Stroke Prevention in AF

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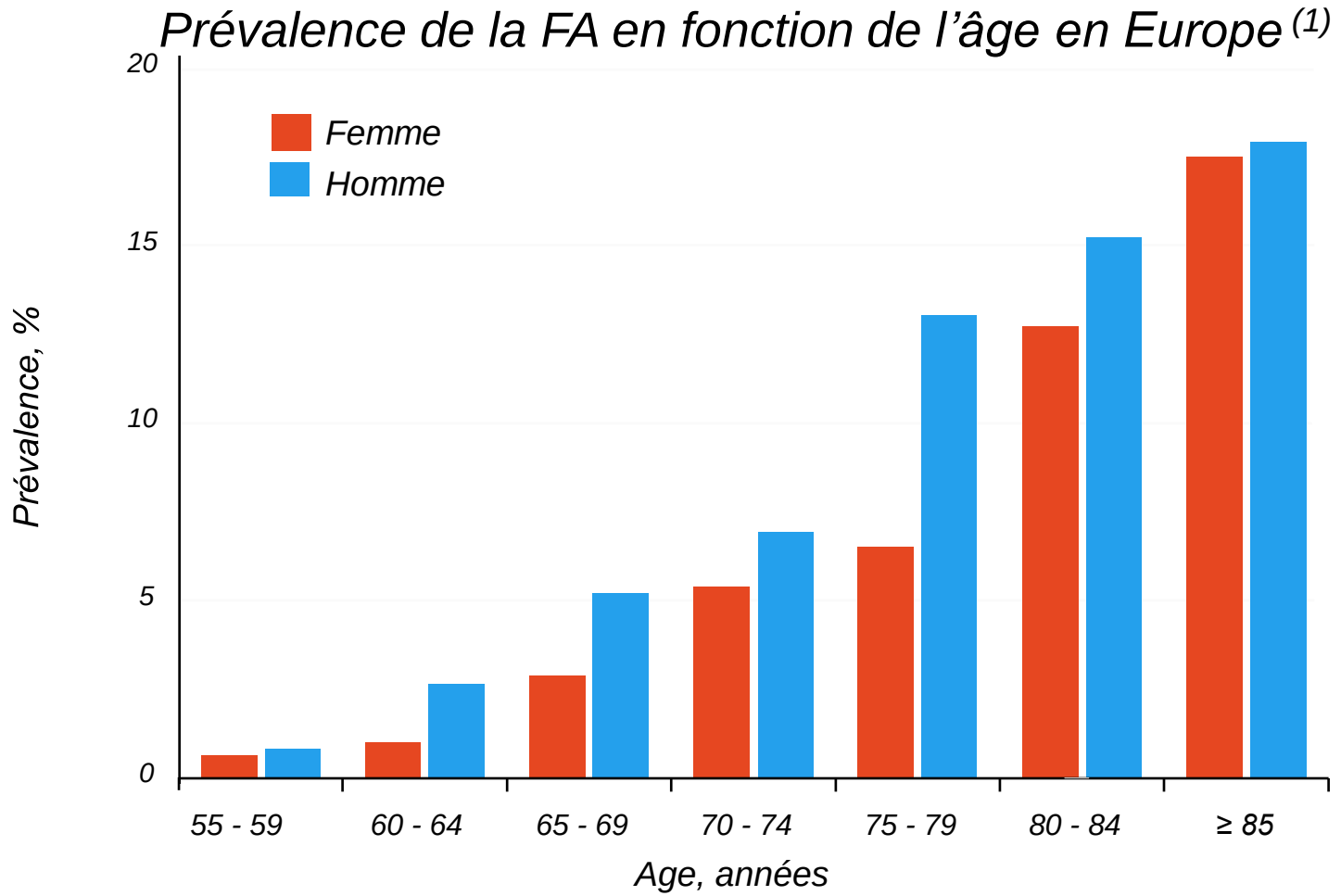
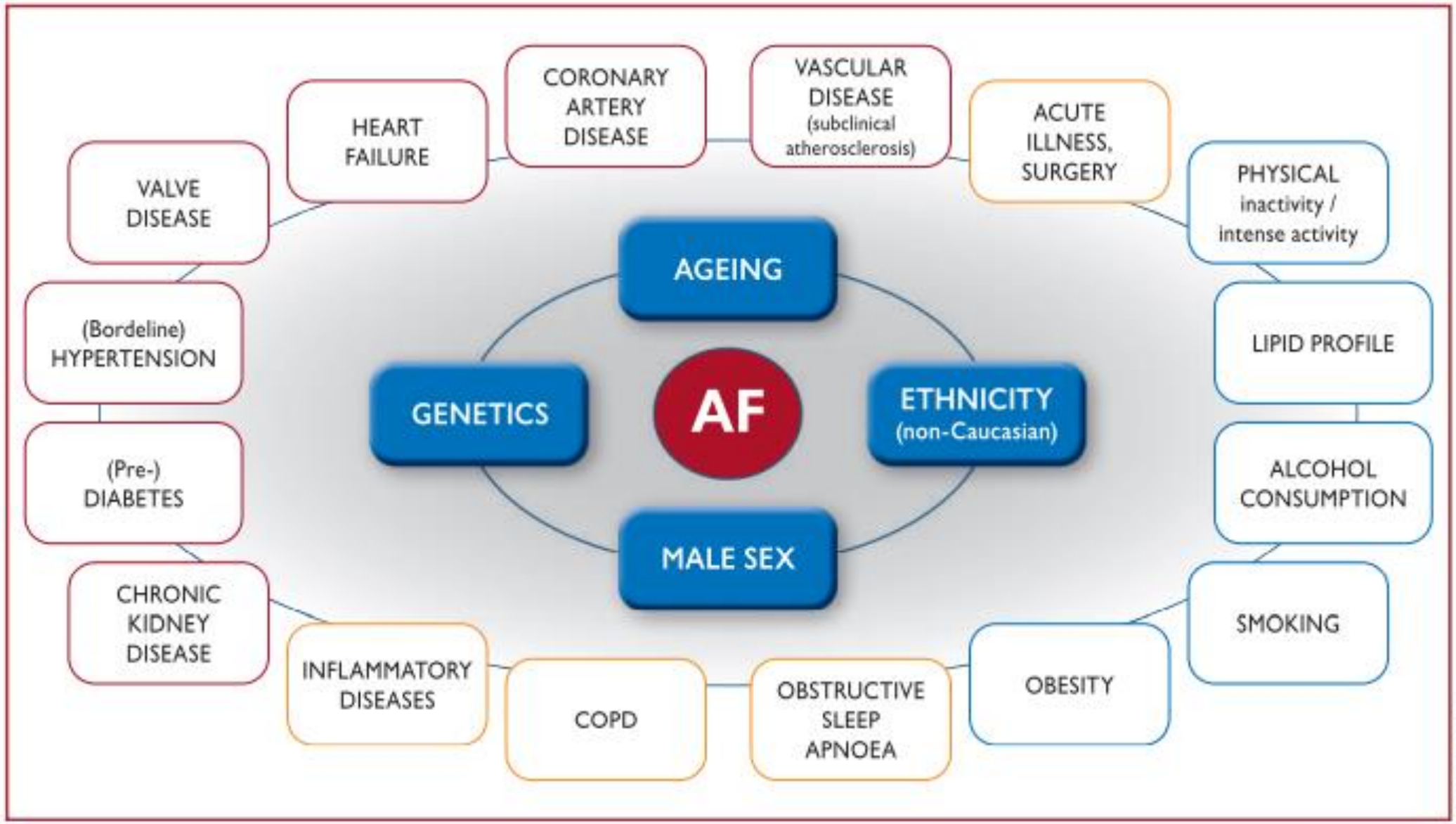
La prévalence de la FA augmente avec l'âge

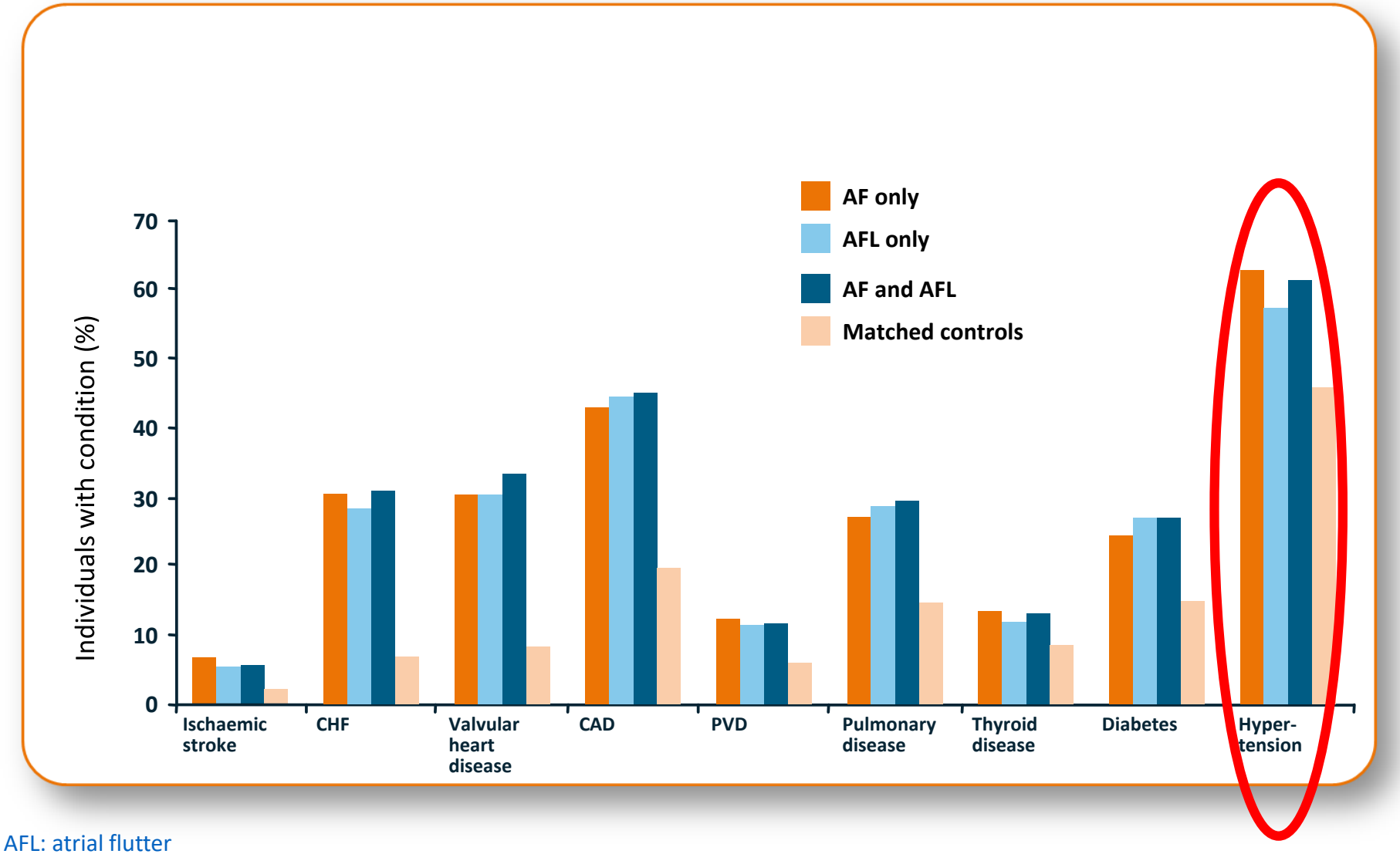


1. Heeringa J et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J 2006 ; 27 : 949-53.

Summary of risk factors for incident AF (ESC 2020)

