

# Relation of Race, Apparent Disability, and Stroke Risk With Warfarin Prescribing for Atrial Fibrillation in Patients Receiving Maintenance Hemodialysis



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Little is known about how warfarin is prescribed for stroke prevention in maintenance dialysis patients with chronic atrial fibrillation (AF). We examined patterns of warfarin use, and associated factors, after AF diagnosis. This retrospective cohort analysis studied US Medicare patients receiving maintenance dialysis January 1, 2008, to June 30, 2010. Demographics, co-morbidity, and a durable medical equipment claims-based disability proxy score predicted warfarin prescription after AF diagnosis. The analysis included 8,964 patients with nonvalvular AF. Compared with nonusers, warfarin users were younger (age  $65.4 \pm 12.1$  vs  $67.0 \pm 12.9$  years) and more likely to be men (54.3% vs 52.8%) and of white race (64.0% vs 59.6%). After adjustment for other factors, nonwhite, versus white, race was associated with significantly less warfarin use within 30 days: odds ratios (ORs), 95% confidence intervals (CIs), were 0.80, 0.71 to 0.91, for black patients; 0.57, 0.43 to 0.76, for Asians; and 0.74, 0.49 to 1.12, for members of other races. Percentages of patients receiving warfarin decreased as Hypertension Abnormal renal and liver function Stroke-Bleeding Labile INR Elderly Drugs or alcohol (HAS-BLED) bleeding risk score increased (OR 0.82, 95% CI 0.73 to 0.92, HAS-BLED score 3 to 4 versus 2; 0.38, 0.26 to 0.57, score  $\geq 5$  vs 2). However, as CHA<sub>2</sub>DS<sub>2</sub>-Vasc stroke-risk score increased, warfarin use tended to decrease (OR 0.90, 95% CI 0.78 to 1.03,  $p = 0.13$ , CHA<sub>2</sub>DS<sub>2</sub>-Vasc score 4 versus 1 to 3; 0.69, 0.61 to 0.78,  $p < 0.0001$ , score 5 vs 1 to 3). In conclusion, providers appear to weigh bleeding risk more heavily than stroke-prevention potential when prescribing warfarin for maintenance dialysis patients. Racial minorities received warfarin substantially less often than whites, even after accounting for other factors. © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:598–604)

Chronic atrial fibrillation (AF) is common in patients receiving maintenance dialysis.<sup>1–3</sup> As in the general population with chronic AF, warfarin is often used to prevent ischemic stroke. However, patients who receive dialysis differ in important ways from those who do not. For example, while their rates of ischemic stroke are high,<sup>4–6</sup> so are their rates of major bleeding events. The efficacy of warfarin for stroke prevention in dialysis patients has never been studied in a randomized clinical trial, meaning that prescribers have been guided only by observational studies that present conflicting results. Because the appropriateness of warfarin for dialysis patients remains the subject of robust debate,<sup>7–10</sup> we sought to investigate warfarin prescribing patterns in these patients. To address this question we used a large, retrospective cohort of maintenance dialysis patients to examine patterns of warfarin use, and factors associated with it, after AF diagnosis. We hypothesized that concerns over bleeding risk would predominate over potential benefits for stroke prevention in prescribing

patterns and, further, that warfarin use would differ substantially by factors such as race and sex even after adjustment of other factors.

## Methods

This study used the United States Renal Data System end-stage renal disease (ESRD) database, which contains data from the Centers for Medicare and Medicaid Services (CMS) ESRD Medical Evidence Report (form CMS-2728), the ESRD Death Notification (form CMS-2746), and Medicare Parts A, B, and D claims.<sup>11</sup> From Medicare, the insurer for most US patients receiving maintenance dialysis, we used billing claims data to determine presence of co-morbid conditions and AF, generate adapted forms of the CHA<sub>2</sub>DS<sub>2</sub>-Vasc and Hypertension Abnormal renal and liver function Stroke-Bleeding Labile INR Elderly Drugs or alcohol (HAS-BLED) scores, and ascertain warfarin use.

