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Atrial Fibrillation

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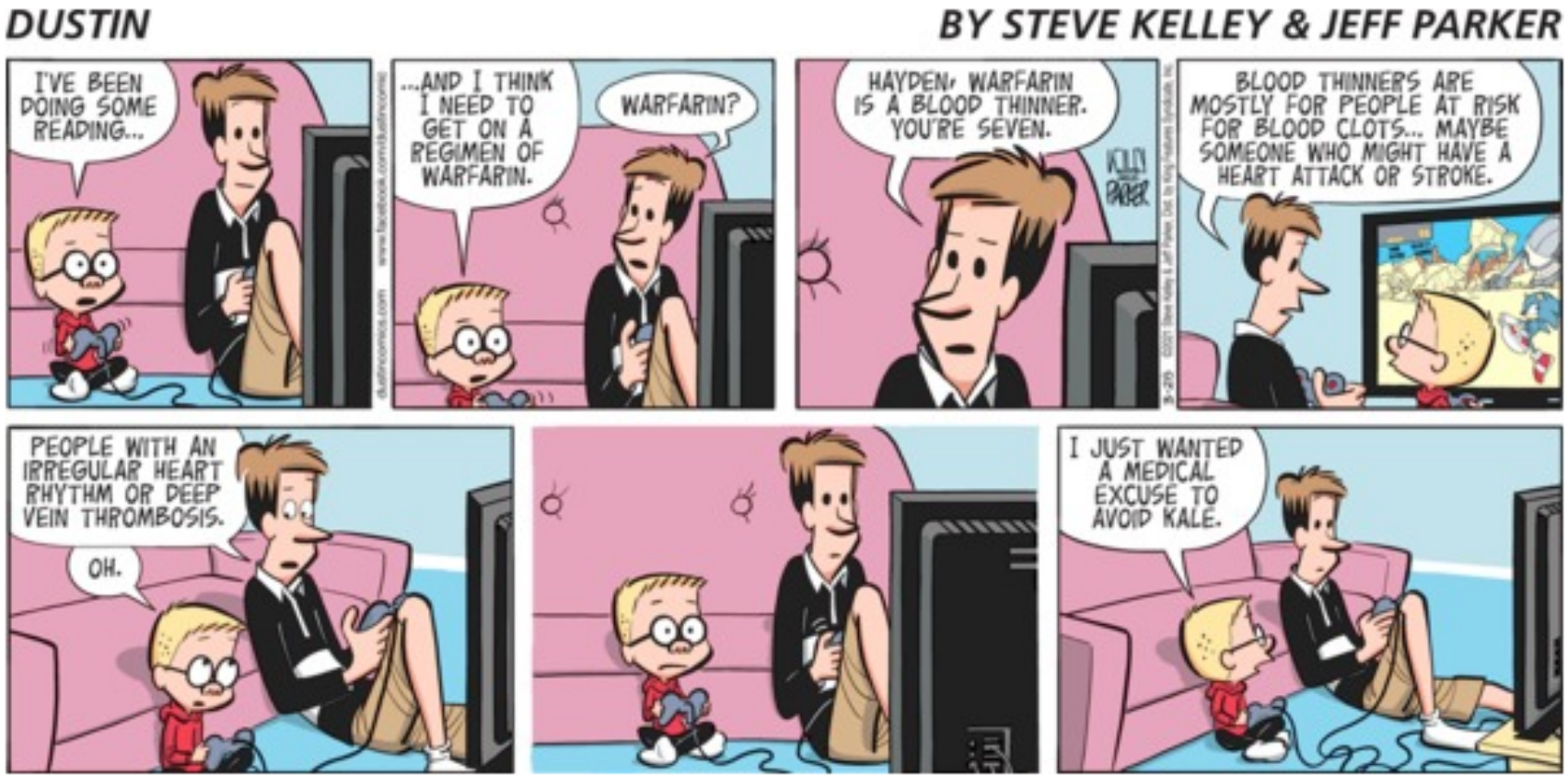
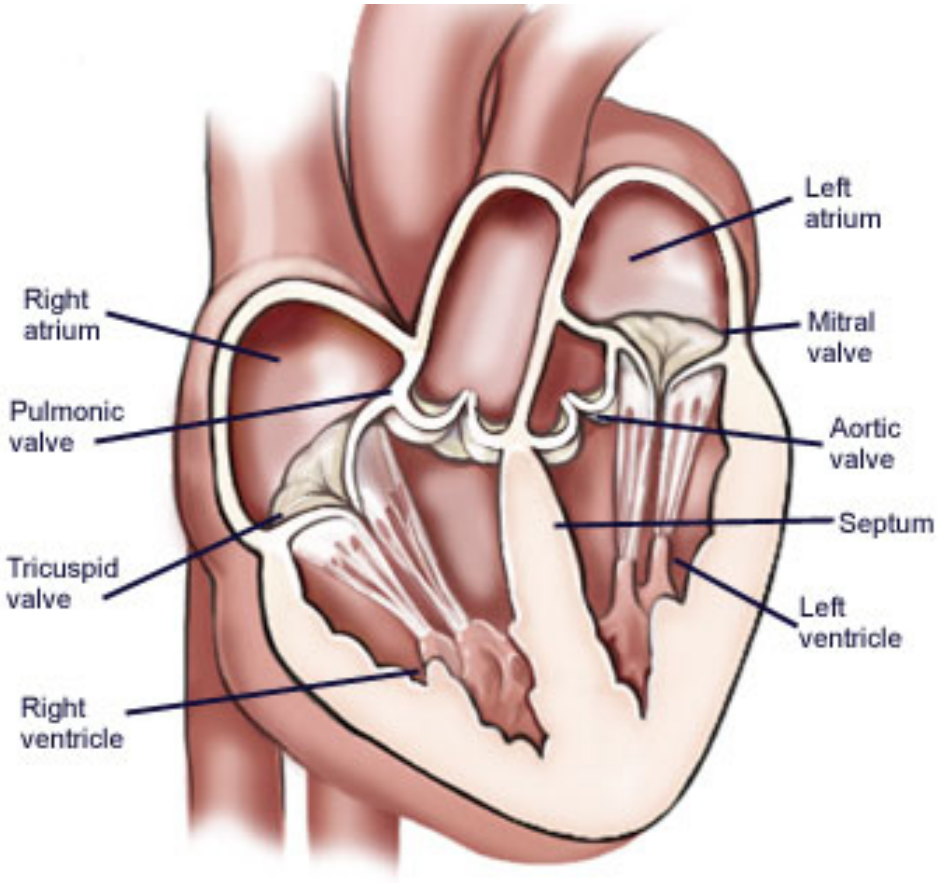