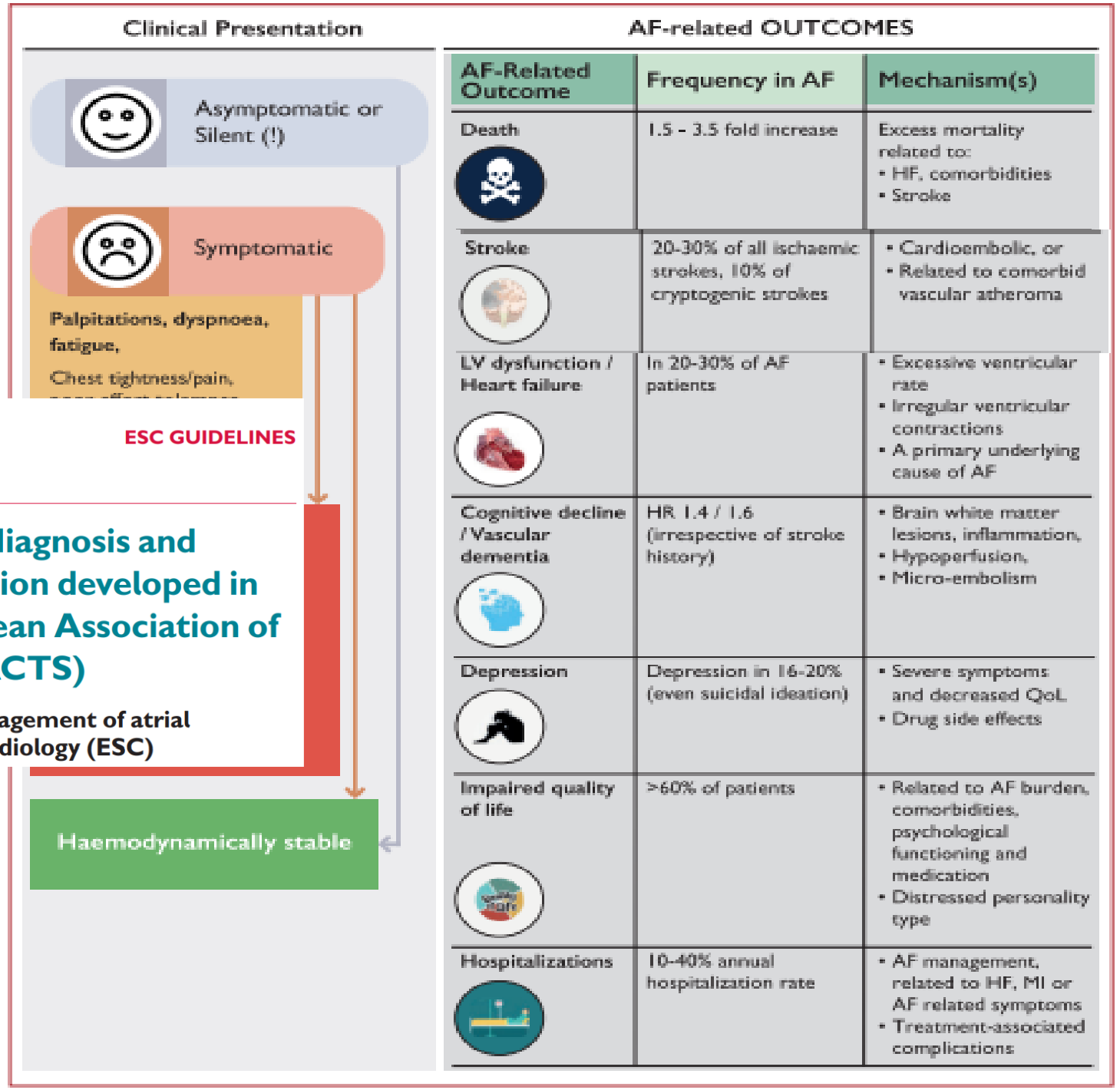


FA: prévalence des comorbidités



AFL: atrial flutter
CAD: coronary artery disease
PVD: peripheral vascular disease

Naccarelli GV, *et al. J Am Coll Cardiol* 2009;53:A104-5 (abs. 1011-52).



ESC European Society of Cardiology

European Heart Journal (2020) **00**, 1–125
doi:10.1093/eurheartj/ehaa612

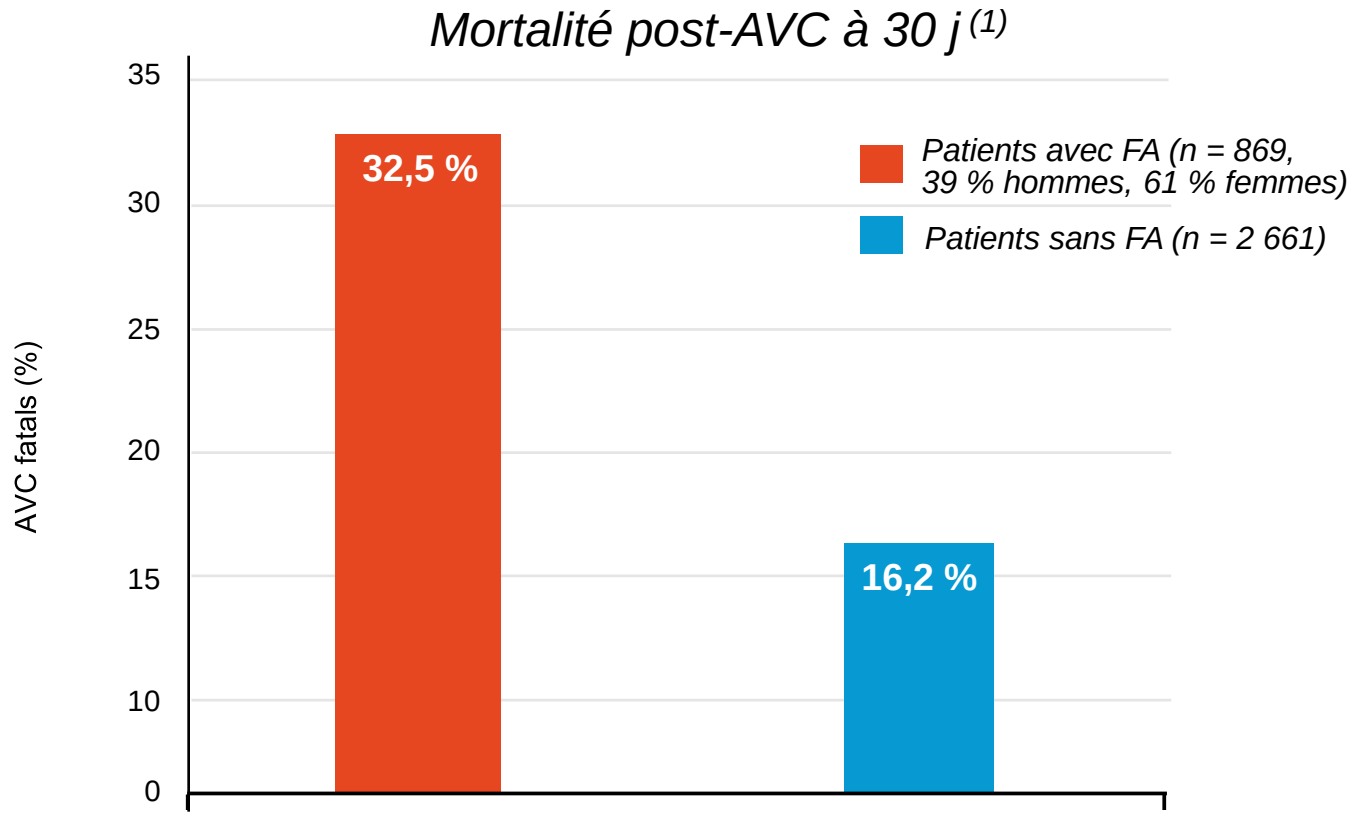
ESC GUIDELINES

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Pronostic des AVC associé à une FA

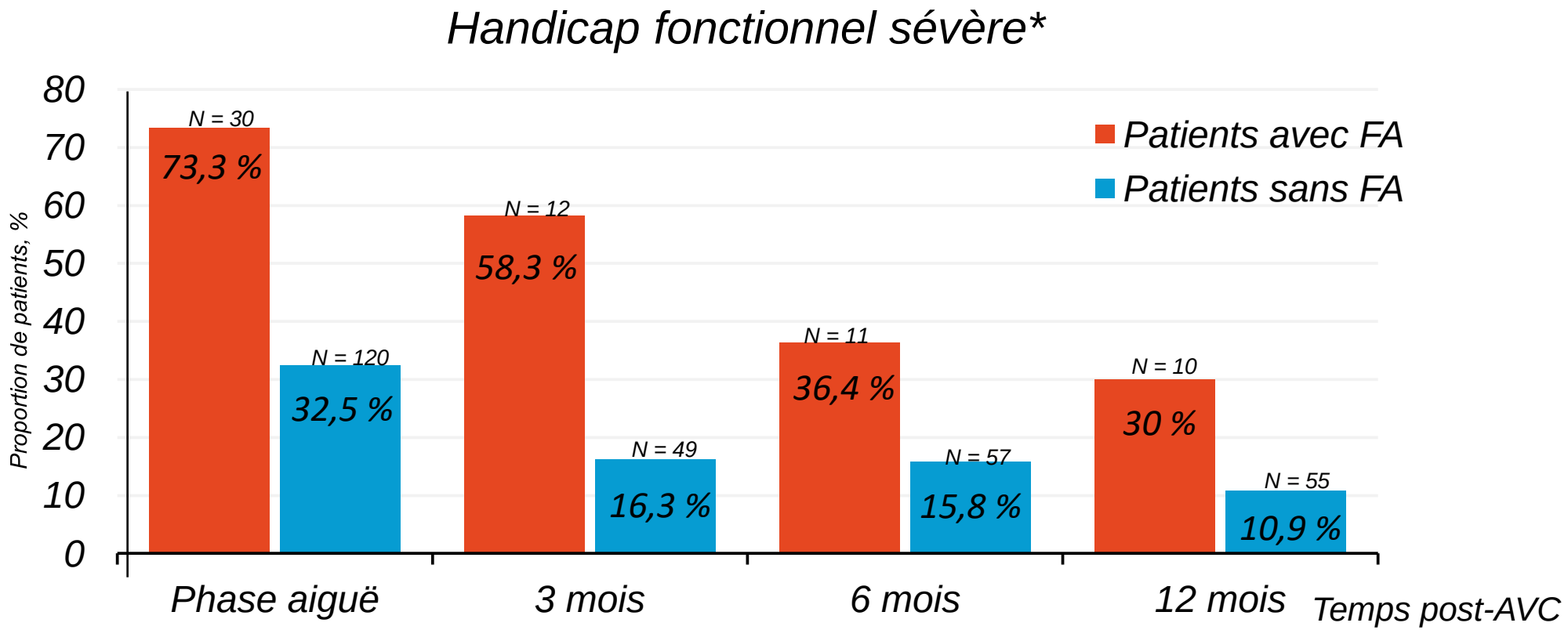
Mortalité à 1 mois des patients atteints d'un AVC associé à une FA



Etude prospective chez 3 530 patients, issus d'un registre de population ayant présenté un 1er AVC (âge moyen de survenue de l'AVC : 78,8 ± 13,3 ans) et évaluant la fréquence et l'impact de la FA sur le pronostic après AVC.

1. Marini C et al. Contribution of Atrial Fibrillation to Incidence and Outcome of Ischaemic Stroke : Results From a Population-Based Study Stroke 2005 ; 36 : 1115-1199.

