CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Strategies for Prevention of Stroke Associated with Atrial Fibrillation

Sunny Kapur MD

Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

Disclosures

- Honoraria / Research Support - Medtronic, Abbott, Biotronik, Novartis, Pfizer, Aziyo

Outline

- *The relationship between Afib and Stroke*
- *Pharmacologic Prevention of CVA in AF*
- *Non-pharmacologic Prevention of CVA in AF*
- *Preventing Recurrent AF strokes*

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

The Relationship Between AF and Stroke

Sunny Kapur MD

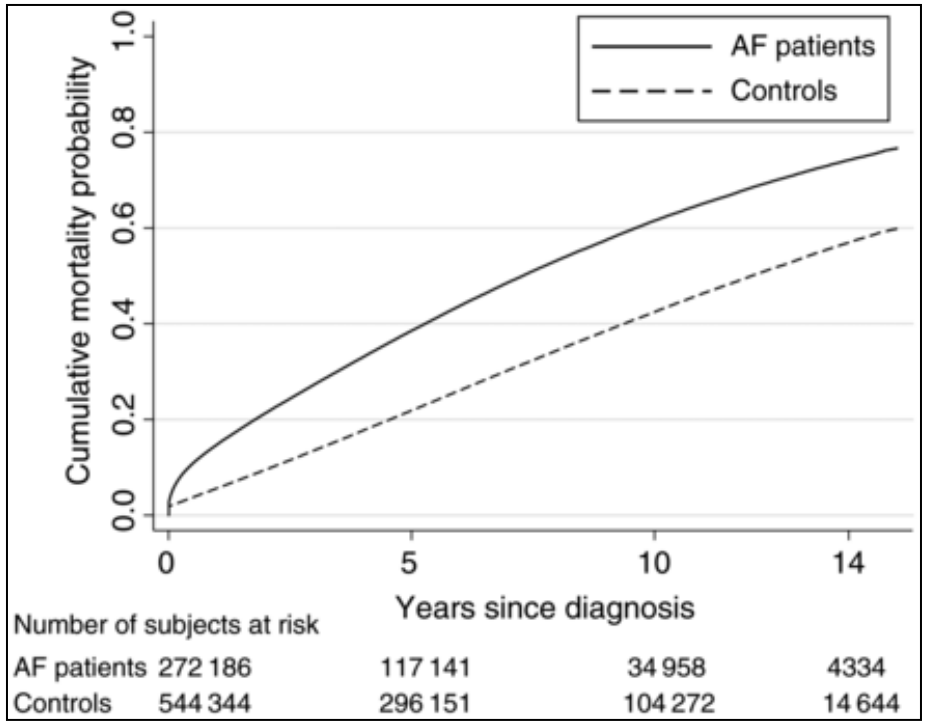
Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

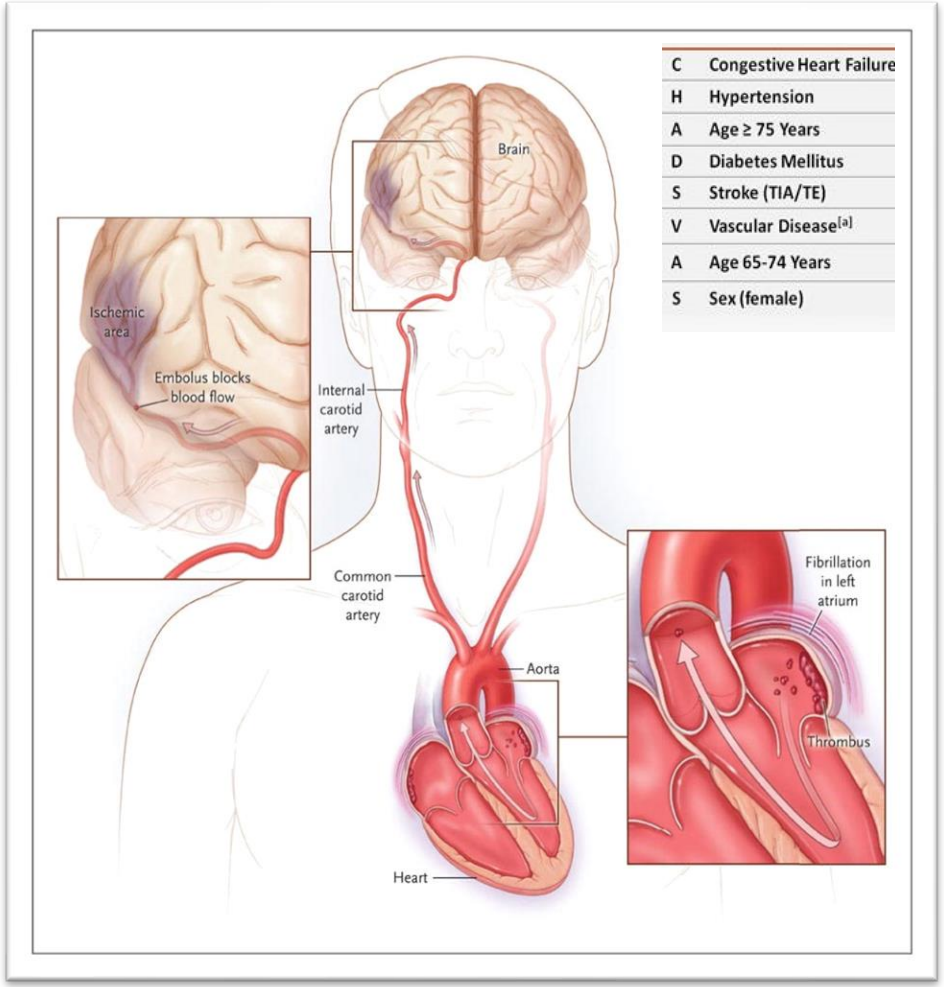
Outline

- ***The relationship between Afib and Stroke***
- *Pharmacologic Prevention of CVA in AF*
- *Non-pharmacologic Prevention of CVA in AF*
- *Preventing Recurrent AF strokes*

AF is associated with significant morbidity and mortality

Classification of AF-related symptoms (EHRA Score)	
EHRA class	**Explanation**
EHRA I	"No symptoms"
EHRA II	" Mild symptoms"; normal daily activity not affected
EHRA III	" Severe symptoms"; normal daily activity affected
EHRA IV	" Disabling symptoms"; normal daily discontinued





Go AS. N Engl J Med 2009;360:2127-2129.

Eur Heart J. 2013 Apr;34(14):1061-7.

AF leads to strokes – AF related strokes are debilitating

Stroke

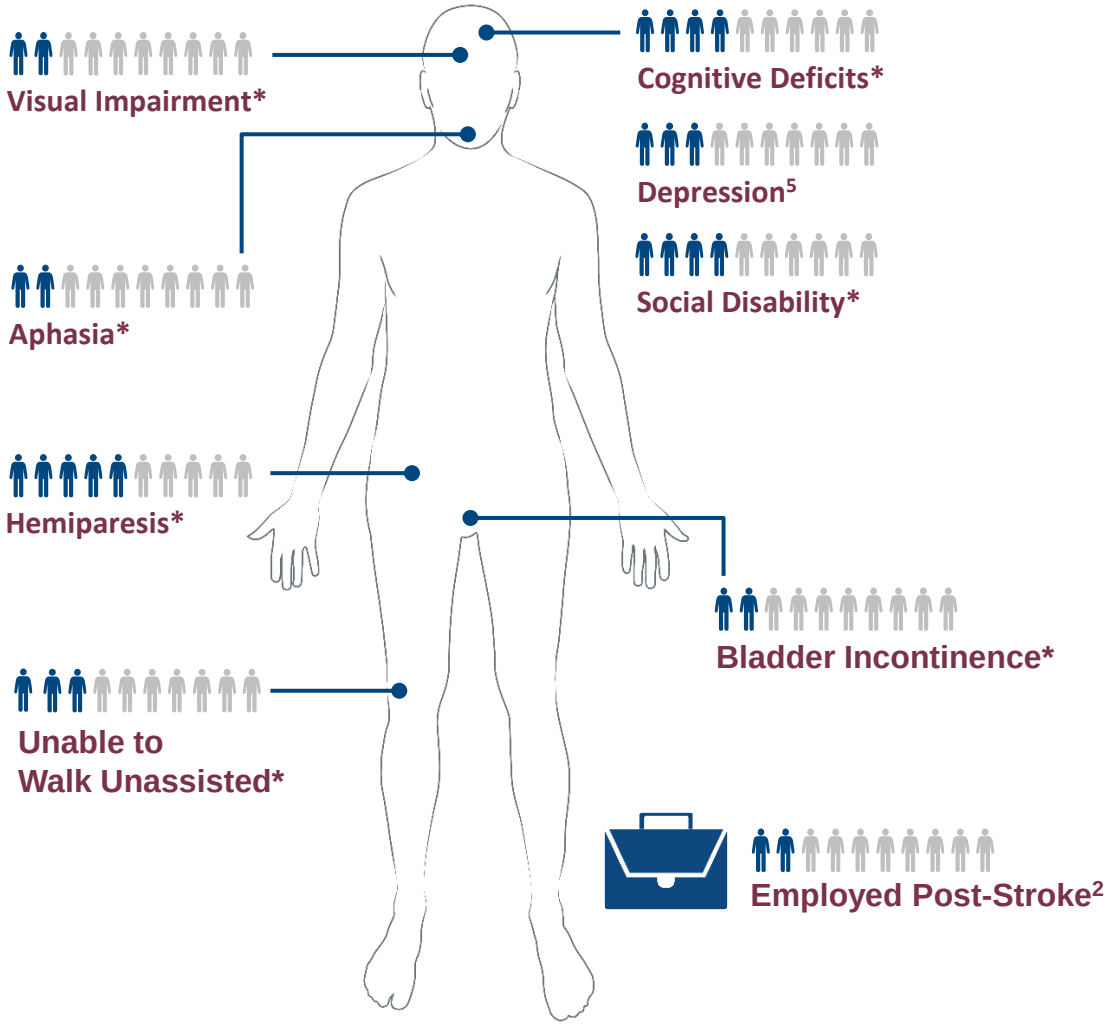
#1 cause of **adult disability** worldwide[1]

AF-related Stroke

1.5X higher **disability**[3**]

2X higher **mortality**[3**]

70% result in **death or permanent disability**[6]

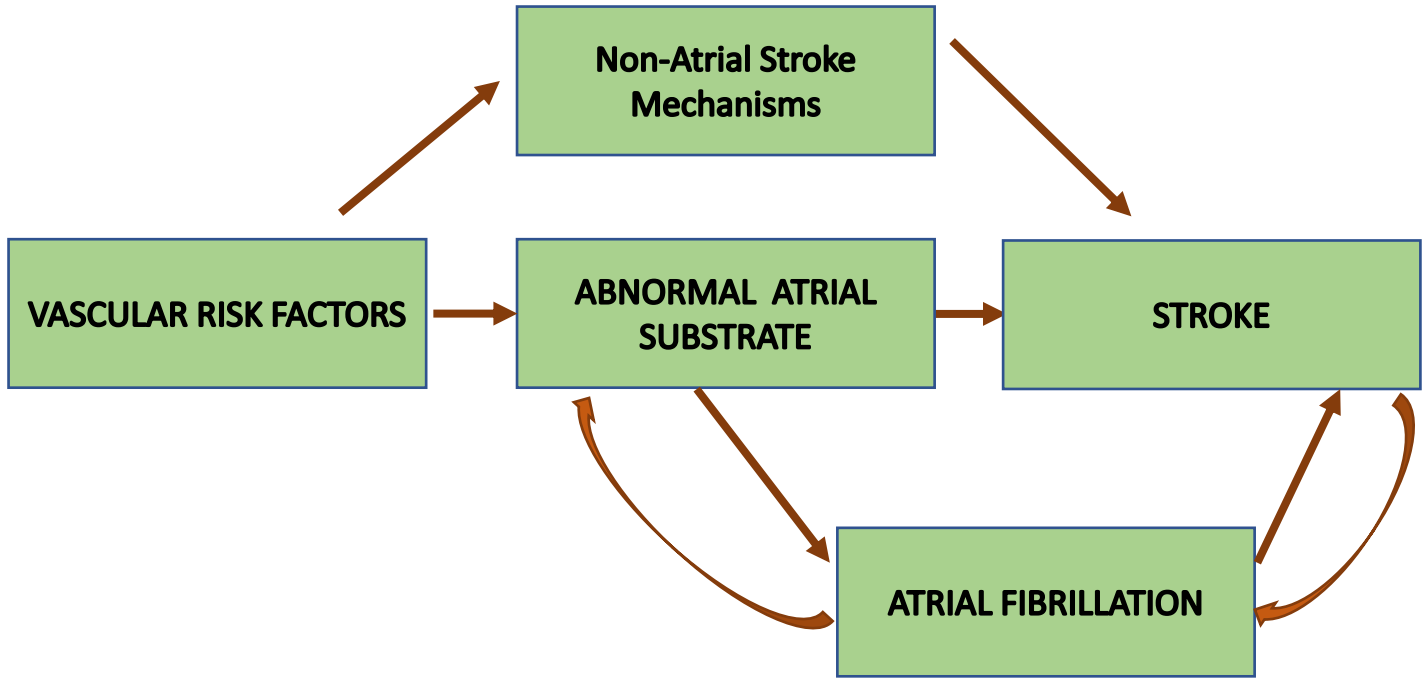


*at 6 months post-stroke[4]

**compared with stroke patients without AF

1. Chee and Tan. "Impact of atrial fibrillation among stroke patients in a Malaysian teaching hospital." Med J Malaysia 69.3 (2014): 119-23.
2. Sreedharan et al. "Employment status, social function decline and caregiver burden among stroke survivors. A South Indian study." Journal of the neurological sciences 332.1 (2013): 97-101.
3. Lamassa et al. "Characteristics, Outcome, and Care of Stroke Associated With Atrial Fibrillation in Europe Data From a Multicenter Multinational Hospital–Based Registry (The European Community Stroke Project)." Stroke 32.2 (2001): 392-398.
4. Kelly-Hayes et al. "The influence of gender and age on disability following ischemic stroke: the Framingham study." Journal of Stroke and Cerebrovascular Diseases 12.3 (2003): 119-126.
5. Loo and Gan. "Burden of stroke in Malaysia." International Journal of Stroke 7.2 (2012): 165-167.
6. Holmes DR, Atrial Fibrillation and Stroke Management: Present and Future, Seminars in Neurology 2010;30:528–536

AF → CVA Mechanisms



Updated model of thromboembolic stroke. This model emphasizes the importance of systemic and atrial substrate as well as rhythm in explaining the relationship between atrial fibrillation (AF) and stroke. In this model, aging and systemic vascular risk factors cause an abnormal atrial tissue substrate, or atrial cardiopathy, that can result in AF and thromboembolism. Once AF develops, the dysrhythmia causes contractile dysfunction and stasis, which further increases the risk of thromboembolism. In addition, over time, the dysrhythmia causes structural remodeling of the atrium, thereby worsening atrial cardiopathy and increasing the risk of thromboembolism even further. In parallel, systemic risk factors increase stroke risk via other mechanisms outside the atrium, such as large-artery atherosclerosis, ventricular systolic dysfunction, and in-situ cerebral small-vessel occlusion. Once stroke occurs, autonomic changes and post-stroke inflammation may transiently increase AF risk.

