
BRIGHAM HEALTH
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Atrial Fibrillation Management:
Update for 2025
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BRIGHAM HEALTH
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- Stanford University School of Medicine (MD/PhD)
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  - Clinical focus – Electrophysiology, Atrial Fibrillation
  - Research focus – Atrial fibrillation, innovations in catheter ablation, non-invasive ablation

# Disclosures

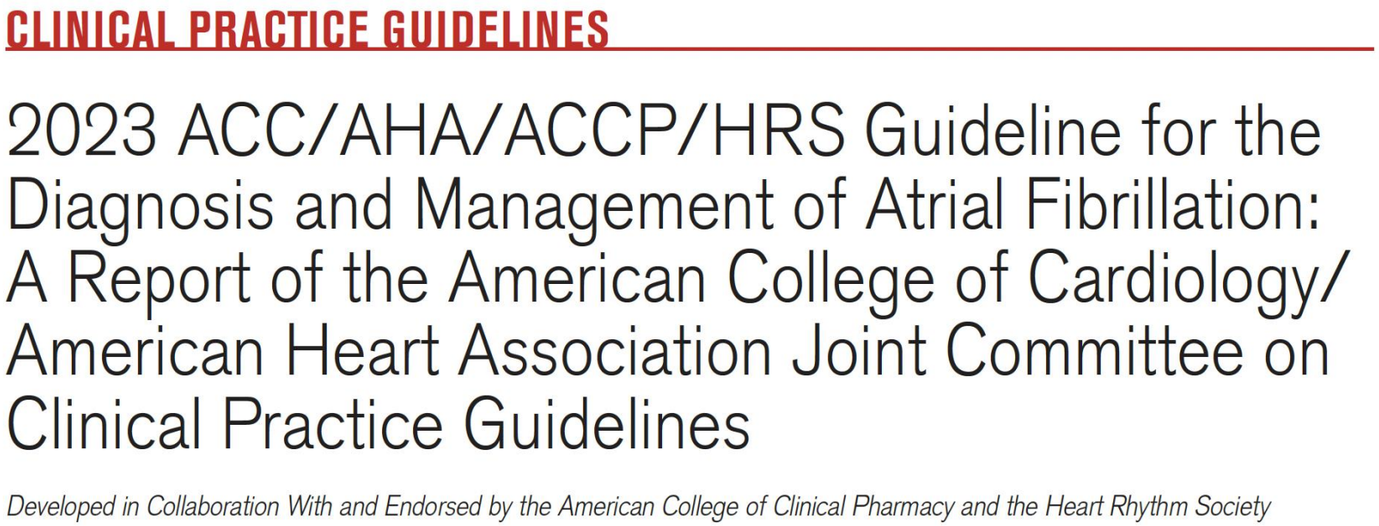


- Biosense Webster, Inc.
  - Research support
  - Scientific Advisory Board
- St Jude Medical/Abbott
  - Consulting
- Varian
  - Research support
  - Scientific Advisory Board
- Medtronic/Affera
  - Consulting
- Volta Medical
  - Consulting
- HRCRS
  - Medical Consultant

# Learning Objectives



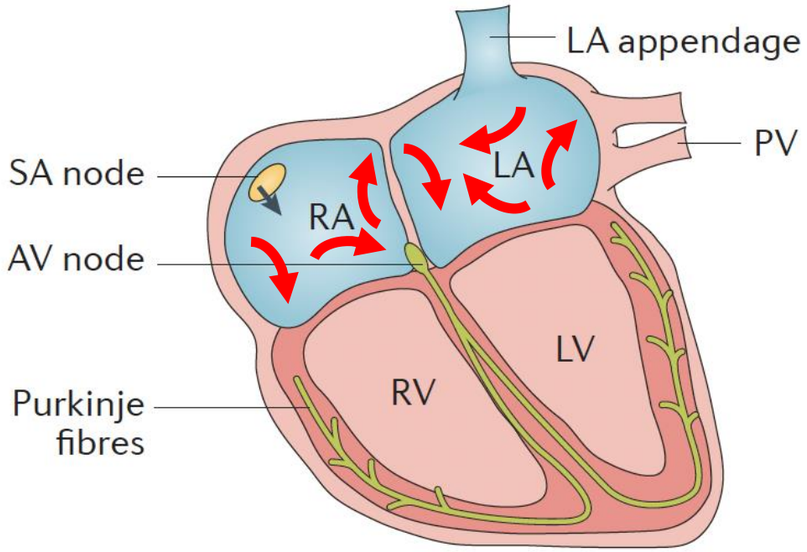
- Understand the current indications, options, risks, and benefits of stroke prevention for atrial fibrillation
- Understand the current indications for medical therapy vs. catheter ablation for the control of rhythm in atrial fibrillation
- Understand the impact of risk factors and risk factor modification on atrial fibrillation clinical outcomes



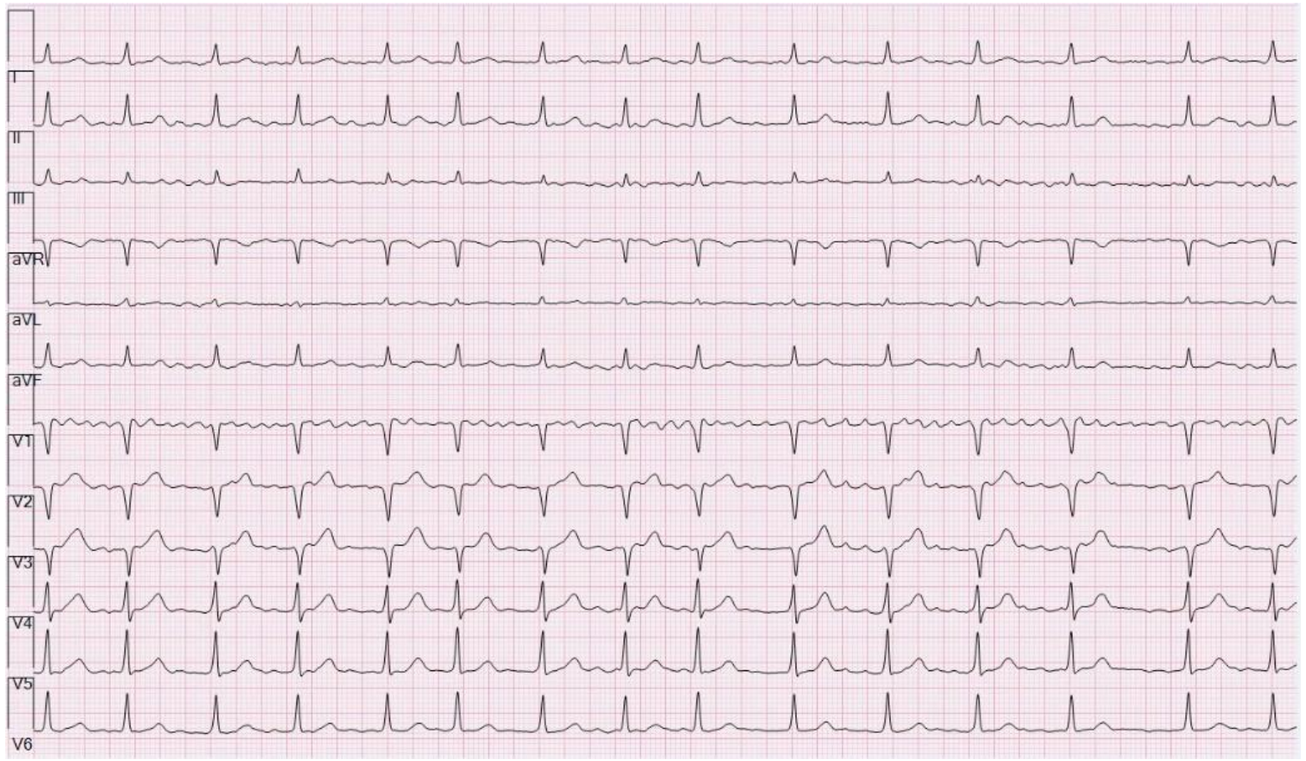
# Atrial Fibrillation



- Rapid irregular electrical activation in the atria
- Irregular rapid (usually) ventricular response




Atrial Fibrillation



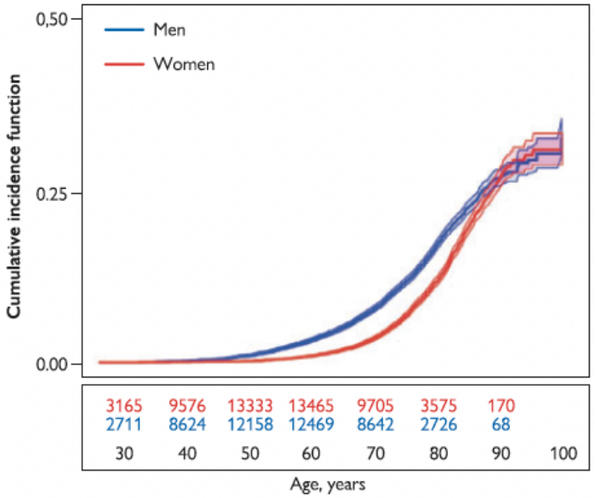

*Adapted from Lip et al Nature, 2016*

# AF: Now the Most Prevalent Arrhythmia Worldwide

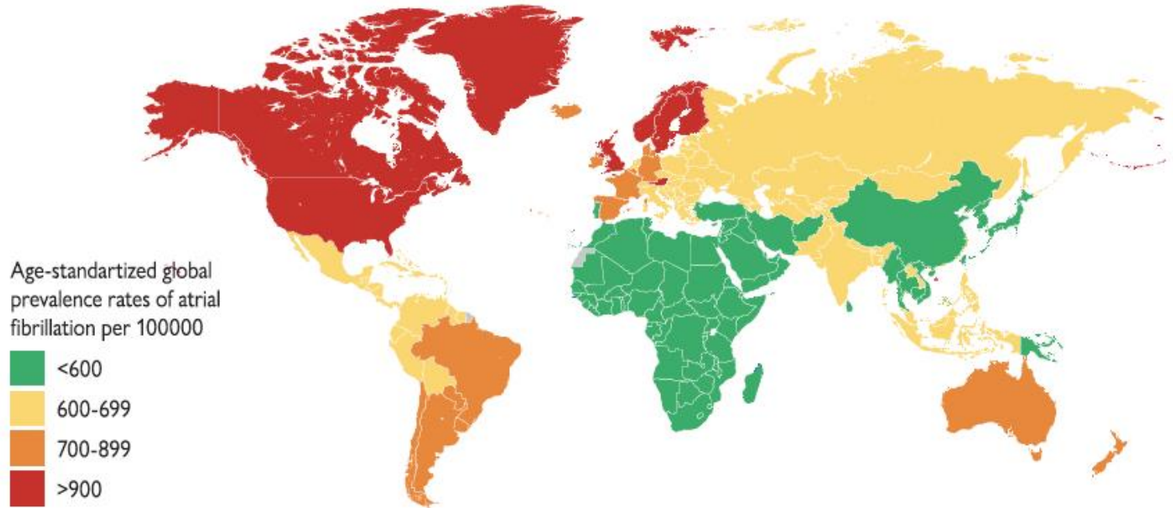
**LIFETIME RISK for AF**
**1 in 3 individuals**

of European ancestry
at index age of 55 years
37.0% (34.3% to 39.6%)

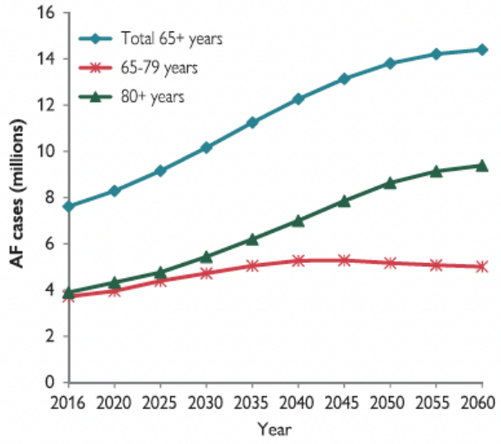
**AF is more common in males**
Cumulative incidence curves and 95% CIs
for AF in women and men with death as a competing risk



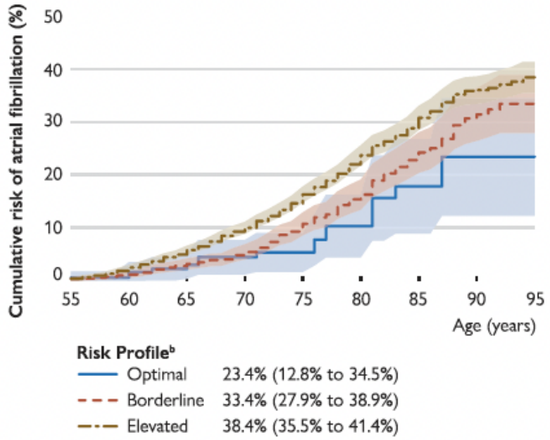

**GLOBAL PREVALENCE OF AF**
(globally, 43.6 million individuals had prevalent AF/AFL in 2016)




**Projected increase in AF prevalence among elderly in EU 2016-2060**




**Lifetime risk of AF increases with increasing risk factor burden[a]**

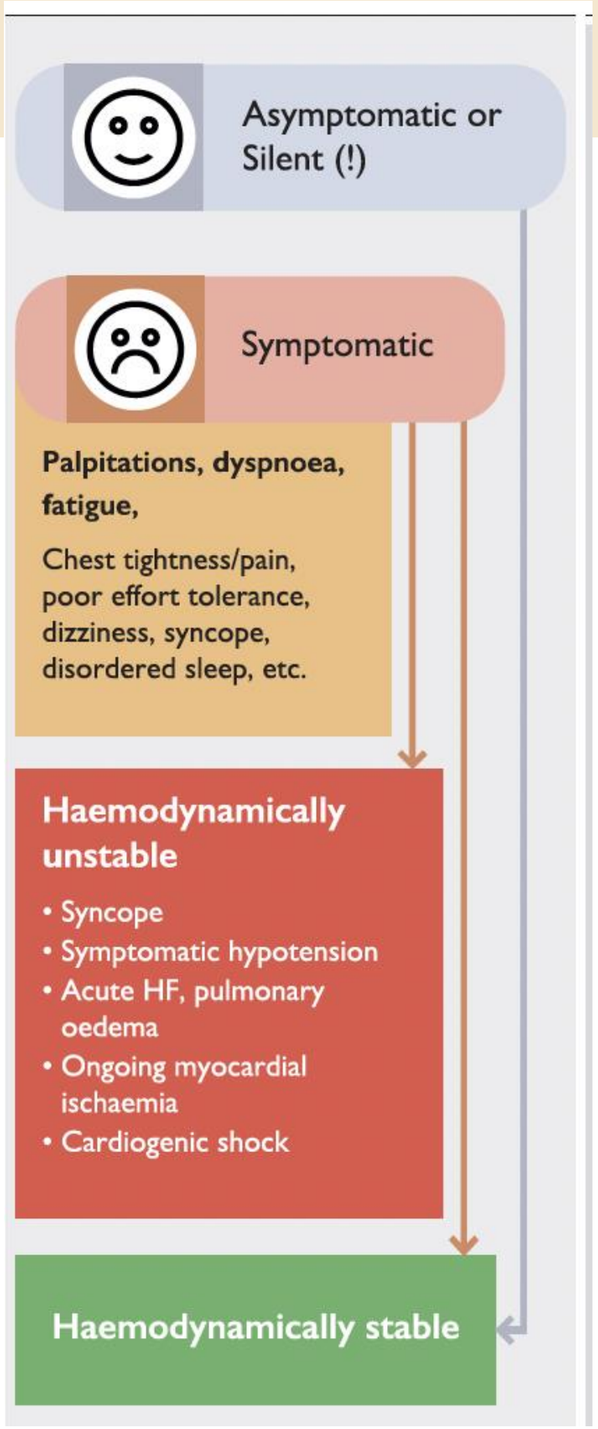



- Higher prevalence in developed countries
- More common with aging, male gender
- Unclear if this is due to diagnosis bias vs. biological underpinnings

*ESC Guidelines 2020*

# Clinical Manifestations and Presentation Vary Significantly

- Reasons for patient-to-patient variation unclear
- Severity of symptoms and impact on quality of life are important factors in decision on rhythm control management
- Conundrum: the asymptomatic patient
  - When is rhythm control indicated?
  - Who should be screened?
  - Concerns for initial presentation as stroke (without other warning signs)




*ESC Guidelines 2020*

# Atrial Fibrillation: Clinical Manifestations



## Major CV Outcomes

| AF-Related Outcome | Frequency in AF | Mechanism(s) |
|---|---|---|
| Death  | 1.5 - 3.5 fold increase | Excess mortality related to:<br>• HF, comorbidities<br>• Stroke |
| Stroke  | 20-30% of all ischaemic strokes, 10% of cryptogenic strokes | • Cardioembolic, or<br>• Related to comorbid vascular atheroma |
| LV dysfunction / Heart failure  | In 20-30% of AF patients | • Excessive ventricular rate<br>• Irregular ventricular contractions<br>• A primary underlying cause of AF |

*ESC Guidelines 2020*

## Additional Manifestations

| AF-Related Outcome | Frequency in AF | Mechanism(s) |
|---|---|---|
| Cognitive decline / Vascular dementia  | HR 1.4 / 1.6 (irrespective of stroke history) | • Brain white matter lesions, inflammation,<br>• Hypoperfusion,<br>• Micro-embolism |
| Depression  | Depression in 16-20% (even suicidal ideation) | • Severe symptoms and decreased QoL<br>• Drug side effects |
| Impaired quality of life  | >60% of patients | • Related to AF burden, comorbidities, psychological functioning and medication<br>• Distressed personality type |
| Hospitalizations  | 10-40% annual hospitalization rate | • AF management, related to HF, MI or AF related symptoms<br>• Treatment-associated complications |