Pronostic fonctionnel des patients atteints d'un AVC associé à un FA

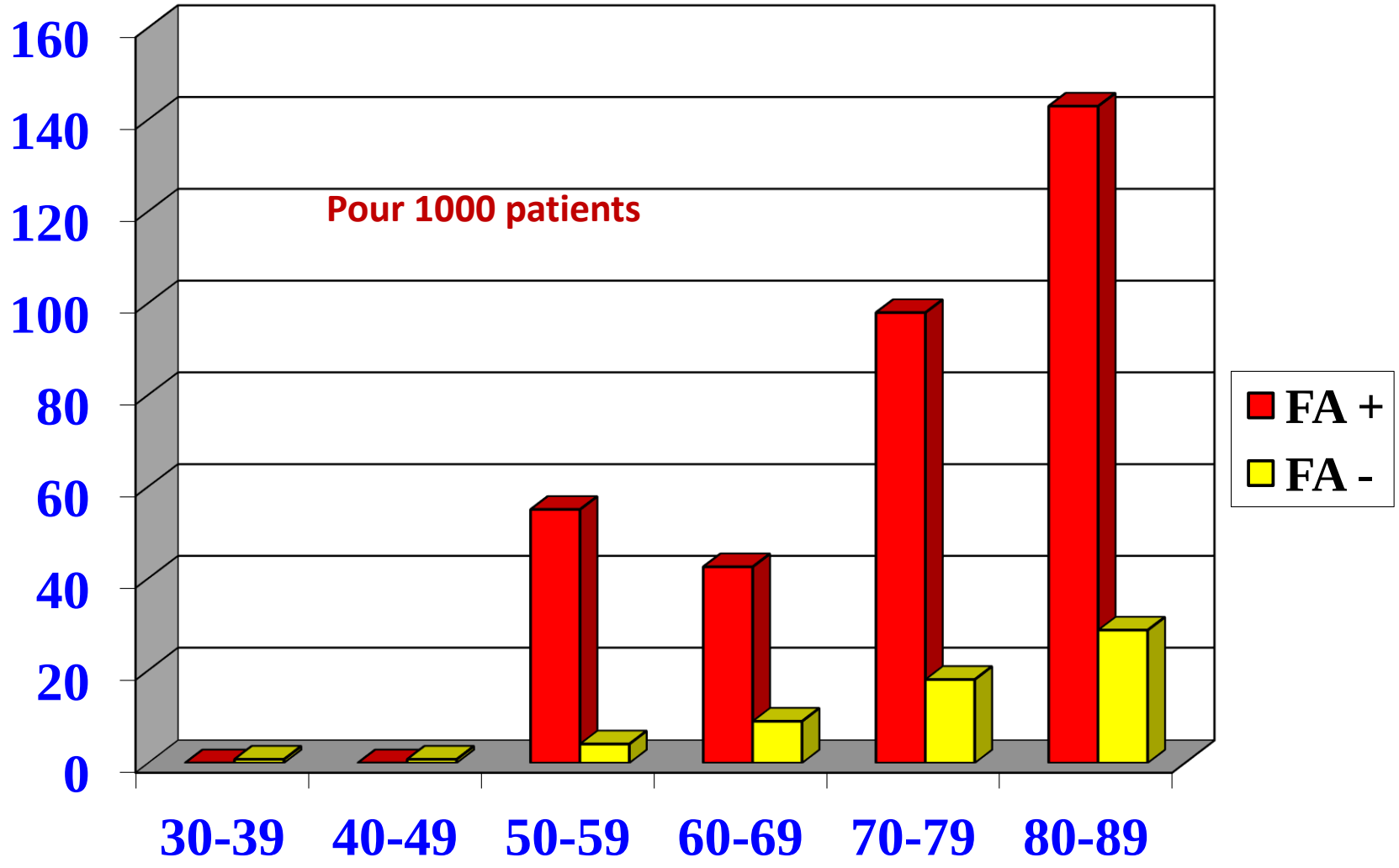


Etude basée sur le suivi de 40 ans de la cohorte originale de Framingham, analyse de 501 patients avec un AVC ischémique incluant 103 patients ayant une FA.
** Le handicap fonctionnel a été évalué chez 150 patients par le score à l'indice de Barthel (score allant de 0 : dépendance complète à 100 : indépendance complète). Un handicap fonctionnel sévère était défini par un score ≤ 40 à l'indice de Barthel.*

Lin HJ, et al. Stroke severity in atrial fibrillation. The Framingham Study. Stroke 1996 ; 27 : 1760-1764.

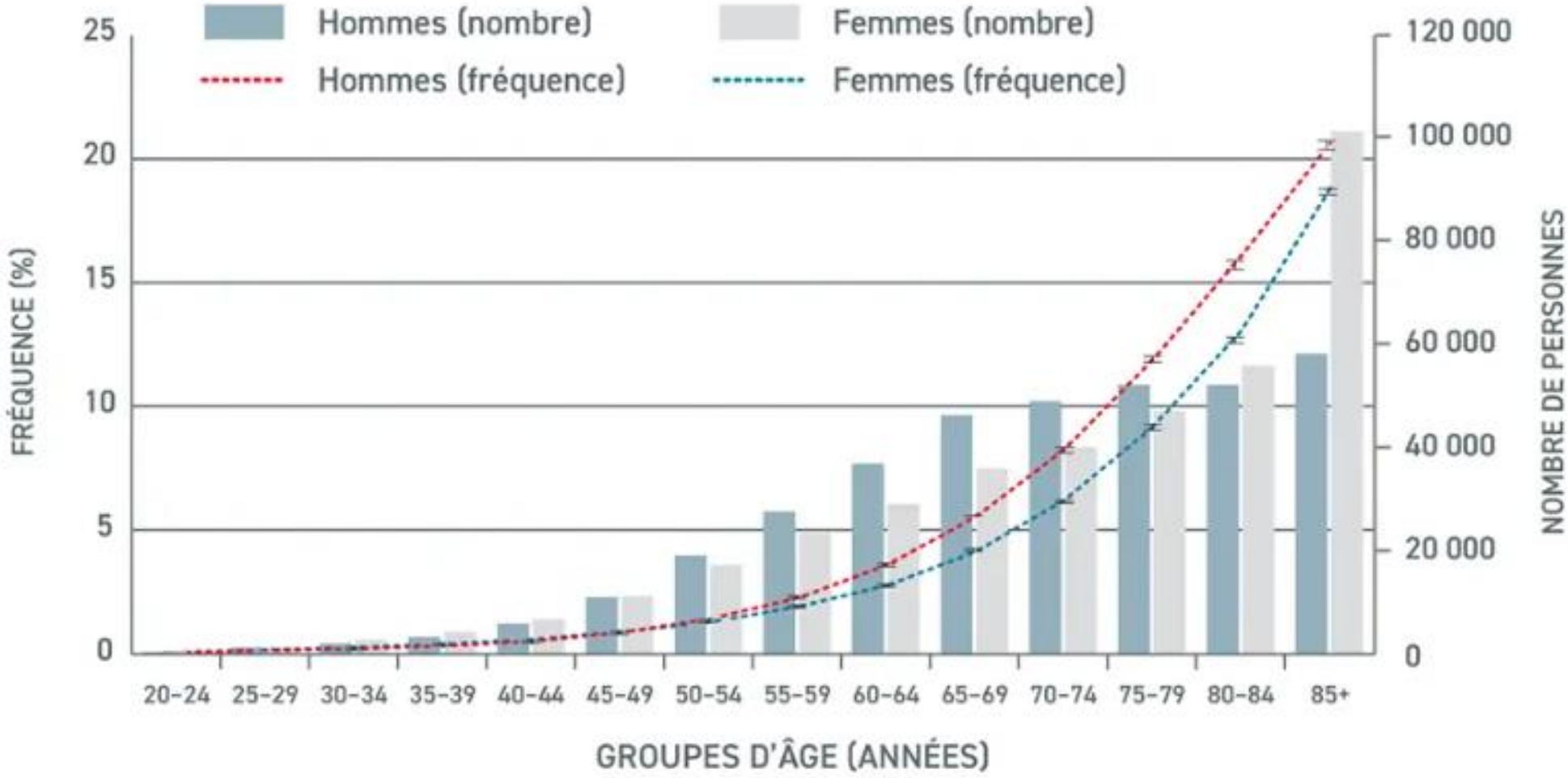
Atrial Fibrillation: A Major Contributor to Stroke in the Elderly
The Framingham Study

Risque d ’AVC à 2 ans en fonction de l’âge

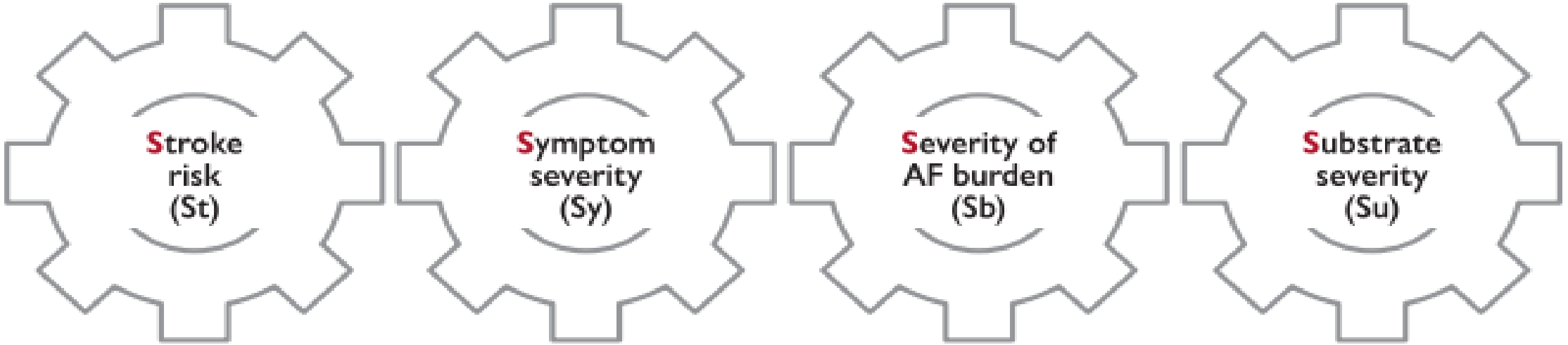


PA Wolf, Arch Intern Med 1987;147:1561-1564

Fréquence des AVC et nombre de victimes, en fonction du groupe d'âge et du sexe



Données canadiennes, de 2012 et 2013; les données du Nouveau-Brunswick et du Yukon n'étaient pas disponibles.
REMARQUE : l'intervalle de confiance à 95 % représente une étendue de valeurs, où selon estimations, la vraie valeur est susceptible de se trouver 19 fois sur 20.



