Supplemental Material Table of Contents

Supplemental Table 1. ICD-9-CM and ICD-10-CM codes used to identify venous thromboembolism

Venous Thromboembolism Diagnosis Codes			
ICD-9-CM Thromboembolic Event			
415.1*	453.4*	453.84	453.87
451.1*	453.82	453.85	453.89
453.2	453.83	453.86	453.9
ICD-10-CM Thromboembolic Event			
I26.0*	I80.23*	I82.44*	I82.890
I26.9*	I80.29*	I82.49*	I82.A1*
I80.1*	I82.40*	I82.4Y*	I82.B1*
I80.20*	I82.41*	I82.4Z*	I82.C1*
I82.210	I82.42*	I82.60*	
I80.22*	I82.43*	I82.62*	

ICD-9-CM, International Classifications of Diseases, Ninth Revision, Clinical Modification;

ICD-10-CM, International Classifications of Diseases, Tenth Revision, Clinical Modification;

VTE, venous thromboembolism

*indicates any digit in this position

Supplemental Table 2. Diagnosis-related group codes used identify recent hospitalization for surgery or trauma

DRG Codes																			
001	026	116	184	234	256	326	346	412	459	479	502	571	617	658	709	744	800	854	929
002	027	117	185	235	257	327	347	413	460	480	503	572	618	659	710	745	801	855	939
003	028	129	215	236	258	328	348	414	461	481	504	573	619	660	711	746	802	856	940
004	029	130	216	239	259	329	349	415	462	482	505	574	620	661	712	747	803	857	941
005	030	131	217	240	260	330	350	416	463	483	506	575	621	662	713	748	804	858	955
006	031	132	218	241	261	331	351	417	464	485	507	576	622	663	714	749	817	870	956
007	032	133	219	242	262	332	352	418	465	486	508	577	623	664	715	750	818	876	957
008	033	134	220	243	263	333	353	419	466	487	509	578	624	665	716	768	819	901	958
010	034	135	221	244	264	334	354	420	467	488	510	579	625	666	717	769	820	902	959
011	035	136	222	245	265	335	355	421	468	489	511	580	626	667	718	770	821	903	963
012	036	137	223	246	266	336	356	422	469	492	512	581	627	668	734	783	822	904	964
013	037	138	224	247	267	337	357	423	470	493	513	582	628	669	735	784	823	905	965
014	038	139	225	248	268	338	358	424	471	494	514	583	629	670	736	785	824	906	969
016	039	163	226	249	269	339	405	425	472	495	515	584	630	671	737	786	825	907	970
017	040	164	227	250	270	340	406	453	473	496	516	585	652	672	738	787	826	908	981
020	041	165	228	251	271	341	407	454	474	497	517	604	653	673	739	788	827	909	982
021	042	166	229	252	272	342	408	455	475	498	518	605	654	674	740	796	828	913	983
022	113	167	231	253	273	343	409	456	476	499	519	614	655	675	741	797	829	914	987
023	114	168	232	254	274	344	410	457	477	500	520	615	656	707	742	798	830	927	988
024	115	183	233	255	296	345	411	458	478	501	570	616	657	708	743	799	853	928	989
025																			

DRG, diagnosis-related group

Supplemental Methods: Approaches used to determine the disability proxy score

Disability Proxy Score: We developed a disability proxy score specifically for use with dialysis patient claims data designed, in part, to attempt to identify disability. While this score has not been validated by medical records review, we have used it in several investigations; details of the development of the score and an example of its application have been previously published (Wetmore et al. *Clin J Am Soc Nephrol.* 2016;11:1413-21; Wetmore et al. *Am J Kidney Dis.* 2018;71:831-41). In brief, established scores, such as the Fried Frailty Score, are excellent tools, but are imperfect for our use because typical measures that might be proxies for frailty, functional status, and disability are not, unfortunately, available in Medicare claims data. We attempted to develop claims-based measures that can potentially assess for disability which (1) use medical claims data and (2) are tailored to dialysis patients. Specifically, we assessed putative disability using evidence of particular diagnoses and the Medicare durable medical equipment (DME) files.