This was a retrospective cohort study of adult patients with newly diagnosed nonvalvular AF who were receiving maintenance dialysis in the United States between January 1, 2008, and June 30, 2010. The date of AF diagnosis was considered the index date. Before this date, we required patients to have been receiving maintenance dialysis and to have had Medicare Parts A and B coverage for  $\geq 1$  year, and to have had Part D coverage for  $\geq 6$  months. The period preceding the index date was used to exclude patients with previous claims for AF, for valvular heart disease, or for warfarin use.

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Covariates were age, race, sex, cause of ESRD, and dialysis duration (all derived from the ESRD Medical Evidence Report). Co-morbid conditions, listed in Table 1, were ascertained from medical claims over the 1-year period preceding the index date by  $\geq 1$  inpatient, home health, or skilled nursing facility claims, or  $\geq 2$  outpatient/Part B claims with corresponding International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes. This method is consistent with previous approaches and has been previously validated for diabetes.<sup>12</sup> Dependence on alcohol or illicit drugs, as per the Medical Evidence Report, was also considered.

We also employed a durable medical equipment (DME) claims-based proxy for putative disability.<sup>13,14</sup> Briefly, potential markers of disability from the DME files were chosen by first limiting to those with prevalence  $>1\%$ , and further limiting to those with an association with mortality, hospitalization, or fracture. Proportional hazards models were used to investigate the association of these markers with mortality, hospitalization, and fracture. The resulting score, which we refer to as a "disability proxy score," was created by taking parameter estimates from the adjusted proportional hazards model, multiplying the parameter estimates by 10, rounding to integer, and summing the markers present in each patient.

Table 1  
Characteristics of atrial fibrillation patients receiving dialysis

Characteristics	Overall n = 8,964		Warfarin n = 1,662		No warfarin n = 7,284	
Age (years)						
0-49	917	(10.2%)	190	(11.3%)	727	(10.0%)
50-64	2833	(31.6%)	564	(33.6%)	2269	(31.2%)
65-74	2698	(30.1%)	531	(31.6%)	2167	(29.8%)
75-84	1970	(22.0%)	339	(20.2%)	1631	(22.4%)
$\geq 85$	546	(6.1%)	56	(3.3%)	490	(6.7%)
Sex						
Male	4758	(53.1%)	912	(54.3%)	3846	(52.8%)
Female	4206	(46.9%)	768	(45.7%)	3438	(47.2%)
Race						
White	5416	(60.4%)	1075	(64.0%)	4341	(59.6%)
Black	2950	(32.9%)	515	(30.7%)	2435	(33.4%)
Asian	429	(4.8%)	61	(3.6%)	368	(5.1%)
Other	169	(1.9%)	29	(1.7%)	140	(1.9%)
Primary cause of ESRD						
Diabetes mellitus	3921	(43.7%)	713	(42.4%)	3208	(44.0%)
Hypertension	2757	(30.8%)	520	(31.0%)	2237	(30.7%)
Glomerulonephritis	901	(10.1%)	200	(11.9%)	701	(9.6%)
Other cause	1385	(15.5%)	247	(14.7%)	1138	(15.6%)
Years on dialysis						
1-2	2681	(29.9%)	468	(27.9%)	2213	(30.4%)
3-4	2275	(25.4%)	416	(24.8%)	1859	(25.5%)
5-9	2582	(28.8%)	485	(28.9%)	2097	(28.8%)
$\geq 10$	1426	(15.9%)	311	(18.5%)	1115	(15.3%)
Atrial fibrillation diagnosis setting						
Inpatient	4840	(54.0%)	1130	(67.3%)	3710	(50.9%)
Outpatient	4124	(46.0%)	550	(32.7%)	3574	(49.1%)
Diabetes mellitus	5885	(65.7%)	1069	(63.6%)	4816	(66.1%)
Atherosclerotic heart disease	4988	(55.6%)	871	(51.8%)	4117	(56.5%)
Congestive heart failure	5361	(59.8%)	978	(58.2%)	4383	(60.2%)
Dysrhythmia	6927	(77.3%)	1382	(82.3%)	5545	(76.1%)
Other cardiac disease	3339	(37.2%)	590	(35.1%)	2749	(37.7%)
Stroke/transient ischemic attack	1733	(19.3%)	276	(16.4%)	1457	(20.0%)
Peripheral vascular disease	3588	(40.0%)	603	(35.9%)	2985	(41.0%)
Chronic obstructive pulmonary disease	2616	(29.2%)	471	(28.0%)	2145	(29.4%)
Gastrointestinal bleeding	933	(10.4%)	96	(5.7%)	837	(11.5%)
Liver disease	796	(8.9%)	123	(7.3%)	673	(9.2%)
Cancer	755	(8.4%)	111	(6.6%)	644	(8.8%)
Drug or alcohol abuse	72	(0.8%)	*	*	65	(0.9%)
Disability proxy score						
$\leq 0$	2955	(33.0%)	727	(43.3%)	2228	(30.6%)
1-2	2316	(25.8%)	453	(27.0%)	1863	(25.6%)
3-4	1894	(21.1%)	292	(17.4%)	1602	(22.0%)
5-6	1100	(12.3%)	131	(7.8%)	969	(13.3%)
$\geq 7$	699	(7.8%)	77	(4.6%)	622	(8.5%)

