10.15	LETTURA (presenta P. Mulatero) Terapia anticoagulante nell'FA del paziente iperteso	M. Bo	*Torino*

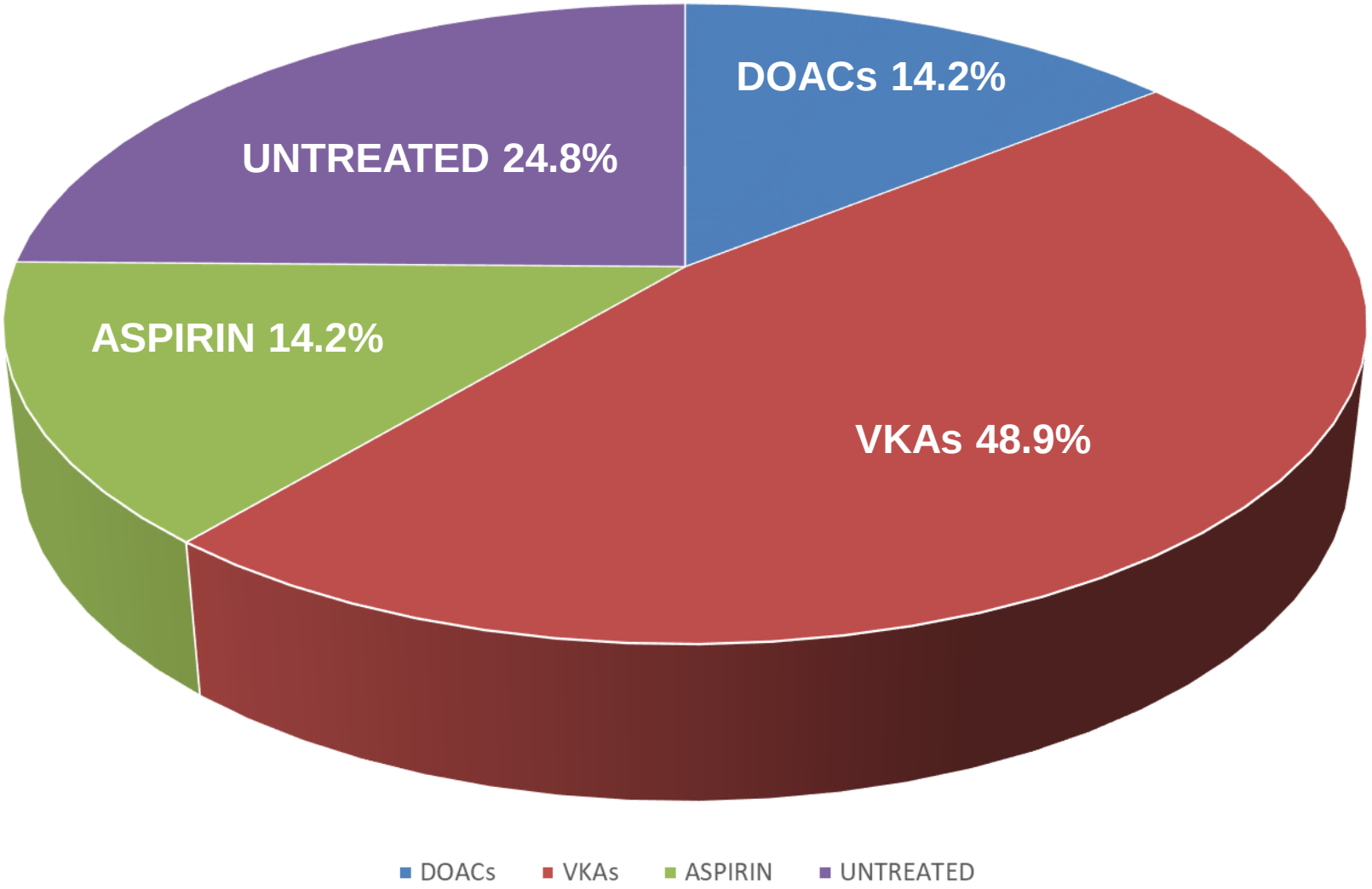
Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI Project

Europace (2019) **21**, 1468–1475

Table 1 Distribution of baseline variables in total sample and by presence of AF: univariate and logistic regression analyses

Variable	Atrial fibrillation *N* = 331	No atrial fibrillation *N* = 4197	Univariate *P*-value	Multivariate *P*-value	OR (95% CI)	Total sample *N* = 4528
Mean age ± SD (years)	78.5 ± 6.9	74.2 ± 6.6	<0.001	<0.001	1.08 (1.06–1.10)	74.5 ± 6.8
Sex (men)	55.3%	46.5%	0.002	0.009	1.40 (1.09–1.79)	47.2%
Home alone	19.0%	14.7%	0.033	0.154	1.25 (0.92–1.71)	15.0%
High-school level or higher	27.5%	36.7%	0.001	0.289	0.87 (0.66–1.13)	35.9%
Hypertension	79.8%	60.5%	<0.001	<0.001	1.94 (1.45–2.60)	62.0%
Previous myocardial infarction	11.2%	6.1%	<0.001	0.654	1.10 (0.74–1.63)	6.5%
Heart failure	13.9%	2.5%	<0.001	<0.001	4.51 (3.02–6.74)	3.4%
Diabetes	23.6%	17.8%	0.009	0.468	1.11 (0.84–1.48)	18.3%
Hypercholesterolaemia[a]	43.5%	38.2%	0.056	0.955	1.01 (0.78–1.30)	38.6%
Hypertriglyceridaemia[b]	12.1%	9.9%	0.201	0.867	0.97 (0.66–1.42)	10.1%
Alcohol consumption	31.1%	25.1%	0.015	0.084	1.27 (0.97–1.66)	25.5%
Peripheral artery disease	8.2%	6.6%	0.274	0.122	0.71 (0.45–1.10)	6.7%
Renal disease[c]	10.6%	4.2%	<0.001	0.184	1.33 (0.87–2.04)	4.7%
Transient ischaemic attack	3.3%	1.9%	0.079	0.851	1.07 (0.54–2.11)	2.0%
Previous stroke	4.8%	1.2%	<0.001	0.002	2.82 (1.49–5.35)	1.5%

170.404 patients with a (primary or secondary) hospital discharge diagnosis of AF (mean age 78 years); inclusion period jan 2015-sept 2018



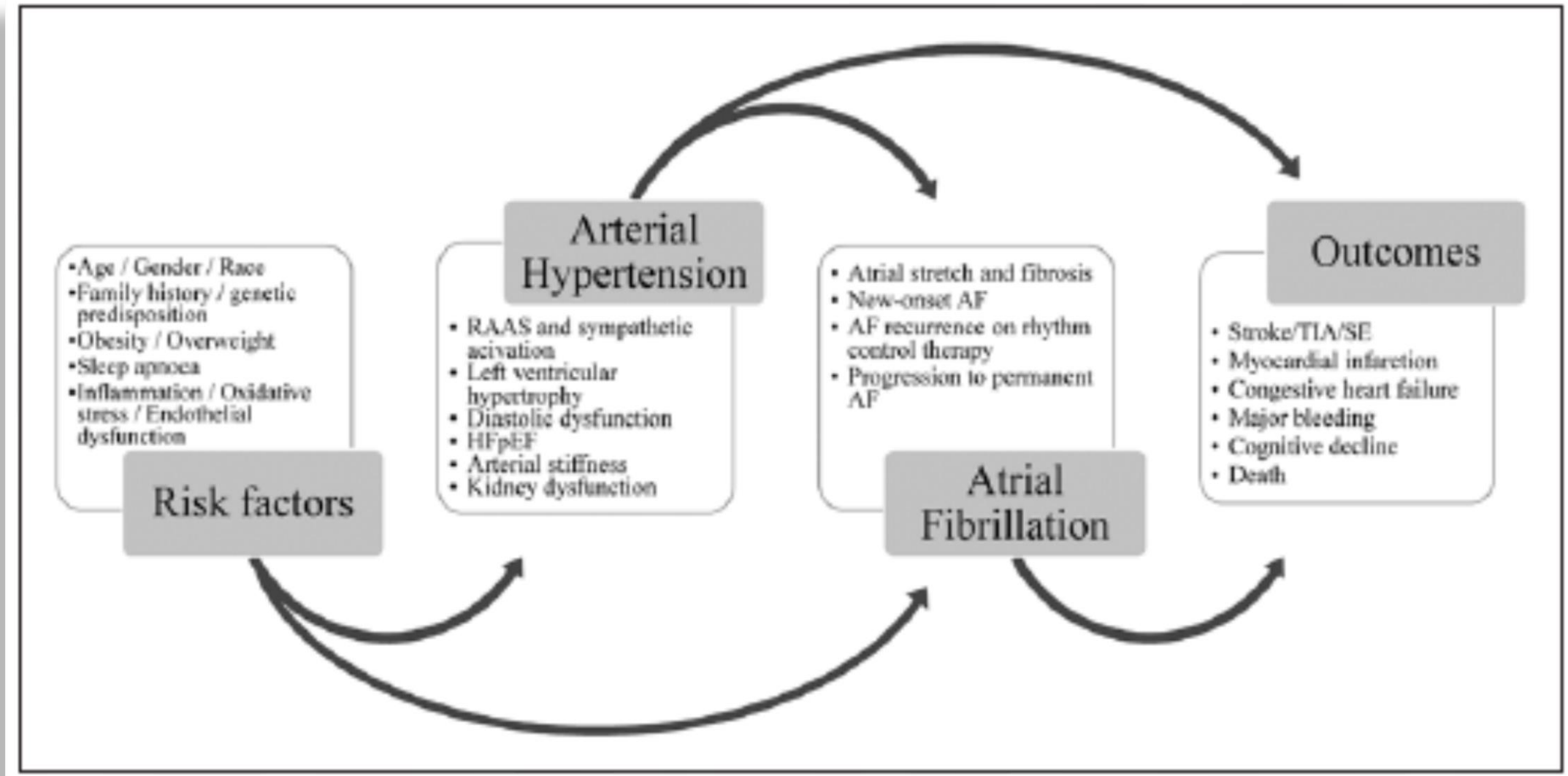
Variables	OVERALL (N=170,404)
Age (mean, SD)	78.7 (10.9)
Female (n, %)	84155 (49.4)
CHA_2DS_2 VASc (mean, SD) **	3.67 (1.42)
CHA_2DS_2 VASc <3 (n, %) **	32058 (18.8)
CHA_2DS_2 VASc =3 (n, %) **	41380 (24.3)
CHA_2DS_2 VASc >3 (n, %) **	96966 (56.9)
HAS BLED (mean, SD) **	2.37 (1.01)
CCI (mean, SD) ***	1.52 (1.60)
- Enrollment year 2015	129713 (76.1)
- Enrollment year 2016	17007 (10.0)
- Enrollment year 2017	15131 (8.9)
- Enrollment year 2018	8553 (5.0)
Hospitalizations pre *	0.25 (0.57)
Drugs pre * (mean, SD)	5.13 (3.62)
Aspirin **	52976 (31.1)
NSAIDS **	41698 (24.5)
P2Y12 inhibitors **	11842 (6.9)
BP lowering drugs **	**141224 (82.9)**
Lipid Lowering drugs **	59346 (34.8)
Cardiovascular drugs **	68615 (40.3)
Oncologic drugs **	8202 (4.8)
Antipsycothics **	5994 (3.5)
Antidepressants **	25110 (14.7)
Anticholinergics **	2381 (1.4)
AF main diagnosis (%)	50818 (29.8)

Bo M, Fumagalli S, Marchionni N, Degli Esposti L

IPERTENSIONE e FA:
FISIOPATOGENESI

Atrial Fibrillation and Hypertension

Mikhail S. Dzeshka, Alena Shantsila, Eduard Shantsila, Gregory Y.H. Lip



(*Hypertension*. 2017;70:854-861

(*Hypertension*. 2021;77:919–928.

Hypertension Burden and the Risk of New-Onset Atrial Fibrillation

A Nationwide Population-Based Study

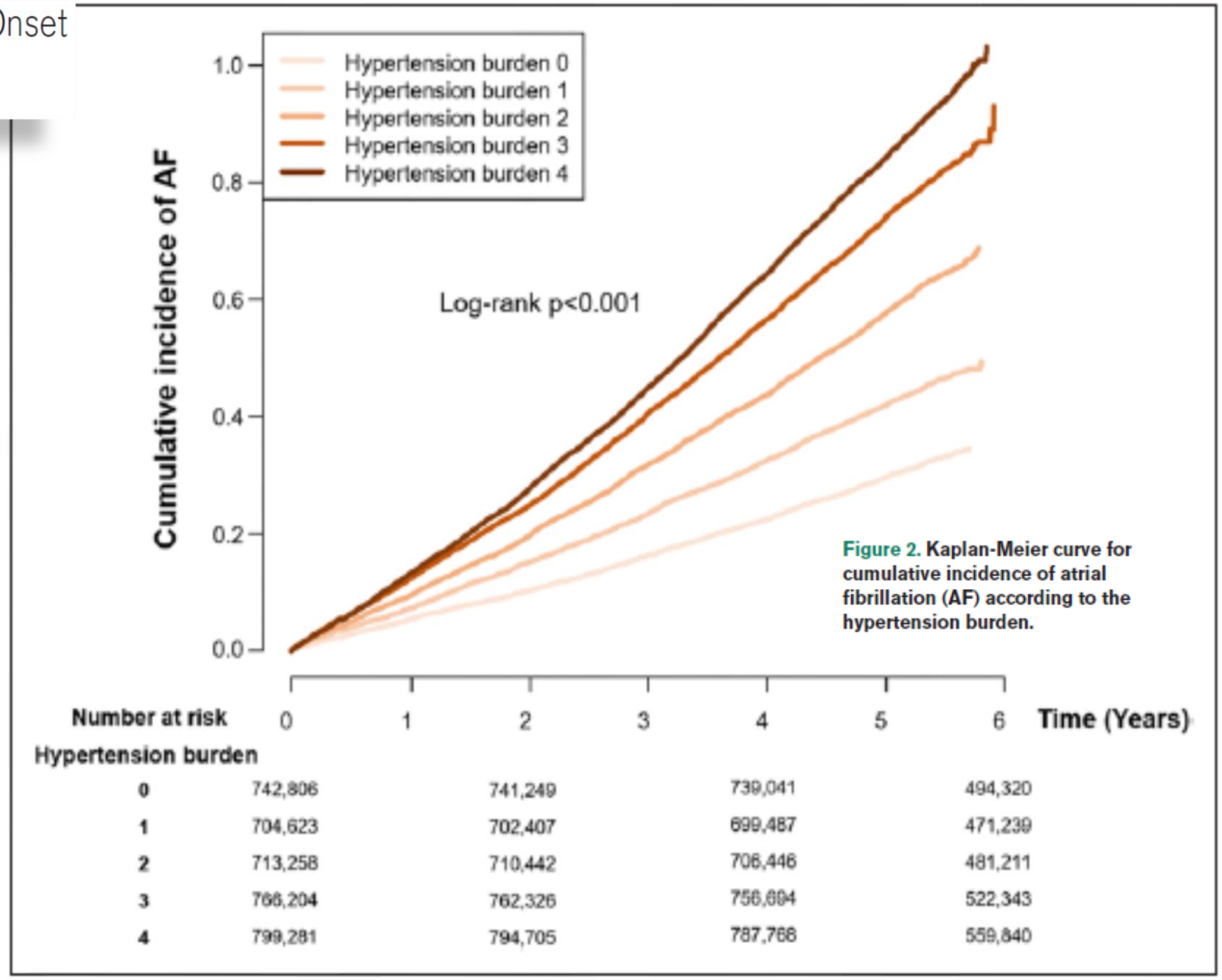


Figure 2. Kaplan-Meier curve for cumulative incidence of atrial fibrillation (AF) according to the hypertension burden.