# Atrial Fibrillation: Detection and Confirmation

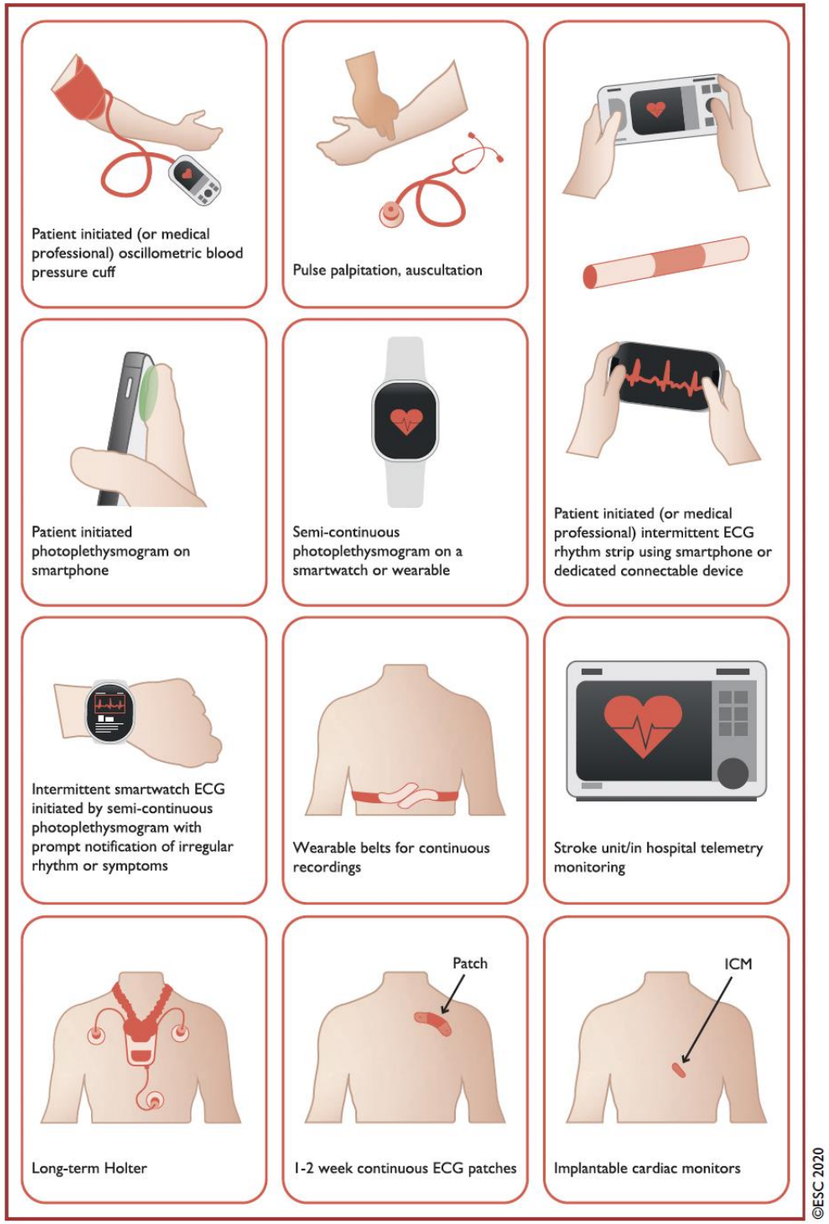
- Pulse measurements – irregular pulse
- ECG detection – in office vs. mobile

**Table 5** Sensitivity and specificity of various AF screening tools considering the 12-lead ECG as the gold standard[173]

| | Sensitivity | Specificity |
|---|---|---|
| **Pulse taking**[203] | 87 - 97% | 70 - 81% |
| **Automated BP monitors**[204–207] | 93 - 100% | 86 - 92% |
| **Single lead ECG**[208–211] | 94 - 98% | 76 - 95% |
| **Smartphone apps**[188,189,191,195,212,213] | 91.5 - 98.5% | 91.4 - 100% |
| **Watches**[196,198,213,214] | 97 - 99% | 83 - 94% |

AF = atrial fibrillation; BP = blood pressure; ECG = electrocardiogram.






*ESC Guidelines 2020*

# CHARGE-AF Score System:
# Predicting incidental atrial fibrillation from the general population:

## Simple Risk Model Predicts Incidenc… and Geographically Diverse Populat…

Alvaro Alonso, MD, PhD;* Bouwe P. Krijthe, MSc;* Thor Aspelund, PhD; Carlee B. Moser, MA; Moritz F. Sinner, MD, MPH; Nona Sotoodehnia, Richard A. Kronmal, PhD; Jared W. Magnani, MD; Jacqueline C. Wittema… Renate B. Schnabel, MD, MSc; Sunil K. Agarwal, MD, PhD; David D. M… Gregory L. Burke, MD, MSc; Lenore J. Launer, PhD; Albert Hofman, MD… Stefan Kääb, MD, PhD; David Couper, PhD; Tamara B. Harris, MD, MS… Bruno H. C. Stricker, MB, PhD; Vilmundur Gudnason, MD, PhD; Susan…

**Table 6. CHARGE-AF Risk Score for Detecting Incident AF***

| Variable (X) | Estimated β Coefficient (SE) | HR (95% CI) |
|---|---|---|
| Age (per 5-y increment) | 0.508 (0.022) | 1.66 (1.59-1.74) |
| White race | 0.465 (0.093) | 1.59 (1.33-1.91) |
| Height (per 10-cm increment) | 0.248 (0.036) | 1.28 (1.19-1.38) |
| Weight (per 15-kg increment) | 0.115 (0.033) | 1.12 (1.05-1.20) |
| Systolic BP (per 20-mm Hg increment) | 0.197 (0.033) | 1.22 (1.14-1.30) |
| Diastolic BP (per 10-mm Hg increment) | −0.101 (0.032) | 0.90 (0.85-0.96) |
| Smoking (current versus former/never) | 0.359 (0.063) | 1.42 (1.25-1.60) |
| Diabetes (yes) | 0.237 (0.073) | 1.27 (1.64-2.48) |
| Myocardial infarction (yes) | 0.496 (0.089) | 1.64 (1.38-1.96) |

- *Data from 3 large US cohorts (A… in Communities [ARIC], the Ca… Study [CHS], and the Framingh… [FHS]*
- *18,556 pts 46-94 y.o. pooled to… models for AF using clinical var…*
- *Model validation was performe… the Age, Gene and Environmen… (AGES) and the Rotterdam Stud… (RS)*

…AF Derived in ARIC, CHS, and FHS*

| | | | Augmented Model | |
|---|---|---|---|---|
| | | HR (95% CI) | Estimated β (SE) | HR (95% CI) |
| | | 1.66 (1.59, 1.74) | 0.501 (0.022) | 1.65 (1.58, 1.72) |
| | | 1.59 (1.33, 1.91) | 0.486 (0.094) | 1.63 (1.35, 1.95) |
| | | 1.28 (1.19, 1.38) | 0.243 (0.037) | 1.28 (1.19, 1.37) |
| | | 1.12 (1.05, 1.20) | 0.121 (0.033) | 1.13 (1.06, 1.20) |
| | | 1.22 (1.14, 1.30) | 0.186 (0.033) | 1.20 (1.13, 1.29) |
| | | 0.90 (0.85, 0.96) | −0.098 (0.032) | 0.91 (0.85, 0.97) |
| | | 1.43 (1.20, 1.71) | 0.365 (0.091) | 1.44 (1.20, 1.72) |
| | | 1.42 (1.25, 1.60) | 0.341 (0.063) | 1.41 (1.24, 1.59) |
| | | 1.27 (1.10, 1.46) | 0.242 (0.073) | 1.27 (1.10, 1.47) |
| | | 2.02 (1.64, 2.48) | 0.678 (0.107) | 1.97 (1.60, 2.43) |
| Myocardial infarction (Yes) | 0.496 (0.089) | 1.64 (1.38, 1.96) | 0.469 (0.090) | 1.60 (1.34, 1.91) |
| LVH by electrocardiogram (Yes) | — | — | 0.401 (0.129) | 1.49 (1.16, 1.92) |
| PR Interval (<120 vs 120 to 199) | — | — | 0.645 (0.200) | 1.91 (1.29, 2.82) |
| PR Interval (>199 vs 120 to 199) | — | — | 0.118 (0.077) | 1.13 (0.97, 1.31) |

*Alonso et al, J Am Heart Assoc. 2013*

# $C_2$HEST Score System
# Predicting incidental atrial fibrillation from the general population:

## A Simple Clinical Risk Score ($C_2$HEST) for Predicting Incident Atrial Fibrillation in Asian Subjects

### Derivation in 471,446 Chinese Subjects, With Internal Validation and External Application in 451,199 Korean Subjects

*Yan-Guang Li, MD, PhD; Daniele Pastori, MD, PhD; Alessio Farcomeni, PhD; Pil-Sung Yang, MD; Eunsun Jang, MD; Boyoung Joung, MD, PhD; Yu-Tang Wang, MD, PhD; Yu-Tao Guo, MD, PhD; and Gregory Y. H. Lip, MD*

Check for updates

**TABLE 4** ] Annual Incidence of AF by $C_2$HEST Score

| Score | No. of Subjects | No. of Incidents of AF | Incidence of AF[a] | Hazard Ratio | 95% CI |
|---|---|---|---|---|---|
| 0 | 310,117 | 246 | 0.18 | 1.00 | ... |
| 1 | 88,825 | 378 | 0.82 | 4.31 | 3.67-5.06 |
| 2 | 19,270 | 148 | 2.31 | 12.8 | 10.4-15.6 |
| 3 | 8,253 | 68 | 3.73 | 22.6 | 17.2-29.6 |
| 4 | 1,373 | 68 | 16.1 | 97.0 | 74.1-127.0 |
| 5 | 90 | 6 | 28.7 | 187.4 | 83.3-421.6 |
| ≥ 6 | 45 | 7 | 59.8 | 332.0 | 156.6-704.0 |

See Table 1 legend for expansion of abbreviation.
[a]Per 1,000 person-years.

**TABLE 3** ] $C_2$HEST Score for Incident Atrial Fibrillation

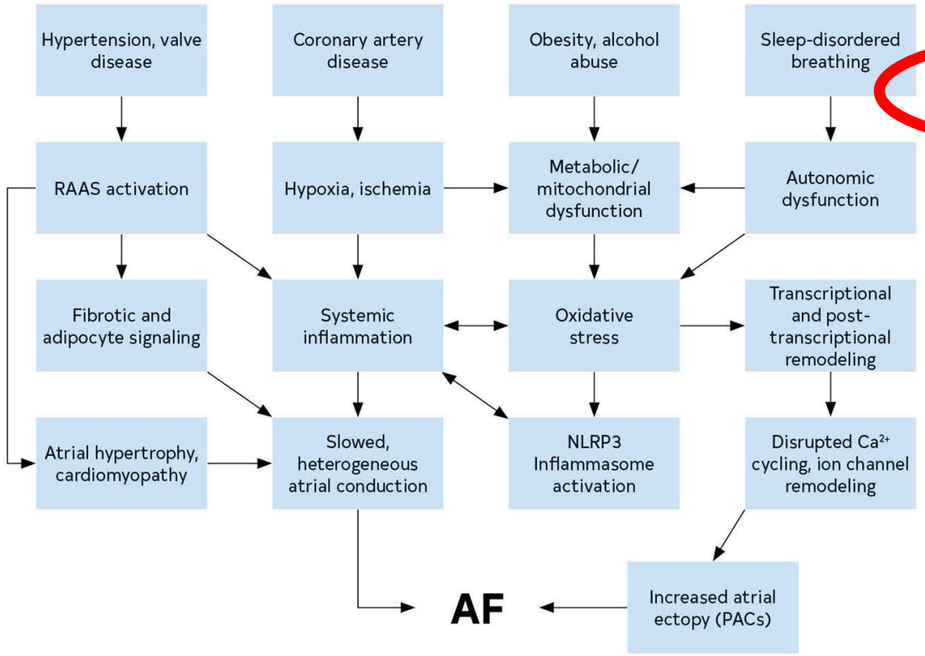
| Acronym | Risk Factor | Points |
|---|---|---|
| $C_2$ | CAD/COPD | 1-2 |
| H | Hypertension | 1 |
| E | Elderly (age ≥ 75 y) | 2 |
| S | Systolic HF | 2 |
| T | Thyroid disease (hyperthyroidism) | 1 |
| | | |
| | Total points | 0-8 |
| | **AUC (C index)** | **95% CI** |
| $C_2$HEST score | 0.749 | 0.729-0.769 |

AUC = area under the curve. See Table 1 legend for expansion of other abbreviations.

*Li et al, CHEST 2019*

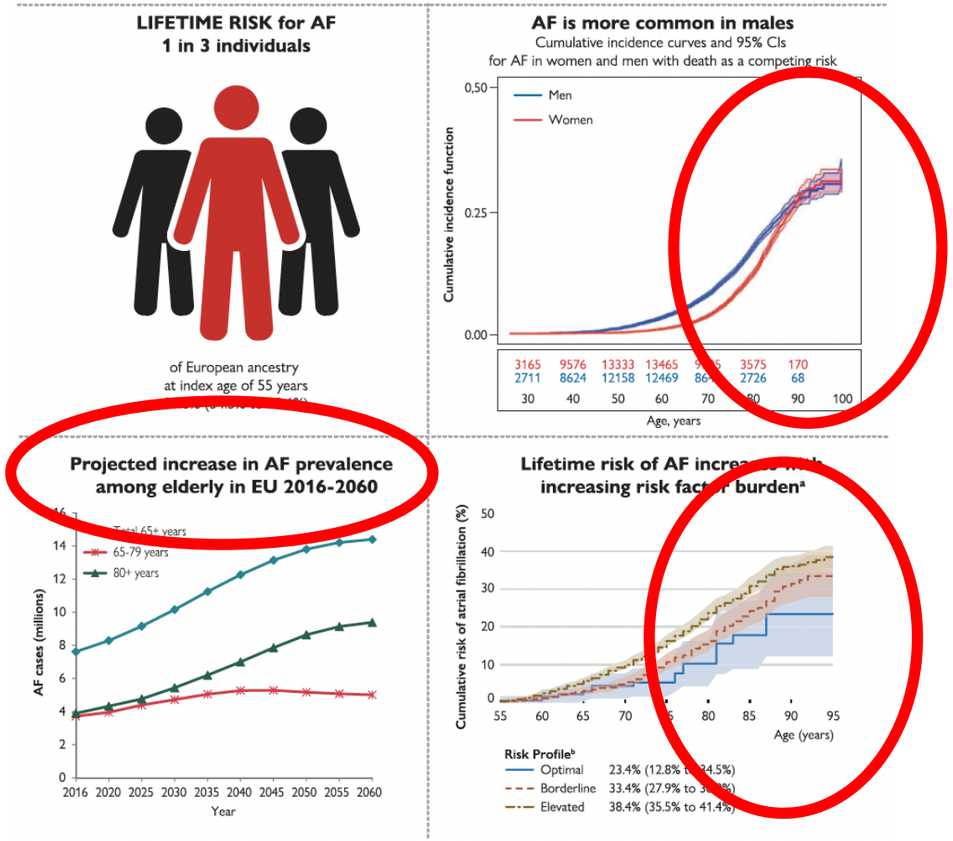
# Atrial Fibrillation: Targeted Population Screening






Major Risk Factors:

- Age
- Race (white)
- HTN
- Weight (obesity)
- Smoking
- Diabetes
- CHF
- MI
- COPD
- Thyroid disease




- Choosing the optimal target population to screen
- Primarily thus far, ***age*** has been utilized
  - Easy to identify and target that population
  - May have lower pretest probability than other population groups, but also results in a larger population screened

*ESC Guidelines 2020, AHA/ACC/HRS Guidelines 2024*

# Apple Watch Study



ORIGINAL ARTICLE

## Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation

Marco V. Perez, M.D., Kenneth W. Mahaffey, M.D., Haley Hedlin, Ph.D., John S. Rumsfeld, M.D., Ph.D., Ariadna Garcia, M.S., Todd Ferris, M.D., Vidhya Balasubramanian, M.S., Andrea M. Russo, M.D., Amol Rajmane, M.D., Lauren Cheung, M.D., Grace Hung, M.S., Justin Lee, M.P.H., Peter Kowey, M.D., Nisha Talati, M.B.A., Divya Nag, Santosh E. Gummidipundi, M.S., Alexis Beatty, M.D., M.A.S., Mellanie True Hills, B.S., Sumbul Desai, M.D., Christopher B. Granger, M.D., Manisha Desai, Ph.D., and Mintu P. Turakhia, M.D., M.A.S., for the Apple Heart Study Investigators*

- In a general population (420k) with an Apple Watch:
  - Irregular heartbeat detection rate is very low (0.52%)
  - Detection rate is highest in those >= 65 years old
  - Subsequent patch monitoring detected AF in ~35%
- Utility as a screening tool undetermined
- What is the appropriate sub-group to focus on?
- Is there any impact on clinical outcomes?

*Perez et al, NEJM Nov 2019*

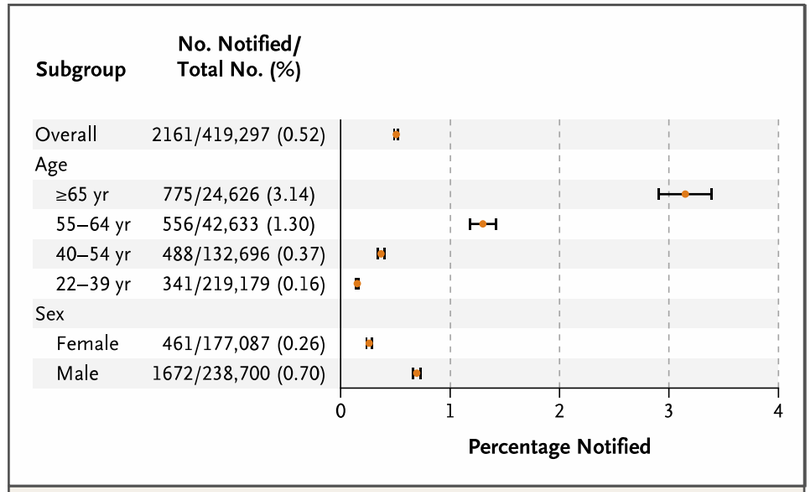



**Figure 2. Irregular Pulse Notifications, According to Age and Sex.**
Horizontal bars indicate 97.5% confidence intervals.

