91st Annual Meeting of the German Cardiac Society

Perspectives on cardiovascular precision medicine – from prevention to intervention

Congress Center Rosengarten , Mannheim April 24, 2025

NIP (IT) IN THE BUD

To stop at an early stage; to take care of a problem in its early stages before it develops into a larger problem

Explanation
A bud is a young flower that has not yet opened. Nip means to "cut". If you nip a bud, you stop the flower (bud) from opening and growing

Example
If a patient presents with AF, sinus rhythm should be restored and maintained as soon as possible rather than let it persist, progress, damage and become refractory to treatment

"im Keim ersticken" or "den Anfängen wehren"

DGK-AFNET Lecture on Arrhythmias

"AF burden, Early AF ablation and Atrial Cardiomyopathy: New Concepts in AF 2025"

"Nipping Atrial Fibrillation in the Bud"

A. John Camm

St George's University of London

Declaration of Competing Interests

Editorial Role: Editor-in-Chief, Clinical Cardiology; Editor-in-Chief, European Textbook of Cardiology and ESC CardioMed.

Charities: Trustee of the Drug Safety Research Unit, the Atrial Fibrillation Association and the Arrhythmia Alliance

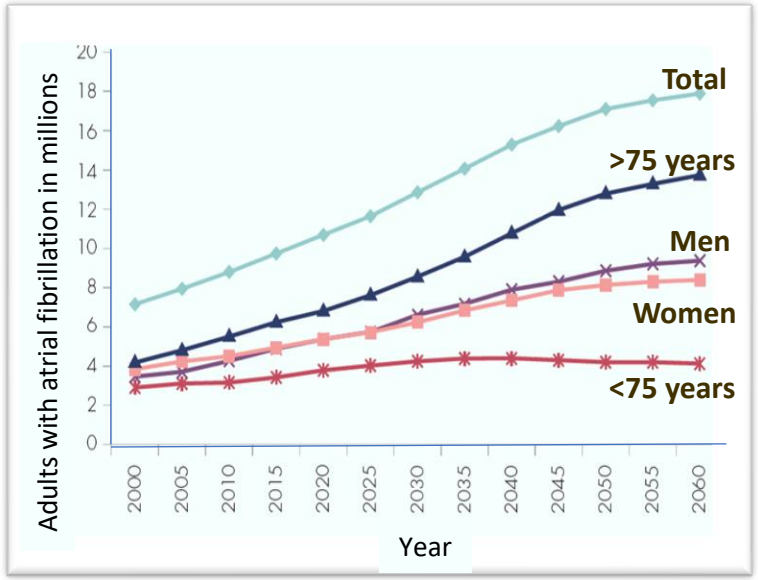
Directorship: Richmond Pharmacology Limited

Consultant/Advisor/Speaker: Acesion, Anthos, Milestone, Abbott, Biosense Webster, Boston Scientific, Johnson and Johnson

A.John Camm
St George's
University of London

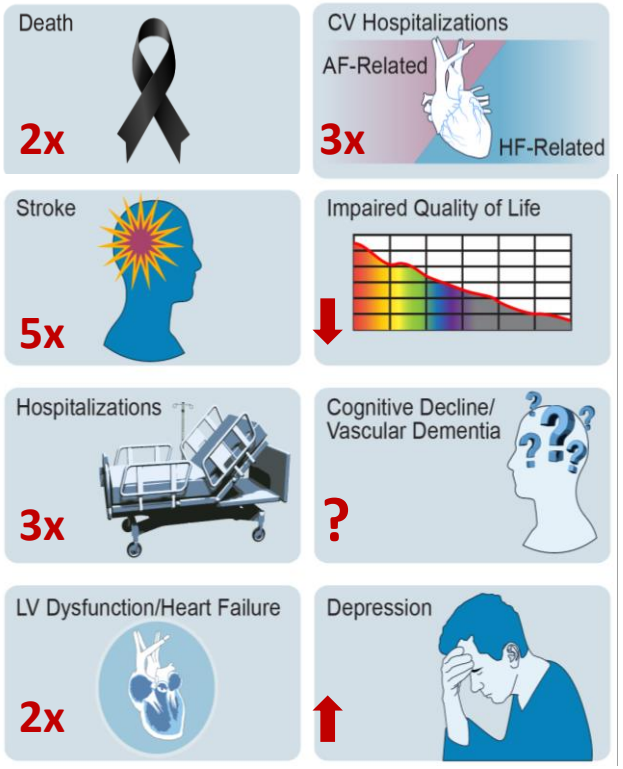
Management of Paroxysmal and Persistent AF

High Prevalence

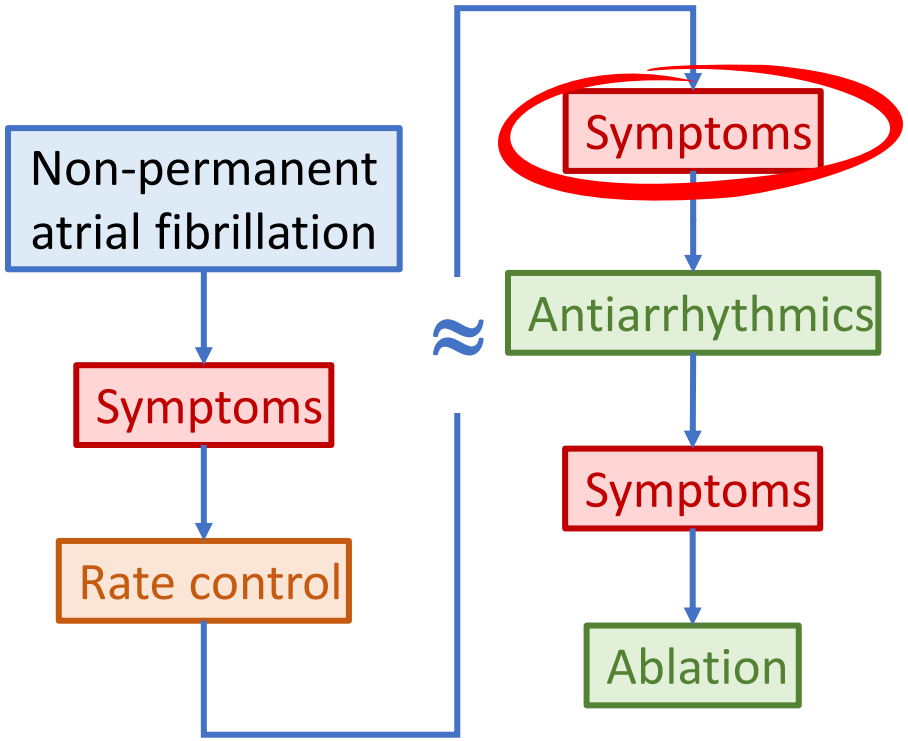


EU AF Prevalence is estimated at 10 million today and is predicted to double by 2060

Adverse Outcomes



Guideline Management



Krijthe, B.P., et al. EHJ 2013; 34: 2746–51; 2) World Health Organization. http://www.euro.who.int/en/health-topics/noncommunicable-diseases 3) Hindricks G, et al. Eur Heart J. 2021;42:373-498, 4) Camm AJ, et al. J Amer Coll Cardiol April 2022

Task Force Report

ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation

A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology

"Conversion to and maintenance of sinus rhythm offers the theoretical advantages of reducing the risk of thromboembolism and consequently the need for chronic anticoagulation, but drugs used to control heart rate are generally considered safer than those with an antiarrhythmic effect. The relative merit of these 2 approaches — rhythm control vs. rate control — is the subject of ongoing clinical trials[178,179]. Limited available data suggest no clear advantage of one approach over the other[179]…"

179: Hohnloser SH, Kuck KH, Lilienthal J. Rhythm or rate control in atrial fibrillation: Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. Lancet 2000; 356: 1789–94.

252 patients; Amiodarone vs Diltiazem, Follow-up 12 months, Amio 23% cardioverted
QOL no difference, Walking distance improved with Amiodarone, Hospitalisation more with Amiodarone

AJC St George's University of London

European Heart Journal (2001) 22, 1852–1923

Rate versus Rhythm Control Trials

AFFIRM

The New England Journal of Medicine

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VOLUME 347 DECEMBER 5, 2002 NUMBER 23

A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS*

ABSTRACT

Background There are two approaches to the treatment of atrial fibrillation: one is cardioversion and treatment with antiarrhythmic drugs to maintain sinus rhythm, and the other is the use of rate-controlling drugs, allowing atrial fibrillation to persist. In both approaches, the use of anticoagulant drugs is recommended.

Methods We conducted a randomized, multicenter comparison of these two treatment strategies in patients with atrial fibrillation and a high risk of stroke or death. The primary end point was overall mortality.

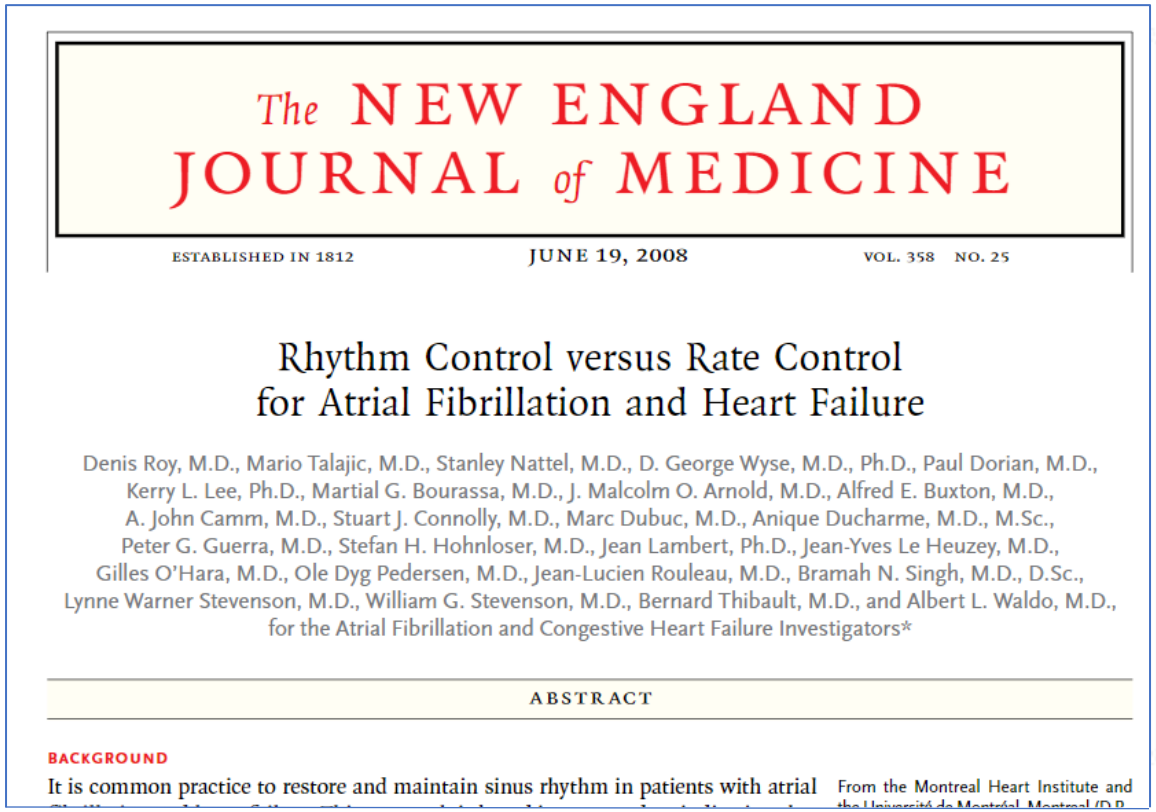
Results A total of 4060 patients (mean [±SD] age, 69.7±9.0 years) were enrolled in the study; 70.8 per-

ATRIAL fibrillation is the most common sustained cardiac arrhythmia, yet the optimal strategy for its management remains uncertain.[1-4] During atrial fibrillation, most symptoms (but perhaps not all) are caused by a poorly controlled or irregular ventricular rate, and the associated risk of death is doubled in patients who have a history of atrial fibrillation.[5-10] Although adequate anticoagulation with warfarin substantially lowers the risk of stroke,[11-13] this drug is frequently not administered.[14]

Initial therapy for atrial fibrillation is often directed toward the maintenance of sinus rhythm by means of

N Engl J Med. 2002 Dec 5;347(23):1825-33

AF-CHF



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 19, 2008 VOL. 358 NO. 25

Rhythm Control versus Rate Control for Atrial Fibrillation and Heart Failure

Denis Roy, M.D., Mario Talajic, M.D., Stanley Nattel, M.D., D. George Wyse, M.D., Ph.D., Paul Dorian, M.D., Kerry L. Lee, Ph.D., Martial G. Bourassa, M.D., J. Malcolm O. Arnold, M.D., Alfred E. Buxton, M.D., A. John Camm, M.D., Stuart J. Connolly, M.D., Marc Dubuc, M.D., Anique Ducharme, M.D., M.Sc., Peter G. Guerra, M.D., Stefan H. Hohnloser, M.D., Jean Lambert, Ph.D., Jean-Yves Le Heuzey, M.D., Gilles O'Hara, M.D., Ole Dyg Pedersen, M.D., Jean-Lucien Rouleau, M.D., Bramah N. Singh, M.D., D.Sc., Lynne Warner Stevenson, M.D., William G. Stevenson, M.D., Bernard Thibault, M.D., and Albert L. Waldo, M.D., for the Atrial Fibrillation and Congestive Heart Failure Investigators*

