



La “migliore terapia” per la prevenzione del rischio tromboembolico nel paziente con FA

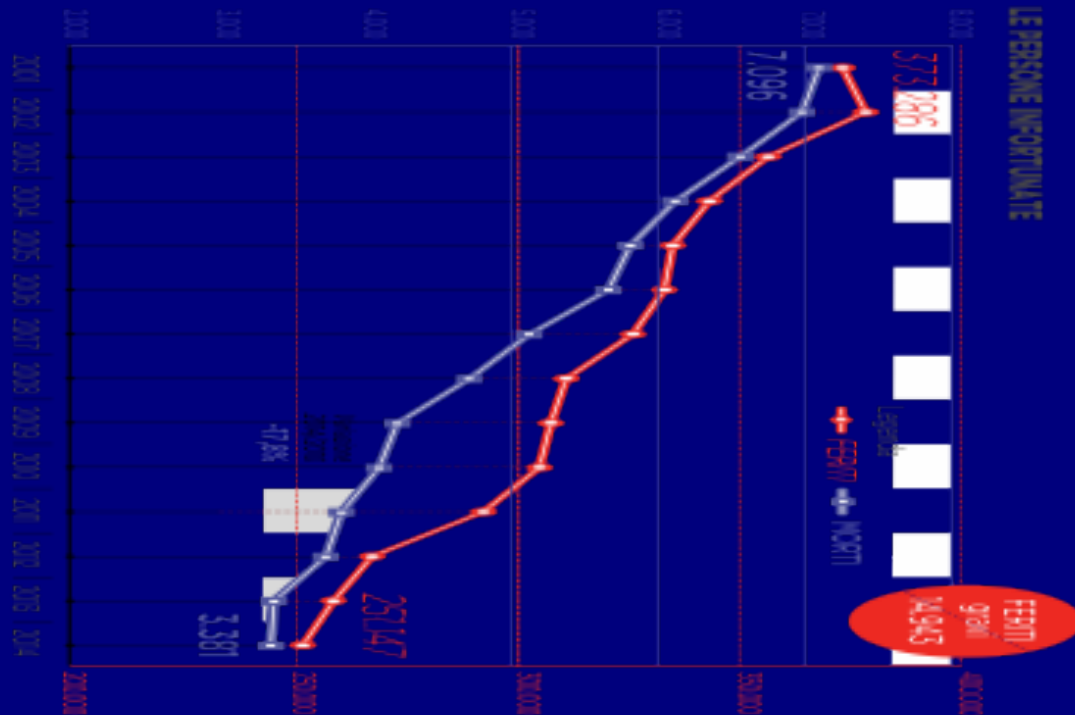
Prof. Fiorenzo Gaita

**Director of the School of Cardiology
University of Turin, Italy**

DATI ISTAT 2014

Incidenti stradali in Italia nel 2014

TOT MORTI 3381



HOW TO REDUCE?



HOW TO REDUCE?



OAT

Management cascade for patients with AF

Treatment

Acute rate and rhythm control

Precipitating factors: lifestyle changes, treatment of underlying cardiovascular

Assess stroke risk: oral anticoagulation if needed

Assess heart rate: rate control

Assess symptoms and comorbidities: rhythm control (antiarrhythmic drugs, cardioversion, TC ablation)

Desired outcome

Hemodynamic stability

Cardiovascular risk reduction

Stroke prevention

Symptoms improvement, LV function preservation

Symptoms improvement, comorbidities prevention

Patient benefit

Improved life expectancy

Improved quality of life, functional capacity

AFFIRM: Total Mortality (at 5 years)

Rate control *vs* Rhythm control

Rate control + TAO *vs* Rhythm control with AAD +/- TAO

4060 pts,

Age 69.7±9 years

528 pts (13%) > 80 y

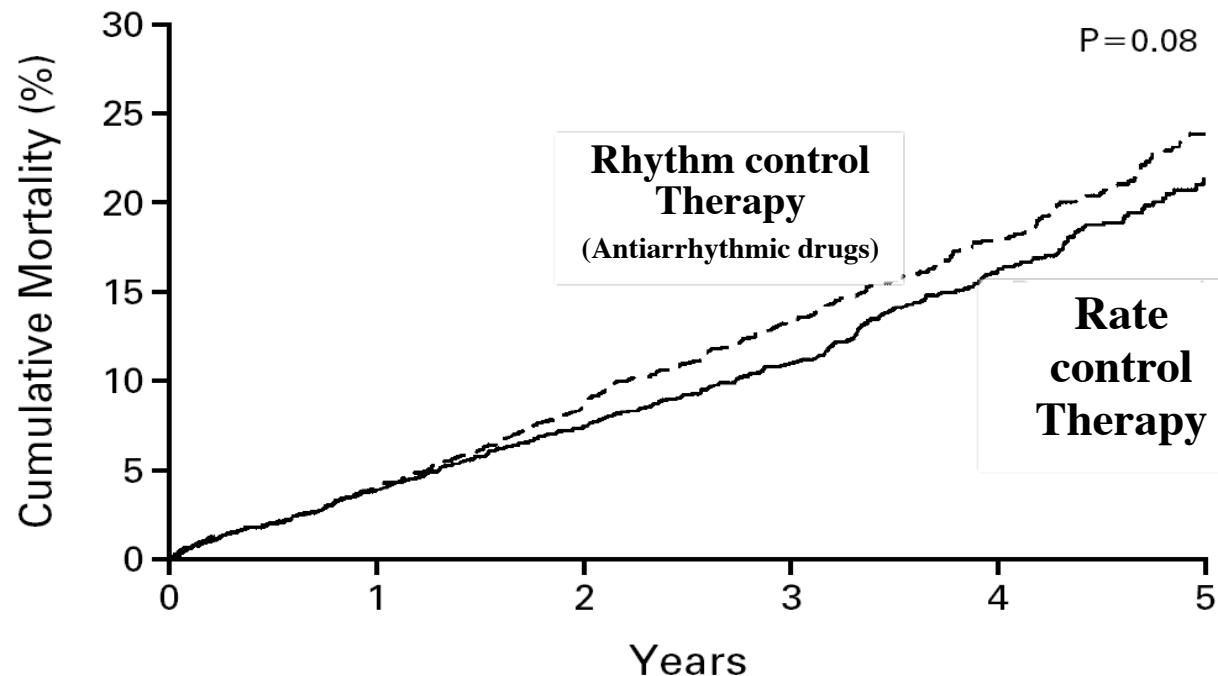
-70.8% Hypertension

-38.2% Ischemic

-↓ EF 26%

-↑ Left atrium 64,7%

Mean FU: 3,5 y



No. OF DEATHS

	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

AFFIRM:

Circulation 2004; 109:1509

Covariates associated to survival:

Covariate	p	HR
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Warfarin	<0.0001	0.50
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Warfarin ↓ of about 50% risk of death

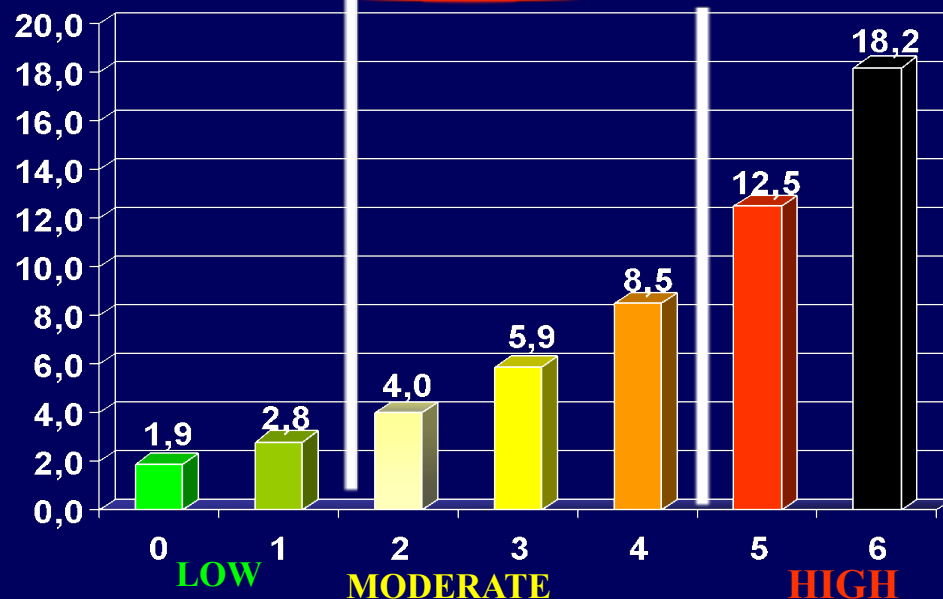
Management of anticoagulation therapy

ESC 2010

Congestive heart failure	1
Hypertension	1
Age > 75 years	1
Diabetes mellitus	1

Expected stroke rate *per 100 pts/y*
 Prior Stroke or TIA ²
 without antithrombotic therapy

