Early Ablation of Atrial Fibrillation: Advances, Approaches, and Outcomes

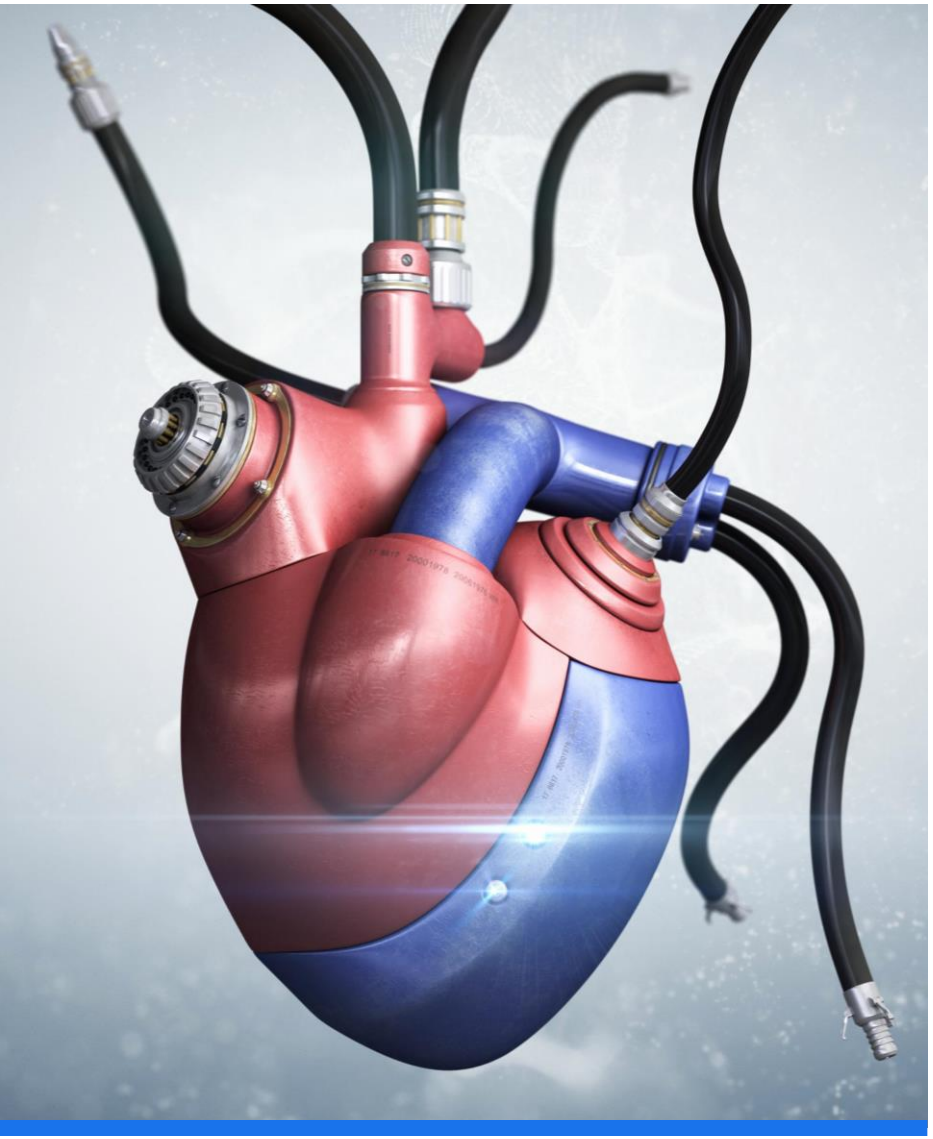
EXPLORING INNOVATIONS AND CLINICAL RESULTS IN AF TREATMENT

SUVEER BAGWE, MD

FMC CV SYMPOSIUM 2025

Disclosure

NONE

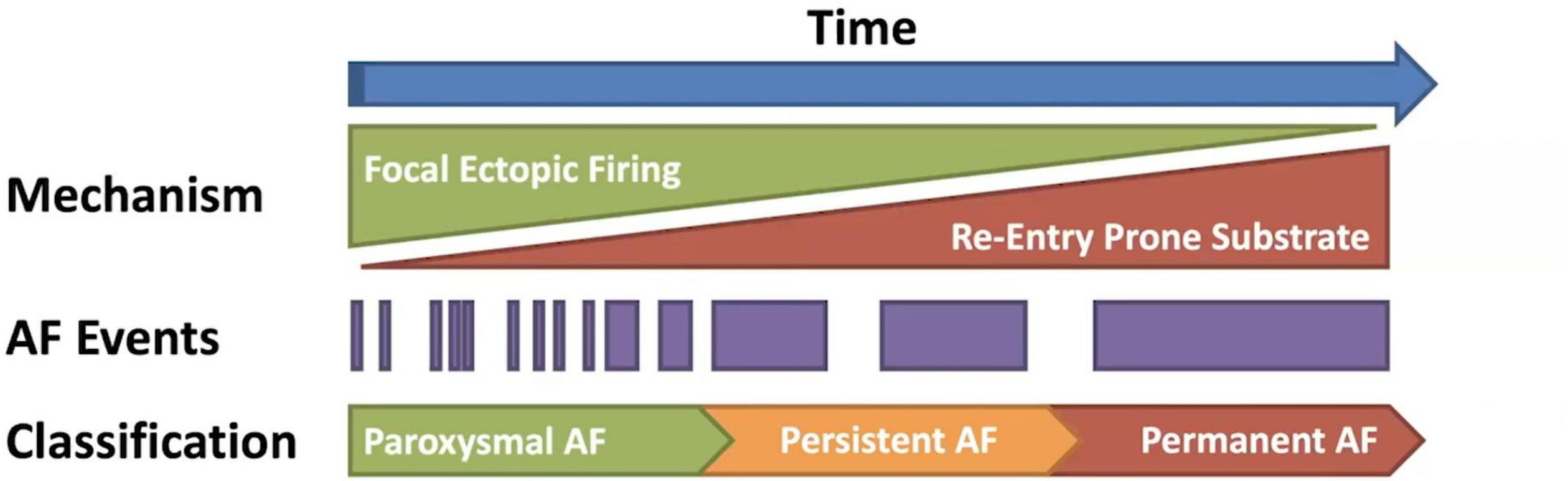


Presentation Agenda

- Understanding Atrial Fibrillation and Its Clinical Significance
- Conventional Management Strategies for Atrial Fibrillation
- Evolution and Rationale for Early Ablation
- Outcomes, Benefits, and Future Directions

Understanding Atrial Fibrillation and Its Clinical Significance

AF IS A CHRONIC PROGRESSIVE DISEASE



- Increased Age
- Structural cardiac pathology (left atrial dilatation)
- Concomitant cardiac conditions (HF, HTN)
- Cardiovascular and Cerebrovascular disease
- Non-cardiac comorbidities (DM, COPD, CKD, OSA)

7% Progression per year

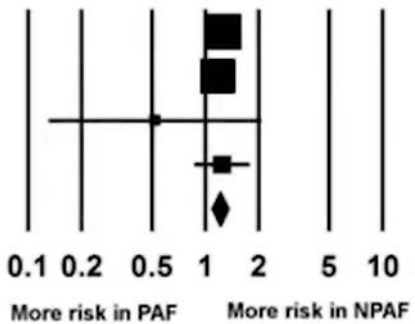
Heart Rhythm 2019;16:502–510

Persistent AF is Associated with Worse Outcomes

B

All-cause mortality (adjusted)

Study name	Hazard ratio	Lower limit	Upper limit	p-Value
ROCKET-AF	1.266	1.069	1.499	0.006
ARISTOTLE	1.176	0.986	1.403	0.071
GISSI-AF	0.520	0.132	2.055	0.351
SPORTIF	1.240	0.871	1.765	0.232
OVERALL	1.217	1.085	1.365	0.001

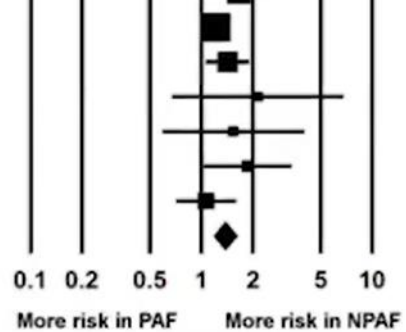


22% adjusted increased risk of Death

B

Stroke or Systemic Embolism (adjusted)

Study name	Hazard ratio	Lower limit	Upper limit	p-Value
ACTIVE A/AVERROES	1.658	1.316	2.089	0.000
ROCKET-AF	1.220	1.060	1.403	0.006
ARISTOTLE	1.429	1.072	1.904	0.015
GISSI-AF	2.141	0.677	6.774	0.195
Euro Heart Survey	1.538	0.595	3.980	0.374
SPORTIF	1.870	1.041	3.359	0.036
Active W	1.064	0.714	1.586	0.761
OVERALL	1.384	1.191	1.608	0.000

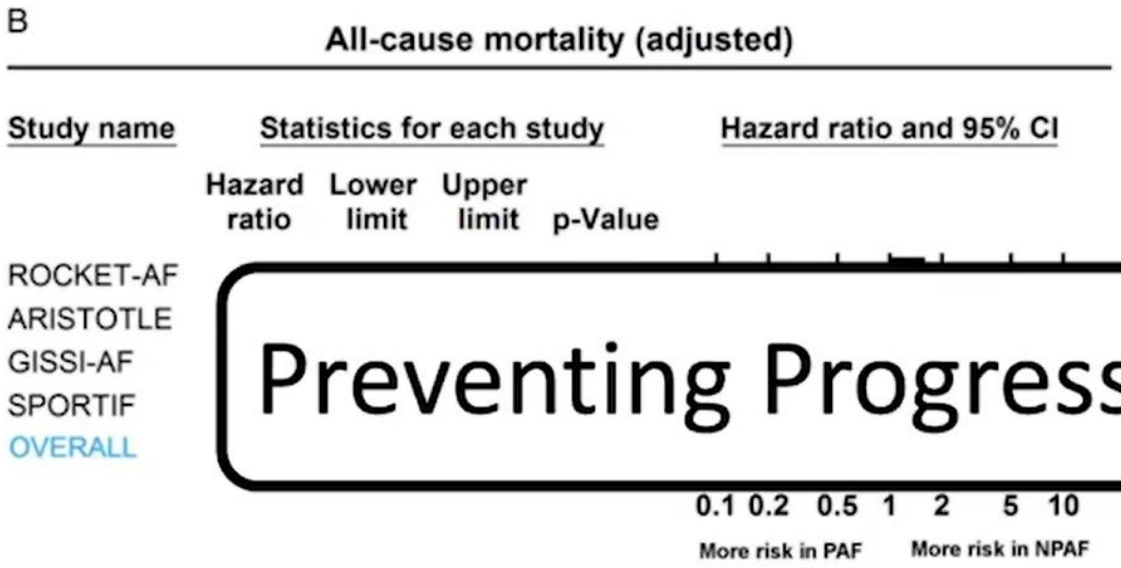


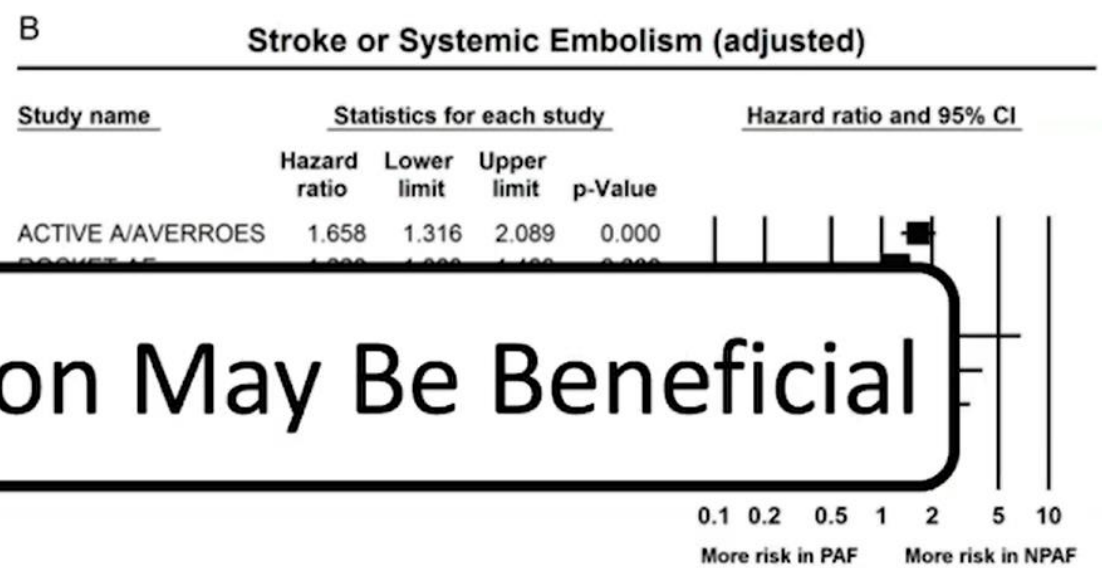
38% adjusted increased risk of Stroke

Classification

European Heart Journal 2016 37, 1591–1602; European Heart Journal 2015 36, 281–287; Circ Arrhythm Electrophysiol. 2017;10:e004267.

Persistent AF is Associated with Worse Outcomes





Preventing Progression May Be Beneficial

22% adjusted increased risk of Death

38% adjusted increased risk of Stroke

Classification Paroxysmal AF → Persistent AF → Permanent AF

European Heart Journal 2016 37, 1591–1602; European Heart Journal 2015 36, 281–287; Circ Arrhythm Electrophysiol. 2017;10:e004267.

Management Options

Anti Arrhythmic drugs

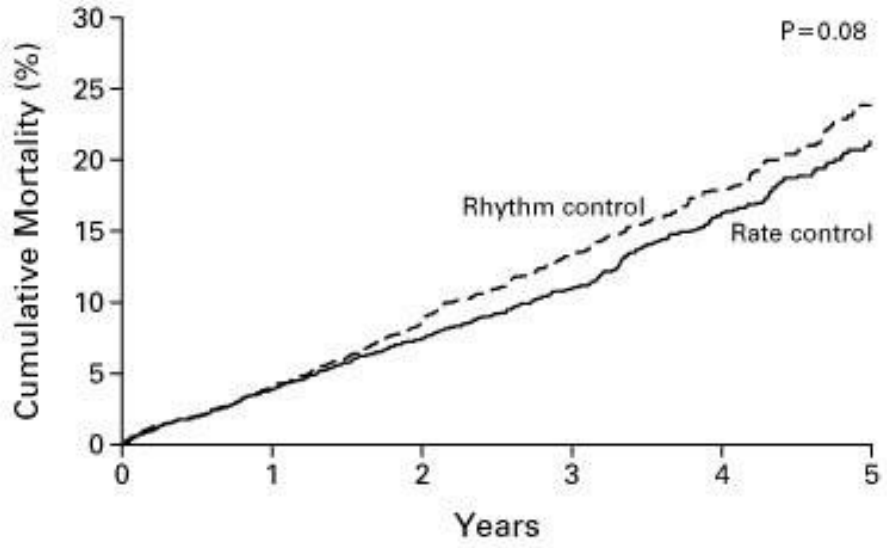
or

Ablation- RF/Cryo/PFA

or

Rate Control

RATE VS RHYTHM
AFFIRM TRIAL



No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

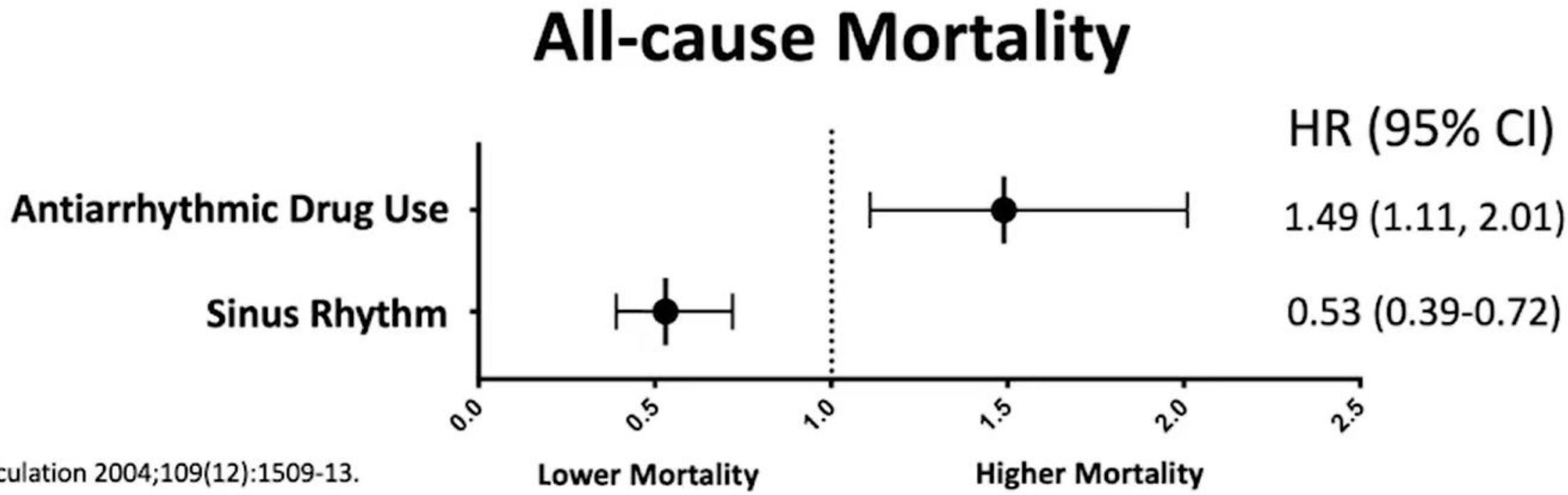
Rate VS Rhythm control
2002
4000 patients
AAD vs rate control
Amiodarone/Sotalol
14 patients underwent ablation

