Who should not receive anticoagulation therapy?

Adherence to guidelines vs. Prejudice

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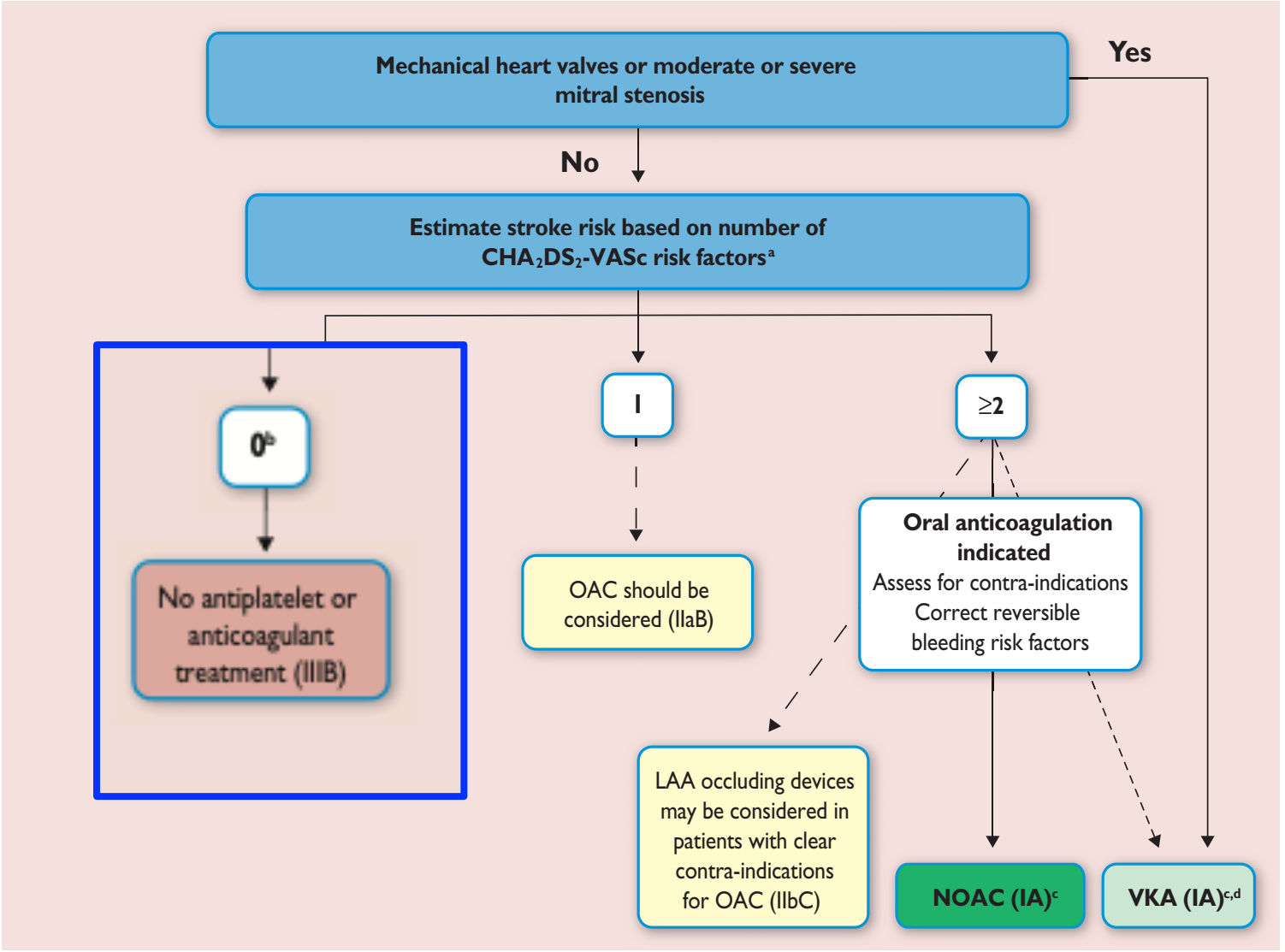
2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Kirchhof P, Eur Heart J 2016

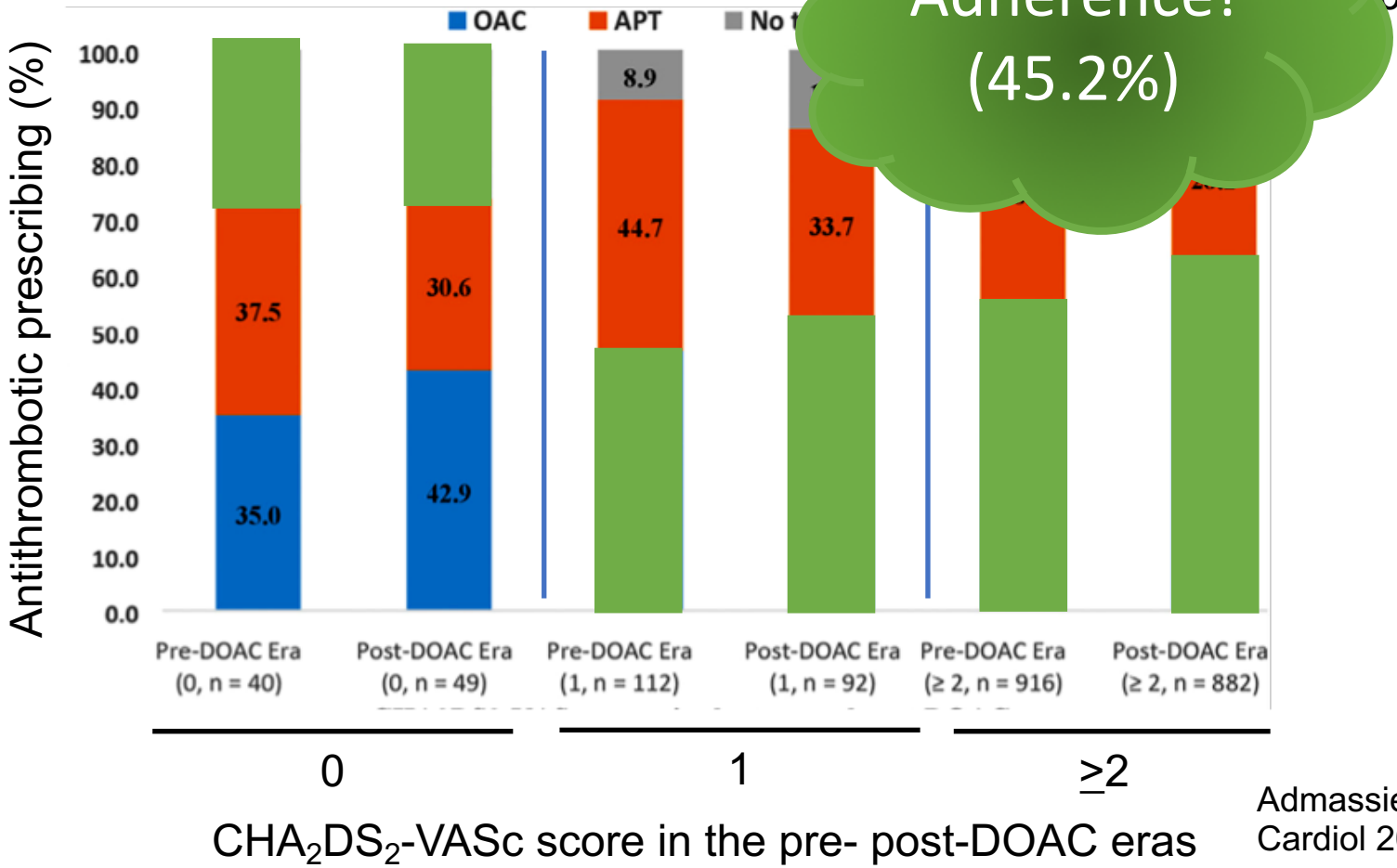
Stroke prevention in atrial fibrillation