ABSTRACT

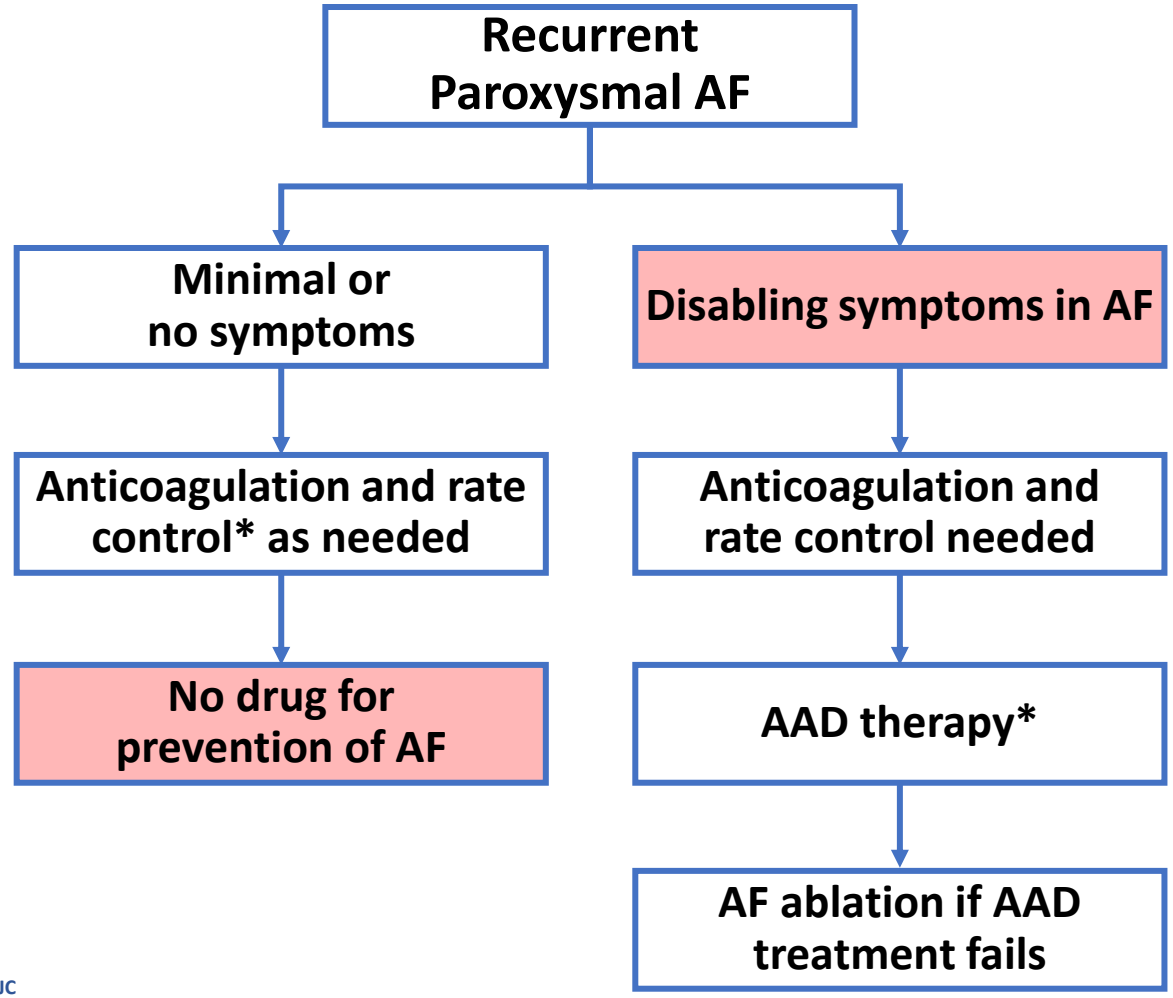
BACKGROUND

It is common practice to restore and maintain sinus rhythm in patients with atrial

From the Montreal Heart Institute and

Roy D, et al. N Engl J Med. 2008 Jun 19;358(25):2667-77

ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation



Persistent AF

When AF persists, one option is to accept progression to permanent AF, with attention to antithrombotic therapy and control of the ventricular rate.

……the decision to attempt restoration of sinus rhythm should be based on the severity of arrhythmia-related symptoms and the potential risk of antiarrhythmic drugs.

Fuster V, et al. 2006 Circulation. 2006;114:e257-e354

These Results Were Not Intuitive

*...the notion of a patient **continuing to live with an auricle incapable of contraction** is a somewhat novel idea...*

….it seems necessary to devote a little study to the condition”

Thomas Lewis, 1902

These Results Were Not Intuitive

Thomas Lewis, 1902

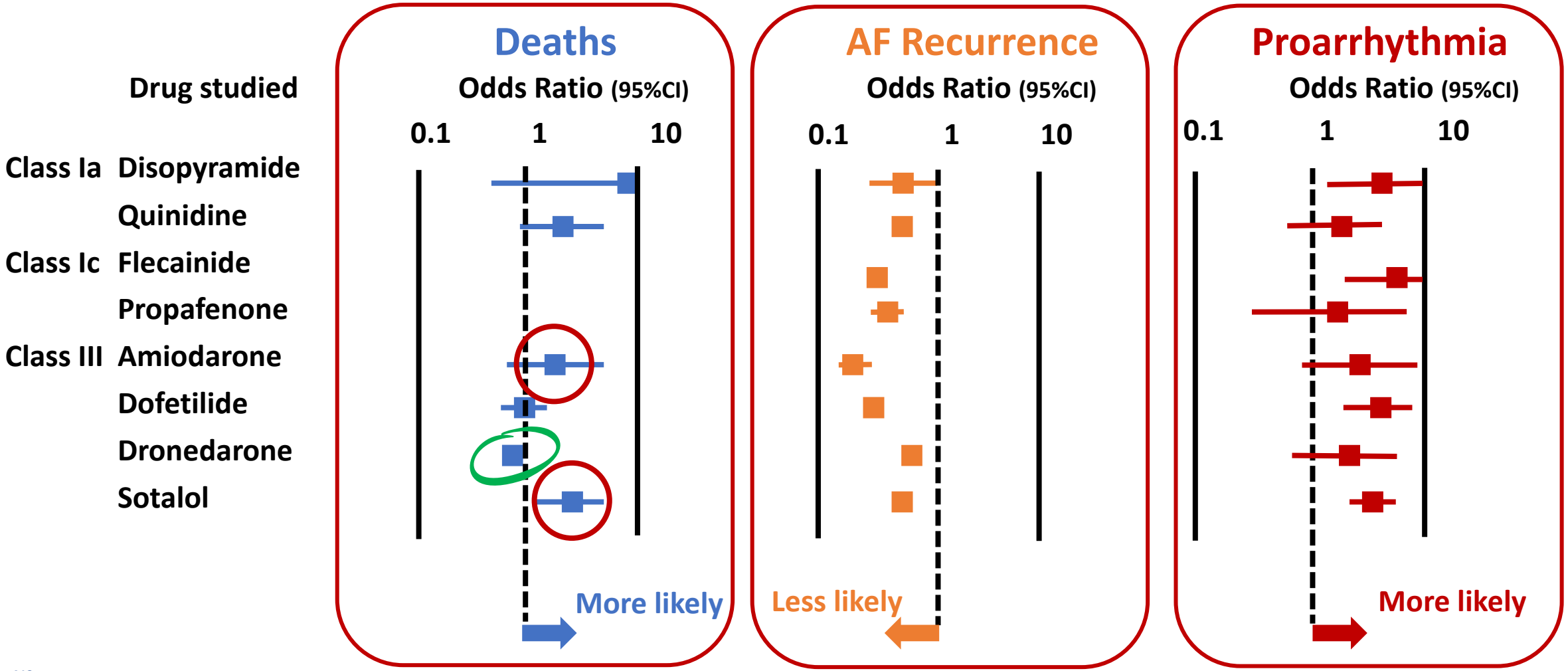
How could this have happened?

*...the notion of a patient **continuing to live with an auricle incapable of contraction** is a somewhat novel idea...*

….it seems necessary to devote a little study to the condition"

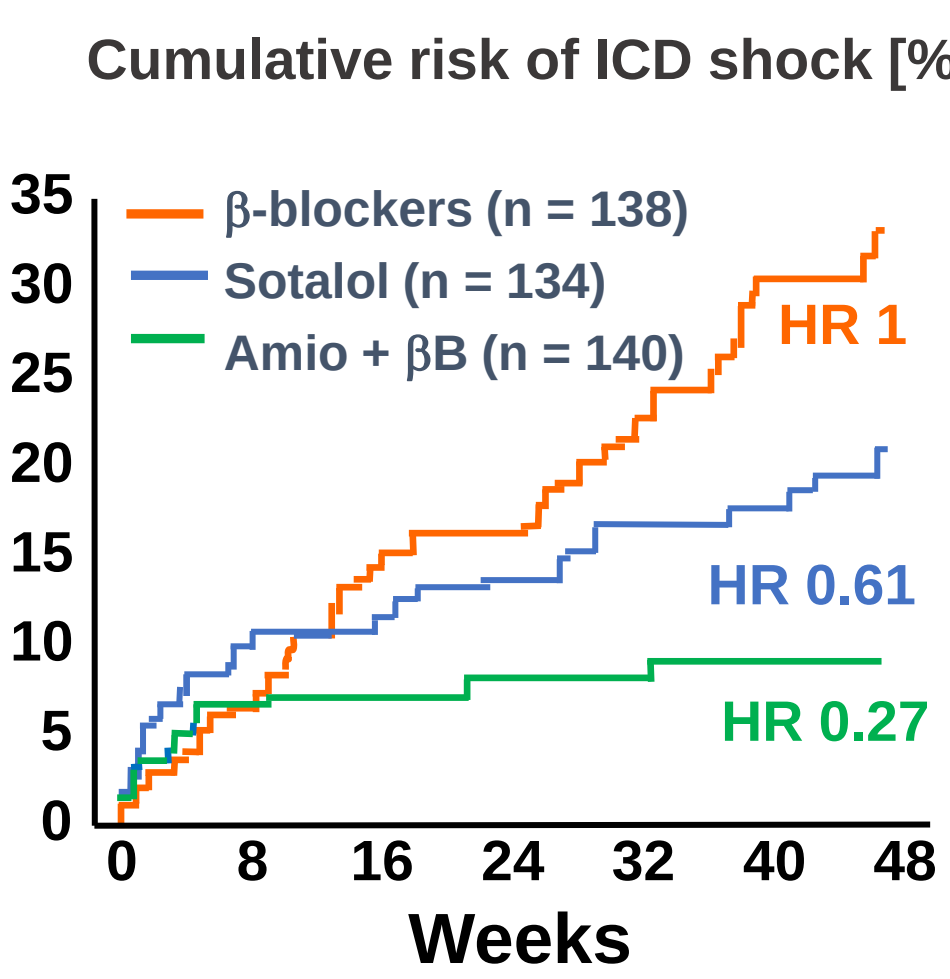
- Oral anticoagulation should not be abandoned after rhythm control
- **Toxic effects of antiarrhythmic drugs**
- Less effective treatment of underlying comorbidities
- Less active management of AF with available AADs
- **Relatively elderly populations**
- **Antiarrhythmic drug with proven value in reducing "hard" cardiovascular outcomes were not available**
- **Left atrial ablation was not a therapeutic option**
- **Trials "relatively" were short compared with a lifetime in AF vs SR**

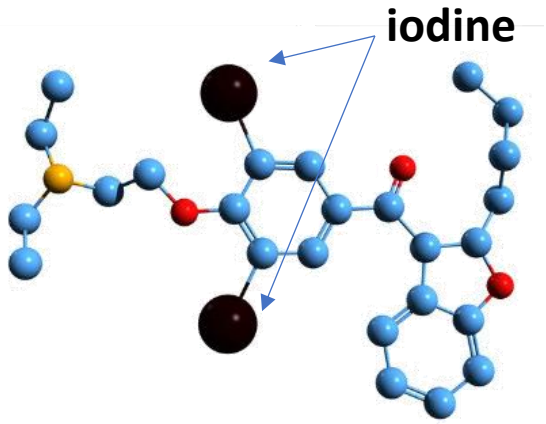
Cochrane Review
Antiarrhythmic Drug Treatment for AF



Lafuente-Lafuente C, et al. Cochrane Database Syst Rev. 2015 28:CD005049

Amiodarone: Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients





Amiodarone
Blue Man Syndrome

- Thyroid abnormalities
- Corneal microdeposits
- Lung fibrosis
- Hepatic dysfunction
- Photosensitivity
- Neuropathy

