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Title

Re-evaluating Safety and Effectiveness of Dabigatran versus Warfarin in a Nationwide Data Environment: A Prevalent New User Design Study

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Concise Title

Prevalent New User Design Study of Dabigatran and Warfarin

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Drugs - Real World Outcomes

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Supplementary Table 1. Diagnosis Codes for comorbidity of interest in International Classification of Diseases Ninth Revision Clinical Modification System (ICD-9-CM)

Diagnosis	ICD-9-CM
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
Pulmonary circulation disorders	415.0, 415.1, 416.x, 417.0, 417.8, 417.9
Hypertension	401.x, 402.x–405.x
Chronic pulmonary disease	416.8, 416.9, 490.x–505.x, 506.4, 508.1, 508.8
Diabetes	250.0–250.3, 250.4–250.9
Hypothyroidism	240.9, 243.x, 244.x, 246.1, 246.8
Renal failure	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x
Mild liver disease	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
Moderate or severe liver disease	456.0–456.2, 572.2–572.8
Peptic ulcer disease excluding bleeding	531.7, 531.9, 532.7, 532.9, 533.7, 533.9, 534.7, 534.9
Solid tumor without metastasis	140.x–172.x, 174.x–195.x
Rheumatoid arthritis/collagen vascular diseases	446.x, 701.0, 710.0–710.4, 710.8, 710.9, 711.2, 714.x, 719.3, 720.x, 725.x, 728.5, 728.89, 729.30
Fluid and electrolyte disorders	253.6, 276.x
Depression	296.2, 296.3, 296.5, 300.4, 309.x, 311
Ischemic stroke	433.x1, 434.x1, 435.9, 436, 437.1x, 437.9x
Intracranial hemorrhage	430, 431, 432
GI-bleeding	456.0, 456.20, 530.21, 530.7, 530.82, 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 535.71, 537.83, 537.84, 569.85, 569.86, 562.02, 562.03, 562.12, 562.13, 569.3, 578, 568.81
Pulmonary embolism	415.1, v12.51, 673.2
Deep vein thrombosis	451.1, 451.2, 451.81, 453.4, 459.1, 671.3, 671.4
Valvular heart disease	093.2, 394.x–397.x, 424.x, 746.3–746.6, V42.2, V43.3

Drugs - Real World Outcomes

Mitral stenosis	746.5, 394.0, 394.2, 396.0, 396.1, 396.8
Myocardial infarction	410.x, 412.x
Arterial embolism/thrombosis	444.x
Vascular disease	410.x, 412.x, 093.0, 437.3, 440.x, 441.x, 443.1-443.9, 447.1, 557.1, 557.9, v43.4
Hemiplegia or paraplegia	334.1, 342.x, 343.x, 344.0– 344.6, 344.9
Dementia	290.x, 294.1, 331.2
Percutaneous coronary intervention ^a	33076A, 33076B, 33077A, 33077B, 33078A, 33078B
Coronary artery bypass surgery ^a	68023A, 68023B, 68024A, 68024B, 68025A, 68025B

^a Taiwan National Health Insurance specific procedure codes

Supplementary Table 2. Drugs of interest in Anatomical Therapeutic Chemical Classification System (ATC)

Drug entity	ATC code
Antiplatelet	B01AC04, B01AC05, B01AC07, B01AC24
Low dose Aspirin	B01AC06
NSAID	M01AA01, M01AB01, M01AB02, M01AB03, M01AB05, M01AB06, M01AB08, M01AB11, M01AB15, M01AB16, M01AB51, M01AB55, M01AC01, M01AC02, M01AC06, M01AC56, M01AE01, M01AE02, M01AE03, M01AE04, M01AE05, M01AE09, M01AE11, M01AE16, M01AE51, M01AE52, M01AE53, M01AE56, M01AG01, M01AG02, M01AG03, M01AG04, M01AX01, M01AX02, M01AX07, M01AX17
Antiepileptics	N03AF01, N03AG01, N03AB02
Antifungal	J02AB02, J02AC02
Diuretics	C03AA01, C03AA03, C03AA04, C03AA06, C03AA07, C03AB01, C03AB02, C03AB03, C03AB04, C03AB05, C03AB06, C03AB07, C03AB08, C03AB09
Beta blockers	C07AA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA07, C07AA12, C07AA15, C07AA19, C07AB02, C07AB03, C07AB04, C07AB05, C07AB07, C07AB09, C07AG01, C07AG02
CCB	C08CA01, C08CA02, C08CA03, C08CA04, C08CA05, C08CA06, C08CA07, C08CA08, C08CA09, C08CA13, C08CA15, C08CA55, C08DA01, C08DA51, C08DB01
ACEI	C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA16
ARB	C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09CA09
Statin	C10AA01, C10AA02, C10AA03, C10AA04, C10AA05, C10AA07, C10AA08
Other lipid lowering agents	C10AB01, C10AB02, C10AB04, C10AB05, C10AB06, C10AB09, C10AB11, C10AC01, C10AC02, C10AD01, C10AD02, C10AD03, C10AD06, C10AD52, C10AX02, C10AX09
Insulin	A10AB01, A10AB02, A10AB03, A10AB04, A10AB05, A10AB06, A10AB30, A10AC01, A10AC02, A10AC03, A10AC04, A10AC30, A10AD01, A10AD02, A10AD03, A10AD04, A10AD05, A10AD06, A10AD30, A10AE01, A10AE02, A10AE03, A10AE04, A10AE05, A10AE06, A10AE30, A10AE56
Other	A10BA02, A10BA03, A10BB01, A10BB02, A10BB03, A10BB04,