Primary endpoint – all cause mortality
FU 42 months
Maintenance of Sinus rhythm WAS NOT the OBJECTIVE

N Engl J Med 2002;347:1825-1833

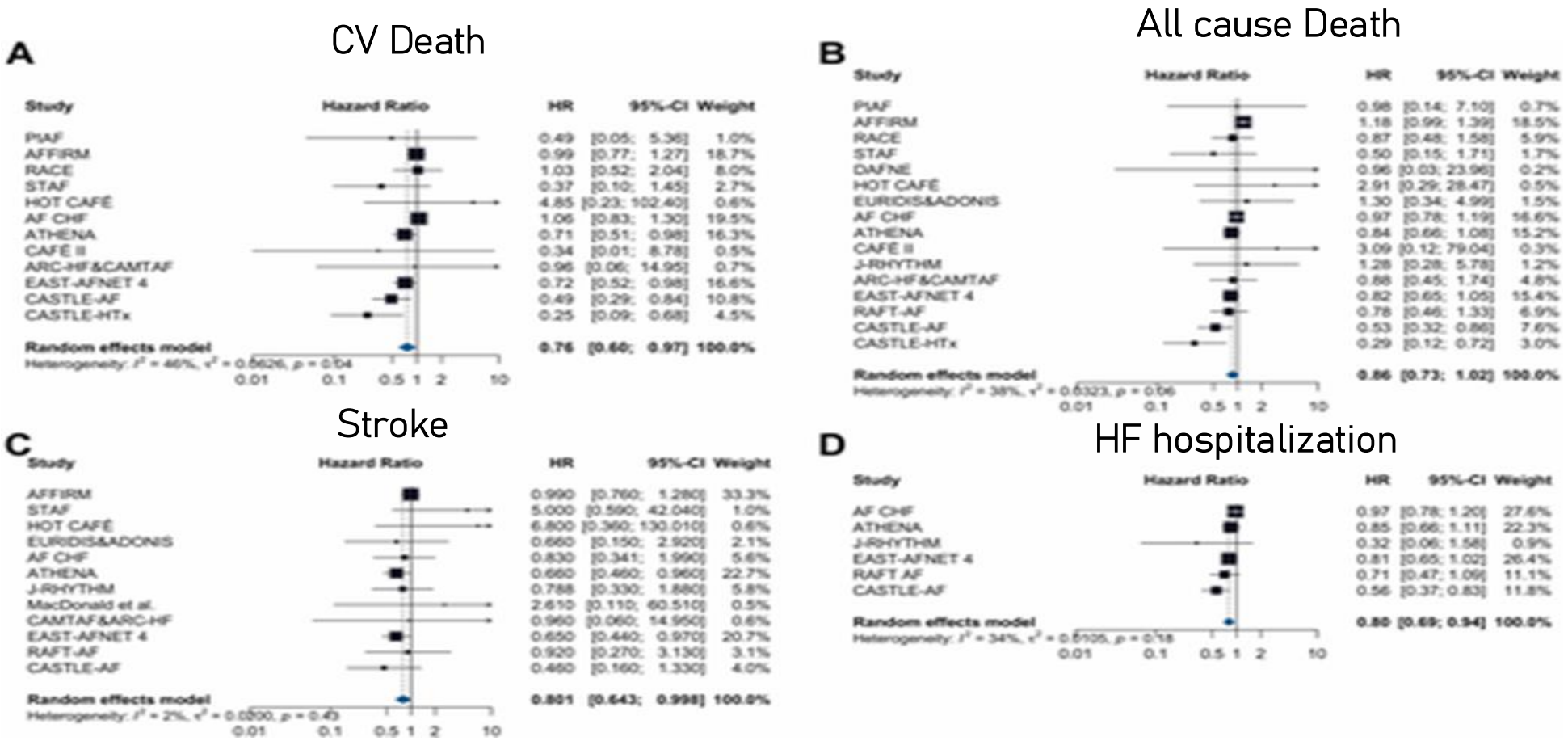
Anti Arrhythmic Drugs

AFFIRM TRIAL



Circulation 2004;109(12):1509-13.

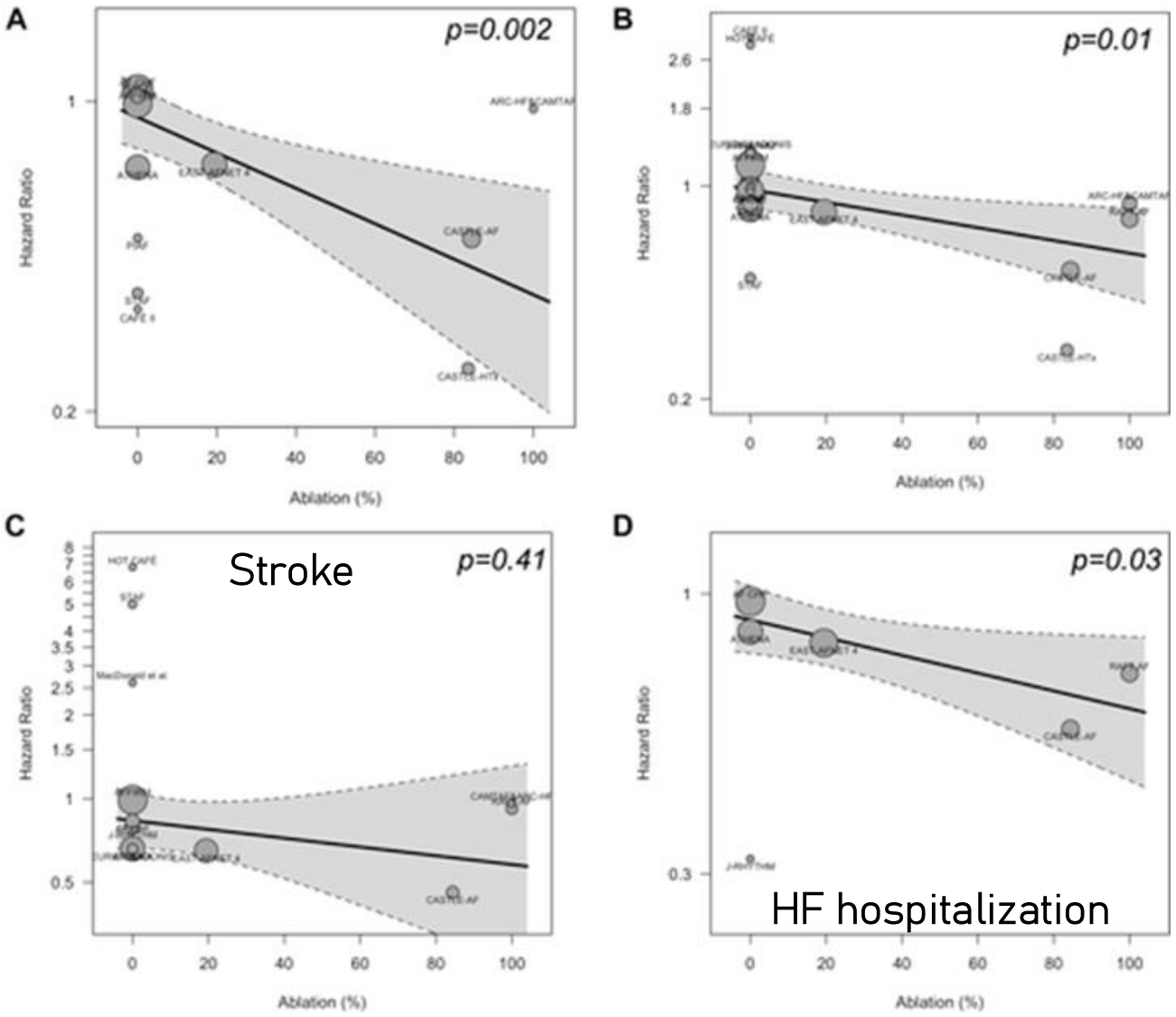
Rhythm vs Rate Control Strategy for Atrial Fibrillation:
A Meta-Analysis of Randomized Controlled Trials

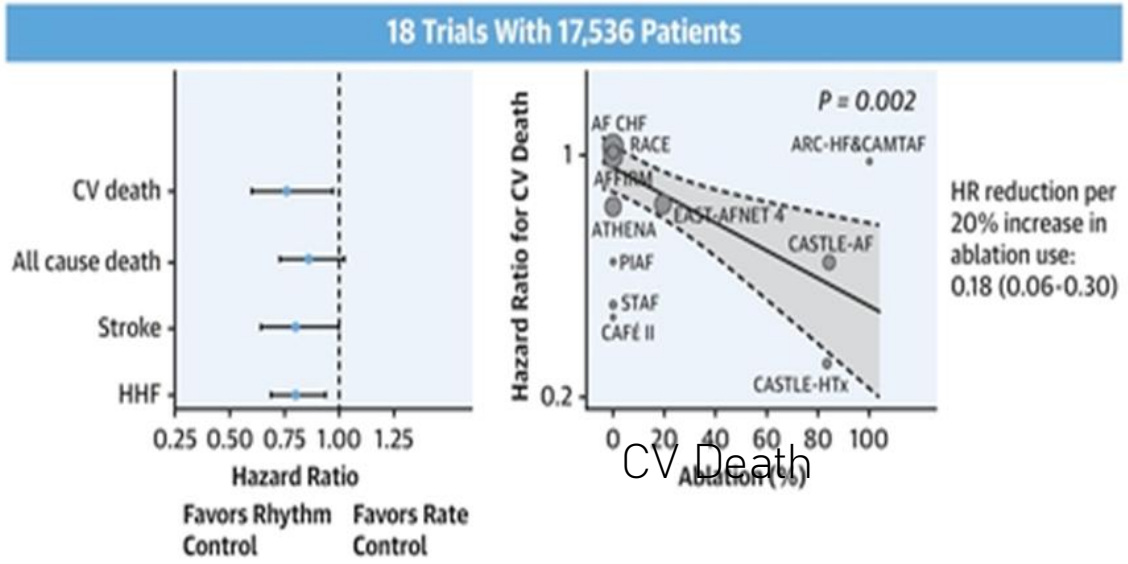


J Am Coll Cardiol EP 2024; 10:1395-1405

CV Death

All cause Death





CV Death

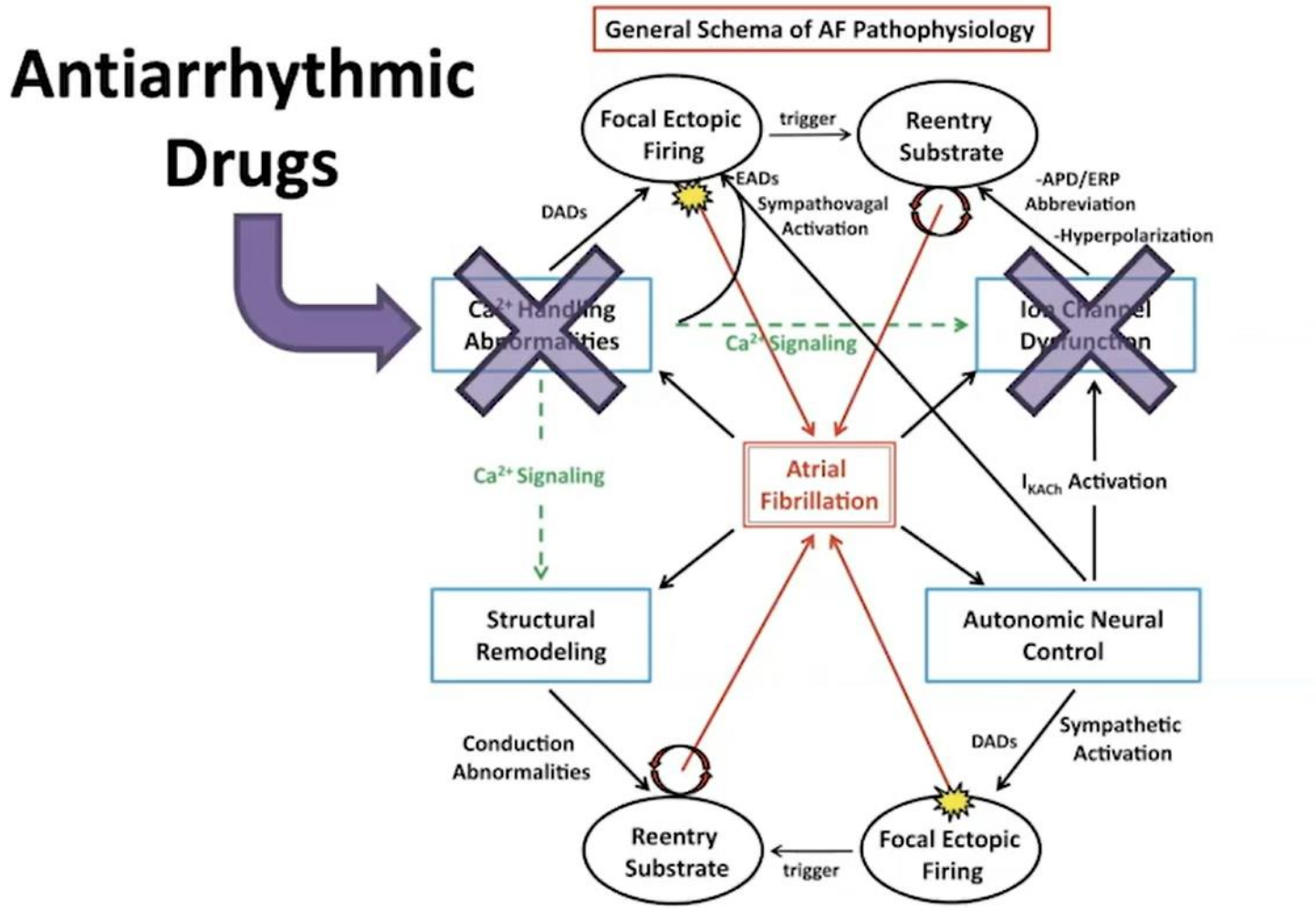
Zafeiropoulos S, et al. J Am Coll Cardiol EP. 2024;10(7):1395-1405.

EDITORIAL

"In conclusion, contemporary trials comparing the effect of early rhythm control by modern antiarrhythmic drugs and catheter-based AF ablation procedures compared with rate control are driving the conceptual paradigm shift that moves rhythm control from a symptom-improving "lifestyle therapy" to a treatment to reduce CV death, stroke, and heart failure hospitalization. "

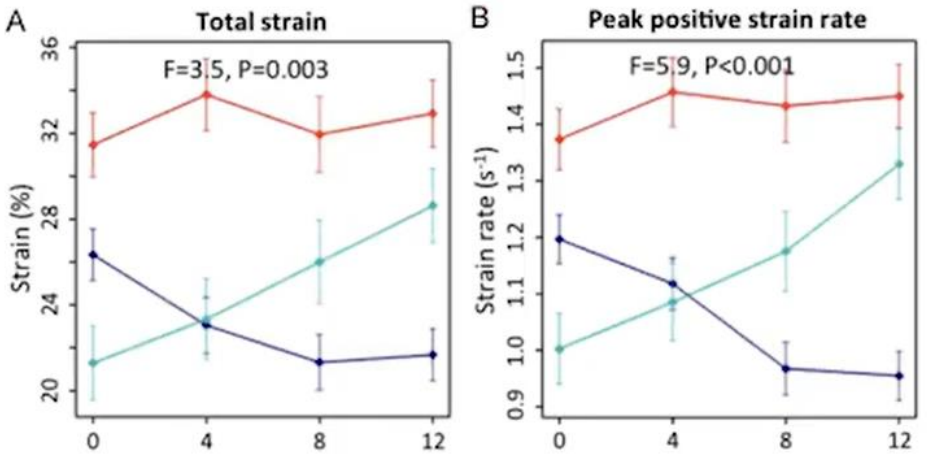
J Am Coll Cardiol EP 2024; 10:1395-1405

Progression - Drugs don't change anything



Andrade et al. Circ Res. 2014 Apr 25;114(9):1453-68.