Changes in Oral Anticoagulant Prescribing for Stroke Prevention in Patients With Atrial Fibrillation

Antithrombotic prescribing, by stroke risk scores, in pre- and post-DOAC era

(Australia, 2011-5; Pre- / Post-DOAC – N=1089 / 1[illegible])



Admassie E, Am J Cardiol 2017

Changes in Oral Anticoagulant Prescribing for Stroke Prevention in Patients With Atrial Fibrillation

Factors associated with OAC prescribing in the

	OR (95% CI)	p
Age	0.98 (0.97-0.99)	<0.001
Men	1.28 (1.05-1.54)	0.012
CHF	1.36 (1.01-1.83)	0.042
VHD	1.71 (1.11-2.70)	0.017
Prior bleeding	0.14 (0.06-0.29)	<0.001
CHA_2DS_2-VASc $\geq$2	1.95 (1.36-2.80)	<0.001
DOAC Era	1.40 (1.17-1.68)	<0.001

VHD: valvular heart disease

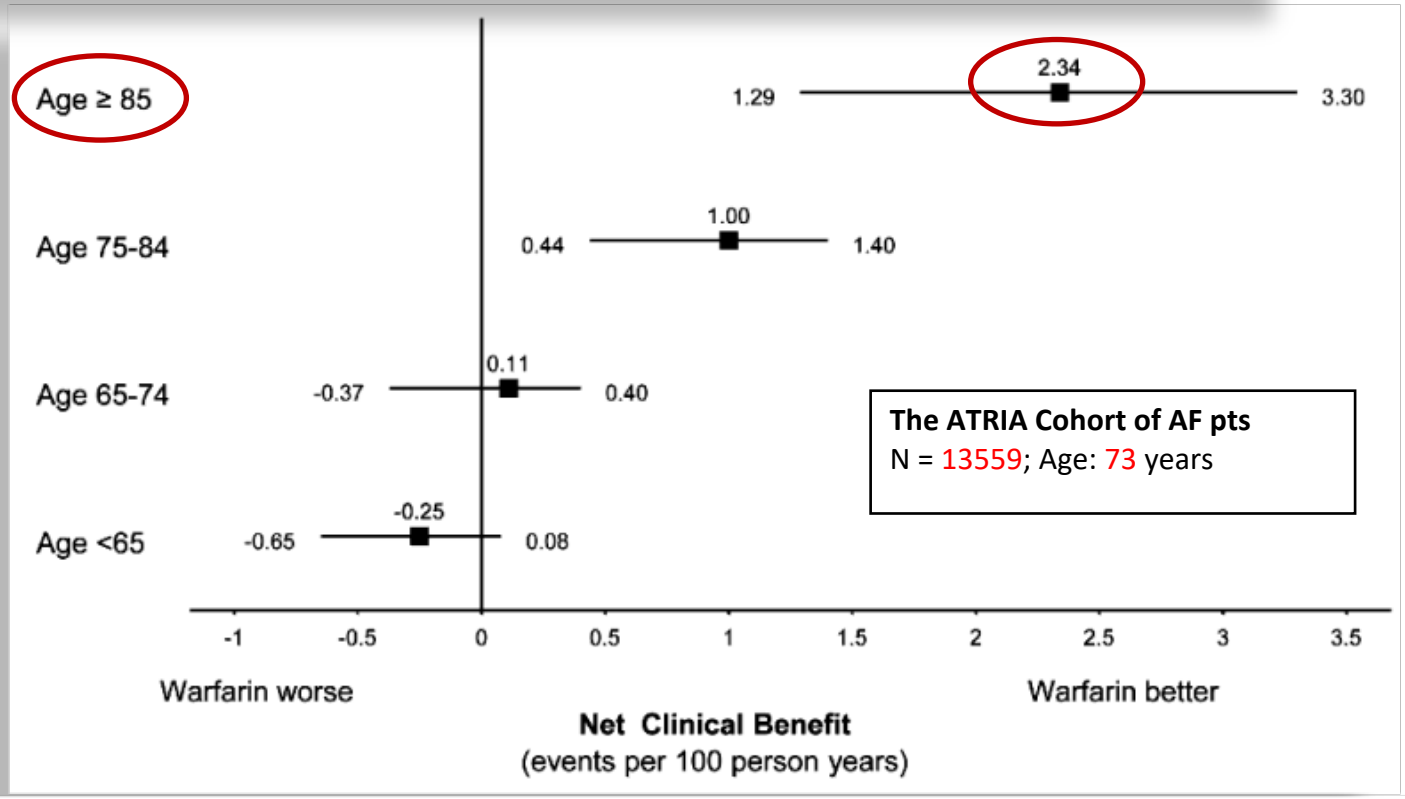
Admassie E, Am J Cardiol 2017

Annals of Internal Medicine | ARTICLE

The Net Clinical Benefit of Warfarin Anticoagulation in Atrial Fibrillation

Ann Intern Med. 2009;151:297-305.

Daniel E. Singer, MD; Yuchiao Chang, PhD; Margaret C. Fang, MD, MPH; Leila H. Borowsky, MPH; Niela K. Pomernacki, RD; Natalia Udaltsova, PhD; and Alan S. Go, MD



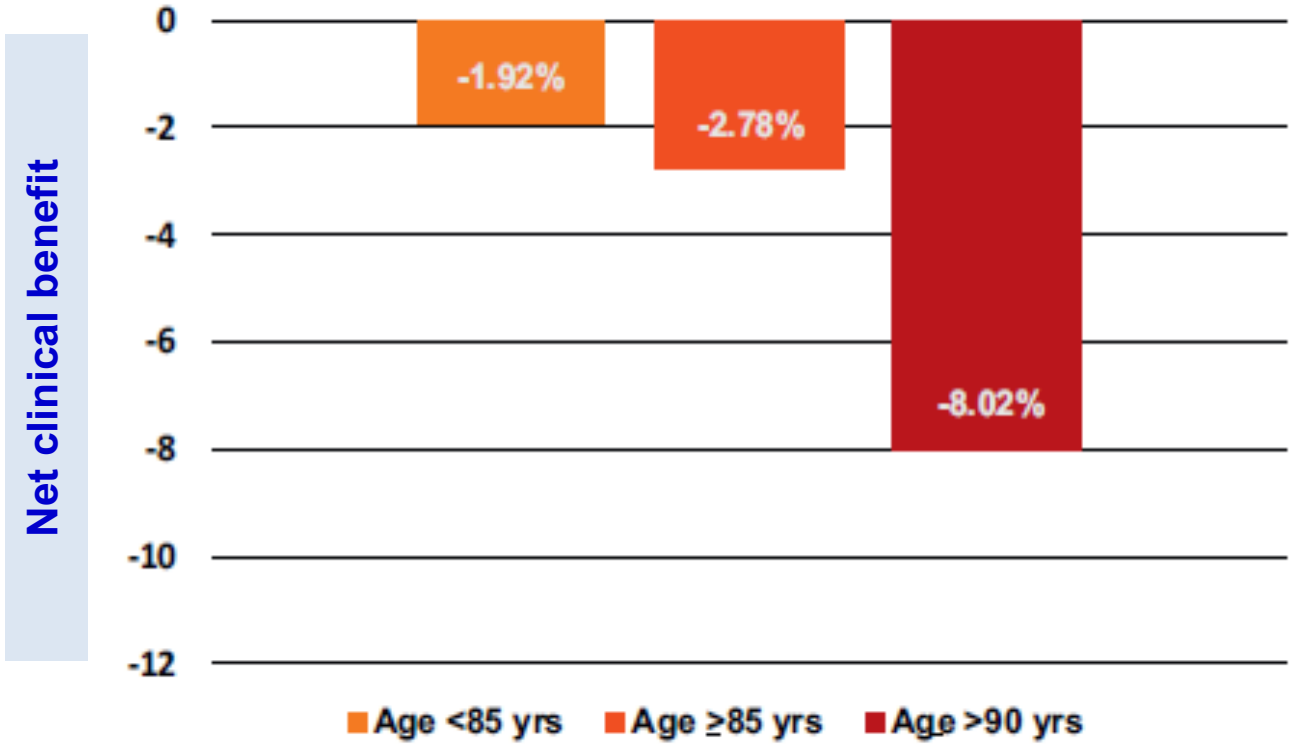
Net Clinical Benefit :

