

## Supplement Material

S1 Table: PZN numbers (Pharmacy central number) of DOACs in standard dose .....	2
S2 Table: International Classification of Diseases version 10 (ICD-10)-codes for effectiveness and safety outcomes. ....	2
S3 Table: International Classification of Diseases version 10 (ICD-10)-codes and Anatomical Therapeutic Chemical (ATC)-codes of covariates for Cox regression analysis and propensity score matching.....	3
S4 Table: Baseline characteristics of phenprocoumon, composite DOAC cohort and subgroups (apixaban, dabigatran, edoxaban and rivaroxaban cohort) after propensity score matching. Standard mean differences (SMD), sample sizes after matching and number of unmatched datasets. ....	4
S5 Table: Mean-follow up time by cohort and outcome. ....	7
S1a Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding death.....	8
S1b Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding thromboembolic events .....	9
S1c Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding bleeding .....	10

S1 Table: PZN numbers (Pharmacy central number) of DOACs in standard dose

<b>B01AF02 Apixaban</b>
1647755, 1647778, 1647809, 1647821, 10218496, 10232906, 11376441, 11376458, 11524829, 11524841, 1647784, 5117273, 10273130, 11174884
<b>B01AE07 Dabigatran</b>
10193371, 10249781, 10261233, 10288114, 10357542, 10395867, 11004550, 11027924, 11027953, 11038299, 11038307, 11130384, 11130409, 11296340, 11296357, 11309120, 11341939, 11341945, 11727107, 12146424, 12605990, 12639115, 12668275, 13059331, 13245080, 13504653, 14015643, 14441759, 14445912, 9707103, 9947988, 10193365, 10390835, 10989779, 9947971, 10206458, 6561946, 6561952, 6561969, 6561981, 8797446
<b>B01AF03 Edoxaban</b>
10714172, 10714203, 10714255, 10714284, 10714309, 12749996, 12750002, 13695877,
<b>B01AF01 Rivaroxaban</b>
4369481, 4369498, 7089606, 8461410, 8461427, 8461433, 8461456, 9724544, 9724550, 9941299, 10005932, 10012174, 10012180, 10012197, 10057490, 10057509, 10072118, 10072124, 10200929, 10297685, 10318631, 10381954, 10381983, 10382008, 10393638, 10393644, 10743802, 10762426, 10852684, 10852690, 10852709, 10853577, 10999341, 10999358, 10999364, 11015714, 11096612, 11559354, 12433514, 12645529, 12645535, 12868703, 13155164, 13331141, 13502507, 13721830, 13902402, 13902879, 14140153, 14253176, 7605025, 10106863, 10106886, 10106892, 10964182

S2 Table: International Classification of Diseases version 10 (ICD-10)-codes for effectiveness and safety outcomes.

ICD-codes for efficiency and safety outcomes	
Cerebral infarction	I63
Stroke, not specified	I64
Transient cerebral ischaemic attacks	G45
Acute vascular disorders of intestine	K55.0
Bleedings in critical areas or organs	H35.6, H43.1, I60, I61, I62, G95.10, K66.1
Bleedings leading to blood transfusion (inpatient billing code 8-800)	D68.3, D69.9, I85.0, I98.3, J94.2, K22.6, K22.81, 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, K29.0, K31.82, K55.22, K57.01, K57.11, K57.13, K57.21, K57.31, K57.33, K57.41, K57.51, K57.53, K57.81, K57.91, K57.93, K62.5, K92.2, K92.0, K92.1, N02.0, N02.1, N02.2, N02.3, N02.4, N02.5, N02.6, N02.7, N02.8, N02.9, N42.1, N95.0, R04, R31, R58

S3 Table: International Classification of Diseases version 10 (ICD-10)-codes and Anatomical Therapeutic Chemical (ATC)-codes of covariates for Cox regression analysis and propensity score matching.

