Supplemental Material

Supplemental Material Figure Legends

Supplemental Material Figure 1: Adherence To The Post-Procedure Anticoagulation And Antiplatelet Therapy Protocol From Pivotal Trials Among 31,944 Patients Who Underwent Watchman LAAO And Enrolled In The NCDR LAAO Registry Between January 1, 2016 And November 31, 2018.

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Supplemental Material Table 1. Adverse Events Collected in the LAAO Registry.

Adverse Events
Myocardial Infarction
Endocarditis
Iatrogenic ASD (requiring intervention)
PCI
Pericardial Effusion (requiring drainage)
Pericardial Effusion with tamponade (requiring percutaneous drainage)
Pericardial Effusion without tamponade (requiring percutaneous drainage)
Pericardial Effusion (requiring open cardiac surgery)
Pericarditis
Unplanned Cardiac Surgery
Unplanned Intervention
LAA Occlusion Reintervention
Systemic Thromboembolism (other than stroke)
New requirement for Dialysis

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Non-Device Related Readmission
Device Related Readmission
Device Related Readmission
Device Fracture
Device Migration
Device Systemic Embolism
Device Thrombus
Hemorrhagic Stroke
Ischemic Stroke
Undetermined Stroke
TIA
Intracranial Hemorrhage (other than hemorrhagic stroke)
Bleeding Event
Other Vascular Complications
Access site Bleeding
Hematoma

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GI Bleeding
Retroperitoneal Bleeding
Other Hemorrhage (non-intracranial)
Major Bleeding
Major Vascular Complication
Device Explant
AV Fistula (requiring surgical repair)
Pseudoaneurysm (requiring endovascular repair)
Pseudoaneurysm (requiring surgical repair)
Pseudoaneurysm (requiring thrombin injection only)
Hemothorax (requiring drainage)

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Supplemental Material Table 2. Definitions of Major Adverse Events in the LAAO Registry.

Adverse Event	Definition
Cardiac Arrest	Cardiac arrest is the cessation of cardiac activity. The patient becomes unresponsive with no normal breathing and no signs of circulation. If corrective measures are not taken rapidly, this condition progresses to sudden death. Cardiac arrest should be used to signify an event as described above that is reversed, usually by CPR and/or defibrillation or cardioversion or cardiac pacing.[1]
Ischemic Stroke	An ischemic stroke is an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of infarction of central nervous system tissue.[2]

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Hemorrhagic Stroke	An acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage. Note: Subdural hematomas are intracranial hemorrhagic events and not strokes.[2]
Undetermined Stroke	A stroke of undetermined origin is defined as an acute episode of focal or global neurological dysfunction caused by presumed brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction but with insufficient information to allow categorization as ischemic or hemorrhagic.[2]
Transient Ischemia Attack	A transient ischemic attack (TIA) is a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.[2]
Intracranial Hemorrhage	Rapidly developing signs of neurologic dysfunction and/or headache due to bleeding into the subarachnoid space (the space

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	between the arachnoid membrane and the pai mater of the brain and spinal cord).
Intracerebral	Intracerebral hemorrhage (ICH) bleeding is usually derived from arterioles. The bleeding is directly into the brain, forming a localized hematoma that spreads along white matter pathways. Accumulation of blood occurs over minutes or hours and the neurologic symptoms usually increase gradually over minutes or a few hours.
Subarachnoid	Subarachnoid hemorrhage (SAH) occurs with the rupture of an aneurysm releasing blood directly into the cerebrospinal fluid (CSF) under arterial pressure. The blood spreads quickly within the CSF, rapidly increasing intracranial pressure. Death or deep coma ensues if the bleeding continues. The bleeding usually lasts only a few seconds, but re-bleeding is common. With causes of SAH other than aneurysm rupture, the bleeding is less abrupt and may continue over a longer period of time.