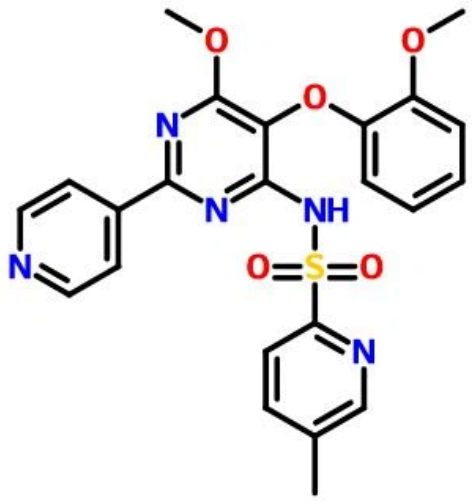
Elimination half-life is of 58 days (ranging from 15 to 142 days)

Metropolitan Museum of Modern ART

AJC St George's University of London

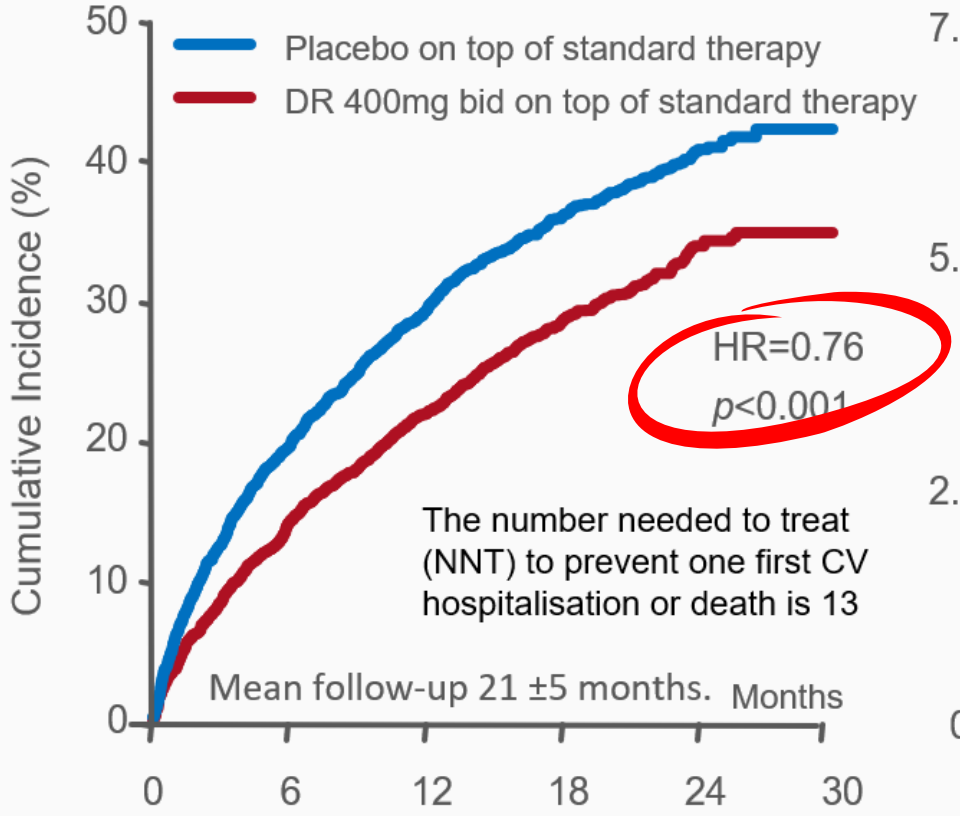
Connolly SJ, et al. JAMA. 2006 Jan 11;295(2):165-71

Dronedarone in the ATHENA Trial

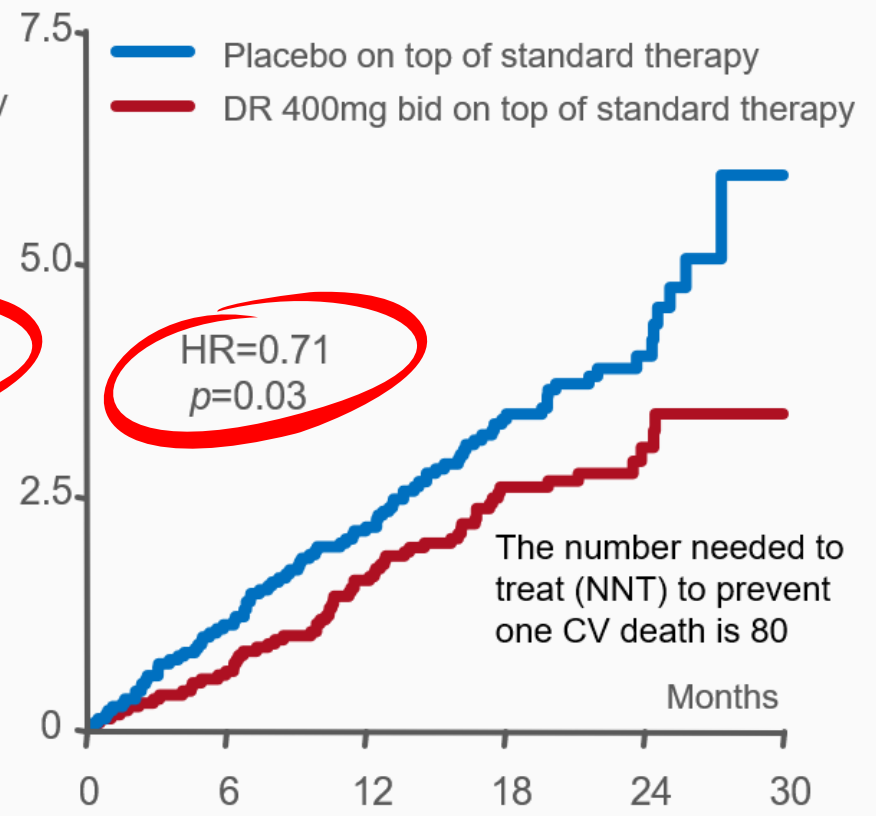


The **only antiarrhythmic drug** to demonstrate in patients with high-risk non-permanent AF a reduction in MACE endpoints in a randomised controlled trial

Dronedarone significantly decreased risk of unplanned CV hospitalisation or death from any cause by 24%

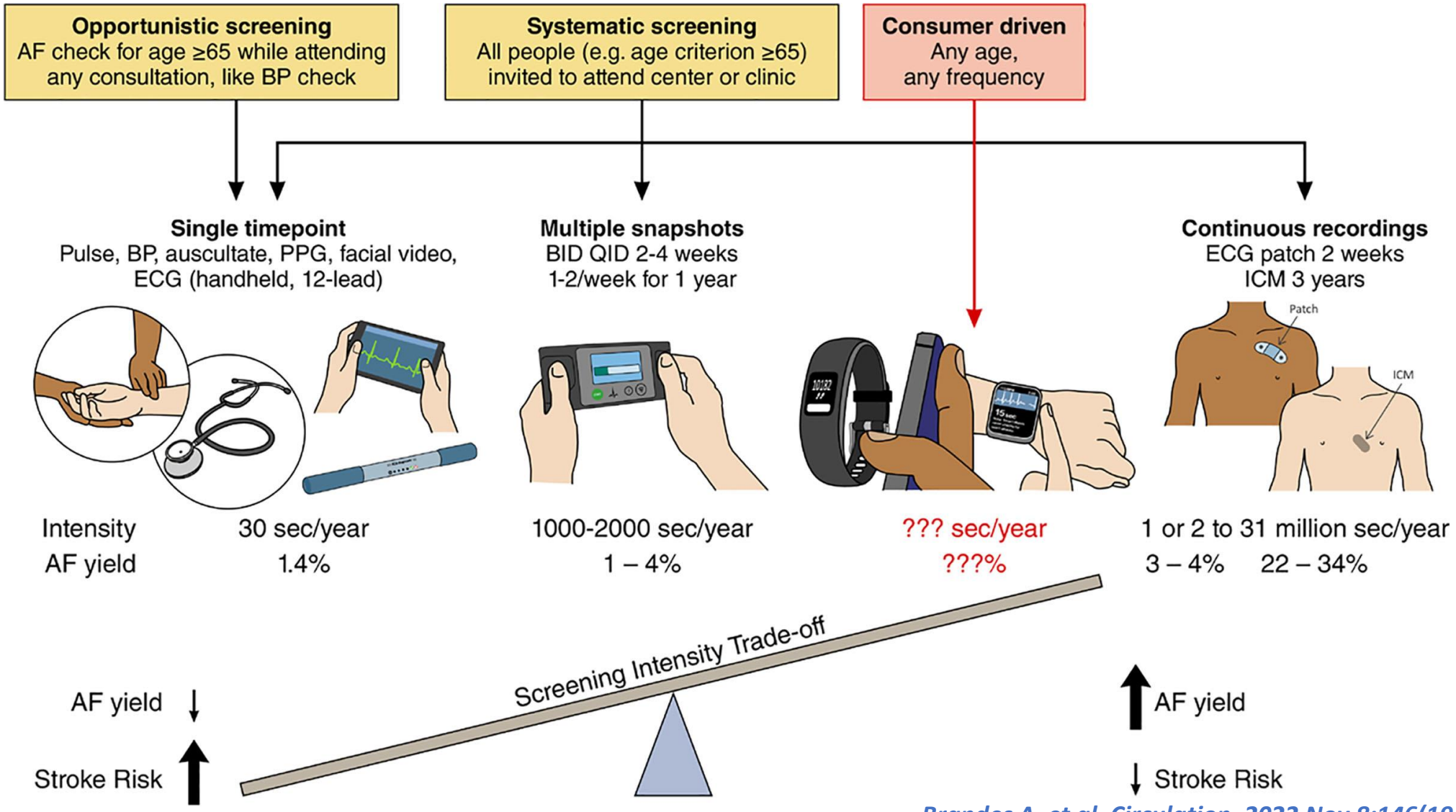


Dronedarone significantly decreased risk of CV death by 29%



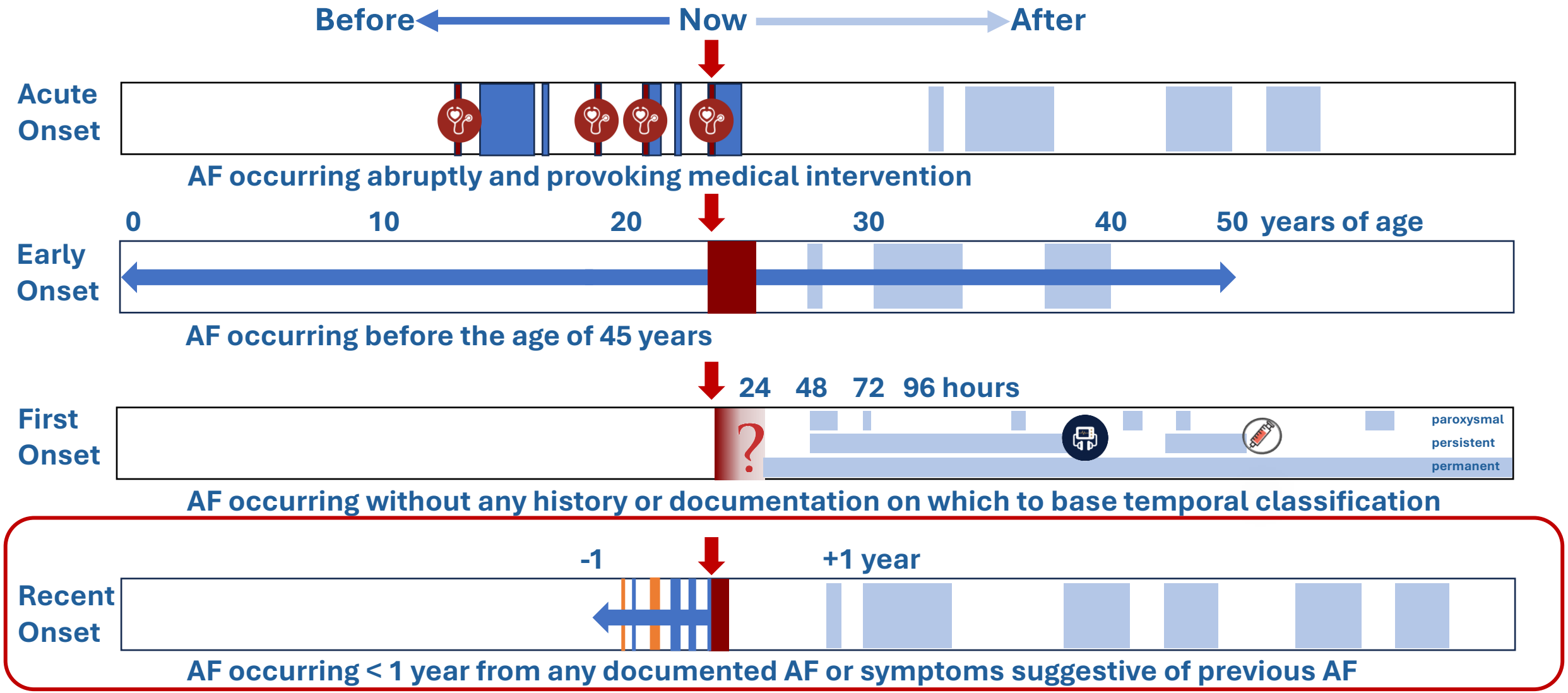
Hohnloser SH, et al. N Engl J Med 2009;360:668-78.

