# Atrial Fibrillation Detection & Treatment


- Kevin P Foley MD FACC FRCP(C)
- Pacific Northwest University
- College of Osteopathic Medicine

# Atrial Fibrillation

- Kevin Foley MD
- No industrial relationships to disclose
- Formerly of the Yakima Heart Center




Yakima
HEART CENTER



Pacific Northwest
University of Health Sciences

# Atrial Fibrillation

- Definition
- Detection and Assessment
- Burden: population and the individual
- Treatment: Rhythm vs Rate Control
- Treatment: Vit K Antag vs NOAC
- Warfarin treatment issues
- Oxidative Stress, Cognitive Impact

# Atrial Fibrillation

- Loss of synchronous atrial contraction
- Fast to slow ventricular rates: no P waves
- Symptoms
  - Rapid Heart Rate
  - Loss of AV synchrony
  - Cannon retrograde pressure waves
  - Changes in neurohormones
- Pathophysiology: electrical, contractile structural remodeling—inflammation (?systemic or local?)

# Predisposing Causes

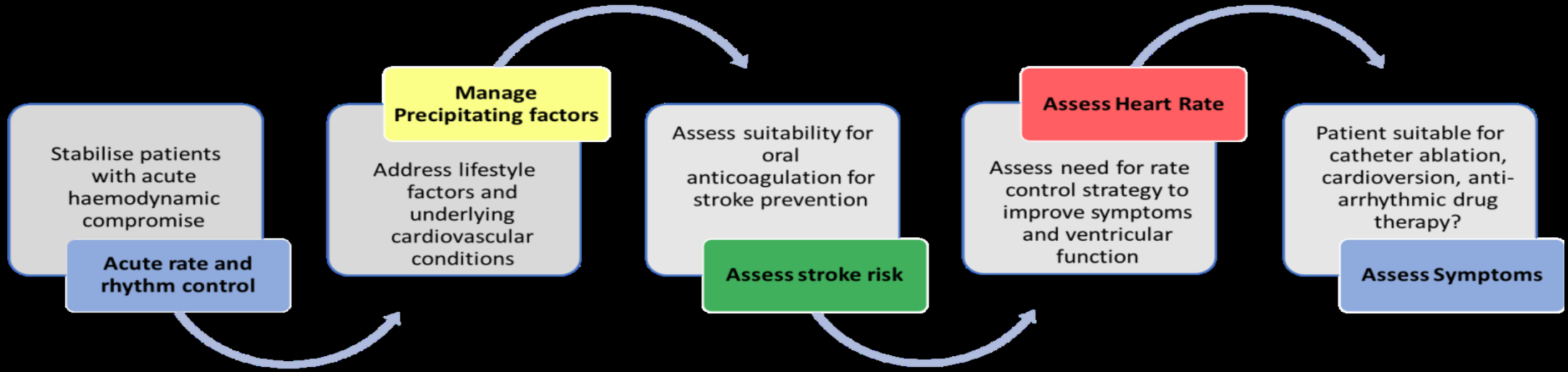
- Ac coronary syndromes
- Valvular heart disease, esp mitral
- CHF
- Hypertension
- Post op surgery/cardiac, other
- Congenital Heart disease (esp ASD)
- WPW
- Other Structural Heart disease

# Predisposing causes—non cardiac

- Pulmonary disease---pneumonia, PE, COPD
- Endocrine: thyrotoxicosis, pheochromocytoma
- Electrolyte imbalance
- Fever/sepsis
- Toxins: alcohol, cocaine

# Atrial Fibrillation

## Paroxysmal: self term <7 days
## Persistent >prolonged >7 Days
## Permanent



# Breathlessness

- 70 year old woman with long history of hypertension, active, walks every day
- Now becomes breathless after walking one block. No chest pain or heaviness, no palpitations
- Exercise ECG: 3 minutes Bruce protocol, atrial fibrillation with ventricular rate of 170  + symptoms
- Echocardiogram: normal LV contractility, slight LA enlargement

# Detection of Atrial Fibrillation—the harder you look, the more likely to find

- Single 12 lead ECG or rhythm strip
- 24-48 hour Holter monitor (battery box or band aid)
- Event recorder—surface or implanted
- Smart watch/smart phone
- Non contact evaluation

# Timeline of Wearable Devices

**1993**
First pacemaker with digital signal processing

**1994**
Physician-prescribed ECG event recorder

**2009**
First major clip-on activity and sleep tracker

**2011**
Shift to wrist-worn devices

**2012**
Early smartwatches

**2013**
Smartphone-connected ECG

**2013-2015**
Smartphone operating system platform watches

**2018**
Irregular rhythm prediagnostic notification and ECG

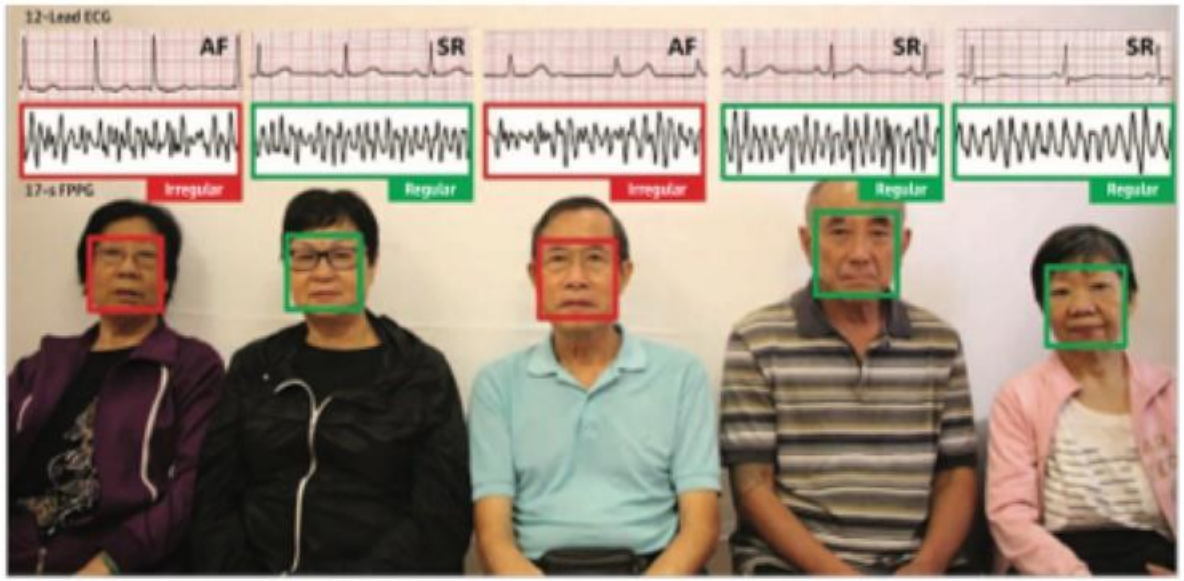
**2019**
Blood pressure monitoring

# Contact-Free Detection of AF (cont)

RESEARCH LETTER

## High-Throughput, Contact-Free Detection of Atrial Fibrillation From Video With Deep Learning

Approaches for atrial fibrillation (AF) detection can screen only 1 patient at a time.[1] In 2018,[2] we demonstrated a novel method of AF detection by analyzing facial photoplethysmographic (FPPG) signals without physical contact using a smartphone




Editor's Note

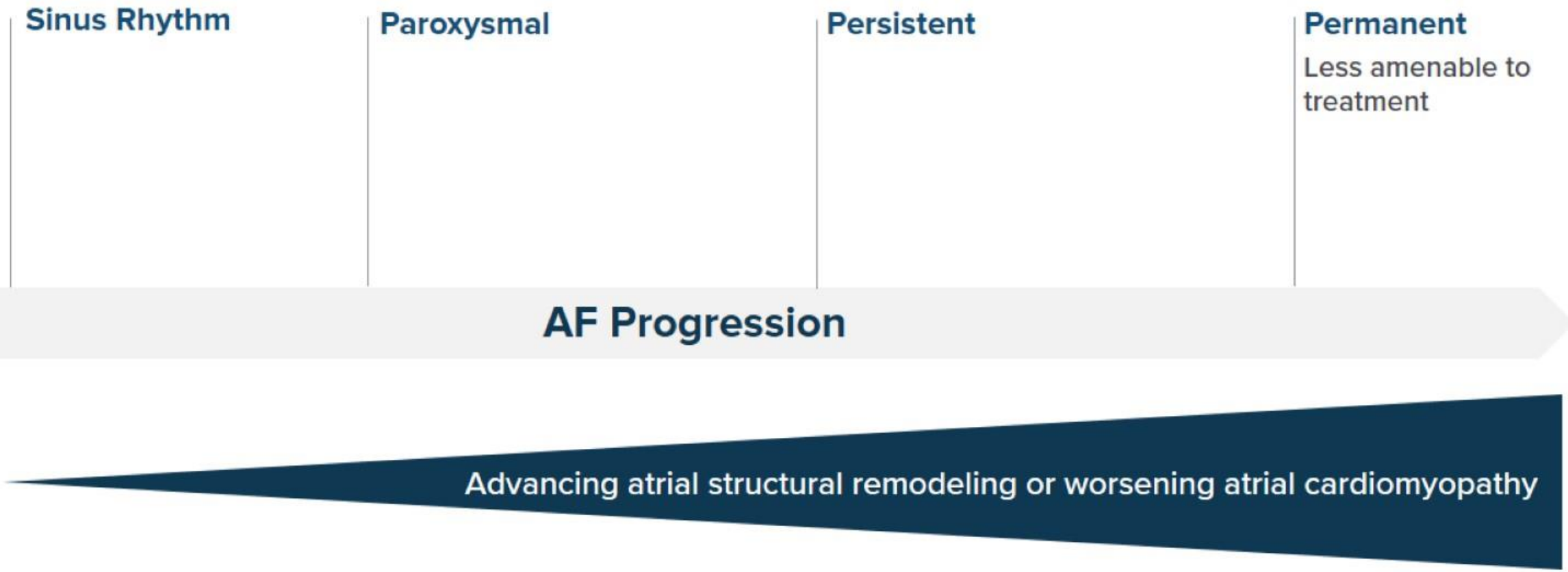
## Diagnosing With a Camera From a Distance—Proceed Cautiously and Responsibly

There have been dramatic advances in diagnosing arrhythmias outside of the clinical setting from sensors widely available to the general public. The placement of a light next to the optical camera sensor on smartphones, a variant of photoplethysmography, can measure pulse rate. By measuring irregularity over longer pulse sequences like some smartwatch devices, atrial fibrillation can also be identified from camera sensors.

Yan BP, et al. *JAMA Cardiol*. 2020;5:105-107. 

