

Supplementary Online Content 2

Yao X, Gersh BJ, Holmes DR, et al. Association of surgical left atrial appendage occlusion with subsequent stroke and mortality among patients undergoing cardiac surgery. *JAMA*. doi:10.1001/jama.2018.6024

eTable 1. Variables Associated With Undergoing LAAO (N=75,782)

eTable 2. Baseline Characteristics in Patients With and Without Prior AF in Propensity Score Matched Cohort

eTable 3. Variables Associated With Post-operative AF in Patients Without Prior AF (N=50,061)

eTable 4. Falsification Endpoint Test in Propensity Score Matched Patients (N=8,590)

eTable 5. Stroke and All-Cause Mortality Using Propensity Score Weighting

eTable 6. AF-Related Health Utilization After Cardiac Surgery Using Propensity Score Weighting

eTable 7. Sensitivity Analysis Stratified by Prior AF and OAC Use During Follow up

eTable 8. Long-term AF-Related Health Utilization Excluding the First 30 Days, Stratified by Whether Patients Had Post-operative AF

eTable 9. Sensitivity Analysis by Whether Patients Developed AF During Follow-up in Patients Without Prior AF in Propensity Score Matched Patients

eTable 10. Sensitivity Analysis Adjusting for Maze Surgery in Patients With Prior AF

eFigure 1. Subgroup Analysis for All-Cause Mortality in Propensity Score Matched Patients With Prior AF

eFigure 2. Subgroup Analysis for All-Cause Mortality in Propensity Score Matched Patients Without Prior AF

eFigure 3. Percentages of Patients on Oral Anticoagulation After Surgery in Propensity Score Matched Cohort

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Variables Associated With Undergoing LAO (N=75,782)

	Odds Ratio, 95% Confidence Interval	P value
Age, per 10 yr increase	1.07 (1.03, 1.10)	<0.001
Race		
Asian	Reference	Reference
Black	1.35 (1.00, 1.82)	0.05
Hispanic/Latino	1.18 (0.86, 1.61)	0.31
White	1.52 (1.13, 2.04)	<0.01
Other/Unknown	1.41 (1.07, 1.85)	0.01
Geographic Region		
Midwest	Reference	Reference
Northeast	0.56 (0.50, 0.62)	<0.001
South	0.70 (0.64, 0.75)	<0.001
West	1.13 (1.02, 1.26)	0.03
Surgery types		
Isolated CABG	Reference	Reference
Mechanical valve replacement	1.17 (1.03, 1.33)	0.02
Tissue valve replacement	1.48 (1.34, 1.62)	<0.001
Valve repair	2.16 (1.90, 2.45)	<0.001
Mitral valve surgery	2.82 (2.56, 3.11)	<0.001
Surgery on both mitral and aortic valve	0.75 (0.60, 0.93)	0.01
On-pump surgery	1.20 (1.11, 1.31)	<0.001
Pre-operative hemodynamic instability	0.56 (0.36, 0.85)	<0.01
Medical History		
Atrial fibrillation	3.60 (3.32, 3.91)	<0.001
Other supraventricular arrhythmia	1.23 (1.15, 1.32)	<0.001
Myocardial infarction	0.76 (0.70, 0.82)	<0.001
Peripheral Artery Disease	0.81 (0.73, 0.89)	<0.001
Major bleeding	1.07 (0.99, 1.17)	0.08
Anemia	1.09 (1.01, 1.18)	0.02
Alcoholism	1.20 (1.04, 1.38)	0.01
Dialysis	0.66 (0.51, 0.86)	<0.01
Cardioversion	1.32 (1.17, 1.48)	<0.001
Ablation	1.23 (1.01, 1.49)	0.04
Pacemaker/ICD	0.78 (0.70, 0.87)	<0.001
PCI	0.89 (0.78, 1.02)	0.08
Liver disease	0.86 (0.78, 0.95)	<0.01
Thyrotoxicosis	1.16 (0.98, 1.37)	0.09

eTable 1 (Continued). Variables Associated With Undergoing LAAO (N=75,782)

	Odds Ratio, 95% Confidence Interval	P value
Baseline medication		
Oral anticoagulant	2.26 (2.07, 2.48)	<0.001
Antiplatelet	0.84 (0.74, 0.96)	0.01
Rate control drugs	1.10 (1.02, 1.18)	0.01
Antiarrhythmic drugs	1.41 (1.26, 1.59)	<0.001
Year of Index Procedure		
2009	Reference	Reference
2010	1.34 (1.12, 1.61)	<0.01
2011	1.31 (1.09, 1.57)	<0.01
2012	1.48 (1.24, 1.76)	<0.001
2013	2.02 (1.71, 2.38)	<0.001
2014	2.20 (1.86, 2.60)	<0.001
2015	2.58 (2.20, 3.03)	<0.001
2016	2.68 (2.28, 3.14)	<0.001
2017	2.54 (2.07, 3.13)	<0.001

Abbreviations: CABG, coronary artery bypass graft; ICD, implantable cardioverter defibrillators; PCI, percutaneous coronary intervention

Odds ratio>1 indicates patients were more likely to receive LAAO. Variables were selected using stepwise forward selection using a threshold of p value of 0.10 for the addition to the model.

eTable 2. Baseline Characteristics in Patients With and Without Prior AF in Propensity Score Matched Cohort

