the Atrial Fibrillation PATIENT

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Commercial Bias

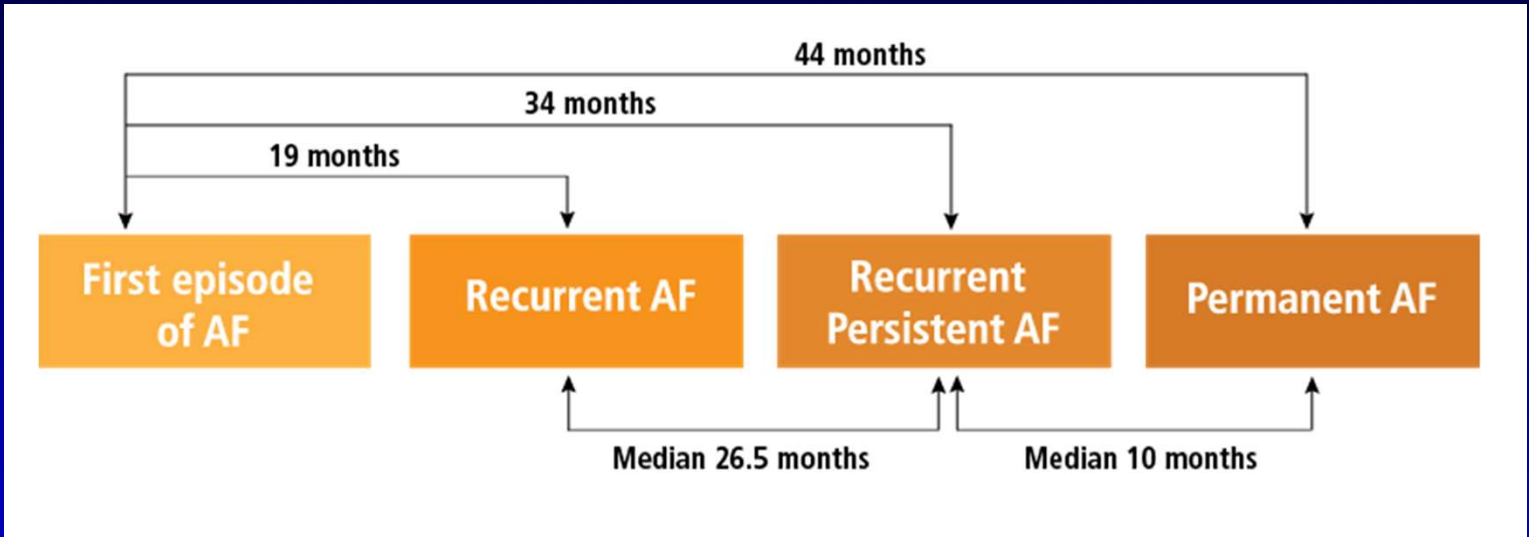
Nothing to disclose

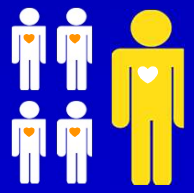
Objectives

- Establish a plan for rate vs rhythm with every patient based on modifiable and non-modifiable risk factors
- Preventing thromboembolism based on risk factors and available treatment options
- Identifying and planning treatment for the atrial fibrillation patient

Establishing Rate vs. Rhythm Control

AF is a Progressive Disease

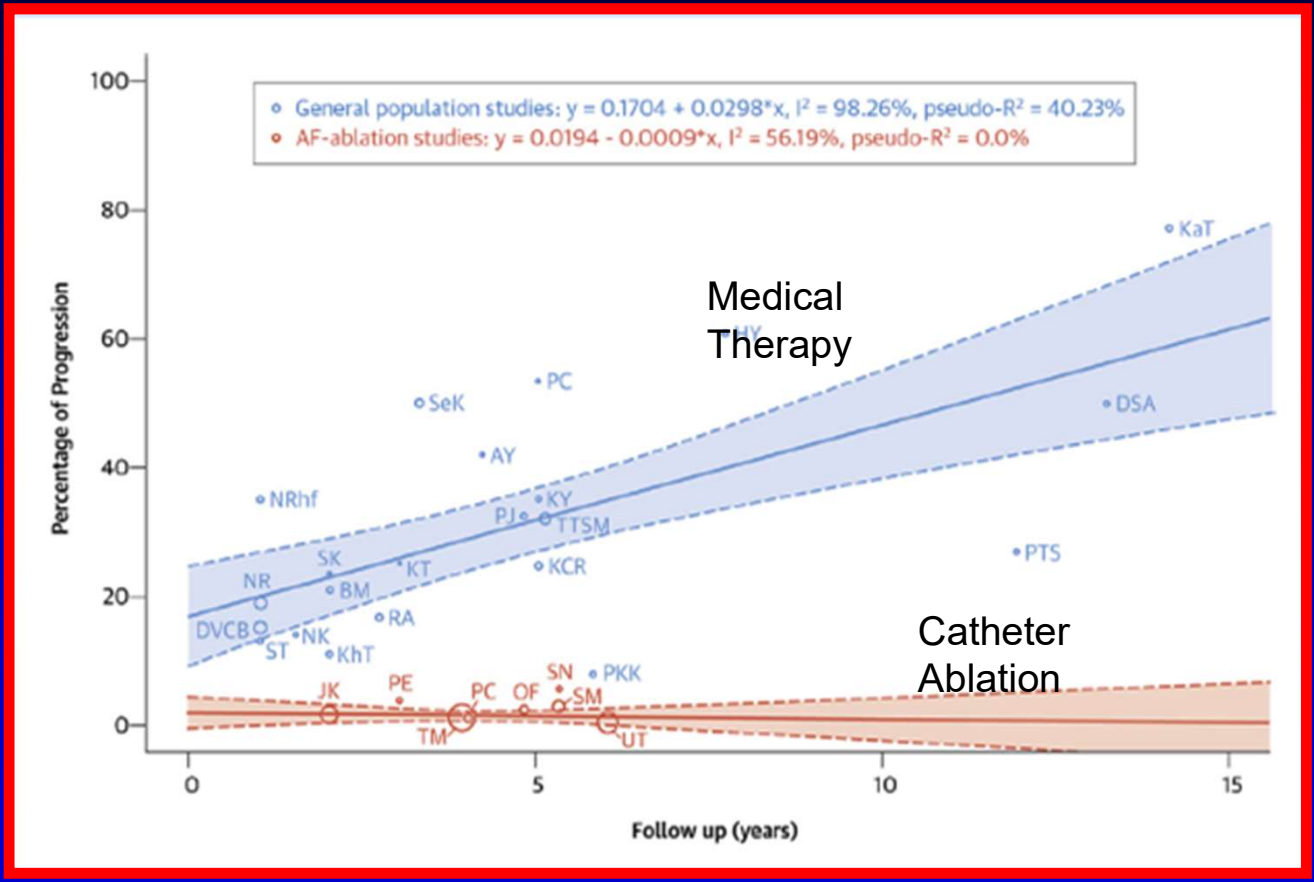




20% **of patients progress from Paroxysmal to Persistent AF within 1 year of diagnosis**

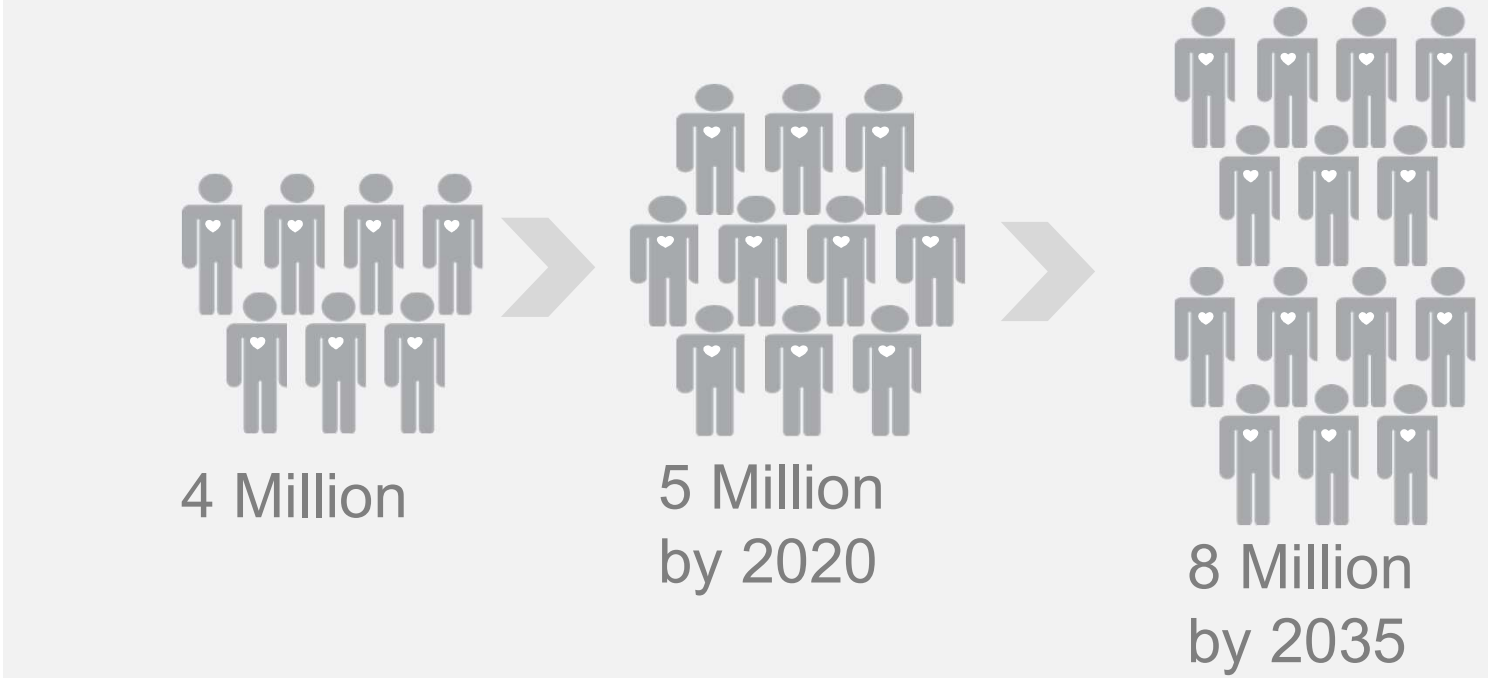
Nieuwlaat R et al. Eur Heart J. 2008 May;29(9):1181-9. doi: 10.1093/eurheartj/ehn139. Epub 2008 Apr 7.

