

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: ICD 9-CM codes for comorbidities

Comorbidity	ICD-9 codes	Ref
For stratification		
Cancer		[21]
-Solid tumor cancer	140-195	
-Blood cancer	200-208	
-Metastatic cancer	196-199	
Renal disease		[8]
-Acute	584.5-584.9	[9]
-Chronic		
Stage 1	585.1	
Stage 2_mild	585.2	
Stage	585.3	
3_moderate	585.4	
Stage 4_severe	585.5	
Stage 5		
ESRD	585.6	[8,10,12,13]
-Dialysis	V45.1, V56.0, V56.1 39.95,54.93,54.98,38.95,39.27, 90935, 90937,90945,90947, 90951-90970, 90989, 90993, 90997, 90999, 90918-90925, 93990	
Liver disease		[14]
-Mild	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570.x, 571.x, 573.3, 573.4, 573.8, 573.9, V42.7	
Mediate or severe	456.0–456.21, 572.2–572.8	
Diabetes		[14]
-without chronic complication	250.0–250.3, 250.8, 250.9	
-with chronic complication	250.4–250.7	
Hypertension	401.x-405.x	[14]
Hyperlipidemia	272.0, 272.1, 272.2, 272.3, 272.4	[15]
Obesity	278.00	[14]
Gastric ulcer	531, 532, 533, 534	[21]
For exclusion criteria		[16]
Mitral stenosis or prosthetic heart valve	394.0, 394.2, 396.0, 396.1, 396.8, V43.3, or V42.2	
Mitral or aortic valve repair or replacement	35.10 to 35.14 or 35.20 to 35.28	[16]

Joint replacement	0080 0081 0082 0083 0084 8141 8142 8143 8144 8146 8147 8154 8155 0070 0071 0072 0073 0074 0075 0076 0077 0085 0086 0087 8151 8152 8153 8169 8148 8149 8156 8157 8159 8171 8172 8173 8174 8175 8179 8180 8181 8182 8183 8184 8185 8186 8187 8188 8197	[21]
For confounding adjusting		
Cardiovascular disease		
-Deep vein thrombosis	451.x, 453.x	[17]
-Pulmonary embolism	415.x	[17]
-Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x	[14]
-Coronary Artery Disease	410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92, 411.0, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.00, 414.01, 414.02, 414.03, 414.04, 414.05, 414.06, 414.07, 414.8, 414.9, V45.81, V45.82	[10]
-Acute MI	410	[1]
-Coronary revascularization	36.01-36.07, 36.09, 00.66, 36.1x	[11]
-Heart failure	402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42, 428.43, 428.9	[10]
-Other ischemic heart disease	410.00, 410.01, 410.02, 410.10, 410.11, 410.12, 410.20, 410.21, 410.22, 410.30, 410.31, 410.32, 410.40, 410.41, 410.42, 410.50, 410.51, 410.52, 410.60, 410.61, 410.62, 410.70, 410.71, 410.72, 410.80, 410.81, 410.82, 410.90, 410.91, 410.92, 411.0, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.00, 414.01, 414.02, 414.03, 414.04, 414.05, 414.06, 414.07, 414.12, 414.2, 414.3, 414.8, 414.9	[15]
-Stroke	433.x1, 434.x1, 436, 430, 431	[7]
-Other cerebrovascular disease	430.x - 438.x	[21]
-TIA	435.x	[7]

- <i>Cardioablation</i>	93650, 93651, 93652, 93653, 93654, 93656, 93655, 93657, 93462	[18]
- <i>Cardioversion</i>	99.61, 99.62, 99.69 92960, 92961	[19]
Other medical conditions		
- <i>Falls</i>	E880-E888, E968.1, E987.0, E987.1, E987.2, E987.9, V15.88	[21]
- <i>Fracture</i>	820–821, 813, 812, 805	[21]
- <i>Syncope</i>	780.2	[20]
- <i>Walker use</i>	E0100, E0105, E0110, E0111, E0112, E0113, E0114, E0116, E0117, E0118, E0130, E0135, E0140, E0141, E0143, E0144, E0147, E0148, E0149, E0153, E0154, E0155, E0156, E0157, E0158	[22]

eTable 2: ICD 9 Codes for HAS-BLED score [7]

HAS-BLED	Score	ICD-9-CM codes
Hypertension	1	401.x-405.x
Abnormal renal function	1	585.3, 585.4
Abnormal liver function	1	070.x, 570, 571.x, 572.x, 573.0-5,
		V42.7
Stroke	1	430, 431, 433.x1, 434.x1, 436
Bleeding history or	1	280.x-287.x, 430, 431, 432.x, 852.x,
predisposition		853.x, 456.0, 456.20, 530.21, 530.7,
		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,
		535.71, 537.83, 537.84, 562.02,
		562.03, 562.12, 562.13, 568.81, 569.3,
		569.85, 578.x, 423.0, 459.0, 596.7,
		599.71, 719.1x, 784.8, 786.3
Elderly (>65)	1	
Antiplatelet or NSAID use	1	
Alcoholism	1	291.x, 303.x, 305.0x, 357.5, 425.5,
		535.3x, 571.0-571.3, 760.71, 980.0,
		V11.3
Maximum score	8	

eTable 3: ICD 9 Codes for CHA₂DS₂-VASc score [7]