\* Subject to the terms of the Data Use Agreement with CMS, cells with  $n < 11$  must be suppressed.

To determine the CHA<sub>2</sub>DS<sub>2</sub>-Vasc and HAS-BLED scores using administrative data, we closely followed a previously used approach.<sup>15</sup> HAS-BLED score was calculated as follows: Since >80% of maintenance dialysis patients have hypertension,<sup>16,17</sup> we assigned 1 point to every patient automatically. We also assigned 1 point to every patient for renal disease, and 1 additional point if liver disease was present. A history of gastrointestinal bleeding (the main source of significant bleeding in dialysis patients) was assigned 1 point, as was history of stroke. Age >65 years at AF diagnosis was assigned 1 point, as was use of drugs or alcohol noted on the CMS-2728 Medical Evidence Report. Because we lacked access to information on history of labile international normalized ratio testing results, this could not be included. A total of 7 points was therefore possible, and every patient had a score of  $\geq 2$ .

The CHA<sub>2</sub>DS<sub>2</sub>-Vasc score was calculated as follows: Every patient again automatically received 1 point for hypertension, and 1 point each for heart failure, diabetes, and history of vascular disease (atherosclerotic heart disease, including myocardial infarction and peripheral vascular disease), if present. Women were assigned 1 point, as were patients aged 65 to 74 years, and patients aged  $\geq 75$  years 2 points. History of stroke was assigned 2 points. A total of 9 points was therefore possible, and every patient had a score of  $\geq 1$ .

International Classification of Diseases, Ninth Revision, Clinical Modification code 427.31 was used to identify AF claims. To establish chronicity of the AF, patients were required to have  $\geq 1$  inpatient or 2 outpatient/Part B claims  $\geq 30$  days apart but within 365 days of each other. AF diagnosis codes could be in any position on the claim. The inpatient discharge date or second outpatient date became the index date, provided there were no AF claims or warfarin claims in the preceding period since January 1, 2007 (the earliest year of data available for this study). Patients with evidence of valvular AF were excluded, as done previously.<sup>2</sup>

The outcome was warfarin use, ascertained at varying time intervals after the index date; 30, 60, and 90 days were selected for analysis. In keeping with the approach of other studies, use at 30 days was selected for the primary analysis, but additional analyses extended this period to 60 and 90 days in the event that patients were discharged from the hospital with a supply of warfarin. As no clear inflection point in patterns of warfarin use emerged as time from initial AF diagnosis elapsed, 90 days was the latest time-point assessed; appearance of a first outpatient warfarin prescription at a later date (e.g., 180 days) might suggest that the indication for the drug was not AF. Warfarin use was ascertained by identifying National Drug Classification codes in the Medicare Part D files. Patients were censored at loss of Part D coverage.

Descriptive statistics (count [n], percentage [%]) were used for demographic characteristics, co-morbid conditions, and disability proxy score for the overall cohort with newly diagnosed nonvalvular AF and for patients who did and did not use warfarin within a 30-day period. To inform the analysis, percentages of patients using warfarin were calculated within 15, 30, 45, 60, 90, and 180 days. Logistic regression was used to model the probability of warfarin use within 30, 60, and 90 days, adjusted for variables listed above. Two additional sensitivity analyses were undertaken. First,

because follow-up time for some patients was shorter due to death, end of study, or other reasons, a time-to-event Cox proportional hazards model was constructed for use within the first 30-day window. Additionally, a Fine-Gray competing risk analysis was performed with death as the competing event for warfarin use. Percentages of warfarin use across the CHA<sub>2</sub>DS<sub>2</sub>-Vasc and HAS-BLED score groups were presented. Univariate logistic regression was performed to evaluate the relation of warfarin use at 30 days with CHA<sub>2</sub>DS<sub>2</sub>-Vasc and HAS-BLED scores. All analyses were conducted using SAS v9.4 (Cary, North Carolina).