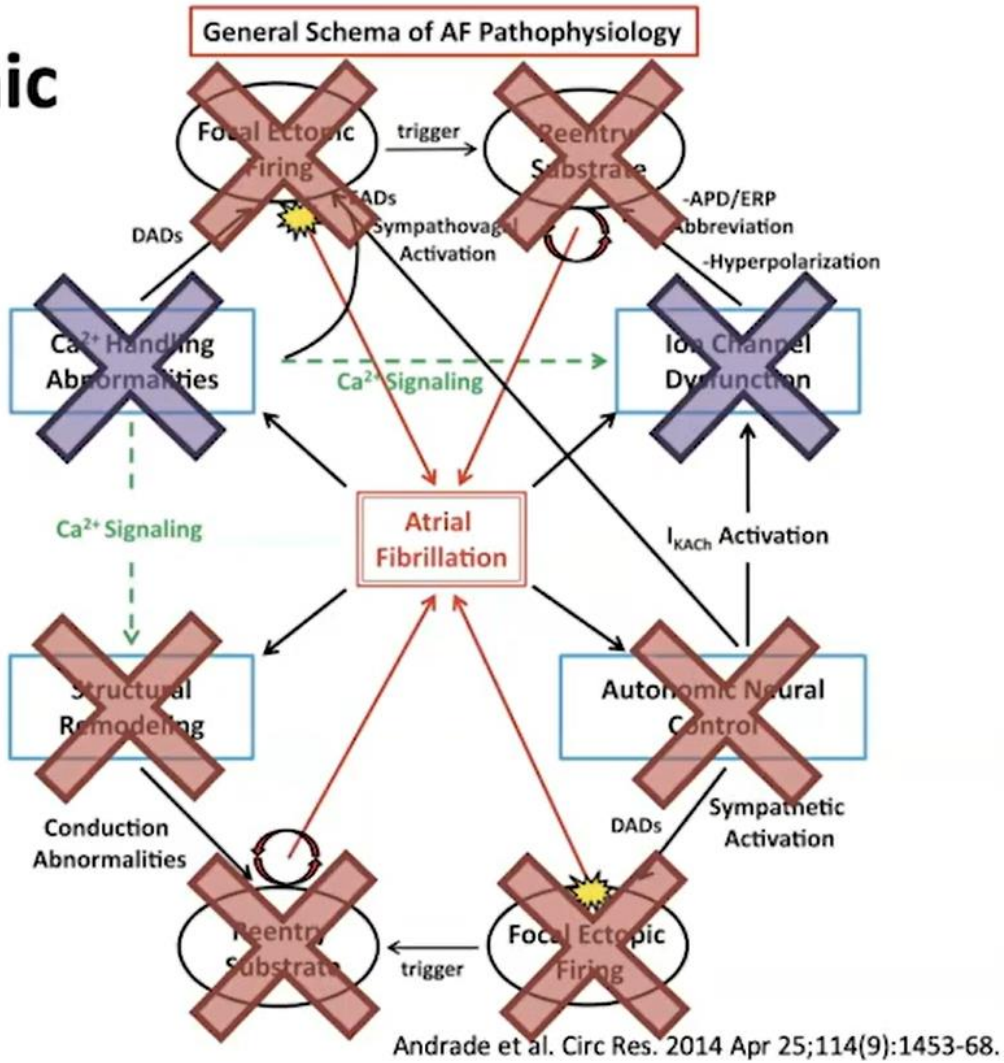
Progression - Drugs don't change anything



Antiarrhythmic Drugs

AF ablation
AF medical Mx
Control

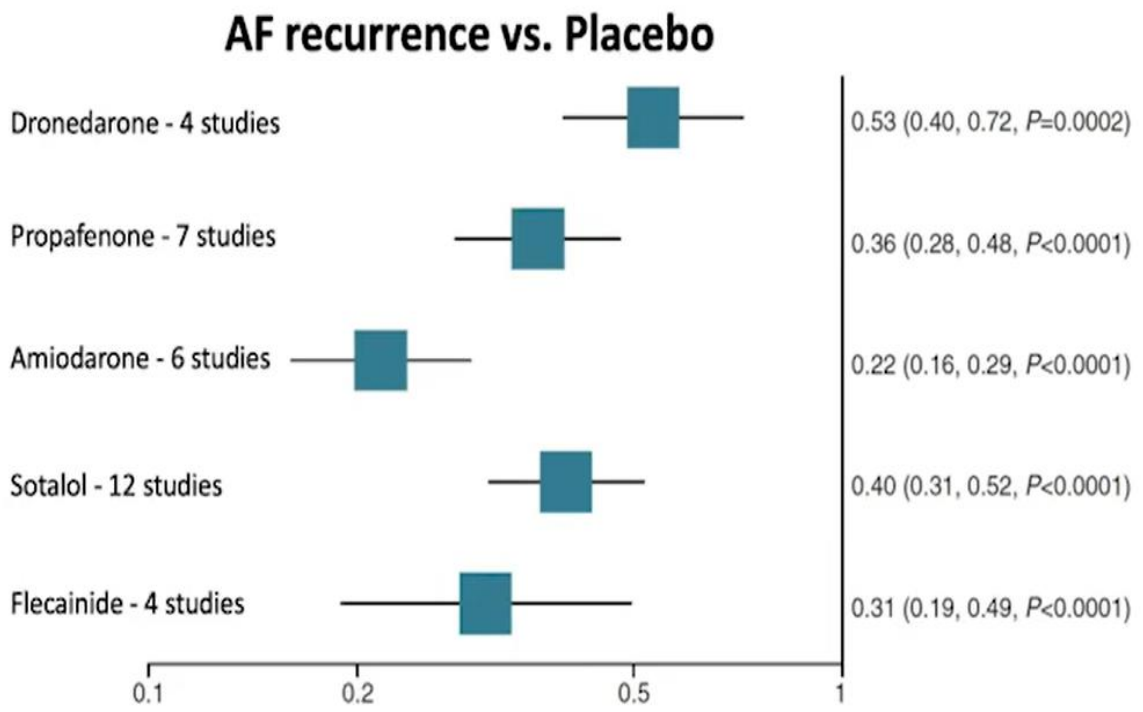
Catheter Ablation



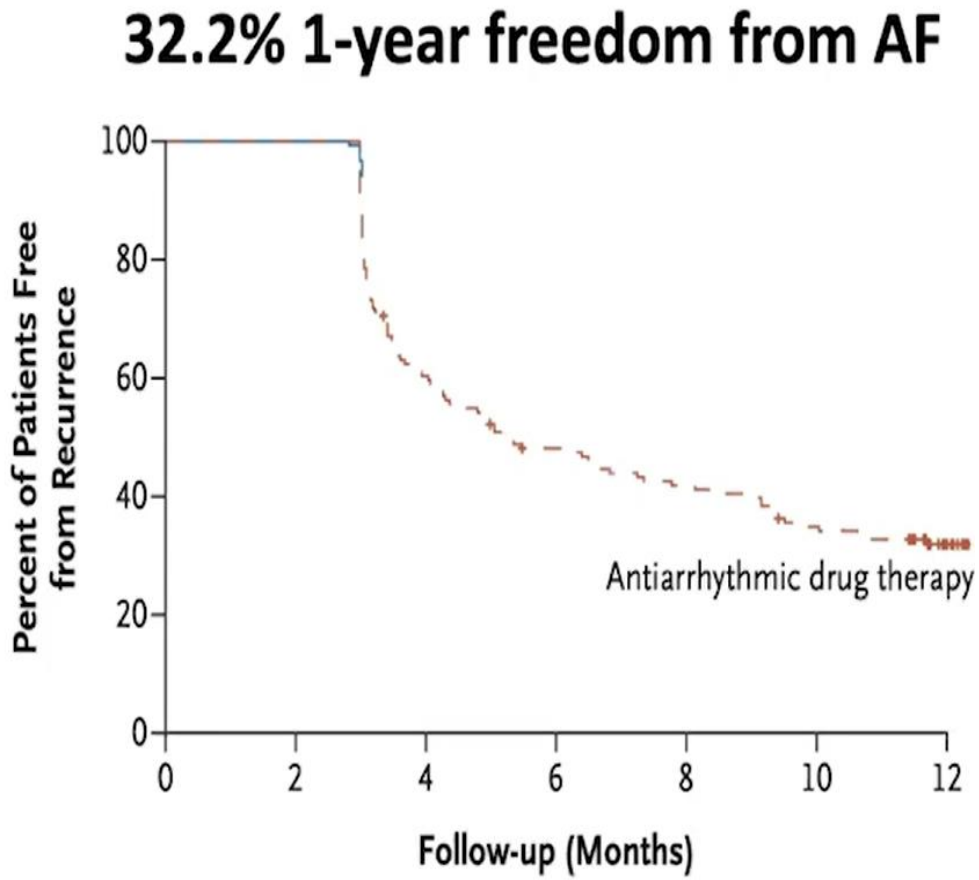
Andrade et al. Circ Res. 2014 Apr 25;114(9):1453-68.

Heart Rhythm 2016:13:331-339

Anti Arrhythmic Drugs

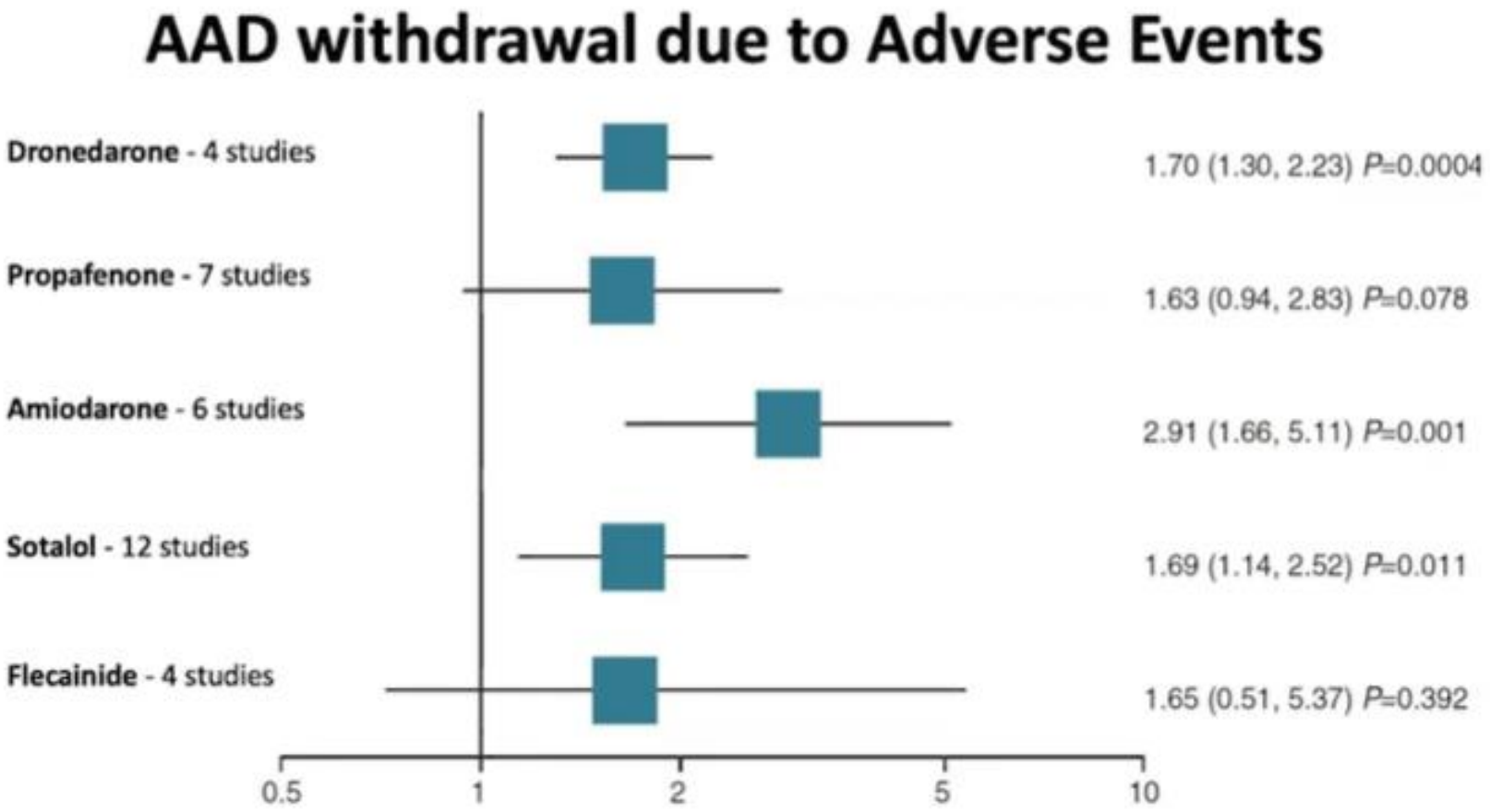


Europace (2011) 13, 329–345

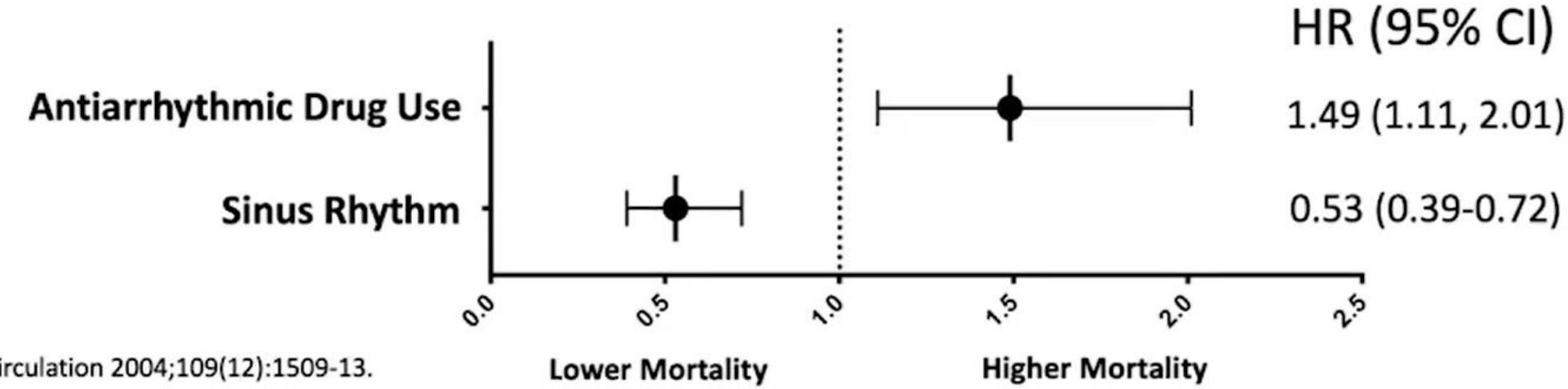


Andrade et al. N Engl J Med 2021; 384:305-315

Anti Arrhythmic Drugs

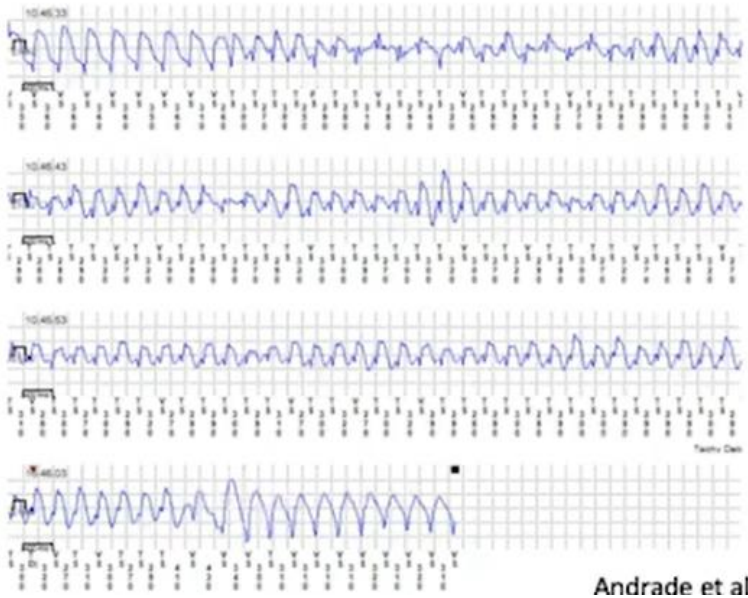


All-cause Mortality

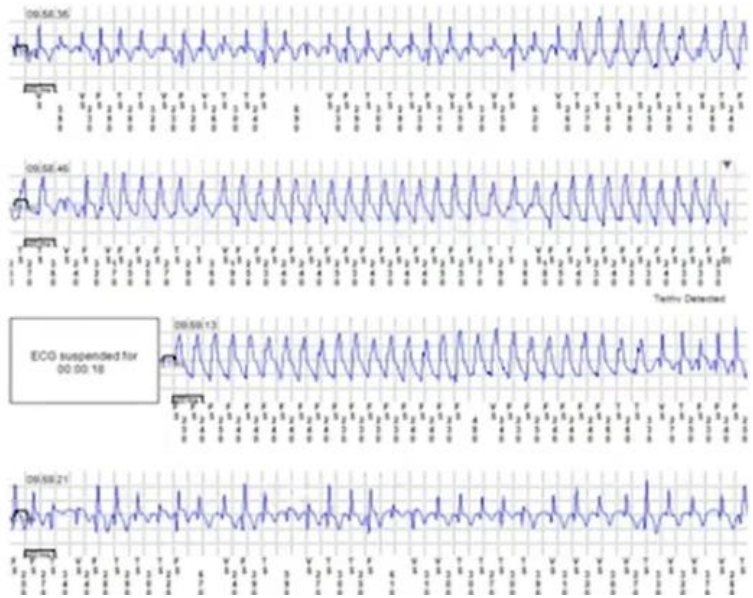


Circulation 2004;109(12):1509-13.