CHA₂DS₂-VASc	Score	ICD-9-CM codes
Congestive heart failure	1	428.x, 402.x1, 404.x1, 404.x3, 398.91
Hypertension	1	401.x-405.x
Diabetes mellitus	1	250.x, 357.2, 362.0x, 366.41
Stroke/TIA/TE	2	430, 431, 433.x1, 434.x1, 436, 435.x,
		444.x
Vascular disease	1	410-414, 443.8,443.9, 440.x
Age≥75	2	
Age 65-74	1	
Female sex	1	
Maximum score	9	

eTable 4: ICD-9-CM codes for study outcomes

Outcomes	ICD-9 codes	Reference
Major bleeding	<i>->Bleeding events in inpatient only and meet the definition for major bleeding: a bleeding event with (i) a critical site code, (ii) a transfusion, or (iii) death</i>	
Overall	Critical site: Intracranial: 430, 431, 432, 852.0, 852.2, 852.4, 853.0; Extracranial: 336.1, 363.6, 372.72, 376.32, 377.42, 379.23, 719.1, 729.92, 729.97, 423.0, 593.81, 772.5, 866.01, 866.02, 866.11, 866.12 Transfusions: a) ICD-9 PRC: 9903, 9904, 9905, 9906, 9907, 9909, b) HCPC: P9010, P9011, P9016, P9017, P9019, P9020	[1]
ICH	430, 431, 432, 852.0, 852.2, 852.4, 853.0	[1]
GI bleeding	<i>->Bleeding at GI site and need a transfusion or lead to death.</i> 455.2, 455.5, 455.8, 456.0x, 456.20, 530.7x, 530.82, 531.00, 531.01, 531.20, 531.21, 531.40, 531.41, 531.60, 531.61, 532.00, 532.01, 532.20, 532.21, 532.40, 532.41, 532.60, 532.61, 533.00, 533.01, 533.20, 533.21, 533.40, 533.41, 533.60, 533.61, 534.00, 534.01, 534.20, 534.21, 534.40, 534.41, 534.60, 534.61, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 537.84, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3x or 569.85, 569.86, 578.0x, 578.1x, 578.9x <i>(combine these with codes for transfusion or death)</i>	[1]
Moderate bleeding	<i>->Bleeding events in inpatient or emergency department that do not meet the criteria for major bleeding</i>	
Overall	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, 456.0, 456.20, 530.7, 530.82, 578.0, 455.2, 455.5, 455.8, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 578.1, 578.9, 593.81, 599.7, 623.8, 626.2, 626.6, 423.0, 459.0, 568.81, 719.1x, 784.7, 784.8, 786.3	[1]
GI bleeding	455.2, 455.5, 455.8, 456.0x, 456.20, 530.7x, 530.82, 531.00, 531.01, 531.20, 531.21, 531.40, 531.41, 531.60, 531.61, 532.00, 532.01, 532.20, 532.21, 532.40, 532.41, 532.60, 532.61, 533.00, 533.01, 533.20, 533.21, 533.40, 533.41, 533.60, 533.61, 534.00, 534.01, 534.20, 534.21, 534.40, 534.41, 534.60, 534.61, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 537.84, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3x or 569.85, 569.86, 578.0x, 578.1x, 578.9x	
Minor bleeding	Bleeding events in outpatient office visits only. Use same codes for moderate bleeding but in outpatients.	

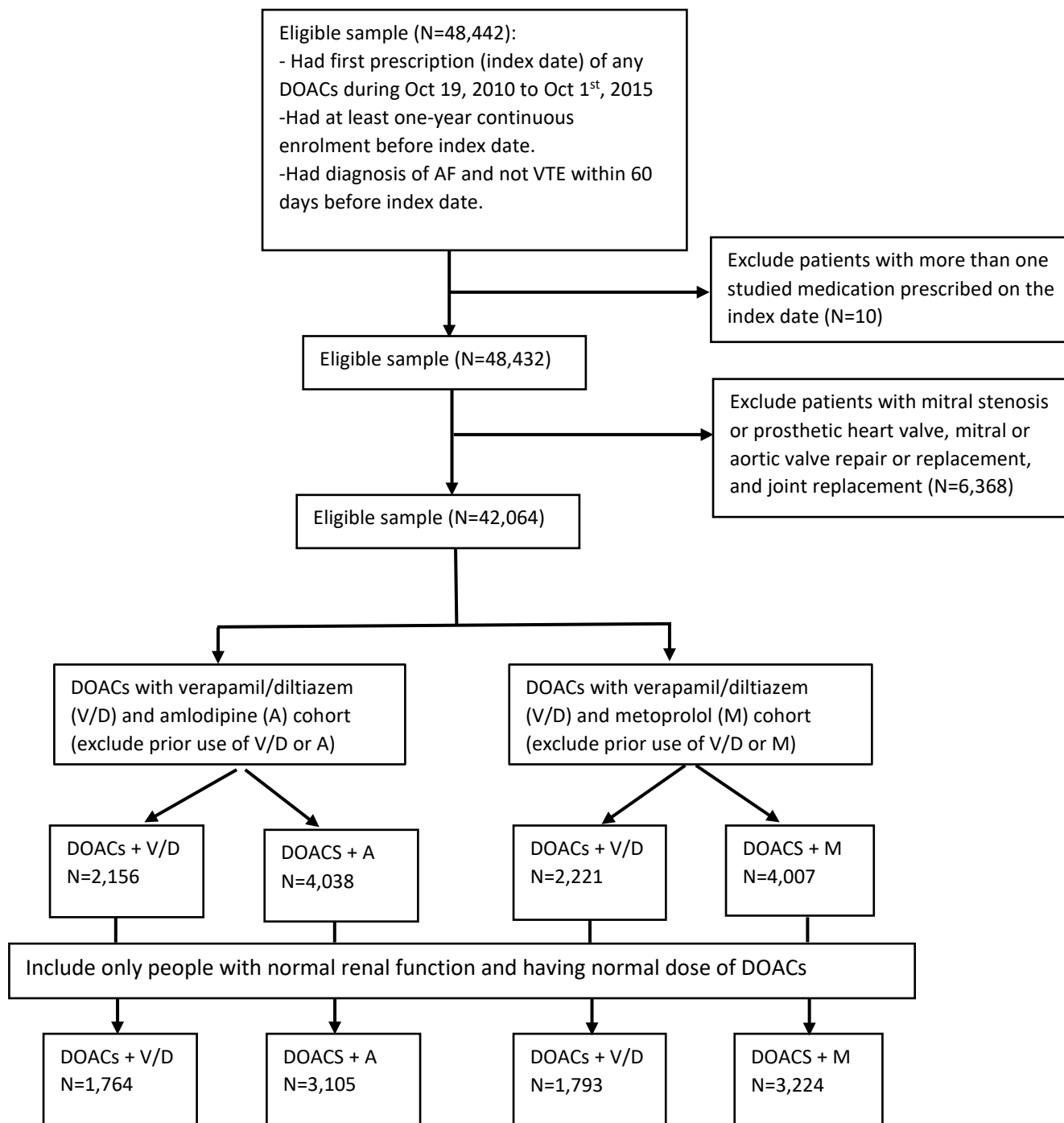
Acute MI	410	[2-6]
Stroke or systemic embolism		[7]
Ischemic stroke	433.x1, 434.x1, or 436	
Hemorrhagic stroke	430, 431	
Systemic embolism	444.x	
TIA	435.x	

