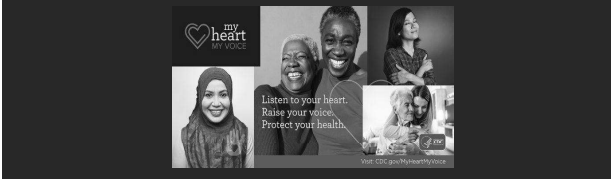


## Cardiac Update 2026: Women, Heart Disease and What's New.

JOHN PAGUNTALAN NP PHD



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### WHY WOMEN AND HEART DISEASE MATTER

- CARDIOVASCULAR DISEASE LEADING CAUSE OF DEATH IN WOMEN
- MORTALITY EXCEEDS ALL CANCERS COMBINED
- GENDER DIFFERENCES EXIST IN CAD, HF, AND AF
- PERSISTENT KNOWLEDGE GAPS AMONG CLINICIANS
- WOMEN EXPERIENCE
  - DELAYED DIAGNOSIS
  - LESS GUIDELINE DIRECTED MEDICAL THERAPY
  - WORSE OUTCOMES AFTER MI, HF AND HIGHER STROKE RISK IN AF

Regits-Zagrosek, Lancet, 2012

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### CORONARY ARTERY DISEASE AND WOMEN

- ATYPICAL SYMPTOMS ARE TYPICAL IN WOMEN
- CHEST PAIN REMAINS COMMON
- MORE FREQUENT
  - DYSPNEA
  - FATIGUE
  - NAUSEA
  - BACK, NECK, JAW PAIN

Canto et al. JAMA

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## PATHOPHYSIOLOGY IN WOMEN

- WOMEN MORE LIKELY TO HAVE
  - DIFFUSE ATHEROSCLEROSIS
  - LESS FOCAL EPICARDIAL OBSTRUCTION
  - ENDOTHELIAL DYSFUNCTION
  - MICROVASCULAR DISEASE

Shaw et al. JACC, 2009

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## INOCA – ISCHEMIA WITH NONOBSTRUCTIVE CORONARY ARTERIES

- UP TO 50-70% OF WOMEN WITH ANGINA HAVE NON-OBSTRUCTIVE DISEASE
- NOT BENIGN
  - INCREASED MACE
  - REDUCED QUALITY OF LIFE
- CORONARY MICROVASCULAR DYSFUNCTION, IMPAIRED CORONARY FLOW RESERVE
  - OFTEN MISSED ON CONVENTIONAL ANGIOGRAPHY
  - SPECIALIZED TESTING: CORONARY FLOW RESERVE, INDEX OF MICROCIRCULATORY RESISTANCE

Bairey et al. JACC, 2017  
Taqueti et al. Circulation 2018

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## DIAGNOSTIC BIAS AND DELAYS

- SYMPTOMS ARE MORE LIKELY ATTRIBUTED TO:
  - ANXIETY
  - GI OR MUSCULOSKELETAL ISSUES
- WOMEN PRESENT LATER
- LONGER DOOR TO BALLOON TIMES

Mehta LS et al. Circulation, 2016

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## ACUTE CORONARY SYNDROME IN WOMEN

- HIGHER IN-HOSPITAL MORTALITY AFTER MI
- YOUNGER WOMEN FARE WORSE
- LESS LIKELY TO RECEIVE:
  - EARLY INVASIVE THERAPIES
  - EVIDENCE-BASED PHARMACOTHERAPY

Mehta LS et al. Circulation, 2016

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## WARRIOR TRIAL (ACC, 2026)

- WOMEN MORE OFTEN PRESENT WITH INOCA. THIS STUDY IS THE LARGEST FOCUSING ON INOCA MANAGEMENT USING INTENSIVE THERAPY VERSUS USUAL CARE
  - INTENSIVE THERAPY – STATIN, ACEI/ARB, AND ASA
- NO SIGNIFICANT REDUCTION IN FIRST MACE VERSUS USUAL CARE
  - Challenge the notion that secondary prevention always work
- DESPITE NEUTRAL OUTCOMES, EVIDENCE SUPPORT ON TREATING RISK FACTORS, HTN, DYSLIPIDEMIA, ETC. IN WOMEN WITH ISCHEMIC SYMPTOMS

