

HKCC 28<sup>th</sup> ASC  
Cardiology Update: What a Primary Care Physician  
Needs to Know in 2020:

# Appropriate Treatment of Clinical & Subclinical AF

5<sup>th</sup> July 2020

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FRCP(Edin)

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Pro-Care Heart Clinic

# Global AF Burden



**Global Burden of Disease Study 2010 (WHO)**

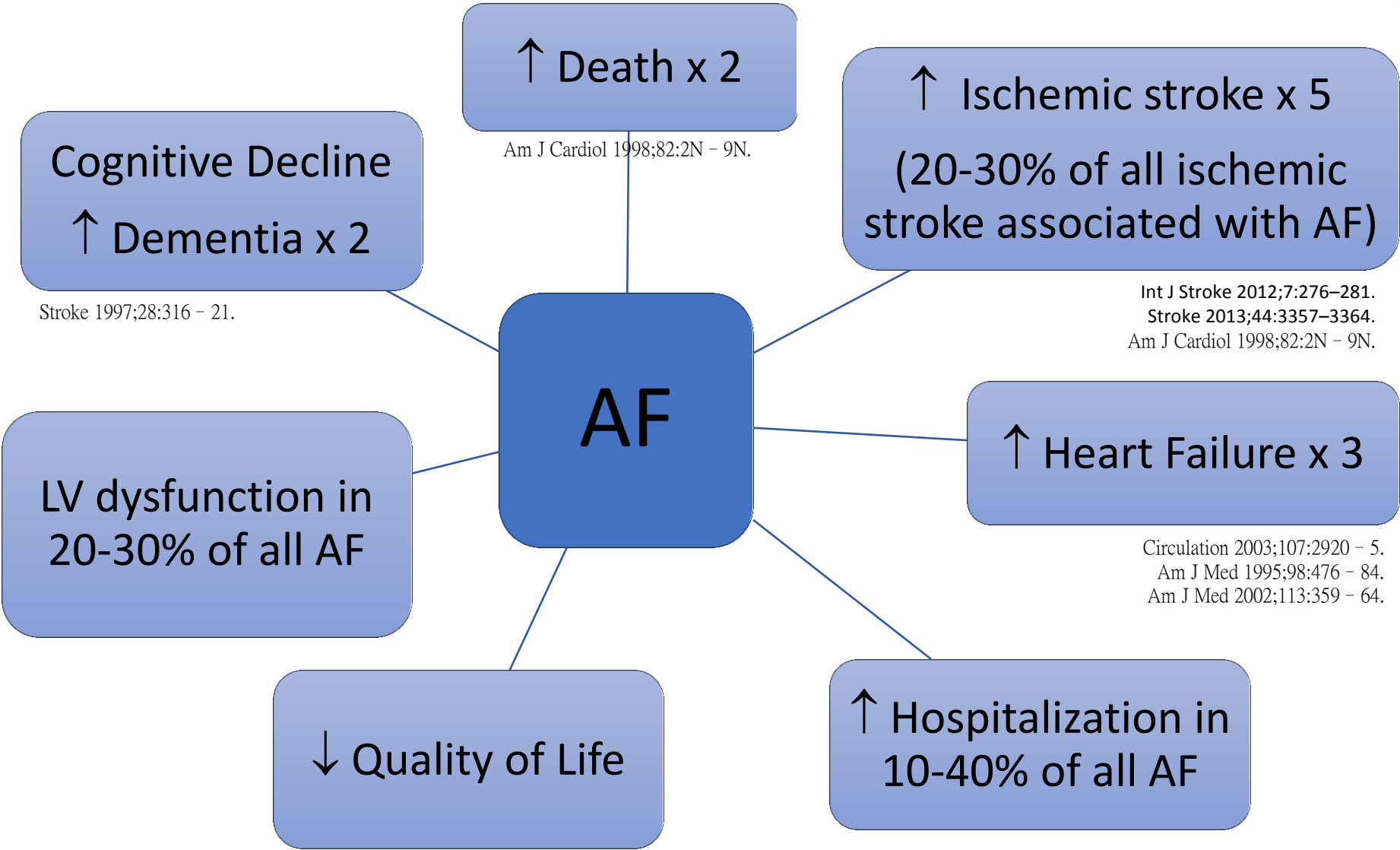
Global Prevalence of AF  
**33.5 million**  
(~0.5% of world's population)

**1 in 4 individuals aged  $\geq 40y$  will develop AF during their lifetime.**

Circulation. 2004 Aug 31. 110 (9):1042-6.  
Cleve Clin J Med. 2004 Jan. 71 (1):40-4.

Circulation. 2014;129:837-847.

# Complications of AF



## Appropriate Treatment of Clinical & Subclinical AF

- Clinical AF

- Risk stratification
- Acute management
- Chronic management

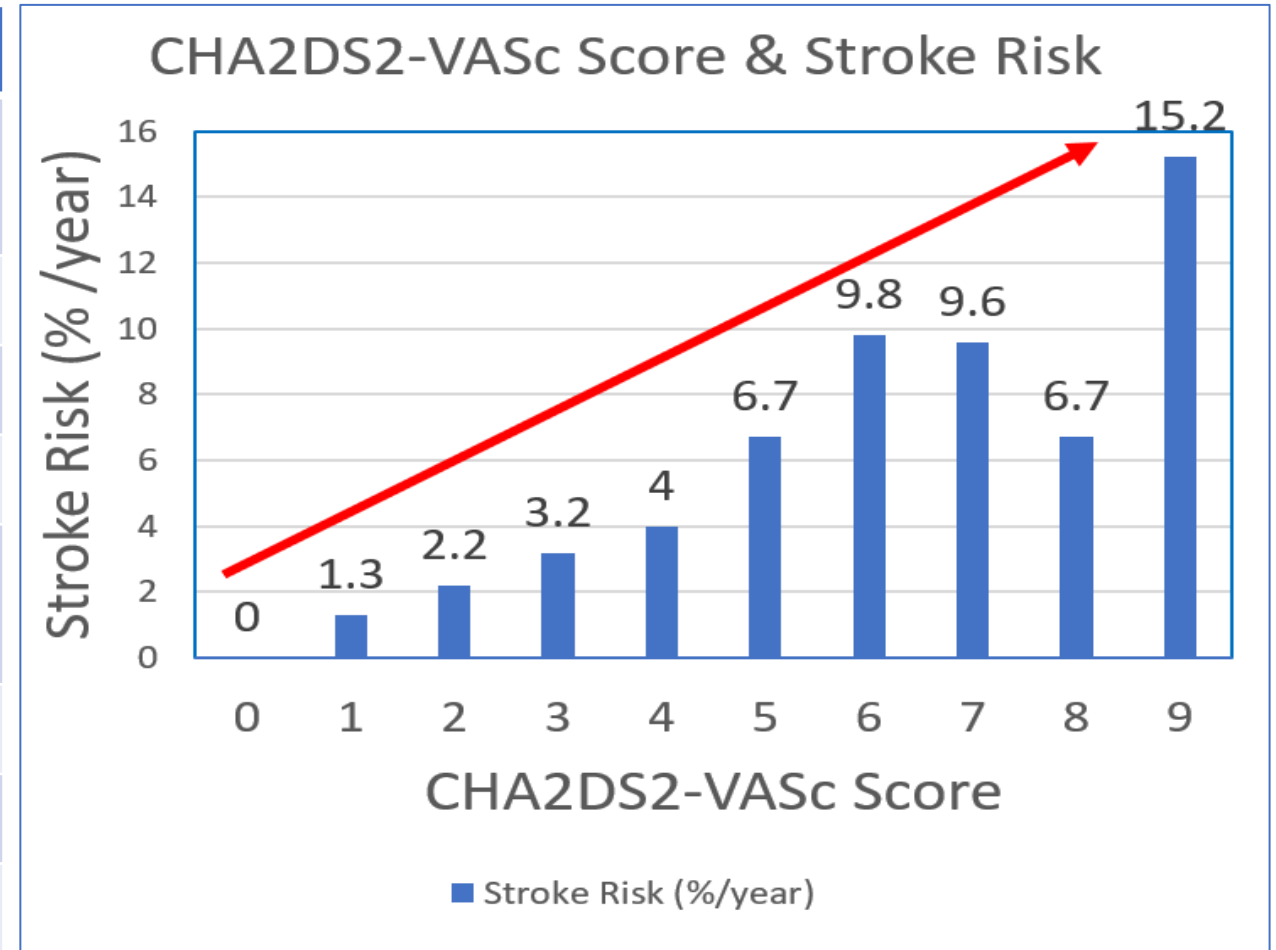
- Subclinical AF

- Definition
- Screening
- Risk stratification
- Anticoagulation strategy
- Mobile technology in AF management

# AF – Stroke Risk Assessment

## CHA2DS2-VASc Score

CHA2DS2-VASc Risk Factors	Score
Congestive Heart Failure or reduced left ventricular ejection fraction	1
Hypertension	1
Age $\geq$ 75y	2
Diabetes Mellitus	1
Previous Stroke/ TIA/ thromboembolism	2
Vascular disease	1
Age 65-74y	1
Sex Category (Female)	1

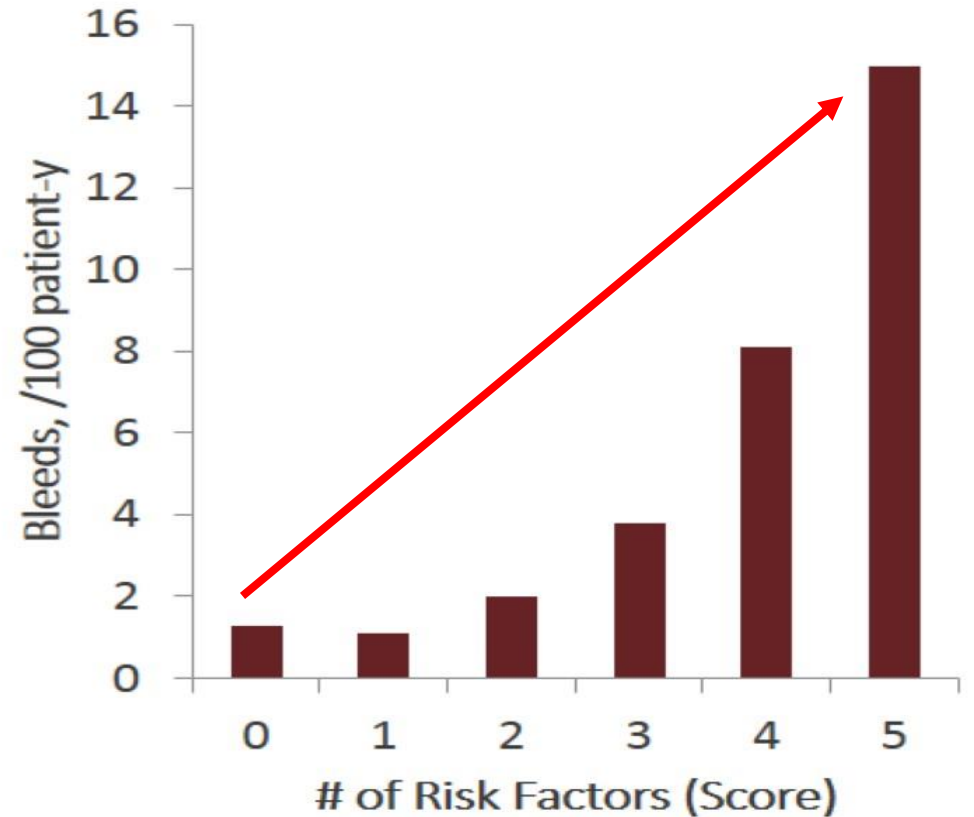


# AF – Bleeding Risk Assessment HAS-BLED Score

Letter	Clinical characteristic	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

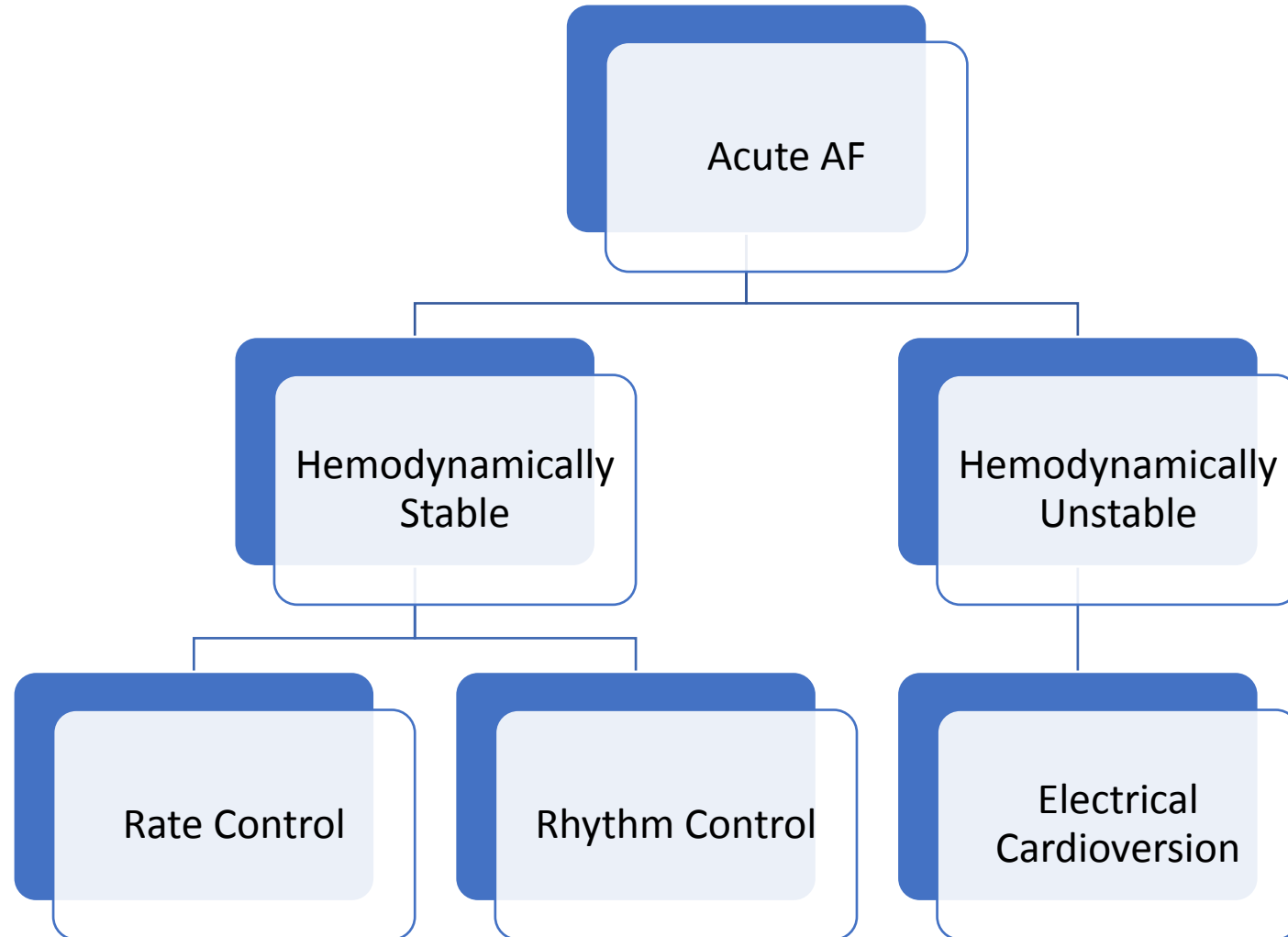
The HAS-BLED score can be used to evaluate major bleeding risk in patients with AF taking warfarin or NOAC therapy.

ESC Guidelines., Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC), *Eur Heart J.* 2010;31:2369-2429. By permission of Oxford University Press.



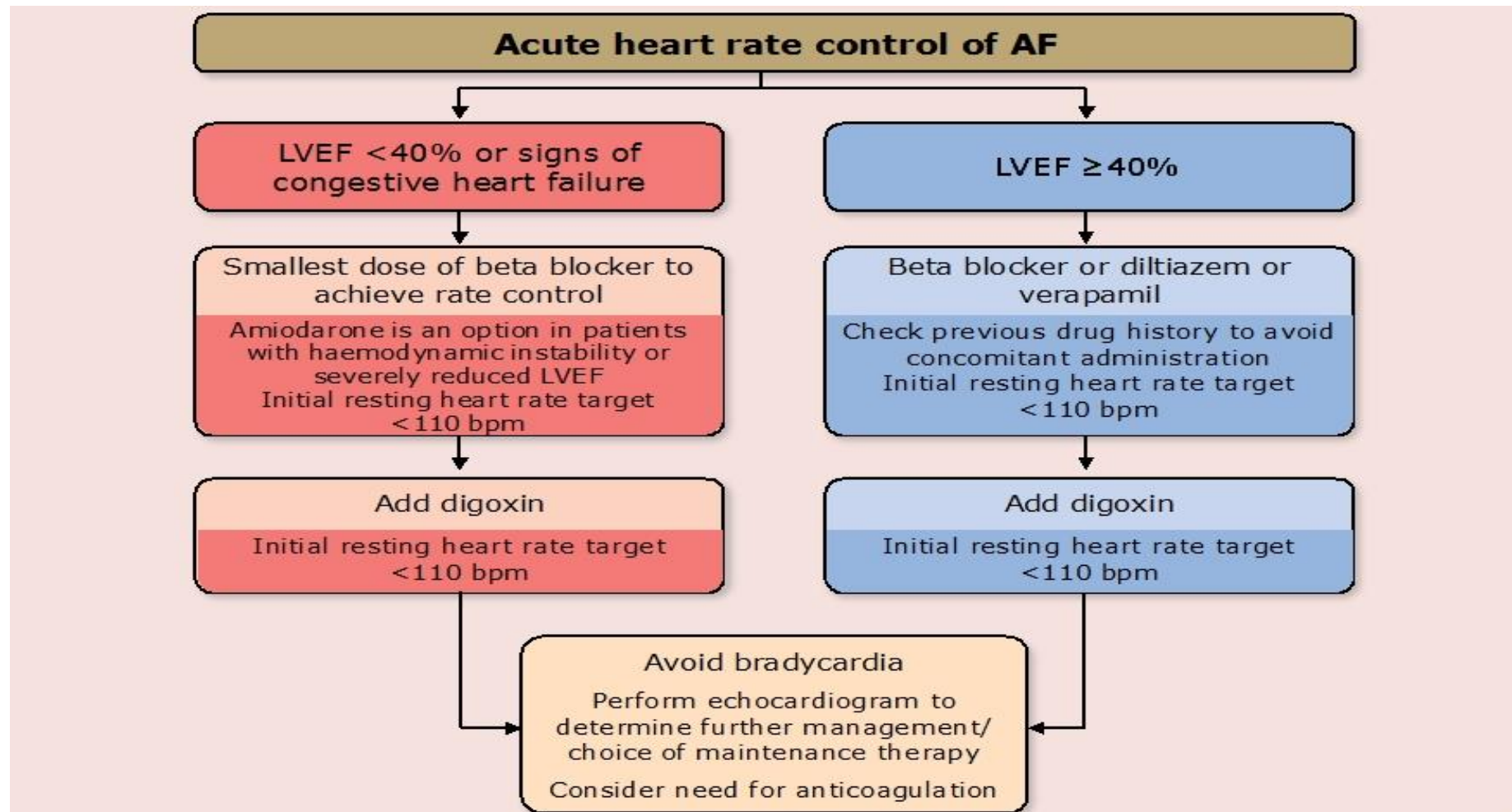
Pisters R, et al. *Chest.* 2010;138: 1093-1100.  
ESC Guidelines. *Eur Heart J.* 2010;31:2369-2429.  
Belen E, et al. *Blood Coagul Fibrinolysis.* 2015;26:793-797.

