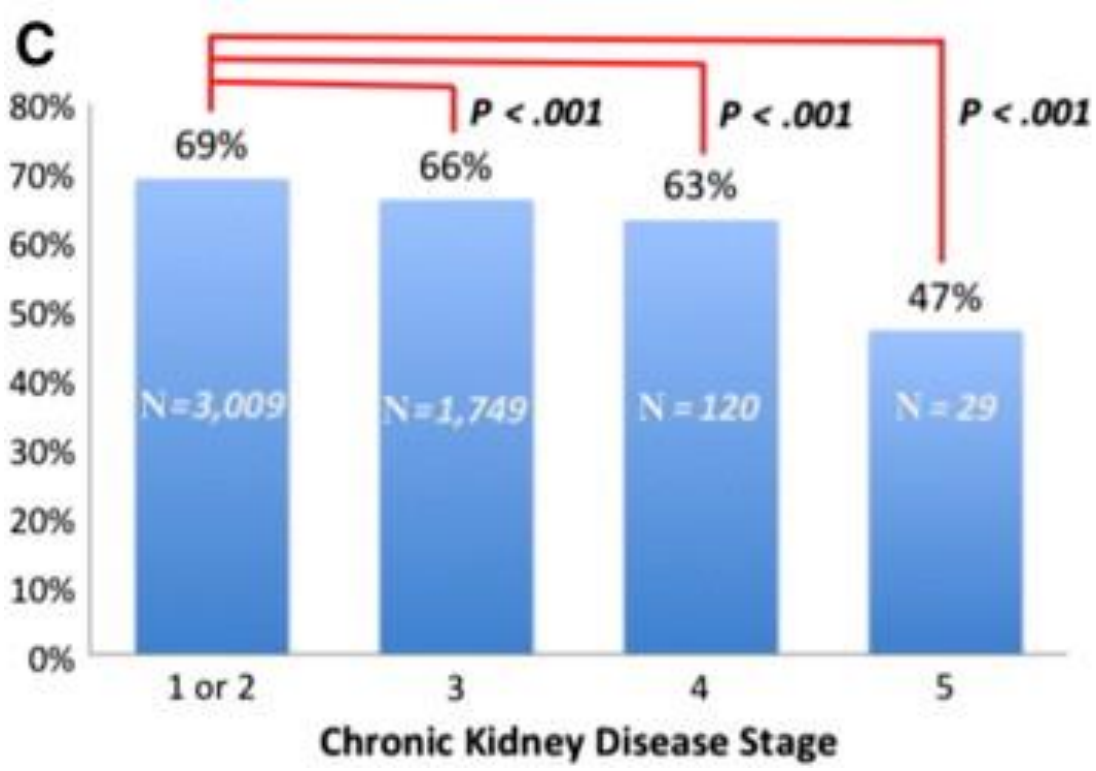
FIBRILLAZIONE ATRIALE E INSUFFICIENZA RENALE END-STAGE

BACKGROUND

- Atrial fibrillation (AF) is more frequent in patients with impaired renal function and occurs in approximately 1 of 5 patients with end-stage renal disease (ESRD)
- Chronic kidney disease is associated with an increased risk of ischemic stroke in patients with AF independent of traditional risk factors for stroke
- The presence of AF complicates the management of ESRD:
  - frequent vascular access
  - prone to bleeding complications, including intracranial hemorrhage
- Significant uncertainty remains regarding the risk-benefit of OAC in patients with ESRD and AF

BACKGROUND

ORBIT-AF registry:
5,210 patients with AF on warfarin



Am Heart J 2015;170: 141–8. 148.e1.