Exertional syncope in a sotalol treated patient

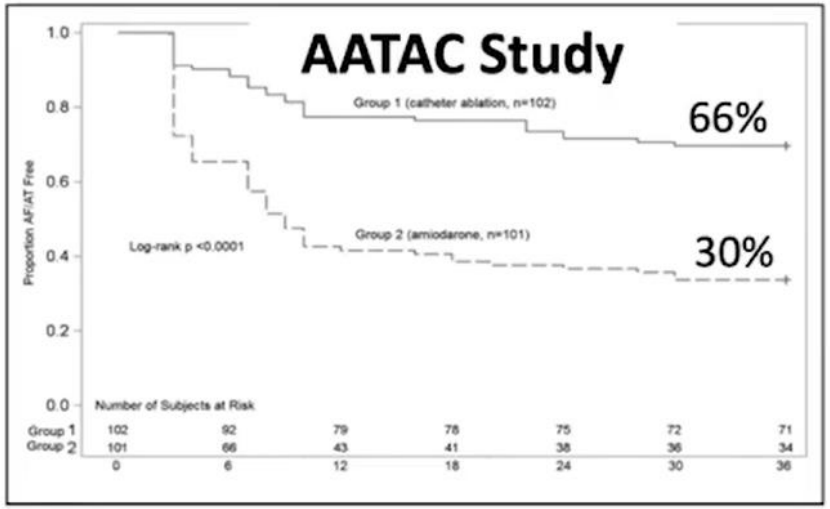


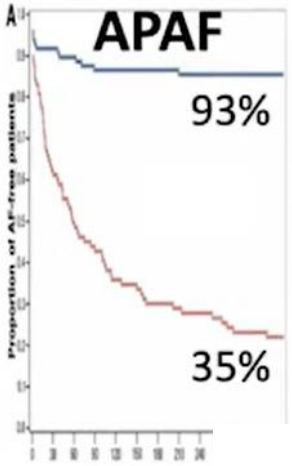
Exertional syncope in a flecainide treated patient

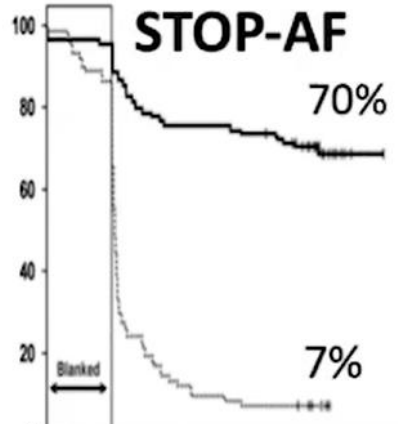


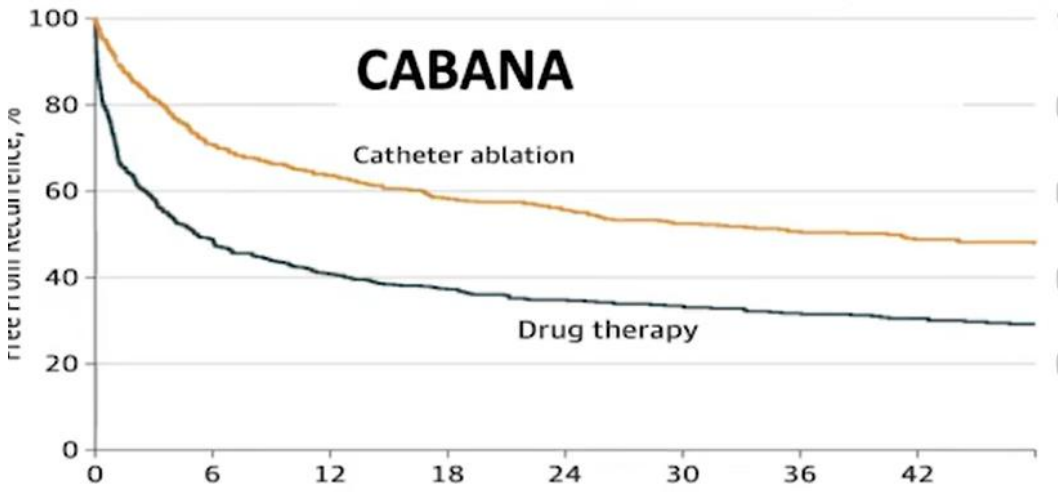
Andrade et al. N Engl J Med 2021; 384:305-315

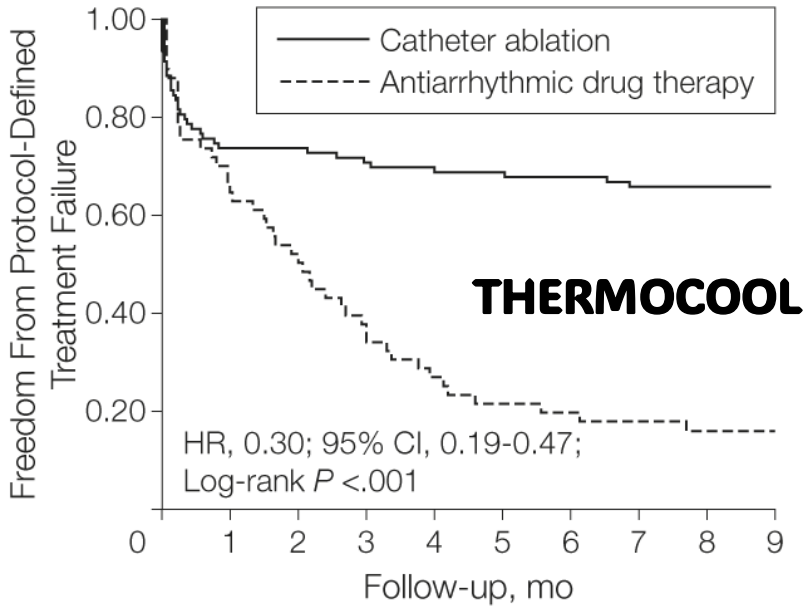
Ablation is more effective than AADs
– *after drugs have failed*





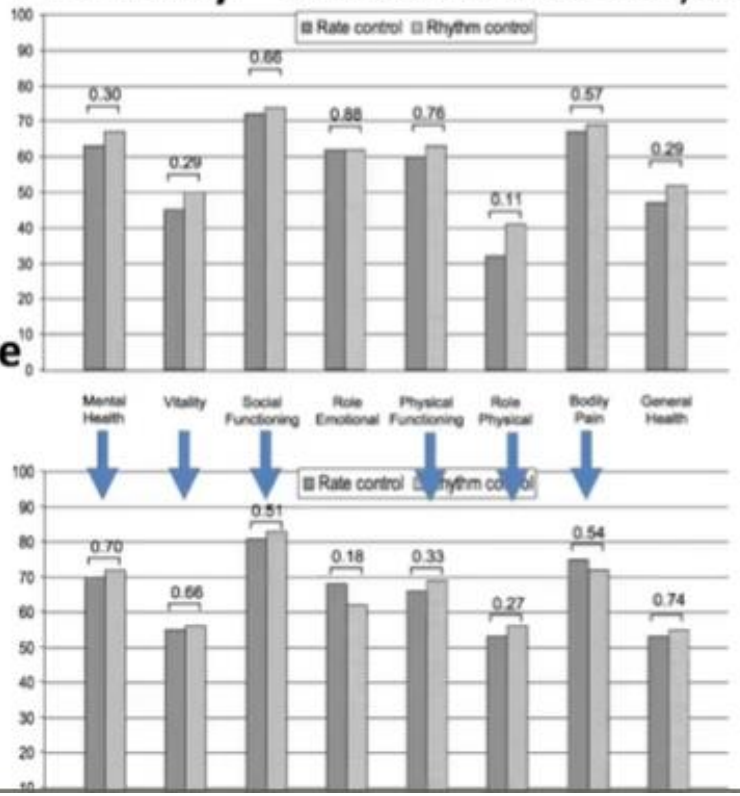






Ablation is more effective than AADs
– *at improving quality of life*

PIAF Study – Intention-to treat analysis



Trial of rate and rhythm control with AAD

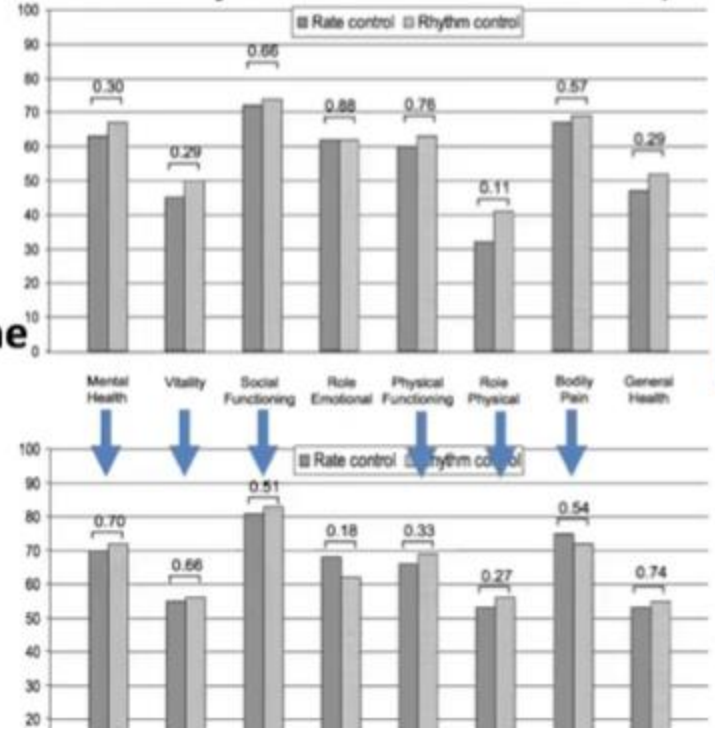
Essentially showing AAD made no difference in improving Quality of Life

Lancet . 2000 Nov 25;356(9244):1789-94.

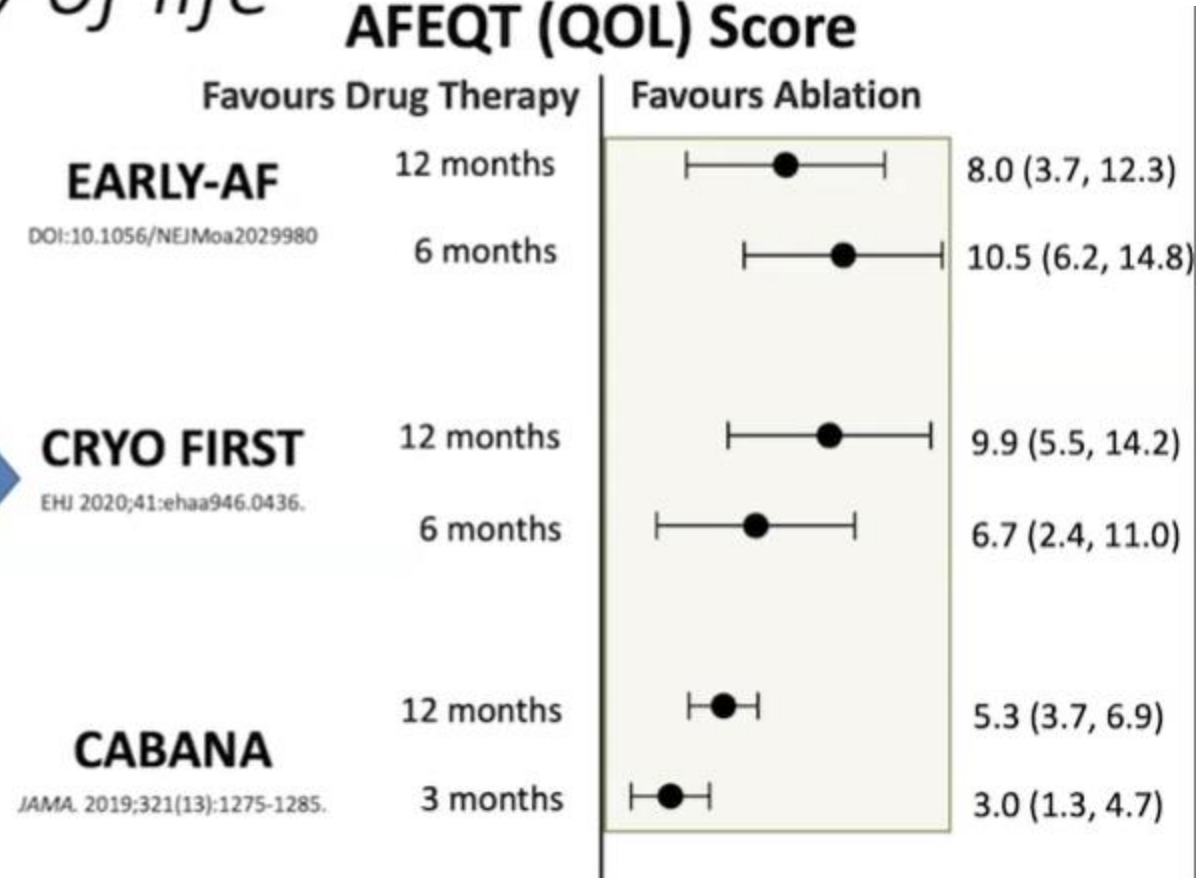
Ablation is more effective than AADs

– *at improving quality of life*

PIAF Study – Intention-to treat analysis



AFEQT (QOL) Score



Lancet . 2000 Nov 25;356(9244):1789-94.

Trial Data

Early Ablation: Early in course of disease?

or

Early ablation after diagnosis??

or

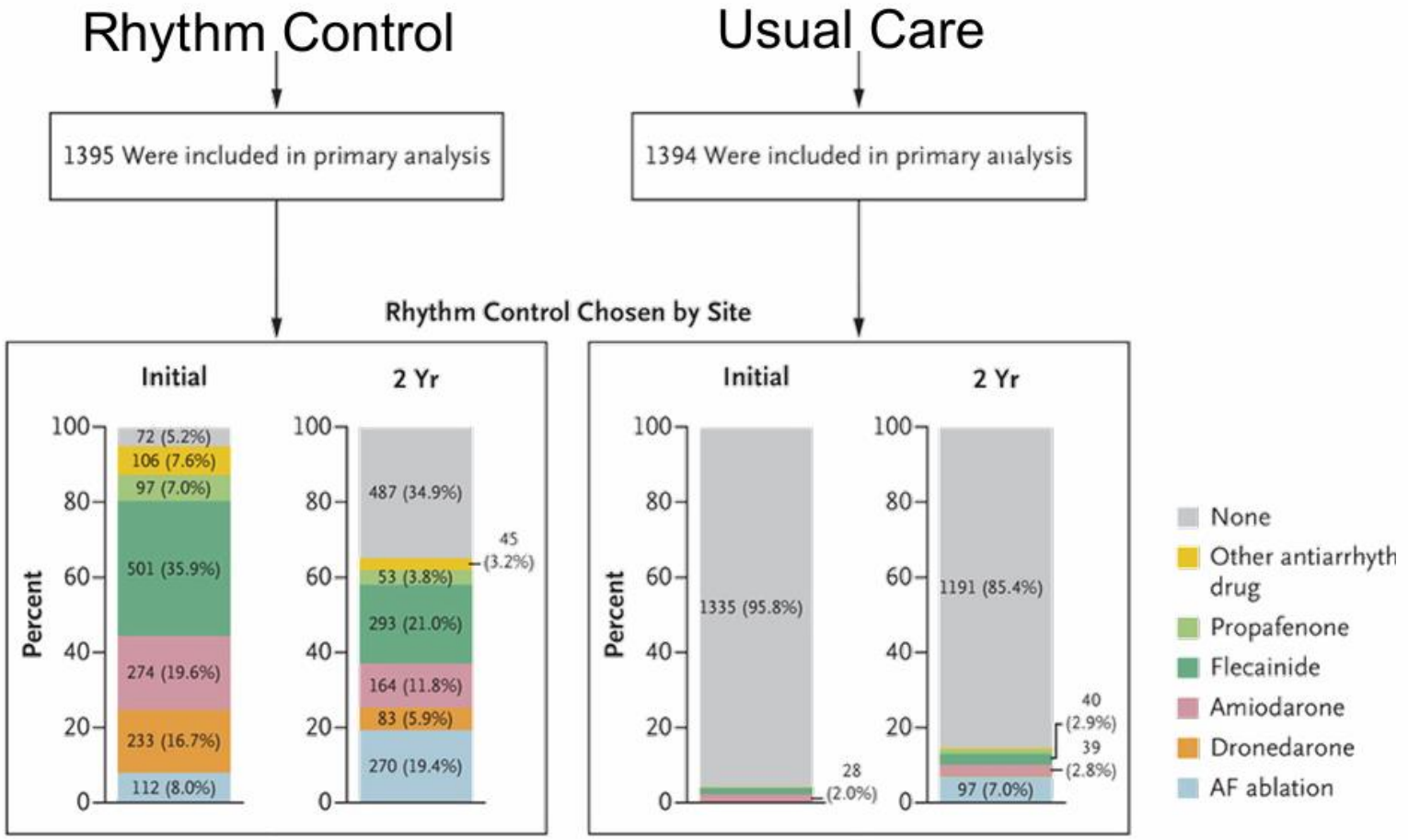
Early ablation in specific subgroups, like CHF???HCM???

or

Just EARLY in life?????