Progression to Persistent AF



JACCCEP. 2015;1(3):105-115. doi:10.1016/j.jacep.2015.04.010

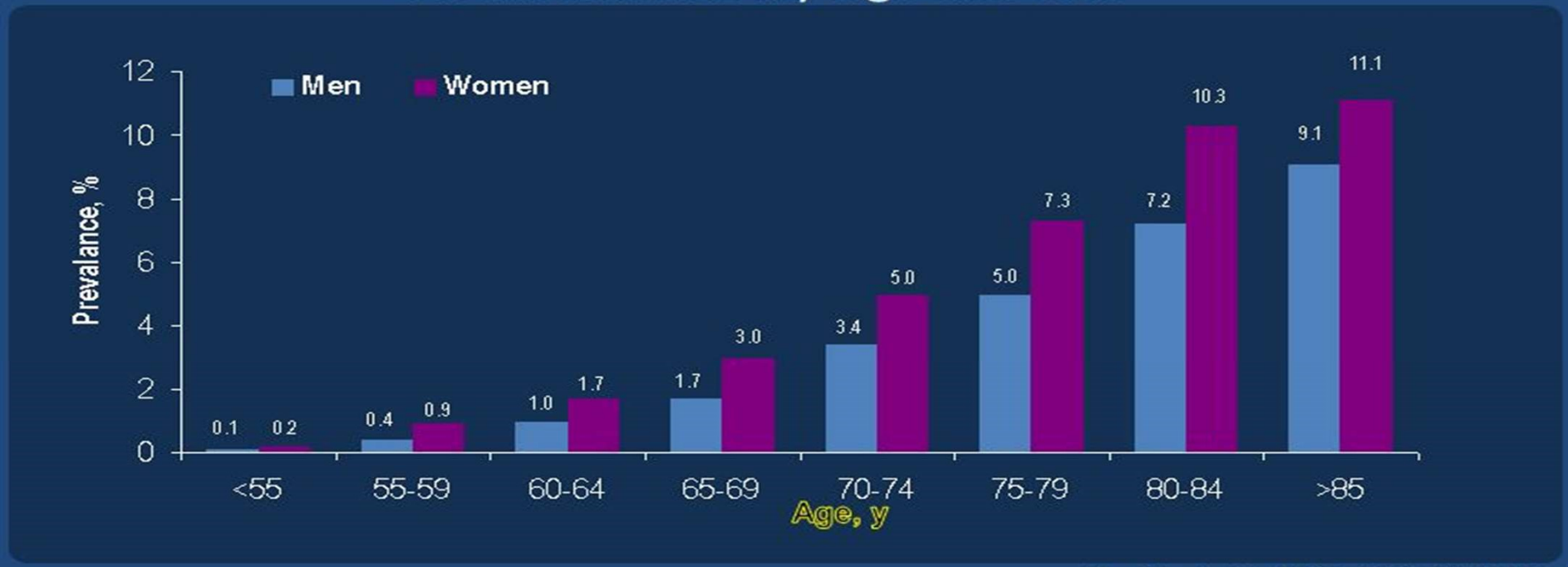
Prevalence of Atrial Fibrillation



Atrial Fibrillation: Prevalence

- Currently: 2.3 - 3.0 millions people have AF in the USA
- In 2050: 7 – 15 millions people will have AF in the USA

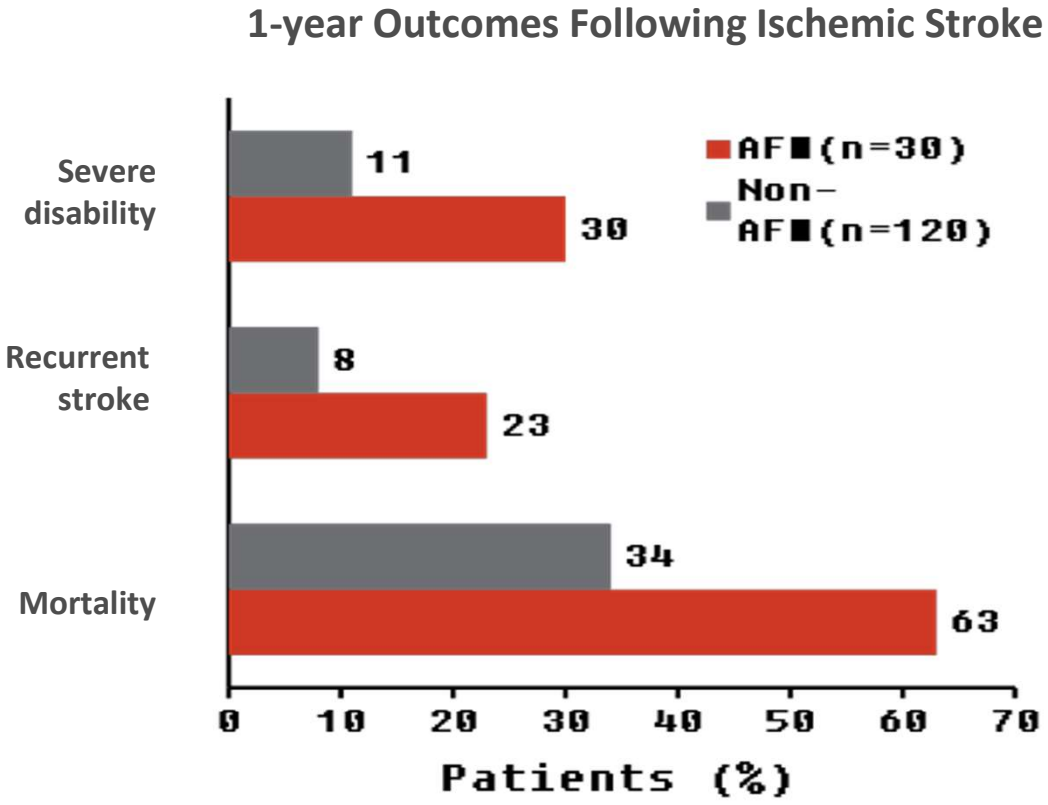
AF Prevalence by Age and Sex



Go AS, et al. *JAMA*. 2001;285:2370-2375.

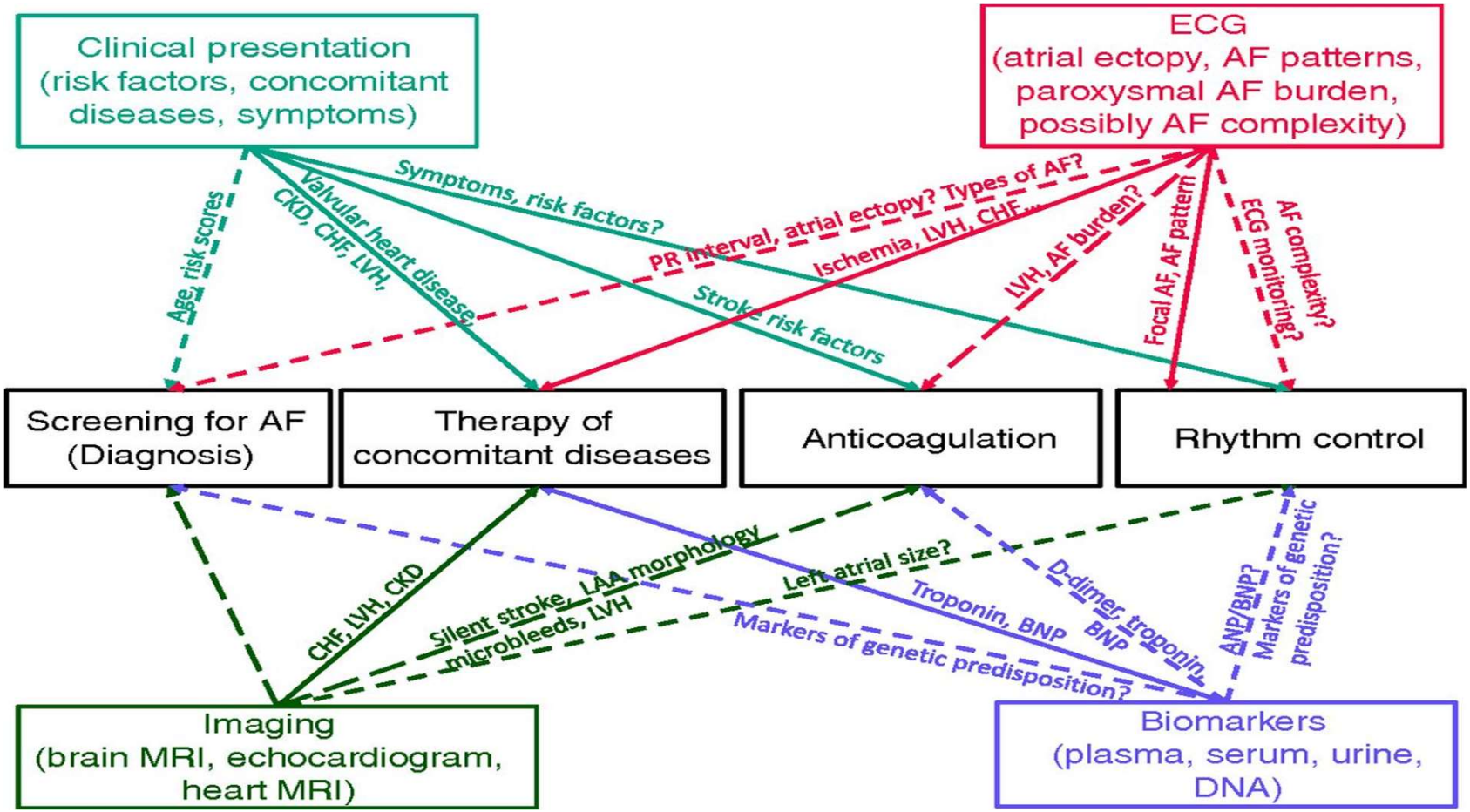
AF and Stroke: A Healthcare Burden

- 2.7 to 6.1 million individuals in the United States had AF in 2010
- AF increases the risk for stroke ≈5-fold
  - 23.5% of strokes in patients
    80 to 89 years old are AF related
- Strokes in patients with AF tend to be more disabling, recur, or be fatal

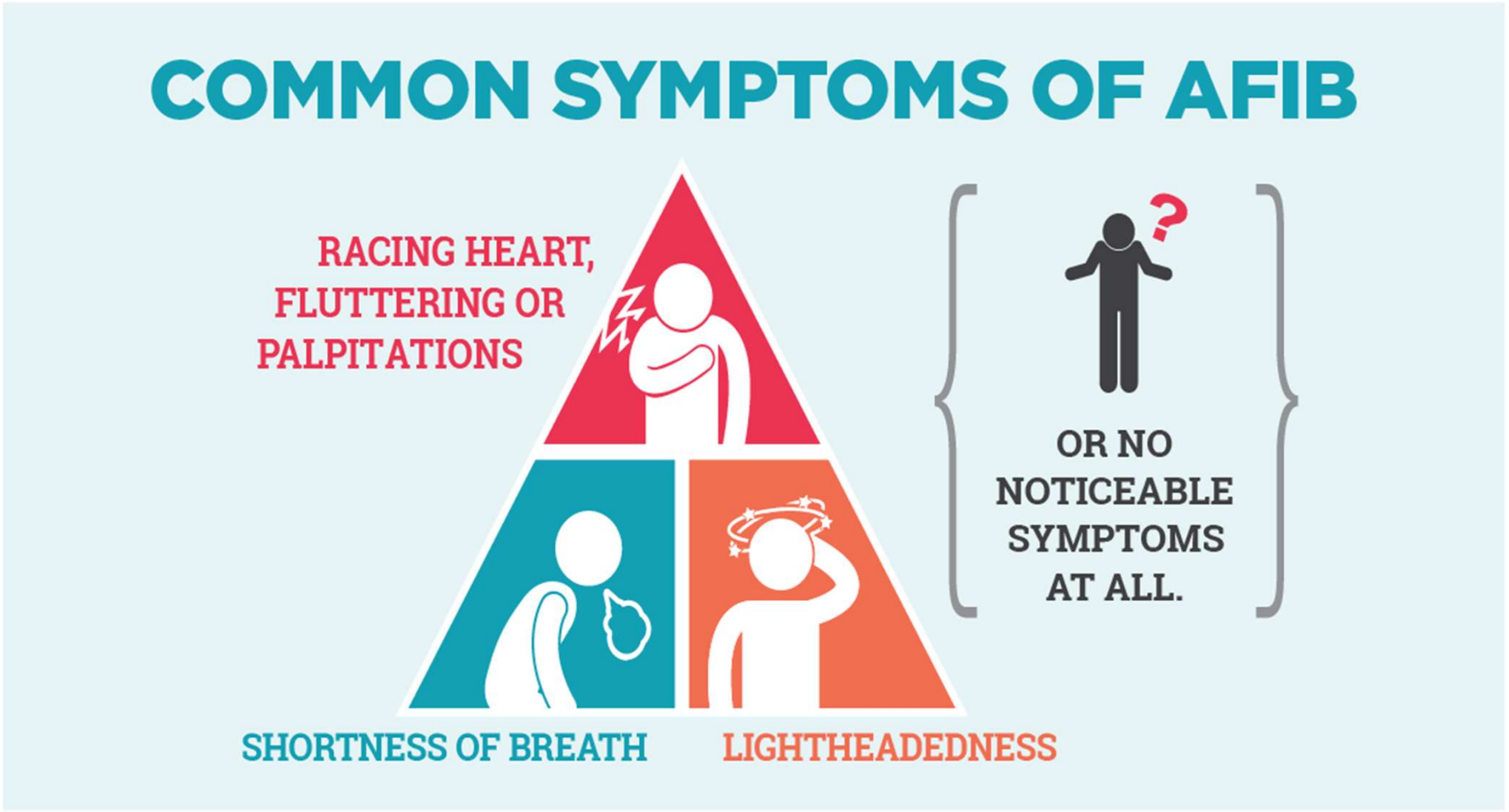


Go AS et al. *Circulation*. 2014;129(3):e28-e292.
Lin HJ et al. *Stroke*. 1996;27(10):1760-1764.