IPERTENSIONE e FA: FISIOPATOGENESI

Hypertension and Atrial Fibrillation
Doubts and Certainties From Basic and Clinical Studies

Paolo Verdecchia, Fabio Angeli, Gianpaolo Reboldi

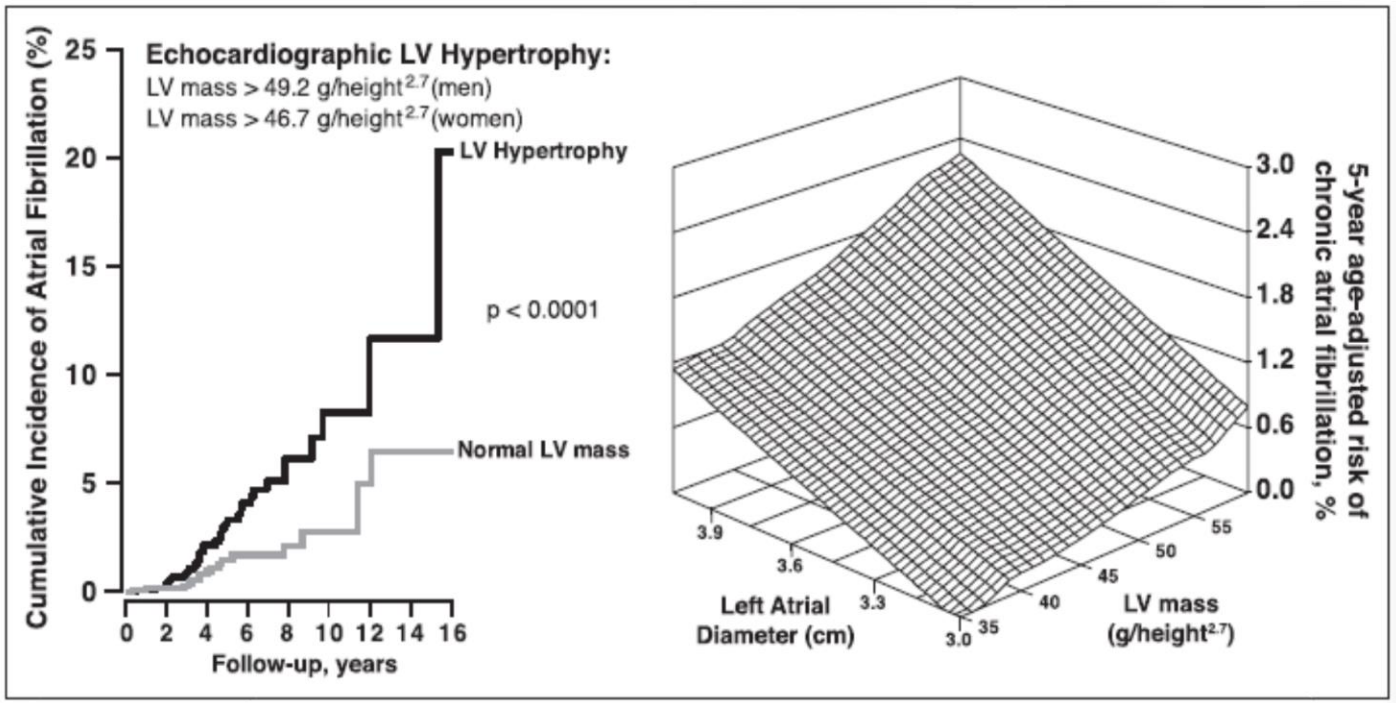


Figure 2. Incidence of new-onset atrial fibrillation in hypertensive patients sorted by absence or presence of left ventricular (LV) hypertrophy at echocardiography (left), and 5-y risk of permanent atrial fibrillation in relation to LV mass and left atrial diameter. Adapted from Verdecchia et al[48] with permission. Copyright © 2003, the American Heart Association. Reported values are the division points for quartiles.

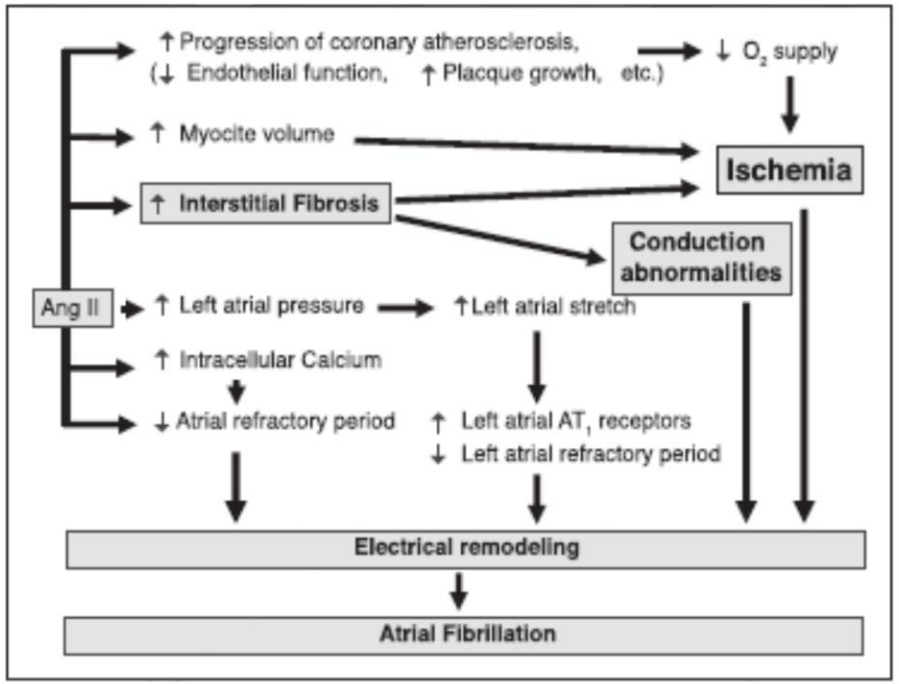


Figure 3. Potential mechanisms by which the renin–angiotensin–aldosterone system may be involved in the onset of atrial fibrillation. Ang II indicates angiotensin II; and AT_1, angiotensin II type I.

(*Circ Res*. 2018;122:352-368.

Hypertension and Atrial Fibrillation

Doubts and Certainties From Basic and Clinical Studies

Paolo Verdecchia, Fabio Angeli, Gianpaolo Reboldi

IPERTENSIONE e FA: FISIOPATOGENESI

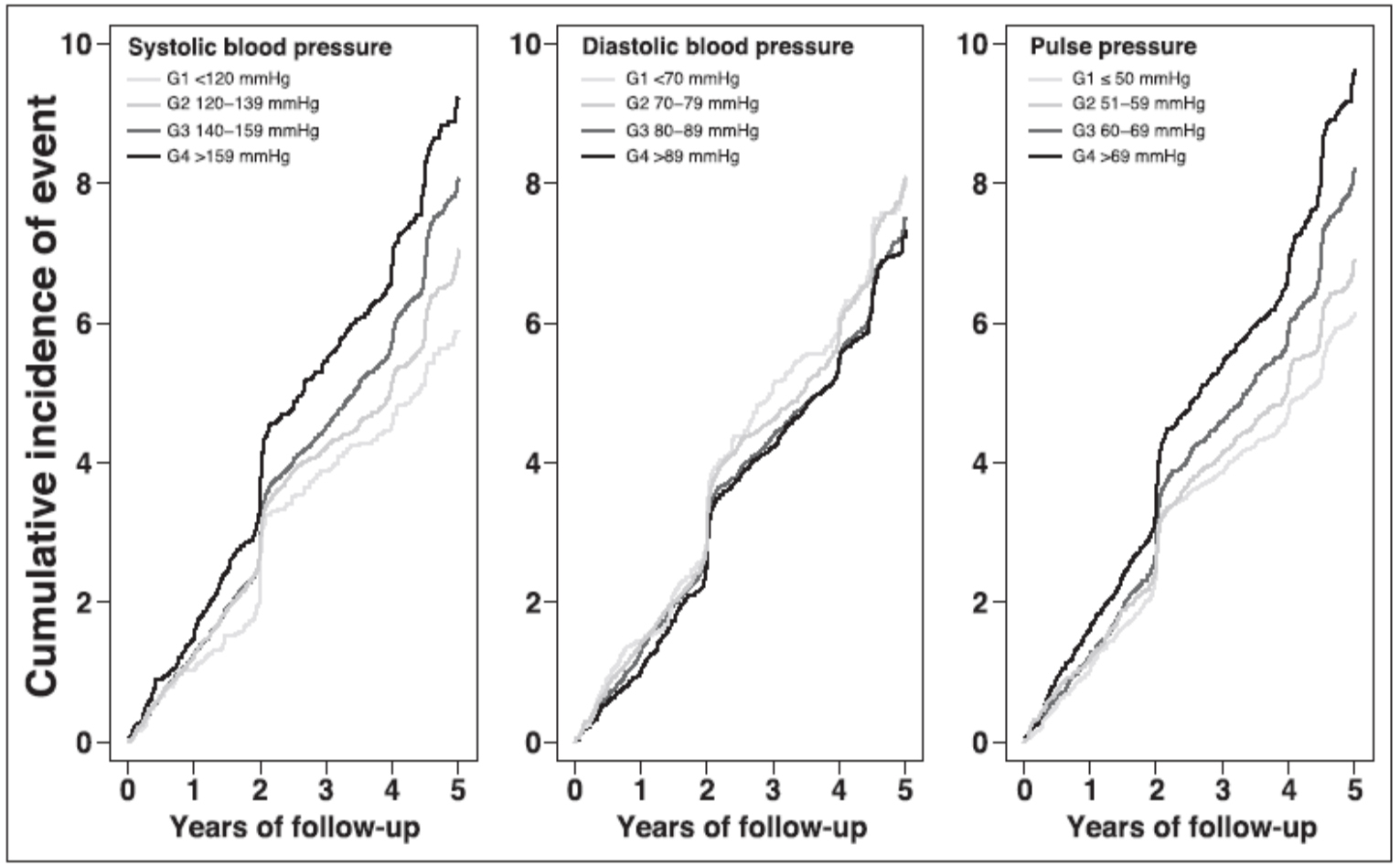


Figure 4. Relation between baseline blood pressure and later occurrence of atrial fibrillation in patients with sinus rhythm at entry enrolled in the ONTARGET (Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial)/TRANSCEND (Telmisartan Randomized Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease). Adapted from Verdecchia et al[84] with permission. Copyright © 2012, Lippincott Williams & Wilkins, Inc.

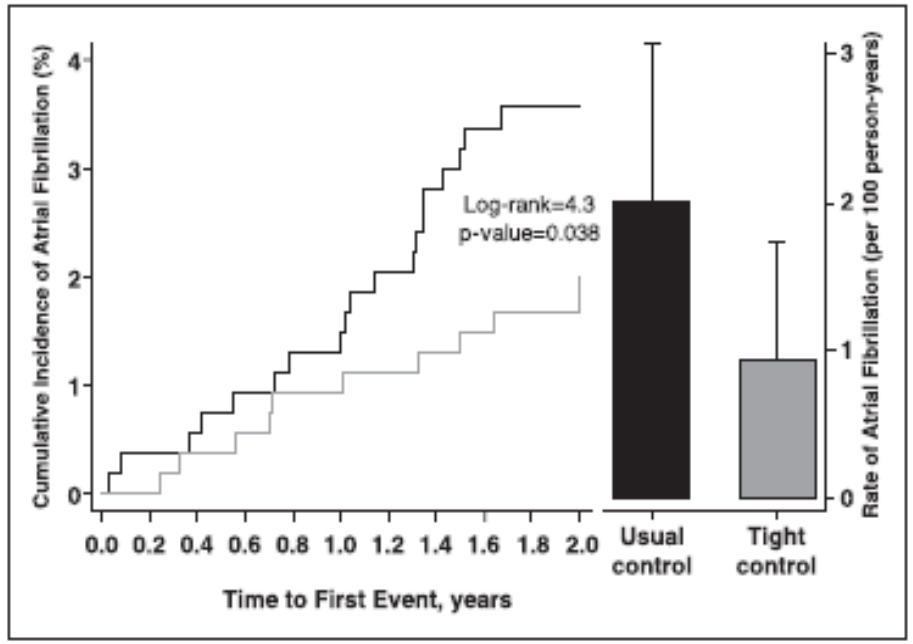


Figure 5. Incidence of new-onset atrial fibrillation in hypertensive patients randomized to a more-tight or less-tight blood pressure control (target systolic blood pressure, <140 vs <130 mm Hg) in the Cardio-Sis study (Studio Italiano Sugli Effetti Cardiovascolari Del Controllo Della Pressione Arteriosa Sistolica).

(*Circ Res*. 2018;122:352-368.

(*Hypertension*. 2020;75:1483

Incidence and Implications of Atrial Fibrillation/Flutter in Hypertension

Insights From the SPRINT Trial

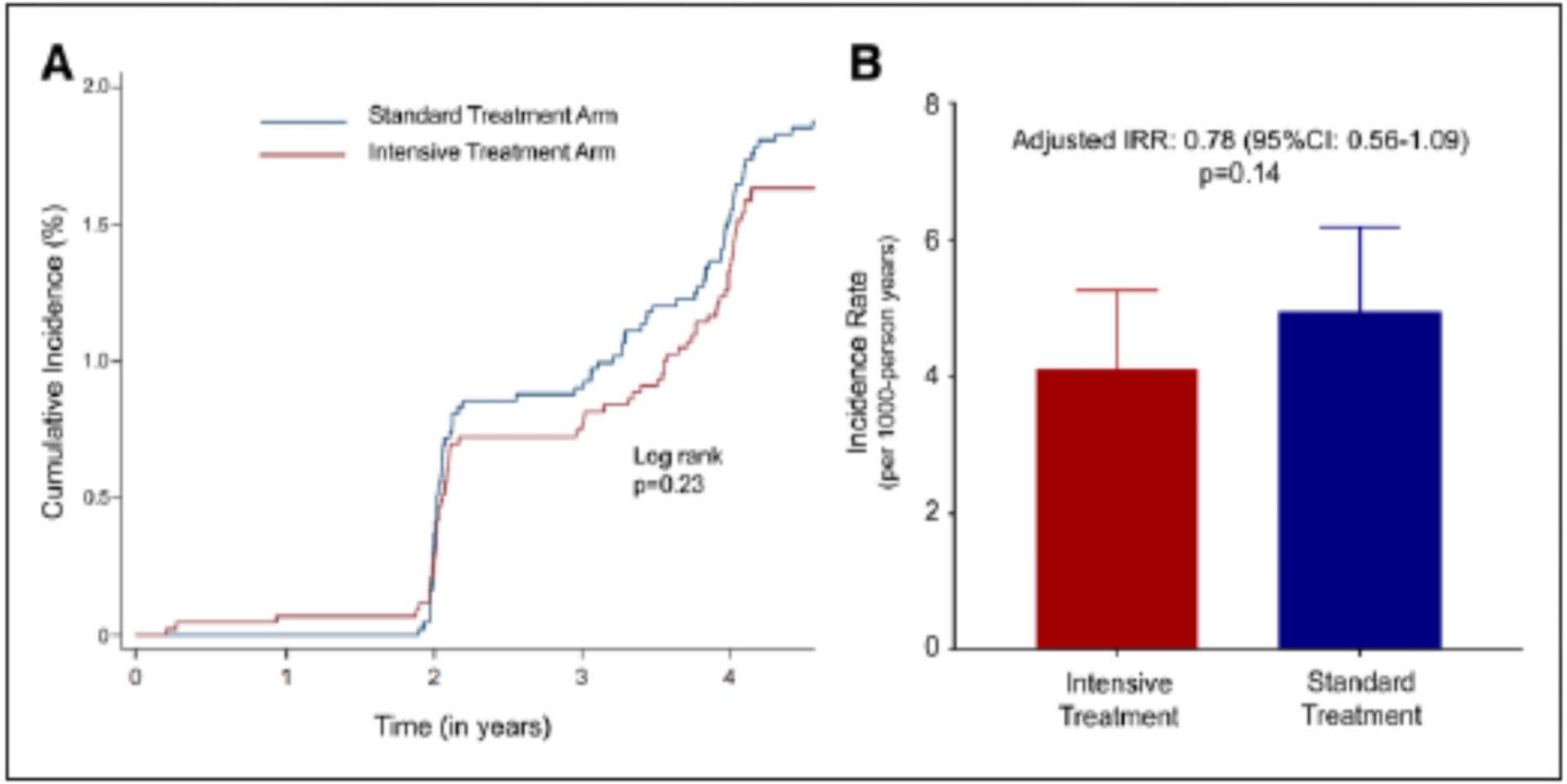


Figure 1. Incidence of new-onset atrial fibrillation/flutter (AF): stratified by treatment strategy. **A**, Cumulative incidence of new-onset atrial fibrillation/flutter stratified by treatment strategy. **B**, Incidence rate of AF in participants randomized to intensive (blue; online) and standard (green; online) blood pressure management. IRR indicates incidence rate ratio.

European Heart Journal (2020) **42**, 373–498

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

AF SCREENING

RISKS

- Abnormal results may cause anxiety
- ECG misinterpretation results may lead to overdiagnosis and overtreatment
- ECG may detect other abnormalities (true or false positives) that may lead to invasive tests and treatments that have the potential for serious harm (e.g., angiography / revascularisation with bleeding, contrast-induced nephropathy and allergic reactions to the contrast)

BENEFITS

Prevention of:
- Stroke/SE using OAC in patients at risk
- Subsequent onset of symptoms

Prevention/reversal of:
- Electrical/mechanical atrial remodelling
- AF-related haemodynamic derangements
- Atrial and ventricular tachycardia-induced cardiopmyopathy

Prevention/reduction of:
- AF-related morbidity; hospitalization; mortality

Reduction of:
- The outcomes associated with conditions / diseases associated with AF that are discovered and treated as a consequence of the examinations prompted by AF detection

Atrial Fibrillation Screening: The Tools Are Ready, But Should We Do It?