# Atrial Fibrillation Acute Management



# Atrial Fibrillation Acute Rate Control

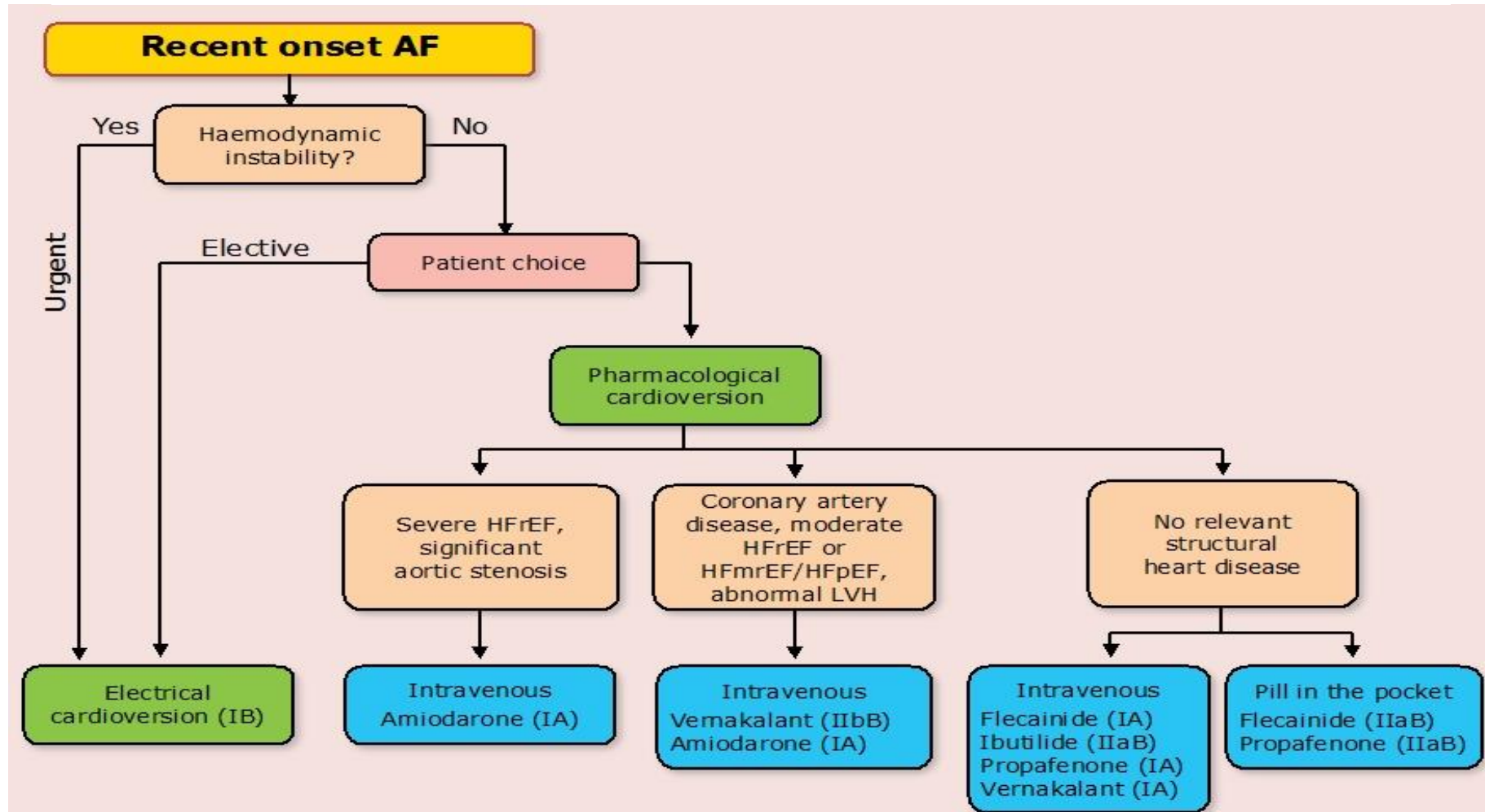
## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS



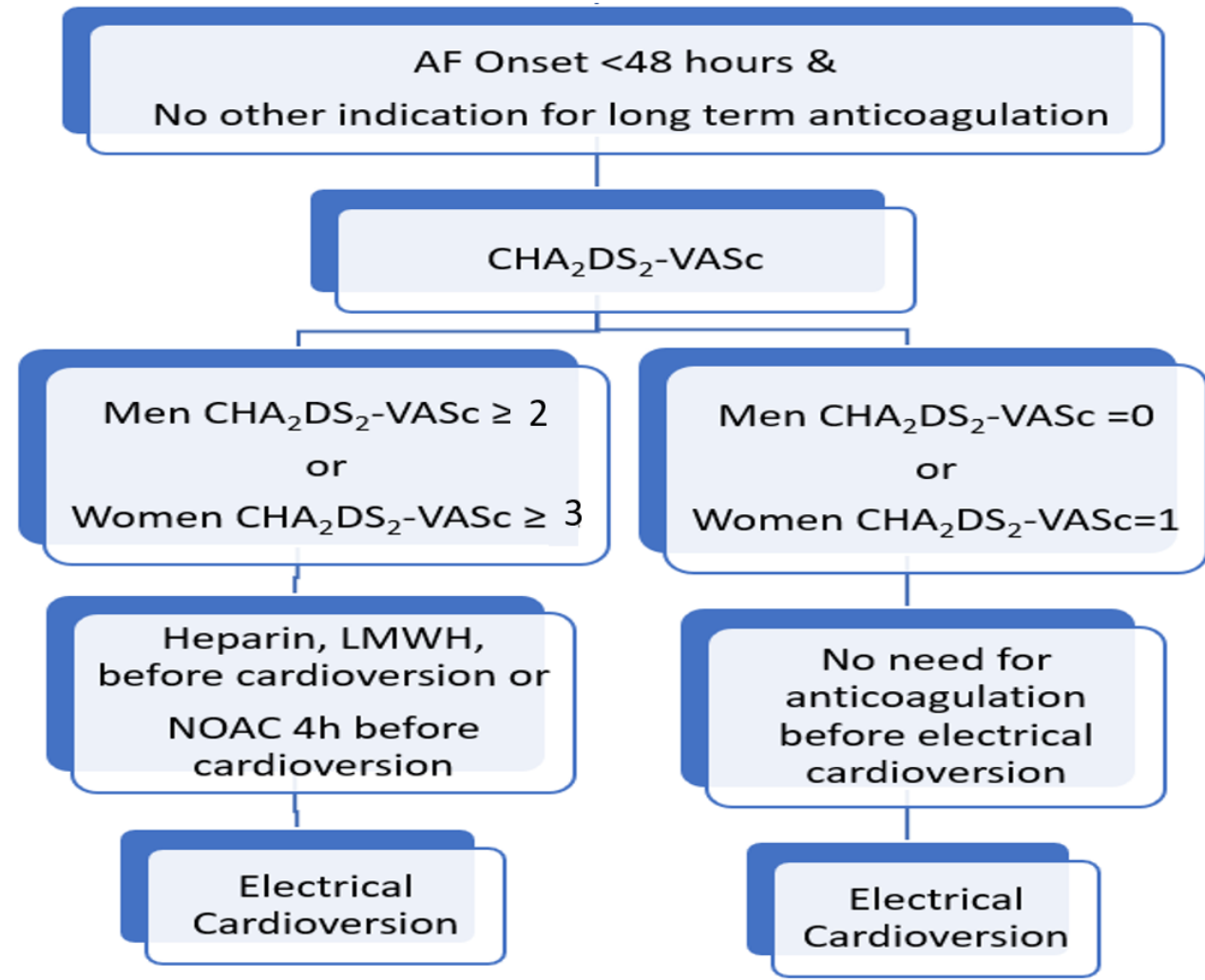


# Atrial Fibrillation Acute Rhythm Control

## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

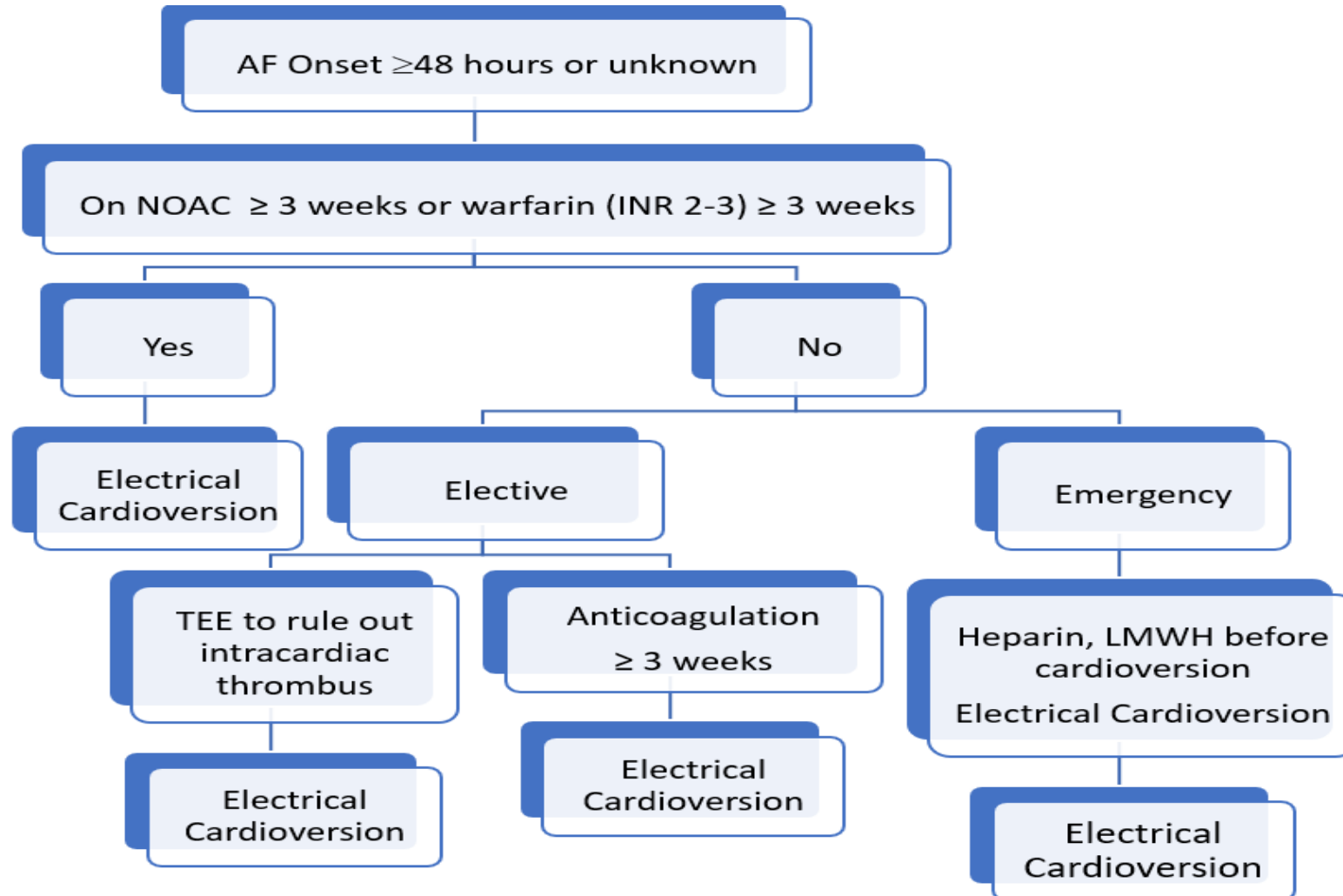


# Cardioversion Anticoagulation Management

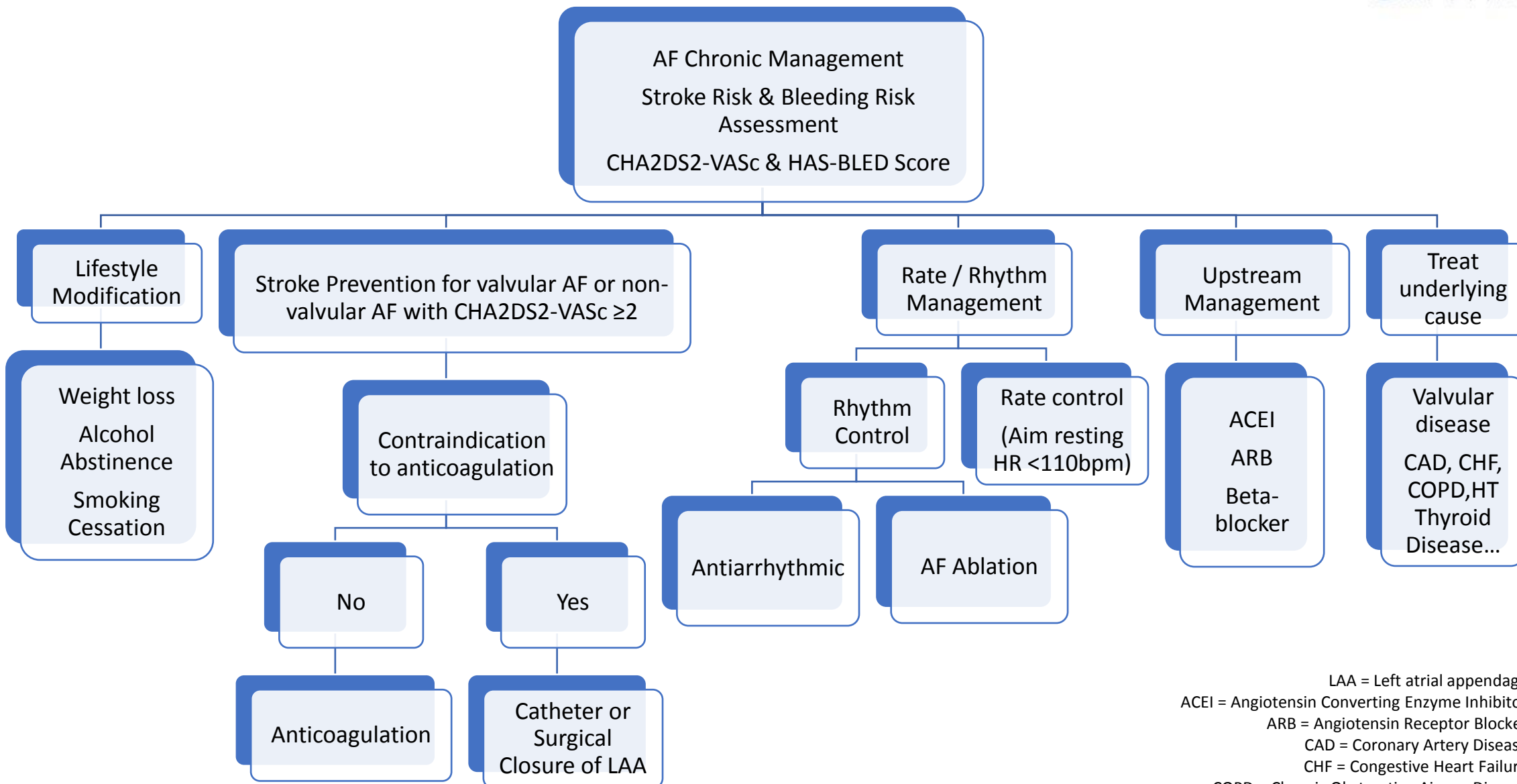


LMWH = Low Molecular Weight Heparin; NOAC = Novel Oral Anticoagulant

# Cardioversion Anticoagulation Management



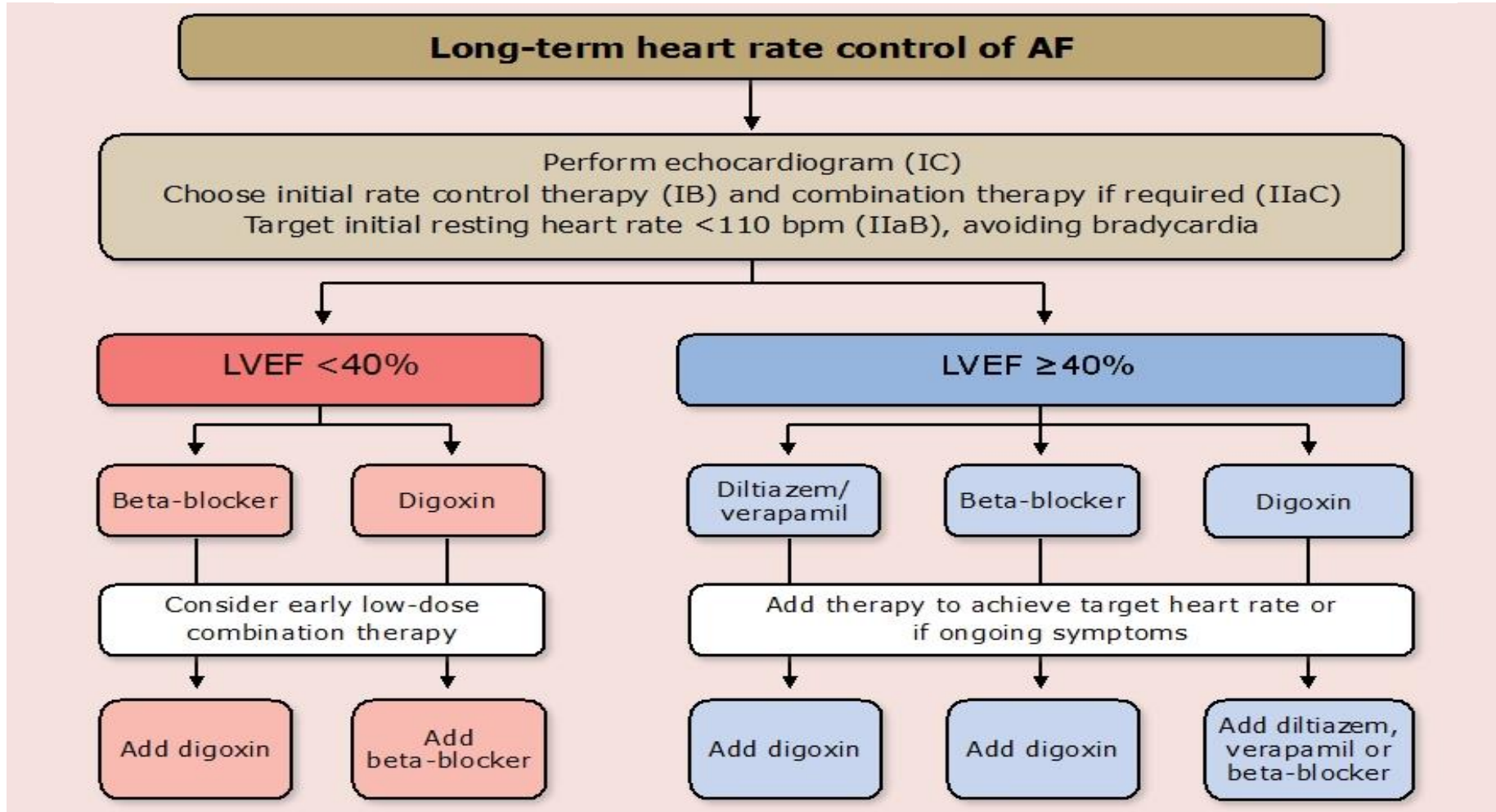
# Atrial Fibrillation Chronic Management



LAA = Left atrial appendage  
ACEI = Angiotensin Converting Enzyme Inhibitor  
ARB = Angiotensin Receptor Blocker  
CAD = Coronary Artery Disease  
CHF = Congestive Heart Failure  
COPD = Chronic Obstructive Airway Disease  
HT = Hypertension