Complexities of AF Management



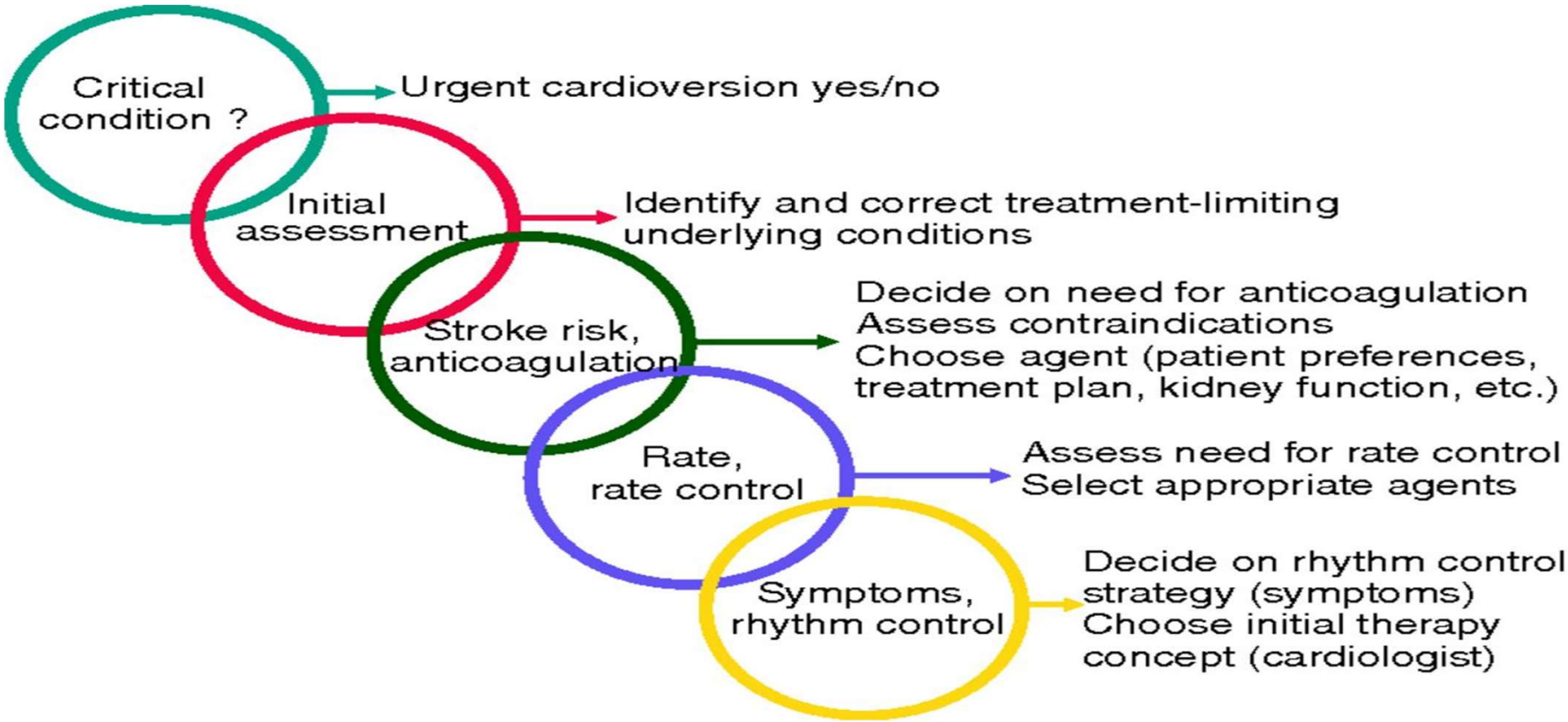
Kirchhof P et al. Europace 2013



Treat Symptoms & Prevent Complications

Symptoms of AF	Related complication of AF	Treatment to prevent symptoms and complications
-	Stroke	Treatment of underlying conditions, oral anticoagulation, possibly left atrial appendage occluders
Fatigue or tiredness	Depression, reduced quality of life	? (possibly rhythm control)
Shortness of Breath	Impaired autonomy, worsening of cardiac function, unplanned hospitalizations	ACE inhibitors, rate control, possibly rhythm control
Palpitations	Tachycardiomyopathy, reduced autonomy	Rate control, rhythm control, possibly anticoagulation
Chest pain	Acute coronary syndrome, unplanned hospitalizations	Treatment of underlying conditions, possibly anticoagulation
Depressed mood, anxiety	Frequent hospitalizations, Impaired cognitive function	Possibly rate control and rhythm control Possibly oral anticoagulation

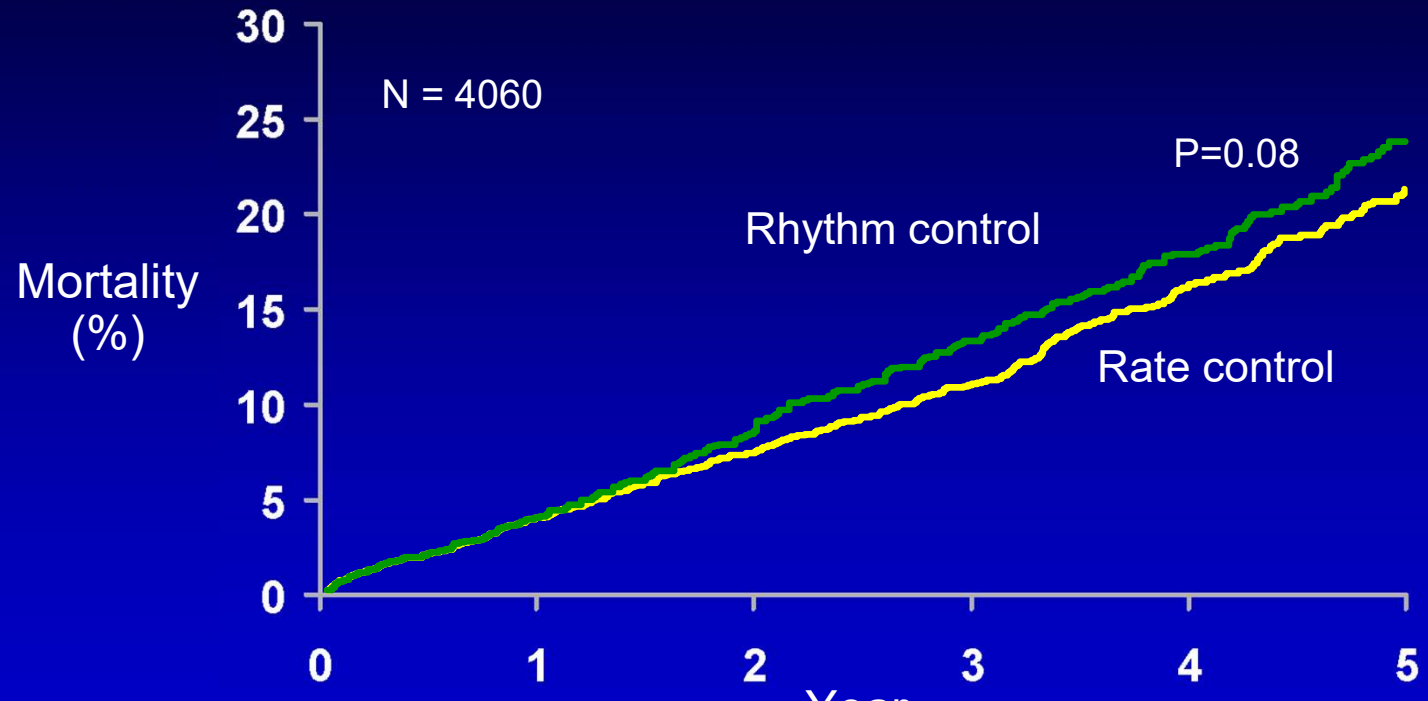
Stepwise decision making in patients with AF



Kirchhof P et al. Europace 2013

AFFIRM Trial

Primary Endpoint: All-Cause Mortality



Deaths (no.)						
Rhythm	**0**	**80 (4)**	**175 (9)**	**257 (13)**	**314 (18)**	**352 (24)**
Rate	**0**	**78 (4)**	**148 (7)**	**210 (11)**	**275 (16)**	**306 (21)**