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Subdural	Subdural hematomas form between the dura and the arachnoid membranes and often require surgical treatment to prevent irreversible brain injury and death caused by hematoma expansion, elevated intracranial pressure, and brain herniation.
Systemic Arterial Embolism	Systemic thromboembolism occurs when a blood vessel (venous or arterial) has been obstructed by a blood clot that was dislodged from another site within the circulatory system.
Major Bleeding	Any bleeding requiring hospitalization, and/or causing a decrease in hemoglobin level > 2g/dL, and/or requiring blood transfusion that was not hemorrhagic stroke.
Major Vascular Complication	Vascular complications can include, but are not limited to, access site occlusions, peripheral embolizations, dissections, pseudoaneurysms and/or AV fistulas. Any noted vascular complication must have had an intervention such as a fibrin injection, angioplasty, or surgical repair to qualify. Prolonged

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	pressure does not qualify as an intervention, but ultrasonic guided compression after making a diagnosis of pseudoaneurysm does qualify. A retroperitoneal bleed or hematoma requiring transfusion is not a vascular complication under this data element. To qualify, this adverse outcome should be attributable to this procedure and not related to a previous or subsequent procedure.
Myocardial Infarction	The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI: ● Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following: o Symptoms of ischemia. o New or presumed new significant ST-segment-T wave (ST-T) changes or

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	new left bundle branch block (LBBB). o Development of pathological Q waves in the ECG. o Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. o Identification of an intracoronary thrombus by angiography or autopsy. ● Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased. ● Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (>5 x 99th percentile URL) in patients with normal baseline values (99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia or (ii) new ischemic ECG changes or (iii) angiographic findings consistent

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	with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required. ● Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL. ● Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>10 x 99th percentile URL) in patients with normal baseline cTn values (99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic documented new graft or new native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.[3]

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Pericardial Effusion Requiring Intervention	Pericardial fluid in the pericardial space compromising cardiac filling and requiring percutaneous drainage. If tamponade occurs there would be fluid in the pericardial space compromising cardiac filling, and requiring intervention such as pericardiocentesis. This should be documented by either: 1. Echo showing pericardial fluid and signs of tamponade such as right heart compromise, or 2. Systemic hypotension due to pericardial fluid compromising cardiac function.[4]
Device Embolization	The device became displaced from its initial annular implantation site. The device is no longer in its original position and has navigated to or past the aortic root and/or ascending/descending aorta.

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Supplemental Material Table 3. Candidate Variables Included in Adjusted Logistic Regression Models.

Age, female, race, CHA_2DS_2-VASC score components (congestive heart failure/ left ventricular dysfunction, hypertension, diabetes mellitus, stroke, transient ischemic attack, thromboembolic event, vascular disease), HAS BLED score components (uncontrolled hypertension, abnormal renal function, abnormal liver function, prior bleeding, labile international normalized ratio (INR), alcohol use, antiplatelet drug, nonsteroidal anti-inflammatory drug, increased risk of falls), valvular atrial fibrillation, prior atrial flutter, cardiomyopathy, chronic lung disease, sleep apnea, prior cardiac structural intervention, coronary artery disease, height, weight, blood pressure, hemoglobin, prothrombin time/INR, serum creatinine, platelet count, baseline medications (warfarin, DOAC, P2Y12 inhibitor, DAPT, bridging anticoagulant therapy, transesophageal echocardiogram (TEE) performed, indication for LAAO (increased thromboembolic stroke risk, history of major bleed, high fall risk, labile INR, patient preference, non-compliance with anticoagulation therapy, procedure canceled, device margin residual leak.

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Supplemental Material Table 4. Baseline Characteristics 31,994 LAAO Registry Patients Between 2016 and 2018.

Characteristic	Total	
	N	(%)
Overall	31,944	(100)
Demographics		
Age, mean (SD), years	75.95	(8.08)
Age categories		
<55	426	(1.33)
55 to 64	1977	(6.18)
65 to 74	10319	(32.25)
75 to 84	14853	(46.42)
>=85	4419	(13.81)
Sex		
Male	18828	(58.85)
Female	13153	(41.11)
Race		