Stroke, Volume 47, Issue 3, March 2016; Pages 895-900

AF → CVA Mechanisms?

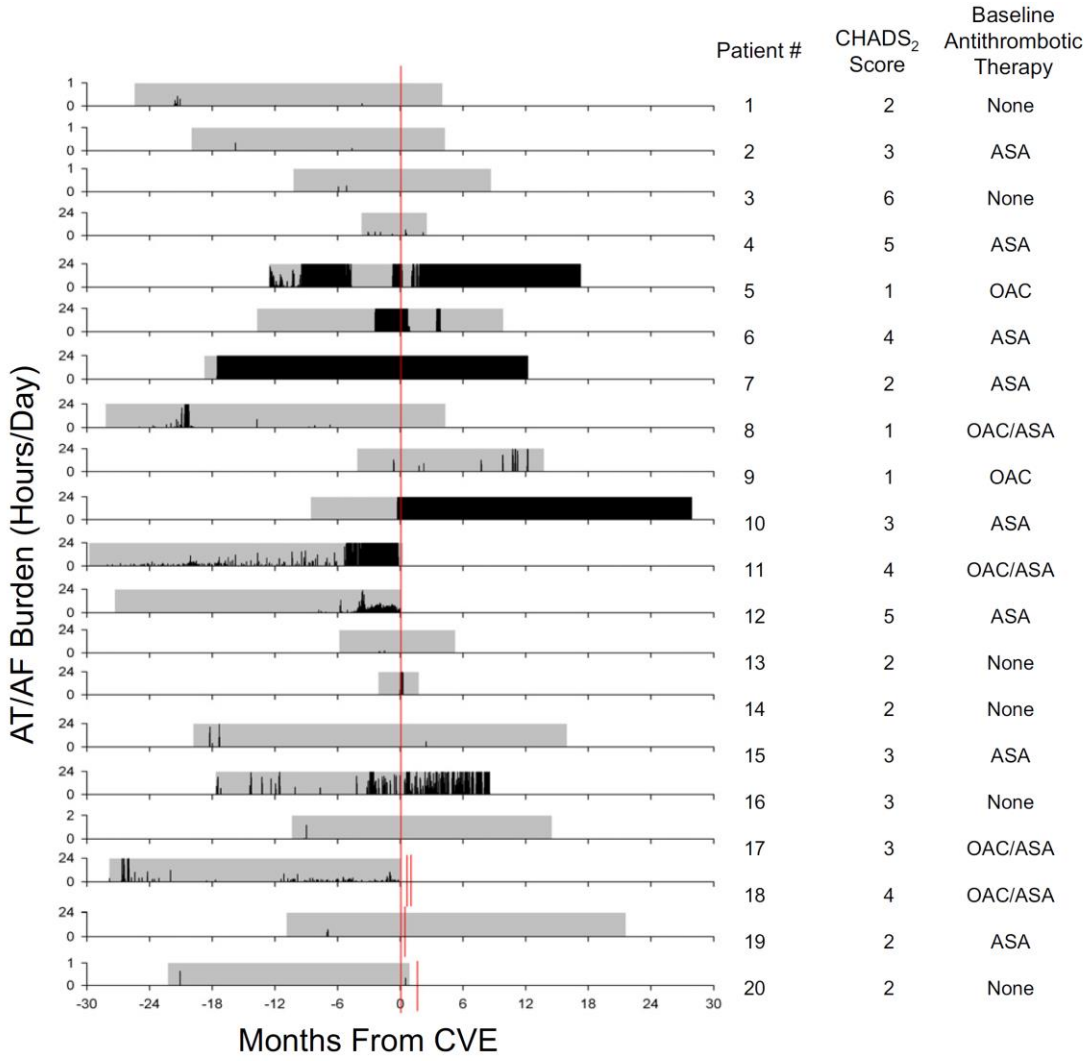
Marker	Authors	Year	Outcome	Association	
				Not Adjusted For AF	Adjusted For AF
ECG markers					
Frequent PACs	Binici et al40	2010	Stroke	1.79 (1.14–2.81)*	1.73 (1.09–2.75)*
PSVT	Kamel et al33	2013	Stroke	N/A	2.10 (1.69–2.62)†
PTFV1	Kamel et al35	2014	Stroke	1.22 (1.03–1.45)‡	1.21 (1.02–1.44)‡
PTFV1	Kamel et al41	2014	Infarct§	1.09 (1.04–1.16)‡	1.09 (1.04–1.15)‡
Frequent PACs	Larsen et al32	2015	Stroke		2.00 (1.16–3.45)‖
PTFV1	Kamel et al34	2015	Non-lacunar stroke	1.44 (1.04–1.99)#	1.49 (1.07–2.07)#
Echocardiographic markers					
Left atrial size	Benjamin et al[37]	1995	Stroke	N/A	2.4 (1.6–3.7)**
Left atrial size	Di Tullio et al[39]	1999	Stroke	N/A	1.47 (1.03–2.11)††
Left atrial size	Karas et al[42]	2012	Stroke	N/A	1.35 (1.12–1.62)‡‡
Left atrial size	Yaghi et al[38]	2015	Cryptogenic or cardioembolic stroke	N/A	1.55 (1.01–2.37)‡‡
Left atrial volume	Barnes et al[43]	2004	Stroke	N/A	1.63 (1.08–2.46)§§
Left atrial volume	Russo et al[44]	2013	Infarct	N/A	1.37 (1.04–1.80)‖‖

Studies Demonstrating an Association Between Markers of Abnormal Atrial Substrate and Incident Stroke Independently of Atrial Fibrillation

AF indicates atrial fibrillation; ECG, electrocardiographic; PACs, premature atrial contractions; PSVT, paroxysmal supraventricular tachycardia; and $PTFV_1$, P-wave terminal force in lead V_1.
*Hazard ratio (HR) and 95% confidence interval (CI) for the primary outcome of death or stroke.
†HR (95% CI) associated with a diagnosis of PSVT.
‡HR (95% CI) per 1-standard deviation (SD) increase in $PTFV_1$.
§Infarct refers to silent brain infarcts detected on magnetic resonance imaging.
‖HR (95% CI) associated with excessive PACs, defined as ≥30 PACs per hour.
#HR (95% CI) associated with ECG-defined left atrial abnormality ($PTFV_1$≥4000 ms μV).
**HR (95% CI) per 10-mm increase in left atrial size in men. The association was not significant in women (HR, 1.4; 95% CI, 0.9–2.1).
††Odds ratio (OR) and 95% CI per 10 mm/1.7 m^2 increase in the left atrial diameter divided by body surface area (left atrial index).
‡‡HR (95% CI) per 1-SD increase in left atrial size.
§§HR (95% CI) for left atrial volume ≥32 mL/m^2.
‖‖HR (95% CI) per 1-SD increase in left atrial minimum volume.
##OR (95% CI) for each 1-SD increase in the left atrial ejection fraction.

Stroke, Volume 47, Issue 3, March 2016; Pages 895-900

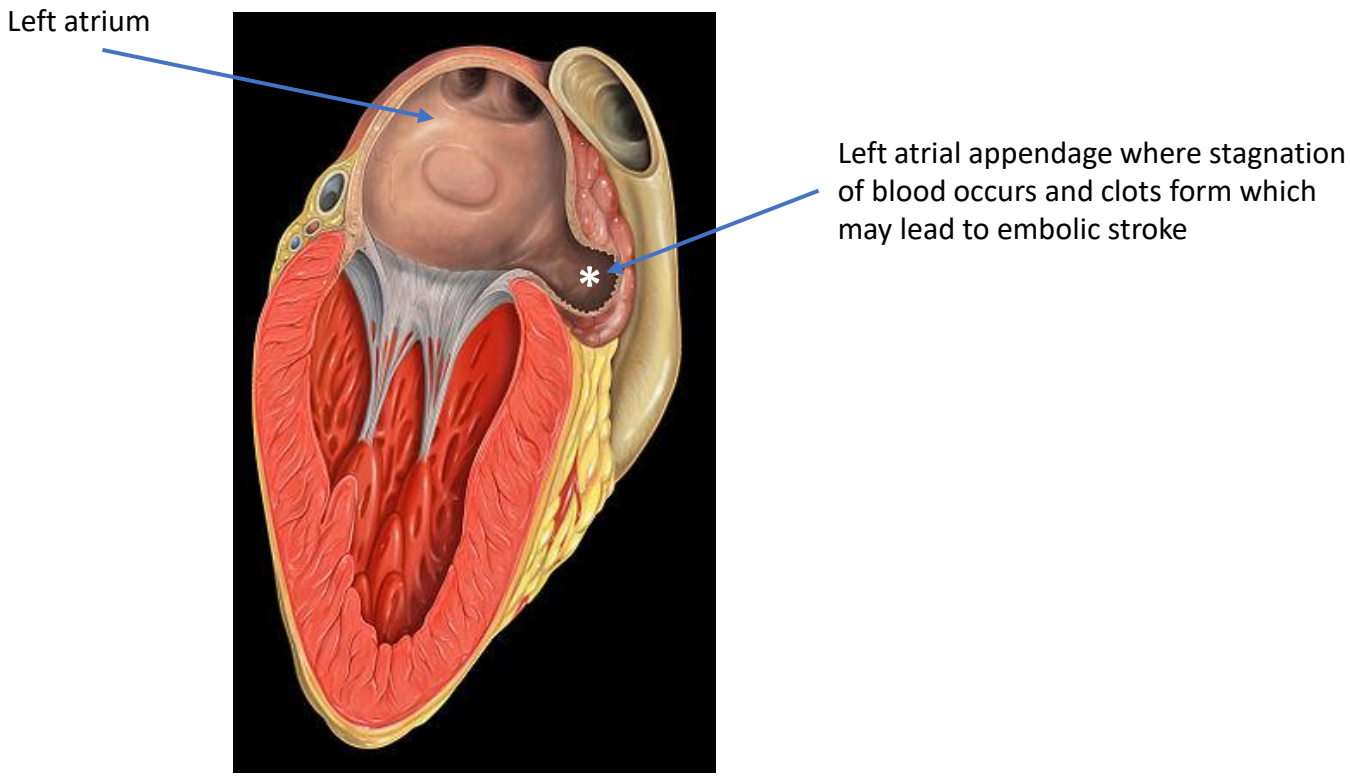
AF → CVA Mechanisms?



Heart Rhythm 2011;8:1416 –1423

Stasis in the LAA?