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*



N=2,789

Age 70±8 yrs

46% Female

26% persistent

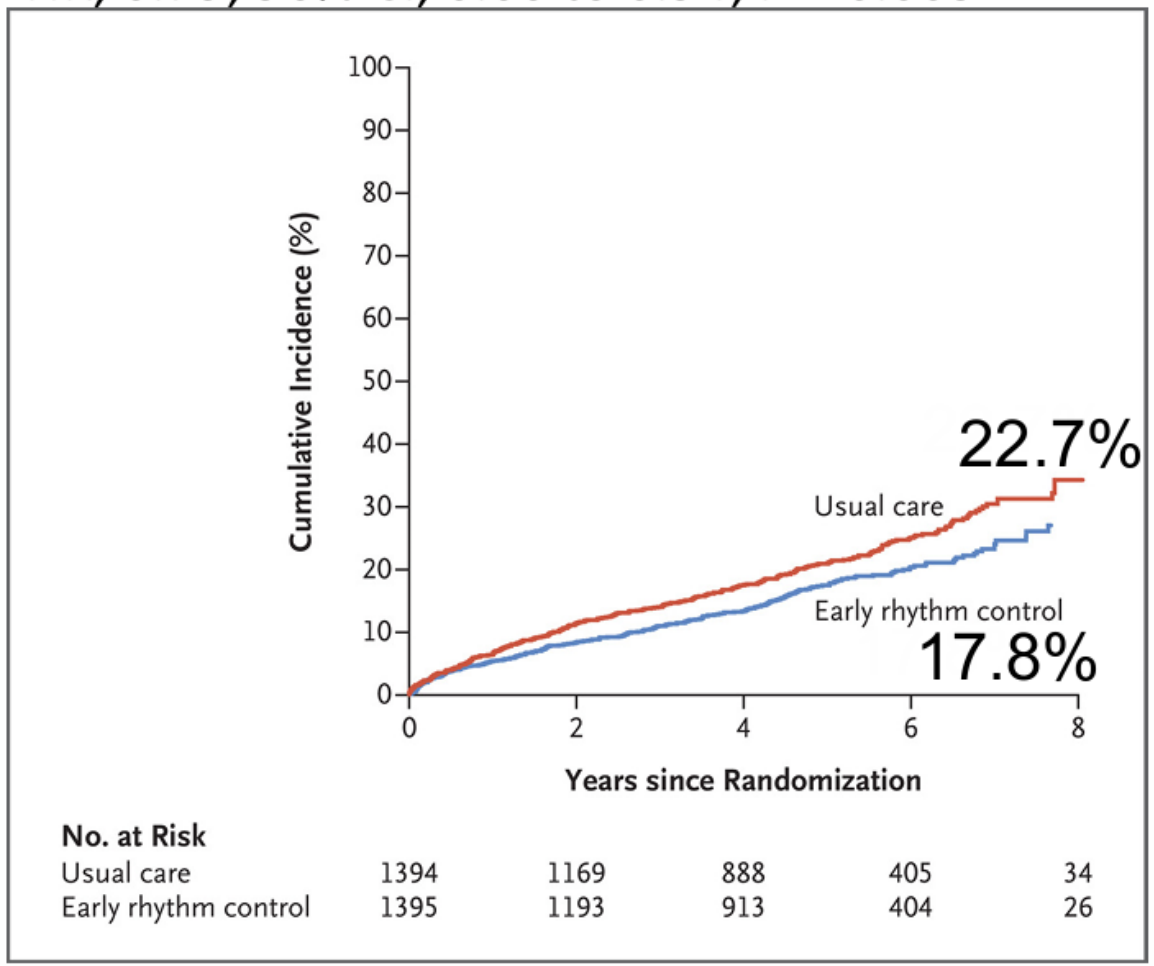
36% Asx

CHADS 2 VASC-3.4

P Kirchhof et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2019422

EAST-AFNET 4 Outcome

HR, 0.79; 96% CI, 0.66 to 0.94; P = 0.005

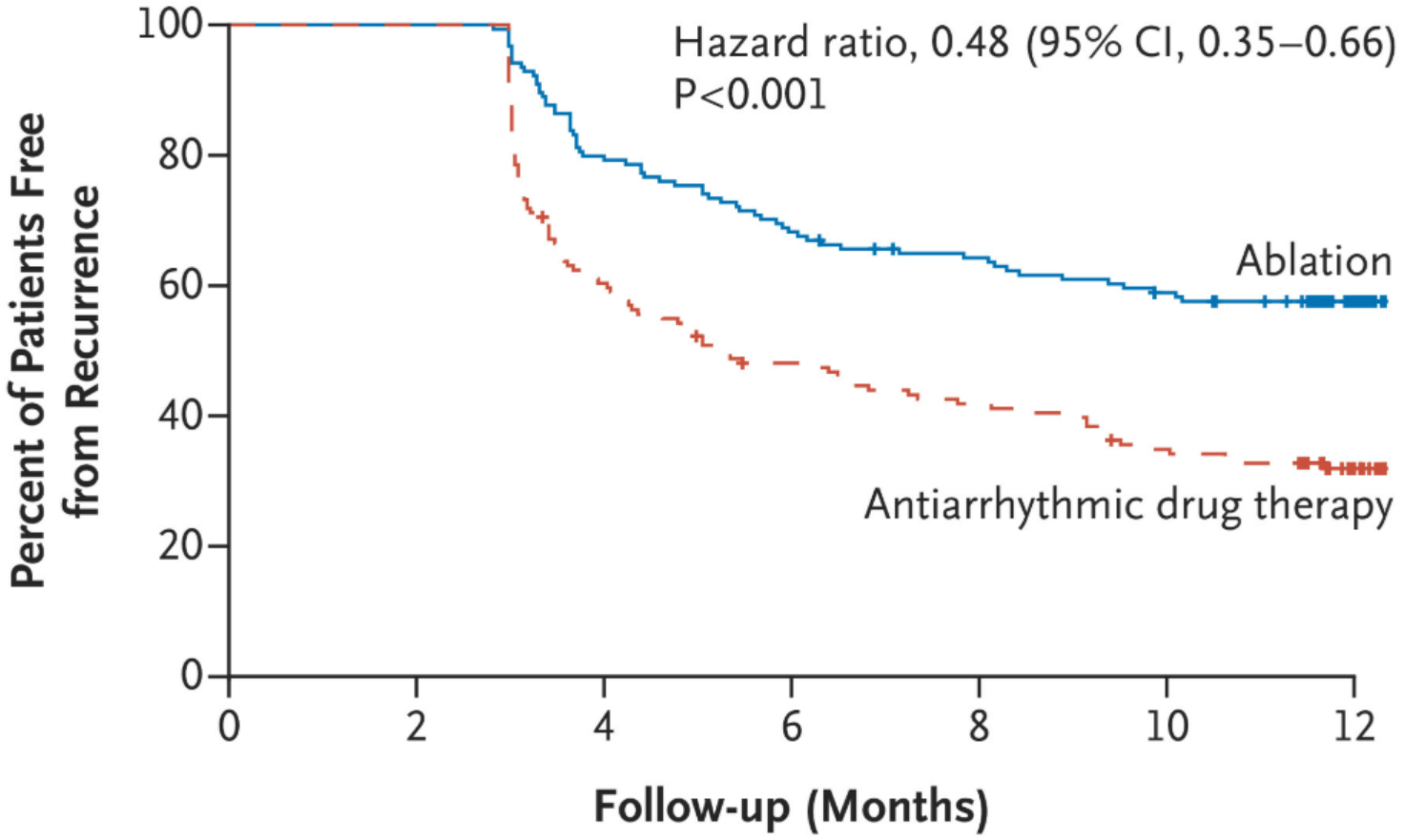


Primary outcome = CV death, stroke, or hospitalization with worsening CHF or ACS.

No diff in hospital nights/yr. (5.8±21.9 vs. 5.1±15.5 days/yr; P = 0.23).

Limitation
Median time in AF- 36 days
No data on success of strategy
Probably most symptomatic patients were not included

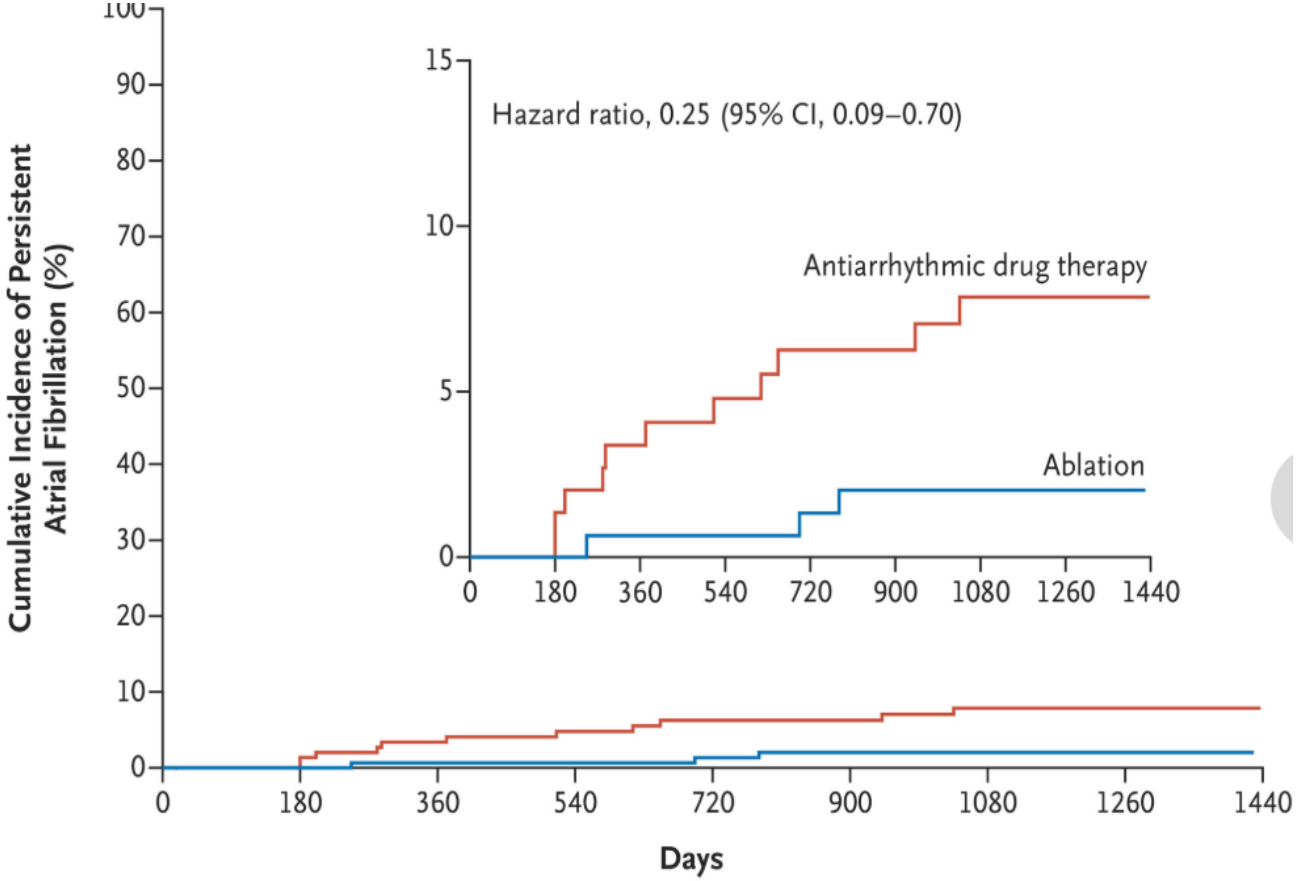
EARLY AF Trial
Ablation as First Line without AAD failure



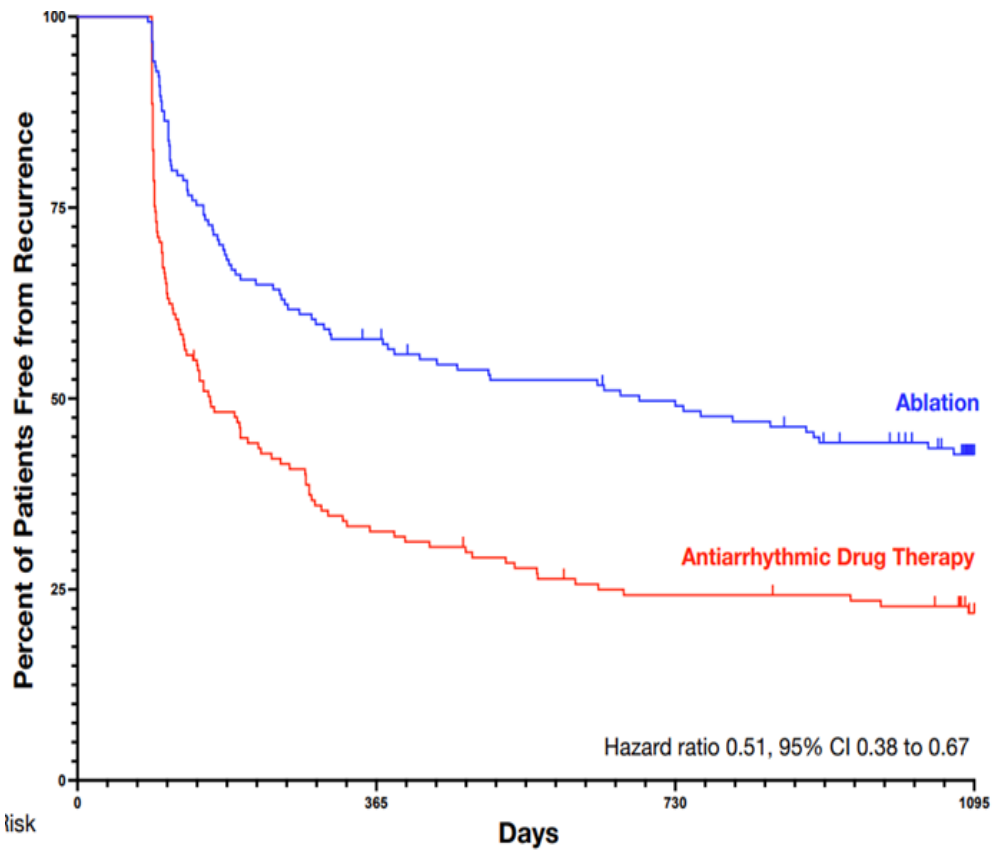
Mean age – 60
CHADS 2 VASC – 2
BMI – 30
PAF – 95%
Female – 30%
Use of AAD – 30%
Median time in AF – 1 year