STUDY SUPPORTING WARFARIN

Table 3. Hazard Ratios for Stroke or Systemic Thromboembolism.*

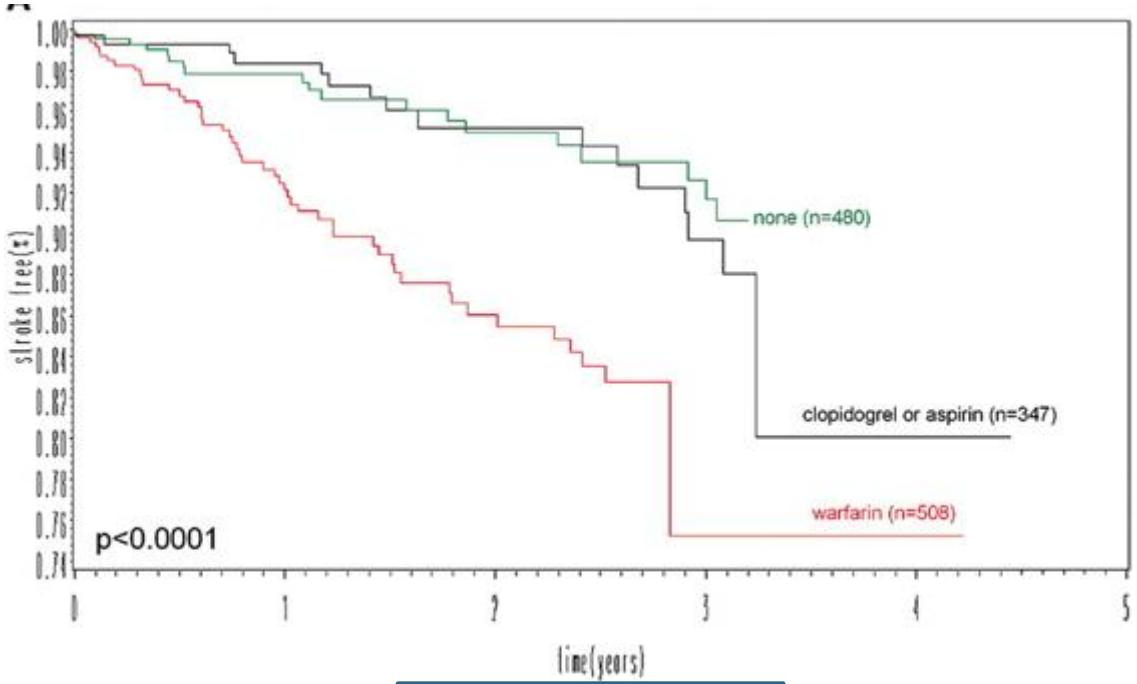
Characteristic	Total Population (N=132,372)		No Renal Disease (N=127,884)†		Non–End-Stage Chronic Kidney Disease (N=3587)†		Disease Requiring Renal-Replacement Therapy (N=901)†	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
All participants			1.00		1.49 (1.38–1.59)	<0.001	1.83 (1.57–2.14)	<0.001
Antithrombotic therapy								
None	1.00		1.00		1.00		1.00	
Warfarin	0.59 (0.57–0.62)	<0.001	0.59 (0.56–0.61)	<0.001	0.84 (0.69–1.01)	0.07	0.44 (0.26–0.74)	0.002
Aspirin	1.11 (1.07–1.15)	<0.001	1.10 (1.06–1.14)	<0.001	1.25 (1.07–1.47)	0.01	0.88 (0.59–1.32)	0.54
Warfarin and aspirin	0.70 (0.65–0.75)	<0.001	0.69 (0.64–0.74)	<0.001	0.76 (0.56–1.03)	0.08	0.82 (0.37–1.80)	0.62
Risk factors for thromboembolism‡								
Congestive heart failure	1.03 (0.99–1.07)	0.18	1.03 (0.99–1.08)	0.11	0.98 (0.84–1.14)	0.78	0.96 (0.64–1.43)	0.84
Hypertension	1.06 (1.03–1.09)	<0.001	1.05 (1.02–1.09)	0.002	1.13 (0.98–1.30)	0.10	1.05 (0.76–1.45)	0.78
Age								
≥75 yr	3.48 (3.31–3.66)	<0.001	3.56 (3.38–3.76)	<0.001	1.87 (1.48–2.36)	<0.001	2.46 (1.60–3.79)	<0.001
65–74 yr	2.02 (1.91–2.14)	<0.001	2.03 (1.92–2.16)	<0.001	1.52 (1.18–1.94)	0.001	2.18 (1.46–3.24)	<0.001
Diabetes	1.32 (1.26–1.38)	<0.001	1.32 (1.25–1.39)	<0.001	1.16 (0.99–1.36)	0.07	1.41 (0.95–2.10)	0.09
History of stroke or systemic thromboembolism	3.20 (3.10–3.31)	<0.001	3.24 (3.14–3.35)	<0.001	2.71 (2.34–3.15)	<0.001	1.99 (1.36–2.91)	<0.001
Vascular disease	1.10 (1.06–1.15)	<0.001	1.12 (1.07–1.16)	<0.001	0.89 (0.76–1.05)	0.17	1.11 (0.78–1.58)	0.57
Female sex	1.12 (1.08–1.15)	<0.001	1.12 (1.08–1.15)	<0.001	1.06 (0.92–1.22)	0.44	1.34 (0.97–1.85)	0.08