# Importance of Early Detection and Initiation of Treatment for AF

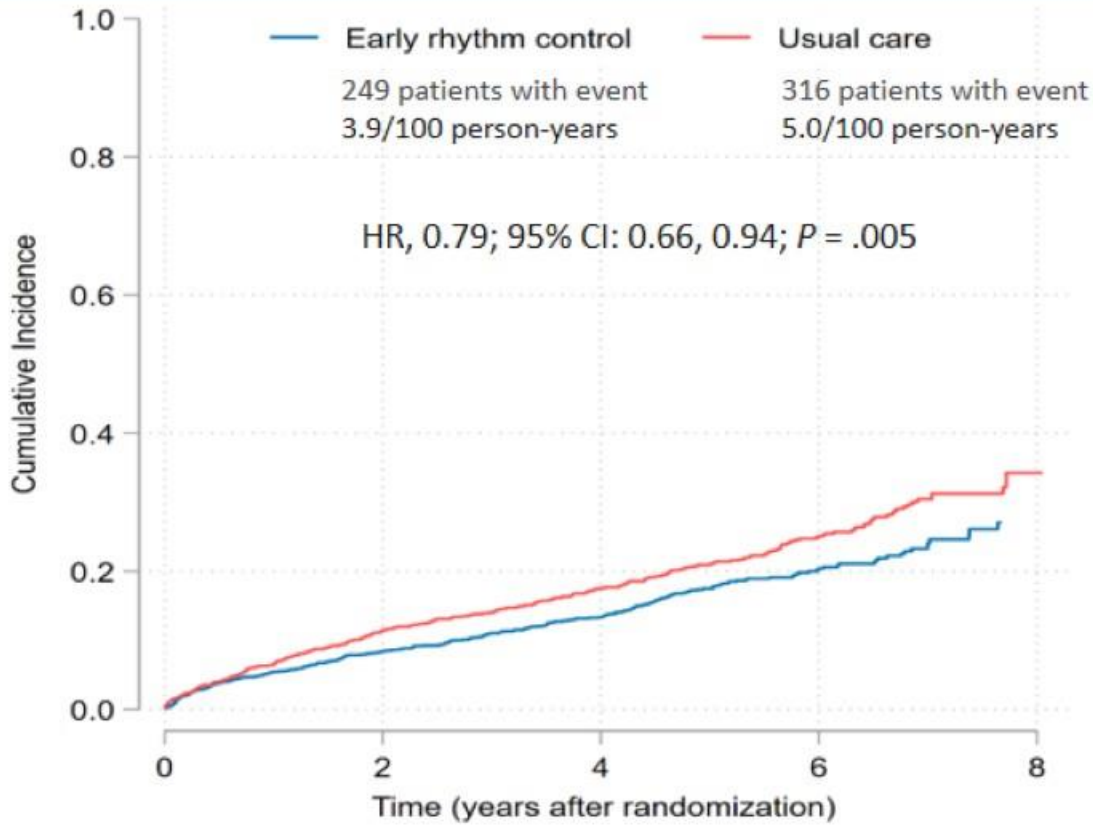
## AF is associated with substantial morbidity and mortality




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

# EAST-AFNET 4
## *First Primary Outcome*

**Early rhythm-control therapy was associated with a 21% lower risk of adverse CV outcomes**



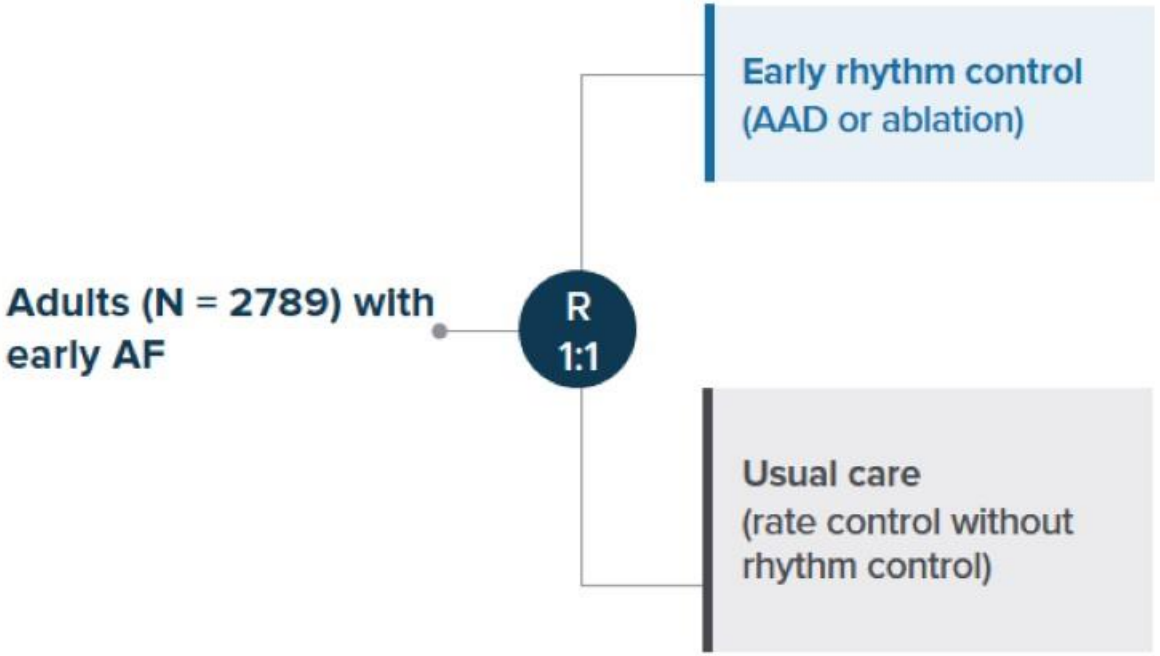

Patients at risk

| | | | | | |
|---|---|---|---|---|---|
| Early rhythm control | 1395 | 1193 | 913 | 404 | 26 |
| Usual care | 1394 | 1169 | 888 | 405 | 34 |

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

# EAST-AFNET 4 Trial
## *Study Design*

### Early rhythm-control therapy vs usual care in patients with AF




**Patients' Baseline Clinical Characteristics**

- OAC: ~90%
- β-blockers: ~80%
- $CHA_2DS_2$-VASc score: ≈ 3.4

**Rhythm control**

- With AADs: 87%
- With ablation: 8% at enrollment; 20% at 2 y in early rhythm control group

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

# EAST-AFNET 4
## *Components of First Primary Outcome*

**Components of first primary outcome with early rhythm control were consistent with overall result**

| | Events in Early Rhythm Control (Incidence/ 100 person-years) | Events in Usual Care (Incidence/ 100 person-years) | Uncorrected HR (95% CI) |
|---|---|---|---|
| CV death | 67 (1.0) | 94 (1.3) | 0.72 (0.52, 0.98) |
| Stroke | 40 (0.6) | 62 (0.9) | 0.65 (0.44, 0.97) |
| Hospitalization with worsening HF | 139 (2.1) | 169 (2.6) | 0.81 (0.65, 1.02) |
| Hospitalization with ACS | 53 (0.8) | 65 (1.0) | 0.83 (0.58, 1.19) |

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

# EAST-AFNET 4
## *Summary*

Results suggest:

**Early rhythm control has the potential to reduce adverse CV outcomes in patients with AF**

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

# Other Studies on Early Rhythm Control

## AFFIRM post hoc analysis[a]

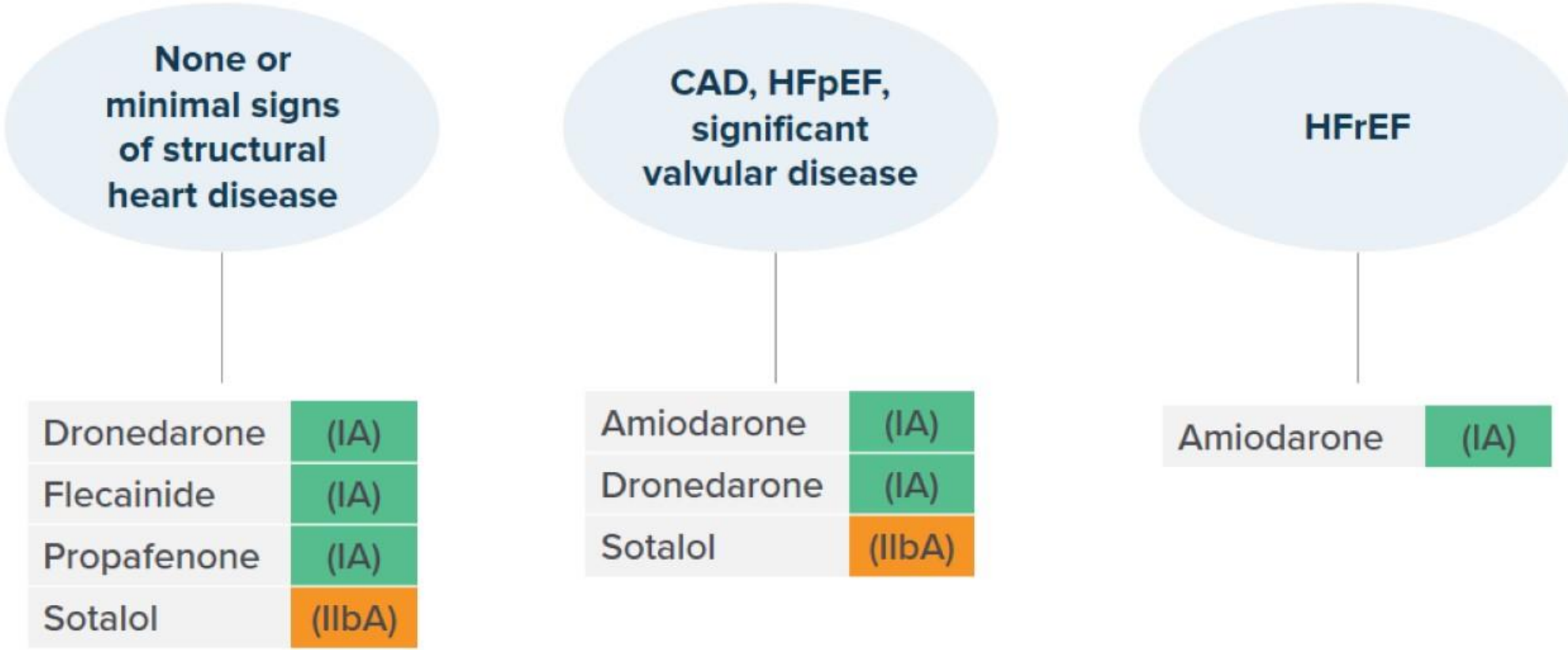
- Found no difference in survival, CV-related hospitalization, or ischemic stroke between rate and rhythm-control strategies in patients diagnosed with AF within 6 months of study enrollment
- Concluded that findings of EAST-AFNET 4 may be more attributable to refinement of AF therapies than to timing of intervention

## EARLY-AF and STOP-AF[b,c]

- Evaluated ablation as first-line therapy vs AADs
- Lower rates of AF recurrence with cryoablation vs AADs
- **Both suggest a role for early rhythm control with ablation**

a. Yang E, et al. *Heart Rhythm*. 2021;18:674-681; b. Andrade JG, et al. *N Engl J Med*. 2021;384:305-315; c. Wazni OM, et al. *N Engl J Med*. 2021;384:316-324.