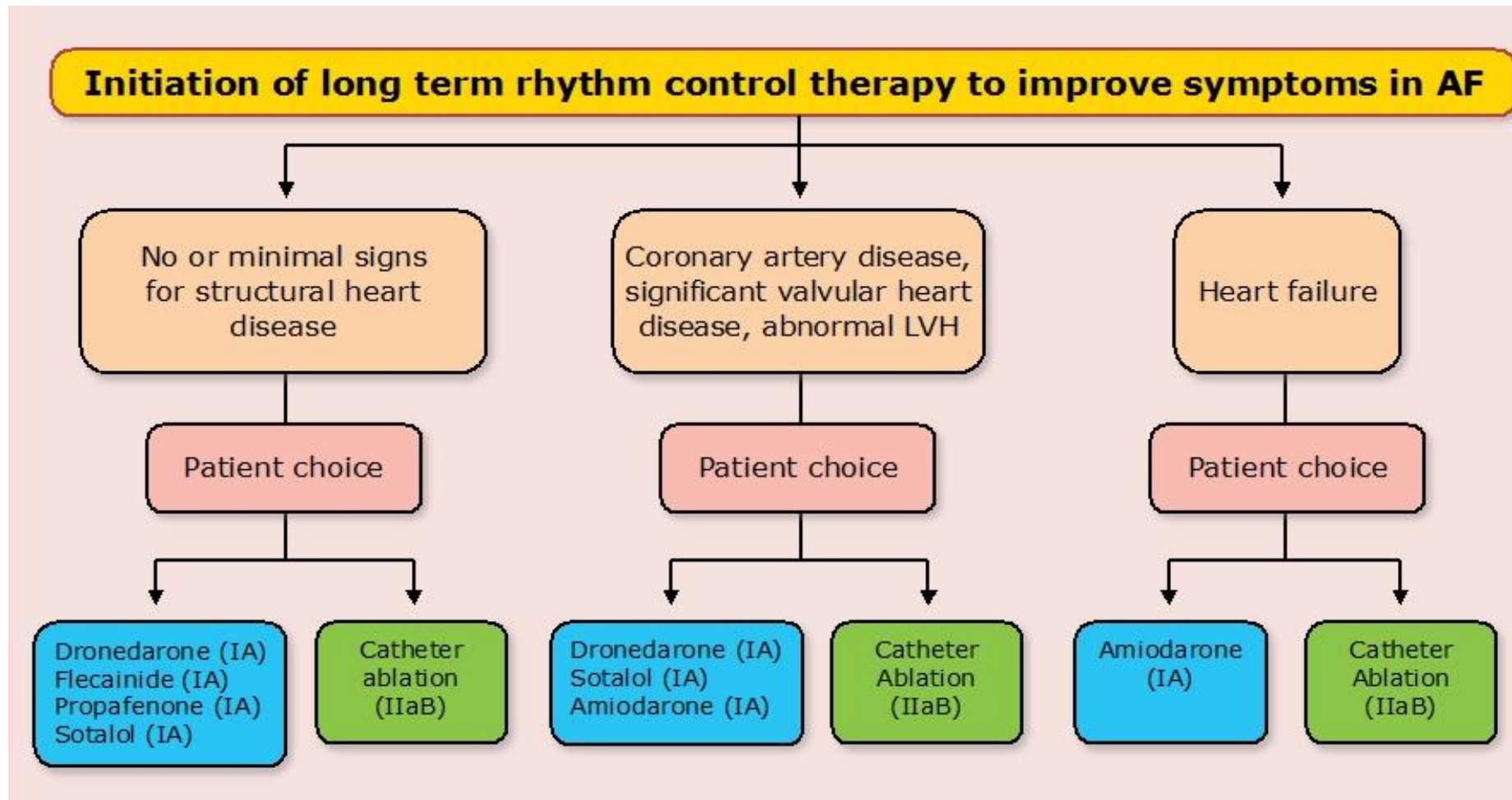
# Atrial Fibrillation Chronic Rate Control

## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

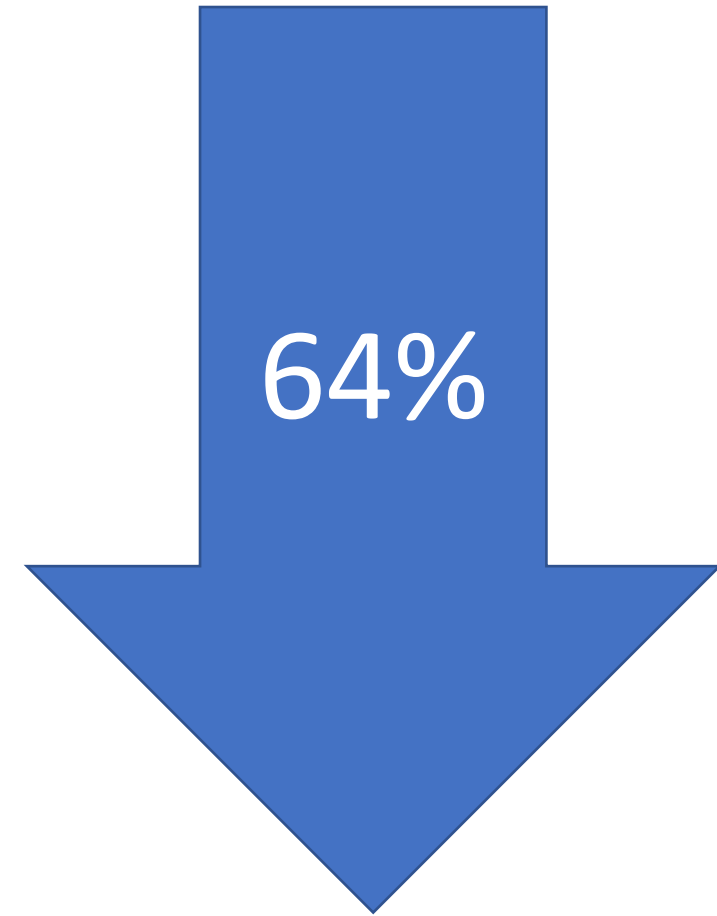
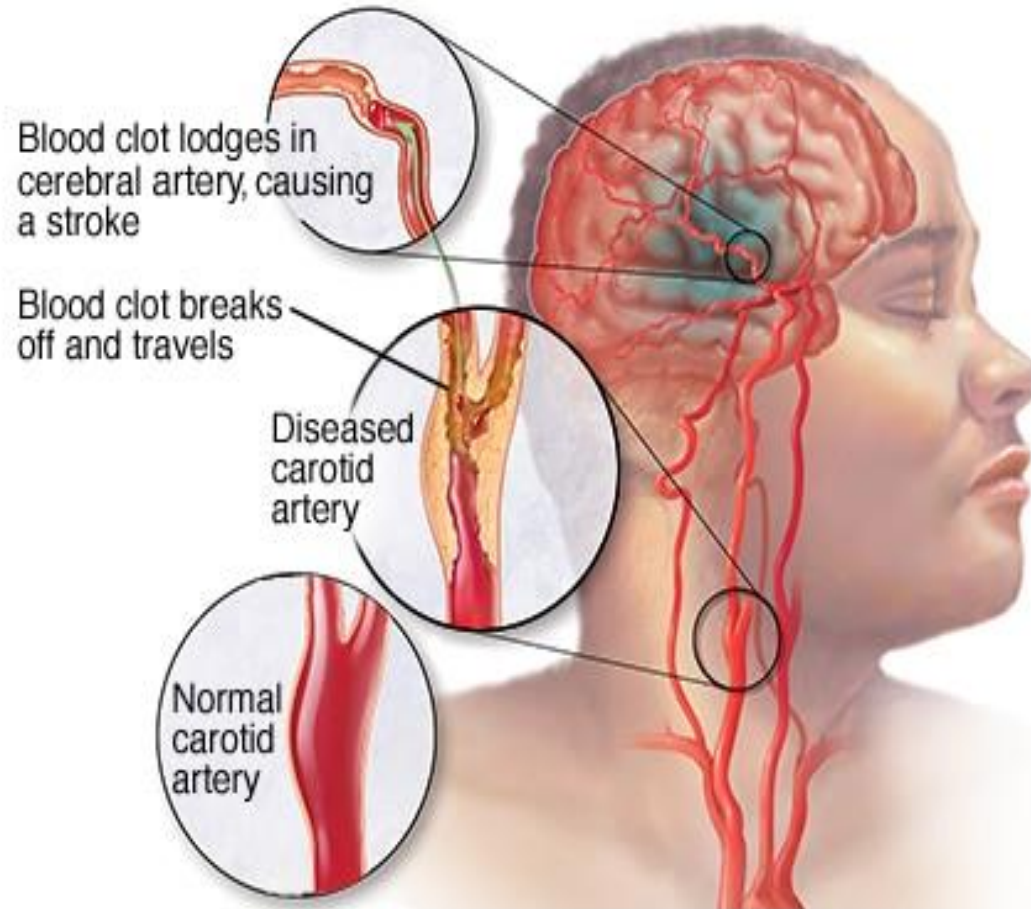


# Atrial Fibrillation Chronic Rhythm Control

## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS



# Oral anticoagulation reduces ischemic stroke risk by 64%



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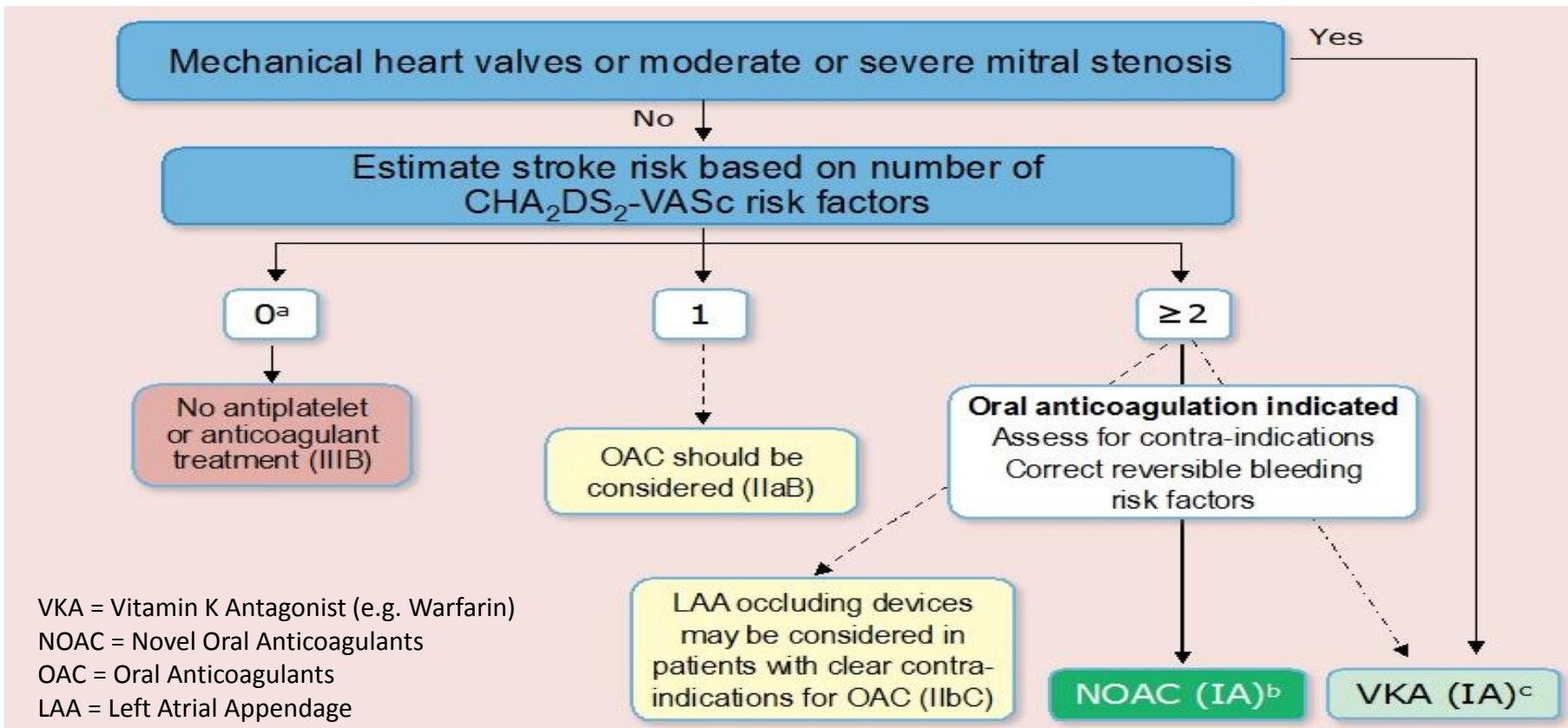
# Stroke Prevention Strategy in AF

## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.

III  
(harm)

A





# Summary - NOAC vs Warfarin

## NOACs are associated with improved outcomes for patients with NVAF compared with warfarin

	Dabigatran (RE-LY <sup>1,2,7</sup> )		Apixaban (ARISTOTLE <sup>3,4</sup> )	Rivaroxaban (ROCKET AF <sup>5</sup> )	Edoxaban (ENGAGE AF-TIMI 48 <sup>6</sup> )
	150 mg BID	110 mg BID	5/2.5 mg BID	20/15 mg OD	60/30 mg OD
Stroke/SE	↓ 35%	Similar	↓ 21%	Similar	Similar
Ischaemic stroke	↓ 24%	Similar	Similar	Similar	Similar
Haemorrhagic stroke	↓ 74%	↓ 69%	↓ 49%	↓ 41%	↓ 46%
Major bleeding	Similar	↓ 20%	↓ 31%	Similar	↓ 20%

Dabigatran 150mg BID is the only NOAC demonstrating superiority to warfarin in ischemic stroke prevention

Apixaban is the only NOAC approved for patients on renal dialysis or eGFR <15ml/min

RE-LY is the only NOAC trial to independently evaluate two fully randomized doses that have then been approved

**No direct head-to-head comparison, outcomes cannot be compared due to different trial designs**

Relative risk reductions vs warfarin. SE, systemic embolism. 1. Connolly SJ et al. N Engl J Med 2014; 2. Connolly SJ et al. N Engl J Med 2010; 3. Granger C et al. N Engl J Med 2011; 4. Lopes RD et al. Lancet 2012; 5. Patel MR et al. N Engl J Med 2011; 6. Giugliano RP et al. N Engl J Med 2013; 7. Pradaxa SPC, 2017

# Choice of Anticoagulant in AF

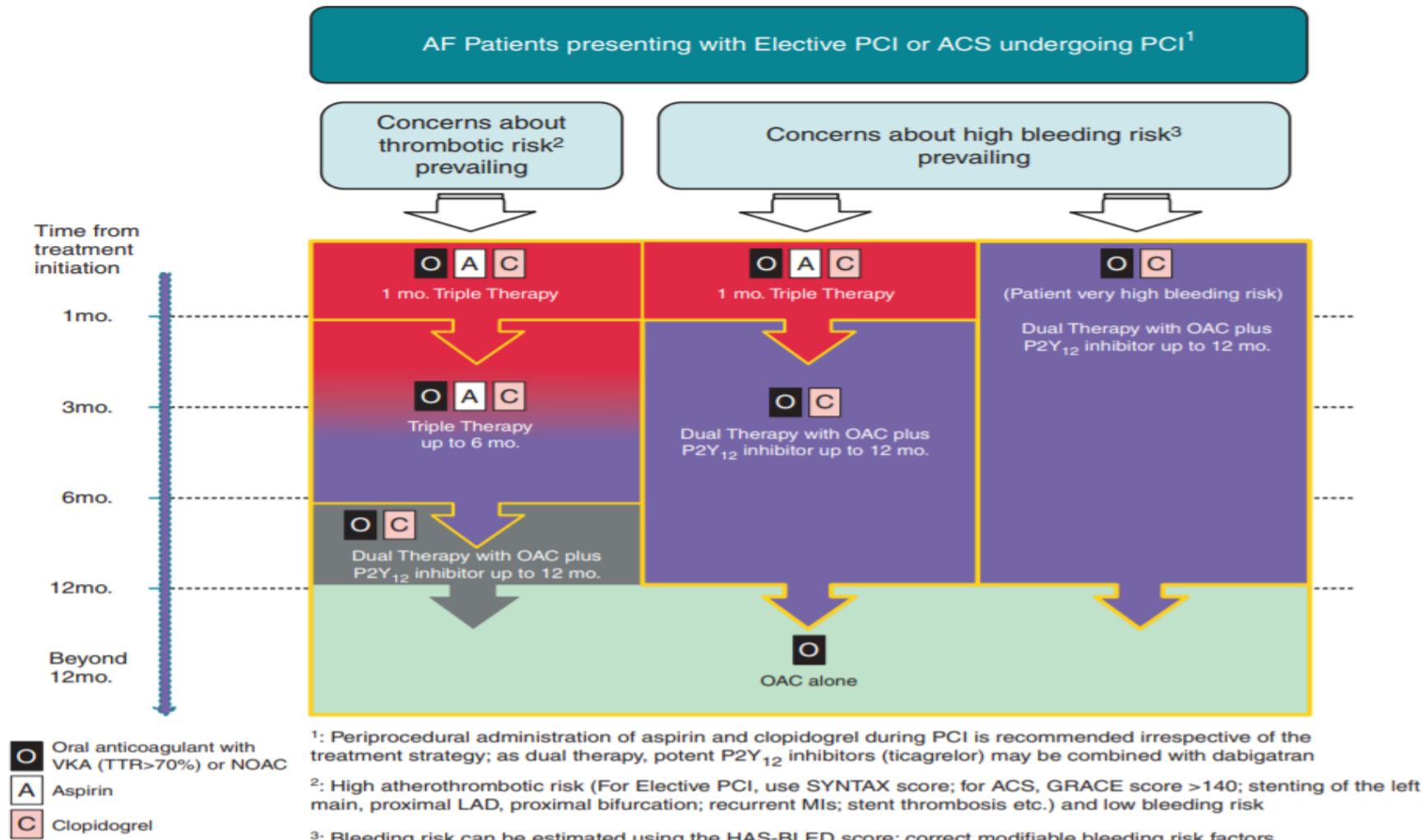
## 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

### Recommendations for Selecting an Anticoagulant Regimen—Balancing Risks and Benefits

Referenced studies that support new or modified recommendations are summarized in [Online Data Supplements 1 and 2](#).