N Engl J Med 2012; 367:625-635

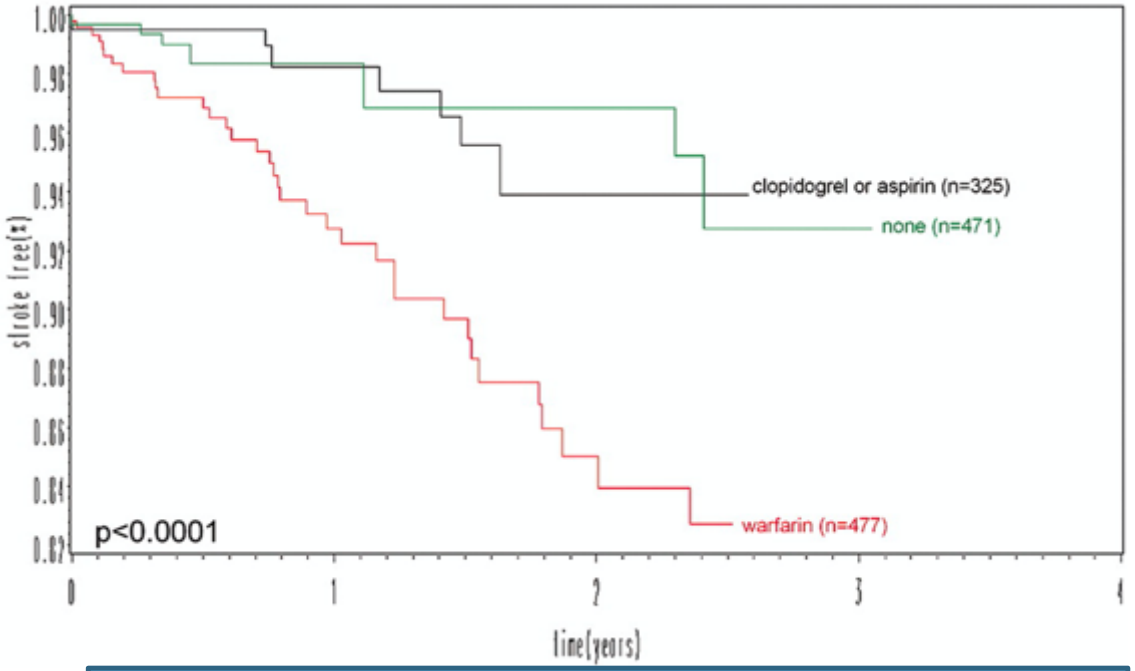
STUDY AGAINST WARFARIN

1671 hemodialysis patients with preexisting atrial fibrillation

Stroke-free survival



Intention-to-treat



Patients censored when they changed prescription

Kevin E. Chan et al. JASN 2009;20:2223-2233

Oral Anticoagulation and Cardiovascular Outcomes in Patients With Atrial Fibrillation and End-Stage Renal Disease

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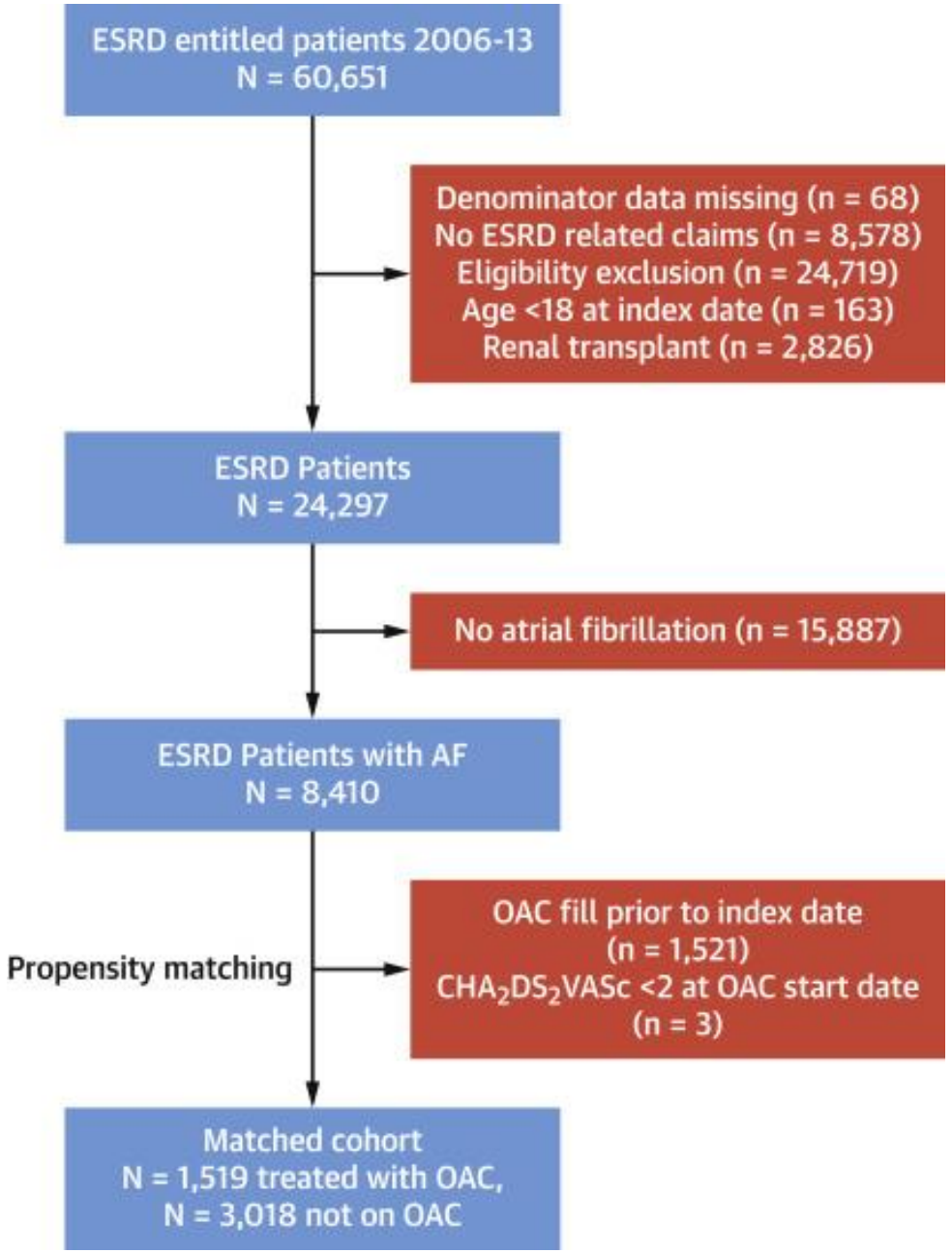
Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

