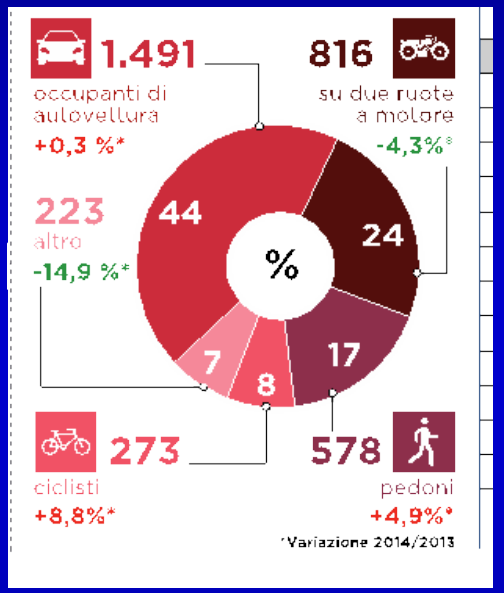
ADVANCES IN CARDIAC ARRHYTHMIAS
and
GREAT INNOVATIONS IN CARDIOLOGY
XXIX GIORNATE CARDIOLOGICHE TORINESI

TURIN
27-28
OCTOBER
2017

Sinus rhythm: a “new” powerful anticoagulant

Prof. Fiorenzo Gaita

IN ITALY 816 DEATHS FOR YEAR BY MOTORCYCLE ACCIDENTS



HOW TO REDUCE?

HOW TO REDUCE?

IN ITALY 196.000 STROKES FOR YEAR

CAUSES OF ISCHEMIC STROKE

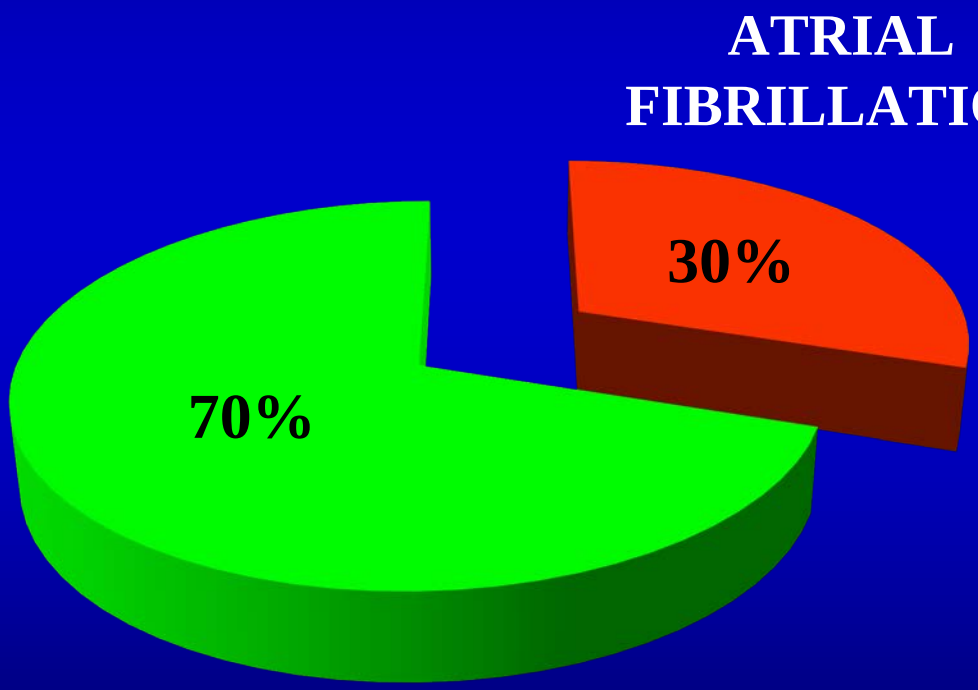
OTHER CAUSES:

30%-50% ATHEROSCLEROSIS OF MAJOR CEREBRAL ARTERIES (ATHEROTHROMBOTIC STROKE)

20% SMALL VESSEL OCCLUSION (LACUNAR STROKE)

5% RARE CAUSES: DISSECTION OF EPIAORTIC VESSELS, VASCULITIS, HEMATOLOGIC DISEASES …

15%-20% UNKNOWN CAUSES



HOW TO REDUCE?