	No Prior AF (N=2152)	Prior AF (N=6438)	p value
Age, yr	64.3 (11.3)	69.7 (10.1)	<0.001
18-64	1058 (49.2)	1815 (28.2)	<0.001
65-74	652 (30.3)	2306 (35.8)	
≥75	442 (20.5)	2317 (36.0)	
Female	737 (34.2)	2284 (35.5)	0.30
Race			<0.01
Asian	33 (1.5)	90 (1.4)	
Black	183 (8.5)	418 (6.5)	
Hispanic/Latino	103 (4.8)	247 (3.8)	
White	1658 (77.0)	5187 (80.6)	
Other/Unknown	175 (8.1)	496 (7.7)	
Geographic Region			<0.001
Midwest	910 (42.3)	2523 (39.2)	
Northeast	175 (8.1)	822 (12.8)	
South	743 (34.5)	2268 (35.2)	
West	324 (15.1)	825 (12.8)	
Medical History			
Other supraventricular arrhythmia	645 (30.0)	3638 (56.5)	<0.001
Thromboembolism	293 (13.6)	1281 (19.9)	<0.001
Heart failure	928 (43.1)	3841 (59.7)	<0.001
Diabetes mellitus	745 (34.6)	2302 (35.8)	0.34
Stage 3-5 CKD	250 (11.6)	948 (14.7)	<0.001
Myocardial infarction	574 (26.7)	1636 (25.4)	0.25
Peripheral artery disease	233 (10.8)	949 (14.7)	<0.001
Major bleeding	425 (19.7)	1672 (26.0)	<0.001
Intracranial bleeding	29 (1.3)	141 (2.2)	0.02
Hypertension	1842 (85.6)	5768 (89.6)	<0.001
Hyperlipidemia	1781 (82.8)	5524 (85.8)	<0.001
Falls	163 (7.6)	699 (10.9)	<0.001
Anemia	1480 (68.8)	4800 (74.6)	<0.001
COPD	235 (10.9)	906 (14.1)	<0.001
Alcoholism	122 (5.7)	412 (6.4)	0.22
Obesity	563 (26.2)	1857 (28.8)	0.02
Smoking	844 (39.2)	2368 (36.8)	0.04
Obstructive sleep apnea	374 (17.4)	1445 (22.4)	<0.001
Non skin cancer	261 (12.1)	1073 (16.7)	<0.001
Ischemic stroke or systemic embolism	225 (10.5)	967 (15.0)	<0.001
TIA	143 (6.6)	681 (10.6)	<0.001
Ventricular arrhythmia	252 (11.7)	1247 (19.4)	<0.001

eTable 2 (continued). Baseline Characteristics in Patients With and Without Prior AF in Propensity Score Matched Cohort

	No Prior AF (N=2152)	Prior AF (N=6438)	p value
Systolic heart failure	422 (19.6)	1782 (27.7)	<0.001
Diabetes requiring insulin	210 (9.8)	518 (8.0)	0.01
Dialysis	33 (1.5)	103 (1.6)	0.83
Cardioversion	22 (1.0)	1204 (18.7)	<0.001
Ablation	12 (0.6)	329 (5.1)	<0.001
Pacemaker/ICD	119 (5.5)	1017 (15.8)	<0.001
PCI	154 (7.2)	541 (8.4)	0.07
Liver disease	231 (10.7)	901 (14.0)	<0.001
Depression	682 (31.7)	2051 (31.9)	0.89
Dementia	44 (2.0)	213 (3.3)	0.00
Hypothyroidism	444 (20.6)	1628 (25.3)	<0.001
Thyrotoxicosis	69 (3.2)	305 (4.7)	<0.01
Ulcer in upper GI tract	106 (4.9)	367 (5.7)	0.17
Pre-operative Endocarditis	43 (2.0)	109 (1.7)	0.35
CHA₂DS₂-VASc			<0.001
0, 1	376 (17.5)	541 (8.4)	
2, 3	857 (39.8)	2023 (31.4)	
≥4	919 (42.7)	3874 (60.2)	
HAS-BLED≥3	1174 (54.6)	4367 (67.8)	<0.001
Baseline Medication			
Oral anticoagulant	54 (2.5)	2562 (39.8)	<0.001
Antiplatelet	192 (8.9)	448 (7.0)	<0.01
Rate control drugs	926 (43.0)	3874 (60.2)	<0.001
Antiarrhythmic drugs	64 (3.0)	1021 (15.9)	<0.001
Other adrenergic blocking agents	90 (4.2)	320 (5.0)	0.14
Other calcium channel blockers	280 (13.0)	861 (13.4)	0.67
Renin angiotensin system antagonists	911 (42.3)	2827 (43.9)	0.20
Loop diuretics	328 (15.2)	1906 (29.6)	<0.001
Thiazides	293 (13.6)	928 (14.4)	0.36
Cholesterol lowering drugs	981 (45.6)	2996 (46.5)	0.44
NSAIDs	236 (11.0)	500 (7.8)	<0.001
Diabetes drugs	299 (13.9)	823 (12.8)	0.19
Antiulcer agents	376 (17.5)	1250 (19.4)	0.05
Pre-operative Medication			
Beta blocker	172 (8.0)	537 (8.3)	0.61
Amiodarone	31 (1.4)	115 (1.8)	0.28
Statin	156 (7.2)	395 (6.1)	0.07
Corticosteroid	44 (2.0)	137 (2.1)	0.82

eTable 2 (continued). Baseline Characteristics in Patients With and Without Prior AF in Propensity Score Matched Cohort