<b>Codes for covariables for Cox regression and propensity score matching</b>	
<b>Prescriptions</b>	<b>ATC-code</b>
Antiarrhythmic medication	C08, C01B, C07AB, C07AG
Antihypertensive medication	C02, C06A
Antiplatelet therapy	B01AC
Antipsychotic medication	N05A
Anti-ulcer therapy	A02B
Cardiac glycosides	C01A
Diuretics	C03
Heparin	B01AB
Lipid lowering medication	C10
NSAIDs	M01
Oral corticosteroids	H02
<b>Comorbidities</b>	<b>ICD-codes</b>
Adiposity	E66
Alcohol abuse	F10
Arterial hypertension	I10, I15
Atherosclerosis	I70
Cachexia	R64
Cancer	C00-C97
Dementia	F00, F01, F02, F03
Diabetes	E10-E14
Liver disease	K70-K77, B15-B19
Myocardial infarction	I21, I22
Nicotine abuse	Z72.2, F17
Orthopaedic implant	Z96.64, Z96.65, T84.04, T84.05
Renal impairment	N18, N19, N17, I12.0, I13.1, I13.2, O08.4, Z99.2, P96.0, Z49.1, N99.0, O90.4, T79.5
- Acute renal impairment	N17
- Moderate chronic impairment	N18.1, N18.2, N18.3
- Severe chronic impairment	N18.4, N18.5
Stroke	I64
Thrombosis	I80-I82

S4 Table: Baseline characteristics of phenprocoumon, composite DOAC cohort and subgroups (apixaban, dabigatran, edoxaban and rivaroxaban cohort) after propensity score matching. Standard mean differences (SMD), sample sizes after matching and number of unmatched datasets.

