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Alosa Health

Balanced information for better care

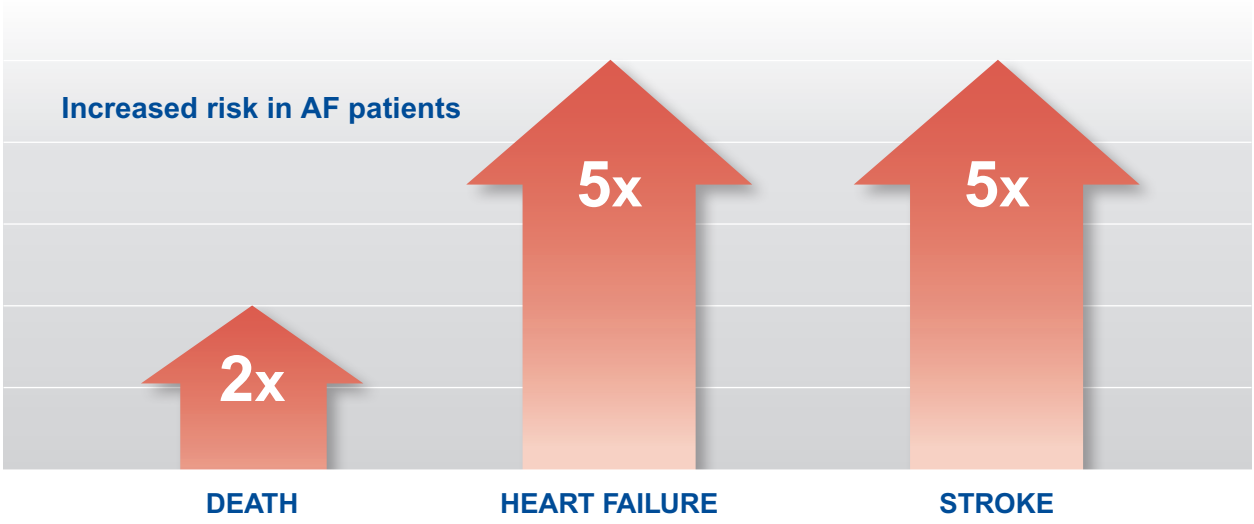
Caring for patients with atrial fibrillation

Current evidence on anticoagulants, rate control, and rhythm control

Atrial fibrillation (AF) sharply increases the risk of stroke and other cardiovascular events

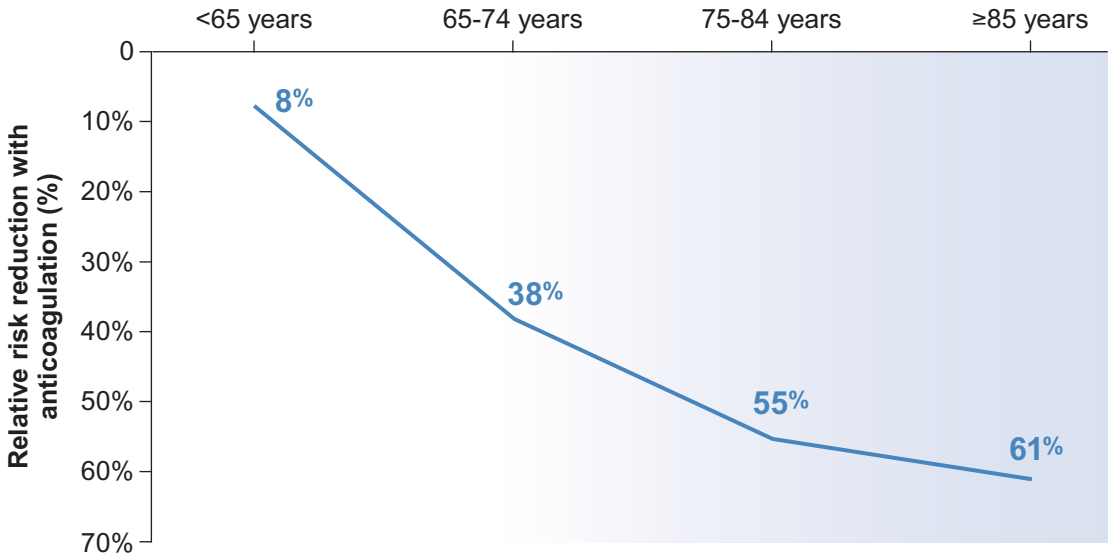
More than 5 million people in the U.S. have AF, particularly the elderly.[1]

