ATRIAL FIBRILLATION AND POTENTIAL GAPS IN CARE

BACKGROUND

Atrial fibrillation (Afib) is the most common sustained cardiac arrhythmia worldwide.[1,2] In 2019, an estimated 2.7 million to 6.1 million individuals living in the United States (US) alone have Afib, with approximately 12 million US cases projected by year 2030.[1,2] Common risk factors for incidence of Afib include advancing age, hypertension, smoking, diabetes and ischemic heart disease.[2] Afib-affected individuals have a four-to-fivefold increased risk of lifetime stroke as compared to individuals not affected by Afib.[3] Afib-associated strokes have consistently been classified as more debilitating, more deadly, and more likely to recur than strokes of other etiologies.[1–3] Given this information, it is not surprising that Afib-associated strokes are also linked to higher hospital, physician, and nursing home-related costs.[1,4] Despite increased risk and severity of Afib-associated stroke, appropriate pharmacological anticoagulation serves as a major modifiable protective factor against stroke in patients living with Afib.[1,3,5]

Figure 1. CHA_2DS_2VASc criteria and scoring system for stroke risk in atrial fibrillation.

Stroke risk factors	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Aged ≥75 years	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease [prior MI, PAD, or aortic plaque]	1
Aged 65–74 years	1
Sex category [i.e. female gender]	1

Pharmacological stroke prophylaxis within the Afib population is achieved through oral anticoagulant therapy.[1,3,5] The chronic use of oral anticoagulants within the Afib population reduces the ability of blood to clot within the atria during fibrillation and decreases stroke risk. In 2019 the American Heart Association (AHA)/ American College of Cardiology (ACC)/ Heart Rhythm Society (HRS) Focused Update of the 2014 Guideline for Management of Patients with Atrial Fibrillation was published. In the selection of appropriate candidates for thromboembolism prophylaxis, emphasis is placed on balancing risks and benefits.[5] The guideline identified the CHA_2DS_2VASc risk assessment criteria (Figure 1) as an appropriate tool to guide pharmacological decision-making within the Afib population.[3,5] CHA_2DS_2 stands for (**C**ongestive heart failure, **H**ypertension, **A**ge (> 65 = 1 point, > 75 = 2 points), **D**iabetes, previous **S**troke/transient ischemic attack (2 points). **VASc** stands for vascular disease (peripheral arterial disease, previous myocardial infarction, aortic atheroma), and sex category (female gender) is also included in this scoring system. For patients with AFib and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended.[3,5] Common therapeutic choices for stroke prevention in atrial fibrillation include non-vitamin K oral anticoagulants, or NOACs, [apixaban (Eliquis), edoxaban (Savaysa), dabigatran (Pradaxa), and rivaroxaban (Xarelto)], and vitamin K antagonists [warfarin (Coumadin)].[3] While the guideline recommends NOAC therapy over warfarin therapy in indicated

populations, the American College of Chest Physicians (CHEST) emphasizes the importance of patient preference and cost in this decision.[3] Detailed tables of the recommendations for selecting an anticoagulant regimen can be found in Appendix A.[5]

MS-DUR conducted an analysis of Medicaid beneficiaries with a diagnosis of Afib to assess potential gaps in care. Beneficiaries with a diagnosis of Afib and indication for chronic antithrombotic therapy based on CHA_2DS_2VASc criteria but not on oral anticoagulant therapy were identified.

METHODS

A retrospective analysis was conducted using Mississippi Medicaid fee-for-service (FFS) and coordinated care organization [CCOs: UnitedHealthcare (UHC), Magnolia (MAG), and Molina (MOL)] claims for the period of December 1, 2018 to November 30, 2019. Medicaid beneficiaries with atrial fibrillation were identified using the CMS Chronic Conditions Warehouse (CCW) algorithm of at least 1 inpatient claim or 2 outpatient claims at least 30 days apart using the first two diagnosis codes. Beneficiaries that were dual-eligible in Medicaid and Medicare at any time during the study period were excluded from the analysis. Information on the beneficiaries' race, gender, age, and health plan (FFS/UHC/MAG/MOL) was summarized in the analysis. Age and health plan were assessed as of the date for the first Afib claim in the analysis period, hereafter referred to as the index Afib diagnosis date.