METHODS

Medicare 5% fee-for-service sample



Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

BASELINE CHARACTERISTICS OF ESRD PATIENTS

	All ESRD Patients (N = 24,297)	Patients With AF (n = 8,410)	Patients Without AF (n = 15,887)	p Value
Demographics				
Age, yrs	65 (53-75)	71 (63-79)	60 (49-70)	<0.0001
Female	50.6 (12,300)	52.2 (4,386)	49.8 (7,914)	0.0005
Black race	35.9 (8,676)	28.7 (2,405)	39.7 (6,271)	<0.0001
Medical history				
Coronary artery disease	52.4 (12,740)	70.9 (5,962)	42.7 (6,778)	<0.0001
Prior MI	18.0 (4,369)	27.1 (2,277)	13.2 (2,092)	<0.0001
Congestive heart failure	54.1 (13,150)	74.0 (6,220)	43.6 (6,930)	<0.0001
Hypertension	93.4 (22,698)	97.2 (8,171)	91.4 (14,527)	<0.0001
Prior stroke or TIA	18.6 (4,514)	24.3 (2,042)	15.6 (2,472)	<0.0001
Diabetes	70.4 (17,109)	73.8 (6,207)	68.6 (10,902)	<0.0001
COPD	33.8 (8,214)	46.4 (3,905)	27.1 (4,309)	<0.0001