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eFigure 1: Cohort selection and attrition



eTable 5: Standardized percent difference of cohort's baseline characteristic after inverse probability of treatment weighting when comparing verapamil/diltiazem versus amlodipine or metoprolol among each DOAC cohort. Differences <10% are considered to indicate well balance covariate distribution between comparison groups.

	Dabigatran	Rivaroxaban	Apixaban	Dabigatran	Rivaroxaban	Apixaban
Patients' characteristic	V/D vs A	V/D vs A	V/D vs A	V/D vs M	V/D vs M	V/D vs M
Demographic						
Age, %						
<65	-3.05	1.62	-11.21	-1.52	0.10	-1.3
65-<70	-1.87	-3.03	1.02	0.78	-0.46	0.48
70-<75	2.10	-0.10	10.15	1.85	-0.07	0.82
75-<80	3.67	1.11	-1.04	-1.38	0.57	0.84
80-<85	1.97	-1.02	7.22	1.85	-0.50	-0.17
≥ 85	-1.57	1.24	5.31	-0.97	0.63	-0.09
Sex, %						
Female	-2.21	-2.16	-0.77	-1.35	1.17	3.57
Medical history, %						
General						
Diabetes w/o complication	-1.74	1.86	-5.59	4.37	0.61	3.77
Diabetes w/complication	-4.09	3.96	1.51	3.02	0.49	-0.10
Hypertension	3.34	2.36	3.79	-1.03	-0.37	-2.71
Hypercholesterolemia	3.99	1.81	-1.92	0.06	-1.10	1.55
Liver failure						
Mild	-0.90	2.25	1.49	5.42	-2.03	2.42
Moderate or severe	0.00	3.27	-4.77	4.37	0.00	-0.05
Cancer						
Solid	-5.05	-1.03	3.67	0.78	1.02	2.21
Fluid	1.31	1.01	-5.41	1.06	-2.60	-2.92
Metastatic	-1.85	2.18	1.37	-1.35	-0.80	2.52
Obesity	3.32	-4.65	-4.73	3.63	-0.27	2.81
Peptic ulcer disease	0.35	1.88	8.36	0.23	-0.58	6.50
Prior hospitalized bleeding event	-0.32	1.31	0.87	0.17	0.77	1.89
Smoking	-1.61	2.04	-2.01	-0.24	-0.78	-0.50
Cardiovascular disease						
Acute myocardial infarction						
Past 1-30 days	-1.41	-2.71	5.56	-3.37	3.01	9.76
Past 31-180 days	-1.11	-1.06	4.82	-1.25	1.85	3.04
Past 181-365 days	2.18	-3.97	4.58	-0.52	3.17	0.83
Coronary revascularization	0.59	0.07	1.26	0.58	0.25	1.33

Heart failure						
Hospitalized	-0.23	-0.35	-0.24	-0.68	1.77	0.12
Outpatient	-4.14	3.21	5.24	-6.89	1.74	2.70
Coronary artery disease	3.78	1.16	1.84	3.91	6.68	5.72
Other ischemic heart disease	3.83	0.23	3.14	4.66	6.67	5.13
Stroke						
Past 1-30 days	-0.36	3.04	1.46	-0.91	1.02	-2.66
Past 31-180 days	-6.22	-3.12	-1.43	-1.75	-7.02	-0.48
Past 181-365 days	-0.62	2.60	3.11	-1.84	0.38	4.43
Other cerebrovascular disease	-5.46	5.05	0.85	-2.01	1.23	-1.61
Transient ischemic attack (TIA)	-3.99	-2.31	0.69	2.64	1.28	-0.90
Cardioversion	3.17	-8.77	-2.76	-5.88	-3.28	1.86
Other medical conditions						
Falls	-5.05	2.84	8.58	2.95	-5.82	1.52
Fractures	-1.39	4.29	1.08	-1.94	0.99	-7.66
Syncope	-3.26	-2.38	-0.04	0.34	-0.54	-0.36
Walker use	-0.93	4.17	-0.84	-0.34	-0.24	2.08
CCI, Mean (SD)	-5.35	3.31	3.91	0.16	0.59	4.69
CHA ₂ DS ₂ -VASc Score						
0-1	-4.10	-3.55	-5.13	0.14	0.12	-2.06
2	4.26	6.03	0.11	5.78	-0.55	0.66
3	1.20	-5.90	4.66	-6.76	0.21	3.13
≥4	-2.96	5.29	0.78	-0.23	0.57	-2.60
HAS-BLED score						
0-1	-1.84	0.20	-5.22	-1.09	-1.12	1.47
2	0.77	0.51	0.52	2.90	-1.08	-5.94
3	-1.66	3.65	-8.36	-4.48	3.40	2.30
≥4	2.07	-3.52	9.94	2.34	-0.88	2.07
Medication use, %						
General						
Estrogen therapy	1.72	-1.52	3.09	1.98	-1.49	1.98
Histamine 2 antagonists	3.80	1.10	0.52	1.08	-1.38	5.81
NSAID	2.57	-1.72	1.02	-6.21	-0.81	4.21
Proton pump inhibitors	0.48	-0.15	0.47	-3.95	-1.31	5.19
SSRI antidepressants	1.09	5.67	-1.89	-7.56	-1.57	1.49
Cardiovascular						
ACE inhibitors	-2.66	-0.80	-2.80	0.83	1.87	-0.07
ARBs	2.61	1.37	4.68	-4.51	0.26	3.46
Antiarrhythmics	-2.62	0.92	-2.60	-3.26	-1.24	-5.85
Other anticoagulants	-0.89	0.45	-0.72	-0.37	-0.10	0.10
Antiplatelet	2.32	-0.97	6.53	3.51	3.40	0.96
B-blocker	1.55	-0.70	6.56	2.47	0.03	1.67