Fabrice Extramiana, MD, PhD; Philippe Gabriel Steg, MD

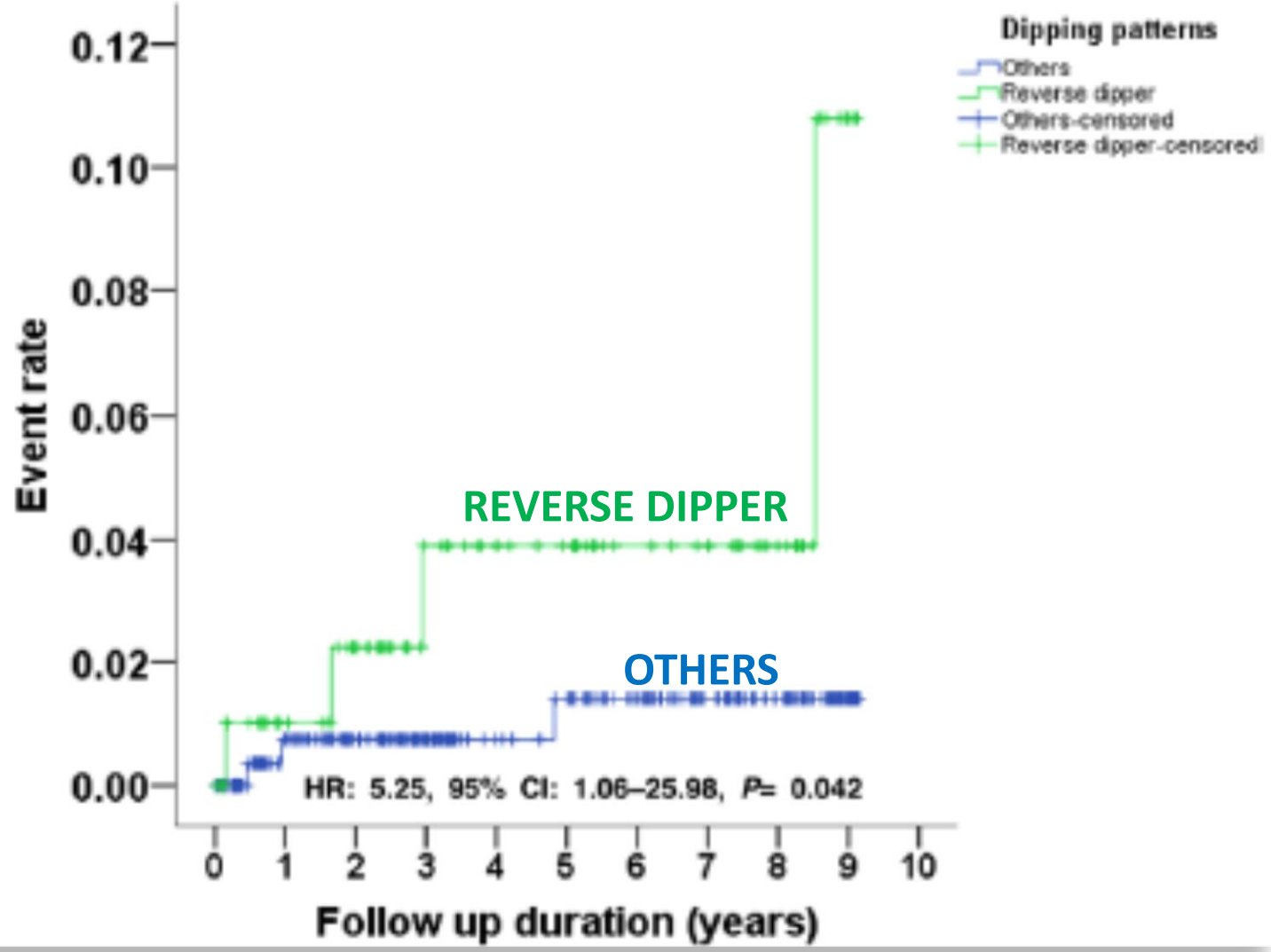
Circulation. 2022;145:955–958.

WHO principles for screening
(1) The condition sought should be an important health problem
(2) There should be an accepted treatment for patients with recognized disease
(3) Facilities for diagnosis and treatment should be available
(4) There should be a recognizable latent or early symptomatic stage
(5) There should be a suitable test or examination
(6) The test should be acceptable to the population
(7) The natural history of the condition, including development from latent to declared disease, should be adequately understood
(8) There should be an agreed policy on whom to treat as patients
(9) The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
(10) Case-finding should be a continuing process and not a "once and for all" project

Prediction of atrial fibrillation in patients with hypertension: A comprehensive comparison of office and ambulatory blood pressure measurements

J Clin Hypertens. 2022;24:838–847.

NEW ONSET AF



IPERTENSIONE e DIAGNOSI PRECOCE della FA

(*Hypertension*. 2022;79:2081–2090.

Systolic Blood Pressure and Effects of Screening for Atrial Fibrillation With Long-Term Continuous Monitoring (a LOOP Substudy)

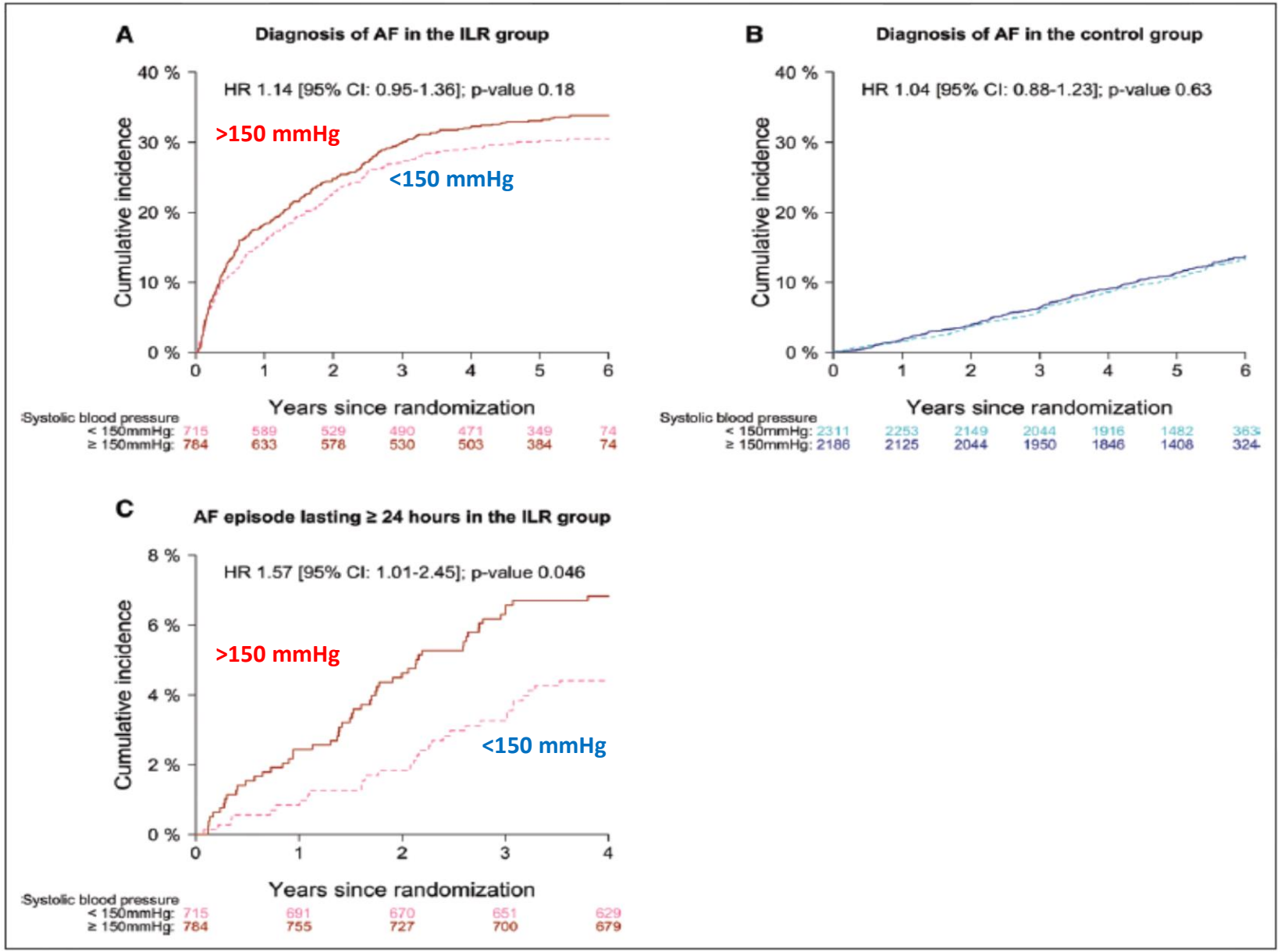


Figure 3. Cumulative incidence of atrial fibrillation (AF) diagnosis and AF episodes lasting ≥24 hours according to systolic blood pressure.

(*Hypertension*. 2022;79:2081–2090.

Systolic Blood Pressure and Effects of Screening for Atrial Fibrillation With Long-Term Continuous Monitoring (a LOOP Substudy)

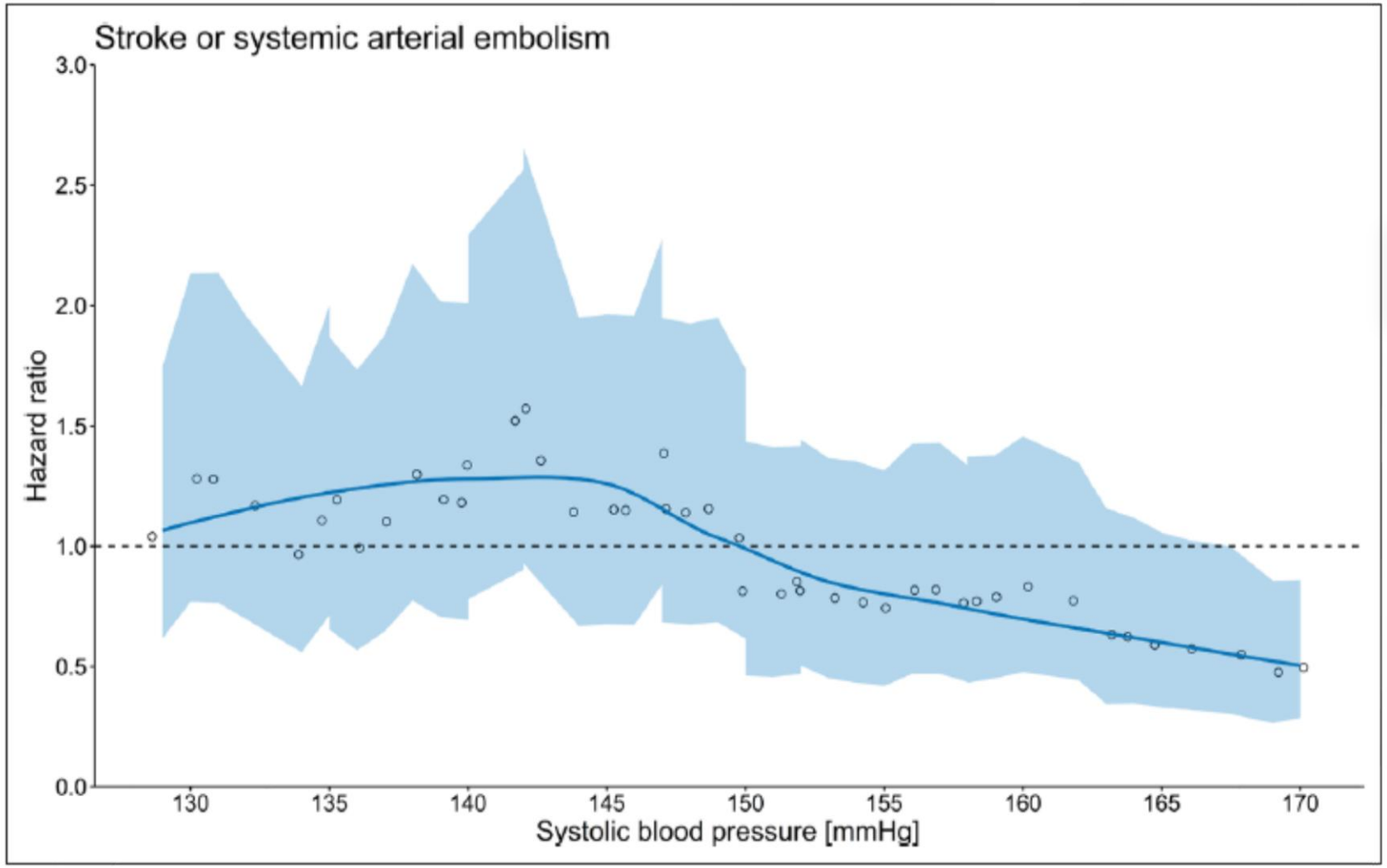


Figure 1. Relation between systolic blood pressure and implantable loop recorder (ILR) screening efficacy on the primary outcome.

What Is New?

We show in an elderly, at-risk population that the benefits of continuous atrial fibrillation screening on stroke prevention increases with elevating systolic blood pressure.

What Is Relevant?

Atrial fibrillation screening with a cutoff of systolic blood pressure ≥150 mmHg is associated with ≈ 50% stroke risk reduction, compared with usual care.

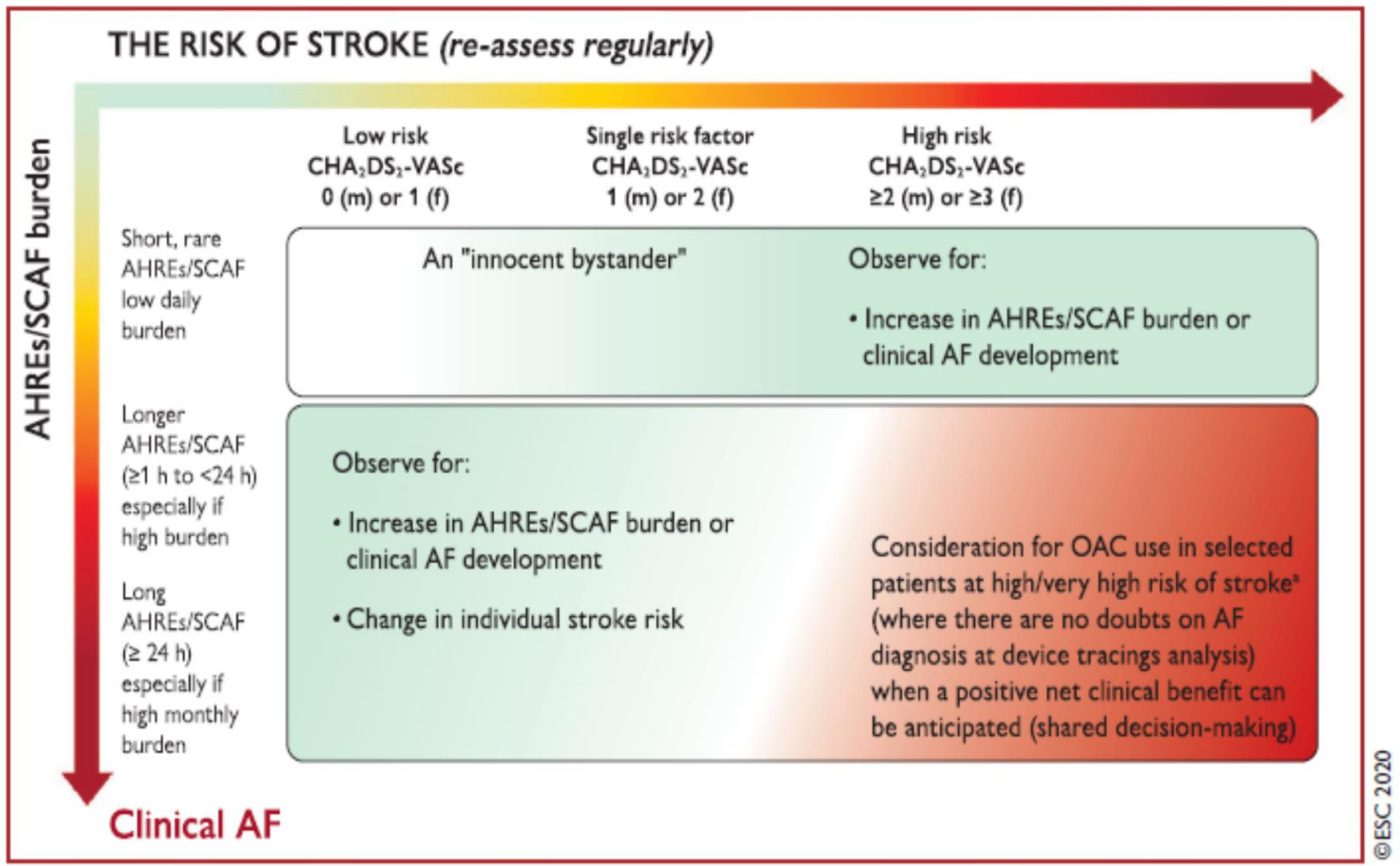
Clinical/Pathophysiological Implications?