Management cascade for patients with AF

Treatment	Desired outcome	Patient benefit
Acute rate and rhythm control	Hemodynamic stability	
Precipitating factors: lifestyle changes, treatment of underlying cardiovascular conditions	Cardiovascular risk reduction	**Improved life expectancy**
Assess stroke risk: oral anticoagulation if needed	**Stroke prevention**	
Assess heart rate: **rate control**	Symptoms improvement, LV function preservation	**Improved quality of life, functional capacity**
Assess symptoms and comorbidities: **rhythm control** (antiarrhythmic drugs, cardioversion, TC ablation)	Symptoms improvement, comorbidities prevention	

ESC 2016 AF guidelines

AFFIRM: Total Mortality (at 5 years)

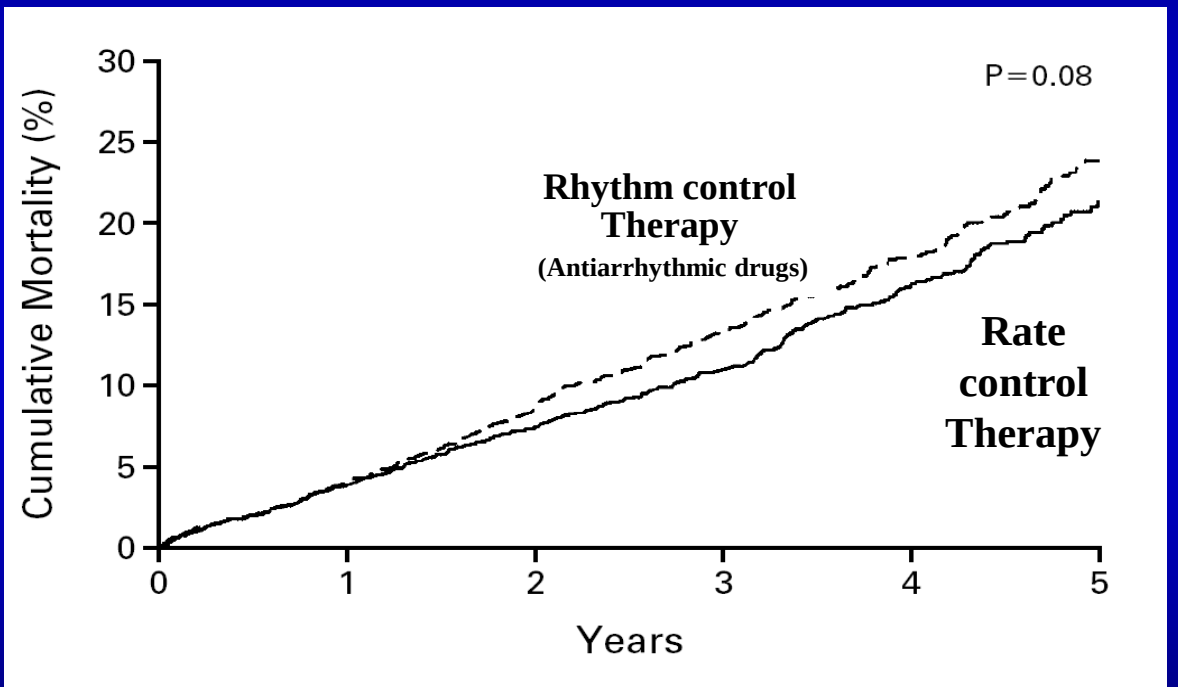
Rate control *vs* Rhythm control

4060 pts,

Age 69.7±9 years

528 pts (13%) > 80 y

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



No. of Deaths		number (percent)				
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)

Mean FU: 3,5 y

New Engl. J. Med 2002;347:1825–1833

AFFIRM:

Circulation 2004; 109:1509

Covariates associated to survival:

Covariate	p	HR
Warfarin	<0.0001	0.50

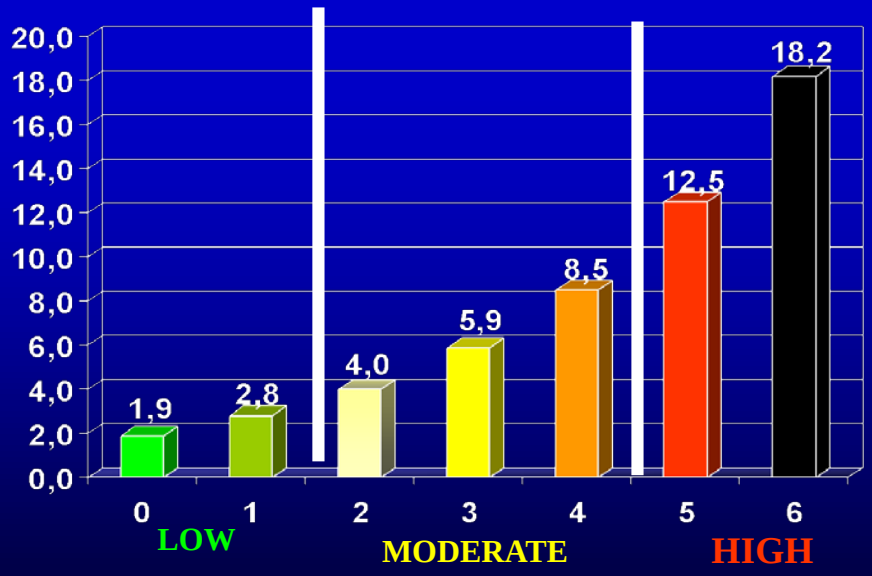
Warfarin ↓of about 50% risk of death

Management of anticoagulation therapy

Using CHADS Score

Congestive heart failure	1
Hypertension	1
Age > 75 years	1
Diabetes mellitus	1
Prior Stroke or TIA	2