AFFIRM Investigators: NEJM 347:1825, 2002

Algorithm for Rate vs Rhythm Control for Patients With Symptomatic AF

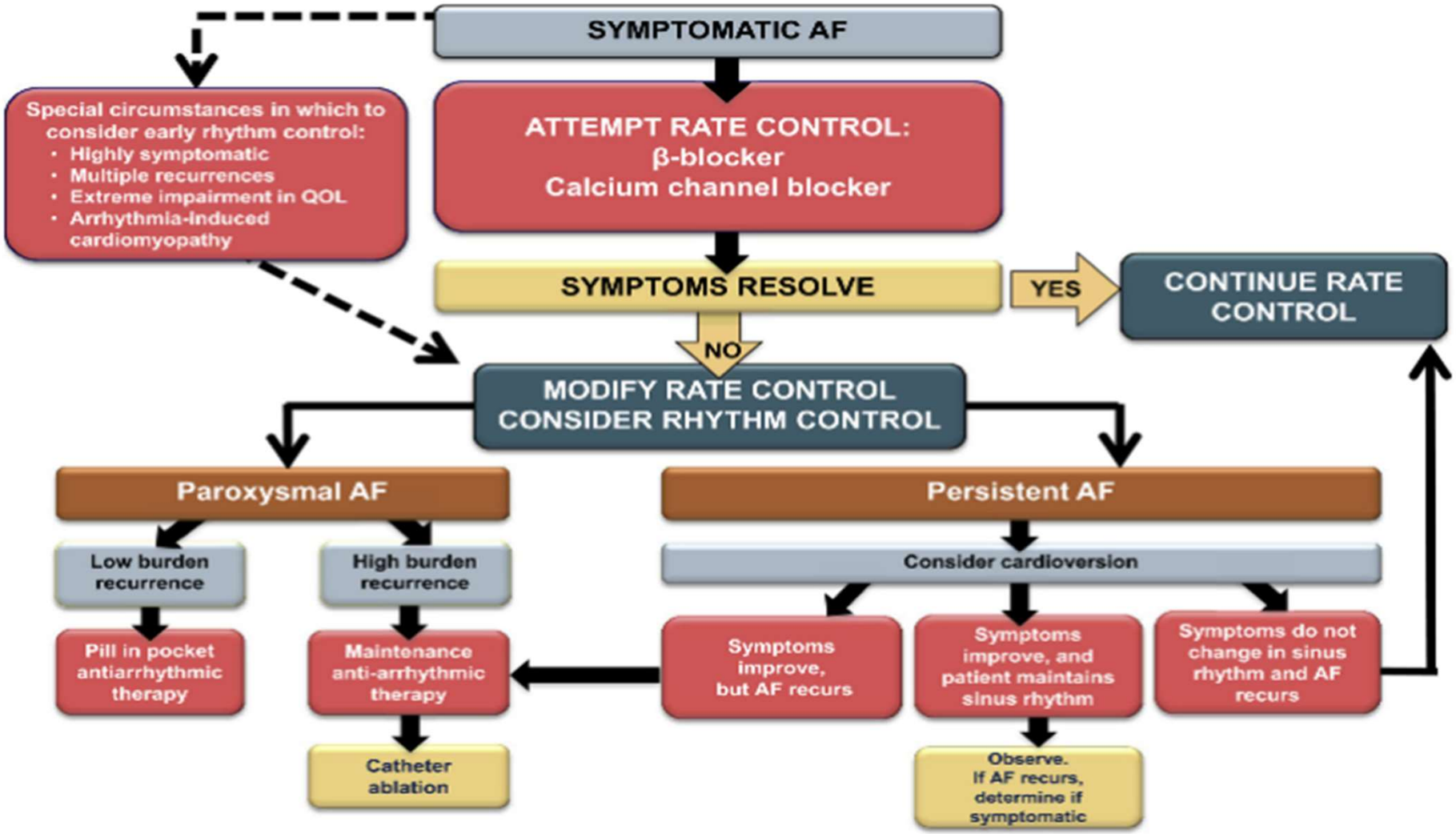
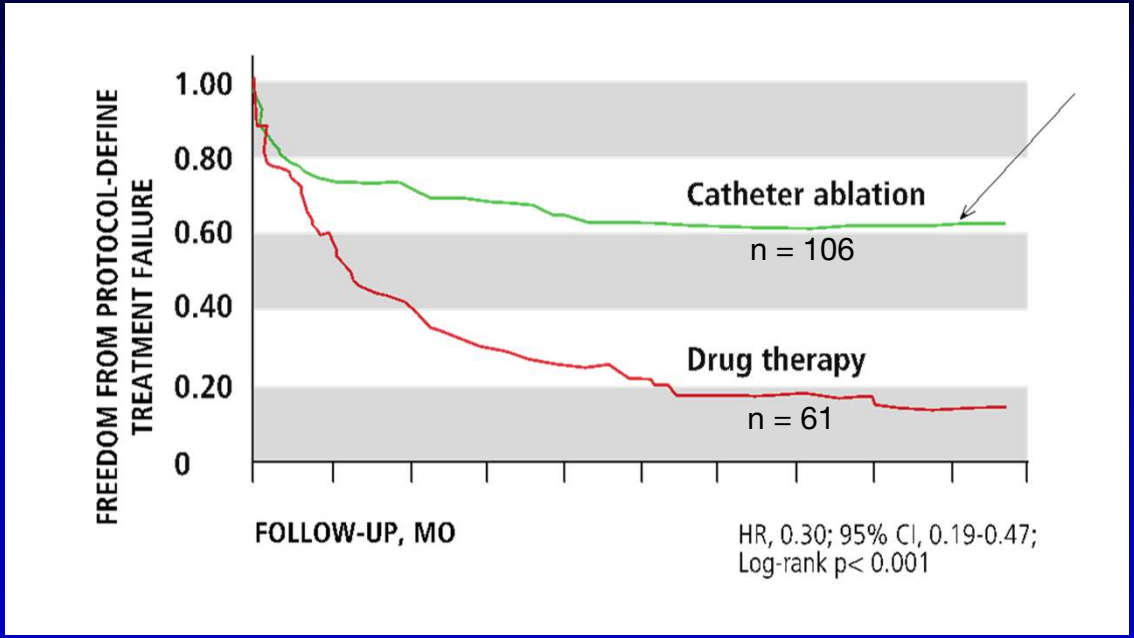


Table 1: Comparison of Rate Control versus Rhythm Control as Management Strategies for Atrial Fibrillation

Therapeutic Strategy	Advantages	Disadvantages
Rate control	• Therapeutically convenient • Less exposure to drug toxicity • Preferred in older, minimally symptomatic AF • Optimal rate control adequate to decrease hospitalisation • Cost-effective	• No effect on disease progression • May not be beneficial in highly symptomatic patients
Rhythm control	• Prevents disease progression • Avoids unfavourable electrical and structural remodelling • Potentially preferable in younger patients • Better quality of life	• Exposure to adverse effects of antiarrhythmic drugs (or risks of ablation procedures) • Generally less cost-effective

AF = atrial fibrillation.

Catheter Ablation vs AAD

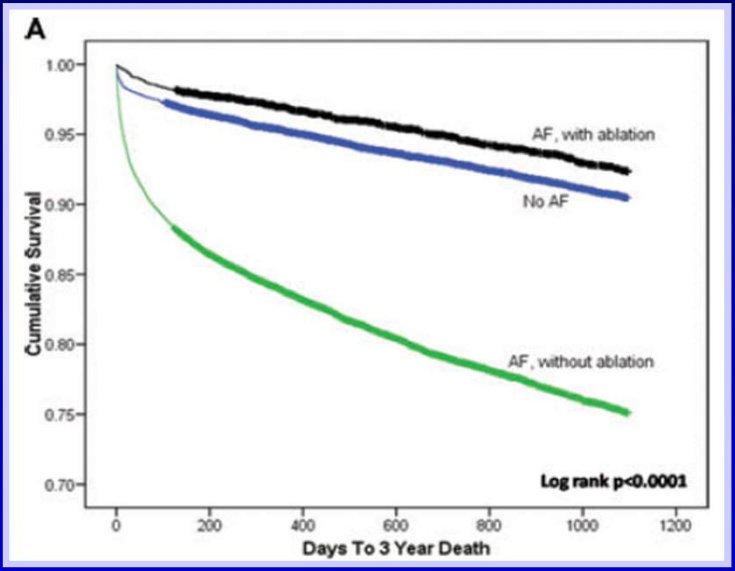


Patients who had catheter ablation had fewer episodes of Afib than patients who took medication

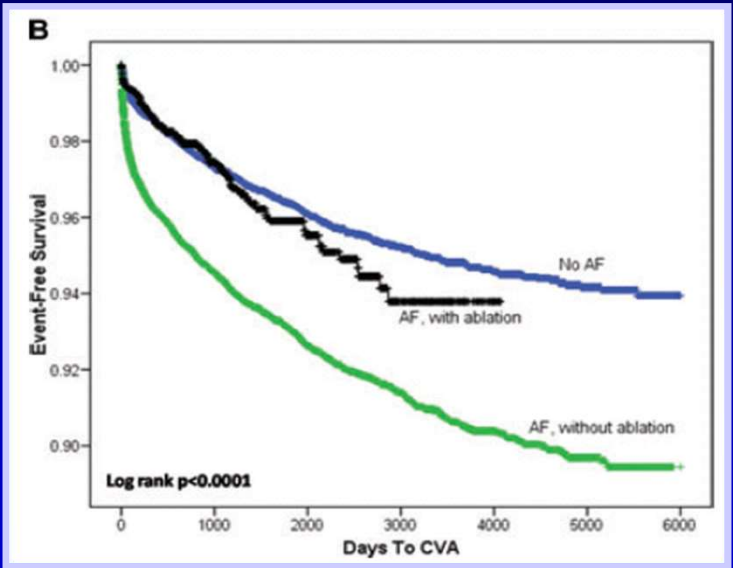
Wilber DJ et. Al. Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation: A Randomized Controlled Trial. *JAMA* 303 (4):333-340.

Impact of Ablation on Death, Stroke and Dementia

Death



Stroke



Over 4000 AF ablation pts were compared to almost 17,000 matched controls without AF and almost 17,000 matched controls with AF, but without ablation.

Bunch, et al. JCE 2011;22:839

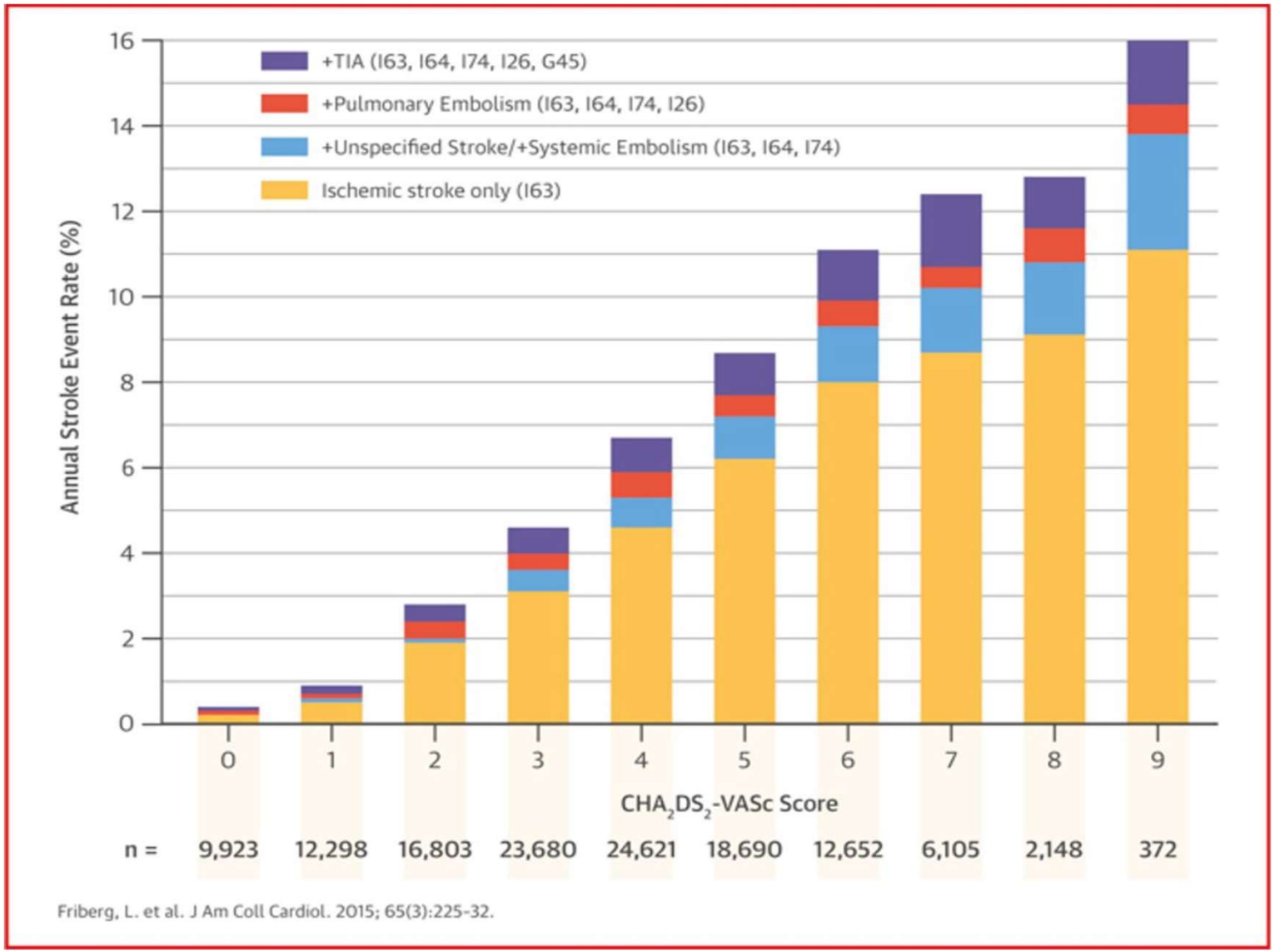
MAYO CLINIC

Incidence of complications

Mayo Clinic
AF ablation
1999-2004
N=623

• Pericardial effusion	70 (11%)
Tamponade	15 (2.4%)
• Stroke/TIA	5 (0.8%)
• Phrenic nerve injury	5 (0.8%)
• Pulmonary vein stenosis	20 (3.2%)
• Myocardial infarction	2 (0.3%)
• Valve injury	1 (0.2%)
• Groin hematoma	14 (2.2%)
• Atrioesophageal fistula	?