- **The Left Atrial Appendage**
  - **91% of thrombus accumulation originates in the LAA (Blackshear et al. *Ann Thorac Surg* 1996)**



CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Pharmacologic Prevention of CVA in AF

Sunny Kapur MD

Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

Outline

- *The relationship between Afib and Stroke*
- ***Pharmacologic Prevention of CVA in AF***
- *Non-pharmacologic Prevention of CVA in AF*
- *Preventing Recurrent AF strokes*

Regardless…the observation exists

Stroke Risk Stratification in AF

$CHADS_2$

Risk Factor	Score
Congestive heart failure	1
Hypertension	1
Age ≥75 y	1
Diabetes	1
Stroke	2

Total Score	Annual Risk of Stroke (%)	
0	1.9	0
1	2.8	1.3
2	4.0	2.2
3	5.9 ← $CHADS_2$	3.2
4	8.5	4.0 ← CHA_2DS_2-VASc
5	12.5	6.7
6	18.2	9.8
7		9.6
8		6.7
9		15.2

CHA_2DS_2-VASc

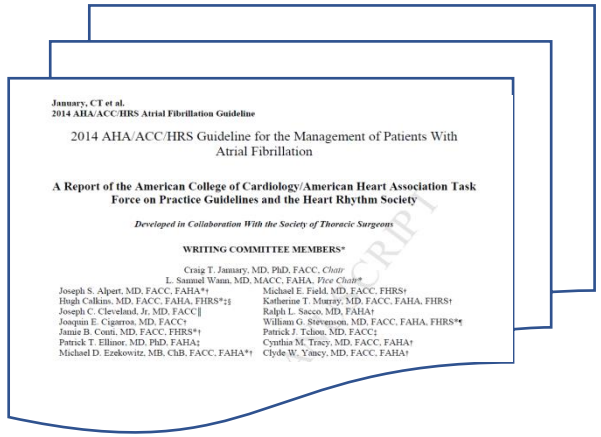
Risk Factor	Score
Congestive heart failure	1
Hypertension	1
Age ≥75 y	2
Diabetes	1
Stroke	2
Vascular disease (MI, PAD, aortic atherosclerosis)	1
AGE 65-74 y	1
Sex category (female)	1

CHA_2DS_2-VASc seems to have 2 major benefits: it more accurately identifies truly low risk pts: it reclassifies many $CHADS_2$ 0-1 pts to a higher Stroke risk

Lip GY, Halperin JL. *Am J Med.* 2010;123(6):484-488. Camm AJ, et al. *Eur Heart J.* 2010;31(19);2369-2429

2014 ACC/AHA/HRS Treatment Guidelines to Prevent Thromboembolism in Patients with AF

- Assess stroke risk with CHA_2DS_2-VASc score
  - *Score 1: Annual stroke risk 1%, oral anticoagulants or aspirin may be considered*
  - *Score ≥2: Annual stroke risk 2%-15%,* ***oral anticoagulants are recommended***
- Balance benefit vs. bleeding risk


January, CT et al.
2014 AHA/ACC/HRS Atrial Fibrillation Guideline

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 Practice Guidelines and the Heart Rhythm Society

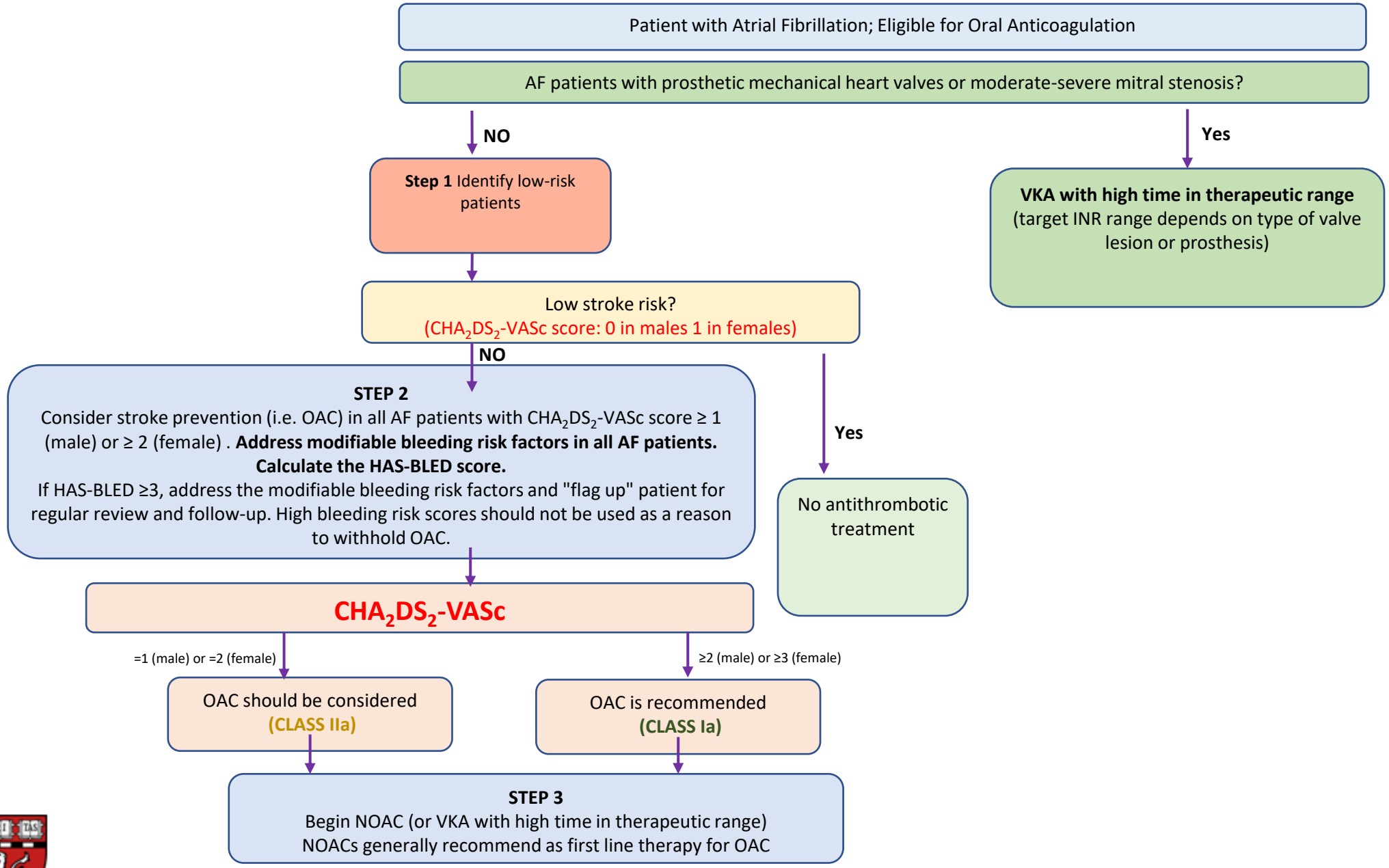
Developed in Collaboration With the Society of Thoracic Surgeons

WRITING COMMITTEE MEMBERS*

Craig T. January, MD, PhD, FACC, Chair
L. Samuel Wann, MD, MACC, FAHA, Vice Chair*
Joseph S. Alpert, MD, FACC, FAHA*†
Hugh Calkins, MD, FACC, FAHA, FHRS*‡§
Joseph C. Cleveland, Jr, MD, FACC‖
Joaquin E. Cigarroa, MD, FACC†
Jamie B. Conti, MD, FACC, FHRS*†
Patrick T. Ellinor, MD, PhD, FAHA‡
Michael D. Ezekowitz, MB, ChB, FACC, FAHA*†
Michael E. Field, MD, FACC, FHRS†
Katherine T. Murray, MD, FACC, FAHA, FHRS†
Ralph L. Sacco, MD, FAHA†
William G. Stevenson, MD, FACC, FAHA, FHRS*¶
Patrick J. Tchou, MD, FACC‡
Cynthia M. Tracy, MD, FACC, FAHA†
Clyde W. Yancy, MD, FACC, FAHA†

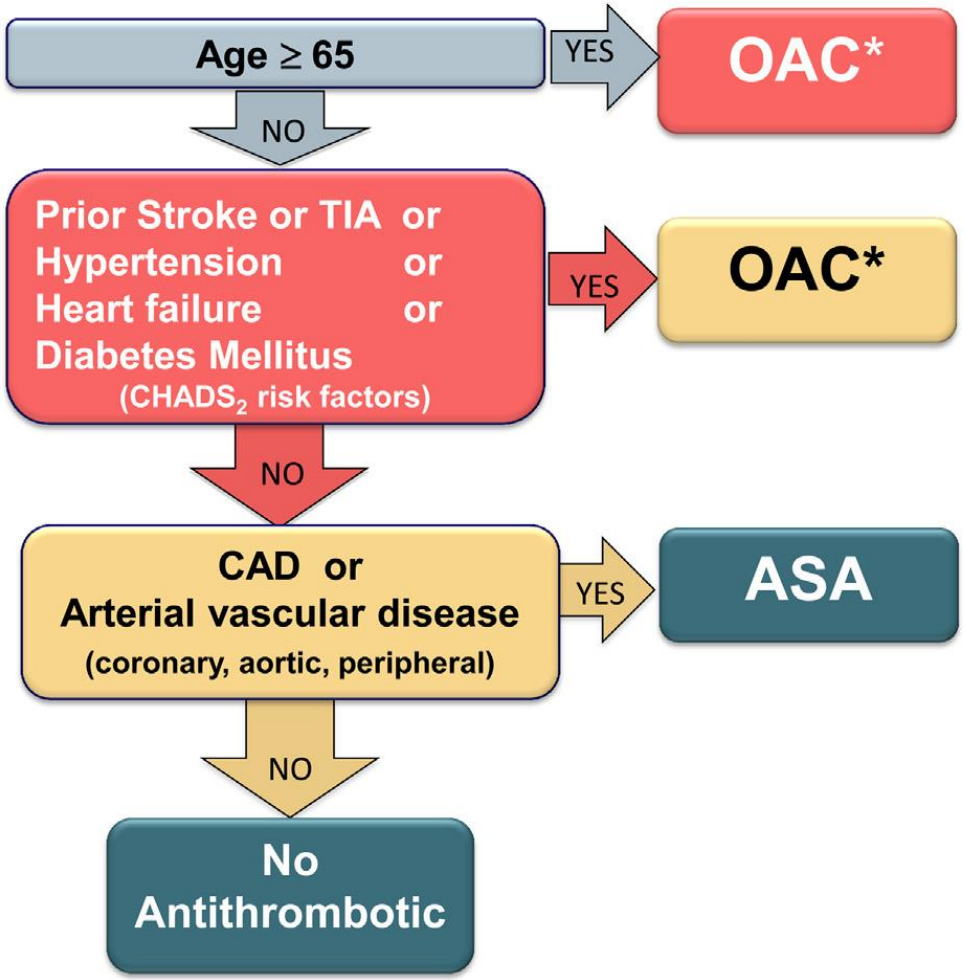
2014 AHA/ACC/HRS Guideline for the Management of Patients with AF

January, CT. et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. JACC. 2014; doi: 10.1016/j.jacc.2014.03.022



European Heart Journal, Volume 42, Issue 5, 1 February 2021, Pages 373–498,

The “CCS Algorithm” for OAC Therapy in AF

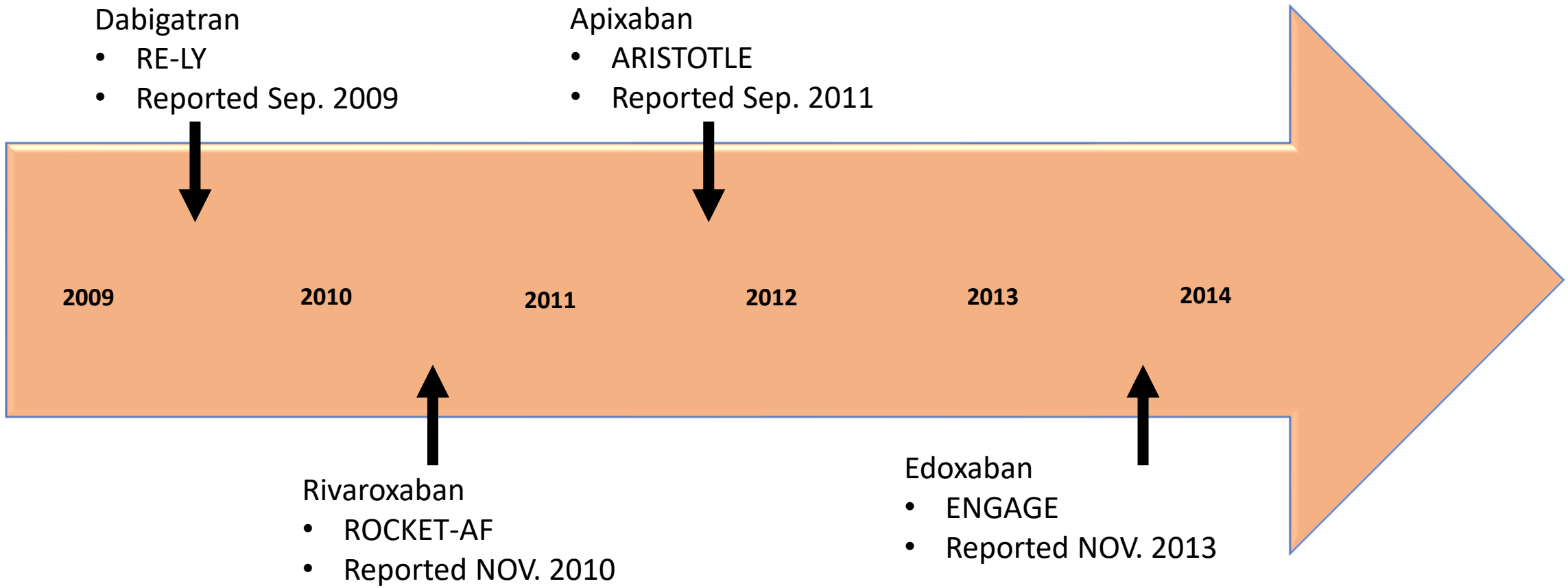


Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥ 75, low body weight).†

- The evidence does not support the use of aspirin as monotherapy for the prevention of thromboembolic events in patients with AF.
- The issue of whether aspirin could be a reasonable antithrombotic monotherapy in very low-risk patients (CHADS2 = 0) has not been well addressed, as the individual trials enrolled very few such patients.
- A 2007 meta-analysis found that aspirin, compared to placebo or no therapy, reduced the risk of stroke by about 20 percent, although this effect was not statistically significant (relative risk reduction 19 percent; 95% CI -1.0 to 35.0).
- Further, aspirin had little effect on reducing the risk of disabling stroke.