FIGURE 1. Patients with AF have increased morbidity and mortality compared to patients of the same age without AF.[2]



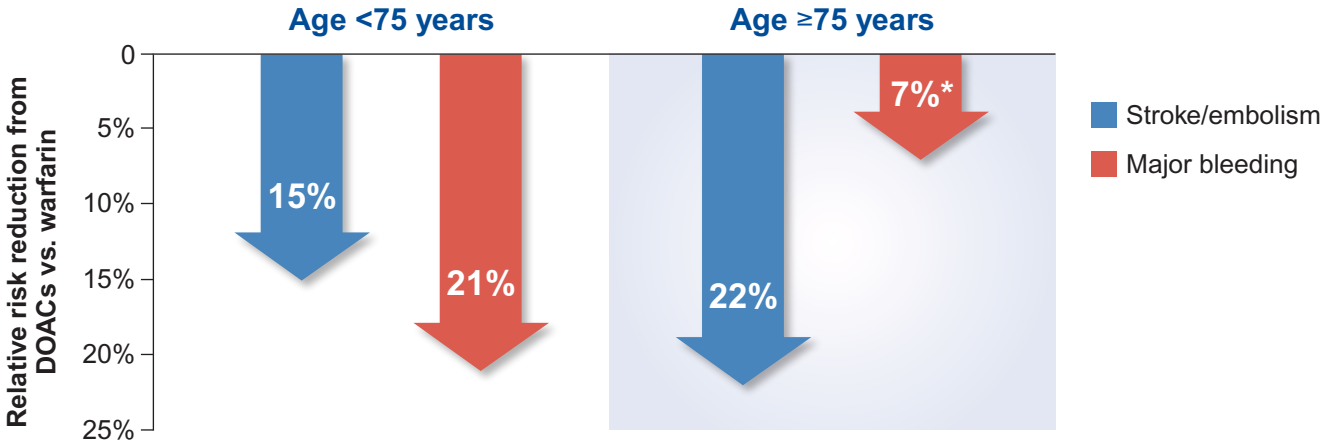
Anticoagulation substantially lowers the risk of stroke, with even more benefits for older adults.

FIGURE 2. As age increases, warfarin significantly reduces the risk of stroke.[3]



Direct oral anticoagulants (DOACs) have proven to be more useful than warfarin

FIGURE 3. A meta-analysis of DOAC trials found patients ≥75 benefited more from DOACs compared to warfarin in preventing stroke and embolism, with a similar risk of bleeding.[4]

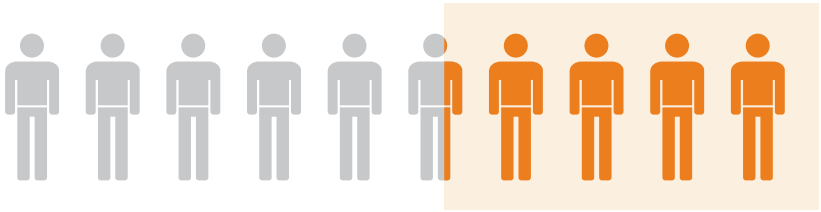


*The reduced bleeding risk with DOACs compared to warfarin was significant in patients <75, but not in those ≥75. In some trials, older patients at higher risk received lower DOAC doses.

For many patients taking warfarin, switching to a DOAC can provide more stroke protection and less bleeding risk.

Despite their benefits, anticoagulants are still under-prescribed in AF.