CHA_2DS_2-VASc *stroke risk score*

For each beneficiary with Afib, CHA_2DS_2-VASc stroke risk score was determined to assess stroke risk. CHA_2DS_2-VASc risk score was calculated in the 12 month period prior to the index Afib diagnosis date based on diagnoses for congestive heart failure, hypertension, diabetes, vascular disease, prior stroke or thromboembolism or transient ischemic attack, age (65-74 years, ≥75 years), and gender. The CHA_2DS_2-VASc risk score was dichotomized into two categories: high and low. For females, the threshold for high CHA_2DS_2-VASc risk score was 3 or more, while it was 2 or more for males.

Prior bleeding events

History of bleeding events was assessed for each beneficiary with Afib in the 12 months prior to the index Afib diagnosis date. A history of major bleeding events as defined by medical claims of gastrointestinal bleeding (MGB), intracranial hemorrhage (ICH), and major bleeding from other sites was assessed for the analyses.

Anticoagulant drug utilization

Finally, for beneficiaries with Afib having high CHA_2DS_2-VASc risk scores and no history of bleeding events, anticoagulant drug utilization was assessed in the study period. Anticoagulant drugs included in the assessment were warfarin, apixaban, dabigatran, rivaroxaban, betrixaban, and edoxaban. (*Although betrixaban does not have an indication for stroke prophylaxis, utilization was assessed. There were no claims found for betrixaban during the study period.)* As a follow-up to our primary analysis, any hospitalization event experienced by beneficiaries with Afib who had a high CHA_2DS_2-VASc risk score, no history of bleeding events, and no anticoagulant drug use during the analysis period was flagged.

RESULTS

Table 1 provides a descriptive summary of Medicaid beneficiaries with a diagnosis of atrial fibrillation during the study period.

TABLE 1: Descriptive Summary of Beneficiaries with Atrial Fibrillation (AFib) Diagnosis Enrolled in Medicaid (FFS and CCOs) Who Are Not Dual Eligible in Medicare (Dec 2018 - Nov 2019)

Characteristics	Category	Fee for Service		United Health Care		Magnolia		Molina		Total (across all plans)	
		N	%	N	%	N	%	N	%	N	%
Race	White	138	40.8%	101	37.4%	135	35.2%	12	38.7%	386	37.8%
	African American	151	44.7%	124	45.9%	170	44.4%	11	35.5%	456	44.6%
	Other	49	14.5%	45	16.7%	78	20.4%	8	25.8%	180	17.6%
	Total	338	100.0%	270	100.0%	383	100.0%	31	100.0%	1022	100.0%
Gender											
Male	CHA_2DS_2-VASc score < 2	45	23.6%	31	20.3%	48	25.1%	6	27.3%	130	23.3%
	CHA_2DS_2-VASc score ≥ 2	146	76.4%	122	79.7%	143	74.9%	16	72.7%	427	76.7%
	Total	191	100.0%	153	100.0%	191	100.0%	22	100.0%	557	100.0%
Female	CHA_2DS_2-VASc score < 3	42	28.6%	41	35.0%	55	28.6%	7	77.8%	145	31.2%
	CHA_2DS_2-VASc score ≥ 3	105	71.4%	76	65.0%	137	71.4%	2	22.2%	320	68.8%
	Total	147	100.0%	117	100.0%	192	100.0%	9	100.0%	465	100.0%
Age (as of index AF diagnosis in the study analysis period)	< 18 years	0	0.0%	0	0.0%	3	0.7%	1	3.3%	4	0.4%
	18-44 years	35	10.4%	41	15.2%	42	11.0%	9	29.0%	127	12.4%
	45-64 years	276	81.7%	229	84.8%	338	88.3%	21	67.7%	864	84.5%
	65-74 years	18	5.3%	0	0.0%	0	0.0%	0	0.0%	18	1.8%
	≥ 75 years	9	2.6%	0	0.0%	0	0.0%	0	0.0%	9	0.9%
	Total	338	100.0%	270	100.0%	383	100.0%	31	100.0%	1022	100.0%
Prior Bleeding Event (in the 12 months prior to the first Afib diagnosis in the study analysis period)											
Yes	Anticoagulant use	68	57.6%	69	71.9%	80	63.0%	5	50.0%	222	63.2%
	No anticoagulant use	50	42.4%	27	28.1%	47	37.0%	5	50.0%	129	36.8%
	Total	118	100.0%	96	100.0%	127	100.0%	10	100.0%	351	100.0%
No	Anticoagulant use	121	55.0%	116	66.7%	181	71%	13	61.9%	431	64.2%
	No anticoagulant use	99	45.0%	58	33.3%	75	29%	8	38.1%	240	35.8%
	Total	220	100.0%	174	100.0%	256	100%	21	100.0%	671	100.0%