N Engl J Med 2021;384:305-315

Progression to persistent AF

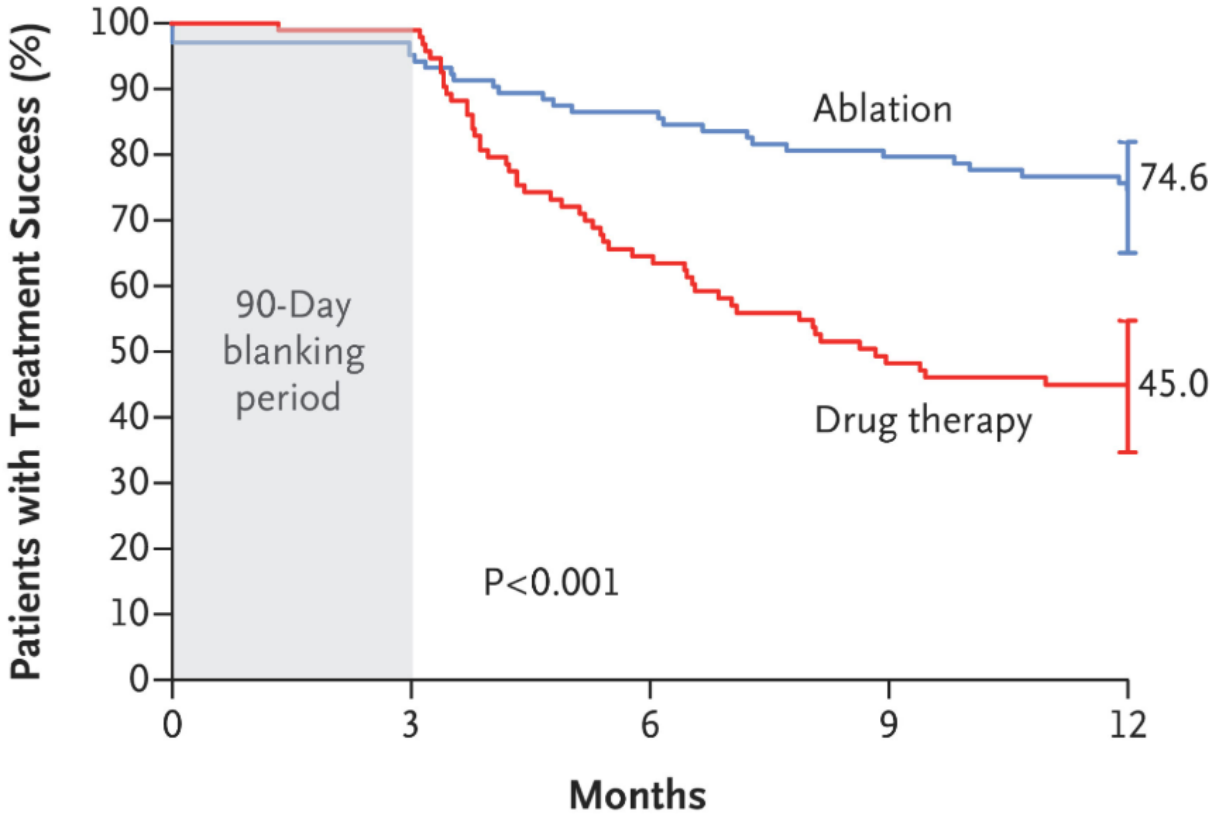


Freedom from any Atrial arrhythmia



STOP AF Trial

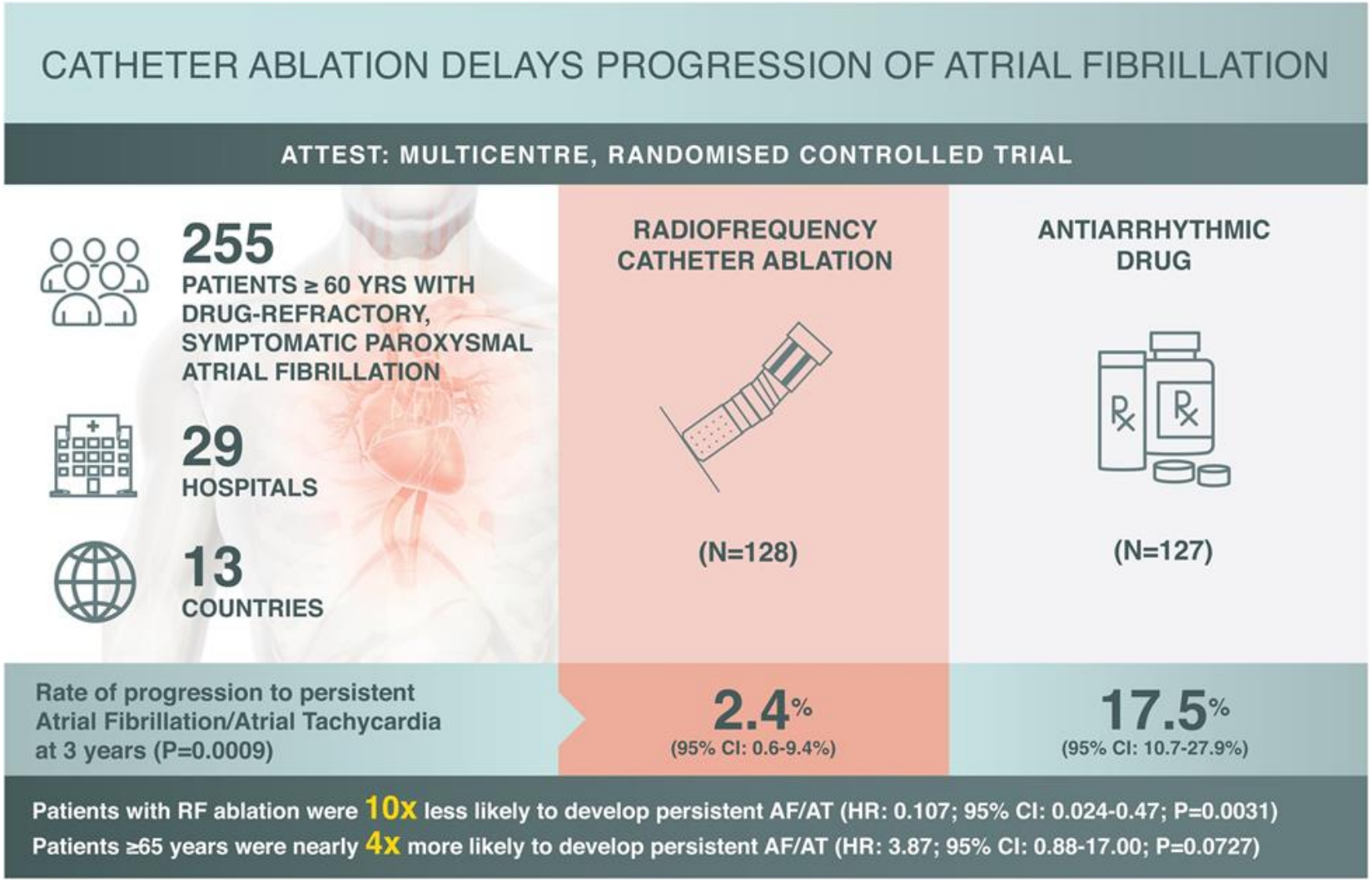
Ablation as First Line without AAD failure



Mean Age - 60
CHADS 2 VASC - 2
BMI - 25-30
Median time in AF - 1.3 years
PAF - 60%
Female - 40%

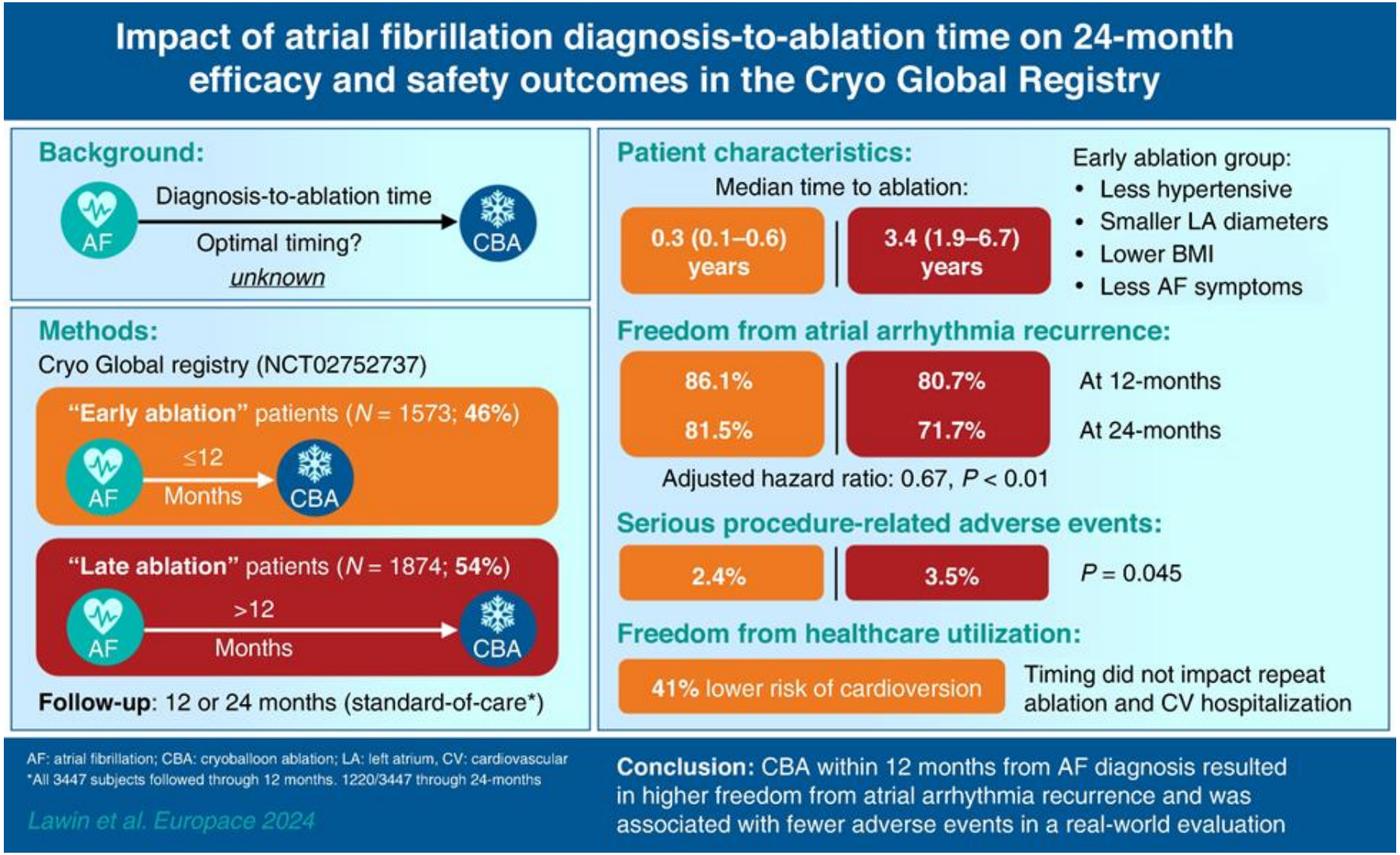
N Engl J Med 2021;384:316-324

Catheter ablation or medical therapy to delay progression of atrial fibrillation: The randomized controlled atrial fibrillation progression trial (ATTEST)



EP Europace, Volume 23, Issue 3, March 2021

Cryo Global Registry



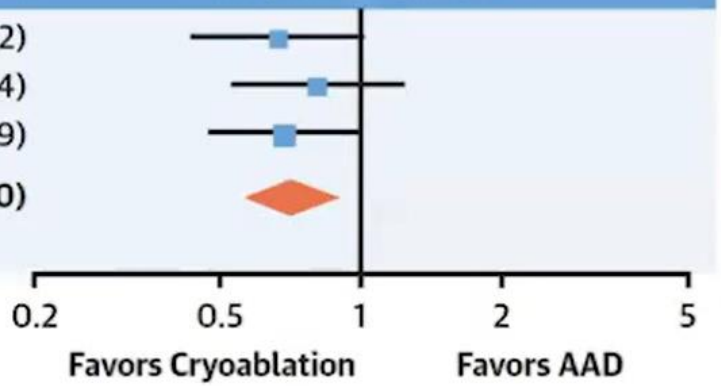
EP Europace, Volume 27, Issue 2, February 2025, euaf008

Ablation Reduced Health Care Utilization

A Health Care Utilization

Study	Cryoablation Events	Cryoablation Total	AAD Events	AAD Total	Weight	Risk Ratio M-H, Random, 95% CI
Cryo-FIRST	25	107	39	111	30.2%	0.66 (0.43-1.02)
EARLY-AF	30	154	36	149	29.8%	0.81 (0.53-1.24)
STOP-AF First	31	104	43	99	39.9%	0.69 (0.47-0.99)
Total (95% CI)		**365**		**359**	**100.0%**	**0.71 (0.56-0.90)**
Total events	86		118			

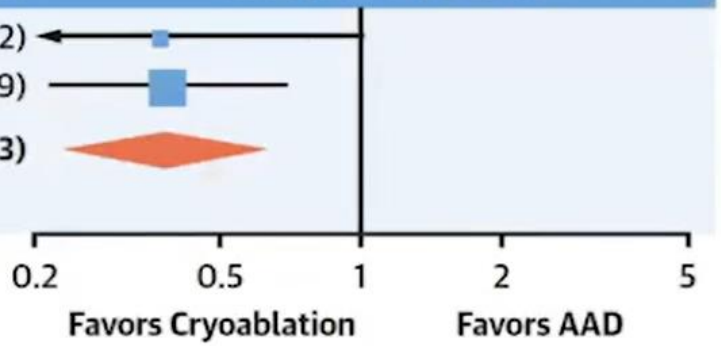
Heterogeneity: $Tau^2 = 0.00$; chi-square = 0.46, df = 2 ($P = 0.79$); $I^2 = 0\%$
Test for overall effect: Z = 2.83 ($P = 0.005$)



B Hospitalization

Study	Cryoablation Events	Cryoablation Total	AAD Events	AAD Total	Weight	Risk Ratio M-H, Random, 95% CI
EARLY-AF	5	154	13	149	25.1%	0.37 (0.14-1.02)
STOP-AF First	13	104	32	99	74.9%	0.39 (0.22-0.69)
Total (95% CI)		**258**		**248**	**100.0%**	**0.38 (0.23-0.63)**
Total events	18		45			

Heterogeneity: $Tau^2 = 0.00$; chi-square = 0.00, df = 1 ($P = 0.95$); $I^2 = 0\%$
Test for overall effect: Z = 3.73 ($P = 0.0002$)



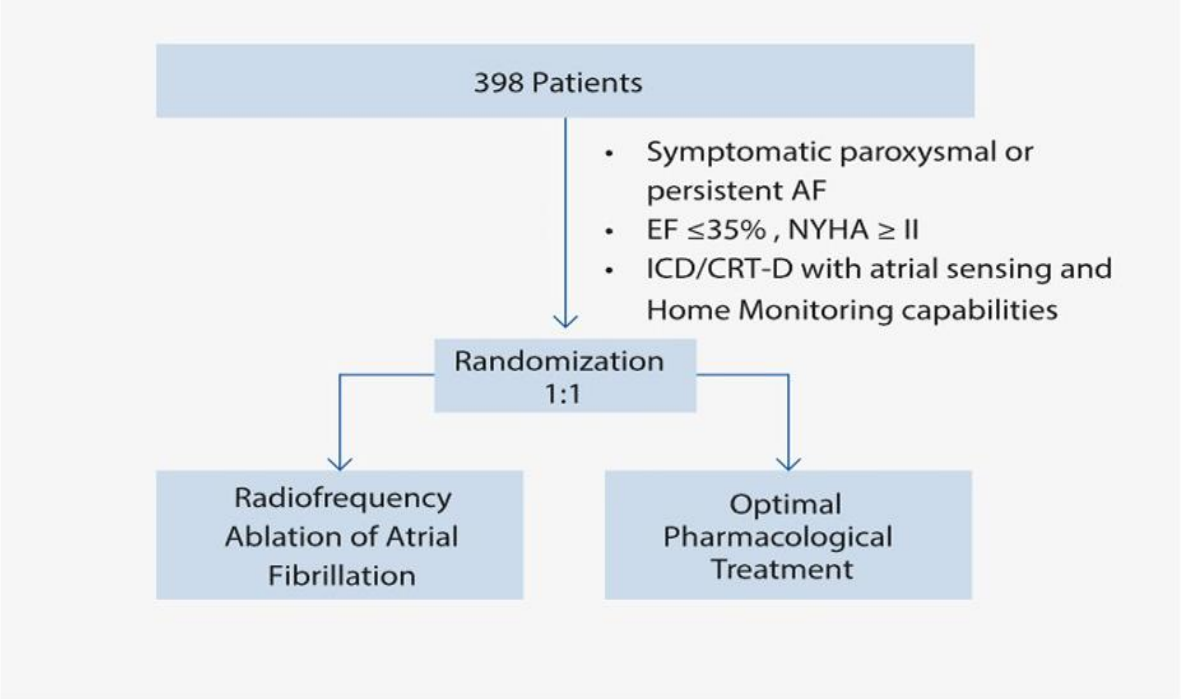
Andrade et al. J Am Coll Cardiol 2021;78:914–930

ALL THESE TRIALS in PAF ARE **NOT POWERED**
TO DETECT MORTALITY/CV mortality/CHF or STROKE benefit