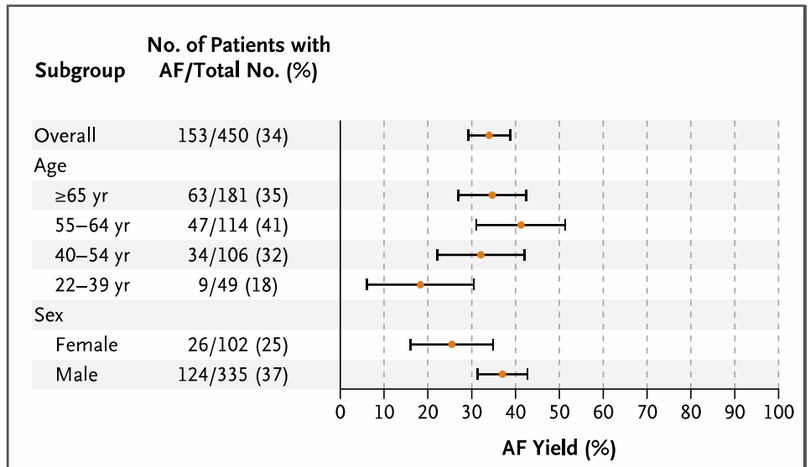
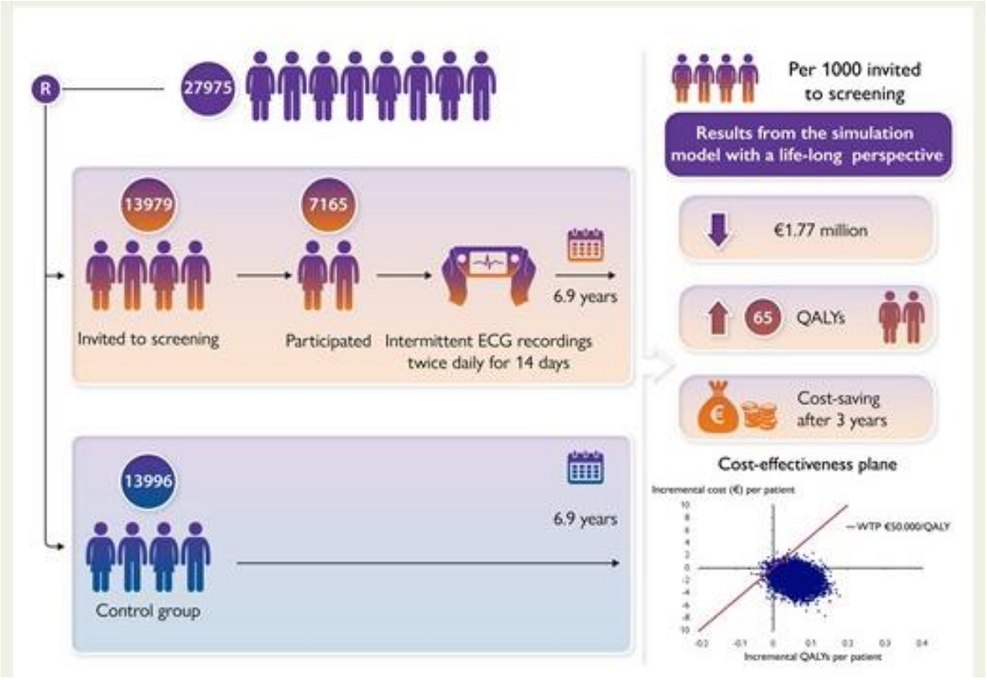


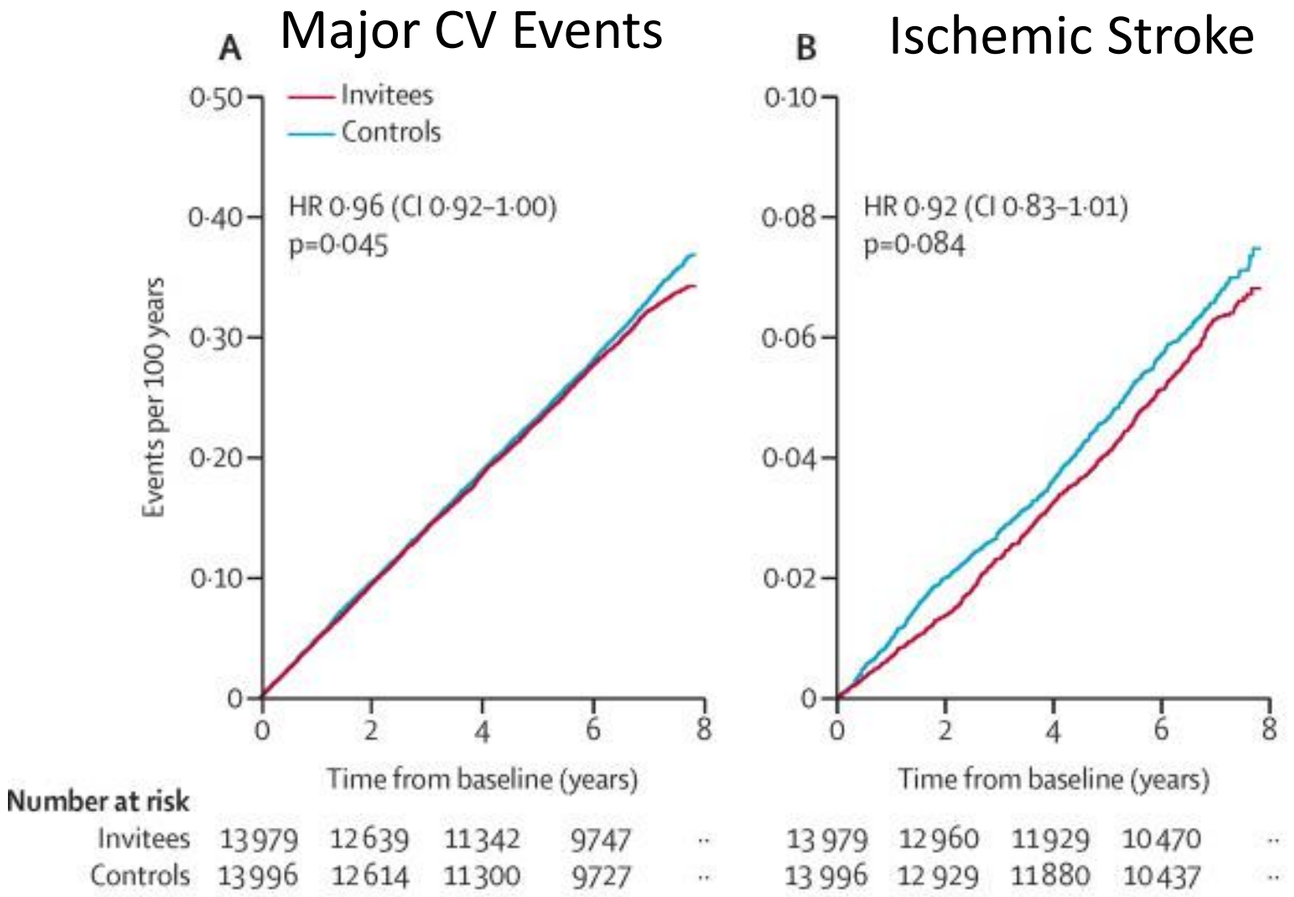

**Figure 3. Yield of Atrial Fibrillation on ECG Patch Monitoring.**
Horizontal bars indicate 97.5% confidence intervals.

# Does General Population Screening Impact Long-term Outcomes?

## Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial

*Emma Svennberg, Leif Friberg, Viveka Frykman, Faris Al-Khalili, Johan Engdahl*, Mårten Rosenqvist**




Svennberg et al, Lancet 2021

# Consolidating Data on AF Screening: Guidelines



## Guideline Recommendations for General Population Screening

- AF screening is cost-effective
- No specific guidance is provided on the specific device to use
- If the screening tool does not provide an interpretable ECG (eg pulse oximetry etc), then a confirmatory ECG showing AF should be obtained if possible
- As with all screening processes, a plan for those ultimately diagnosed with AF is needed

** ESC and US AF Guidelines 2020, 2024*

- Abnormal resu
- ECG misinterp to overdiagnos
- ECG may dete (true or false p invasive tests a the potential f (e.g., angiograp bleeding, contr and allergic rea

- *Spe* ***opportunity*** *and* ***age***

*ESC Guidelines 2020*

*AHA/ACC/HRS Guidelines Joglar et al 2024*

**Recommendations for screening to detect AF**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Opportunistic screening for AF by pulse taking or ECG rhythm strip is recommended in | I | B |
| | | B |
| | | B |
| ≥30 s or 12-lead ECG and if shows AF. | | |
| Systematic ECG screening should be considered to detect AF in individuals aged ≥75 years, or those at high risk of stroke.[212,224,227] | IIa | B |

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# Initial Evaluation of the Patient Diagnosed With AF



Initial evaluation:

- Exclude common treatable etiologies
- Evaluate for underlying cardiac structural pathology
- Evaluate medical comorbidities that will impact stroke risk and decisions for anticoagulation

Specific recommendations regarding coronary artery disease evaluation:

- Ischemic evaluation is appropriate if signs or symptoms suggesting CAD are present
- Routine ischemic evaluation is otherwise not indicated

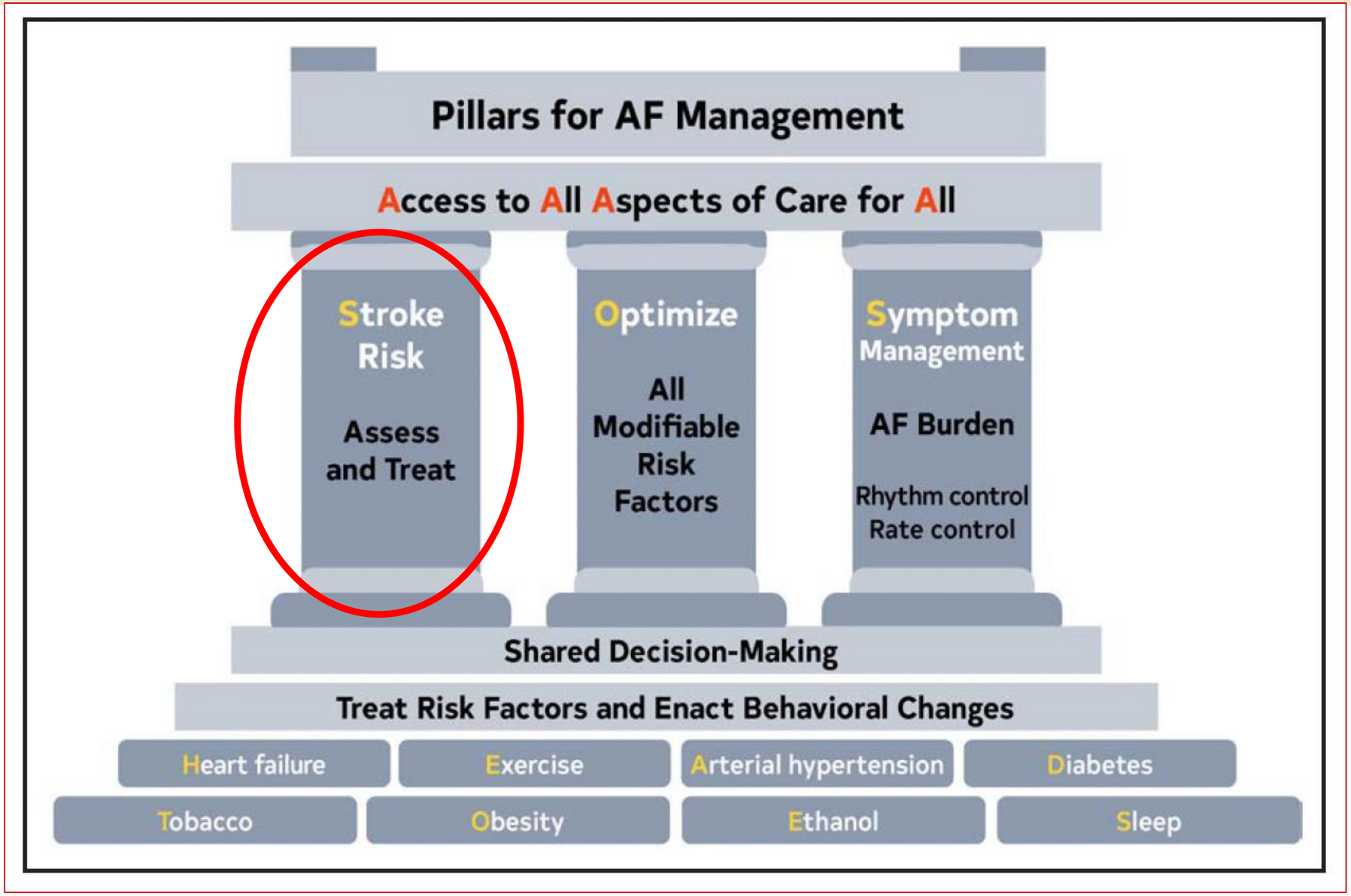
## *4.2.1. Basic Clinical Evaluation*

**Recommendations for Basic Clinical Evaluation**
**Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

| COR | LOE | Recommendations |
|---|---|---|
| 1 | B-NR | 1. In patients with newly diagnosed AF, a transthoracic echocardiogram[1–4] to assess cardiac structure, laboratory testing to include a complete blood count, metabolic panel, and thyroid function,[5–7] and when clinical suspicion exists, targeted testing to assess for other medical conditions associated with AF are recommended to determine stroke and bleeding risk factors, as well as underlying conditions that will guide further management. |
| 3: No benefit | B-NR | 2. In patients with newly diagnosed AF, protocolized testing for ischemia, acute coronary syndrome (ACS), and pulmonary embolism (PE) should not routinely be performed to assess the etiology of AF unless there are additional signs or symptoms to indicate those disorders.[8–10] |

# Beyond Initial Workup: AHA/ACC Guidelines






Joglar J, et al. *AHA/ACC/HRS 2024 guideline for the management of patients with atrial fibrillation.* Circulation, 2024.

# Stroke Risk: ~90% of stroke in AF is caused by blood clots that form in the left atrial appendage (LAA)[1]



**Loss of mechanical atrial contraction of the LAA leads to blood flow stasis**

↓

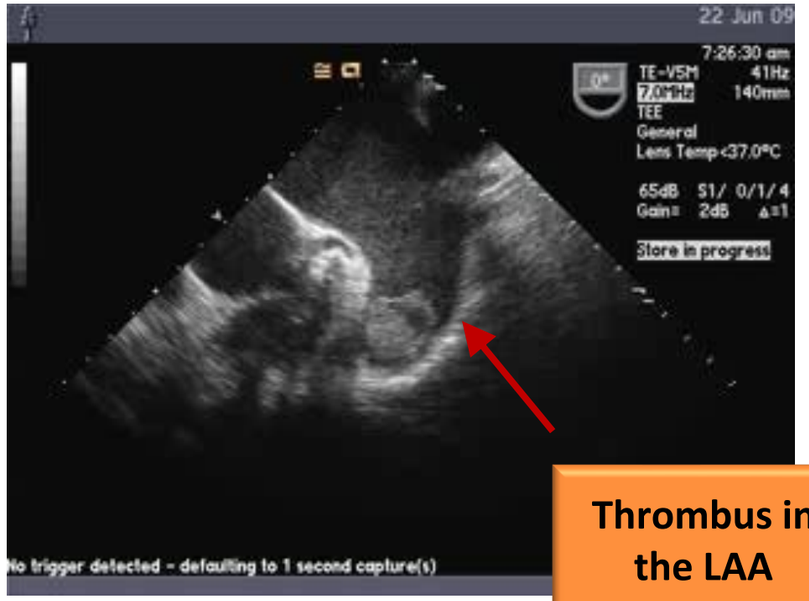
**The stagnant blood may coagulate and form thrombus**

↓

**Dislodgement of the thrombus, with distal embolization in the cerebral circulation**

↓

**Occlusion of the cerebral circulation leads to stroke**




**Thrombus in the LAA**

**Thrombus Revealed by Transesophageal Echocardiography**

A total of 76 patients (13.8 percent) with right or left heart thrombi were identified among the 549 patients who underwent a transesophageal echocardiographic examination. Of these 76 patients with thrombi, 67 (88.2 percent) had a thrombus in the left atrial appendage. None of the patients with thrombi had an embolic event during the eight-week study, although four of these patients died from various

The New England Journal of Medicine



VOLUME 344 MAY 10, 2001 NUMBER 19

USE OF TRANSESOPHAGEAL ECHOCARDIOGRAPHY TO GUIDE CARDIOVERSION IN PATIENTS WITH ATRIAL FIBRILLATION

ALLAN L. KLEIN, M.D., RICHARD A. GRIMM, D.O., R. DANIEL MURRAY, PH.D., CAROLYN APPERSON-HANSEN, M.STAT., RICHARD W. ASINGER, M.D., IAN W. BLACK, M.D., RAVIN DAVIDOFF, M.B., B.CH., RAIMUND ERBEL, M.D., JONATHAN L. HALPERIN, M.D., DAVID A. ORSINELLI, M.D., THOMAS R. PORTER, M.D., AND MARCUS F. STODDARD, M.D., FOR THE ASSESSMENT OF CARDIOVERSION USING TRANSESOPHAGEAL ECHOCARDIOGRAPHY INVESTIGATORS*

[1] *Blackshear JL. Odell JA., Annals of Thoracic Surgery. 1996*

[2] *Klein et al., NEJM 2001*

# AF and stroke



- Risk without anticoagulation 0-15% annually
- Impact of duration of AF episodes on stroke risk: uncertain, but probably yes
- Strokes from AF are more severe
  - Greater long-term disability and mortality
- Therefore, all AF patients should be considered for long-term anticoagulation – but which ones?