High systolic blood pressure and dysregulated hypertension may assist in identifying the appropriate population who will benefit from atrial fibrillation screening.

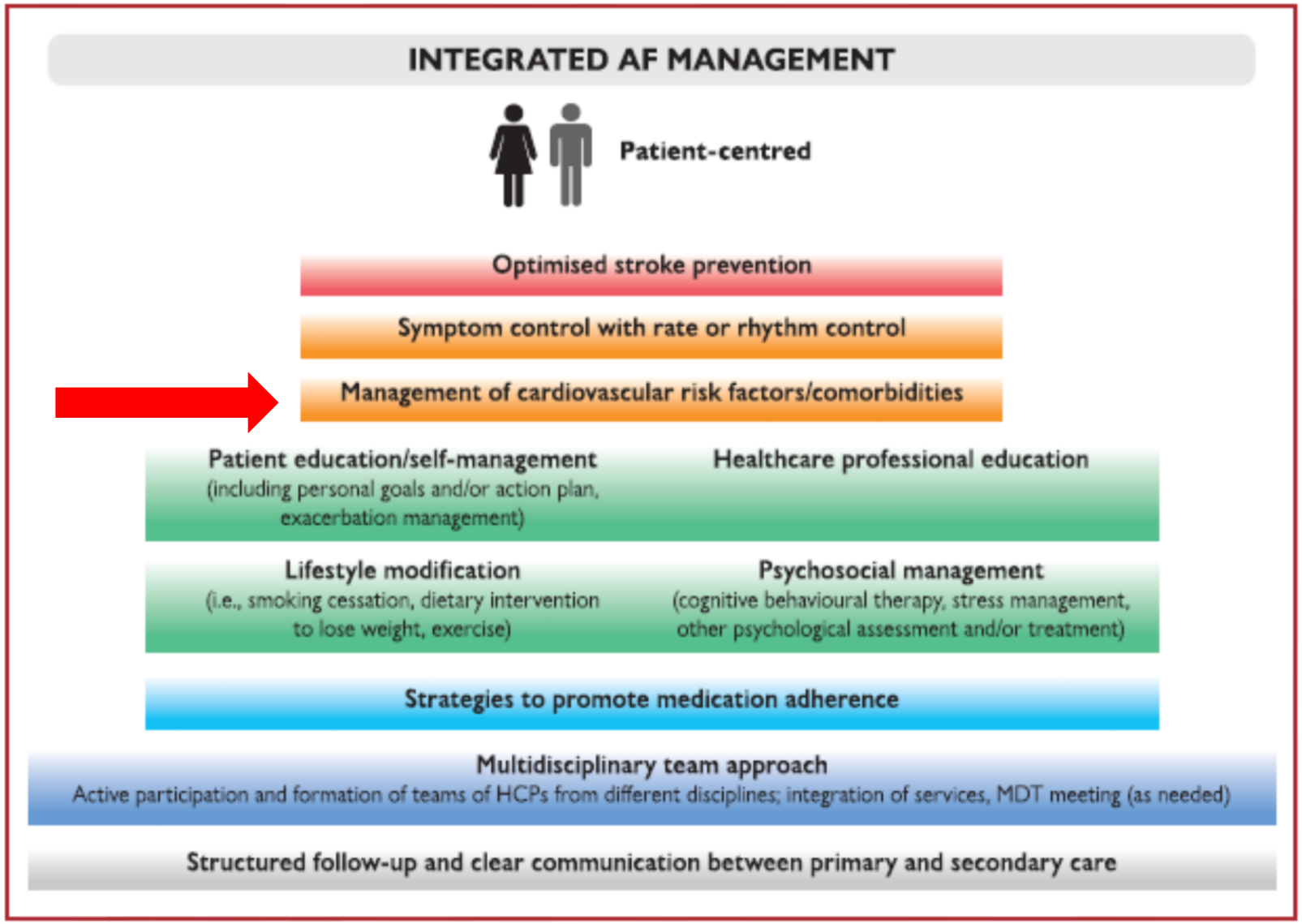
European Heart Journal (2020) **42**, 373–498

IPERTENSIONE e DIAGNOSI PRECOCE della FA

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



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



Journal of Hypertension 2021, 39:1670–1677

Blood pressure levels and risk of haemorrhagic stroke in patients with atrial fibrillation and oral anticoagulants: results from The Swedish Primary Care Cardiovascular Database of Skaraborg

TRATTAMENTO del PAZIENTE IPERTESO con FA

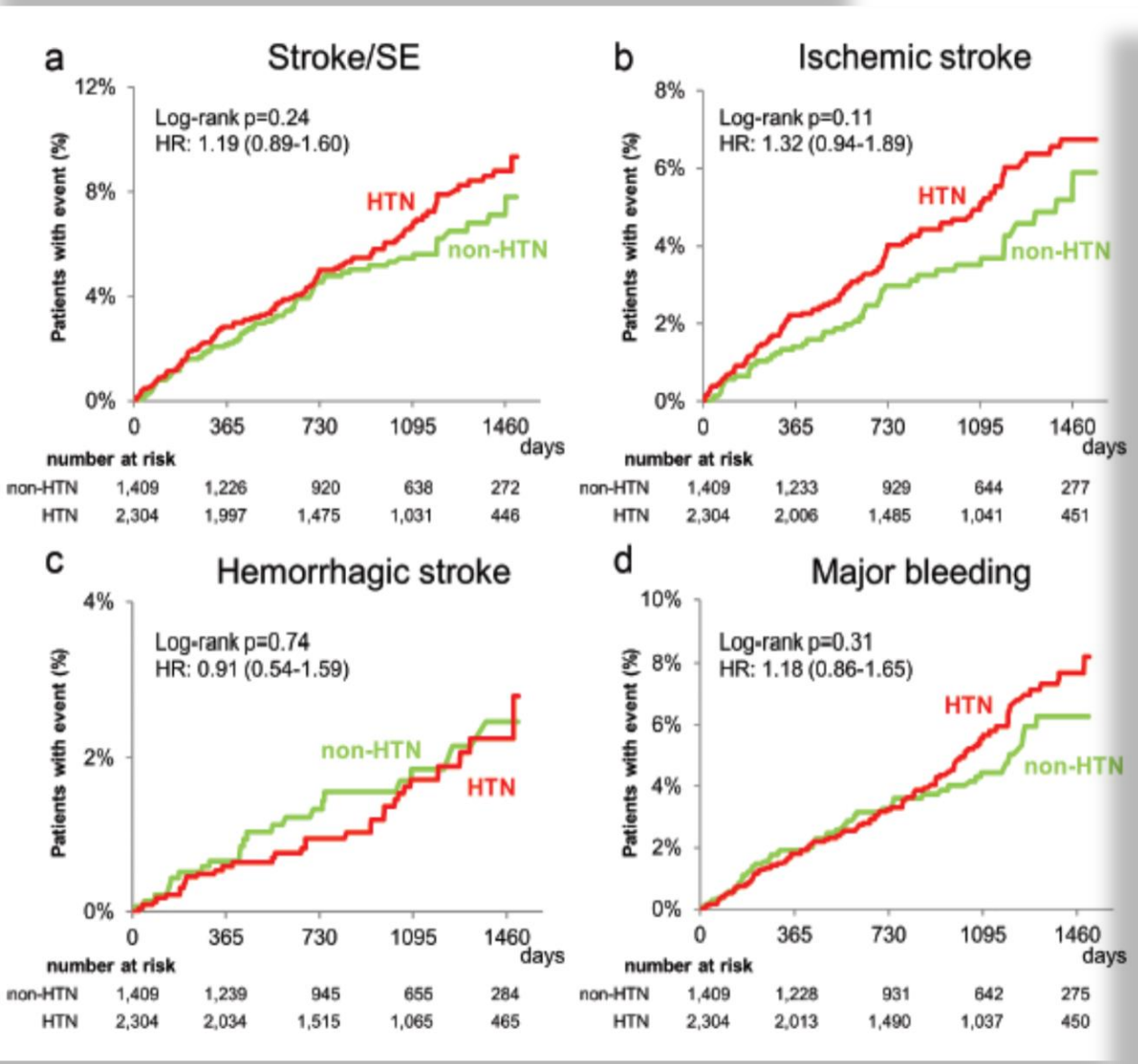
TABLE 3. Hazard ratios, per SBP category, for outcomes with 95% confidence intervals

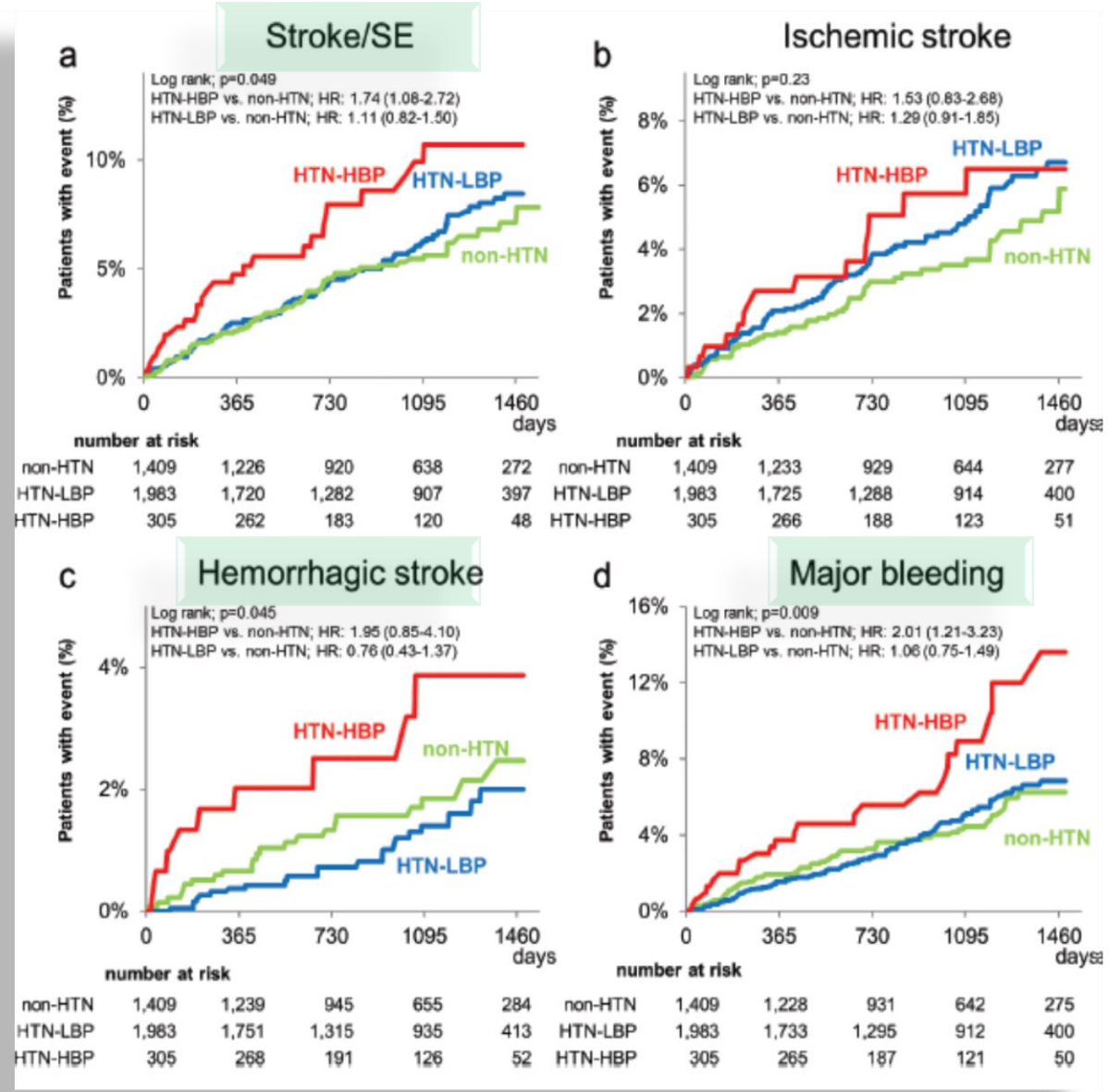
	130–139 mmHg, *n* = 829	<130 mmHg, *n* = 1031	140–159 mmHg, *n* = 1440	160–179 mmHg, *n* = 497	≥180 mmHg, *n* = 175
Haemorrhagic stroke	1 (ref)	0.72 (0.22–2.36)	1.32 (0.51–3.44)	3.53 (1.35–9.23)	0.66 (0.08–5.54)
All stroke	1 (ref)	1.02 (0.65–1.59)	1.15 (0.77–1.72)	1.71 (1.1–2.67)	1.3 (0.67–2.51)
Ischaemic stroke	1 (ref)	1.11 (0.69–1.78)	1.16 (0.75–1.79)	1.46 (0.88–2.42)	1.43 (0.71–2.86)
Any bleed	1 (ref)	1.11 (0.69–1.78)	1.16 (0.75–1.79)	1.46 (0.88–2.42)	1.43 (0.71–2.86)
Gastrointestinal bleed	1 (ref)	1.33 (0.78–2.29)	1.22 (0.73–2.03)	1.16 (0.61–2.2)	0.54 (0.16–1.81)
Death	1 (ref)	1.1 (0.86–1.41)	1.1 (0.87–1.38)	0.89 (0.66–1.21)	1.22 (0.8–1.84)

American Journal of Hypertension 30(11) November 2017

Relationship of Hypertension and Systolic Blood Pressure With the Risk of Stroke or Bleeding in Patients With Atrial Fibrillation: The Fushimi AF Registry

TRATTAMENTO del PAZIENTE IPERTESO con FA





PLOS Medicine | https://doi.org/10.1371/journal.pmed.1003599 June 1, 2021

Blood pressure-lowering treatment for the prevention of cardiovascular events in patients with atrial fibrillation: An individual participant data meta-analysis

