

## **Supplemental Material Table of Contents**

**Supplemental Table 1.** Condition-specific ICD-9 and ICD-10 diagnostic codes used in this study

**Supplemental Table 2.** Time to event data for each outcome in the apixaban and the no anticoagulation group.

**Supplemental Table 3.** Baseline characteristics of the unmatched and matched cohort for patients on hemodialysis

**Supplemental Table 4.** Clinical outcomes for patients on hemodialysis

**Supplemental Table 5.** Sensitivity analyses

**Supplemental Table 6.** Clinical outcomes in the prevalent atrial fibrillation dataset

**Supplemental Table 7.** Effect of apixaban on any stroke, transient ischemic attack, or systemic thromboembolism and major bleeding in selected strata (prevalent atrial fibrillation dataset)

**Supplemental Table 1.** Condition-specific ICD-9 and ICD-10 diagnostic codes used in this study

Cardiovascular Mortality	<b>DEATHFM:</b> 23, 25, 26, 27, 28, 29, 30, 31, 32
Ischemic stroke or transient ischemic attack	<b>ICD-9-CM:</b> 362.3x, 433.x1, 434.x1, 436 <b>ICD-10 CM:</b> H34.1, I63
Systemic embolism	<b>ICD-9-CM:</b> 434.1, 444.xx, 445.xx <b>ICD-10 CM:</b> I74, I75
Myocardial infarction	<b>ICD-9-CM:</b> 410.xx <b>ICD-10 CM:</b> I21.x(x), I22.x(x)
Hemorrhagic stroke	<b>ICD-9-CM:</b> 430, 431, 432 <b>ICD-10 CM:</b> I60, I61, I62
<b><u>Major bleeding</u></b>	
1. Resulting in death	<b>DEATHFM:</b> 38, 39, 40, 41, 42, 43, 72
2. Intracranial	<b>ICD-9-CM:</b> 430, 431, 432.x <b>ICD-10 CM:</b> I60, I61, I62
<b><u>Clinically significant bleeding</u></b>	
1. Resulting in death	<b>DEATHFM:</b> 38, 39, 40, 41, 42, 43, 72
2. In a critical site:	
- Intracranial	<b>ICD-9-CM:</b> 430, 431, 432.x <b>ICD-10 CM:</b> I60, I61, I62
- Intraocular	<b>ICD-9-CM:</b> 360.43, 362.43, 362.81, 363.61, 363.62, 363.72, 376.32, 377.42, 379.23 <b>ICD-10 CM:</b> H44.81, H35.73x, H35.6x, H31.30x, H31.31x, H31.41x, H05.23x, H43.1x, H47.02x
- Pericardial	<b>ICD-9-CM:</b> 423.0 // <b>ICD-10 CM:</b> I31.2
- Airway	<b>ICD-9-CM:</b> 784.8, 786.30, 786.39 // <b>ICD-10 CM:</b> R04.x(x)
- Intra-articular	<b>ICD-9-CM:</b> 719.1x // <b>ICD-10 CM:</b> M25.0x(x)
- Retroperitoneal	<b>ICD-9-CM:</b> 568.81// <b>ICD-10 CM:</b> K66.1
3. Resulting in hospitalization:	One of the following codes in the institutional inpatient files:
- GI	<b>ICD-9-CM:</b> 456.0, 456.20, 530.21, 530.7, 530.82, 531.0x, 531.2x, 531.4x, 531.5x, 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.x1, 537.83, 537.84, 578.x, 562.x2, 562.x3, 569.3, 569.85 <b>ICD-10 CM:</b> I85.x1, K22.11, K22.6, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.x1, K31.811, K31.82, K92.0, K92.1, K92.2, K57.x1, K57.x3, K62.5, K55.21
- Urinary	<b>ICD-9-CM:</b> 596.7, 602.1, 599.7x <b>ICD-10 CM:</b> N42.1, R31.0, R31.9
- Gynecological	<b>ICD-9-CM:</b> 620.7, 621.4, 623.6, 624.5, 626.6, 626.8, 626.9, 627.0, 627.1 <b>ICD-10 CM:</b> N83.6, N83.7, N85.7, N92.0, N92.1, N92.4, N92.5, N93.8, N93.9, N95.0
- Other	<b>ICD-9-CM:</b> 459.0, 958.2, 729.92, 285.1
<b>Pneumonia</b> (viral or bacterial)	<b>ICD-9-CM:</b> 480.x, 481, 482.x(x), 483.x, 484.x, 485, 486, 487.0, 488.x1

Hip fracture

**ICD-10-CM:** J09.X1, J10.0\_, J11.0\_, J12, J13, J14, J15, J16, J18

**ICD-9-CM:** 820.x(x), 821.xx

**ICD-10-CM:** S72.x

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**Supplemental Table 2.** Time to event data for each outcome in the apixaban and the no anticoagulation group.