# Stroke Risk and AF: $CHA_2DS_2$-VASc



| CHA2DS2-VASc Risk Criteria | Points |
|---|---|
| **C**ongestive Heart Failure/LV Dysfunction | 1 |
| **H**ypertension | 1 |
| **A**ge ≥ 75 Years | 2 |
| **D**iabetes Mellitus | 1 |
| Prior **S**troke, TIA, thromboembolism | 2 |
| Peripheral **V**ascular Disease or Coronary Artery Disease | 1 |
| **A**ge 65-74 Years | 1 |
| **S**ex Category (i.e., Female Sex) | 1 |

| Score | Adjusted stroke rate (%/year) based on $CHA_2DS_2$-VASc score |
|---|---|
| 0 | 0 |
| 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 |

- Complicated
- Limited external validation
- Limited reclassification improvement

*Camm AJ, ESC Guidelines, Eur Heart J 2010*

# Bleeding Risk on Anticoagulation



**Table 10 Clinical risk factors in the HAS-BLED score[395]**

| Risk factors and definitions | | Points awarded |
|---|---|---|
| **H** | **Uncontrolled hypertension**<br>SBP >160 mmHg | 1 |
| **A** | **Abnormal renal and/or hepatic function**<br>Dialysis, transplant, serum creatinine >200 μmol/L, cirrhosis, bilirubin > × 2 upper limit of normal, AST/ALT/ALP >3 × upper limit of normal | 1 point for each |
| **S** | **Stroke**<br>Previous ischaemic or haemorrhagic[a] stroke | 1 |
| **B** | **Bleeding history or predisposition**<br>Previous major haemorrhage or anaemia or severe thrombocytopenia | 1 |
| **L** | **Labile INR[b]**<br>TTR <60% in patient receiving VKA | 1 |
| **E** | **Elderly**<br>Aged >65 years or extreme frailty | 1 |
| **D** | **Drugs or excessive alcohol drinking**<br>Concomitant use of antiplatelet or NSAID; and/or excessive[c] alcohol per week | 1 point for each |
| **Maximum score** | | **9** |

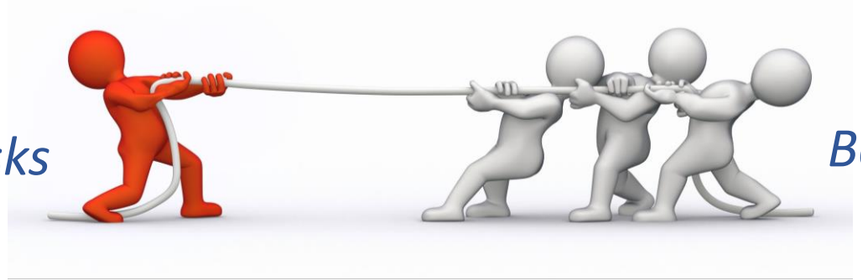


**These factors also affect risk of stroke**

ESC Guidelines 2020

# When to anticoagulate: current guidelines





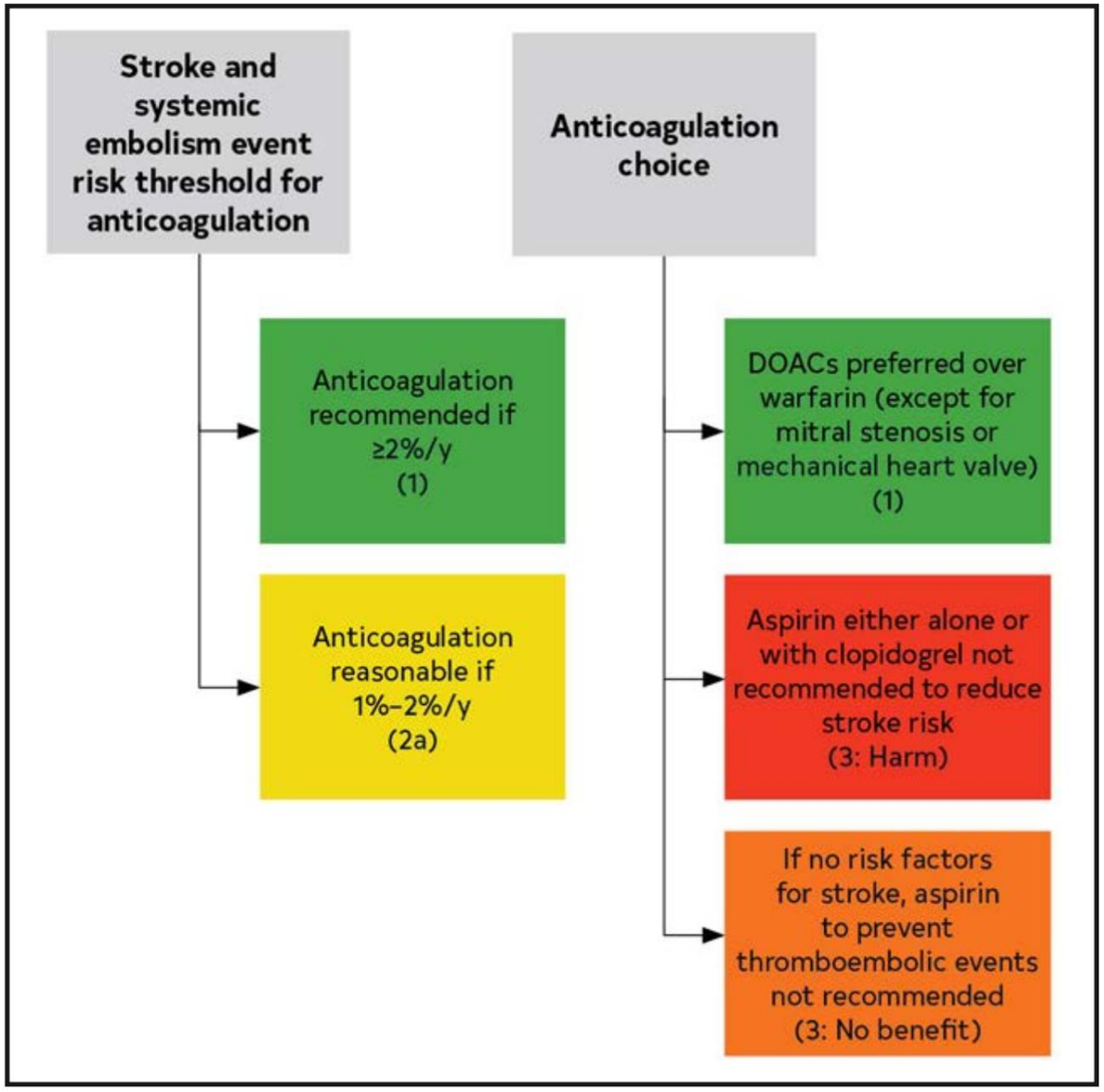

| $CHA_2DS_2$-Vasc Score | |
|---|---|
| 0 men, 1 women | "reasonable to omit anticoagulation" |
| 1 men, 2 women | "anticoagulation may be considered" |
| >= 2 | "anticoagulation is recommended" |

*Anticoagulation decision is therefore based on $CHA_2DS_2$-Vasc Score*
*Irrespective of AF burden*

*AHA/ACC/HRS AF Guidelines 2023*

# Options for Stroke Prevention in AF

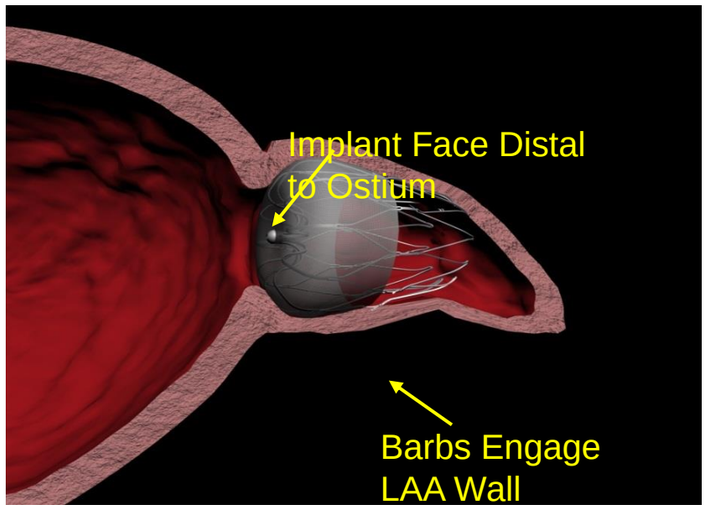





- **Anticoagulation considered for all regardless of whether a rhythm or rate control strategy is chosen**
- AF pts with mitral stenosis or a mechanical valve should be treated with **warfarin**
- $CHA_2DS_2$-Vasc Score
  - 0(M)/1(F) – no anticoagulation
  - 1(M)/2(F) – anticoagulation may be considered
  - >=2(M)/3(F) – anticoagulation is recommended
- ***Where does Left Atrial Appendage Occlusion (LAAO) fit into this scheme?***

# Guideline Recommendations






## Percutaneous LAAO

- FDA approved in patients with AF and a contraindication or intolerance for anticoagulation (IIa/b level of evidence)

## Surgical LAAO

- LAAO with continued AC is Class I indication
- LAAO with discontinuation of AC is IIb indication

### 6.5.1. Percutaneous Approaches to Occlude the LAA

**Recommendations for Percutaneous Approaches to Occlude the LAA Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

| COR | LOE | Recommendations |
|---|---|---|
| 2a | B-NR | 1. In patients with AF, a moderate to high risk of stroke ($CHA_2DS_2$-VASc score ≥2), and a contraindication (Table 14) to long-term oral anticoagulation due to a nonreversible cause, percutaneous LAAO (pLAAO) is reasonable.[1–4] |
| 2b | B-R | 2. In patients with AF and a moderate to high risk of stroke and a high risk of major bleeding on oral anticoagulation, pLAAO may be a reasonable alternative to oral anticoagulation based on patient preference, with careful consideration of procedural risk and with the understanding that the evidence for oral anticoagulation is more extensive.[1–3,5,6] |

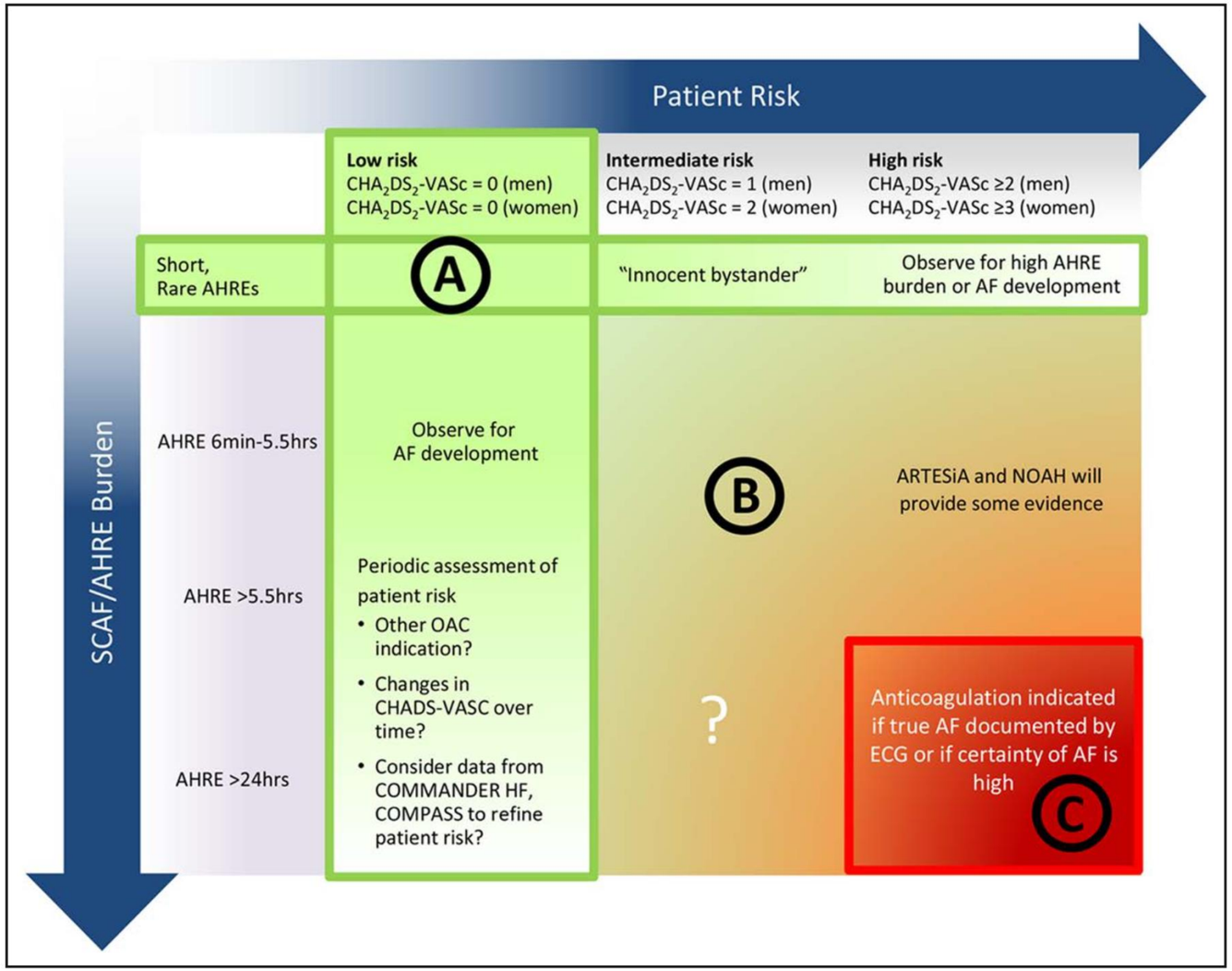
### 6.5.2. Cardiac Surgery—LAA Exclusion/Excision

**Recommendations for Cardiac Surgery—LAA Exclusion/Excision Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

| COR | LOE | Recommendations |
|---|---|---|
| 1 | A | 1. In patients with AF undergoing cardiac surgery with a $CHA_2DS_2$-VASc score ≥2 or equivalent stroke risk, surgical LAA exclusion, in addition to continued anticoagulation, is indicated to reduce the risk of stroke and systemic embolism.[1–3] |
| 1 | A | 2. In patients with AF undergoing cardiac surgery and LAA exclusion, a surgical technique resulting in absence of flow across the suture line and a stump of <1 cm as determined by intraoperative transesophageal echocardiography should be used.[1,4,5] |
| 2b | A | 3. In patients with AF undergoing cardiac surgery with $CHA_2DS_2$-VASc score ≥2 or equivalent stroke risk, the benefit of surgical LAA exclusion in the absence of continued anticoagulation to reduce the risk of stroke and systemic embolism is uncertain.[1–3] |

# Device-detected AF






- AHA/ACC Guidelines 2023

## Emerging findings

- AF Burden is emerging as an important determinant of stroke risk
- Burden is yet to be incorporated into guideline recommenations

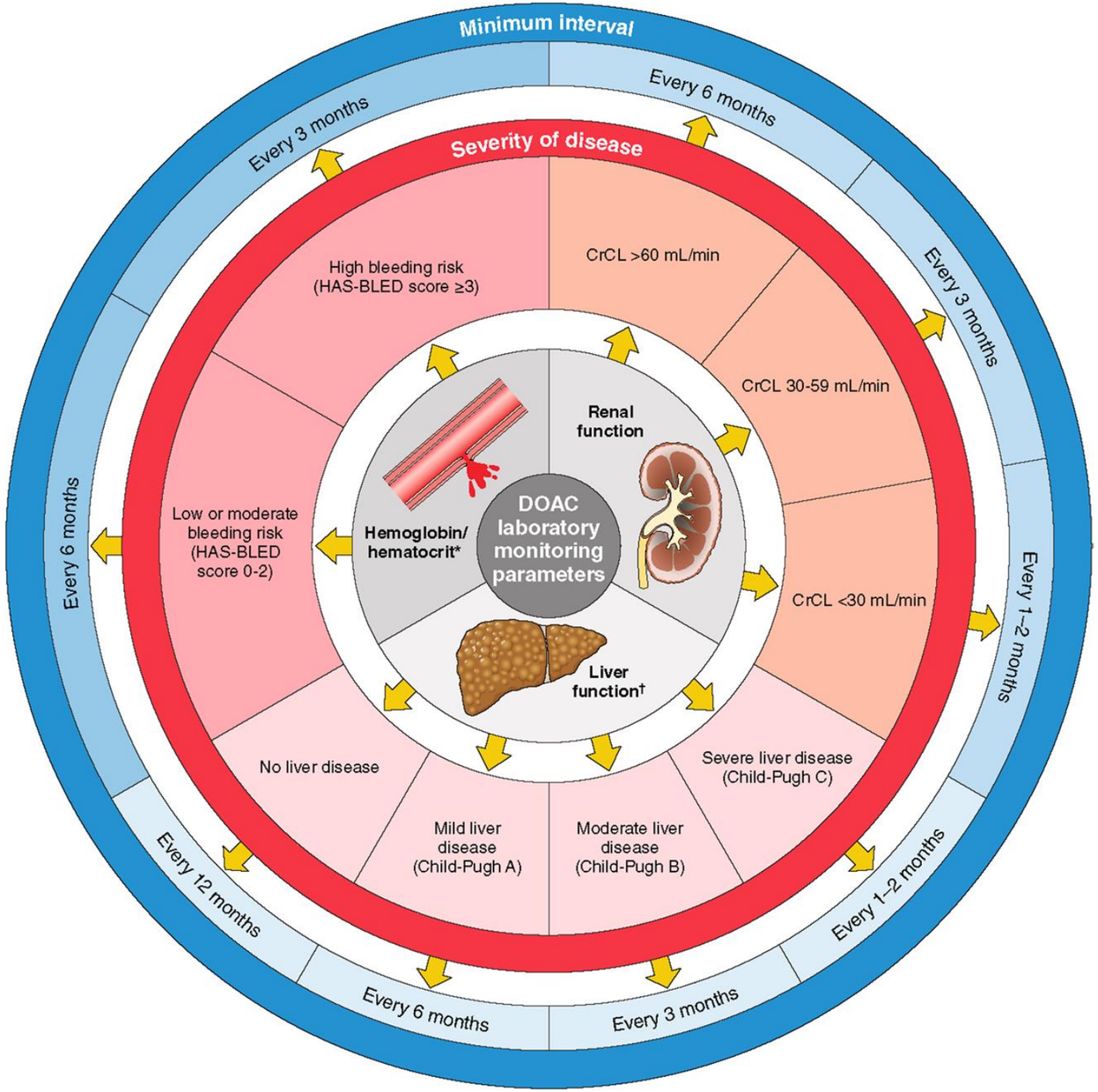
Potential Implications for management: AF seen on pre-existing device (pacemaker, ICD, monitor)