WE CAN show reduction in symptoms and
progression to persistent AF

CLASS I/IIA indication in 2023 ACC/HRS Guidelines

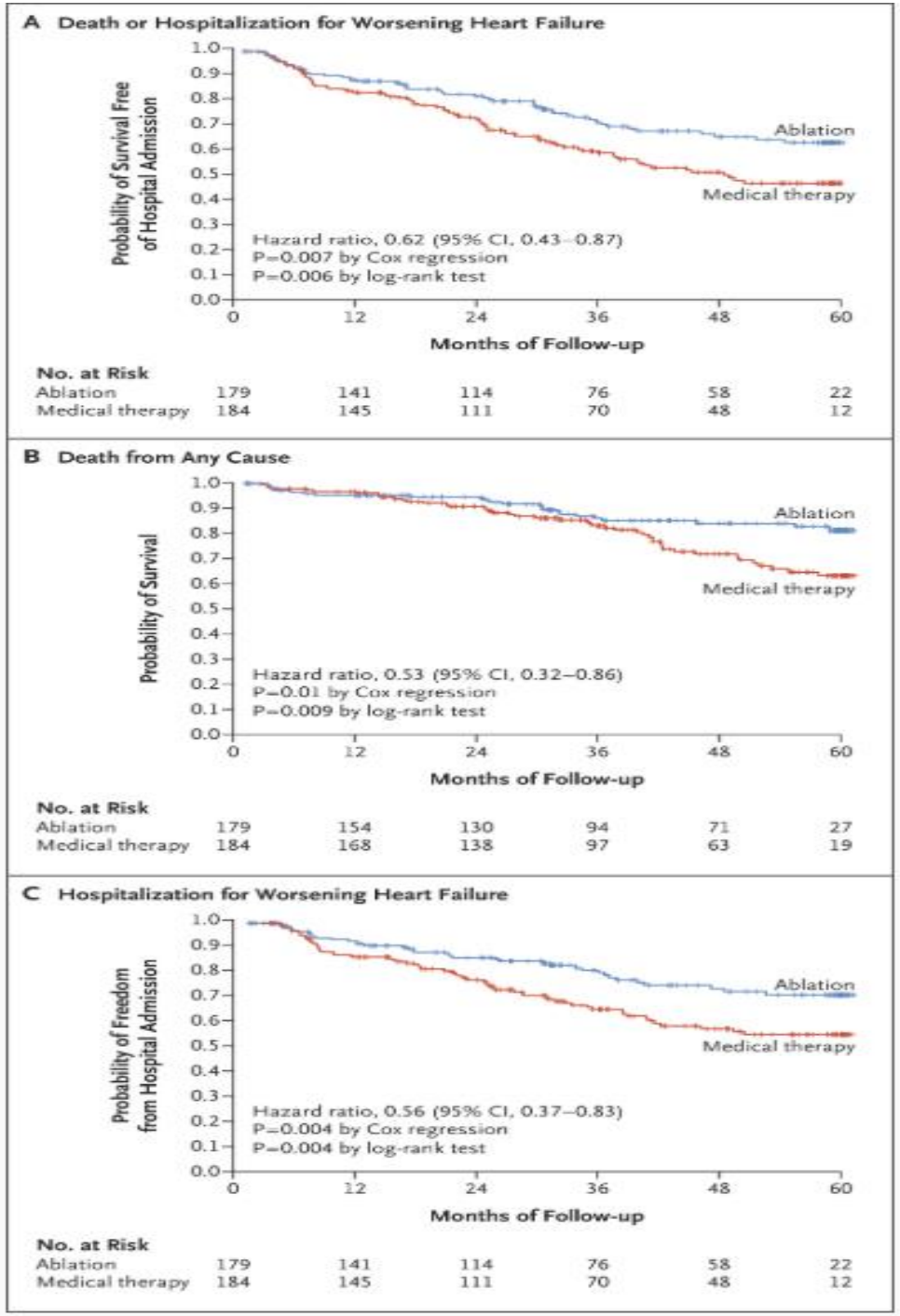
Catheter Ablation for Atrial Fibrillation with Heart Failure-CASTLE HF



Age - 64
BMI- 29
CHF - Class 2-60%
NICM - 60%
Persistent AF - 70%
LVEF - 32%
Amio failure - 45%
ICD/CRTD - 100%

Primary endpoint: All-cause death or unplanned hospitalization due to worsening of heart failure

N Engl J Med 2018;378:417-427



N Engl J Med 2018;378:417-427

Table S9. AF Burden Derived from the Memory of Implanted Devices*

	AF Burden per Patient (in % of Time) at Different Follow-Ups							
	Baseline	3 M	6 M	12 M	24 M	36 M	48 M	60 M
Mean ± SD								
Ablation	51 ± 47	27 ± 39	23 ± 37	20 ± 38	23 ± 39	25 ± 40	27 ± 41	27 ± 42
Pharmacological	51 ± 46	51 ± 47	51 ± 46	52 ± 46	48 ± 47	50 ± 47	54 ± 47	64 ± 45

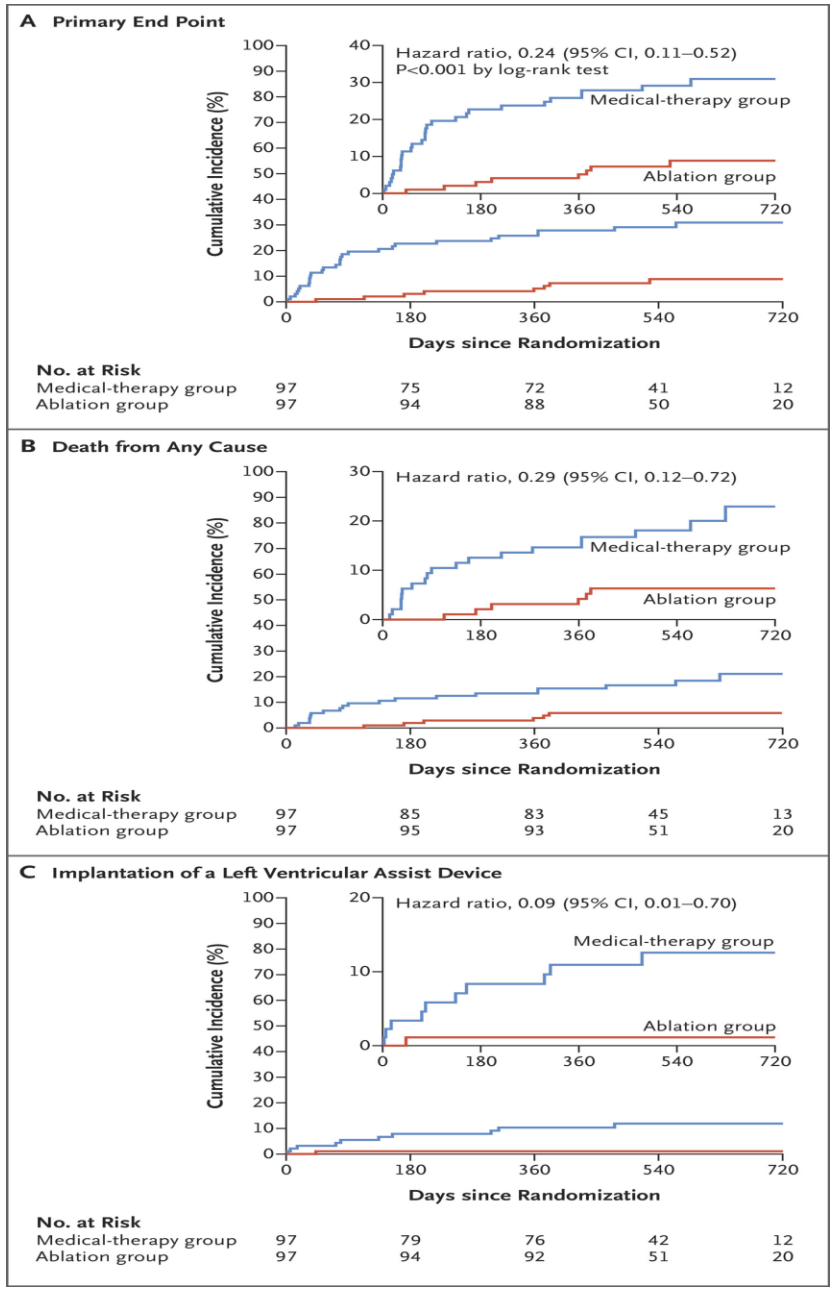
Table S10. Patients with Consistent Levels of AF Burden

	AF Burden at All Follow-Ups*				
	≥5%	≥10%	≥25%	≥50%	≥90%
Patients					
Ablation group – no. (% of 163†)	31 (19)	30 (18)	30 (18)	20 (12)	15 (9)
Pharmacological group – no. (% of 178†)	85 (48)	80 (45)	80 (45)	69 (39)	56 (32)

N Engl J Med 2018;378:417-427

CASTLE HTX Trial

Death/LVAD/HT



Age - 62
NYHA Class – 3/4

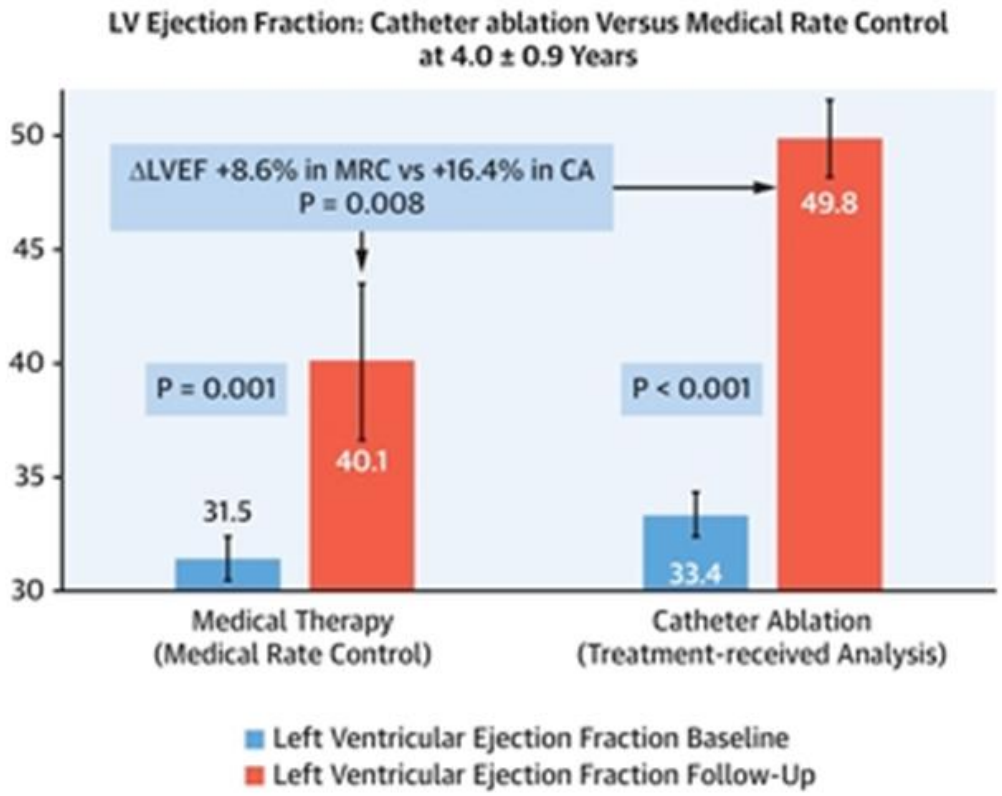
Patients with end stage CHF
Referred for LVAD/HT

LVEF - 25%
NICM - 60%
Persistent AF - 56%
Duration of AF - 4 years

N Engl J Med 2023;389:1380-1389

CAMERA-MRI Study

CENTRAL ILLUSTRATION: Impact of CA Versus Medical Therapy on LVEF in AF-HFrEF



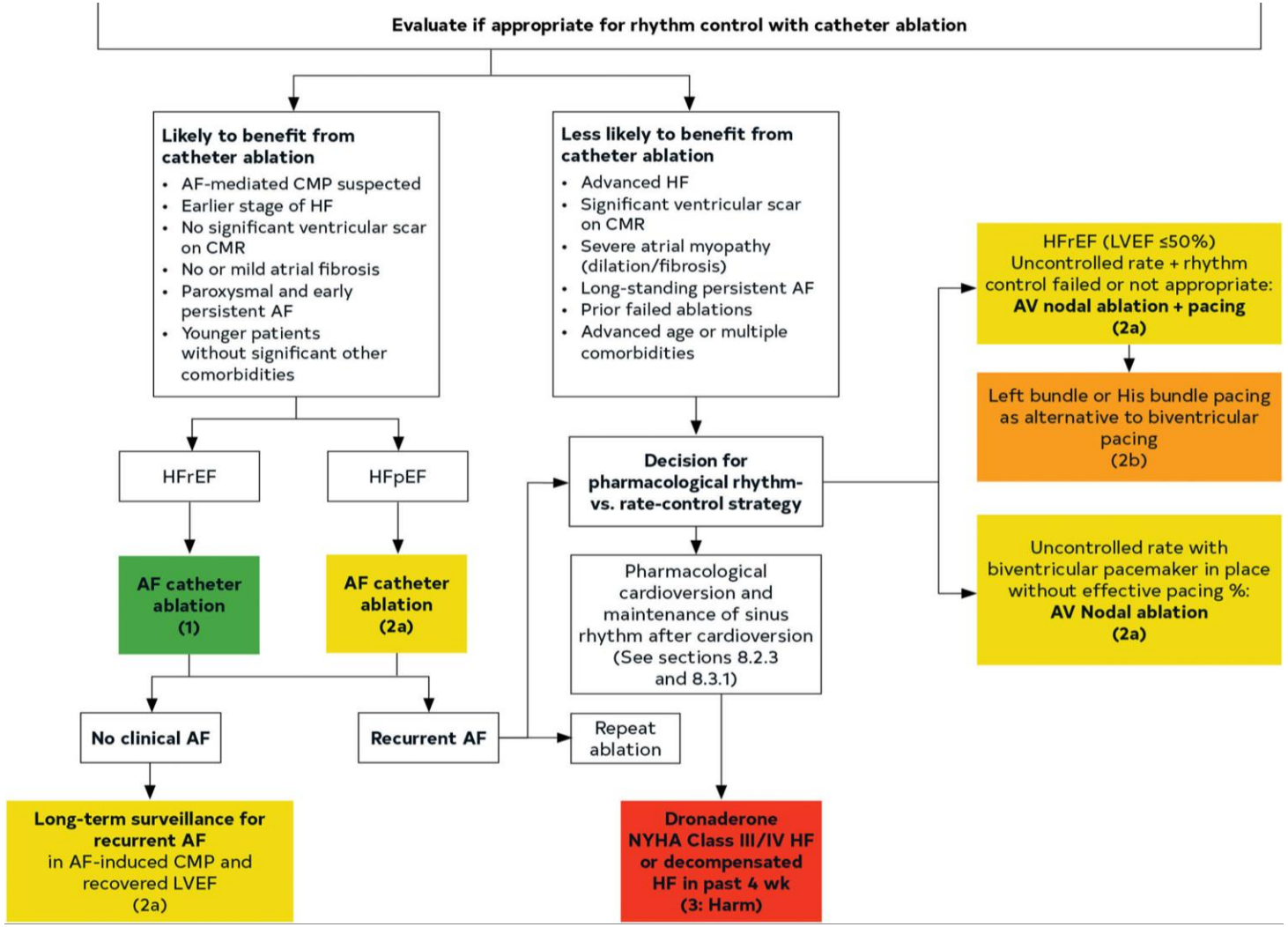
Sugumar, H. et al. J Am Coll Cardiol EP. 2020;6(13):1721-31.