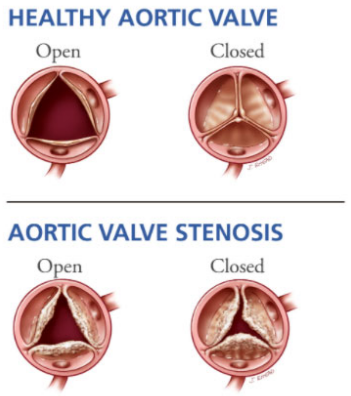
https://www.arcamax.com/thefunnies/dustin/s-2495070 3/28/21

Heart Valves

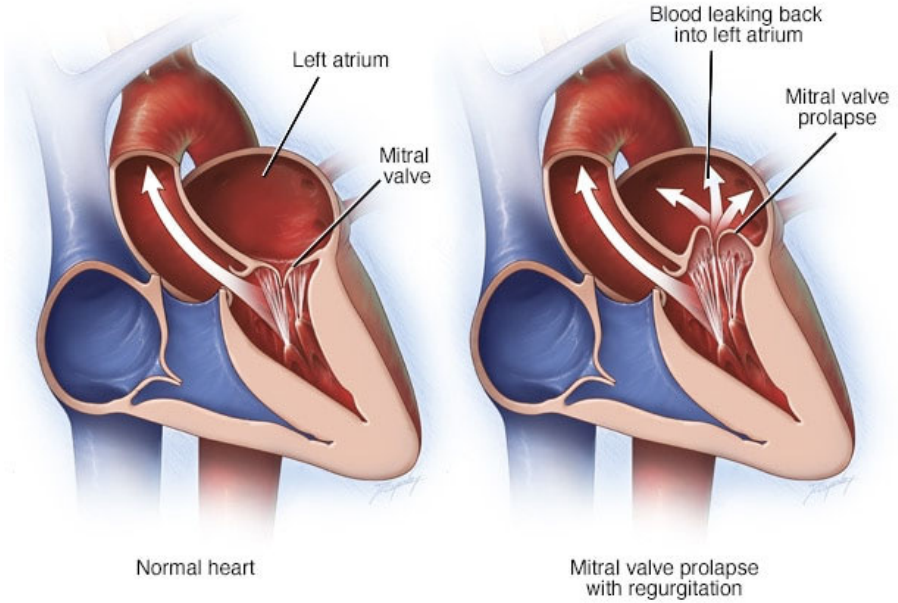
- Aortic
- Mitral
- Tricuspid
- Pulmonic