	Stroke risk (St)	Symptom severity (Sy)	Severity of AF burden (Sb)	Substrate severity (Su)
DESCRIPTION	Truly low risk of stroke • Yes • No	• Asymptomatic/mildly symptomatic • Moderate • Severe or disabling	• Spontaneously terminating • AF duration and density of episodes per unit of time	• Comorbidities/ cardiovascular risk factors • Atrial cardiomyopathy (atrial enlargement / dysfunction / fibrosis)
Commonly used assessment tool(s)	**CHA_2DS_2-VASc score**	**EHRA symptom score** QoL questionnaires	• **Temporal pattern of AF** (Paroxysmal, Persistent, Long-standing persistent, Permanent) • **Total AF burden** (total time in AF per monitoring period, the longest episode, number of episodes, etc.)	• **Clinical assessment** Incident AF risk scores, AF progression risk scores • **Imaging** (TTE, TOE, CT, cardiac MRI), biomarkers

Table 7 Stroke risk factors in patients with AF

Most commonly studied clinical risk factors (a systematic review)	Positive studies/All studies	Other clinical risk factors	Imaging biomarkers	Blood/urine biomarkers
Stroke/TIA/systemic embolism	15/16	Impaired renal function/CKD	*Echocardiography*	Cardiac troponin T and I Natriuretic peptides Cystatin C Proteinuria CrCl/eGFR CRP IL-6 GDF-15 von Willebrand factor D-dimer
Hypertension	11/20	OSA	LA dilatation Spontaneous contrast or thrombus in LA Low LAA velocities Complex aortic plaque	
Ageing (per decade)	9/13	Hypertrophic cardiomyopathy		
Structural heart disease	9/13	Amyloidosis in degenerative cerebral and heart diseases		
Diabetes mellitus	9/14	Hyperlipidaemia		
Vascular disease	6/17	Smoking	*Cerebral imaging*	
CHF/LV dysfunction	7/18	Metabolic syndrome	Small-vessel disease	
Sex category (female)	8/22	Malignancy		

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

Table 9 factors for bleeding with OAC and antiplatelet therapy

Non-modifiable	Potentially modifiable	Modifiable	Biomarkers
Age >65 years	Extreme frailty ± excessive risk of falls[a]	Hypertension/elevate SBP	GDF-15
Previous major bleeding	Anaemia	Concomitant antiplatelet/NSAID	Cystatin C / CKD-EPI
Severe renal impairment (on dialysis or renal transplant)	Reduced platelet count or function	Excessive alcohol intake	cTnT-hs
Severe hepatic dysfunction (cirrhosis)	Renal impairment with CrCl <60 mL/min	Non-adherence to OAC	Von Willebrand factor (+ other coagulation markers)
Malignancy	VKA management strategy[b]	Hazardous hobbies / occupations	
Genetic factors (e.g., CYP 2C9 polymorphisms)		Bridging therapy with heparin	
Previous stroke, small-vessel disease, etc.		INR control (target 2.0–3.0), target TTR >70%[c]	
Diabetes mellitus		Appropriate choice of OAC and correct dosing[d]	
Cognitive impairment/dementia			

[a]Walking aids; appropriate footwear; home review to remove trip hazards; neurological assessment where appropriate. [b]Increased INR monitoring, dedicated OAC clinicals, self-monitoring/self-management, educational/behavioural interventions. [c]For patients receiving VKA treatment. [d]Dose adaptation based on patient's age, body weight, and serum creatinine level.

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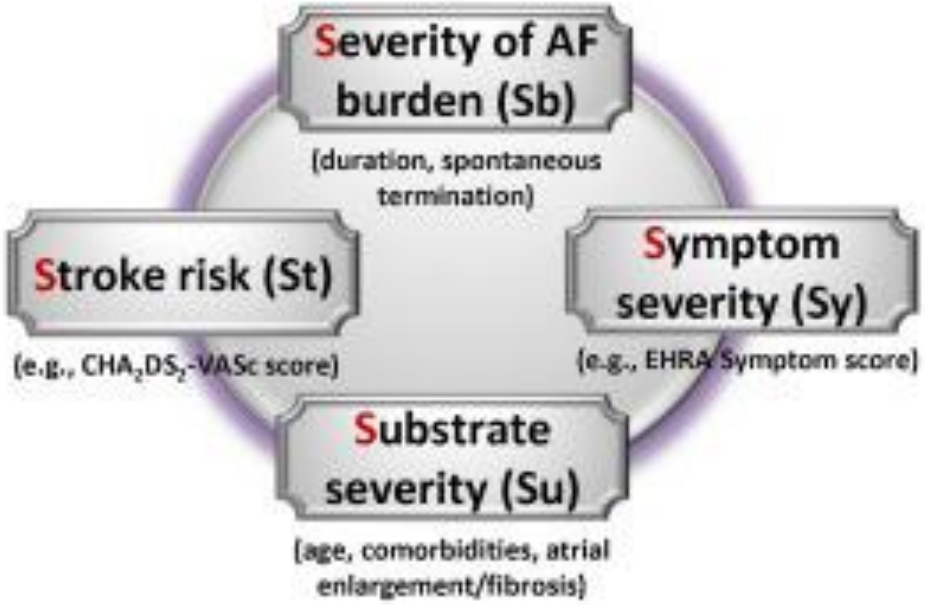
CC To ABC

Confirm AF

A 12-lead ECG or a rhythm strip showing AF pattern for ≥30 s

Characterise AF (the 4S-AF scheme)



The ABC pathway for integrated care management

'A' Avoid stroke
Optimize stroke prevention

'Atrial fibrillation 3-step'

Step 1
- Identify low risk patients

Step 2
- Offer stroke prevention to patients with one or more risk factors for stroke
- Assess bleeding risk

Step 3
- Decide on OACs (either a DOAC [preferred] or VKA with well-managed TTR)

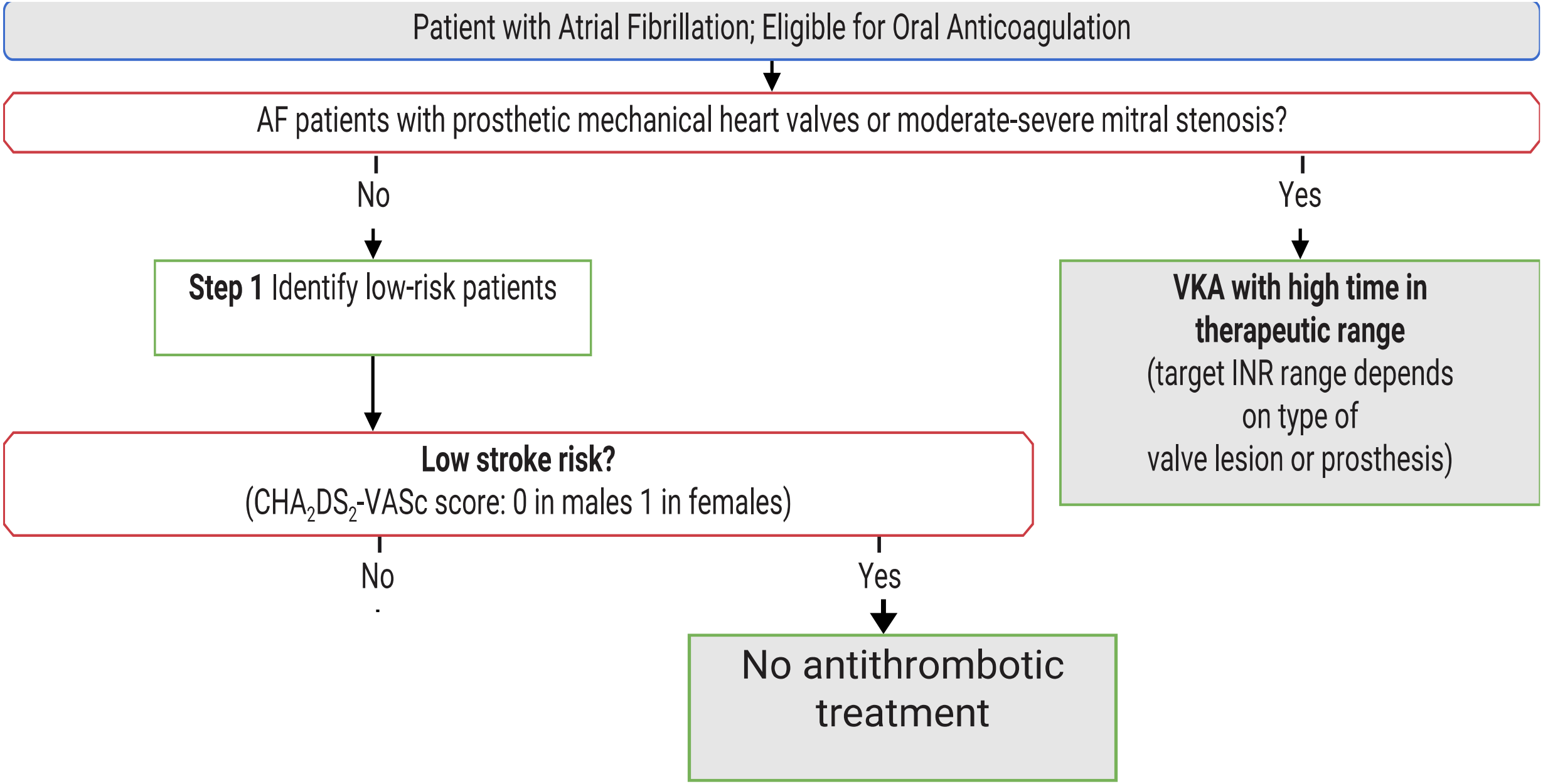
'B' Better symptom management
Treat symptoms

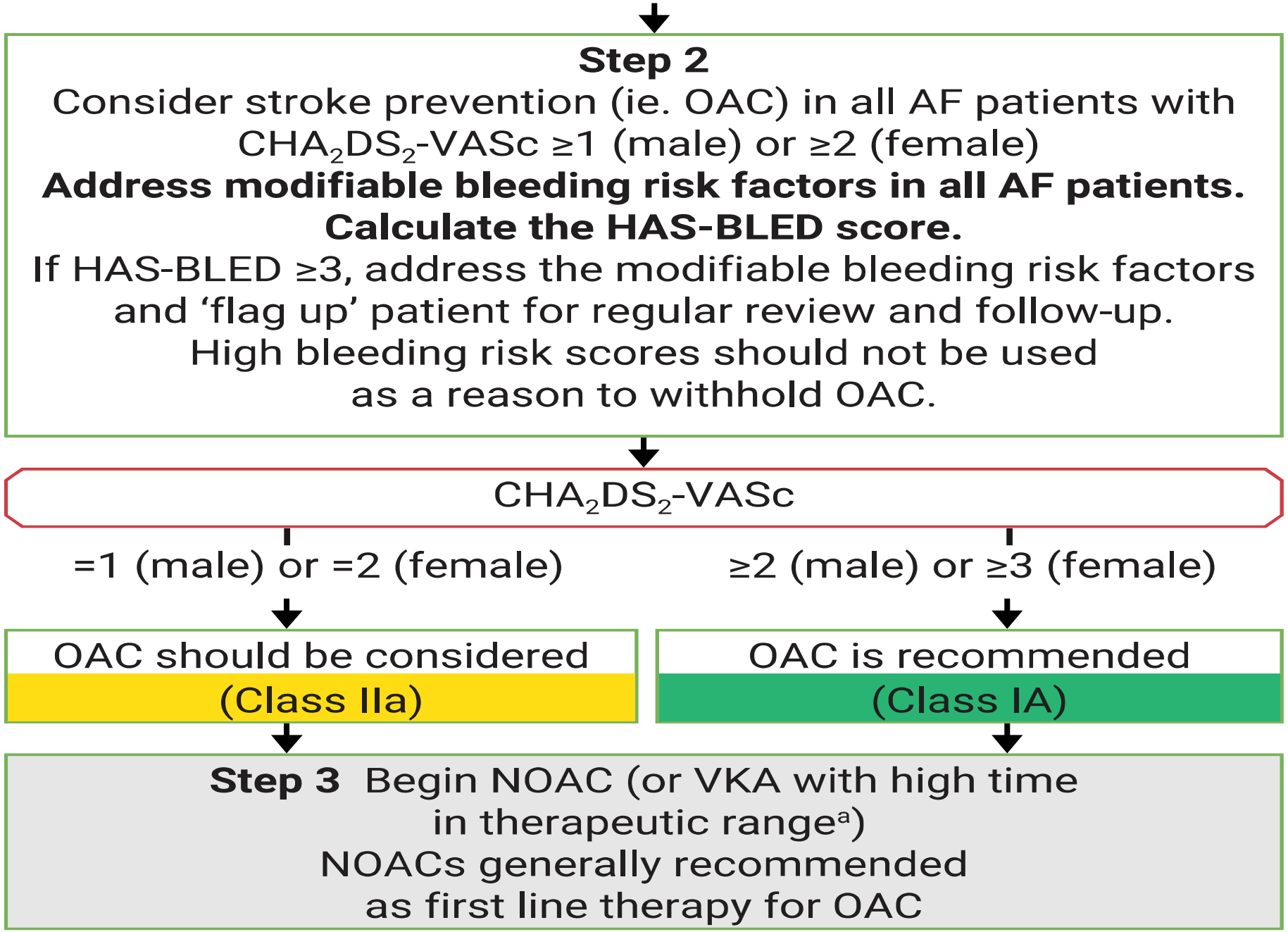
Patient-centered and symptom-directed decisions on rate or rhythm control