The research protocol was approved by the institutional review board at Hennepin Healthcare. Data Use Agreements between the Hennepin Healthcare Research Institute and the United States Renal Data System were in place.

## Results

We identified 68,349 patients with AF who had complete information (Figure 1). After exclusions, a cohort of 8,964 patients with apparent newly diagnosed nonvalvular AF and no previous warfarin use remained.

Characteristics of warfarin users and nonusers at 30 days (primary analysis) are shown in Table 1. Compared with nonusers, users were more likely to be younger, men, and of white rather than black race, and to have longer (i.e.,  $\geq 10$  years) dialysis duration, generally less co-morbidity, and a lower disability proxy score.

Timing of warfarin use by site of diagnosis is shown in Table 2. Use at 30 days was 18.7% overall, increasing modestly each month to 27.7% at 180 days. Percentages of patients who died after AF diagnosis, by site of diagnosis, are shown in Table S1. At 30 days, 1.9% of patients had died. The percentage increased to 8.5% at 90 days.

Factors associated with warfarin use at 30, 60, and 90 days are shown in Table 3. Results were highly consistent for each time-point assessed. After adjustment for other factors, age was associated with less warfarin use, but only in the oldest dialysis patients; for example, at 30 days, the odds ratio (OR) was 0.53 (95% confidence interval [CI], 0.38 to 0.75) for patients aged 85 years or older compared with those aged 49 years or younger, but was 0.96 (0.77 to 1.20) for patients aged 75 to 84 years. Nonwhite, as compared with white, race was associated with substantially lower use; the ORs were 0.80 (0.71 to 0.91) for black patients, 0.57 (0.43 to 0.76) for Asians, and 0.74 (0.49 to 1.12) for members of other races at 30 days; the pattern was similar at 60 and 90 days. Gastrointestinal bleeding was associated with significantly lower likelihood of warfarin use at each time period examined. Additionally, increasing disability proxy score (indicating greater DME use and therefore greater presumed disability) was associated with progressively lower likelihood of warfarin use.

We examined the potential interaction of race with age and, separately, with sex by recalculating the Cox proportional hazards models with these interaction terms for the primary (30-day) analysis; p values were not significant (0.91 and 0.065, respectively).

In 2 additional sensitivity analyses, factors associated with warfarin use were examined using Cox proportional hazards and Fine-Gray competing risk models. Hazard

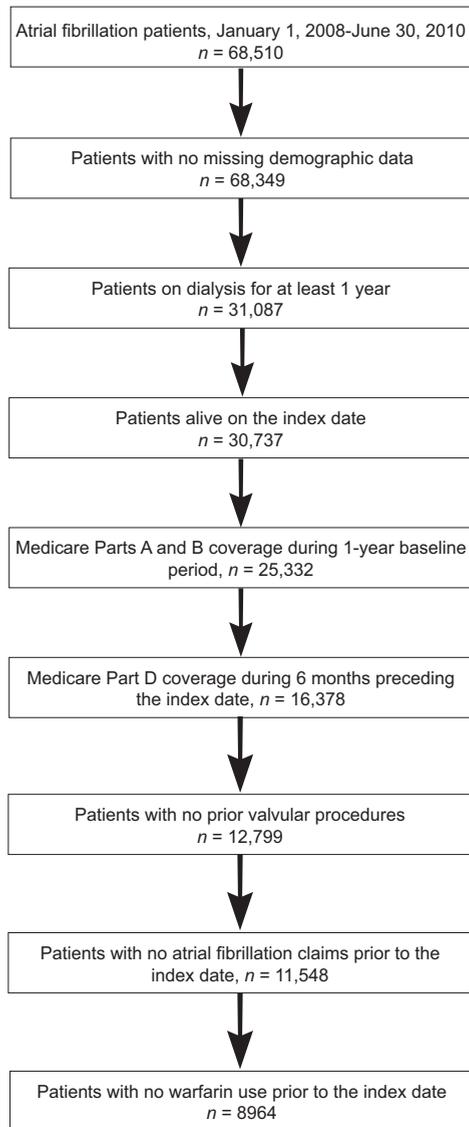


Figure 1. Construction of the study cohort.

ratios were generally highly consistent with those derived from the primary approach (Table S2).