66 Patients
Ablation vs rate control

CHF - Class 2/3
On GDMT - 98%
Persistent AF median duration - 2.3 years
LVEF - 32%

½ rate control group crossed over to ablation

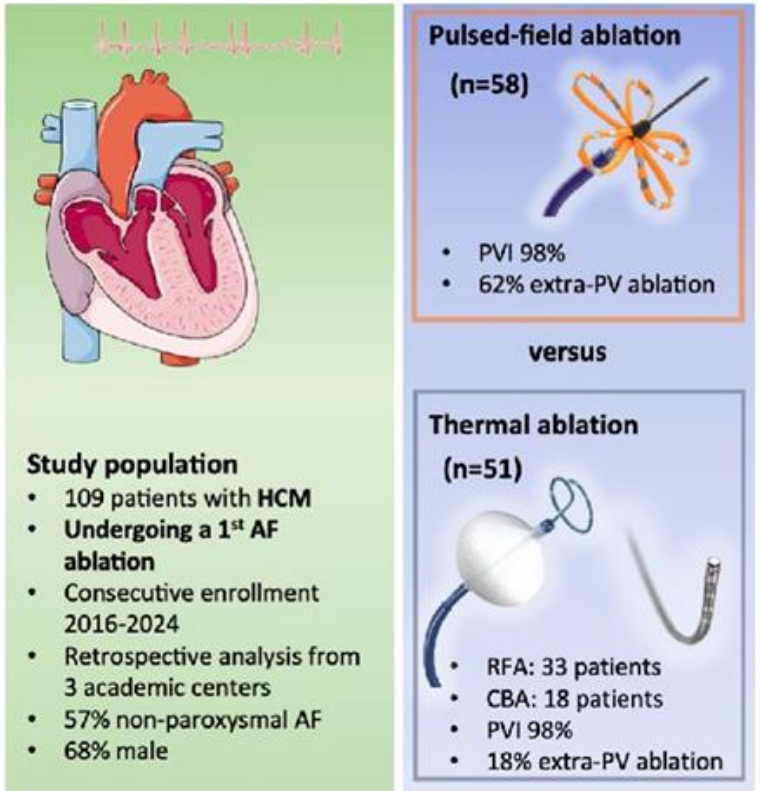
AF ablation may show mortality/morbidity benefit in CHF
Class I/II A indication in guidelines

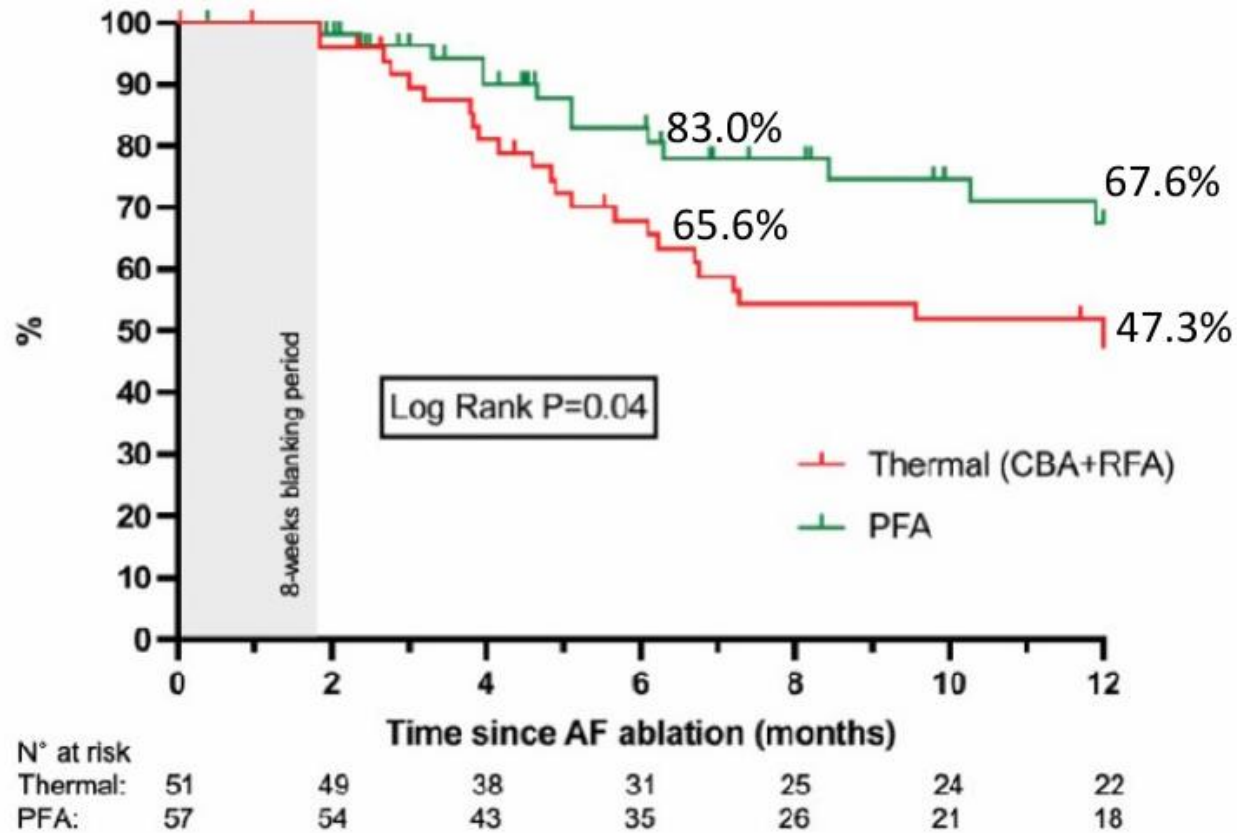


2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation

Pulsed-Field vs Thermal Catheter Ablation of Atrial Fibrillation in Patients with Hypertrophic Cardiomyopathy

Samy Gribissa, MD[1], Thomas Kueffer, PhD[2], Sven Knecht, PhD[3], Xavier Waintraub, MD[1]; Nicolas Badenco, MD[1], Philippe Charron, MD, PhD[1,4], Pauline Pinon, MD[1], Raphael King, MSc[2], Estelle Gandjbakhch, MD, PhD[1,4], Guillaume Duthoit, MD[1], Christian Sticherling, MD[3], Tobias Reichlin, MD, PhD[2], Mikael Laredo, MD, PhD[1]





JACC:CEP *in press*

Efficacy and Risk of Atrial Fibrillation Ablation Before 45 Years of Age

Peter Leong-Sit, MD; Erica Zado, PA-C; David J. Callans, MD; Fermin Garcia, MD; David Lin, MD; Sanjay Dixit, MD; Rupa Bala, MD; Michael P. Riley, MD, PhD; Mathew D. Hutchinson, MD; Joshua Cooper, MD; Edward P. Gerstenfeld, MD; Francis E. Marchlinski, MD

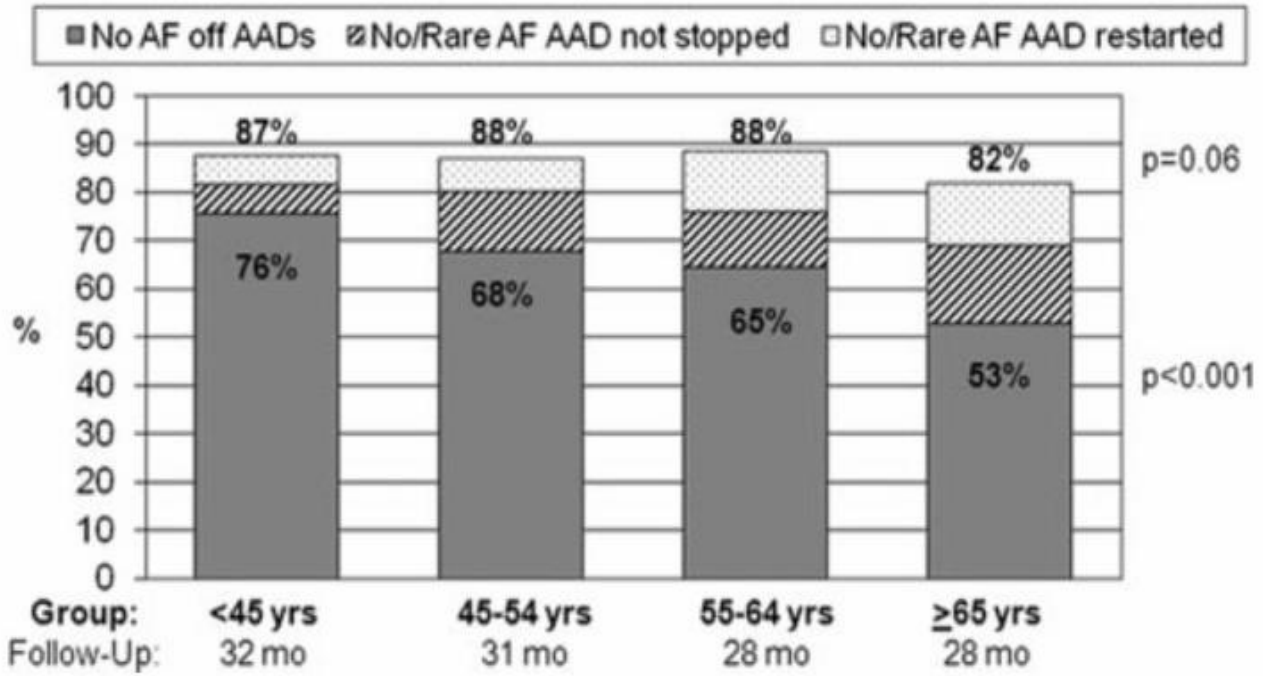


Figure 1. Control of AF after AF ablation on the basis of age

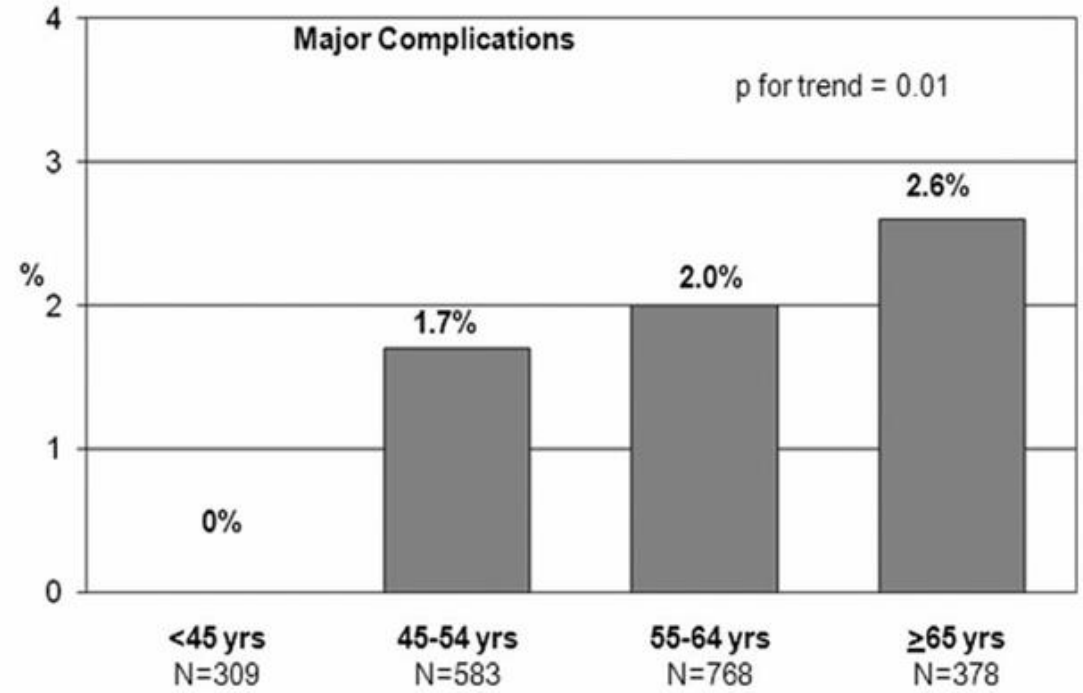


Figure 2. Rate of major complications after AF ablation

Circ Arrhythm Electrophysiol. 2010 Oct;3(5):452-7.

Ablations are getting safer

Contemporary ablation is safe

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation

Jason G. Andrade, M.D., George A. Wells, Ph.D., Marc W. Deyell, M.D., Matthew Bennett, M.D., Vidal Essebag, M.D., Ph.D., Jean Champagne, M.D., Jean-Francois Roux, M.D., Derek Yung, M.D., Allan Skanes, M.D., Yaariv Khaykin, M.D., Carlos Morillo, M.D., Umjeet Jolly, M.D., Paul Novak, M.D., Evan Lockwood, M.D., Guy Amit, M.D., Paul Angaran, M.D., John Sapp, M.D., Stephan Wardell, M.D., Sandra Lauck, Ph.D., Laurent Macle, M.D., and Atul Verma, M.D., for the EARLY-AF Investigators*

Outcome at 12 months	Ablation Group n=154	Antiarrhythmic Group n=149	RR (95% CI)
Any safety endpoint	14 (9.1%)	24 (16.1%)	0.59 (0.29–1.21)
Serious adverse events	5 (3.2%)	6 (4.0%)	0.81 (0.25–2.59)

Andrade et al. N Engl J Med 2021; 384:305-315

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Progression of Atrial Fibrillation after Cryoablation or Drug Therapy

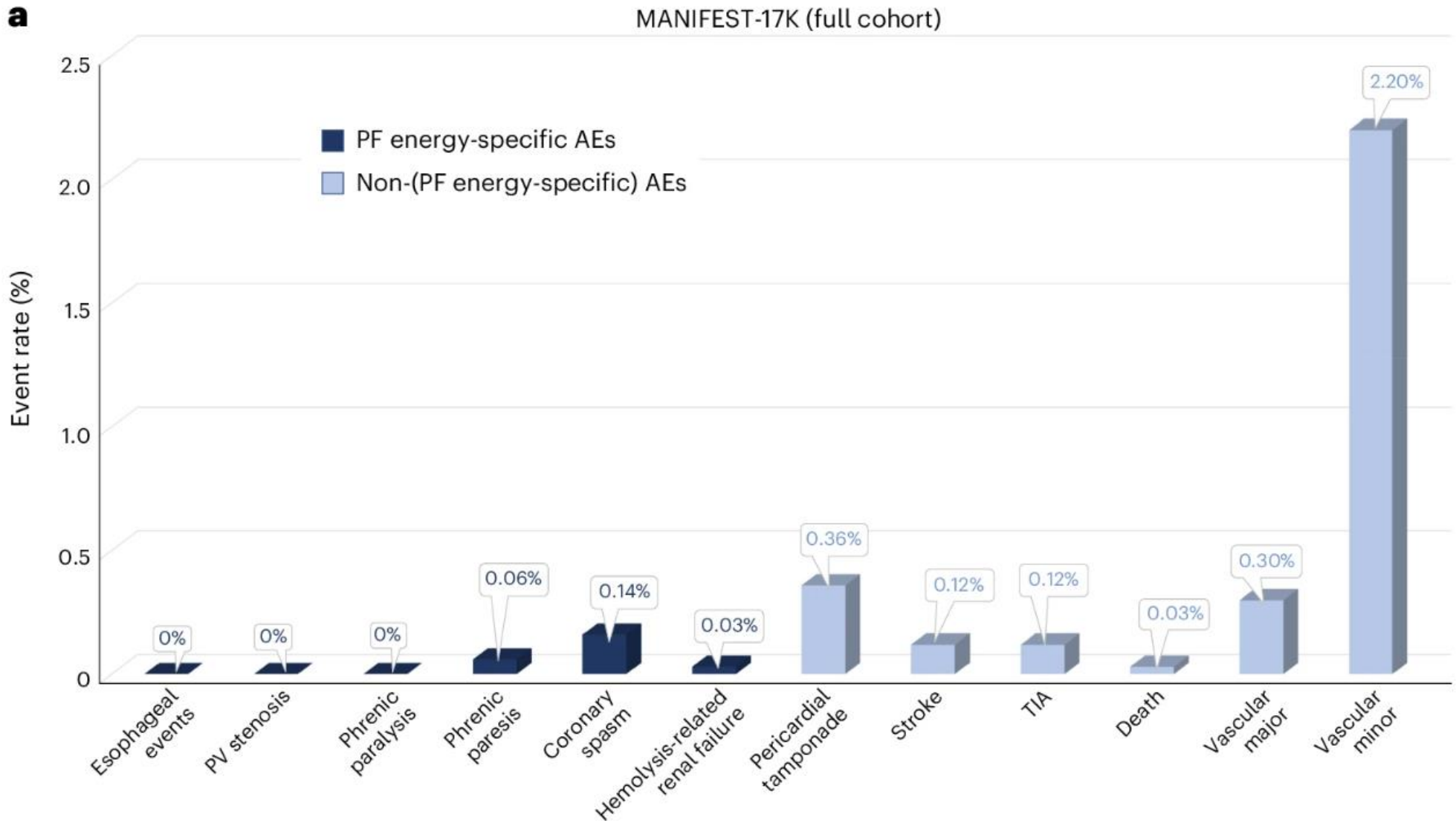
J.G. Andrade, M.W. Deyell, L. Macle, G.A. Wells, M. Bennett, V. Essebag, J. Champagne, J.-F. Roux, D. Yung, A. Skanes, Y. Khaykin, C. Morillo, U. Jolly, P. Novak, E. Lockwood, G. Amit, P. Angaran, J. Sapp, S. Wardell, S. Lauck, J. Cadrin-Tourigny, S. Kochhäuser, and A. Verma, for the EARLY-AF Investigators*

ABSTRACT

Outcome at 36 months	Ablation Group n=154	Antiarrhythmic Group n=149	RR (95% CI)
Any safety endpoint	17 (11.0%)	35 (23.5%)	**0.47 (0.28, 0.79)**
Serious adverse events	7 (4.5%)	15 (10.1%)	0.45 (0.19, 1.05)

Andrade et al. N Engl J Med 2023; 388:105-116

Safety of pulsed field ablation in more than 17,000 patients with atrial fibrillation in the MANIFEST-17K study



Nature Medicine volume 30, pages2020–2029 (2024)

Atrial Fibrillation Ablation:

Lessons learned

1. Treatment of AF results in improved outcomes

2. Ablation as a first line-treatment is better than AAD for preventing recurrence

3. Ablation as a first line-treatment is better than AAD for preventing progression

Thank You