'C' Cardiovascular and other comorbidities
Manage risk factors

- Manage hypertension, heart failure, diabetes mellitus, cardiac ischemia, and sleep apnea
- Lifestyle changes: obesity reduction, regular exercise, and reduction of alcohol and stimulant use
- Patient psychological morbidity
- Consider patient values and preferences

(ESC 2020)


Patient with Atrial Fibrillation; Eligible for Oral Anticoagulation
AF patients with prosthetic mechanical heart valves or moderate-severe mitral stenosis?
No
Yes
Step 1 Identify low-risk patients
VKA with high time in therapeutic range (target INR range depends on type of valve lesion or prosthesis)
Low stroke risk?
(CHA2DS2-VASc score: 0 in males 1 in females)
No
Yes
No antithrombotic treatment

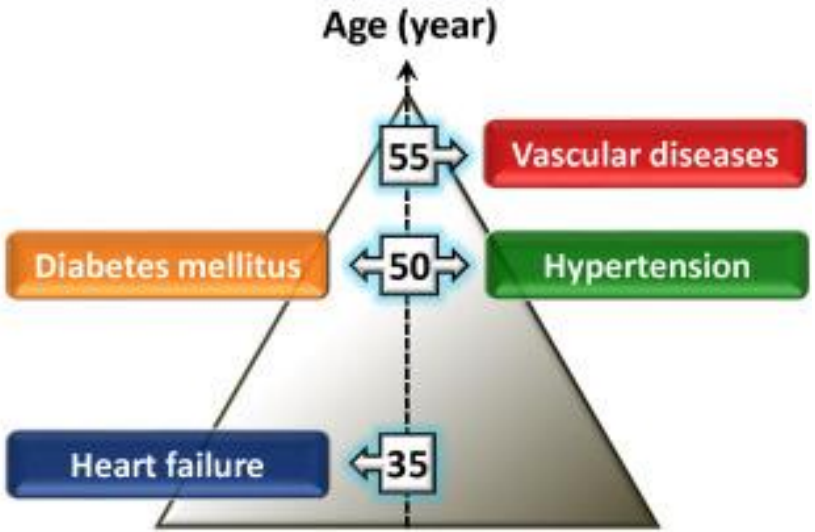

Step 2
Consider stroke prevention (ie. OAC) in all AF patients with CHA2DS2-VASc ≥1 (male) or ≥2 (female)
Address modifiable bleeding risk factors in all AF patients.
Calculate the HAS-BLED score.
If HAS-BLED ≥3, address the modifiable bleeding risk factors and 'flag up' patient for regular review and follow-up.
High bleeding risk scores should not be used as a reason to withhold OAC.
CHA2DS2-VASc
=1 (male) or =2 (female)
≥2 (male) or ≥3 (female)
OAC should be considered
(Class IIa)
OAC is recommended
(Class IA)
Step 3 Begin NOAC (or VKA with high time in therapeutic range[a])
NOACs generally recommended as first line therapy for OAC

Recommandations sur la prévention des accidents vasculaires cérébraux dans les lignes directrices ESC, ACC/AHA et APHRS. ACC/AHA

CHA_2DS_2-VASc score 1 for Males and 2 for Females

2016/2020 ESC AF guidelines	2019 ACC/AHA focused update
OACs should be considered (IIa)	OACs may be considered (IIb)

2021 APHRS consensus guidelines
Different age thresholds to initiate DOACs for different comorbidities



Annals of Internal Medicine | Review

Meta-analysis: Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular Atrial Fibrillation

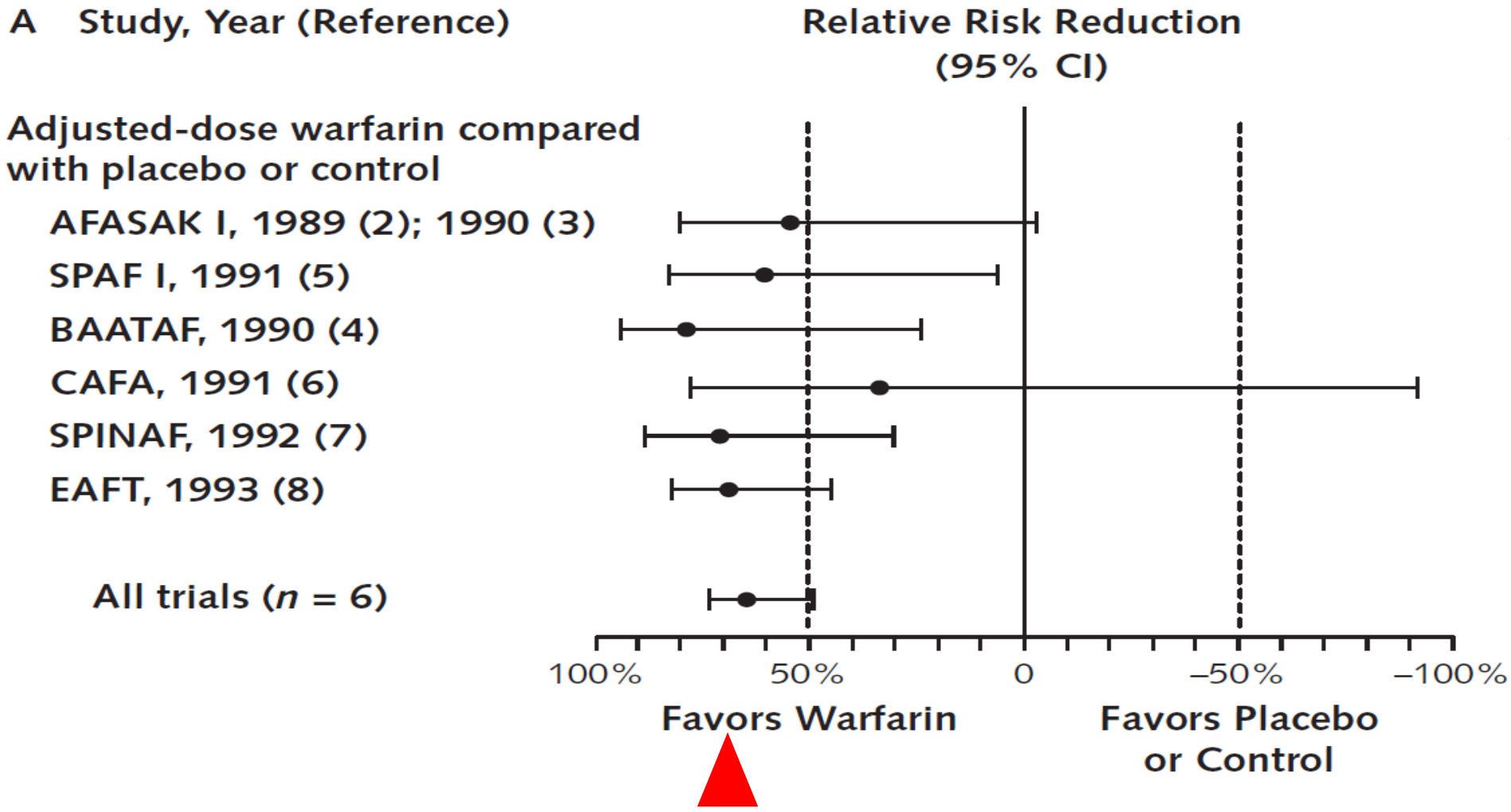
Robert G. Hart, MD; Lesly A. Pearce, MS; and Maria I. Aguilar, MD

Background: Atrial fibrillation is a strong independent risk factor for stroke.

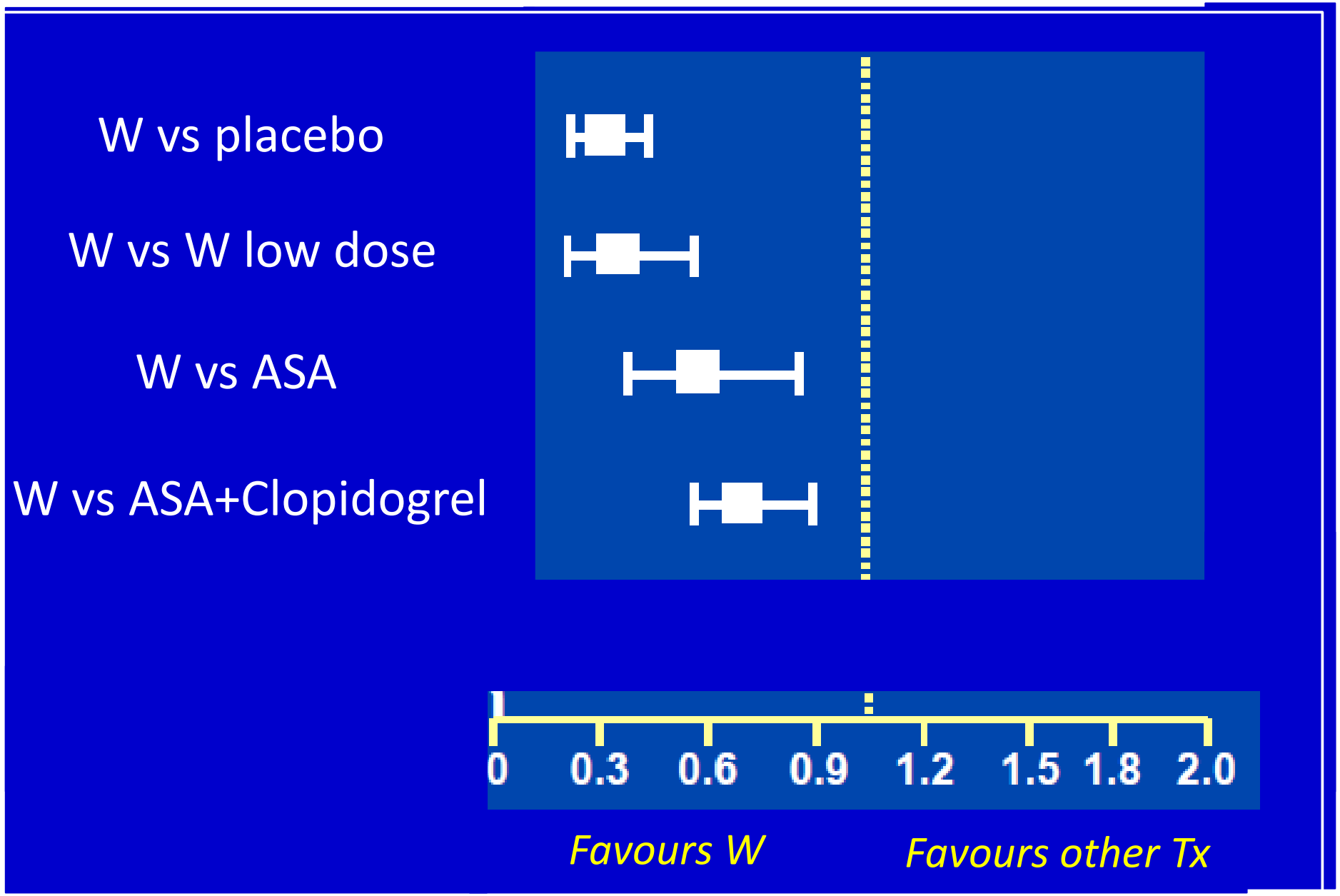
Purpose: To characterize the efficacy and safety of antithrombotic agents for stroke prevention in patients who have atrial fibrillation, adding 13 recent randomized trials to a previous meta-analysis.

