.00	71.1	70.4	0.02
Calcium channel blockers	45.7	44.6	0.02	45.7	46.1	-0.01
Diuretics	52.3	57.4	-0.10	52.9	52.6	0.01
Drugs for acid related disorders	30.3	33.4	-0.07	30.6	30.4	0.00
Drugs for obstructive airway diseases	25.8	25.9	0.00	25.6	25.7	0.00
Drugs used in diabetes	20.2	23.7	-0.08	20.4	19.9	0.01
Immunosuppressants	3.2	3.0	0.01	3.1	3.0	0.00
Lipid-modifying agents	53.2	56.4	-0.06	53.6	53.7	0.00
Opioids	20.4	24.1	-0.09	20.7	20.4	0.01
Psycholeptics	23.4	23.8	-0.01	23.0	22.9	0.00
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	0.9	0.7	0.02	0.8	0.9	-0.01

AF, atrial fibrillation; PS, propensity score.

Online Resource 8. Baseline characteristics before and after 1:1 PS matching in the AF population in the Optum database: Rivaroxaban vs Apixaban

Characteristic	Before matching			After matching		
	Rivaroxaban %	Apixaban %	Std. diff	Rivaroxaban %	Apixaban %	Std. diff
Age group, years						
20-24	0.0	0.0	0.00	0.0	0.0	-0.01
25-29	0.0	0.0	0.02	0.0	0.0	0.01
30-34	0.1	0.0	0.02	0.1	0.0	0.02
35-39	0.2	0.1	0.03	0.1	0.1	0.02
40-44	0.4	0.2	0.02	0.4	0.3	0.02
45-49	0.8	0.5	0.04	0.7	0.6	0.02
50-54	1.9	1.1	0.06	1.7	1.5	0.01
55-59	3.9	2.6	0.07	3.6	3.6	0.00
60-64	6.6	4.9	0.07	6.3	6.3	0.00
65-69	14.8	12.5	0.07	14.5	14.5	0.00
70-74	18.8	18.4	0.01	18.9	18.5	0.01
75-79	18.7	18.8	0.00	19.1	19.0	0.00
80-84	18.2	18.0	0.01	16.7	16.2	0.01
85-89	15.7	22.8	-0.18	17.9	19.3	-0.04
Medical history: General						
Acute respiratory disease	24.5	27.8	-0.07	24.9	25.1	0.00
Attention-deficit/hyperactivity disorder	0.2	0.2	0.00	0.2	0.2	-0.01
Chronic liver disease	1.5	1.4	0.01	1.4	1.3	0.01
Chronic obstructive lung disease	18.7	22.2	-0.08	19.6	19.4	0.00
Crohn's disease	0.3	0.4	-0.02	0.3	0.4	-0.02
Dementia	6.1	7.8	-0.07	6.5	6.3	0.00
Depressive disorder	16.2	19.1	-0.07	17.3	16.9	0.01
Diabetes mellitus	30.4	33.0	-0.06	30.9	30.7	0.00
Gastroesophageal reflux disease	22.0	26.4	-0.10	23.2	22.7	0.01
Gastrointestinal hemorrhage	2.5	3.3	-0.05	2.7	2.6	0.01
Human immunodeficiency virus infection	0.1	0.0	0.01	0.1	0.0	0.02
Hyperlipidemia	64.2	69.1	-0.10	64.6	64.2	0.01
Hypertensive disorder	82.0	85.5	-0.10	82.3	82.2	0.00
Lesion of liver	1.0	1.2	-0.02	1.0	1.0	0.01
Obesity	18.5	20.4	-0.05	19.7	19.3	0.01
Osteoarthritis	32.7	37.3	-0.10	33.6	33.1	0.01
Pneumonia	10.3	12.7	-0.07	10.5	10.4	0.00
Psoriasis	1.2	1.2	-0.01	1.2	1.2	0.00
Renal impairment	20.9	28.7	-0.18	22.3	22.1	0.01
Rheumatoid arthritis	2.9	3.1	-0.01	3.0	2.9	0.00
Schizophrenia	0.2	0.3	-0.01	0.3	0.2	0.01
Ulcerative colitis	0.4	0.5	-0.01	0.5	0.5	0.00
Urinary tract infectious disease	17.4	20.6	-0.08	17.7	17.4	0.01
Viral hepatitis C	0.4	0.5	-0.01	0.5	0.5	0.00
Visual system disorder	37.6	39.7	-0.04	38.4	37.7	0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	94.5	96.0	-0.07	94.7	94.9	-0.01
Cerebrovascular disease	15.3	19.5	-0.11	15.6	15.3	0.01
Coronary atherosclerosis	24.6	30.1	-0.12	24.8	24.3	0.01
Heart disease	98.4	99.3	-0.08	98.5	98.6	-0.01
Heart failure	27.6	33.6	-0.13	28.2	27.9	0.01
Ischemic heart disease	16.5	20.5	-0.10	16.7	16.6	0.00
Peripheral vascular disease	8.3	10.5	-0.08	8.7	8.7	0.00
Venous thrombosis	0.7	0.9	-0.02	0.8	0.7	0.00
Medical history: Neoplasms						
Hematologic neoplasm	1.6	2.0	-0.03	1.7	1.7	0.00
Malignant lymphoma	0.9	1.1	-0.02	0.9	0.8	0.01
Malignant neoplasm of anorectum	0.2	0.2	-0.01	0.2	0.2	0.00
Malignant neoplastic disease	11.7	13.0	-0.04	11.9	11.8	0.00
Malignant tumor of breast	4.0	4.2	-0.01	3.9	3.9	0.00
Malignant tumor of colon	0.6	0.8	-0.02	0.7	0.6	0.01
Malignant tumor of lung	0.8	1.1	-0.03	0.9	0.9	0.00
Malignant tumor of urinary bladder	0.3	0.4	-0.01	0.3	0.3	0.00
Medication use						
Agents acting on the renin-angiotensin system	55.5	58.0	-0.05	55.6	55.2	0.01

Antibacterials for systemic use	48.9	52.0	-0.06	49.2	48.6	0.01
Antidepressants	28.2	30.9	-0.06	29.1	28.5	0.01
Anti-epileptics	16.2	18.9	-0.07	17.1	16.6	0.01
Anti-inflammatory and antirheumatic products	18.8	18.6	0.00	18.7	18.6	0.00
Antineoplastic agents	3.9	4.3	-0.02	4.0	3.8	0.01
Antipsoriatics	0.6	1.0	-0.04	0.7	0.7	0.00
Antithrombotic agents	17.2	20.9	-0.09	17.9	17.6	0.01
Beta-blocking agents	70.6	73.6	-0.07	71.1	71.1	0.00
Calcium channel blockers	44.6	47.5	-0.06	44.7	44.7	0.00
Diuretics	51.6	55.3	-0.07	51.9	52.5	-0.01
Drugs for acid related disorders	32.8	36.0	-0.07	33.3	32.6	0.01
Drugs for obstructive airway diseases	28.7	30.1	-0.03	29.4	29.2	0.00
Drugs used in diabetes	20.8	23.1	-0.05	21.4	21.5	0.00
Immunosuppressants	3.6	3.8	-0.01	3.6	3.7	-0.01
Lipid-modifying agents	53.9	58.7	-0.10	54.8	54.3	0.01
Opioids	22.1	24.2	-0.05	22.7	22.3	0.01
Psycholeptics	26.1	27.2	-0.02	26.4	26.0	0.01
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	1.0	1.0	0.00	1.0	1.2	-0.02

AF, atrial fibrillation; PS, propensity score.

Online Resource 9. Baseline characteristics before and after 1:1 PS matching in the AF population in the Optum database: Rivaroxaban vs Dabigatran

Characteristic	Before matching			After matching		
	Rivaroxaban %	Dabigatran %	Std. diff	Rivaroxaban %	Dabigatran %	Std. diff
Age group, years						
25-29	0.0	<0.1	0.02	<0.1	<0.1	0.00
30-34	0.1	<0.1	0.02	0.1	<0.1	0.03
35-39	0.2	0.2	0.00	0.1	0.2	-0.02
40-44	0.4	0.3	0.01	0.4	0.2	0.03
45-49	0.8	0.9	-0.01	0.9	0.8	0.01
50-54	1.9	2.3	-0.03	1.9	1.8	0.01
55-59	3.9	4.7	-0.04	4.7	4.4	0.01
60-64	6.6	8.5	-0.07	7.5	7.6	0.00
65-69	14.8	14.7	0.00	15.9	15.3	0.02
70-74	18.8	18.6	0.00	18.3	19.1	-0.02
75-79	18.7	17.5	0.03	17.8	18.4	-0.02
80-84	18.2	23.8	-0.14	22.0	20.9	0.03
85-89	15.7	8.4	0.22	10.3	11.2	-0.03
Medical history: General						
Acute respiratory disease	24.5	23.5	0.02	24.0	23.9	0.00
Attention-deficit/hyperactivity disorder	0.2	0.2	-0.01	0.1	0.3	-0.03
Chronic liver disease	1.5	1.7	-0.02	1.5	1.8	-0.02
Chronic obstructive lung disease	18.7	16.9	0.05	17.0	17.7	-0.02
Crohn's disease	0.3	0.3	0.00	0.3	0.3	0.01
Dementia	6.1	4.6	0.07	5.1	5.1	0.00
Depressive disorder	16.2	13.5	0.08	14.8	14.4	0.01
Diabetes mellitus	30.4	29.8	0.01	30.3	30.2	0.00
Gastroesophageal reflux disease	22.0	18.4	0.09	20.4	19.6	0.02
Gastrointestinal hemorrhage	2.5	3.0	-0.03	2.8	3.0	-0.02
Human immunodeficiency virus infection	0.1	<0.1	0.02	<0.1	<0.1	0.00
Hyperlipidemia	64.2	66.0	-0.04	66.3	65.7	0.01
Hypertensive disorder	82.0	82.7	-0.02	82.3	82.3	0.00
Lesion of liver	1.0	1.0	0.00	0.9	1.2	-0.03
Obesity	18.5	14.4	0.11	16.6	15.8	0.02
Osteoarthritis	32.7	28.5	0.09	30.2	29.7	0.01
Pneumonia	10.3	9.1	0.04	9.9	9.4	0.01
Psoriasis	1.2	0.9	0.02	1.2	1.0	0.02
Renal impairment	20.9	17.0	0.10	18.2	18.4	0.00
Rheumatoid arthritis	2.9	3.0	-0.01	3.5	3.0	0.03
Schizophrenia	0.2	0.2	0.00	0.3	0.3	0.00
Ulcerative colitis	0.4	0.4	0.00	0.4	0.4	0.01
Urinary tract infectious disease	17.4	16.5	0.02	17.9	16.7	0.03
Viral hepatitis C	0.4	0.3	0.03	0.3	0.3	0.00
Visual system disorder	37.6	37.4	0.00	37.1	37.6	-0.01
Medical history: Cardiovascular disease						
Atrial fibrillation	94.5	96.0	-0.07	95.1	95.4	-0.02
Cerebrovascular disease	15.3	18.8	-0.09	19.0	18.0	0.03
Coronary arteriosclerosis	24.6	26.1	-0.04	26.1	25.7	0.01
Heart disease	98.4	98.9	-0.04	98.7	98.5	0.02
Heart failure	27.6	25.5	0.05	26.4	26.0	0.01
Ischemic heart disease	16.5	16.3	0.00	16.8	16.2	0.02
Peripheral vascular disease	8.3	6.8	0.06	7.2	6.9	0.01
Venous thrombosis	0.7	0.8	0.00	0.9	0.7	0.02
Medical history: Neoplasms						
Hematologic neoplasm	1.6	1.3	0.02	1.4	1.5	0.00
Malignant lymphoma	0.9	0.6	0.04	0.7	0.6	0.00
Malignant neoplasm of anorectum	0.2	0.2	0.00	0.3	0.3	0.02
Malignant neoplastic disease	11.7	11.6	0.00	11.2	11.7	-0.02
Malignant tumor of breast	4.0	4.1	-0.01	3.9	4.1	-0.01
Malignant tumor of colon	0.6	0.6	0.00	0.7	0.7	0.00
Malignant tumor of lung	0.8	0.7	0.02	0.6	0.6	0.00
Malignant tumor of urinary bladder	0.3	0.2	0.02	0.3	0.2	0.01
Medication use						
Agents acting on the renin-angiotensin system	55.5	55.6	0.00	55.3	55.6	-0.01
Antibacterials for systemic use	48.9	48.1	0.02	48.7	48.0	0.01