Potential markers of disability from the DME files were chosen by first limiting to those with prevalence greater than 1%, and then further limiting to those with an association with fracture, hospitalization, or mortality. Proportional hazards models were first used to investigate unadjusted associations of these markers with death, and adjusted associations (adjusted for demographics, comorbidity, erythropoietin dose, hemoglobin). The resulting potential markers of disability were: bed, oxygen, wheelchair, continuous positive airway pressure (CPAP) device, nebulizer, walker, commode, dressings, enteral supplies, diabetic shoes, diabetic supplies, suction canister, home health claim, hospice claim, skilled nursing facility claim, rehab claim,

myocardial infarction, history of stroke, depression, visual impairment, hip fracture, history of thyroid disease, and dementia.

Using this list, we constructed another proportional hazards model, with mortality as the outcome, to determine the additional contribution of these potential disability markers beyond demographic characteristics and comorbidity. The model was then reduced, and the following variables remained significant for mortality in the model, after adjusting for other patient characteristics and comorbidity:

- hospital bed
- wheelchair
- walker
- commode
- home oxygen
- CPAP device
- suction canister
- wound dressings
- enteral supplies
- home health claims
- hospice claims
- skilled nursing facility claims
- acute myocardial infarction (AMI)
- stroke
- hip fracture
- visual impairment

- dementia
- depression

Use of hospital bed, wheelchair, walker, commode, home oxygen, CPAP device, suction canister, wound dressings, and enteral supplies was ascertained from Medicare DME claim files based on Healthcare Common Procedure Coding System (HCPCS) codes. To define AMI, stroke, hip fracture, visual impairment, dementia, and depression, we required one or more inpatient, skilled nurse facility, home health, or hospice claims with a corresponding diagnosis code or two or more outpatient/Part B claims with corresponding diagnosis codes within a year. The HCPCS and International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes are listed in **Supplemental Table 3**.

The disability proxy score was created by taking parameter estimates from the adjusted proportional hazards model (including demographics, comorbid conditions, and the above potential markers of disability), multiplying the parameter estimates by 10, setting to zero if between -0.5 and +0.5, rounding to integer, and summing. The C-statistic in the developmental cohort was 0.736. While the score was developed using hemodialysis patients who were incident in 2008, the performance characteristics of the score were assessed by applying the resulting score to a separate validation Medicare cohort. The validation cohort consisted of patients initiating hemodialysis the following year (that is, incident to dialysis in 2009), who therefore had virtually identical underlying case-mix characteristics. The resulting C-statistic in the validation cohort was 0.741.

The final score was calculated using the following formula: based on presence/absence of disease and/or equipment use: score = 1 × hospital bed + 1 × wheelchair – 1 × walker – 1 ×

commode + 3 × oxygen – 2 × CPAP device + 2 × suction canister + 1 × wound dressings + 3 × enteral feedings + 1 × home health claim + 10 × hospice service claim + 2 × SNF claim + 2 × AMI + 1 × history of stroke + 1 × hip fracture + 2 × dementia + 2 × depression

Supplemental Table 3. HCPCS and ICD-9-CM diagnosis codes used to define the disability proxy score