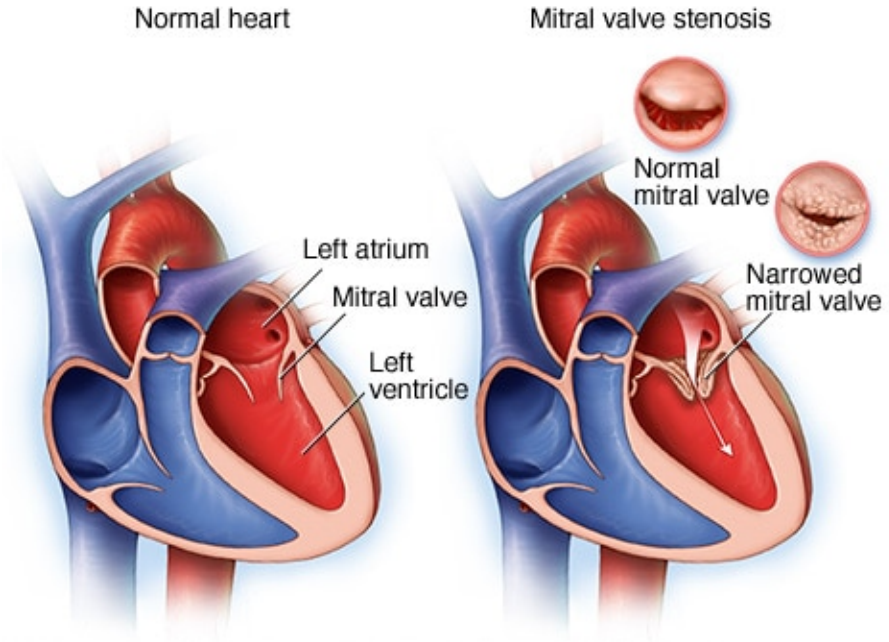
Valvular Heart Disease



Regurgitation

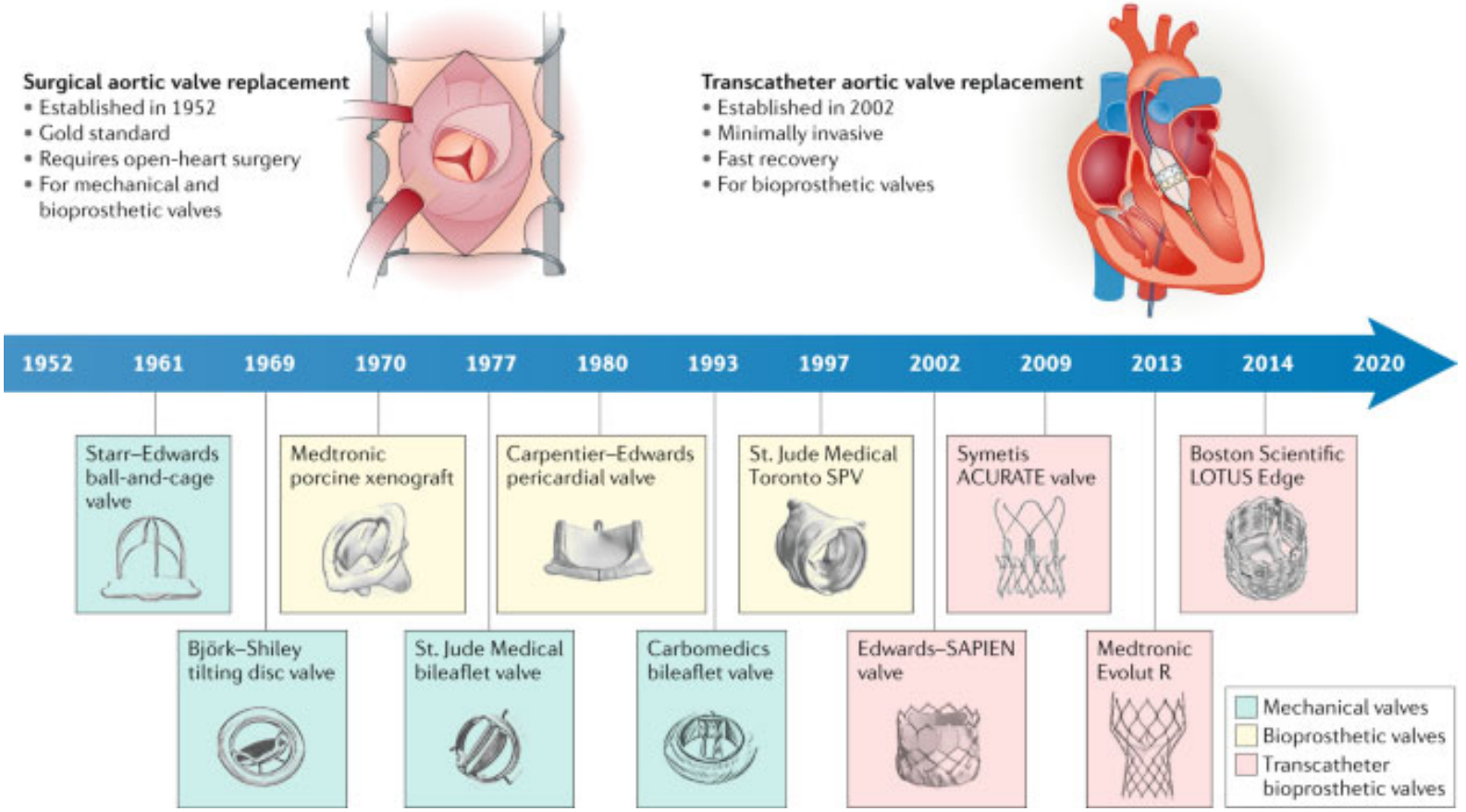


Stenosis



Valvular Heart Disease

- Disease vs. Valve Repair/Replacement



Nature Reviews Cardiology 2021. 18,92-116.

Valvular Heart Disease and Anticoagulation

- Mechanical prosthetic valves: warfarin

INR goal 2-3	• Mechanical bileaflet or current generation single-tilting disk AVR (no additional risk factors for TE)
INR goal 2.5-3.5	• Mechanical AVR + risk factors for TE or older-generation mechanical AVR • Mechanical MVR

Risk factors: AF, previous thromboembolism, LV dysfunction, hypercoagulable conditions

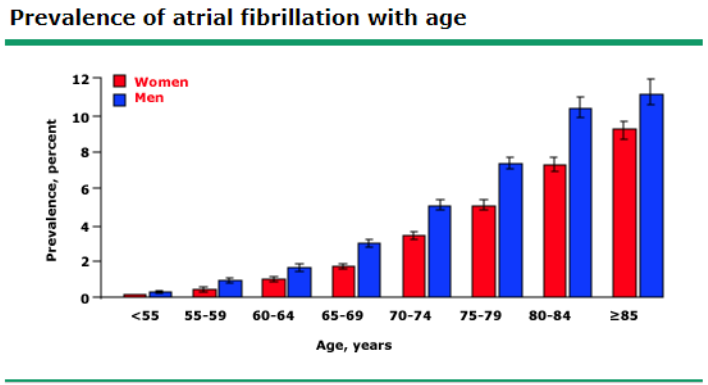
- Aspirin 75-100mg daily + warfarin in patients with a mechanical valve
- Aspirin 75-100mg daily reasonable for all patients with a bioprosthetic aortic or mitral valve
  - Warfarin (INR goal 2-3) at least 3 months, up to 6 months after bioprosthetic MVR or AVR in patients at low risk of bleeding
  - Lifelong anticoagulation not required in many patients