Using CHADS Score



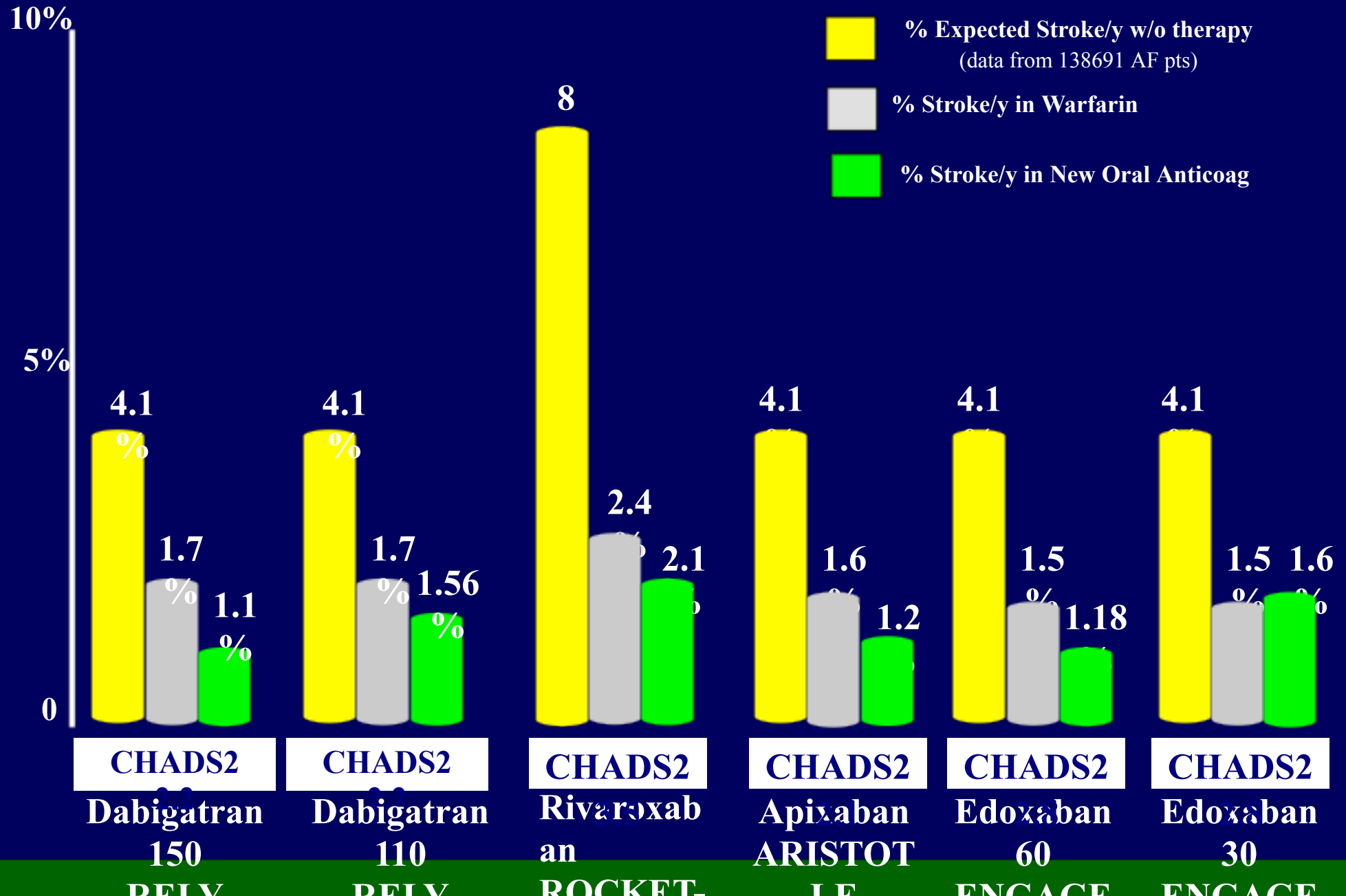
**Recommended
antithrombotic therapy**

CHADS2 score	Antithrombotic therapy
≥ 2	Oral Anticoagulation
1	Either OAC or aspirin 75-325 mg.
0	Aspirin 75-325 mg

	DABIGATRAN 150 bid or 110 bid	APIXABAN 5 bid or 2.5 bid	RIVAROXABAN 20 or 15 od	EDOXABAN 30 or 60 od
<i>Name</i>	<u>Pradaxa</u> <u>2009</u>	<u>Eliquis</u> <u>2012</u>	<u>Xarelto</u> <u>2011</u>	<u>Lixiana</u> <u>2015</u>
Mean CHADS	2.1	2.1	3.5	2.8
<i>Bioavailability</i>	7%	60%	60-80%	40%
<i>Half-life (T_½)</i>	12-17 h	12 h	5-9 h young 11-13 h elderly	10-14
<i>T_{max} h</i>	2-4 h	3-4 h	2-4 h	1-5 h
<i>Clearance</i>	80% renal	25% renal 75% biliary	60% renal 33% biliary	40% renal
<i>Drug interaction</i> <i>P-gp competition</i> <i>CYP3A4 inhibition</i>	Amiodarone (↑) Quinidine (↑) Verapamil (↑)	Diltiazem (↑) Ketoconazole(↑)	Ritonavir(↑) Ketokonazole(↑) Quinidine(↑)	Quinidine(↑) Verapamil(↑)

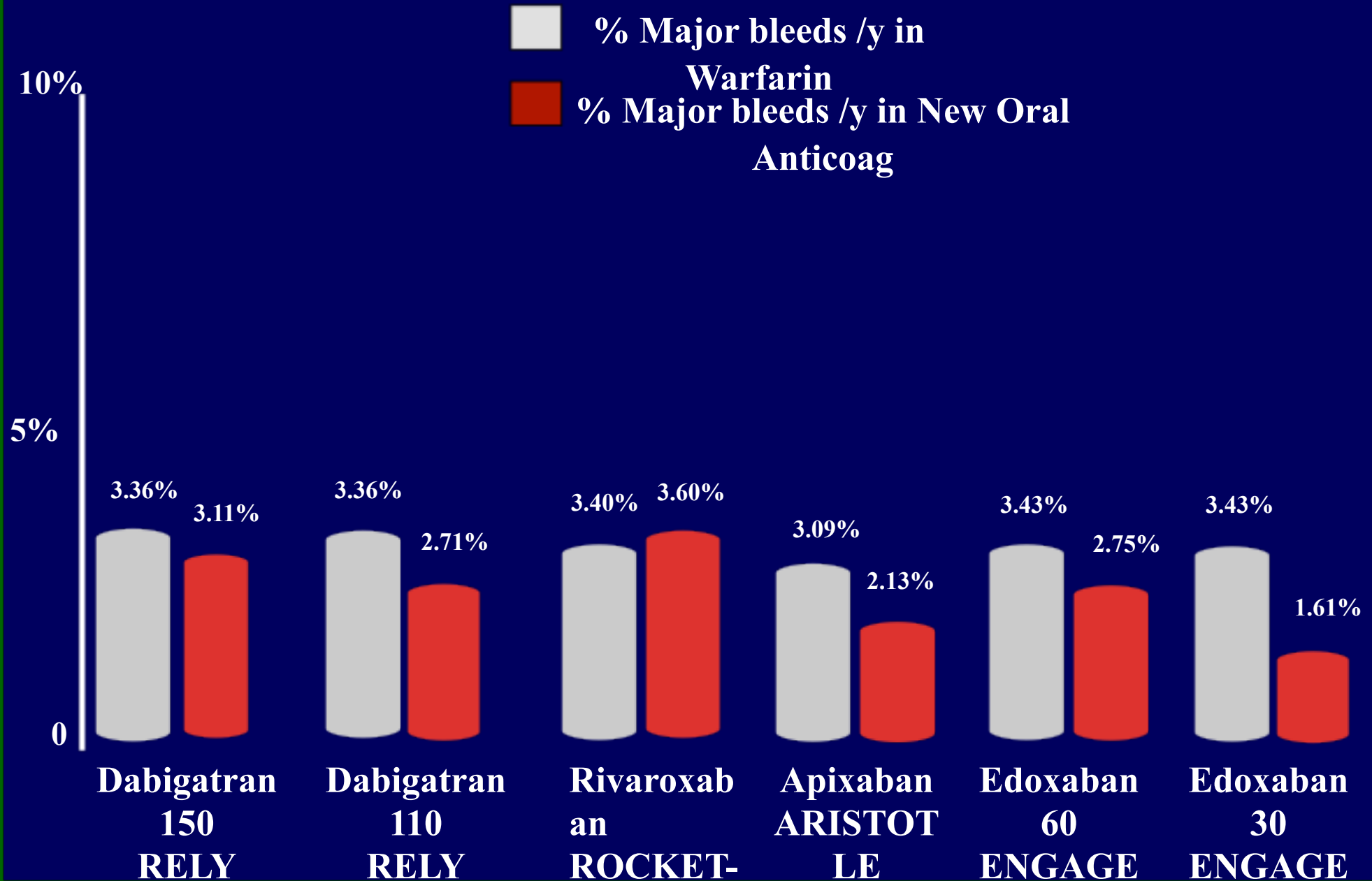
NON VALVULAR AF: ANNUAL THROMBOEMBOLIC RISK

No Treated vs Warfarin vs **New Oral Anticoagulants**



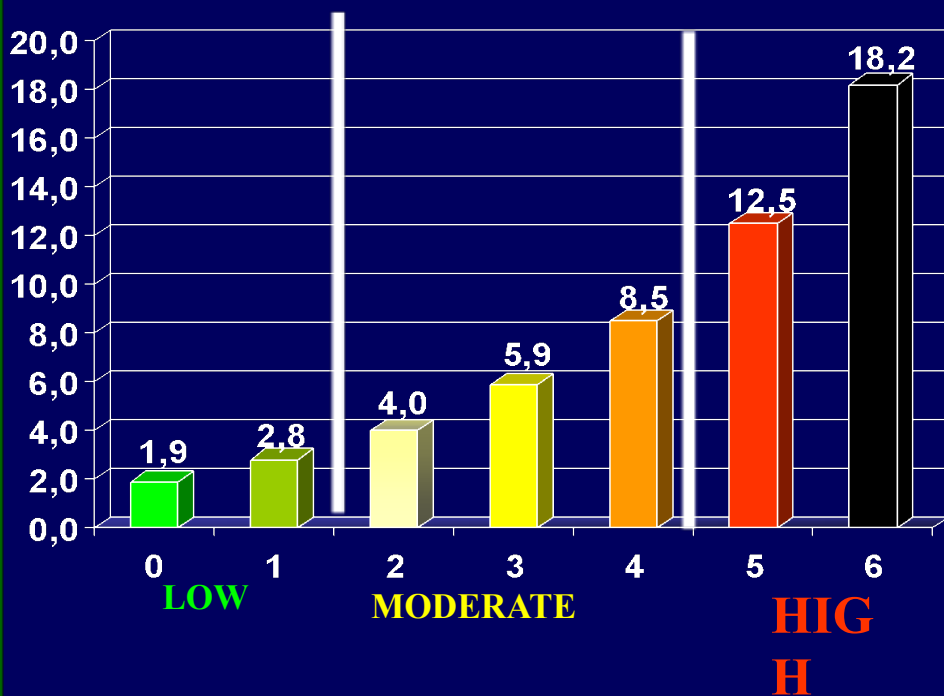
Direct Oral anticoagulation: ANNUAL MAJOR BLEEDS RISK