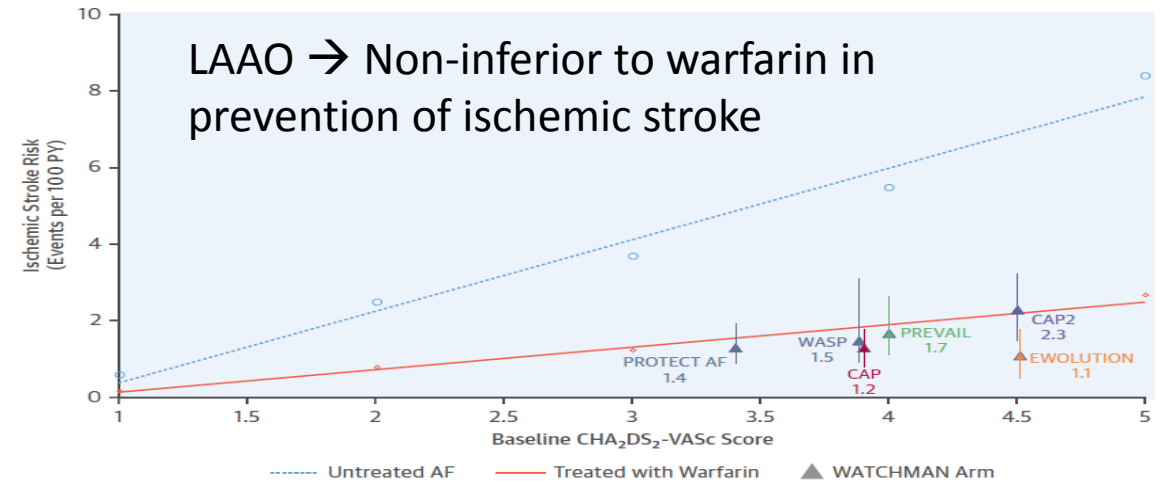
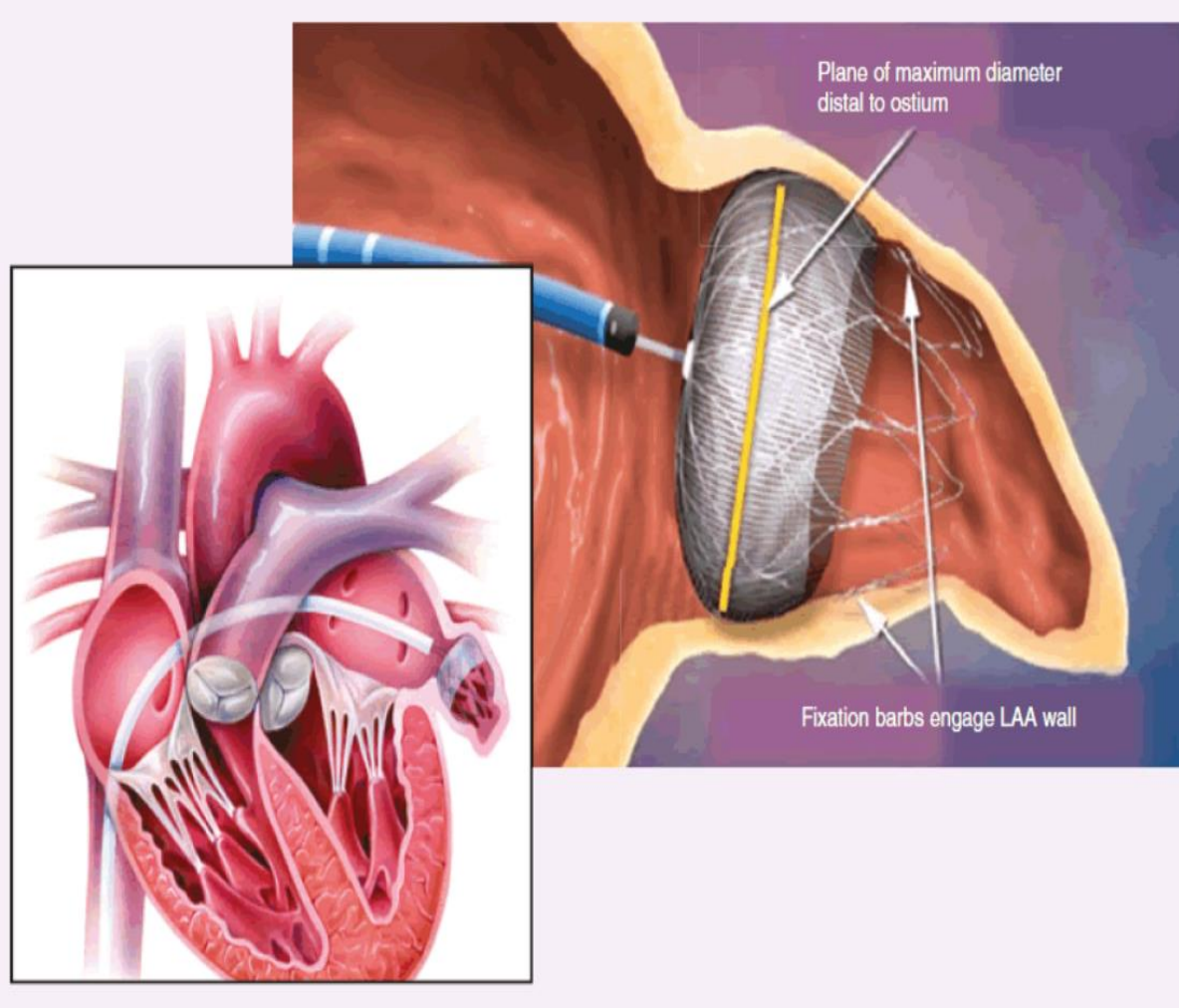
COR	LOE	Recommendations
I	A	<p>1. For patients with AF and an elevated CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended.</p> <p>Options include:</p> <ul style="list-style-type: none"> <li>• Warfarin (LOE: A) (S4.1.1-5–S4.1.1-7)</li> <li>• Dabigatran (LOE: B) (S4.1.1-8)</li> <li>• Rivaroxaban (LOE: B) (S4.1.1-9)</li> <li>• Apixaban (LOE: B) (S4.1.1-10), or</li> <li>• Edoxaban (LOE: B-R) (S4.1.1-11)</li> </ul>
	B	
	B	
	B	
I		<p>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) (S4.1.1-8–S4.1.1-11).</p>
I	C-EO	<p>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.</p>

# 2018 Joint European Consensus Document on the Management of Antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI: A Joint Consensus Document of the EHRA, EAPCI, & ACCA



# 5-Year Outcomes After Left Atrial Appendage Closure

From the PREVAIL and PROTECT AF Trials



LAO ↓ → hemorrhagic stroke, disabling/fatal stroke, CV death / unexplained death, major bleeding & all-cause death vs warfarin; in patients with non-valvular AF

	HR	p-value
<b>Efficacy</b>		
All stroke or SE	0.82	0.3
Ischemic stroke or SE	0.96	0.9
Hemorrhagic stroke	1.7	0.08
Ischemic stroke or SE >7 days	0.2	0.0022
Disabling/Fatal Stroke (MRS change of ≥2)	1.4	0.3
Non-Disabling Stroke	1.79	0.1
CV/unexplained death	0.41	0.03
<b>Safety</b>		
All-cause death	0.59	0.03
Major bleed, all	0.73	0.04
Major bleeding, non procedure-related	0.91	0.6
	0.48	0.0003

Favors WATCHMAN ← → Favors Warfarin

Hazard Ratio (95% CI)

Blackshear: Ann Thoracic Surg 61, 1996  
Johnson: Eur J Cardiothoracic Surg 17, 2000  
Fagan: Echocardiography 17, 2000  
Manning WJ. Clin Cardiol. 1995; 18:58, 114

## Left Atrial Appendage Occlusion (LAAO)

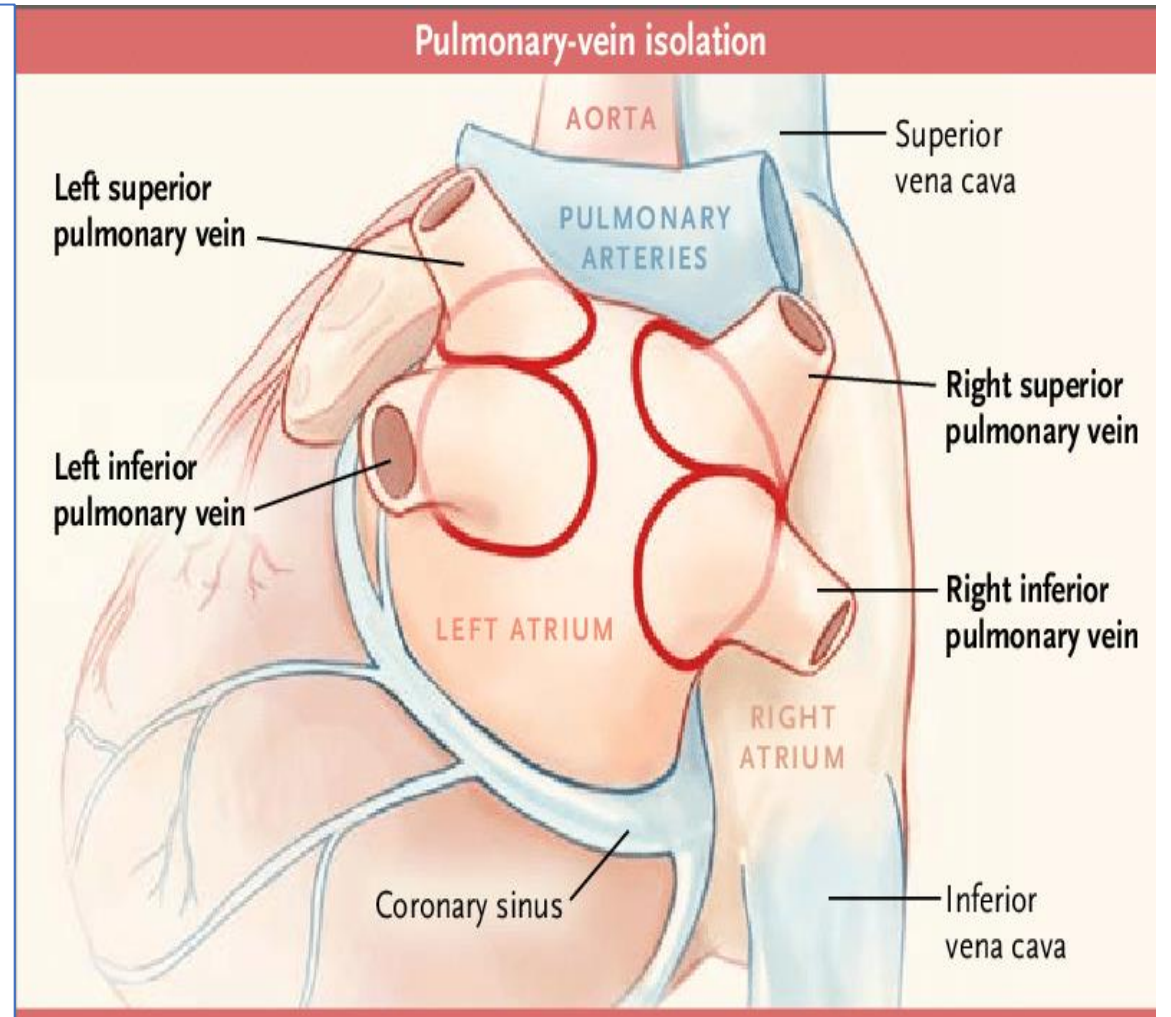
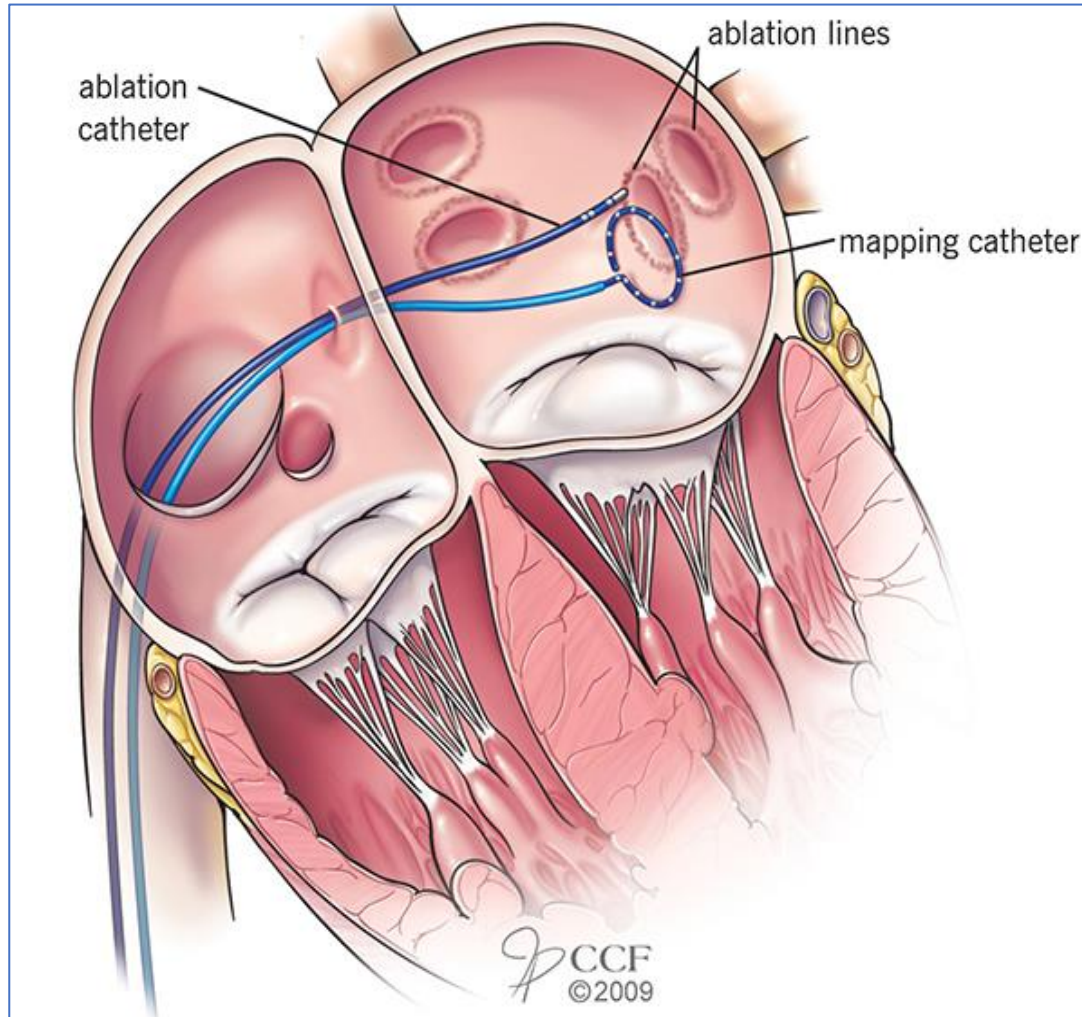
### 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).	<b>IIb</b>	<b>B</b>
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### 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

COR	LOE	Recommendation
<b>IIb</b>	<b>B-NR</b>	1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5).

# Pulmonary Vein Isolation Cornerstone of AF Ablation

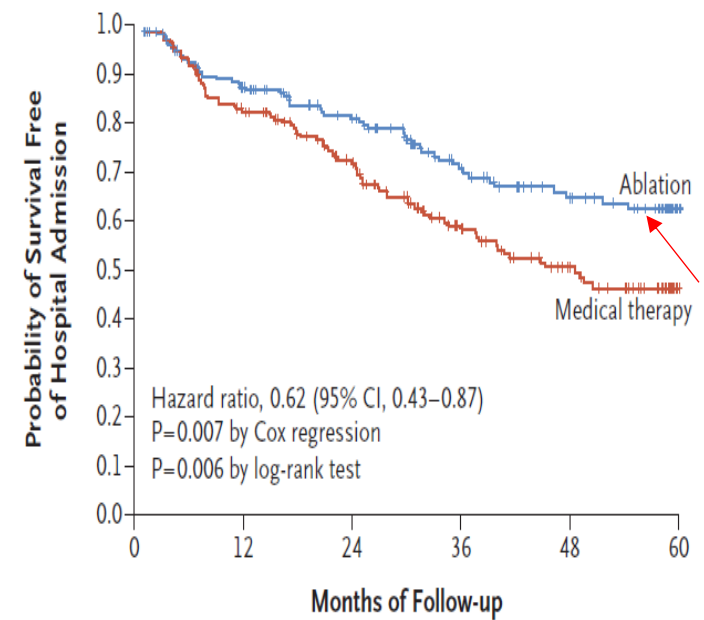


# Catheter Ablation for Atrial Fibrillation with Heart Failure

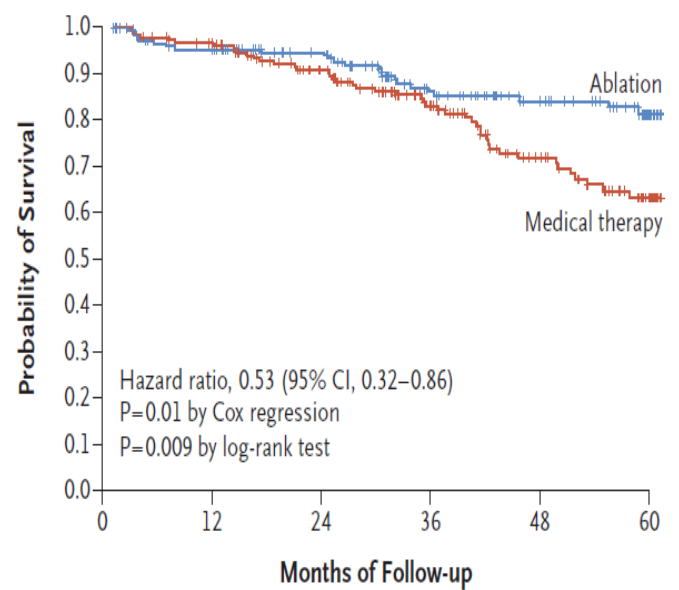
## CASTLE - AF Trial

In patients with paroxysmal / persistent AF and heart failure (LVEF ≤35%):  
 AF Ablation → ↓ Death by ~50% & ↓ Hospitalization for CHF by 44% vs drug therapy  
 ↓ Combined endpoint of death or hospitalization for CHF by 38%

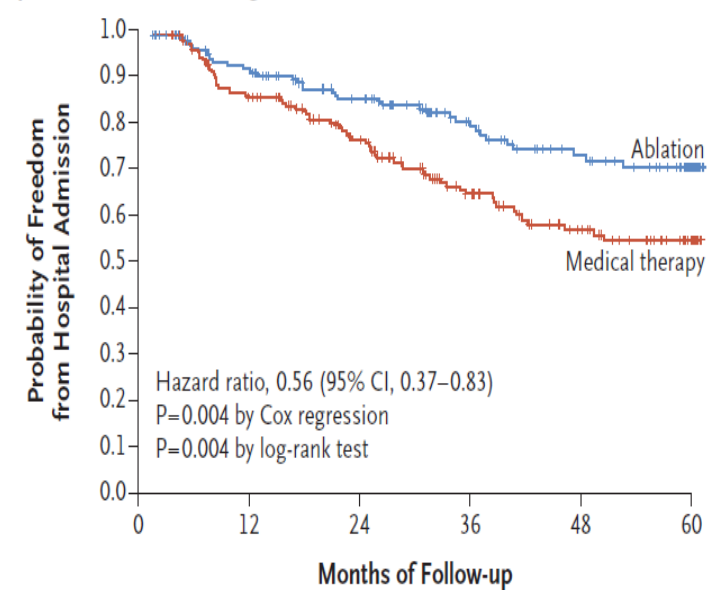
**A** Death or Hospitalization for Worsening Heart Failure



**B** Death from Any Cause



**C** Hospitalization for Worsening Heart Failure



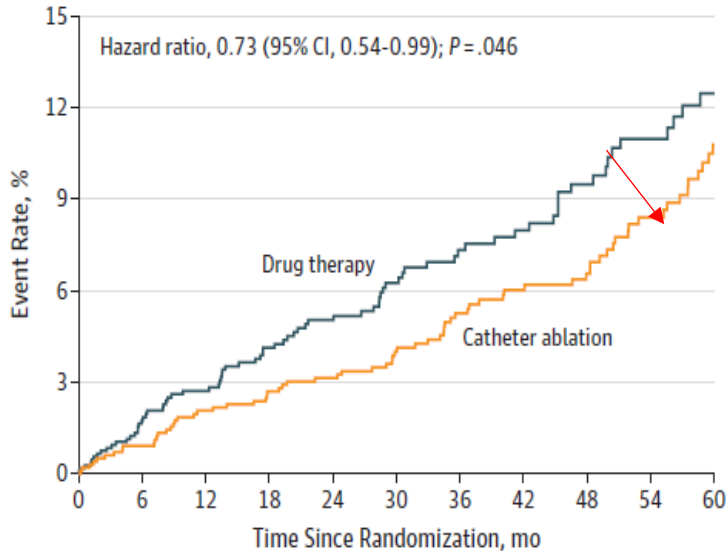
AF Ablation (N = 179); Medical therapy (N=184)

# Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation

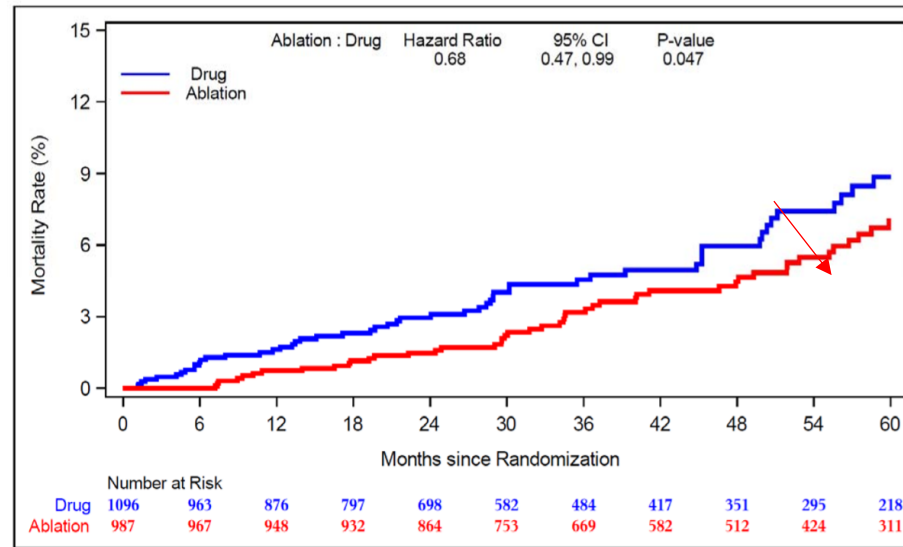
## The CABANA Randomized Clinical Trial

By per-protocol analysis (Treatment received):  
 AF Ablation ↓ primary endpoints and mortality by ~ 30% vs drug therapy  
 By intention-to-treat analysis:  
 AF Ablation ↓ recurrent AF by ~50% vs drug therapy