FIGURE 4. At one academic center, just over 40% of patients who had a CHA_2DS_2-VASc score of 2 or greater were not receiving anticoagulation.[5]



Prescribed anticoagulation (57%) **No anticoagulation (43%)**

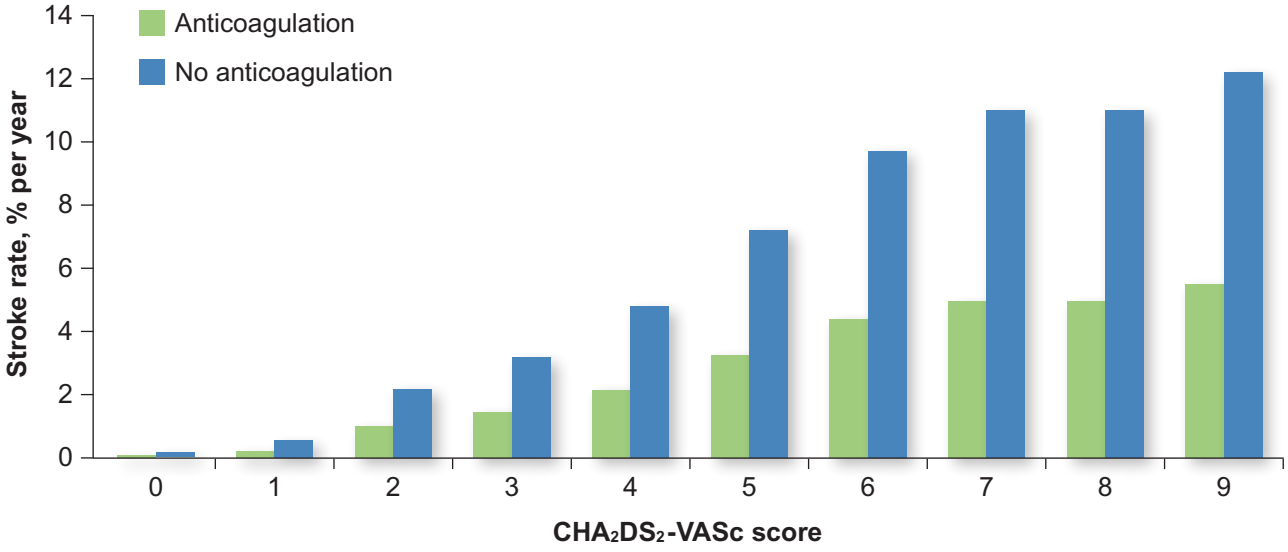
Estimate the need for treatment with the CHA_2DS_2-VASc score in patients with AF

TABLE 1. The CHA_2DS_2-VASc score is based on readily available clinical characteristics.[6]

Letter	Characteristic	Points (if yes)
C	congestive heart failure*	1
H	hypertension	1
A	age ≥75 years old	2
D	diabetes	1
S	stroke, TIA, or thromboembolism	2
V	vascular disease**	1
A	age 65-74 years	1
S	sex: female	1
		Maximum 9 points

* **Congestive heart failure:** left ventricle ejection fraction ≤40
** **Vascular disease:** myocardial infarction, peripheral vascular disease, or aortic plaque