(annual rate of ischemic strokes / systemic emboli prevented by warfarin) **minus** (intracranial hemorrhages due to warfarin) * impact weight

The impact weight was 1.5, reflecting the greater clinical impact of intracranial hemorrhage versus thromboembolism

The safety and efficacy of non-vitamin K antagonist oral anticoagulants in atrial fibrillation in the elderly

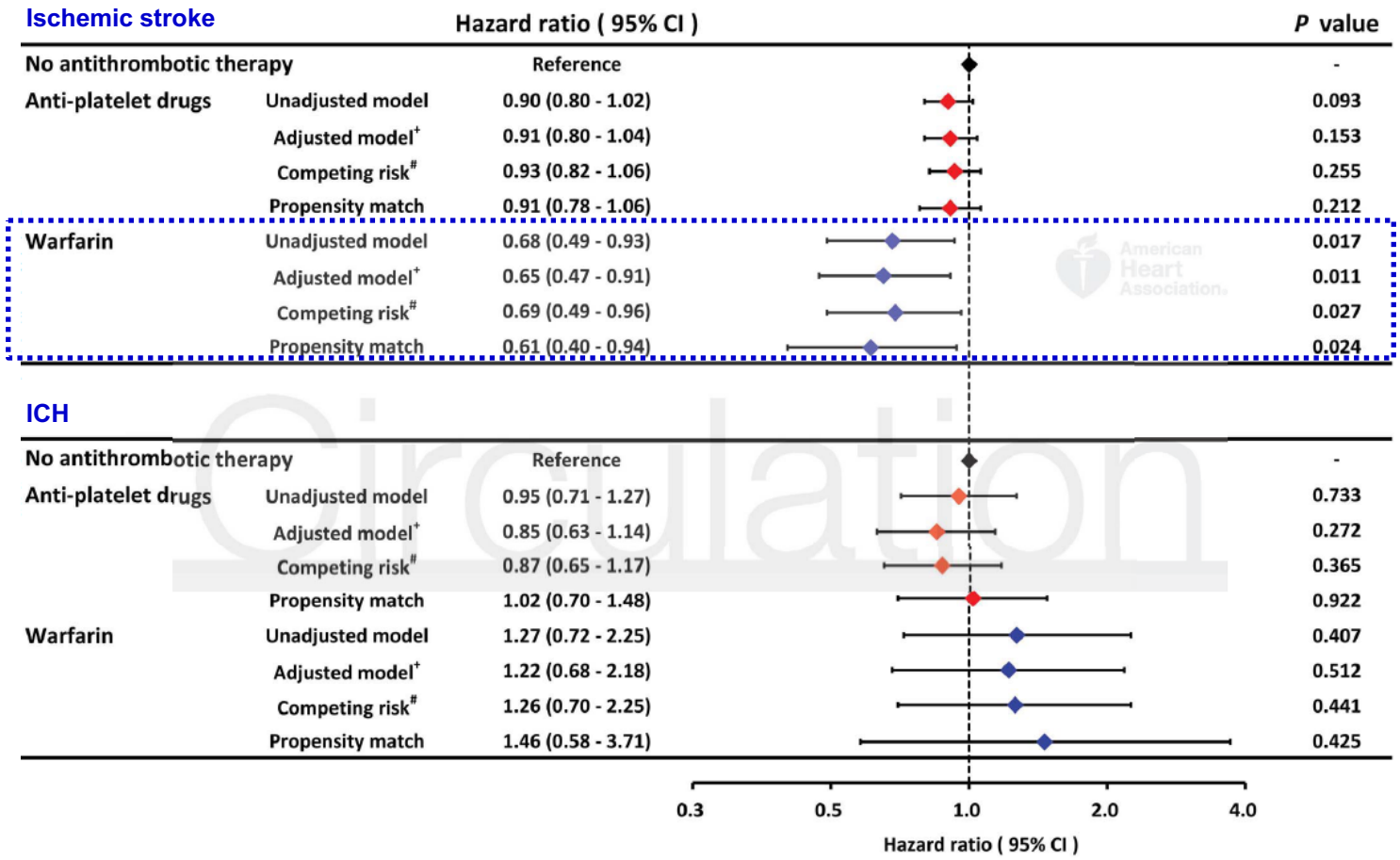
Net clinical benefit, adjusted for the risk of subsequent death, of OACs vs. no OACs according to different age groups (the PREFER in AF)



Patti G Int J Cardiol 2018

Oral Anticoagulation in Very Elderly (≥ 90 years) Patients with Atrial Fibrillation - A Nationwide Cohort Study

Risk of ischemic stroke and ICH by treatment (era without NOACs, years 1996-2011)

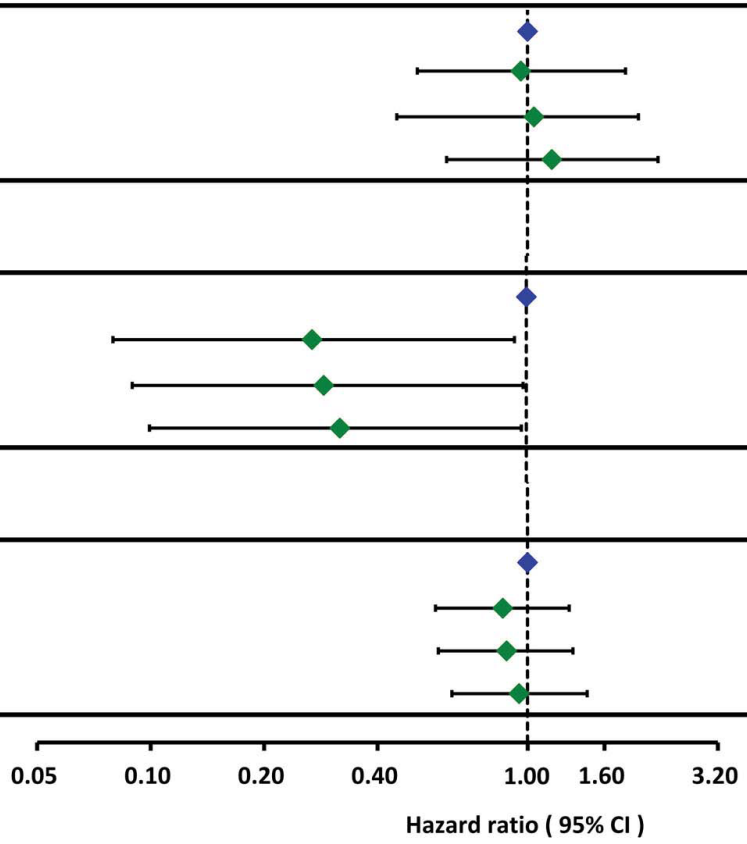


Chao TF, Lip GYH Circulation 2018

Oral Anticoagulation in Very Elderly (≥ 90 years) Patients with Atrial Fibrillation - A Nationwide Cohort Study