Expected stroke rate ***per 100 pts/y***
without antithrombotic therapy



Gage, JAMA 2001; 285:2864-2870

ESC 2010

Recommanded antithrombotic therapy

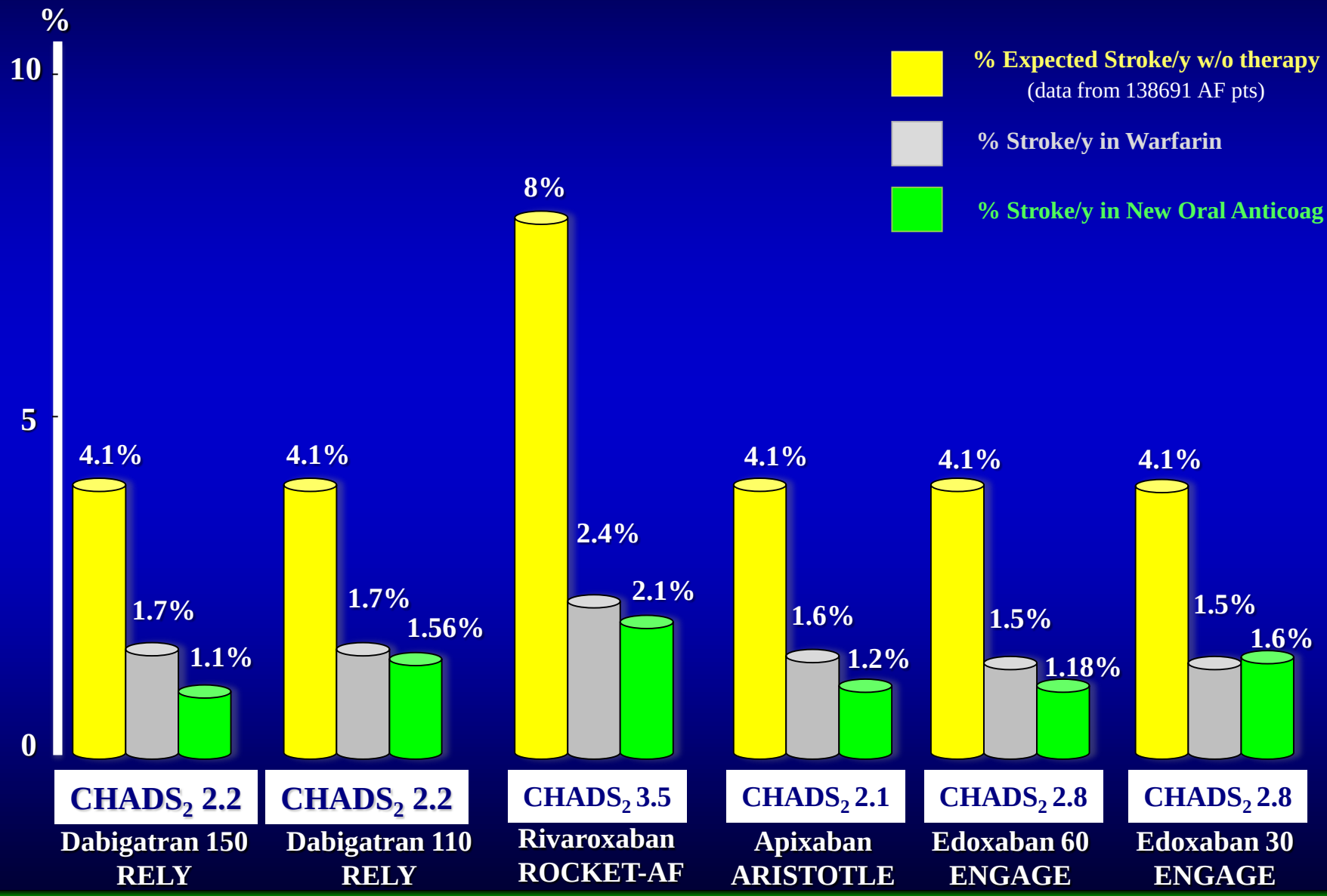
$CHADS_2$ score	Antithrombotic therapy
≥ 2	Oral Anticoagulation
1	Either OAC or aspirin 75-325 mg.
0	Aspirin 75-325 mg

ACC/AHA/ESC AF Guidelines 2010

	DABIGATRAN 150 bid or 110 bid	APIXABAN 5 bid or 2.5 bid	RIVAROXABAN 20 or 15 od	EDOXABAN 30 or 60 od
Name	***Pradaxa 2009***	***Eliquis 2012***	***Xarelto 2011***	***Lixiana 2015***
Mean CHADS	**2.1**	**2.1**	**3.5**	**2.8**
Bioavailability	**7%**	**60%**	**60-80%**	**40%**
Half-life (T ½)	**12-17 h**	**12 h**	**5-9 h young 11-13 h elderly**	**10-14**
T max h	**2-4 h**	**3-4 h**	**2-4 h**	**1-5 h**
Clearence	**80% renal**	**25% renal 75% biliary**	**60% renal 33% biliary**	**40% renal**
Drug interaction P-gp competition CYP3A4 inhibition	**Amiodarone (↑) Quinidine (↑) Verapamil (↑)**	**Diltiazem (↑) Ketoconazolo(↑)**	**Ritonavir(↑) Ketokonazole(↑) Quinidine(↑)**	**Quinidine(↑) Verapamil(↑)**