Percentages of patients receiving warfarin decreased as HAS-BLED score increased. In distinction, as  $CHA_2DS_2$ -Vasc score increased, warfarin use tended to decrease (OR 0.90, 95% CI 0.78 to 1.03,  $p = 0.13$  for  $CHA_2DS_2$ -Vasc

Table 2  
Percentages of patients initiating warfarin use after atrial fibrillation diagnosis

Days after diagnosis	All atrial fibrillation patients	Diagnosis setting	
		Inpatient	Outpatient
15	16.5	21.5	10.6
30	18.7	23.3	13.3
45	20.5	25.0	15.3
60	21.8	26.0	16.9
90	23.9	27.7	19.3
180	27.7	31.3	23.6

score of 4 vs 1 to 3, OR 0.69, 95% CI 0.61 to 0.78,  $p < 0.0001$  for score 5 vs 1 to 3). The relation between levels of  $CHA_2DS_2$ -Vasc and HAS-BLED was explored, and patterns of use within 30 days are shown as percentages in Table 4; while percentage of patients prescribed warfarin appeared to decrease as HAS-BLED score increased, warfarin prescription appeared to decrease, or at least did not increase, as  $CHA_2DS_2$ -Vasc score increased. The pattern was similar for warfarin use within 60 and 90 days (Table S3). This relation was further explored in subgroups of race (white vs black), sex, and diabetes status (Table S4); whereas many cell sizes were small, the overall patterns appeared similar.

## Discussion

Little work has explored the determinants of warfarin prescription in patients receiving maintenance dialysis. We found, first, that although likelihood of warfarin use decreased as bleeding risk increased, warfarin use did not increase as stroke risk increased. Second, warfarin appears to be used much less commonly in members of racial minorities than in white patients. These findings have no readily apparent justification.

Although we anticipated the clear signal of decreasing warfarin use with increasing HAS-BLED score at all levels of  $CHA_2DS_2$ -Vasc score, we were surprised to find no signal of increasing warfarin use with increasing stroke risk. This finding suggests that prescribers appear to weigh bleeding risk substantially more than the potential benefits of stroke prevention. The reasons for this are uncertain; however, development, validation, and widespread use of stroke-risk scores for dialysis patients is important, given the high stroke rates in this population,<sup>4-6</sup> and introduction of new oral anticoagulants for stroke prevention in AF.<sup>18,19</sup>

Although several findings of our warfarin use models were expected, such as decreasing likelihood of use with increasing age, worsening apparent disability, and history of gastrointestinal bleeding or liver disease, our finding concerning the association of use with race was dismaying. We had originally hypothesized that putative disability might account, in part, for differential likelihood of warfarin use by race. Therefore, we sought to augment traditional claims-based co-morbidity assessment by adjusting for putative disability using our novel disability proxy score. However, even after extensive multivariable adjustment, including for the disability proxy score, likelihood of warfarin use was substantially lower in blacks, Asians, and members of other races relative to whites. This suggests that other factors, presumably unrelated to disability, may be largely responsible for the differential prescribing rates. There is no obvious clinical justification for this phenomenon, given that neither the  $CHA_2DS_2$ -Vasc nor HAS-BLED scores incorporate race into the risk stratification assessment. While the literature is replete with examples of racial differences regarding medications, other therapies, and outcomes,<sup>20-23</sup> including a smaller previous study of warfarin use in dialysis patients,<sup>24</sup> we are careful to note that our finding cannot be considered *prima facie* evidence of racial disparity because this term connotes inappropriate barriers to therapy. Nonetheless, providers may judge blacks,

Table 3

Odds ratios for patient characteristics associated with warfarin use after atrial fibrillation diagnosis