<b>Time to outcome (days)</b>	<b>No anticoagulation</b>	<b>Apixaban</b>
Time to stroke, TIA, or embolism	212 (65-523)	173 (49-379)
Time to stroke	214 (65-532)	173 (48-384)
Time to ischemic stroke	216 (67-532)	174 (49-384)
Time to hemorrhagic stroke	218 (68-538)	180 (52-386)
Time to clinically significant bleeding	140 (42-357)	124 (32-272)
Time to ischemic stroke-MI	184 (55-462)	163 (43-348)
Time to death	293 (87-636)	184 (52-387)

Results are shown as median (interquartile range). TIA, transient ischemic attack; MI, myocardial infarction

**Supplemental Table 3.** Baseline characteristics of the unmatched and matched cohort for patients on hemodialysis

Characteristics	Unmatched cohort			Matched cohort		
	No anticoagulation	Apixaban	St. dif.	No anticoagulation	Apixaban	St. dif.
Number of patients	9831	453		1374	453	
<i>Demographics</i>						
Age	68 ± 13	67 ± 11	-0.01	68 ± 13	67 ± 11	-0.08
Male sex	5283 (54%)	241 (53%)	-0.01	722 (53%)	241 (53%)	0.01
Black race	3151 (32%)	108 (24%)	-0.19	310 (23%)	108 (24%)	0.03
Dialysis vintage (months)	26 (10-59)	19 (6-33)	-0.32	19 (5-39)	19 (6-33)	0.00
<i>Comorbidities</i>						
Hypertension	9781 (100%)	452 (100%)	0.05	1370 (100%)	452 (100%)	0.02
Diabetes	7934 (81%)	375 (83%)	0.05	1111 (81%)	375 (83%)	0.05
Coronary disease	7514 (76%)	342 (76%)	-0.02	1036 (75%)	342 (76%)	0.00
Heart failure	7559 (77%)	351 (78%)	0.01	1076 (78%)	351 (78%)	-0.02
Myocardial infarction	2684 (27%)	102 (23%)	-0.11	315 (23%)	102 (23%)	-0.01
Stroke history	4010 (41%)	161 (36%)	-0.11	511 (37%)	161 (36%)	-0.04
PVD	5973 (61%)	257 (57%)	-0.08	771 (56%)	257 (57%)	0.01
Dyslipidemia	8365 (85%)	414 (91%)	0.20	1249 (91%)	414 (91%)	0.02
Malignancy	2793 (28%)	123 (27%)	-0.03	391 (29%)	123 (27%)	-0.03

Alcohol-related disease	1481 (15%)	51 (11%)	-0.11	161 (12%)	51 (11%)	-0.01
Liver disease	3240 (33%)	118 (26%)	-0.15	335 (24%)	118 (26%)	0.04
COPD	4375 (45%)	187 (41%)	-0.06	570 (42%)	187 (41%)	0.00
Bleeding history	5716 (58%)	224 (49%)	-0.18	675 (49%)	224 (49%)	0.01
<i>Medication</i>						
ACEI	2975 (30%)	120 (27%)	-0.08	335 (24%)	120 (27%)	0.05
ARB	1819 (19%)	87 (19%)	0.02	252 (18%)	87 (19%)	0.02
Antiplatelet agent	2450 (25%)	106 (23%)	-0.04	324 (24%)	106 (23%)	0.00
Beta-blocker	6777 (69%)	330 (73%)	0.09	997 (73%)	330 (73%)	0.00
Statin	5183 (53%)	274 (61%)	0.16	830 (60%)	274 (61%)	0.00

Results are presented as mean  $\pm$  standard deviation, median (interquartile range) or number (percentage). Standardized differences  $<0.10$  are considered to be negligible.

St. dif., standardized difference; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker

**Supplemental Table 4.** Clinical outcomes for patients on hemodialysis (453 patients on apixaban matched with 1374 patients without any anticoagulation)

Outcome	Incidence in apixaban users	Incidence in non-users	Crude HR (95% CI)	<i>p</i> value	Adjusted* HR (95% CI)	<i>p</i> value
Any stroke or TIA or embolism	8.5 (13)	7.3 (105)	1.36 (0.75-2.46)	0.31	1.41 (0.78-2.55)	0.26
Any stroke	6.5 (<11)	6.1 (88)	1.24 (0.64-2.42)	0.53	1.27 (0.65-2.49)	0.48
Major bleeding	4.4 (<11)	1.6 (41)	<b>2.42 (1.12-5.23)</b>	<b>0.03</b>	<b>2.44 (1.13-5.28)</b>	<b>0.02</b>
Clinically important bleeding	58.9 (69)	57.5 (621)	1.15 (0.89-1.48)	0.30	1.15 (0.89-1.49)	0.28
Ischemic stroke- MI	27.3 (38)	25.9 (341)	1.20 (0.85-1.69)	0.30	1.19 (0.85-1.67)	0.31
Ischemic stroke	3.9 (<11)	5.2 (75)	0.88 (0.38-2.07)	0.78	0.91 (0.39-2.15)	0.84
Hemorrhagic stroke	2.6 (<11)	1.3 (19)	2.19 (0.75-6.46)	0.15	2.21 (0.75-6.51)	0.15