Warfarin vs New Oral Anticoagulants

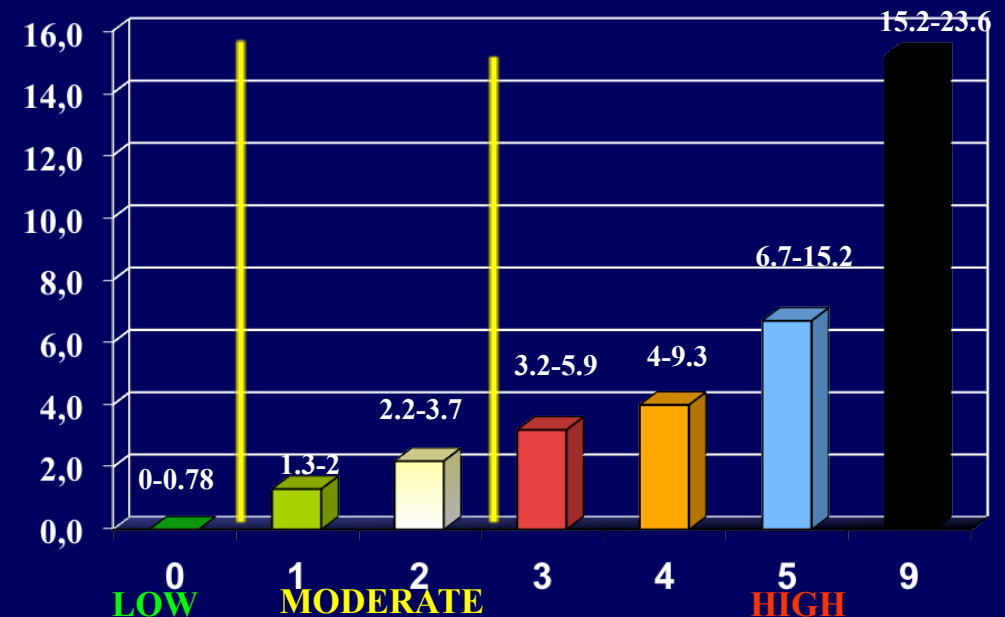


Expected stroke rate per 100 pt/y without antithrombotic therapy

**FROM
CHADS2**



TO CHA2DS2VASC



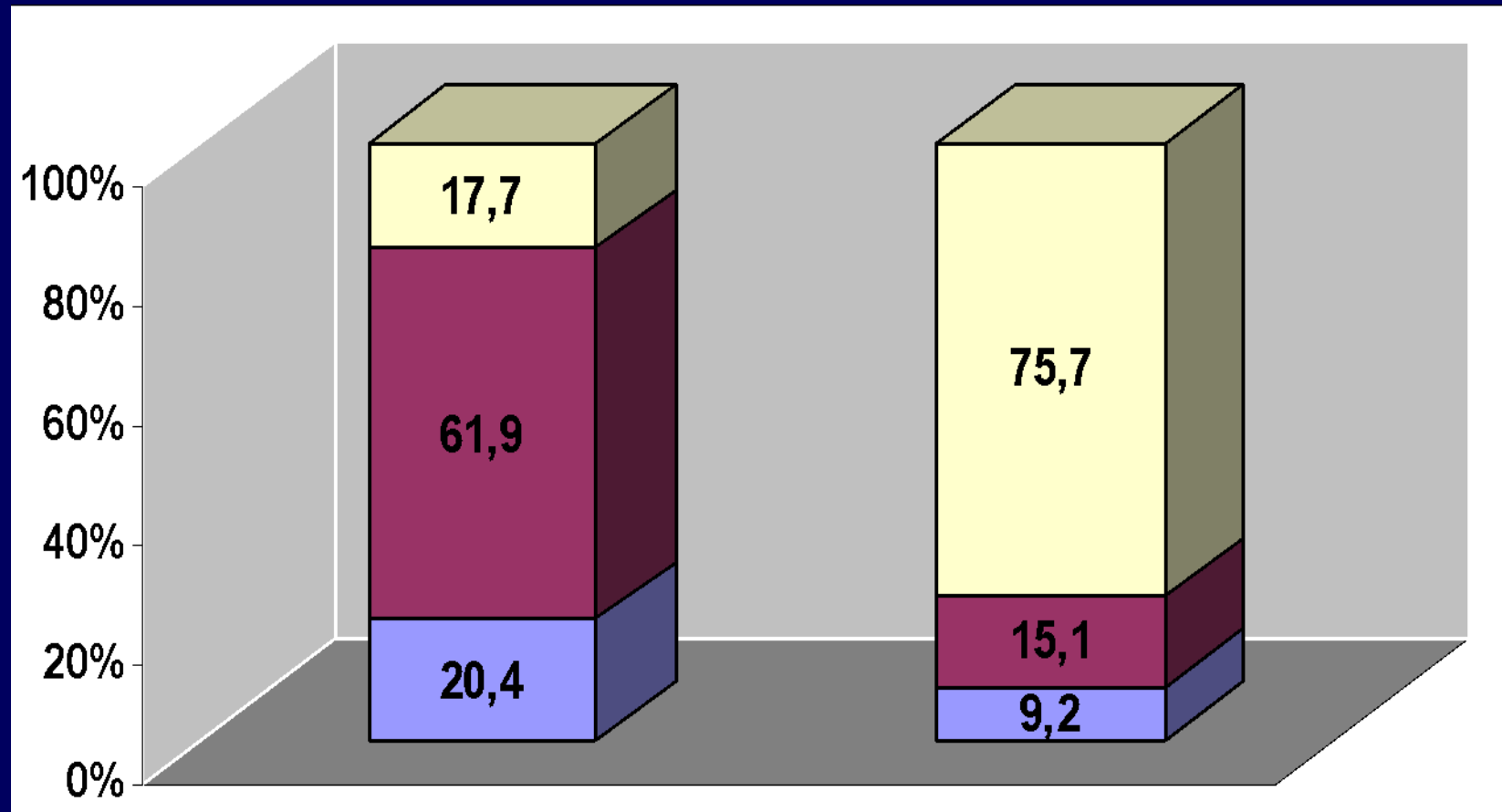
Gage, JAMA 2001; 285:2864-2870

ESC GL for the Management of AF 2010

Risk Categorization for CHADS2 Score and CHA2DS2 VASc Score:

Euro Heart Survey pts who did not receive OAC at baseline

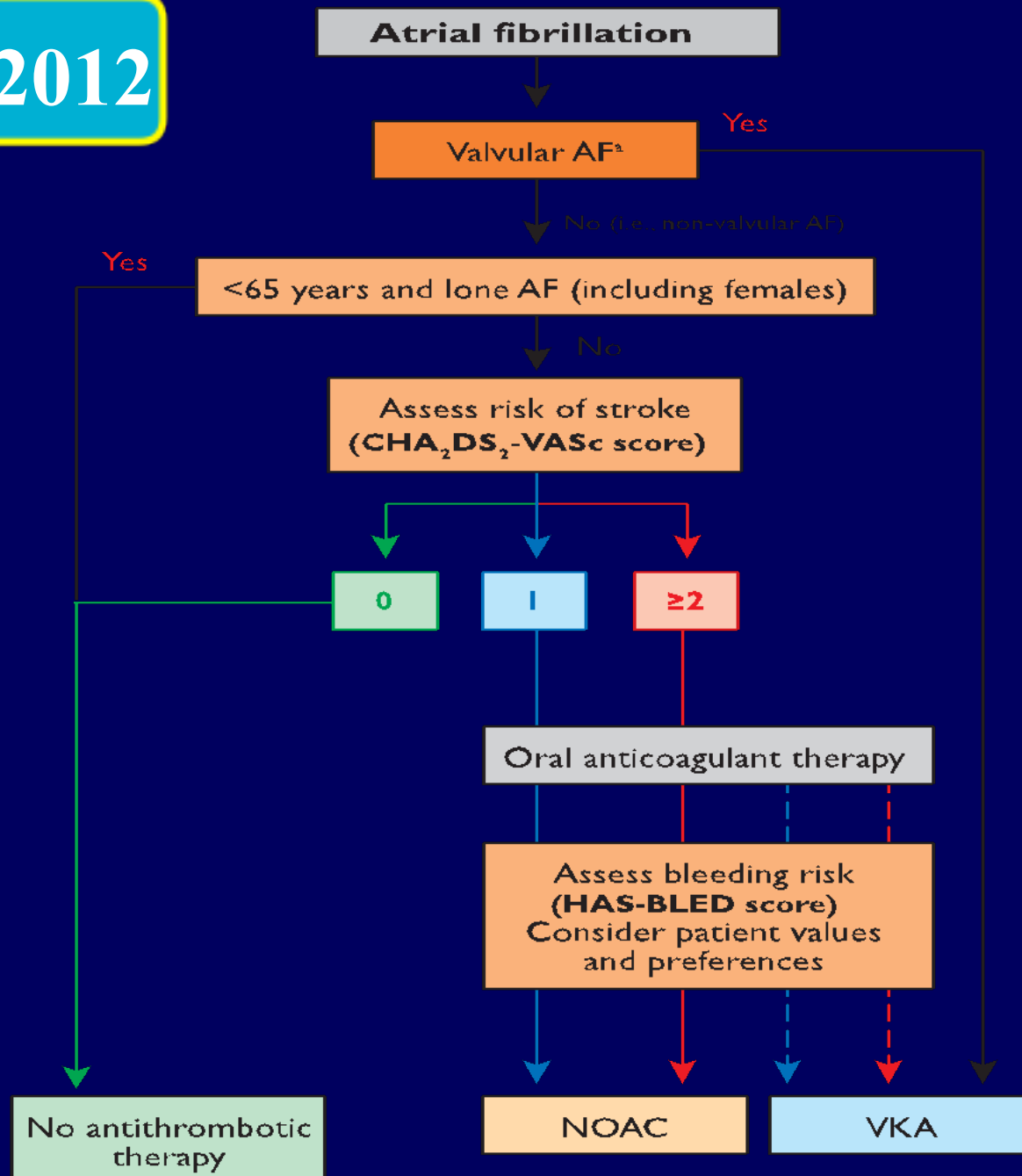
% in Risk of Thromboembol



- High Risk (score ≥ 2)
- Intermediate Risk (score 1)
- Low Risk (score 0)