# AAD Therapy for Rhythm Control
## *2020 ESC Guidelines*



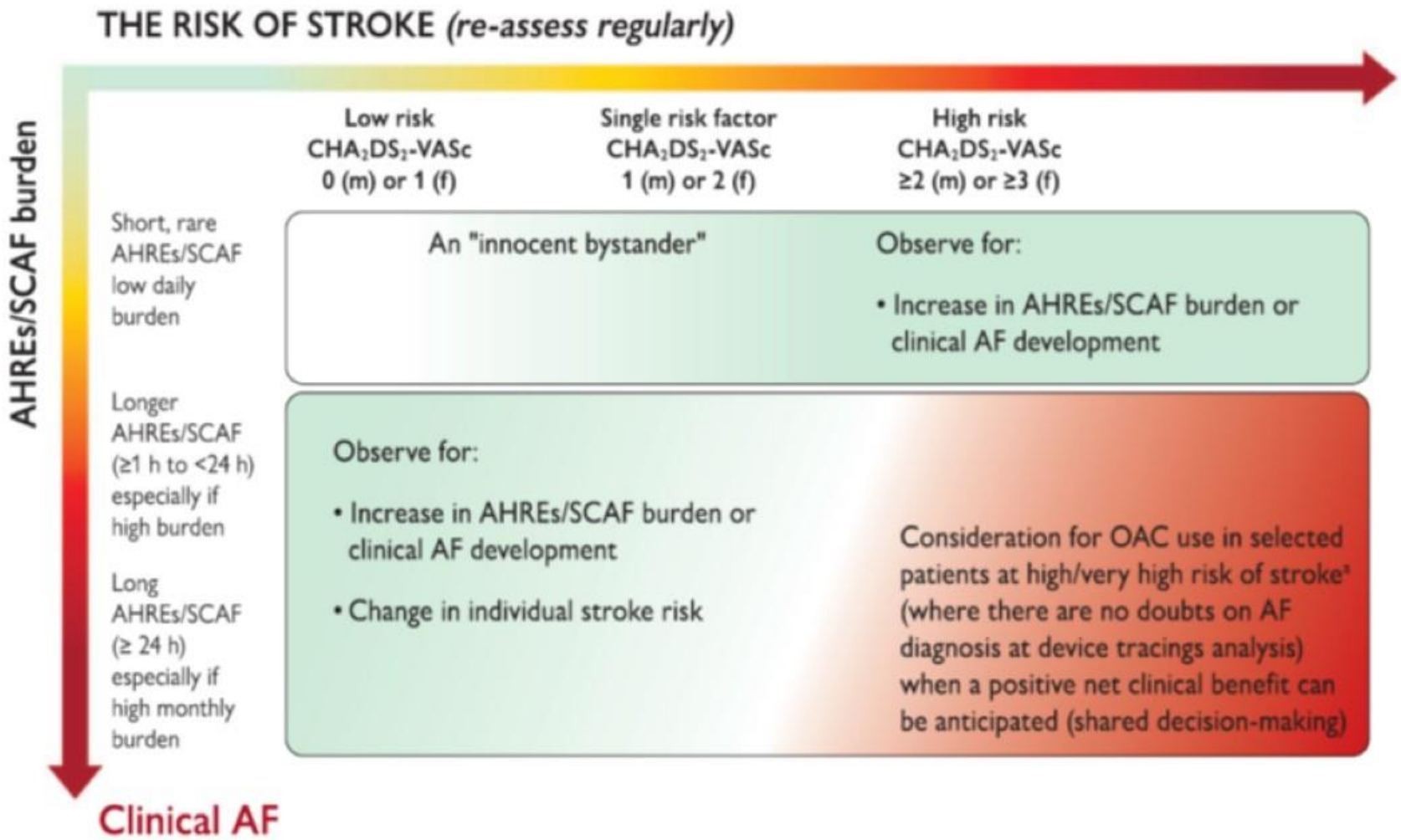

*Dofetilide is available in the United States

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

# Atrial Fibrillation and Anticoagulation

- CHADS2 score for stroke risk—Mod =1,2, High Risk >3
  - CHF Yes=1
  - Hypertension Yes=1
  - Age >75 Yes=1
  - Diabetes Hx  Yes=1
  - TIA or prev stroke Yes=2
- Also: Cha2DS2VASc Score
- HAS-BLED score for bleeding risk (hypertension, crf, liver disease, hx stroke, previous bleed, labile INR)

# Management of Subclinical AF
## *2020 ESC Guidelines*




Hindricks G, et al, 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS), *Eur Heart J*, 2021, p76. By permission of Oxford University Press.

# Anticoagulants and Atrial Fib

- DO NOT offer stroke prevention therapy <65 with AF and no risk factors other than gender
- Consider anticoag for men with CHA2DS2VASc score of 1
- Offer anticoagulation to ALL with CHA2DS2VASc 2 or above
- DO NOT OFFER ASPIRIN FOR STROKE PREVENTION REGARDLESS OF SCORE
- DO NOT COMBINE ASPIRIN WITH WARFARIN

Atrial Fibrillation Risk

Stroke

Cognitive Decline
Silent stroke

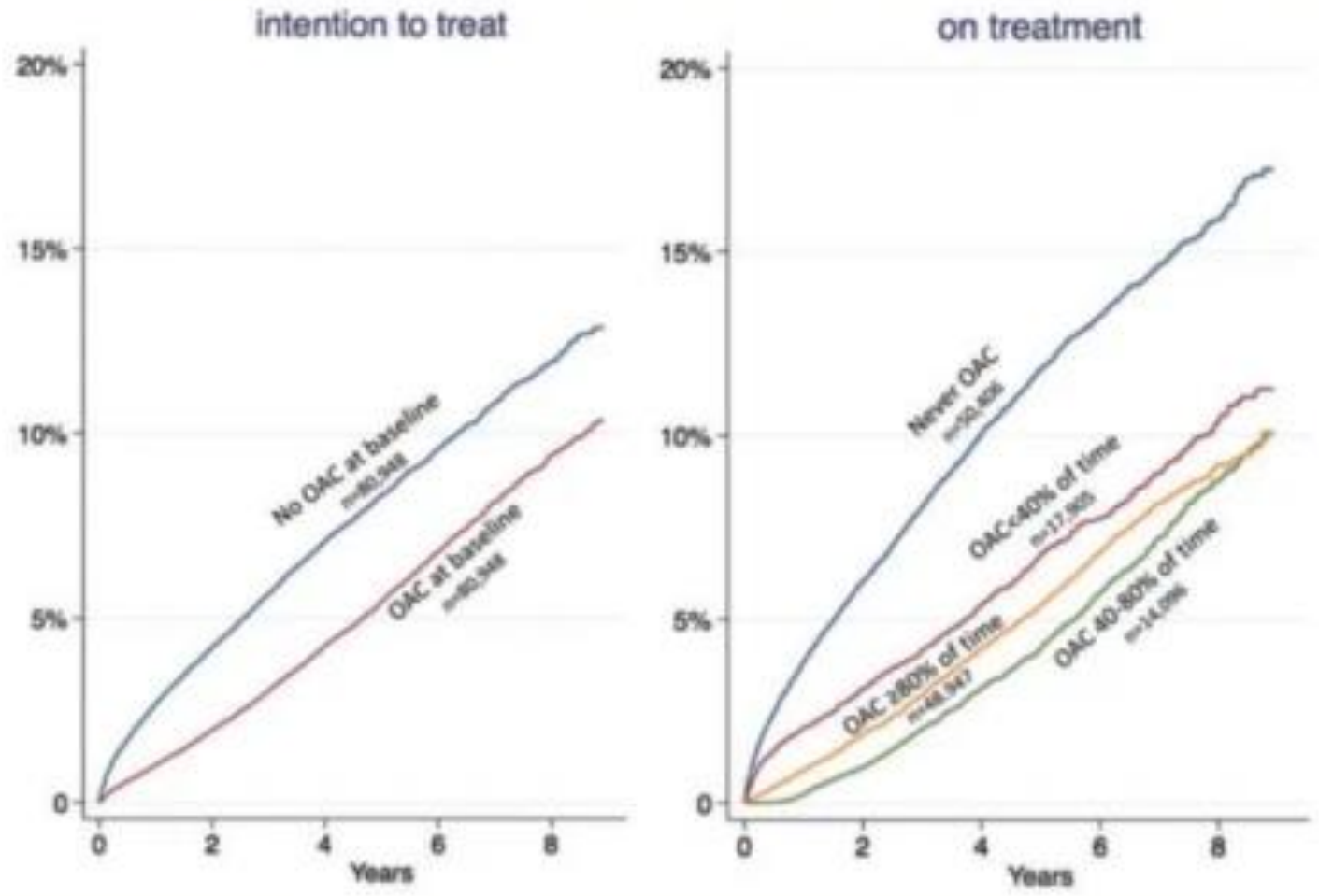



**Figure 1** Unadjusted incidence of dementia in relation to oral anticoagulant treatment among 161 896 patients with atrial fibrillation and no previous diagnosis of dementia who were propensity score matched for the likelihood of oral anticoagulation treatment at baseline.

# Atrial Fibrillation and Anticoagulation

- Vitamin K antagonist—warfarin
- Long acting drug
- Monitor with prothrombin time (INR)
- Readily available reversal with Vit K or FFP

- Novel Oral Anticoagulants (NOAC)—Direct Oral Anticoag (DOAC)
- No monitoring test
- Reversal varies with drug

# Oral Anticoagulation Compliance

41,430 (68%) patients on VKA

19,548 (32%) on DOAC

Inadequate prescription

- 36% VKA poor control in therapeutic range—ICH 2.2%
- 67.6% DOAC (no history thromboemb event or ICH.) 22% no GFR adjustment

Poor adequacy to current criteria

Int J Environ Res Public Health 2021 Feb 24: 18(5):2244

# Following Warfarin/ VKA treatment

- Patient schedules blood draw for INR
- Patient comes to lab facility
- Patient has venous blood drawn
- Result returns to practitioner’s office, compared to record
- Phone call to patient
- Elapsed time—36 to 48 hours—approx. 5 phone calls, delay, errors, hassle

# Self measurement of INR

- Commercial system (e.g, Coagchek 2)
- Finger stick
- Run test
- Inform practitioner’s office

# Warfarin = Vitamin K Antagonist
# low vit K->reduced bone density
# CRF: increased vascular calcification
# Lower Fx risk with DOAC

- Vitamin K1
- Poor placental transport
- Carboxylates clotting factors
- Green leafy veg
- Animals can covert to K2

- Vitamin K2—low intake even in healthy diet
- improves bone density
- Reduces arterial calification
- Many subtypes: MK4, MK7
- May lower protime in patient taking warfarin

# Vitamin K content of foods

- K1
- Spinach ½ c: 445 mcg cooked, 145 mcg raw
- Brussel Sprouts: 110
- Blueberries: 21 mcg
- Carrots: 17 mcg

- K2
- Natto: 1103 mcg
- Goose 31 mcg
- Pork: 2.1 mcg
- Egg Yolk 32 mcg

# Warfarin Cautions

- Scrupulous Diet: NO---stay with same general diet—no major spinach binges
- Long medication half life---3 to 5 days to see effect of dosage change
- More frequent INR testing—may lead to too many dose changes, increased risk of bleeding
- Simplify dosing
- Interacts with everything: ASA contraindicated.  Topical salicylates, everything interacts—follow INR
- Caution patients to report unusual abdominal pain, lightheadedness, change in bowel habits
- Caution to avoid head injuries

# NOACs in AF-Related Stroke Prevention

## Stroke or SE Events

| | Drug/ Dose | RR (95% CI) | *P* Value |
|---|---|---|---|
| RE-LY | Dabigatran 150 mg twice daily | 0.66 (0.53, 0.82) | .0001 |
| ROCKET AF | Rivaroxaban 20 mg daily | 0.88 (0.75, 1.03) | .12 |
| ARISTOTLE | Apixaban 5 mg twice daily | 0.80 (0.67, 0.95) | .012 |
| ENGAGE AF-TIMI 48 | Edoxaban 60 mg once daily | 0.88 (0.75, 1.02) | .10 |
| **COMBINED** | | **0.81 (0.73, 0.91)** | **< .0001** |

Ruff CT, et al. *Lancet.* 2014;383:955-962.

# Real-World Evidence

- US Administrative Database (N = 14,865)
  - Patients with AF taking apixaban, dabigatran, or rivaroxaban
  - Among patients with a renal indication for dose reduction, 43.0% received standard doses
  - In patients with no renal indication for dose reduction, 13.3% received reduced doses

Yao X, et al. *J Am Coll Cardiol*. 2017;69:2779-2790.

# Non-Vitamin K Antagonist Oral Anticoagulants vs Warfarin in Atrial Fibrillation

## Individual Patient Data From the Pivotal Randomized Trials

**Anthony P. Carnicelli, MD**

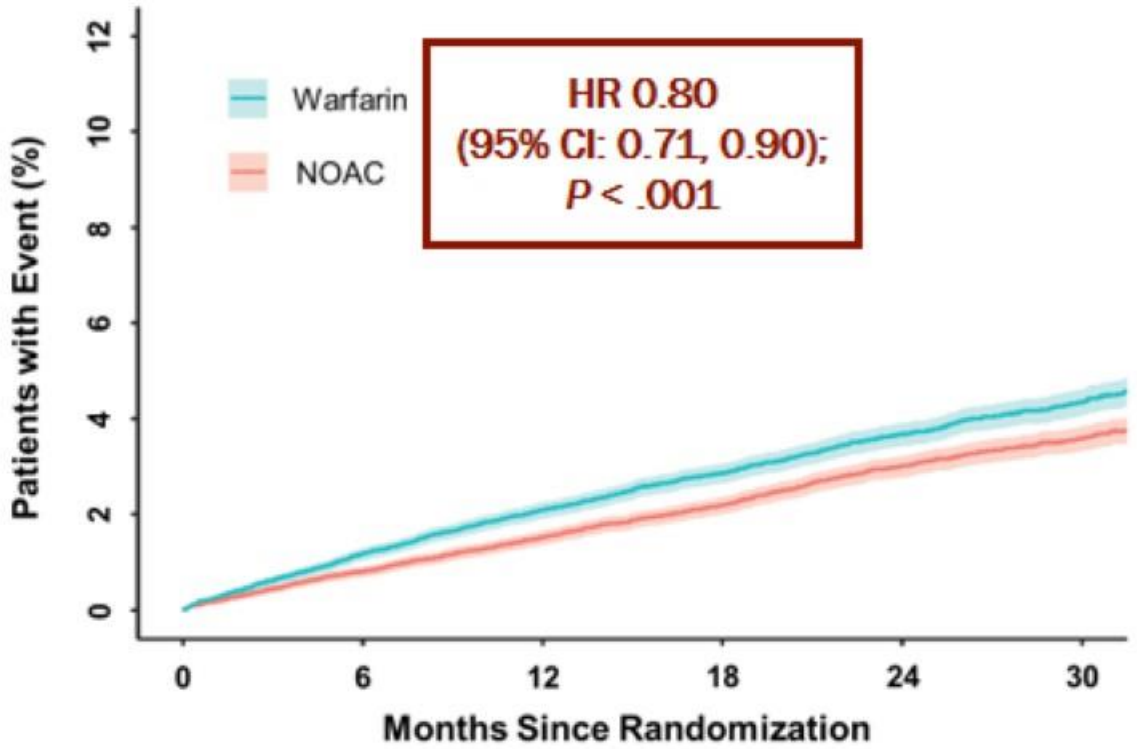
**On behalf of the COMBINE AF Investigators**


(A COllaboration between Multiple institutions to Better Investigate Non-vitamin K antagonist oral anticoagulant usE in Atrial Fibrillation)

Carnicelli AP, et al. ESC Congress 2020.