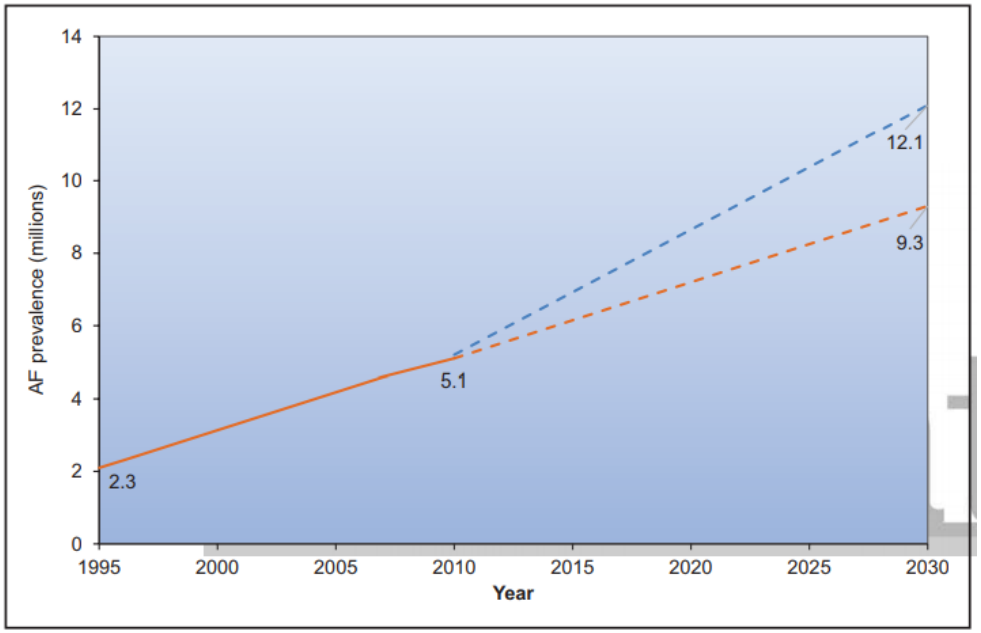
Objectives

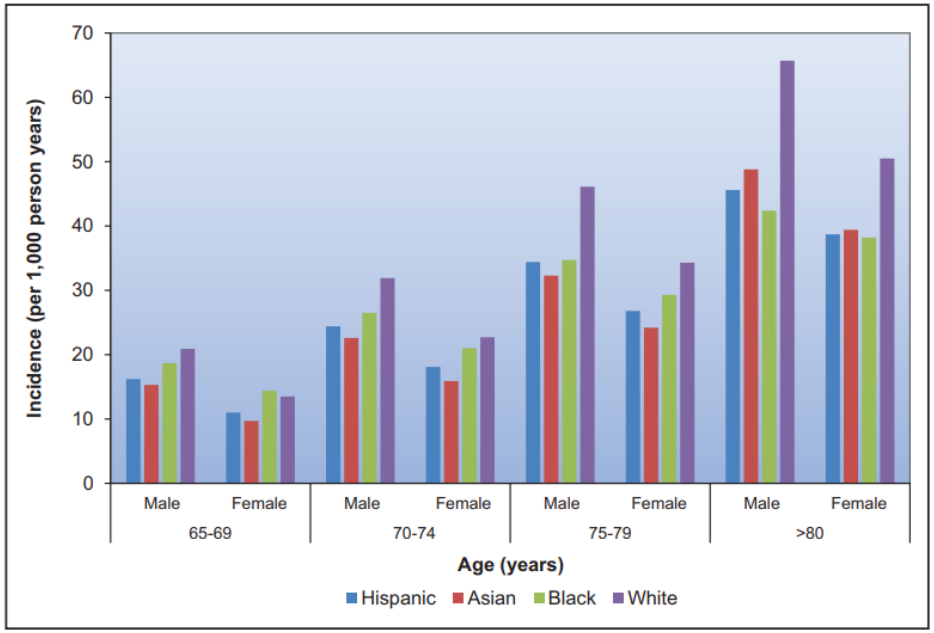
- Understand the pathophysiology of atrial fibrillation
- Select appropriate antithrombotic therapy for ischemic stroke prevention for patients with atrial fibrillation
- Select appropriate medications for ventricular rate control in patients with atrial fibrillation
- Select appropriate medications for rhythm control in patients with atrial fibrillation
- Discuss appropriate therapies for rhythm control in patients with atrial fibrillation