Verma A. et al. Can J Cardiol. 2014: 1114-1130

Priority #4 – Cardioembolic stroke prevention



Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation

Connolly, Stuart J., et al. New England Journal of Medicine 361.12 (2009): 1139-1151.
Patel, Manesh R., et al. New England Journal of Medicine 365.10 (2011): 883-891.
Granger, Christopher B., et alNew England Journal of Medicine 365.11 (2011): 981-992.
Giugliano, Robert P., et al. New England Journal of Medicine 369.22 (2013): 2093-2104.

Anticoagulation Regimen – Balancing Risks and Benefits

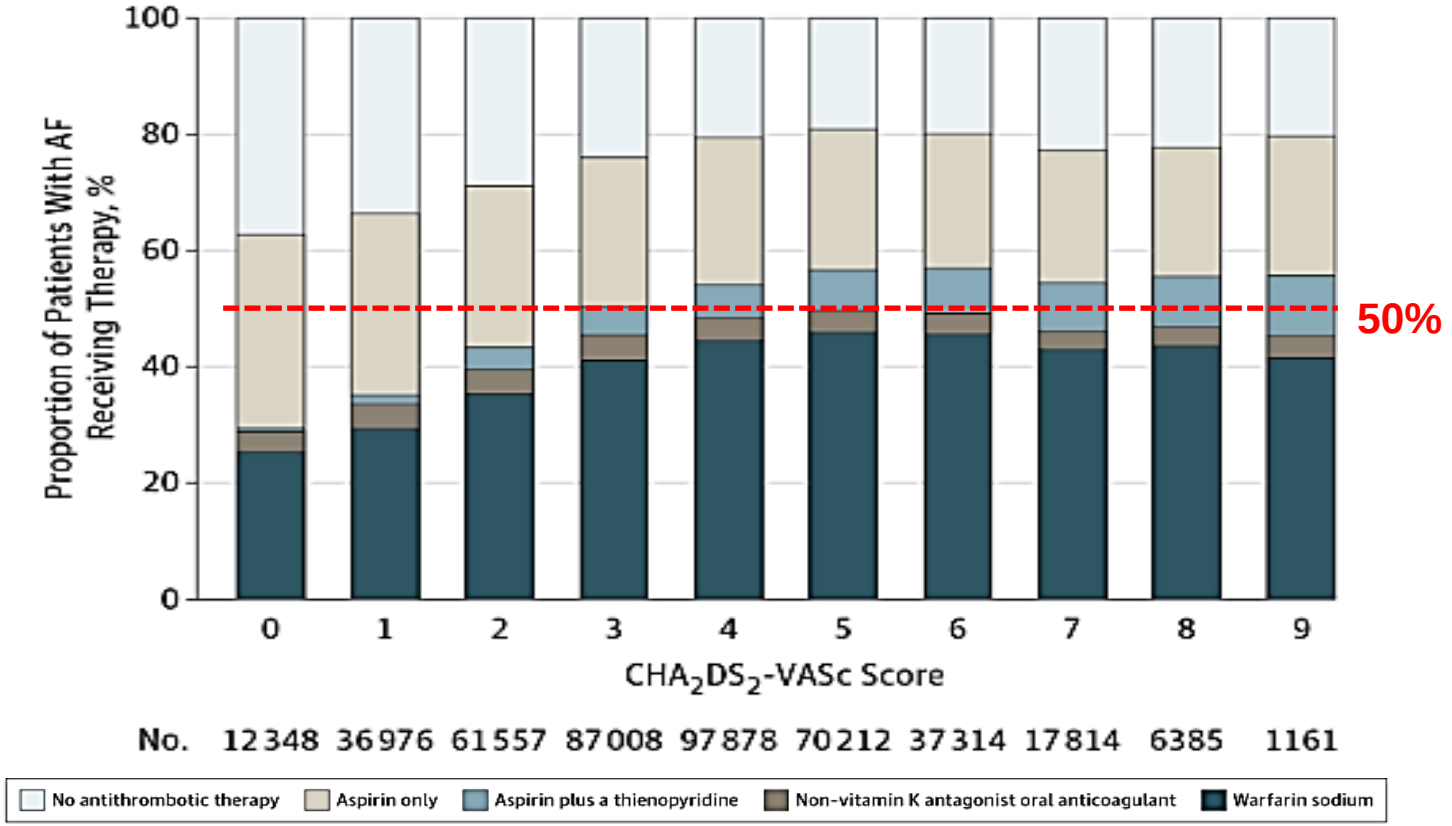
Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits		
COR	**LOE**	**Recommendations**
I	**A**	**NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a 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.

January et al. Circulation. 2019140:e125-e151

Oral Anticoagulation is Standard of Care, But Not for All

NCDR Pinnacle Registry: >400,000 Outpatients w AF

<50% of Patients with AF at Highest Risk of Stroke were Prescribed an OAC



Warfarin
Bleeding risk
Daily regimen
High non-adherence rates
Regular INR monitoring
Food and drug interaction issues
Complicates surgical procedures

Novel Oral Anticoagulants
Bleeding risk
Daily regimen
High non-adherence rates
Complicates surgical procedures
Lack of reversal agents
High cost

1. Hsu, J et al. JAMA Cardiol. Published online March 16, 2016. doi:10.1001/jamacardio.2015.0374

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Non-pharmacologic Prevention of CVA in AF

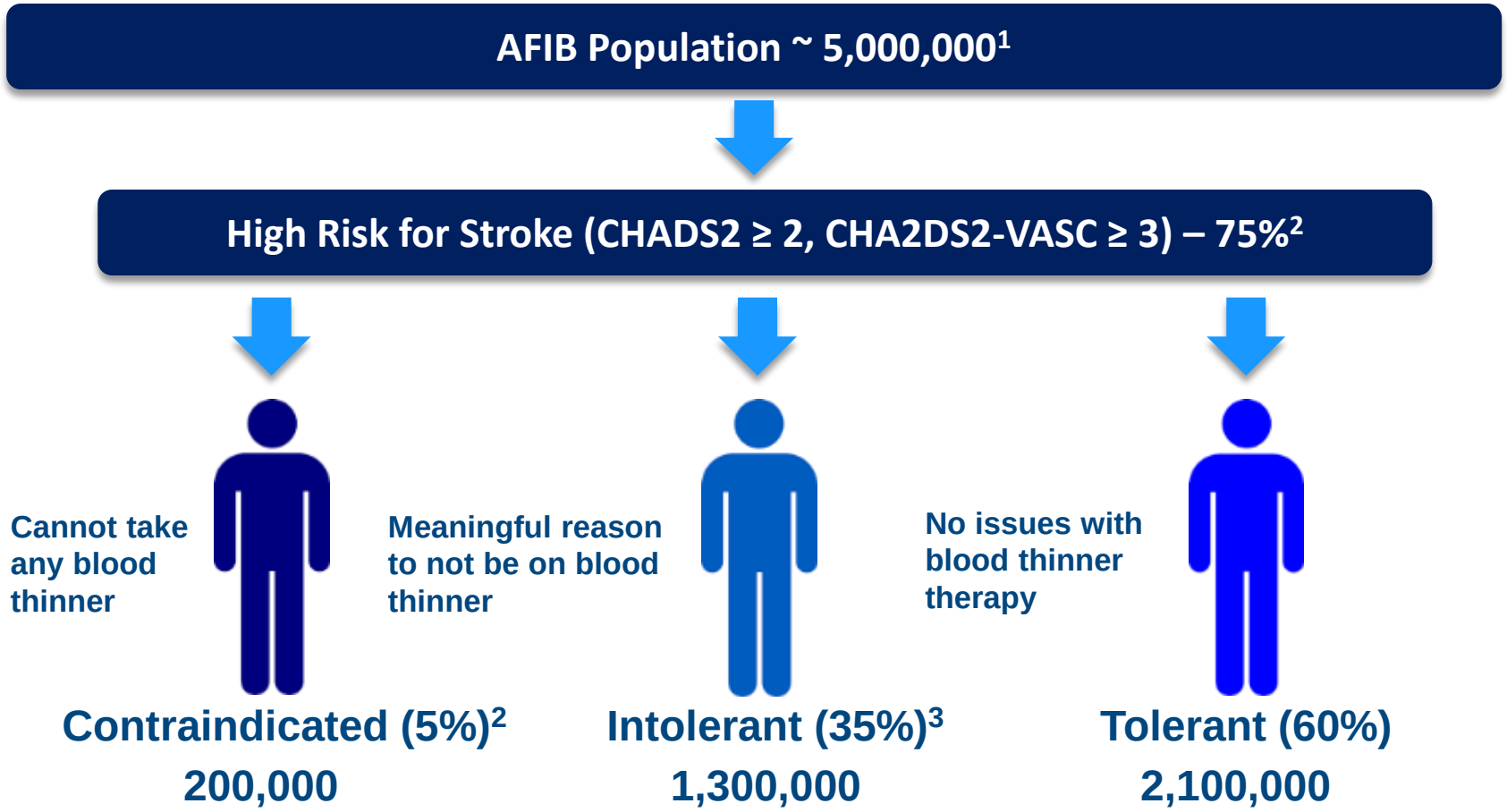
Sunny Kapur MD

Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

Outline

- *The relationship between Afib and Stroke*
- *Pharmacologic Prevention of CVA in AF*
- ***Non-pharmacologic Prevention of CVA in AF***
- *Preventing Recurrent AF strokes*

The Problem with Anticoagulation



1. the AnTicoagulation and Risk Factors In Atrial Fibrillation (ATRIA) Study JAMA. 2001;285(18):2370-2375. doi:10.1001/jama.285.18.2370 2. Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk JAMA Cardiol. Published online March 16,2016.doi:10.1001/jamacardio.2015.0374 3. PINNACLE Q4 2015 national summary report, Data on File

Bleeding Risks Compound Over Time

CHA_2DS_2-VASc* Score	Annual % Stroke Risk
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7

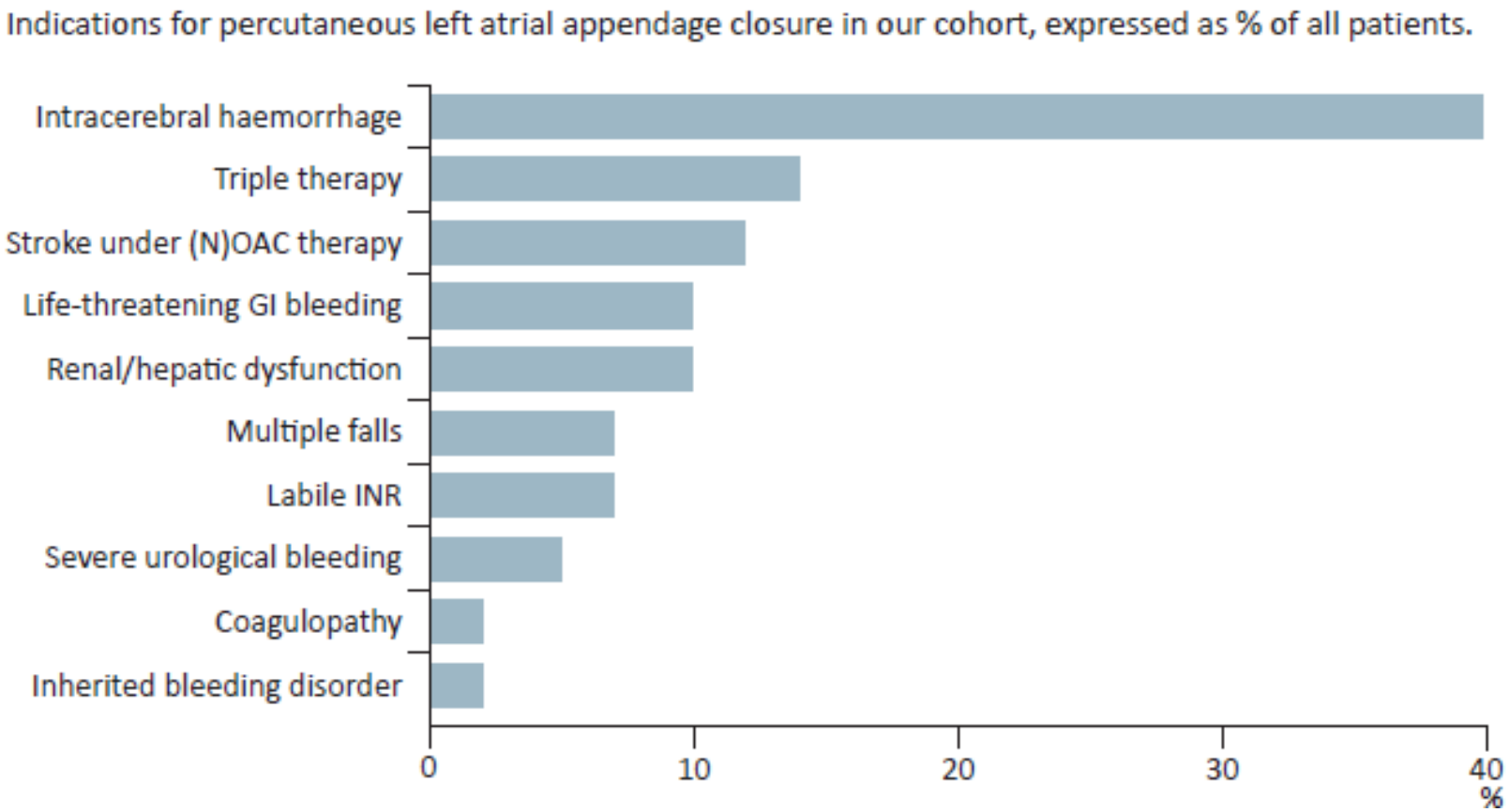
HAS-BLED** Score	Annual % Bleed Risk
0	0.9
1	3.4
2	4.1
3	5.8
4	8.9
5	9.1