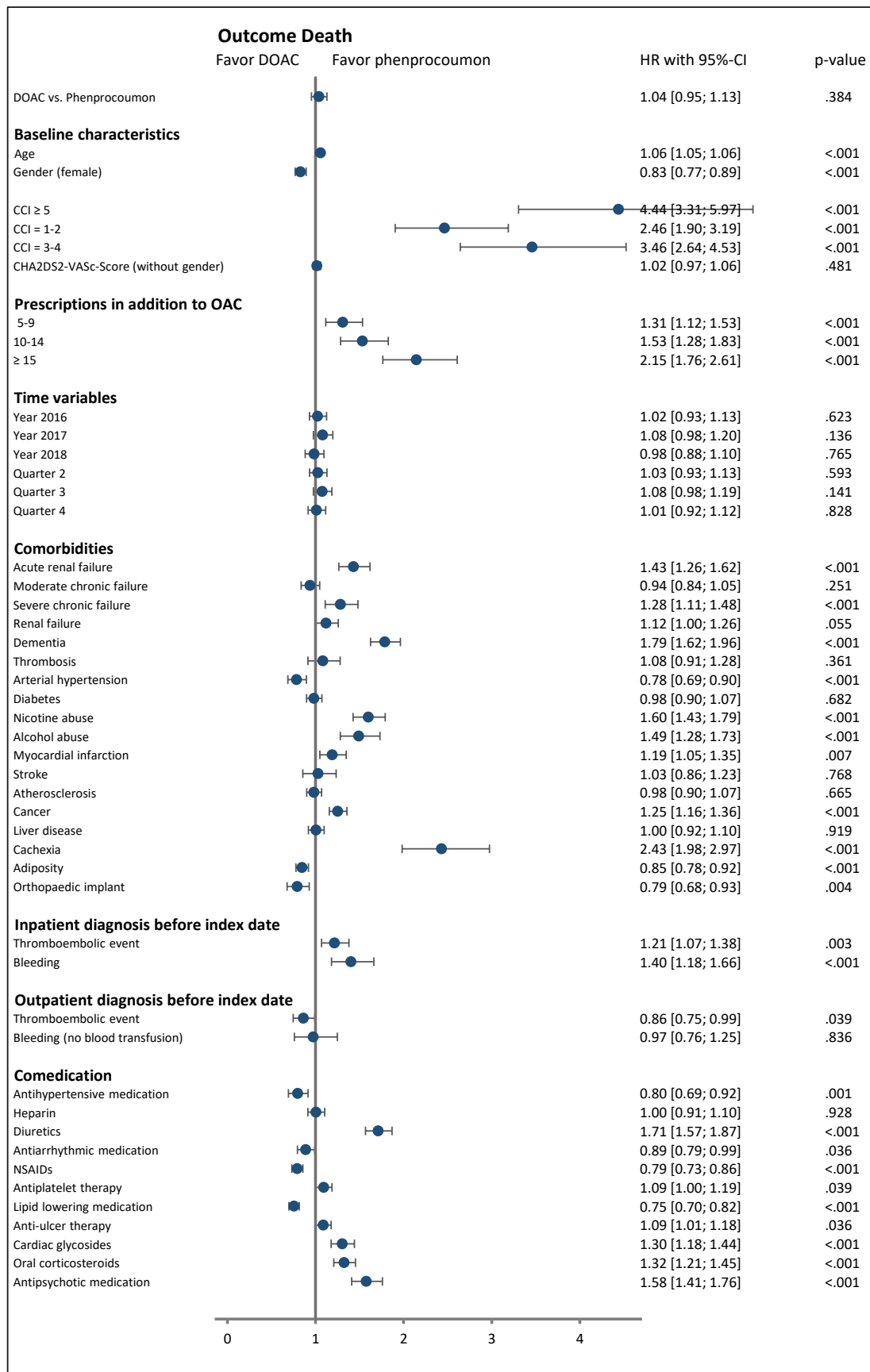
After Matching	Phenprocoumon	DOAC	SMD			
<i>n</i>	17,752	17,752				
<i>n</i> (unmatched)	2,427	34,030				
Distance	0.65	0.67	0.09			
<b>Baseline characteristics (mean ± SD):</b>						
Age	74.14 (10.24)	73.41 (10.22)	-0.06			
Female persons (%)	41.46	40.99	-0.01			
CCI = 0	10.40	9.17	-0.03			
CCI ≥ 5	20.07	19.97	0.00			
CCI = 1-2	38.77	39.33	0.01			
CCI = 3-4	30.75	31.53	0.02			
CHA <sub>2</sub> DS <sub>2</sub> -VASC-Score (without gender)	3.56 (1.56)	3.52 (1.61)	-0.02			
<b>Prescriptions in addition to OAC (%):</b>						
≤ 4	15.76	14.67				
5-9	41.97	42.32	0.01			
10 -14	27.68	28.18	0.01			
≥ 15	14.59	14.83	0.01			
<b>Comorbidities: Proportion of patients with ... (%)</b>						
Acute renal failure	4.78	4.64	-0.01			
Moderate chronic failure	18.89	18.79	0.00			
Severe chronic failure	1.82	1.57	-0.03			
Renal failure	28.42	27.81	-0.02			
Dementia	8.04	7.94	0.00			
Thrombosis	3.52	3.57	0.00			
Arterial hypertension	88.72	88.33	-0.01			
Diabetes	34.83	35.30	0.01			
Nicotine abuse	8.40	9.48	0.04			
Alcohol abuse	3.17	3.55	0.02			
Myocardial infarction	7.76	7.90	0.01			
Stroke	4.04	4.24	0.01			
Atherosclerosis	18.41	18.59	0.00			
Cancer	20.92	21.09	0.00			
Liver disease	18.34	19.48	0.03			
Cachexia	0.61	0.67	0.01			
Adiposity	27.97	29.66	0.04			
Orthopaedic implant	3.66	4.46	0.03			
<b>Comedication: Proportion of patients with ... (%)</b>						
Antihypertensive medication	6.61	6.87	0.01			
Heparin	20.54	19.20	-0.05			
Diuretics	50.96	50.12	-0.02			
Antiarrhythmic medication	87.11	86.76	-0.01			
NSAIDs	33.71	35.87	0.04			
Antiplatelet therapy	24.48	25.06	0.01			
Lipid lowering medication	45.96	46.74	0.02			
Anti-ulcer therapy	44.94	46.44	0.03			
Cardiac glycosides	10.25	9.81	-0.02			
Oral corticosteroids	12.26	12.92	0.02			
Antipsychotic medication	4.20	4.20	0.00			
<b>Inpatient diagnosis before index date ... (%)</b>						
Thromboembolic event	6.14	7.07	0.03			
Bleeding	1.84	1.88	0.00			
<b>Outpatient diagnosis before index date ... (%)</b>						
Thromboembolic event	10.12	10.29	0.01			
Bleeding (no blood transfusion)	1.39	1.52	0.01			
<b>After Matching</b>	<b>Phenprocoumon</b>	<b>Apixaban</b>	<b>SMD</b>	<b>Phenprocoumon</b>	<b>Dabigatran</b>	<b>SMD</b>
<i>n</i>	14,939	14,939		2,083	2,083	
<i>n</i> (unmatched)	5,240	8,404		18,096	122	
Distance	0.53	0.55	0.10	0.24	0.25	0.01
<b>Baseline characteristics (mean ± SD):</b>						