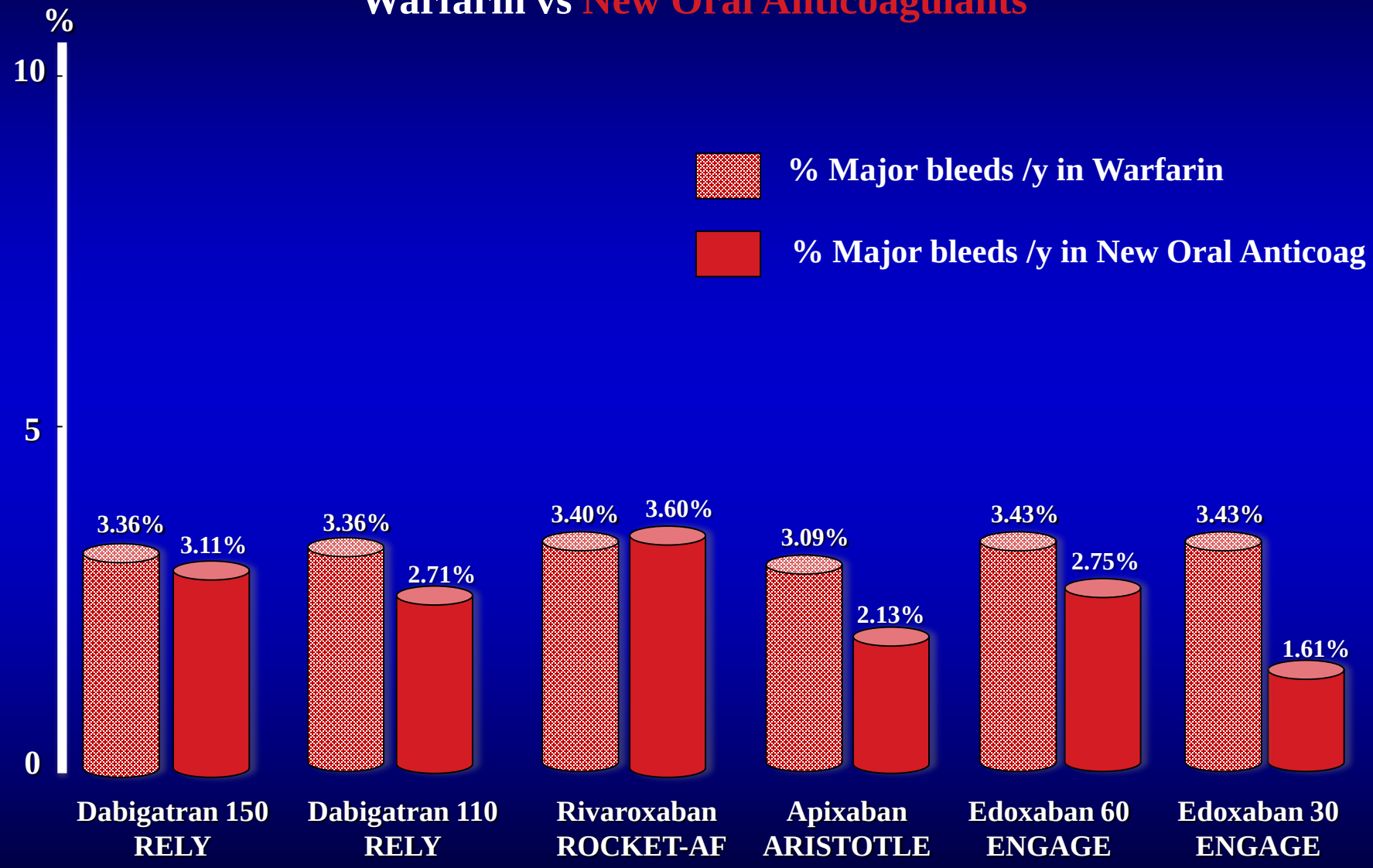
NON VALVULAR AF: ANNUAL THROMBOEMBOLIC RISK