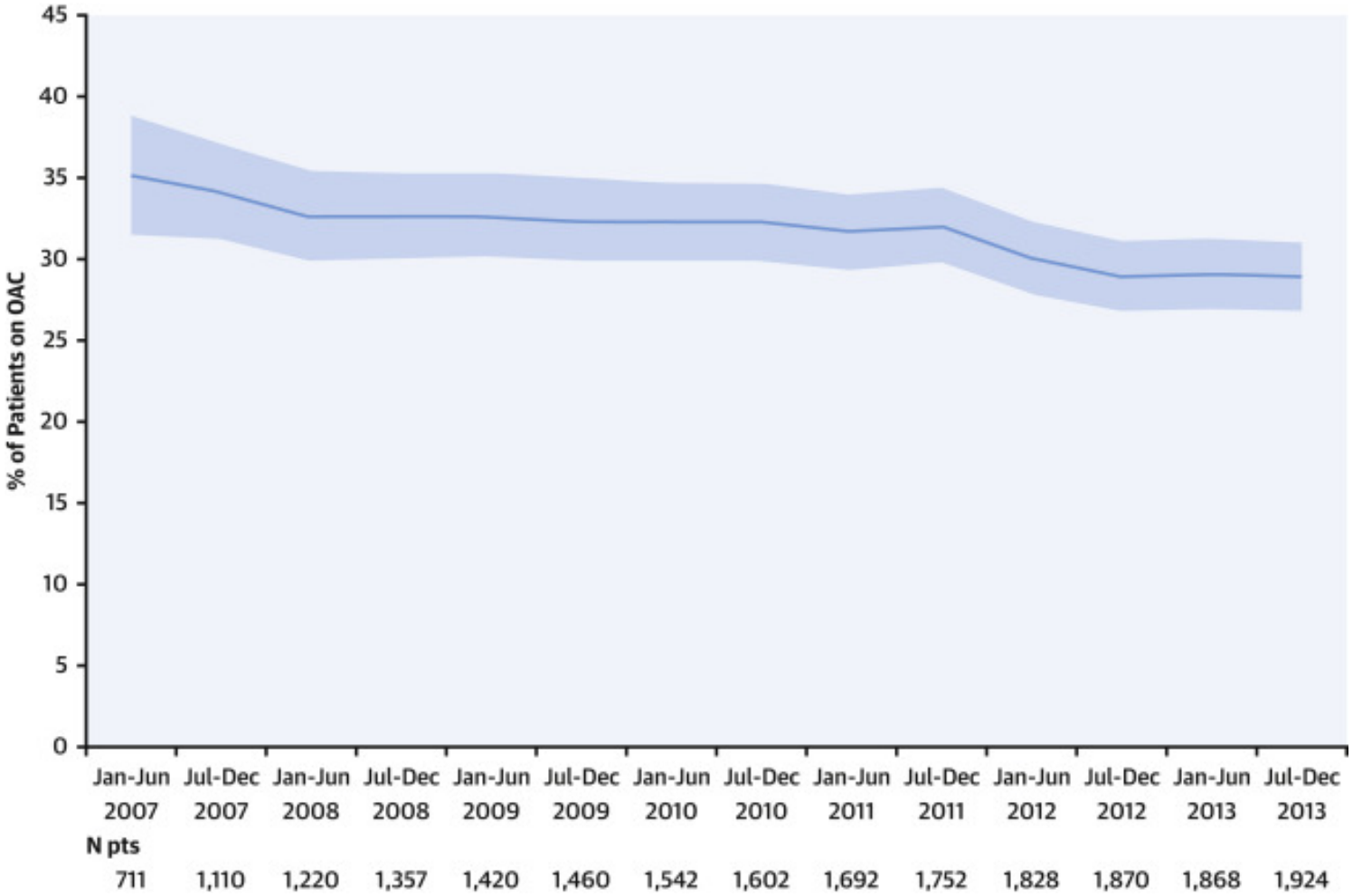
Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

BASELINE CHARACTERISTICS OF ESRD PATIENTS WITH AF

	All ESRD AF Patients (N = 8,410)	Patients With OAC (n = 3,043)	Patients Without OAC (n = 5,367)	p Value
Demographics				
Age, yrs	71 (63-79)	70 (61-78)	72 (63-80)	<0.0001
Female	52.2 (4,386)	51.9 (1,579)	52.3 (2,807)	0.72
Black race	28.7 (2,405)	28.1 (854)	29.0 (1,551)	0.40
Medical history				
Coronary artery disease	70.9 (5,962)	69.4 (2,112)	71.7 (3,850)	0.024
Prior MI	27.1 (2,277)	24.3 (738)	28.7 (1,539)	<0.0001
Prior CABG	2.7 (228)	2.6 (78)	2.8 (150)	0.53
Congestive heart failure	74.0 (6,220)	73.6 (2,239)	74.2 (3,981)	0.55
Hypertension	97.2 (8,171)	96.7 (2,942)	97.4 (5,229)	0.047
Prior stroke or TIA	24.3 (2,042)	21.7 (659)	25.8 (1,383)	<0.0001
Diabetes	73.8 (6,207)	73.6 (2,239)	73.9 (3,968)	0.72
COPD	46.4 (3,905)	44.5 (1,353)	47.5 (2,552)	0.0064
Stroke and bleeding risk				
CHA_2DS_2-VASc score				
Median (IQR)	6 (4-7)	6 (4-7)	6 (4-7)	0.010
0 (low risk)	0.3 (22)	0.2 (7)	0.3 (15)	
1 (medium risk)	1.5 (122)	1.5 (47)	1.4 (75)	
2 or greater (high risk)	98.3 (8,266)	98.2 (2,989)	98.3 (5,277)	
Prior hospitalization for bleeding	8.0 (673)	6.0 (182)	9.1 (491)	<0.0001
ATRIA bleeding score				
Median (IQR)	8 (7-9)	8 (7-9)	8 (7-9)	<0.0001
0-3 (low risk)	0.7 (63)	0.5 (16)	0.9 (47)	
4 (medium risk)	5.8 (486)	6.6 (200)	5.3 (286)	
5 or greater (high risk)	93.5 (7,861)	92.9 (2,827)	93.8 (5,034)	