Risk of ischemic stroke, ICH and major bleeding by treatment. (era with NOACs, years 2012-2015)

		Hazard ratio (95% CI)	*P* value
Ischemic stroke			
Warfarin		Reference	-
NOACs	Unadjusted model	0.96 (0.51 - 1.82)	0.900
	Adjusted model[+]	1.04 (0.45 - 1.97)	0.905
	Competing risk[#]	1.16 (0.61 - 2.22)	0.654
ICH			
Warfarin		Reference	-
NOACs	Unadjusted model	0.27 (0.08 - 0.93)	0.038
	Adjusted model[+]	0.29 (0.09 - 0.98)	0.046
	Competing risk[#]	0.32 (0.10 - 0.97)	0.044
Major bleeding			
Warfarin		Reference	-
NOACs	Unadjusted model	0.86 (0.57 - 1.29)	0.455
	Adjusted model[+]	0.88 (0.58 - 1.32)	0.536
	Competing risk[#]	0.95 (0.63 - 1.44)	0.866



Chao TF, Lip GYH Circulation 2018

Changes in Oral Anticoagulant Prescribing for Stroke Prevention in Patients With Atrial Fibrillation

Summary of documented reasons for not prescribing an OAC

	Pre		p
Fall risk			0.154
Refusal			1.000
ADR (current bleeding)	16%	13%	0.765
Anemia & other hematologic disorders	6%	9%	0.54
Non-compliance, labile INR	8%	12%	0.631
Aging, dementia, psychiatric disorders, palliative care, CKD	5%	10%	0.26
Fear / high risk / history of bleeding	2%	6%	0.406

Prejudice!

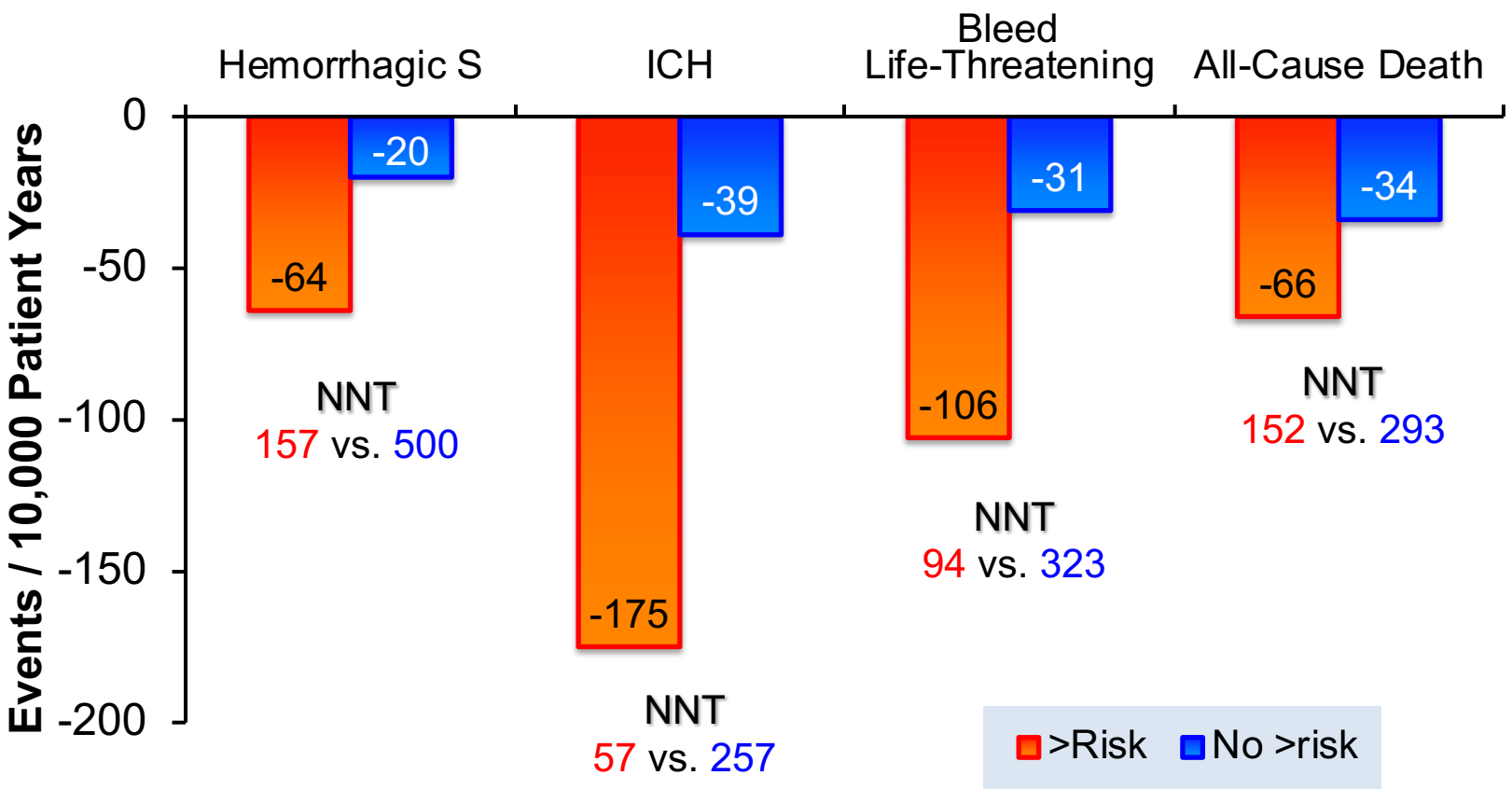
ADR: adverse drug reaction; **CKD:** chronic kidney disease

Admassie E, Am J Cardiol 2017

Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling

ENGAGE AF–TIMI 48 Analysis

Absolute Risk Reduction of 60 mg Edoxaban Compared With Warfarin in Patients at Increased Versus Not at Increased Fall Risk

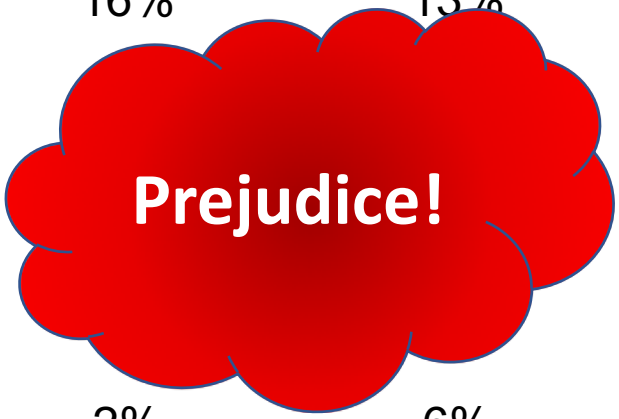


Steffel J, JACC 2016

Changes in Oral Anticoagulant Prescribing for Stroke Prevention in Patients With Atrial Fibrillation

Summary of documented reasons for not prescribing an OAC

	Pre-DOAC (N=86)	Post-DOAC (N=68)	p
Fall risk	42%	29%	0.154
Refusal	21%	21%	1.000
ADR (current bleeding)	16%	13%	0.765
Anemia & other hematologic disorders			0.54
Non-compliance, labile INR			0.631
Aging, dementia, psychiatric disorders, palliative care, CKD			0.26
Fear / high risk / history of bleeding	2%	6%	0.406