Expected vs Warfarin vs New Oral Anticoagulants



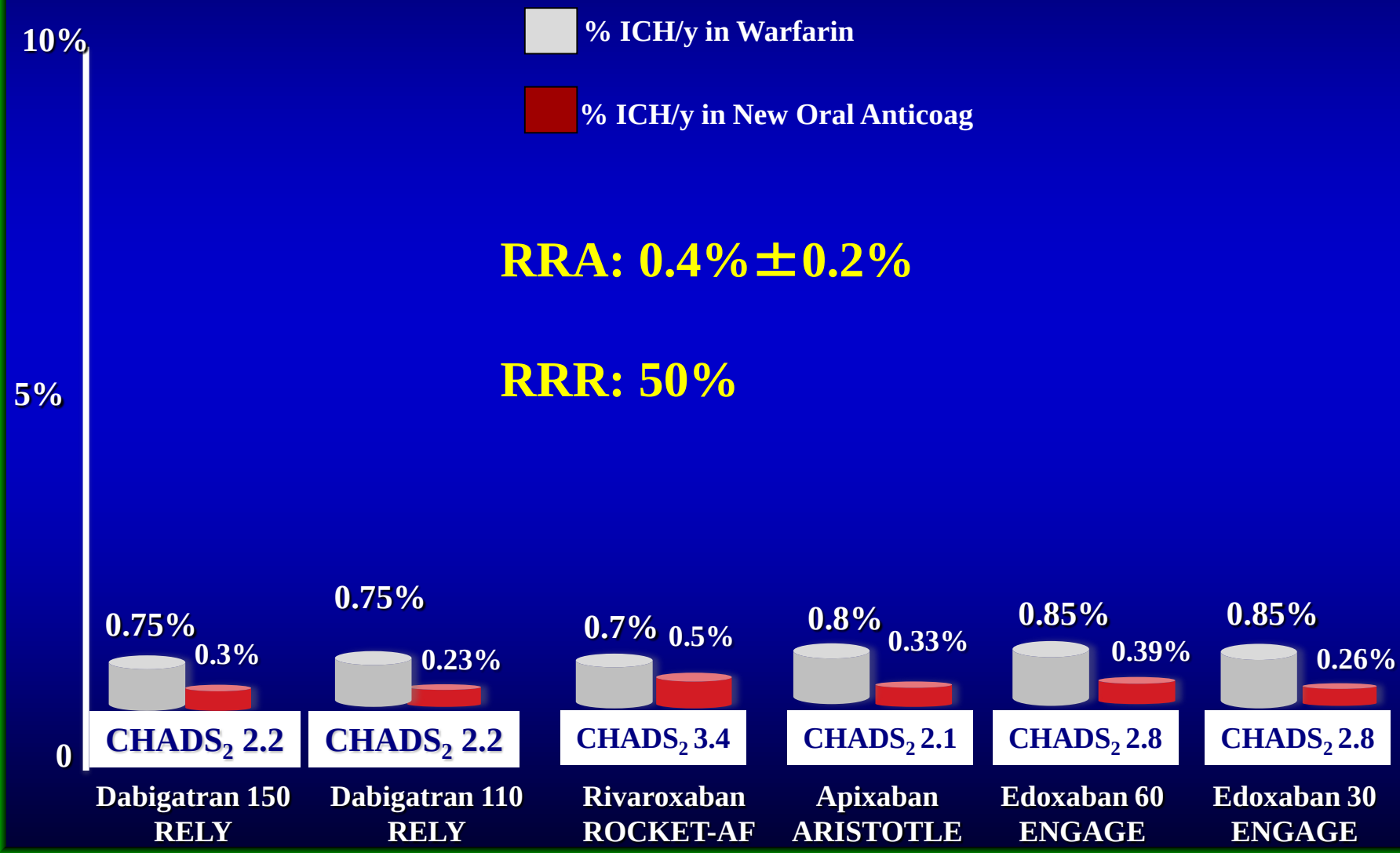
Direct Oral anticoagulation: ANNUAL MAJOR BLEEDS RISK