Table 1: Stroke and bleeding risk stratification with the CHA_2DS_2-VASc and HAS-BLED schemas

CHA_2DS_2-VASc	Score	HAS-BLED	Score
Congestive heart failure/LV dysfunction	1	Hypertension i.e. uncontrolled BP	1
Hypertension	1	Abnormal renal/liver function	1 or 2
Aged ≥75 years	2	Stroke	1
Diabetes mellitus	1	Bleeding tendency or predisposition	1
Stroke/TIA/TE	2	Labile INR	1
Vascular disease [prior MI, PAD, or aortic plaque]	1	Age (e.g. >65)	1
Aged 65-74 years	1	Drugs (e.g. concomitant aspirin or NSAIDSs) or alcohol	1
Sex category [i.e. female gender]	1		
Maximum score	**9**		**9**

* 2014 AHA / ACC / HRS Guidelines
** Lip. JACC (2011)

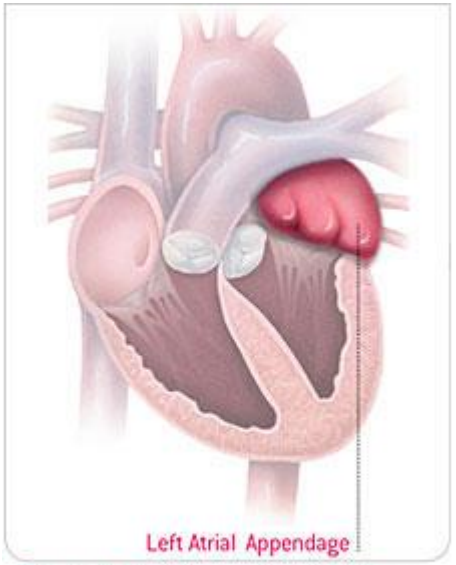
Relative or Absolute Contraindications



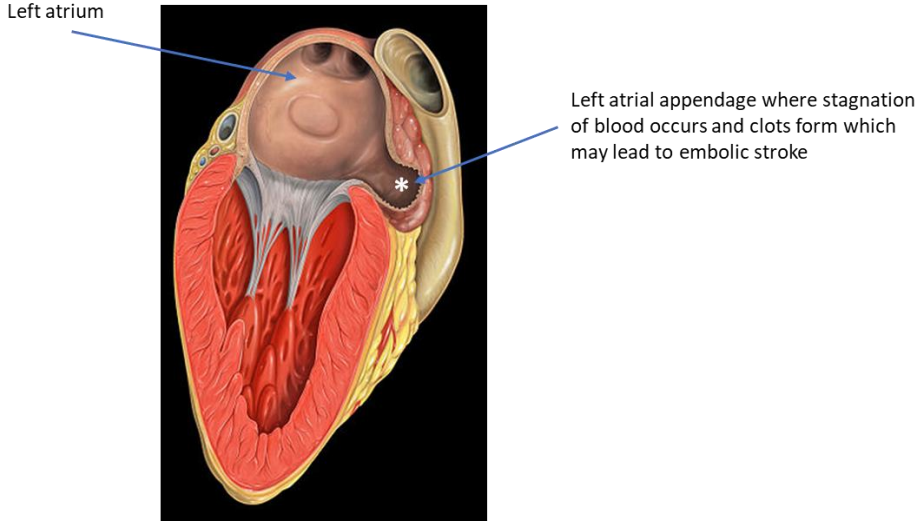
*Lifestyle contraindications

So what do we do?

- Over 70 years ago, we realized that most clots form in one specific corner of the heart – the left atrial appendage or LAA
  - 91% of thrombus accumulation originates in the LAA



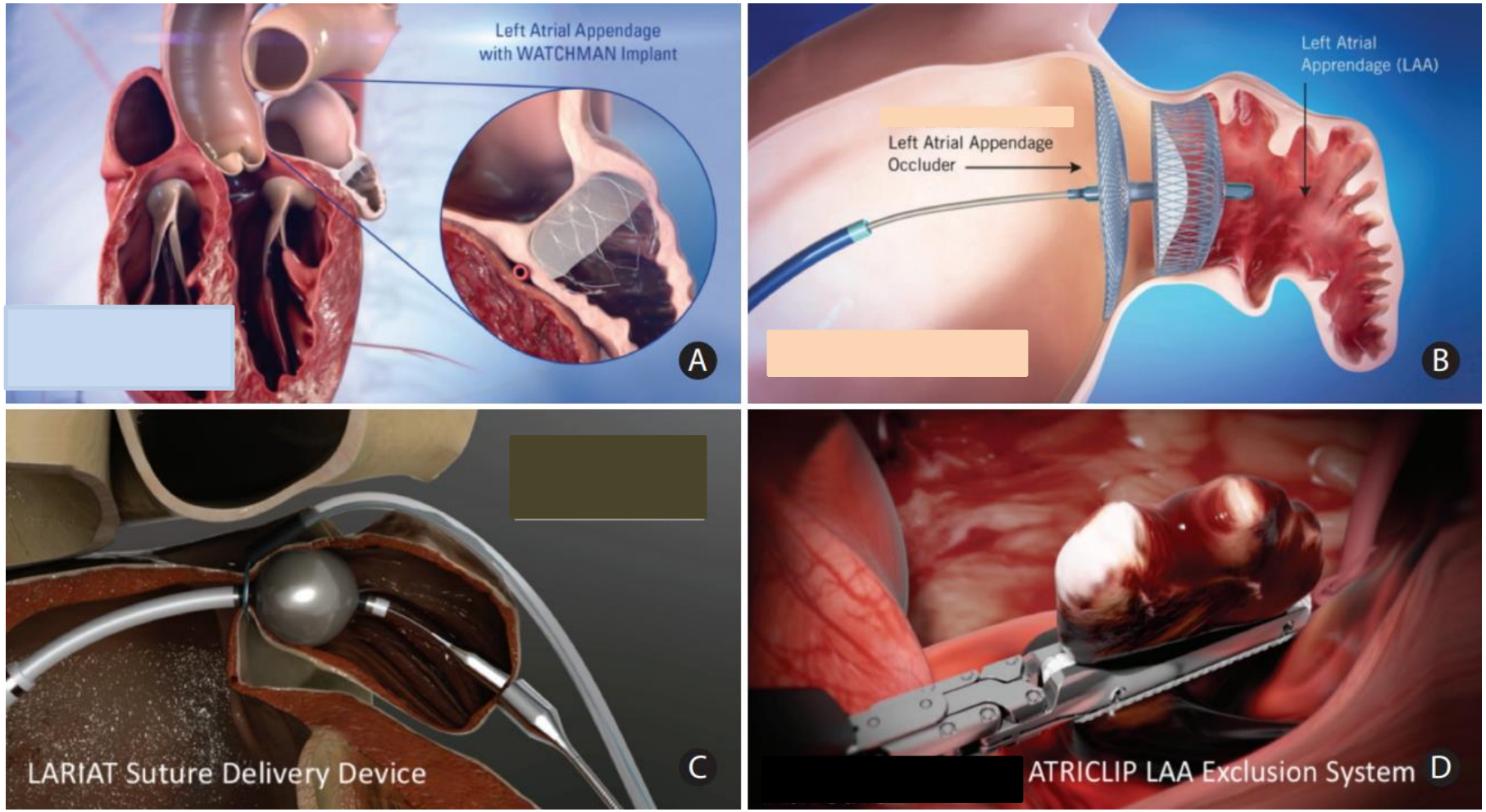
The Left Atrial Appendage (LAA) is a pouch like extension on the left side of the heart



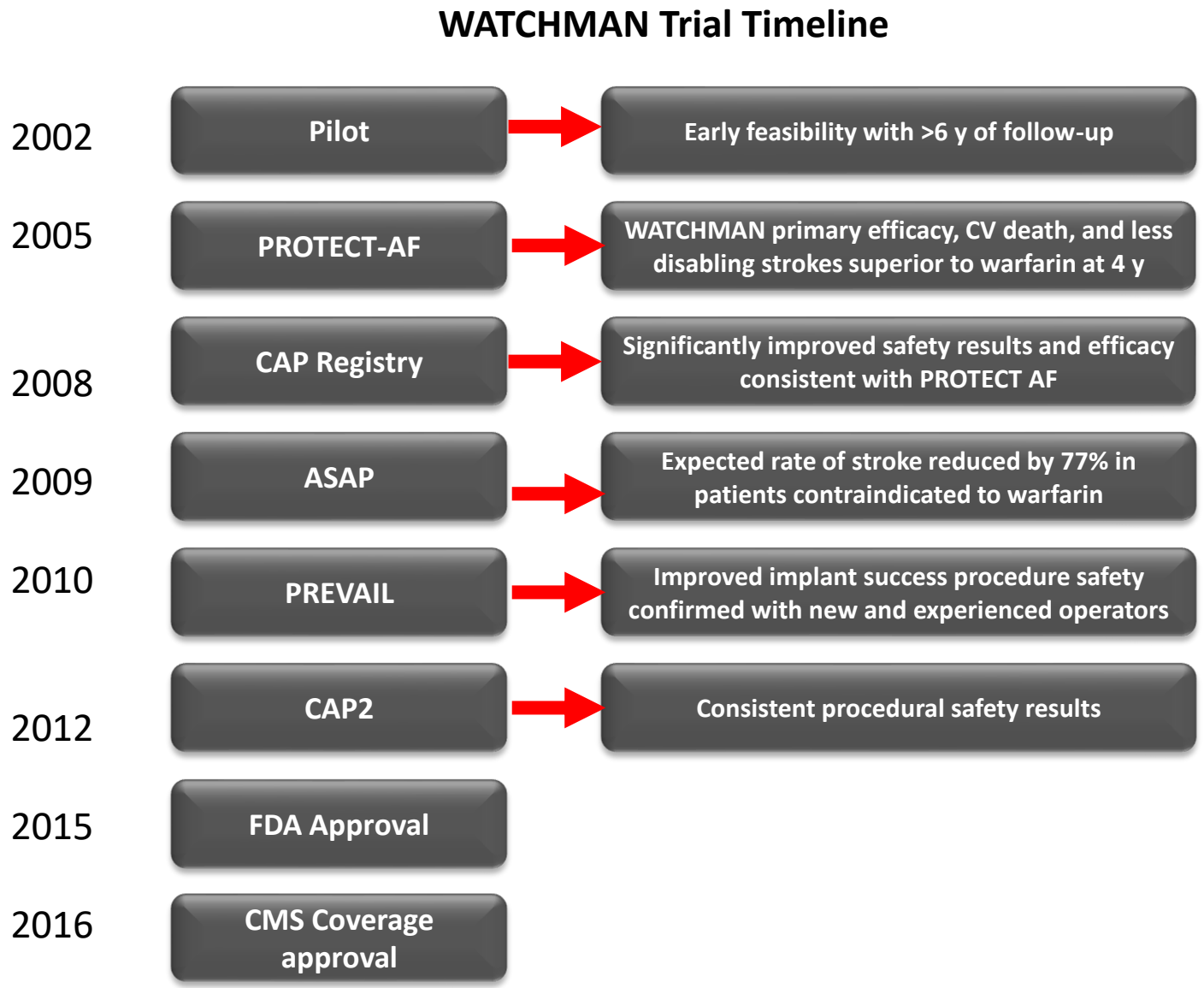
- Open heart surgery to remove the LAA has been done for decades
  - The first report was from two patients with AF in **1949.**