	No Prior AF (N=2152)	Prior AF (N=6438)	p value
Laboratory Test Results			
Serum creatinine, mg/dL	1.0±0.4	1.1±0.5	0.01
Serum calcium, mg/dL	9.4±0.4	9.4±0.5	0.10
Serum albumin, g/dL	4.2±0.4	4.2±0.4	<0.001
Hemoglobin, g/dL	13.6±1.8	13.4±1.8	0.01
LDL-C, mg/dL	103.5±36.6	94.3±34.5	<0.001
HbA1c, %	7.0±1.9	6.5±1.3	<0.01
Surgery Types			
CABG	1125 (52.3)	2805 (43.6)	<0.001
Mechanical valve replacement	159 (7.4)	635 (9.9)	0.00
Bioprosthetic valve replacement	621 (28.9)	2403 (37.3)	<0.001
Valve repair	645 (30.0)	1699 (26.4)	0.00
CABG+valve surgery	398 (18.5)	1104 (17.1)	0.15
Types of Valves Treated During Valve Surgery*			
Aortic	544 (38.2)	1880 (39.7)	0.31
Mitral	877 (61.5)	2861 (60.4)	0.44
Tricuspid or pulmonary	152 (10.7)	702 (14.8)	<0.001
Both mitral and aortic valves	48 (3.4)	205 (4.3)	0.11
On-pump Surgery	1664 (77.3)	5114 (79.4)	0.04
Pre-operative Hemodynamic Instability	13 (0.6)	42 (0.7)	0.81
Year of Index Procedure			0.42
2009	131 (6.1)	362 (5.6)	
2010	160 (7.4)	476 (7.4)	
2011	162 (7.5)	523 (8.1)	
2012	178 (8.3)	635 (9.9)	
2013	302 (14.0)	885 (13.7)	
2014	300 (13.9)	858 (13.3)	
2015	363 (16.9)	1127 (17.5)	
2016	444 (20.6)	1270 (19.7)	
2017	112 (5.2)	302 (4.7)	
Length of Baseline Period, yr	3.8 (3.2)	3.9 (3.3)	0.06

Abbreviations: AF, atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HbA1c, hemoglobin A1c; ICD, implantable cardioverter defibrillators; LAAO, surgical occlusion of the left atrial appendage; LDL-C, low-density lipoprotein cholesterol; NSAID, nonsteroidal anti-inflammatory drug; PCI, percutaneous coronary intervention; TIA, transient ischemic attack. The CHA2DS2-VASc score is a 0- to 9-point stroke risk score where a higher point score indicates higher risk of stroke. The point score is calculated as follows: 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex and 2 points for age 75 years or older and prior stroke, TIA or thromboembolism. The HAS-BLED score is a 0- to 9-point bleeding risk score where a higher point score indicates higher risk of bleeding. The point score is calculated as follows: 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio, age>65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider international normalized ratio, so the range is 0-8. Chi-square analysis was used to compare categorical variables and Kruskal-Wallis was used to compare continuous variables. The baseline period refers to the time period before the surgery, which was used to establish patients' medical history. Although there were differences in baseline characteristics between patients with and without prior AF, the characteristics of patients receiving LAAO vs. not receiving LAAO were similar in patients with or without prior AF.

eTable 3. Variables Associated With Post-operative AF in Patients Without Prior AF (N=50,061)

		No. of Patients	No. of Events	Person Years	Event Rate	Hazard Ratio, 95 CI	p value
LAAO	No	48985	6990	3583	1.95	Reference	
	Yes	1076	298	70	4.27	1.48 (1.31, 1.67)	<0.001
Age, per 10 yr increase						1.44 (1.40, 1.47)	<0.001
Sex	Male	35702	4951	2617	1.89	Reference	
	Female	14359	2337	1036	2.26	0.91 (0.87, 0.96)	<0.001
Race	Nonwhite	12202	1720	889	1.93	Reference	
	White	37859	5568	2764	2.01	1.07 (1.01, 1.13)	0.01
Surgery types							
Isolated CABG		34458	3778	2575	1.47	Reference	Ref
Mechanical valve replacement		3803	811	266	3.05	2.02 (1.86, 2.19)	<0.001
Tissue valve replacement		8513	1965	585	3.36	1.75 (1.64, 1.86)	<0.001
Valve repair		3287	734	227	3.23	1.60 (1.44, 1.78)	<0.001
Mitral valve surgery	No	45905	6115	3378	1.81	Reference	
	Yes	4156	1173	274	4.27	1.54 (1.42, 1.67)	<0.001
Medical History							
Other supraventricular arrhythmia	No	39363	4946	2916	1.70	Reference	
	Yes	10698	2342	737	3.18	1.55 (1.47, 1.63)	<0.001
Heart failure	No	32525	3638	2434	1.49	Reference	
	Yes	17536	3650	1219	2.99	1.30 (1.23, 1.38)	<0.001
Myocardial infarction	No	29055	4176	2126	1.96	Reference	
	Yes	21006	3112	1526	2.04	1.13 (1.08, 1.19)	<0.001
COPD	No	44379	6219	3250	1.91	Reference	
	Yes	5682	1069	403	2.65	1.11 (1.04, 1.19)	<0.01
Obesity	No	35410	5175	2584	2.00	Reference	
	Yes	14651	2113	1069	1.98	1.11 (1.05, 1.17)	<0.001
Smoking	No	28109	4360	2037	2.14	Reference	
	Yes	21952	2928	1616	1.81	0.93 (0.89, 0.98)	<0.01
Thromboembolism	No	42483	5907	3116	1.90	Reference	
	Yes	7578	1381	537	2.57	1.11 (1.04, 1.18)	<0.001
Ventricular arrhythmia	No	45107	6163	3315	1.86	Reference	
	Yes	4954	1125	338	3.33	1.37 (1.28, 1.46)	<0.001
Systolic heart failure	No	42781	5586	3156	1.77	Reference	
	Yes	7280	1702	496	3.43	1.17 (1.09, 1.25)	<0.001
Dialysis	No	48986	6981	3582	1.95	Reference	
	Yes	1075	307	70	4.36	1.52 (1.35, 1.71)	<0.001
Cardioversion	No	49736	7173	3633	1.97	Reference	
	Yes	325	115	20	5.89	2.10 (1.74, 2.53)	<0.001

eTable 3 (continued). Variables Associated With Post-operative AF in Patients Without Prior AF (N=50,061)