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White	29616	(92.57)
Black	1502	(4.69)
Hispanic	114	(0.36)
Asian	523	(1.63)
American Indian/ Alaskan Native	83	(0.26)
Native Hawaiian/ Pacific Islander	43	(0.13)
Other	113	(0.35)
Primary insurance payer		
Medicare/Medicaid	27813	(86.93)
Private health insurance	3726	(11.65)
Other	455	(1.42)
CHA_2DS_2- VASC score, mean (SD)	4.55	(1.46)
Congestive heart failure	11834	(36.99)
Congestive heart failure class		
NYHA class I	2863	(8.95)
NYHA class II	5439	(17.00)

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NYHA class III	2542	(7.95)
NYHA class IV	165	(0.52)
Hypertension	29521	(92.27)
Diabetes mellitus	12138	(37.94)
Prior transient ischemic attack	4625	(14.46)
Prior thromboembolic event	5861	(18.32)
Vascular disease	13728	(42.91)
Prior myocardial infarction	6533	(20.42)
Peripheral arterial disease	4604	(14.39)
Known aortic plaque	1363	(4.26)
HAS-BLED score, mean (SD)	3.01	(1.13)
Uncontrolled hypertension	8407	(26.28)
Abnormal renal function	4358	(13.62)
Abnormal liver function	1012	(3.16)
Prior stroke	8694	(27.17)
Ischemic	4817	(15.06)

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Hemorrhagic	2346	(7.33)
Undetermined	1970	(6.16)
Prior bleeding	22451	(70.17)
Labile INR	3805	(11.89)
Alcohol use	1787	(5.59)
Antiplatelet medication use	8927	(27.90)
Non-steroidal inflammatory drug use	9606	(30.02)
Other history and risk factors		
Clinically relevant prior bleeding	22278	(69.63)
Intracranial	3806	(11.90)
Epistaxis	2059	(6.44)
Gastrointestinal	13407	(41.90)
Other	4820	(15.07)
Fall risk	12571	(39.29)
Genetic coagulopathy	258	(0.81)
Cardiomyopathy	6741	(21.07)

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Ischemic	3447	(10.77)
Non-ischemic	2344	(7.33)
Chronic lung disease	6757	(21.12)
Coronary artery disease	15225	(47.59)
Sleep apnea	8242	(25.76)
Arrhythmia history		
Atrial fibrillation type		
Paroxysmal	16665	(52.09)
Persistent (>7 days)	6794	(21.24)
Long-standing persistent (>1 year)	3111	(9.72)
Permanent	5304	(16.58)
Atrial flutter	4427	(13.84)

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Supplemental Material Table 5. Odds of Adverse Events from Discharge Through 45 +/- 14 Mutually Exclusive Discharge Medication Groupings.

	Unadjusted			Adjusted		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Any adverse event						
Warfarin and Aspirin	reference					
Warfarin	**0.716**	**0.596-0.860**	**<0.001**	**0.637**	**0.525-0.774**	**<0.001**
DOAC and Aspirin	0.936	0.809-1.084	0.377	1.130	0.936-1.364	0.202
DOAC	**0.702**	**0.575-0.857**	**0.001**	**0.734**	**0.579-0.931**	**0.011**
DAPT (P2Y12 and Aspirin)	1.045	0.810-1.347	0.736	0.892	0.674-1.181	0.425
Any major adverse event						
Warfarin and Aspirin	reference					
Warfarin	**0.763**	**0.624-0.933**	**0.008**	**0.656**	**0.530-0.812**	**<0.001**
DOAC and Aspirin	0.980	0.835-1.149	0.802	1.212	0.986-1.491	0.068
DOAC	**0.736**	**0.592-0.914**	**0.006**	**0.766**	**0.591-0.993**	**0.044**
DAPT (P2Y12 and Aspirin)	1.027	0.774-1.363	0.853	0.846	0.618-1.158	0.296