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## HEART FAILURE AND WOMEN

- HEART FAILURE WITH PRESERVED EJECTION FRACTION PREDOMINATES
- STRONG LINKS TO:
  - HYPERTENSION
  - OBESITY
  - DIABETES
- WOMEN LIVE LONGER WITH HF BUT EXPERIENCE:
  - MORE SYMPTOMS
  - LOWER QUALITY OF LIFE

Dunlay SM et al. Circulation 2017

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## HEART FAILURE Update (2022 ACC/AHA Heart Failure Guidelines)

- Chronic progressive condition that occurs when the heart is not able to meet the body's need for oxygen
- Based on Stage of HF
  - Stage A: At-risk for Heart Failure
  - Stage B: Pre-Heart Failure
  - Stage C: Symptomatic-Heart Failure
  - Stage D: Advanced Heart Failure
- Based on LVEF
  - HFrEF: <40% (HFmrEF: >40%)
  - HFmrEF: 41% to 49%
  - HFpEF: >50%

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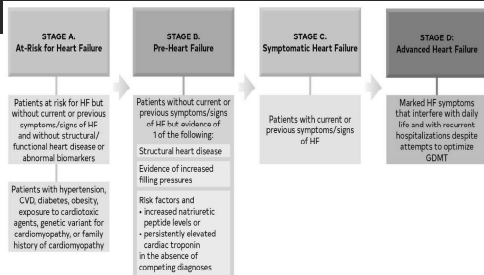


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## Stages of HF




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## HEART FAILURE SEVERITY

- Based on LVEF Criteria
  - HFrEF: <= 40%
  - HFmrEF: 41% to 49%
  - HFpEF: >= 50%
- HFimpEF >40% (previously HFrEF)

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## HEART FAILURE - MANAGEMENT

- Non-Pharmacologic - Dietary and Lifestyle changes
  - Sodium restriction
  - Regular physical activity/cardiac rehab – Class 2
- Pharmacologic Treatment
  - Diuretics – loop and thiazide diuretics
  - 4 PILLARS OF GDMT in HFrEF – ARNI, SGLT2i, BB, and MRA

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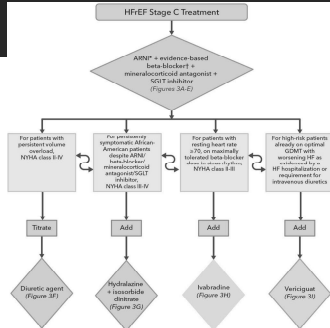


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### ■ HFREF




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## STEP – HFpEF Trial (JACC, 2024)

- In patients with obesity-related heart failure with preserved ejection fraction (HFpEF), women have greater symptom severity, greater exercise limitation, and more severe systemic inflammation than men.
- Semaglutide not only improved outcomes in women but resulted in higher weight loss than men
- Findings from STEP-HFpEF trial (Research Study to Investigate How Well Semaglutide Works in People Living With Heart Failure and Obesity) demonstrate that treatment with semaglutide reduced body weight in both women and men but resulted in greater weight loss in women.

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## SUMMIT TRIAL (NEJM, 2025)

- Obesity increases the risk of heart failure with preserved ejection fraction. Tirzepatide, causes considerable weight loss, but data are lacking with respect to its effects on cardiovascular outcomes.
- Treatment with tirzepatide led to a lower risk of a composite of death from cardiovascular causes or worsening heart failure and improved health status in patients with heart failure with preserved ejection fraction and obesity.
- IN WOMEN WITH HFPEF, OBESITY IS THE DISEASE ENGINE AND SUMMIT SHOWS TREATING THE ENGINE IMPROVES OUTCOMES

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## ATRIAL FIBRILLATION AND WOMEN