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

RATES OF ANTICOAGULATION IN PATIENTS WITH ESRD



Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

TABLE 3 Characteristics That Are Associated With OAC Utilization (Propensity Model)

	HR (95% CI)	Wald Chi-Square	p Value
Age	0.87 (0.83-0.91) (per 10 yrs)	38.5706	<0.0001
Female	1.09 (0.98-1.21)	2.6999	0.1004
Black race	1.00 (0.90-1.13)	0.0063	0.9367
Region		5.1001 (3 df)	0.1646
Northeast vs. West	1.17 (0.98-1.41)		
Midwest vs. West	1.20 (1.01-1.43)		
South vs. West	1.11 (0.95-1.30)		
Time since AF diagnosis		0.3897 (3 df)	0.9424
<3 months vs. >9 months	1.02 (0.79-1.31)		
3-6 months vs. >9 months	1.09 (0.81-1.47)		
6-9 months vs. >9 months	1.01 (0.72-1.40)		
Time since ESRD diagnosis		5.4914 (3 df)	0.1392
<3 months vs. >9 months	0.90 (0.72-1.13)		
3-6 months vs. >9 months	1.18 (0.89-1.58)		
6-9 months vs. >9 months	1.01 (0.73-1.40)		
Dialysis type		1.8255 (2 df)	0.4014
Hemodialysis vs. none	1.02 (0.51-2.05)		
Peritoneal vs. none	0.77 (0.34-1.72)		
CAD	1.02 (0.89-1.18)	0.0997	0.7522
Prior MI	1.13 (1.00-1.29)	3.8372	0.0501
Prior CABG	1.40 (1.09-1.80)	6.8722	0.0088
Congestive heart failure	1.24 (1.06-1.45)	7.1502	0.0075
Hypertension	1.23 (0.55-2.76)	0.2484	0.6182
Stroke or TIA	1.03 (0.90-1.17)	0.1738	0.6768
Diabetes	0.99 (0.87-1.12)	0.0258	0.8723
COPD	1.00 (0.90-1.11)	0.0009	0.9755
Cancer	1.06 (0.93-1.20)	0.8273	0.3631
Dementia	0.75 (0.61-0.93)	7.0742	0.0078
Prior bleeding hospitalization	0.64 (0.51-0.81)	14.3654	0.0002
CHA_2DS_2-VASc high risk (≥2)	3.27 (1.04-10.33)	4.0891	0.0432
ATRIA score high risk (≥5)	1.36 (0.98-1.90)	3.3527	0.0671

PROPENSITY MODEL

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

VARIABLES USED IN PROPENSITY MODEL FOR OAC USE

Baseline Characteristics†	Pre-Match			Matched 1:2		
	OAC (n = 1,522)	No OAC (n = 5,367)	Standardized Difference (%)	OAC* (n = 1,519)	No OAC (n = 3,018)†	Standardized Difference (%)
Age	69 (60-77)	69 (63-80)	24.9	70 (61-78)	70 (62-79)	6.3
Female	54 (825)	52 (2,807)	3.8	54 (825)	54 (1,638)	0.1
Black race	32 (481)	29 (1,551)	5.9	32 (480)	30 (917)	2.6
Southern region	44 (666)	45 (2,405)	2.1	44 (665)	45 (1,350)	1.9
Medical history‡						
CAD	76 (1,158)	80 (4,295)	9.5	82 (1,249)	82 (2,478)	0.3
Prior MI	22 (328)	25 (1,337)	8.0	24 (361)	25 (748)	2.4
Prior CABG	4 (64)	4 (193)	3.1	4 (67)	4 (135)	0.3
CHF	82 (1,248)	83 (4,472)	3.5	87 (1,323)	88 (2,648)	1.9
Hypertension	99 (1,511)	100 (5,345)	4.2	100 (1,513)	100 (3,010)	2.3
Stroke or TIA	16 (244)	21 (1,143)	13.5	20 (302)	21 (620)	1.6
Diabetes	77 (1,174)	77 (4,131)	0.4	79 (1,206)	79 (2,399)	0.2
COPD	50 (764)	55 (2,954)	9.7	57 (863)	57 (1,716)	0.1
Cancer	19 (294)	22 (1,195)	7.3	21 (319)	21 (623)	0.9
Dementia	5 (75)	9 (468)	15.1	7 (99)	6 (196)	0.1
Stroke and bleeding risk‡						
CHA_2DS_2-VASc high risk (≥2)	99 (1,510)	99 (5,328)	0.7	100 (1,519)	100 (3,018)	–§
Prior bleeding hospitalization	5 (74)	9 (472)	15.6	5 (79)	5 (162)	0.7
ATRIA score high risk (≥5)	96 (1,456)	97 (5,196)	6.0	98 (1,483)	98 (2,957)	2.4