# COMBINE-AF
## *Efficacy of NOACs vs Warfarin*

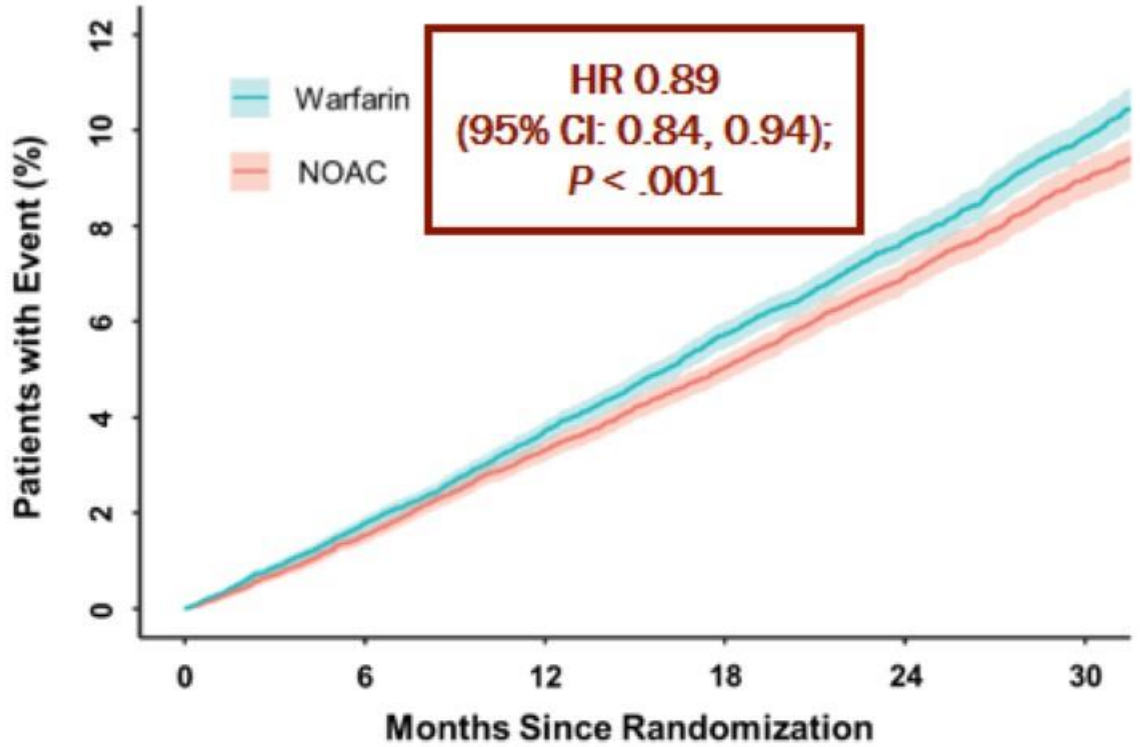
### Stroke/Systemic Embolism




**Number at Risk (number of events)**

| | | | | | | |
|---|---|---|---|---|---|---|
| Warfarin | 29229 (0) | 28027 (336) | 27051 (591) | 21654 (786) | 15324 (944) | 8870 (1031) |
| NOAC | 29312 (0) | 28256 (231) | 27328 (431) | 21907 (602) | 15595 (761) | 9027 (837) |

### All-Cause Death



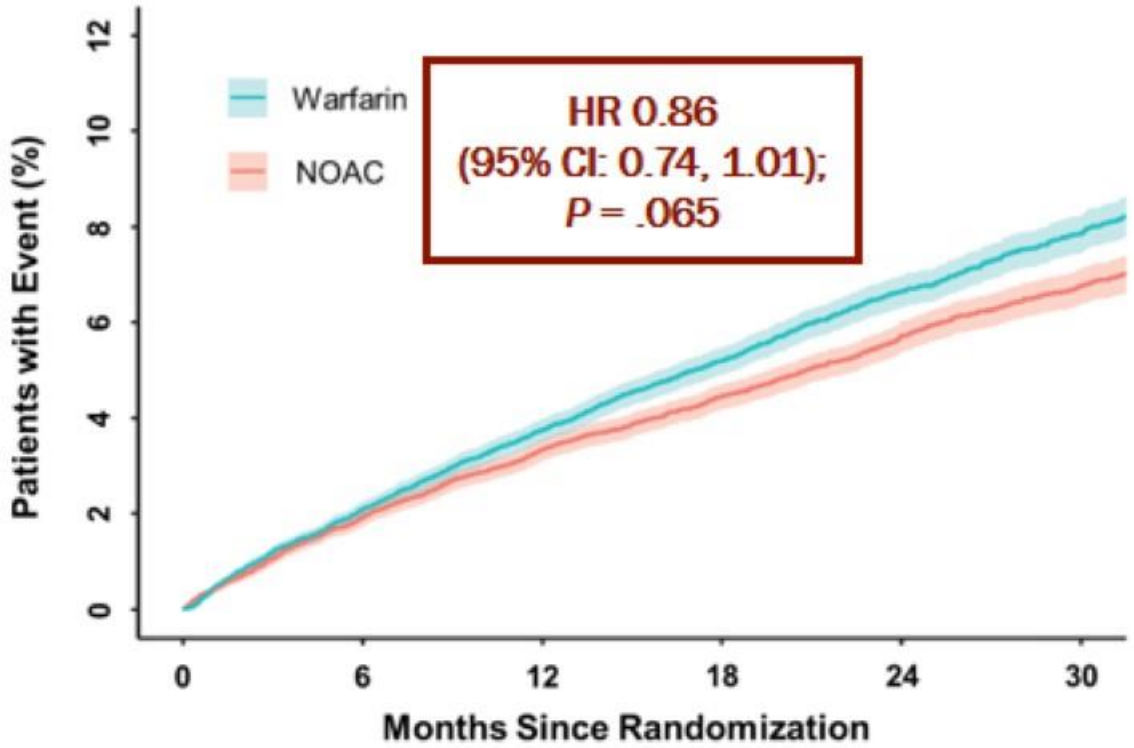

**Number at Risk (number of events)**

| | | | | | | |
|---|---|---|---|---|---|---|
| Warfarin | 29229 (0) | 28302 (512) | 27476 (1067) | 22120 (1587) | 15735 (1987) | 9139 (2289) |
| NOAC | 29312 (0) | 28462 (442) | 27654 (956) | 22276 (1404) | 15951 (1794) | 9271 (2080) |

Carnicelli AP, et al. ESC Congress 2020.

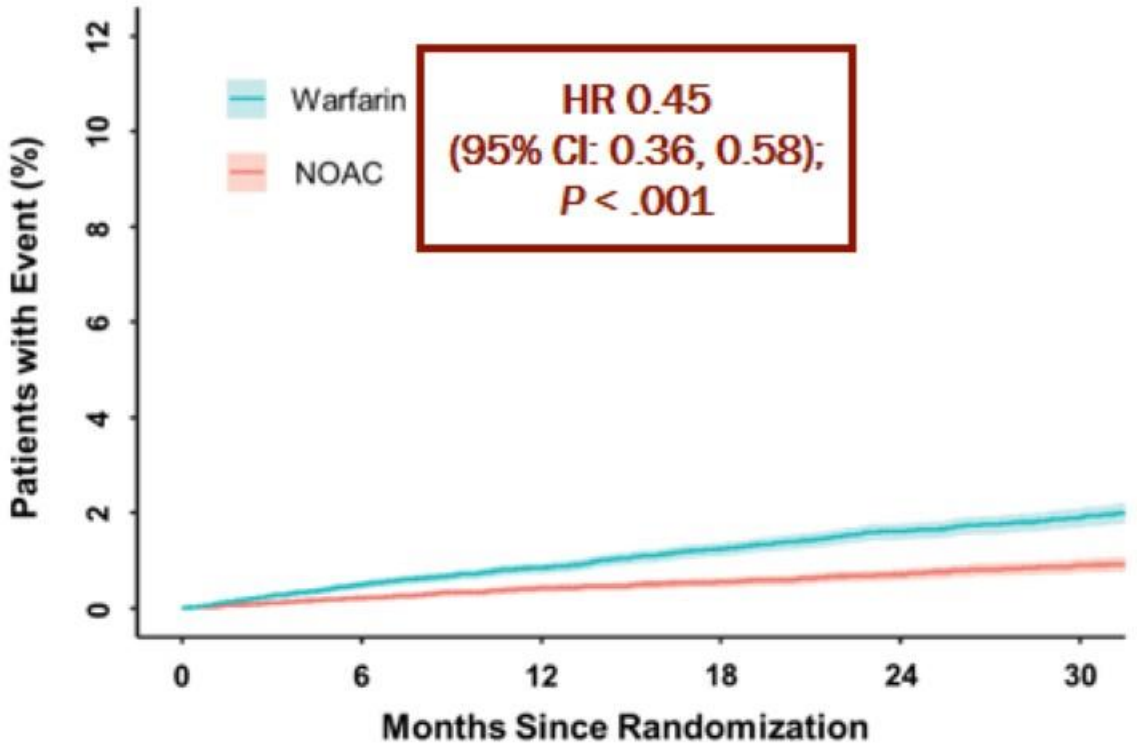
# COMBINE-AF
## *Safety of NOACs vs Warfarin*

### Major Bleeding




| Number at Risk (number of events) | | | | | | |
|---|---|---|---|---|---|---|
| Warfarin | 29187 (0) | 25639 (572) | 23562 (992) | 18382 (1311) | 12618 (1555) | 7009 (1686) |
| NOAC | 29270 (0) | 25375 (521) | 23456 (877) | 18258 (1117) | 12577 (1321) | 7050 (1434) |