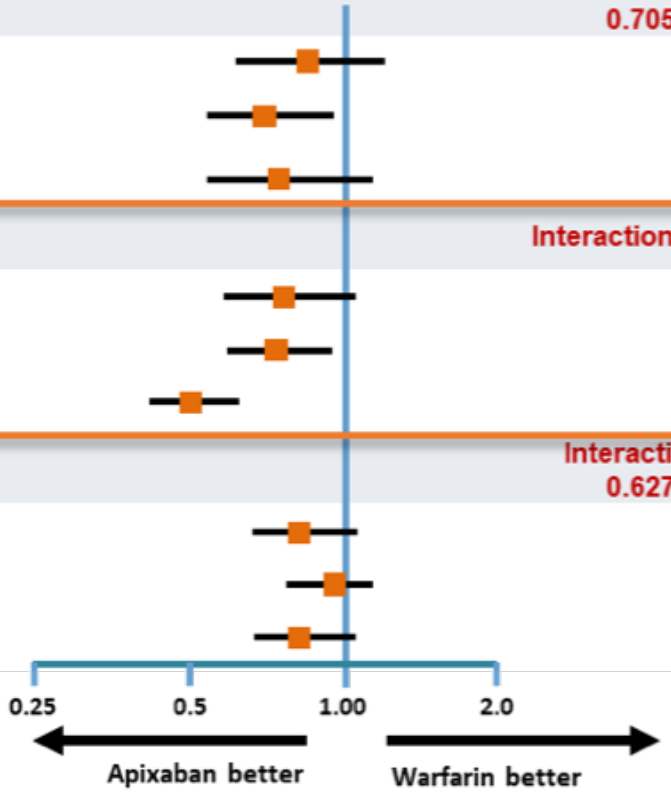


ADR: adverse drug reaction; **CKD:** chronic kidney disease

Admassie E, Am J Cardiol 2017

Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial

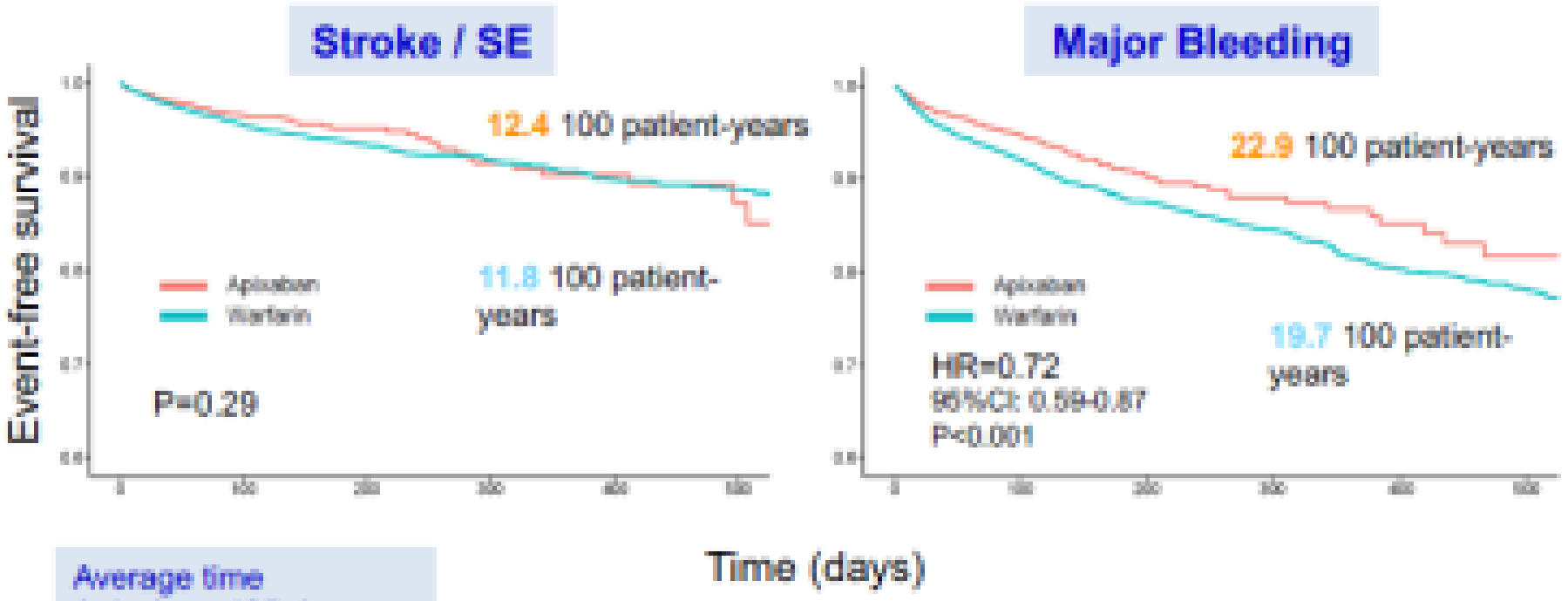
	Apixaban	Warfarin	Hazard Ratio (95% CI)	P value
	%/yr (No. of events)			
Stroke / SE				Interaction: 0.705
eGFR >80 mL/min[1]	0.99% (70)	1.12% (79)		
eGFR >50-80 mL/min[2]	1.24% (87)	1.69% (116)		
eGFR ≤50 mL/min[3]	2.11% (54)	2.67% (69)		
Major Bleeding				Interaction: 0.03
eGFR >80 mL/min[1]	1.46% (96)	1.84% (119)		
eGFR >50-80 mL/min[2]	2.45% (157)	3.21% (199)		
eGFR ≤50 mL/min[3]	3.21% (73)	6.44% (142)		
All-cause death				Interaction: 0.627
eGFR >80 mL/min[1]	2.33% (169)	2.71% (195)		
eGFR >50-80 mL/min[2]	3.41% (244)	3.56% (251)		
eGFR ≤50 mL/min[3]	7.12% (188)	8.30% (221)		



Adapted from Hohnloser et al. Eur Heart J 2012; 2012;e-published August 29, doi:10.1093/eurheartj/ehs274.

Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States

Event-free survival in apixaban (n= 2351) and prognostic score–matched warfarin (n=7053) cohorts - Medicare beneficiaries in the US Renal Data System; 2010 - 2015



Average time
Apixaban: 105 days
Warfarin: 157 days

Siontis KC,
Circulation 2018

Changes in Oral Anticoagulant Prescribing for Stroke Prevention in Patients With Atrial Fibrillation

Summary of documented reasons for not prescribing an OAC

	Pre-DOAC (N=86)	Post-DOAC (N=68)	p
Fall risk	42%	29%	0.154
Refusal	21%		1.000
ADR (current bleeding)			65
Anemia & other hematologic disorders			4
Non-compliance, labile INR			0.631
Aging, dementia, psychiatric disorders, palliative care, CKD	5%	%	0.26
Fear / high risk / history of bleeding	2%	6%	0.406

Adherence ?
(assess further)