Data Sources: Randomized trials identified by using the Cochrane Stroke Group search strategy, 1966 to March 2007, unrestricted by language.

Adjusted dose warfarin vs placebo/control



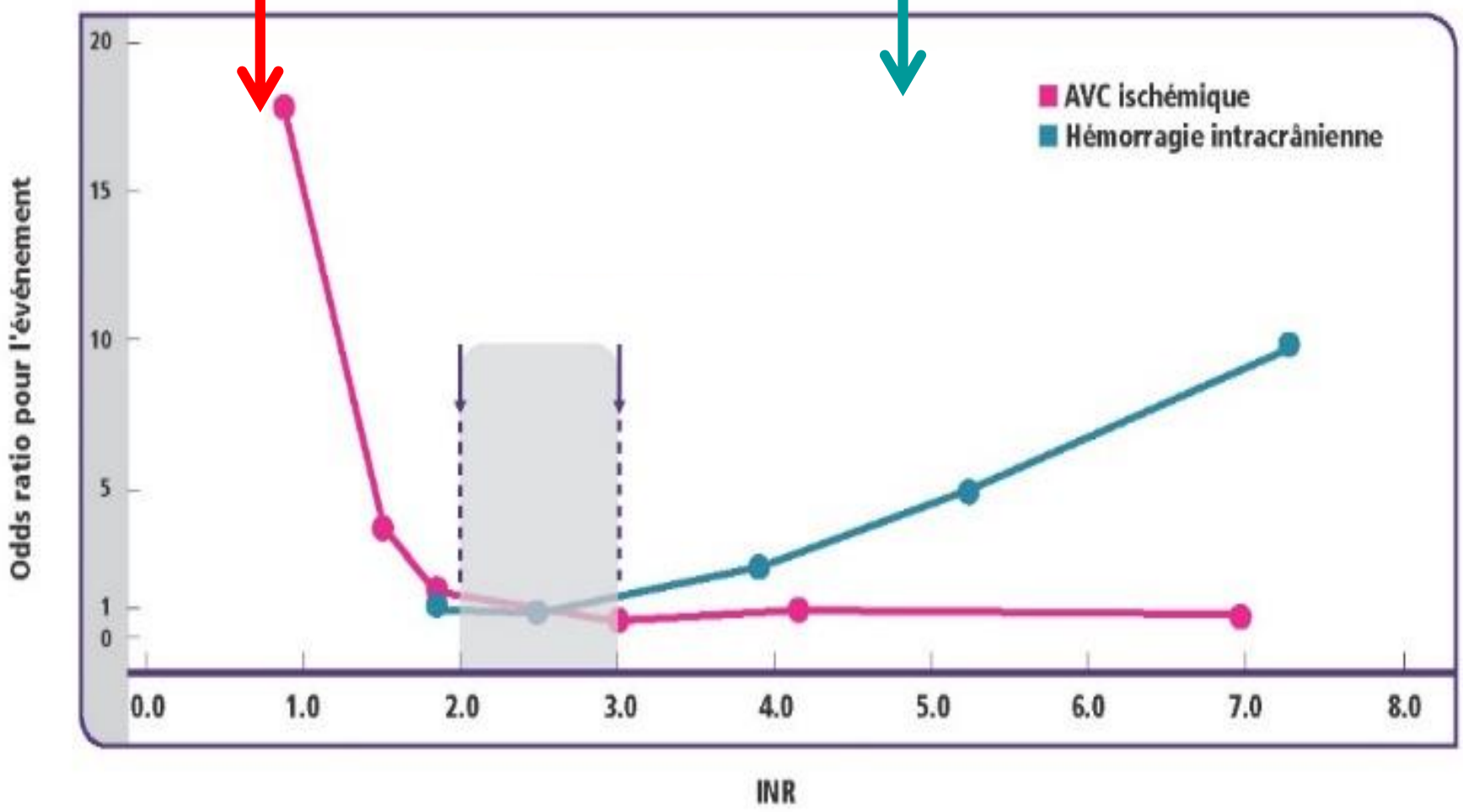
Hart et al, *Ann Intern Med.* 2007;146:857-867



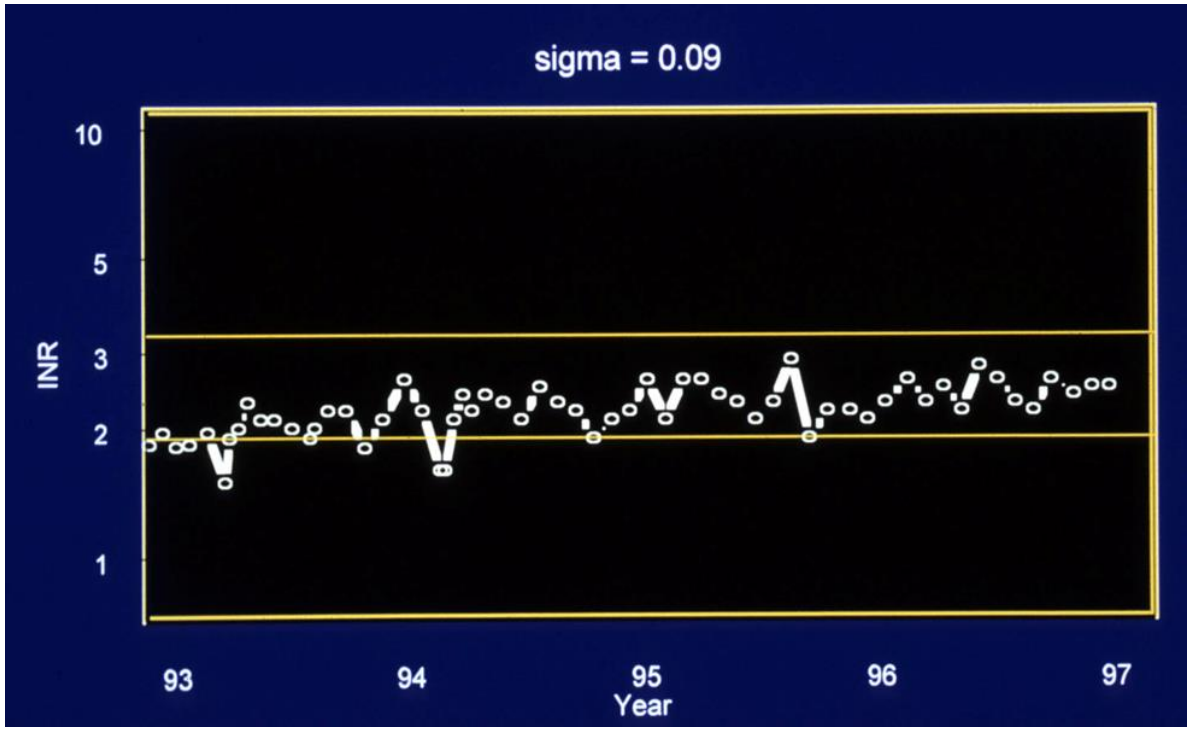
From Camm AJ et al., ESC 2009

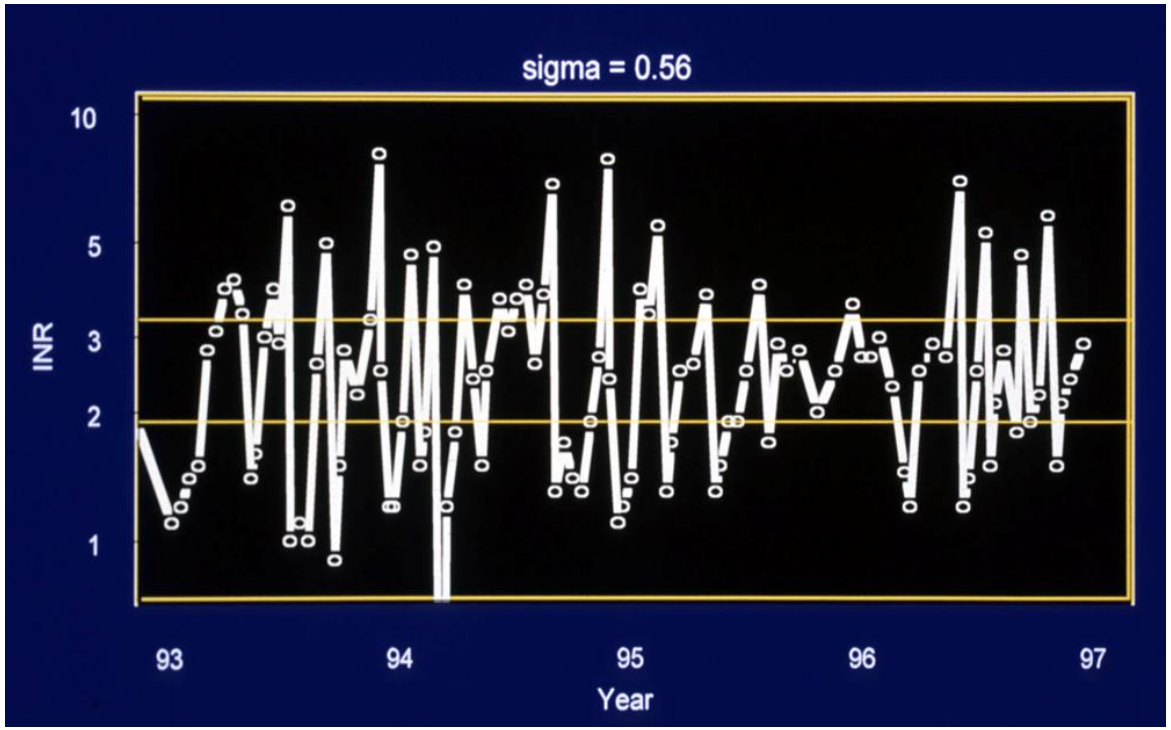
Risque embolique x1.9

Risque d'hémorragie majeure x3.2



Stabilité – Instabilité de l'INR sous AVK





Anticoagulants : responsables de **31%** des cas d'accidents iatrogènes graves * *
au 1er rang des médicaments responsables !

