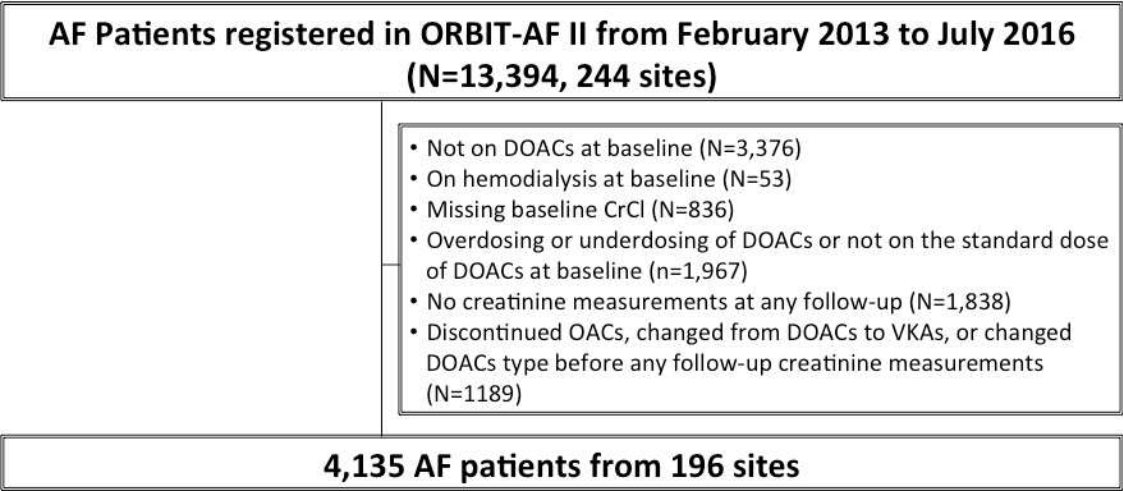


eAppendix 1. Analysis strategy to evaluate, in patients treated with DOACs, the proportion of patients eligible for dose adjustment during follow-up, and of these, the proportion of patients who received a reduction in dose

- Identify patients whose renal function declines enough to meet the dose adjustment criteria and provide the frequency and percentage of patients meeting the criteria by DOAC type and overall:
 - **Dabigatran:** CrCl from >30 at baseline to ≤30 at any follow-up time
 - **Rivaroxaban:** CrCl from >50 at baseline to ≤50 at any follow-up time
 - **Edoxaban:** CrCl from >50 at baseline to ≤50 at any follow-up time
 - **Apixaban:** Serum creatinine from ≤1.5 at baseline to >1.5 at any follow-up time.
- In above identified patients, evaluate whether the dose of DOACs are appropriately reduced or not and provide the frequency and percentage of patients based on the below criteria:
 - **Dabigatran**
 - 150 mg twice daily is standard dose.
 - CrCl 15 to 30 mL/min: 75 mg twice daily unless patient receiving concomitant dronedarone, then avoid concurrent use.
 - CrCl <15 mL/min or on dialysis: not recommended.
 - **Rivaroxaban**
 - 20 mg once daily is standard dose.
 - CrCl 15 to 50 mL/min: 15 mg once daily.
 - CrCl <15 mL/min or on dialysis: Avoid use.
 - **Edoxaban**
 - 60 mg once daily is standard dose.
 - CrCl 15 to 50 mL/min: 30 mg once daily.
 - CrCl <15 mL/min or on dialysis: Avoid use.
 - CrCl >95 mL/min: Avoid use.
 - **Apixaban**
 - 5 mg twice daily unless patient has any 2 of the following: Age ≥80 years, body weight ≤60 kg, or serum creatinine >1.5 mg/dL, then reduce dose to 2.5 mg twice daily.
 - **Note** – Patients who are taken off drug because CrCl creatinine decreases below the threshold in which the drug is recommended are considered appropriately dosed.

eFigure 1. Cohort creation for the specific aim evaluating, in patients treated with DOACs, the proportion of patients eligible for dose adjustment during follow-up, and of these, the proportion of patients who received a reduction in dose

Abbreviation: AF, atrial fibrillation; OAC, oral anticoagulants; CrCl, creatinine clearance; DOACs, direct oral anticoagulants



eTable 1. Numbers of patients who were censored at each time-point

	No of patients	Percent	Cumulative Frequency	Cumulative Percent
6 months	279	4.2%	279	4.2%
12 months	3519	52.7%	3798	56.8%
18 months	1162	17.4%	4960	74.2%
24 months	1722	25.8%	6682	100.0%

eTable 2. Numbers of patients who were defined as SRF and WRF at each time-point

	Visit at which patient was censored				Total
	6 months	12 months	18 months	24 months	
SRF	235	2776	878	1250	5139
	84.2%	78.9%	75.6%	72.6%	
WRF	44	743	284	472	1543
	15.8%	21.1%	24.4%	27.4%	
Total	279	3519	1162	1722	6682