Antidepressants	28.2	26.7	0.03	27.1	27.5	-0.01
Anti-epileptics	16.2	13.4	0.08	14.0	14.9	-0.02
Anti-inflammatory and antirheumatic products	18.8	18.1	0.02	17.9	18.0	0.00
Antineoplastic agents	3.9	3.6	0.02	3.8	3.8	0.00
Antipsoriatics	0.6	0.6	0.00	0.5	0.7	-0.02
Antithrombotic agents	17.2	15.8	0.04	15.5	15.7	0.00
Beta-blocking agents	70.6	70.8	0.00	70.3	70.2	0.00
Calcium channel blockers	44.6	45.7	-0.02	44.1	45.7	-0.03
Diuretics	51.6	52.3	-0.01	50.8	51.8	-0.02
Drugs for acid related disorders	32.8	30.3	0.05	31.9	31.6	0.01
Drugs for obstructive airway diseases	28.7	25.8	0.07	26.8	26.9	0.00
Drugs used in diabetes	20.8	20.2	0.02	19.7	20.2	-0.01
Immunosuppressants	3.6	3.2	0.02	3.5	3.1	0.02
Lipid-modifying agents	53.9	53.2	0.02	53.7	53.3	0.01
Opioids	22.1	20.4	0.04	20.2	21.3	-0.03
Psycholeptics	26.1	23.4	0.06	25.2	25.2	0.00
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	1.0	0.9	0.01	1.0	1.0	0.00

AF, atrial fibrillation; PS, propensity score.

Online Resource 10. Baseline characteristics before and after 1:1 PS matching in the AF population in the Optum database: Apixaban vs Dabigatran

Characteristic	Before matching			After matching		
	Apixaban %	Dabigatran %	Std. diff	Apixaban %	Dabigatran %	Std. diff
Age group, years						
25-29	0.0	<0.1	0.00	0.0	<0.2	0.00
30-34	0.0	<0.1	0.00	<0.2	<0.2	0.00
35-39	0.1	0.2	-0.03	<0.2	<0.2	-0.01
40-44	0.2	0.3	-0.02	0.4	0.2	0.03
45-49	0.5	0.9	-0.05	0.6	0.9	-0.04
50-54	1.1	2.3	-0.09	1.6	1.8	-0.02
55-59	2.6	4.7	-0.11	3.7	4.0	-0.01
60-64	4.9	8.5	-0.14	7.3	7.1	0.01
65-69	12.5	14.7	-0.06	14.9	15.2	-0.01
70-74	18.4	18.6	0.00	18.0	19.2	-0.03
75-79	18.8	17.5	0.03	18.7	19.0	-0.01
80-84	18.0	23.8	-0.14	17.8	17.8	0.00
85-89	22.8	8.4	0.40	16.9	14.6	0.06
Medical history: General						
Acute respiratory disease	27.8	23.5	0.10	24.9	24.3	0.01
Attention-deficit/hyperactivity disorder	0.2	0.2	-0.01	<0.2	0.4	-0.05
Chronic liver disease	1.4	1.7	-0.03	1.2	2.0	-0.06
Chronic obstructive lung disease	22.2	16.9	0.13	17.4	18.8	-0.04
Crohn's disease	0.4	0.3	0.02	0.3	0.2	0.02
Dementia	7.8	4.6	0.13	6.2	5.8	0.02
Depressive disorder	19.1	13.5	0.15	15.9	16.2	-0.01
Diabetes mellitus	33.0	29.8	0.07	30.6	31.3	-0.02
Gastroesophageal reflux disease	26.4	18.4	0.19	19.9	20.9	-0.02
Gastrointestinal hemorrhage	3.3	3.0	0.02	2.8	3.6	-0.05
Human immunodeficiency virus infection	0.0	<0.1	0.01	0.0	<0.2	0.00
Hyperlipidemia	69.1	66.0	0.07	66.2	66.7	-0.01
Hypertensive disorder	85.5	82.7	0.08	83.5	82.9	0.02
Lesion of liver	1.2	1.0	0.02	0.9	1.4	-0.05
Obesity	20.4	14.4	0.16	16.9	17.6	-0.02
Osteoarthritis	37.3	28.5	0.19	30.5	31.1	-0.01
Pneumonia	12.7	9.1	0.11	9.3	9.7	-0.02
Psoriasis	1.2	0.9	0.03	1.2	0.9	0.04
Renal impairment	28.7	17.0	0.28	18.4	20.1	-0.04
Rheumatoid arthritis	3.1	3.0	0.01	3.1	3.2	-0.01
Schizophrenia	0.3	0.2	0.01	<0.2	0.3	-0.03
Ulcerative colitis	0.5	0.4	0.01	0.5	0.5	0.00
Urinary tract infectious disease	20.6	16.5	0.11	17.3	17.3	0.00
Viral hepatitis C	0.5	0.3	0.04	0.3	0.4	-0.02
Visual system disorder	39.7	37.4	0.05	36.4	38.3	-0.04
Medical history: Cardiovascular disease						
Atrial fibrillation	96.0	96.0	0.00	95.5	95.1	0.02
Cerebrovascular disease	19.5	18.8	0.02	18.3	19.5	-0.03
Coronary arteriosclerosis	30.1	26.1	0.09	26.2	26.9	-0.02
Heart disease	99.3	98.9	0.04	98.4	98.4	0.00
Heart failure	33.6	25.5	0.18	26.2	26.9	-0.02
Ischemic heart disease	20.5	16.3	0.11	16.0	16.9	-0.02
Peripheral vascular disease	10.5	6.8	0.13	7.2	7.3	0.00
Venous thrombosis	0.9	0.8	0.01	0.9	0.7	0.01
Medical history: Neoplasms						
Hematologic neoplasm	2.0	1.3	0.05	1.7	1.6	0.00
Malignant lymphoma	1.1	0.6	0.06	0.9	0.6	0.03
Malignant neoplasm of anorectum	0.2	0.2	0.00	0.3	0.2	0.03
Malignant neoplastic disease	13.0	11.6	0.04	11.5	11.5	0.00
Malignant tumor of breast	4.2	4.1	0.00	4.2	4.1	0.01
Malignant tumor of colon	0.8	0.6	0.02	0.7	0.7	0.00
Malignant tumor of lung	1.1	0.7	0.05	0.7	0.7	-0.01
Malignant tumor of urinary bladder	0.4	0.2	0.03	0.4	0.3	0.03
Medication use						
Agents acting on the renin-angiotensin system	58.0	55.6	0.05	55.5	55.1	0.01
Antibacterials for systemic use	52.0	48.1	0.08	47.6	49.3	-0.03

Antidepressants	30.9	26.7	0.09	29.0	28.7	0.01
Anti-epileptics	18.9	13.4	0.15	16.5	16.7	-0.01
Anti-inflammatory and antirheumatic products	18.6	18.1	0.01	17.7	17.9	-0.01
Antineoplastic agents	4.3	3.6	0.04	3.8	3.5	0.02
Antipsoriatics	1.0	0.6	0.04	0.6	0.6	0.00
Antithrombotic agents	20.9	15.8	0.13	15.9	16.8	-0.02
Beta-blocking agents	73.6	70.8	0.06	69.5	71.1	-0.03
Calcium channel blockers	47.5	45.7	0.04	44.1	44.0	0.00
Diuretics	55.3	52.3	0.06	50.3	52.0	-0.04
Drugs for acid related disorders	36.0	30.3	0.12	32.3	32.7	-0.01
Drugs for obstructive airway diseases	30.1	25.8	0.10	26.7	27.3	-0.02
Drugs used in diabetes	23.1	20.2	0.07	21.0	21.0	0.00
Immunosuppressants	3.8	3.2	0.04	3.8	3.3	0.02
Lipid-modifying agents	58.7	53.2	0.11	53.0	54.4	-0.03
Opioids	24.2	20.4	0.09	21.3	22.7	-0.03
Psycholeptics	27.2	23.4	0.09	26.1	26.7	-0.01
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	1.0	0.9	0.01	1.3	1.1	0.02

AF, atrial fibrillation; PS, propensity score.

Online Resource 11. Baseline characteristics before and after 1:1 PS matching in the VTE population in the Optum database: Apixaban vs Warfarin

Characteristic	Before matching			After matching		
	Apixaban %	Warfarin %	Std. diff	Apixaban %	Warfarin %	Std. diff
Age group, years						
20-24	0.2	0.5	-0.05	0.3	0.4	-0.01
25-29	0.5	0.9	-0.05	0.6	0.5	0.01
30-34	0.8	1.3	-0.05	1.0	0.8	0.02
35-39	1.3	2.0	-0.05	1.5	1.3	0.01
40-44	2.0	2.9	-0.05	2.3	1.6	0.04
45-49	2.9	4.1	-0.06	3.0	3.3	-0.02
50-54	4.1	5.3	-0.06	4.5	3.8	0.03
55-59	6.2	7.2	-0.04	5.8	6.6	-0.03
60-64	8.0	9.0	-0.04	7.9	8.0	0.00
65-69	14.3	14.0	0.01	14.3	14.3	0.00
70-74	17.0	14.3	0.07	16.8	17.2	-0.01
75-79	14.9	12.8	0.06	14.7	14.3	0.01
80-84	12.3	16.9	-0.13	12.2	12.5	-0.01
85-89	15.4	8.6	0.21	15.2	15.4	0.00
Medical history: General						
Acute respiratory disease	34.8	30.7	0.09	34.5	34.9	-0.01
Attention-deficit/hyperactivity disorder	0.7	0.5	0.02	0.6	0.6	-0.01
Chronic liver disease	1.7	3.7	-0.12	2.2	2.3	-0.01
Chronic obstructive lung disease	23.2	20.5	0.06	23.1	23.8	-0.02
Crohn's disease	0.8	1.0	-0.02	0.9	0.9	0.00
Dementia	12.5	10.5	0.06	12.8	12.6	0.01
Depressive disorder	27.5	24.0	0.08	27.4	28.9	-0.04
Diabetes mellitus	33.3	30.1	0.07	33.9	35.0	-0.02
Gastroesophageal reflux disease	35.0	26.4	0.19	32.9	33.7	-0.02
Gastrointestinal hemorrhage	5.8	6.2	-0.02	6.5	6.8	-0.01
Human immunodeficiency virus infection	0.2	0.2	-0.01	0.2	0.3	-0.02
Hyperlipidemia	58.1	51.4	0.14	57.5	57.8	-0.01
Hypertensive disorder	75.0	70.5	0.10	75.1	75.4	-0.01
Lesion of liver	3.8	3.9	0.00	3.8	4.0	-0.01
Obesity	27.3	20.7	0.16	27.8	28.0	0.00
Osteoarthritis	47.4	38.1	0.19	45.9	46.0	0.00
Pneumonia	17.7	16.5	0.03	17.8	18.5	-0.02
Psoriasis	1.0	1.0	0.00	0.9	1.3	-0.04
Renal impairment	32.7	27.1	0.12	34.7	35.4	-0.01
Rheumatoid arthritis	4.9	4.5	0.02	4.5	4.8	-0.02
Schizophrenia	0.6	0.7	0.00	0.7	0.8	0.00
Ulcerative colitis	0.9	1.0	-0.01	1.0	1.0	0.00
Urinary tract infectious disease	25.7	26.5	-0.02	27.2	28.4	-0.03
Viral hepatitis C	0.7	0.6	0.00	0.9	0.9	0.00
Visual system disorder	32.7	29.2	0.08	31.7	32.4	-0.01
Medical history: Cardiovascular disease						
Cerebrovascular disease	12.0	13.2	-0.04	12.1	13.1	-0.03
Coronary arteriosclerosis	19.4	16.4	0.08	19.5	19.7	-0.01
Heart disease	59.0	52.1	0.14	58.4	59.0	-0.01
Heart failure	27.3	19.5	0.19	27.0	27.6	-0.02
Ischemic heart disease	15.5	12.8	0.08	15.7	15.6	0.00
Peripheral vascular disease	12.6	12.1	0.02	12.9	13.3	-0.01
Venous thrombosis	68.8	74.8	-0.14	70.1	70.4	-0.01
Medical history: Neoplasms						
Hematologic neoplasm	6.2	5.5	0.03	5.6	6.3	-0.03
Malignant lymphoma	1.9	1.5	0.03	1.8	1.8	0.00
Malignant neoplasm of anorectum	1.0	1.2	-0.02	0.8	0.9	-0.01
Malignant neoplastic disease	24.1	22.5	0.04	22.4	23.5	-0.03
Malignant tumor of breast	7.3	6.8	0.02	6.5	6.4	0.01
Malignant tumor of colon	2.3	2.4	-0.01	2.2	2.4	-0.01
Malignant tumor of lung	4.7	3.6	0.05	4.0	3.7	0.02
Malignant tumor of urinary bladder	0.5	0.5	0.00	0.6	0.5	0.02
Medication use						
Agents acting on the renin-angiotensin system	46.2	42.7	0.07	45.8	46.3	-0.01