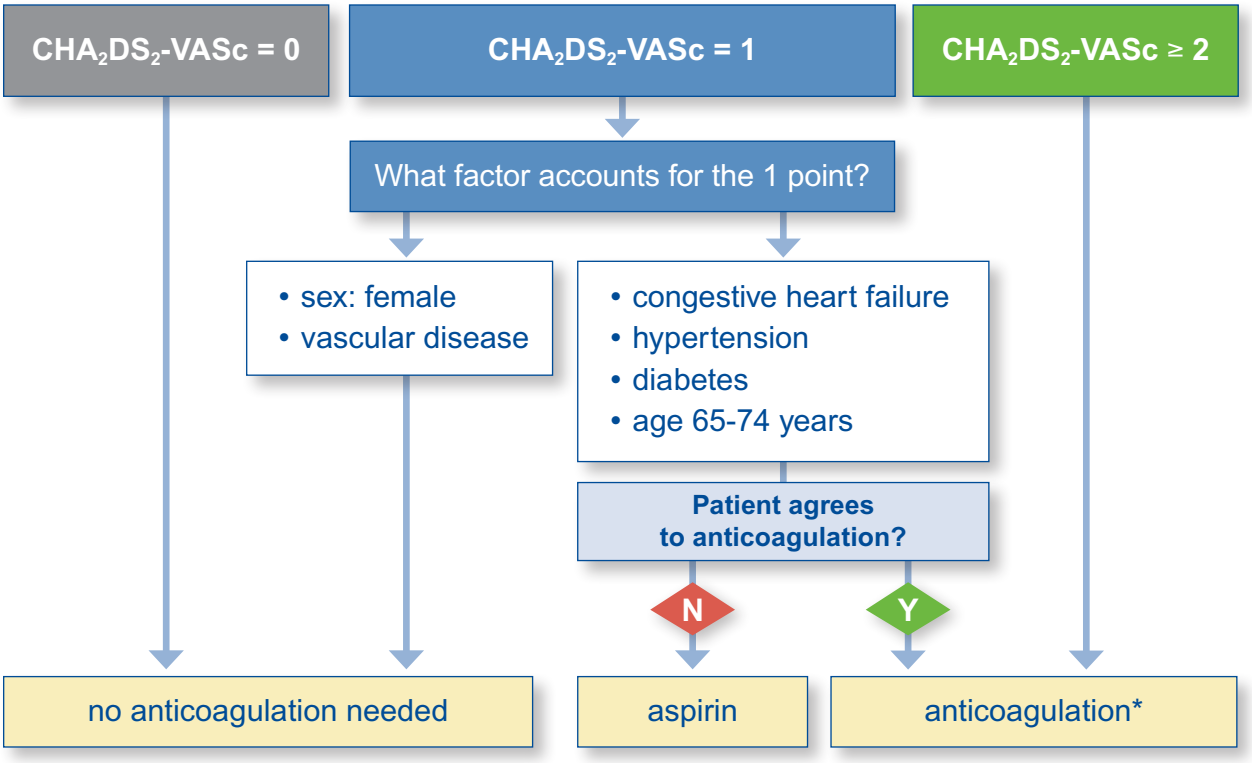
FIGURE 5. The risk of stroke and the benefit of anticoagulation both increase sharply with CHA_2DS_2-VASc score.[7]



At every CHA_2DS_2-VASc score, anticoagulation reduces the risk of stroke by about half.

Anticoagulate based on stroke risk

FIGURE 6. Recommend an anticoagulation plan based on CHA_2DS_2-VASc score.[8,9]



*DOAC preferred over warfarin, unless unaffordable or contraindicated.

Reduce the risk of bleeding.

Address modifiable risk factors.

- Control blood pressure.
- Stop or reduce alcohol use.
- Change or modify other medications that increase bleeding risk, if possible.
- Use a DOAC instead of warfarin, unless unaffordable or contraindicated.

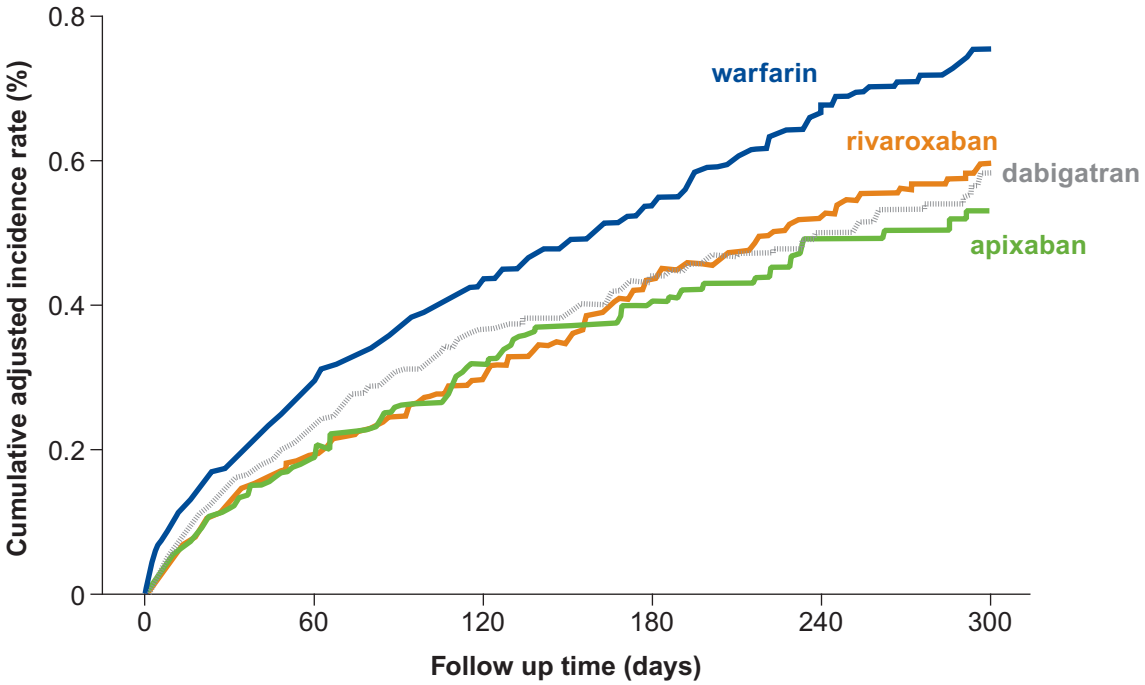
Monitor renal and liver function.