ADR: adverse drug reaction; **CKD:** chronic kidney disease

Admassie E, Am J Cardiol 2017

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Kirchhof P, EHJ, 2016

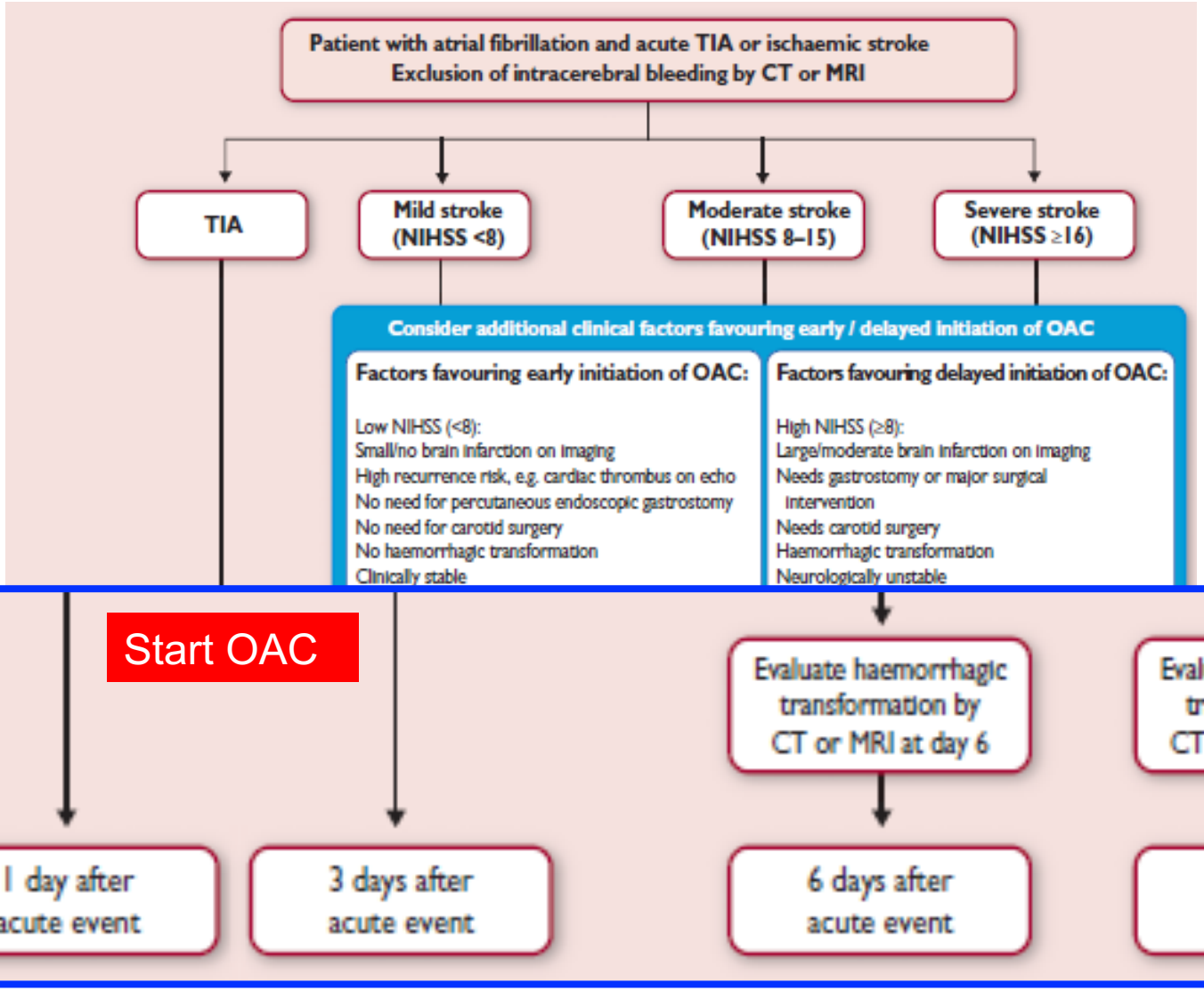
Risk factors for bleeding in anticoagulated patients

Modifiable bleeding risk factors
Hypertension (especially when systolic blood pressure is >160 mmHg)
Labile INR or TTR <60% (VKA) / Medication predisposing to bleeding
Excess alcohol (≥8 drinks/week)
Potentially modifiable bleeding risk factors
Anaemia / Reduced platelet count or function
Impaired renal and liver function
Non-modifiable bleeding risk factors
Age >65 years or ≥75 years
History of major bleeding / Previous stroke
Dialysis-dependent kidney disease or renal transplant
Cirrhotic liver disease / Malignancy / Genetic factors
Biomarker-based bleeding risk factors
High-sensitivity troponin / Serum creatinine / estimated CrCl
Growth differentiation factor-15

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Kirchhof P, Eur Heart J 2016

Initiation or continuation of OAC in atrial fibrillation patients after an **ischemic** stroke or transient ischemic attack



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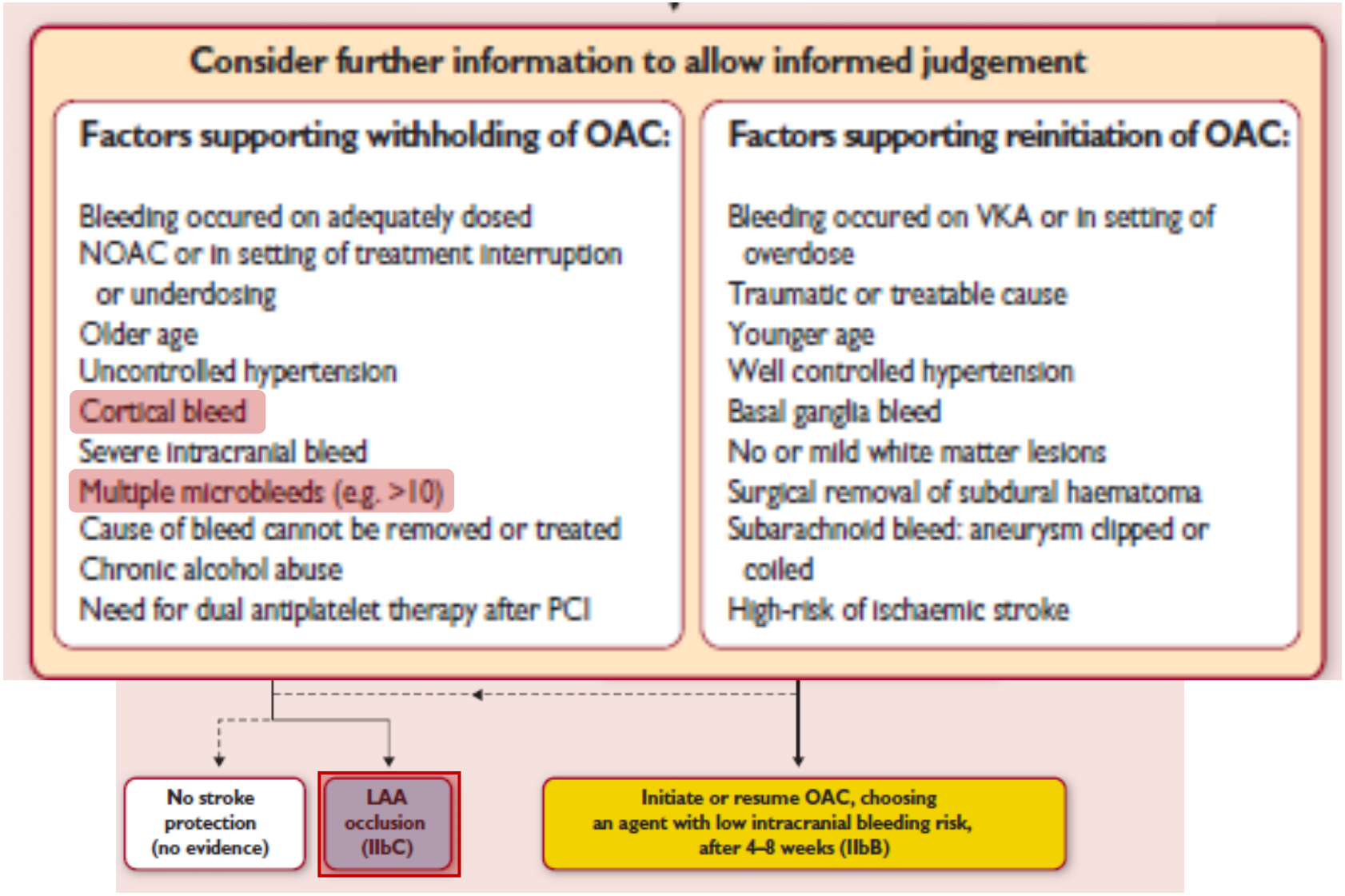
Kirchhof P, Eur Heart J 2016