Drugs - Real World Outcomes

antidiabetics	A10BB05, A10BB07, A10BB08, A10BB09, A10BB12, A10BB31, A10BF01, A10BF02, A10BG02, A10BG03, A10BH01, A10BH02, A10BH03, A10BH04, A10BH05, A10BJ01, A10BJ02, A10BJ05, A10BK01, A10BK03, A10BX01, A10BX02, A10BX03, A10BX08, A10XA01
Warfarin	B01AA03
NOAC	B01AE07, B01AF01 , B01AF02

NSAID: Nonsteroidal anti-inflammatory drug; CCB: Calcium channel blocker; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; NOAC: Non-vitamin K oral anticoagulant

Supplementary Table 3. Characteristics of Before Propensity Score Matched Dabigatran and Warfarin Users in Time and Prescription-based Exposure Sets (One Year Prior Index Prescription)

	Before propensity score match				Standardized difference
	Dabigatran		Warfarin		
n, %	10811		10811		
Mean age(SD)	74.51	10.16	70.60	12.47	0.34
Male	6349	59%	6299	58%	0.01
CHA ₂ DS ₂ -VASc					
Mean(SD)	3.90	1.64	3.59	1.95	0.17
Median(Q1-Q3)	4.00	(3-5)	4.00	(2-5)	
Congestive heart failure	3219	30%	3681	34%	-0.09
Hypertension	7790	72%	7404	68%	0.08
Chronic pulmonary disease	2320	21%	2396	22%	-0.02
Diabetes	3249	30%	3434	32%	-0.04
Renal failure	1173	11%	2058	19%	-0.23
Liver disease	922	9%	1045	10%	-0.04
Peptic ulcer disease excluding bleeding	1261	12%	1267	12%	0.00
Ischemic stroke	3241	30%	2651	25%	0.12
Intracranial hemorrhage	214	2%	201	2%	0.01
Gastrointestinal bleeding	586	5%	705	7%	-0.05
Myocardial infarction	352	3%	538	5%	-0.09
Vascular disease	1645	15%	1953	18%	-0.08
Hemiplegia or paraplegia	583	5%	585	5%	0.00
Dementia	606	6%	532	5%	0.03
Gout	1016	9%	1125	10%	-0.03
Percutaneous coronary intervention	216	2%	370	3%	-0.09
Coronary artery bypass surgery	7	0%	50	0%	-0.08
Antiplatelet	3279	30%	3584	33%	-0.06
Low dose Aspirin	7160	66%	6782	63%	0.07

Drugs - Real World Outcomes

NSAID	7122	66%	7238	67%	-0.02
Antiepileptics	295	3%	346	3%	-0.03
Antifungal	131	1%	191	2%	-0.05
Diuretics	2685	25%	2655	25%	0.01
Beta blockers	6957	64%	7258	67%	-0.06
CCB	7360	68%	7316	68%	0.01
ACEI	2377	22%	2634	24%	-0.06
ARB	6307	58%	5909	55%	0.07
Statin	3821	35%	3627	34%	0.04
Other lipid lowering agents	680	6%	736	7%	-0.02
Insulin	1202	11%	1928	18%	-0.19
Other oral antidiabetics	2978	28%	3090	29%	-0.02
Dabigatran new users	8385	78%			
Dabigatran switchers	2426	22%			