CHADS-Vasc >=2

- >24h episodes: anticoagulate
- 5m-24h: may anticoagulate
- <5m: no benefit

# Monitoring Anticoagulation

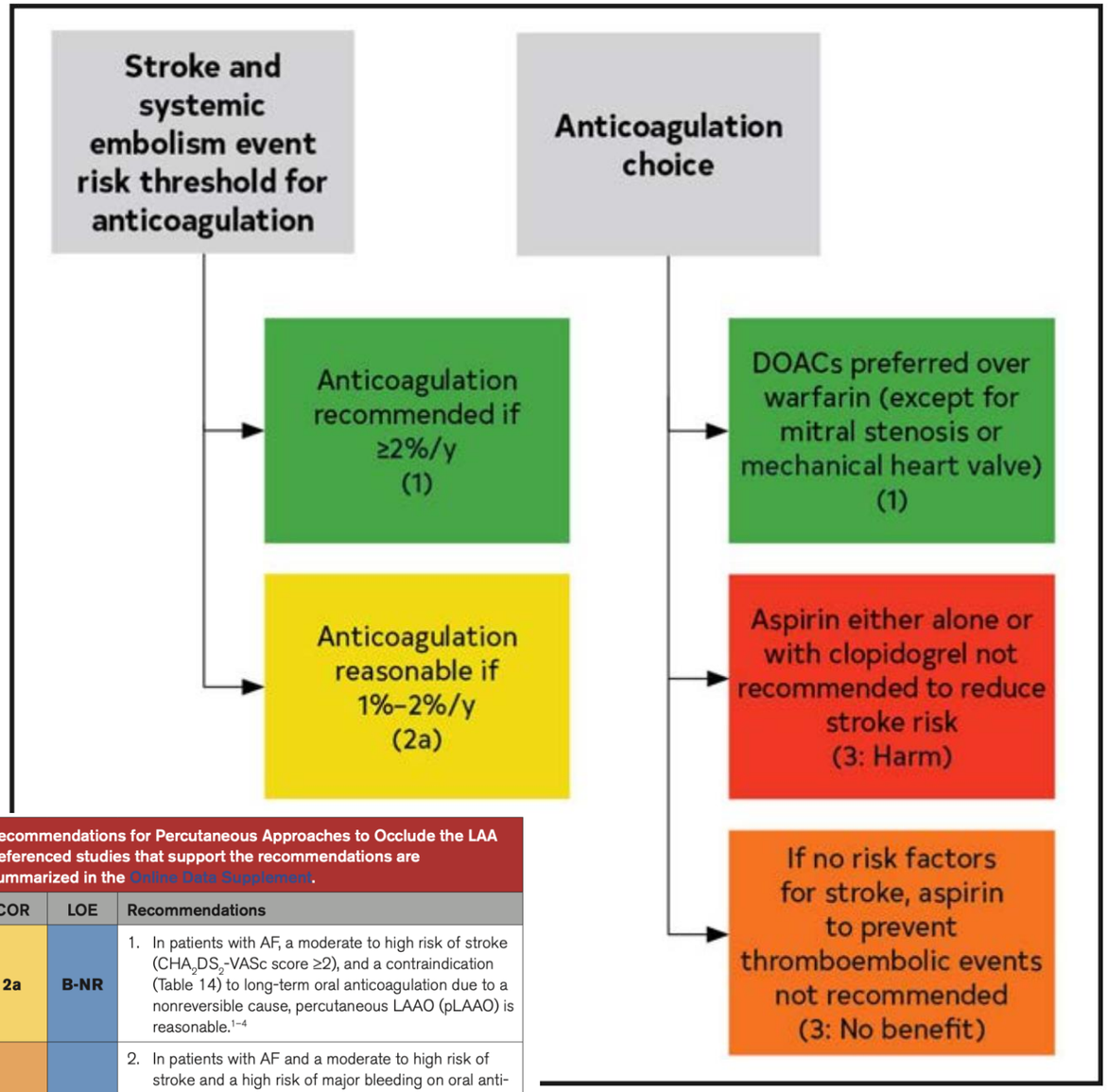
- Basic monitoring interval: q 6 months
- With increased hepatic or renal disease, increase monitoring frequency
- With higher bleed risk, monitor more frequently




- AHA/ACC Guidelines 2023

# Options for stroke prevention in AF






**Recommendations for Percutaneous Approaches to Occlude the LAA**
**Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

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- **Anticoagulation considered for all regardless of whether a rhythm or rate control strategy is chosen**
- AF pts with mitral stenosis or a mechanical valve should be treated with **warfarin**
- $CHA_2DS_2$-Vasc Score
  - 0(M)/1(F) – no anticoagulation
  - 1(M)/2(F) – anticoagulation may be considered
  - >=2(M)/3(F) – anticoagulation is recommended
- Mechanical left atrial appendage exclusion in select patients

# Rhythm vs. Rate Control?



- **That Was Then:**
  - The AFFIRM, RACE, and AF-CHF trials showed no mortality benefit to a rhythm control strategy compared to a rate control strategy.
  - But these studies are >20-30 years old, before current ablation strategies, anticoagulation recommendations (AC was typically stopped in patients in the rhythm control arm)

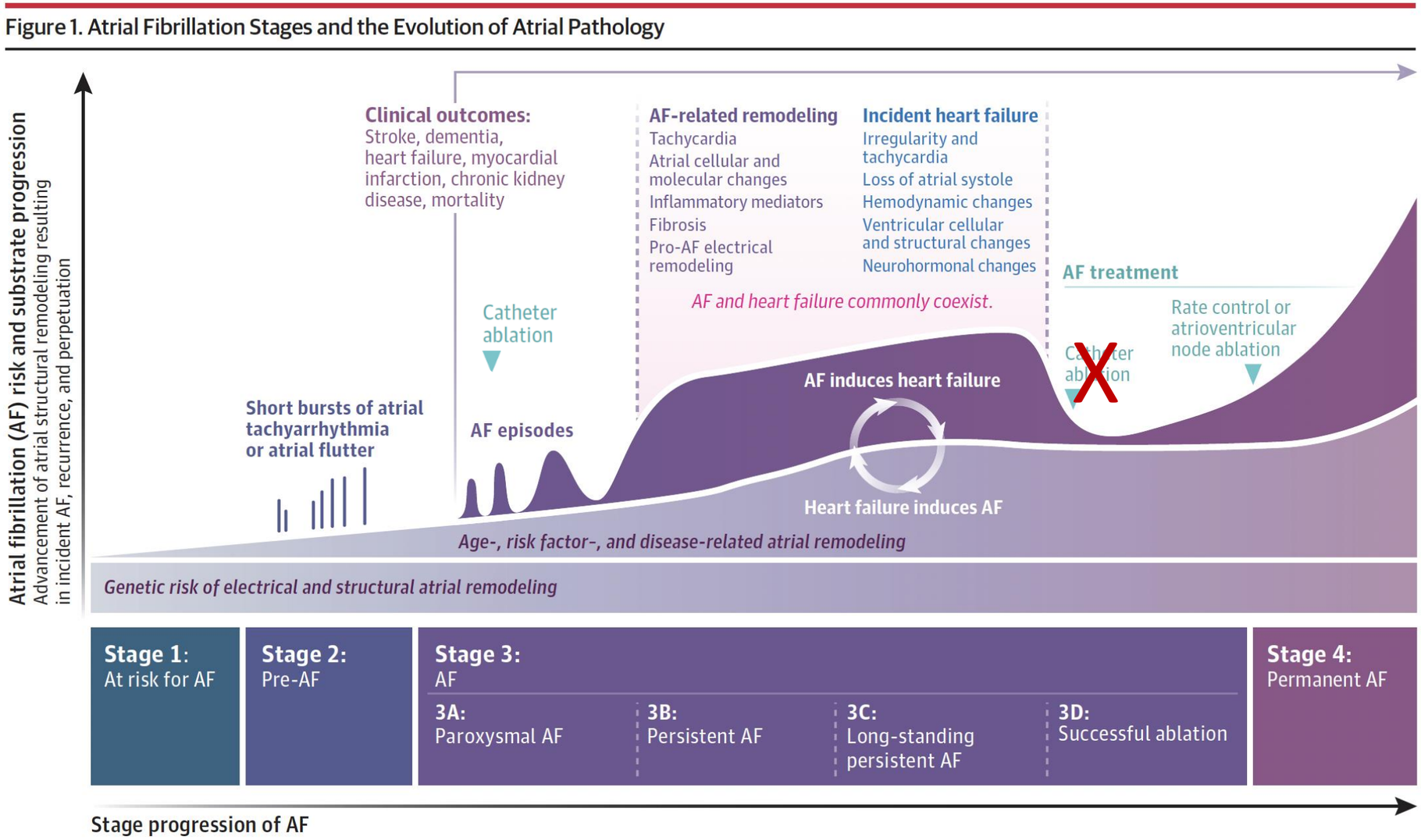
- **This is Now:**
  - Newest studies demonstrate across the board benefit to *early* rhythm control/ablation strategy
  - Benefit includes not only ability to maintain sinus rhythm, but reduced hospitalizations, improved morbidity, improved *mortality*

The Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Investigators. *A comparison of rate control and rhythm control in patients with atrial fibrillation.* N Engl J Med. 2002;347: 1825-1833.

# AF Progression Over Time



## That Was Then  This is Now




Chung et al, JAMA 2024

# EARLY Rhythm vs. Rate Control? EAST-AF



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 1, 2020 VOL. 383 NO. 14

## Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators*

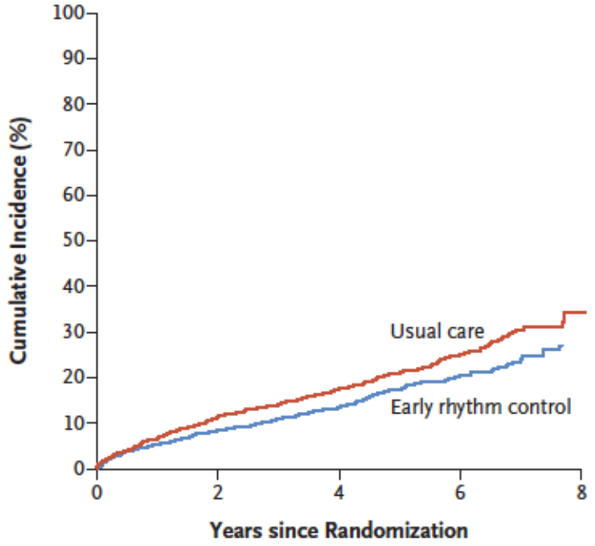



**Figure 2. Aalen–Johansen Cumulative-Incidence Curves for the First Primary Outcome.**

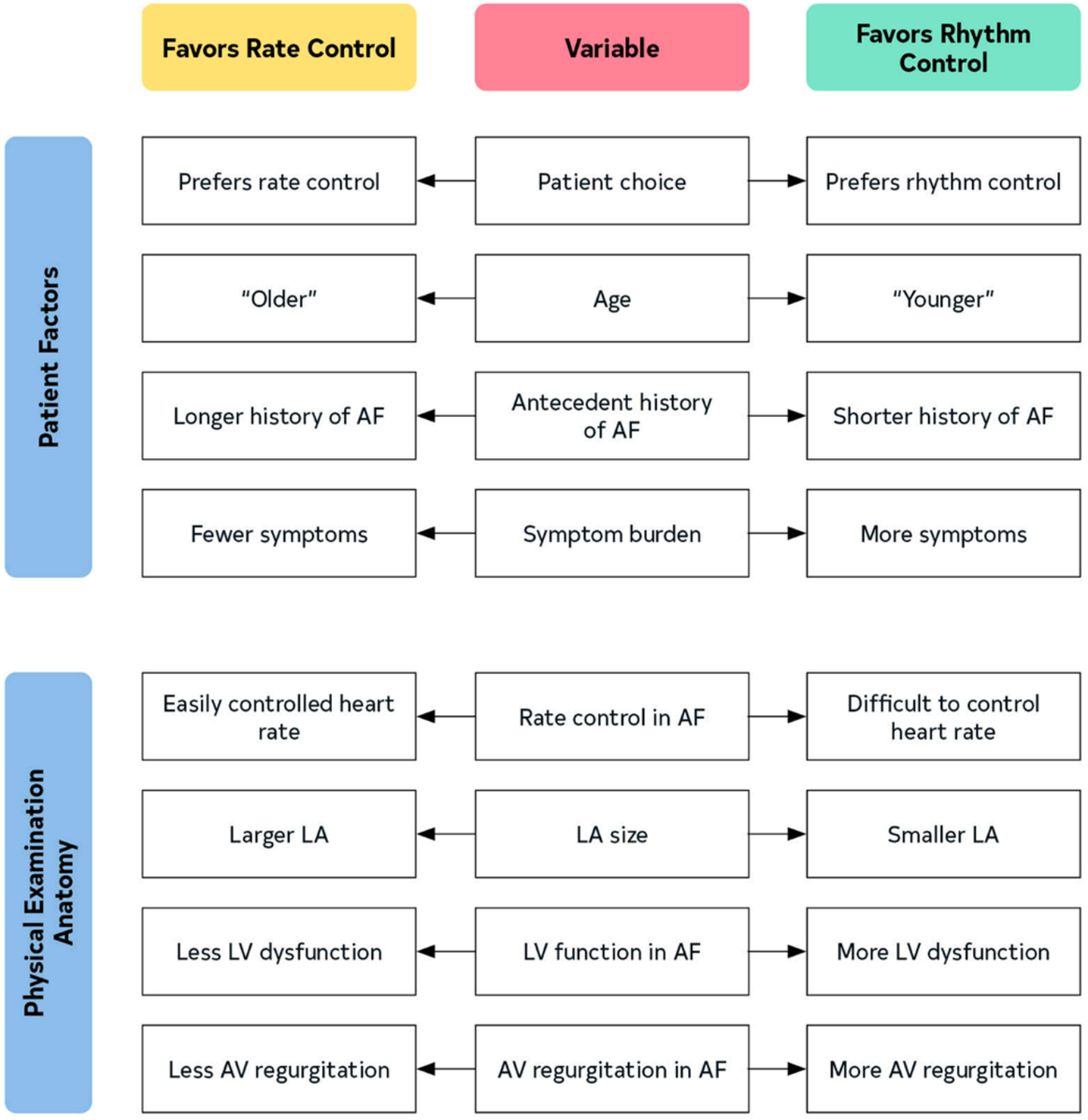
The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome.

**Table 2. Efficacy Outcomes.***

| Outcome | Early Rhythm Control | Usual Care | Treatment Effect |
|---|---|---|---|
| First primary outcome — events/person-yr (incidence/100 person-yr) | 249/6399 (3.9) | 316/6332 (5.0) | 0.79 (0.66 to 0.94)† |
| Components of first primary outcome — events/person-yr (incidence/100 person-yr) | | | |
| Death from cardiovascular causes | 67/6915 (1.0) | 94/6988 (1.3) | 0.72 (0.52 to 0.98)‡ |
| Stroke | 40/6813 (0.6) | 62/6856 (0.9) | 0.65 (0.44 to 0.97)‡ |
| Hospitalization with worsening of heart failure | 139/6620 (2.1) | 169/6558 (2.6) | 0.81 (0.65 to 1.02)‡ |
| Hospitalization with acute coronary syndrome | 53/6762 (0.8) | 65/6816 (1.0) | 0.83 (0.58 to 1.19)‡ |
| Second primary outcome — nights spent in hospital/yr | 5.8±21.9 | 5.1±15.5 | 1.08 (0.92 to 1.28)§ |
| Key secondary outcomes at 2 yr | | | |
| Change in left ventricular ejection fraction — % | 1.5±9.8 | 0.8±9.8 | 0.23 (−0.46 to 0.91)¶ |
| Change in EQ-5D score‖ | −1.0±21.4 | −2.7±22.3 | 1.07 (−0.68 to 2.82)¶ |
| Change in SF-12 Mental Score** | 0.7±10.6 | 1.6±10.1 | −1.20 (−2.04 to −0.37)¶ |
| Change in SF-12 Physical Score** | 0.3±8.5 | 0.1±8.2 | 0.33 (−0.39 to 1.06)¶ |
| Change in MoCA score | 0.1±3.3 | 0.1±3.2 | −0.14 (−0.39 to 0.12)¶ |
| Sinus rhythm — no. of patients with feature/total no. (%) | 921/1122 (82.1) | 687/1135 (60.5) | 3.13 (2.55 to 3.84)†† |
| Asymptomatic — no. of patients with feature/total no. (%)‡‡ | 861/1159 (74.3) | 850/1171 (72.6) | 1.14 (0.93 to 1.40)†† |

# Rhythm Control Indications






Joglar J, et al. *AHA/ACC/HRS 2024 guideline for the management of patients with atrial fibrillation.* Circulation, 2024.

# A two-slide primer on antiarrhythmic drugs



**Vaughan Williams Class I** - Na channel blockade

- Flecainide PO: 50-150mg every 12 hrs
- Propafenone PO: 150-300mg every 8 hrs, or sustained release 225-425mg every 12 hrs

**Vaughan Williams Class III** – K channel blockade

- Amiodarone PO: 200mg TID x 2 weeks, 200mg BID x 2wks, then 200mg daily. Take with meals.
  - Monitor for hepatic, thyroid, pulmonary, ophthalmologic, skin toxicity
- Dofetilide PO: 125-500mcg every 12 hrs, based on renal function and QTc;
  - must be initiated in the hospital
- Dronedarone PO: 400mg twice daily with meals
  - Monitor for hepatotoxicity; contraindicated in permanent AF, low EF
- Sotalol PO: 80mg BID, to a maximum of 240-320mg/day, based on renal function and QTc
  - In-hospital initiation favored

- Less commonly prescribed: disopyramide, quinidine

# AAD considerations – slide 2

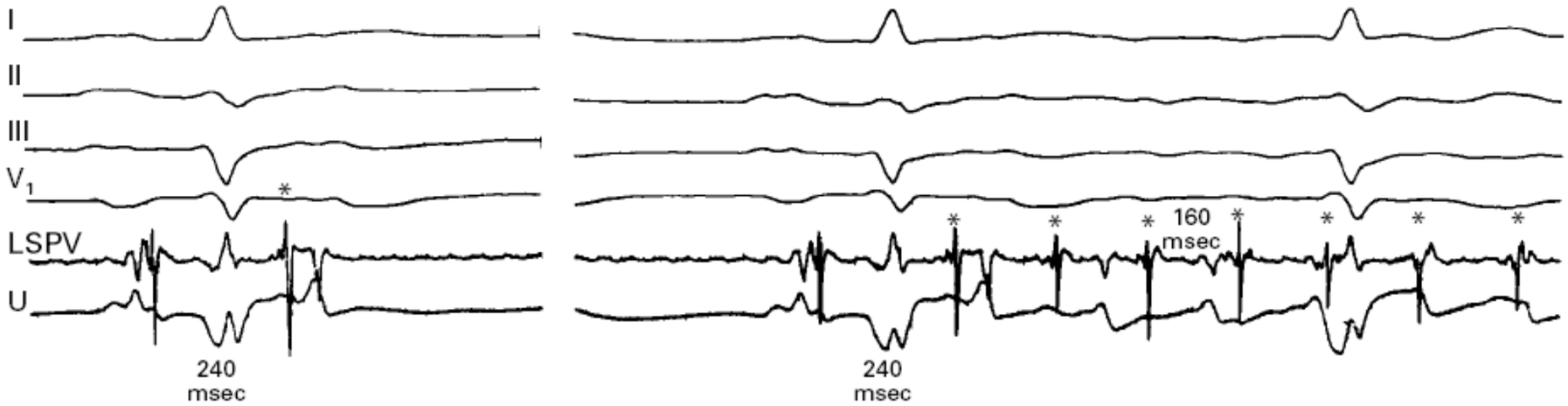


- Class IC agents
  - Contraindicated in patients with "structural heart disease"
  - May be used as maintenance or "pill in the pocket"
  - Should be given with concomitant rate control agent to prevent rapidly conducting atrial flutter
- Class III agents
  - All agents can prolong QT interval (amiodarone less so)
  - Dofetilide and sotalol should be initiated in the hospital
  - Patients taking amiodarone should have periodic monitoring for organ toxicity

# SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÉLÈZE HOCINI, M.D., GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOUROUX, M.D., PHILIPPE LE MÉTAYER, M.D., AND JACQUES CLÉMENTY, M.D.