Digoxin	1.46	3.55	-0.67	2.19	-0.19	0.20
Diuretics						
Loop	-3.29	3.16	-1.48	-6.00	1.51	-1.55
Potassium sparing	0.29	-4.18	1.68	-0.41	-1.65	4.11
Thiazide and other	0.79	0.81	1.51	-5.00	-3.39	0.47
Nitrates	-0.02	6.29	8.05	2.76	4.06	9.88
Statins	1.75	1.44	-2.13	-3.87	3.44	3.36
Fibrates	3.01	2.33	-0.02	-4.44	1.69	2.68
Other antihyperlipidemic	0.31	0.07	6.32	-6.00	1.51	-1.55
Diabetes related						
Insulin	-1.35	-2.28	-0.96	-0.07	-0.22	-0.47
Metformin	2.11	0.11	0.37	-3.54	0.22	2.36
Sulfonylurea	-0.82	-5.87	-1.78	1.04	-0.69	1.61
Other	-1.03	6.53	-6.23	3.14	1.10	2.15
Metabolic inhibitors						
Amiodarone	-2.80	0.59	4.67	-1.03	0.98	-1.18
Dronedarone	-0.50	-0.31	-0.63	-4.94	0.38	-6.19
Azole antifungals	0.95	1.70	0.59	1.00	-0.39	-1.21
Metabolic inducers						
Carbamazepine	-0.83	1.93	6.82	0.44	-1.00	7.96
Phenytoin	-5.33	2.96	-4.77	-5.31	-1.27	0.00
Phenobarbital	0.13	0.17	0.00	-3.06	-3.21	0.00
Prescriber specialty				0.44	-1.00	7.96
Internal medicine	0.84	-10.95	1.87	1.51	-0.38	-2.92
Family practice	-0.43	-1.39	2.25	-0.51	-1.04	0.71
Geriatric medicine	3.15	3.27	0.00	3.09	0.00	0.00
Cardiology	2.00	6.04	-1.89	-3.70	1.58	1.66
Critical care medicine	3.15	-4.49	4.82	4.37	-0.45	0.00
Hematology	-1.65	-3.18	0.00	-3.06	-0.04	4.59
Oncology	-4.35	0.19	0.00	-0.20	-3.21	4.59
Healthcare utilization						
Outpatient visits, %						
≤ 9	2.26	4.23	-0.46	-2.87	2.44	-6.03
>9-16	0.42	-7.74	0.68	0.25	0.40	1.72
>16-29	-2.64	0.25	-1.45	2.11	-2.51	0.35
>29	0.11	4.46	1.34	0.21	-0.02	3.66
Inpatient visits, Mean (SD)	-1.67	-1.28	-0.82	1.70	-2.39	2.49
ER visits	-2.39	2.41	2.99	5.35	-2.32	-1.32
Number of Rx, %						
≤ 6	-0.14	2.70	-2.78	2.05	4.08	-5.93
>6-9	-1.37	-2.45	-1.11	-5.42	-0.34	3.16
>9-13	4.01	-1.11	-0.70	-0.71	-1.68	0.74
>13	-2.45	1.25	4.02	4.50	-1.44	1.37

V/D: verapamil/diltiazem; A: amlodipine;

CCI: Charlson comorbidity index; NSAID: nonsteroidal anti-inflammatory drugs; SSRI: selective serotonin reuptake inhibitors; ACE inhibitors: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin II receptor blockers; ER: emergency room