Deluge of Recent Onset AF



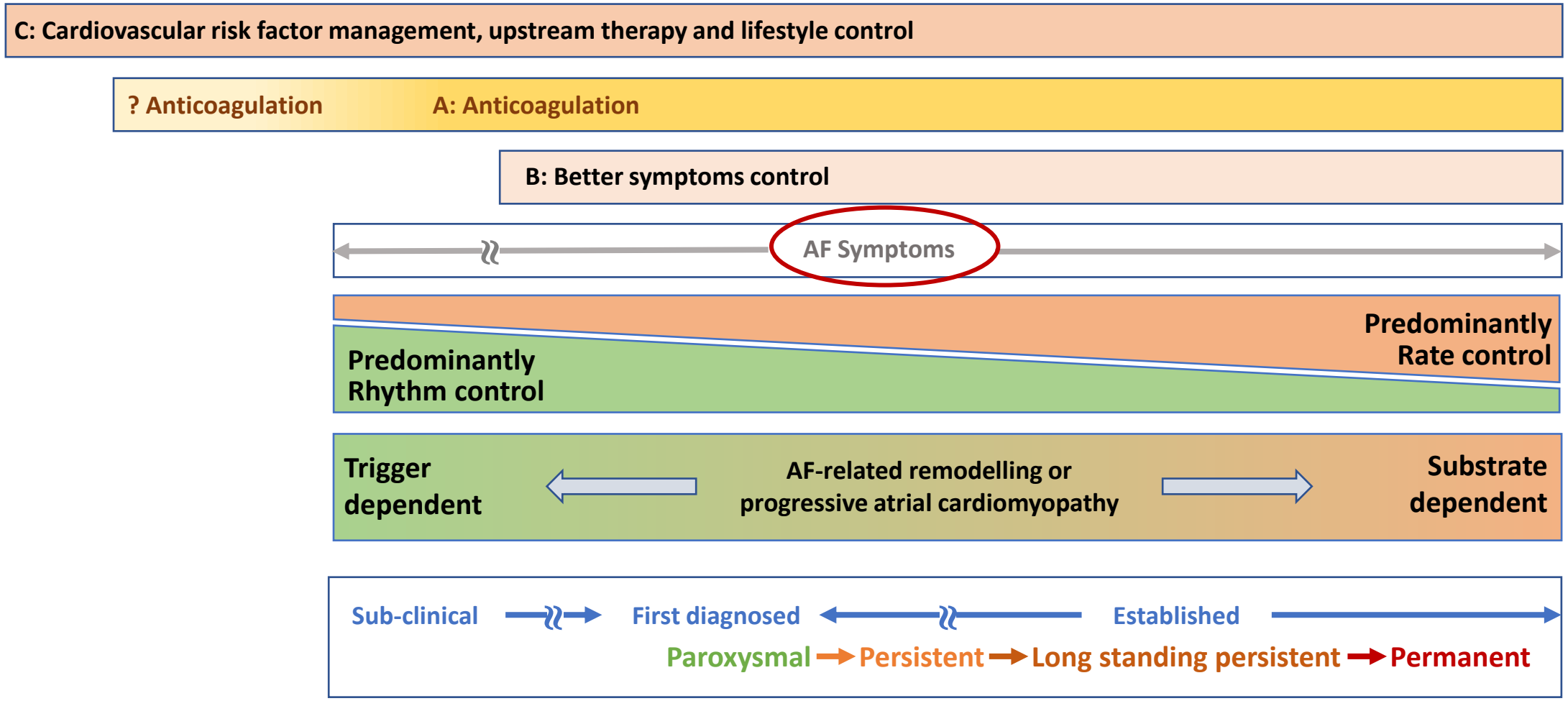
Brandes A, et al. Circulation. 2022 Nov 8;146(19):1461-1474

Acute, Early, First and Recent-Onset AF*



** these forms of AF are not mutually exclusive*

Atrial Fibrillation is a Dynamic Disease



Camm AJ, et al. J Amer Coll Cardiol April 2022

New Onset AF in Large USA Academic Centre

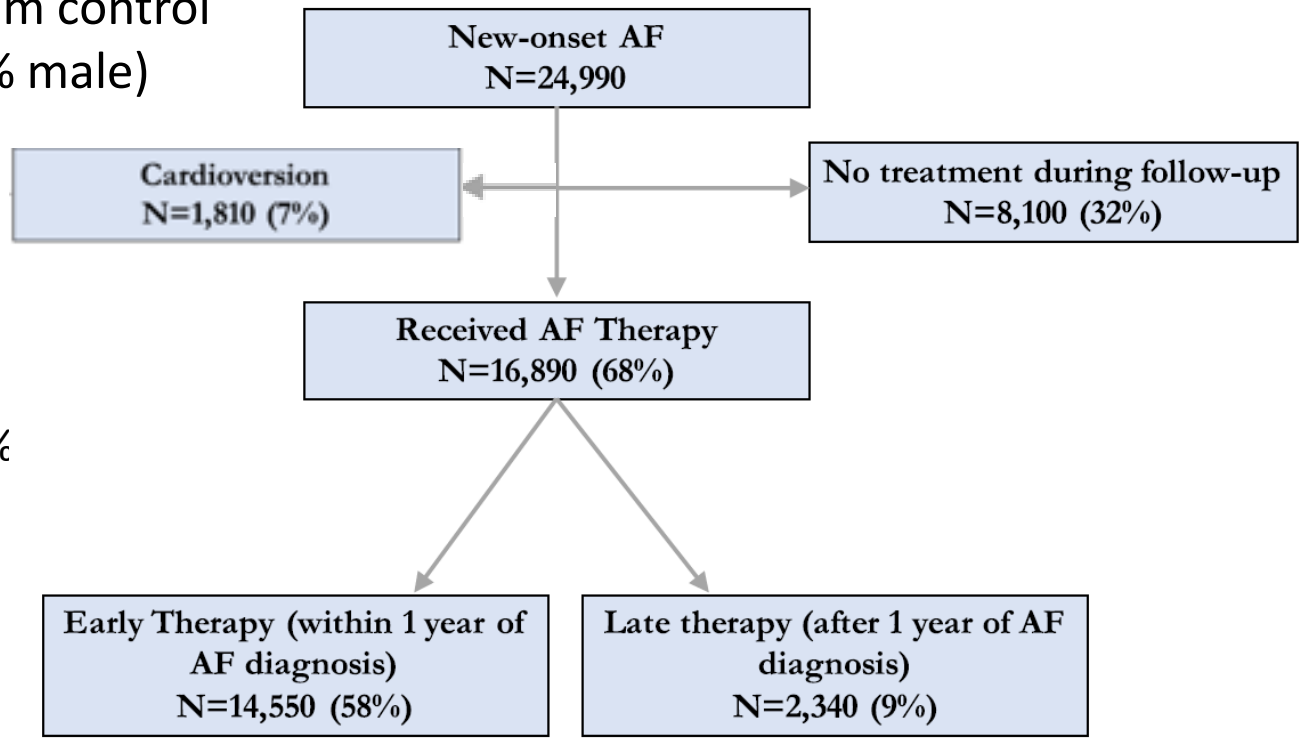
- New onset AF between January 2018 and January 2023
- 3 lines of treatment: no treatment, rate- or rhythm control
- **24 990** patients (mean age 69.8 ± 13.1 years, 58% male)

First line therapy

None: 8,100 (32%)
Rate-control: 12 055 (48%)
Rhythm control: 4835 (20%)
AADs 3919 (16%) and
AF ablation 916 (4%)

During FU

None: 8100 (32%)
Rate-control: 9760 (39%)
Rhythm-control: 7130 (29%
AADs: 4610 (18%)
AF ablation: 2530 (10%)

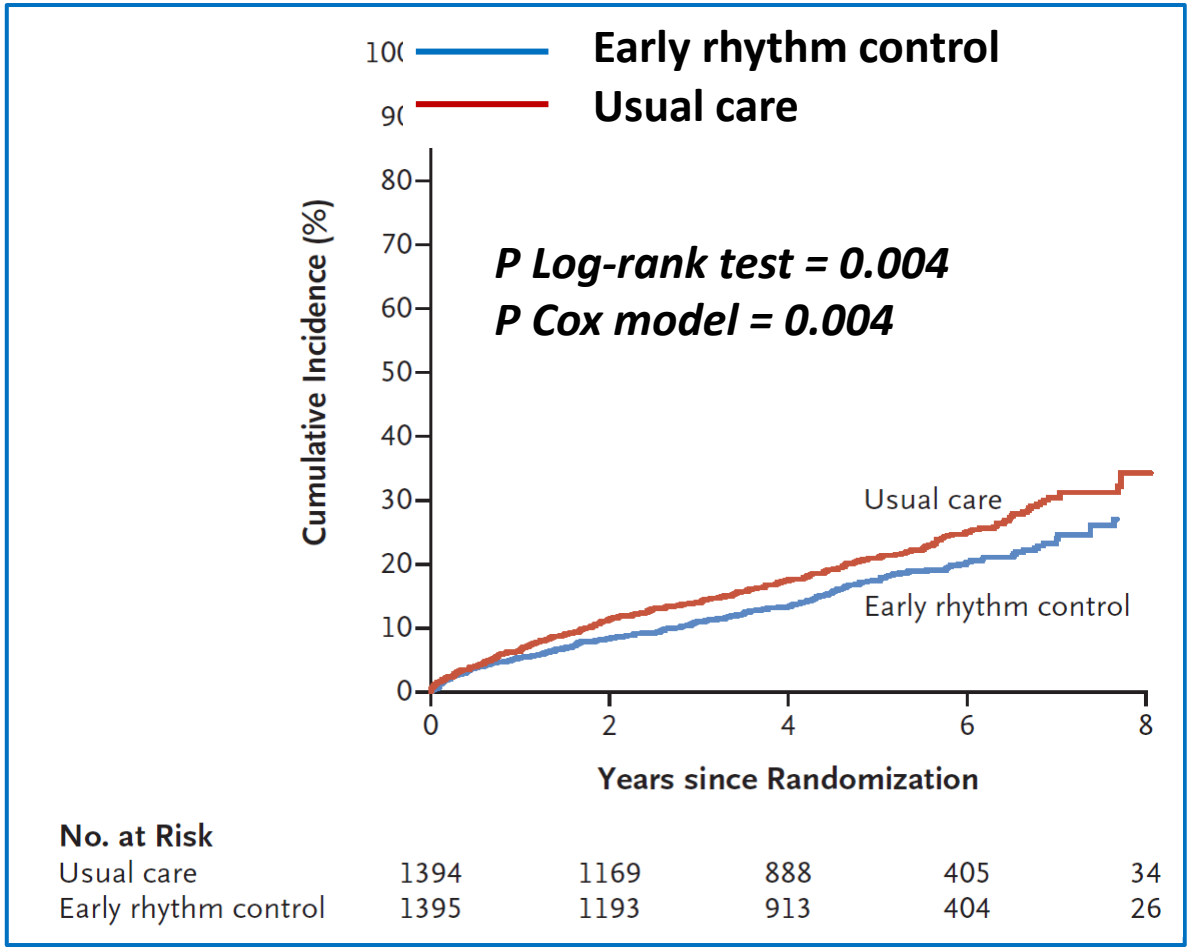


"Most contemporary patients with incident AF at a large US academic tertiary center either received no rate or rhythm intervention or only rate-control."

AJC St George's University of London

Zghaib T, et al. J Cardiovasc Electrophysiol. 2025;36:824-829

Primary Outcomes and Components



	Events / person-years (Incidence rate per 100 person years)		HR adjusted for the group-sequential design
First 1⁰ outcome	249 / 6399 (3.9)	316 / 6332 (5.0)	0.79 [0.66-0.94]
Components of 1st 1⁰ outcome			
CV death	67 /6915 (1.0)	94 / 6988 (1.3)	0.72 [0.52-0.98]
Stroke	40 / 6813 (0.6)	62 / 6856 (0.9)	0.65 [0.44-0.97]
Hospitalization for worsening HF	139 / 6620 (2.1)	169 / 6558 (2.6)	0.81 [0.65-1.02]
Hospitalization with ACS	53 / 6762 (0.8)	65 / 6816 (1.0)	0.83 [0.58-1.19]
Second 1⁰ outcome	Mean ± SD		IRR [99% CI]†
Nights spent in hospital pa	5.8 ± 21.9	5.1 ± 15.5	1.08 [0.92-1.28]

The 1st primary outcome was a composite of CV death, stroke, or hospitalization with worsening of HF or ACS