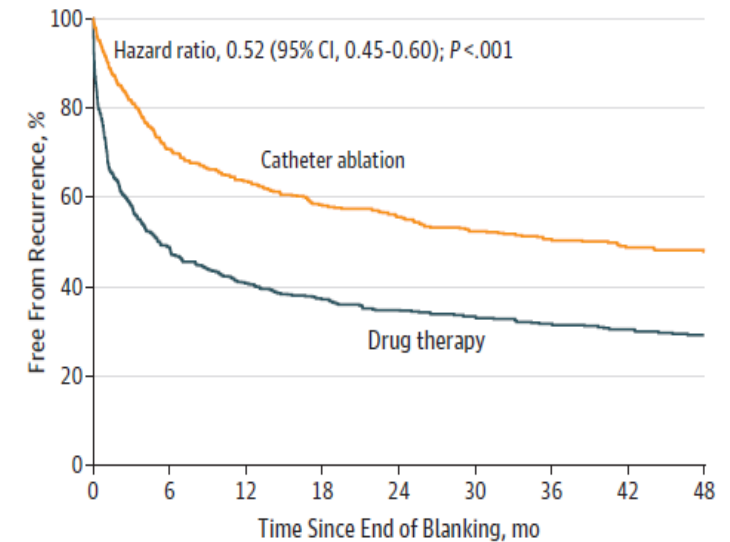
Death, disabling stroke, serious bleeding, or cardiac arrest



All-cause mortality



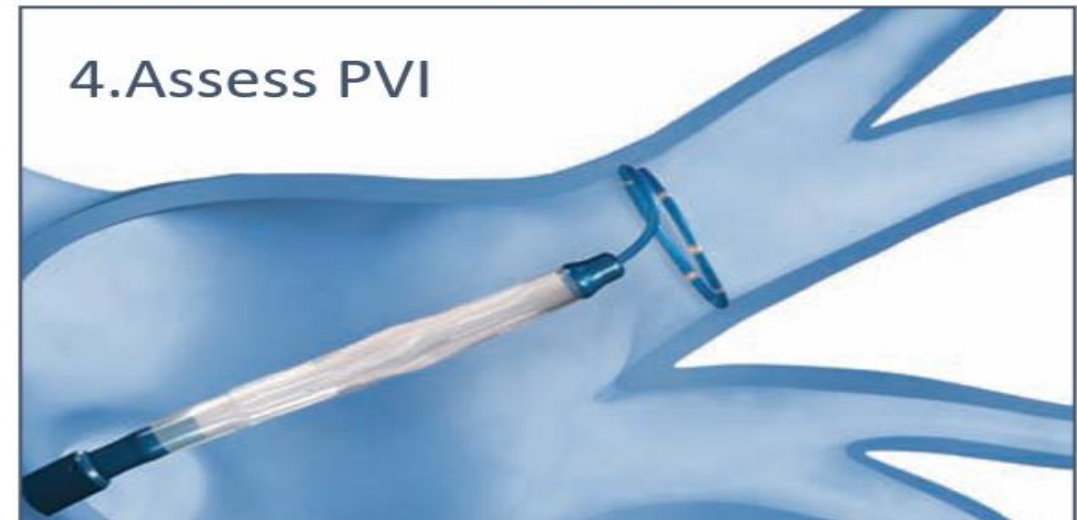
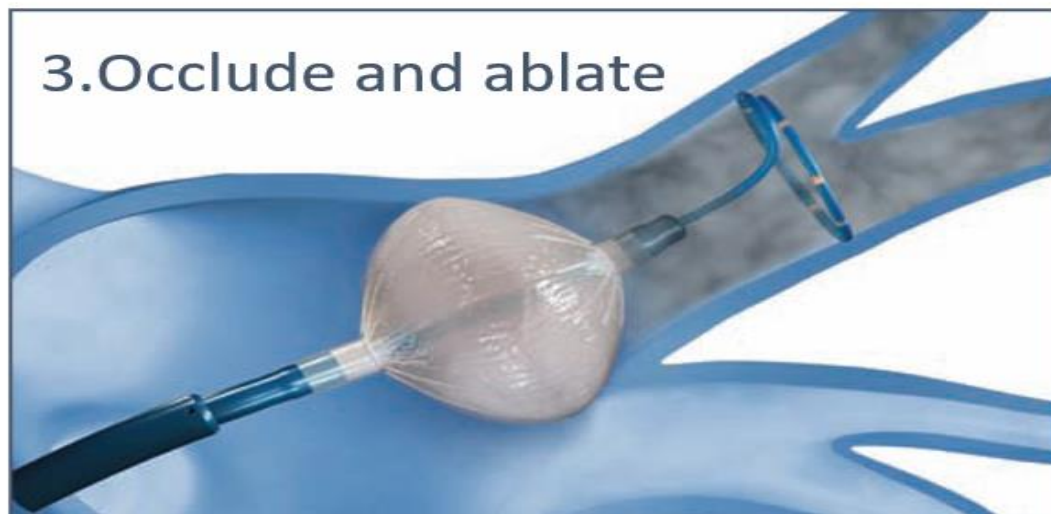
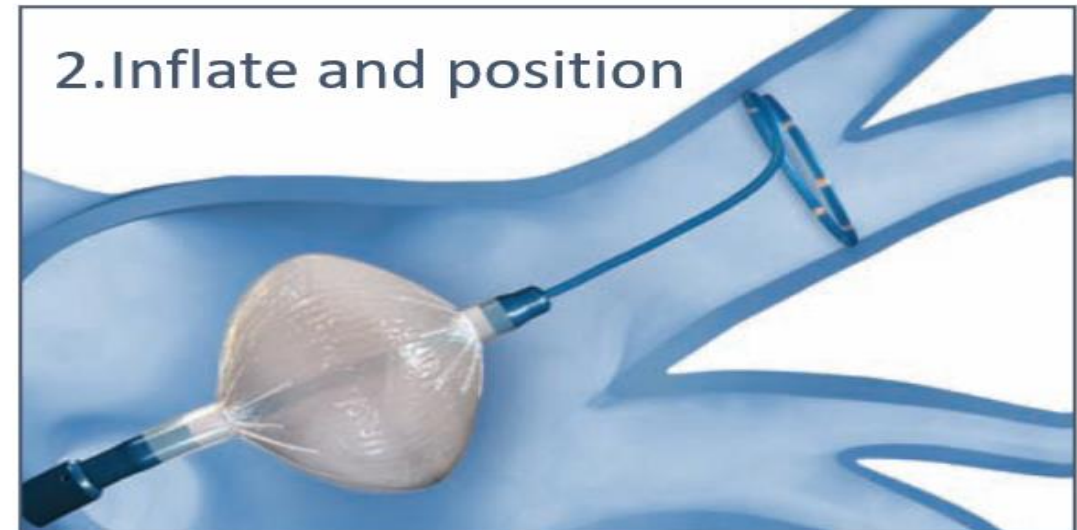
Recurrent AF



AF Ablation ( N = 1108); Drug therapy (N=1096)



# Cryoballoon AF Ablation

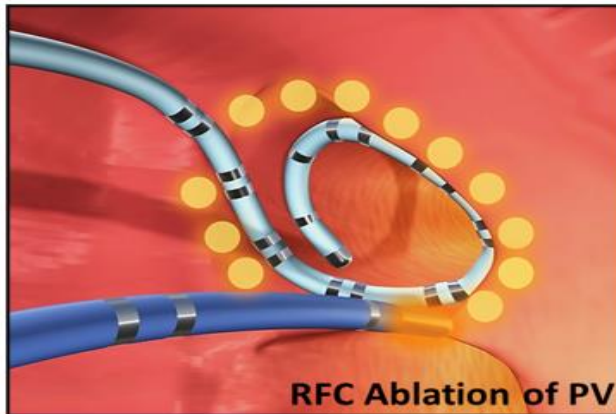


# Cryoballoon or Radiofrequency Ablation for Paroxysmal AF

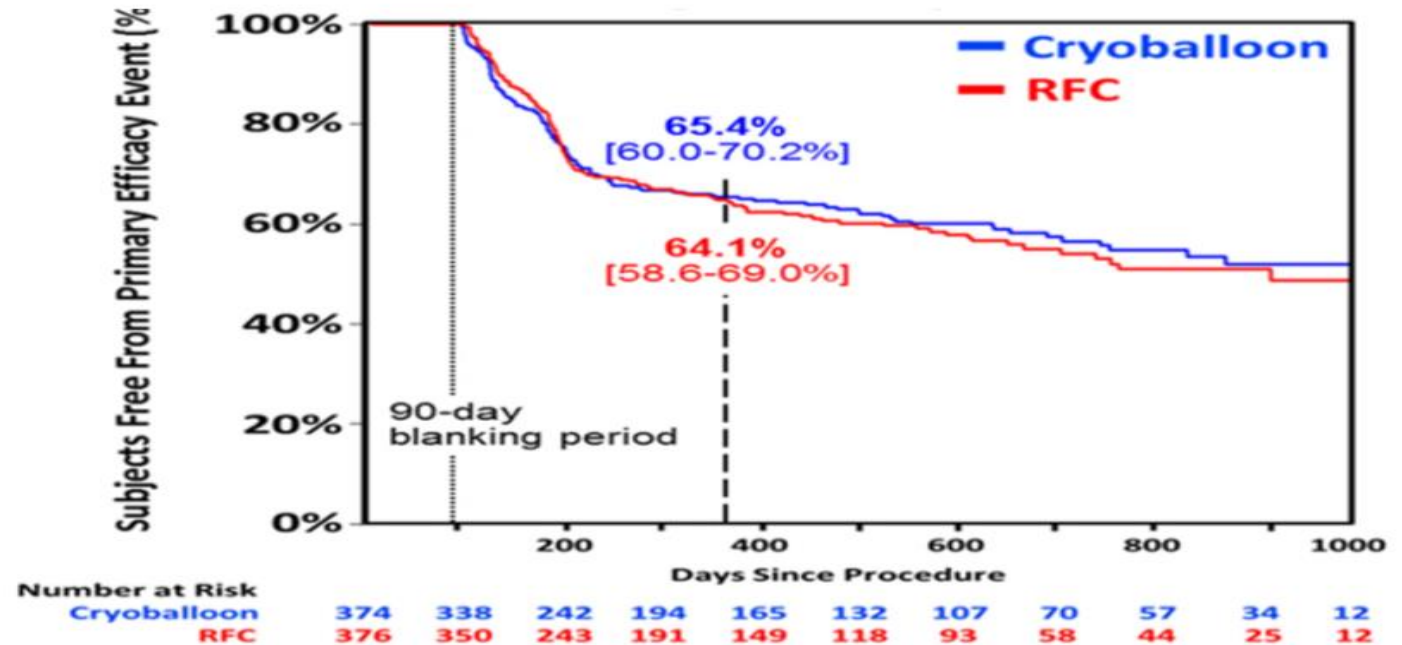
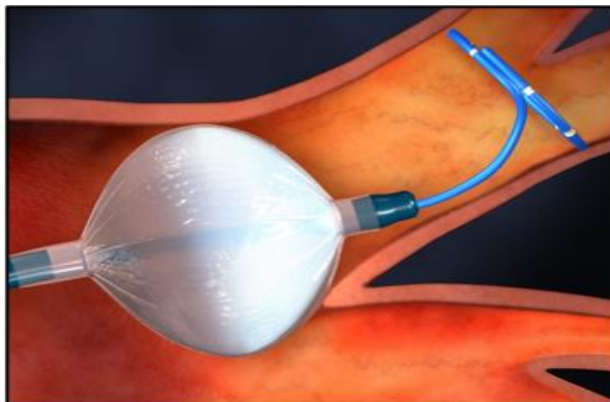
FIRE AND ICE Trial

Cryoballoon vs Radiofrequency AF Ablation → Similar efficacy

RFC Ablation (“FIRE”)



Cryoballoon Ablation (“ICE”)



Efficacy End Point Type	Cryo (N=374)	RFC (N=376)
Recurrent atrial arrhythmia	80	87
Antiarrhythmic drug prescription	51	49
Re-ablation	7	7

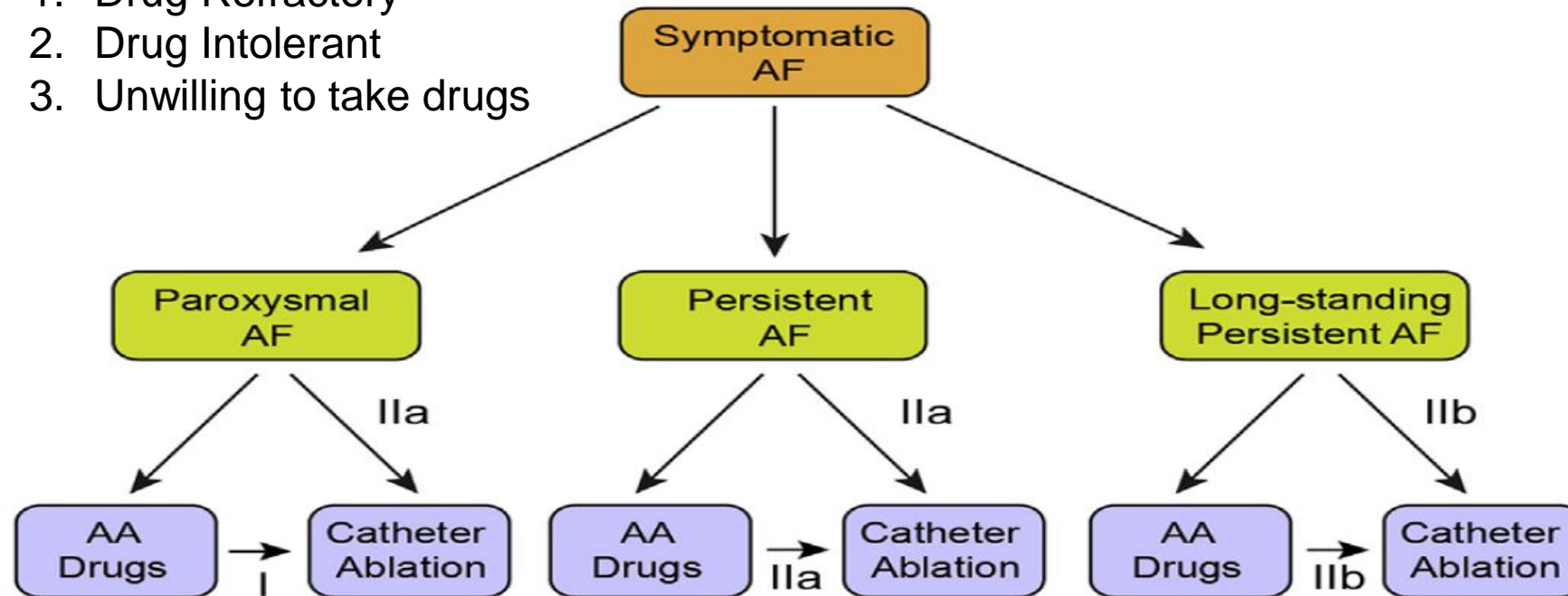
# Atrial Fibrillation Catheter Ablation

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary <sup>e</sup>



## Indications for Catheter Ablation of Symptomatic Atrial Fibrillation

1. Drug Refractory
2. Drug Intolerant
3. Unwilling to take drugs



AA = Antiarrhythmic

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

Recommendation for Catheter Ablation in HF		
COR	LOE	Recommendation
IIb	B-R	<b>AF catheter ablation</b> may be reasonable in selected patients with symptomatic <b>AF and Heart Failure (HF) with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF.</b>

An iceberg floating in the ocean. The tip of the iceberg is above the water surface, and the much larger, jagged base is submerged below. The sky is blue with scattered white clouds. The water is a clear, deep blue.

**Symptomatic AF**

**Asymptomatic /  
Subclinical AF**

**Up to 30-90%  
Asymptomatic**

Lancet Neurol. 2015;14(9):903-13.  
N Engl J Med. 2014; 26;370(26):2478-86.  
Circulation. 1994; 89(1):224-7.  
Int J Cardiol. 2017 Jan 15;227:583-588.  
Curr Pharm Des 2015;21:659-66.

J Interv Card Electrophysiol 2000;4:369-82.  
Int J Clin Pract 2014;68:444-52.  
Pacing Clin Electrophysiol 2009;32:91-8.  
Circulation 1994;89:224-7.  
J Am Coll Cardiol 2004;43:47-52.



**Screening for atrial fibrillation: a European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLAECE)**

## Definition of Different Subtypes of AF

Asymptomatic or clinically silent AF	Episode of at least 30 s of ECG documented absolutely irregular RR intervals with no discernable, distinct P waves, in the absence of symptoms typically associated with AF (i.e. palpitations, shortness of breath, lightheadedness, chest pain, pre-syncope, or syncope)
AHRE	Episodes of at least 5 min of AT/AF with an atrial rate >180 bpm, detected by the continuous monitoring of CIEDs
Subclinical AF	Episodes of AT/AF with duration between 5 min and 24 h, detected in patients without clinical history or clinical symptoms of AF

CIED = Cardiac Implantable Electronic Device

AHRE = Atrial High Rate Episodes

# AF & Cryptogenic Stroke

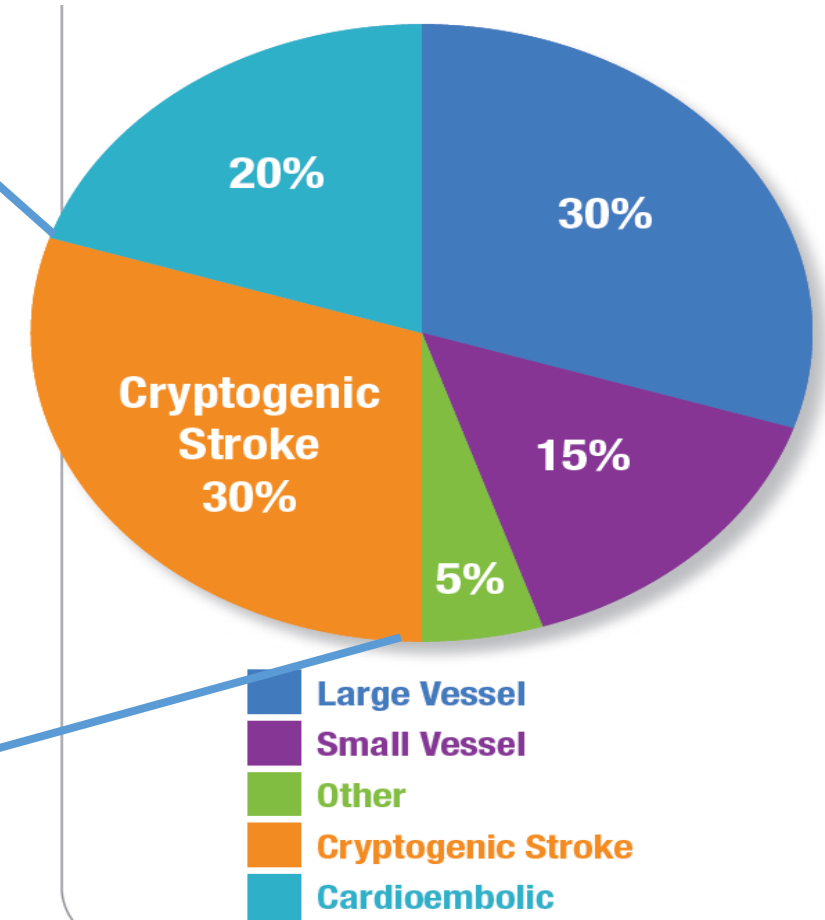
## The “30% Rule”