eTable 6: Standardized difference of cohort's baseline characteristic after inverse probability of treatment weighting when comparing DOAC together among cohort of verapamil/diltiazem, amlodipine or metoprolol						
Patients' characteristic	Verapamil/Diltiazem		Amlodipine		Metoprolol	
	D vs A	R vs A	D vs A	R vs A	D vs A	R vs A
Demographic						
Age, %						
<65	-0.96	-0.96	1.86	0.62	-0.43	-0.97
65-<70	-2.12	-1.7	-0.82	-0.75	-0.26	0.05
70-<75	3.19	1.56	1.97	1.7	0.04	0.07
75-<80	-0.46	-0.07	-3.28	-1.22	-1.59	-1.46
80-<85	1.05	2	-2.4	-3.32	1.44	2.05
≥ 85	1.48	1.72	2.16	3.87	4.1	3.93
Sex, %						
Female	1.46	0.34	0.72	0.37	2.58	3.74
Medical history, %						
General						
Diabetes w/o complication	-0.4	-1.41	-2.77	-3.71	-0.19	0.13
Diabetes w/complication	2.04	2.23	-0.43	-1.27	-1.65	-1
Hypertension	-0.66	-1.36	-1.5	-1.32	1.77	2.29
Hypercholesterolemia	1.97	1.25	-3.61	-3.47	-3.84	-4.02
Liver failure						
Mild	1.18	1.4	0.71	0.5	-1.64	-1.01
Moderate or severe	-3.35	-3.35	0	2.54	2.68	0
Cancer						
Solid	0.43	0.77	-0.43	0.12	2.18	2.14
Fluid	1.34	1.45	-0.11	-0.06	0.73	0.03
Metastatic	1.25	0.72	-1.14	-0.6	-0.52	0.91
Obesity	-2.2	-1.86	0.14	-0.69	-0.28	-1.03
Peptic ulcer disease	10.54	10.5	-3.81	-4.4	-2.83	-2.83
Prior hospitalized bleeding event	1.79	2.23	0.08	0.15	2.5	2.75
Smoking	-4.01	-4.24	2.1	1.4	3.99	2.51
Cardiovascular disease						
Acute myocardial infarction						
Past 1-30 days	-1.67	-3.17	1.52	1.43	4.12	2.86
Past 31-180 days	0.53	-0.84	1.22	0.65	-0.05	-0.26
Past 181-365 days	6.43	6.14	-0.71	-1.29	-4.49	-5.46
Coronary revascularization	-0.8	-1.79	2.36	3.82	-1.13	-0.37
Heart failure						
Hospitalized	2.33	1.79	-0.02	0.47	1.62	1.46
Outpatient	2.87	1.2	1.7	0.33	-3.38	-2.1

Coronary artery disease	1.55	0.31	3.43	3.95	0.89	0.22
Other ischemic heart disease	3.06	2.48	3.7	3.72	1.63	0.66
Stroke						
Past 1-30 days	-2.3	-5.26	0.78	1.74	2.43	1.99
Past 31-180 days	-3.59	-4.27	3.14	5.7	-0.98	0.04
Past 181-365 days	4.58	3.46	3.21	2.85	0.74	0.24
Other cerebrovascular disease	-1.37	-1.33	5.01	4.86	0.38	-0.79
Transient ischemic attack (TIA)	-0.22	-0.33	4.95	5.85	1.3	2.09
Cardioversion	2.38	3.2	0.1	-0.36	1.43	0.3
Other medical conditions						
Falls	1.1	0.29	1.76	-0.18	0.67	4.95
Fractures	-0.55	-2.11	-0.07	3.43	-0.67	4.22
Syncope	2.22	2.23	0.18	-0.22	2	3.3
Walker use	-2.3	-1.96	1.32	1.1	0.15	1.28
CCI, Mean (SD)	3.11	2.01	-0.54	-1.12	1.79	3.37
CHA ₂ DS ₂ -VASc Score						
0-1	-4.87	-3.9	-0.67	-1.77	0.58	-1.03
2	3.21	2.95	-0.9	-0.63	-1.51	-1.99
3	3.79	3.99	-0.58	0.11	0.48	2.05
≥4	-3.03	-4.97	4.16	4.37	1.22	2.85
HAS-BLED score						
0-1	-0.35	-0.31	2.43	1.72	4.13	2.99
2	-0.16	-0.47	-0.1	-0.96	-3.75	-2.16
3	0.17	0.24	-4.02	-4.06	-2.81	-2.55
≥4	0.3	0.46	1.74	2.94	2.03	1.48
Medication use, %						
General						
Estrogen therapy	2.05	2.66	2.84	2.29	0.03	0.03
Histamine 2 antagonists	-2.03	-2.39	3.21	3.33	4.76	1.77
NSAID	-0.06	-1.76	2.28	2.52	-0.69	2.67
Proton pump inhibitors	1.54	2.44	-0.26	0.67	2.04	2.17
SSRI antidepressants	2.8	0.01	-1.32	-0.29	0.26	0.51
Cardiovascular						
ACE inhibitors	-5.15	-4.27	2.78	2.51	1.21	0.78
ARBs	4.64	5.51	0.31	1.07	1.05	2.2
Antiarrhythmics	-1.8	-0.79	2.86	3.04	0.39	-1.79
Other anticoagulants	6.58	6.56	0.08	-0.54	-3.16	-4.46
Antiplatelet	-0.05	0.33	3.18	4.62	1.37	0.94
B-blocker	2.92	1.9	2.06	2.21	1.46	1.8
Digoxin	-1.37	-1.35	-0.74	-2.1	1.05	1.91