Characteristics	Warfarin use					
	Within 30 days		Within 60 days		Within 90 days	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age, years						
0-49	1.00 (ref)		1.00 (ref)		1.00 (ref)	
50-64	1.03 (0.85-1.25)	0.7443	1.04 (0.86-1.25)	0.6952	1.03 (0.86-1.23)	0.7476
65-74	1.09 (0.89-1.33)	0.4054	1.10 (0.91-1.33)	0.3261	1.08 (0.90-1.30)	0.4036
75-84	0.96 (0.77-1.20)	0.7361	0.99 (0.81-1.22)	0.9349	0.99 (0.81-1.20)	0.8842
≥85	0.53 (0.38-0.75)	0.0003	0.49 (0.35-0.68)	< 0.0001	0.52 (0.38-0.71)	<0.0001
Sex						
Male	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Female	1.01 (0.90-1.13)	0.9122	0.96 (0.86-1.07)	0.4764	0.99 (0.89-1.09)	0.7790
Race						
White	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Black	0.80 (0.71-0.91)	0.0006	0.80 (0.71-0.90)	0.0002	0.79 (0.70-0.88)	<0.0001
Asian	0.57 (0.43-0.76)	0.0002	0.61 (0.47-0.79)	0.0003	0.63 (0.49-0.81)	0.0003
Other	0.74 (0.49-1.12)	0.1504	0.74 (0.50-1.10)	0.1386	0.88 (0.61-1.26)	0.4817
Primary cause of end-stage renal disease						
Diabetes mellitus	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Hypertension	1.02 (0.87-1.19)	0.7982	0.98 (0.85-1.14)	0.8222	0.97 (0.84-1.12)	0.7037
Glomerulonephritis	1.03 (0.83-1.27)	0.8110	0.99 (0.81-1.21)	0.9299	1.04 (0.85-1.26)	0.7191
Other cause	0.84 (0.69-1.02)	0.0714	0.82 (0.68-0.98)	0.0311	0.83 (0.70-0.99)	0.0359
Years on dialysis						
1-2	1.00 (ref)		1.00 (ref)		1.00 (ref)	
3-4	1.02 (0.88-1.19)	0.7747	1.02 (0.88-1.17)	0.8138	0.99 (0.86-1.13)	0.8776
5-9	1.07 (0.92-1.24)	0.3919	1.07 (0.93-1.23)	0.3502	1.06 (0.92-1.21)	0.4272
≥10	1.15 (0.97-1.38)	0.1166	1.15 (0.97-1.36)	0.1088	1.10 (0.94-1.30)	0.2410
Atrial fibrillation diagnosis setting						
Inpatient	1.00 (ref)		1.00 (ref)		1.00 (ref)	
Outpatient	0.47 (0.40-0.54)	< 0.0001	0.52 (0.45-0.59)	< 0.0001	0.58 (0.50-0.66)	<0.0001
Diabetes mellitus	1.00 (0.86-1.16)	0.9930	0.99 (0.86-1.14)	0.8782	0.99 (0.87-1.14)	0.9103
Atherosclerotic heart disease	0.93 (0.83-1.05)	0.2533	0.88 (0.79-0.99)	0.0281	0.88 (0.79-0.98)	0.0200
Congestive heart failure	1.07 (0.95-1.20)	0.2944	1.08 (0.97-1.22)	0.1669	1.10 (0.98-1.23)	0.0908
Dysrhythmia	0.91 (0.75-1.09)	0.3025	0.86 (0.72-1.02)	0.0768	0.91 (0.78-1.07)	0.2609
Other cardiac disease	0.97 (0.86-1.09)	0.6129	0.95 (0.85-1.06)	0.3844	0.96 (0.86-1.07)	0.4577
Stroke/transient ischemic attack	1.03 (0.88-1.20)	0.7237	1.04 (0.90-1.20)	0.5856	1.08 (0.94-1.25)	0.2519
Peripheral vascular disease	0.94 (0.84-1.06)	0.3531	1.00 (0.89-1.12)	0.9598	1.03 (0.93-1.15)	0.5665
Chronic obstructive pulmonary disease	1.12 (0.99-1.28)	0.0814	1.10 (0.98-1.25)	0.1195	1.10 (0.98-1.24)	0.1110
Gastrointestinal bleeding	0.52 (0.42-0.65)	< 0.0001	0.58 (0.48-0.71)	< 0.0001	0.60 (0.50-0.73)	<0.0001
Liver disease	0.82 (0.67-1.01)	0.0665	0.86 (0.71-1.04)	0.1194	0.80 (0.66-0.97)	0.0206
Cancer	0.81 (0.65-1.00)	0.0553	0.91 (0.74-1.11)	0.3303	0.87 (0.72-1.06)	0.1720
Drug or alcohol abuse	0.43 (0.20-0.96)	0.0397	0.36 (0.16-0.79)	0.0111	0.32 (0.15-0.71)	0.0049
Disability proxy score						
≤0	1.00 (ref)		1.00 (ref)		1.00 (ref)	
1-2	0.76 (0.66-0.87)	0.0001	0.76 (0.67-0.87)	< 0.0001	0.75 (0.66-0.86)	<0.0001
3-4	0.57 (0.49-0.68)	< 0.0001	0.61 (0.53-0.72)	< 0.0001	0.62 (0.53-0.71)	<0.0001
5-6	0.42 (0.34-0.53)	< 0.0001	0.49 (0.40-0.60)	< 0.0001	0.51 (0.42-0.62)	<0.0001
≥7	0.44 (0.33-0.58)	< 0.0001	0.45 (0.35-0.59)	< 0.0001	0.46 (0.36-0.58)	<0.0001