Blackshear et al. Ann Thorac Surg 1996

The development of minimally invasive LAA occlusion/ligation devices started…

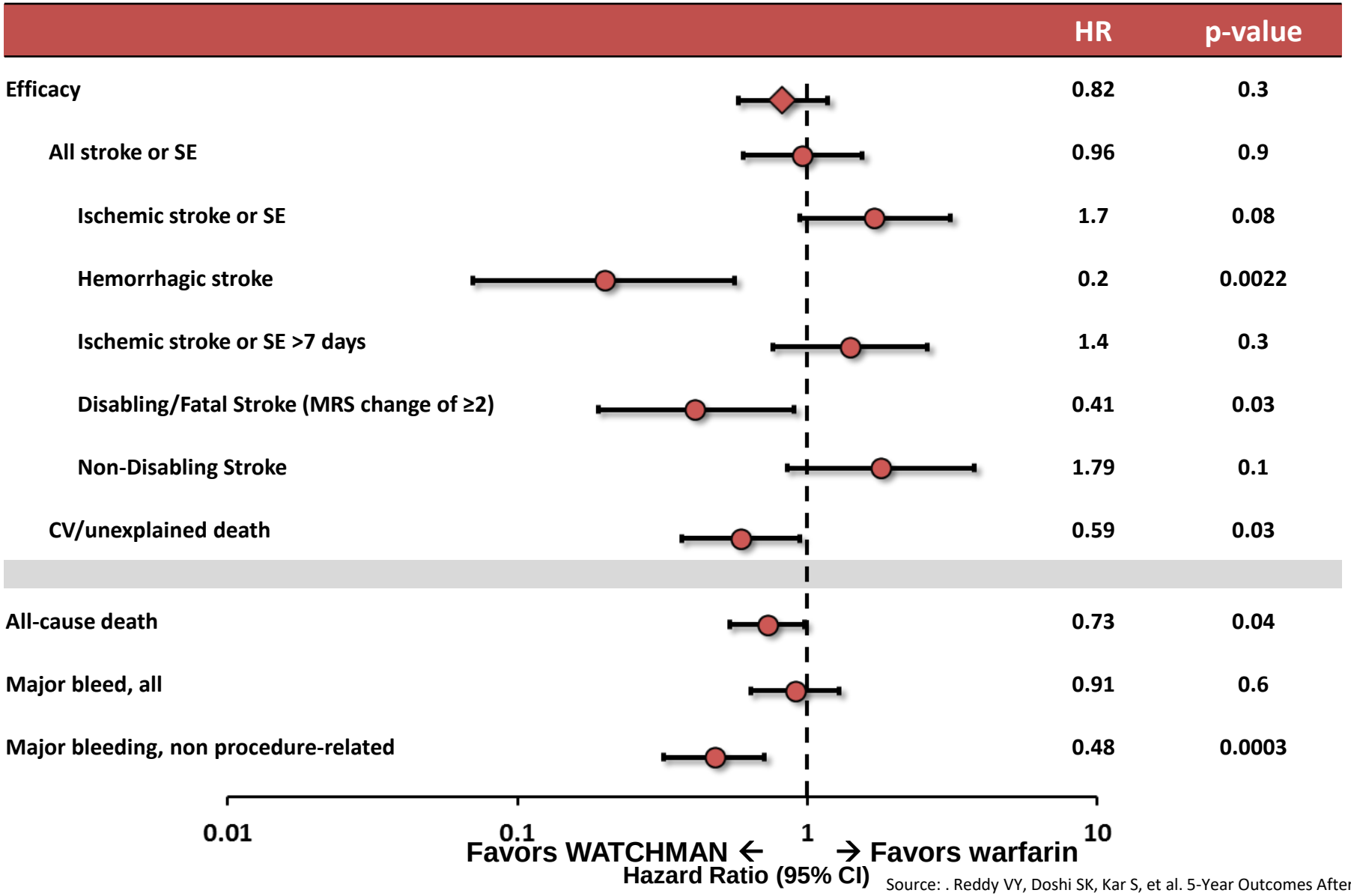


The first device approved in the USA: WATCHMAN



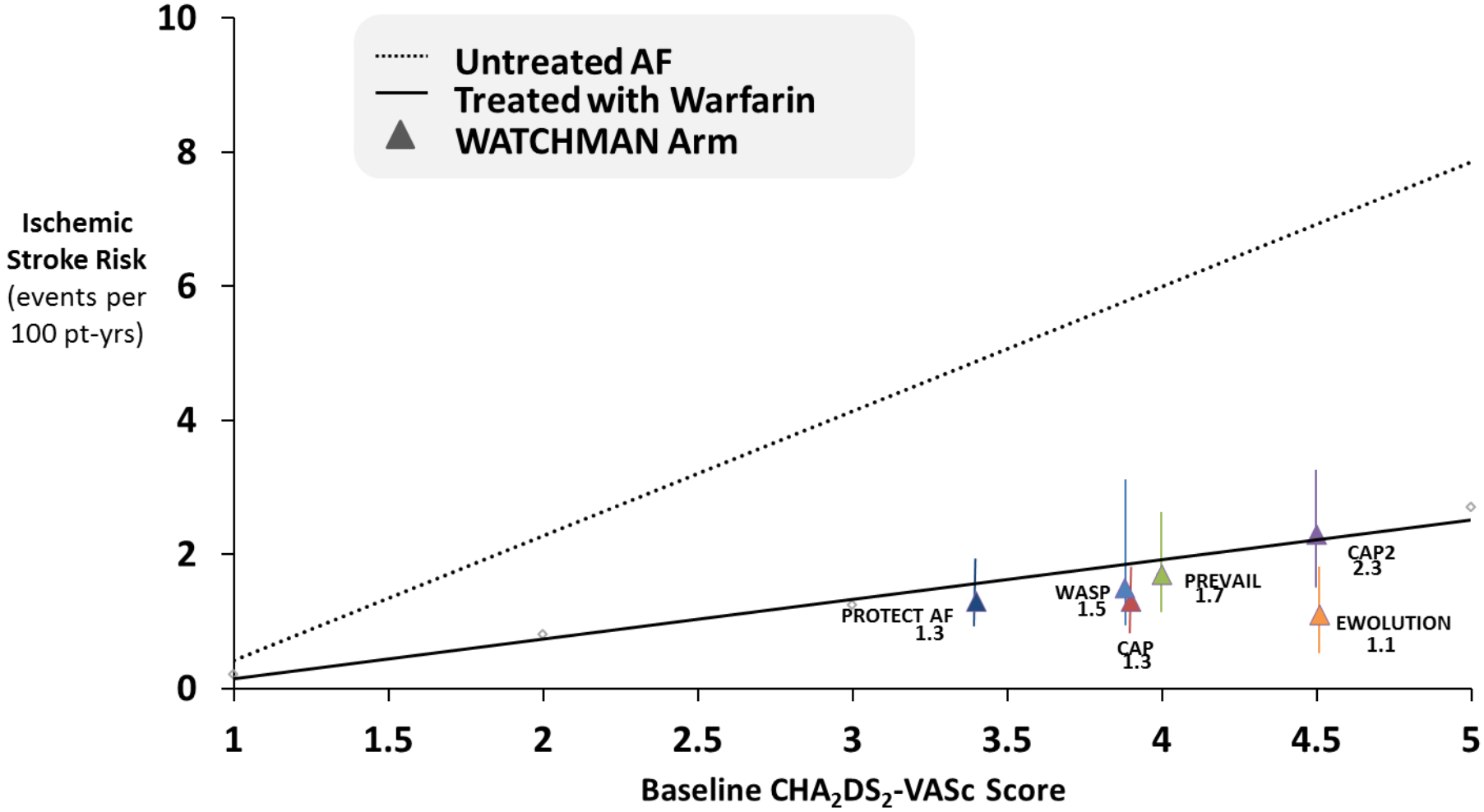
Patient Level Meta-Analysis
PROTECT AF, PREVAIL 5 Years

BRIGHAM AND WOMEN'S HOSPITAL
Heart & Vascular Center



Source: . Reddy VY, Doshi SK, Kar S, et al. 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. J. Am Coll Cardiol. 2017; In Press

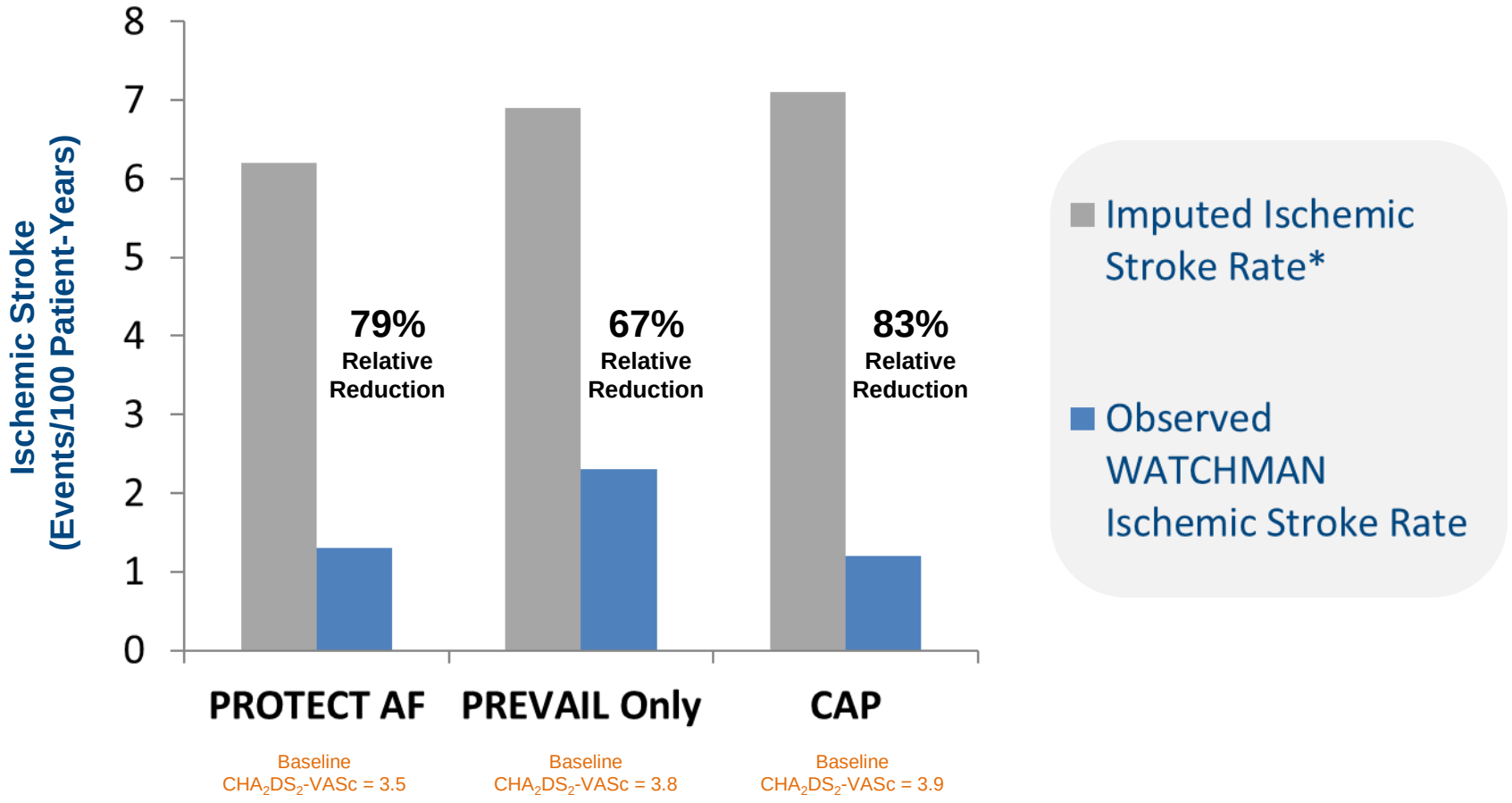
WATCHMAN Comparable to warfarin for Ischemic Stroke in 2 RCT, 4 Registries



Source: . Reddy VY, Doshi SK, Kar S, et al. 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. J. Am Coll Cardiol. 2017; In Press

WATCHMAN™ Device Reduces Ischemic Stroke Over No Therapy

BRIGHAM AND WOMEN'S HOSPITAL
Heart & Vascular Center



* Imputation based on published rate with adjustment for CHA2DS2-VASc score (3.0); Olesen JB. Thromb Haemost (2011)

FDA Oct 2014 Panel Sponsor Presentation. Hanzel G, et al. TCT 2014 (abstract)

Is LAA occlusion right for you?

BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

Patient Selection Considerations

FDA Indication

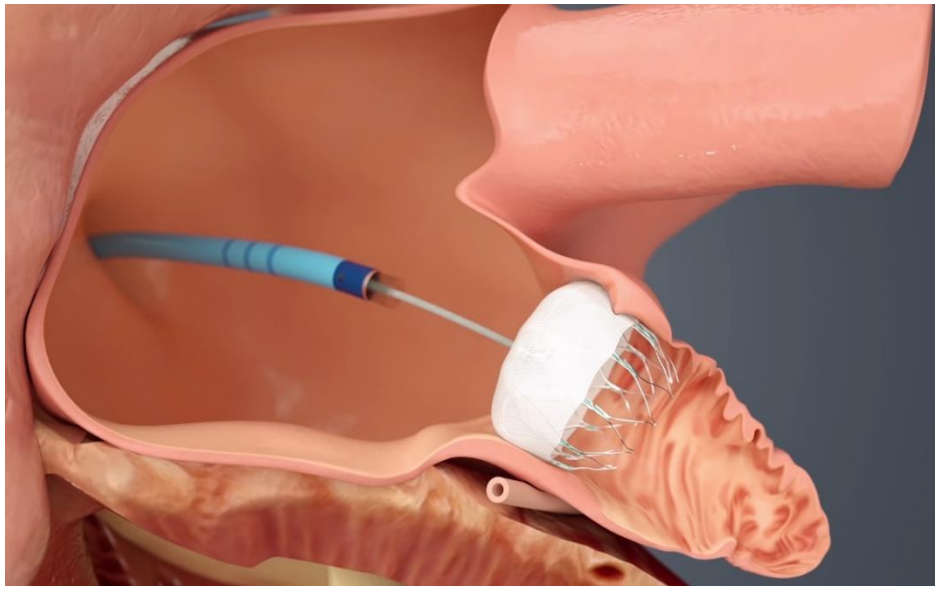
- The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:
  - Are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for anticoagulation therapy;
  - Are deemed by their physicians to be suitable for warfarin; and
  - **Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin**, taking into account the safety and effectiveness of the device compared to warfarin

CMS Coverage

- CHADS2 score ≥2 or a CHA2DS2-VASc score ≥3
- Patients must be suitable for short-term warfarin, but **deemed unable to take long-term oral anticoagulation**
- Documented evidence of a formal shared decision interaction between the patient and an independent, non-interventional physician