Age	73.64 (10.38)	72.94 (10.14)	-0.06	66.48 (12.14)	66.72 (10.30)	0.02
Female persons	41.78	41.31	-0.01	33.65	33.89	0.01
CCI = 0	11.20	10.38	-0.02	17.71	18.24	0.01
CCI ≥ 5	19.02	18.54	-0.01	13.06	12.34	-0.02
CCI = 1-2	39.64	41.33	0.03	44.22	44.46	0.00
CCI = 3-4	30.14	29.76	-0.01	25.01	24.96	0.00
CHA <sub>2</sub> DS <sub>2</sub> -VASc-Score (without gender)	3.49 (1.56)	3.44 (1.60)	-0.03	2.89 (1.71)	2.87 (1.73)	-0.01
<b>Prescriptions in addition to OAC (%):</b>						
≤ 4	17.19	17.09		26.55	26.69	
5-9	42.26	42.57	0.01	45.56	45.51	0.00
10 -14	26.55	26.56	0.00	20.64	20.07	-0.01
≥ 15	14.00	13.78	-0.01	7.25	7.73	0.02
<b>Comorbidities: Proportion of patients with ... (%)</b>						
Acute renal failure	4.20	4.26	0.00	1.68	1.54	-0.01
Moderate chronic failure	17.60	16.71	-0.03	9.17	7.06	-0.08
Severe chronic failure	1.28	1.10	-0.02	0.67	0.34	-0.06
Renal failure	26.15	25.09	-0.03	13.59	11.57	-0.06
Dementia	7.89	7.60	-0.01	3.94	3.41	-0.03
Thrombosis	3.28	3.41	0.01	2.69	2.64	0.00
Arterial hypertension	88.31	87.86	-0.01	82.96	82.33	-0.02
Diabetes	34.14	34.11	0.00	26.60	26.21	-0.01
Nicotine abuse	8.51	9.27	0.03	10.51	9.65	-0.03
Alcohol abuse	3.23	3.53	0.02	4.99	4.51	-0.02
Myocardial infarction	6.94	6.49	-0.02	3.98	3.98	0.00
Stroke	3.93	4.22	0.01	7.78	7.06	-0.03
Atherosclerosis	17.84	17.74	0.00	13.49	13.68	0.01
Cancer	20.42	20.38	0.00	17.67	17.33	-0.01
Liver disease	18.06	18.61	0.01	17.76	17.71	0.00
Cachexia	0.54	0.54	0.00	0.24	0.24	0.00
Adiposity	28.34	28.98	0.01	29.67	27.89	-0.04
Orthopaedic implant	4.00	4.84	0.04	3.79	3.84	0.00
<b>Comedication: Proportion of patients with ... (%)</b>						
Antihypertensive medication	6.40	6.38	0.00	5.04	4.51	-0.03
Heparin	12.79	12.30	-0.02	8.21	7.78	-0.02
Diuretics	48.97	47.41	-0.03	29.19	29.28	0.00
Antiarrhythmic medication	87.14	86.88	-0.01	85.31	85.50	0.01
NSAIDs	33.99	35.30	0.03	39.32	38.89	-0.01
Antiplatelet therapy	23.85	23.41	-0.01	17.47	16.42	-0.03
Lipid lowering medication	45.42	45.16	-0.01	44.41	44.22	0.00
Anti-ulcer therapy	44.11	44.52	0.01	39.51	39.56	0.00
Cardiac glycosides	8.60	8.07	-0.02	5.71	5.42	-0.01
Oral corticosteroids	12.22	12.64	0.01	11.09	11.09	0.00
Antipsychotic medication	4.28	4.32	0.00	2.98	2.83	-0.01
<b>Inpatient diagnosis before index date ... (%)</b>						
Thromboembolic event	6.85	8.37	0.05	22.13	22.18	0.00
Bleeding	1.79	1.80	0.00	1.01	1.20	0.02
<b>Outpatient diagnosis before index date ... (%)</b>						
Thromboembolic event	10.11	10.86	0.02	18.92	18.19	-0.02
Bleeding (no blood transfusion)	1.39	1.43	0.00	1.30	1.15	-0.01
<b>After Matching</b>	<b>Phenprocoumon</b>	<b>Edoxaban</b>	<b>SMD</b>	<b>Phenprocoumon</b>	<b>Rivaroxaban</b>	<b>SMD</b>
n	7,384	7,384		12,942	12,942	
n (unmatched)	12,795	452		7,237	5,456	
Distance	0.37	0.37	0.04	0.49	0.51	0.08
<b>Baseline characteristics (mean ± SD):</b>						
Age	71.40 (10.90)	71.08 (10.55)	-0.03	72.56 (10.45)	71.87 (10.17)	-0.06
Female persons	39.18	38.48	-0.01	40.53	40.20	-0.01
CCI = 0	16.45	16.75	0.01	12.92	12.94	-0.02
CCI ≥ 5	11.88	11.66	-0.01	15.38	14.33	-0.03
CCI = 1-2	45.50	45.94	0.01	42.38	43.80	0.03
CCI = 3-4	26.16	25.65	-0.01	29.32	28.92	-0.01
CHA <sub>2</sub> DS <sub>2</sub> -VASc-Score (without gender)	3.01 (1.50)	2.97 (1.54)	-0.03	3.29 (1.50)	3.21 (1.55)	-0.05
<b>Prescriptions in addition to OAC (%):</b>						