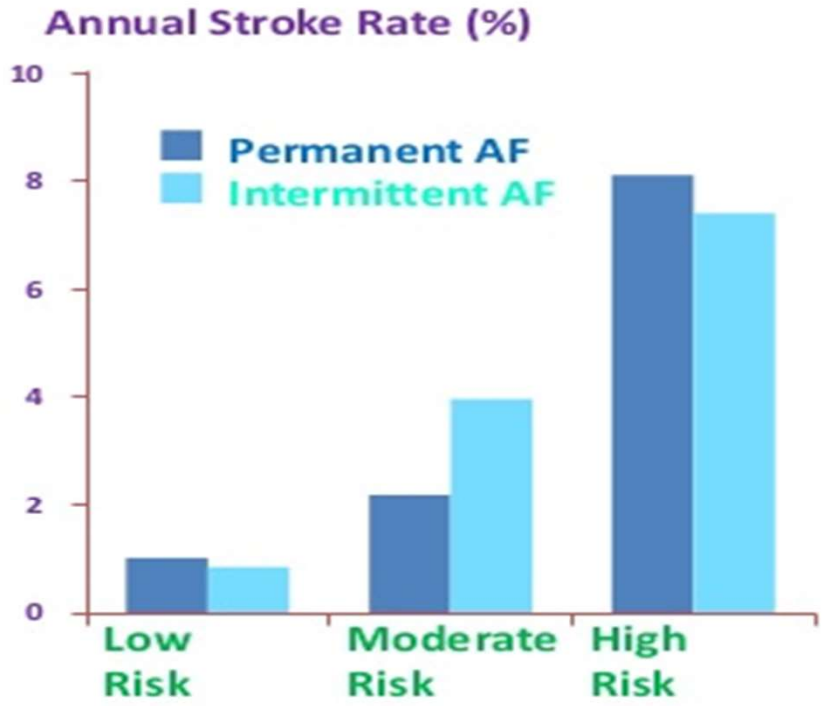
Preventing Thromboembolism



Friberg, L. et al. J Am Coll Cardiol. 2015; 65(3):225-32.

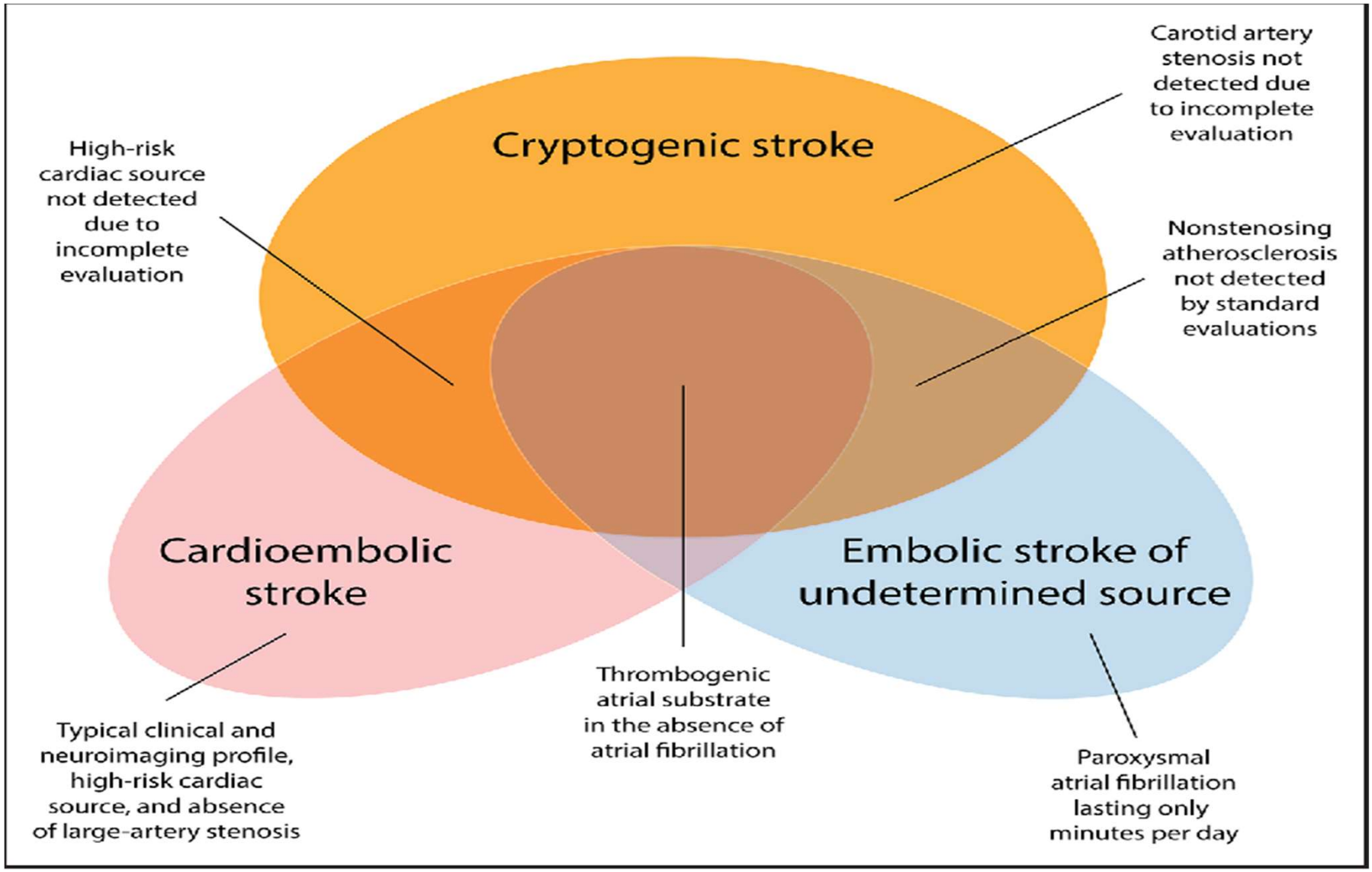
AF and Stroke

- AF increases stroke risk 4- to 5-fold
- Stroke is the most common and devastating complication of AF
  - Incidence of all-cause stroke in patients with AF is 5%
- AF is an independent risk factor for stroke
  - Approximately 15% of all strokes in the United States caused by AF
  - Risk for stroke increases with age
- Stroke risk persists even in asymptomatic AF
- Stroke risk persists in patients with a "high-risk" profile despite a strategy of rhythm control (AFFIRM study, RACE study)

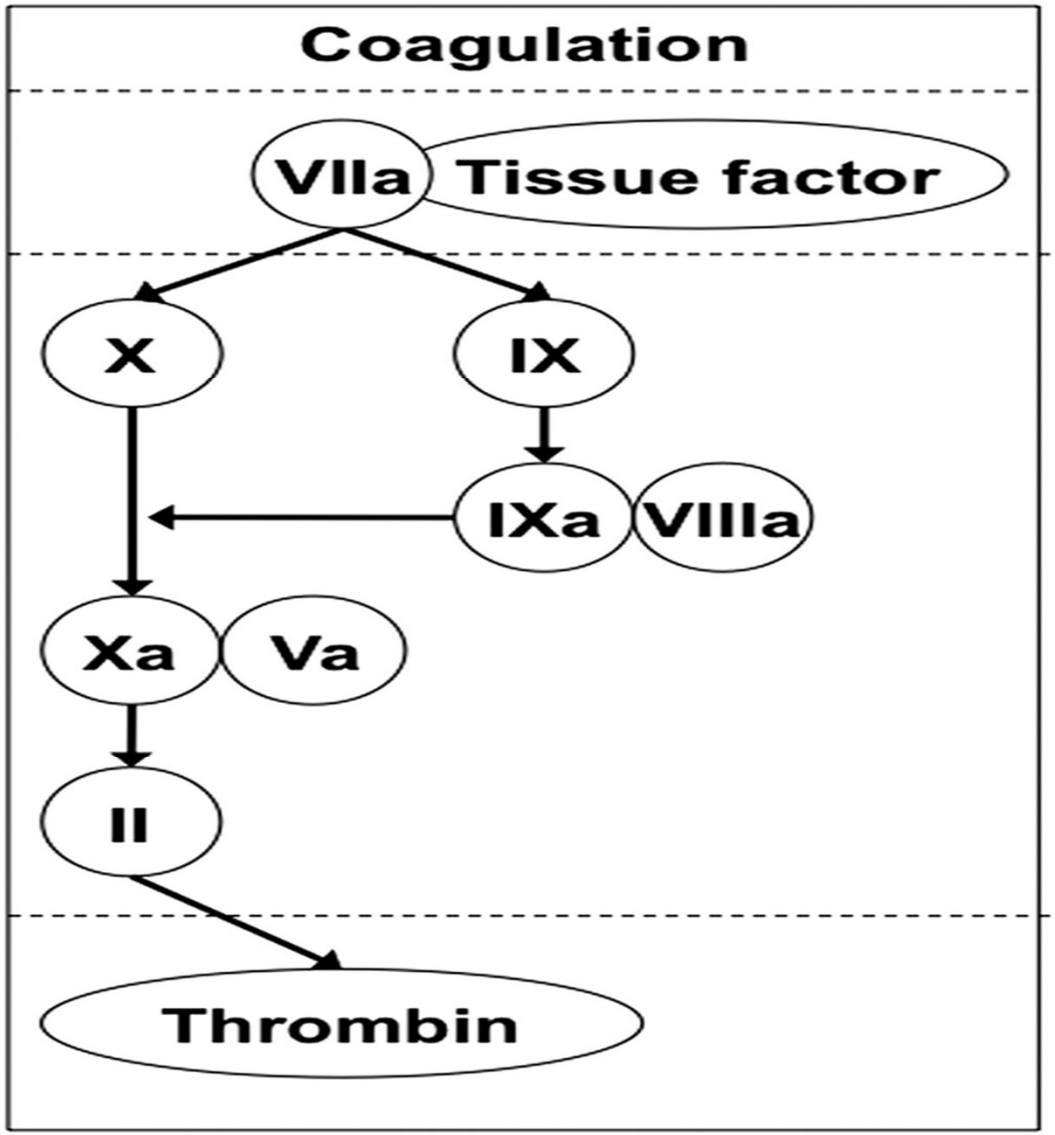


RACE II = Rate Control Efficacy in Permanent Atrial Fibrillation.