Note: Patients with Afib were identified using the CMS Chronic Conditions warehouse algorithm of at least 1 inpatient or 2 outpatient claims for Afib in the first two diagnosis codes

History of bleeding was identified from medical claims (inpatient and outpatient) using all diagnosis codes for any of the three following categories: major gastrointestinal bleeding, intracranial hemorrhage, other bleeding events

Anticoagulant drugs included: warfarin, apixaban, dabigatran, rivaroxaban, betrixaban*, and edoxaban (*No claims were found for betrixaban)

- A total of 1022 beneficiaries had a diagnosis of AFib during the study period.
- Of the 1022 beneficiaries, 54.5% (557) were males and 45.5% (465) were females.

- 73.1% (747) of beneficiaries with Afib diagnosis were calculated to have a high CHA_2DS_2-VASc risk score ($\geq$ 2 for males or $\geq$ 3 for females).
- The majority of beneficiaries (84.5%) were ages 45-64 years.
- 65.7% (671) of beneficiaries with an Afib diagnosis had no history of bleeding events with 35.8% (240) of those beneficiaries not having a claim for anticoagulant therapy.

Table 2 combines CHA_2DS_2-VASc risk scores and history of prior bleeding events to identify beneficiaries that are candidates for anticoagulant therapy based on claims data.

TABLE 2: Current Anticoagulant Use Among Medicaid Beneficiaries with Afib with High CHA_2DS_2-VASc Risk Score and No Prior History of Bleeding (Dec 2018 - Nov 2019)

Plan (at index AF diagnosis)	Gender	High CHA_2DS_2-VASc Risk Score*	No prior bleeding**	Anticoagulant use***	
				Yes	No
Fee for Service	Male	146	82	51	31
	Female	105	67	39	28
	Total	251	149	90	59
United Health Care	Male	122	73	52	21
	Female	76	41	30	11
	Total	198	114	82	32
Magnolia	Male	143	89	66	23
	Female	137	87	60	27
	Total	280	176	126	50
Molina	Male	16	11	8	3
	Female	2	1	1	0
	Total	18	12	9	3
Total		747	451	307	**144**

*High CHA_2DS_2-VASc risk score = $\geq$ 2 for males, $\geq$ 3 females.

**History of prior bleeding events were checked for during the 12-month period prior to the index AFib diagnosis date among those that had high CHA_2DS_2-VASc risk scores.

***Anti-thrombin use in the current analysis period was assessed for those that had high CHA_2DS_2-VASc risk scores and no prior bleeding events.