- ATRIAL FIBRILLATION MOST PREVALENT ARRHYTHMIAS:
  - HIGHER STROKE RISK IN WOMEN
  - LESS LIKELY REFERRED TO CARDIOLOGY, AND STARTED ON OAC
  - SEX DIFFERENCES IN AAD/RHYTHM CONTROL
- GREATER SUSCEPTIBILITY TO DRUG INDUCED QT PROLONGATION

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## PROGNOSIS AND COMPLICATIONS

Event	Association with AF
Death	Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke
Stroke	20-30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with latent, paroxysmal AF
Hospitalizations	15-40% of AF patients are hospitalized every year
Quality of life	Quality of life is impaired in AF patients independent of other cardiovascular conditions
Left ventricular dysfunction and heart failure	Left ventricular dysfunction is found in 20-30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF
Cognitive decline and vascular dementia	Cognitive decline and vascular dementia can develop even in unimpaired AF patients. Brain white matter lesions are more common in AF patients than in patients without AF

- Stroke
- Quality of Life
- LV dysfunction and HF
- Cognitive decline and vascular dementia

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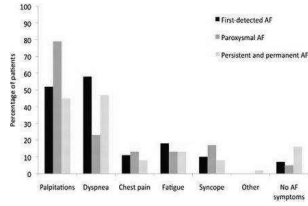
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## DIAGNOSIS

- Presentation – Signs and Symptoms
- History and Physical Exam
- 12 Lead ECG
- Heart Monitor
- Echocardiogram
- Stress Test
- Other tests: CXR, CCTA, heart cath (not routinely done)
- Labs: CMP, Mag, TSH reflex, CBC (also BNP, troponin, D-dimer)




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## AF GUIDELINE UPDATE 2023 (ACC,AHA,ACCP,HRS)



Stages of AF

At Risk, Pre-AF, AF sub-stages, Permanent AF



Substages of AF

Paroxysmal, Persistent, Long-standing Persistent, Successful Ablation



Diagnostic AND Treatment Algorithm

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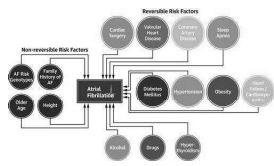


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## RISK FACTORS



- Reversible RF
  - Cardiac surgery, valvular disease, CAD, sleep apnea
  - DM, HTN, Obesity, HF, CM
  - Alcohol, Drugs, Hyperthyroidism
- Non-reversible RF
  - AF risk genotypes, family history
  - Older age -
  - Gender -
  - Height -

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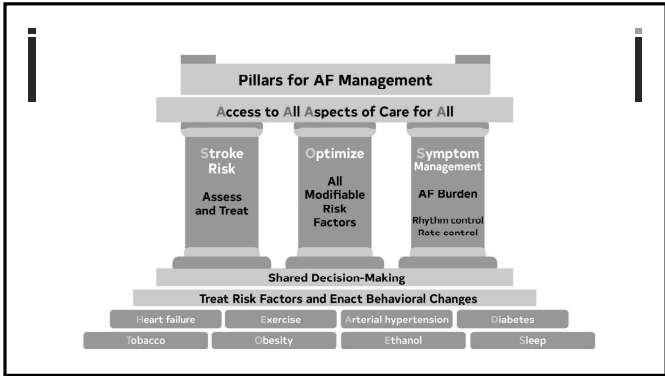
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### STROKE RISK AND ANTICOAGULATION – 1st pillar

- Oral anticoagulation for patients at risk for stroke
  - NOAC
  - VKA
- Risk prediction tool
  - CHADSVASC
  - HASBLED

CHADSVASC			
Congestive heart failure	1		
Hypertension	1		
Age >74	2		
Age 65-74	1		
Diabetes Mellitus	1		
Stroke/TIA	2		
Vascular disease	1		
Female	1		

HAS-BLED			
Hypertension (>160mmHg)	1		
Renal (dialysis, Transplant Cr >200)	1		
Liver (cirrhosis, LFTs Bil x2 or others x3)	1		
Stroke history	1		
Prior major bleed/predisposition	1		
High/Unstable INR	1		
Age >65 years	1		
Medication pre-empting to bleed	1		
Alcohol/Drugs (≥3 drinks/week)	1		