Atrial Fibrillation

- Estimated ~2.7-6.1 million people in US
- Overall prevalence of 0.4-1%



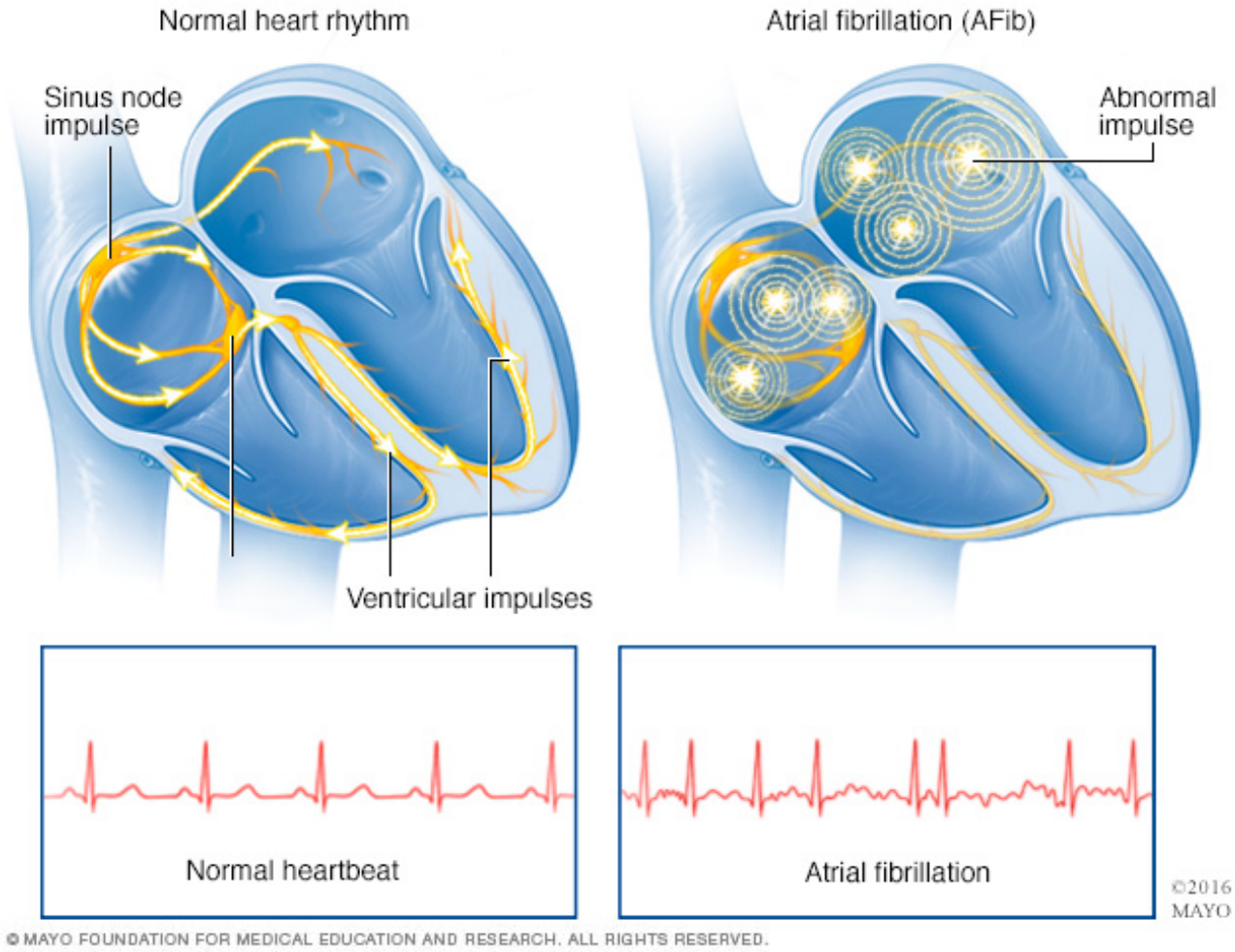




2017 AHA Heart Disease and Stroke Statistics

Atrial Fibrillation

- Disorganized atrial activation
- Irregularly irregular rhythm
- Extremely rapid atrial rate: 400-600 beats/min
- Rapid ventricular rate: 120-180 beats/min



Atrial Fibrillation Video

https://www.medtronic.com/us-en/patients/conditions/atrial-fibrillation-afib.html

AF Definitions

Acute	Onset within 48 hours
Paroxysmal	Terminates spontaneously or with intervention within 7 days of onset
Persistent	Duration longer than 7 days and does not terminate spontaneously
Longstanding persistent	Continuous AF > 12 months in duration
Permanent	• Does not terminate with attempts at pharmacologic or electrical cardioversion • Decision to accept AF; no further attempts to restore and/or maintain sinus rhythm
Recurrent	Two or more episodes
Lone	AF in absence of structural heart disease
Nonvalvular	AF in absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair

Atrial fibrillation vs. Atrial flutter

	Atrial Fibrillation	Atrial Flutter
Rhythm	Irregularly irregular supraventricular	Regular supraventricular
Atrial Rate	400-600 bpm	270-330 bpm
Ventricular Rate	Irregular	Regular ratio of A:V conduction (i.e. 2:1, or 3:1)
EKG	No consistent atrial activity (p waves)	Sawtooth pattern

Risk Factors for AF

- Increasing age
- HTN
- Diabetes mellitus
- Myocardial infarction
- Valvular heart disease
- Heart failure
- Obesity
- Obstructive sleep apnea
- Cardiothoracic surgery
- Smoking
- Exercise
- Alcohol use
- Hyperthyroidism
- Congenital heart disease
- Hypertrophic cardiomyopathy
- VTE
- CKD
- Abnormal QT or P-wave duration

Signs/Symptoms of AF

- May be asymptomatic
- Rapid HR/palpitations
- Fatigue, weakness
- Dizziness, lightheadedness, syncope
- Dyspnea
- Chest pain
- Embolic event (stroke or TIA)
- Heart failure symptoms (pulmonary/peripheral edema, weight gain, ascites)