Equipment Use/Disease	HCPCS/ICD-9-CM Diagnosis codes
Hospital bed	E0250, E0251, E0255, E0256, E0260, E0261, E0265, E0266, E0270, E0290-E0297, E0301-E0304
Wheelchair	A0130, E0971, E0973, E1089, E1090, E1250, E1260, E1285, E1290, E2365, E2601, K0001, K0003-K0007, K0010, K0011, K0195, K0813-K0898
Walker	E0100, E0105, E0130, E0135, E0140, E0141, E0143, E0144, E0147-E0149
Commode	E0163, E0165, E0168, E0170, E0171, E0275, E0276
Home oxygen	E0425, E0430, E0431, E0433-E0435, E0439, E0440, E1390, K0738, K0741
CPAP device	A7027, A7034-A7039, A7044-A7046, E0470, E0561, E0562, E0601, E0618, E0619
Suction canister	A7000-A7002
Dressings	A6021-A6024, A6196-A6205, A6209-A6214, A6216-A6239, A6242-A6247, A6251-A6259, A6266, A6402-A6404, A6442-A6456
Enteral supplies	B3034-B3036, B4081-4083, B4087, B4088, B4100, B4102, B4104, B4149, B4150, B4152-B4155, B4157, B9000, B9002
AMI	410.x1
Stroke	430, 431, 432, 434.x1, 436.xx, V12.54
Hip fracture	733.14, 808.xx, 820.xx
Visual impairment	361.xx, 362.xx, 365.xx, 366.xx, 369.xx
Dementia	290.xx
Depression	296.xx, 298.0, 300.4, 301.1x, 309.0, 309.1, 311

AMI, acute myocardial infarction; CPAP, continuous positive airway pressure; HCPCS, Healthcare Common Procedure Coding System; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification.

Supplemental Table 4. Baseline characteristics of the study sample prior to inverse probability of treatment weighting

	Treatment group		
	Warfarin	Apixaban	Standardized difference*
n	9088	3118	
Age in years, %			
18-44	1207 (13)	357 (11)	5.6
45-64	3458 (38)	1108 (36)	5.2
65-74	2488 (27)	877 (28)	-1.7
75-79	879 (10)	356 (11)	-5.7
80+	1056 (12)	420 (13)	-5.6
Female sex, %	4804 (53)	1693 (54)	-2.9
Race, %			
White	4572 (50)	1570 (50)	-0.1
Black	4204 (46)	1418 (46)	1.6
Other	312 (3)	130 (4)	-3.9
Urban residence, %	7296 (80)	2480 (80)	1.9
Medicaid coverage, %	5258 (58)	1952 (63)	-9.2
Low-income subsidy, %	6450 (71)	2343 (75)	-9.4
Modality/vascular access, %			
HD-catheter	4403 (48)	1504 (48)	0.4
HD-AVG	1369 (15)	504 (16)	-3.0
HD-AVF	2708 (31)	934 (30)	1.4
PD	536 (6)	176 (6)	1.1
Time on dialysis, %			
0 -< 6 months	1600 (18)	515 (17)	2.9
6 -< 12 months	646 (7)	223 (7)	-0.2
1 -< 3 years	2198 (24)	733 (24)	1.6
3 -< 5 years	1556 (17)	575 (18)	-3.5
5 -< 8 years	1631 (18)	512 (16)	4.1
≥8 years	1457 (16)	560 (18)	-5.1
Primary cause of kidney failure, %			
Diabetes	4087 (45)	1517 (49)	-7.4
Hypertension	2775 (31)	1001 (32)	-3.4
Glomerulonephritis	919 (10)	213 (7)	11.8
Other	1307 (14)	387 (12)	5.8
VTE type, %			
DVT only	6624 (73)	2394 (77)	-9.0
PE with or without DVT	2464 (27)	724 (23)	9.0
Provoking VTE factors, %			