at

ESC 2012





ESC 2016

**Mechanical heart valve,
moderate/sever mitral stenosis?**

yes

NO

CHA2DS2VASC

0

**no treatment
(IIB)**

**CHA2DS2-VASc
Male: 0
Female: 1**

1

**OAC should be
considered
(IIaB)**

**CHA2DS2-VASc
Male: 1
Female: 2**

**Vitamin K
Antagonist
(IA)**



ESC 2016

**Mechanical heart valve,
moderate/sever mitral stenosis?**

yes

NO

CHA2DS2VASC

0

**no treatment
(IIB)**

**CHA2DS2-VASc
Male: 0
Female: 1**

1

**OAC should be
considered
(IIaB)**

**CHA2DS2-
VASc
Male: 1
Female: 2**

≥ 2

**Oral anticoagulation
indicated**

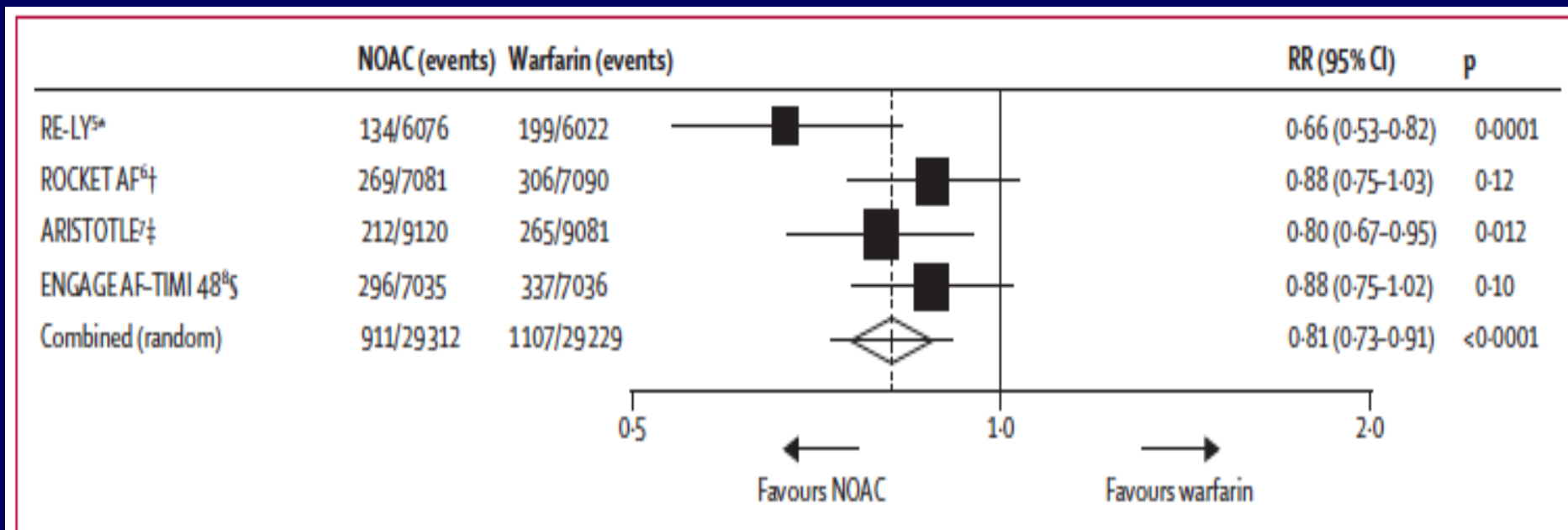
**Direct oral
anticoagulants
(IA)**

**Vitamin K
Antagonist
(IA)**

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



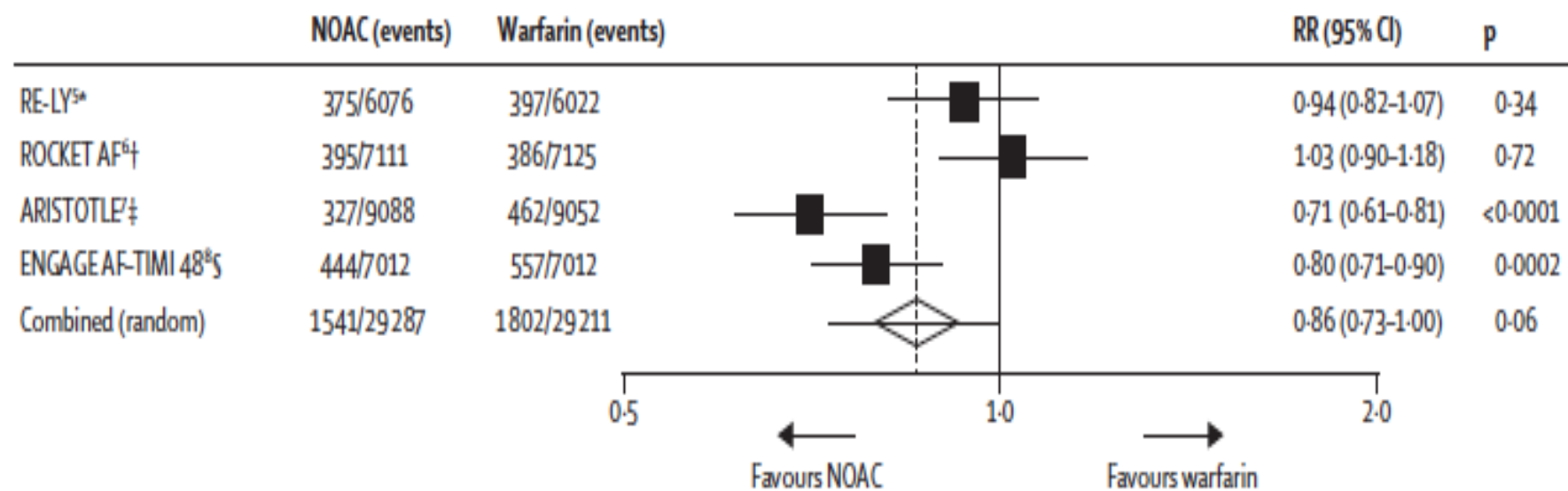
STROKE OR SYSTEMIC EMBOLISM



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



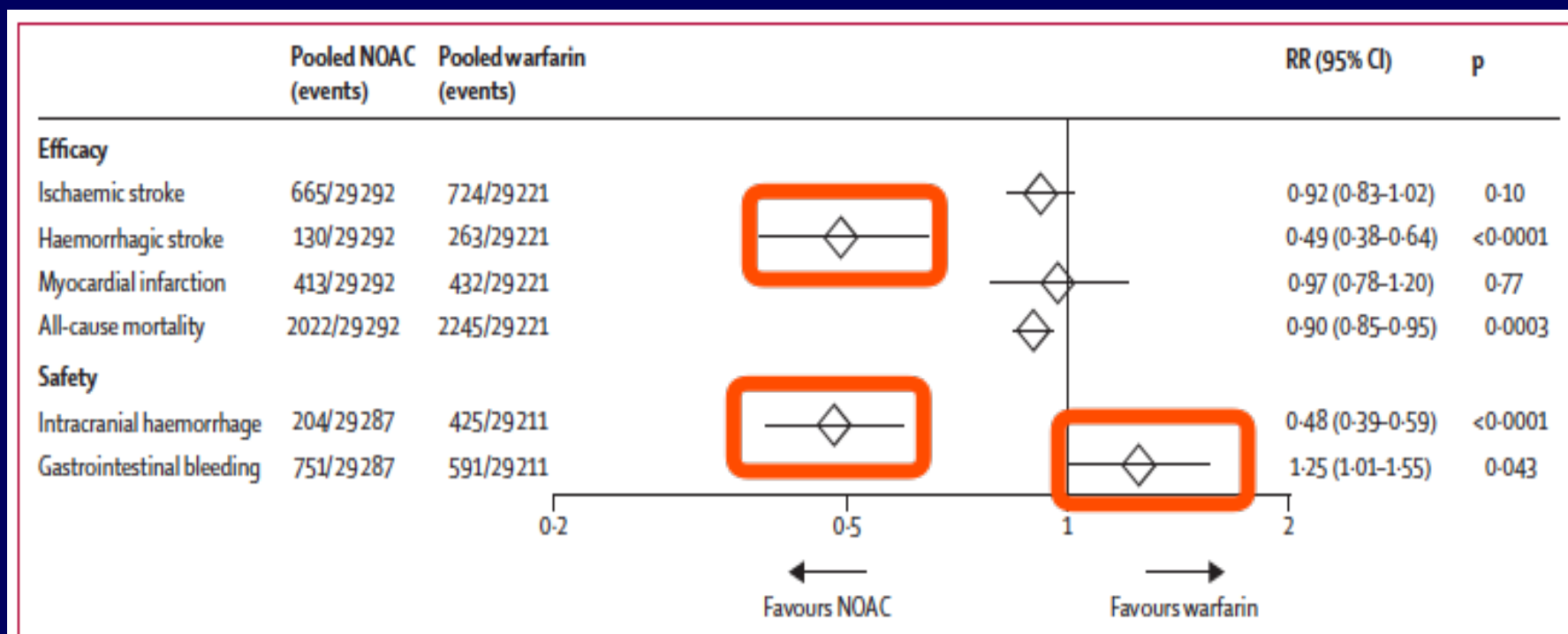
MAJOR BLEEDING



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



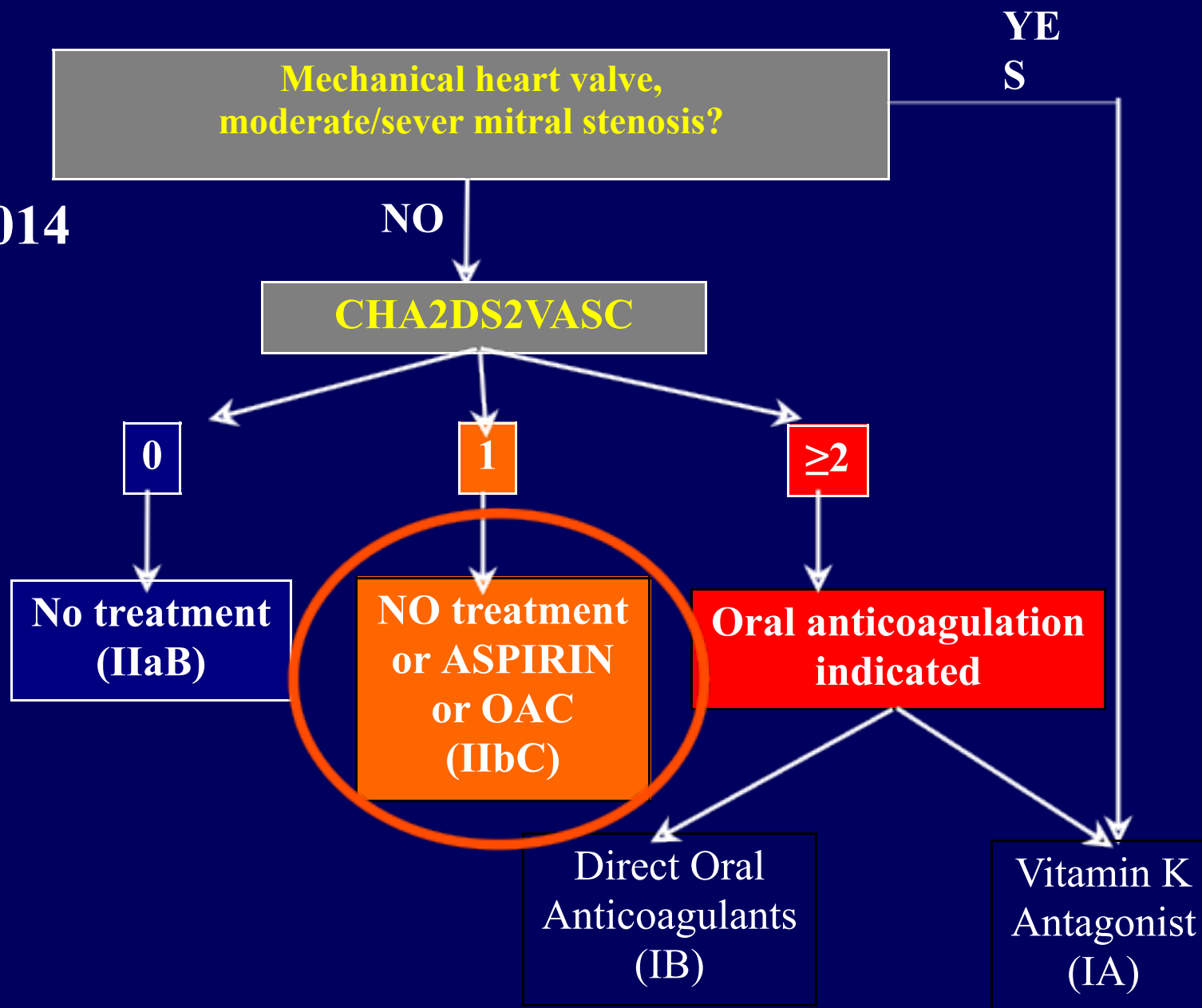
SECONDARY EFFICACY AND SAFETY OUTCOMES



AHA/ACC/HRS Guidelines for the Management of patients with AF



Circulation 2014



HOW TO REDUCE?



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AF ABLATION