Antibacterials for systemic use	61.0	57.9	0.06	58.8	60.1	-0.03
Antidepressants	38.8	35.9	0.06	37.6	38.9	-0.03
Anti-epileptics	30.3	23.9	0.14	29.3	30.3	-0.02
Anti-inflammatory and antirheumatic products	27.1	24.1	0.07	24.4	23.8	0.01
Antineoplastic agents	10.7	9.8	0.03	9.2	9.4	0.00
Antipsoriatics	1.1	1.0	0.01	1.2	1.5	-0.02
Antithrombotic agents	25.9	54.4	-0.61	36.5	34.5	0.04
Beta-blocking agents	37.4	34.7	0.06	37.8	37.5	0.01
Calcium channel blockers	28.6	25.7	0.06	28.9	28.4	0.01
Diuretics	44.7	42.6	0.04	45.1	45.7	-0.01
Drugs for acid related disorders	42.2	37.6	0.10	41.1	42.7	-0.03
Drugs for obstructive airway diseases	32.4	27.6	0.10	30.5	31.3	-0.02
Drugs used in diabetes	22.7	20.4	0.06	22.7	24.0	-0.03
Immunosuppressants	6.0	5.1	0.04	5.6	5.6	0.00
Lipid-modifying agents	45.4	40.6	0.10	45.5	45.4	0.00
Opioids	41.5	40.0	0.03	42.4	41.9	0.01
Psycholeptics	36.2	33.9	0.05	35.6	36.7	-0.02
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	2.4	2.1	0.02	2.1	1.6	0.04

PS, propensity score; VTE, venous thromboembolism.

Online Resource 12. Baseline characteristics before and after 1:1 PS matching in the VTE population: Dabigatran vs Warfarin

Characteristic	Before matching			After matching		
	Dabigatran %	Warfarin %	Std. diff	Dabigatran %	Warfarin %	Std. diff
Age group, years						
20-24	<1.2	0.5	-0.05	<1.2	0.0	0.00
25-29	<1.2	0.9	-0.05	<1.2	<1.2	-0.06
30-34	1.8	1.3	0.04	1.9	1.6	0.02
35-39	2.1	2.0	0.01	2.1	2.6	-0.03
40-44	3.2	2.9	0.02	3.2	3.2	0.00
45-49	4.8	4.1	0.03	4.9	5.6	-0.03
50-54	7.1	5.3	0.07	7.2	6.0	0.05
55-59	9.2	7.2	0.07	9.0	9.0	0.00
60-64	9.4	9.0	0.02	9.5	11.1	-0.05
65-69	13.6	14.0	-0.01	13.7	13.9	-0.01
70-74	16.4	14.3	0.06	16.2	13.7	0.07
75-79	12.7	12.8	0.00	12.8	10.4	0.07
80-84	8.3	16.9	-0.26	8.4	12.8	-0.14
85-89	10.6	8.6	0.07	10.4	9.0	0.05
Medical history: General						
Acute respiratory disease	31.3	30.7	0.01	31.1	33.6	-0.06
Attention-deficit/hyperactivity disorder	1.2	0.5	0.07	1.2	1.2	0.00
Chronic liver disease	4.1	3.7	0.02	4.2	3.2	0.05
Chronic obstructive lung disease	20.3	20.5	-0.01	20.2	21.1	-0.02
Crohn's disease	1.4	1.0	0.04	1.4	<1.2	0.10
Dementia	6.5	10.5	-0.14	6.5	5.8	0.03
Depressive disorder	25.1	24.0	0.03	25.1	30.4	-0.12
Diabetes mellitus	27.6	30.1	-0.05	27.8	30.6	-0.06
Gastroesophageal reflux disease	30.2	26.4	0.08	30.2	30.6	-0.01
Gastrointestinal hemorrhage	5.8	6.2	-0.02	5.8	6.7	-0.04
Human immunodeficiency virus infection	<1.2	0.2	0.00	<1.2	0.0	0.00
Hyperlipidemia	52.5	51.4	0.02	52.7	51.3	0.03
Hypertensive disorder	70.0	70.5	-0.01	70.1	69.4	0.02
Lesion of liver	5.5	3.9	0.08	5.6	7.0	-0.06
Obesity	24.7	20.7	0.10	24.6	26.2	-0.04
Osteoarthritis	45.2	38.1	0.14	44.8	47.8	-0.06
Pneumonia	13.8	16.5	-0.08	13.7	13.7	0.00
Psoriasis	1.2	1.0	0.01	1.2	2.6	-0.10
Renal impairment	22.1	27.1	-0.12	22.0	20.4	0.04
Rheumatoid arthritis	1.6	4.5	-0.17	1.6	2.1	-0.03
Schizophrenia	<1.2	0.7	0.00	<1.2	1.4	-0.07
Ulcerative colitis	1.6	1.0	0.05	1.6	<1.2	0.09
Urinary tract infectious disease	24.4	26.5	-0.05	24.4	25.1	-0.02
Viral hepatitis C	<1.2	0.6	0.01	<1.2	<1.2	0.00
Visual system disorder	29.5	29.2	0.01	29.2	28.8	0.01
Medical history: Cardiovascular disease						
Cerebrovascular disease	10.1	13.2	-0.10	9.7	12.1	-0.07
Coronary arteriosclerosis	14.7	16.4	-0.04	14.4	16.7	-0.06
Heart disease	51.6	52.1	-0.01	51.5	52.9	-0.03
Heart failure	20.7	19.5	0.03	20.9	19.7	0.03
Ischemic heart disease	12.0	12.8	-0.02	11.8	13.9	-0.06
Peripheral vascular disease	10.6	12.1	-0.05	10.4	10.4	0.00
Venous thrombosis	69.8	74.8	-0.11	69.6	67.5	0.04
Medical history: Neoplasms						
Hematologic neoplasm	6.7	5.5	0.05	6.7	10.2	-0.12
Malignant lymphoma	1.8	1.5	0.02	1.9	2.3	-0.03
Malignant neoplasm of anorectum	<1.2	1.2	-0.05	<1.2	<1.2	-0.03
Malignant neoplastic disease	29.0	22.5	0.15	29.0	32.7	-0.08
Malignant tumor of breast	7.1	6.8	0.01	7.2	11.1	-0.14
Malignant tumor of colon	4.1	2.4	0.10	4.2	3.0	0.06
Malignant tumor of lung	5.5	3.6	0.09	5.6	6.0	-0.02
Malignant tumor of urinary bladder	<1.2	0.5	0.00	<1.2	<1.2	-0.04
Primary malignant neoplasm of prostate	0.0	0.0	0.00	0.0	<1.2	0.00
Medication use						

Agents acting on the renin-angiotensin system	41.9	42.7	-0.02	41.8	41.1	0.01
Antibacterials for systemic use	61.1	57.9	0.06	60.8	61.9	-0.02
Antidepressants	37.1	35.8	0.03	37.1	39.2	-0.04
Anti-epileptics	29.5	23.9	0.13	29.2	30.6	-0.03
Anti-inflammatory and antirheumatic products	24.4	24.1	0.01	24.4	23.7	0.02
Antineoplastic agents	11.5	9.8	0.06	11.6	9.5	0.07
Antipsoriatics	<1.2	1.0	-0.07	<1.2	<1.2	-0.03
Antithrombotic agents	29.3	54.4	-0.53	29.2	26.0	0.07
Beta-blocking agents	29.5	34.6	-0.11	29.7	32.7	-0.06
Calcium channel blockers	24.0	25.7	-0.04	23.9	21.6	0.06
Diuretics	36.4	42.6	-0.13	36.4	38.1	-0.03
Drugs for acid related disorders	38.0	37.6	0.01	37.6	42.9	-0.11
Drugs for obstructive airway diseases	28.1	27.6	0.01	27.6	31.8	-0.09
Drugs used in diabetes	20.5	20.4	0.00	20.6	21.8	-0.03
Immunosuppressants	5.8	5.1	0.03	5.8	4.4	0.06
Lipid-modifying agents	41.5	40.6	0.02	41.5	41.3	0.00
Opioids	42.4	40.0	0.05	42.5	45.7	-0.06
Psycholeptics	36.9	33.9	0.06	36.9	40.8	-0.08
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	3.9	2.1	0.11	3.9	1.6	0.14

PS, propensity score; VTE, venous thromboembolism.