		No. of Patients	No. of Events	Person Years	Event Rate	Hazard Ratio, 95 CI	p value
Ablation	No	49967	7256	3647	1.99	Reference	
	Yes	94	32	6	5.72	1.80 (1.27, 2.56)	<0.001
PCI	No	43457	6417	3167	2.03	Reference	
	Yes	6604	871	486	1.79	0.91 (0.85, 0.99)	0.03
Liver disease	No	43866	6237	3209	1.94	Reference	
	Yes	6195	1051	444	2.37	1.08 (1.01, 1.15)	0.03
Hyperlipidemia	No	5980	901	435	2.07	Reference	
	Yes	44081	6387	3218	1.99	0.89 (0.82, 0.95)	<0.01
Depression	No	34494	5074	2516	2.02	Reference	
	Yes	15567	2214	1136	1.95	0.93 (0.88, 0.98)	<0.01
On-pump surgery	No	16299	2492	1188	2.10	Reference	
	Yes	33762	4796	2465	1.95	0.90 (0.85, 0.94)	<0.001
Pre-operative hemodynamic instability	No	49579	7174	3621	1.98	Reference	
	Yes	482	114	32	3.56	1.35 (1.12, 1.63)	<0.01
Baseline medication							
Oral anticoagulant	No	49302	7115	3600	1.98	Reference	
	Yes	759	173	52	3.30	1.35 (1.16, 1.57)	<0.001
Antiplatelet	No	43053	6326	3138	2.02	Reference	
	Yes	7008	962	514	1.87	0.93 (0.86, 1.00)	0.06
Rate control drugs	No	28911	4019	2120	1.90	Reference	
	Yes	21150	3269	1533	2.13	1.09 (1.03, 1.14)	<0.001
Other adrenergic blocking agents	No	47599	6811	3479	1.96	Reference	
	Yes	2462	477	174	2.74	1.10 (1.00, 1.21)	0.04
Other calcium channel blockers	No	42162	5968	3086	1.93	Reference	
	Yes	7899	1320	567	2.33	1.09 (1.03, 1.16)	<0.01
Diabetes drug	No	40253	5814	2940	1.98	Reference	
	Yes	9808	1474	713	2.07	1.06 (1.00, 1.13)	0.06
Antiulcer agents	No	41194	5958	3009	1.98	Reference	
	Yes	8867	1330	644	2.07	0.92 (0.86, 0.98)	<0.01

Event rate was calculated as number of events per person-year.

Abbreviations: AF, atrial fibrillation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; ICD, implantable cardioverter defibrillators; LAAO, surgical occlusion of the left atrial appendage; PCI, percutaneous coronary intervention.

This is a multivariable Cox proportional hazards regression. Hazard ratio>1 indicates patients were more likely to develop post-operative AF.

Variables were selected using stepwise forward selection using a threshold of p value of 0.10 for the addition to the model

eTable 4. Falsification Endpoint Test in Propensity Score Matched Patients (N=8,590)

	No LAAO					LAAO				Hazard Ratio Comparing LAAO to No LAAO (95% CI)	P Value
	No. of Patients	No. of Events	Person Years	Event Rate		No. of Patients	No. of Events	Person Years	Event Rate		
COPD											
Overall	4295	130	7567	1.72		4295	123	7895	1.56	0.94 (0.73, 1.20)	0.60
No AF at baseline	1076	31	1953	1.59		1076	24	1881	1.28	0.80 (0.47, 1.36)	0.41
AF at baseline	3219	99	5613	1.76		3219	99	6014	1.65	0.98 (0.74, 1.29)	0.86
Pneumonia											
Overall	4295	466	7135	6.53		4295	435	7476	5.82	0.92 (0.81, 1.05)	0.20
No AF at baseline	1076	91	1851	4.92		1076	78	1818	4.29	0.87 (0.64, 1.17)	0.35
AF at baseline	3219	375	5285	7.10		3219	357	5658	6.31	0.93 (0.80, 1.07)	0.30
Fracture											
Overall	4295	207	7482	2.77		4295	191	7769	2.46	0.91 (0.75, 1.11)	0.34
No AF at baseline	1076	38	1960	1.94		1076	39	1845	2.11	1.10 (0.70, 1.71)	0.69
AF at baseline	3219	169	5523	3.06		3219	152	5924	2.57	0.86 (0.69, 1.07)	0.19

Abbreviations: AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease

Outcomes were captured by a primary diagnosis during an emergency department visit or any primary or secondary diagnosis during an inpatient stay. No statistically significant results suggested no evidence for residual confounding.