MACE

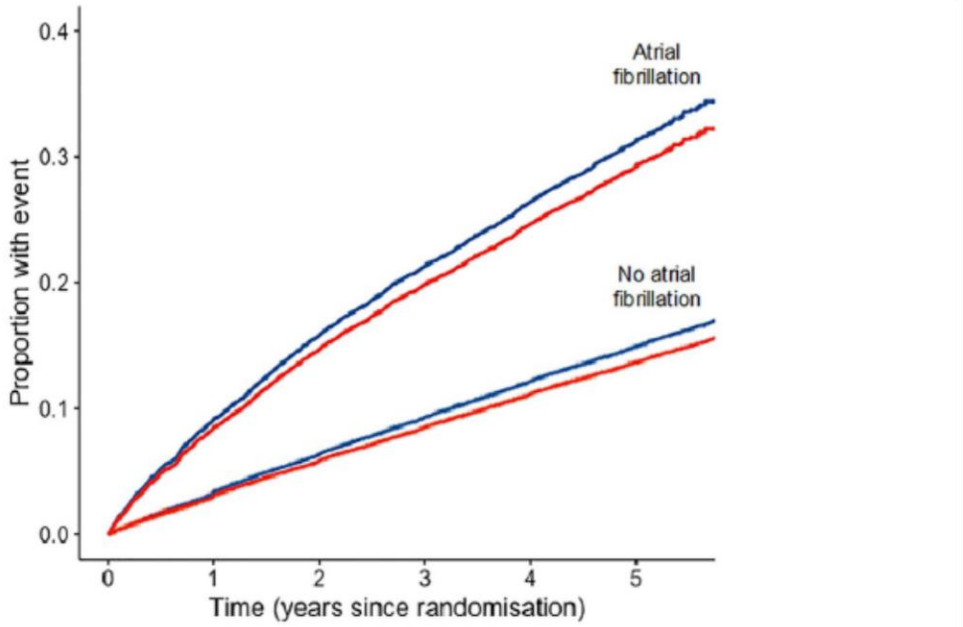
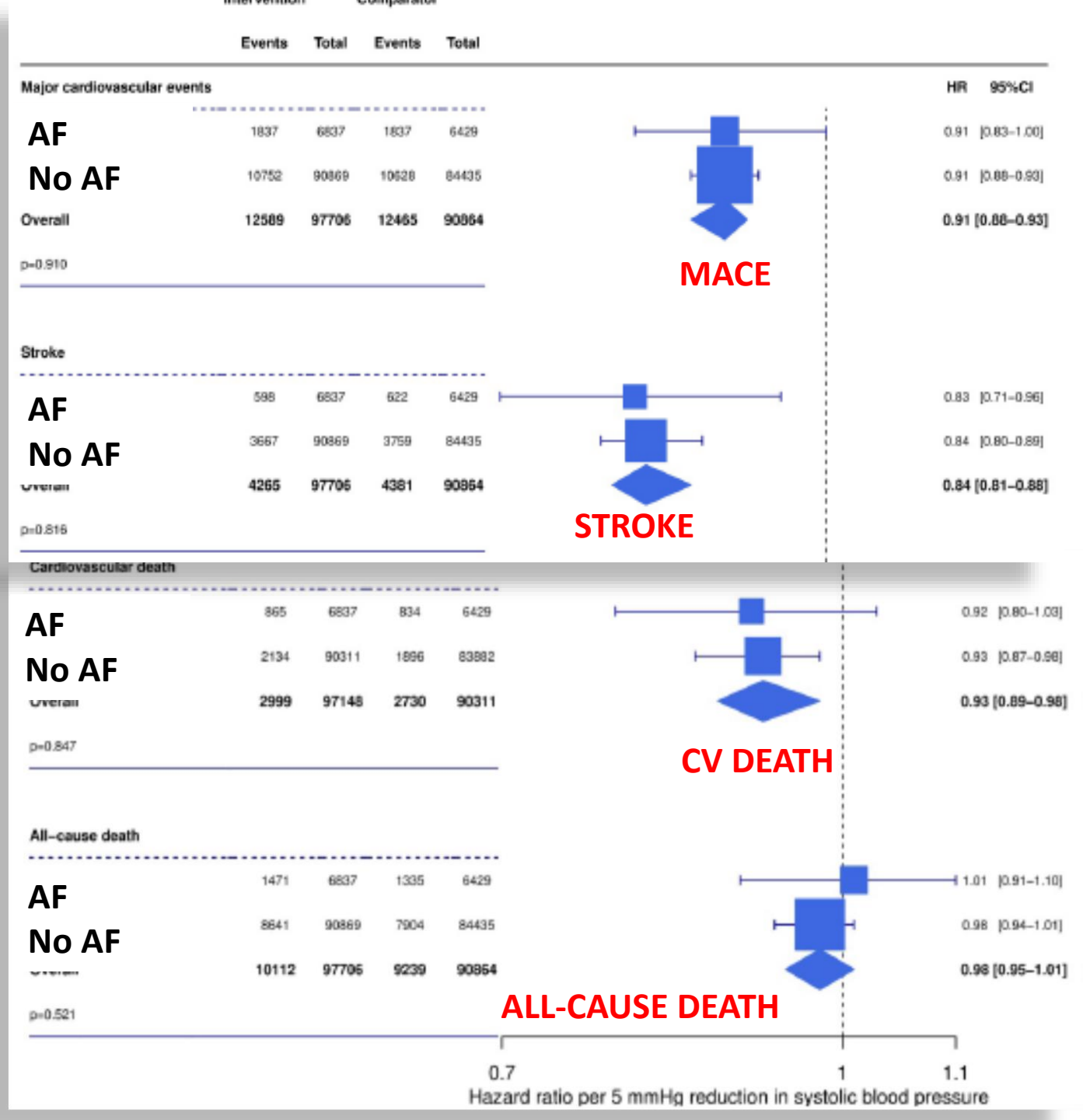


Fig 3. Cumulative event rates for the primary outcome (major cardiovascular events) by treatment arm, stratified by presence of atrial fibrillation at baseline. Shown are estimates of the proportions of patients with major



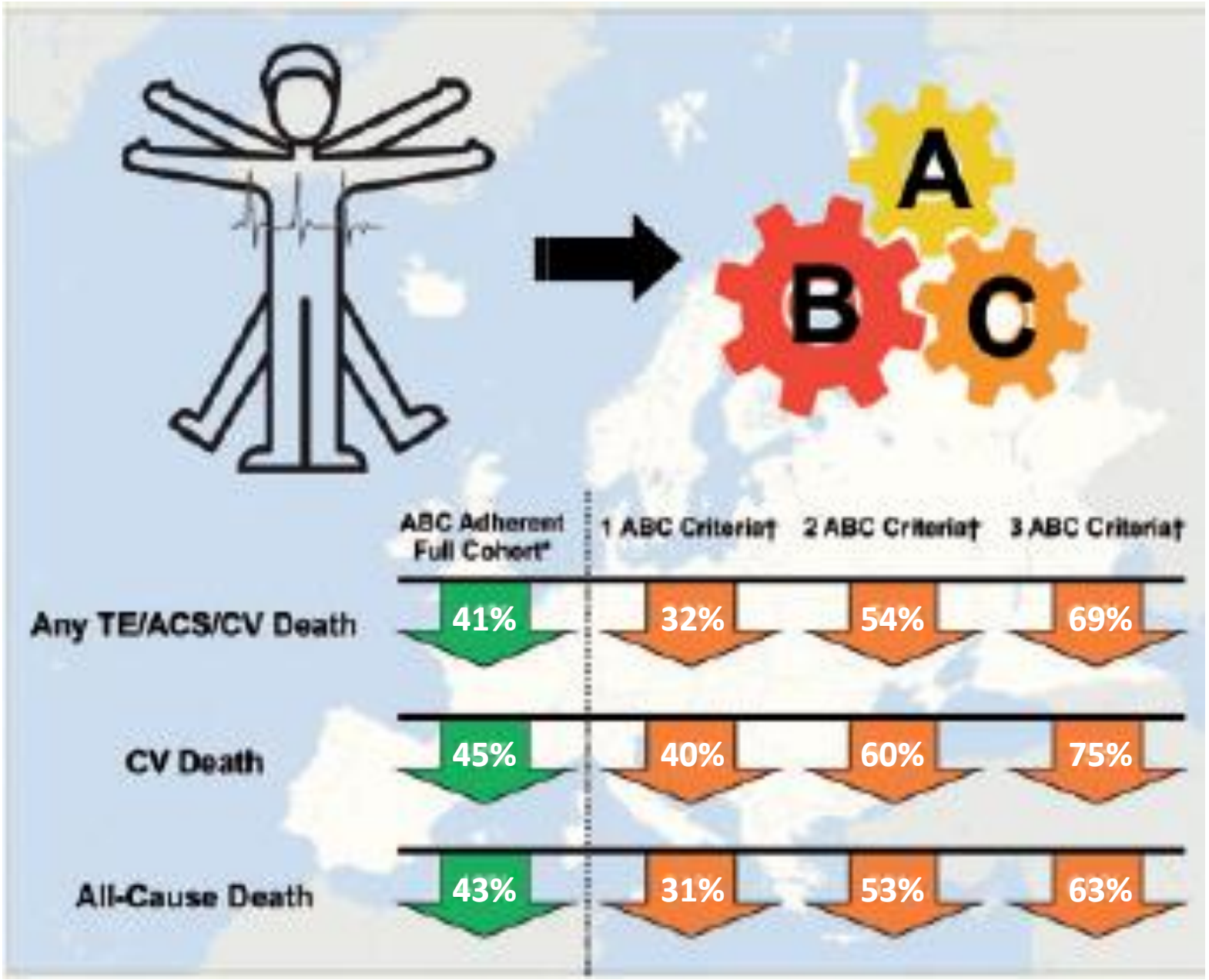
TRATTAMENTO del PAZIENTE con FA IPERTESO

Relation of outcomes to ABC (Atrial Fibrillation Better Care) pathway adherent care in European patients with atrial fibrillation: an analysis from the ESC-EHRA EORP Atrial Fibrillation General Long-Term (AFGen LT) Registry

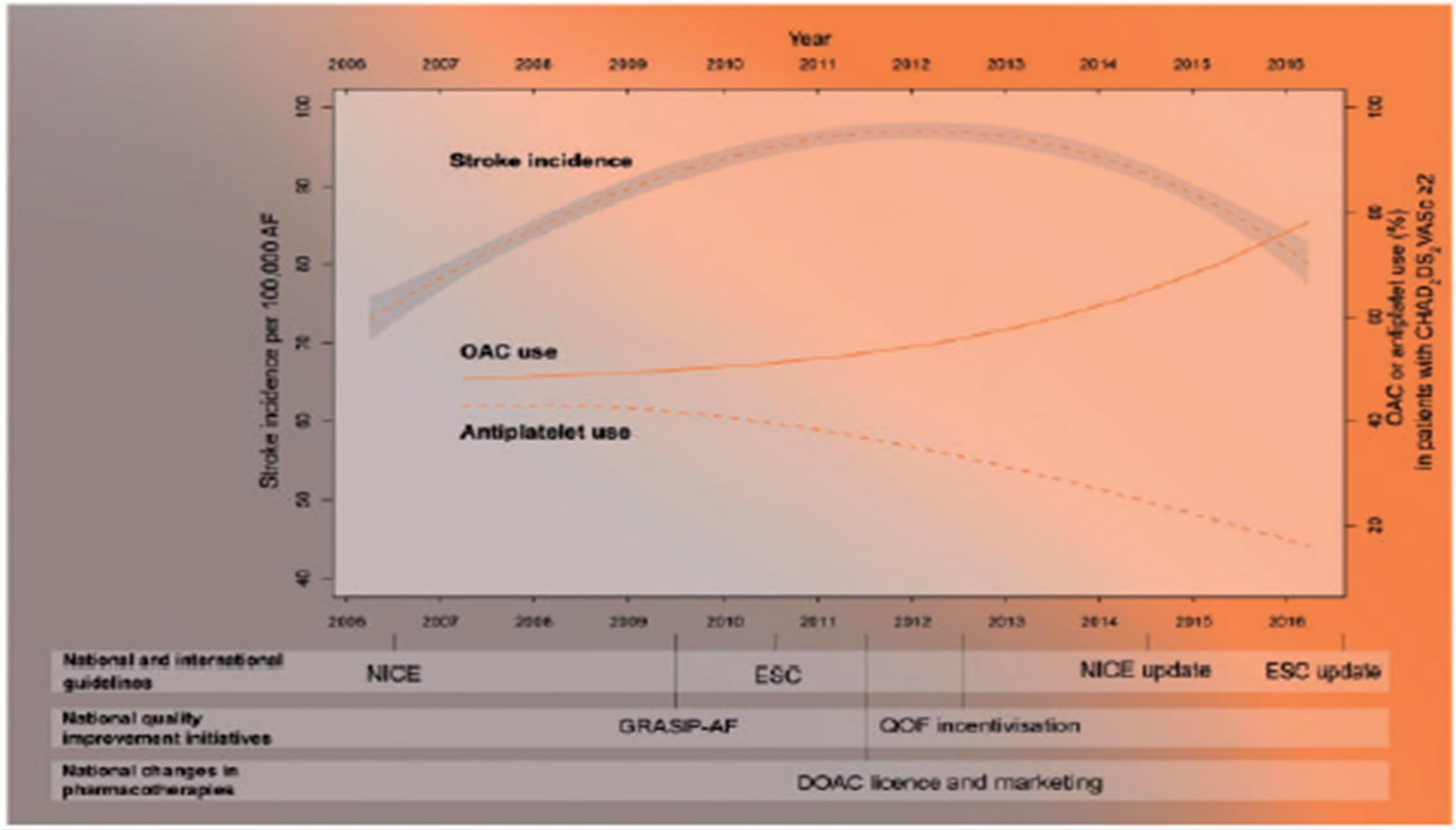
Europace (2021) **23**, 174–183

What's new?

- Integrated care is part of in atrial fibrillation (AF) management.
- The 'Atrial Fibrillation Better Care' (ABC) pathway has been proposed to streamline integrated care in AF patients.
- In a cohort of contemporary AF patients, an ABC adherent care was evident in 30.0% of patients.
- Clinical management adherent to ABC pathway was associated with a lower risk of cardiovascular events, cardiovascular death, and all-cause death.

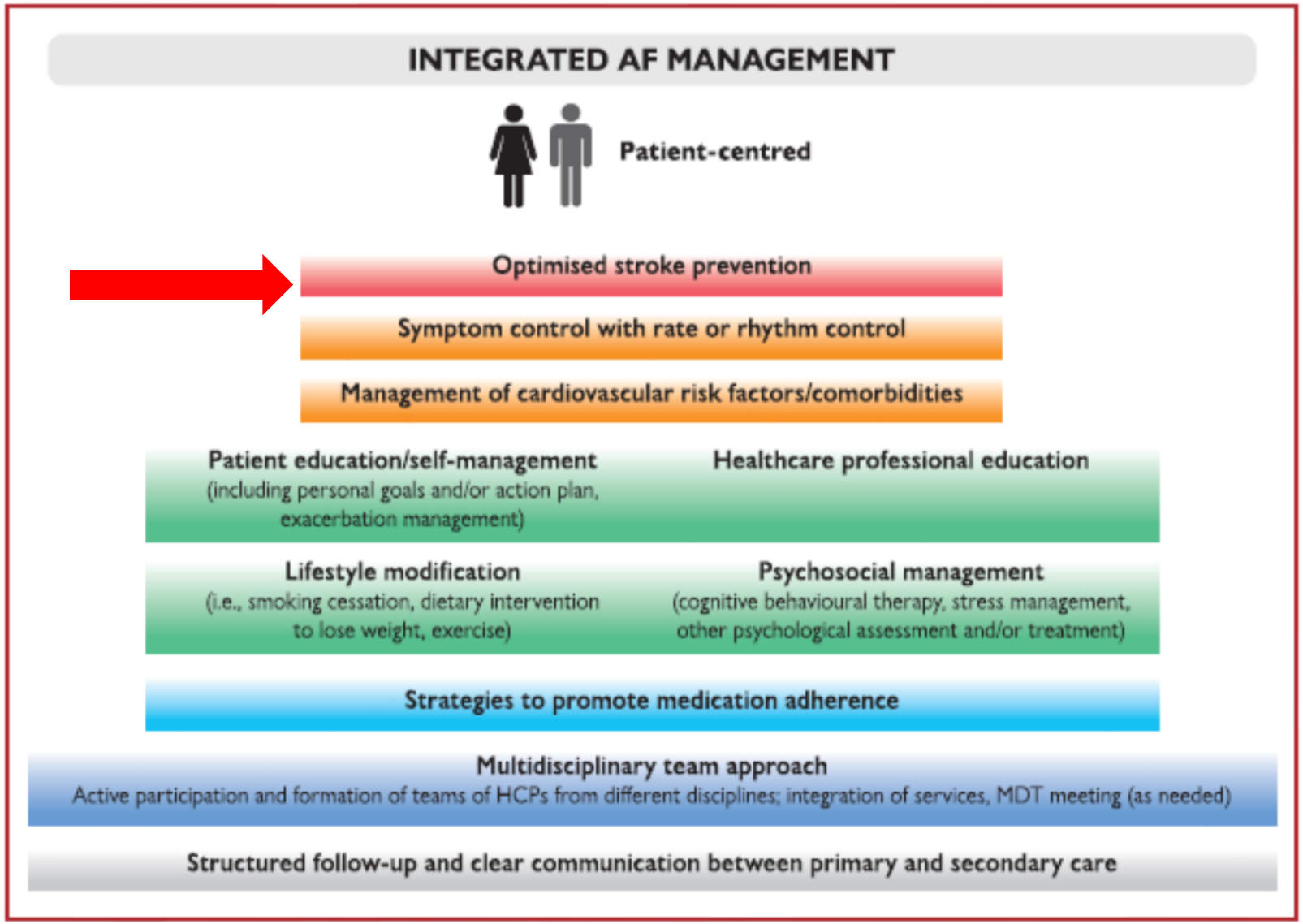


A 10 year study of hospitalized atrial fibrillation-related stroke in England and its association with uptake of oral anticoagulation