Incidence rates are presented as number of events per 100 patient-years (total number of events). The number of outcomes per group is shown in parentheses. For the outcomes of any stroke, any stroke or TIA or thromboembolism, major bleeding, clinically important bleeding, ischemic stroke or myocardial infarction, ischemic stroke, and hemorrhagic stroke, patients were followed up to the date of death, kidney transplantation, on December 31<sup>st</sup>, 2015, loss of Medicare A-B or D coverage, or at the date of the last available apixaban prescription (plus drug supply days). Death was considered as a competing risk.

\*, Hazard ratios were adjusted for: CHA<sub>2</sub>DS<sub>2</sub>-Vasc score for the composite outcome of any stroke, any stroke or TIA or systemic thromboembolism and for the outcome of ischemic stroke; modified HAS-BLED score for major bleeding, hemorrhagic stroke, and clinically-important bleeding;

history of hypertension, diabetes mellitus, dyslipidemia, and myocardial infarction for the composite outcome of ischemic stroke or myocardial infarction.

HR, hazard ratio; CI, confidence interval; TIA, transient ischemic attack; MI, myocardial infarction



**Supplemental Table 5.** Sensitivity analyses

Outcome	Crude HR (95% CI)	<i>p</i> value	Adjusted* HR (95% CI)	<i>p</i> value
<b>Intention to treat analysis</b>				
Stroke or embolism	1.09 (0.68-1.72)	0.73	1.07 (0.67-1.70)	0.78
Major bleeding	1.16 (0.58-2.31)	0.68	1.13 (0.57-2.27)	0.73
Clinically important bleeding	1.02 (0.83-1.25)	0.86	1.00 (0.81-1.22)	0.94
Ischemic stroke or MI	0.94 (0.71-1.24)	0.66	0.93 (0.70-1.23)	0.59
<b>Time-distribution matching analysis</b>				
Stroke or embolism	0.88 (0.48-1.61)	0.68	0.93 (0.51-1.71)	0.83
Major bleeding	1.92 (0.88-4.18)	0.10	1.94 (0.89-4.23)	0.10
Clinically important bleeding	0.95 (0.74-1.21)	0.66	0.95 (0.74-1.21)	0.66
Ischemic stroke or MI	0.99 (0.71-1.38)	0.93	1.00 (0.72-1.40)	0.99
<b>Marginal structural model</b>				
Stroke or embolism	1.21 (0.67-2.20)	0.53	1.08 (0.60-1.92)	0.81
Major bleeding	3.29 (0.46-23.62)	0.24	3.16 (0.44-22.70)	0.25
Clinically important bleeding	0.88 (0.65-1.17)	0.37	0.83 (0.63-1.10)	0.20
Ischemic stroke or MI	1.12 (0.74-1.70)	0.58	1.03 (0.70-1.53)	0.87

For the intention to treat analysis, patients were followed up to the date of death, kidney transplantation, or on December 31<sup>st</sup>, 2015. Death was considered as a competing risk.

For the time-distribution matching analysis, patients were censored at the date of the last available apixaban prescription (plus drug supply days) for all outcomes.

For the marginal structural models, the following parameters were used to calculate the inverse probability weights: age, sex, race, dialysis modality, dialysis vintage, stroke history, MI history, bleeding history, hypertension, diabetes, heart failure, coronary disease, dyslipidemia, peripheral vascular disease, liver disease, alcohol-related disease, cancer, chronic obstructive lung disease, and use of medication (renin-angiotensin-aldosterone inhibitors, beta-blockers, statins, or antiplatelet agents).

\* Hazard ratios were adjusted for: CHA<sub>2</sub>DS<sub>2</sub>-Vasc score for the outcomes of stroke (ischemic or hemorrhagic, transient ischemic) or systemic thromboembolism; modified HAS-BLED score for major bleeding and clinically important bleeding; history of hypertension, diabetes mellitus, dyslipidemia, and myocardial infarction for the outcome of ischemic stroke or myocardial infarction.

HR, hazard ratio; CI, confidence interval; MI, myocardial infarction

**Supplemental Table 6.** Clinical outcomes in the prevalent atrial fibrillation dataset: 1266 patients on apixaban and 3797 patients without any anticoagulation.