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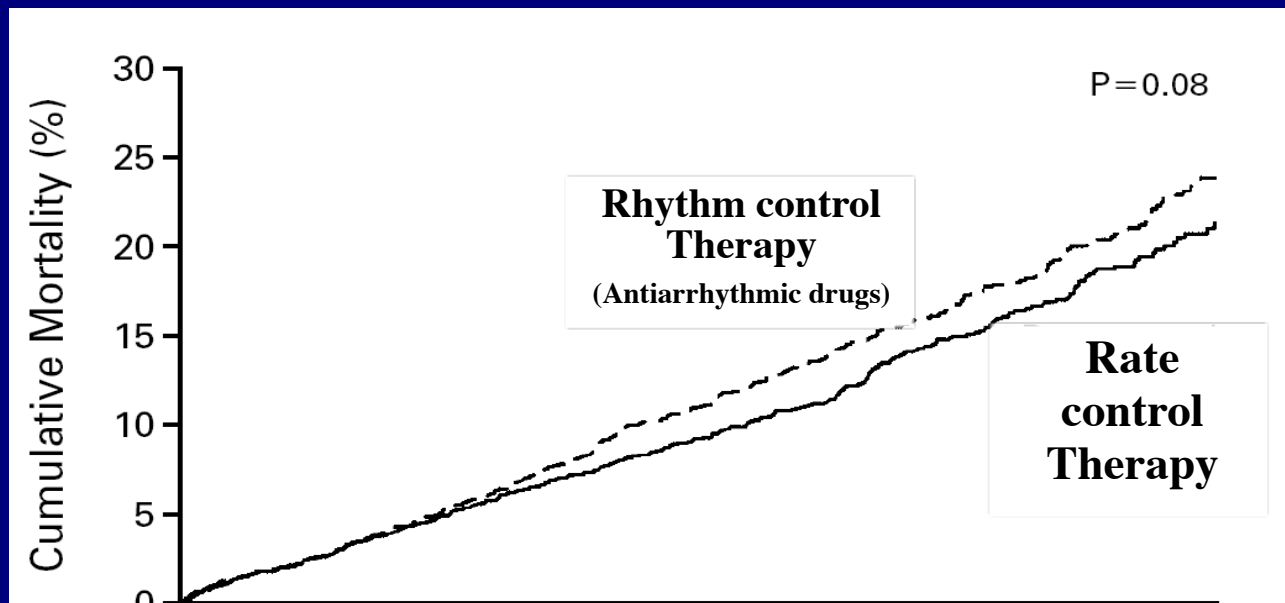
AFFIRM: Total Mortality (at 5 years)

Rate control *vs* Rhythm control

Rate control + TAO *vs* Rhythm control with AAD +/- TAO

4060 pts,
Age 69.7 ± 9 years
528 pts (13%) > 80 y

-70.8% Hypertension
-38.2% Ischemic
-↓ EF 26%
-↑ Left atrium 64,7%



21% pts treated with:
Procainamide, Disopiramide,
Chinidine, Morizine

2 (24)
6 (21)

AFFIRM: Circulation 2004; 109:1509

Covariates associated to survival:

Covariate	p	HR
Warfarin	<0.0001	0.50

Warfarin ↓ of about 50% risk of death

Sinus Rhythm	<0.0001	0.53
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Sinus rhythm ↓ of about 50% risk of death

RS or Warfarin

↓ of about 50%

risk of death; if both of them a risk ↓ of **73%**

ROCKET AF Trial patients enrollment – 14264 pts



Physician's choice of rhythm control

Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation

Physician's choice of rhythm control

Out of 14.264 **ROCKET-AF** pts



Paroxysmal AF

2802 (20%)



?

Rhythm control

176 pts (6,3%)

(cardioversion or ablation)



Persistent AF

11462 (80%)



?

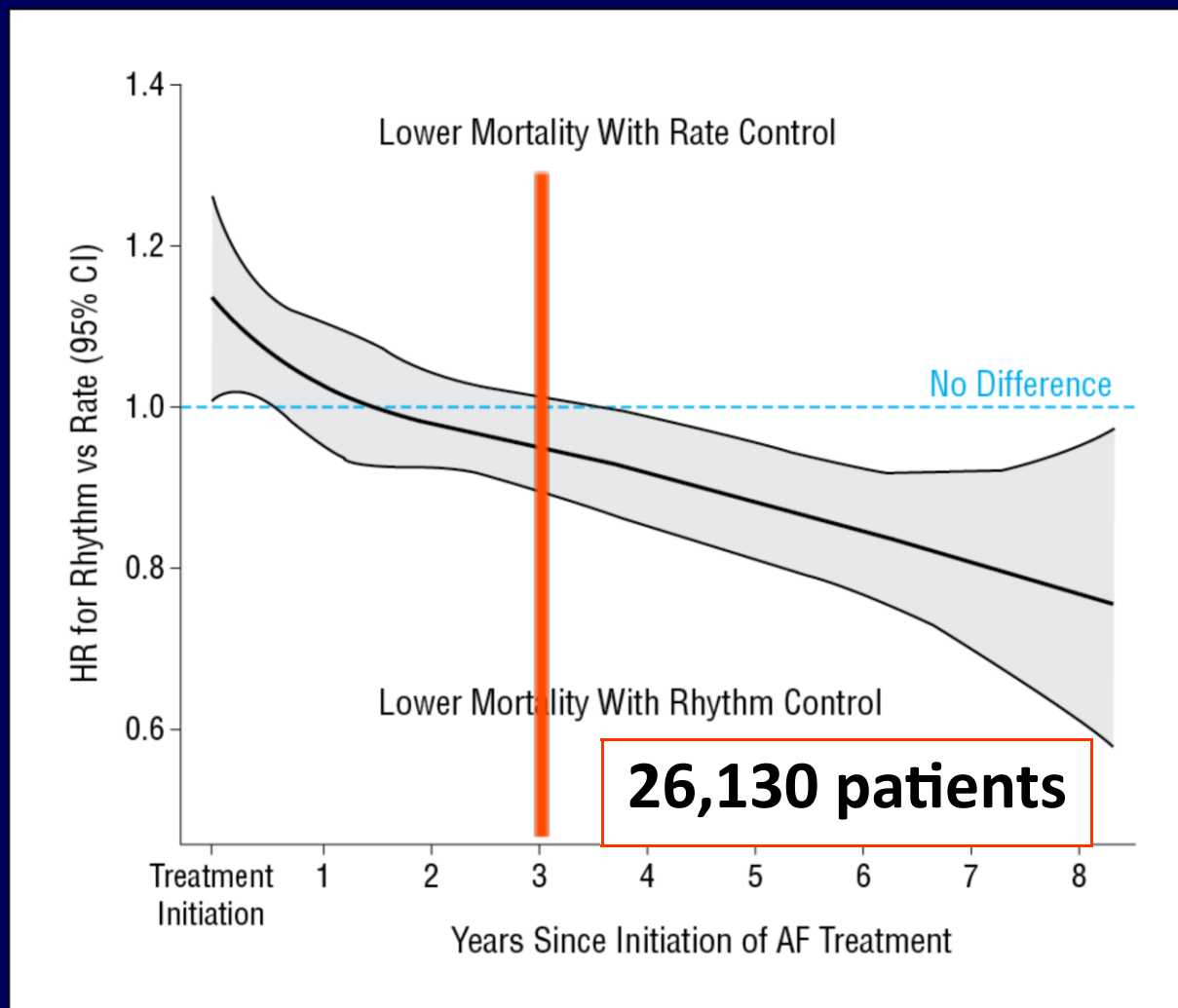
Rhythm control

154 pts (1,3%)