- Arrhythmogenic triggers for AF in the pulmonary vein musculature demonstrated in 45 patients with PAF




- Ablation of these PV triggers resulted in reduction/elimination of AF

*Haissaguerre et al. NEJM 1998*

# Why do we differentiate between paroxysmal vs. persistent AF when it comes to ablation?

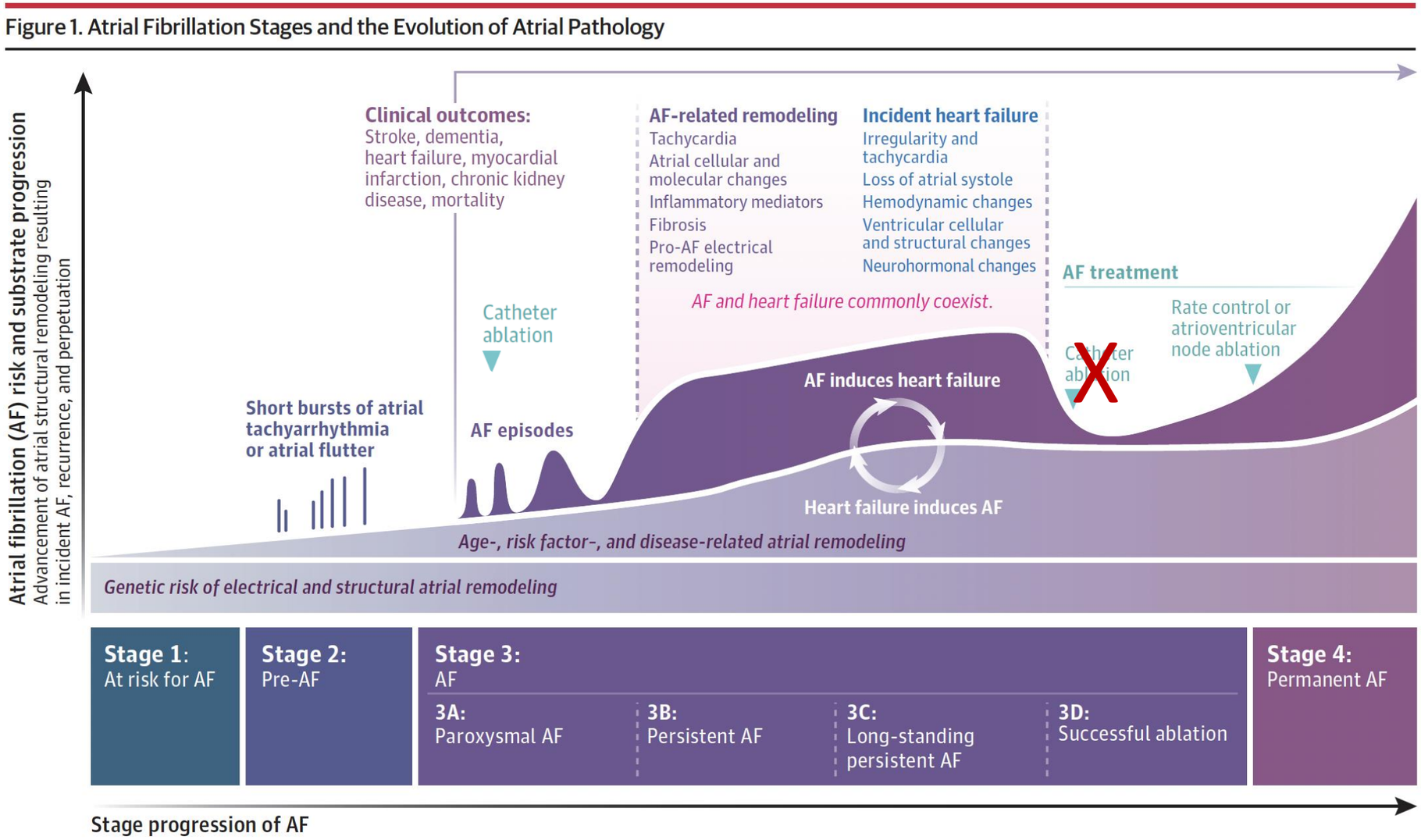


| | Paroxysmal AF | Persistent AF | Long-standing persistent AF |
|---|---|---|---|
| Definition | Episodes self terminate or via CV <7d | Episodes do not self terminate < 7d | Persistent AF >1 year |
| LA size | Normal to mildly enlarged | Mild to severely enlarged | Severely enlarged |
| LA scar burden | Low | Moderate | high |
| Efficacy of AAD | Often effective | Not as effective | Usually refractory |
| When to offer ablation? | First-line therapy | First-line OK, but after AAD failure best | After AAD failure |
| Ablation technique | PV isolation alone | PV isolation only probably still best | PV isolation; additional ablation likely needed |
| Catheter ablation efficacy | Excellent | Not quite excellent, but still good | ?, but likely low with current approaches |

# AF Progression Over Time



## That Was Then  This is Now




Chung et al, JAMA 2024

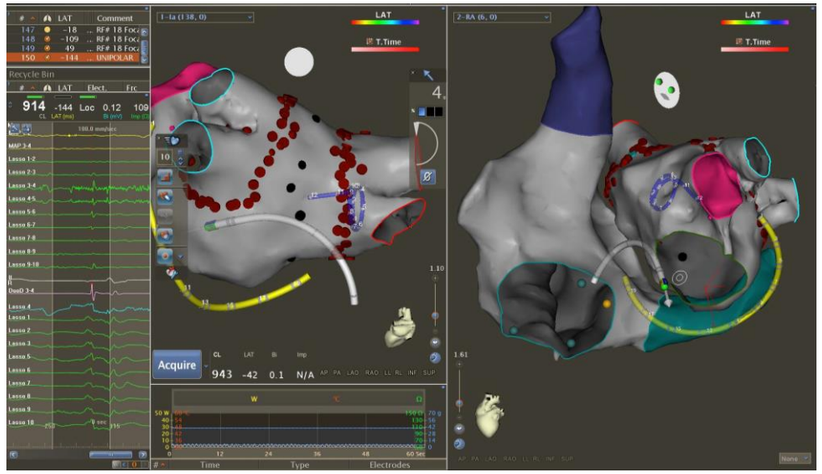
# What happens during catheter ablation for AF?

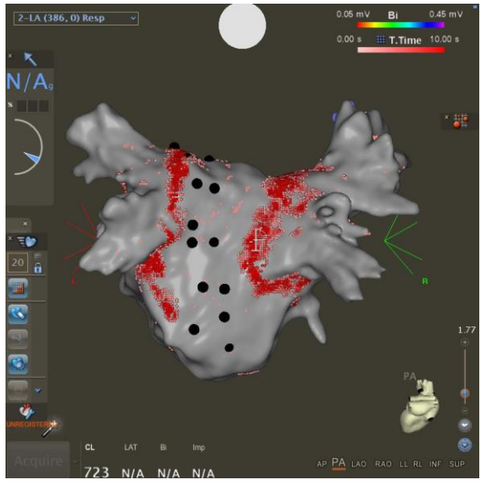


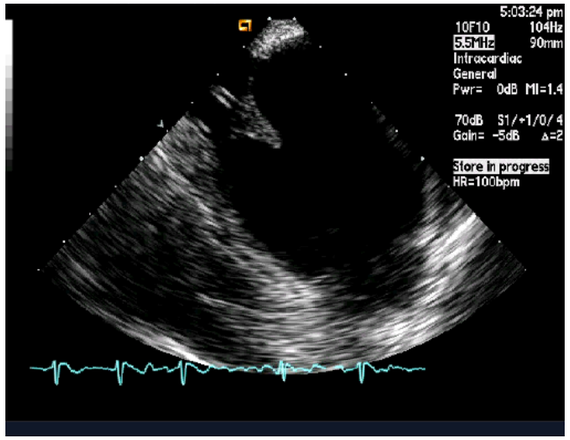
- Typically performed under general anesthesia
- Vascular access (venous)
- Catheter advancement into the heart (RA)
- Transseptal puncture to access the left atrium (LA)
- Tools utilized – almost all cases performed using either radiofrequency energy (RF) or cryothermy (freezing), with a goal of creating permanent scar and resultant electrical conduction block
- Ablation delivered to circumferentially electrically isolate all pulmonary veins
- Additional ablation beyond PV isolation may be performed, particularly in patients with persistent or long-standing persistent AF

# What happens during catheter ablation for AF?



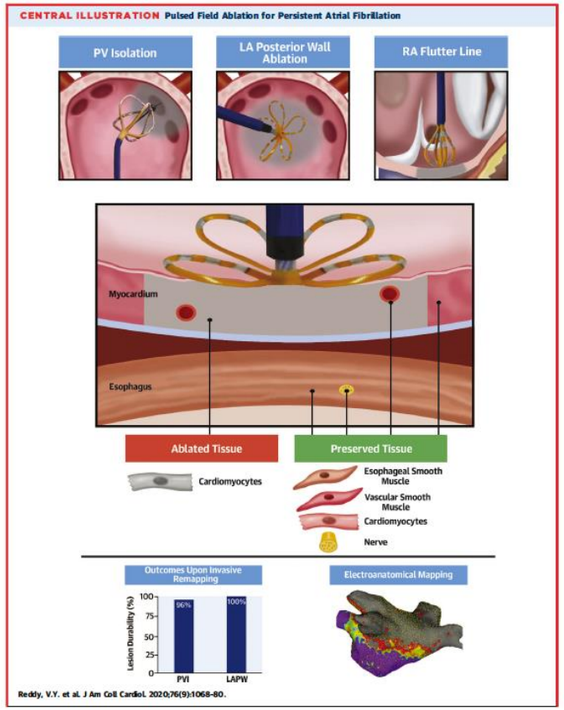


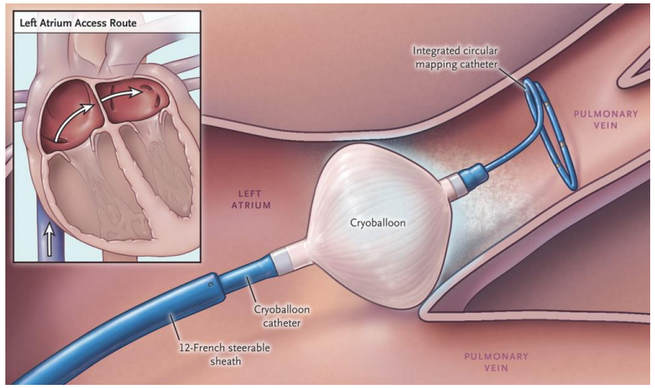




Commonly used tools:

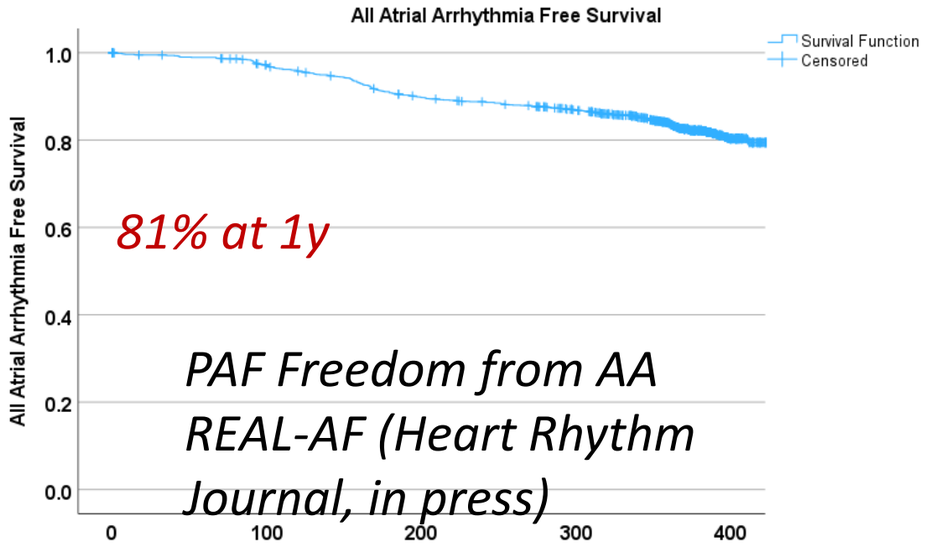
- Electroanatomic mapping
- RF energy: irrigated tip, contact force
- Cryoablation: balloon catheter
- Pulsed Field Ablation (PFA)
- ICE (intracardiac ultrasound)

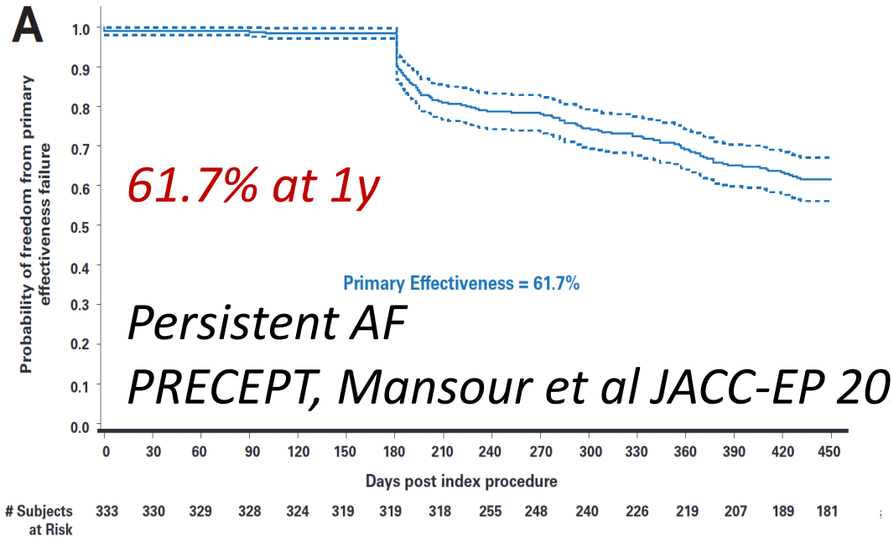


# What are the risks and benefits of AF ablation?






## Benefits of Rhythm Control (specifically ablation)

- Symptom improvement
- Reduction in hospitalization, heart failure
- Improved mortality in select patients
- Possible decreased long-term risks of dementia, cognitive decline

# What to expect after AF ablation?



- **Atrial tachyarrhythmias can occur** in the first three months after ablation during the healing phase. These arrhythmias can be treated with medical therapy and often resolve. However, a repeat ablation procedure should be considered if atrial tachyarrhythmias persist.
- Patients should be **anticoagulated for at least two months** after ablation. **Long-term oral anticoagulation should be considered** in patients with a CHA2DS2-VASc score ≥2 regardless of the outcome after ablation.
  - Data supporting discontinuation after ablation not available yet

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Calkins et al., Heart Rhythm Vol 14, No 10, October 2017

# Current/Pipeline PFA Systems (USA and EU)



| System | Company | Key Features | | Dedicated Mapping System? * |
|---|---|---|---|---|
| Farapulse | Boston Scientific | OTW Flower/Basket |  | **Yes (new) *** |
| Pulse Select | Medtronic | OTW fixed circular loop |  | No |
| Varipulse | Biosense | Variable loop |  | **Yes** |
| Omnypulse | Biosense | Small spheroid |  | **Yes** |
| STSF Dual Energy | Biosense | Point catheter (STSF) |  | **Yes** |
| Affera | Medtronic | Large spheroid |  | **Yes** |
| Others are under development/evaluation | Various | Various |  | Various |

# PFA Clinical Outcomes Data



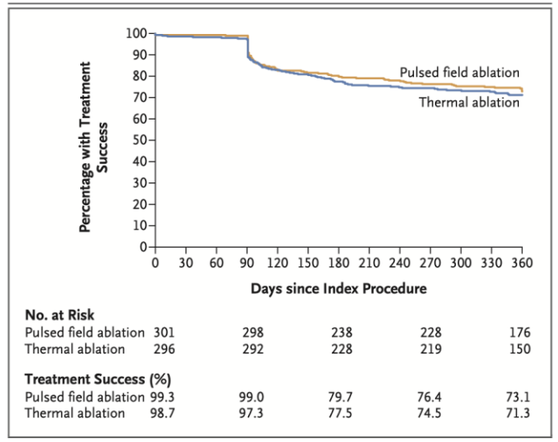
73% freedom from AA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation

Vivek Y. Reddy, M.D., Edward P. Gerstenfeld, M.D., Andrea Natale, M.D., William Whang, M.D., Frank A. Cuoco, M.D., Chinmay Patel, M.D., Stavros E. Mountantonakis, M.D., Douglas N. Gibson, M.D., John D. Harding, M.D., Christopher R. Ellis, M.D., Kenneth A. Ellenbogen, M.D., David B. DeLurgio, M.D., Jose Osorio, M.D., Anitha B. Achyutha, M.Tech., M.S.E., Christopher W. Schneider, M.Eng., Andrew S. Mugglin, Ph.D., Elizabeth M. Albrecht, Ph.D., Kenneth M. Stein, M.D., John W. Lehmann, M.D., M.P.H., and Moussa Mansour, M.D., for the ADVENT Investigators*



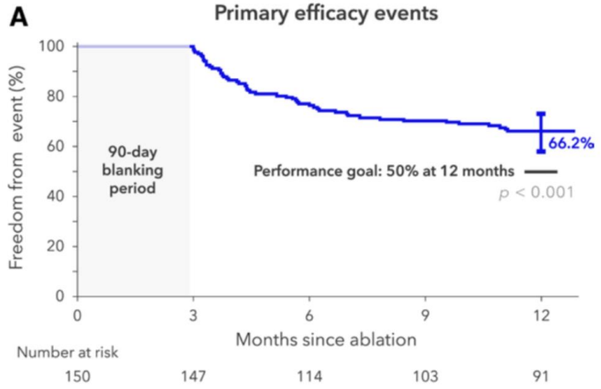

66.2% freedom from AA

Circulation

ORIGINAL RESEARCH ARTICLE

## Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial

Atul Verma, MD; David E. Haines, MD; Lucas V. Boersma, MD; Nitesh Sood, MD; Andrea Natale, MD; Francis E. Marchlinski, MD; Hugh Calkins, MD; Prashanthan Sanders, MBBS; Douglas L. Packer, MD; Karl-Heinz Kuck, MD; Gerhard Hindricks, MD; Birce Onal, PhD; Jeffrey Cerkvenik, MS; Hiroshi Tada, MD; David B. DeLurgio, MD; on behalf of the PULSED AF Investigators



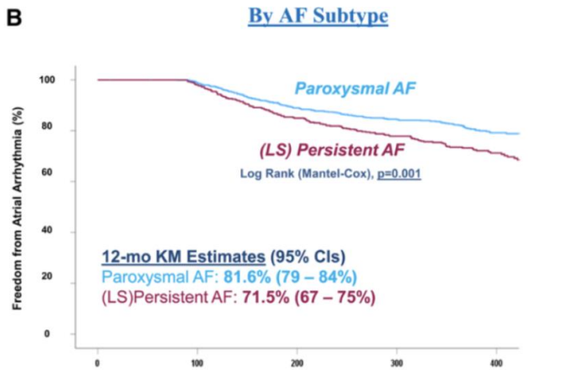

81.6% freedom from AA
- But only 66% pts >1 24h Holters

Circulation

ORIGINAL RESEARCH ARTICLE

## Safety and Effectiveness of Pulsed Field Ablation to Treat Atrial Fibrillation: One-Year Outcomes From the MANIFEST-PF Registry

Mohit K. Turagam, MD; Petr Neuzil, MD PhD; Boris Schmidt, MD; Tobias Reichlin, MD; Kars Neven, MD; Andreas Metzner, MD; Jim Hansen, MD; Yuri Blaauw, MD; Philippe Maury, MD; Thomas Arentz, MD; Philipp Sommer, MD; Ante Anic, MD; Frédéric Anselme, MD; Serge Boveda, MD, PhD; Tom Deneke, MD; Stephan Willems, MD; Pepijn van der Voort, MD; Roland Tilz, MD; Moritoshi Funasako, MD; Daniel Scherr, MD; Reza Wakili, MD; Daniel Steven, MD; Josef Kautzner, MD; Johan Vijgen, MD; Pierre Jais, MD; Jan Petru, MD; Julian Chun, MD; Laurent Roten, MD; Anna Füting, MD; Marc D. Lemoine, MD; Martin Ruwald, MD; Bart A Mulder, MD; Anne Rollin, MD; Heiko Lehrmann, MD; Thomas Fink, MD; Zrinka Jurisic, MD; Corentin Chaumont, MD; Raquel Adeliño, MD; Karin Nentwich, MD; Melanie Gunawardene, MD; Alexandre Ouss, MD; Christian-Hendrik Heeger, MD; Martin Manninger, MD; Jan-Eric Bohnen, MD; Arian Sultan, MD; Petr Peichl, MD; Pieter Koopman, MD; Nicolas Derval, MD; Thomas Kueffer, MD; Gilbert Rahe, MD; Vivek Y. Reddy, MD




## PFA Data

- Short/intermediate term efficacy comparable to RF/Cryo
- Complication risks similar as well
- Theoretical risk of collateral injury, esp esophageal injury leading to AEF is reduced
- Procedure times significantly shorter

# What are the risks and benefits of AF ablation?



**Risks:** between <1 to 10% reported depending on the experience of the center, operator

- "Generic" risks – vascular complications, thromboembolic complications, pericardial effusion and tamponade
- AF ablation specific risks
  - Pulmonary vein (PV) stenosis – nearly unheard of today due to more antral ablation techniques
  - Phrenic nerve injury – risk using cryo >>> RF, most recover within weeks to months
  - Atrio-esophageal injury – unpredictable, but high mortality (nearly 100% without intervention, 50-60% with surgical repair; true event rate is unknown, but probably in the range of 1:500 to 1:1000

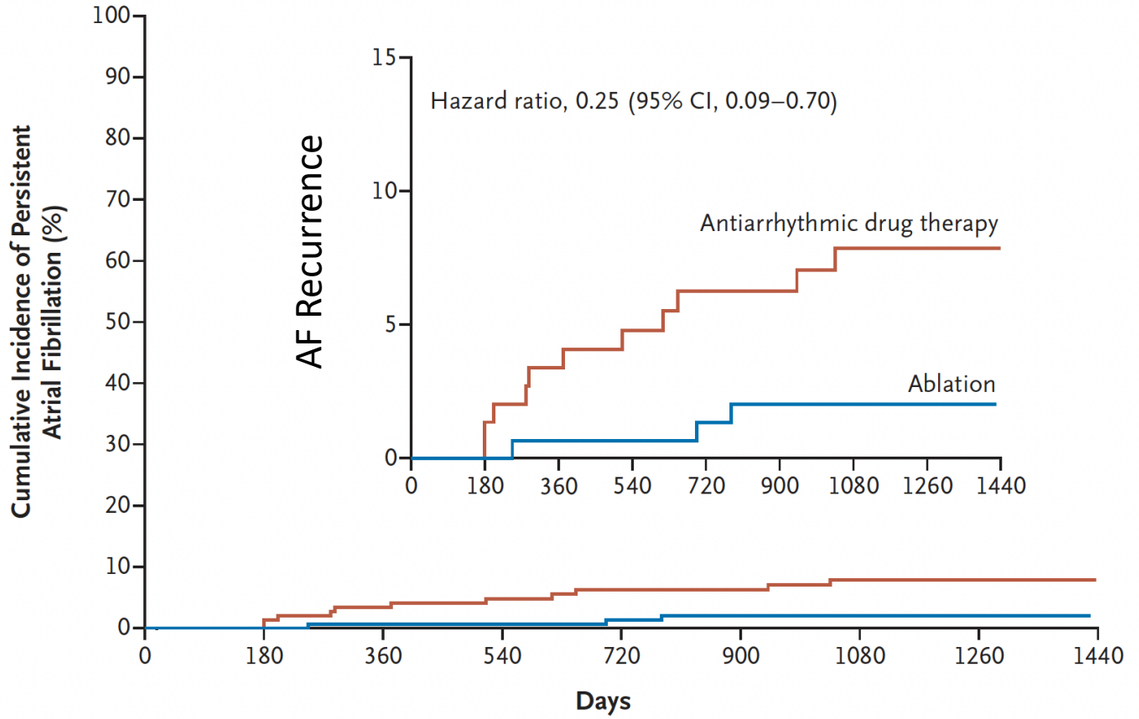
# First Line Catheter Ablation: Ready for Prime Time?

- Accumulating data in the modern era of ablation supports early ablation
- Early ablation improves freedom from AF long-term
- Consensus supports outcomes regardless of ablation modality (cryo, RF, other)
- Newer data incorporated into the newest guidelines (2020, 2024)

ORIGINAL ARTICLE

## Progression of Atrial Fibrillation after Cryoablation or Drug Therapy

J.G. Andrade, M.W. Deyell, L. Macle, G.A. Wells, M. Bennett, V. Essebag, J. Champagne, J.-F. Roux, D. Yung, A. Skanes, Y. Khaykin, C. Morillo, U. Jolly, P. Novak, E. Lockwood, G. Amit, P. Angaran, J. Sapp, S. Wardell, S. Lauck, J. Cadrin-Tourigny, S. Kochhäuser, and A. Verma, for the EARLY-AF Investigators*




*NEJM Nov 2022*

# AHA/ACC Guideline recommendations for ablation: 2025



## Class IA Recommendation:

- In patients failed/intolerant of AAD
- First line in select (younger, healthier) patients

## Class II Recommendation:

- 2A: *persistent* AF ablation as first line therapy in younger, healthier patients
- 2B: in select patients to prevent progression to permanent AF

| COR | LOE | Recommendations |
|---|---|---|
| 1 | A | 1. In patients with symptomatic AF in whom anti-arrhythmic drugs have been ineffective, contra-indicated, not tolerated or not preferred, and continued rhythm control is desired, cath-eter ablation is useful to improve symptoms.[1–10] |
| 1 | A | 2. In selected patients (generally younger with few comorbidities) with symptomatic parox-ysmal AF in whom rhythm control is desired, catheter ablation is useful as first-line therapy to improve symptoms and reduce progression to persistent AF.[11–16] |
| 1 | A | 3. In patients with symptomatic or clinically significant AFL, catheter ablation is useful for improving symptoms.[17–19] |

Joglar J, et al. *AHA/ACC/HRS 2024 guideline for the management of patients with atrial fibrillation.* Circulation, 2024.

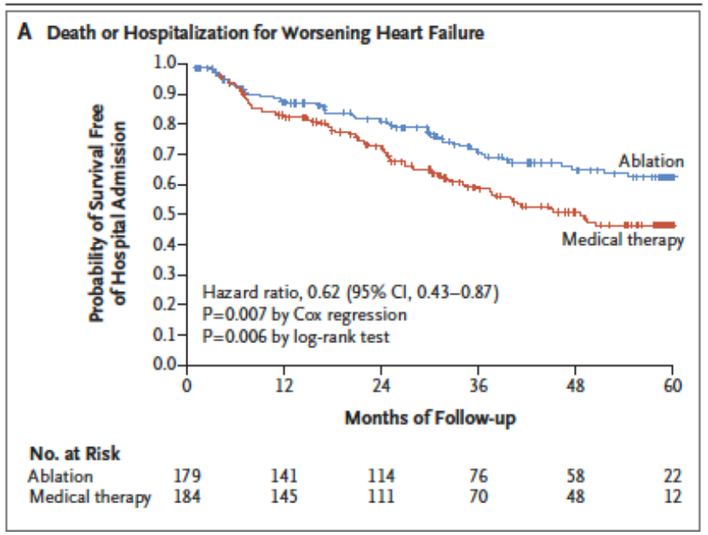
# Specific Population: AF in the Setting of CHF

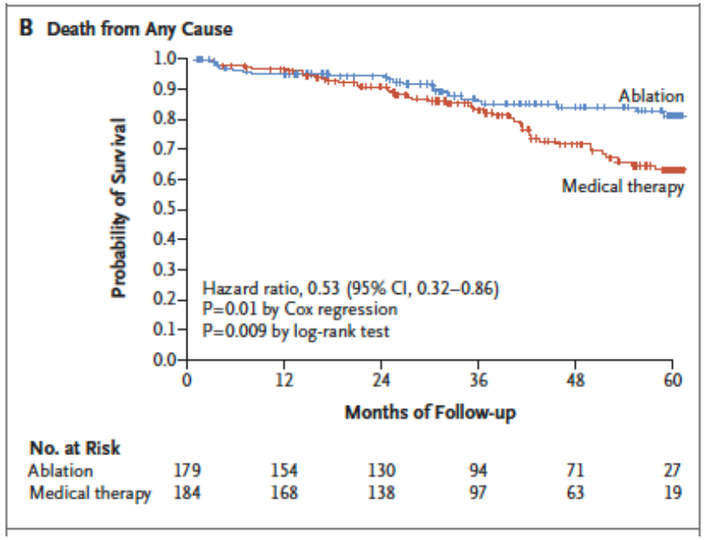


- **CASTLE-AF study** *(NEJM 2018)*
- 179 patients with HFpEF randomized to AAD vs. catheter ablation
- All outcomes favor ablation: composite death, HF hospitalization, all-cause mortality
- F/U Study **CASTLE-HTX** (NEJM 2023) demonstrates mortality benefit in advanced HFrEF patients

| | | |
|---|---|---|
| 1 | B-NR | 1. In patients who present with a new diagnosis of HFrEF and AF, arrhythmia-induced cardiomyopathy should be suspected, and an early and aggressive approach to AF rhythm control is recommended.[1,2] |
| 1 | A | 2. In appropriate patients with AF and HFrEF who are on GDMT, and with reasonable expectation of procedural benefit (Figure 24), catheter ablation is beneficial to improve symptoms, QOL, ventricular function, and cardiovascular outcomes.[3–13] |

Joglar J, et al. *AHA/ACC/HRS 2024 guideline for the management of patients with atrial fibrillation.* Circulation, 2024.



# 2025 Current Best Practices for Rhythm Control



- **Paroxysmal AF**
  - Ablation after failing medication is a Class IA indication
  - Ablation first line is a Class IA indication in younger, healtier patients, or with HFrEF
- **Persistent AF**
  - Ablation after failing medication is a Class IA indication
  - Ablation first line is a Class IIA indication in younger, healthier patients
- Overall AF: early rhythm control is superior to a "wait and see" approach (not incorporated in guidelines *yet*)
- As we are improving outcomes with ablation for rhythm control, a signal for **mortality benefit** is emerging

## Reduction in Major CV Outcomes

| AF-Related Outcome | Frequency in AF | Mechanism(s) |
|---|---|---|
| Death  | 1.5 - 3.5 fold increase | Excess mortality related to:<br>• HF, comorbidities<br>• Stroke |
| Stroke  | 20-30% of all ischaemic strokes, 10% of cryptogenic strokes | • Cardioembolic, or<br>• Related to comorbid vascular atheroma |
| LV dysfunction / Heart failure  | In 20-30% of AF patients | • Excessive ventricular rate<br>• Irregular ventricular contractions<br>• A primary underlying cause of AF |

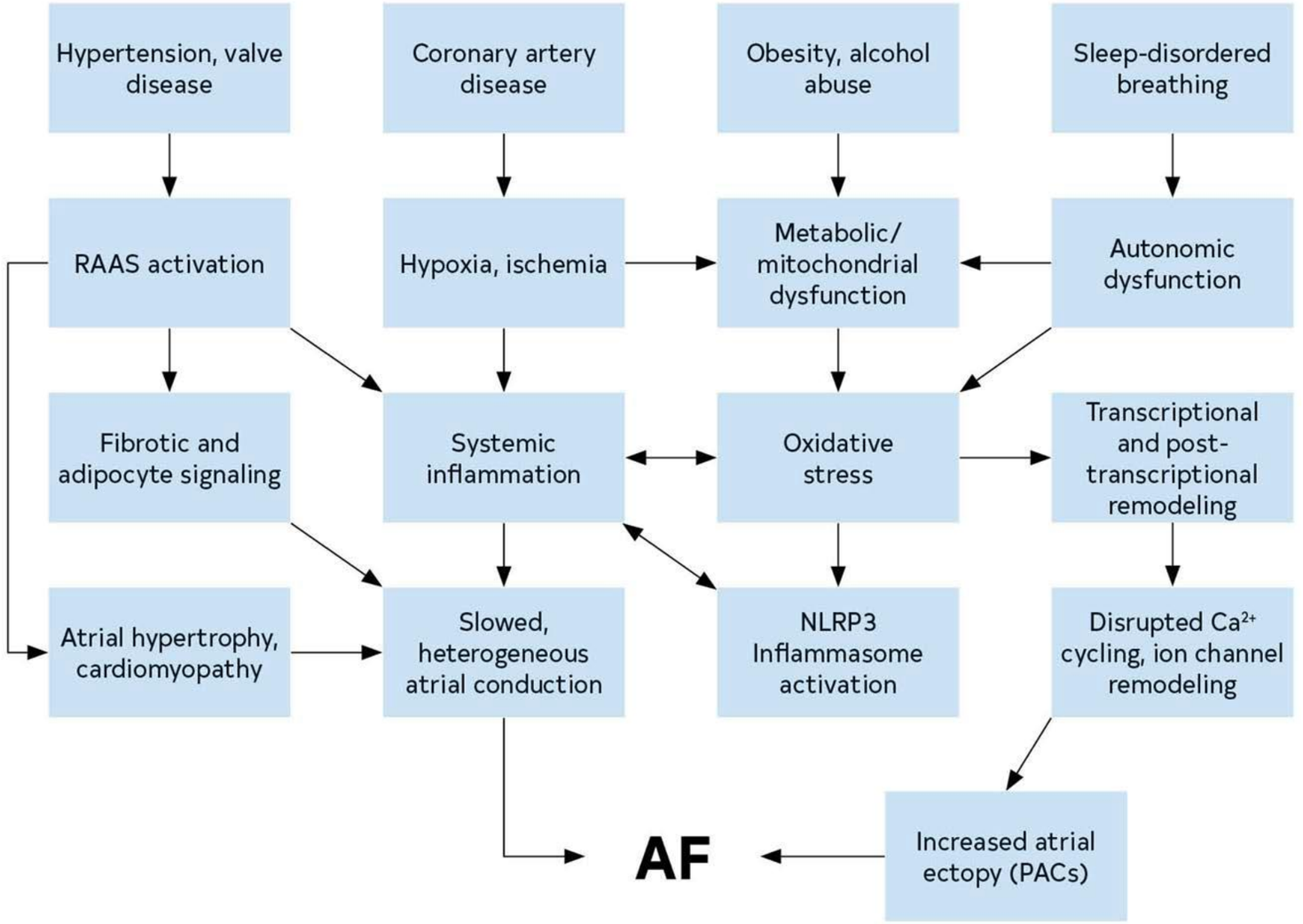
*ESC Guidelines 2020*

# Proposed mechanism for AF promotion in at-risk populations



The known modifiable MEDICAL risk factors in AF:

- Hypertension
- Obesity
- Diabetes
- Sleep apnea
- CAD

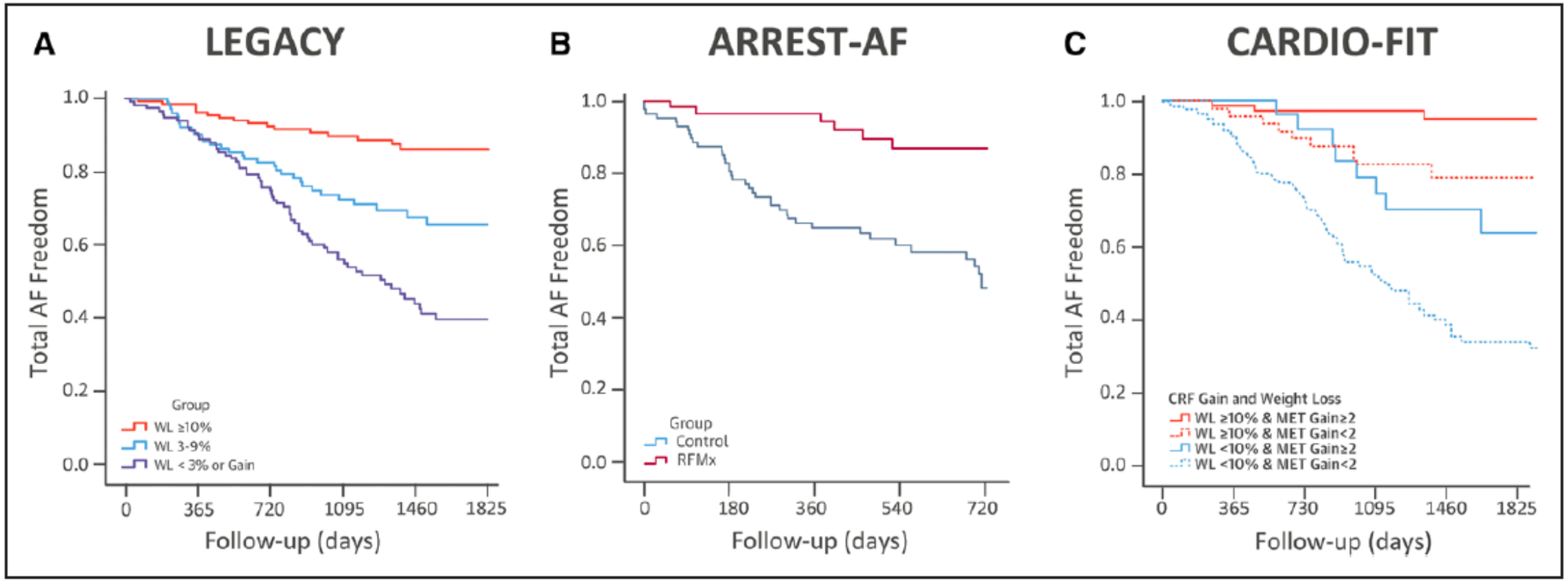



Treating the upstream inputs: Can we reduce AF incidence with reduction of these risk factors?

*AHA/ACC AF Guidelines 2024*

# Data supporting risk factor modification






- LEGACY – **weight loss** leads to reduced AF burden w/o ablation
- ARREST-AF – improved control of **multiple risk factors** reduces AF burden after AF ablation (HTN, DM, weight)
- CARDIO-FIT – improved **CV fitness** leads to decreased AF burden after AF ablation

*Sanders et al, Circ 2017*

# Data supporting lifestyle modification



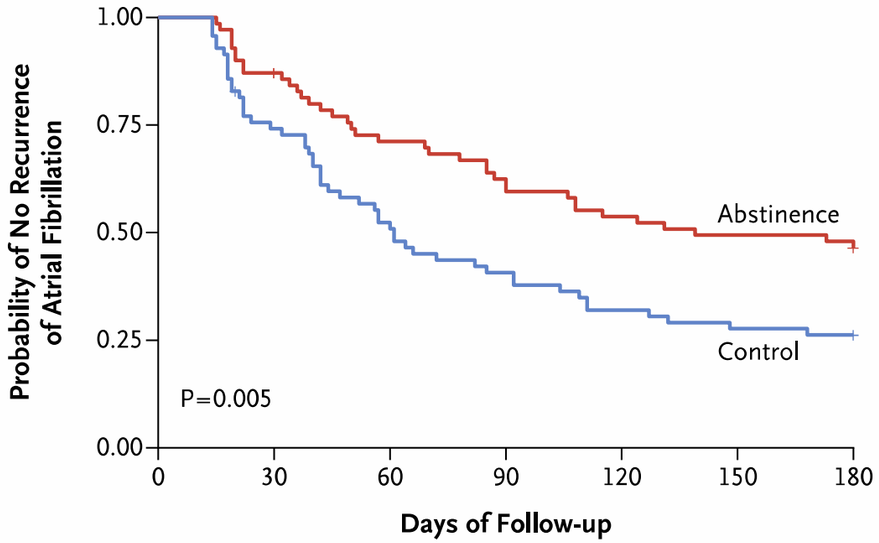


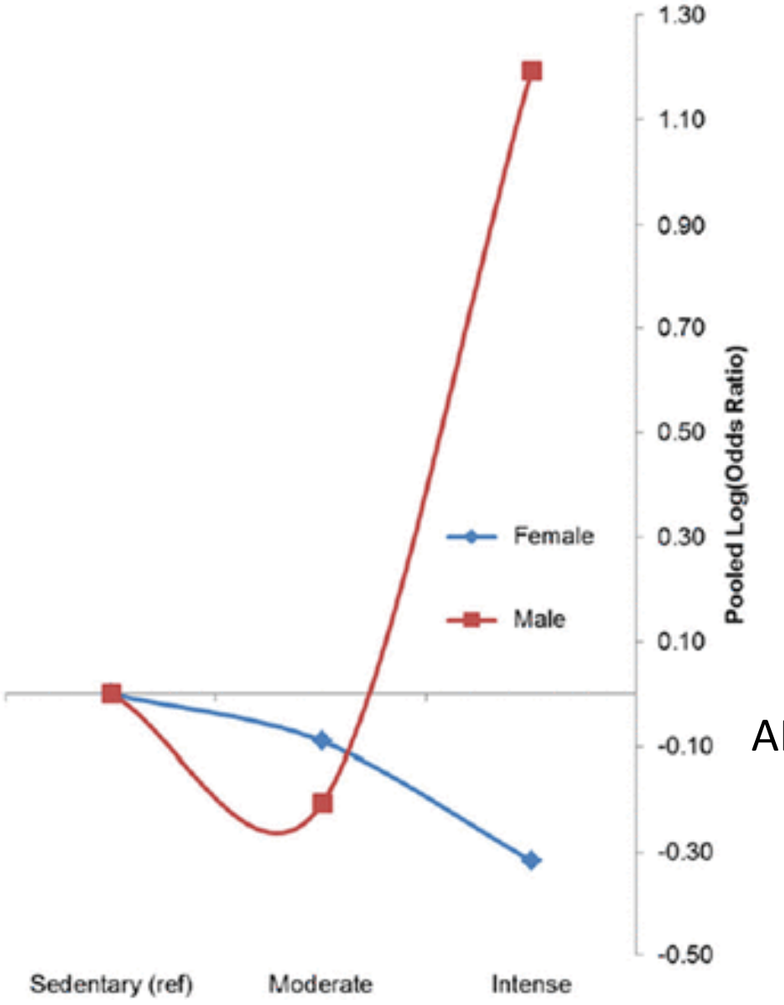

**Figure 2.** **Time to Recurrence of Atrial Fibrillation.**

- **Moderate to heavy alcohol drinkers** with AF: abstinence significantly reduces AF recurrence
- On the other hand, no studies to date have demonstrated an association between caffeine intake and AF risk or burden
- We are often asked about stress level and AF burden/risk, but this has been very challenging to study

*Voskoboinik et al, NEJM 2020*

# Exercise and AF burden

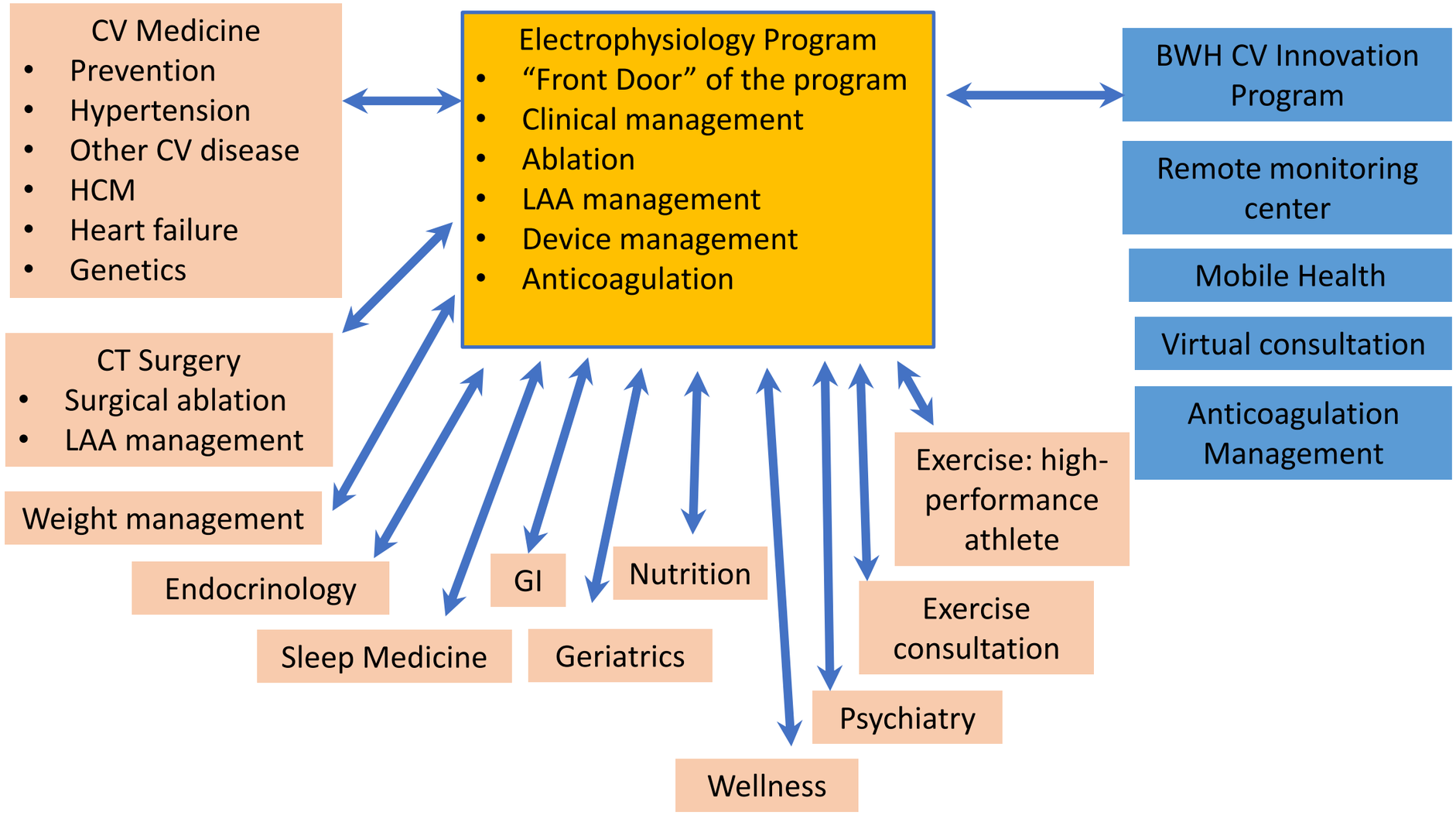





- Exercise quantity/burden demonstrates a ”U-shaped” relationship with AF incidence in males
- In females, data suggests decreasing incidence of AF with increasing AF burden
- In males, data suggest that there is such a thing as “too much exercise” as far as AF risk goes

# The New AF Treatment Paradigm: BWH Comprehensive AF Program

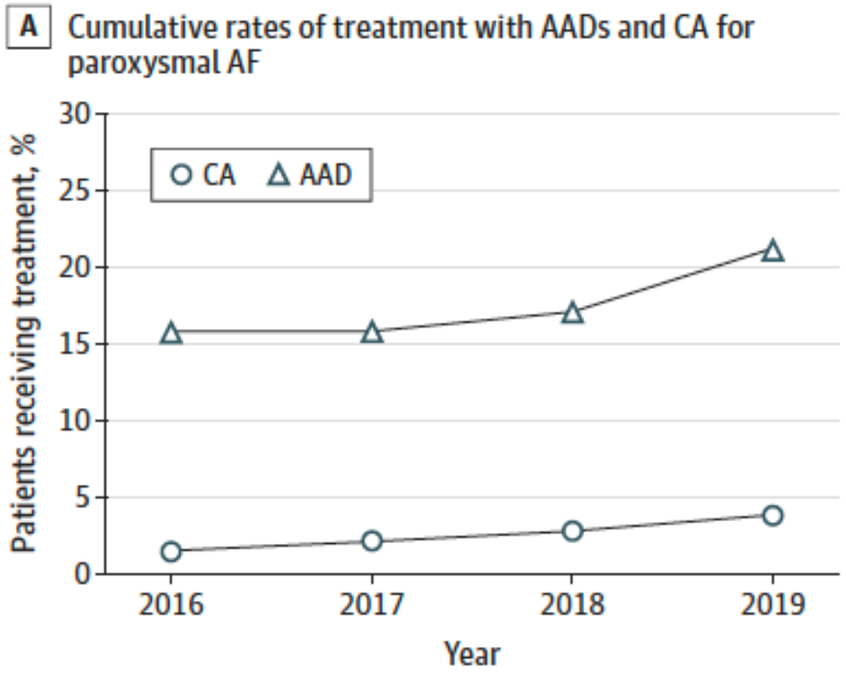


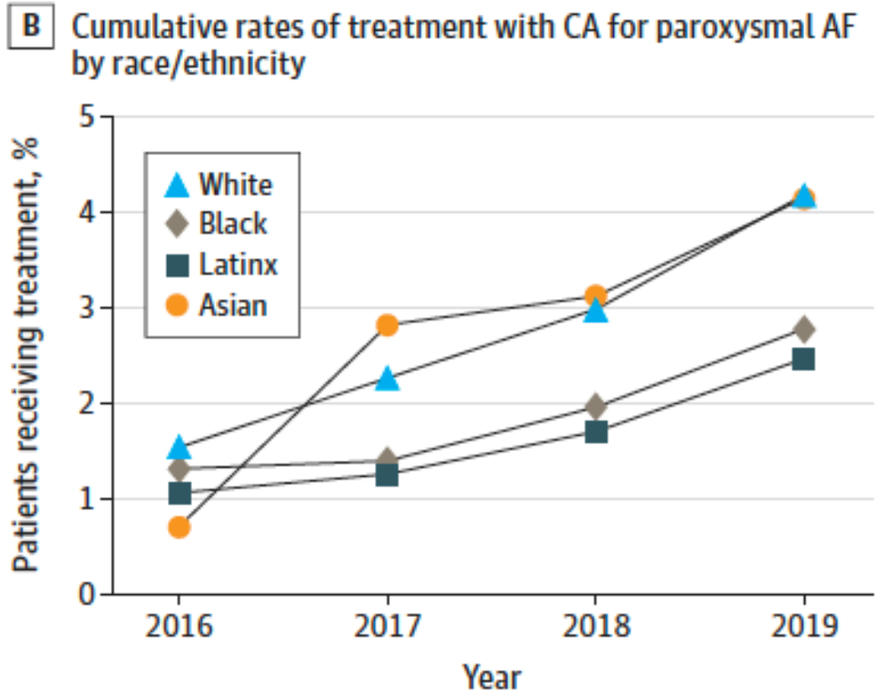


# Additional Challenges with AF Patient Management



RACE: Disparities persist in treatment for AF
- AAD and catheter ablation are relatively under-utilized among Blacks, Latinx




Eberly et al. *JAMA Network Open*. 2021

# Sex Differences in AF

## AF in Women:

- Lower incidence/prevalence compared to White men
- More likely to be symptomatic than men with AF
- More likely to receive rate control than rhythm control
- Less likely to receive stroke reduction therapies including:
  - Oral Anticoagulation
  - Left Atrial Appendage Occlusion
- Higher risk of stroke and heart failure
- Higher mortality compared to men

*Nat Rev Cardiol. 2017 Feb; 14 (2):113-124*
*Curr Cardiol Rev. 2019 May; 15(2): 136-144*
*JCE. 2020 Dec; 32(10): 2793-2807*

# Key Updates on the Management of Atrial Fibrillation in 2025



## Diagnosing AF, Clinical Manifestations

- AF clinical presentation is variable
- Clinicians will be seeing more and more patients with personal ECG devices
- What to do about personal data remains unclear – for now it is reasonable to take data into account in the course of standard medical diagnosis and management

## Cornerstones of therapy for AF:

- **Stroke prevention**
  - CHA2DS2-Vasc should guide anticoagulation (with patient individualization)
  - DOAC agents are recommended (except pts with mitral stenosis or mechanical heart valves)
- **Rhythm Control** – catheter ablation is superior to medication for maintaining sinus rhythm
  - Early rhythm control strategy results in mortality benefit and improved ability to maintain sinus rhythm
  - Current guidelines are moving gradually towards ablation as initial rhythm control in select patients
- **Risk factor modification**
  - Evaluation and treatment of known modifiable risk factors is indicated
  - Reduction of alcohol intake may improve AF outcomes
  - Exercise vs. AF burden has a complex relationship

# References



Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, Eckhardt LL, Goldberger ZD, Gopinathannair R, Gorenek B, Hess PL, Hlatky M, Hogan G, Ibeh C, Indik JH, Kido K, Kusumoto F, Link MS, Linta KT, Marcus GM, McCarthy PM, Patel N, Patton KK, Perez MV, Piccini JP, Russo AM, Sanders P, Streur MM, Thomas KL, Times S, Tisdale JE, Valente AM, Van Wagoner DR; Peer Review Committee Members. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024 Jan 2;149(1):e1-e156.

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# Thank you!



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