Diuretics						
Loop	1.28	2.09	0.74	2.21	-0.7	1.68
Potassium sparing	-2.16	-3.42	0.98	0.78	1.87	1.2
Thiazide and other	-1.47	-2.51	2.32	2.9	0.41	0.92
Nitrates	2.95	1.86	2.48	2.64	2.39	0.16
Statins	-0.9	-1.88	-0.19	0.89	0.3	1.01
Fibrates	2.61	5.6	1.46	1.61	3.97	3.05
Other antihyperlipidemic	6.17	6.45	-0.31	0.44	1.01	-0.11
<i>Diabetes related</i>						
Insulin	0.11	1.42	0.6	0.29	1.14	0.54
Metformin	2.65	1.51	-2.99	-3.06	-1.98	-1.07
Sulfonylurea	2.3	2.41	0.13	1.15	-2.95	-3.21
Other	-3.09	-5.7	-3.42	-4.35	-2.66	-1.67
<i>Metabolic inhibitors</i>						
Amiodarone	2.58	3.09	0.12	-0.4	2.65	0.35
Dronedarone	-0.26	-0.01	1.04	1.34	-4.35	-3.56
Azole antifungals	1.48	2.84	2.32	1.38	-3.72	-4.7
<i>Metabolic inducers</i>						
Carbamazepine	6.44	6.23	0.2	1.42	1.2	4.68
Phenytoin	2.62	1.57	0	5.08	0.00	2.67
Phenobarbital	4.16	4.17	3.53	3.53	0.00	0.00
<i>Prescriber specialty</i>						
Internal medicine	-3.37	-2.37	-0.84	-0.40	1.86	-0.05
Family practice	-0.48	-1.99	2.76	3.33	0.21	1.09
Geriatric medicine	0.00	0.00	4.04	4.03	2.68	0.00
Cardiology	-1.96	-1.21	-1.27	-1.93	2.49	0.98
Critical care medicine	0.00	4.72	-0.03	-4.23	3.50	3.49
Hematology	6.23	6.14	3.60	0.00	-3.70	-0.01
Oncology	5.95	6.69	0.00	2.54	0.00	-3.31
<i>Healthcare utilization</i>						
Outpatient visits, %						
≤ 9	3.35	2.89	0.23	-0.88	-0.35	-0.21
>9-16	5.5	6.61	-4.75	-4.06	2.84	0.39
>16-29	-6.84	-6.23	0.54	0.4	-2.23	-0.68
>29	-1.39	-2.87	4.97	5.6	-0.36	0.6
Inpatient visits, Mean (SD)	0.01	-1.81	6.92	8.36	4.66	5.33
ER visits	-2.17	-2.9	3.49	2.5	1.43	2.3
Number of Rx, %						
≤ 6	0.24	0.88	1.57	0.43	-3.31	-4.36
>6-9	0.42	-0.95	-2.49	-2.71	-0.29	-0.14
>9-13	-3.58	-2.86	0.72	1.11	-0.06	1.14
>13	2.94	3.04	0.45	1.18	3.6	3.19

V/D: verapamil/diltiazem; A: amlodipine;

CCI: Charlson comorbidity index; NSAID: nonsteroidal anti-inflammatory drugs; SSRI: selective serotonin reuptake inhibitors; ACE inhibitors: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin II receptor blockers; ER: emergency room

eTable 7: Number and incident rate of adverse bleeding events among concomitant users of DOACs with verapamil/diltiazem and with amlodipine									
Bleeding categories	Dabigatran			Rivaroxaban			Apixaban		
	Event (N)	Crude ER	Adj ER	Event (N)	Crude ER	Adj ER	Event (N)	Crude ER	Adj ER
Verapamil/Diltiazem									
Overall bleed	51	256.2	244.9	56	274.8	270.5	17	159.1	165.3
Overall GI bleed	30	146.0	149.7	23	108.0	84.0	6	54.8	50.0
Major/moderate bleed	12	56.9	54.4	15	69.4	73.0	4	36.5	32.5
Major/moderate GI bleed	7	33.2	29.6	5	23.0	19.0	1	9.1	9.9
Minor bleed	49	245.3	239.4	52	254.4	246.7	15	140.2	152.9
GI minor bleed	29	141.3	145.6	22	103.3	77.4	6	54.8	50.0
Stroke + SE	0	NA	NA	1	4.4	8.8	0	NA	NA
Amlodipine									
Overall bleed	71	177.0	158.4	98	270.1	273.4	34	207.7	185.1
Overall GI bleed	32	77.7	68.6	47	125.9	131.4	14	82.1	71.9
Major/moderate bleed	12	28.8	24.1	22	58.0	59.9	4	23.0	20.8
Major/moderate GI bleed	7	16.8	13.1	12	31.4	37.2	1	5.8	4.7
Minor bleed	68	169.4	151.1	93	255.5	258.4	32	194.9	174.5
GI minor bleed	31	75.6	66.8	44	117.5	123.7	14	82.1	71.9
Stroke + SE	0	NA	NA	1	2.6	2.2	1	5.5	12.8
Abbreviations: ER=event rate; Adj: adjusted; GI=gastrointestinal; SE: systemic embolism; D=dabigatran; R=rivaroxaban; A=apixaban; DOAC=direct acting oral anticoagulants. *rate per 1000 person years									

eTable 8: Number and incident rate of adverse bleeding event among concomitant users of DOACs with verapamil/diltiazem and with metoprolol									
Bleeding categories	Dabigatran			Rivaroxaban			Apixaban		
	Event (N)	Crude ER	Adj ER	Event (N)	Crude ER	Adj ER	Event (N)	Crude ER	Adj ER
Verapamil/Diltiazem									
Overall bleed	53	248.2	291.3	62	278.5	234.7	19	163.9	170.5
Overall GI bleed	30	139.1	171.6	25	108.0	84.7	7	62.1	88.7
Major/moderate bleed	12	54.4	85.0	15	66.4	55.8	5	44.2	29.6
Major/moderate GI bleed	7	31.8	50.0	5	21.9	18.6	1	8.8	4.7
Minor bleed	51	237.6	275.6	58	258.4	223.4	17	145.3	140.2
GI minor bleed	29	134.3	167.5	24	103.3	82.1	7	62.1	88.7
Stroke +SE	0	NA	NA	1	4.4	3.3	0	NA	NA
Metoprolol									
Overall bleed	80	201.1	199.7	127	316.8	314.6	45	223.4	219.4
Overall GI bleed	32	76.7	72.3	53	122.6	119.0	19	94.5	104.0
Major/moderate bleed	11	24.5	25.2	23	55.8	57.3	4	15.3	20.1
Major/moderate GI bleed	5	9.9	9.1	11	26.3	26.3	2	5.1	11.0
Minor bleed	78	196.0	194.9	122	302.6	300.4	42	211.7	209.5
GI minor bleed	30	74.1	70.4	51	117.5	114.2	18	94.5	104.0
Stroke + SE	1	2.2	2.6	1	2.2	2.2	0	NA	NA
Abbreviations: ER=event rate; Adj: adjusted; GI=gastrointestinal; SE: systemic embolism; D=dabigatran; R=rivaroxaban; A=apixaban; DOAC=direct acting oral anticoagulants. *rate per 1000 person years									