≤ 4	24.87	24.52		19.20	19.18	
5-9	43.68	44.72	0.02	42.97	43.86	0.02
10 -14	21.63	21.28	-0.01	25.19	24.66	-0.01
≥ 15	9.82	9.48	-0.01	12.64	12.30	-0.01
<u>Comorbidities: Proportion of patients with ... (%)</u>						
Acute renal failure	1.94	1.79	-0.01	3.45	3.07	-0.02
Moderate chronic failure	10.70	10.96	0.01	13.88	12.88	-0.03
Severe chronic failure	0.51	0.45	-0.01	0.74	0.60	-0.02
Renal failure	16.44	16.52	0.00	21.09	19.83	-0.04
Dementia	5.07	4.74	-0.02	6.80	6.38	-0.02
Thrombosis	2.74	2.55	-0.01	3.36	3.54	0.01
Arterial hypertension	85.39	85.32	0.00	87.54	86.59	-0.03
Diabetes	29.08	28.94	0.00	32.91	32.21	-0.02
Nicotine abuse	8.06	8.36	0.01	8.96	9.28	0.01
Alcohol abuse	3.18	3.28	0.01	3.41	3.73	0.02
Myocardial infarction	3.60	3.75	0.01	5.76	5.66	0.00
Stroke	3.52	3.20	-0.02	3.38	3.29	-0.01
Atherosclerosis	15.87	15.93	0.00	16.35	15.86	-0.01
Cancer	19.11	19.11	0.00	20.03	19.56	-0.01
Liver disease	18.19	18.55	0.01	18.11	18.08	0.00
Cachexia	0.34	0.34	0.00	0.67	0.66	0.00
Adiposity	28.58	28.35	-0.01	28.43	28.71	0.01
Orthopaedic implant	5.48	6.07	0.02	3.79	4.04	0.01
<u>Comedication: Proportion of patients with ... (%)</u>						
Antihypertensive medication	5.55	5.62	0.00	5.94	5.93	0.00
Heparin	8.83	8.82	0.00	12.83	11.86	-0.03
Diuretics	35.04	34.47	-0.01	44.60	42.70	-0.04
Antiarrhythmic medication	84.33	84.53	0.01	86.93	86.69	-0.01
NSAIDs	35.97	36.08	0.00	34.98	35.87	0.02
Antiplatelet therapy	18.49	18.24	-0.01	22.10	21.41	-0.02
Lipid lowering medication	38.72	38.54	0.00	41.96	41.24	-0.02
Anti-ulcer therapy	36.94	36.38	-0.01	42.54	42.72	0.00
Cardiac glycosides	5.39	5.07	-0.02	8.26	7.90	-0.02
Oral corticosteroids	11.94	11.67	-0.01	12.15	12.42	0.01
Antipsychotic medication	3.28	3.20	0.00	4.05	3.96	-0.01
<u>Inpatient diagnosis before index date ... (%)</u>						
Thromboembolic event	5.58	5.42	-0.01	5.80	5.84	0.00
Bleeding	0.96	0.83	-0.02	1.27	1.08	-0.02
<u>Outpatient diagnosis before index date ... (%)</u>						
Thromboembolic event	8.86	8.52	-0.01	8.64	8.46	-0.01
Bleeding (no blood transfusion)	1.12	1.18	0.01	1.24	1.20	0.00