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Any readmissions						
Warfarin and Aspirin	reference					
Warfarin	1.032	0.879-1.224	0.719	1.013	0.844-1.215	0.891
DOAC and Aspirin	1.039	0.895-1.206	0.614	1.112	0.913-1.355	0.293
DOAC	1.001	0.827-1.211	0.993	1.077	0.851-1.362	0.539
DAPT (P2Y12 and Aspirin)	1.070	0.820-1.395	0.619	0.885	0.660-1.188	0.416
Any stroke or TIA						
Warfarin and Aspirin	reference					
Warfarin	1.048	0.616-1.782	0.863	1.013	0.844-1.215	0.891
DOAC and Aspirin	1.429	0.941-2.168	0.094	1.112	0.913-1.355	0.293
DOAC	1.030	0.590-1.796	0.918	1.077	0.851-1.362	0.539
DAPT (P2Y12 and Aspirin)	1.378	0.672-2.827	0.381	0.885	0.660-1.188	0.416
Device-related thrombus						
(among those with TEE)						
Warfarin and Aspirin	reference					
Warfarin	0.797	0.582-1.090	0.156	0.806	0.580-1.120	0.200

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DOAC and Aspirin	0.943	0.728-1.220	0.654	1.021	0.738-1.412	0.902
DOAC	1.019	0.747-1.389	0.906	1.113	0.764-1.621	0.578
DAPT (P2Y12 and Aspirin)	1.801	1.236-2.262	0.002	1.424	0.929-2.183	0.104
Peri-device leak >5mm (among those with TEE)						
Warfarin and Aspirin	Reference					
Warfarin	0.675	0.412-1.107	0.120	0.659	0.392-1.106	0.114
DOAC and Aspirin	0.721	0.479-1.086	0.117	0.775	0.461-1.305	0.338
DOAC	0.893	0.563-1.415	0.630	0.963	0.539-1.719	0.898
DAPT (P2Y12 and Aspirin)	0.532	0.213-1.331	0.178	0.697	0.284-1.711	0.431

OR=odds ratio

95% CI=95% confidence

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Supplemental Material Table 6. Odds of Adverse Events from Discharge Through 6 Months In Mutually Exclusive Discharge Medication Groupings.

Adverse event	Unadjusted			Adjusted		
	OR	95% CI	P value	OR	95% CI	P value
Any adverse event						
Warfarin and Aspirin	reference					
Warfarin	**0.864**	**0.758-0.986**	**0.030**	**0.804**	**0.699-0.925**	**0.002**
DOAC and Aspirin	0.884	0.789-0.991	0.034	1.095	0.945-1.269	0.227
DOAC	0.844	0.731-0.974	0.020	0.949	0.797-1.131	0.562
DAPT (P2Y12 and Aspirin)	0.965	0.790-1.178	0.724	0.823	0.660-1.026	0.083
Any major adverse event						
Warfarin and Aspirin	reference					
Warfarin	**0.917**	**0.804-1.046**	**0.195**	**0.847**	**0.735-0.976**	**0.022**
DOAC and Aspirin	0.913	0.815-1.024	0.120	1.105	0.952-1.283	0.189
DOAC	0.839	0.726-0.970	0.018	0.920	0.769-1.100	0.358
DAPT (P2Y12 and Aspirin)	1.033	0.848-1.260	0.744	0.835	0.669-1.042	0.110

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Any readmission						
Warfarin and Aspirin	reference					
Warfarin	0.992	0.882-1.115	0.888	0.975	0.860-1.105	0.692
DOAC and Aspirin	1.023	0.923-1.133	0.667	1.052	0.916-1.207	0.474
DOAC	1.093	0.962-1.241	0.172	1.124	0.957-1.320	0.153
DAPT (P2Y12 and Aspirin)	**0.995**	**0.831-1.192**	**0.956**	**0.806**	**0.658-0.986**	**0.036**
Any stroke or TIA						
Warfarin and Aspirin	reference					
Warfarin	1.003	0.729-1.379	0.986	1.019	0.727-1.428	0.912
DOAC and Aspirin	1.228	0.948-1.591	0.120	1.118	0.804-1.557	0.507
DOAC	1.144	0.832-1.573	0.408	0.990	0.669-1.465	0.961
DAPT (P2Y12 and Aspirin)	1.154	0.730-1.826	0.540	0.897	0.540-1.490	0.675