Event rate was calculated as the number of events per 100 person-years.

eTable 5. Stroke and All-Cause Mortality Using Propensity Score Weighting

	No LAAO					LAAO				Hazard Ratio (95% CI)	P Value
	No. of Patients	No. of Events	Person Years	Event Rate		No. of Patients	No. of Events	Person Years	Event Rate		
Ischemic stroke or systemic embolism											
Overall	71408	96	6392	1.51		4374	73	6509	1.13	0.76 (0.61, 0.95)	0.02
No AF at baseline	48985	25	1847	1.36		1076	22	1783	1.22	0.89 (0.59, 1.35)	0.59
AF at baseline	22423	71	4545	1.56		3298	52	4725	1.09	0.72 (0.55, 0.93)	0.01
Death											
Overall	71408	258	6514	3.96		4374	205	6647	3.09	0.78 (0.68, 0.90)	<0.001
No AF at baseline	48985	49	1881	2.60		1076	42	1817	2.34	0.89 (0.66, 1.20)	0.46
AF at baseline	22423	209	4634	4.52		3298	163	4830	3.37	0.75 (0.65, 0.88)	<0.001

Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage

Event rate was calculated as the number of events per 100 person-years. The number of events, person years and event rates were all calculated using weights.

eTable 6. AF-Related Health Utilization After Cardiac Surgery Using Propensity Score Weighting

	No LAAO					LAAO				Absolute Rate Difference (95% CI)	Incident Rate Ratio, 95% CI	P Value
	No. of Patients	No. of Events	Person Years	Event Rate		No. of Patients	No. of Events	Person Years	Event Rate			
AF-related outpatient visits												
Overall	71408	59189	6514	9.09	4374	74955	6647	11.28	2.19 (1.67, 2.72)	1.24 (1.18, 1.30)	<0.001	
No AF at baseline	48985	3555	1881	1.89	1076	5401	1817	2.97	1.08 (0.51, 1.65)	1.57 (1.29, 1.91)	<0.001	
AF at baseline	22423	55634	4634	12.01	3298	69555	4830	14.40	2.40 (1.75, 3.04)	1.20 (1.14, 1.26)	<0.001	
AF-related hospitalization												
Overall	71408	1908	6514	0.29	4374	2264	6647	0.34	0.05 (0.03, 0.07)	1.16 (1.10, 1.24)	<0.001	
No AF at baseline	48985	116	1881	0.06	1076	145	1817	0.08	0.02 (0.00, 0.04)	1.29 (1.02, 1.64)	0.03	
AF at baseline	22423	1792	4634	0.39	3298	2120	4830	0.44	0.05 (0.03, 0.08)	1.13 (1.07, 1.21)	<0.001	

Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage

Event rate was calculated as the number of events per person-year. The number of events, person years and event rates were all calculated using weights.

eTable 7. Sensitivity Analysis Stratified by Prior AF and OAC Use During Follow up

	No LAAO					LAAO				Hazard Ratio LAAO vs No LAAO (95% CI)	P Value
	No. of Patients	No. of Events	Person Years	Event Rate		No. of Patients	No. of Events	Person Years	Event Rate		
Ischemic stroke or systemic embolism											
No AF and No OAC	890	22	1600	1.37		870	18	1460	1.23	0.87 (0.46, 1.61)	0.65
No AF and OAC	186	--	--	0.79		206	--	--	1.20	1.52 (0.37, 6.27)	0.56
AF and No OAC	1670	54	2879	1.88		1647	32	3059	1.05	0.58 (0.38, 0.90)	0.02
AF and OAC	1549	43	2804	1.53		1572	35	2972	1.18	0.80 (0.51, 1.24)	0.31
Death											
No AF and No OAC	890	45	1624	2.77		870	38	1488	2.55	0.91 (0.59, 1.40)	0.66
No AF and OAC	186	--	--	1.30		206	--	--	1.42	1.10 (0.34, 3.57)	0.88
AF and No OAC	1670	156	2934	5.32		1647	115	3115	3.69	0.71 (0.56, 0.90)	<0.01
AF and OAC	1549	129	2848	4.53		1572	84	3056	2.75	0.62 (0.47, 0.81)	<0.001

Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage; OAC, oral anticoagulant

Event rate was calculated as the number of events per 100 person-years.

OAC use was defined as a prescription of oral anticoagulant within 14 days of the surgery. The results remained largely unchanged if OAC use was defined as a prescription within 30 days of the surgery, or a prescription at any time during follow up, or proportion of days covered (PDC)≥80%.

To maintain de-identification (referring to the cells with dashes), OptumLabs does not allow researchers to disclose the number of events when the number is 10 or fewer. Medicare data has similar requirements.

eTable 8. Long-term AF-Related Health Utilization Excluding the First 30 Days, Stratified by Whether Patients Had Post-operative AF

	Overall (N=2,047)	Patients with Post-operative AF (N=495)	Patients without Post-operative AF (N=1,552)	p value
Patients with late AF, N (%)	565 (27.6)	358 (72.3)	207 (13.3)	<0.001
Person-years	3749	897	2852	
N of AF-related outpatient visits	7730	5989	1741	
Event rate for AF-related outpatient visits	2.06	6.68	0.61	<0.001
N of AF-related hospitalization	186	128	58	
Event rate for AF-related hospitalization	0.05	0.14	0.02	<0.001

Abbreviation: AF, atrial fibrillation

Event rate was calculated as the number of events per person-year. This analysis aimed to assess whether post-operative AF developed to late AF, and was restricted to patients in the propensity score matched cohort who did not have prior AF and had more than 30 days of follow up. Late AF was defined as any AF diagnosis beyond the first 30 days after the surgery over an average of 1.8 years of follow up.

eTable 9. Sensitivity Analysis by Whether Patients Developed AF During Follow-up in Patients Without Prior AF in Propensity Score Matched Patients