European Heart Journal (2018) **39**, 2975–2983

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



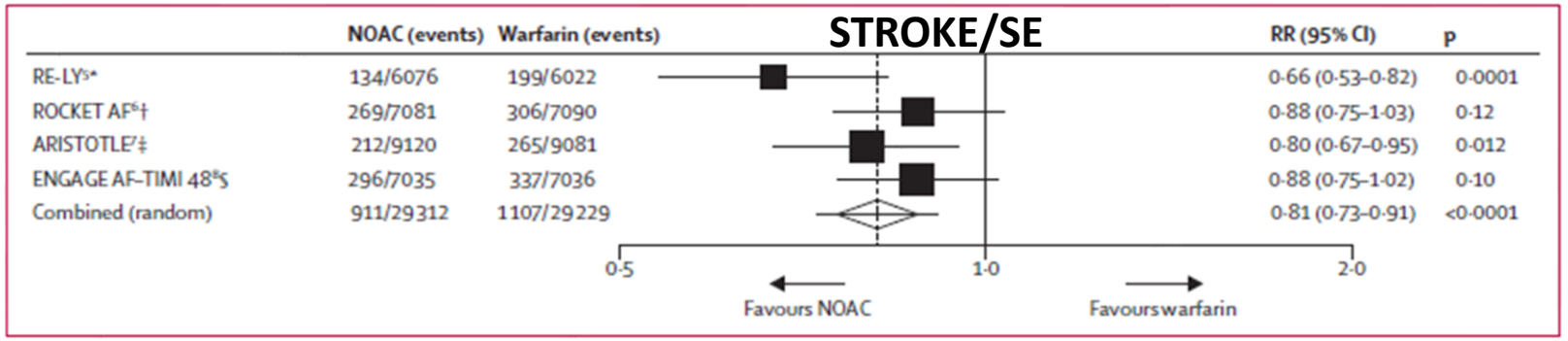
IMPLICAZIONI CLINICHE

Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

Christian T Ruff, Robert P Giugliano, Eugene Braunwald, Elaine B Hoffman, Naveen Deenadayalu, Michael D Ezekowitz, A John Camm, Jeffrey I Weitz, Basil S Lewis, Alexander Parkhomenko, Takeshi Yamashita, Elliott M Antman

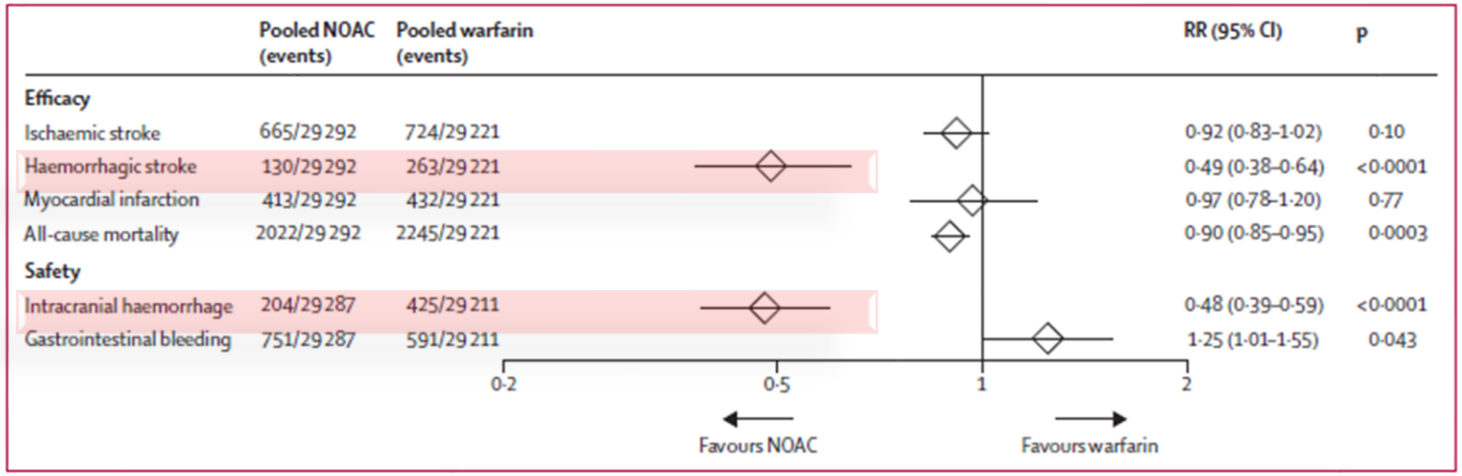
Lancet 2014; 383: 955–62

STROKE/SE



	NOAC (events)	Warfarin (events)	RR (95% CI)	p
RE-LY[5]*	134/6076	199/6022	0·66 (0·53–0·82)	0·0001
ROCKET AF[6]†	269/7081	306/7090	0·88 (0·75–1·03)	0·12
ARISTOTLE[7]‡	212/9120	265/9081	0·80 (0·67–0·95)	0·012
ENGAGE AF–TIMI 48[8]§	296/7035	337/7036	0·88 (0·75–1·02)	0·10
Combined (random)	911/29312	1107/29229	0·81 (0·73–0·91)	<0·0001

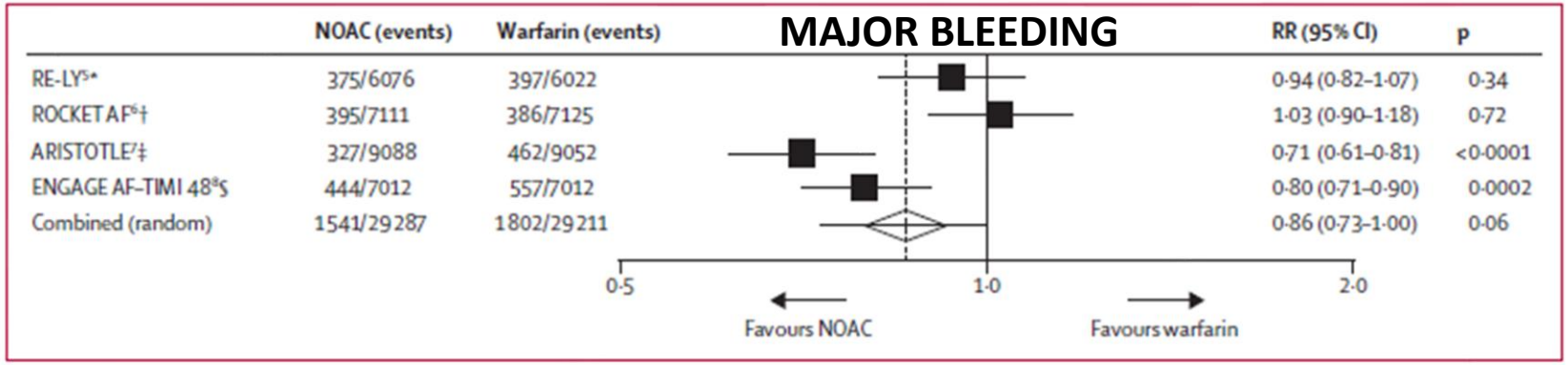
47%; p=0·13. NOAC=new oral anticoagulant. RR=risk ratio. *Dabigatran 150 mg twice daily. †Rivaroxaban
) mg once daily.



	Pooled NOAC (events)	Pooled warfarin (events)	RR (95% CI)	p
Efficacy				
Ischaemic stroke	665/29292	724/29221	0·92 (0·83–1·02)	0·10
Haemorrhagic stroke	130/29292	263/29221	0·49 (0·38–0·64)	<0·0001
Myocardial infarction	413/29292	432/29221	0·97 (0·78–1·20)	0·77
All-cause mortality	2022/29292	2245/29221	0·90 (0·85–0·95)	0·0003
Safety				
Intracranial haemorrhage	204/29287	425/29211	0·48 (0·39–0·59)	<0·0001
Gastrointestinal bleeding	751/29287	591/29211	1·25 (1·01–1·55)	0·043

***Figure 2*: Secondary efficacy and safety outcomes**
Data are n/N, unless otherwise indicated. Heterogeneity: ischaemic stroke I^2=32%, p=0·22; haer
p=0·13; all-cause mortality I^2=0%, p=0·81; intracranial haemorrhage I^2=32%, p=0·22; gastrointe
RR=risk ratio.

MAJOR BLEEDING



	NOAC (events)	Warfarin (events)	RR (95% CI)	p
RE-LY[5]*	375/6076	397/6022	0·94 (0·82–1·07)	0·34
ROCKET AF[6]†	395/7111	386/7125	1·03 (0·90–1·18)	0·72
ARISTOTLE[7]‡	327/9088	462/9052	0·71 (0·61–0·81)	<0·0001
ENGAGE AF–TIMI 48[8]§	444/7012	557/7012	0·80 (0·71–0·90)	0·0002
Combined (random)	1541/29287	1802/29211	0·86 (0·73–1·00)	0·06

***Figure 3*: Major bleeding**
Data are n/N, unless otherwise indicated. Heterogeneity: I^2=83%; p=0·001. NOAC=new oral anticoagulant. RR=risk ratio. *Dabigatran 150 mg twice daily. †Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. §Edoxaban 60 mg once daily.

Oral anticoagulant therapy for older patients with atrial fibrillation: a review of current evidence

European Journal of Internal Medicine 41 (2017) 18–27

Mario Bo [a], Enrica Grisoglio [a], Enrico Brunetti [a,*], Yolanda Falcone [a], Niccolò Marchionni [b]

Efficacy and safety outcomes in patients >=75 years

	RE-LY		ROCKET-AF	ARISTOTLE	ENGAGE-AF	
Patients>75 years, n (%)	7528/18113 (40.1%)		6229/14624 (43.7%)	5678/18201 (31.2%)	8474/21105	(40.2%)
	Dabi 150	Dabi 110	Rivaroxaban	Apixaban	Edoxaban HD	Edoxaban LD
STROKE/SE	0.67 (0.49-0.90)	0.88 (0.66-1.17)	0.80 (0.63-1.02)	0.71 (0.53-0.95)	0.83 (0.67-1.04)	1.12 (0.91-1.40)
MAJOR BLEEDING	1.18 (0.98-1.42)	1.01 (0.83-1.23)	1.11 (0.92-1.34)	0.64 (0.52-0.79)	0.83 (0.70-0.99)	0.47 (0.38-0.58)
IC BLEEDING	0.42 (0.25-0.70)	0.37 (0.21-0.64)	0.80 (0.50-1.28)	0.34 (0.20-0.57)	0.40 (0.26-0.62)	0.31 (0.19-0.49)

European Heart Journal - Cardiovascular Pharmacotherapy (2017) **3**, 28–36

A nationwide registry study to compare bleeding rates in patients with atrial fibrillation being prescribed oral anticoagulants

32 675 AF patients (58% men, median age 75 years)

Conclusion

In this nationwide cohort study on AF patients being prescribed OAC, use of apixaban and dabigatran were associated with a lower risk of major or CRNM bleeding compared with the use of warfarin. The risk of GI bleeding was higher among users of dabigatran and rivaroxaban compared with warfarin, whereas users of apixaban and dabigatran had a lower risk of ICH compared with users of warfarin. The risk of stroke was not addressed in this study, and hence the optimal benefit to risk balance between stroke prevention and bleeding could not be evaluated.

Overall sample

OAC Major or CRNM	IR	HR (95% CI)	P
Warfarin	11.44	1 (ref.)	
Dabigatran 110	9.76	0.81 (0.69,0.95)	0.009
Dabigatran 150	5.12	0.68 (0.58,0.80)	<0.001
Warfarin	11.44	1 (ref.)	
Rivaroxaban 15	15.86	1.12 (0.96,1.31)	0.158
Rivaroxaban 20	9.84	1.01 (0.89,1.15)	0.853
Warfarin	11.44	1 (ref.)	
Apixaban 2.5	10.60	0.64 (0.52,0.80)	<0.001
Apixaban 5	7.78	0.73 (0.62,0.86)	<0.001

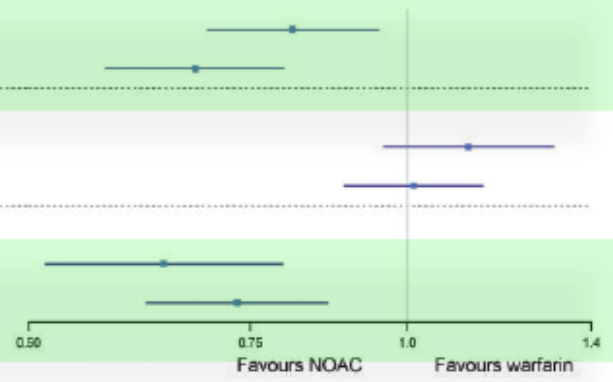


Figure 4 Risk of major or CRNM bleeding for the reduced and standard dose of dabigatran, rivaroxaban, and apixaban compared with warfarin. Crude IR for first bleeding episode are given as events per 100 person-years. CI, confidence interval; CRNM, clinically relevant non-major bleeding; HR, adjusted hazard ratio; IR, incidence rate; OAC, oral anticoagulant.

=>75 years

OAC Major or CRNM	IR	HR (95% CI)	P
Warfarin	14.64	1 (ref.)	
Dabigatran	10.00	0.84 (0.72,0.99)	0.036
Rivaroxaban	14.68	1.14 (0.99,1.30)	0.067
Apixaban	10.82	0.72 (0.61,0.86)	<0.001

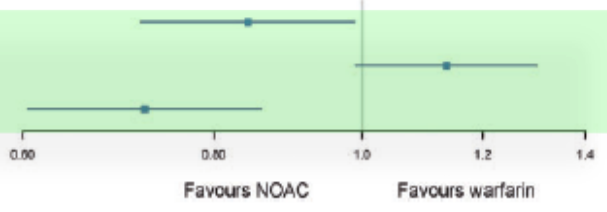


Figure 5 Risk of major or CRNM bleeding for dabigatran, rivaroxaban, and apixaban compared with warfarin in the subgroup of patients ≥75 years. Crude IR for first bleeding episode are given as events per 100 person-years. CI, confidence interval; CRNM, clinically relevant non-major bleeding; HR, adjusted hazard ratio; IR, incidence rate; OAC, oral anticoagulant.

Comparison of dabigatran, rivaroxaban, and apixaban for effectiveness and safety in atrial fibrillation: a nationwide cohort study

65 563 new users of OACs, 38% > 75 years

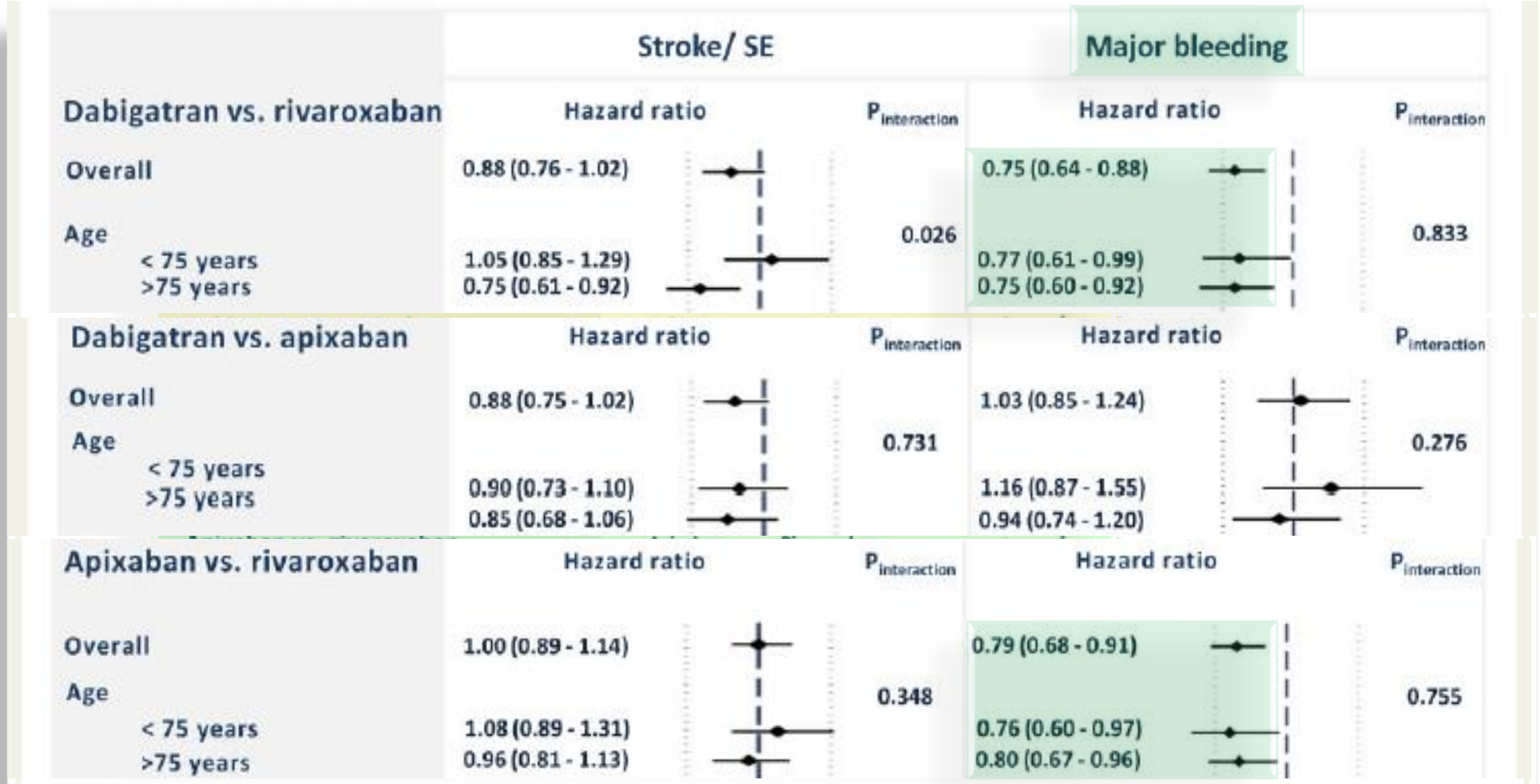


Figure 5 The risk of stroke or systemic embolism and major bleeding for patients using standard or reduced dose non-vitamin K antagonist oral anticoagulants. CI, confidence interval; Pys., person-years.