Online Resource 13. Baseline characteristics before and after 1:1 PS matching in the VTE population: Rivaroxaban vs Apixaban

Characteristic	Before matching			After matching		
	Rivaroxaban %	Apixaban %	Std. diff	Rivaroxaban %	Apixaban %	Std. diff
Age group, years						
20-24	0.7	0.2	0.07	0.5	0.3	0.04
25-29	1.0	0.5	0.06	0.7	0.6	0.01
30-34	1.3	0.8	0.05	0.9	1.1	-0.01
35-39	2.6	1.3	0.09	1.8	1.6	0.02
40-44	3.5	2.0	0.09	2.4	2.5	0.00
45-49	5.0	2.9	0.11	3.7	3.4	0.02
50-54	6.5	4.1	0.11	5.0	4.8	0.01
55-59	8.8	6.2	0.10	7.2	7.3	0.00
60-64	10.1	8.0	0.07	8.9	8.8	0.01
65-69	14.2	14.3	0.00	14.3	14.9	-0.02
70-74	15.0	17.0	-0.06	16.5	17.2	-0.02
75-79	11.9	14.9	-0.09	14.1	13.9	0.00
80-84	9.7	12.3	-0.08	11.1	11.2	0.00
85-89	9.7	15.4	-0.17	12.7	12.6	0.00
Medical history: General						
Acute respiratory disease	28.8	34.8	-0.13	31.8	31.6	0.00
Attention-deficit/hyperactivity disorder	0.8	0.7	0.01	0.5	0.8	-0.04
Chronic liver disease	2.1	1.7	0.03	1.7	1.5	0.02
Chronic obstructive lung disease	17.4	23.2	-0.15	20.5	19.9	0.01
Crohn's disease	0.9	0.8	0.01	0.9	0.7	0.02
Dementia	8.4	12.5	-0.13	10.5	10.3	0.01
Depressive disorder	24.1	27.5	-0.08	26.7	26.6	0.00
Diabetes mellitus	26.0	33.3	-0.16	30.5	28.8	0.04
Gastroesophageal reflux disease	27.3	35.0	-0.17	32.0	31.5	0.01
Gastrointestinal hemorrhage	4.4	5.8	-0.07	4.8	5.0	-0.01
Human immunodeficiency virus infection	0.2	0.2	0.00	0.2	0.2	-0.01
Hyperlipidemia	49.0	58.1	-0.18	55.5	53.8	0.03
Hypertensive disorder	64.0	75.0	-0.24	71.6	70.2	0.03
Lesion of liver	4.2	3.8	0.02	4.1	3.9	0.01
Obesity	23.4	27.3	-0.09	26.9	25.4	0.03
Osteoarthritis	40.1	47.4	-0.15	45.5	44.7	0.02
Pneumonia	13.0	17.7	-0.13	15.1	15.0	0.00
Psoriasis	1.2	1.0	0.02	1.3	1.0	0.03
Renal impairment	18.8	32.7	-0.32	25.5	23.6	0.04
Rheumatoid arthritis	4.4	4.9	-0.02	4.7	4.4	0.01
Schizophrenia	0.6	0.6	0.00	0.7	0.6	0.01
Ulcerative colitis	0.8	0.9	-0.02	0.8	0.9	-0.01
Urinary tract infectious disease	20.5	25.7	-0.12	22.8	21.9	0.02
Viral hepatitis C	0.5	0.7	-0.02	0.6	0.6	0.01
Visual system disorder	28.1	32.7	-0.10	31.6	30.6	0.02
Medical history: Cardiovascular disease						
Cerebrovascular disease	8.6	12.0	-0.11	9.9	9.8	0.00
Coronary arteriosclerosis	13.1	19.4	-0.17	16.2	15.3	0.02
Heart disease	44.8	59.0	-0.29	53.0	51.6	0.03
Heart failure	16.2	27.3	-0.27	21.7	21.2	0.01
Ischemic heart disease	10.0	15.5	-0.16	12.4	12.3	0.00
Peripheral vascular disease	10.2	12.6	-0.08	11.7	10.9	0.03
Venous thrombosis	73.4	68.8	0.10	69.2	70.2	-0.02
Medical history: Neoplasms						
Hematologic neoplasm	6.8	6.2	0.03	6.7	6.4	0.01
Malignant lymphoma	1.8	1.9	-0.01	2.0	2.0	0.00
Malignant neoplasm of anorectum	1.2	1.0	0.02	1.1	1.1	0.00
Malignant neoplastic disease	24.9	24.1	0.02	24.7	24.6	0.00
Malignant tumor of breast	8.0	7.3	0.02	7.4	7.6	-0.01
Malignant tumor of colon	2.4	2.3	0.00	2.3	2.6	-0.02
Malignant tumor of lung	4.8	4.7	0.00	4.9	5.1	-0.01
Malignant tumor of urinary bladder	0.5	0.5	0.00	0.6	0.4	0.02
Medication use						
Agents acting on the renin-angiotensin system	39.5	46.2	-0.14	44.6	42.7	0.04
Antibacterials for systemic use	58.7	61.0	-0.05	60.3	59.4	0.02

Antidepressants	35.6	38.8	-0.06	37.3	37.8	-0.01
Anti-epileptics	25.2	30.3	-0.11	28.3	28.1	0.00
Anti-inflammatory and antirheumatic products	27.1	27.1	0.00	26.8	27.4	-0.01
Antineoplastic agents	12.0	10.7	0.04	11.5	11.2	0.01
Antipsoriatics	0.4	1.1	-0.08	0.6	0.6	0.00
Antithrombotic agents	23.0	25.9	-0.07	24.8	24.1	0.01
Beta-blocking agents	29.4	37.4	-0.17	33.5	32.5	0.02
Calcium channel blockers	21.0	28.6	-0.18	25.2	24.1	0.02
Diuretics	37.3	44.7	-0.15	41.8	40.3	0.03
Drugs for acid related disorders	35.2	42.2	-0.14	39.0	38.7	0.01
Drugs for obstructive airway diseases	27.9	32.4	-0.10	30.4	30.5	0.00
Drugs used in diabetes	17.8	22.7	-0.12	20.7	19.7	0.03
Immunosuppressants	5.3	6.0	-0.03	5.9	5.7	0.01
Lipid-modifying agents	37.2	45.4	-0.17	42.2	41.0	0.02
Opioids	40.6	41.5	-0.02	41.1	41.7	-0.01
Psycholeptics	36.8	36.2	0.01	35.9	36.3	-0.01
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	2.7	2.4	0.02	2.2	2.7	-0.03

PS, propensity score; VTE, venous thromboembolism.

Online Resource 14. Baseline characteristics before and after 1:1 PS matching in the VTE population: Rivaroxaban vs Dabigatran

Characteristic	Before matching			After matching		
	Rivaroxaban %	Dabigatran %	Std. diff	Rivaroxaban %	Dabigatran %	Std. diff
Age group, years						
20-24	0.7	<1.2	0.07	<1.2	<1.2	0.10
25-29	1.0	<1.2	0.06	<1.2	<1.2	0.00
30-34	1.3	1.8	-0.04	1.5	2.0	-0.04
35-39	2.6	2.1	0.03	2.2	2.0	0.02
40-44	3.5	3.2	0.02	3.5	3.2	0.01
45-49	5.0	4.8	0.01	4.2	5.2	-0.05
50-54	6.5	7.1	-0.03	4.7	6.9	-0.10
55-59	8.8	9.2	-0.02	8.2	8.2	0.00
60-64	10.1	9.4	0.02	10.4	9.4	0.03
65-69	14.2	13.6	0.02	15.6	13.1	0.07
70-74	15.0	16.4	-0.04	14.6	17.1	-0.07
75-79	11.9	12.7	-0.02	12.9	12.9	0.00
80-84	9.7	8.3	0.05	8.7	8.2	0.02
85-89	9.7	10.6	-0.03	12.1	11.1	0.03
Medical history: General						
Acute respiratory disease	28.8	31.3	-0.06	35.1	31.2	0.08
Attention-deficit/hyperactivity disorder	0.8	1.2	-0.04	<1.2	<1.2	-0.06
Chronic liver disease	2.1	4.1	-0.12	2.5	4.2	-0.10
Chronic obstructive lung disease	17.4	20.3	-0.08	25.2	21.0	0.10
Crohn's disease	0.9	1.4	-0.05	<1.2	1.2	-0.12
Dementia	8.4	6.5	0.08	7.9	6.9	0.04
Depressive disorder	24.1	25.1	-0.02	28.2	25.7	0.06
Diabetes mellitus	26.0	27.6	-0.04	28.2	28.2	0.00
Gastroesophageal reflux disease	27.3	30.2	-0.06	36.6	30.7	0.13
Gastrointestinal hemorrhage	4.4	5.8	-0.06	8.4	5.7	0.11
Human immunodeficiency virus infection	0.2	<1.2	-0.01	<1.2	<1.2	0.00
Hyperlipidemia	49.0	52.5	-0.07	54.5	53.0	0.03
Hypertensive disorder	64.0	70.0	-0.13	72.3	70.3	0.04
Lesion of liver	4.2	5.5	-0.06	5.9	5.7	0.01
Obesity	23.4	24.7	-0.03	27.2	24.8	0.06
Osteoarthritis	40.1	45.2	-0.10	47.3	45.5	0.04
Pneumonia	13.0	13.8	-0.02	14.1	14.1	0.00
Psoriasis	1.2	1.2	0.00	1.5	1.2	0.02
Renal impairment	18.8	22.1	-0.08	24.3	22.5	0.04
Rheumatoid arthritis	4.4	1.6	0.16	3.2	1.5	0.12
Schizophrenia	0.6	<1.2	-0.01	<1.2	<1.2	0.03
Ulcerative colitis	0.8	1.6	-0.08	1.5	1.2	0.02
Urinary tract infectious disease	20.5	24.4	-0.10	23.5	24.8	-0.03
Viral hepatitis C	0.5	<1.2	-0.02	<1.2	<1.2	-0.07
Visual system disorder	28.1	29.5	-0.03	29.0	30.9	-0.04
Medical history: Cardiovascular disease						
Cerebrovascular disease	8.6	10.1	-0.05	14.1	9.9	0.13
Coronary arteriosclerosis	13.1	14.7	-0.05	16.6	14.1	0.07
Heart disease	44.8	51.6	-0.14	55.9	51.0	0.10
Heart failure	16.2	20.7	-0.12	20.3	21.0	-0.02
Ischemic heart disease	10.0	12.0	-0.06	16.1	11.6	0.13
Peripheral vascular disease	10.2	10.6	-0.01	10.4	10.4	0.00
Venous thrombosis	73.4	69.8	0.08	66.1	68.8	-0.06
Medical history: Neoplasms						
Hematologic neoplasm	6.8	6.7	0.00	8.7	6.2	0.10
Malignant lymphoma	1.8	1.8	0.00	1.5	1.7	-0.02
Malignant neoplasm of anorectum	1.2	<1.2	0.05	1.7	<1.2	0.09
Malignant neoplastic disease	24.9	29.0	-0.09	30.7	28.5	0.05
Malignant tumor of breast	8.0	7.1	0.03	6.7	6.4	0.01
Malignant tumor of colon	2.4	4.1	-0.10	3.5	4.5	-0.05
Malignant tumor of lung	4.8	5.5	-0.03	5.0	4.5	0.02
Malignant tumor of urinary bladder	0.5	<1.2	0.01	<1.2	<1.2	0.06
Medication use						
Agents acting on the renin-angiotensin system	39.5	41.9	-0.05	40.8	41.3	-0.01

Antibacterials for systemic use	58.7	61.1	-0.05	59.7	59.7	0.00
Antidepressants	35.6	37.1	-0.03	37.9	37.4	0.01
Anti-epileptics	25.2	29.5	-0.10	30.2	29.7	0.01
Anti-inflammatory and antirheumatic products	27.1	24.4	0.06	22.0	24.5	-0.06
Antineoplastic agents	12.0	11.5	0.02	11.1	11.1	0.00
Antipsoriatics	0.4	<1.2	0.00	0.0	<1.2	0.00
Antithrombotic agents	23.0	29.3	-0.14	34.7	29.0	0.12
Beta-blocking agents	29.4	29.5	0.00	33.7	29.0	0.10
Calcium channel blockers	21.0	24.0	-0.07	20.5	24.0	-0.08
Diuretics	37.3	36.4	0.02	34.9	35.4	-0.01
Drugs for acid related disorders	35.2	38.2	-0.06	39.6	38.6	0.02
Drugs for obstructive airway diseases	27.9	28.1	0.00	30.4	28.7	0.04
Drugs used in diabetes	17.8	20.5	-0.07	18.3	20.0	-0.04
Immunosuppressants	5.3	5.8	-0.02	3.7	5.4	-0.08
Lipid-modifying agents	37.2	41.7	-0.09	44.3	41.8	0.05
Opioids	40.6	42.4	-0.04	44.3	41.8	0.05
Psycholeptics	36.8	36.9	0.00	35.4	36.9	-0.03
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	2.7	3.9	-0.07	3.7	3.5	0.01

PS, propensity score; VTE, venous thromboembolism.