	No LAAO (N=1,076)				LAAO (N=1,076)				Hazard Ratio (95% CI)	P Value
	No. of Patients	No. of Events	Person Years	Event Rate	No. of Patients	No. of Events	Person Years	Event Rate		
Ischemic stroke or systemic embolism										
All patients	1076	25	1982	1.26	1076	23	1877	1.23	0.95 (0.54, 1.68)	0.87
No AF during follow up	762	12	1347	0.89	668	11	1092	1.01	1.10 (0.48, 2.49)	0.82
AF during follow up	314	13	635	2.05	408	12	784	1.53	0.74 (0.34, 1.62)	0.45
Death										
All patients	1076	50	2010	2.49	1076	44	1912	2.30	0.92 (0.61, 1.37)	0.67
No AF during follow up	762	26	1362	1.91	668	22	1107	1.99	1.03 (0.58, 1.82)	0.92
AF during follow up	314	24	647	3.71	408	22	805	2.73	0.73 (0.41, 1.30)	0.28

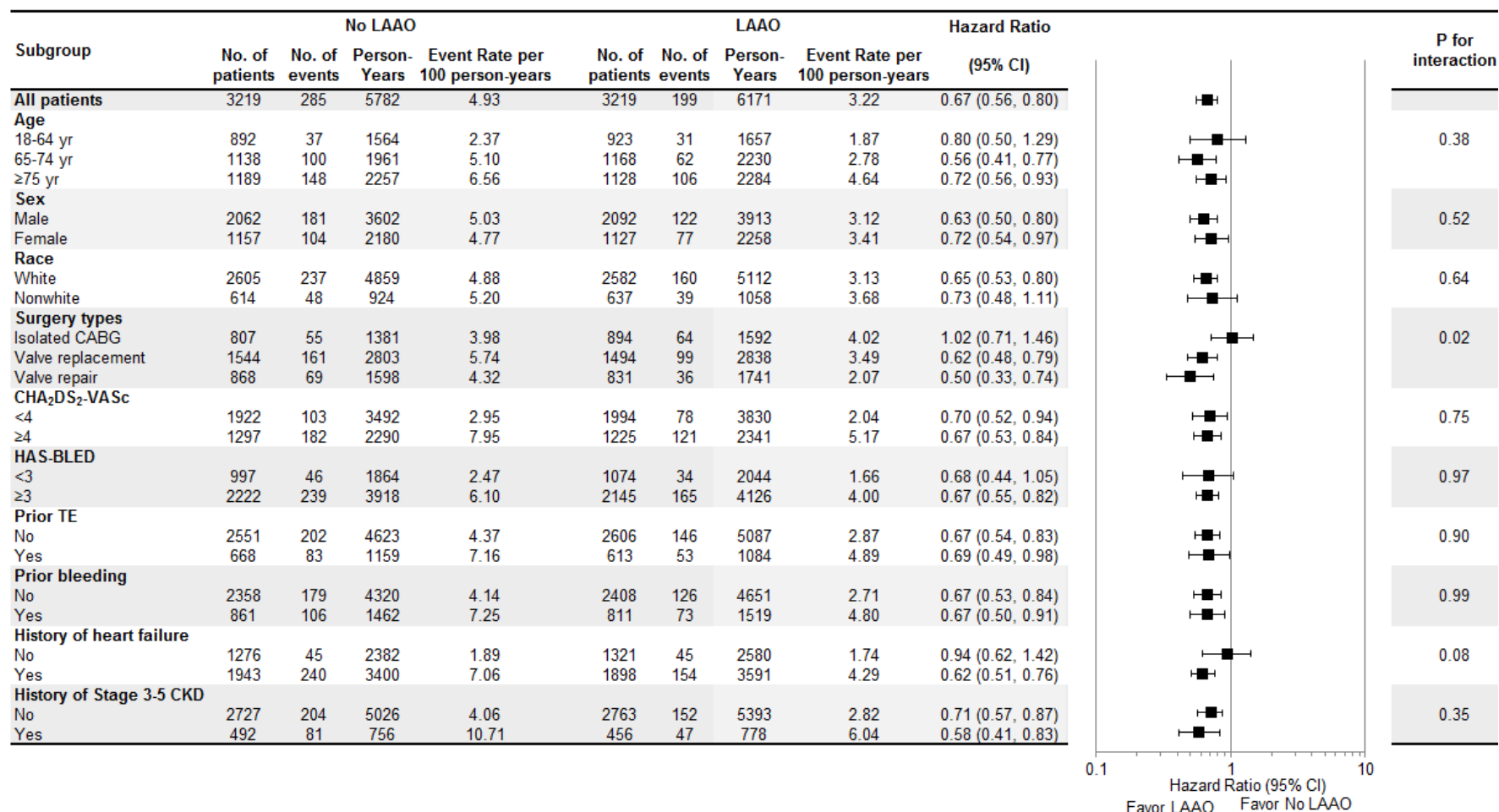
Abbreviations: AF, atrial fibrillation; LAAO, surgical occlusion of the left atrial appendage
Event rate was calculated as the number of events per 100 person-years.

eTable 10. Sensitivity Analysis Adjusting for Maze Surgery in Patients With Prior AF

	No LAAO				LAAO				Hazard Ratio (95% CI)	P Value
	No. of Patients	No. of Events	Person Years	Event Rate	No. of Patients	No. of Events	Person Years	Event Rate		
Ischemic stroke or systemic embolism	3219	97	5683	1.71	3219	67	6032	1.11	0.71 (0.51, 0.98)	0.04
Death	3219	285	5782	4.93	3219	199	6171	3.22	0.69 (0.57, 0.83)	<0.001
AF-related outpatient visit	3219	75825	5782	13.11	3219	90927	6171	14.74	1.12 (1.05, 1.19)	<0.001
AF-related hospitalization	3219	2360	5782	0.41	3219	2738	6171	0.44	1.08 (1.00, 1.16)	0.06