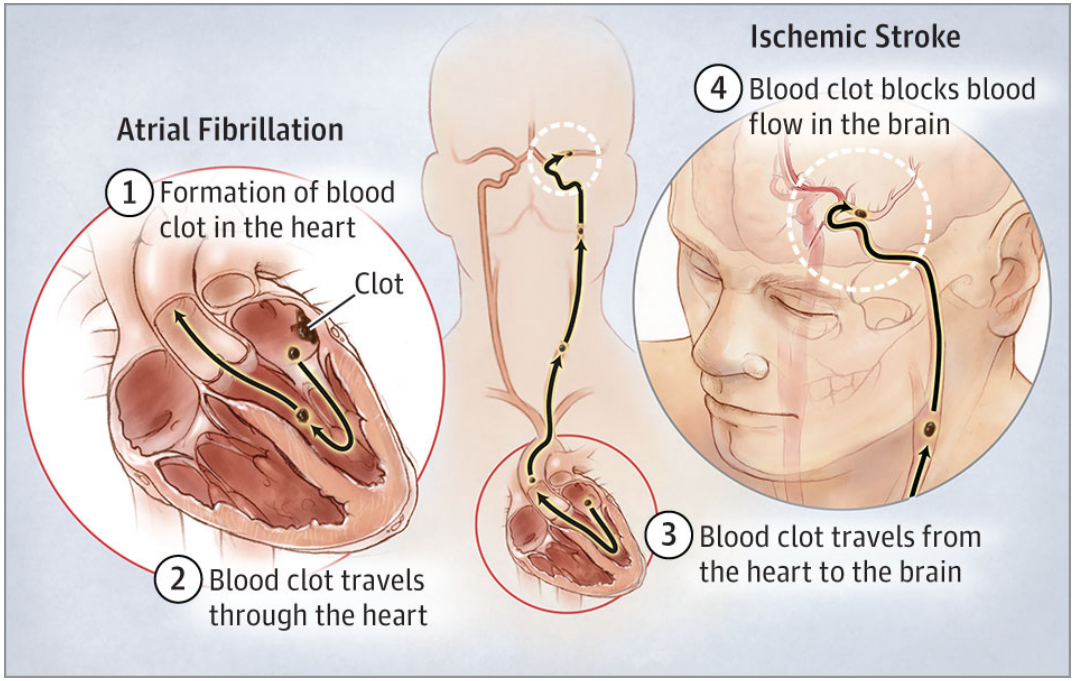
http://www.medtronic.com/us-en/patients/conditions/atrial-fibrillation-afib.html

Atrial Fibrillation Treatment Strategies

1. Prevention of thromboembolism
2. Rate control
3. Rhythm control

Treatment Strategy #1: Stroke Prevention

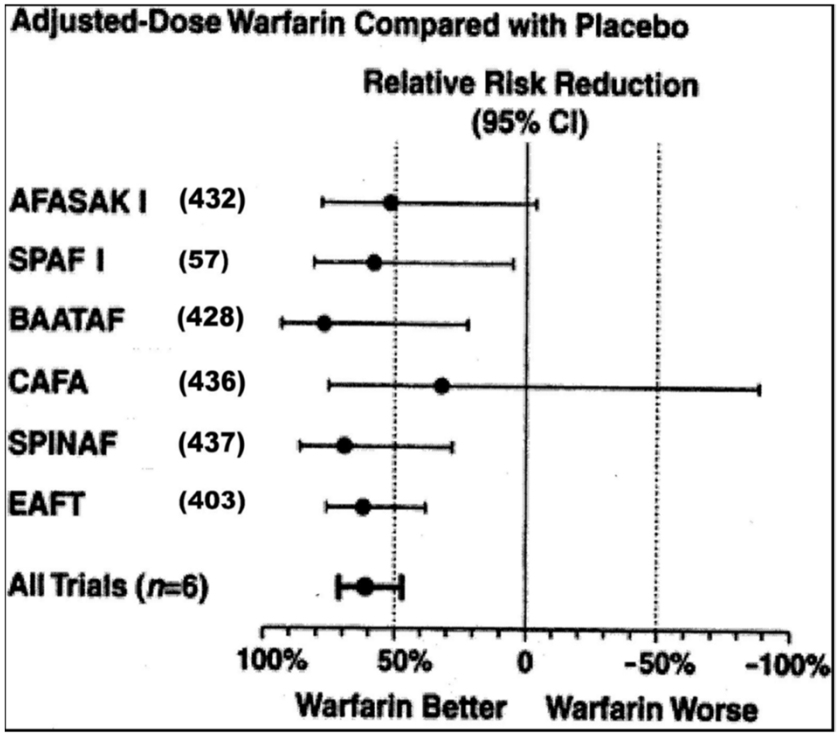
- ~5% average risk of ischemic stroke in patients not on antithrombotic therapy
- Significantly increases with age
- Pathophysiology
  - Blood not ejected from left atrium to left ventricle
  - Blood pools in the left atrium, especially in left atrial appendage
  - Thrombus formation
    - →Travels through mitral valve
    - →Left ventricle
    - →Ejected during systole

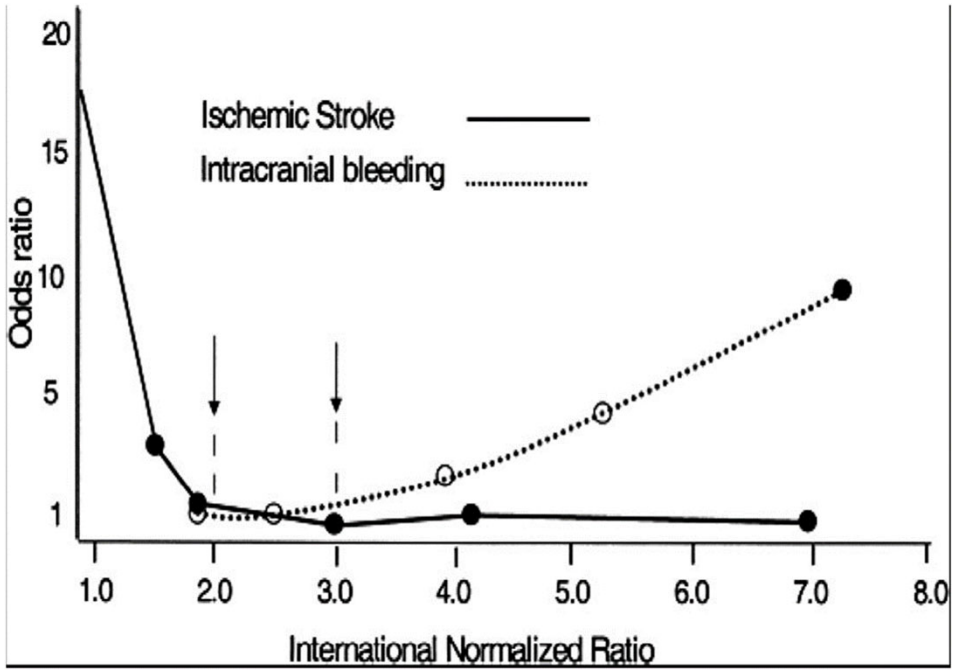


Treatment Strategy #1: Stroke Prevention

- Medications – Antithrombotics
  - Antiplatelets
    - Aspirin 81mg or 325mg daily
    - Aspirin + clopidogrel 75mg daily
  - Anticoagulants
    - Warfarin (goal INR of 2-3)
    - Direct thrombin inhibitor
      - Dabigatran
    - Factor Xa inhibitors
      - Apixaban
      - Rivaroxaban
      - Edoxaban