For patients with a prior major bleed, use an anticoagulant option with the lowest risk of bleeding. *See next page.*

Age increases the risk of bleeding, but also increases the risk of stroke.

Stroke and bleeding risks differ among commonly prescribed anticoagulants

FIGURE 7. In a 2019 FDA study of over 180,000 Medicare patients, all DOACs reduced the risk of stroke more than warfarin.[10]



Bleeding risks vary significantly among anticoagulant options.

TABLE 2. Relative risk of bleeding event for three DOACs compared to warfarin[10]

	Intracranial hemorrhage	Major extracranial bleed	Major gastrointestinal bleed
apixaban	++	++	++
dabigatran	+++	–*	–
rivaroxaban	++	––	––

+ More symbols indicate less bleeding risk compared to warfarin. – More symbols indicate greater bleeding risk compared to warfarin.

* Difference is not statistically significant for this comparison.

Among the DOACs, apixaban has the most favorable bleeding profile overall while dabigatran has the lowest risk of intracranial bleeding.[10]

After over a decade of use, DOACs appear to be the best choice for most patients

TABLE 3. Comparison of DOACs and warfarin

	dabigatran	rivaroxaban	apixaban	edoxaban	warfarin
Mechanism	direct thrombin inhibitor	direct factor Xa inhibitor	direct factor Xa inhibitor	direct factor Xa inhibitor	vitamin K antagonist
Dosing frequency	twice daily	once daily	twice daily	once daily	once daily
Standard dose	150 mg	20 mg	5 mg	60 mg	based on INR
Dose adjustment	CrCl* 15-30: 75 mg+	CrCl 15-49: 15 mg	**Two of:** age ≥80, weight ≤60 kg, or SCr** ≥1.5: 2.5 mg	CrCl 15-49: 30 mg	based on INR
Renal contraindications	CrCl <15	CrCl <15	none	CrCl <15 or >95	none
FDA-approved reversal agent	idarucizumab (Praxbind)	andexanet alfa (Andexxa)	andexanet alfa (Andexxa)	none	vitamin K
Other considerations	can cause dyspepsia—consider PPI	should be taken with evening meal	safe to use in patients with severe kidney disease or on dialysis[11]	do not use in normal renal function	drug-diet interactions; requires INR monitoring

*CrCl: creatinine clearance, mL/min
**SCr: serum creatinine, mg/dL
+Dosing reflects FDA labeling, but this dose was not studied in randomized trials.

Patients may benefit from warfarin over DOACs if they:[8]