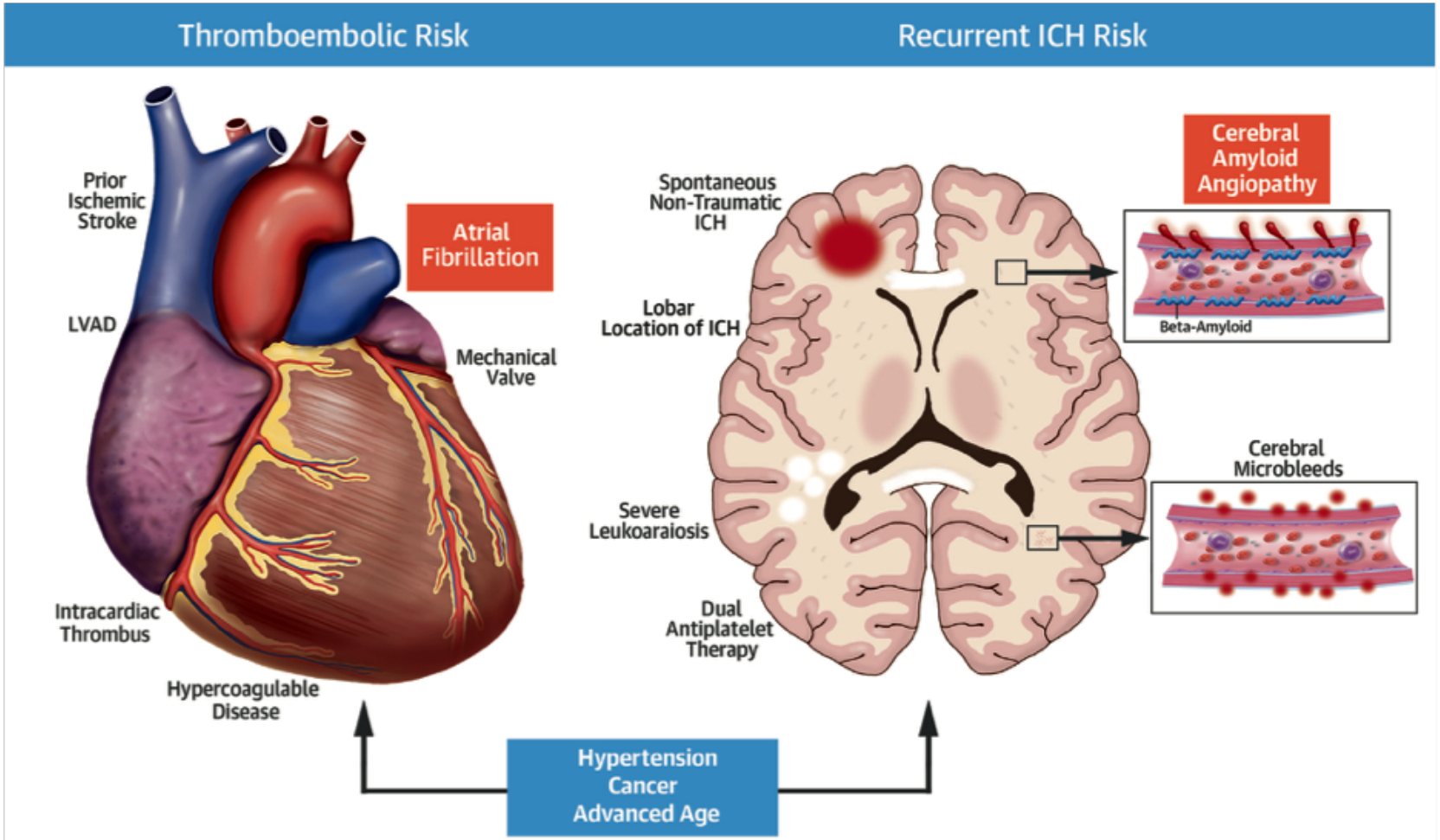
Withholding or reinitiating OAC in atrial fibrillation patients after an **intracranial bleeding**



Cerebral Amyloid Angiopathy

Diagnosis, Clinical Implications, and Management Strategies in Atrial Fibrillation

CAA and AF: Factors Associated with Increased Risk of Thromboembolism and Intracerebral Hemorrhage