SD: standard deviation; Q1-Q3: quartile 1-quartile 3; NSAID: Nonsteroidal anti-inflammatory drug; CCB: Calcium channel blocker; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker

Supplementary Table 4. Characteristics After Propensity Score Matched Dabigatran and Warfarin Users in Time and Prescription-based Exposure Sets (One Year Prior to Index Prescription)

	Incident new users					Prevalent new users				
	Dabigatran		Warfarin		Standardized difference	Dabigatran		Warfarin		Standardized difference
n, %	8385		8385			2396		2396		
Mean age(SD)	74.98	9.95	74.04	10.91	0.09	72.89	10.71	72.90	11.18	0.00
Male	4932	59%	4885	58%	0.01	1397	58%	1391	58%	0.01
CHA ₂ DS ₂ -VASc										
Mean(SD)	3.83	1.62	3.72	1.85	0.06	4.14	1.70	3.95	1.83	0.11
Median(Q1-Q3)	4.00	(3-5)	4.00	(2-5)		4.00	(3-5)	4.00	(3-5)	
Congestive heart failure	2381	28%	2373	28%	0.00	828	35%	928	39%	-0.09
Hypertension	6027	72%	5949	71%	0.02	1741	73%	1725	72%	0.01
Chronic pulmonary disease	1792	21%	1746	21%	0.01	516	22%	502	21%	0.01
Diabetes	2510	30%	2472	29%	0.01	727	30%	783	33%	-0.05
Renal failure	910	11%	967	12%	-0.02	260	11%	320	13%	-0.08
Liver disease	722	9%	711	8%	0.00	198	8%	213	9%	-0.02
Peptic ulcer disease excluding bleeding	985	12%	1000	12%	-0.01	275	11%	258	11%	0.02

Drugs - Real World Outcomes

Ischemic stroke	2172	26%	2234	27%	-0.02	1057	44%	776	32%	0.24
Intracranial hemorrhage	139	2%	157	2%	-0.02	71	3%	52	2%	0.05
Gastrointestinal bleeding	422	5%	461	5%	-0.02	162	7%	151	6%	0.02
Myocardial infarction	271	3%	295	4%	-0.02	79	3%	88	4%	-0.02
Vascular disease	539	6%	565	7%	-0.01	167	7%	170	7%	0.00
Hemiplegia or paraplegia	366	4%	408	5%	-0.02	213	9%	197	8%	0.02
Dementia	476	6%	470	6%	0.00	129	5%	135	6%	-0.01
Gout	760	9%	811	10%	-0.02	253	11%	255	11%	0.00
Percutaneous coronary intervention	163	2%	170	2%	-0.01	52	2%	50	2%	0.01
Coronary artery bypass surgery	a	a	14	0%	-0.03	a	a	11	0%	-0.07
Antiplatelet	2565	31%	2519	30%	0.01	706	29%	692	29%	0.01
Low dose Aspirin	5636	67%	5549	66%	0.02	1508	63%	1374	57%	0.11
NSAID	5513	66%	5632	67%	-0.03	1588	66%	1556	65%	0.03
Antiepileptics	203	2%	209	2%	0.00	89	4%	81	3%	0.02
Antifungal	101	1%	90	1%	0.01	29	1%	36	2%	-0.03

Drugs - Real World Outcomes

Diuretics	2059	25%	2066	25%	0.00	618	26%	592	25%	0.02
Beta blockers	5315	63%	5386	64%	-0.02	1623	68%	1593	66%	0.03
CCB	5714	68%	5699	68%	0.00	1627	68%	1607	67%	0.02
ACEI	1736	21%	1813	22%	-0.02	633	26%	591	25%	0.04
ARB	4844	58%	4697	56%	0.04	1440	60%	1467	61%	-0.02
Statin	2840	34%	2786	33%	0.01	972	41%	908	38%	0.05
Other lipid lowering agents	515	6%	540	6%	-0.01	165	7%	153	6%	0.02
Insulin	925	11%	927	11%	0.00	275	11%	344	14%	-0.09
Other oral antidiabetics	2294	27%	2235	27%	0.02	673	28%	735	31%	-0.06

SD: standard deviation; Q1-Q3: quartile 1-quartile 3; NSAID: Nonsteroidal anti-inflammatory drug; CCB: Calcium channel blocker; ACEI:

Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; ^a Due to data protection regulation in Taiwan, sparse numbers in a cell are not allowed to be retrieved from Health and Welfare Data Science Center