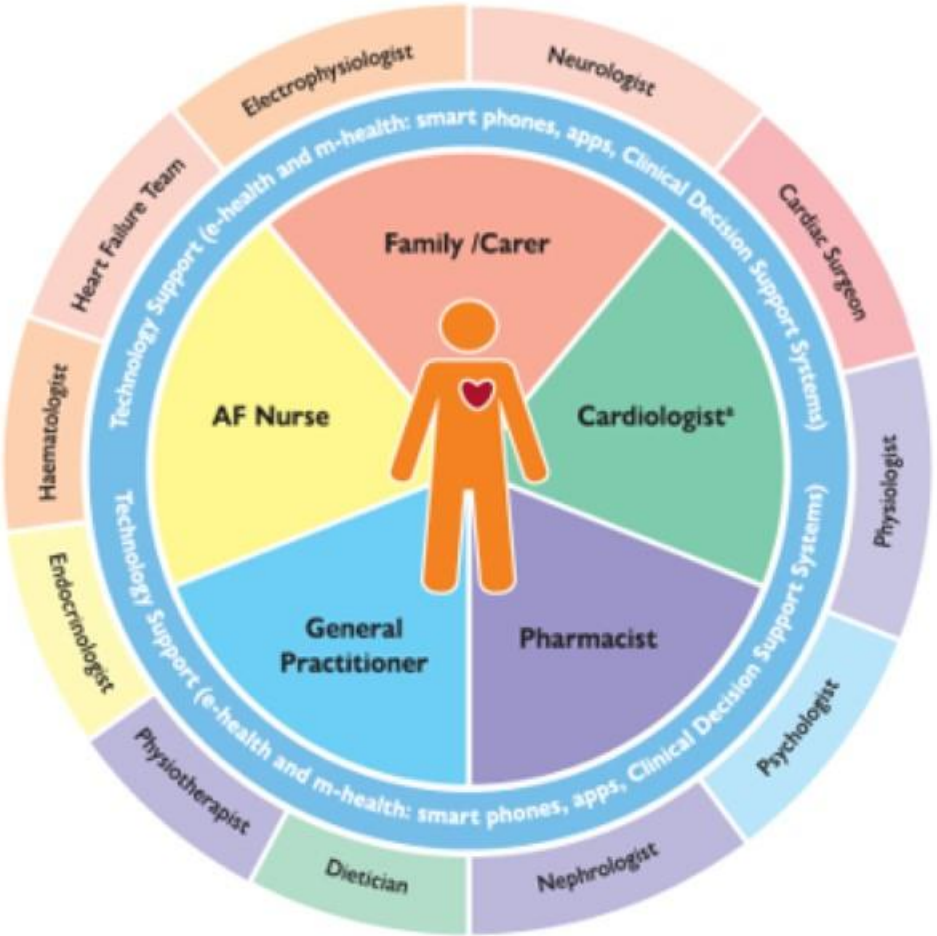
### Intracranial Bleeding

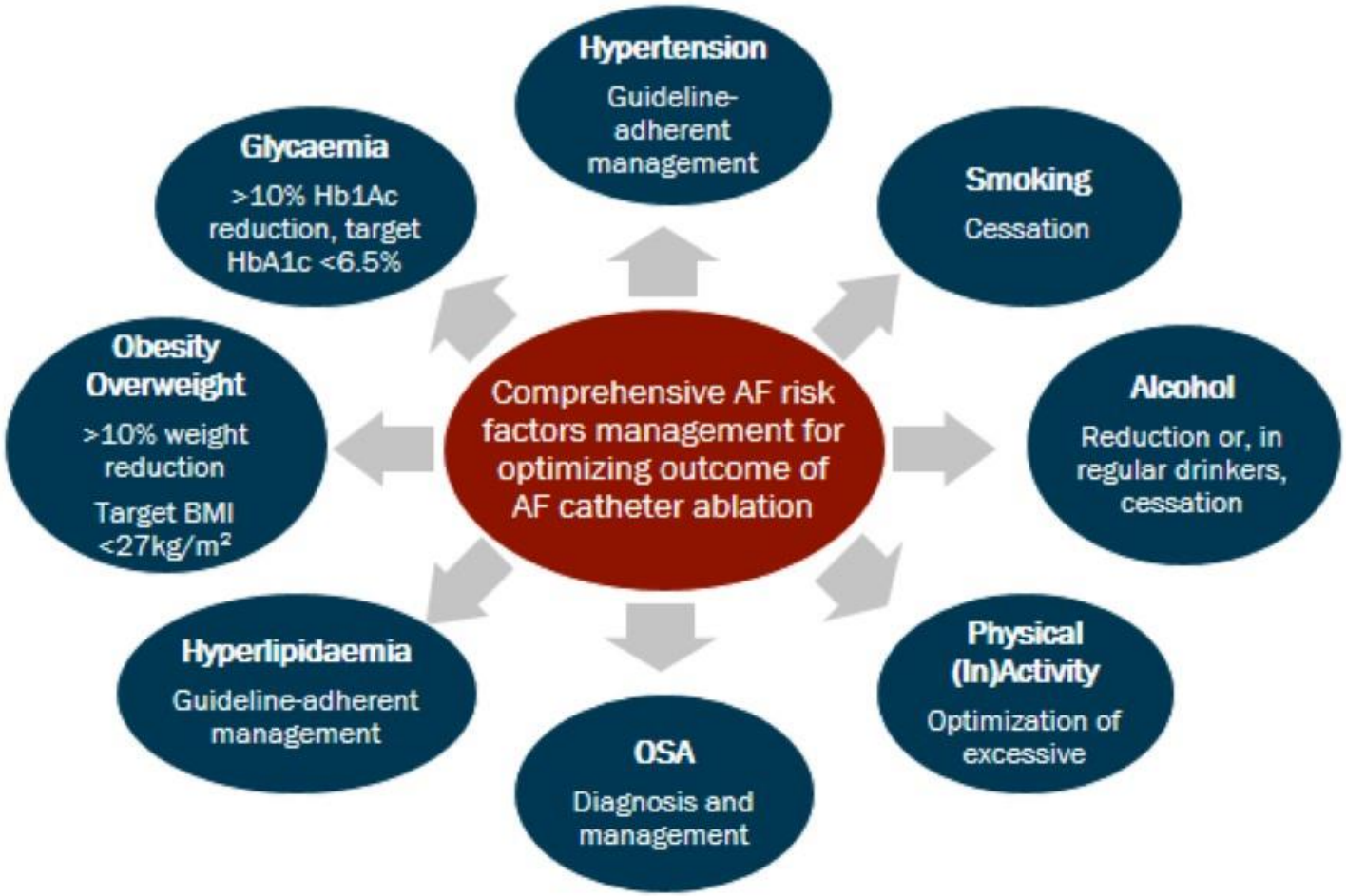



| Number at Risk (number of events) | | | | | | |
|---|---|---|---|---|---|---|
| Warfarin | 29187 (0) | 25900 (132) | 23995 (219) | 18854 (306) | 13037 (369) | 7299 (398) |
| NOAC | 29270 (0) | 25624 (55) | 23863 (107) | 18685 (133) | 12986 (159) | 7317 (179) |

Carnicelli AP, et al. ESC Congress 2020.

# ESC Guidelines
## *Integrated Management*




Hindricks G, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS), *Eur Heart J*, 2021, 373-498. By permission of Oxford University Press.

# ESC Guidelines
## *Class III Recommendations*

| Recommendations | Class | Level |
|---|---|---|
| Antiplatelet therapy alone (monotherapy or aspirin in combination with clopidogrel) is not recommended for stroke prevention in AF. | III | A |
| Estimated bleeding risk, in the absence of absolute contraindications to OAC, should not in itself guide treatment decisions to use OAC for stroke prevention. | III | A |
| Clinical pattern of AF (i.e. first detected, paroxysmal, persistent, long-standing persistent, permanent) should not condition the indication to thromboprophylaxis. | III | B |

Hindricks G, et al. *Eur Heart J.* 2020:ehaa612.

# ESC Guidelines
## *Modifiable Bleeding Risk Factors*

| Modifiable Bleeding Risk Factors |
| --- |
| Hypertension/elevated SBP |
| Concomitant antiplatelet/NSAID |
| Excessive alcohol intake |
| Nonadherence to OAC |
| Hazardous hobbies/occupations |
| Bridging therapy with heparin |
| INR control (target 2.0 to 3.0), target TTR > 70%* |
| Appropriate choice of OAC and correct dosing† |

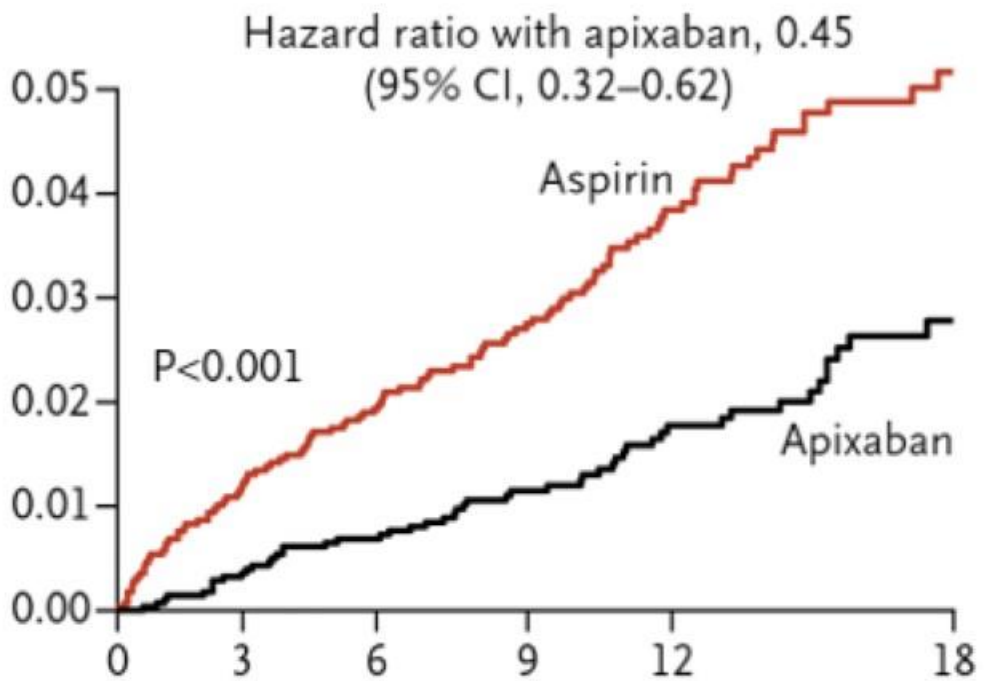
*For patients receiving VKA treatment; †Dose adaptation based on patient's age, body weight, and serum creatinine level.
Hindricks G, et al. *Eur Heart J.* 2020:ehaa612.

# Opportunities to Improve Care

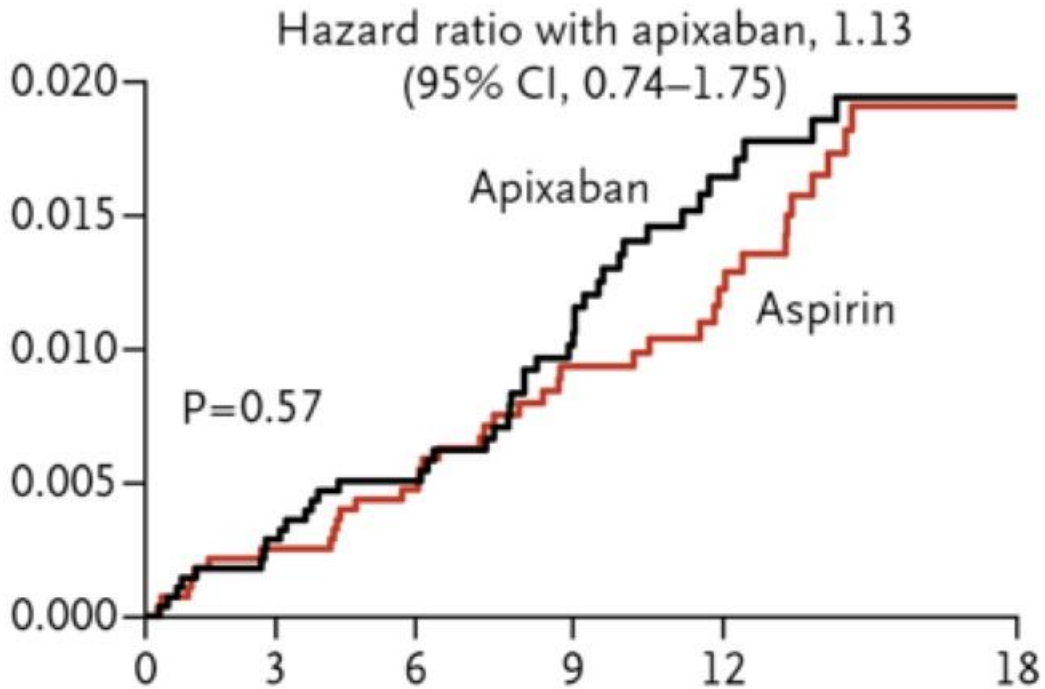
If your patient is on aspirin, switch it to OAC