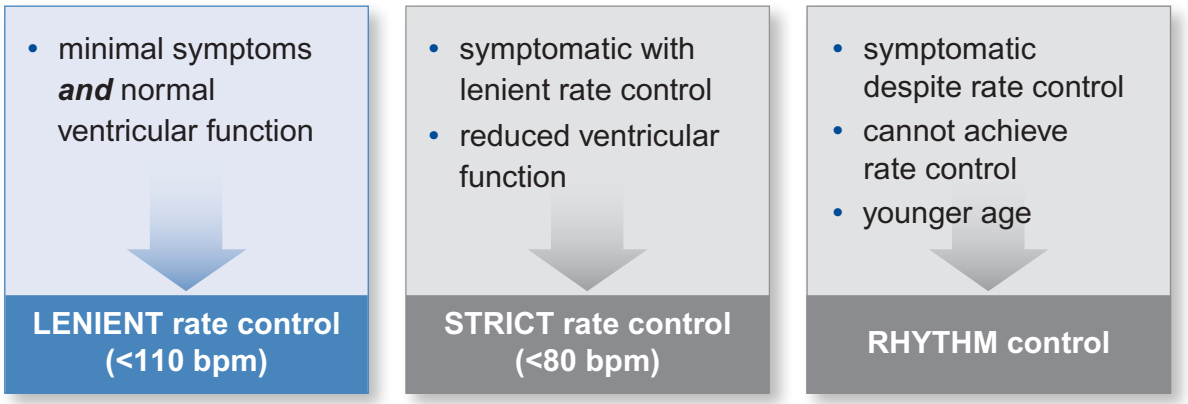
- ✓ **have a contraindication to DOACs (e.g., mechanical heart valves)**
- ✓ **have severe liver dysfunction**
- ✓ **cannot afford a DOAC**

Managing AF:

Control the rate

Randomized trials found that lenient rate control is the best approach for most patients.[12]

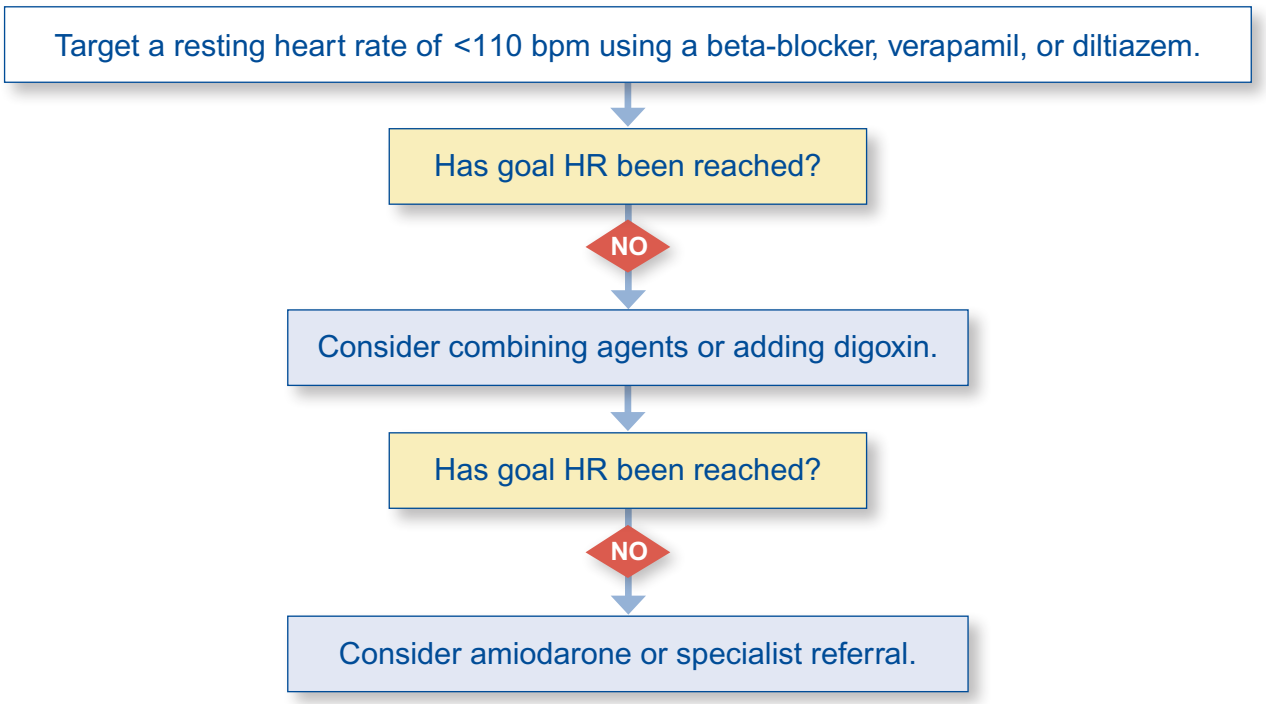
FIGURE 8. Patient factors that determine whether it is better to control rate or rhythm



Establishing rate control

Beta-blockers and non-dihydropyridine calcium channel blockers (i.e., diltiazem, verapamil) are similarly effective in controlling heart rate. Digoxin is less effective when used alone, but can be useful with other medications.