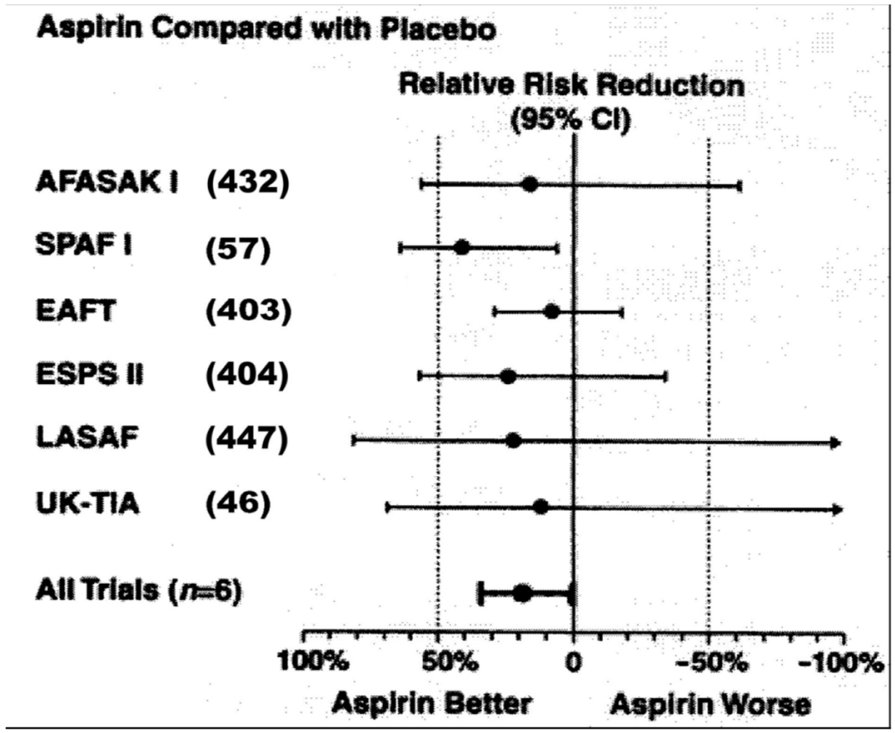
Warfarin





AHA/ACC AF Guidelines 2006

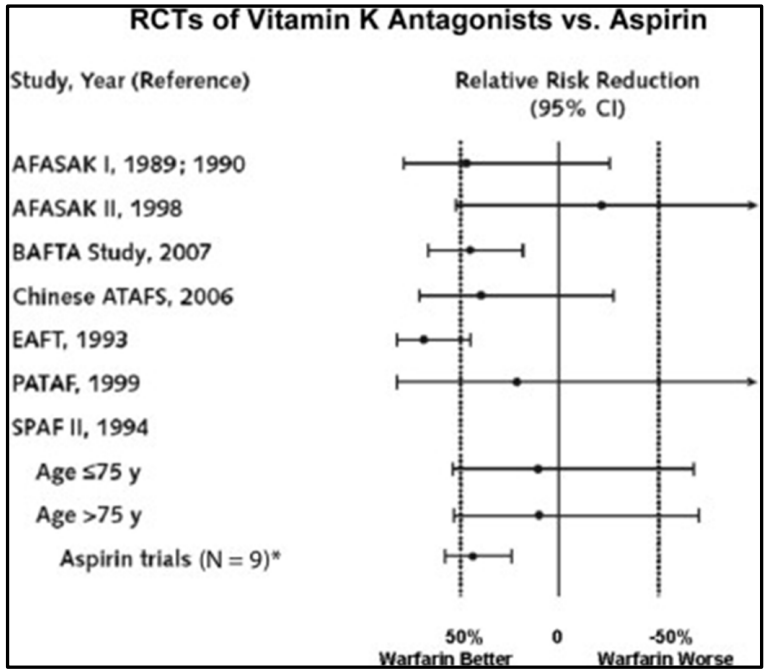
Aspirin



- Aspirin is superior to placebo at reducing stroke
- 20% RRR in meta- analysis
- No evidence that 81 mg or 325 mg is better

AHA/ACC AF Guidelines 2006

Warfarin vs. Aspirin



- Warfarin is superior to aspirin at reducing stroke
- 39% RRR in meta- analysis

CCS AF Guidelines 2010

Warfarin vs. Aspirin + Clopidogrel

Trial	End Point	Conclusion
ACTIVE W n=3371 AF and ≥ 1 RF for stroke Warfarin with INR 2-3 vs. clopidogrel 75mg + aspirin 75-100mg	Combined: first occurrence of stroke, non-CNS systemic embolism, MI, vascular death	Prematurely stopped: Warfarin (165 events) vs. Clopidogrel + aspirin (234 events) (p=0.0003) Major bleeding was similar
ACTIVE A n=7554 AF unsuitable for warfarin treatment Aspirin alone vs. clopidogrel 75mg + aspirin 75-100mg	Combined: first occurrence of stroke, non-CNS systemic embolism, MI, vascular death	Decreased events with aspirin + clopidogrel 6.8% vs. 7.6% (p=0.01) Increased major bleeding with aspirin + clopidogrel 2% vs. 1.3% (p<0.001)