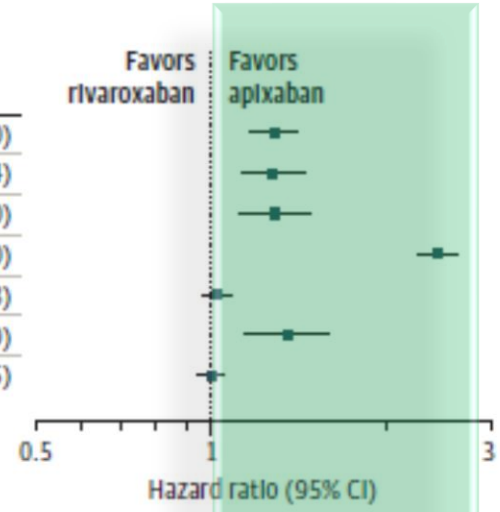
European Heart Journal - Cardiovascular Pharmacotherapy (2020) **6**, 75–85

IMPLICAZIONI CLINICHE

Figure 3. Outcomes by Medication Dose in a Study of the Association of Rivaroxaban vs Apixaban With Major Ischemic or Hemorrhagic Events in Atrial Fibrillation

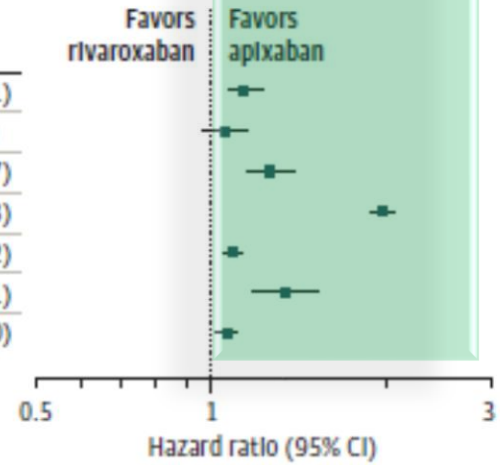
A Reduced dose

Outcome	Rate per 1000 person-years		Rate difference (95% CI)	Hazard ratio (95% CI)
	Rivaroxaban	Apixaban		
Major ischemic/hemorrhagic event	27.4	21.0	6.4 (4.1 to 8.7)	1.28 (1.16 to 1.40)
Ischemic	15.5	11.9	3.6 (1.9 to 5.3)	1.27 (1.13 to 1.44)
Hemorrhagic	11.9	9.1	2.8 (1.3 to 4.3)	1.28 (1.11 to 30.0)
Nonfatal extracranial bleeding	57.5	22.5	35.0 (31.9 to 38.1)	2.44 (2.26 to 34.0)
Total mortality	87.0	82.7	4.2 (-0.1 to 8.6)	1.02 (0.97 to 1.08)
Fatal ischemic/hemorrhagic event	8.5	6.2	2.3 (1.1 to 3.6)	1.35 (1.14 to 1.59)
Other death during follow-up	78.4	76.5	1.9 (-2.3 to 6.0)	1.00 (0.95 to 1.05)



B Standard dose

Outcome	Rate per 1000 person-years		Rate difference (95% CI)	Hazard ratio (95% I)
	Rivaroxaban	Apixaban		
Major ischemic/hemorrhagic event	13.2	11.4	1.8 (1.0 to 2.6)	1.13 (1.06 to 1.21)
Ischemic	6.8	6.4	0.5 (-0.1 to 1.0)	1.05 (.96 to 1.14)
Hemorrhagic	6.3	5.0	1.3 (0.8 to 1.8)	1.25 (1.14 to 1.37)
Nonfatal extracranial bleeding	35.0	17.5	17.5 (16.3 to 18.7)	1.94 (1.85 to 2.03)
Total mortality	32.9	29.7	3.1 (1.9 to 4.4)	1.08 (1.04 to 1.12)
Fatal ischemic/hemorrhagic event	3.4	2.5	0.9 (0.5 to 1.3)	1.33 (1.17 to 1.51)
Other death during follow-up	29.4	27.2	2.2 (1.0 to 3.4)	1.06 (1.01 to 1.10)



Adjusted incidence of study outcomes according to anticoagulant dose. Rates, rate differences, and hazard ratios were adjusted with inverse probability of treatment weighting; the variables used in the adjustment are shown in eTable 5 in the Supplement. See eTable 9 in the Supplement for numbers of events.

Stroke. 2022;53:1873–1882.

Effectiveness and Safety of Anticoagulation Therapy in Frail Patients With Atrial Fibrillation

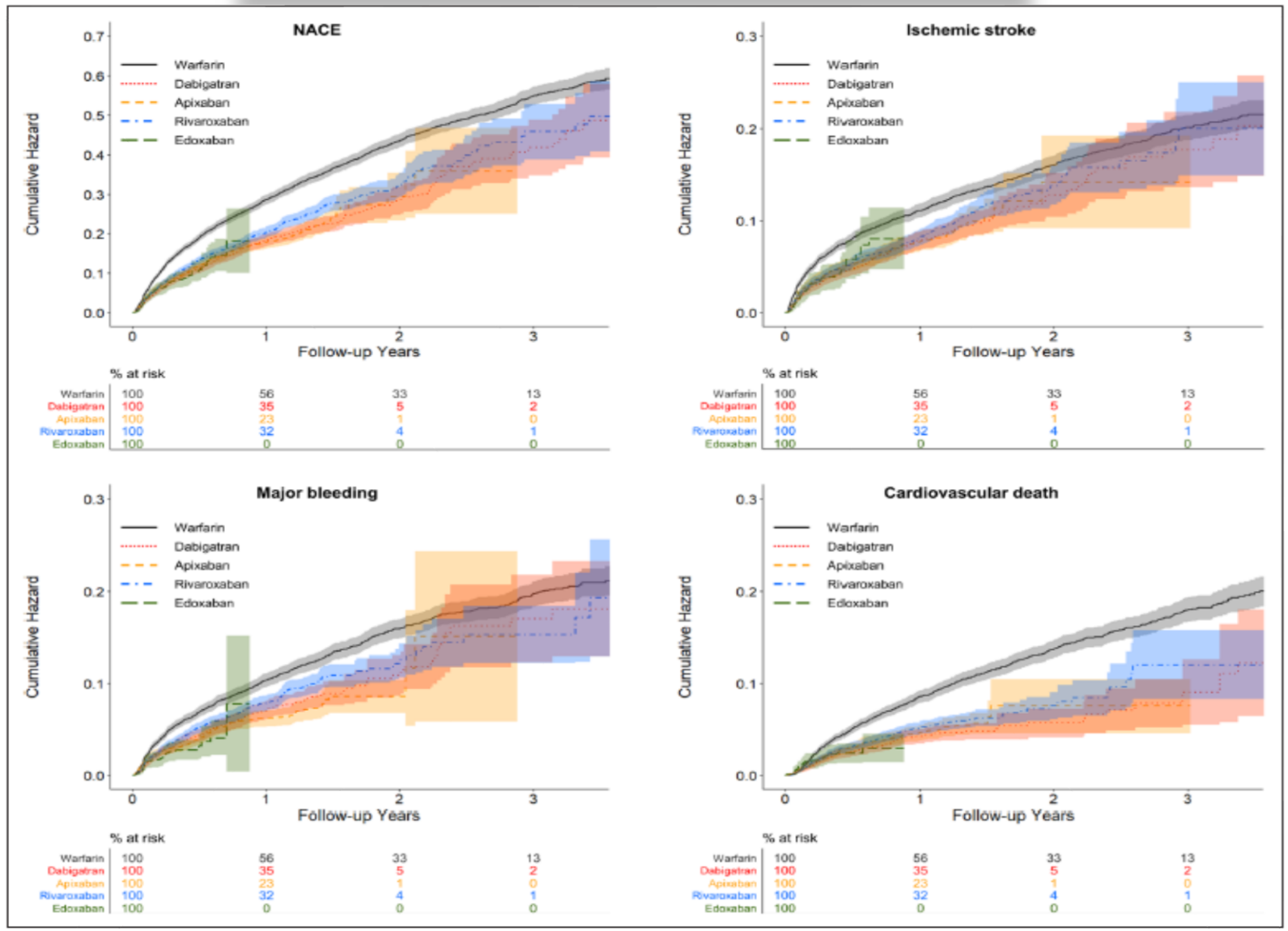


Figure 3. Weighted cumulative hazards of clinical outcomes for frail patients with atrial fibrillation receiving direct oral anticoagulants or warfarin.
NACE indicates net adverse clinical event.

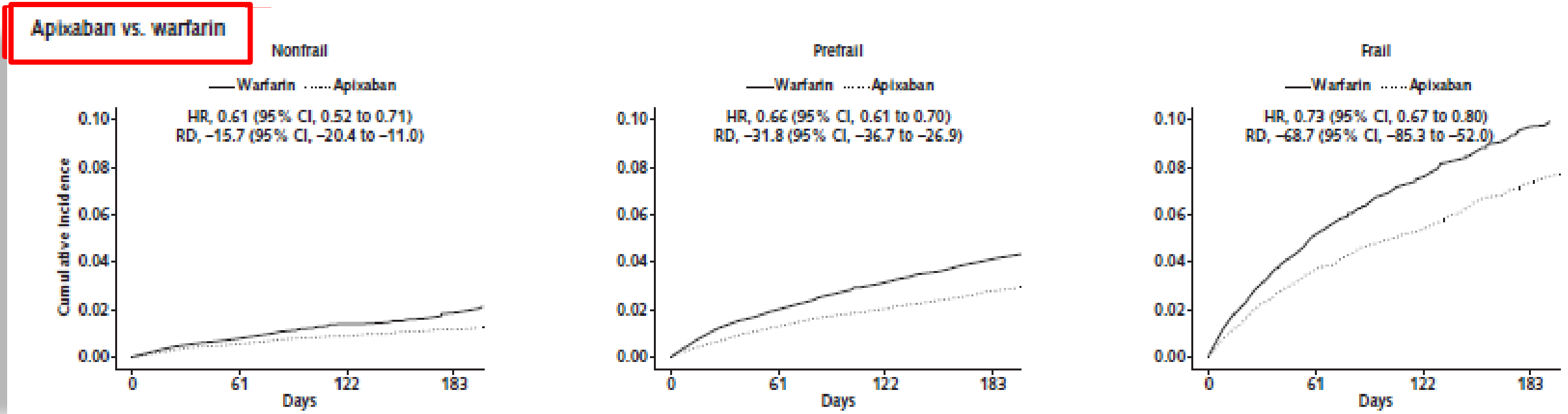
Frailty and Clinical Outcomes of Direct Oral Anticoagulants Versus Warfarin in Older Adults With Atrial Fibrillation

A Cohort Study

Ann Intern Med. doi:10.7326/M20-7141

1:1 PSM analysis AF **Medicare beneficiaries** (mean age 76 years) with **frailty (CFI)** who initiated warfarin or DOACs

Figure. Cumulative incidence plots of a composite end point of death, ischemic stroke, or major bleeding in older adults with atrial fibrillation newly treated with direct oral anticoagulants versus warfarin, by frailty level.



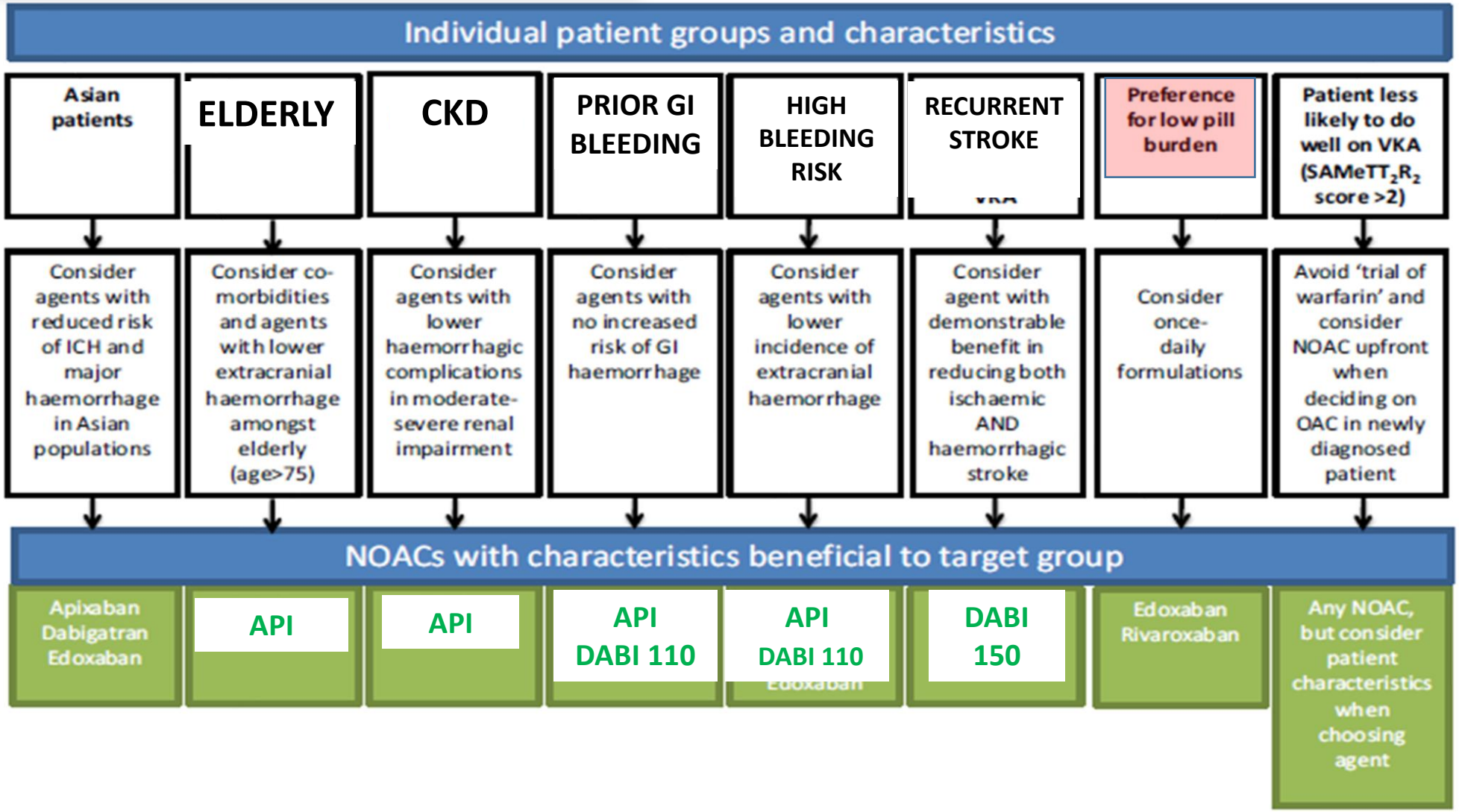
IMPLICAZIONI CLINICHE

Review ● Journal of INTERNAL MEDICINE

doi: 10.1111/joim.12360

Choosing the right drug to fit the patient when selecting oral anticoagulation for stroke prevention in atrial fibrillation

A. M. Shields[1] & G. Y. H. Lip[2,3]



Intern Med 2015; **278**: 1–18.

Non-vitamin K oral anticoagulants and age

European Heart Journal Advance Access published February 4, 2016

First choice	In patients older than 75 years, we suggest apixaban 5 mg twice daily [2.5 mg if ≥2 of the following: age ≥80 years, body weight ≤60 kg, or creatinine ≥1.5 mg/dL (133 μmol/L)]
Second choice	Dabigatran 110 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily

Appropriateness of Oral Anticoagulants for the Long-Term Treatment of Atrial Fibrillation in Older People: Results of an Evidence-Based Review and International Consensus Validation Process (OAC-FORTA 2016)

and missing for all other compounds. Apixaban was rated FORTA-A (highly beneficial). Other non-vitamin K antagonist oral anticoagulants (including low/high-intensity dabigatran and high-intensity edoxaban) and warfarin were assigned to FORTA-B (beneficial). Phenprocoumon, acenocoumarol and fluindione were rated FORTA-C (questionable), mainly reflecting the absence of data.