Fuster V, et al. *J Am Coll Cardiol*. 2006;48(4):e149-e246. Kannel WB, et al. *Med Clin North Am*. 2008;92(1):17-42. Page RL, et al. *Circulation*. 2003;107(8):1141-1145. Hart RG, et al. *J Am Coll Cardiol*. 2000; 35(1):183-187. Dulli DA, et al. *Neuroepidemiology*. 2003;22(2):118-123.


Carotid artery stenosis not detected due to incomplete evaluation
Cryptogenic stroke
High-risk cardiac source not detected due to incomplete evaluation
Nonstenosing atherosclerosis not detected by standard evaluations
Cardioembolic stroke
Embolic stroke of undetermined source
Thrombogenic atrial substrate in the absence of atrial fibrillation
Typical clinical and neuroimaging profile, high-risk cardiac source, and absence of large-artery stenosis
Paroxysmal atrial fibrillation lasting only minutes per day


CONSIDER
Coumadin!
COUMADIN
IMPOSSIBLE TO DOSE!
TOUGH TO MONITOR!
CAUSES DEATH WHEN USED PROPERLY.
BUT... LIFESAVING!!
...WHEN IT'S NOT TRYING TO KILL YOU....
IT'S A TOUGH SELL.



New Drugs

Direct Xa inhibitors
(rivaroxaban, apixaban)

Direct thrombin inhibitors
(dabigatran)

Methods

	RE-LY	ROCKET-AF	ARISTOTLE
Study design	PROBE (warfarin open label, dabigatran blinded)	Double-blind, double-dummy	Double-blind, double-dummy
Comparison	**Dabigatran 110 or 150 mg bid vs. warfarin**	**Rivaroxaban 20 mg qd vs. warfarin**	**Apixaban 5 mg bid vs. warfarin**
Initial dose adjustment		15 mg qd if Clcr 30–49 mL/min	2.5 mg bid for 2 or more of: • age ≥80 • weight ≤60 kg • Scr ≥ 1.5 mol/L
Inclusion criteria	Af and at least one risk factor for embolization†	Nonvalvular Af and $CHADS_2 \geq 2$	Atrial fibrillation or flutter and $CHADS_2 \geq 1$
Key exclusion criteria	Valvular Af Acute stroke **Clcr <30 ml/min**	Valvular Af Acute stroke **Clcr <30 ml/min**	Valvular Af Acute stroke **Scr >2.5 mg/dl or Clcr <25 ml/min**
Populations analyzed	ITT (intention-to-treat analysis)	PPOT(per-protocol, on-treatment analysis)	ITT (intention-to-treat analysis)
Primary end point	Stroke or systemic embolism	Stroke or systemic embolism	Stroke or systemic embolism

†Previous stroke or TIA, LEVF< 40%, symptoms of heart failure, age ≥75 years or 65–74 years plus DM, HTN, or CAD

Apixaban

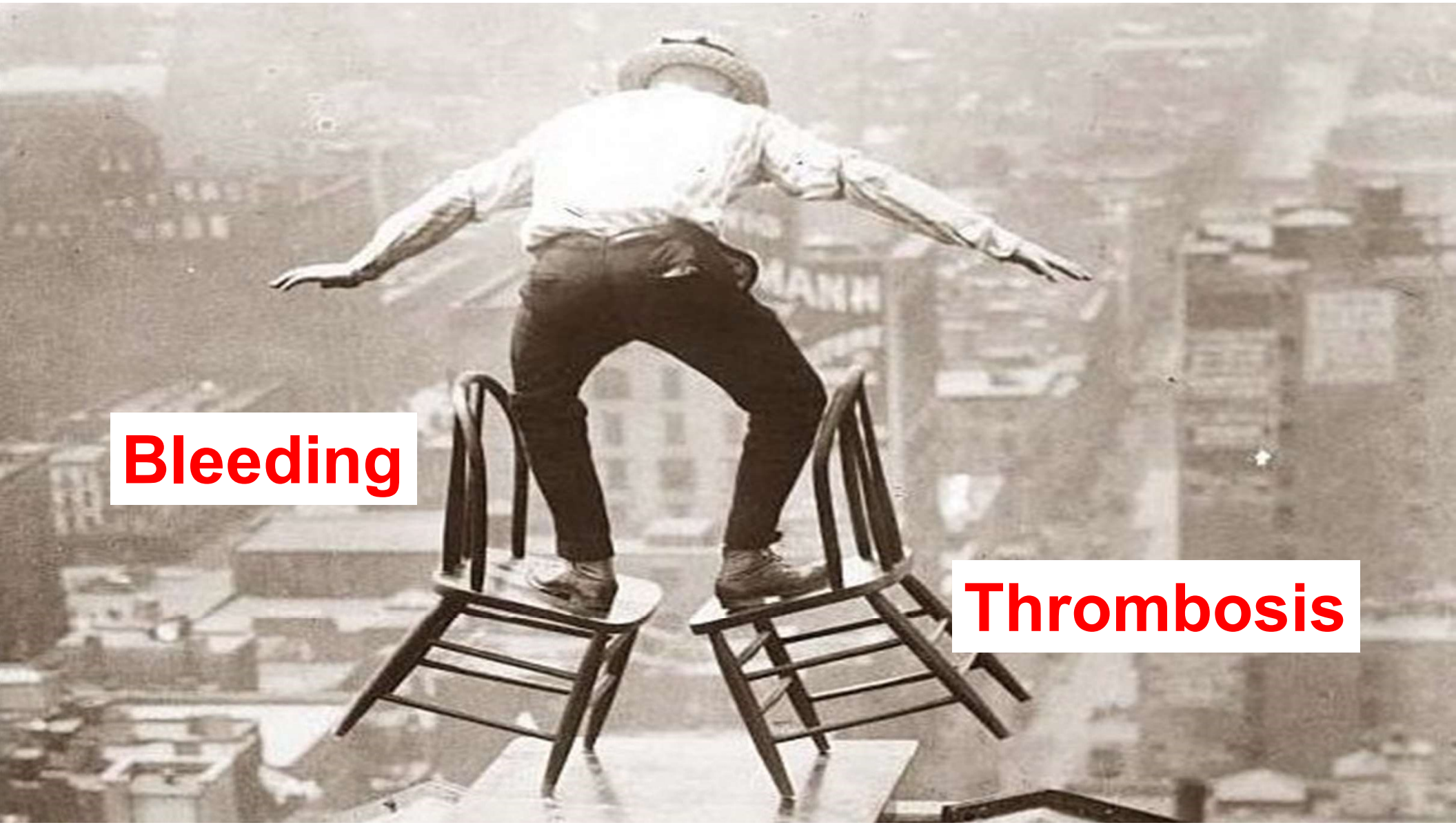
- Drugs expected to significantly increase bleeding risk if coadministered:
  - Systemic treatment with strong inhibitors of both CYP3A4 and P-gp (e.g., ritonavir, ketaconazole)
  - Other anticoagulants
  - Antiplatelet agents and NSAIDs including ASA

Rivaroxaban

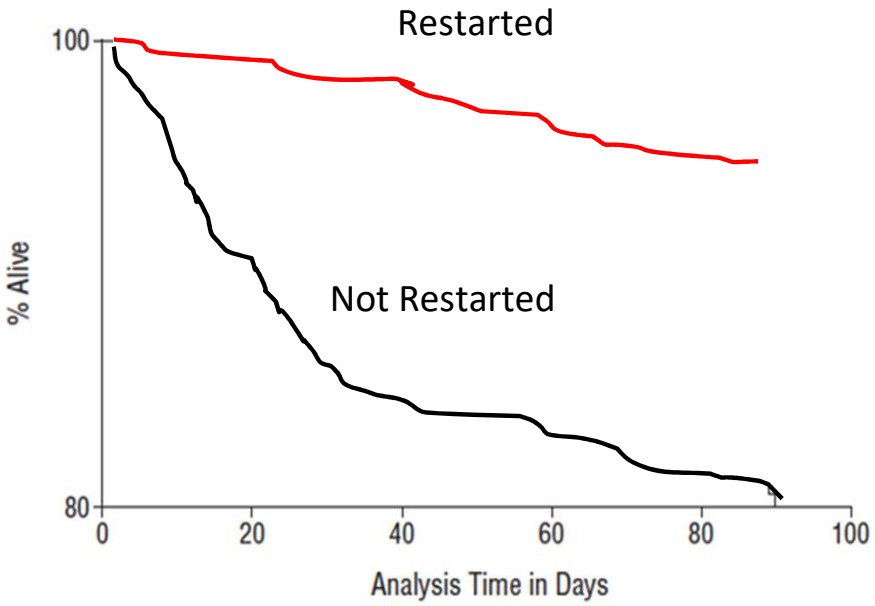
- Drugs expected to significantly increase bleeding risk if coadministered:
  - Systemic treatment with strong inhibitors of both CYP3A4 and P-gp (e.g., ritonavir, ketaconazole)
  - Other anticoagulants
  - Dual antiplatelet therapy (ASA plus a thienopyridine)
- Caution to be taken when coadministering NSAIDs, including ASA
- Not recommended owing to lack of data:
  - Dronedarone

Dabigatran

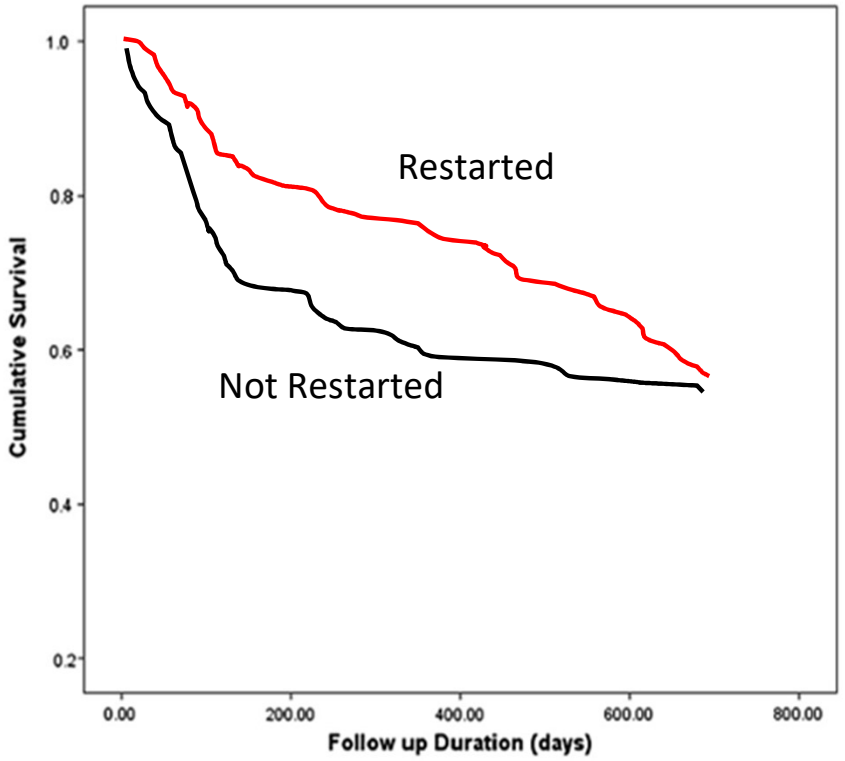
- Drugs expected to significantly increase bleeding risk if coadministered:
  - Systemic treatment with ketoconazole, cyclosporine, itraconazole, or tacrolimus, or quinidine
  - Other anticoagulants
- Contraindicated:
  - Dronedarone
- Dose reduction recommended in patients with moderate renal impairment:
  - Receiving comedications that are strong P-gp inhibitors
  - Taking verapamil, ASA, and/or clopidogrel