Left Atrial Appendage Closure

- LAA occlusion is an option to reduce the risk of stroke in patient with AF
- LAA occlusion is reserved for patients who "cannot" take anticoagulation
- WATCHMAN and Amulet are minimally invasive procedures to occlude the LAA

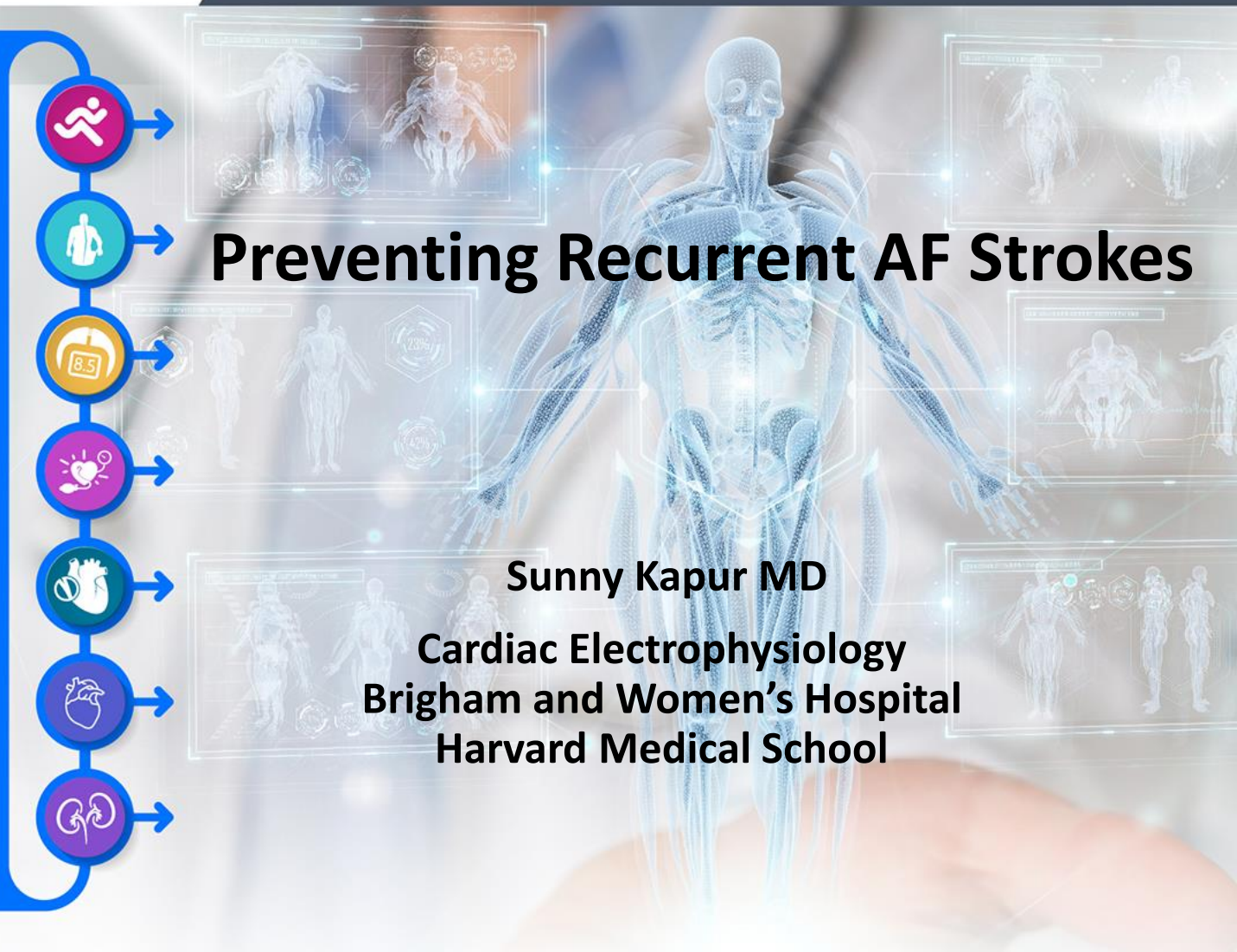


CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)



Preventing Recurrent AF Strokes

Sunny Kapur MD

Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

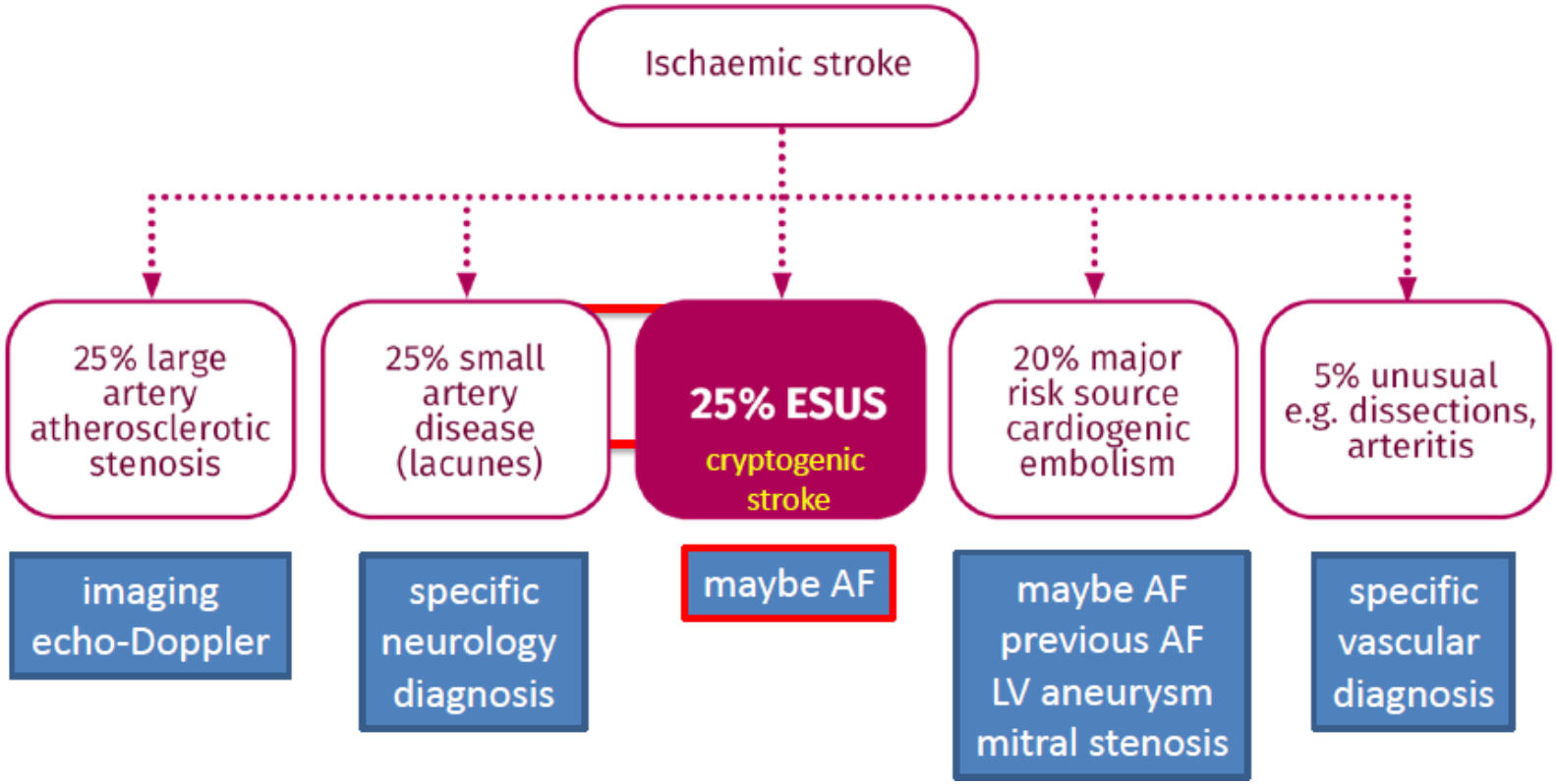
Outline

- *The relationship between Afib and Stroke*
- *Pharmacologic Prevention of CVA in AF*
- *Non-pharmacologic Prevention of CVA in AF*
- ***Preventing Recurrent AF strokes***

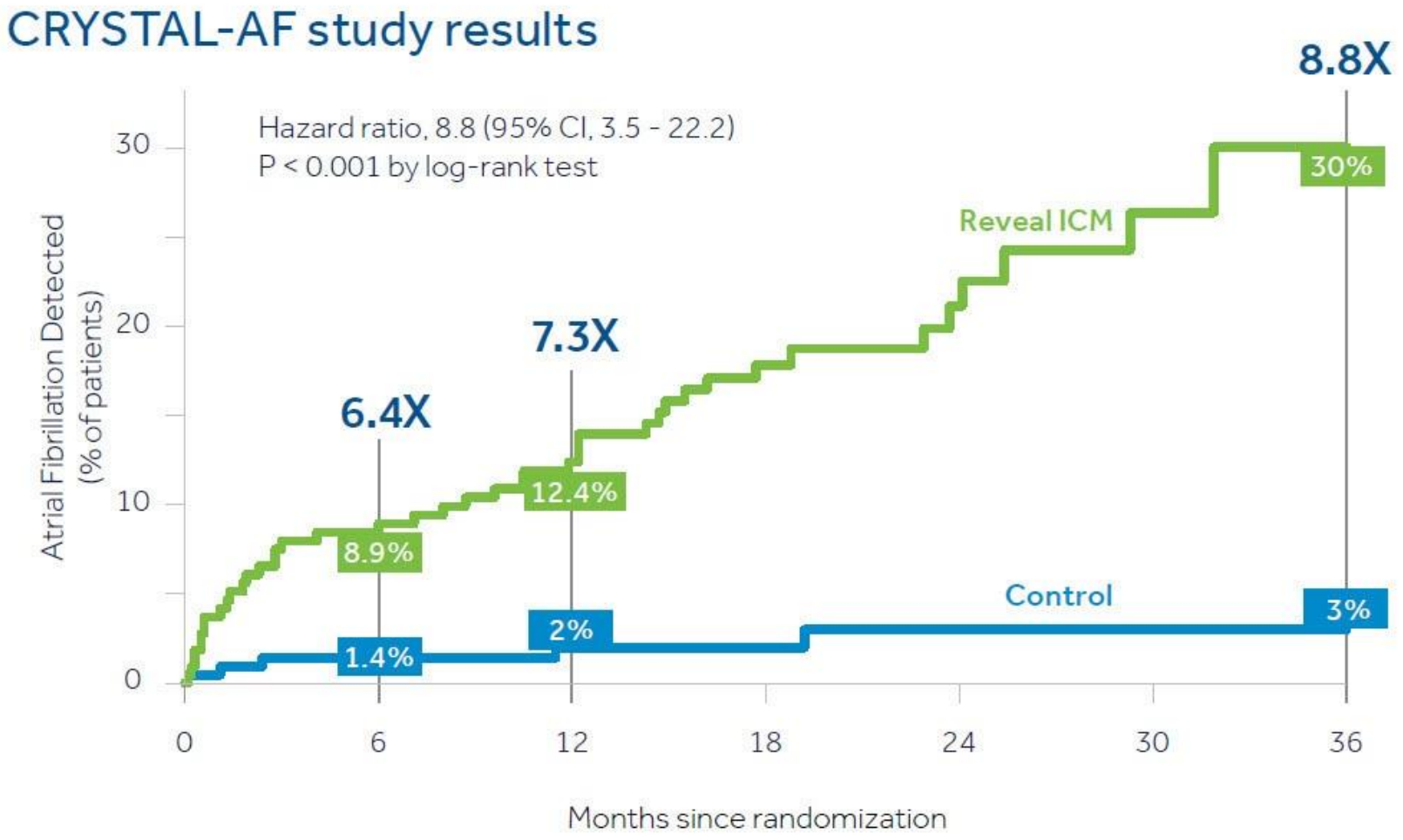
An ounce of prevention…

- 68 y/o man with h/o diabetes, HTN, TIA, admitted with stroke
- Head MRI showed multiple foci of restricted diffusion within mid and posterior aspect of left MCA distribution. CTA showed no stenosis of major arteries of head and neck
- TEE mild MR, no PFO
- EKG and telemetry normal.
- Implantable loop recorder implanted.