(cardioversion or ablation)

Mortality: rate vs. rhythm control

Population-based administrative databases from Quebec (Canada) **from 1999 to 2007** to select **patients 66 years or older**



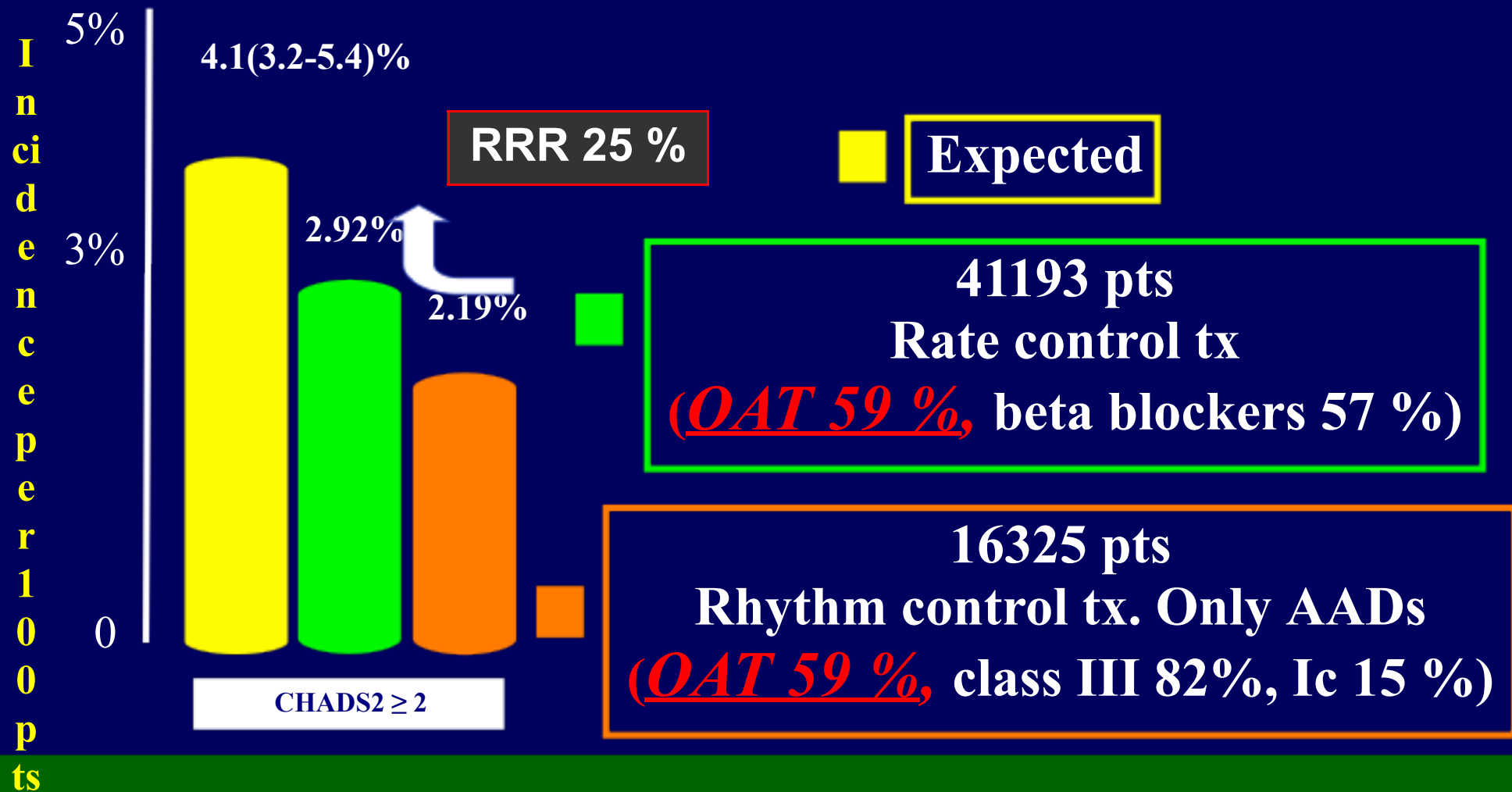
Rhythm Versus Rate Control Therapy and Subsequent Stroke or Transient Ischemic Attack in Patients With Atrial Fibrillation

Meytal Avgil Tsadok, Cynthia A. Jackevicius, Vidal Essebag, Mark J. Eisenberg, Elham Rahme, Karin H. Humphries, Jack V. Tu, Hassan Behloul and Louise Pilote

Circulation 2012;126:2680-87

57518 AF Quebec pts, aged > 65 y, mean CHADS2 2 (1999-2007)

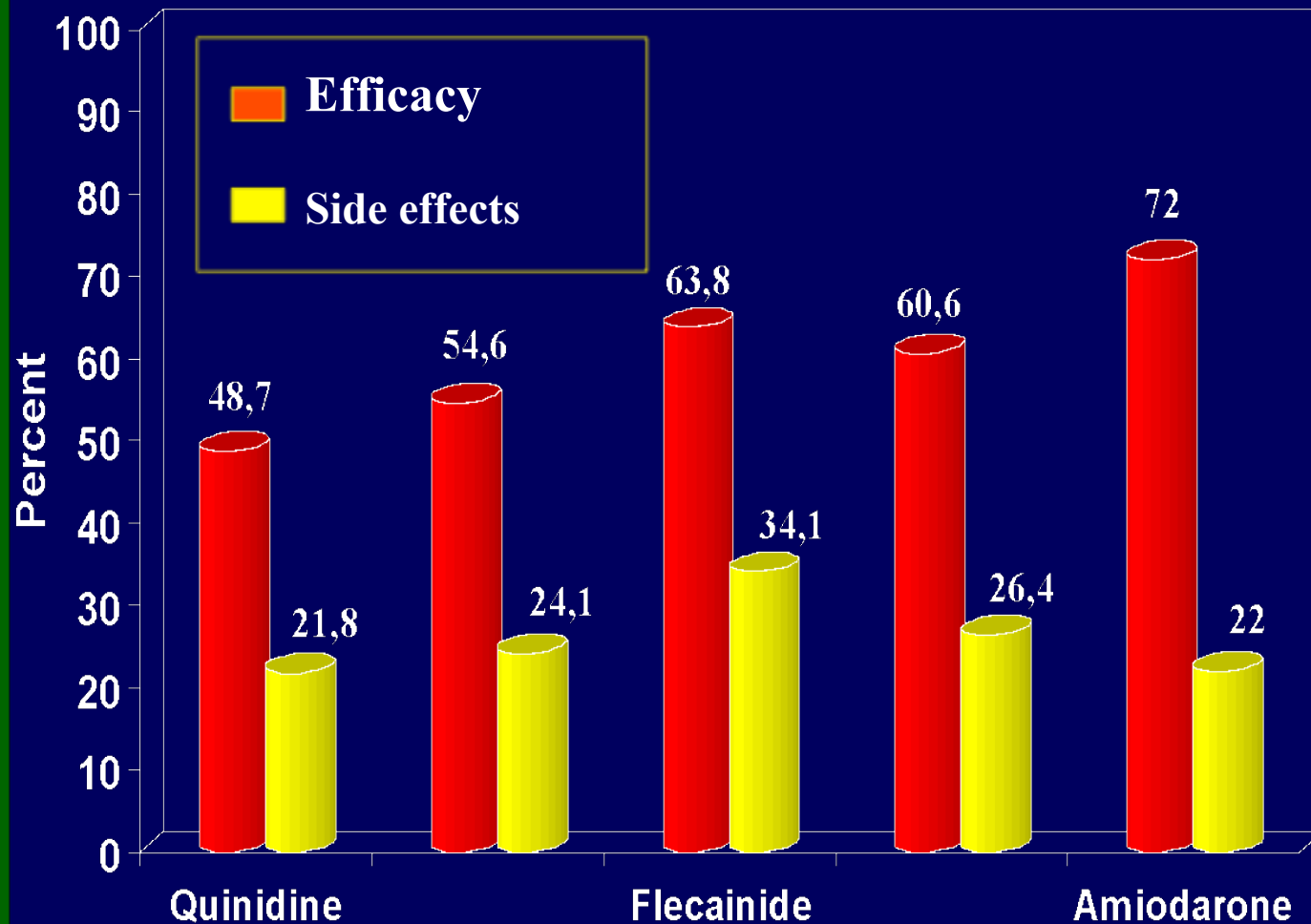
Less incidence of stroke/TIA in rhythm control