- For the 747 Afib beneficiaries with a high CHA_2DS_2-VASc risk score, 451 had no prior bleeding events identified.
- **Of those with a high CHA_2DS_2-VASc risk score and no prior bleeding events identified, 144 beneficiaries had no anticoagulant claim during the study period.**

For additional analysis, MS-DUR examined hospitalization events experienced by beneficiaries with Afib who had a high CHA_2DS_2-VASc risk score, no history of bleeding events, and no anticoagulant drug use during the analysis period. (Table 3)

TABLE 3: Hospitalizations Among Afib Beneficiaries with High CHA_2DS_2-VASc Risk Score, No Prior Bleeding, and No Anticoagulant Use (Dec 2018 - Nov 2019)

Gender	Any hospitalization	FFS	UHC	MAG	MOL	Total
Female	Yes	16	3	14	-	33
	No	12	8	13	-	33
Male	Yes	17	11	6	3	37
	No	14	10	17	0	41

- 48.6% (70) of beneficiaries with high risk scores, no prior bleeding events identified, and no anticoagulant use were hospitalized during the study.
- Regardless of the reason for the hospitalizations, these hospitalizations represent opportunities for transitions of care services to recognize and initiate oral anticoagulant therapy for these 70 beneficiaries.

CONCLUSIONS

Although a small number of Medicaid beneficiaries have a diagnosis of Afib, these individuals are at a significantly increased risk of lifetime stroke compared to those without Afib. Afib-associated strokes have been shown to be more debilitating, have higher mortality, and are associated with higher costs than strokes of other etiologies. Preventing even a small number of Afib-associated strokes can have a significant impact. Opportunities exist for beneficiaries diagnosed with Afib to be properly treated with anticoagulants for stroke prophylaxis.