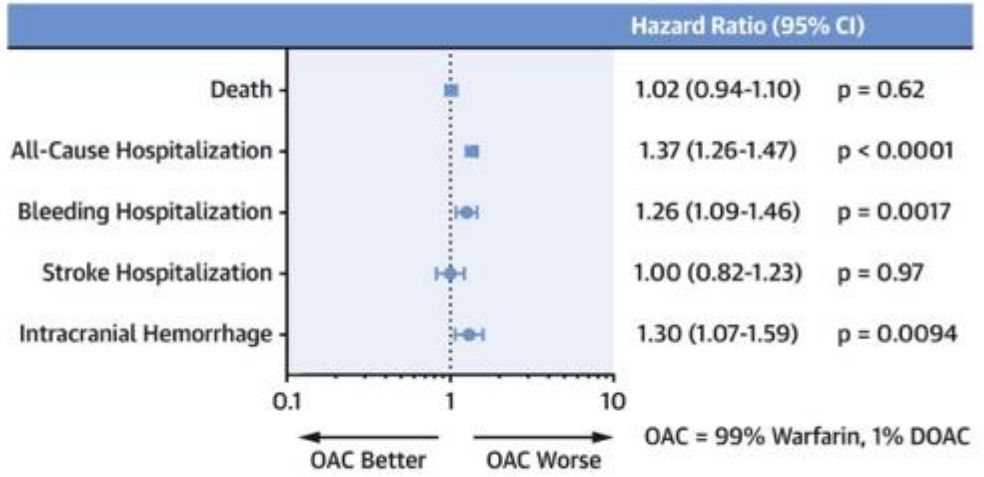
Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

OUTCOMES AMONG MATCHED COHORT

TABLE 5 Unadjusted Risk of Relevant Outcomes Among Matched Cohort of ESRD Patients With AF by Anticoagulant Use

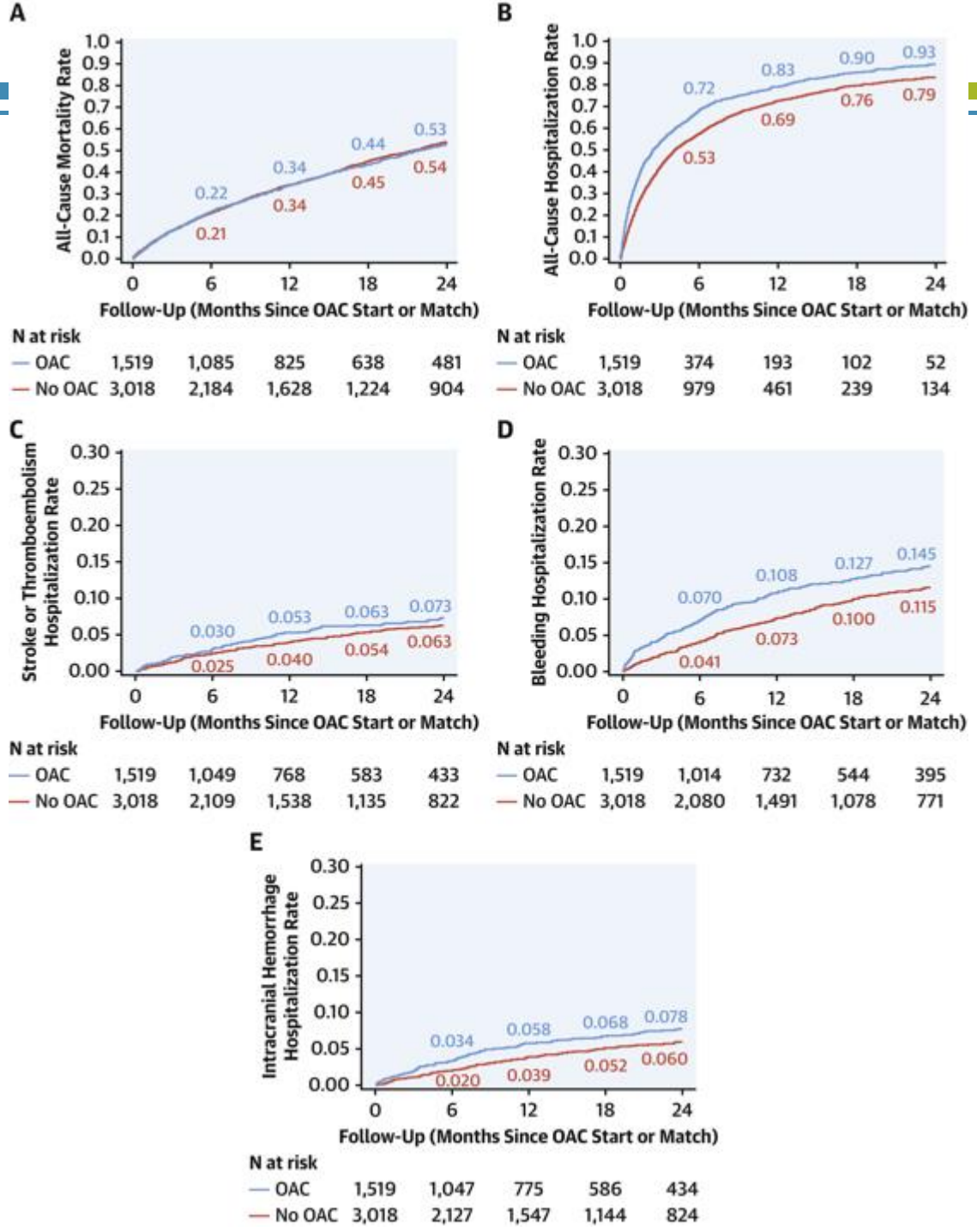
Event Risk*	OAC (n = 1,519)†	No OAC (n = 3,018)†
Death		
Total events	922	1,817
1-yr risk	33.9 (31.5-36.5)	34.2 (32.4-36.0)
2-yr risk	53.0 (50.2-55.8)	54.1 (52.1-56.1)
Hospital admission for any reason		
Total events	1,297	2,395
1-yr risk	79.2 (77.1-81.4)	72.7 (71.0-74.4)
2-yr risk	89.3 (87.7-91.0)	83.5 (82.0-85.0)
Hospital admission for bleeding		
Total events	230	375
1-yr risk	10.8 (9.3-12.6)	7.3 (6.4-8.4)
2-yr risk	14.5 (12.7-16.5)	11.5 (10.4-12.9)
Hospital admission for stroke or thromboembolic event		
Total events	117	211
1-yr risk	5.3 (4.2-6.6)	4.0 (3.3-4.8)
2-yr risk	7.3 (6.1-8.9)	6.3 (5.4-7.3)
Hospital admission for ICH‡		
Total events	129	198
1-yr risk	5.8 (4.7-7.1)	3.9 (3.2-4.7)
2-yr risk	7.8 (6.5-9.4)	6.0 (5.1-7.0)