**What is the thromboembolic risk
after AF ablation?**

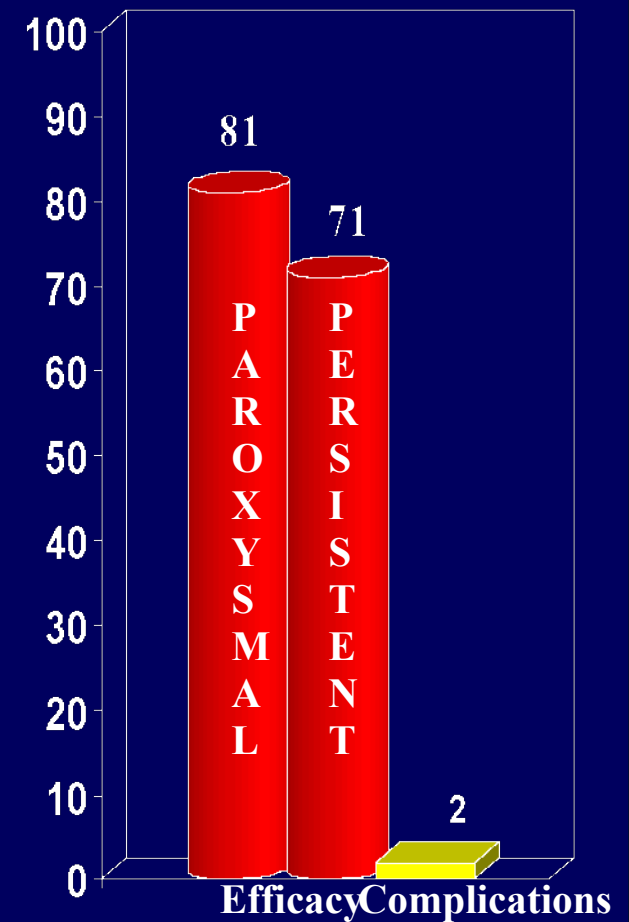
AADs for AF

(~1 year F-up)



AF ablation

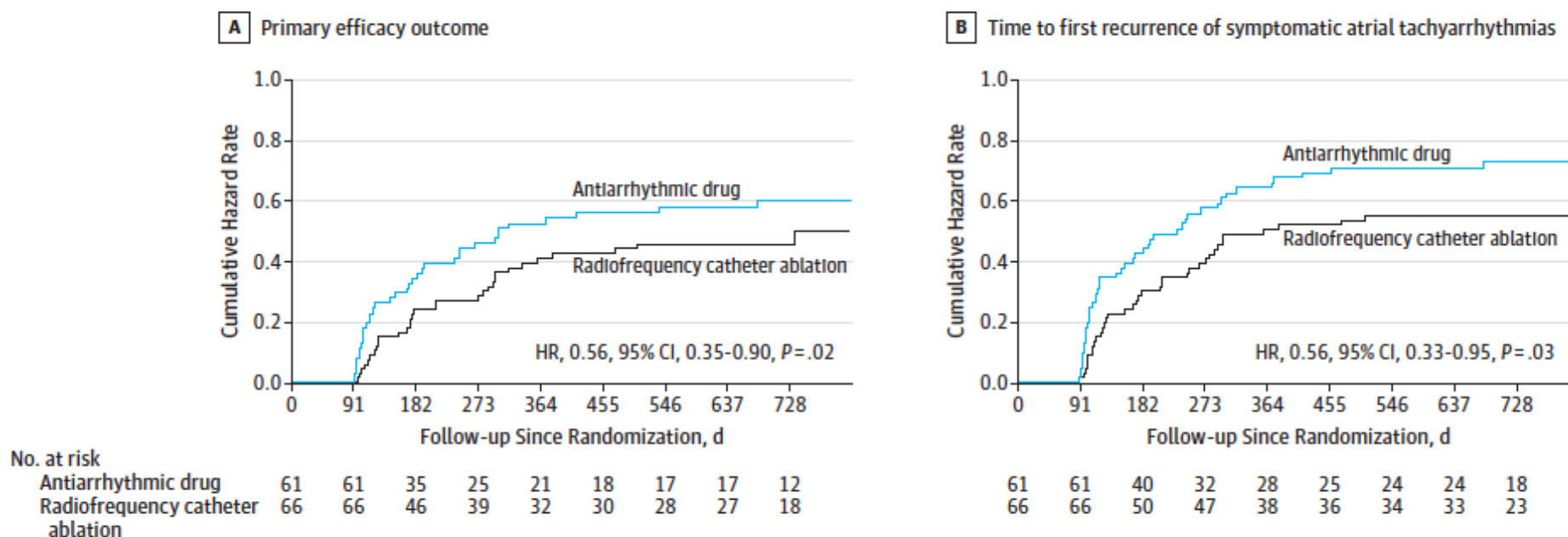
(~1 year F-up)



Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2) A Randomized Trial

Carlos A. Morillo, MD, FRCPC; Atul Verma, MD, FRCPC; Stuart J. Connolly, MD, FRCPC; Karl H. Kuck, MD, FHRS; Girish M. Nair, MBBS, FRCPC; Jean Champagne, MD, FRCPC; Laurence D. Sterns, MD, FRCPC; Heather Beresh, MSc; Jeffrey S. Healey, MD, MSc, FRCPC; Andrea Natale, MD; for the RAAFT-2 Investigators

Figure 2. Kaplan-Meier Curves of Time to First Recurrence of Any Atrial Tachyarrhythmias (A) and Time to First Recurrence of Symptomatic Atrial Tachyarrhythmias (B)



Tachyarrhythmias include atrial fibrillation, tachycardia, and flutter. HR indicates hazard ratio.



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

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

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Endorsed by the European Stroke Organisation (ESO)



ablation, heparin should be given to maintain an activated clotting time >300 s. Anticoagulation should be maintained for at least 8 weeks after ablation for all patients. The true incidence of thromboembolic events after catheter ablation has never been systematically studied and the expected stroke risk has been adopted from non-ablation AF cohorts. Although observational studies suggest a relatively low stroke rate in the first few years after catheter ablation of AF,^{737,771–776} the long-term risk of recurrent AF and the safety profile of anticoagulation in ablated patients need to be considered. In the absence of controlled trial data, OAC after catheter ablation should follow general anticoagulation recommendations, regardless of the presumed rhythm outcome.

Long-term events following atrial fibrillation rate control or transcatheter ablation: a multicenter observational study

Cristina Gallo^a, Alberto Battaglia^a, Matteo Anselmino^a, Francesca Bianchi^c, Stefano Grossi^c, Giulia Nangeroni^a, Elisabetta Toso^a, Luca Gaido^a, Marco Scaglione^b, Federico Ferraris^a and Fiorenzo Gaita^a

JCM 2016

Long-term events following atrial fibrillation rate control or transcatheter ablation: a multicenter observational study

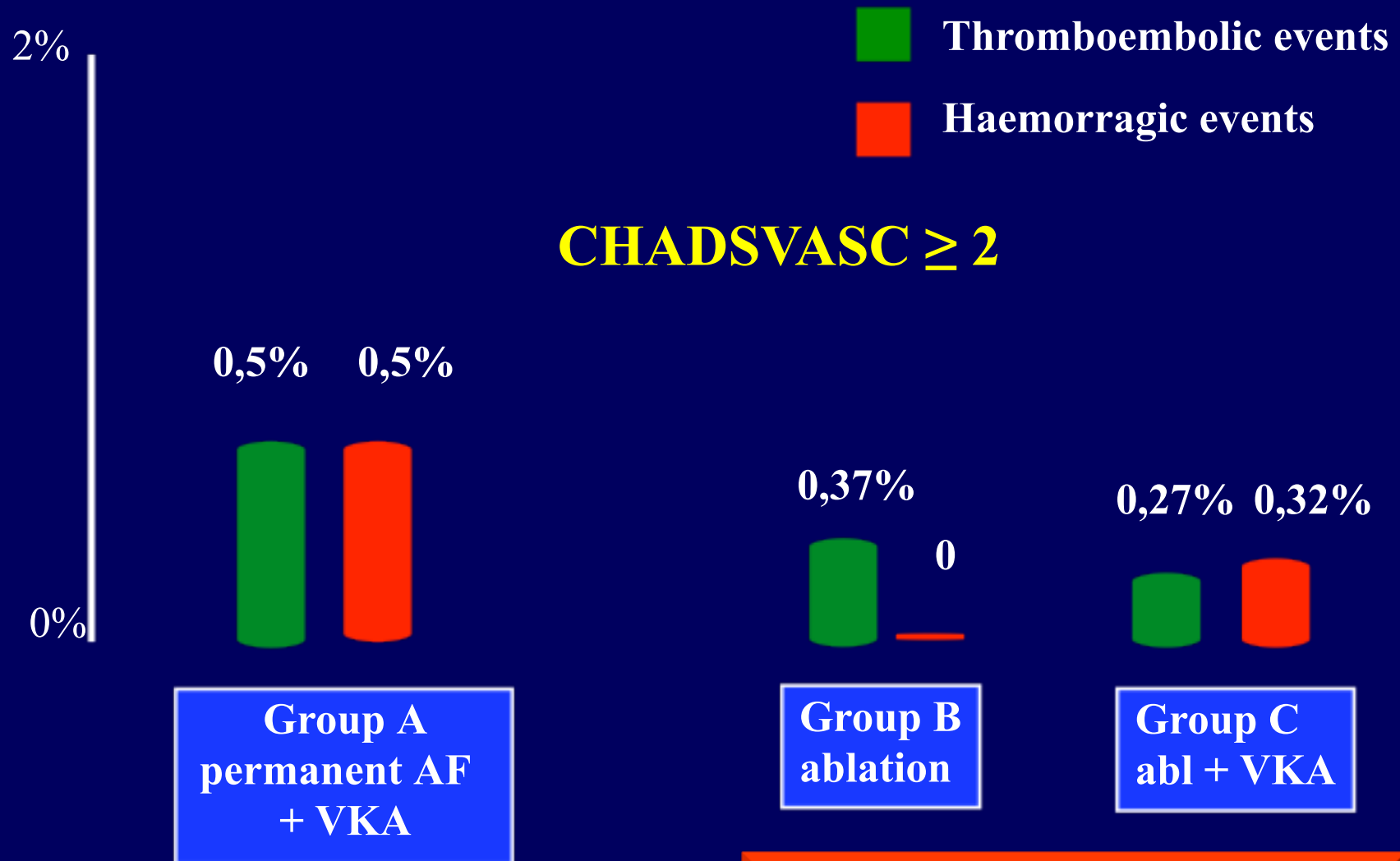
1500 patients – mean CHADSVASC 2.4

- Group A: permanent AF+ VKA* – 500 pts
- Group B: AF ablation – 500 pts
- Group C: AF ablation + VKA* – 500 pts