# AVERROES
## *Efficacy and Safety*

### Stroke or SEE




### Major Bleeding



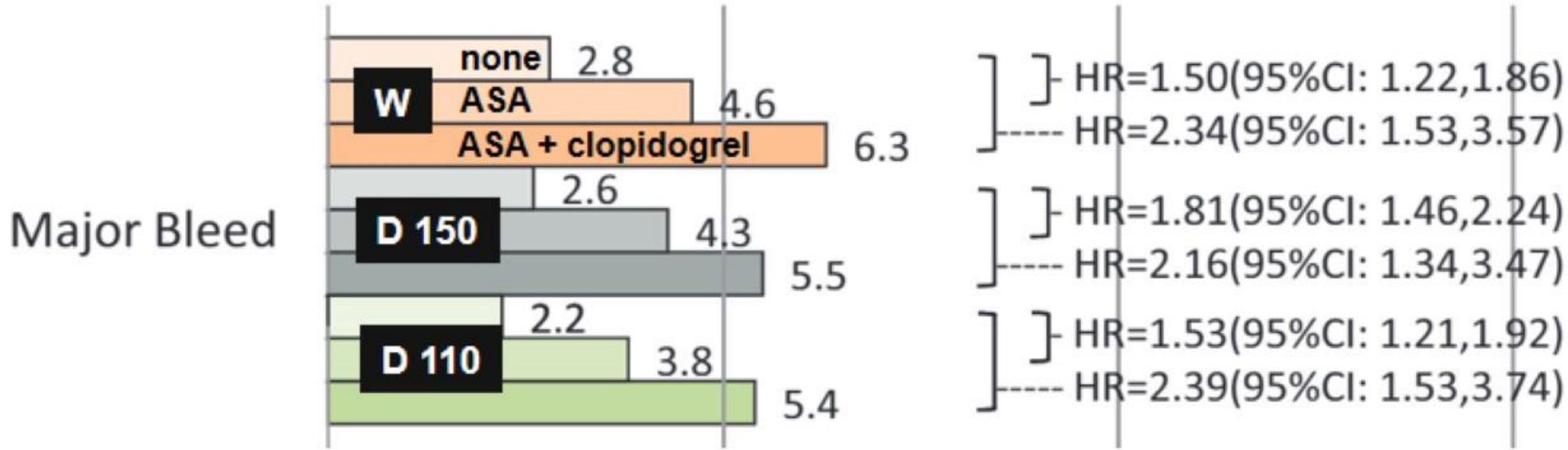

**ICH: 11 apixaban, 13 ASA**

Connolly SJ, et al. *N Engl J Med*. 2011;364:806-817; Flaker GC, et al. *Stroke*. 2012;43:3291-3297.

# Opportunities to Improve Care

The risk of adding aspirin to OAC is substantial

# Bleeding According to Antiplatelet Treatment



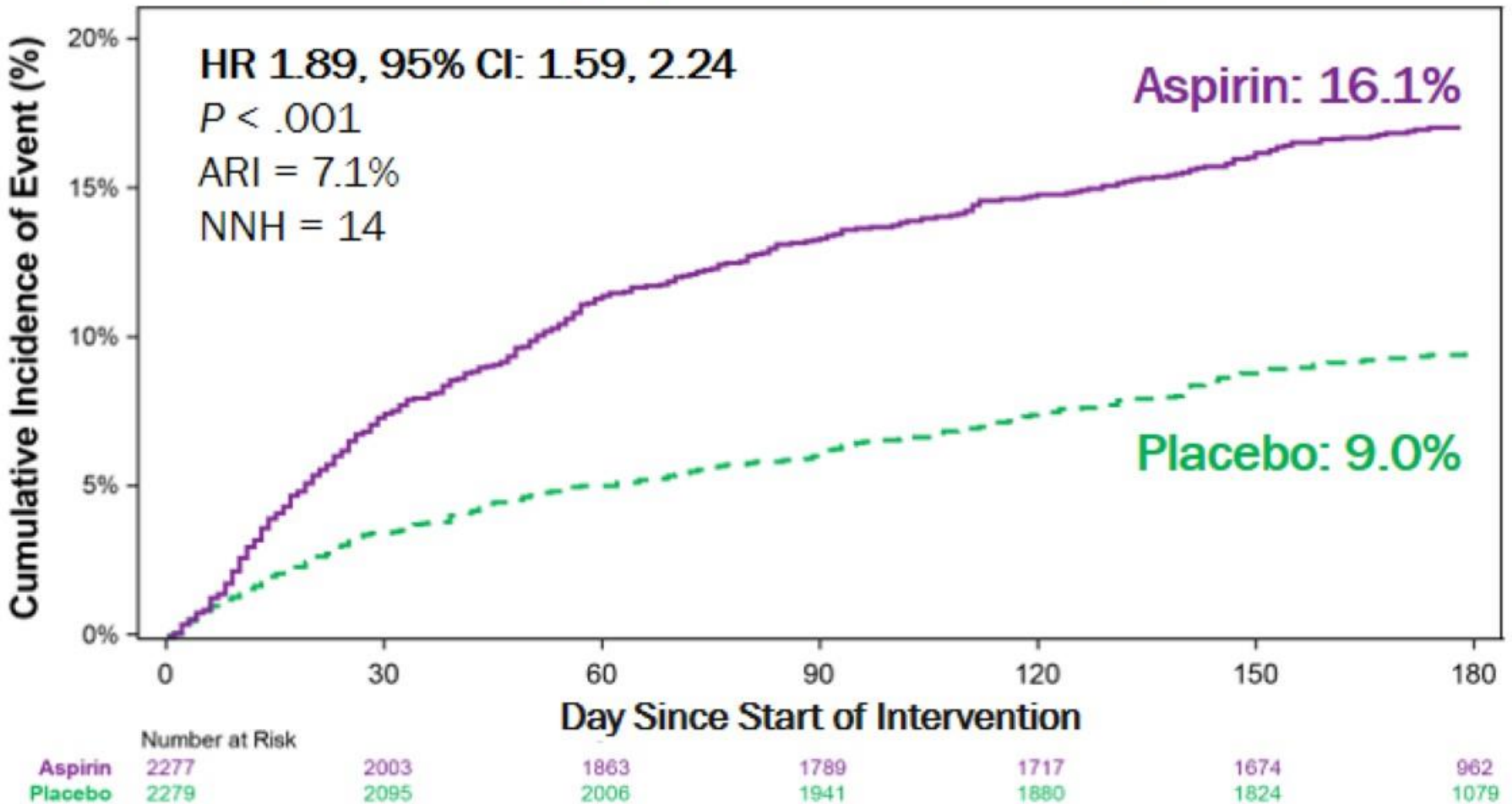

**Series of no, single, and dual antiplatelet therapy**

**HRs adjusted for age, gender, warfarin experience, SBP, CAD, HF, hypertension, diabetes, TIA, CrCl, and statin use**

Circulation. Published online December 27, 2012.

# AUGUSTUS
## *Antithrombotic Therapy After ACS or PCI in AF*

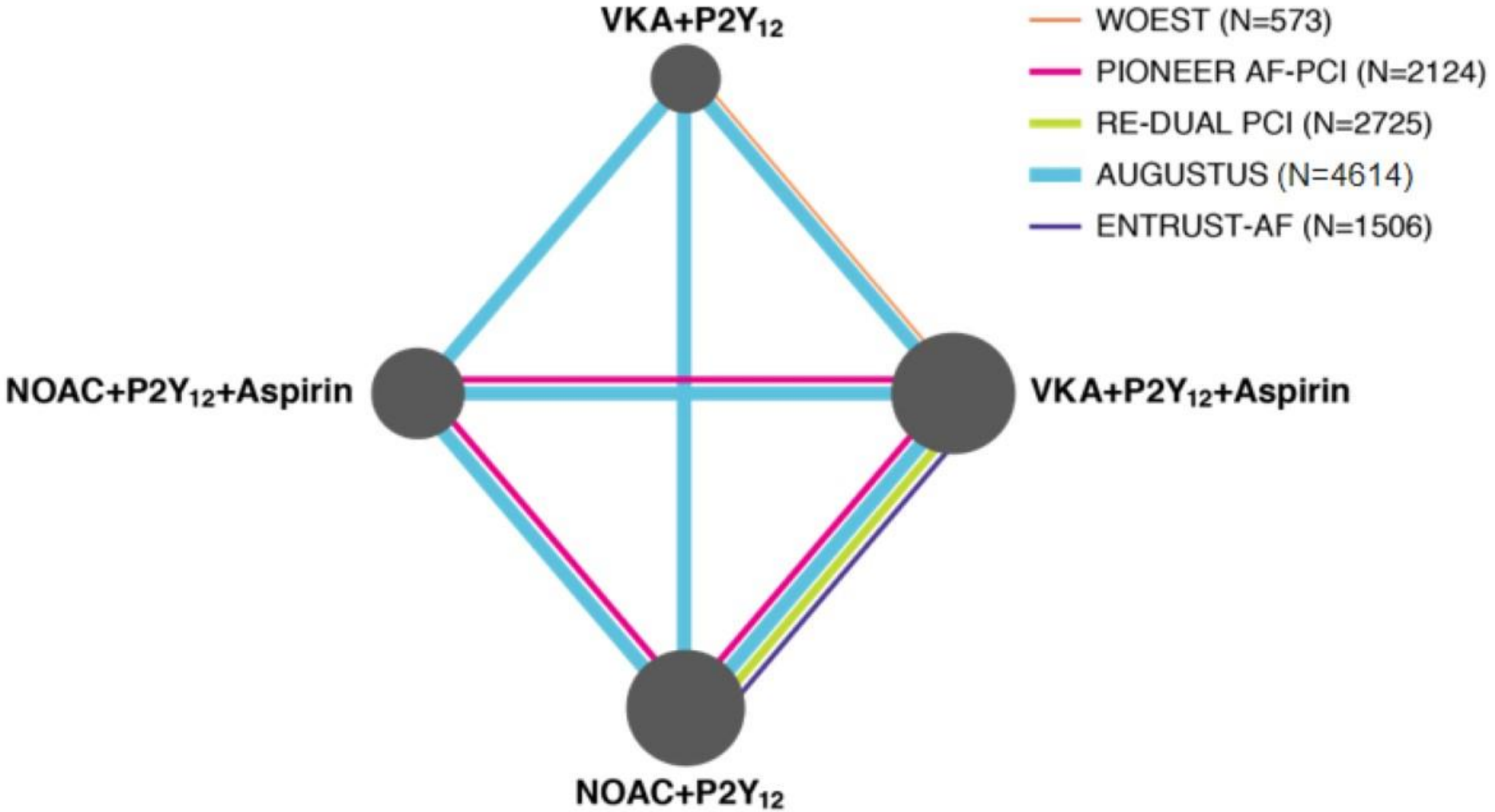
### Major/CRNM Bleeding




Lopes RD, et al. *N Engl J Med*. 2019;380:1509-1524.