Yearly risk of Stroke, by score			
1	1.1%	2.2 (2%)	3.2 (2%)
4	4.0%	5.0 (7%)	6.0 (8%)
7	7.0 (6%)	8.0 (7%)	9.0 (5.2%)

Yearly risk of Major Bleed, by score			
0-1	1.0%		
2	1.8%		
3	3.7%		
≥4	>8%		

NICE recommend consideration of anticoagulation if score ≥0

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation  
 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;63:2268-80

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### LEFT ATRIAL APPENDAGE OCCLUSION DEVICE

Alternative to anticoagulation in patients with AF who are at high risk for stroke but has contraindications to anticoagulation

- PROTECTAF (Am Heart J, 2006) - non inferior to warfarin
- PREVAIL Trial (Lancet, 2009) - < 2% procedural complication, per cardiac diffusion
- ASAP Trial (JACC, 2013) - reasonable to transition without warfarin, 1.7% stroke rate, Superior to warfarin in CV mortality and hemorrhagic stroke prevention
- Longest studied closure device, FDA cleared device for use in March 2015.
- 2023 AF Guideline Update (ACA-AHA-ACC/HRS): LAO devices receive higher level Class of Recommendation, upgraded to Class 2A

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## RISK FACTOR MODIFICATION – 2nd pillar

- OBESITY
- OSA
- ALCOHOL AND SMOKING
- HTN
- DM
- PHYSICAL ACTIVITY
- Heart Failure
- Stress!
  - More pronounced in women
  - Several observational studies in PubMed support assertion that psych stress can trigger AF

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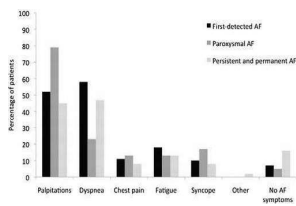


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## SYMPTOM CONTROL



- Rate control – leave patient in AF but keep heart rate under control to alleviate symptoms, prevent tachycardia mediated cardiomyopathy, control HR < 110 bpm
  - AFFIRM Trial 2002
  - RACE II Trial 2010
- Rhythm control – attempt to convert and keep patient in sinus rhythm
  - DCCV, AAD, ablation

Mitchell RN, et al. Clinical Status of Patients With Atrial Fibrillation. *Journal of Intensive Care Medicine*. 2010;25(1):1-10. DOI: 10.1177/0885066609349450

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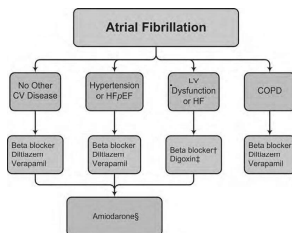


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## RATE CONTROL: AVN BLOCKING AGENTS



2014 AHA/ACC/HRS AF Guidelines

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## RHYTHM CONTROL

- RESTORATION AND MAINTENANCE OF SINUS RHYTHM
  - Cardioversion – acute symptoms, prognostication
  - AAD – antiarrhythmic drug therapy
    - Class Ic
    - Class IIIa
    - **Black Box Warning** – increase mortality and proarrhythmic effects
  - Catheter ablation

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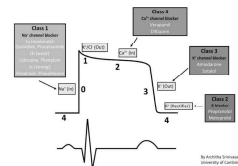
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## RHYTHM CONTROL: ANTI -ARRHYTHMIC DRUGS (AAD)

- Class Ic – Sodium channel blockers:
  - Flecainide (Tambacor) – 50 to 150 mg BID
  - Propafenone (Rythmol) – 225 mg ER BID, 150-300 BID
- Class III – Potassium channel blockers
  - Sotalol – (Betapace) 80-160 mg BID
  - Dofetilide (Tikosyn) – 125 to 500 mcg BID
  - Dronedarone (Multaq) – 400 mg BID
  - Amiodarone (Cordarone) – loading dose, various combinations, both IV and PO 400 mg BID for 5 days, 200 mg daily