*** FOR CHADSVASC $\geq$ 2**

Follow up 5 years

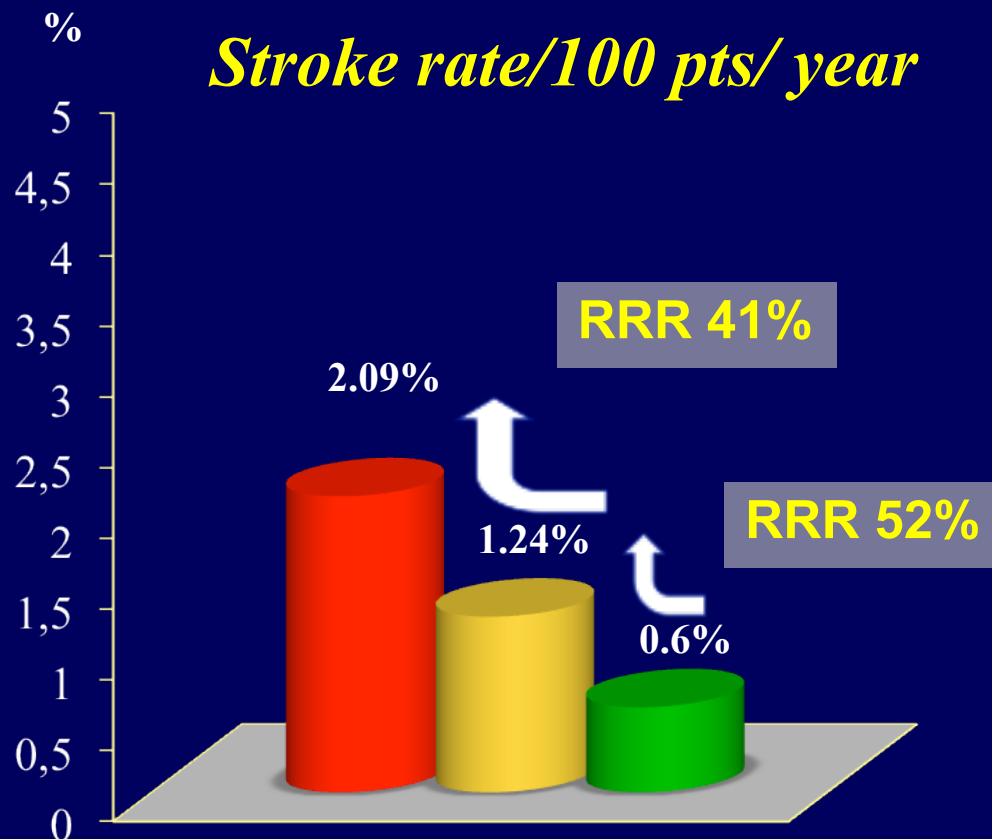
Thromboembolic or Haemorrhagic events/ 100 pts/ year



**36% RRR of TE by
TC ablation**

TE event rate following AF ablation vs oral anticoagulation: a Metanalysis

46 studies, **387379** AF pts, mean FU 2,4 y
MEAN CHADS 2

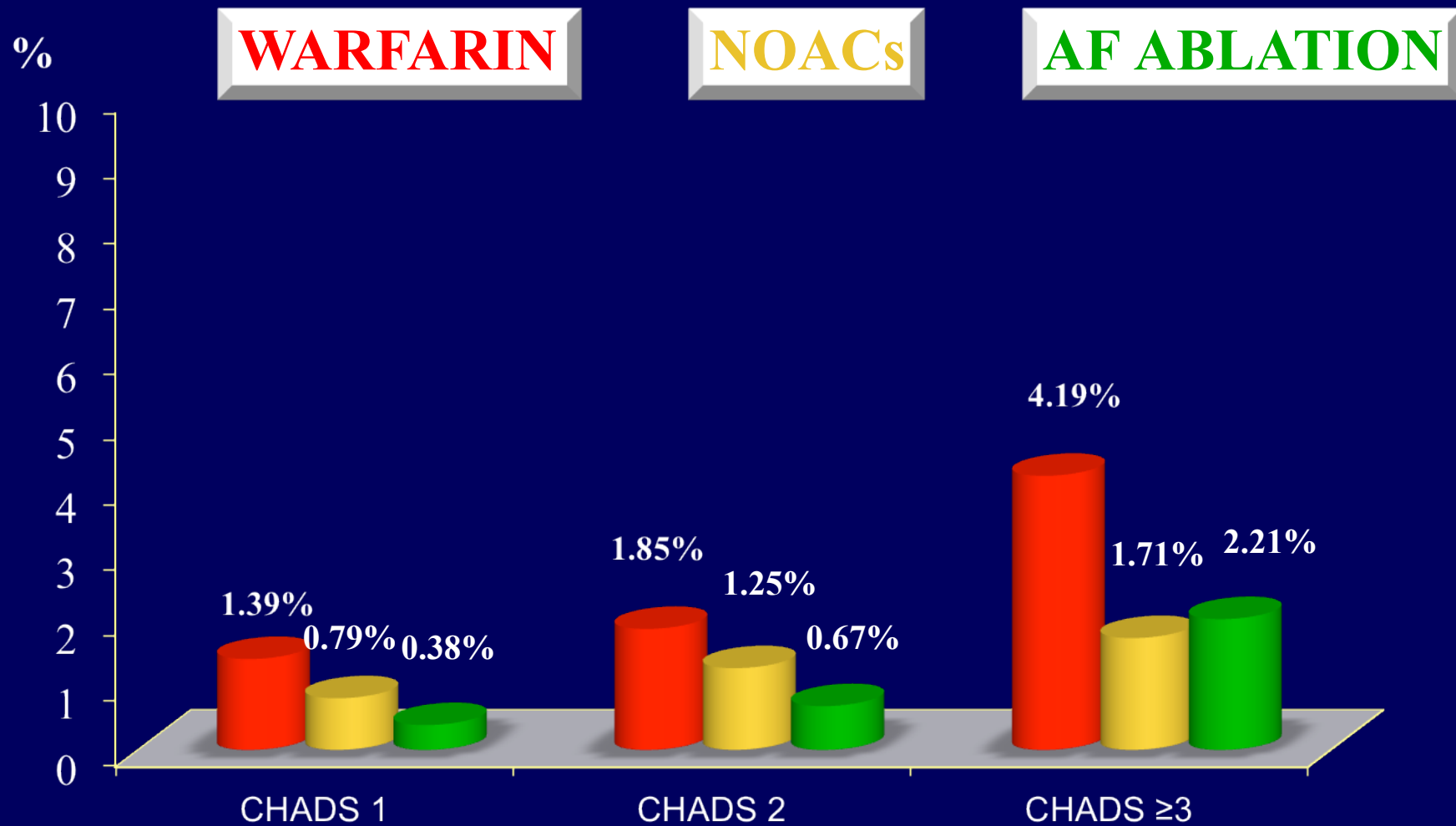


281595 pts WARFARIN

54811 pts NOACs

**50973 pts AF
ABLATION**

TE event rate following AF ablation vs oral anticoagulation according to CHADS score

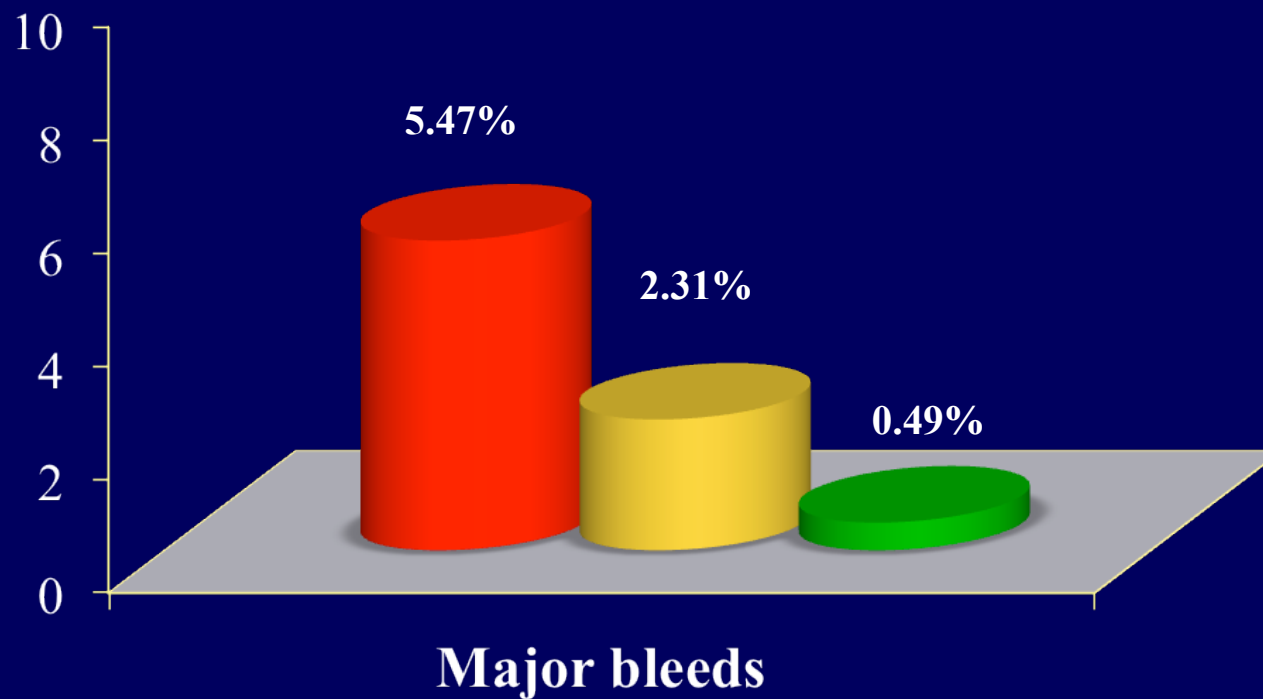


Bleeding event rate following AF ablation vs oral anticoagulation

WARFARIN

NOACs

AF ABLATION



Conclusions

**Oral anticoagulant therapy is the first
therapeutical step in the TE risk prevention**

**Synus rhythm maintenance by means
of TC ablation reduce TE RR of about 50%**

Conclusions

**In pts with CHADS2 0-1
the best therapy to reduce TE risk is
AF ablation without OAT**

**In pts with CHADS2 ≥ 2
the best therapy to reduce TE risk could be
AF ablation associated with OAT**

Thank you for your attention