Warfarin vs New Oral Anticoagulants



ANNUAL INTRACRANIAL HEMORRAGE RISK

Warfarin vs New Oral Anticoagulants

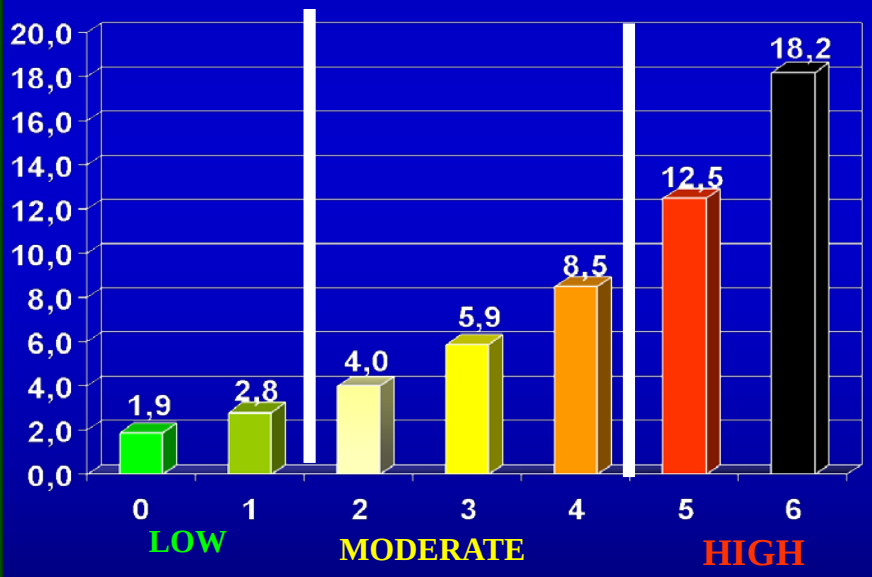


Expected stroke rate per *100 pt/y* without antithrombotic therapy

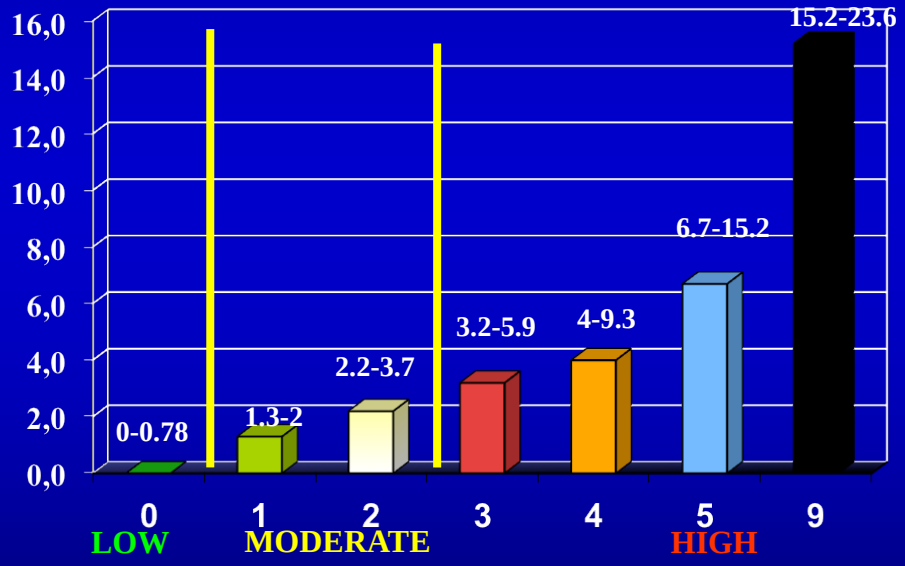
FROM $CHADS_2$