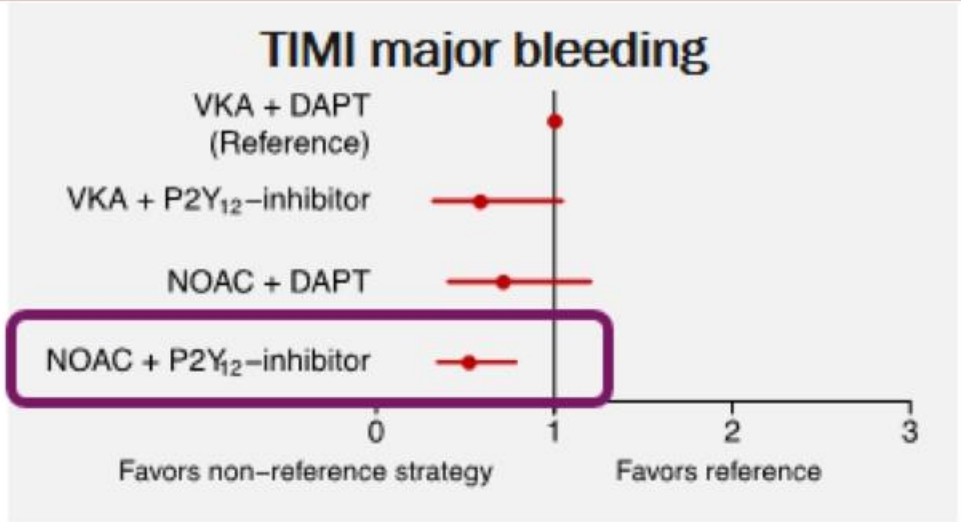
# AF With PCI

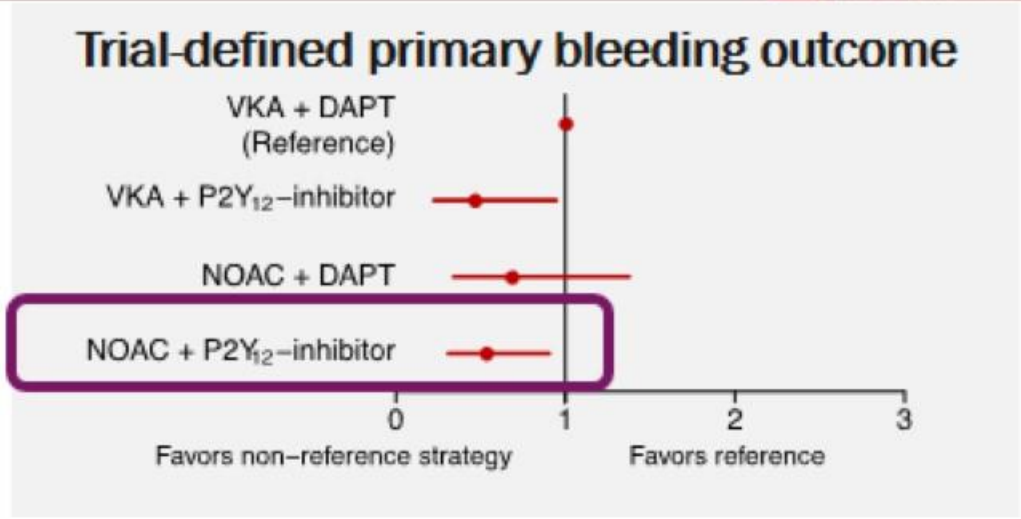
## *Network Meta-Analysis of 4 Antithrombotic Treatment Regimens*

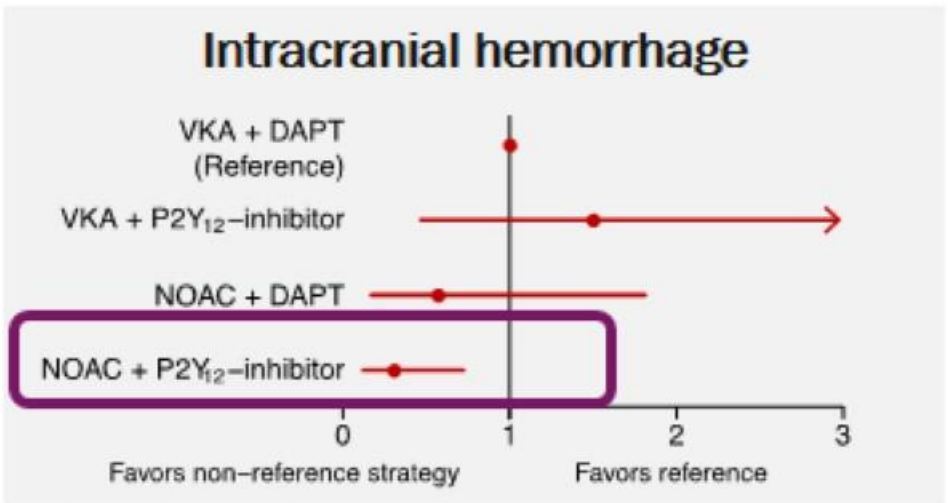


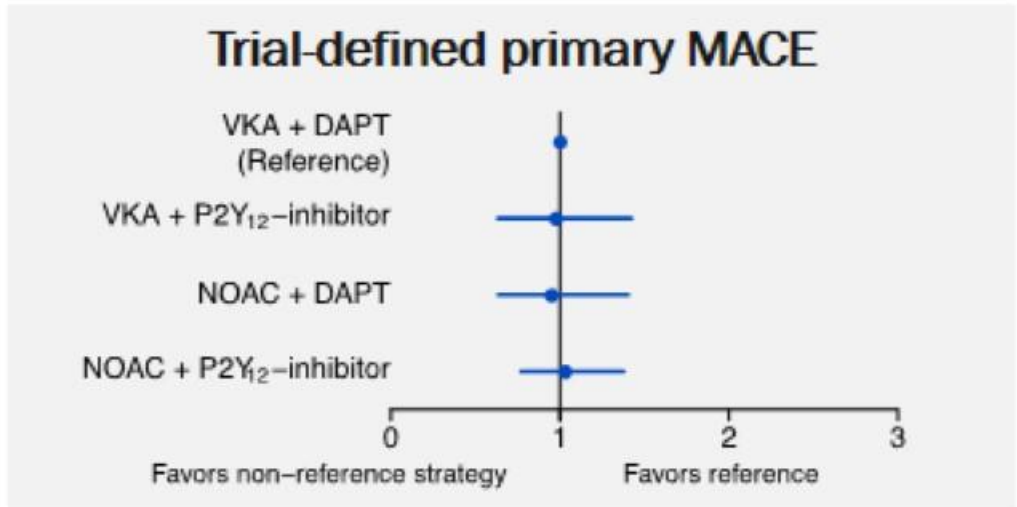

Lopes RD, et al. *JAMA Cardiol*. 2020;5:582-589. Copyright © 2020 American Medical Association. All rights reserved.

# Meta-Analysis
## *Patients With AF Undergoing PCI*



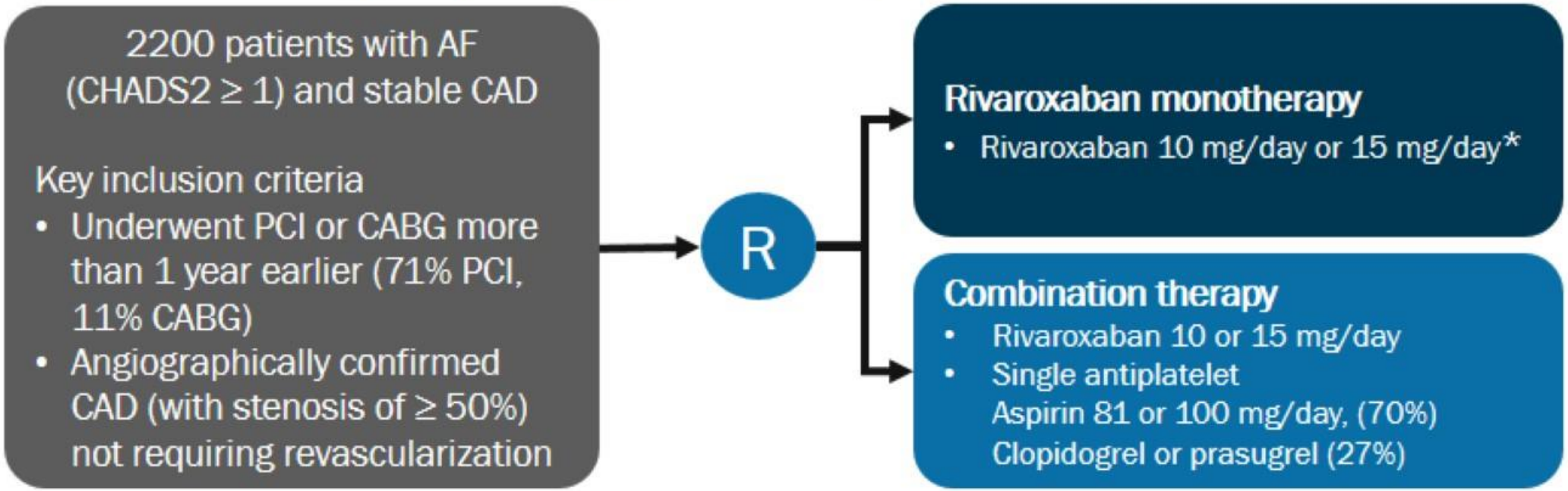




Lopes RD, et al. *JAMA Cardiol*. 2020;5:582-589.

# AFIRE

## *Antithrombotic Therapy for AF with Stable Coronary Disease*

A multicenter, prospective, randomized, open-label, parallel-group trial

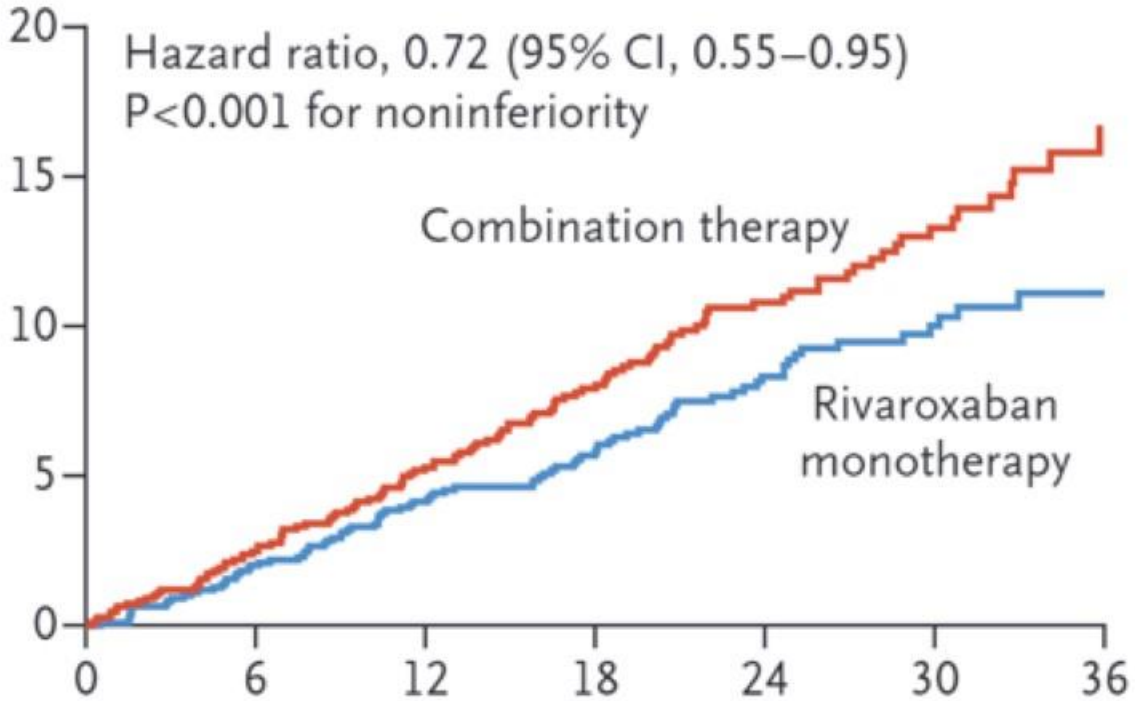



**Noninferiority for primary outcome: stroke, SE, MI, USA requiring revascularization, death; stopped early due to excess death with combination therapy**

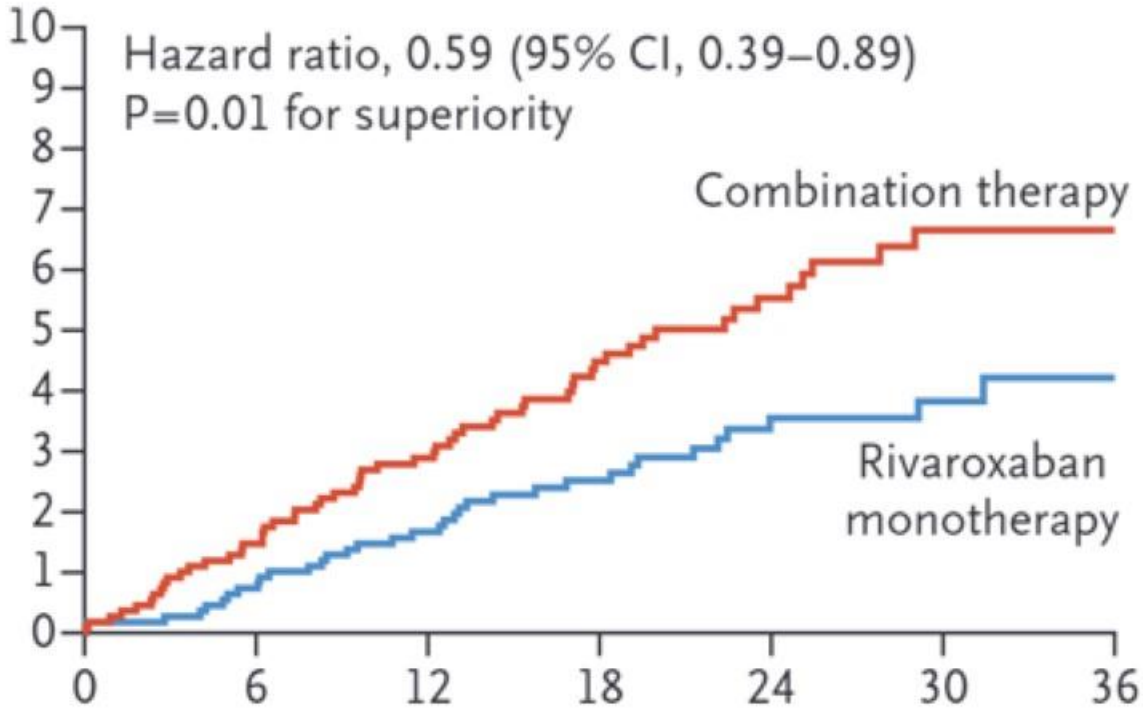
*The level of rivaroxaban in blood samples obtained from Japanese patients who were taking rivaroxaban at the 15-mg dose was similar to the level in white patients who were taking the 20-mg dose.