Prevalence & Subtypes of Ischemic Stroke

AF causes up to 30% of ischemic stroke <sup>1, 2, 3</sup>

Up to 30% of ischemic strokes are cryptogenic <sup>4</sup>

Up to 30% cryptogenic stroke → has previously undetected PAF<sup>5</sup>



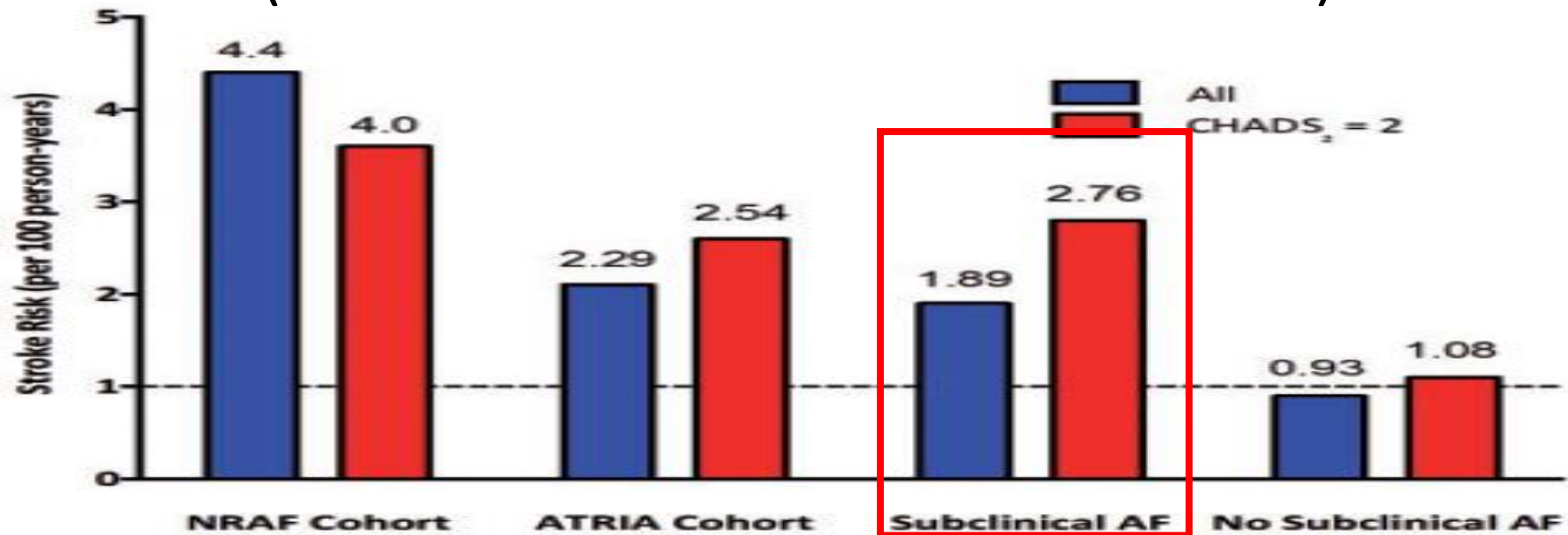
1. Wolf PA et al. Stroke 1991;22:983-988.  
2. Arch Intern Med 1994;154:1449-1457.  
3. Arch Intern Med 1987; 147:1561-1564

5. N Engl J Med. 2014;370:2478-2486  
4. Stroke. 1993;24:35-41

# Why to screen for subclinical AF ?

## Subclinical device-detected atrial fibrillation and stroke risk: a systematic review and meta-analysis

Subclinical AF → ↑ Stroke risk x 2.4  
(Absolute annual risk of stroke 1.89%)



### Subclinical AF and stroke risk



# Why to screen for subclinical AF ?

## CIED-detected new-onset atrial tachyarrhythmia

→ ↑ Risk of thromboembolism x 3

**22,330 Patients**  
28 studies in implantable cardiac device patients with no known history of atrial tachyarrhythmia (AT)  
**23% Incidence of DDAT**  
Developed any device-detected atrial tachyarrhythmia (DDAT) over  $21.8 \pm 18.6$  months

Thromboembolic Event (TE) risk in DDAT patients

**8,181 Patients**  
9 studies reporting TE incidence  
2,023 with new-onset DDAT

**RR 2.88**  
**(1.79-4.64,  $p < 0.001$ )**  
Risk of TE with any DDAT

**RR 3.60**  
**(2.06-6.30,  $p < 0.001$ )**  
Risk of TE with adjudicated DDAT

**RR 2.05**  
**(1.06-3.97,  $p = 0.03$ )**  
Risk of TE with non-  
adjudicated DDAT

TE risk was correlated with DDAT duration:

- DDAT  $\geq 5$ min: RR 3.86 (95% CI 2.04–7.30;  $P < 0.001$ )
- DDAT  $< 1$  min: RR 1.77 (95% CI, 1.15–2.74;  $P = 0.01$ )

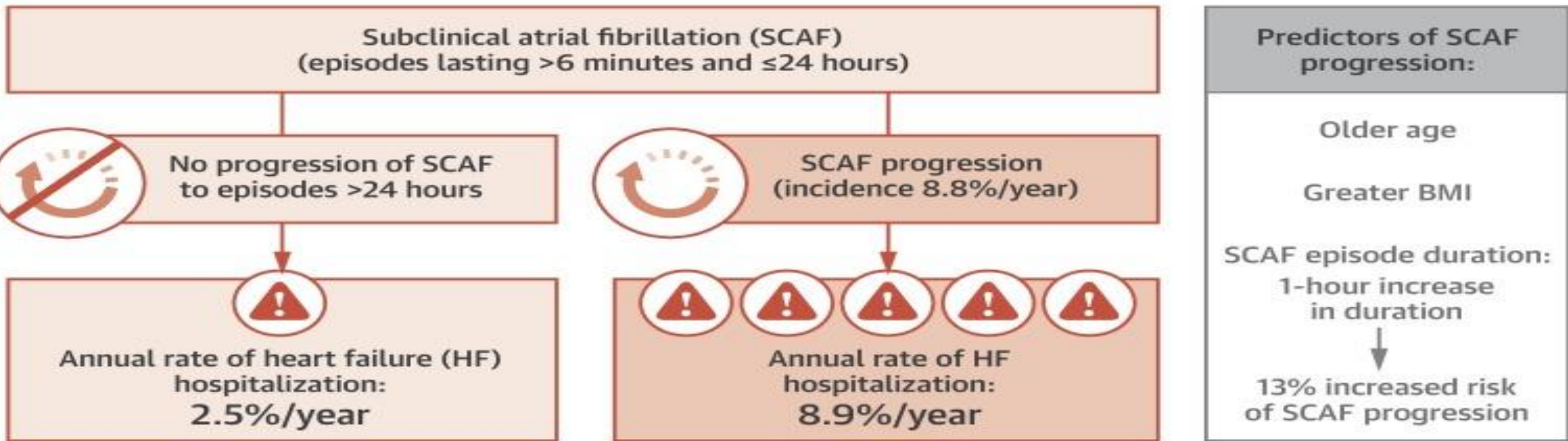
- Absolute incidence of TE: 2.1%
- TE rate was ~ 3 times higher in patients with DDAT



# Why to screen for subclinical AF ?

Subclinical AF progression is associated with increased risk of heart failure

## CENTRAL ILLUSTRATION: Subclinical Atrial Fibrillation Progression and the Risk of Heart Failure Hospitalization



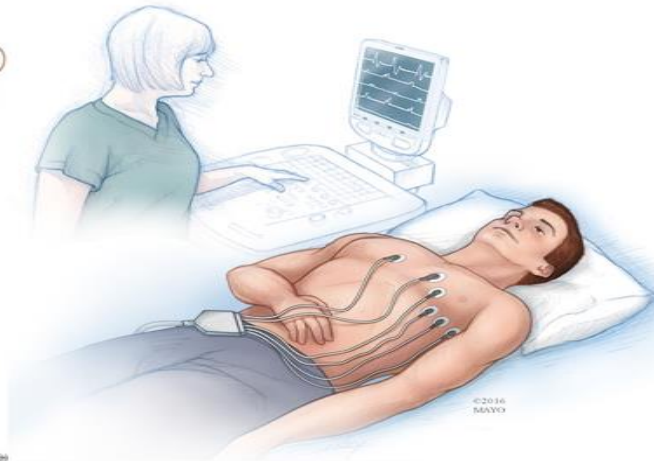
SCAF progression associated with increased risk of HF hospitalization  
[HR: 4.58; 95% CI: 1.64 - 12.8; p = 0.004]

# How to screen for asymptomatic / subclinical AF ?

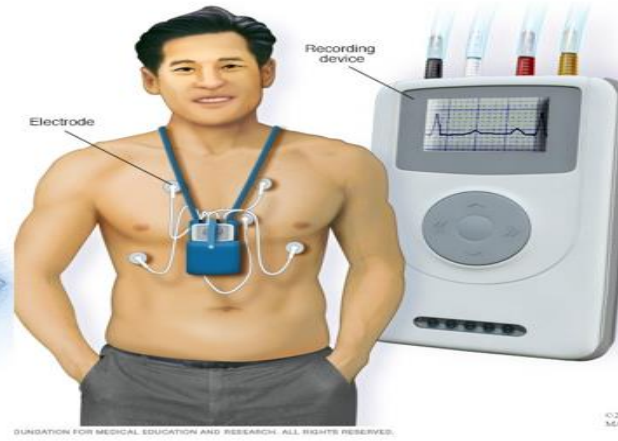
Pulse Check



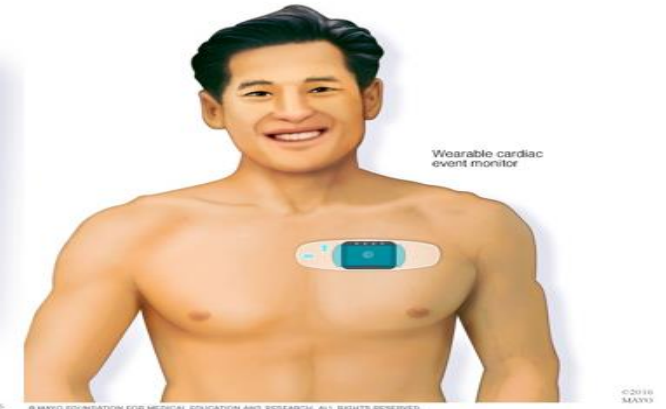
ECG



Holter



Wearable Cardiac Monitor



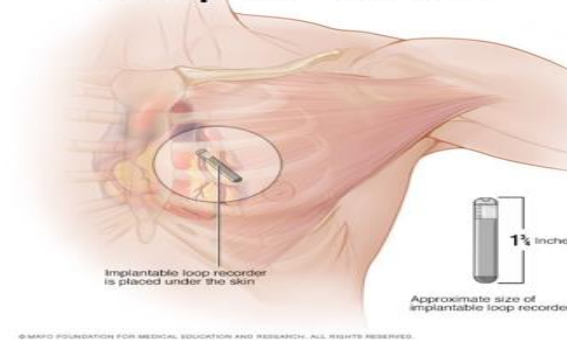
AliveCor Kardia



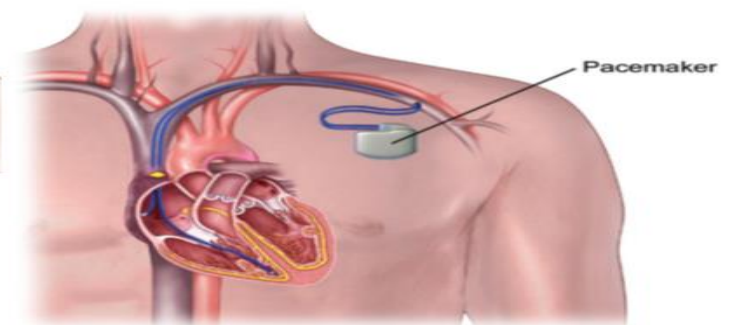
Apple Watch



Implantable Loop Recorder



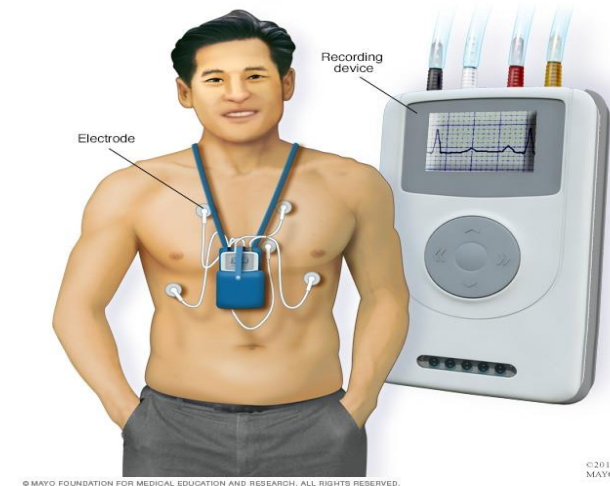
Pacemaker / ICD / CRT



# Incidence of newly-detected AF in cryptogenic stroke by 30-day event recorder Embrace Trial

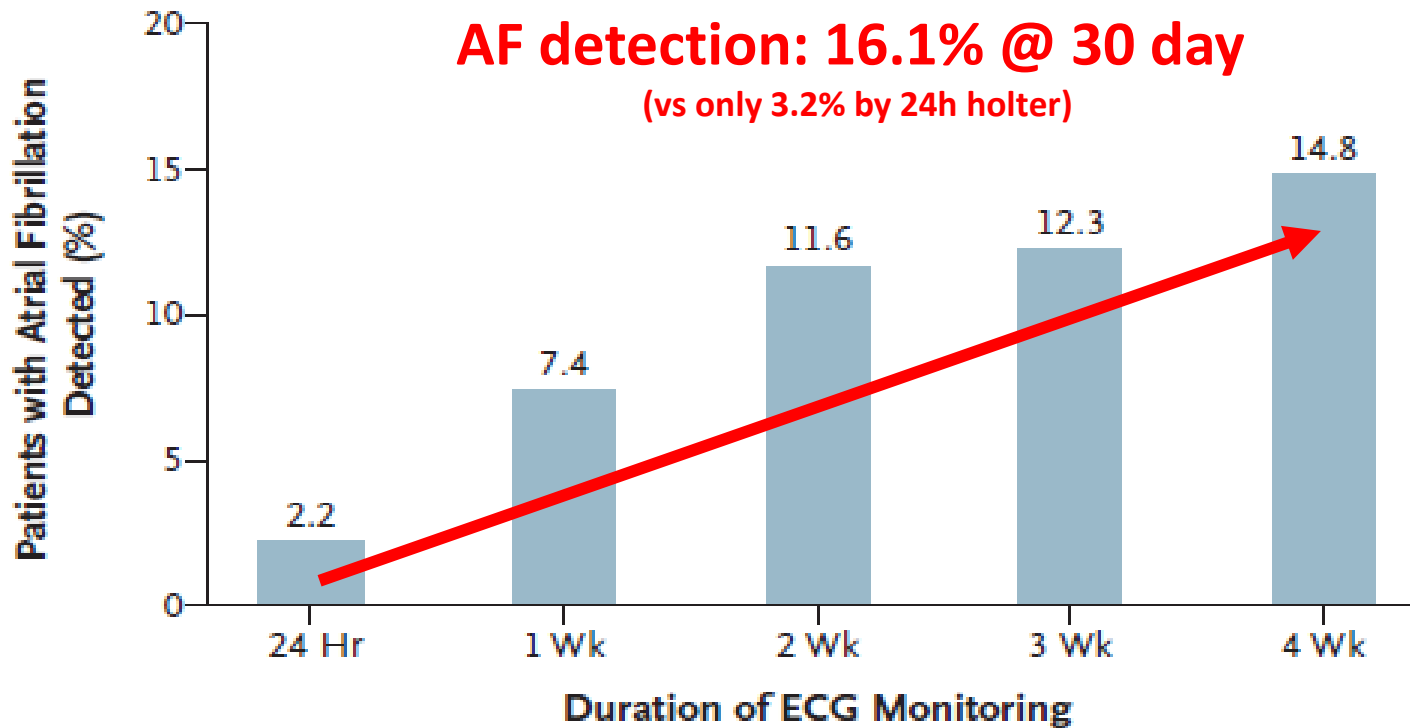
N = 572 Cryptogenic stroke/TIA Patients (in past 6 months).  
Received event recorder for 30d vs 24h.

30d vs 24h Event Recorder



**ER910, 920 AF**

Arrhythmia Event Monitor

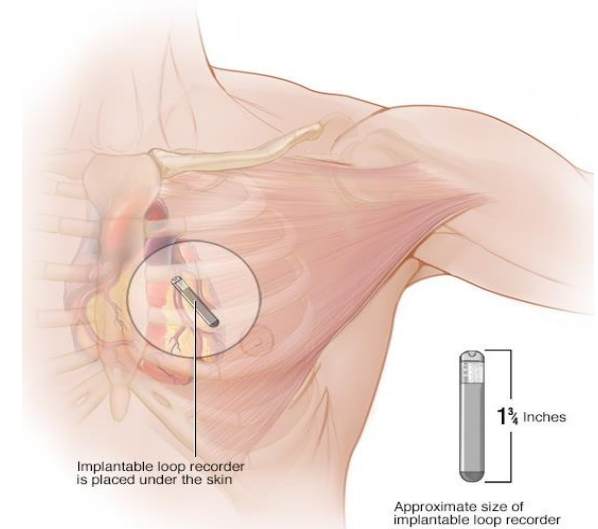
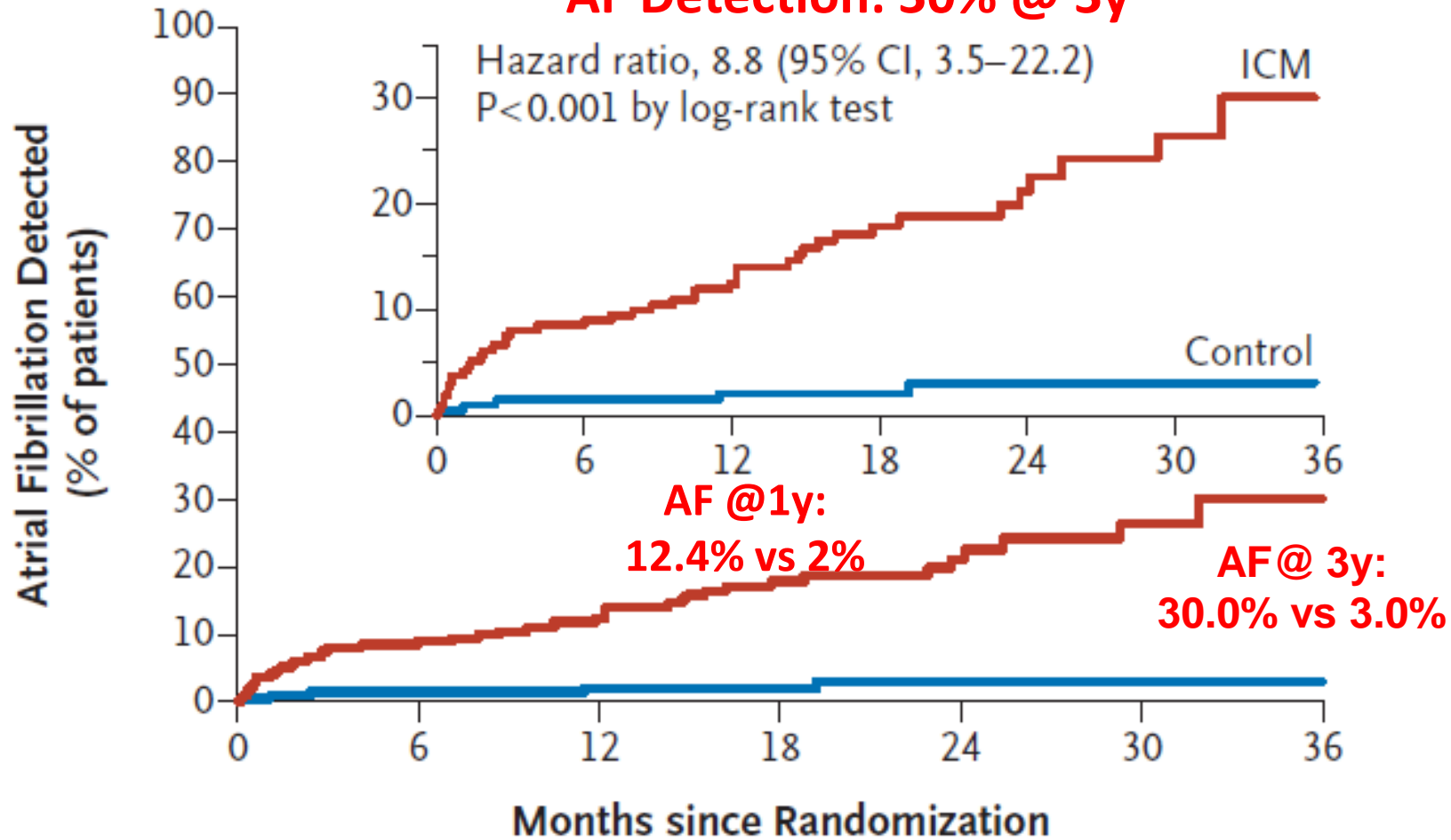


AF ≥30s: 16.1% (30d) vs 3.2% (24h)  
AF ≥ 2.5 minute: 9.9% (30d) vs 2.5%(24h)

# Incidence of newly detected AF in cryptogenic stroke by ILR Crystal AF Trial

N =441 Cryptogenic stroke/ TIA in past 90 days.