Asians, and other minorities as being less likely to benefit from, and more likely to be harmed by, warfarin than whites; the reasons for, and appropriateness of, this phenomenon remain uncertain.

Our claims-based disability proxy score, which relies heavily on claims for DME (and which we posit is therefore a marker of disability),<sup>13,14</sup> may serve as a proxy for difficult-to-assess markers of health, such as functional status, frailty, or perhaps even social support. Increasing disability is not an explicit factor considered by stroke-risk

calculators or, especially, by bleeding-risk calculators. However, our results suggest that prescribers appear to consider disability outside of more formal risk-stratification tools. A future framework design to guide decision making regarding initiation of systemic anticoagulation in dialysis patients might benefit from explicit consideration of markers of disability or frailty.

Our study has important limitations. Only temporal antecedence, and not causality, can be inferred. In conducting a claims-based study, we lacked granular clinical detail that

Table 4

Percentages of patients using warfarin within 30 days of atrial fibrillation diagnosis by CHA<sub>2</sub>DS<sub>2</sub>-Vasc and HAS-BLED scores

CHA <sub>2</sub> DS <sub>2</sub> -Vasc score <sup>†</sup>	HAS-BLED score*		
	2	3-4	≥5
1-3	21.8	21.6	12.5
4	20.9	19.8	0.00
≥5	17.4	16.4	10.0

\* See text for details of the assignment of points for the HAS-BLED score.

<sup>†</sup> See text for details of the assignment of points for the CHA<sub>2</sub>DS<sub>2</sub>-Vasc score.

undoubtedly influences bedside decision making, although our disability proxy score attempted to consider the potential role of traditionally neglected factors. Misclassification of patients as having, or not having, AF is also possible, although none of these potential weaknesses would be likely to demonstrate differential associations by race. Additionally, there may be clinically important differences in patient characteristics that both vary by race and inform physicians' warfarin prescribing decisions to which our administrative database does not have access. Finally, despite considerable clinical appeal, our disability proxy score, while used in previous studies, has not been validated.

Our study also has important strengths. Our study sample was relatively large and our approach to identification of AF from claims is well established. Our findings were robust to varying time horizons (30, 60, and 90 days), and the findings from the primary analysis were strongly supported by both the time-to-event and competing-risk analyses.

In conclusion, we found evidence that providers appear to weight bleeding risk more heavily than stroke-prevention potential in patients newly diagnosed with nonvalvular AF receiving maintenance dialysis. Our disability proxy score appears to be a factor influencing prescribing decisions and provides crucial covariate control. Lastly, racial minorities are prescribed warfarin substantially less often than whites, even after accounting for co-morbidity burden and putative markers of disability; whether this represents inappropriate withholding of therapy or prudent decision making remains uncertain, but there is, at present, no obvious basis for this distinction.

## Disclosures

The authors have no conflicts of interest to disclose.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi:10.1016/j.amjcard.2018.11.020>.

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