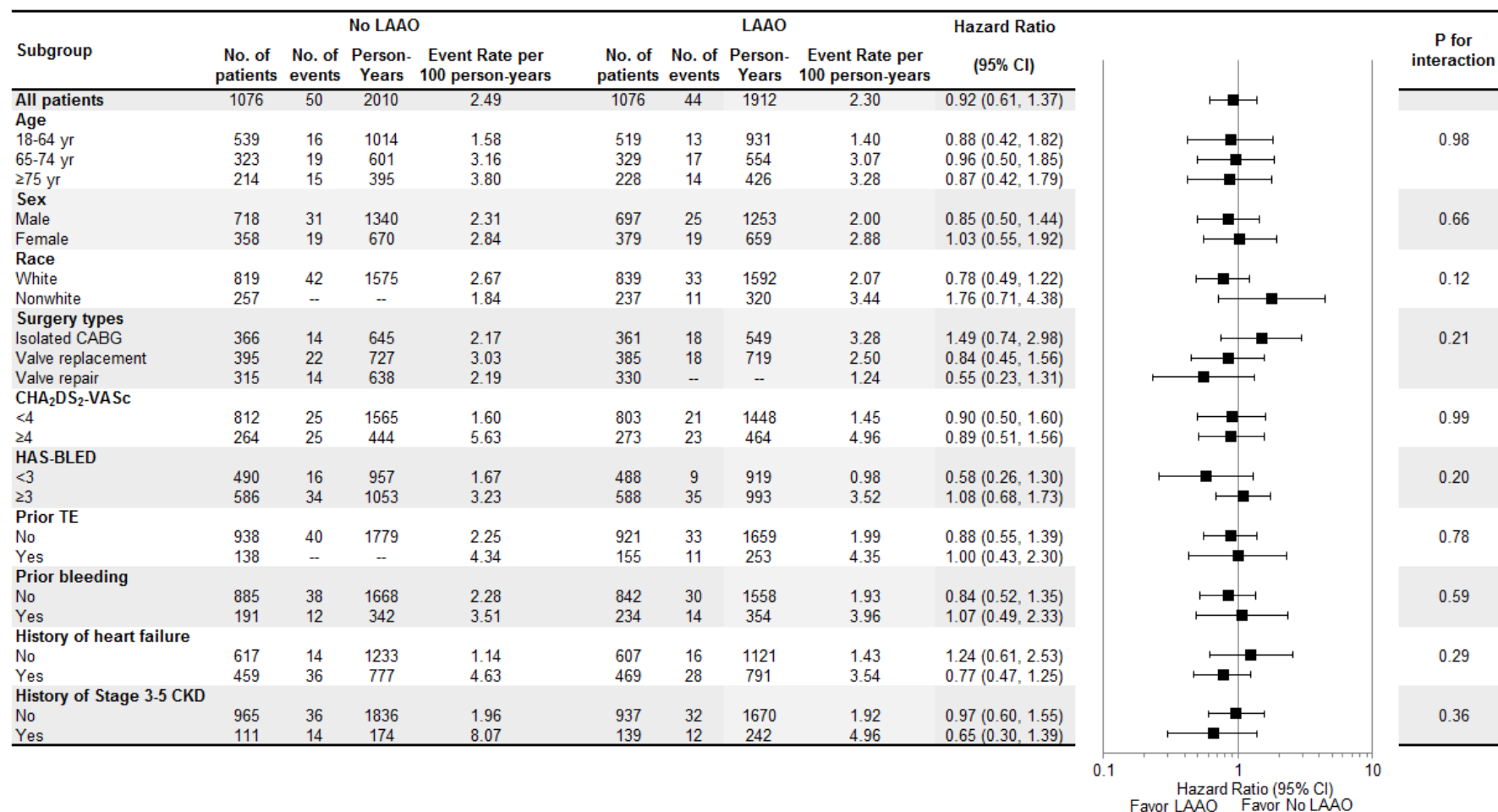
Whether patients received concomitant Maze surgery was adjusted in the regression models. The maze procedure was not statistically associated with any outcomes in the models. The event rates for ischemic stroke or systemic embolism and death were calculated as the number of events per 100 person-years, and the event rates for AF-related outpatient visit and AF-related hospitalization were calculated as the number of events per person-year.

eFigure 1. Subgroup Analysis for All-Cause Mortality in Propensity Score Matched Patients With Prior AF