Online Resource 15. Baseline characteristics before and after 1:1 PS matching in the VTE population: Apixaban vs Dabigatran

Characteristic	Before matching			After matching		
	Apixaban %	Dabigatran %	Std. diff	Apixaban %	Dabigatran %	Std. diff
Age group, years						
20-24	0.2	<1.2	0.00	<1.3	<1.3	0.07
25-29	0.5	<1.2	0.00	1.3	<1.3	0.08
30-34	0.8	1.8	-0.09	<1.3	2.1	-0.11
35-39	1.3	2.1	-0.06	1.9	1.6	0.02
40-44	2.0	3.2	-0.07	4.3	3.2	0.06
45-49	2.9	4.8	-0.10	4.0	4.5	-0.03
50-54	4.1	7.1	-0.13	5.9	6.9	-0.04
55-59	6.2	9.2	-0.11	7.2	7.7	-0.02
60-64	8.0	9.4	-0.05	9.0	9.6	-0.02
65-69	14.3	13.6	0.02	13.8	13.3	0.02
70-74	17.0	16.4	0.02	15.7	18.1	-0.06
75-79	14.9	12.7	0.06	10.9	12.2	-0.04
80-84	12.3	8.3	0.13	11.7	8.2	0.12
85-89	15.4	10.6	0.14	12.8	11.7	0.03
Medical history: General						
Acute respiratory disease	34.8	31.3	0.07	29.3	32.2	-0.06
Attention-deficit/hyperactivity disorder	0.7	1.2	-0.05	<1.3	<1.3	-0.06
Chronic liver disease	1.7	4.1	-0.14	2.1	3.7	-0.10
Chronic obstructive lung disease	23.2	20.3	0.07	22.9	21.8	0.03
Crohn's disease	0.8	1.4	-0.06	<1.3	1.3	-0.08
Dementia	12.5	6.5	0.21	10.6	7.2	0.12
Depressive disorder	27.5	25.1	0.06	27.4	26.6	0.02
Diabetes mellitus	33.3	27.6	0.12	31.9	29.3	0.06
Gastroesophageal reflux disease	35.0	30.2	0.10	34.6	31.6	0.06
Gastrointestinal hemorrhage	5.8	5.8	0.00	6.9	6.4	0.02
Human immunodeficiency virus infection	0.2	<1.2	-0.01	<1.3	<1.3	0.00
Hyperlipidemia	58.1	52.5	0.11	50.0	53.2	-0.06
Hypertensive disorder	75.0	70.0	0.11	71.3	71.0	0.01
Lesion of liver	3.8	5.5	-0.08	4.8	5.6	-0.04
Obesity	27.3	24.7	0.06	24.7	25.5	-0.02
Osteoarthritis	47.4	45.2	0.04	49.5	46.8	0.05
Pneumonia	17.7	13.8	0.10	14.4	13.8	0.02
Psoriasis	1.0	1.2	-0.02	<1.3	<1.3	-0.03
Renal impairment	32.7	22.1	0.24	26.3	23.9	0.06
Rheumatoid arthritis	4.9	1.6	0.19	4.5	1.6	0.17
Schizophrenia	0.6	<1.2	0.00	<1.3	<1.3	0.00
Ulcerative colitis	0.9	1.6	-0.06	<1.3	1.6	-0.10
Urinary tract infectious disease	25.7	24.4	0.03	25.3	25.0	0.01
Viral hepatitis C	0.7	<1.2	0.00	<1.3	<1.3	0.06
Visual system disorder	32.7	29.5	0.07	28.2	31.6	-0.08
Medical history: Cardiovascular disease						
Cerebrovascular disease	12.0	10.1	0.06	12.0	9.8	0.07
Coronary arteriosclerosis	19.4	14.7	0.12	14.6	13.8	0.02
Heart disease	59.0	51.6	0.15	53.7	51.6	0.04
Heart failure	27.3	20.7	0.16	22.3	21.8	0.01
Ischemic heart disease	15.5	12.0	0.10	14.1	11.2	0.09
Peripheral vascular disease	12.6	10.6	0.06	10.9	11.2	-0.01
Venous thrombosis	68.8	69.8	-0.02	66.2	67.8	-0.03
Medical history: Neoplasms						
Hematologic neoplasm	6.2	6.7	-0.02	7.4	6.4	0.04
Malignant lymphoma	1.9	1.8	0.01	2.1	1.9	0.02
Malignant neoplasm of anorectum	1.0	<1.2	0.03	<1.3	<1.3	0.03
Malignant neoplastic disease	24.1	29.0	-0.11	27.9	28.2	-0.01
Malignant tumor of breast	7.3	7.1	0.01	8.0	6.6	0.05
Malignant tumor of colon	2.3	4.1	-0.10	3.7	4.3	-0.03
Malignant tumor of lung	4.7	5.5	-0.04	6.1	4.5	0.07
Malignant tumor of urinary bladder	0.5	<1.2	0.00	<1.3	<1.3	0.03
Medication use						
Agents acting on the renin-angiotensin system	46.2	41.9	0.09	39.1	41.2	-0.04
Antibacterials for systemic use	61.0	61.1	0.00	58.0	60.1	-0.04

Antidepressants	38.8	37.1	0.03	35.4	38.0	-0.06
Anti-epileptics	30.3	29.5	0.02	25.8	30.6	-0.11
Anti-inflammatory and antirheumatic products	27.1	24.4	0.06	26.9	25.0	0.04
Antineoplastic agents	10.7	11.5	-0.03	11.4	11.4	0.00
Antipsoriatics	1.1	<1.2	0.08	<1.3	<1.3	0.03
Antithrombotic agents	25.9	29.3	-0.08	34.3	30.3	0.08
Beta-blocking agents	37.4	29.5	0.17	31.1	29.0	0.05
Calcium channel blockers	28.6	24.0	0.10	26.3	25.5	0.02
Diuretics	44.7	36.4	0.17	37.8	35.1	0.06
Drugs for acid related disorders	42.2	38.2	0.08	40.7	39.6	0.02
Drugs for obstructive airway diseases	32.4	28.1	0.09	29.0	28.2	0.02
Drugs used in diabetes	22.7	20.5	0.05	22.3	21.3	0.03
Immunosuppressants	6.0	5.8	0.01	5.9	5.9	0.00
Lipid-modifying agents	45.4	41.7	0.08	34.3	42.3	-0.16
Opioids	41.5	42.4	-0.02	44.1	42.8	0.03
Psycholeptics	36.2	36.9	-0.01	39.1	36.7	0.05
Psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics	2.4	3.9	-0.08	3.7	4.0	-0.01

PS, propensity score; VTE, venous thromboembolism.

Online Resource 16. After matching (adjusted) incidence rates by indication and exposure group; on-treatment, 1:100 PS matching

Indication	T vs C	Database	Patients		TAR		Events		IR		MDRR
			T	C	T	C	T	C	T	C	
AF	Rivaroxaban vs Warfarin	CCAIE	2,909	6,495	719	1,931	6	18	8.34	9.32	3.45
		MDCR	9,362	20,817	3,063	6,894	12	16	3.92	2.32	3.14
		Optum	13,891	34,511	4,249	13,552	22	27	5.18	1.99	2.42
		Meta-analysis	26,162	61,823	8,032	22,378	40	61	4.98	2.73	1.84
	Apixaban vs Warfarin	CCAIE	1,971	3,924	487	1,231	5	14	10.26	11.37	3.91
		MDCR	6,554	12,901	2,164	4,334	<5	10	<2.31	2.31	>4.62
		Optum	13,282	25,981	4,052	10,396	11	21	2.71	2.02	2.85
		Meta-analysis	21,807	42,806	6,704	15,961	<21	45	<3.13	2.82	>2.07
	Dabigatran vs Warfarin	CCAIE	3,086	8,440	722	2,464	<5	21	<6.92	8.52	>3.46
		MDCR	7,949	27,637	2,357	9,103	6	17	2.54	1.87	4.07
		Optum	7,126	38,367	1,876	14,817	<5	29	<2.66	1.96	>3.75
		Meta-analysis	18,161	74,444	4,957	26,386	<16	67	<3.23	2.54	>2.17
	Rivaroxaban vs Apixaban	CCAIE	5,091	8,240	1,335	2,202	16	12	11.98	5.45	2.97
		MDCD	2,009	3,345	427	695	<5	0	<11.69	0.00	>13.30
		MDCR	9,444	18,474	3,064	6,210	11	12	3.59	1.93	3.44
		Optum	17,478	39,594	5,563	12,534	26	38	4.67	3.03	2.14
		Meta-analysis	32,013	66,308	9,963	20,948	53	62	5.32	2.96	1.75
	Rivaroxaban vs Dabigatran	MDCR	4,028	6,135	1,382	1,775	7	<5	5.06	<2.82	>57.40
		Optum	4,729	5,991	1,439	1,554	10	<5	6.95	<3.22	>12.47
		Meta-analysis	8,757	12,126	2,822	3,329	17	<10	6.02	<3.00	>8.55
	Apixaban vs Dabigatran	MDCR	2,172	2,453	751	700	<5	<5	<6.65	<7.14	>Inf
		Optum	3,102	3,476	973	921	5	<5	5.14	<5.43	>Inf
		Meta-analysis	5,274	5,929	1,725	1,622	<10	<10	<5.80	<6.16	>Inf
	VTE	Rivaroxaban vs Warfarin	CCAIE	5,027	17,425	937	4,778	28	50	29.87	10.46
MDCD			2,606	7,136	414	1,720	6	16	14.47	9.30	3.85
Optum			6,921	22,402	1,516	7,042	22	39	14.51	5.54	2.33
Meta-analysis			14,554	46,963	2,868	13,541	56	105	19.52	7.75	1.68
Apixaban vs Warfarin		CCAIE	1,922	7,633	392	2,115	6	22	15.29	10.40	3.75
		MDCD	1,214	4,565	200	1,093	<5	10	<24.97	9.15	>5.90
		Optum	4,087	12,615	964	4,076	9	22	9.33	5.40	3.22
		Meta-analysis	7,223	24,813	1,557	7,285	<20	54	<12.84	7.41	>2.18
Rivaroxaban vs Apixaban		CCAIE	4,590	5,197	908	1,056	25	10	27.50	9.47	2.58
		MDCR	2,265	2,920	498	705	<5	<5	<10.02	<7.09	>Inf
		Optum	7,678	10,012	1,768	2,490	24	14	13.57	5.62	2.50
		Meta-analysis	14,533	18,129	3,176	4,252	<54	<29	<17.00	<6.82	>3.09

AF, atrial fibrillation; C, comparator; CCAIE, IBM MarketScan® Commercial Database; Inf, infinity; IR, incidence rate; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; MDRR, minimal detectable relative risk; T, treatment; TAR, time-at-risk; VTE, venous thromboembolism.