The problem: 25% of ischemic strokes are cryptogenic

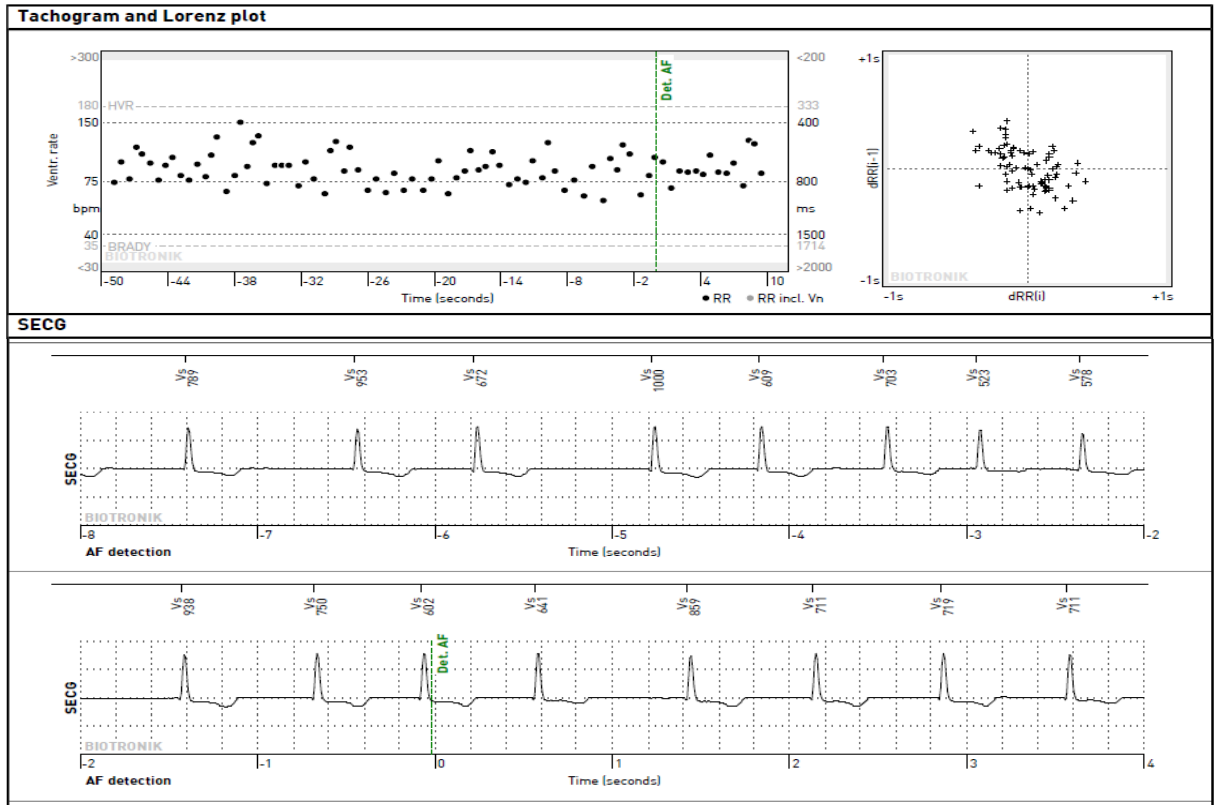


CRYSTAL-AF study results



Sanna T. et al. *NEJM*. 2014: 2478-2846

Indications / Use Cases for ILRs

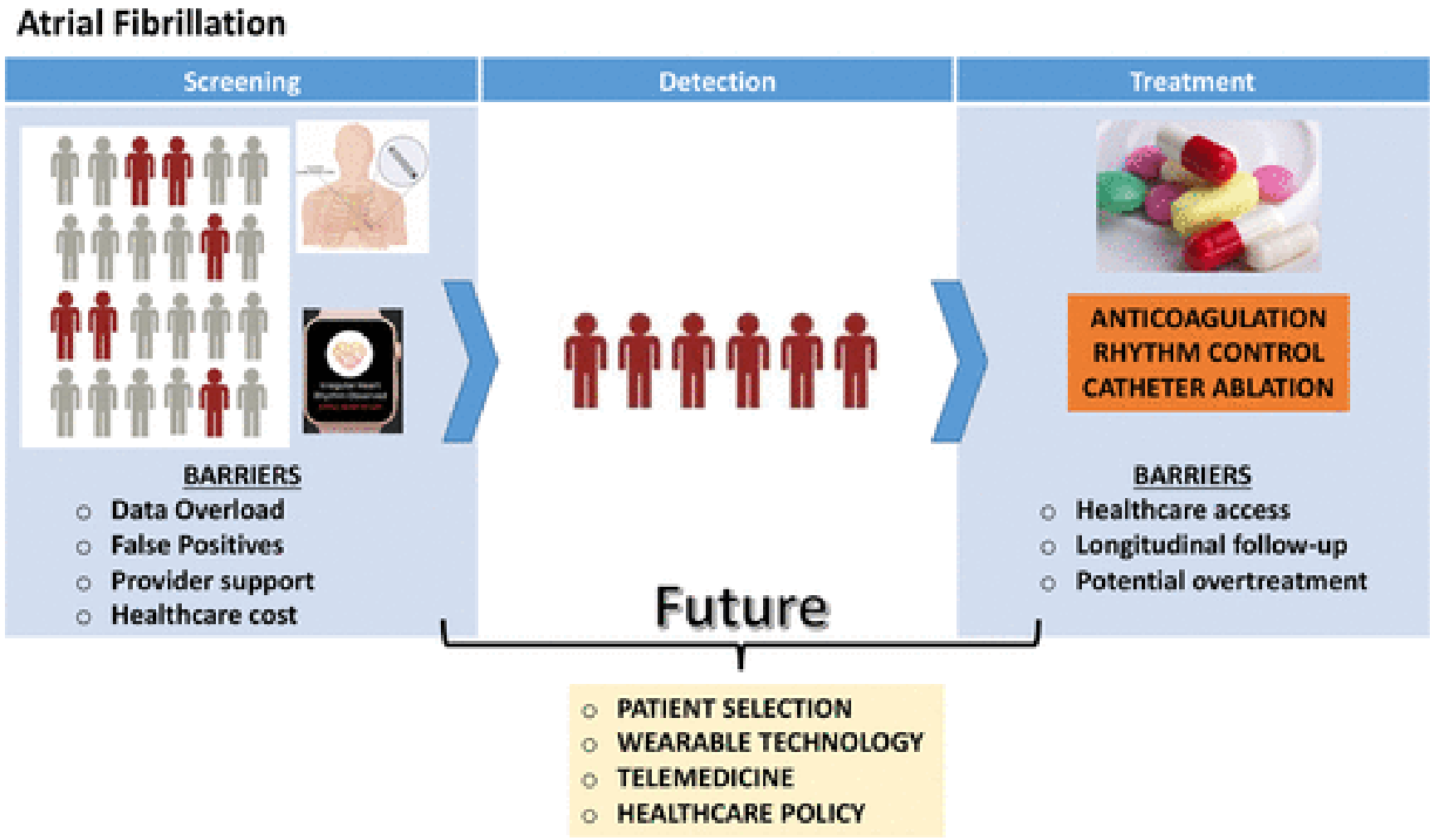


2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Recommendations for Device Detection of AF and Atrial Flutter		
COR	LOR	Recommendations
I	B-NR	In patients with cardiac implantable electronic devices (pacemakers or implanted cardioverter-defibrillators), the presence of recorded atrial high-rate episodes (AHREs) should prompt further evaluation to document clinically relevant AF to guide treatment decisions
IIa	B-R	In patients with cryptogenic stroke (i.e., stroke of unknown cause) in whom external ambulatory monitoring is inconclusive, implantation of a cardiac monitor (loop recorder) is reasonable to optimize detection of silent AF

January, Craig T., et al. Journal of the American College of Cardiology 74.1 (2019): 104-132.

Can this be extrapolated to screening for Afib in patients prior to stroke?



Summary

- Atrial fibrillation is a heterogenous disorder that requires tailoring of clinical therapy
- The relationship between AF and cardio embolism is well documented if poorly understood.
- Pharmacologic and Non-pharmacologic approaches to cardioembolic protection of AF patients are important considerations
- Identifying patients with AF and instiuting appropriate therapy prior to a stroke (or recurrent stroke) is an important goal

Supplemental Reference Slide

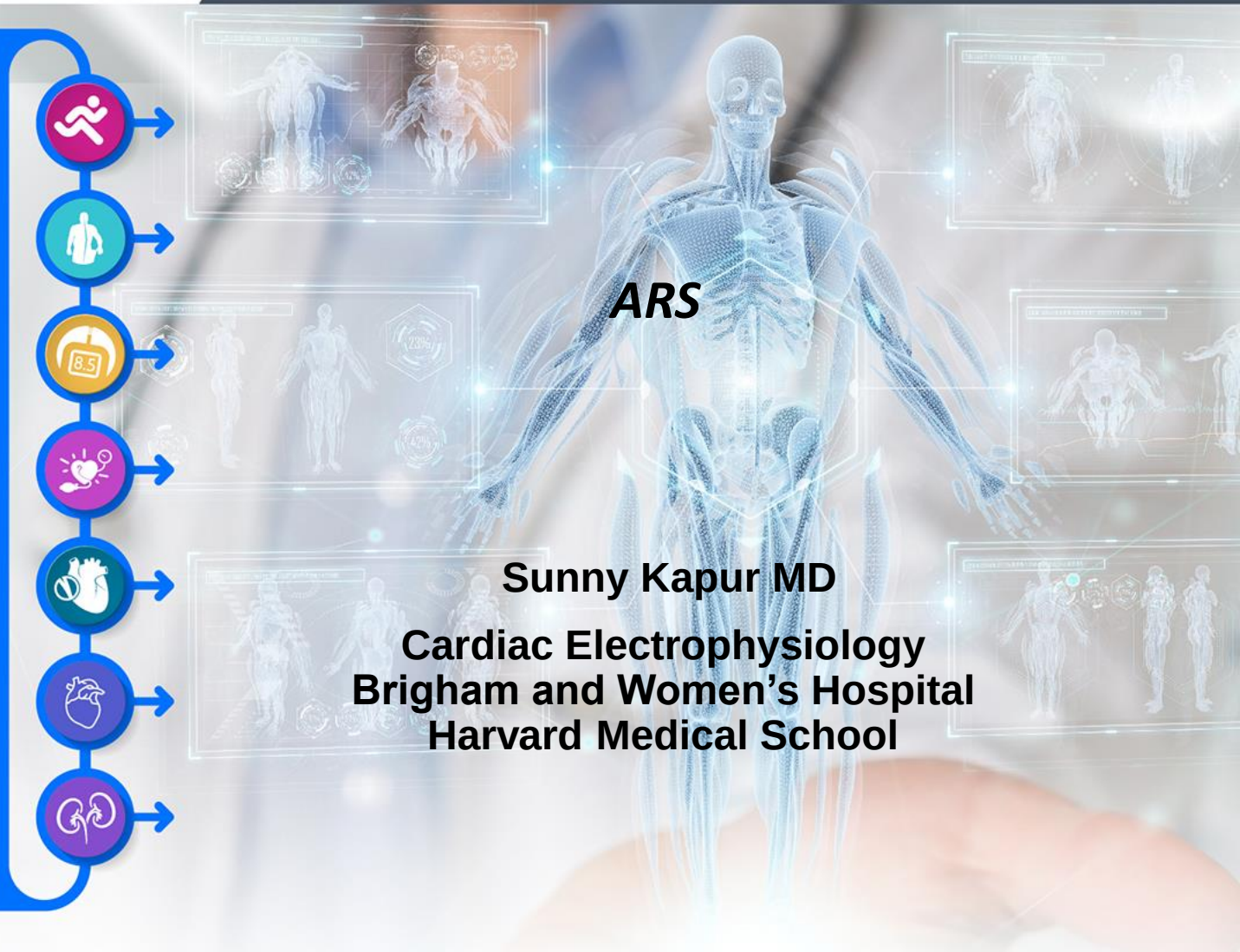
- Pritchett EL. Management of atrial fibrillation. N Engl J Med 1992; 326:1264.
- Atrial fibrillation: current understandings and research imperatives. The National Heart, Lung, and Blood Institute Working Group on Atrial Fibrillation. J Am Coll Cardiol 1993; 22:1830.
- Lip GY, Metcalfe MJ, Rae AP. Management of paroxysmal atrial fibrillation. Q J Med 1993; 86:467.

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)



ARS

Sunny Kapur MD

Cardiac Electrophysiology
Brigham and Women's Hospital
Harvard Medical School

Question #1

A 70-year-old woman with type 2 diabetes mellitus and rheumatic mitral stenosis is evaluated for dyspnea and fatigue. She has a history of atrial fibrillation that has resulted in these symptoms in the past. She has had successful cardioversions, most recently about 2 years ago. She has hypertension controlled with medication. She also has mild left-ventricular dysfunction related to coronary artery disease and history of myocardial infarction. Her current medications include atenolol, lisinopril, aspirin, atorvastatin, and insulin. Physical examination demonstrates an irregularly irregular rhythm with a heart rate of 78 beats per minute. Blood pressure is 130/80 mm Hg. The cardiovascular and pulmonary examinations are otherwise unremarkable.

What medication should this patient receive for at least 3-4 weeks before cardioversion?

A. Warfarin

B. Clopidogrel

C. Rivaroxaban

D. No additional medication is needed

Answer #1

A. **Warfarin**
B. Clopidogrel
C. Rivaroxaban
D. No additional medication is needed

Prior to cardioversion, anticoagulation prevents cardioembolic risk. With rheumatic heart disease warfarin is the preferable choice. Dual antiplatelet therapy is inferior to warfarin for anticoagulation in atrial fibrillation.

Question #2

A 70-year-old man with diabetes, hypertension and arthritis presents with a stroke. No clear etiology is defined. He is discharged on aspirin and Plavix. External ambulatory monitoring shows normal sinus rhythm with frequent PACs.

What would by the best next step?

A. Initiate warfarin
B. Initiate apixaban
C. Implantable loop recorder
D. Permanent Pacemaker
E. No additional changes

Answer #2

A. Initiate warfarin
B. Initiate apixaban
C. Implantable loop recorder
D. Permanent Pacemaker
E. No additional changes

An implantable loop recorder to look for atrial fibrillation after cryptogenic stroke is a reasonable next step. Without documented AF, triple anticoagulation therapy would not be of benefit. There is no indication for a pacemaker described.