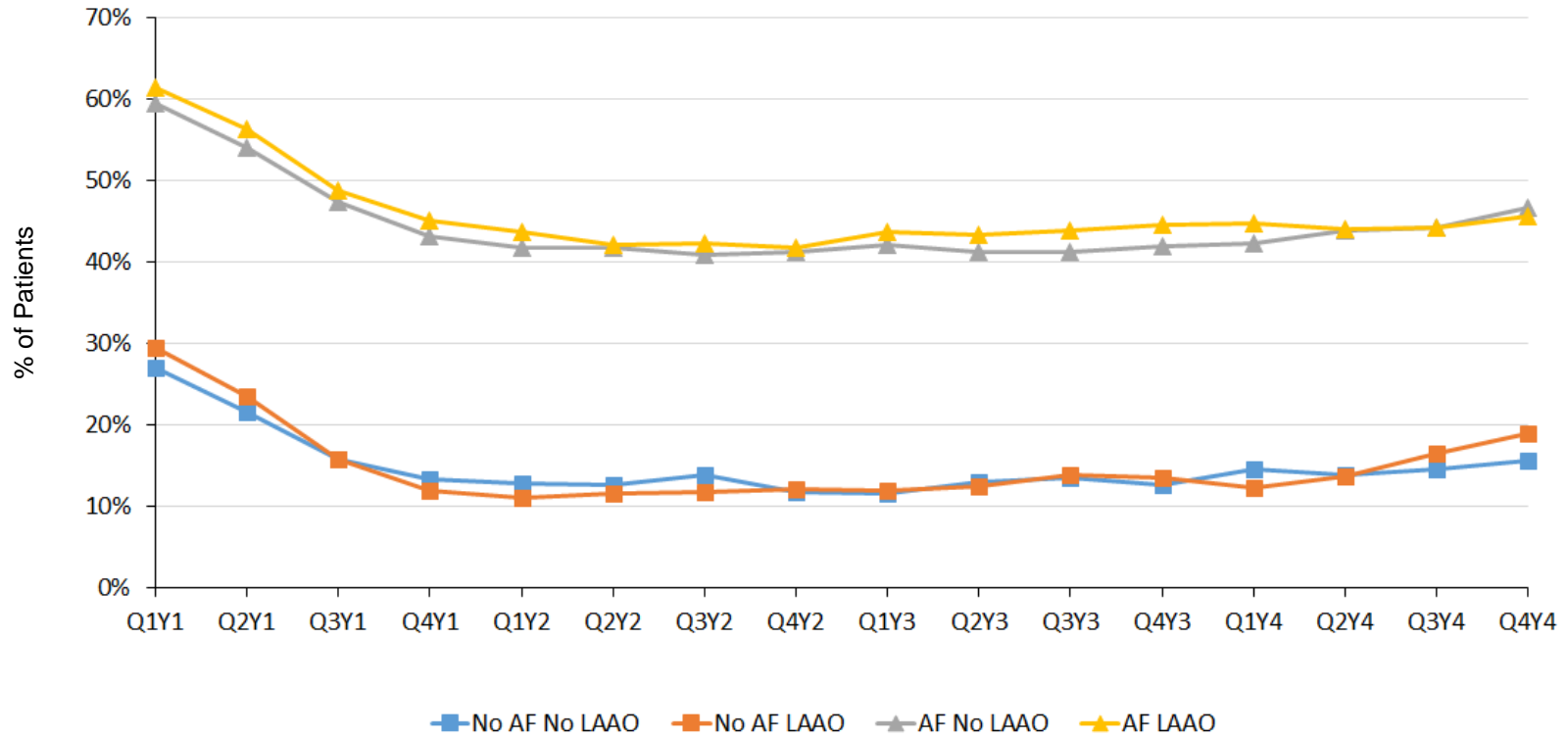
Abbreviations: AF, atrial fibrillation; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LAAO, surgical occlusion of the left atrial appendage; TE, thromboembolism. The CHA₂DS₂-VASc score is a 0- to 9-point stroke risk score where a higher point score indicates higher risk of stroke. The point score is calculated as follows: 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex and 2 points for age 75 years or older and prior stroke, transient ischemic attack or thromboembolism. The HAS-BLED score is a 0- to 9-point bleeding risk score where a higher point score indicates higher risk of bleeding. The point score is calculated as follows: 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio, age>65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider international normalized ratio, so the range is 0-8.

eFigure 2. Subgroup Analysis for All-Cause Mortality in Propensity Score Matched Patients Without Prior AF



Abbreviations: AF, atrial fibrillation; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LAAO, surgical occlusion of the left atrial appendage; TE, thromboembolism. The CHA₂DS₂-VASc score is a 0- to 9-point stroke risk score where a higher point score indicates higher risk of stroke. The point score is calculated as follows: 1 point each for heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, and female sex and 2 points for age 75 years or older and prior stroke, transient ischemic attack or thromboembolism. The HAS-BLED score is a 0- to 9-point bleeding risk score where a higher point score indicates higher risk of bleeding. The point score is calculated as follows: 1 point each for hypertension, abnormal kidney function, abnormal liver function, prior stroke, prior bleeding or bleeding predisposition, labile international normalized ratio, age>65 years, medication usage predisposing to bleeding, and alcohol use. This study did not consider international normalized ratio, so the range is 0-8. To maintain de-identification (referring to the cells with dashes), OptumLabs does not allow researchers to disclose the number of events when the number is 10 or fewer. Medicare data has similar requirements.

eFigure 3. Percentages of Patients on Oral Anticoagulation After Surgery in Propensity Score Matched Cohort



Abbreviations: Q=Quarter Y=Year

No. of Patients	Q1Y1	Q2Y1	Q3Y1	Q4Y1	Q1Y2	Q2Y2	Q3Y2	Q4Y2	Q1Y3	Q2Y3	Q3Y3	Q4Y3	Q1Y4	Q2Y4	Q3Y4	Q4Y4
No AF No LAO	1023	946	812	716	653	582	517	448	391	333	297	256	214	189	158	141
No AF LAO	1010	920	807	698	609	521	459	418	364	323	277	238	204	183	153	127
AF No LAO	3063	2781	2430	2112	1848	1639	1421	1257	1087	922	808	706	622	551	466	412
AF LAO	3075	2833	2476	2201	1935	1736	1548	1365	1174	1034	913	803	688	594	522	454