Online Resource 17. After matching (adjusted) incidence rates by indication and exposure group; on-treatment (30d gap), 1:100 PS matching

Indication	T vs C	Database	Patients		TAR		Events		IR		MDRR
			T	C	T	C	T	C	T	C	
AF	Rivaroxaban vs Warfarin	CCAIE	2,909	6,495	1,908	3,475	25	33	13.10	9.50	2.22
		MDCR	9,362	20,817	8,302	13,271	28	23	3.37	1.73	2.34
		Optum	13,891	34,511	12,358	27,886	54	61	4.37	2.19	1.78
		Meta-analysis	26,162	61,823	22,569	44,633	107	117	4.74	2.62	1.51
	Apixaban vs Warfarin	CCAIE	1,971	3,924	1,484	2,212	11	22	7.41	9.95	2.81
		MDCR	6,554	12,901	6,206	8,037	13	16	2.09	1.99	3.01
		Optum	13,282	25,981	12,602	20,534	32	44	2.54	2.14	1.97
		Meta-analysis	21,807	42,806	20,292	30,784	56	82	2.76	2.66	1.66
	Dabigatran vs Warfarin	CCAIE	3,086	8,440	1,765	4,448	13	40	7.36	8.99	2.38
		MDCR	7,949	27,637	6,369	17,593	23	28	3.61	1.59	2.56
		Optum	7,126	38,367	5,947	31,381	15	69	2.52	2.20	2.32
	Rivaroxaban vs Apixaban	CCAIE	5,091	8,240	3,419	5,949	36	41	10.53	6.89	1.93
		MDCR	9,444	18,474	7,849	16,317	27	32	3.44	1.96	2.16
		Optum	17,478	39,594	14,321	33,323	63	82	4.40	2.46	1.66
		Meta-analysis	32,013	66,308	25,590	55,590	126	155	4.92	2.79	1.43
	Rivaroxaban vs Dabigatran	CCAIE	1,972	2,939	1,339	1,568	20	10	14.93	6.38	2.84
		MDCR	4,028	6,135	3,836	4,606	17	14	4.43	3.04	2.80
		Optum	4,729	5,991	4,525	4,782	23	14	5.08	2.93	2.53
		Meta-analysis	10,729	15,065	9,701	10,956	60	38	6.18	3.47	1.78
	Apixaban vs Dabigatran	CCAIE	1,044	1,136	805	633	11	6	13.65	9.47	3.90
		MDCR	2,172	2,453	2,309	1,850	<5	9	<2.17	4.86	>4.48
		Optum	3,102	3,476	3,072	2,690	11	8	3.58	2.97	3.62
		Meta-analysis	6,318	7,065	6,187	5,174	<27	23	<4.36	4.45	>2.21
	VTE	Rivaroxaban vs Warfarin	CCAIE	5,027	17,425	2,487	8,383	54	84	21.71	10.02
MDCD			2,606	7,136	1,093	3,182	14	30	12.80	9.43	2.60
MDCR			3,376	12,081	1,844	6,641	9	16	4.88	2.41	3.88
Optum			6,921	22,402	3,847	12,969	43	69	11.18	5.32	1.87
Meta-analysis			17,930	59,044	9,273	31,176	120	199	12.94	6.38	1.45
Apixaban vs Warfarin		CCAIE	1,922	7,633	962	3,565	13	37	13.50	10.38	2.69
		MDCD	1,214	4,565	485	1,953	<5	21	<10.30	10.75	>3.85
		Optum	4,087	12,615	2,279	7,179	12	37	5.26	5.15	2.54
		Meta-analysis	7,223	24,813	3,728	12,698	<30	95	<8.05	7.48	>1.82
Rivaroxaban vs Apixaban		CCAIE	4,590	5,197	2,152	2,426	47	23	21.83	9.48	1.96
		MDCR	2,265	2,920	1,166	1,548	<5	5	<4.28	3.23	>5.97
		Optum	7,678	10,012	3,931	5,334	45	22	11.45	4.12	1.99
		Meta-analysis	14,533	18,129	7,251	9,310	<97	50	<13.38	5.37	>1.59

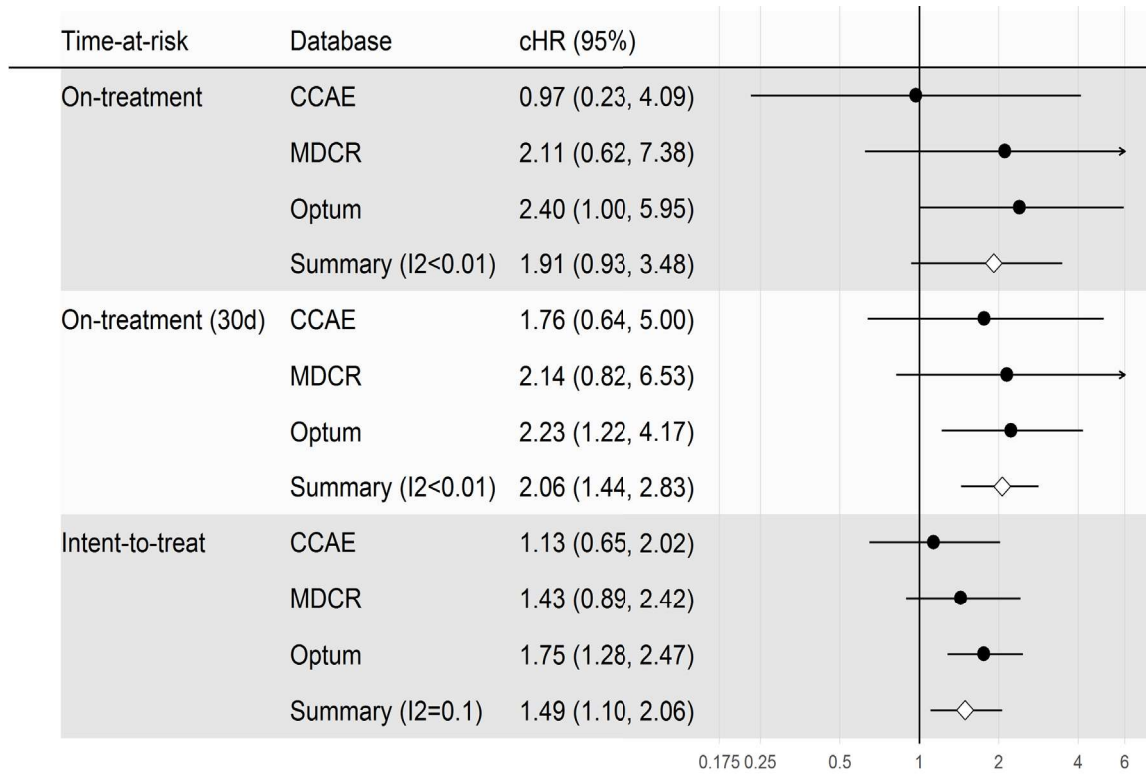
AF, atrial fibrillation; C, comparator; CCAIE, IBM MarketScan® Commercial Database; IR, incidence rate; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; MDRR, minimal detectable relative risk; T, treatment; TAR, time-at-risk; VTE, venous thromboembolism.

Online Resource 18. After matching (adjusted) incidence rates by indication and exposure group; intent-to-treat, 1:100 PS matching

Indication	T vs C	Database	Patients		TAR		Events		IR		MDRR
			T	C	T	C	T	C	T	C	
AF	Rivaroxaban vs Warfarin	CCAIE	2,909	6,495	5,230	11,139	53	93	10.13	8.35	1.65
		MDCR	9,362	20,817	20,161	44,369	54	76	2.68	1.71	1.70
		Optum	13,891	34,511	34,204	90,924	119	170	3.48	1.87	1.44
		Meta-analysis	26,162	61,823	59,596	146,434	226	339	3.79	2.32	1.29
	Apixaban vs Warfarin	CCAIE	1,971	3,924	3,285	6,548	29	53	8.83	8.09	1.93
		MDCD	1,518	3,732	2,406	7,205	12	33	4.99	4.58	2.51
		MDCR	6,554	12,901	12,548	25,338	29	35	2.31	1.38	2.10
		Optum	13,282	25,981	28,572	61,240	52	115	1.82	1.88	1.58
	Meta-analysis	CCAIE	23,325	46,538	46,812	100,333	122	236	2.61	2.35	1.37
		MDCR	3,086	8,440	6,038	15,341	48	124	7.95	8.08	1.62
		Optum	7,949	27,637	20,940	62,248	47	110	2.24	1.77	1.71
	Dabigatran vs Warfarin	CCAIE	7,126	38,367	21,969	108,418	60	204	2.73	1.88	1.61
		MDCR	18,161	74,444	48,948	186,008	155	438	3.17	2.35	1.34
		Meta-analysis	5,091	8,240	8,077	11,992	82	95	10.15	7.92	1.54
	Rivaroxaban vs Apixaban	MDCD	2,009	3,345	2,908	4,329	20	25	6.88	5.77	2.37
		MDCR	9,444	18,474	17,578	29,716	51	62	2.90	2.09	1.75
		Optum	17,478	39,594	34,657	67,124	118	143	3.40	2.13	1.46
		Meta-analysis	34,022	69,653	63,220	113,162	271	325	4.29	2.87	1.28
	Rivaroxaban vs Dabigatran	CCAIE	1,972	2,939	3,564	5,621	38	39	10.66	6.94	1.92
		MDCR	4,028	6,135	9,306	15,374	30	29	3.22	1.89	2.11
		Optum	4,729	5,991	13,055	17,502	57	54	4.37	3.09	1.71
		Meta-analysis	10,729	15,065	25,925	38,498	125	122	4.82	3.17	1.44
	Apixaban vs Dabigatran	CCAIE	1,044	1,136	1,858	2,117	25	12	13.45	5.67	2.51
		MDCR	2,172	2,453	4,562	5,257	10	15	2.19	2.85	3.07
Optum		3,102	3,476	7,397	8,661	19	28	2.57	3.23	2.27	
VTE	Rivaroxaban vs Warfarin	CCAIE	5,027	17,425	9,083	33,154	121	331	13.32	9.98	1.37
		MDCD	2,606	7,136	5,041	16,015	51	156	10.12	9.74	1.55
		MDCR	3,376	12,081	6,551	25,653	18	47	2.75	1.83	2.32
		Optum	6,921	22,402	14,390	54,436	95	245	6.60	4.50	1.43
		Meta-analysis	17,930	59,044	35,067	129,259	285	779	8.13	6.03	1.23
	Apixaban vs Warfarin	CCAIE	1,922	7,633	2,880	13,356	27	131	9.37	9.81	1.74
		MDCD	1,214	4,565	1,695	8,398	11	86	6.49	10.24	2.01
		Optum	4,087	12,615	6,766	26,193	25	116	3.69	4.43	1.73
		Meta-analysis	7,223	24,813	11,342	47,947	63	333	5.55	6.95	1.40
	Rivaroxaban vs Apixaban	CCAIE	4,590	5,197	6,018	6,583	86	61	14.29	9.27	1.59
		MDCD	2,095	2,407	2,411	2,683	35	16	14.51	5.96	2.20
		MDCR	2,265	2,920	3,138	3,703	6	9	1.91	2.43	4.30
		Optum	7,678	10,012	10,998	13,454	75	47	6.82	3.49	1.67
		Meta-analysis	16,628	20,536	22,565	26,425	202	133	8.95	5.03	1.36