Yasuda S, et al. *N Engl J Med*. 2019;381:1103-1113.

# AFIRE
## *Efficacy and Safety*




Primary: stroke, SE, MI, USA/revasc, death:
39% increased with aspirin




ISTH major bleeding:
70% increased with aspirin

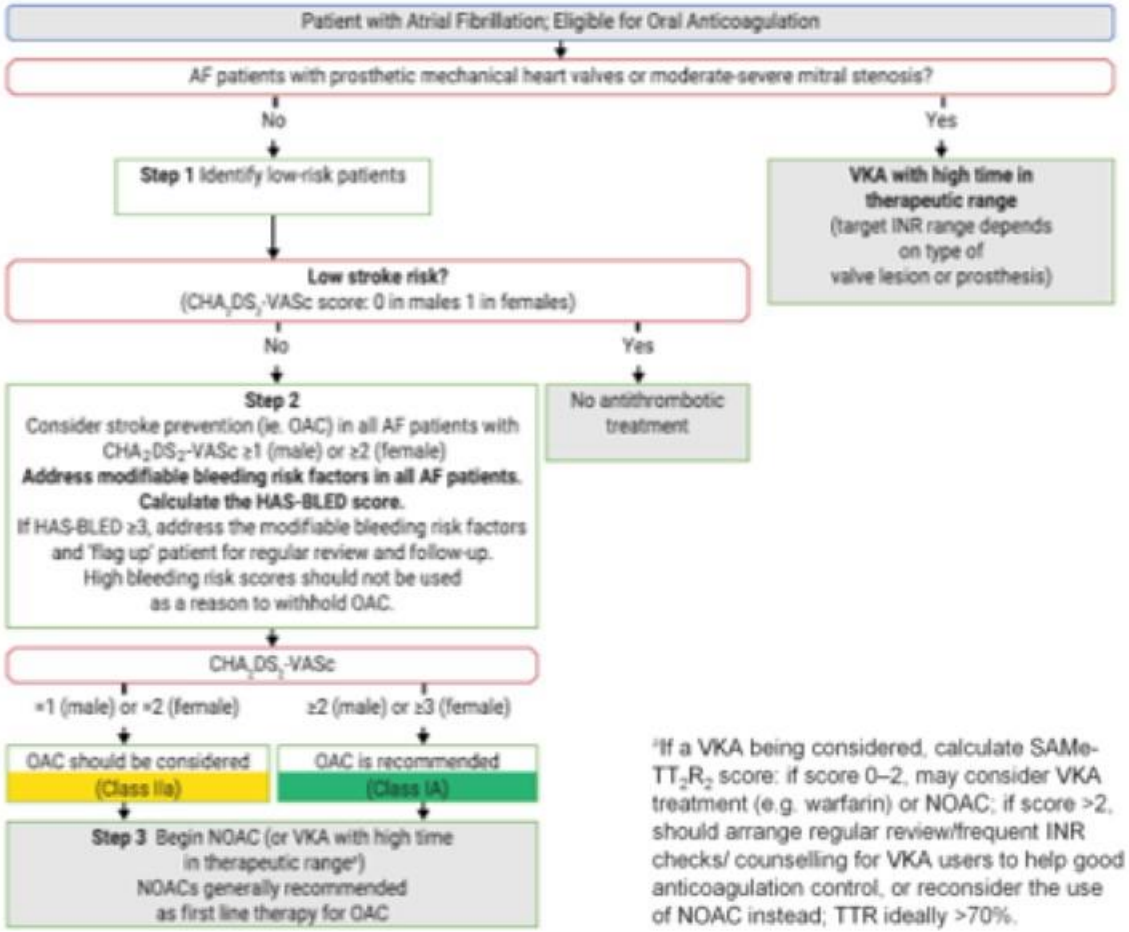
Yasuda S, et al. *N Engl J Med*. 2019;381:1103-1113.

# ESC Guidelines
## *LAA Occlusion*

| Recommendations for occlusion or exclusion of the LAA | Class | Level |
|---|---|---|
| LAA occlusion may be considered for stroke prevention in patients with AF and contraindications for long-term anticoagulant treatment (e.g. intracranial bleeding without a reversible cause). | IIb | B |

Hindricks G, et al. *Eur Heart J*. 2020:ehaa612.

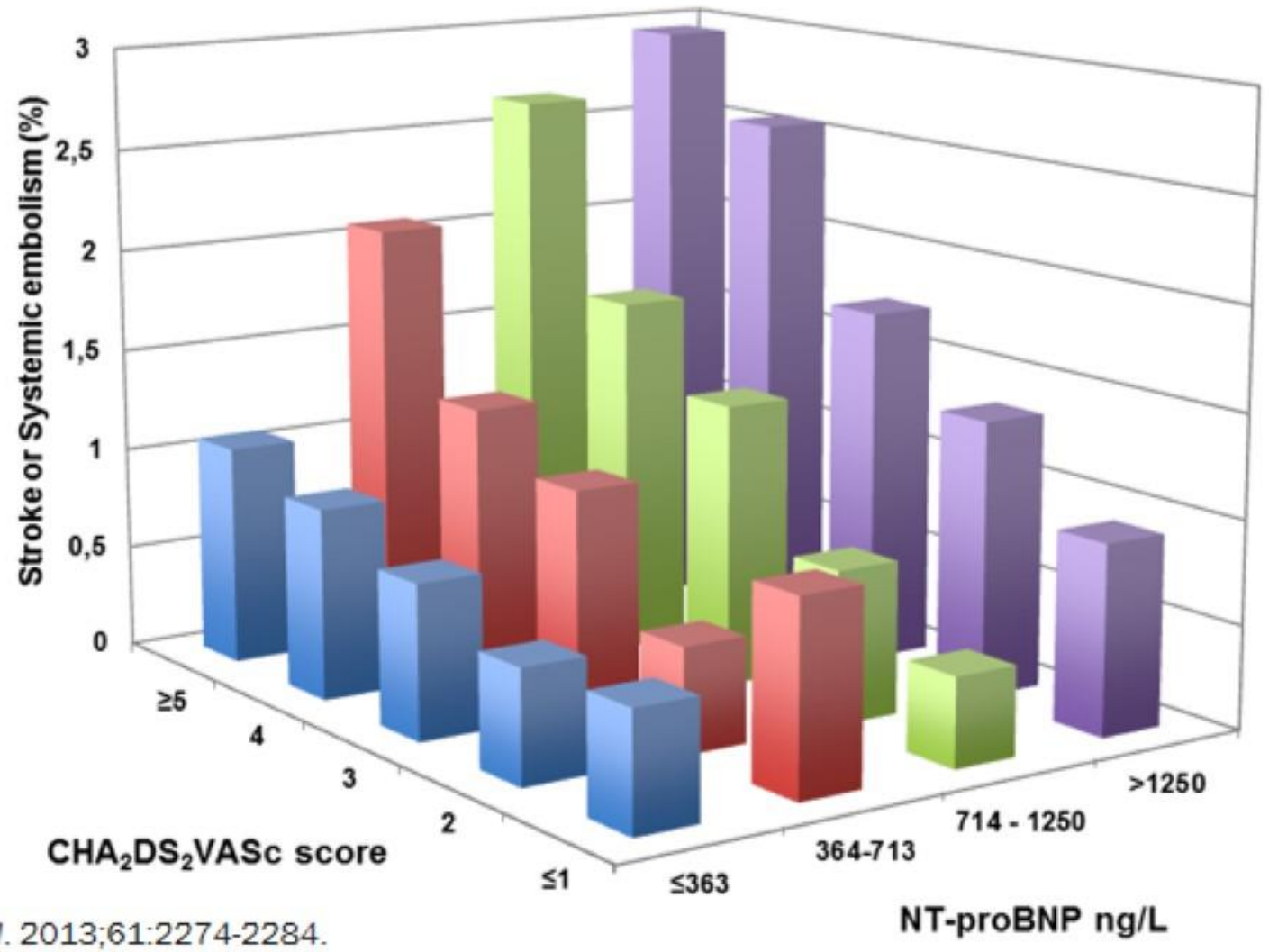
# ESC Guidelines
## *Anticoagulation*




[a]If a VKA being considered, calculate SAMe-$TT_2R_2$ score: if score 0–2, may consider VKA treatment (e.g. warfarin) or NOAC; if score >2, should arrange regular review/frequent INR checks/ counselling for VKA users to help good anticoagulation control, or reconsider the use of NOAC instead; TTR ideally >70%.

Hindricks G, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS), *Eur Heart J*, 2021, 373-498. By permission of Oxford University Press.

# Risk of Stroke by Quartiles of NT-proBNP




Hijazi Z, et al. *J Am Coll Cardiol*. 2013;61:2274-2284.

# Opportunities to Improve Care

Importance of using the dose shown to be safe and effective in randomized trials

# Dose Selection Criteria for NOACs

| | Dabigatran | Rivaroxaban | Apixaban | Edoxaban |
|---|---|---|---|---|
| Standard dose | 150 mg twice daily | 20 mg once daily | 5 mg twice daily | 60 mg once daily |
| Lower dose | 110 mg twice daily | | | 30 mg once daily |
| Reduced dose | | 15 mg once daily | 2.5 mg twice daily | 30 mg once daily |
| Dose-reduction criteria | Dabigatran 110 mg bid in patients with:<br>• Age ≥ 80 years<br>• Concomitant use of verapamil, or<br>• Increased bleeding risk | CrCl 15 mL/min to 49 mL/min | At least 2 of 3 criteria:<br>• Age ≥ 80 years,<br>• Body weight ≤ 60 kg, or<br>• Serum creatinine ≥ 1.5 mg/dL (133 µmol/L) | If any of the following:<br>• CrCl 15-50 mL/min,<br>• Body weight ≤ 60 kg,<br>• Concomitant use of dronedarone, ciclosporin, erythromycin, or ketoconazole |

Hindricks G, et al. *Eur Heart J.* 2020:ehaa612.

# Under-Dosing of NOACs

- There is more use of lower-dose NOACs in practice than directed by the evidence and guidelines
- Low-dose NOACs are less effective at preventing stroke
  - 43% increased risk of ischemic stroke with low-dose edoxaban vs warfarin in ENGAGE
- Dose adjustment as done in the outcome trials provides best evidence of what should be done in practice

Graham DJ, et al. *Circulation*. 2015;131:157-164; Giugliano RP, et al. *NEJM*. 2013; 369:2093-2104.