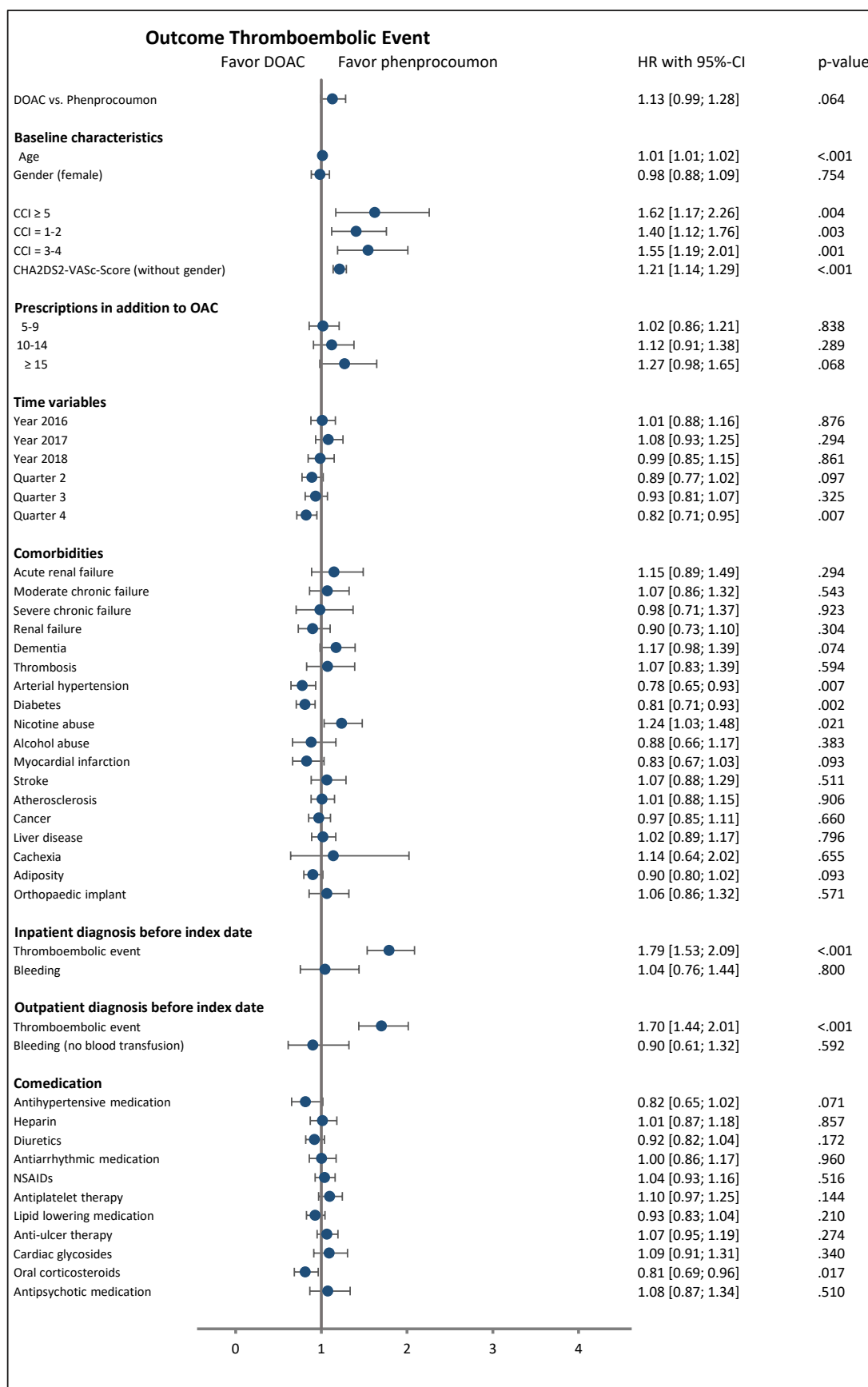
S5 Table: Mean-follow up time by cohort and outcome.

Mean follow-up time	Phenprocoumon vs. DOAC			
	VKA	DOAC		
<b>N</b>	17,752	17,752		
Thromboembolic events	315.9	302.7		
Deceased	318.8	305.9		
Bleeding	314.9	303.3		
Mean follow-up time	Phenprocoumon vs. Apixaban		Phenprocoumon vs. Dabigatran	
	VKA	Apixaban	VKA	Dabigatran
<b>N</b>	14,939	14,939	2,083	2,083
Thromboembolic events	316.8	312.8	318.0	294.7
Deceased	319.8	316.4	322.1	300.1
Bleeding	316.0	314.5	319.9	298.8
Mean follow-up time	Phenprocoumon vs. Edoxaban		Phenprocoumon vs. Rivaroxaban	
	VKA	Edoxaban	VKA	Rivaroxaban
<b>N</b>	7,384	7,384	12,942	12,942
Thromboembolic events	321.8	316.1	318.5	297.9
Deceased	324.2	318.9	321.3	300.4
Bleeding	321.3	317.0	317.9	297.8