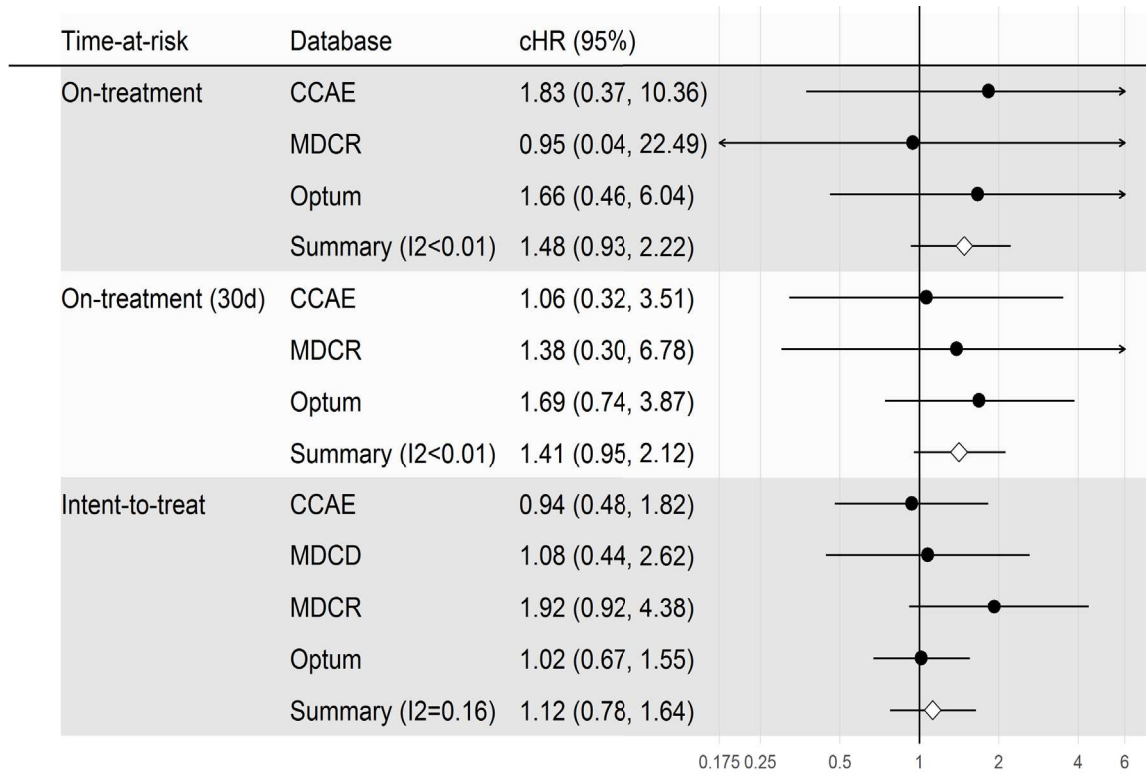
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Online Resource 19. AF population: Rivaroxaban vs Warfarin, 1:100 PS matching



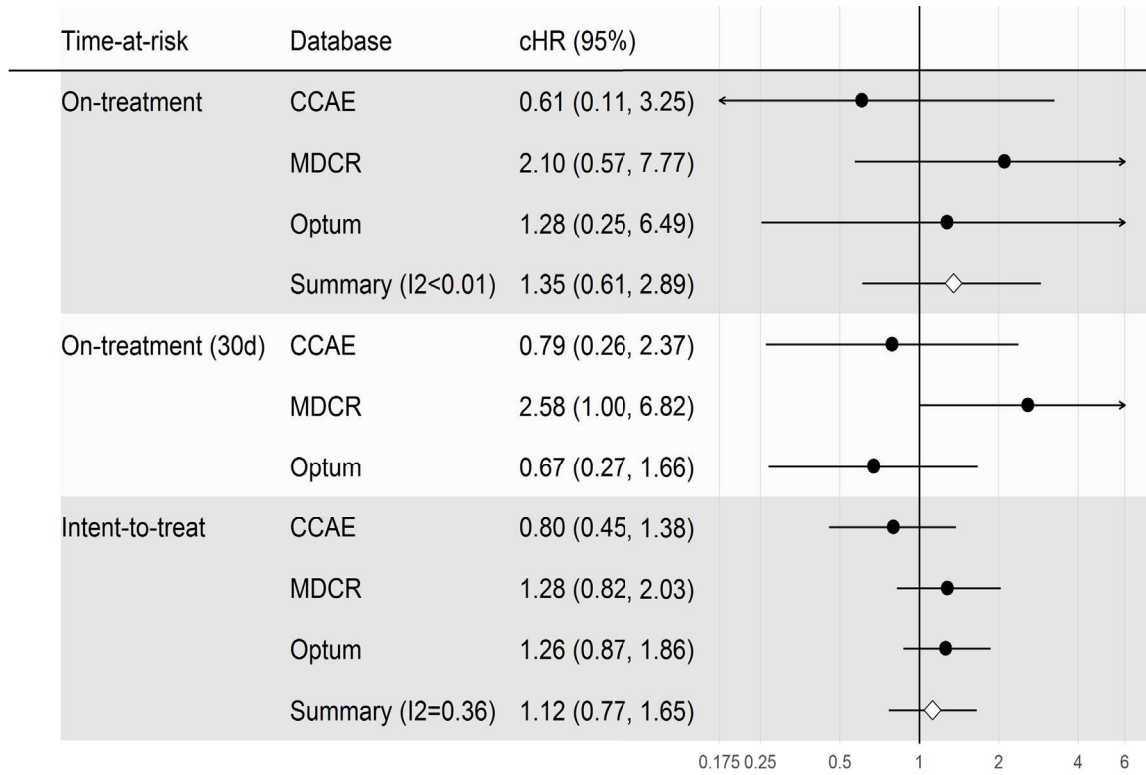
AF, atrial fibrillation; CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 20. AF population: Apixaban vs Warfarin, 1:100 PS matching



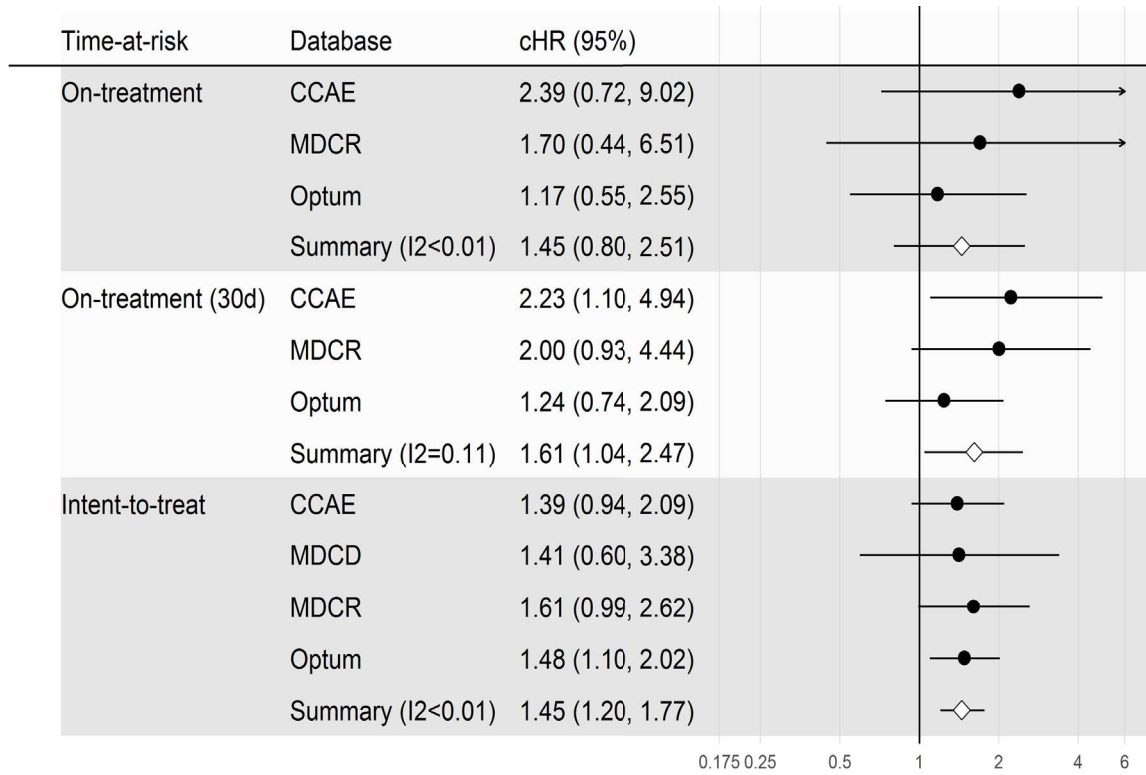
AF, atrial fibrillation; CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 21. AF population: Dabigatran vs Warfarin, 1:100 PS matching



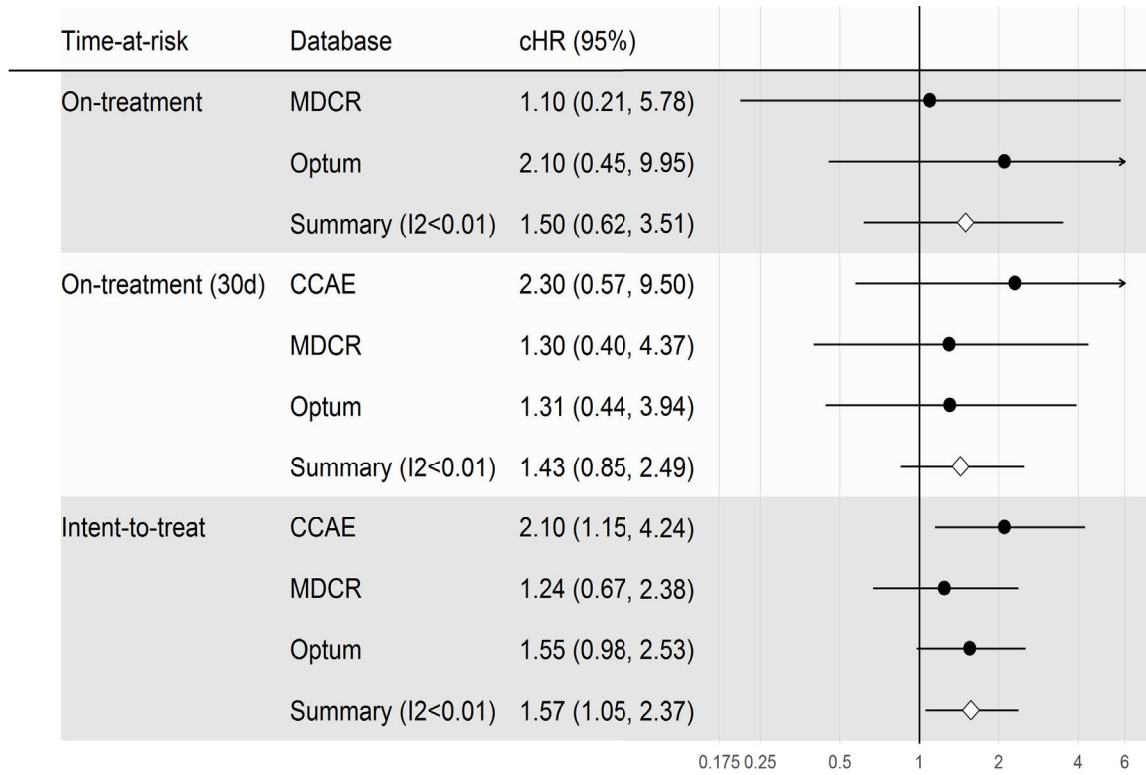
AF, atrial fibrillation; CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 22. AF population: Rivaroxaban vs Apixaban, 1:100 PS matching