CENTRAL ILLUSTRATION: Adjusted Outcomes Among Matched End-Stage Renal Disease-Atrial Fibrillation Patients by Anticoagulant Use at 2 Years



Pokorney, S.D. et al. J Am Coll Cardiol. 2020;75(11):1299-308.

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.



CUMULATIVE INCIDENCE CURVES FOR PROPENSITY-MATCHED OUTCOMES

(A) all-cause mortality
(B) all-cause hospitalization
(C) stroke or thromboembolic hospitalization
(D) bleeding hospitalization,
(E) intracranial hemorrhage

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

CONCLUSIONS

- 1 of 3 patients with ESRD had AF.
- Patients with ESRD and concomitant AF were older and had more comorbid illness than those without AF.
- Only 1 of 3 patients with AF, ESRD, and a CHA2DS2-VASc $\geq$ 2 were treated with OAC.
- There was no evidence of an association between OAC therapy and lower risk of stroke.
- One-third of patients with ESRD and AF who were treated with OAC discontinued therapy at 1 year, and patients treated with OAC experienced an increased risk for all-cause bleeding and intracranial hemorrhage.

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

LIMITATIONS

- Because our analysis is based on administrative claims data for determination of outcomes and comorbidities, it is possible that unmeasured confounders such as over-the-counter medication use (e.g., aspirin) may have affected results.
- Information about TTR and adherence to warfarin therapy in patients prescribed OAC were not available
- The analysis does not include socio-economic information, certain clinical variables (blood pressure, weight), or information regarding smoking and alcohol use.
- Limited number of patients treated with direct-acting oral anticoagulants

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.

CONCLUSIONS

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL OUTCOMES: Patients with AF and ESRD are at increased risk of thromboembolic and bleeding complications. Observational studies of oral vitamin K antagonist therapy have reported conflicting effects on mortality, thrombotic, and bleeding events in these patients.

TRANSLATIONAL OUTLOOK: Further investigation is needed to establish the safety and efficacy of target-specific oral anti-coagulants and left atrial appendage occlusion in these patients.

Pokorney et al., J Am Coll Cardiol 2020;75:1299–308.