Outcome	Crude HR (95% CI)	<i>p</i> value	Adjusted* HR (95% CI)	<i>p</i> value
Any stroke or TIA or embolism	0.98 (0.65-1.48)	0.91	0.96 (0.64-1.46)	0.87
Any stroke	0.82 (0.52-1.30)	0.40	0.80 (0.51-1.27)	0.35
Major bleeding	<b>3.19 (2.00-5.09)</b>	<b>&lt;0.001</b>	<b>3.18 (2.00-5.08)</b>	<b>&lt;0.001</b>
Clinically important bleeding	<b>1.36 (1.15-1.59)</b>	<b>&lt;0.001</b>	<b>1.34 (1.14-1.58)</b>	<b>&lt;0.001</b>
Ischemic stroke or MI	<b>1.26 (1.01-1.57)</b>	<b>0.04</b>	1.21 (0.97-1.50)	0.09
Ischemic stroke	1.01 (0.65-1.56)	0.98	0.99 (0.63-1.53)	0.95
Hemorrhagic stroke	<b>3.11 (1.89-5.13)</b>	<b>&lt;0.001</b>	<b>3.09 (1.88-5.10)</b>	<b>&lt;0.001</b>

For the outcomes of any stroke, any stroke or transient ischemic attack or thromboembolism, major bleeding, clinically important bleeding, ischemic stroke or myocardial infarction, ischemic stroke, and hemorrhagic stroke, patients were followed up to the date of death, kidney transplantation, on December 31<sup>st</sup>, 2015, loss of Medicare A-B or D coverage, or at the date of the last available apixaban prescription (plus drug supply days). Death was considered as a competing risk.

\*, Hazard ratios were adjusted for: CHA<sub>2</sub>DS<sub>2</sub>-Vasc score for the outcome of any stroke, the composite outcome of any stroke or transient ischemic attack or systemic thromboembolism, and the outcome of ischemic stroke; modified HAS-BLED score for major bleeding, hemorrhagic stroke, and clinically important bleeding; history of hypertension, diabetes mellitus, dyslipidemia, and myocardial infarction for the composite outcome of ischemic stroke or myocardial infarction.

HR, hazard ratio; CI, confidence interval; TIA, transient ischemic attack; MI, myocardial infarction

**Supplemental Table 7.** Effect of apixaban compared with no anticoagulation on any stroke and major bleeding in selected strata (prevalent atrial fibrillation dataset: 1266 patients on apixaban and 3797 patients without any anticoagulation).

Outcome	Stratum	HR (95% CI)	<i>p</i> value	<i>p</i> for interaction
Any stroke or transient ischemic attack or systemic embolism	Age ≥ 75	0.54 (0.22-1.33)	0.18	0.11
	Age < 75	1.23 (0.77-1.97)	0.39	
	Males	1.19 (0.69-2.04)	0.53	0.30
	Females	0.80 (0.42-1.54)	0.50	
	Black race	1.82 (0.85-3.89)	0.12	0.11
	Other races	0.79 (0.48-1.30)	0.35	
	Prior stroke	0.99 (0.55-1.78)	0.97	0.80
	No prior stroke	0.94 (0.52-1.71)	0.84	
	High risk for stroke*	1.09 (0.71-1.67)	0.70	0.14
	Low risk for stroke*	0.24 (0.03-1.70)	0.15	
Fatal or intracranial bleeding	Age ≥ 75	1.15 (0.36-3.70)	0.81	0.04
	Age < 75	4.47 (2.66-7.52)	<0.001	
	Males	3.27 (1.85-5.79)	<0.001	0.85
	Females	2.88 (1.29-6.45)	0.01	
	Black race	3.44 (1.78-10.03)	0.02	0.80
	Other races	3.06 (1.82-5.14)	<0.001	
	Prior stroke	3.59 (1.68-7.70)	0.001	0.60
	No prior stroke	2.90 (1.60-5.28)	<0.001	
	High risk for bleeding <sup>#</sup>	2.64 (1.38-5.05)	0.003	0.36
	Low risk for bleeding <sup>#</sup>	3.89 (1.99-7.62)	<0.001	

\* High risk for stroke was defined as a CHA<sub>2</sub>DS<sub>2</sub>-Vasc score ≥5 and low risk for stroke as a CHA<sub>2</sub>DS<sub>2</sub>-Vasc score <5.

# High risk for bleeding was defined as a HAS-BLED score >3 and low risk for stroke as a HAS-BLED score ≤3.

Crude hazard ratios are reported. Death was considered as a competing risk. Patients were followed up to the date of death, kidney transplantation, on December 31<sup>st</sup>, 2015, loss of Medicare A-B or D coverage, or

at the date of the last available apixaban prescription (plus drug supply days). HR, hazard ratio; CI, confidence interval