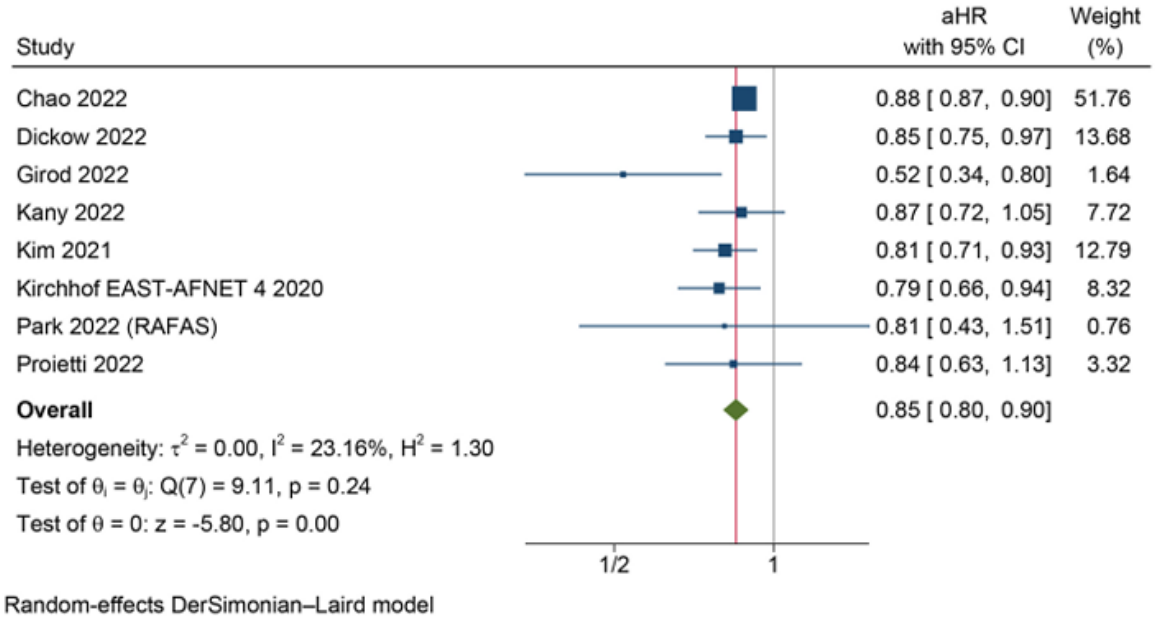
Kirchhof P, et al. N Engl J Med. 2020;383:1305-1316

Early Rhythm Control Compared to Rate Control in AF – A Systematic review and Meta-analysis

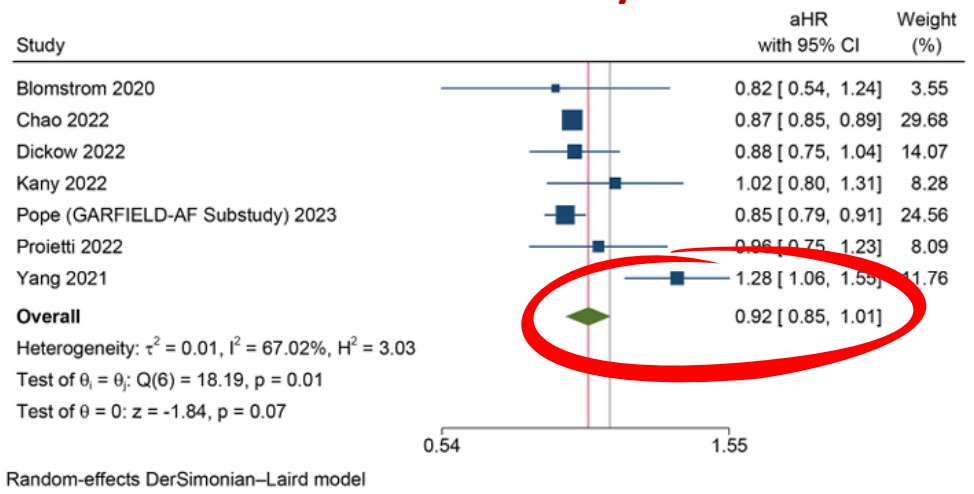
504,124 patients from 11 studies were included in this systematic review and meta-analysis

MAACE:

composite of mortality, S/SE, HF hospitalization and ACS

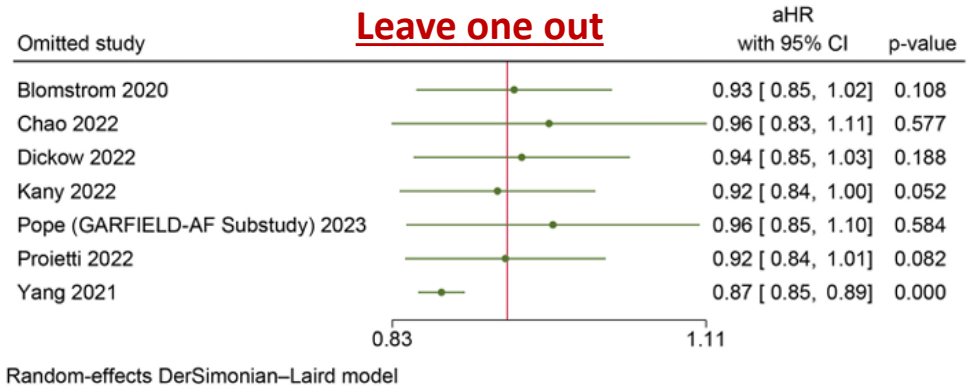


Mortality



Mortality (Sensitivity Analysis)

Leave one out



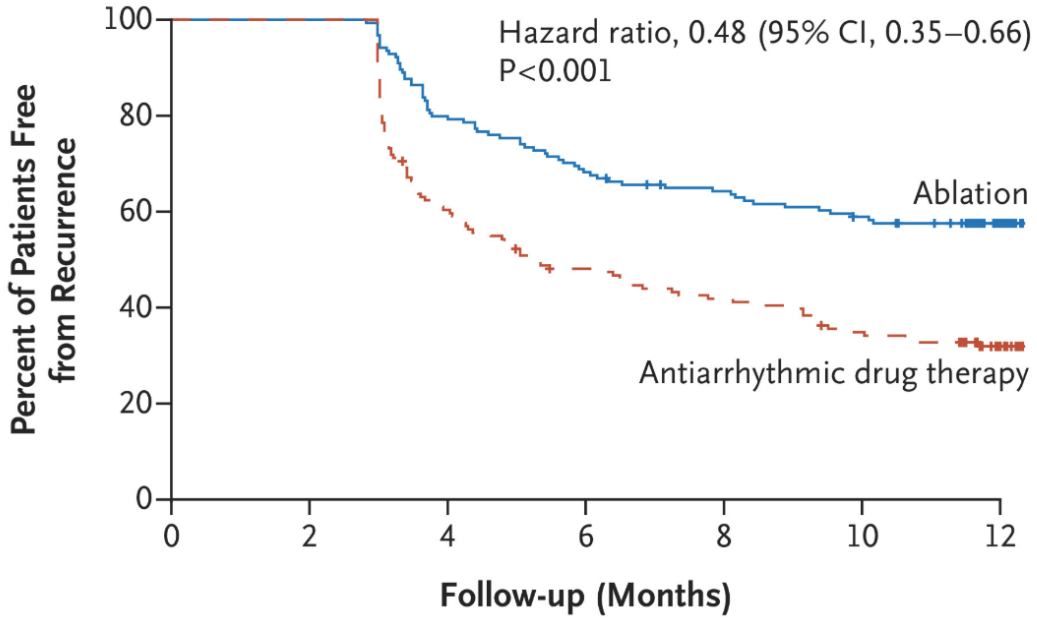
AJC St George's University of London

Hermanto K et al. doi: 10.1016/j.ipej.2025.02.003. Epub ahead of print

Initial Therapy for Paroxysmal AF

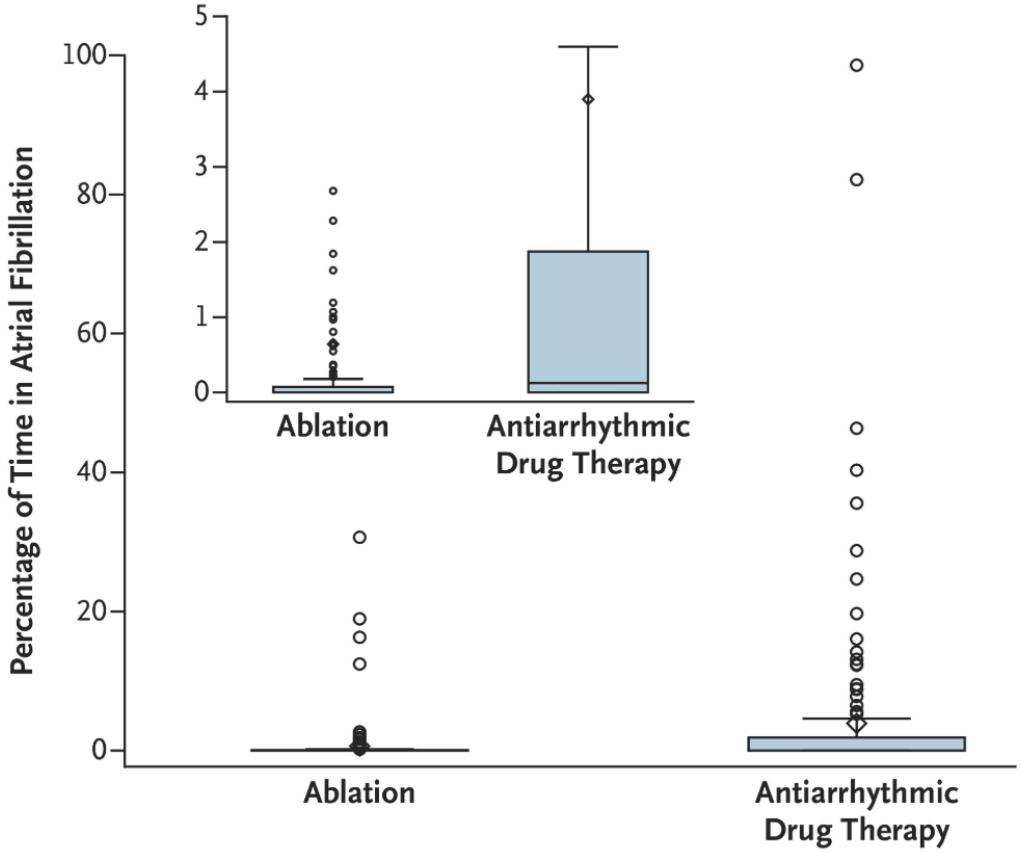
Early Aggressive Invasive Intervention for Atrial Fibrillation (EARLY-AF)

303 pts with symptomatic, paroxysmal, untreated AF: catheter ablation with a cryothermy balloon or AAD



No. at Risk

Ablation	154	154	123	105	96	86	55
Antiarrhythmic drug therapy	149	149	89	69	60	49	27

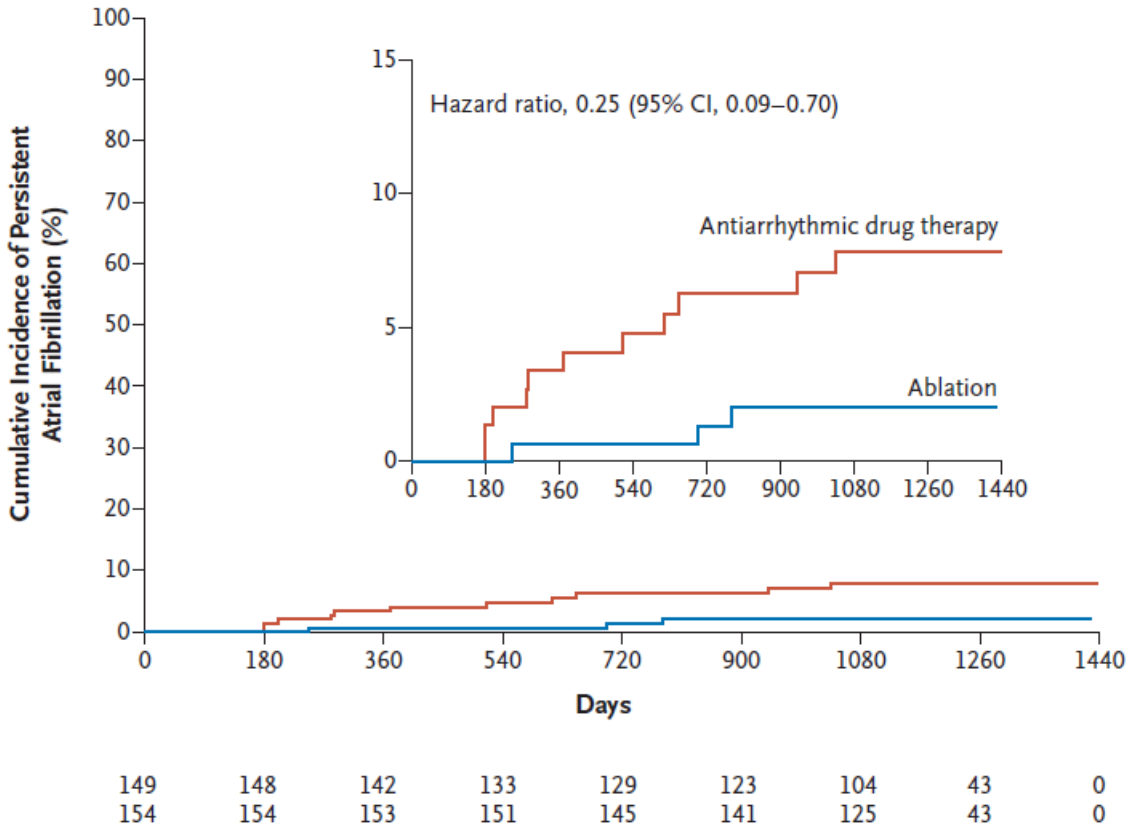


Andrade AJ, et al N Engl J Med. 2021;384(4):305-315

Cumulative Incidence of First Episode of Persistent Atrial Fibrillation

- 3-year follow-up of pts with paroxysmal, untreated atrial fibrillation
- Enrolled in CRT (EARLY-AF) assigned to: Initial rhythm-control therapy with cryoballoon ablation or AAD therapy
- Implantable loop recorders
- Downloaded daily recordings
- 303 pts enrolled, with 154 pts assigned to initial rhythm-control therapy with cryoablation and 149 assigned to AAD therapy.