Drugs Affecting the Cardiac Action Potential



**Side effects:** dizziness, fatigue, bradycardia, N/V, abdominal pain, hypotension, asthenia, sinus arrest, asystole, VT, Torsades, QT prolongation, HF, severe bradycardia, MI if abrupt DC

**BLACK BOX WARNING** - Increased mortality

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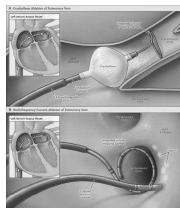
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## RHYTHM CONTROL – CATHETER ABLATION

- CATHETER Ablation - Procedure to modify, remove or terminate faulty electrical pathways using thermal energy
- RF ablation – conventional procedure
  - Heat energy to create transmural lesions
  - Long procedural and fluoroscopy time
- Cryoablation
  - Cold energy to isolate PV, alternative to RF
  - Limited to PV ostia
- Generally safe but invasive and tedious
  - Procedural risks - hematoma, pseudoANEURYSM, bleeding perforation, effusion, PV stenosis, phrenic nerve palsy, aorto-esophageal fistula, retroperitoneal bleeding, cardiac arrest, stroke, perforation, arrhythmias, and death
- **Pulse Field Ablation** – newest approach




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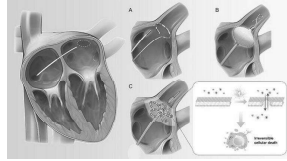
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## PULSE FIELD ABLATION

- Pulsed Field Ablation, is an innovative technique in cardiac electrophysiology for treating arrhythmias.
- Unlike traditional thermal energy, pulsed electric fields to induce irreversible electroporation (IRE).
- This approach selectively destroys abnormal heart tissue while preserving the structural integrity of surrounding healthy tissue.
- Less life-threatening complications
- Shorter procedural time



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## ADVENT Trial — Pulsed Field Ablation (PFA) for Paroxysmal Atrial Fibrillation. (NEJM, 2023)

- First randomized clinical trial to directly compare FARAPULSE™ Pulsed Field Ablation (PFA) with standard-of-care thermal ablation (radiofrequency or cryoballoon) for paroxysmal atrial fibrillation (PAF)
- **Efficacy:** At 1 year, PFA was **noninferior** to thermal ablation for freedom from recurrence, cardioversion, or repeat ablation [LCTMD](#).
- **Safety:** No long-term safety concerns; lower risk of esophageal or phrenic nerve injury compared to thermal ablation [American College of Cardiology](#).
- **Procedure times:** Less pulmonary vein narrowing with PFA, leading to shorter ablation and total procedure times
- **Clinical Implications:** PFA offers **noninferior efficacy** to thermal ablation with **improved safety and reduced collateral tissue injury**.
  - Long-term data show **comparable or better effectiveness** and **fewer hospital-based interventions**.
  - Lower AA burden may support a shift in ablation goals from "cure" to **successful management of AF** [American College of Cardiology](#).

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## A PARADIGM SHIFT IN AF TREATMENT

- Recent AF guideline UPDATE (2023 ACC/AHA/ACCP/HRS, 2024 ESC) emphasize early rhythm control over strict rate control to improve outcomes.
  - Class I recommendation for symptomatic paroxysmal AF
  - Class I recommendation for symptomatic AF and HFrEF
- Early intervention (within 12 months of diagnosis) is prioritized to reduce mortality, stroke, and heart failure hospitalization, especially in younger patients or those with heart failure, via [catheter ablation](#) or [antiarrhythmic drugs \(AADs\)](#).
  - Prevent progression of disease
  - Paroxysmal AF from turning into persistent AF, lowers success rate of interventions.