TO CHA_2DS_2VASC

Gage, JAMA 2001

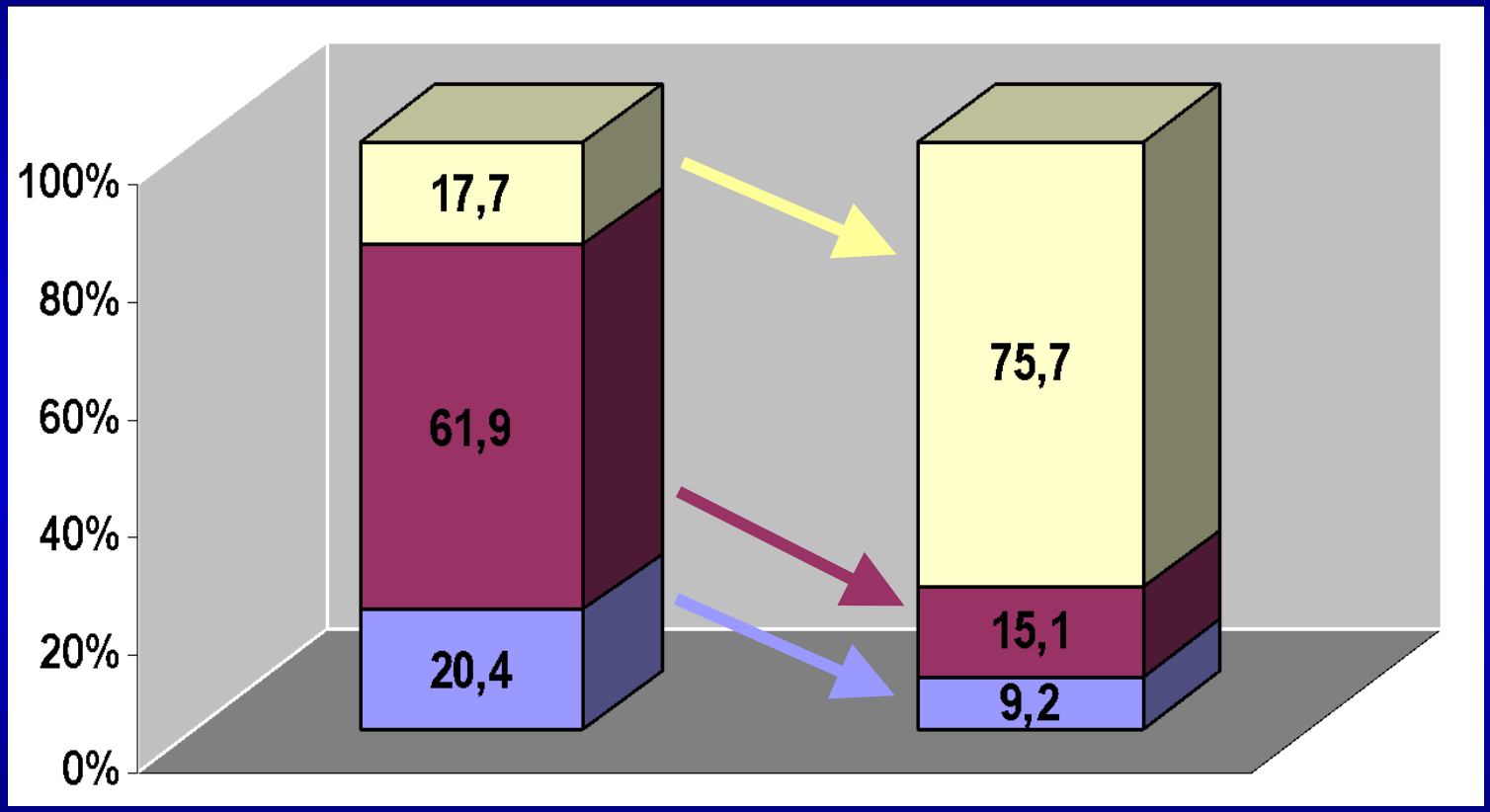


ESC GL for AF 2010



Risk Categorization for $CHADS_2$ Score and CHA_2DS_2 VASc Score:

Euro Heart Survey pts who did not receive OAC at baseline



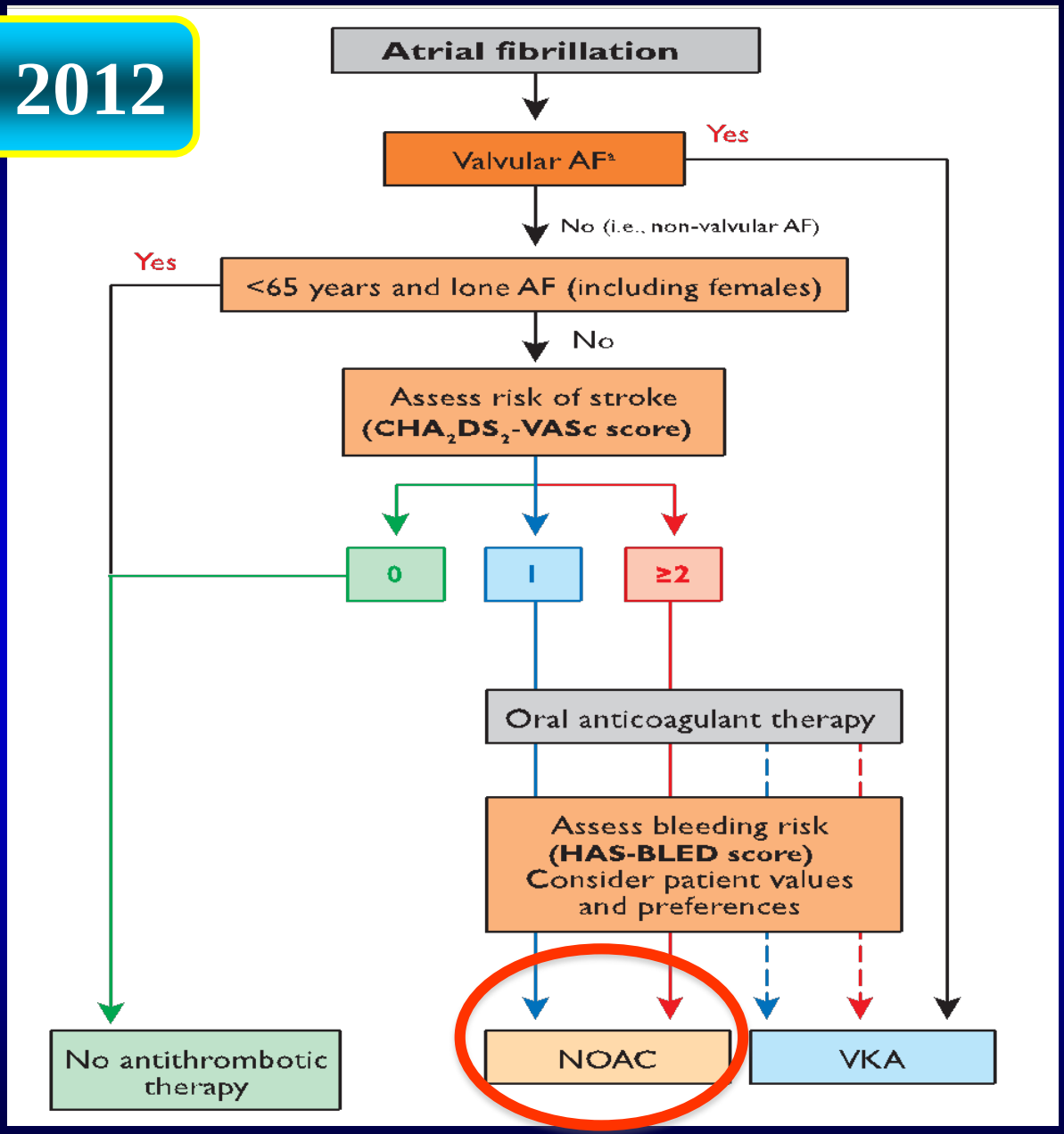
High **Risk (score ≥** 2)