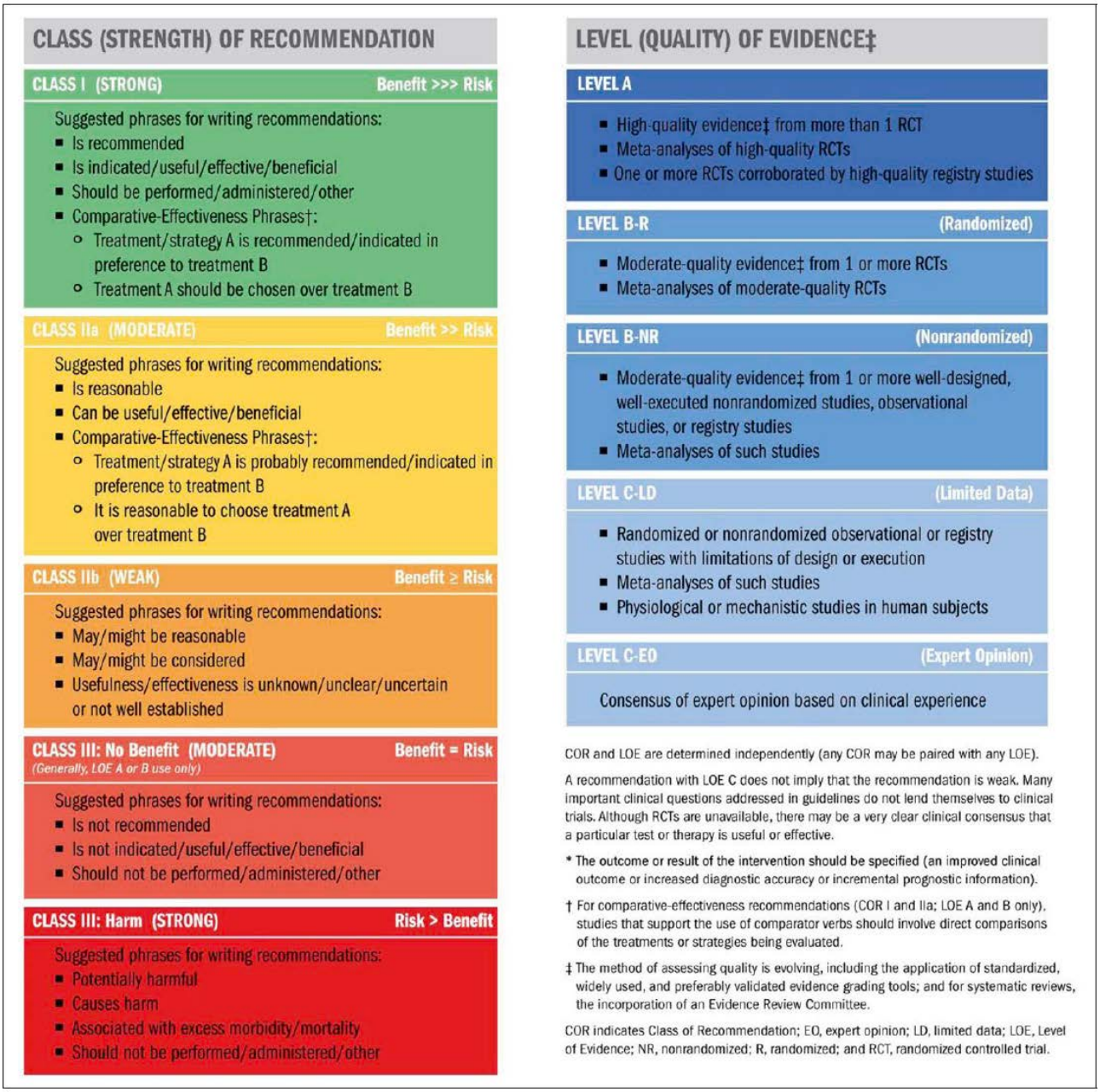
RECOMMENDATIONS

1) DOM should implement an educational intervention notifying prescribers of those beneficiaries diagnosed with Afib that are potential candidates for anticoagulant therapy.

References:

1. Alkhouli M, Noseworthy PA, Rihal CS, Holmes DR. Stroke Prevention in Nonvalvular Atrial Fibrillation: A Stakeholder Perspective. *J Am Coll Cardiol*. 2018;71(24):2790-2801. doi:10.1016/j.jacc.2018.04.013
2. CDC. Atrial Fibrillation | cdc.gov. Centers for Disease Control and Prevention. https://www.cdc.gov/heartdisease/atrial_fibrillation.htm. Published December 9, 2019. Accessed February 3, 2020.
3. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. *CHEST*. 2018;154(5):1121-1201. doi:10.1016/j.chest.2018.07.040
4. Wang G, Tong X, George MG. Atrial Fibrillation Associated Costs for Stroke Hospitalizations of Medicare Beneficiaries in the Stroke Belt of the United States. *J Atr Fibrillation*. 2013;5(6):7-11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539299/. Accessed February 18, 2020.
5. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2019;74(1):104-132. doi:10.1016/j.jacc.2019.01.011

APPENDIX A



CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Note: COR – Class of Recommendation; LOE – Level of Evidence

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(1 of 3)*

COR	LOE	Recommendations
I	A B B B B-R	**1. For patients with AF and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended. Options include:** • **Warfarin [Coumadin, Jantoven] - (LOE: A)** • **Dabigatran [Pradaxa] - (LOE: B)** • **Rivaroxaban [Xarelto] - (LOE: B)** • **Apixaban [Eliquis] - (LOE: B) or** • **Edoxaban [Savaysa] - (LOE: B-R)** **MODIFIED**: This recommendation has been updated in response to the approval of edoxaban, a new factor Xa inhibitor. More precision in the use of CHA_2DS_2-VASc scores is specified in subsequent recommendations. The LOEs for warfarin, dabigatran, rivaroxaban, and apixaban have not been updated for greater granularity as per the new LOE system. (Section 4.1. in the 2014 AF Guideline) The original text can be found in Section 4.1 of the 2014 AF guideline. Additional information about the comparative effectiveness and bleeding risk of NOACs can be found in Section 4.2.2.2.
I	A	**2. NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve).** **NEW**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. When the NOAC trials are considered as a group, the direct thrombin inhibitor and factor Xa inhibitors were at least noninferior and, in some trials, superior to warfarin for preventing stroke and systemic embolism and were associated with lower risks of serious bleeding.
I	A	**3. Among patients treated with warfarin, the international normalized ratio (INR) should be determined at least weekly during initiation of anticoagulant therapy and at least monthly when anticoagulation (INR in range) is stable.** **MODIFIED:** "Antithrombotic" was changed to "anticoagulant."
I	B	**4. In patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve), the CHA_2DS_2-VASc score is recommended for assessment of stroke risk.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. Patients with AF with bioprosthetic heart valves are addressed in the supportive text. (Section 4.1. in the 2014 AF guideline)
I	B	**5. For patients with AF who have mechanical heart valves, warfarin is recommended.** **MODIFIED:** New information is included in the supportive text.
I	B	**6. Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent.** **MODIFIED:** "Antithrombotic" was changed to "anticoagulant."