eTable 9: Hazard ratio of adverse bleed events among concomitant users of direct oral anticoagulant and verapamil/diltiazem versus amlodipine			
Bleeding categories	Dabigatran HR (95% CI)	Rivaroxaban HR (95% CI)	Apixaban HR (95% CI)
Unadjusted analysis			
Overall bleed	1.40 (0.98-2.01)	1.02 (0.74-1.42)	0.77 (0.43-1.37)
Overall GI bleed	1.84 (1.12-3.03) *	0.85 (0.52-1.41)	0.67 (0.26-1.75)
Major/moderate bleed	1.95 (0.87-4.34)	1.22 (0.63-2.36)	1.60 (0.40-6.41)
Major/moderate GI bleed	1.97 (0.69-5.64)	0.73 (0.26-2.08)	1.79 (0.11-28.69)
Minor bleed	1.40 (0.97-2.03)	1.00 (0.71-1.41)	0.72 (0.39-1.32)
GI minor bleed	1.84 (1.11-3.06) *	0.87 (0.52-1.46)	0.67 (0.26-1.75)
Diltiazem alone			
Overall bleed	1.56 (1.06-2.30) *	1.06 (0.75-1.51)	1.11 (0.60-2.04)
Overall GI bleed	2.06 (1.20-3.54) *	0.58 (0.32-1.08)	0.81 (0.28-2.37)
Major/moderate bleed	2.30 (0.95-5.55)	1.42 (0.73-2.76)	2.02 (0.44-9.17)
Major/moderate GI bleed	2.17 (0.65-7.27)	0.64 (0.21-1.93)	2.80 (0.14-55.74)
Minor bleed	1.61 (1.09-2.39) *	1.01 (0.70-1.46)	1.08 (0.57-2.03)
GI minor bleed	2.12 (1.23-3.64) *	0.55 (0.29-1.05)	0.81 (0.28-2.37)
Verapamil alone			
Overall bleed	1.34 (0.64-1.82)	0.71 (0.35-1.44)	0.13 (0.01-1.94)
Overall GI bleed	2.70 (1.15-6.34) *	0.83 (0.32-2.13)	0.33 (0.02-5.18)
Major/moderate bleed	2.12 (0.46-9.74)	0.51 (0.09 -2.93)	NA
Major/moderate GI bleed	2.79 (0.43-17.98)	NA	NA
Minor bleed	1.29 (0.60-2.80)	0.74 (0.36-1.51)	0.14 (0.01-2.08)
GI minor bleed	2.44 (0.99-6.01)	0.87 (0.34-2.25)	0.33 (0.02-5.18)
15-day gap			
Overall bleed	1.35 (0.97-1.88)	0.85 (0.62-1.17)	1.02 (0.58-1.81)
Overall GI bleed	1.87 (1.19-2.93) *	0.60 (0.35-1.00)	0.71 (0.25-2.01)
Major/moderate bleed	2.52 (1.18- 5.41) *	1.18 (0.64-2.18)	2.41 (0.60-9.64)
Major/moderate GI bleed	3.58 (1.25-10.21) *	0.64 (0.24-1.68)	2.17 (0.11-43.09)
Minor bleed	1.36 (0.98-1.90)	0.84 (0.60-1.16)	0.98 (0.54-1.77)
GI minor bleed	1.83 (1.16 -2.90) *	0.57 (0.34-0.98) *	0.71 (0.25-2.01)
Any diagnosis code position for outcome			
Overall bleed	1.74 (1.49-2.02)	0.87 (0.77-0.99) †	1.01 (0.81-1.27)
Overall GI bleed	1.93 (1.55-2.41) †	0.46 (0.36-0.57) †	0.45 (0.29-0.71) †
Major/moderate bleed	1.89 (1.07-3.32) †	1.06 (0.74-1.55)	1.92 (0.71-5.16)
Major/moderate GI bleed	1.97 (0.75-5.17)	0.30 (0.15-0.58) †	5.66 (0.42-75.69)
Minor bleed	1.75 (1.50-2.05) *	0.87 (0.76-0.99) †	1.02 (0.81-1.29)
GI minor bleed	1.91 (1.53-2.39) †	0.43 (0.34-0.54) †	0.41 (0.25-0.65) †
Standardized mortality ratio weight			
Overall bleed	1.31 (0.97-1.77)	1.45 (0.86-1.53)	0.48 (0.13-1.80)
Overall GI bleed	2.16 (1.43-3.26) *	1.19 (0.76-1.87)	0.56 (0.24-1.30)
Major/moderate bleed	2.34 (1.21-4.52) *	1.64 (0.92-2.90)	1.23 (0.41-3.69)
Major/moderate GI bleed	2.60 (1.08-6.24) *	1.15 (0.44-3.00)	1.03 (0.12-8.78)
Minor bleed	1.32 (0.97-1.79)	1.11 (0.82-1.49)	0.60 (0.35-1.03)
GI minor bleed	2.29 (1.50-3.49) *	1.20 (0.75-1.89)	0.56 (0.24-1.30)