**AF Detection: 30% @ 3y**



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ICM = Insertable Cardiac Monitor or Implantable Loop Recorder (ILR)

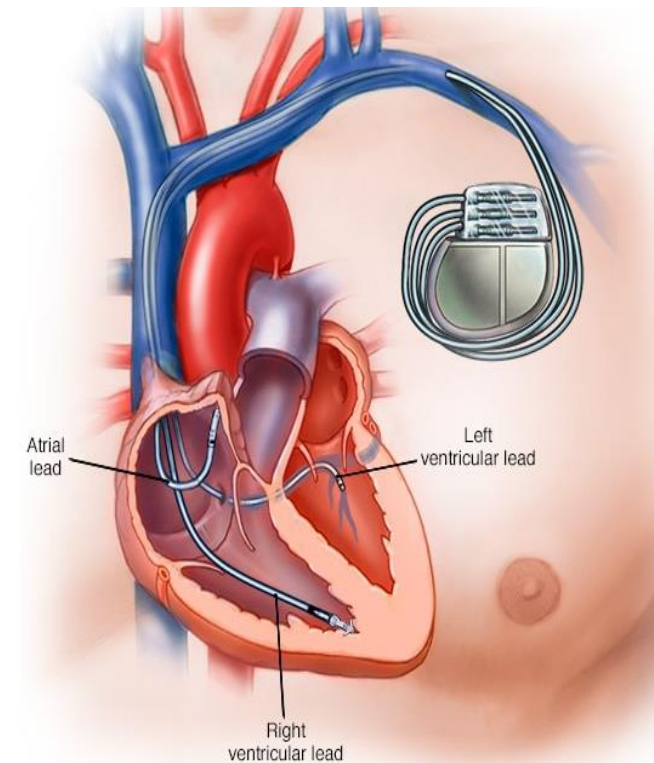
# Incidence of AF detected by cardiac implantable electronic devices (CIED)

CIED detected new-onset AF: 28-35% at ~ 1-2.5 years follow-up

**Table 4** Incidence of atrial fibrillation in the implanted device population

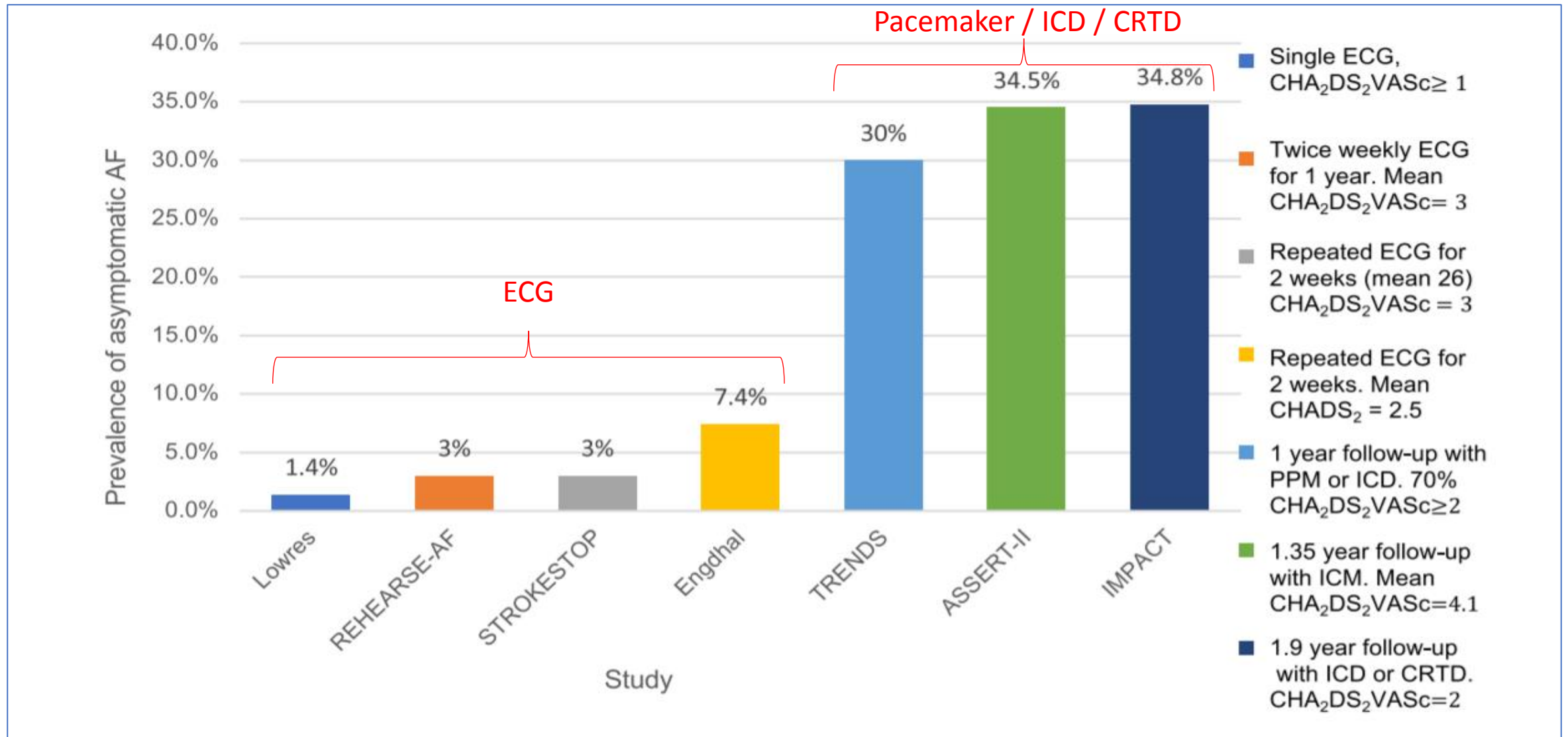
Year	Study	Device Indication	Clinical Profile of Patients	Follow-up	Incidence of AF
2002	Gillis <i>et al.</i> <sup>16</sup>	PPMs for sinus node disease	All	718±383 days	157/231 (68%)
2003	MOST <sup>5</sup>	PPMs for sinus node disease	All	median 27 months	156/312 (50%)
2006	BEATS <sup>21</sup>	PPMs for all indications	All	Prospective, 12 months	137/254 (54%)
2010	TRENDS <sup>17</sup>	PPMs and ICDs All indications	History of prior stroke No history of AF No OAC use ≥1 stroke risk factor	Mean 1.4 years	45/163 (28%)
2012	TRENDS <sup>6</sup>	PPMs and ICDs All indications	No history of prior stroke No history of AF No OAC use ≥1 stroke risk factor	1.1±0.7 years	416/1368 (30%)
2012	ASSERT <sup>7</sup>	PPMs and ICDs All indications	History of hypertension No history of AF No OAC use	2.5 years	895/2580 (34.7%)
2013	Healey <i>et al.</i> <sup>4</sup>	PPMs All indications	All	Single center retrospective	246/445 (55.3%)

AF, atrial fibrillation; ICD, implantable cardioverter-defibrillator; OAC, oral anticoagulation; PPM, permanent pacemaker; ASSERT, ASymptomatic atrial fibrillation and Stroke Evaluation in pacemaker patients and atrial fibrillation Reduction atrial pacing Trial; BEATS, Balanced Evaluation of Atrial Tachyarrhythmias in Stimulated patients; MOST, MODE Selection Trial; TRENDS, The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke.



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# Prevalence of asymptomatic AF by screening method and stroke risk score



# Incidence of AF detected by mobile device in general population

Large scale assessment of a Smartwatch to identify AF

## Apple Watch - Apple Heart Study

N = 419,297 FU 8 months (median of 117 days)

Irregular Pulse notification: **0.52%** (N = 2161)

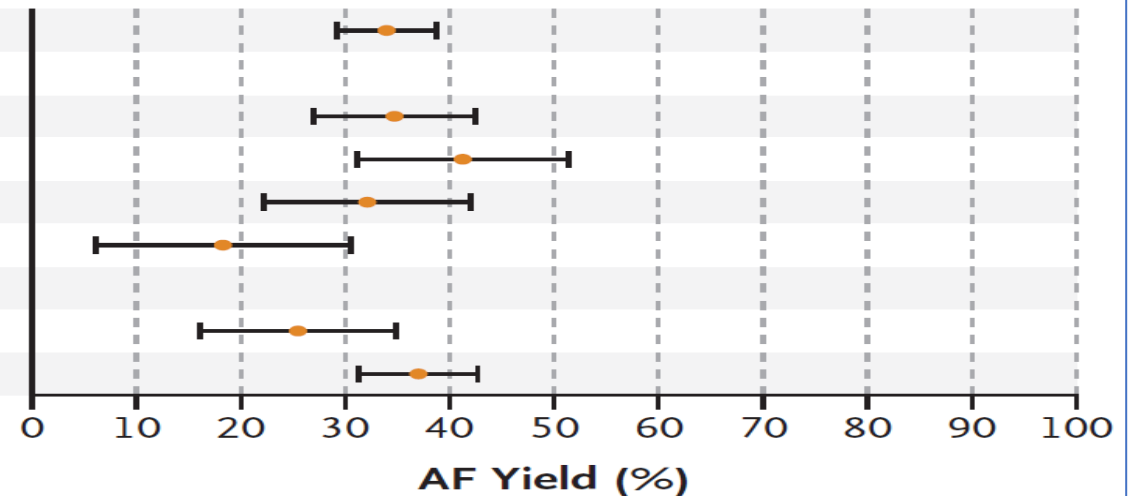
Among 450 participants with ECG patches (7d) recording:

**AF present in 34%** ( Positive predictive value 0.84 )



**Subgroup**      **No. of Patients with AF/Total No. (%)**

Overall	153/450 (34)
<b>Age</b>	
≥65 yr	63/181 (35)
55–64 yr	47/114 (41)
40–54 yr	34/106 (32)
22–39 yr	9/49 (18)
<b>Sex</b>	
Female	26/102 (25)
Male	124/335 (37)

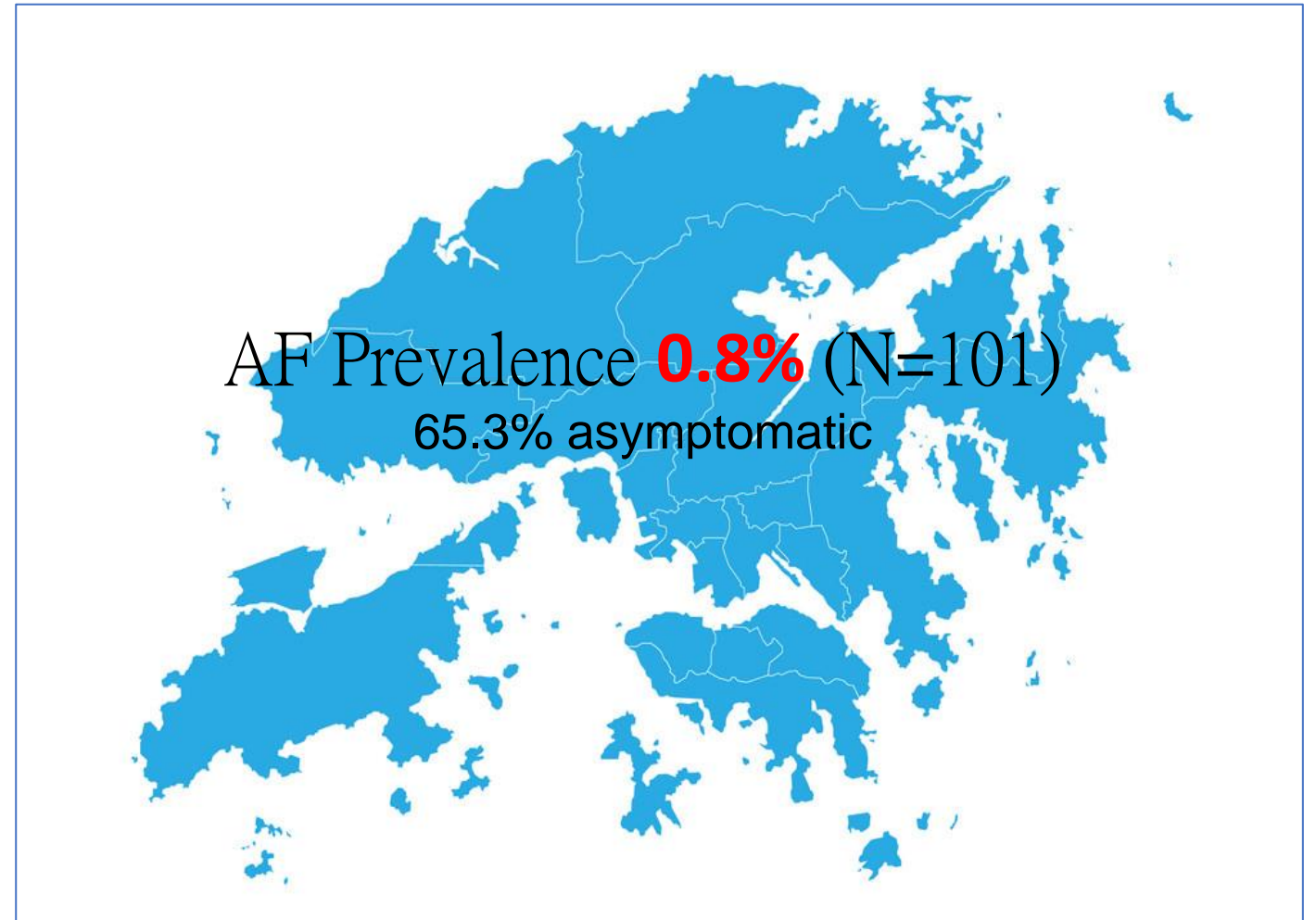




# Incidence of AF detected by mobile device in general population

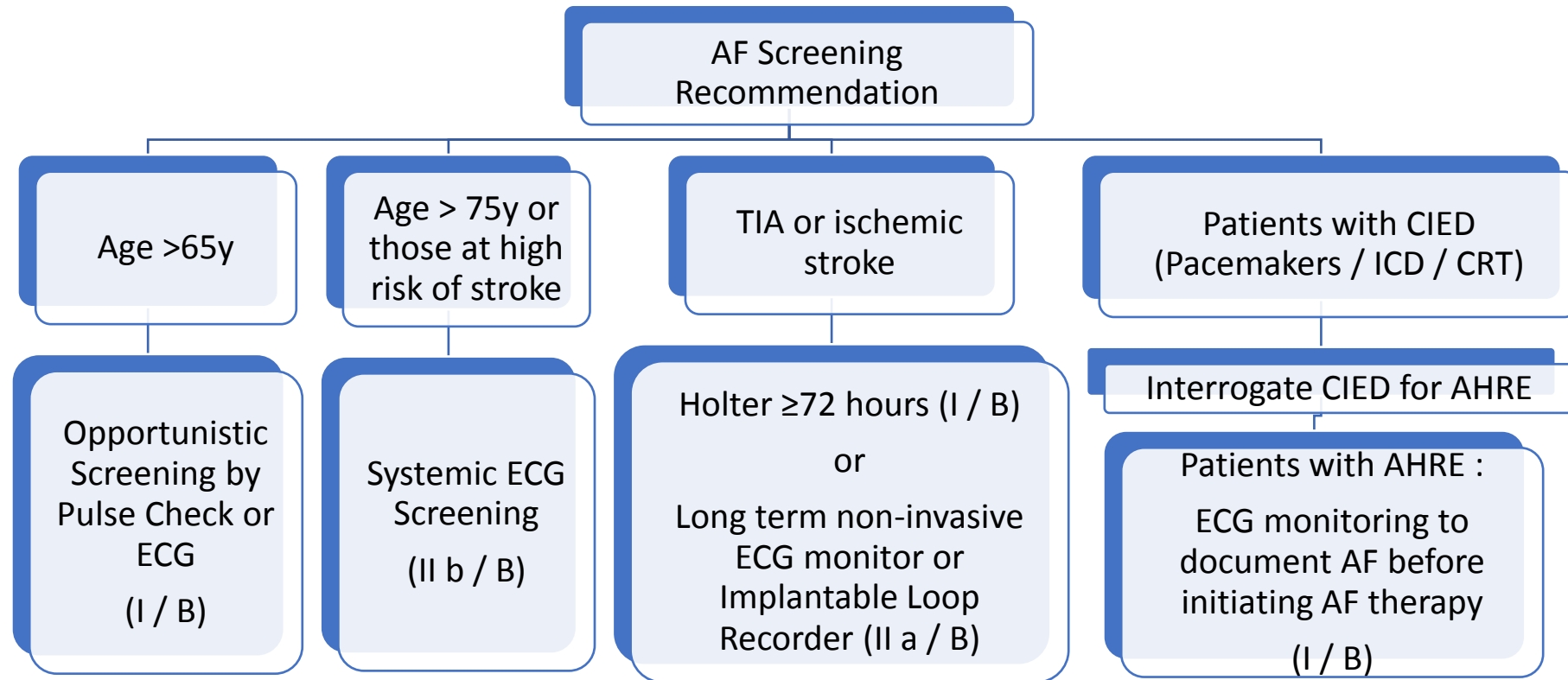
## Screening for atrial fibrillation by AliveCor in 13,122 Hong Kong citizens with smartphone electrocardiogram

AliveCor Kardia



# Subclinical AF - Who to screen? AF Screening General Recommendation

## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS



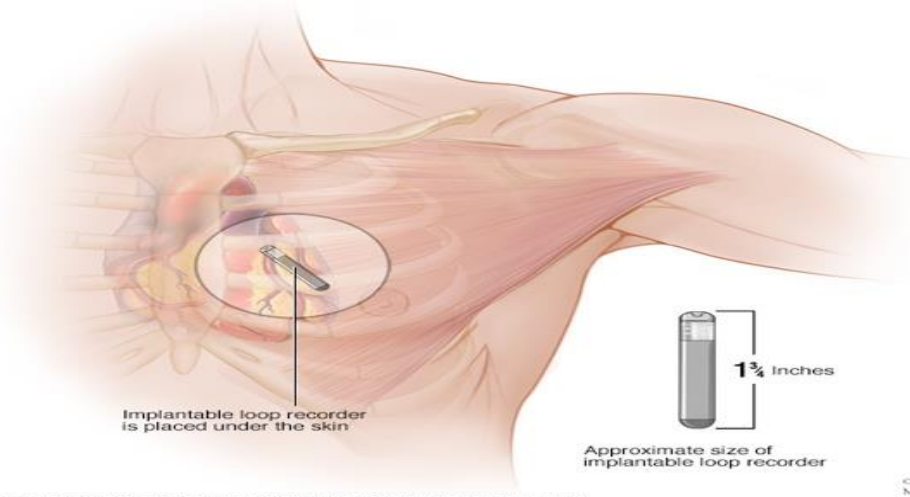
CIED = Cardiac Implantable Electronic Devices  
AHRE = Atrial High Rate Episodes