Bleeding
Thrombosis

Mortality After GI Bleed

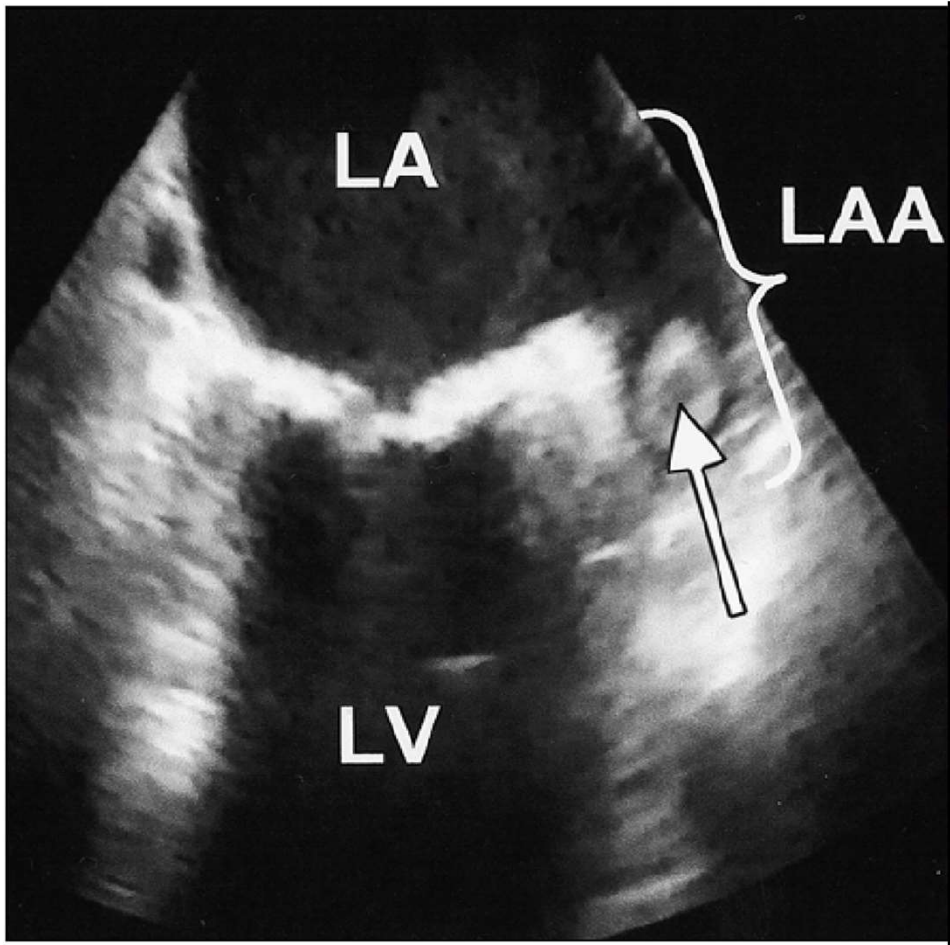


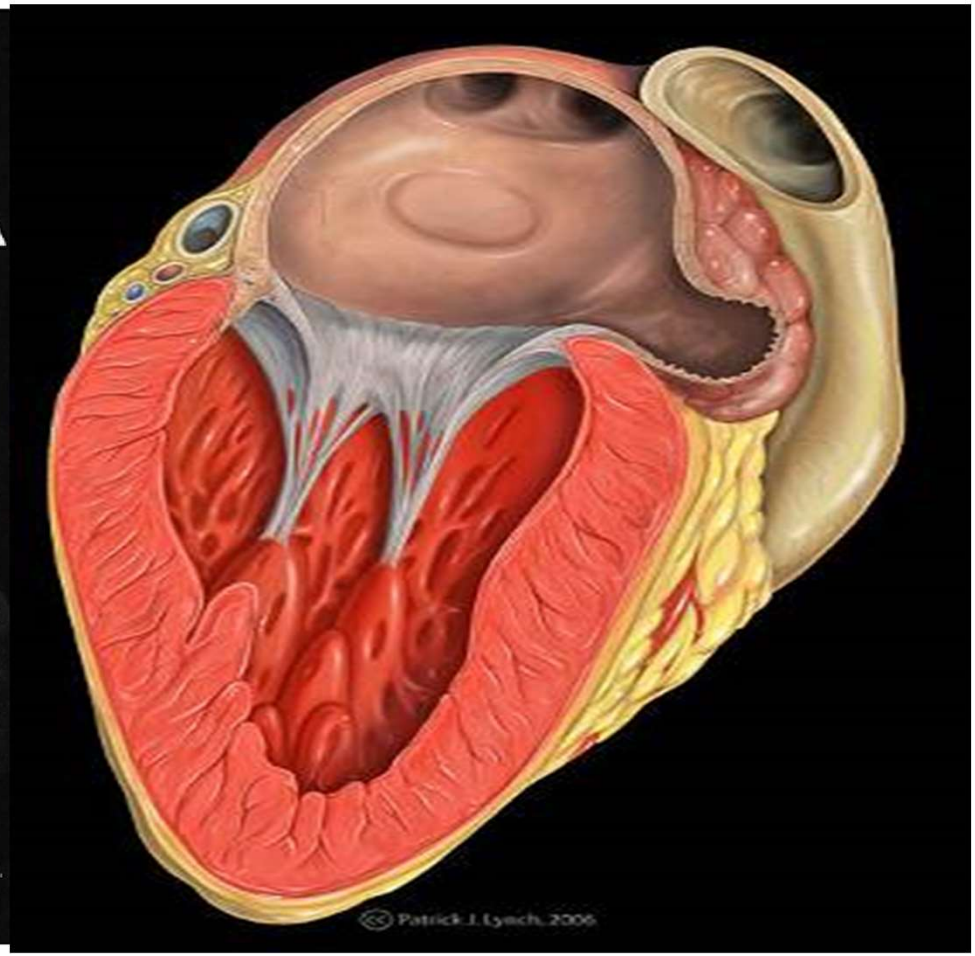
Witt DM et al *Arch Intern Med.* 2012;172(19):1484



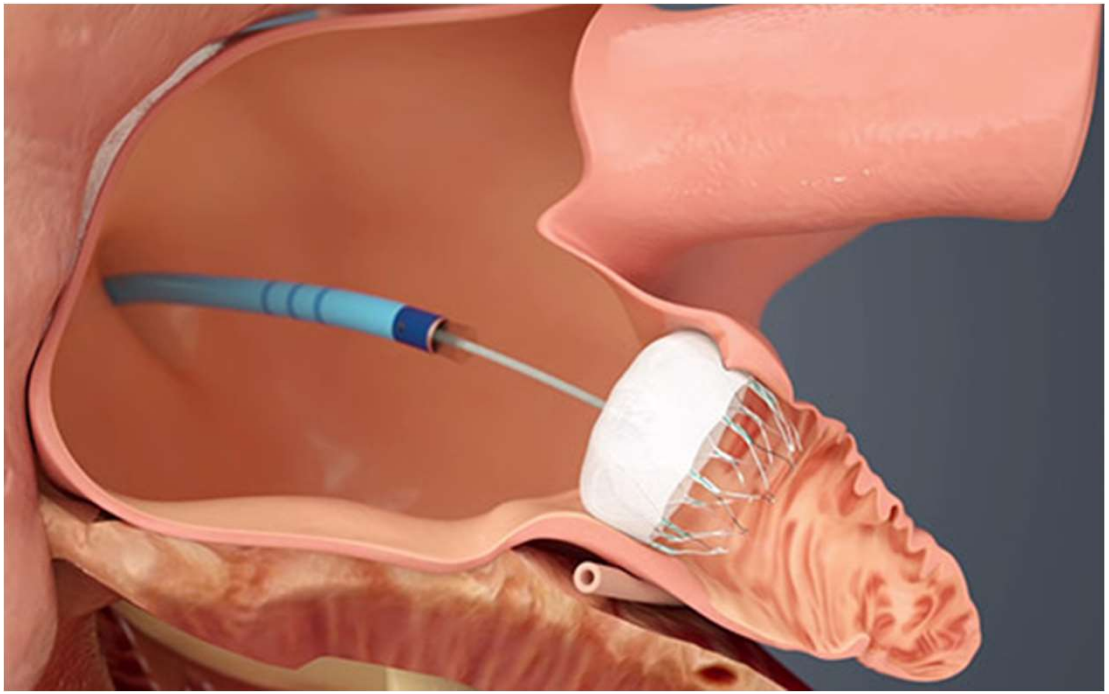
Qureshi W et al *Am J Cardiol* 2014;113:662