Assessing Stroke Risk: CHA_2DS_2-VASc

Risk Factor	Score
C ongestive heart failure	1
H ypertension	1
A ge ≥ 75 years	2
D iabetes mellitus	1
S troke/TIA/ Thromboembolism	2
V ascular disease (prior MI, PAD, aortic plaque)	1
A ge 65-74	1
S ex **c**ategory (ie, female sex)	1

CHA_2DS_2-VASc Score	Adjusted ischemic stroke rate (% per yr)
0	0.2%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.2%

Friberg L, Rosenqvist M, Lip GY. Eur Heart J 2012; 33:1500.
January CT, Wann LS, Alpert JS, et al. J Am Coll Cardiol 2014.

Stroke Risk and Anticoagulation

CHEST 2018 Atrial Fibrillation Guidelines

CHA_2DS_2 – VASc Score	Recommendation
0 (male) 1 (female)	No antithrombotic therapy
1 (male) 2 (female)	Oral anticoagulation (OAC) recommended

- In patients eligible for OAC, recommend DOACs over VKA
- Recommend against antiplatelet therapy alone regardless of stroke risk
- HAS-BLED to assess bleeding risk

CHEST. 2018;154(5):1121-1201.

AHA/ACC/HRS 2019 Atrial Fibrillation Guidelines

CHA_2DS_2 – VASc Score	Recommendation
0 (male) 1 (female)	No antithrombotic therapy
1 (male) 2 (female)	Anticoagulation may be considered
2 (male) 3 (female)	Oral anticoagulation (OAC) recommended

- NOACs recommended over warfarin in NOAC-eligible patients
- Nonvalvular afib: absence of moderate-to-severe mitral stenosis or a mechanical heart valve

Circulation. 2019;139.online

Patient Case

- JM is an 82 yo female with PMH of DM, HTN, increased lipids, h/o NSTEMI with PCI 6 years ago, and osteoporosis.

- **What is the patient's CHA_2DS_2-VASc score?**

Assessing Anticoagulation: Warfarin

Risk Factor	Score
S ex (female)	1
A ge (< 60 years)	1
Me dical history (≥ 2 comorbidities: hypertension, diabetes mellitus, coronary artery disease/myocardial infarction, peripheral artery disease, heart failure, prior stroke, pulmonary disease, and liver or renal disease)	1
T reatment (interacting drugs, such as amiodarone)	1
T obacco use (within 2 years)	2
R ace (non-Caucasian)	2

Patients with score >2 may not achieve high TTRs and DOACs may want to be considered instead of warfarin.

Apostolakis S, Sullivan RM, Olshansky B, et al. Factors affecting quality of anticoagulation control among patients with atrial fibrillation on warfarin: the same-tt2r2 score. CHEST. 2013;144(5)1555-1563.

Assessing Bleeding Risk: HAS-BLED

	Clinical Characteristic	Points
H	Hypertension (ie, uncontrolled blood pressure, SBP > 160mmHg)	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding tendency or predisposition	1
L	Labile INRs (for patients taking warfarin)	1
E	Elderly (age greater than 65 years)	1
D	Drugs (concomitant aspirin or NSAIDs) or excess alcohol use (1 point each)	1 or 2

HAS-BLED Score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5 to 9	Insufficient data

Lip GY. Am J Med 2011; 124:111. Lip GY. ACC, 9/17/2012.
Pisters R. Chest 2010; 138:1093

Major Outcomes of DOACs vs. Warfarin

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
	RE-LY	ROCKET-AF	ARISTOTLE	ENGAGE AF
Mean $CHADS_2$ Score	2.1	3.5	2.1	2.8
Mean TTR	64%	55%	62%	65%
Efficacy				
Stroke/SE	Superior	Non-inferior	Superior	Non-inferior
Ischemic Stroke	Superior	Non-inferior	Non-inferior	Non-inferior
Hemorrhagic stroke	Superior	Superior	Superior	Superior
Safety				
Major bleeding	Non-inferior	Non-inferior	Superior	Superior
Intracranial hemorrhage	Superior	Superior	Superior	Superior
GI Bleeding	Inferior	Inferior	Non-inferior	Inferior

Dosing for Non-Valvular Atrial Fibrillation

Drug	Dose
Dabigatran	• CrCL >30mL/min: 150mg BID • CrCL 15-30 mL/min: 75mg BID † • CrCL <15mL/min or patients on dialysis: not recommended
Rivaroxaban	To be given with evening meal: • CrCL > 50 mL/min: 20mg po daily • CrCL 15-50 mL/min: 15mg po daily • Avoid in patients with CrCL < 15 mL/min, not recommended in dialysis
Apixaban	5mg BID - OR - 2.5mg BID in patients with at least 2 of the following characteristics: • age ≥80 years, bodyweight ≤60kg, serum creatinine ≥1.5 mg/dL ESRD with dialysis: no dosage adjustment necessary unless age ≥80 years or bodyweight ≤60kg, then reduce dose
Edoxaban	• CrCL 51-95mL/min: 60mg daily • CrCL 15-50 mL/min: 30 mg daily • CrCL < 15 mL/min: not recommended Not used if CrCL > 95mL/min

*For dabigatran, rivaroxaban, and edoxaban, patients with CrCl <30 mL/min were excluded from clinical trials; for apixaban, patients with CrCl <25 mL/min (or Scr >2.5 mg/dL) were excluded.

†Was not evaluated in clinical trials, but is an FDA-approved dose