Abbreviations: HR=hazard ratio; CI=confidence interval; GI=gastrointestinal; D=dabigatran; R=rivaroxaban; A=apixaban; DOAC=direct acting oral anticoagulants
NA: no event in one of the comparison groups
*Denotes statistically significant results at $P<0.05$
†Denotes proportional hazard assumption violated as the interaction between treatment and time was significant

eTable 10: Hazard ratio of adverse bleed events among concomitant use of direct oral anticoagulant and verapamil/diltiazem versus metoprolol			
Bleeding categories	Dabigatran HR (95% CI)	Rivaroxaban HR (95% CI)	Apixaban HR (95% CI)
Unadjusted result			
Overall bleed	1.21 (0.85-1.72)	0.89 (0.65-1.21)	0.73 (0.42-1.28)
Overall GI bleed	1.78 (1.08-2.95) *	0.88 (0.54-1.44)	0.67 (0.28-1.59)
Major/moderate bleed	2.21 (0.95-5.11)	1.21 (0.63-2.33)	2.87 (0.68-12.02)
Major/moderate GI bleed	3.19 (0.93-10.91)	0.84 (0.29-2.43)	1.75 (0.11-28.04)
Minor bleed	1.19 (0.83-1.70)	0.86 (0.63-1.19)	0.68 (0.38-1.23)
GI minor bleed	1.78 (1.07-2.97) *	0.88 (0.53-1.45)	0.67 (0.28-1.59)
Diltiazem alone			
Overall bleed	1.35 (0.93-1.95)	0.77 (0.54-1.10)	0.72 (0.39-1.34)
Overall GI bleed	2.17 (1.28-3.68) *	0.76 (0.43-1.34)	0.52 (0.19-1.44)
Major/moderate bleed	2.67 (1.15-6.20) *	1.07 (0.52-2.20)	1.86 (0.42-8.15)
Major/moderate GI bleed	4.31 (1.20-15.49) *	0.91 (0.29-2.80)	0.54 (0.03-11.09)
Minor bleed	1.36 (0.94-1.97)	0.75 (0.52-1.09)	0.57 (0.28-1.13)
GI minor bleed	2.23 (1.31-3.78) *	0.76 (0.43-1.36)	0.52 (0.19-1.44)
Verapamil alone			
Overall bleed	1.76 (1.01-3.06) *	0.72 (0.37-1.40)	1.00 (0.40-2.52)
Overall GI bleed	2.92 (1.40-6.11) *	0.52 (0.15-1.78)	2.06 (0.77-5.48)
Major/moderate bleed	5.84 (2.20-15.49) *	0.71 (0.15-3.26)	NA
Major/moderate GI bleed	9.82 (1.40-40.10) *	NA	NA
Minor bleed	1.49 (0.82-2.72)	0.75 (0.39-1.47)	1.04 (0.41-2.62)
GI minor bleed	2.71 (1.26-5.87) *	0.54 (0.16-1.85)	2.06 (0.77-5.48)
15-day gap			
Overall bleed	1.35 (0.98-1.86)	0.70 (0.51-0.96) *	0.83 (0.49-1.38)
Overall GI bleed	2.01 (1.26-3.20) *	0.60 (0.36-0.99) *	0.77 (0.36-1.65)
Major/moderate bleed	2.71 (1.36-5.38) *	0.96 (0.50-1.83)	2.09 (0.54-8.06)
Major/moderate GI bleed	4.75 (1.69-13.39) *	0.92 (0.33-2.51)	0.41 (0.02-8.48)
Minor bleed	1.31 (0.95-1.81)	0.70 (0.51-0.96) *	0.69 (0.40-1.21)
GI minor bleed	2.01 (1.25-3.22) *	0.60 (0.36-1.00)	0.77 (0.36-1.65)
Any diagnosis code position for outcome			
Overall bleed	1.23 (1.07-1.40) †	0.91 (0.81-1.03) †	0.67 (0.52-0.87) †
Overall GI bleed	1.92 (1.56-2.37) †	0.63 (0.51-0.79) †	0.35 (0.23-0.55) *
Major/moderate bleed	1.72 (1.06-2.77) *	0.88 (0.59-1.31)	1.71 (0.73-4.00)
Major/moderate GI bleed	3.78 (1.64-8.72) *	0.36 (0.16-0.82) †	0.26 (0.03-2.14)
Minor bleed	1.21 (1.06-1.38) †	0.91 (0.80-1.03) †	0.64 (0.49-0.84) †
GI minor bleed	1.90 (1.54-2.35) †	0.62 (0.49-0.78) †	0.35 (0.22-0.55) *
Standardized mortality ratio weight			
Overall bleed	1.26 (0.93-1.72)	0.87 (0.66-1.15)	0.86 (0.52-1.43)
Overall GI bleed	2.01 (1.31-3.09) *	0.80 (0.52-1.22)	1.09 (0.48-2.50)
Major/moderate bleed	3.69 (1.72-7.91) *	1.26 (0.72-2.21)	10.77 (2.12-54.73) *
Major/moderate GI bleed	3.27 (1.24-8.63) *	0.72 (0.28-1.84)	10.28 (0.29-355.88)

Minor bleed	1.27 (0.92-1.73)	0.85 (0.64-1.13)	0.78 (0.46-1.33)
GI minor bleed	2.12 (1.36-3.29) *	0.79 (0.51-1.23)	1.09 (0.48-2.50)
<p>Abbreviations: HR=hazard ratio; CI=confidence interval; GI=gastrointestinal; D=dabigatran; R=rivaroxaban; A=apixaban; DOAC=direct acting oral anticoagulants NA: no event in one of the comparison groups *Denotes statistically significant results at $P<0.05$ †Denotes proportional hazard assumption violated as the interaction between treatment and time was significant and a covariate for time was entered into the model.</p>			