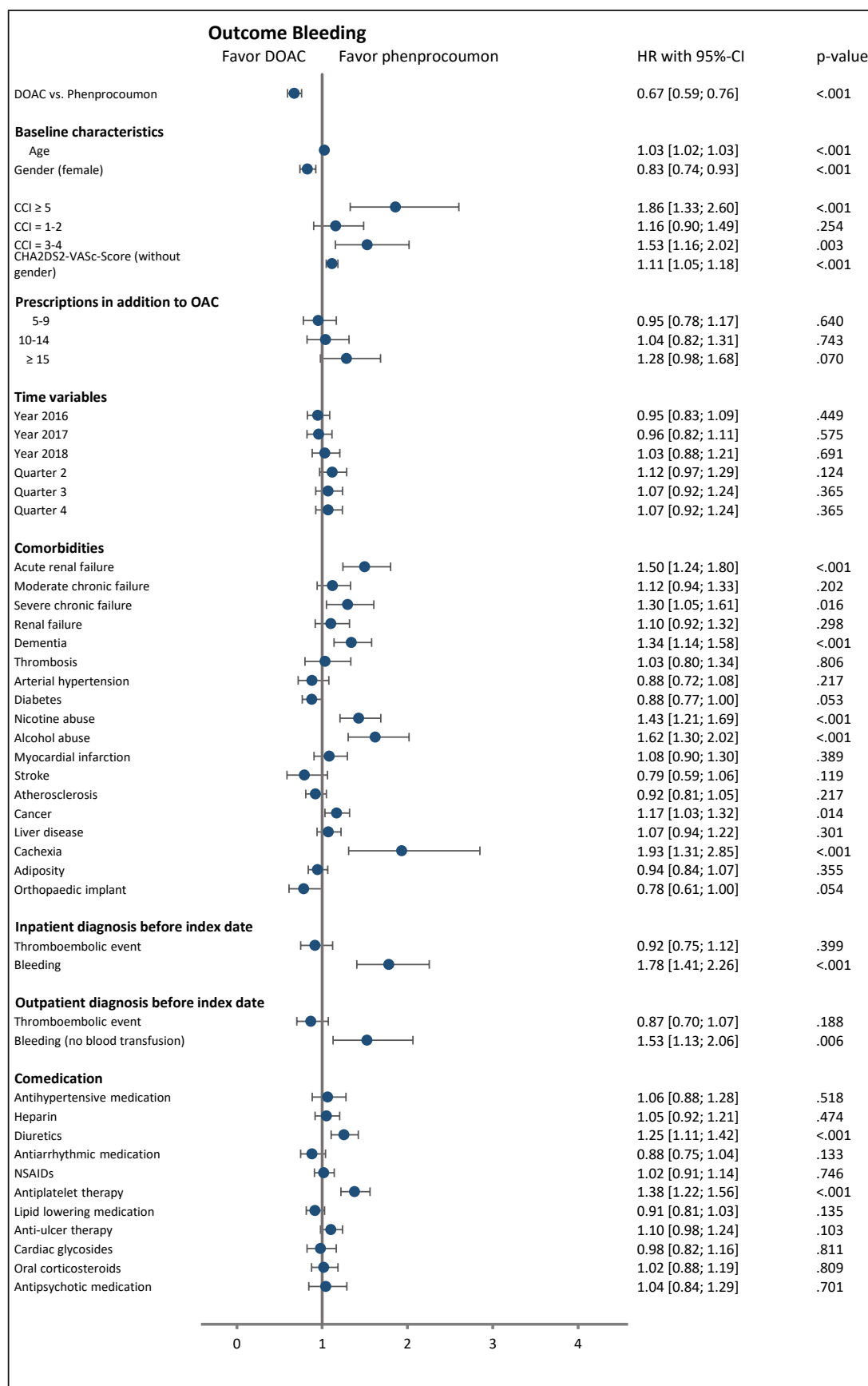


S1a Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding death





S1b Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding thromboembolic events 9



S1c Figure: Cox-Regression analysis for DOAC vs. phenprocoumon regarding bleeding