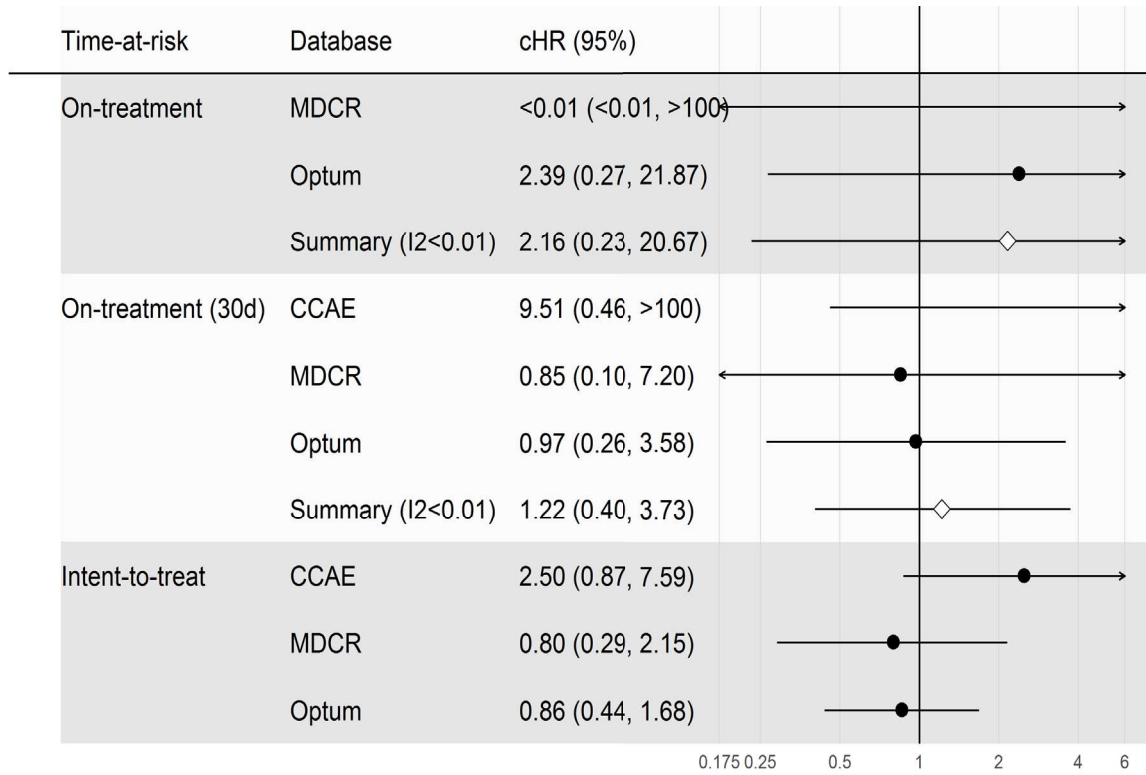
AF, atrial fibrillation; CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 23. AF population: Rivaroxaban vs Dabigatran, 1:100 PS matching



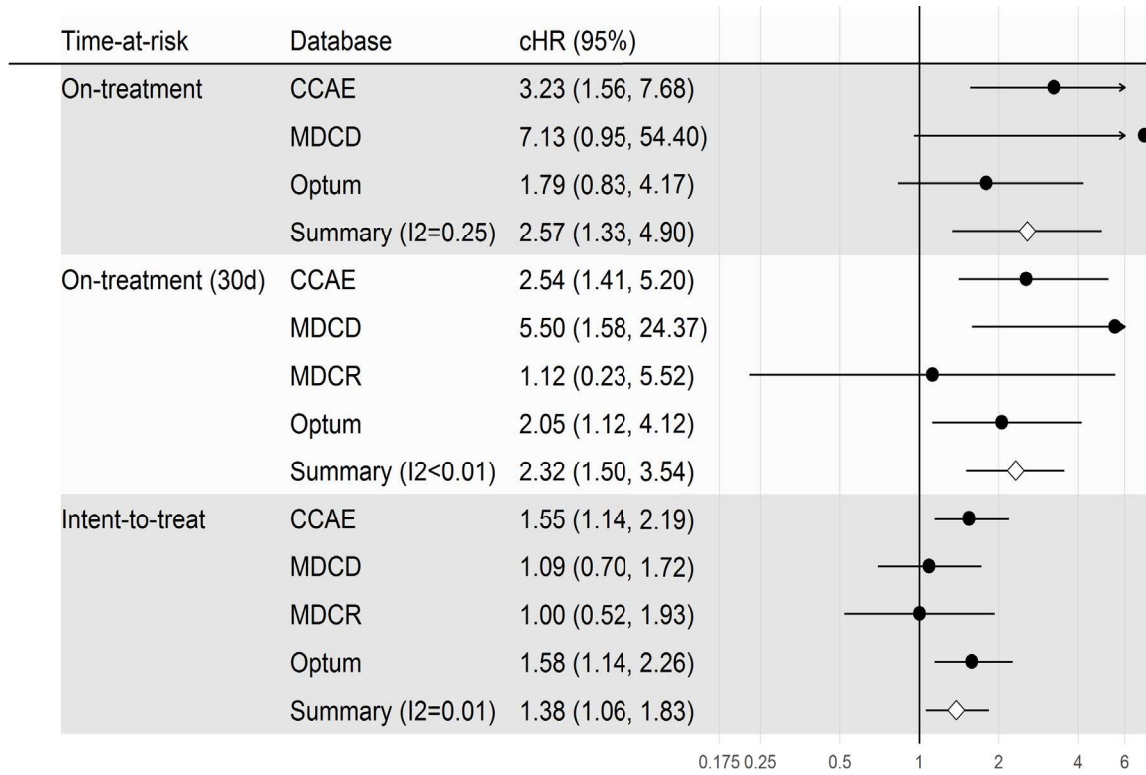
AF, atrial fibrillation; CCAE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 24. AF population: Apixaban vs Dabigatran, 1:100 PS matching



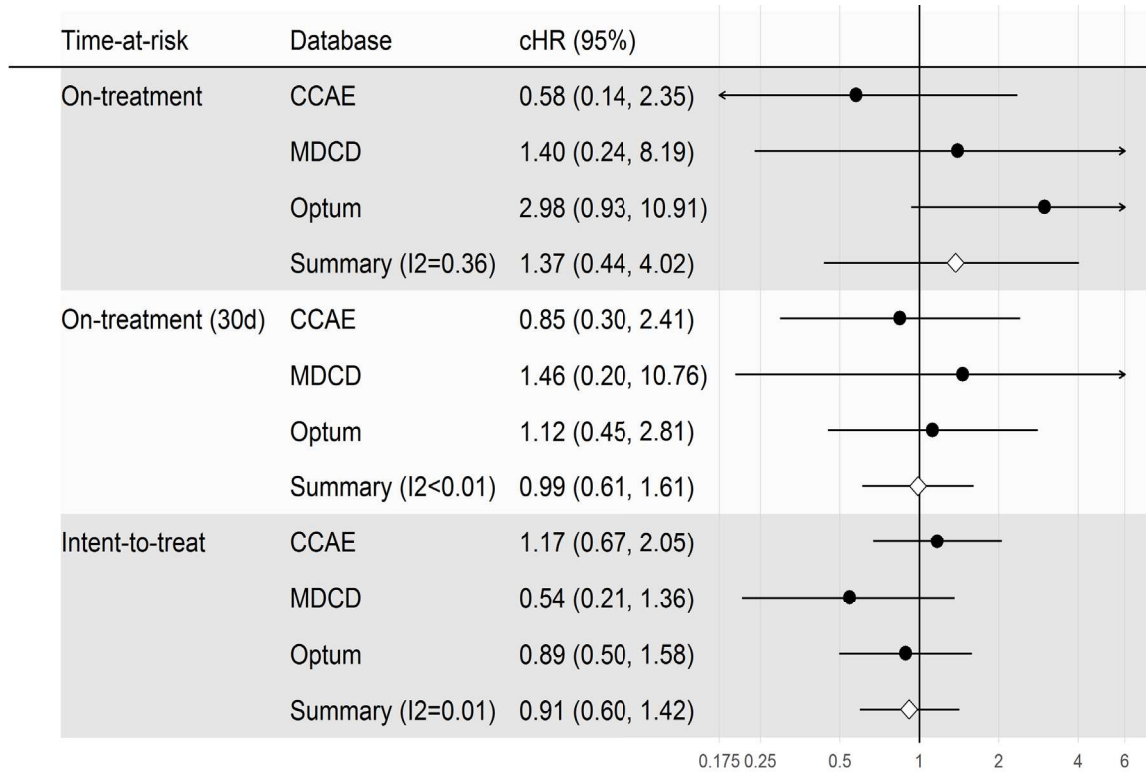
AF, atrial fibrillation; CCAE, IBM MarketScan[®] Commercial Database; cHR, calibrated hazard ratio; MDCR, IBM MarketScan[®] Medicare Supplemental Beneficiaries; PS, propensity score.

Online Resource 25. VTE population: Rivaroxaban vs Warfarin, 1:100 PS matching



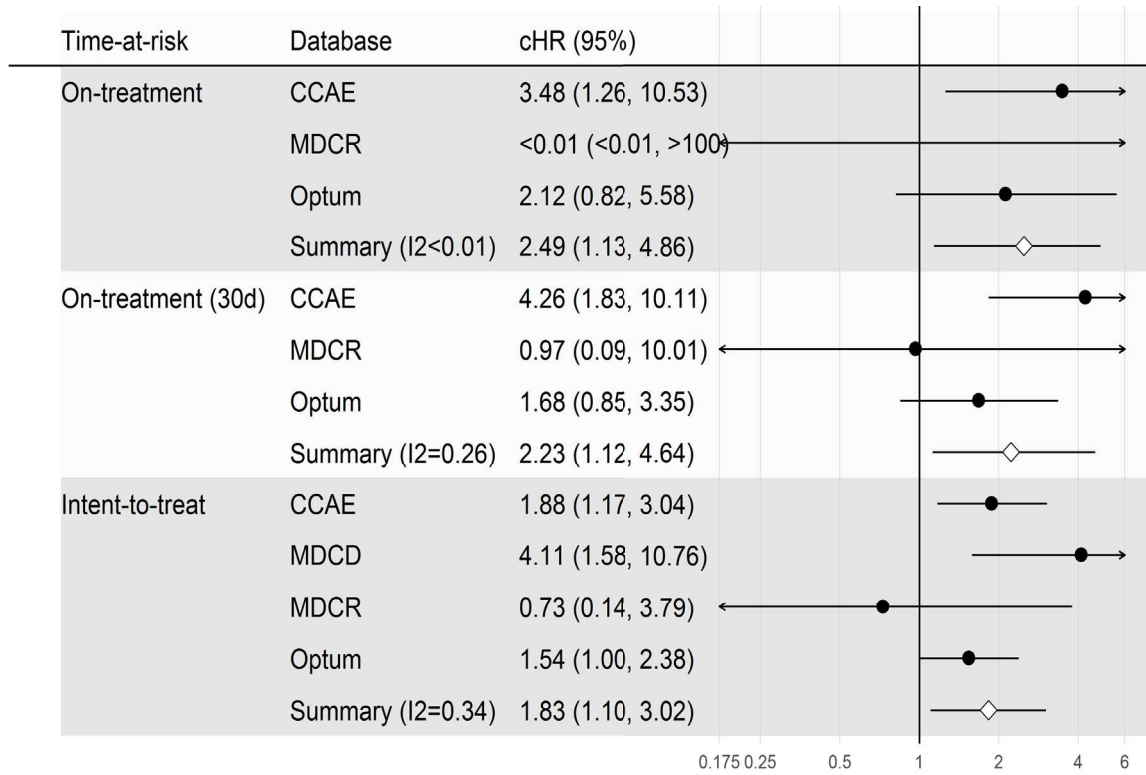
CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score; VTE, venous thromboembolism.

Online Resource 26. VTE population: Apixaban vs Warfarin, 1:100 PS matching



CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCD, IBM MarketScan® Multi-state Medicaid; PS, propensity score; VTE, venous thromboembolism.

Online Resource 27. VTE population: Rivaroxaban vs Apixaban, 1:100 PS matching



CCAIE, IBM MarketScan® Commercial Database; cHR, calibrated hazard ratio; MDCD, IBM MarketScan® Multi-state Medicaid; MDCR, IBM MarketScan® Medicare Supplemental Beneficiaries; PS, propensity score; VTE, venous thromboembolism.