OR=odds ratio

95% CI=95% confidence intervals

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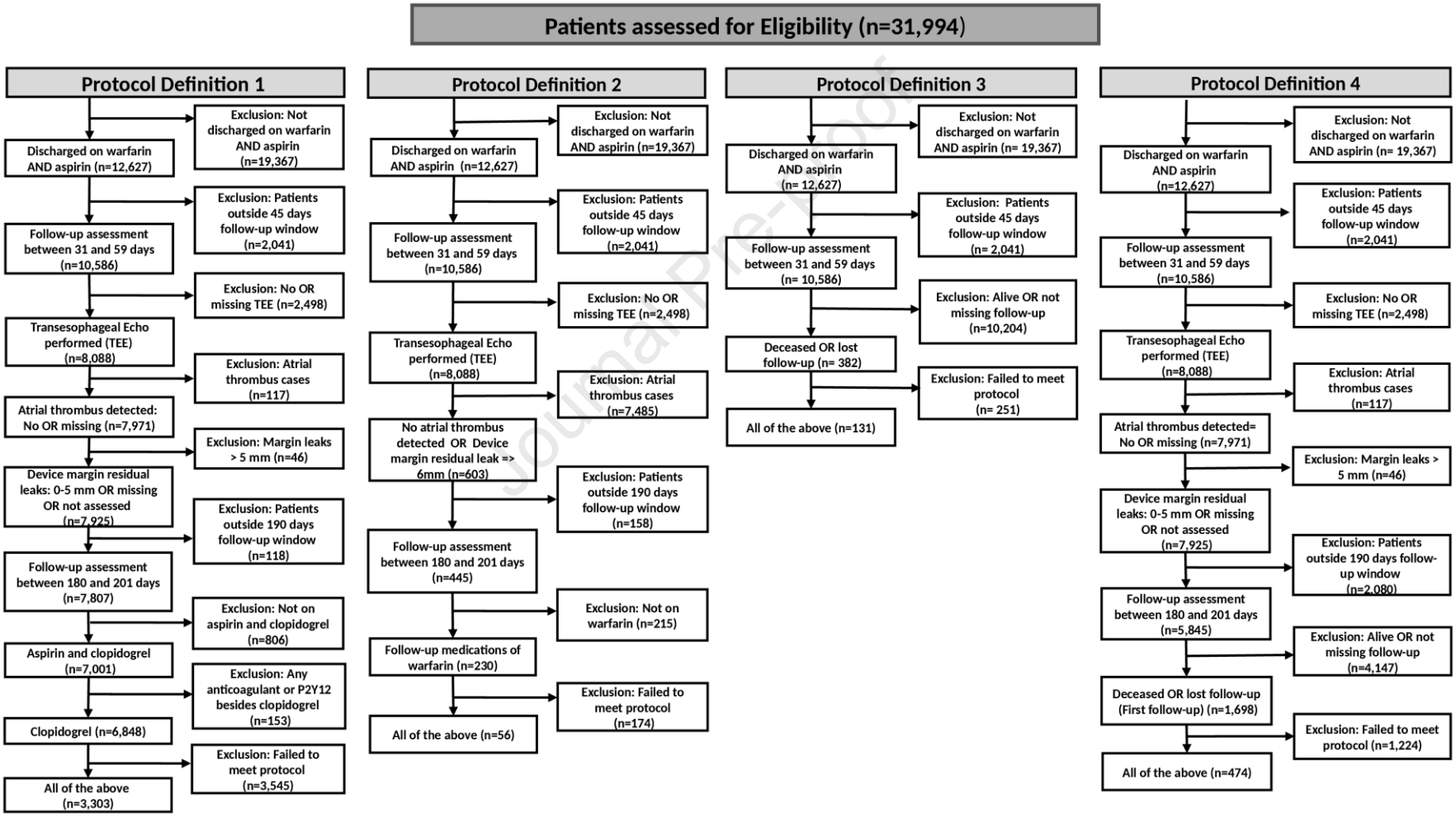
Supplemental Material Figure 1. Adherence to the Post-Procedure Anticoagulation And Antiplatelet Therapy Protocol From Pivotal Trials Among 31,944 Patients Who Underwent Watchman LAAO and Enrolled in the NCDR LAAO Registry Between January 1, 2016 and November 31, 2018.



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