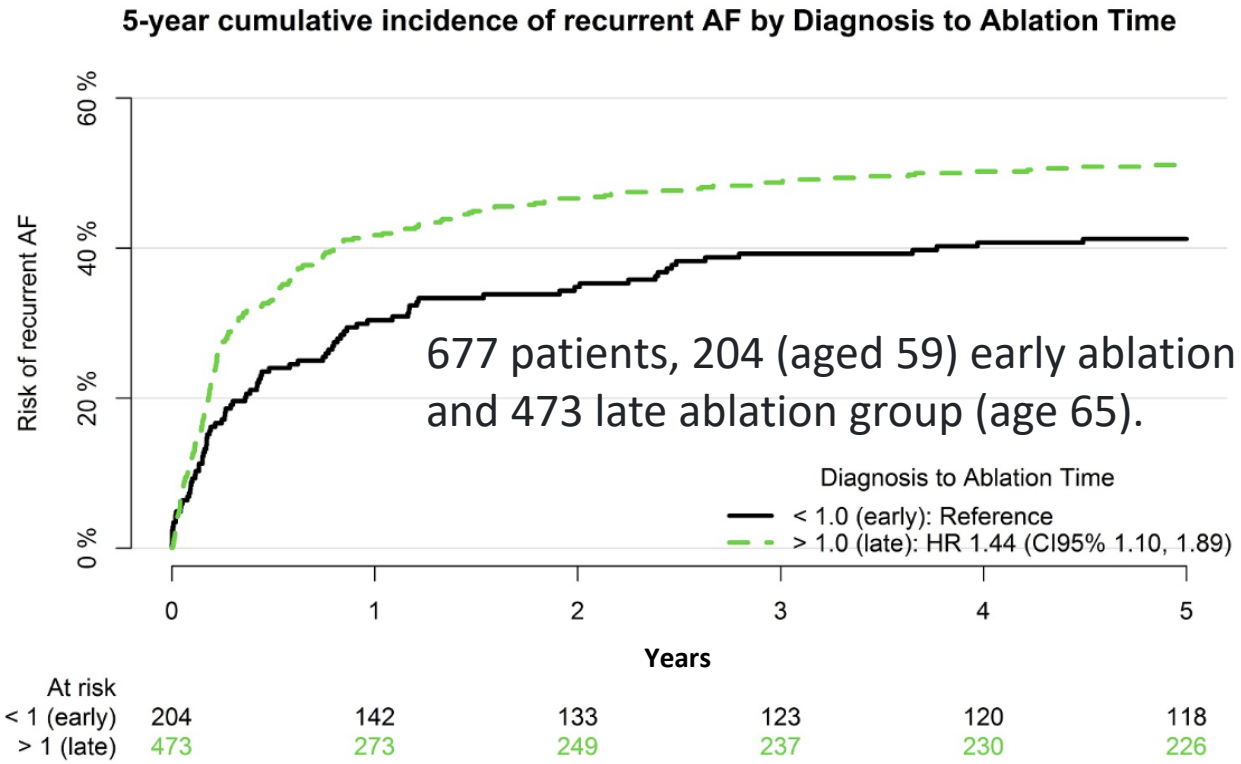
First Episode of Persistent AF

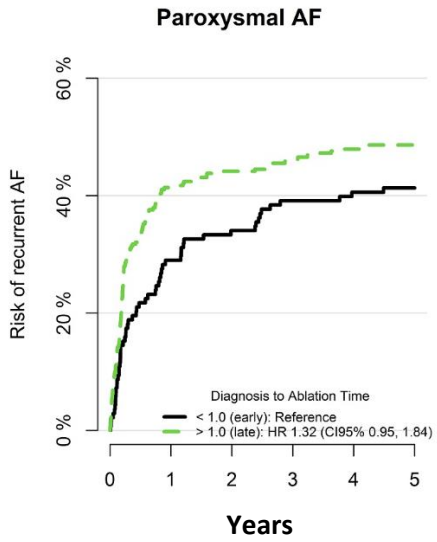


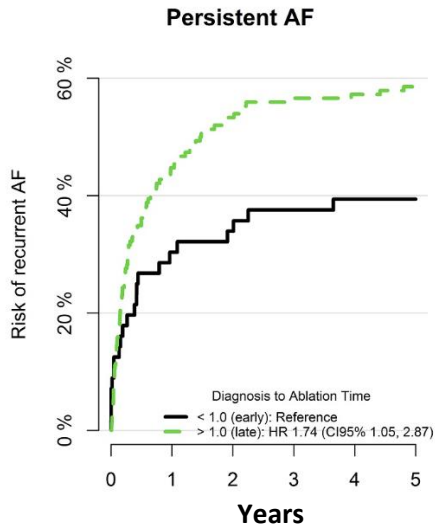
Andrade J, et al N Engl J Med. 2023 Jan 12;388(2):105-116

Effect of Early Cryoballoon Ablation on AF Recurrence A Nationwide Register Study

- Danish nationwide register-based study
- Cryoablation for AF 2012-2018
- Stratified by Diagnosis to Ablation Time (DAT)
- ≤ 1 year and 1 year







Conclusions

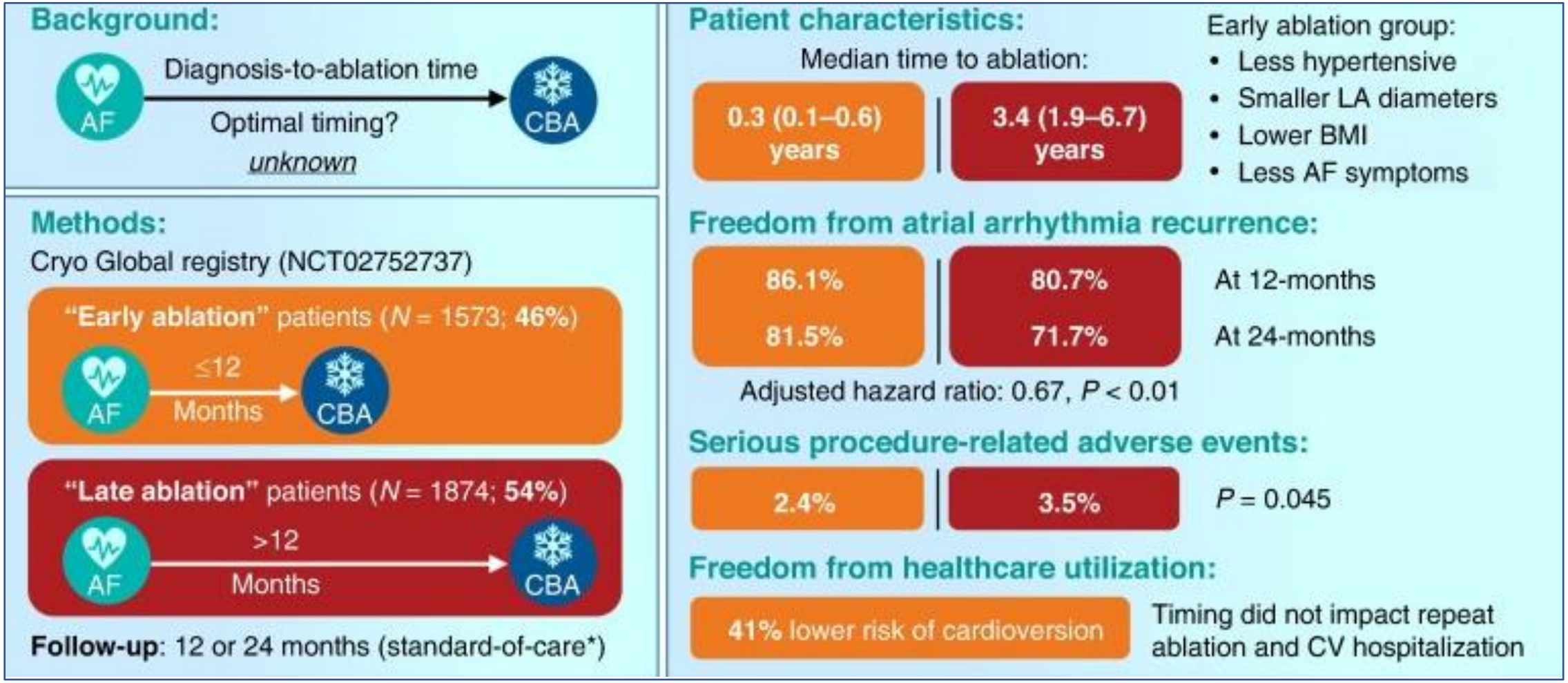
Early cryoballoon ablation could provide considerable benefits and improve outcomes after ablation, indicating that cryoballoon ablation as first-line therapy might be ideal

AJC St George's University of London

R Hein, et al. J Cardiovasc Electrophysiol. 2024 May 16. doi: 10.1111/jce.16303.

Impact of AF Diagnosis to Ablation Time on 24 m

Efficacy and Safety Outcomes in the Cryo Global Registry

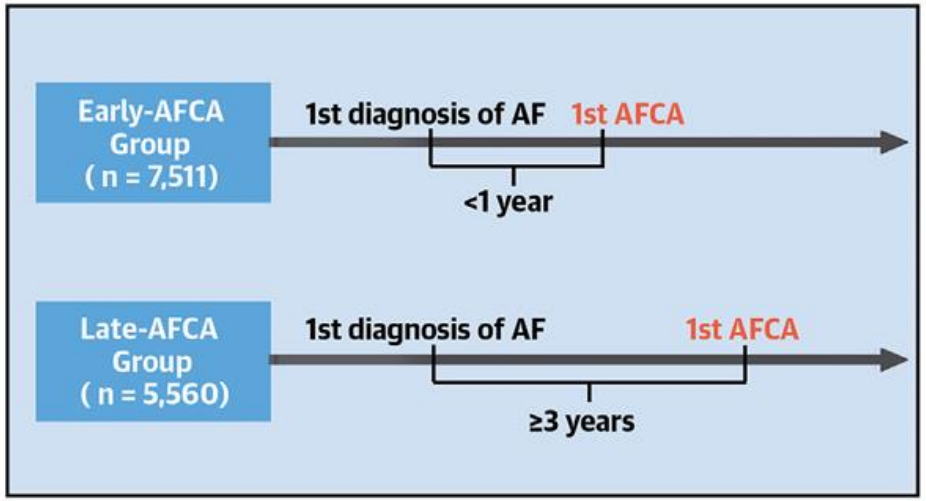


Lawin D, et al. Europace. 2025 Feb 5;27(2):euaf008.

Early vs Late Atrial Fibrillation Catheter Ablation for the Clinical Outcomes

- Korean claims database, 944,710 AF patients without previous AFCA
- Categorized into 3 groups based on duration from AF diagnosis to AFCA

A retrospective nationwide cohort of pateints underwent AFCA
(n = 19,268)



Outcomes	HR (95% CI)	
Composite outcome	1.38 (1.14-1.67)	X
MACE	1.37 (1.07-1.74)	X
Myocardial stroke	1.28 (0.63-2.58)	
Ischemic stroke	0.96 (0.69-1.35)	
HF hospitalization	2.29 (1.53-3.42)	X
All-cause death	1.49 (1.13-1.98)	X
AF recurrence	1.28 (1.15-1.42)	X

Key Messages

- Late AFCA showed poorer clinical outcomes, primarily due to increased risks of HF hospitalization and AF recurrence
- These findings underscore the benefits of catheter ablation for early rhythm control of AF

AJC St George's University of London

Kwon S, et al. JACC Clin Electrophysiol. 2025 Jan 21:S2405-500X(24)01092-2

Early Rhythm Control in Patients With Incident Atrial Fibrillation Who Had a Prior Stroke

- Korean nationwide claims database
- Newly diagnosed AF and history of prior stroke
- Early (< 1 yr) rhythm control cf. usual care
- Primary outcome: incident stroke /Propensity score weighting
- 53,509 pts were included (ERC: 12,455 UC: 41,054)
- All patients on OAC / Median FU = 2.6 years

Among patients with stroke history
N= 53,509

- **41% of recent strokes within 6 months**
- **36% of disabling stroke requiring rehabilitation**
- **7% of severe strokes**