Abbreviations: SRF, stable renal function; WRF, worsening renal function

eTable 3. Comparison of baseline characteristics and provider specialty between patients with appropriately reduced NOACs and those without

	Overall N=145	Not Appropriately Reduced N=116	Appropriately Reduced N=29
<u>Demographics</u>			
Age, median (IQR)	79.0 (75.0, 82.0)	79.0 (74.5, 83.0)	80.0 (77.0, 82.0)
Male	62 (42.8%)	48 (41.4%)	14 (48.3%)
Race			
White	127 (87.6%)	102 (87.9%)	25 (86.2%)
Black/African American	7 (4.8%)	6 (5.2%)	1 (3.4%)
Hispanic	4 (2.8%)	3 (2.6%)	1 (3.4%)
<u>Medical History</u>			
Current smoker	6 (4.1%)	5 (4.3%)	1 (3.4%)
Former / recent smoker	64 (44.1%)	47 (40.5%)	17 (58.6%)
Hypertension	127 (87.6%)	100 (86.2%)	27 (93.1%)
Hyperlipidemia	109 (75.2%)	85 (73.3%)	24 (82.8%)
Diabetes	33 (22.8%)	26 (22.4%)	7 (24.1%)
Chronic kidney disease	54 (37.2%)	36 (31.0%)	18 (62.1%)
Gastrointestinal bleed	6 (4.1%)	6 (5.2%)	0 (0.0%)
Congestive heart failure	43 (29.7%)	37 (31.9%)	6 (20.7%)
Pacemaker	14 (9.7%)	12 (10.3%)	2 (6.9%)
Cerebrovascular disease	30 (20.7%)	20 (17.2%)	10 (34.5%)
History of coronary artery disease	57 (39.3%)	46 (39.7%)	11 (37.9%)
Prior myocardial infarction	20 (13.8%)	16 (13.8%)	4 (13.8%)
<u>Risk Score</u>			
CHA ₂ DS ₂ VASc score, median (IQR)	4.0 (4.0, 5.0)	4.0 (4.0, 5.0)	5.0 (4.0, 6.0)
ATRIA bleeding score, median (IQR)	3.0 (3.0, 5.0)	3.0 (3.0, 6.0)	3.0 (3.0, 4.0)
ORBIT bleeding score, median (IQR)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	3.0 (2.0, 4.0)

Vital Signs and AF Status

BMI (kg/m ²), median (IQR)	28.2 (24.8, 31.2)	28.4 (24.7, 31.3)	27.7 (25.1, 29.1)
Heart rate (bpm), median (IQR)	72.0 (64.0, 86.0)	73.0 (62.0, 87.5)	72.0 (64.0, 79.0)
SBP (mm Hg), median (IQR)	132.0 (120.0, 142.0)	132.0 (120.0, 146.0)	130.0 (122.0, 136.0)
DBP (mm Hg), median (IQR)	72.0 (66.0, 80.0)	72.0 (66.0, 80.0)	74.0 (68.0, 80.0)

Echocardiographic Assessment

LVEF, median (IQR)	55.0 (50.0, 60.0)	55.0 (50.0, 60.0)	60.0 (50.0, 60.0)
LA diameter (cm), median (IQR)	4.2 (3.7, 4.7)	4.2 (3.8, 4.6)	3.9 (3.3, 5.0)

Laboratory Data

sCr (mg/dL), median (IQR)	1.0 (0.8, 1.3)	0.9 (0.8, 1.2)	1.1 (1.0, 1.3)
Hemoglobin (g/dL), median (IQR)	12.7 (11.5, 14.1)	12.6 (11.5, 14.0)	13.3 (11.4, 14.6)
CrCl (ml/min), median (IQR)	59.0 (53.9, 69.6)	59.8 (54.0, 71.9)	55.7 (51.7, 59.2)

Type of AF

First Detected / New Onset	56 (38.6%)	45 (38.8%)	11 (37.9%)
Paroxysmal Atrial Fibrillation	47 (32.4%)	33 (28.4%)	14 (48.3%)
Persistent Atrial Fibrillation	28 (19.3%)	25 (21.6%)	3 (10.3%)
Permanent Atrial Fibrillation	14 (9.7%)	13 (11.2%)	1 (3.4%)

Provider Specialty

Internal Medicine / Primary Care	21 (14.5%)	17 (14.7%)	4 (13.8%)
Cardiology	113 (77.9%)	90 (77.6%)	23 (79.3%)
Electrophysiology	41 (28.3%)	35 (30.2%)	6 (20.7%)

Region

West	19 (13.1%)	15 (12.9%)	4 (13.8%)
Northeast	30 (20.7%)	25 (21.6%)	5 (17.2%)
Midwest	24 (16.6%)	17 (14.7%)	7 (24.1%)
South	72 (49.7%)	59 (50.9%)	13 (44.8%)

Abbreviations: IQR, interquartile range; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction; LA, left atrium; serum Cr, serum creatinine; CrCl, creatinine clearance; AF, atrial fibrillation