AVK : 12,3% des hospitalisations pour effet indésirable médicamenteux (1ère cause d'hospitalisation)

AVK : 5000 à 6000 accidents hémorragiques mortels/an

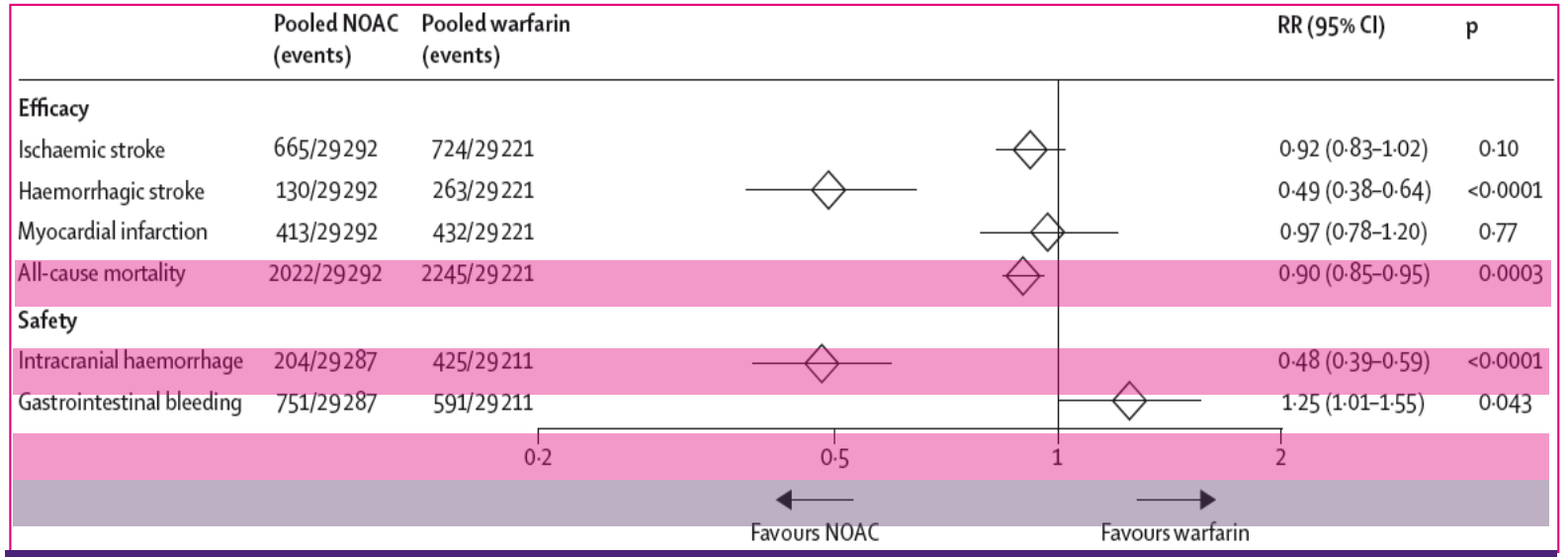
* www.ansm.sante.fr : Les anticoagulants en France en 2014 : état des lieux, synthèse et surveillance.

** Étude Nationale sur les Événements Indésirables graves liés aux Soins. DREES. Études et Résultats n° 398, mai 2005 et Série Étude et Recherche n° 110, septembre 2011

AOD et sécurité d'emploi

Méta-analyse RE-LY, Rocket AF, ARISTOTLE et ENGAGE AF-TIMI 48 :

71 683 patients inclus



Réduction de 52 % des hémorragies IC vs AVK

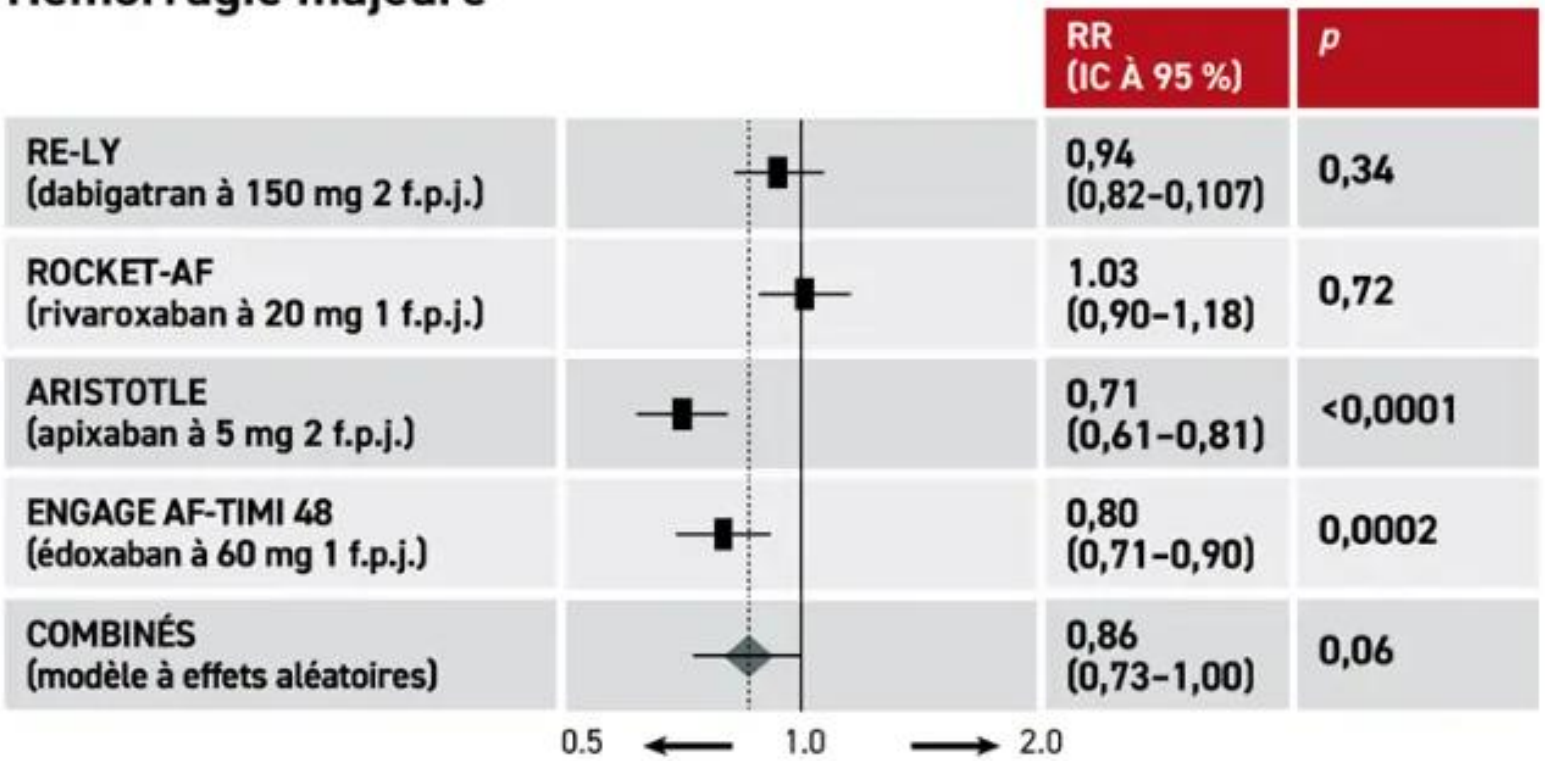
Réduction de 10 % des décès toutes causes

Augmentation de 25 % des hémorragies gastro-intestinales vs AVK

Ruff CT, Giugliano RP, Braunwald E *et al.* *Lancet.* 4 décembre 2013

Les NACO, aussi sûrs que la warfarine pour ce qui est du risque relatif d'hémorragie

Méta-analyse sur l'efficacité des NACO *vs* celle de la warfarine :
Hémorragie majeure

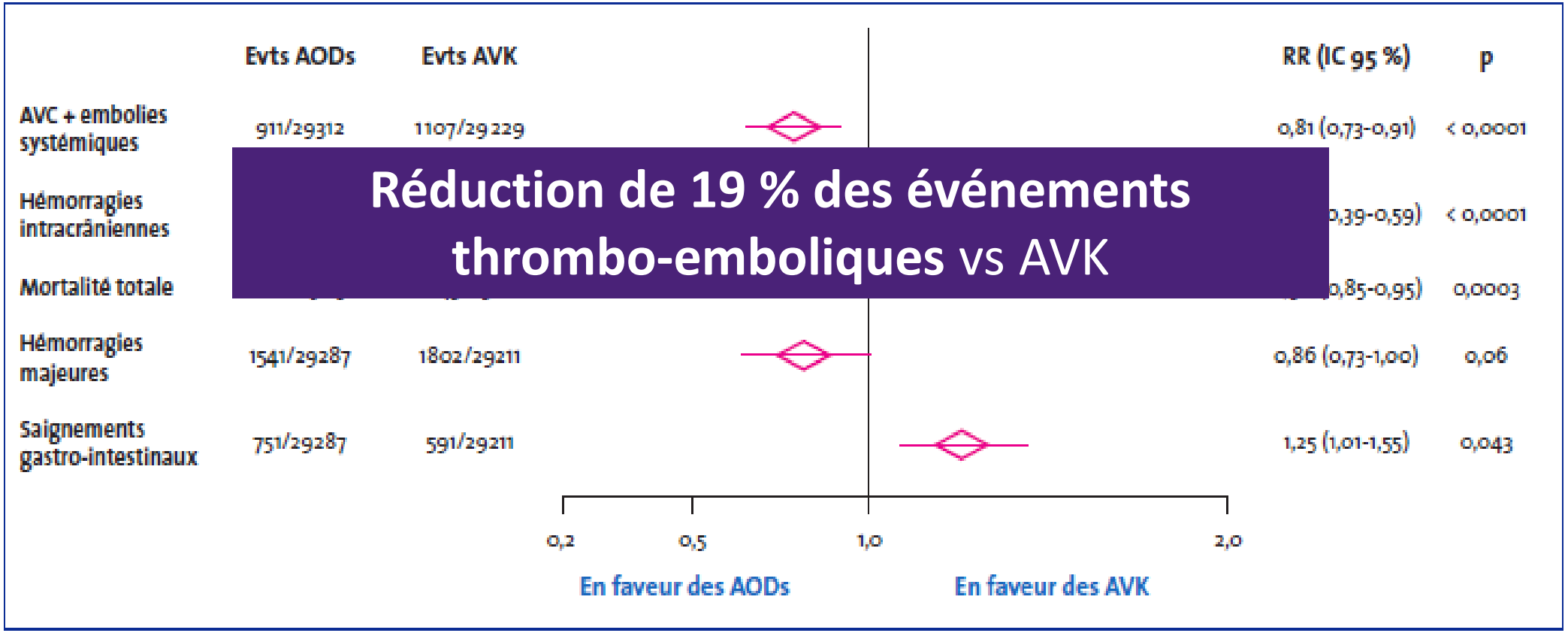


Les données sont exprimées en n/N, à moins d'indication contraire.
Hétérogénéité : I^2 = 83 %; p = 0,001. NACO : nouvel anticoagulant oral (anticoagulant pour voie orale qui n'est pas un antagoniste de la vitamine K); RR = risque relatif.

AOD et évènements thrombo-emboliques

Méta-analyse RE-LY, Rocket AF, ARISTOTLE et ENGAGE AF-TIMI 48 :

71 683 patients inclus



Ruff CT, Giugliano RP, Braunwald E *et al.* *Lancet.* 4 décembre 2013

Recommendations for the prevention of thromboembolic events in AF (1)

Recommendations	Class	Level
For stroke prevention in AF patients who are eligible for OAC, NOACs are recommended in preference to VKAs (excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis).	I	A
For stroke risk assessment, a risk-factor–based approach is recommended, using the CHA_2DS_2-VASc clinical stroke risk score to initially identify patients at 'low stroke risk' (CHA_2DS_2-VASc score = 0 in men, or 1 in women) who should not be offered antithrombotic therapy.	I	A
OAC is recommended for stroke prevention in AF patients with CHA_2DS_2-VASc score ≥2 in men or ≥3 in women.	I	A