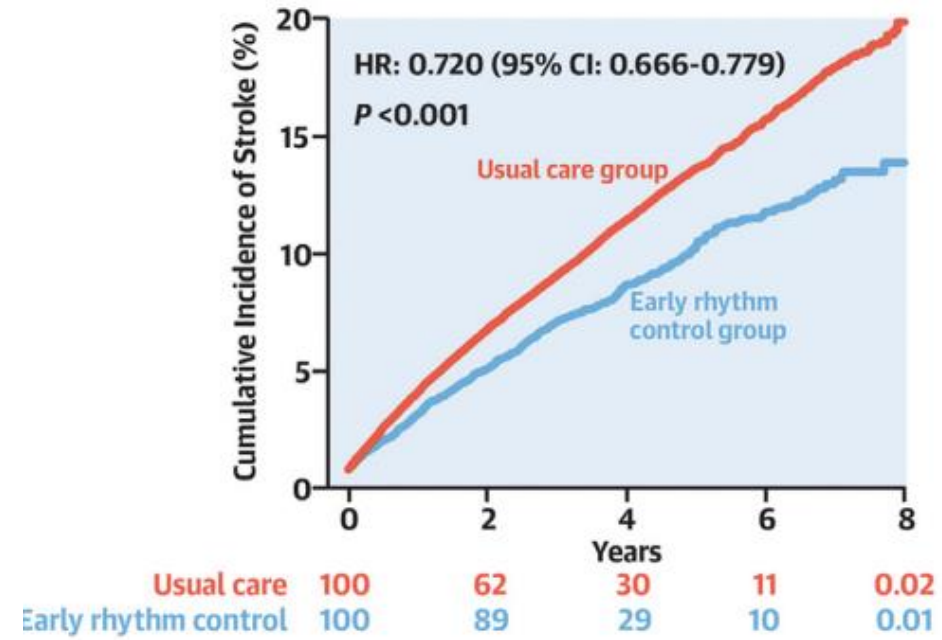
Early Rhythm Control Within 1 Year After AF Diagnosis

Compared to usual care (non-rhythm control)

Recurrent Ischemic Stroke Risk 28%

Lower risk of ischemic stroke
(HR: 0.72, 95% CI: 0.666-0.779)

Weighted Cumulative Incience Curves of Recurrent Ischemic Stroke According to Early Rhythm Control



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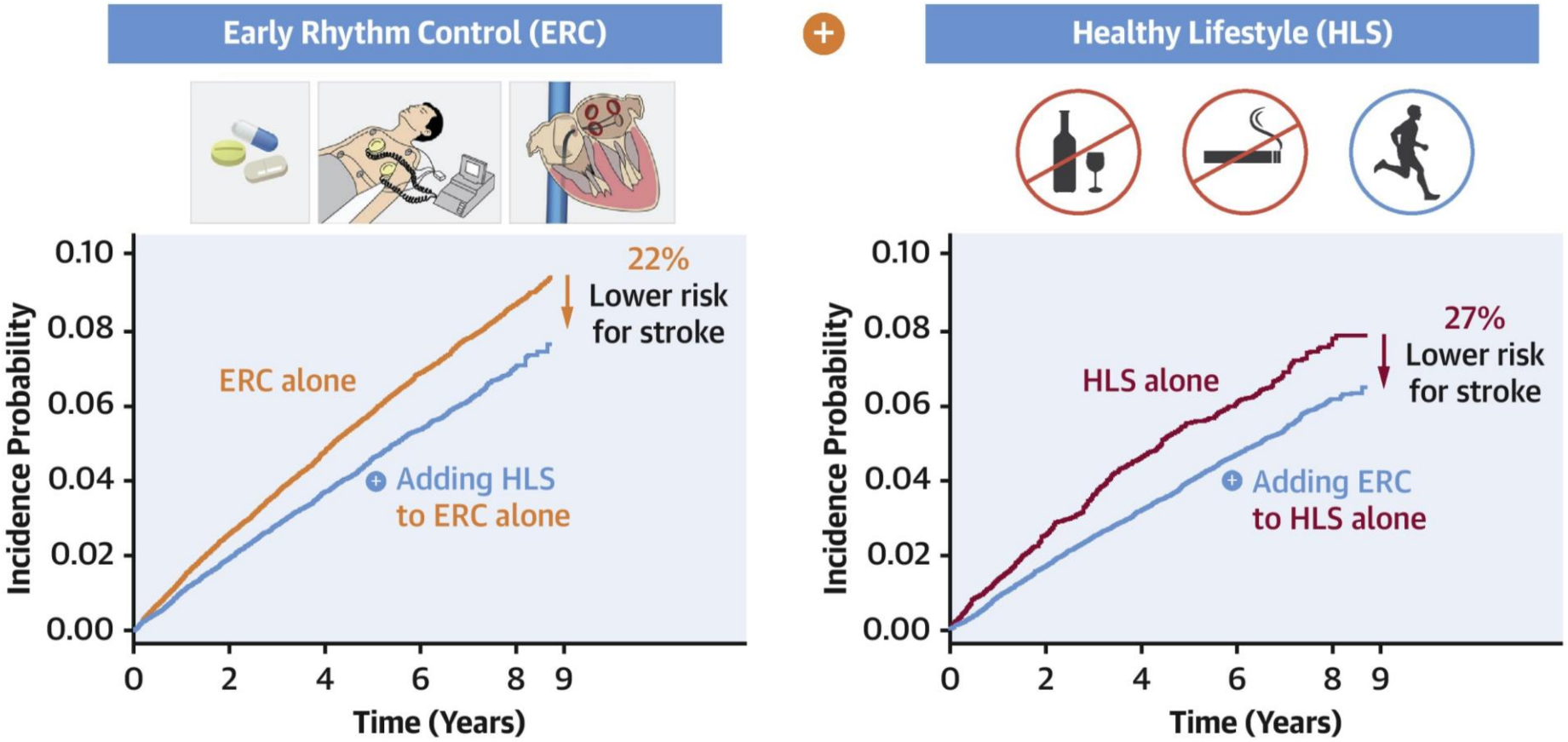
Lee SR, et al. J Am Coll Cardiol EP 2023;9:1121–1133

Impact of Adding ERC and HLS on Ischaemic Stroke Risk Reduction

Association between both ERC and HLS and the Risk of ischemic stroke in patients with newly diagnosed AF



Lee S-R, et al J. Am. Coll Cardiol 10.1016. jacep.2024,02,016 2024

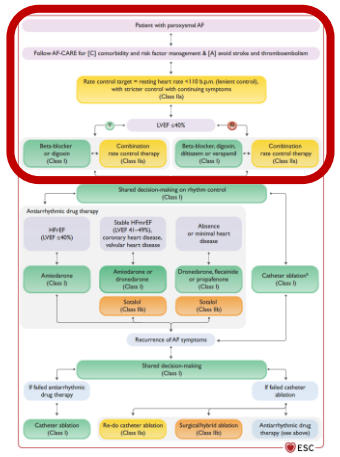
Pathway for Paroxysmal and Persistent AF - Part 1

Patients with paroxysmal or persistent AF

↓

Follow AF-CARE for [C] comorbidity and risk factor management & [A] avoid stroke and thromboembolism

↓



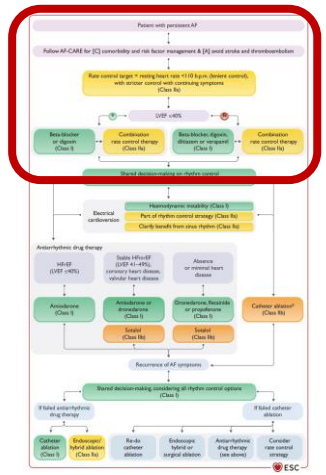
Rate control target = resting heart rate <110 b.p.m. (lenient control),
with stricter control with continuing symptoms
(Class IIa)

↓

LVEF ≤40%

Y → Beta-blocker or digoxin (Class I) → Combination rate control therapy (Class IIa)

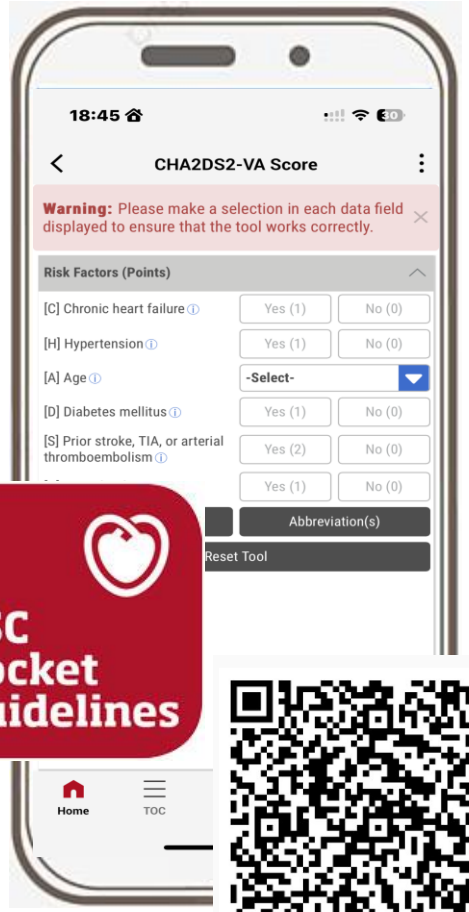
N → Beta-blocker, digoxin, diltiazem or verapamil (Class I) → Combination rate control therapy (Class IIa)



European Heart Journal 2024 – doi: 10.1093/eurheartj/ehae176

ESC Guidelines

Rate and Rhythm Control



Implementation of a rhythm control strategy should be considered within 12 months of diagnosis in selected patients with AF at risk of thromboembolic events to reduce the risk of cardiovascular death or hospitalization.	IIa	B

Catheter ablation

CA is recommended in patients with paroxysmal or persistent **AF resistant or intolerant to antiarrhythmic drug therapy** to reduce symptoms, recurrence, and progression of AF.	I	A
CA is recommended as **a first-line option within a shared decision-making rhythm control strategy in patients with paroxysmal AF**, to reduce symptoms, recurrence, and progression of AF.	I	A
CA may be considered as **a first-line option within a shared decision-making rhythm control strategy in selected patients with persistent AF** to reduce AF symptoms, recurrence, and progression	IIb	C
AF catheter ablation is recommended in patients with **AF and HFrEF with high probability of tachycardia-induced cardiomyopathy** to reverse left ventricular dysfunction.	I	B

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European Heart Journal 2024 – doi: 10.1093/eurheartj/ehae176

Rhythm Control - When and Why?

- Tachycardia mediated cardiomyopathy
- Younger age
- 1st AF episode or short history
- Normal – moderate increased LAVI / atrial conduction delay (left atrial myopathy)
- AF precipitated by a temporary event (acute illness)
- No or few comorbidities / heart disease
- Rate control difficult to achieve
- Patient's choice

Hindricks G, et al. Eur Heart J. 2021;42:373-498

ESC
European Society of Cardiology

ESC Guidelines on Atrial Fibrillation 2020

Rhythm Control - When and Why?