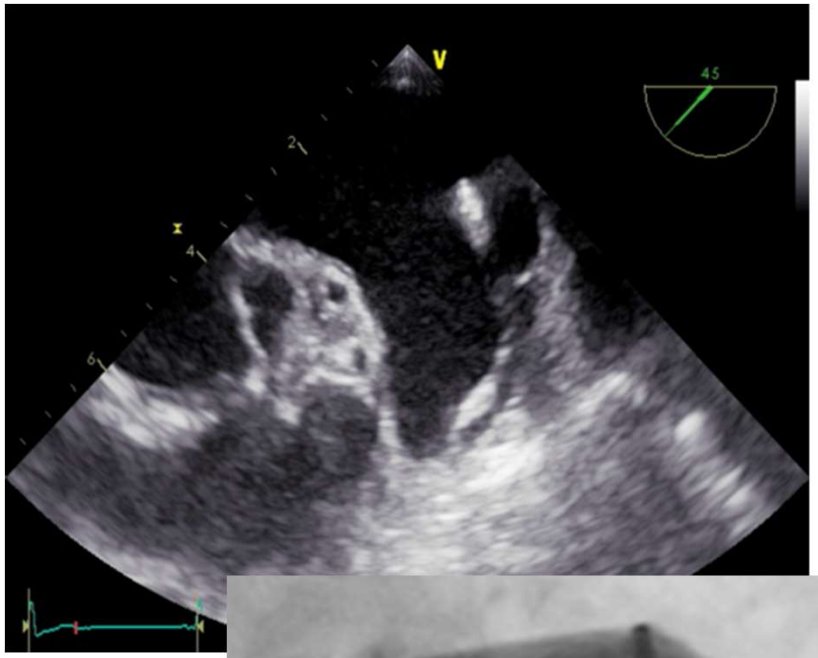
Left Atrial Appendage

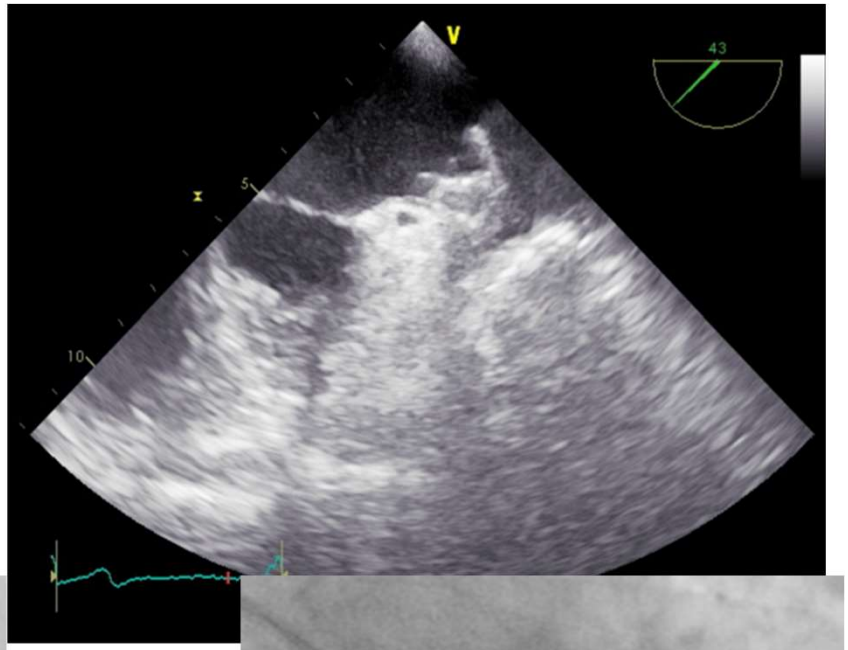


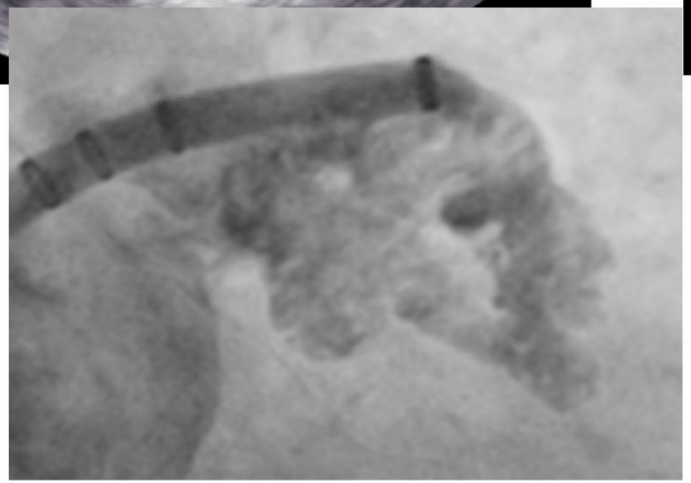


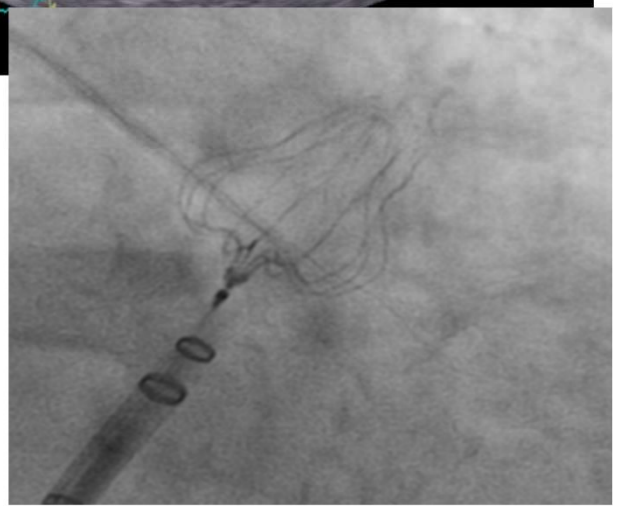
Concept:
Exclude the LAA from central circulation




V
45
2
4
6


V
43
5
10





Evidence Based Follow Up and Plan

Example of AF Referral Patterns

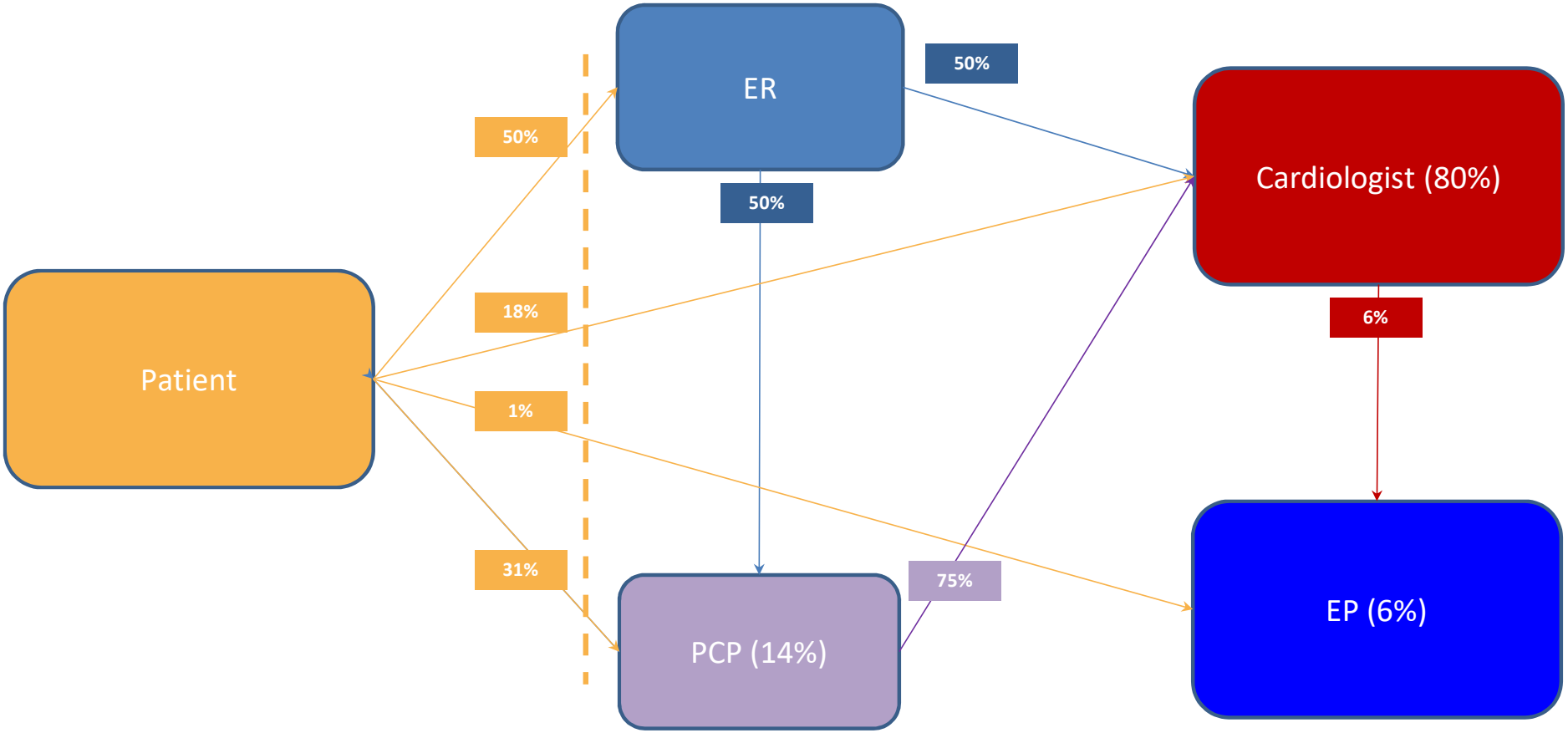


*Chart is based on BWI internal analysis of HMS/IMS claims data from Jan 1, 2012 to Apr 1. 2013.

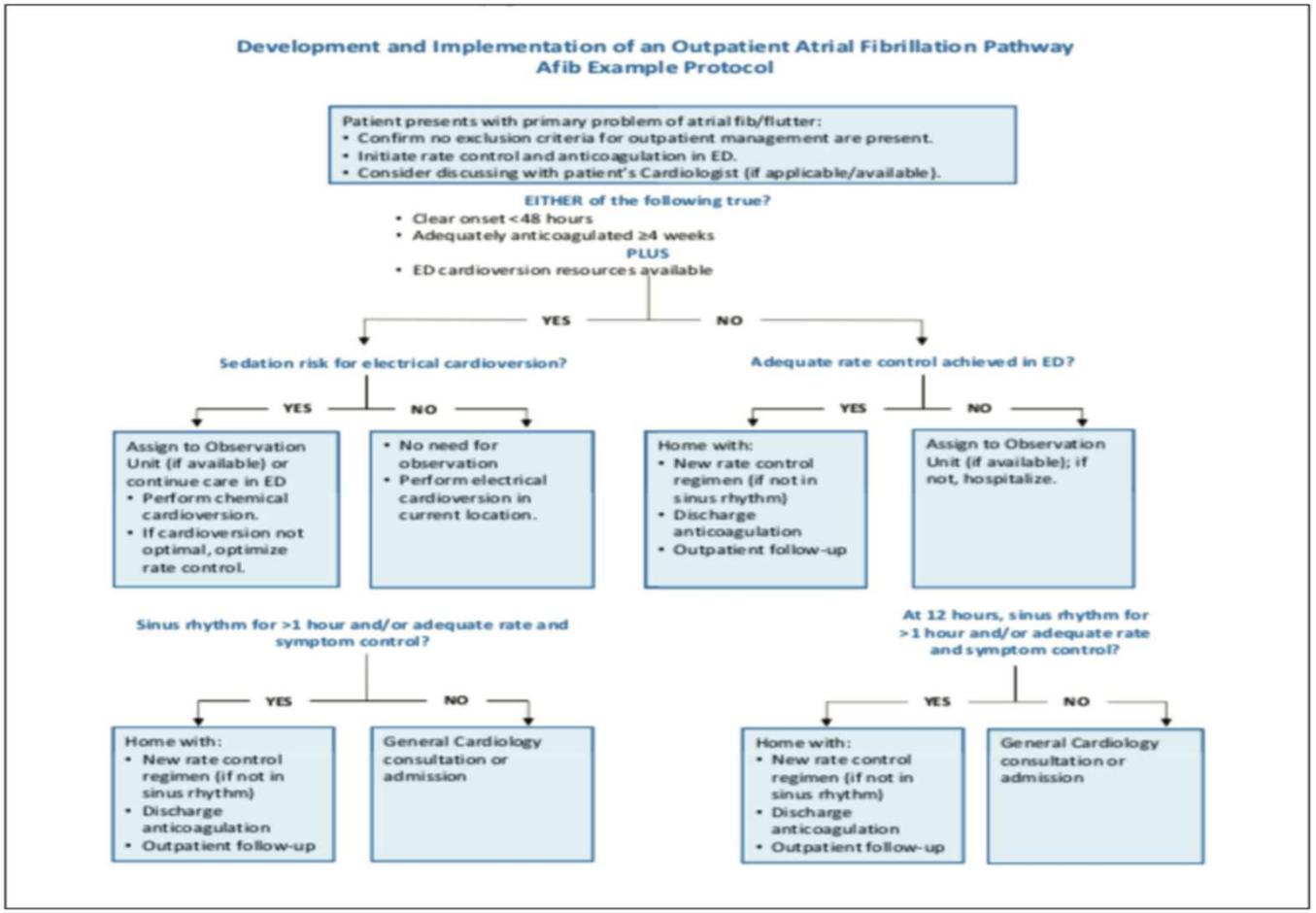


Figure 1: Sample atrial fibrillation outpatient pathway *(Reprinted with permission from Baugh CW, Clark CL, Wilson JW, et al. Creation and Implementation of an Outpatient Pathway for Atrial Fibrillation in the Emergency Department Setting: Results of an Expert Panel. Acad Emerg Med. 2018;25(9):1065-1075).*

Implementation of an ED Atrial Fibrillation and Flutter Pathway

Improved Rates of Appropriate Anticoagulation

48.6% → 70.2%

(Percent of Patients)

Shorter ED Length of Stay

262 → 218

(Minutes)

Decreased 30-day Revisit Rates for CHF

13.2% → 2.3%

(Percent of Patients)

Take Home Message: AF pathways can reduce system resource use and improve patient oriented outcomes

Barbic et al. *CJEM*. May 2018
https://doi.org/10.1017/cem.2017.418
Created by S. Huang and A. Chin. Editor: B. Thoma. CanadiEM.

canadiem CJEM JCMU