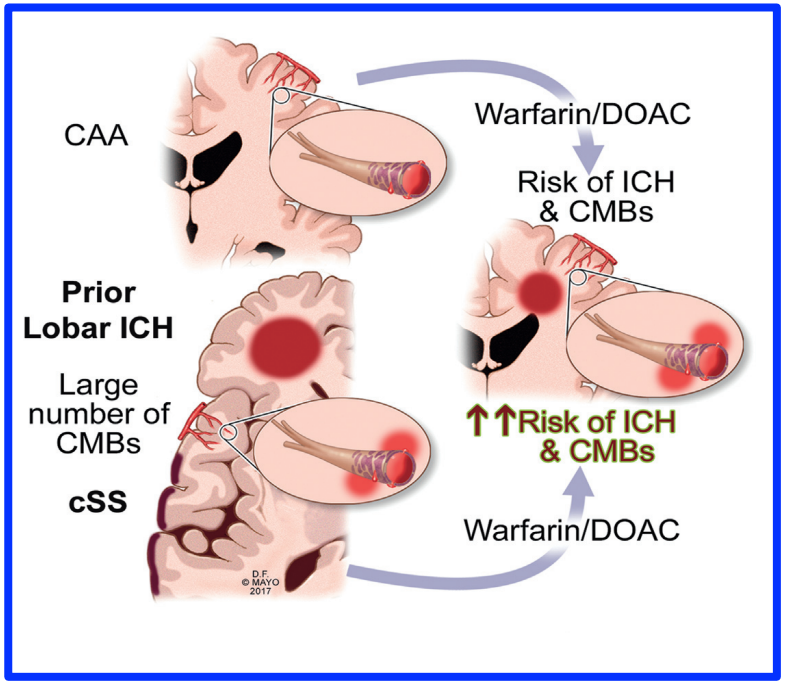


DeSimone CV, JACC 2017

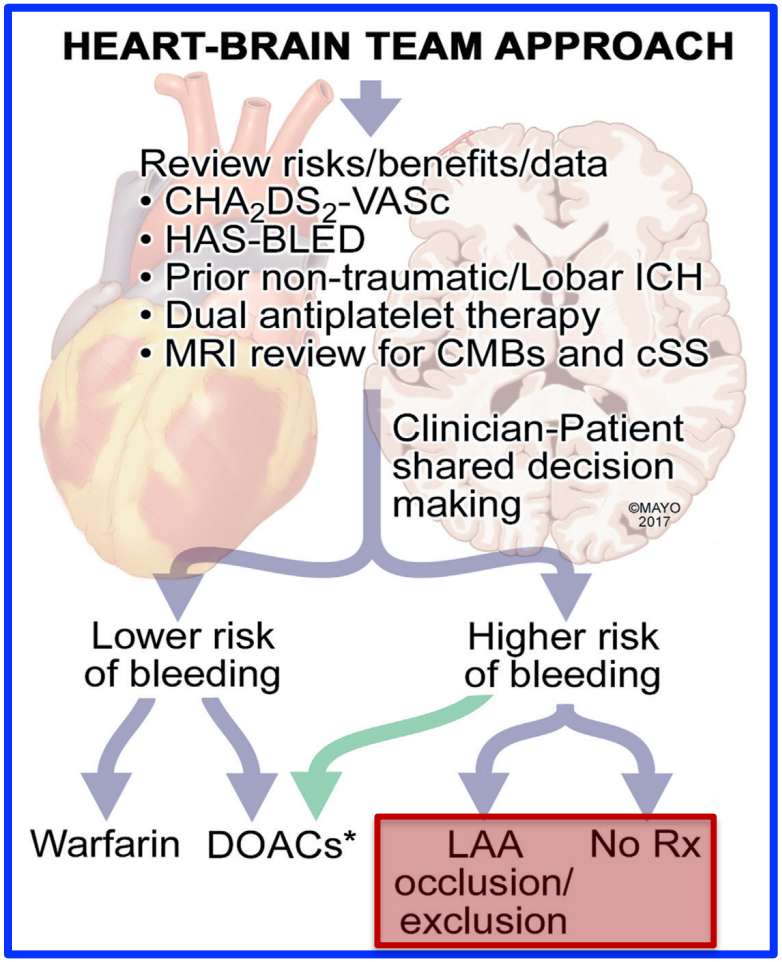
Cerebral Amyloid Angiopathy

Diagnosis, Clinical Implications, and Management Strategies in Atrial Fibrillation

Risk Factors Associated With ICH and Heart–Brain Team Schema for Consideration of Pharmacologic and Nonpharmacologic Therapies in a Patient With AF and CAA



cSS: cortical superficial siderosis
CMBs: cerebral microbleeds



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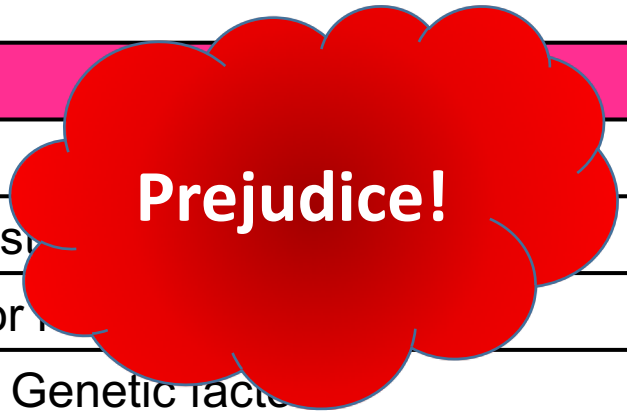
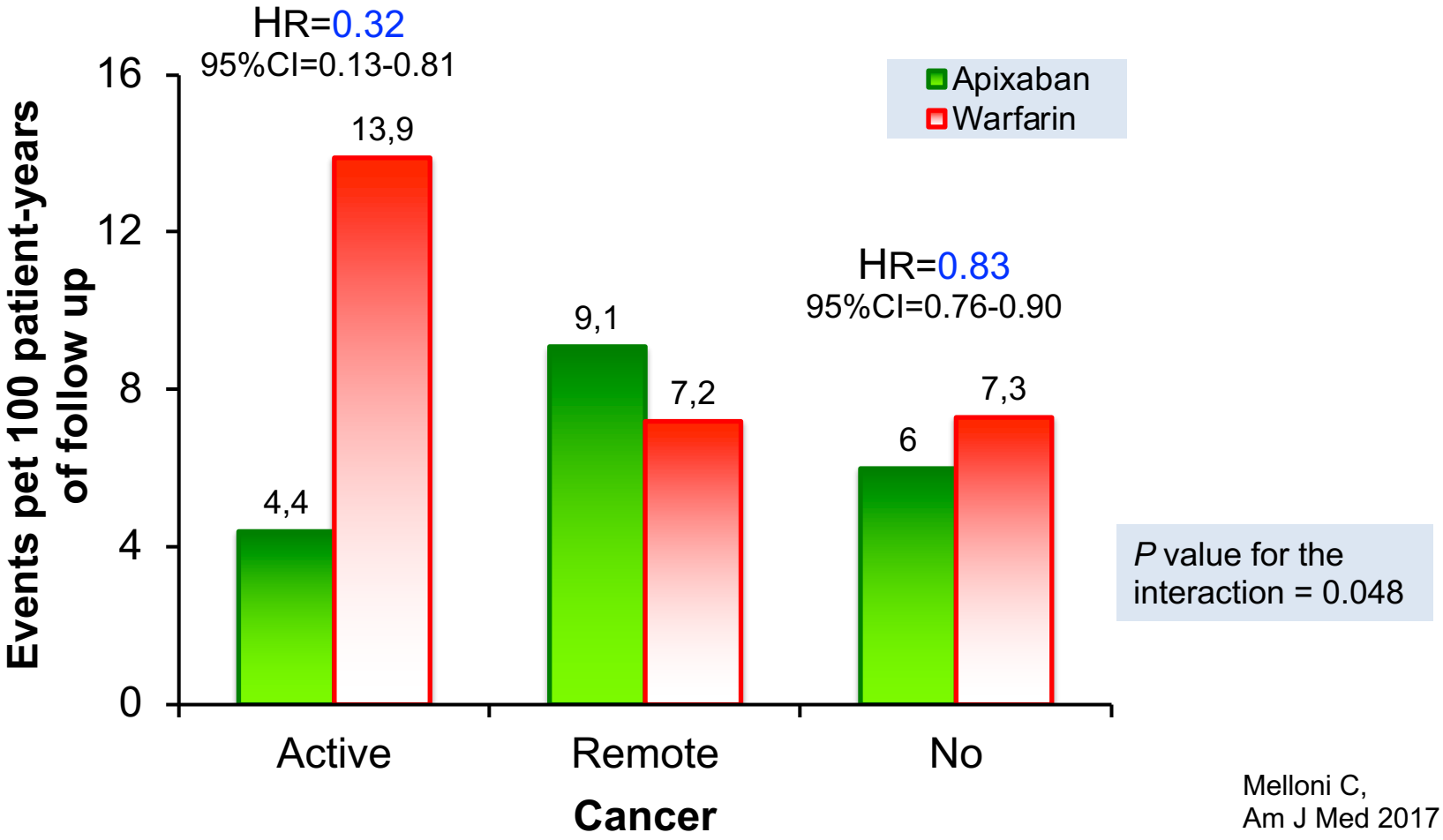
Growth differentiation factor-15



Efficacy and Safety of Apixaban Versus Warfarin in Patients with Atrial Fibrillation and a History of Cancer: Insights from the ARISTOTLE Trial

Effects of Apixaban Versus Warfarin by Cancer Status
Composite end point (Stroke/SE, MI, death, and ISTH major bleeding)



Melloni C,
Am J Med 2017

Adherence to Guidelines vs. **Prejudice**: Conclusions

- According to guidelines, CHA_2DS_2-VASc = 0 patients with AF **should NOT** receive OAC therapy, but real world data show they do receive OAC in more than 1/3 of cases
- Among all others, who should receive OAC with few exceptions, there is substantial under treatment, mostly due to prejudice driven by:
  - Older Age
  - Risk of falling
  - CKD
  - Recent ischemic stroke
  - Previous or active malignancy
- High risk of bleeding (not HAS-BLED!) and intra-cranial hemorrhage associated with cerebral amyloid angiopathy are potential reasons for **NOT prescribing** OAC therapy, after multi-professional assessment leading to individually tailored decision making, including LAA occlusion