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### EAST AFNET 4 TRIAL, NEJM 2020

- The Early Treatment of AF for Stroke Prevention Trial (EAST-AFNET 4) was designed to test whether a strategy of early rhythm-control therapy that includes AF ablation would be associated with better outcomes in patients with early AF than contemporary, evidence-based usual care.
- Early-rhythm control therapy in patients with early AF and CV conditions was associated with a lower risk of death from cardiovascular causes, stroke, or hospitalization for heart failure or acute coronary syndrome than usual care over a follow-up time of more than 5 years, without affecting the number of nights spent in the hospital.
- Most patients (>70%) were asymptomatic at 1 and 2 years in both treatment groups, and the magnitude of change in LV function did not differ between the groups at 2 years.
- The incidence of the overall safety outcome events was similar in the two groups.

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### RECENT Studies – Favor Early Rhythm Control and Ablation

- Superiority of Early rhythm control (AAD,Ablation) in **symptomatic paroxysmal AF** compared to rate control strategy (EAST AFNET 4 Trial, 2020)
  - Rhythm control soon after diagnosis reduce CV death (not all cause) and complications, HF,ACS
  - First trial to challenge AFFIRM trial that rhythm control not superior to rate control
- Superiority of ablation in **symptomatic paroxysmal AF** compared to AAD
  - STOP AF 2021 - cryoablation superior to AAD in maintenance of SR
  - Early AF 2021 - cryoablation superior to AAD in preventing recurrence of AF
  - ATTEST trial, 2021 - early radiofrequency superior to AAD

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### Significant AF TRIALS

- HOLIDAY Monitor Study 2021
  - Alcohol intake increase the risk of AF, a glass of wine doubles the risk of AF
- ACTIVE AF Trial 2021
  - Supervised exercise program up to 210 min per week reduce AF recurrence by 33%
- APP - Based AF management program shows favorable outcomes in AF
  - eBRAVE-AF Trial 2022 app-based program better in detecting new onset AF than usual care, FDA-approved AF detection algorithm in Apple watch
- Sleep AF Trial 2022
  - CPAP reduce and reverse atrial remodeling
- Stroke AF Trial 2023 (January)
  - AF detection rate at 22% in 3 years using implantable cardiac monitoring devices/ILR versus 2.4% in usual care
  - highlights importance of continuous and extended monitoring in cryptogenic stroke

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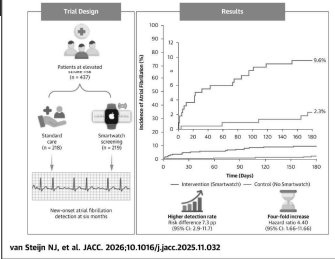
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## EQUAL TRIAL (JACC 2026)

- SMARTWATCH VERSUS USUAL CARE
- 47% WOMEN IN STUDY
- IMPROVED DETECTION OF AF
  - NEW ONSET
  - ASYMPTOMATIC

CENTRAL ILLUSTRATION: A Randomized Controlled Trial Investigating Smartwatch-Based Screening for Atrial Fibrillation




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## KEY POINTS

- ATYPICAL SYMPTOMS ARE TYPICAL IN WOMEN WITH CAD
- HIGHER INCIDENCE OF MICROVASCULAR DYSFUNCTION
- EXPERIENCE DELAYS IN DIAGNOSIS AND WORSE OUTCOMES IN MI
- HFpEF MORE COMMON IN WOMEN
- WOMEN MORE SYMPTOMATIC WITH HFpEF
- HIGHER RISK FOR STROKE IN AF
- LESS LIKELY TO RECEIVE OAC, TIMELY REFERRAL TO CARDIOLOGY CARE
- Most RECENT STUDIES with clinical implications in women
  - TREATING RISK FACTORS OF INOCA MAKES A DIFFERENCE IN WOMEN WITH CAD, Warrior Trial 2026
  - TREATING OBESITY IN HFpEF IMPROVE SYMPTOMS AND OUTCOMES IN WOMEN WITH HF, STEP-HFpEF, SUMMIT Trial 2025
  - USE OF SMARTWATCH OR PROLONGED MONITORING IMPROVE DETECTION OF AF, 47% women in study, EQUAL Trial 2026

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"It's easy to focus on mastering the science of medicine but the real art of medicine is to see the whole person in front of you."

John Paguntalan NP PhD

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