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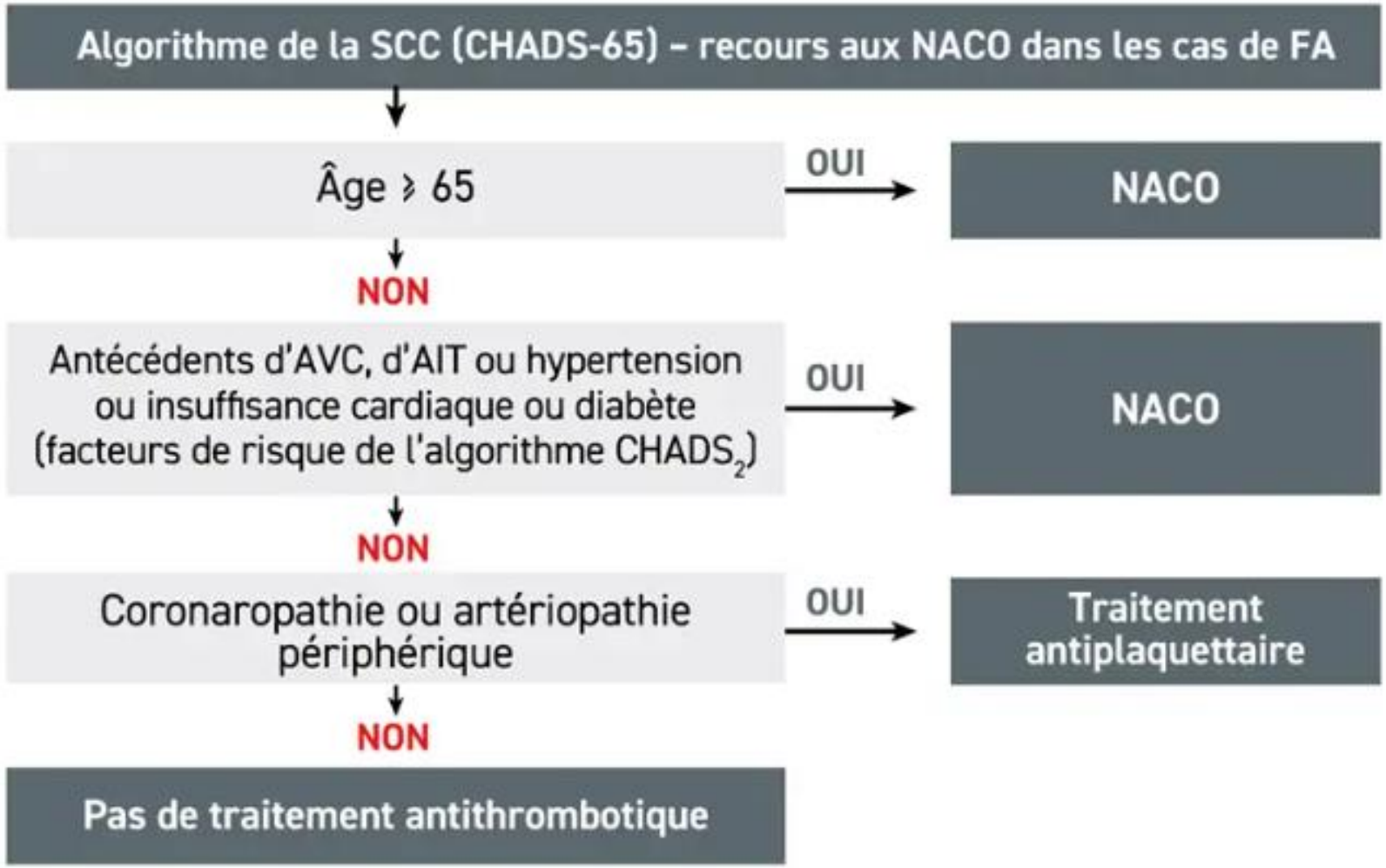
(European Heart Journal 2020-doi/10.1093/eurheartj/ehaa612)

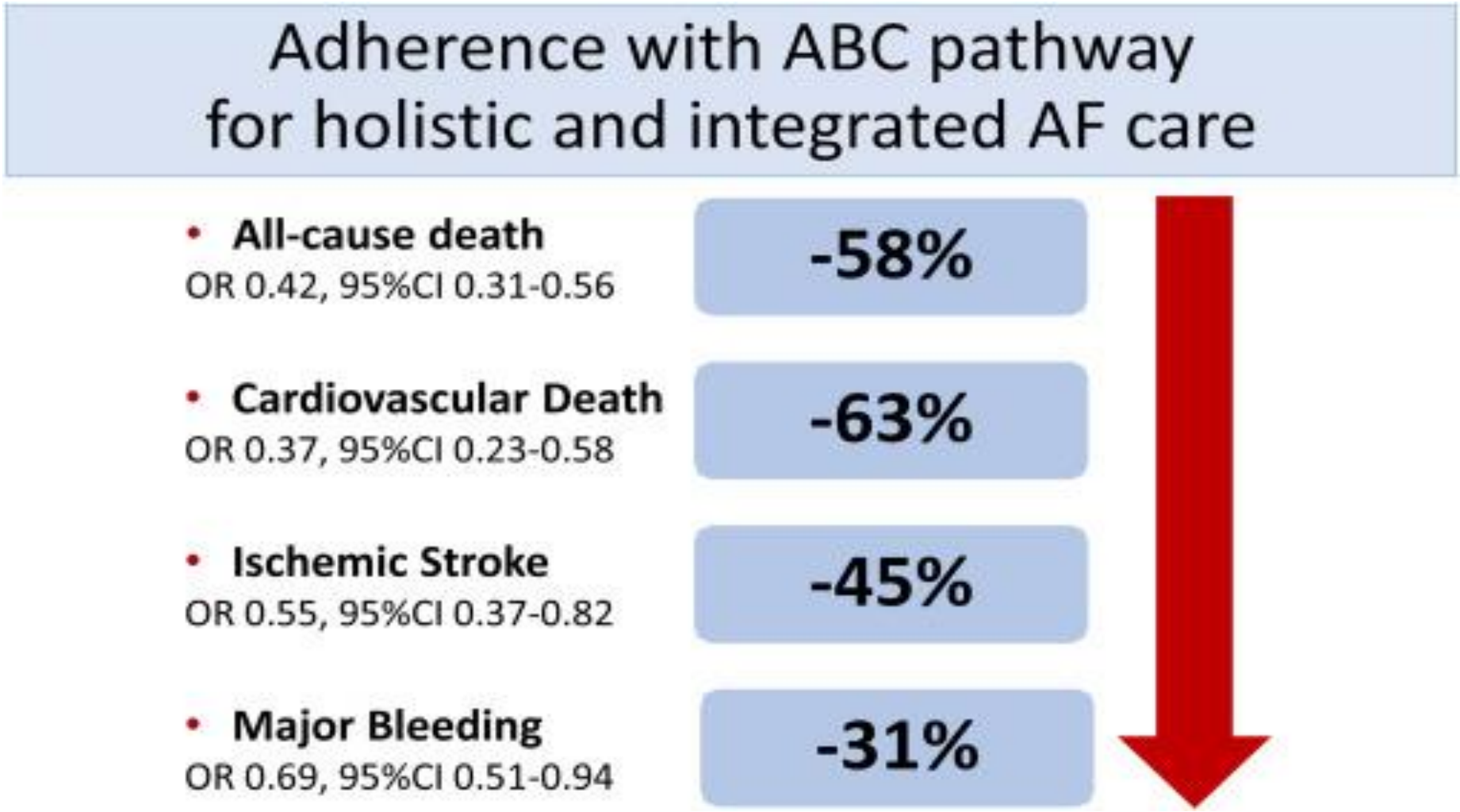
Les lignes directrices de la SCC recommandent les NACO de préférence à la warfarine pour la plupart des patients atteints de FA



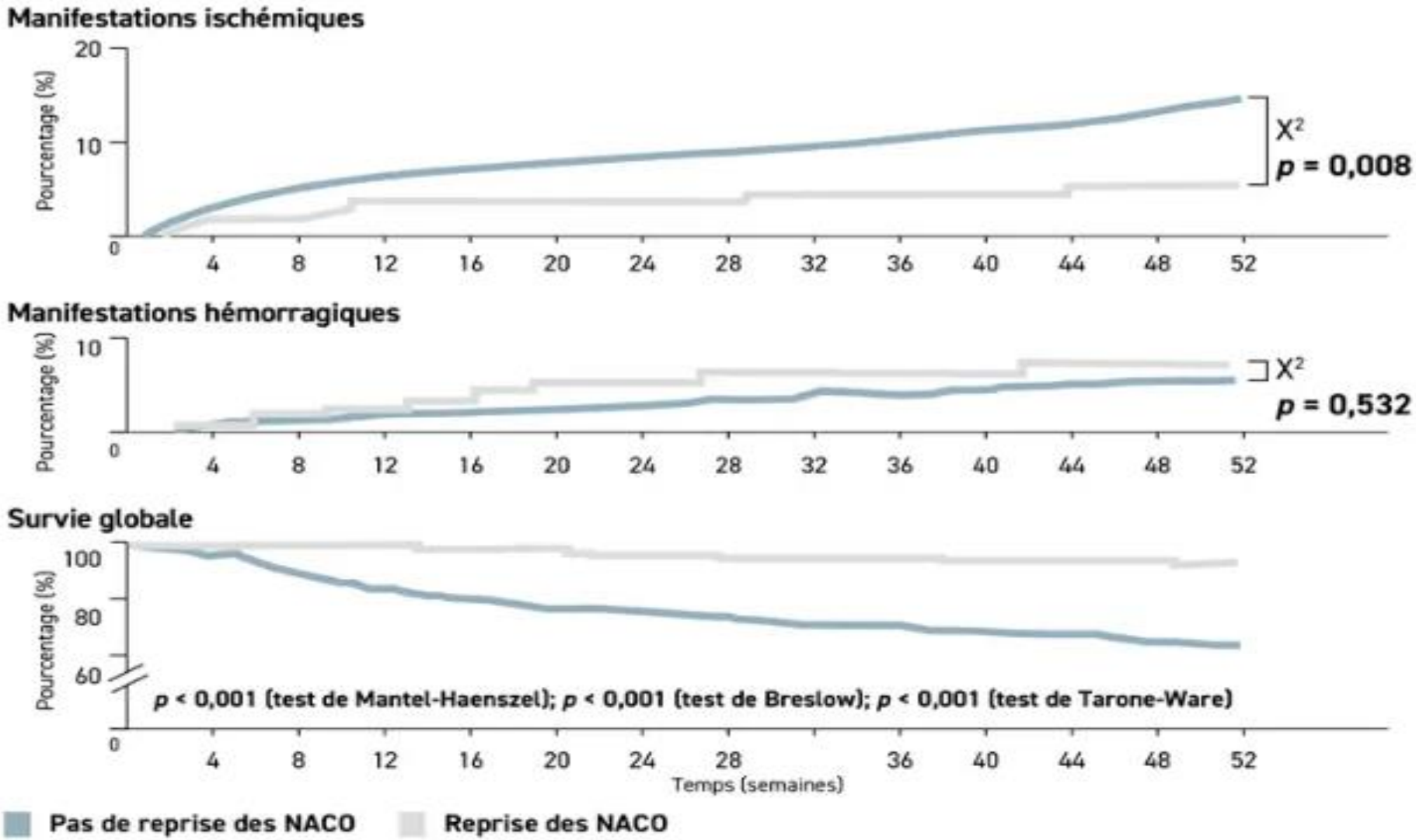
Effets des traitements selon le schéma 4S-AF

The 4S-AF scheme	EORP-AF General Long-Term Registry		APHRS AF registry	
Treatment	Risk of mortality HR (95% CI)		Composite risk of ischemic stroke/SEE, heart failure, ACS, significant CAD requiring coronary intervention and mortality OR (95% CI)	
(St = 1) Anticoagulation therapy	↓ 27%	0.73 (0.54-0.98)	↓ 43%	0.57 (0.38-0.84)
(Sy = 2) Rhythm control during follow-up	↓ 78%	0.22 (0.09-0.54)	↓ 74%	0.26 (0.03-1.95)
(Su ≥ 1) Risk factor management	↓ 17%	0.83 (0.66-1.05)	↓ 62%	0.38 (0.16-0.94)
All 4S-AF domains treated	↓ 29%	0.71 (0.55-0.92)	↓ 62%	0.38 (0.23-0.65)

Impacts de l'adhésion au parcours ABC sur les résultats cliniques chez les patients atteints de FA



Lien entre la reprise de l'administration des NACO après une HC associée à ces agents et une raréfaction des manifestations ischémiques et une prolongation de la survie



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