Drugs Aging (2017) 34: 499.
doi.org/10.1007/s40266-017-0466-6

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel**

Table 4. 2019 American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medications: Drugs To Be Used With Caution in Older Adults[a]

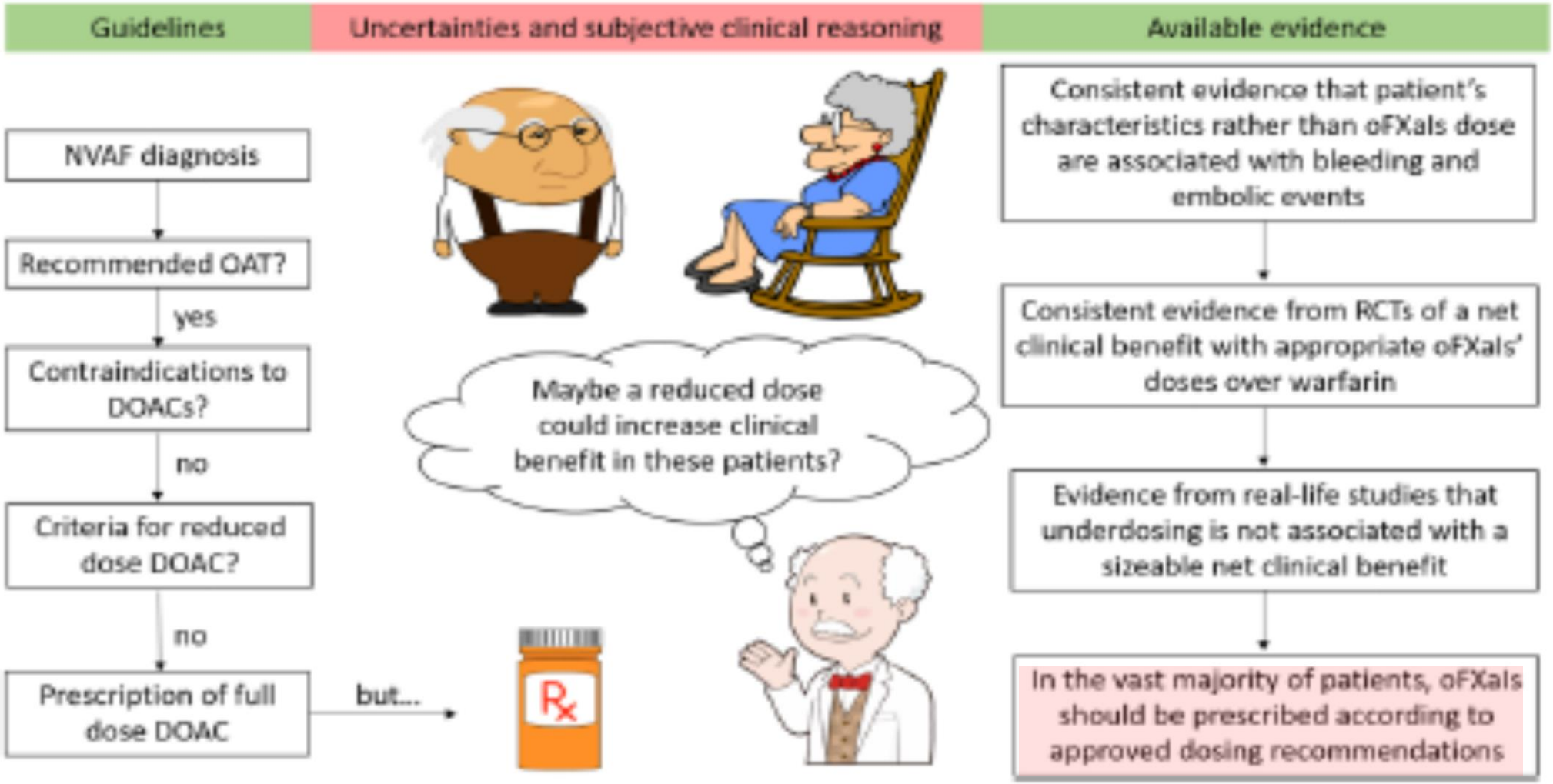
Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Dabigatran Rivaroxaban	Increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other direct oral anticoagulants when used for long-term treatment of VTE or atrial fibrillation in adults ≥75 years.	Use with caution for treatment of VTE or atrial fibrillation in adults ≥75 years	Moderate	Strong

JAGS 67:674–694, 2019

Off-label use of reduced dose direct oral factor Xa inhibitors in subjects with atrial fibrillation: a review of clinical evidence

Mario Bo [1]*, Alberto Corsini [2,3], Enrico Brunetti [1], Gianluca Isaia[1], Maddalena Gibello[1], Nicola Ferri [4], Daniela Poli[5], Niccolò Marchionni [6], Gaetano Maria De Ferrari [7]

European Heart Journal - Cardiovascular Pharmacotherapy (2021) **7**, 334–345



Circulation. 2022;145:242–255.

Direct Oral Anticoagulants Versus Warfarin in Patients With Atrial Fibrillation: Patient-Level Network Meta-Analyses of Randomized Clinical Trials With Interaction Testing by Age and Sex

Clinical Perspective

What Is New?

- When individual patient data from randomized trials of direct oral anticoagulants (DOACs) versus warfarin are analyzed collectively, standard-dose DOAC use results in lower incidence of stroke, death, and intracranial hemorrhage with no difference in major bleeding.
- The relative benefits of standard-dose DOACs over warfarin for stroke prevention were consistent across nearly all subgroups, including across the entire continuous spectrum of age, with no evidence of interaction by sex. These benefits may be greater in patients with lower creatinine clearance.
- For major bleeding, younger patients and patients with lower body weight may derive a greater benefit from standard-dose DOAC over warfarin.

What Are the Clinical Implications?

- The totality of efficacy and safety data from randomized clinical trials supports the use of standard-dose DOACs over warfarin for stroke prevention in nonvalvular atrial fibrillation, regardless of age or sex.

IMPLICAZIONI CLINICHE

(*Stroke*. 2019;50:2093-2100.

Anticoagulation After Stroke in Patients With Atrial Fibrillation

To Bridge or Not With Low-Molecular-Weight Heparin?

Table 4. PS Matching: Outcomes

	No Bridging Therapy (n=323)	Bridging Therapy (n=323)	HR (95% CI)	*P* Value
Combined outcome	13 (4.0%)	40 (12.3%)	Unadjusted, 3.08 (95% CI, 1.68–5.64)	0.0001
			Adjusted, 2.23 (95% CI, 1.41–3.52)	0.0001
Ischemic outcome	6 (1.9%)	27 (8.3%)	Unadjusted, 4.50 (95% CI, 1.88–10.75)	0.003
			Adjusted, 2.23 (95% CI, 1.29–3.88)	0.003
Hemorrhagic outcome	7 (2.2%)	19 (5.9%)	Unadjusted, 2.71 (95% CI, 1.16–6.37)	0.017
			Adjusted, 2.24 (95% CI, 1.15–4.36)	0.017

HR indicates hazard ratio; and PS, propensity score.

Stroke. 2020;51:2724–2732. DOI: 10.1161/STROKEAHA.120.028867

Anticoagulation Type and Early Recurrence in Cardioembolic Stroke

The IAC Study

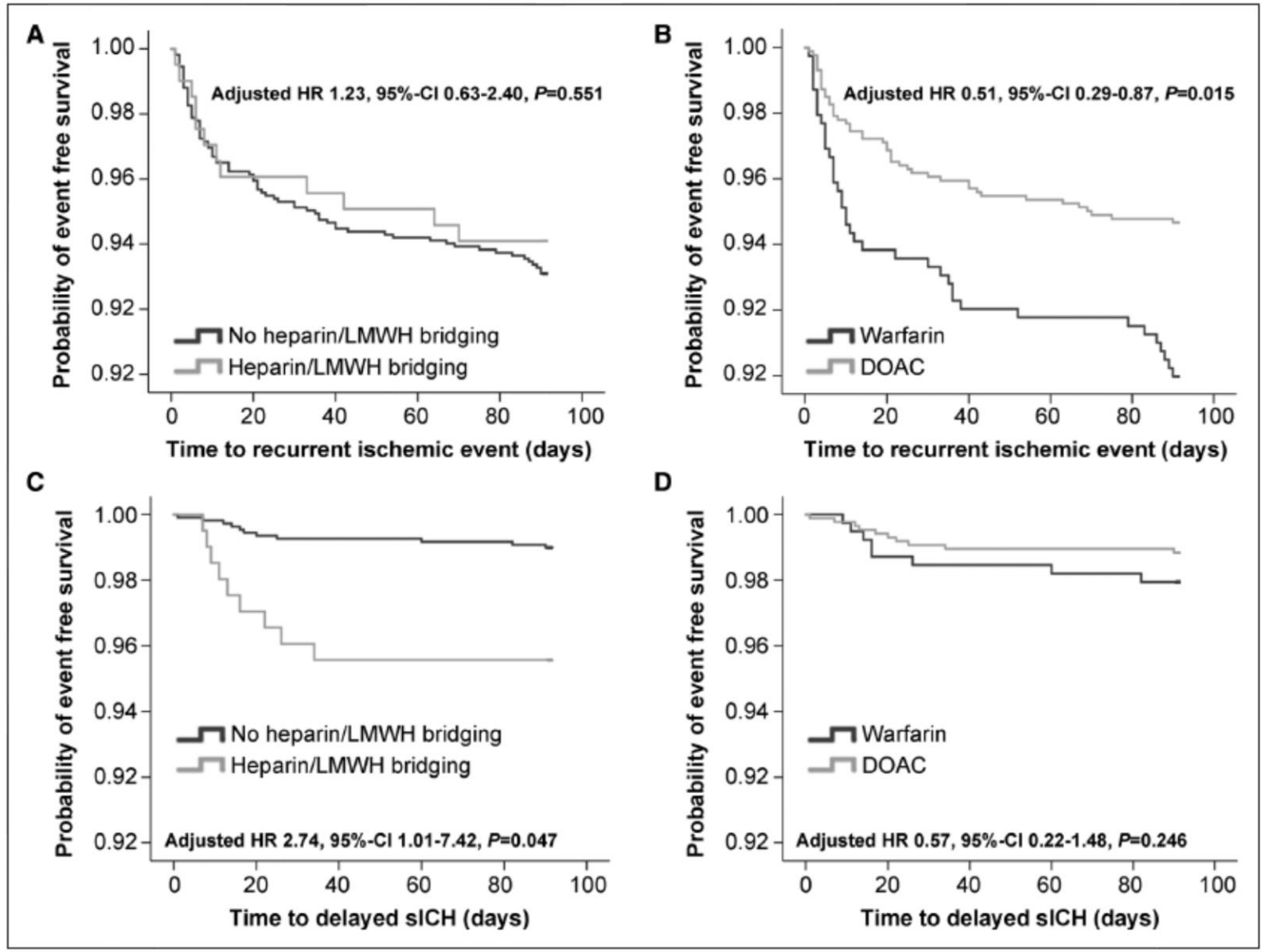


Figure 2. KM survival analyses of the risk of delayed symptomatic intracranial hemorrhage and recurrent ischemic events based on treatment type: left side shows bridging vs no bridging and right side shows direct oral anticoagulant (DOAC) vs warfarin treatment.

HR indicates hazard ratio; LMWH, low molecular weight heparin; and sICH, symptomatic intracranial hemorrhage.

Practical "1-2-3-4-Day" Rule for Starting Direct Oral Anticoagulants After Ischemic Stroke With Atrial Fibrillation: Combined Hospital-Based Cohort Study

Stroke. 2022;53:1540–1549.

«1-2-3-4-day» vs «1-3-6-12-day» rule for starting DOAC after ischemic stroke with AF

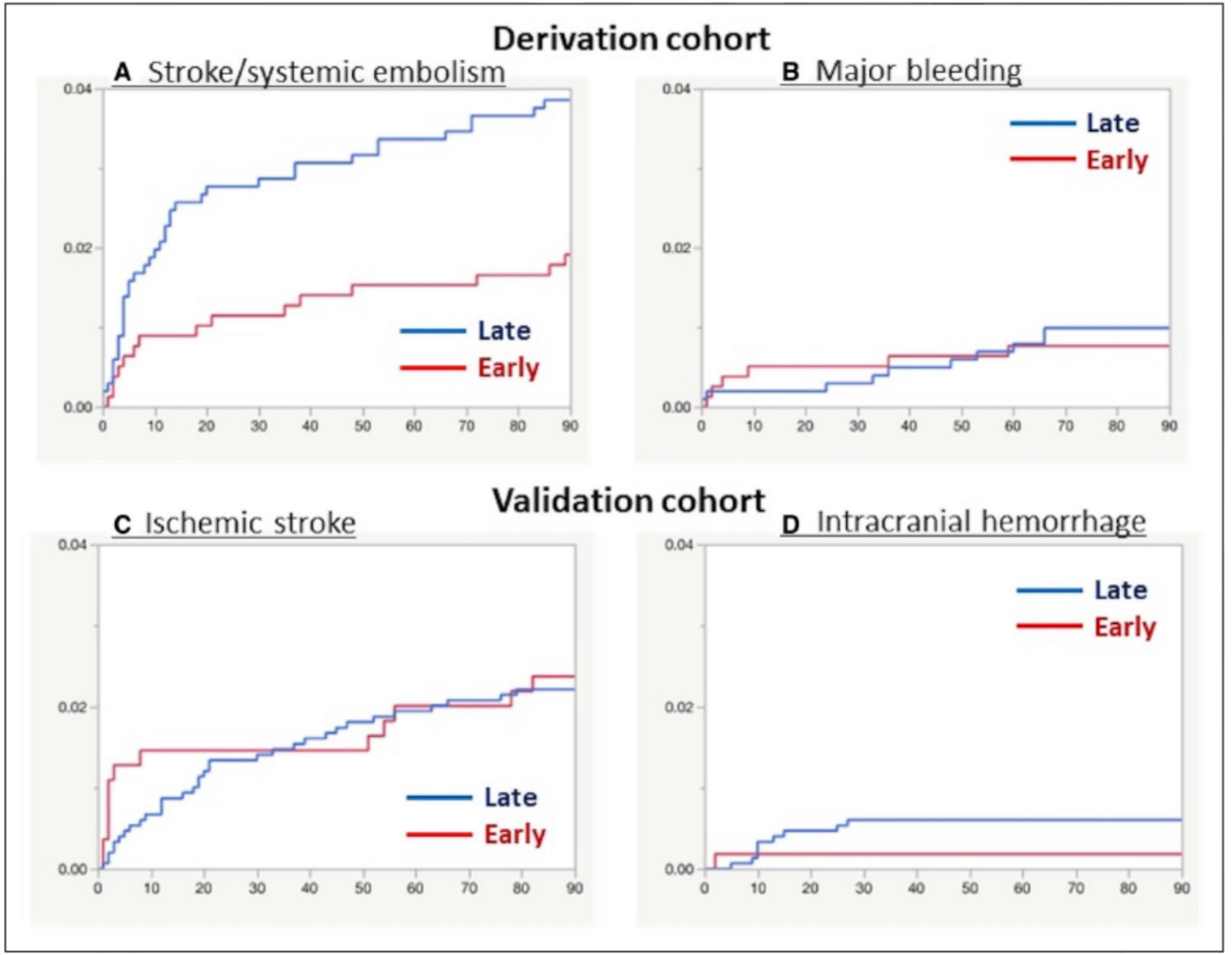


Figure 2. Kaplan-Meier analysis of outcomes.
The Kaplan-Meier curves for the time to the first event of stroke or systemic embolism (**A**) and major bleeding (**B**) for the derivation cohort and that of ischemic stroke (**C**) and intracranial hemorrhage (**D**) in the validation cohort are shown. NIHSS indicates National Institutes of Health Stroke Scale.

10.15	LETTURA (presenta P. Mulatero) Terapia anticoagulante nell'FA del paziente iperteso	**THM**	M. Bo	*Torino*

L'ipertensione arteriosa è «**intrinsecamente» legata alla FA**

Vi sono discrete evidenze che la **riduzione del burden ipertensivo e del danno d'organo** possano **ridurre l'incidenza o ritardare l'insorgenza della FA**

Esistono elementi suggestivi di un **potenziale beneficio clinico dal trattamento appropriato della FA «subclinica» precocemente identificata in soggetti ipertesi** ad elevata probabilità di FA

Vi sono discrete evidenze che **un'efficace trattamento dell'ipertensione possa ridurre l'incidenza dei MACE nei pazienti ipertesi con FA**

I **DOACs offrono un miglior benefico clinico netto** rispetto agli AVK, prevalentemente legato ad una **minor incidenza di sanguinamenti intracranici**. Tuttavia evidenze concordi dimostrano che vi sono **sostanziali differenze in termini di «safety» tra i diversi DOACs**.