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(2 of 3)*

I	B-NR	**7. Renal function and hepatic function should be evaluated before initiation of a NOAC and should be reevaluated at least annually.** **MODIFIED**: Evaluation of hepatic function was added. LOE was updated from B to B-NR. New evidence was added. (Section 4.1. in the 2014 AF Guideline)
I	C	**8. In patients with AF, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risks and relative risks of stroke and bleeding, as well as the patient's values and preferences.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C	**9. For patients with atrial flutter, anticoagulant therapy is recommended according to the same risk profile used for AF.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C	**10. Reevaluation of the need for and choice of anticoagulant therapy at periodic intervals is recommended to reassess stroke and bleeding risks.** **MODIFIED: "**Antithrombotic" was changed to "anticoagulant."
I	C-EO	**11. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) who are unable to maintain a therapeutic INR level with warfarin, use of a NOAC is recommended.** **MODIFIED:** Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. (Section 4.1. in the 2014 AF Guideline)
IIa	B	**12. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 0 in men or 1 in women, it is reasonable to omit anticoagulant therapy.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve. (Section 4.1. in the 2014 AF Guideline)
IIb	B-NR	**13. For patients with AF who have a CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage chronic kidney disease (CKD; creatinine clearance [CrCl] <15 mL/min) or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0 to 3.0) or apixaban for oral anticoagulation.** **MODIFIED**: New evidence has been added. LOE was updated from B to B-NR. (Section 4.1. in the 2014 AF Guideline)

Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits *(3 of 3)*

IIb	B-R	**14. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and moderate-to-severe CKD (serum creatinine ≥1.5 mg/dL [apixaban], CrCl 15 to 30 mL/min [dabigatran], CrCl ≤50 mL/min [rivaroxaban], or CrCl 15 to 50 mL/min [edoxaban]) with an elevated CHA_2DS_2-VASc score, treatment with reduced doses of direct thrombin or factor Xa inhibitors may be considered (e.g., dabigatran, rivaroxaban, apixaban, or edoxaban).** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and this recommendation has been changed in response to the approval of edoxaban. LOE was updated from C to B-R. (Section 4.1. in the 2014 AF Guideline)
IIb	C- LD	**15. For patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) and a CHA_2DS_2-VASc score of 1 in men and 2 in women, prescribing an oral anticoagulant to reduce thromboembolic stroke risk may be considered.** **MODIFIED**: Exclusion criteria are now defined as moderate-to-severe mitral stenosis or a mechanical heart valve, and evidence was added to support separate risk scores by sex. LOE was updated from C to C-LD. (Section 4.1. in the 2014 AF Guideline)
III: No Benefit	C-EO	**16. In patients with AF and end-stage CKD or on dialysis, the direct thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban or edoxaban are not recommended because of the lack of evidence from clinical trials that benefit exceeds risk.** **MODIFIED**: New data have been included. Edoxaban received FDA approval and has been added to the recommendation. LOE was updated from C to C-EO. (Section 4.1. in the 2014 AF Guideline)
III: Harm	B-R	**17. The direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve.** **MODIFIED**: Evidence was added. LOE was updated from B to B-R. Other NOACs are addressed in the supportive text. (Section 4.1. in the 2014 AF Guideline)