# AF screening for patients with ischemic / cryptogenic stroke

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

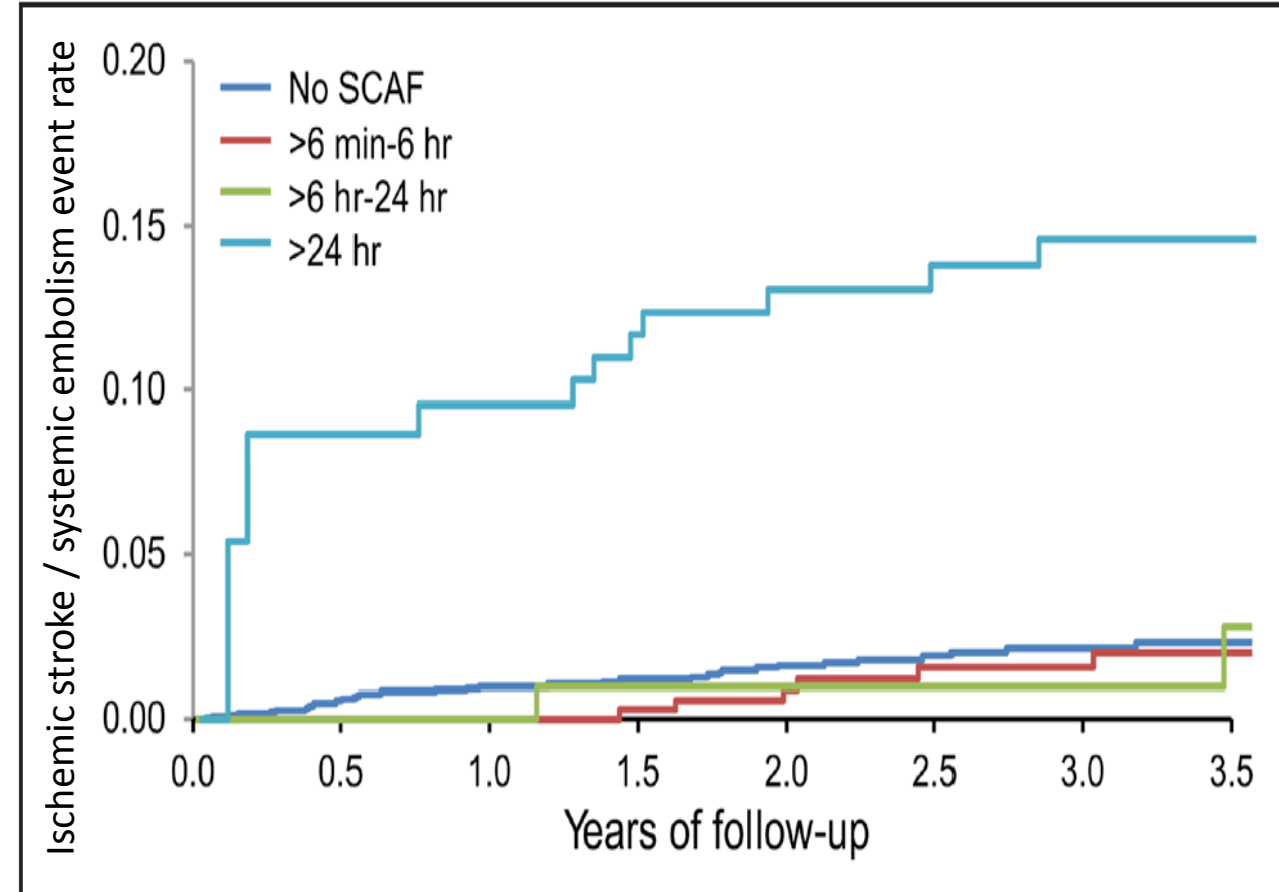
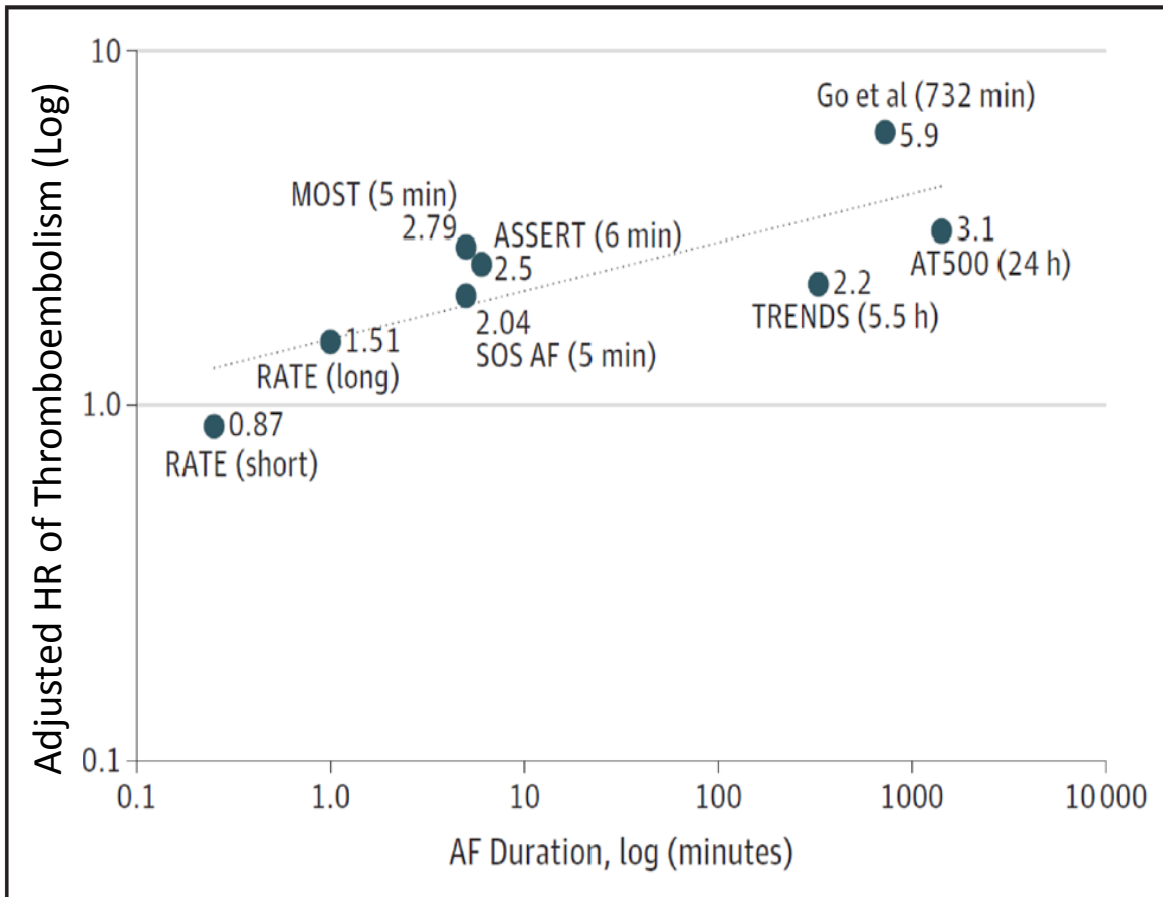
### Recommendations for Device Detection of AF and Atrial Flutter

COR	LOE	Recommendations
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 ( <b>loop recorder</b> ) is reasonable to optimize detection of silent AF.



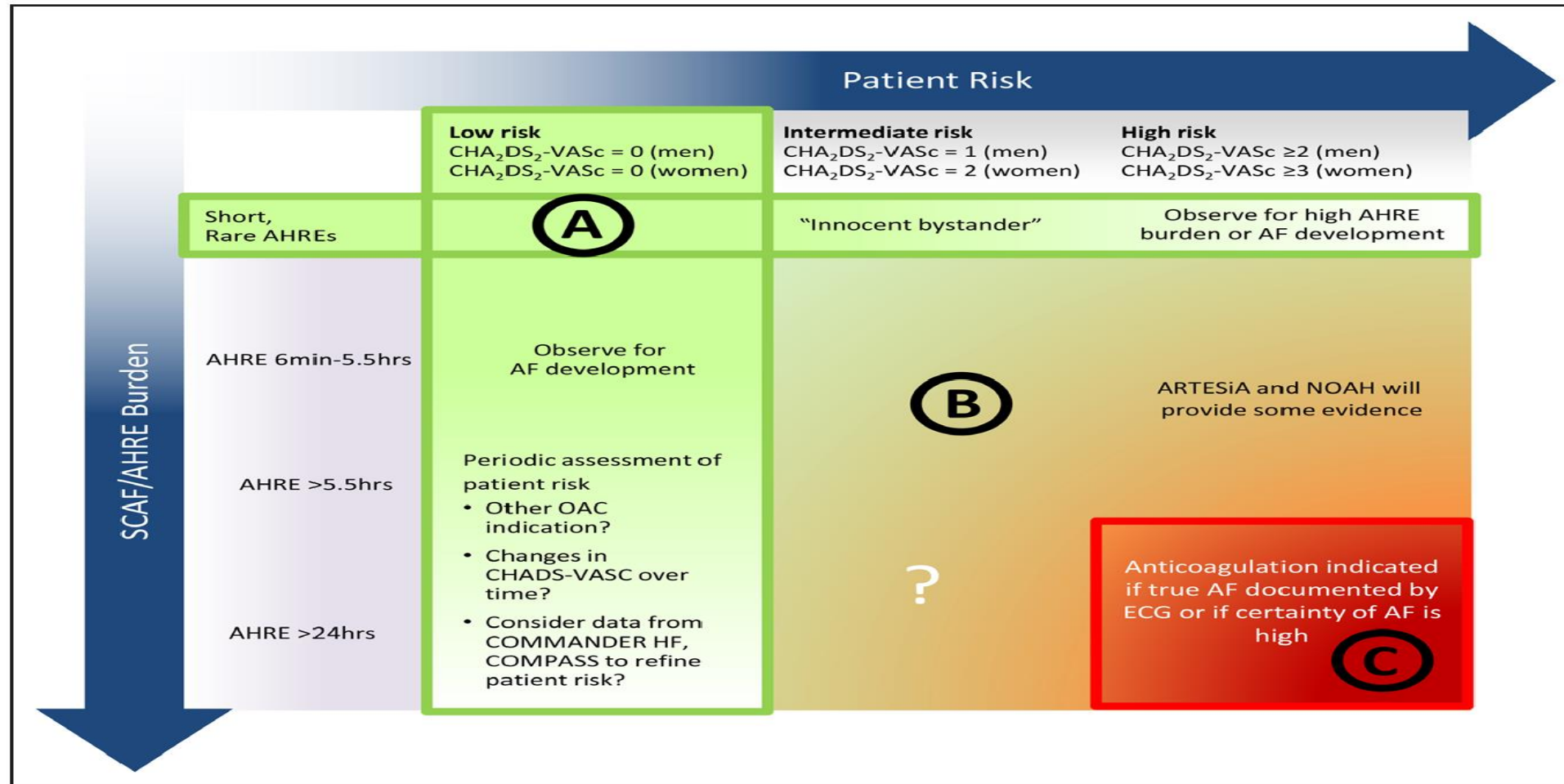
# When to treat subclinical AF ?

Longer duration of CIED-detected subclinical AF is associated with higher risk of stroke / thromboembolic event



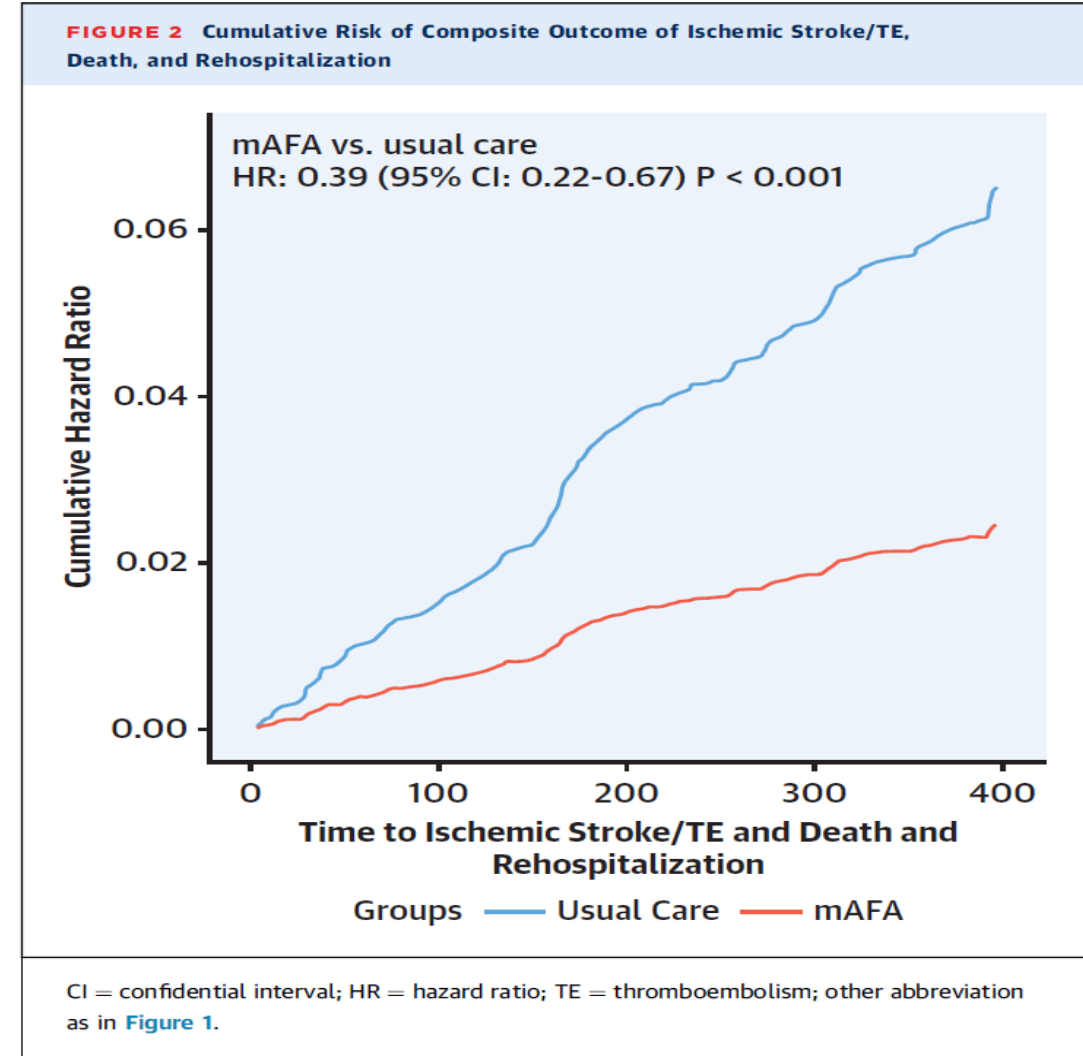
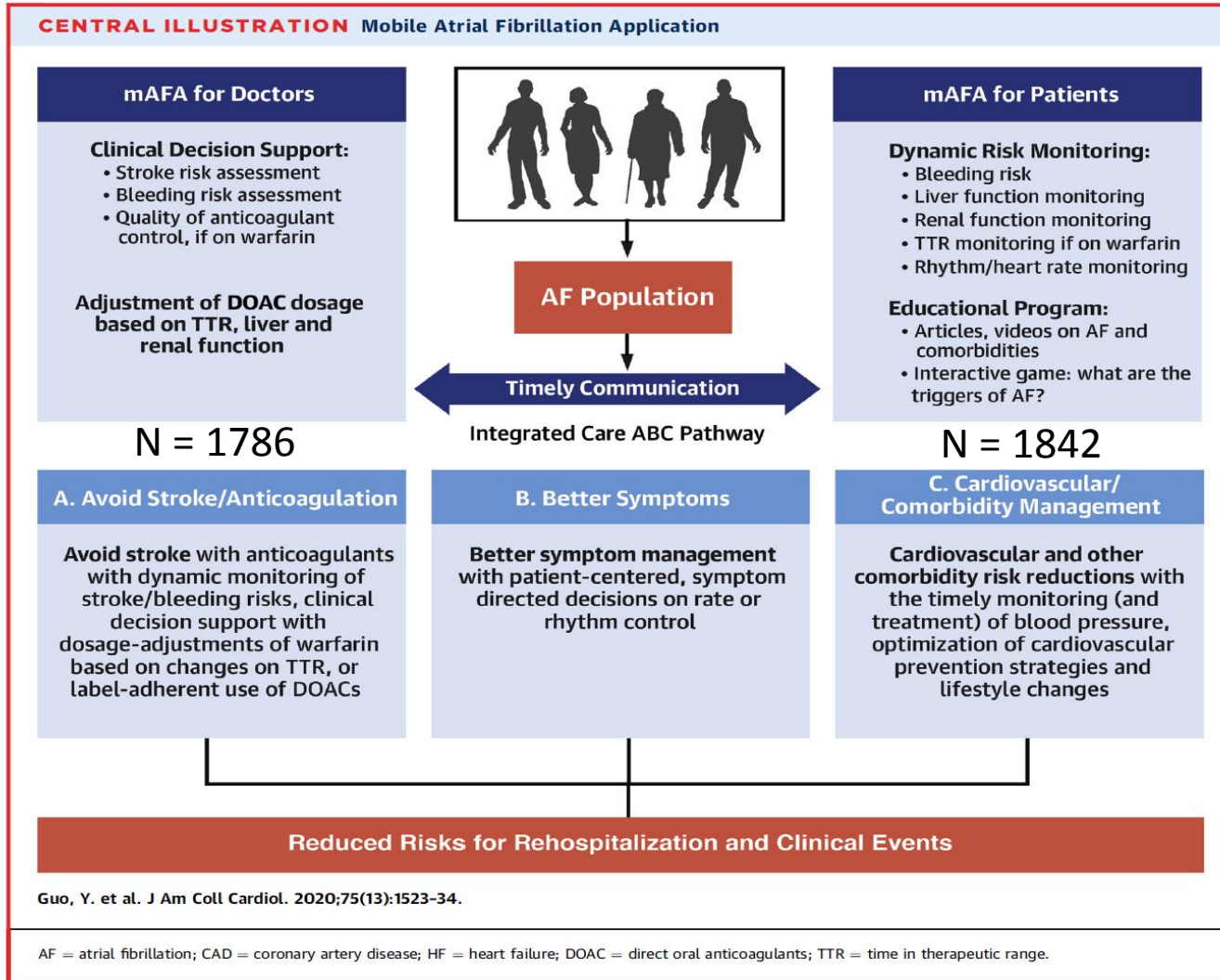
# Subclinical and Device-Detected Atrial Fibrillation: Pondering the Knowledge Gap

A Scientific Statement From the American Heart Association



# Mobile Health Technology to Improve Care for Patients With Atrial Fibrillation

Mobile AF application (mAFA) integrated AF management ↓ ischemic stroke / thromboembolism, death & rehospitalization



# Take Home Messages (1)

- AF ↑ Death x2, ↑CHF x 3, ↑ Stroke x 5
- 30% of ischemic strokes & cryptogenic stroke are associated with AF
- Anticoagulation ↓ stroke by 60-70%
- AF acute management: rate/rhythm control, cardioversion
- AF chronic management: risk factors control, upstream management, rate/rhythm control, anticoagulation, treatment of underlying cause
- Symptomatic AF patients who are drug intolerant, drug refractory or who are unwilling to take drugs
  - AF Ablation
    - ↓ AF symptom
    - ↓ Mortality & CHF hospitalization (esp in CHF patients)

# Take Home Messages (2)

- Up to 90% AF are asymptomatic / subclinical
- Subclinical AF → ↑ risk of stroke x 2-3 times
- AF symptom and subtype should not be used to guide decision on anticoagulation
- Patients ≥ 65y or with history of TIA / ischemic stroke should receive AF screening
- Anticoagulation is recommended for patients with subclinical AF duration >5.5 - 24 hours with ↑ stroke risk , & should be considered for patients with subclinical AF duration > 6 min with ↑ stroke risk
- Benefit of anticoagulation in subclinical AF should be balanced against the risk of bleeding
- Mobile technology could help early AF detection & optimization of AF management