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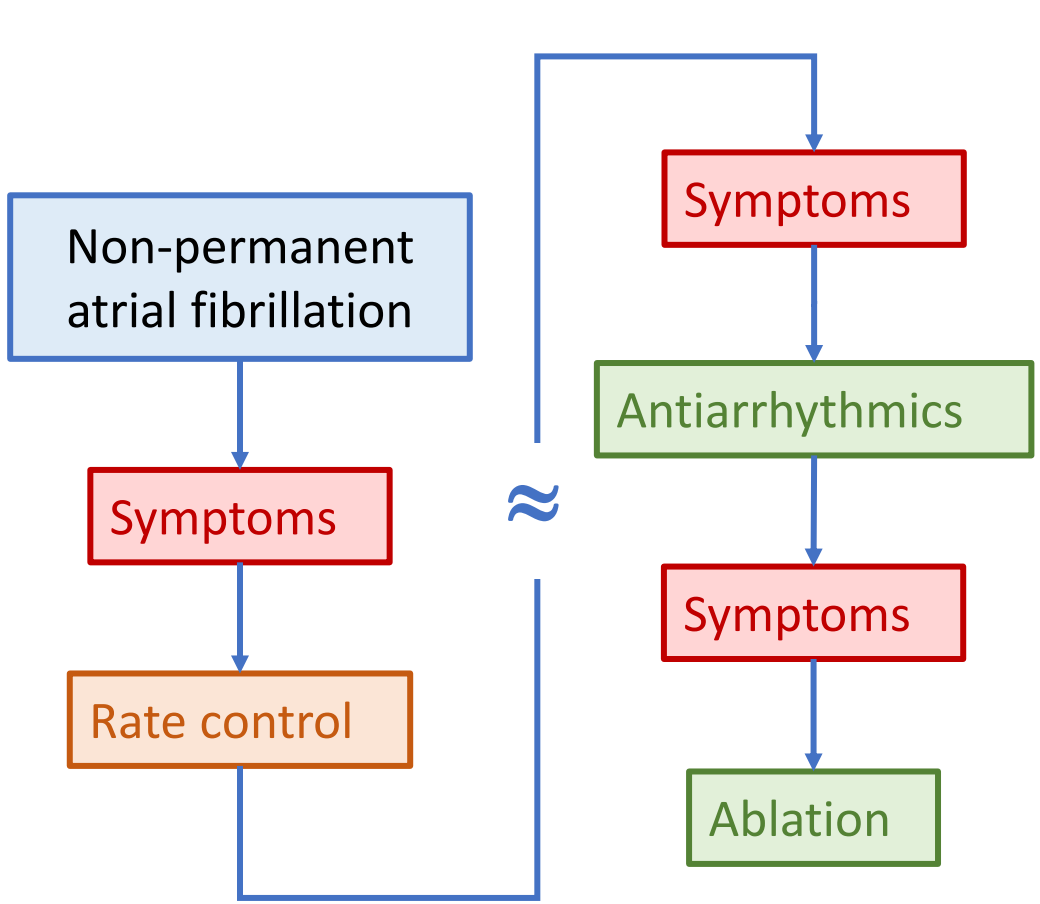
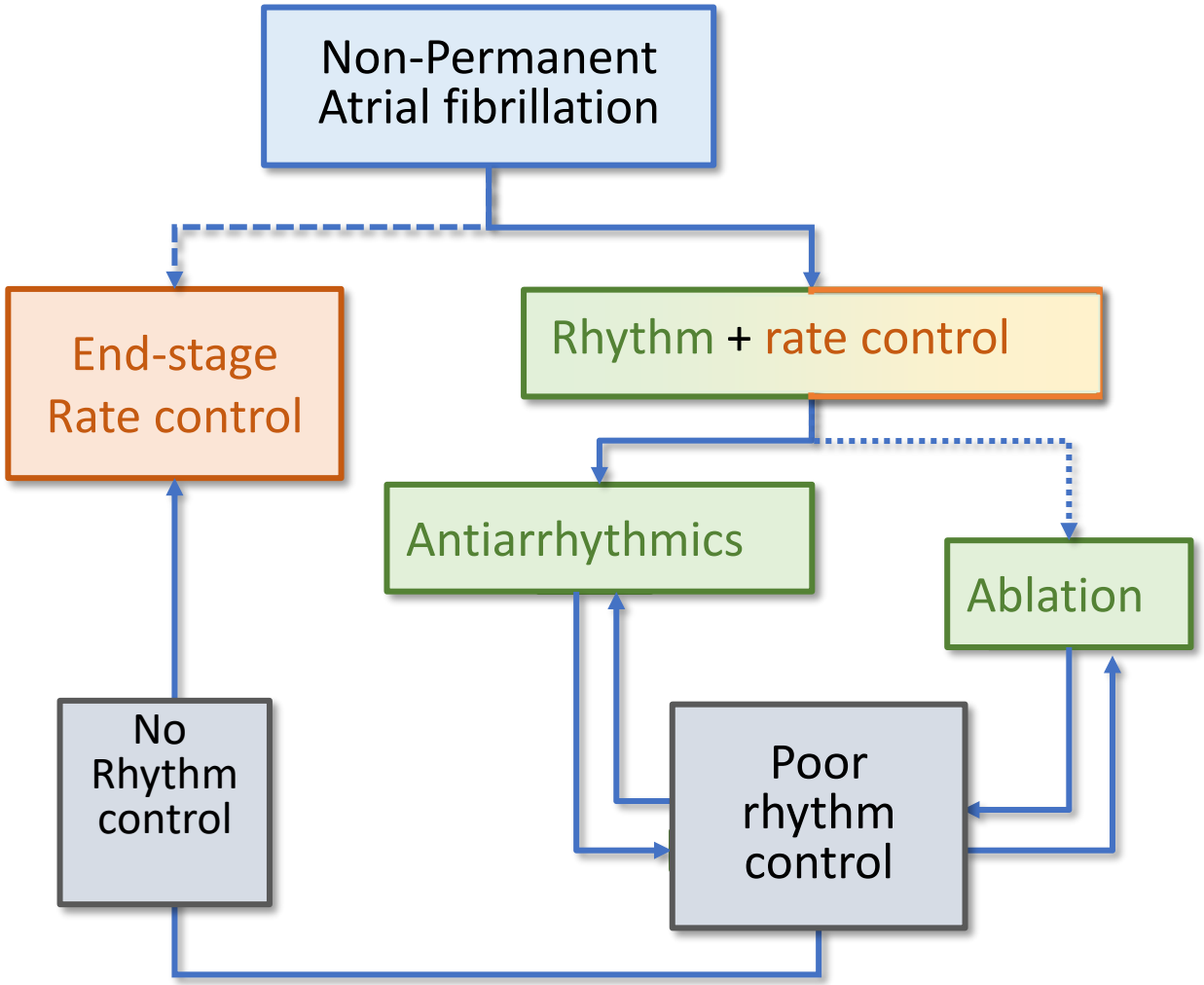
Implications of More Effective Rhythm Control Using Left Atrial Catheter Ablation





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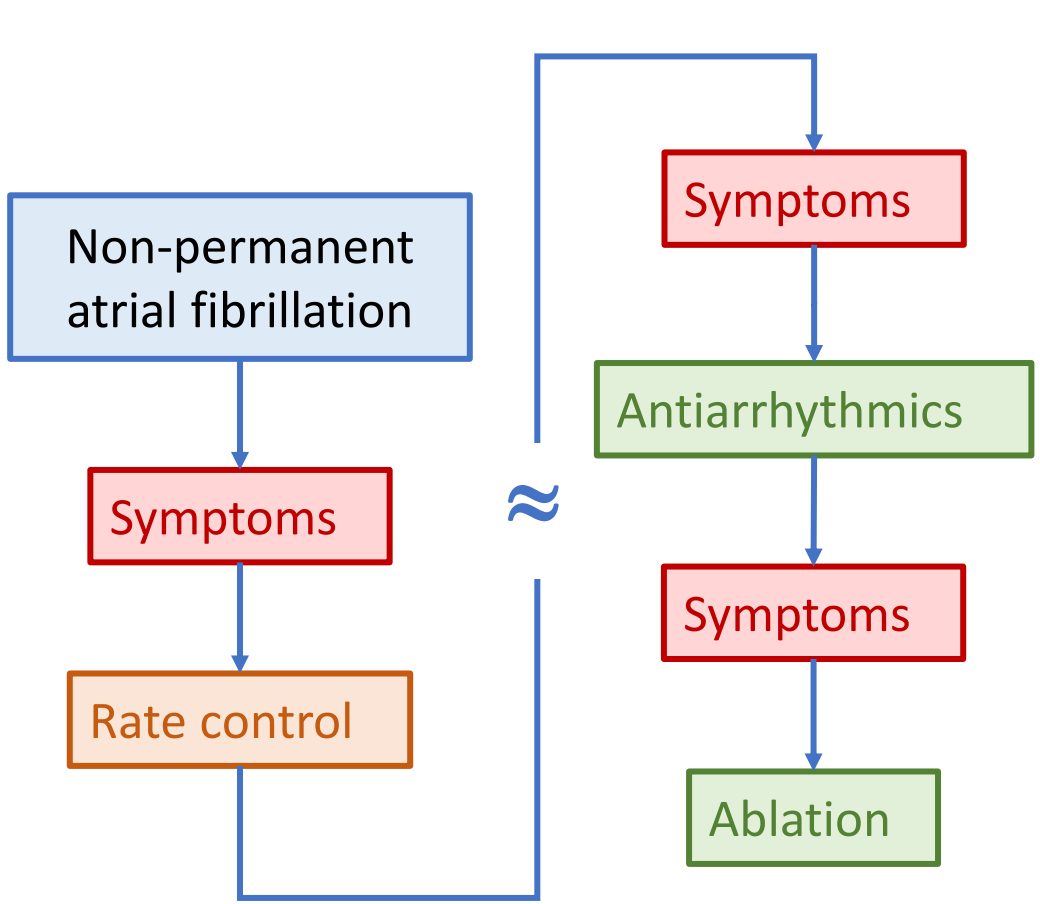
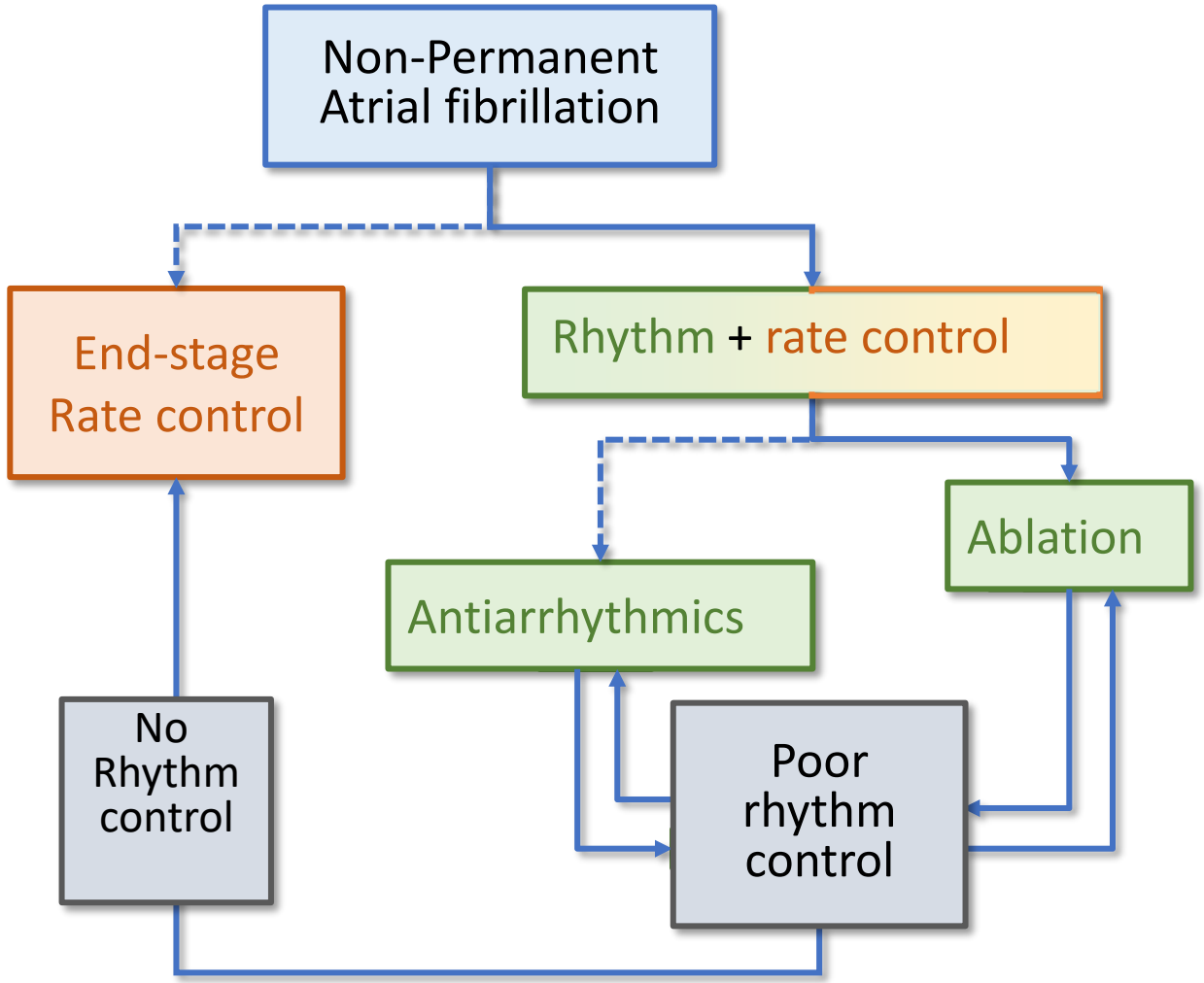
Implications of More Effective Rhythm Control Using Left Atrial Catheter Ablation





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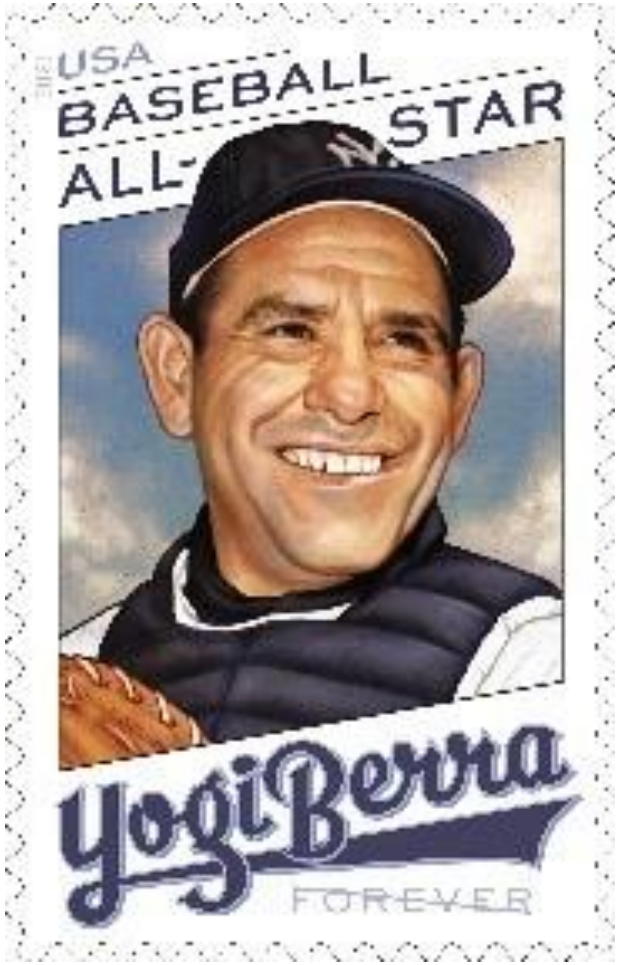
Yogi-isms – Yogi Berra – Baseball Star



"When you come to a fork in the road take it"

Make the right decision **(about rate versus rhythm control)**

"The future ain't what it used to be"

New life ahead **(with rhythm control as 1st line therapy for many with AF)**

"The Yogi Book: I Really Didn't Say Everything I Said!"

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Thank you for your attention…

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