Surgery	2150 (24)	766 (25)	-2.1
Institutional stay of ≥3 days	4731 (52)	1628 (52)	-0.3
Active cancer or chemotherapy	1243 (14)	442 (14)	-1.4
Comorbid conditions, %			
Heart failure	5374 (59)	1858 (60)	-0.9
Myocardial infarction	2167 (24)	689 (22)	4.2
Cerebrovascular disease	2109 (23)	734 (24)	-0.8
Peripheral artery disease	3525 (39)	1286 (41)	-5.0
COPD	3822 (42)	1268 (41)	2.8
Peptic ulcer	383 (4)	117 (4)	2.4
Liver disease	1328 (15)	419 (13)	3.4
Coagulopathy	2368 (26)	713 (23)	7.4
Alcohol abuse	306 (3)	96 (3)	1.6
Tobacco use	4215 (46)	1396 (45)	3.2
History of falls	1599 (18)	628 (20)	-6.5
Disability proxy score, %			
≤0	2127 (23)	730 (23)	0.0
1-2	2461 (27)	788 (25)	4.1
3-4	2025 (22)	732 (24)	-2.8
5-6	1411 (16)	494 (16)	-0.9
7+	1064 (12)	374 (12)	-0.9
Medication use on index date, %			
Antidiabetic	2112 (23)	819 (26)	-7.0
Antihypertensive	3503 (39)	1230 (39)	-1.9
Antiarrhythmic	463 (5)	198 (6)	-5.4
Statin	3217 (35)	1248 (40)	-9.6
Antiplatelet	1170 (13)	494 (16)	-8.5
NSAID	107 (1)	54 (2)	-4.6
Corticosteroid	586 (6)	204 (7)	-0.4
SSRI/SNRI	1309 (15)	522 (17)	-3.9
Proton pump inhibitor	2700 (30)	988 (32)	-4.3
Antineoplastic	248 (3)	100 (3)	-2.8
ED/observation visits, mean (SD)	1.6 (2.7)	1.7 (2.6)	-2.4
Inpatient visits, mean (SD)	2.4 (1.8)	2.3 (1.8)	5.0
Hospitalization days, mean (SD)	24.4 (22.2)	21.3 (22.1)	14.3

*The standardized difference (reported as a percentage) represents the difference in means or proportions of the two groups scaled by the pooled standard deviation.

AVF, arteriovenous fistula; AVG, arteriovenous graft; COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; ED, emergency department; KF, kidney failure; HD, hemodialysis; NSAID, non-steroidal anti-inflammatory drug; PD, peritoneal dialysis; PE, pulmonary embolism; SD, standard deviation; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, serotonin selective reuptake inhibitor

Supplemental Table 5. Pattern of drug discontinuation or switching over time

	N (%)	
Initial Drug Prescribed	6-month follow-up	3-month follow-up
Warfarin	9088	9088
Switch to apixaban or other DOAC	293 (3%)	259 (3%)
Discontinue	6730 (74%)	4991 (55%)
Apixaban label-concordant	3118	3118
Switch to warfarin or other DOAC	93 (3%)	86 (3%)
Discontinue	2333 (75%)	1934 (62%)

DOAC, direct oral anticoagulants

Supplemental Table 6. Reasons for the end of follow-up for the ITT analysis

	N (%)	
Cause	6-month follow-up	3-month follow-up
Death	1956 (16%)	1221 (10%)
End of Medicare coverage	486 (4%)	271 (2%)
Modality change/transplant	278 (2%)	169 (1%)
End of follow-up (Dec 31, 2018)	9486 (78%)	10,545 (86%)

ITT, intention-to-treat

Supplemental Figure 1. Comparisons, adjusted using IPT and IPC weighting for sociodemographic factors, comorbid conditions, disability proxy score, concomitant medications, and healthcare utilization, for apixaban vs. warfarin in the 3-month follow-up analysis.

CAS, censored-at-switching; CI, confidence interval; HR, hazard ratio; IPC, inverse-probability-of-censoring; IPT, inverse-probability-of-treatment; ITT, intention-to-treat; PY, person-years; VTE, venous thromboembolism

Supplemental Figure 1

Outcome	Analysis	Warfarin Crude N events	Warfarin Event rate per 100 PY	Apixaban Crude N events	Apixaban Event rate per 100 PY	HR (95% CI)
VTE hospitalization	ITT	231	11.5	45	7.0	0.60 (0.43, 0.84)
	CAS	172	12.5	27	7.1	0.52 (0.34, 0.80)
Major bleeding	ITT	282	14.3	71	10.6	0.74 (0.56, 0.97)
	CAS	221	16.2	58	13.4	0.78 (0.58, 1.06)
All-cause mortality	ITT	892	44.3	329	47.8	1.08 (0.94, 1.23)
	CAS	521	38.0	179	42.4	1.07 (0.89, 1.27)