FIGURE 9. Managing rate control in AF



If rhythm control is appropriate, choose a regimen based on symptoms

Managing antiarrhythmic medications will often require consultation with a cardiologist, as will intervention procedures.

What the PCP needs to know about specialist interventions

TABLE 4. Rhythm control strategies

	Cardioversion	AF ablation	AV node ablation
Which patients benefit?	patients with newly diagnosed, symptomatic AF	patients with symptomatic, recurrent AF	patients not eligible for AF ablation
Will anticoagulation be required?	yes, at least 4 weeks post cardioversion: longer-term decisions driven by CHA_2DS_2-VASc score	yes*	yes
Additional comments	recurrence of AF is common	recurrence of AF is common	patient is pacemaker dependent

*Guidelines recommend continuing anticoagulation, but trial evidence is lacking.

Medications

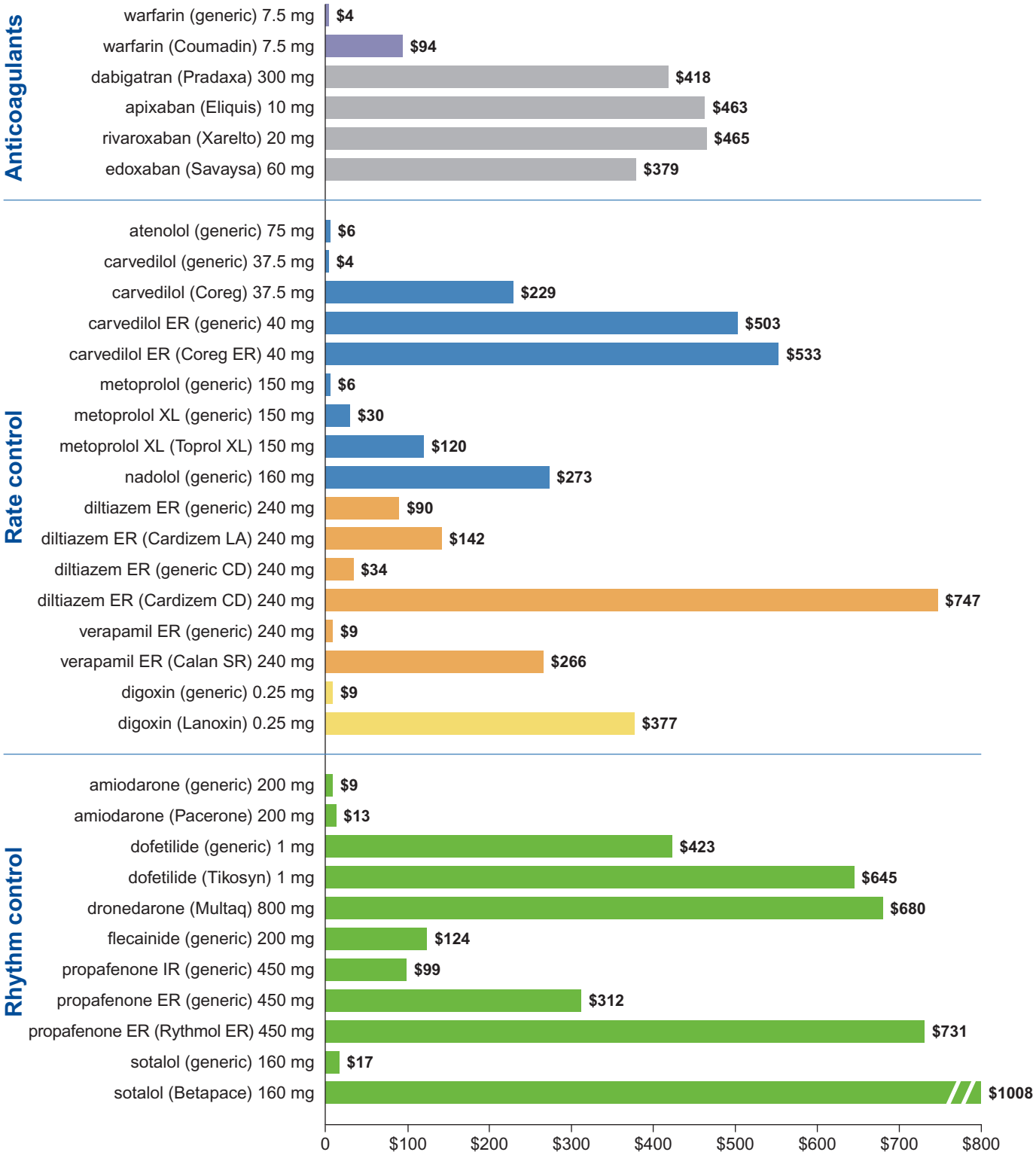
Antiarrhythmics (e.g., propafenone, flecainide, sotalol, amiodarone) confer several risks, including arrhythmia and toxicity, and relatively low long-term success rates. Anticoagulation is continued in patients taking antiarrhythmics.

Other specialist interventions include left atrial appendage (LAA) devices (e.g., Watchman).

- LAA devices were found to be no less effective than warfarin at two years.[13]
- Indicated in patients who cannot take long-term anticoagulation.
  - — Anticoagulation is required in the short term after device placement.
  - — The Centers for Medicare and Medicaid Services suggests these devices be restricted to patients with a CHA_2DS_2-VASc score ≥3.

Prices of these regimens vary widely

FIGURE 10. Cost of a 30-day drug supply



Prices from goodrx.com, October 2019. Listed doses are based on Defined Daily Doses by the World Health Organization and should not be used for dosing in all patients. All doses shown are for generics when available, unless otherwise noted. These prices are a guide; patient costs will be subject to copays, rebates, and other incentives.

Key points

- **Atrial fibrillation sharply increases the risk of stroke,** but this risk is markedly reduced by anticoagulation.
- **Older patients with AF are at the greatest risk of stroke** and benefit the most from anticoagulation.
- **Use the CHA_2DS_2-VASc score** to predict stroke risk and guide prescribing.
- **Address modifiable risks for bleeding.**
- **Direct oral anticoagulants (DOACs) reduce both stroke and bleeding risk** compared to warfarin in most patients.
- **Patients taking warfarin can be switched to a DOAC** unless there are contraindications or financial concerns that prevent the change.
- **Rate control is preferred over rhythm control for most patients,** targeting a heart rate of <110 bpm. Patients with continued symptoms may require a target rate of <80 bpm.

Visit AlosaHealth.org/AtrialFibrillation

for links to risk calculators, other resources, and a longer evidence document.

References:

(1) Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *Am J Cardiol.* 2013;112(8):1142-1147. **(2)** Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation.* 2019;139(10):e56-e528. **(3)** Singer DE, Chang Y, Fang MC, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. *Ann Intern Med.* 2009;151(5):297-305. **(4)** Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet.* 2014;383(9921):955-962. **(5)** Ashburner J, Atlas S, Khurshid S, et al. Electronic physician notifications to improve guideline-based anticoagulation in atrial fibrillation: a randomized controlled trial. *J Gen Intern Med.* 2018;33(12):2070-7. **(6)** Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest.* 2010;137(2):263-272. **(7)** Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *Eur Heart J.* 2012;33(12):1500-1510. **(8)** 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 in Collaboration With the Society of Thoracic Surgeons. *Circulation.* 2019;140(2):e125-e151. **(9)** Olesen JB, Lip GY, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. *BMJ.* 2011;342:d124. **(10)** Graham DJ, Baro E, Zhang R, et al. Comparative Stroke, Bleeding, and Mortality Risks in Older Medicare Patients Treated with Oral Anticoagulants for Nonvalvular Atrial Fibrillation. *Am J Med.* 2019;132(5):596-604.e511. **(11)** Siontis KC, Zhang X, Eckard A, et al. Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States. *Circulation.* 2018;138(15):1519-1529. **(12)** Van Gelder IC, Groenveld HF, Crijns HJ, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med.* 2010;362(15):1363-1373. **(13)** Reddy VY, Doshi SK, Sievert H, et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial. *Circulation.* 2013;127(6):720-729.

About this publication

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at AlosaHealth.org.

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