Intermediate Risk (score 1)

Low Risk (score 0)

CHEST 2010; 137(2):263–272

ESC 2012



2012 Update of the ESC AF Guidelines

ESC 2016

Mechanical heart valve, moderate/sever mitral stenosis?

yes

NO

CHA_2DS_2VASC

- **0** → **no treatment (IIIB)**
- **1** → **OAC should be considered (IIaB)**
- **≥2** → **Oral anticoagulation indicated**
  - Direct oral anticoagulants (IA)
  - Vitamin K Antagonist (IA)

ESC AF Guidelines 2016

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

Circulation 2014

Mechanical heart valve, moderate/sever mitral stenosis?

YES

NO

CHA2DS2VASC

0

1

≥2

No treatment (IIaB)

NO treatment or ASPIRIN or OAC (IIbC)

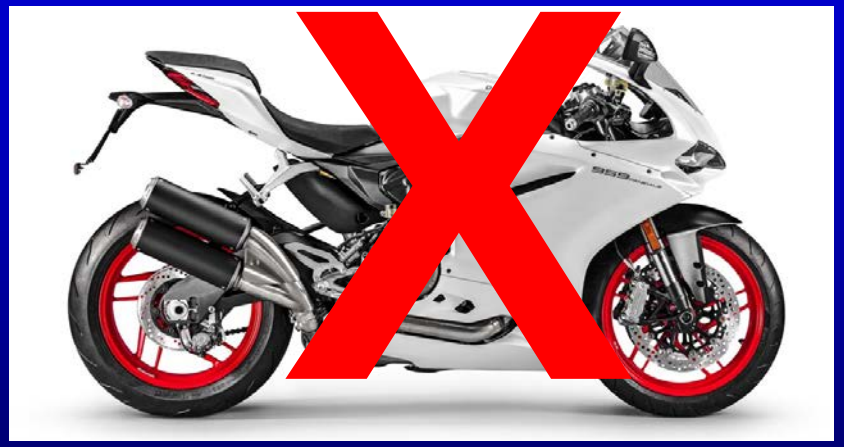
Oral anticoagulation indicated

Direct Oral Anticoagulants (IB)

Vitamin K Antagonist (IA)

HOW TO REDUCE EVEN MORE THE RISK?

ATRIAL FIBRILLATION



ANTICOAGULANT THERAPY

SINUS RHYTHM:

DRUGS OR AF ABLATION

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

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	Persistent AF
2802 (20%)	11462 (80%)
?	?
Rhythm control	Rhythm control
176 pts (6,3%)	154 pts (1,3%)
(cardioversion or ablation)	(cardioversion or ablation)

Piccini JP; J Am Coll Cardiol 2013

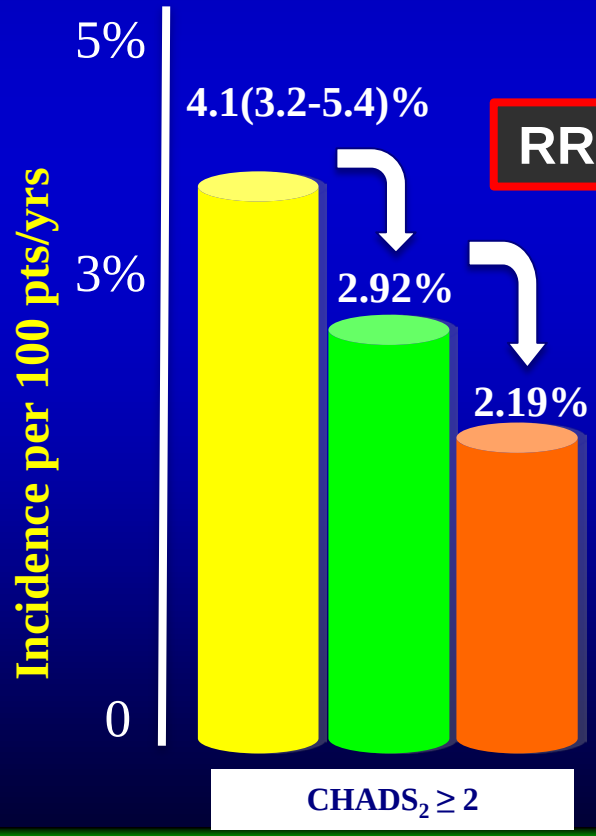
Rhythm Versus Rate Control Therapy and Subsequent Stroke or Transient Ischemic Attack in Patients With Atrial Fibrillation

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

Circulation 2012;126:2680-87

***57518** AF Quebec pts, aged > 65 y, mean CHADS$_2$ 2 (1999-2007)*

Less incidence of stroke/TIA in rhythm control



Expected

41193 pts

Rate control tx

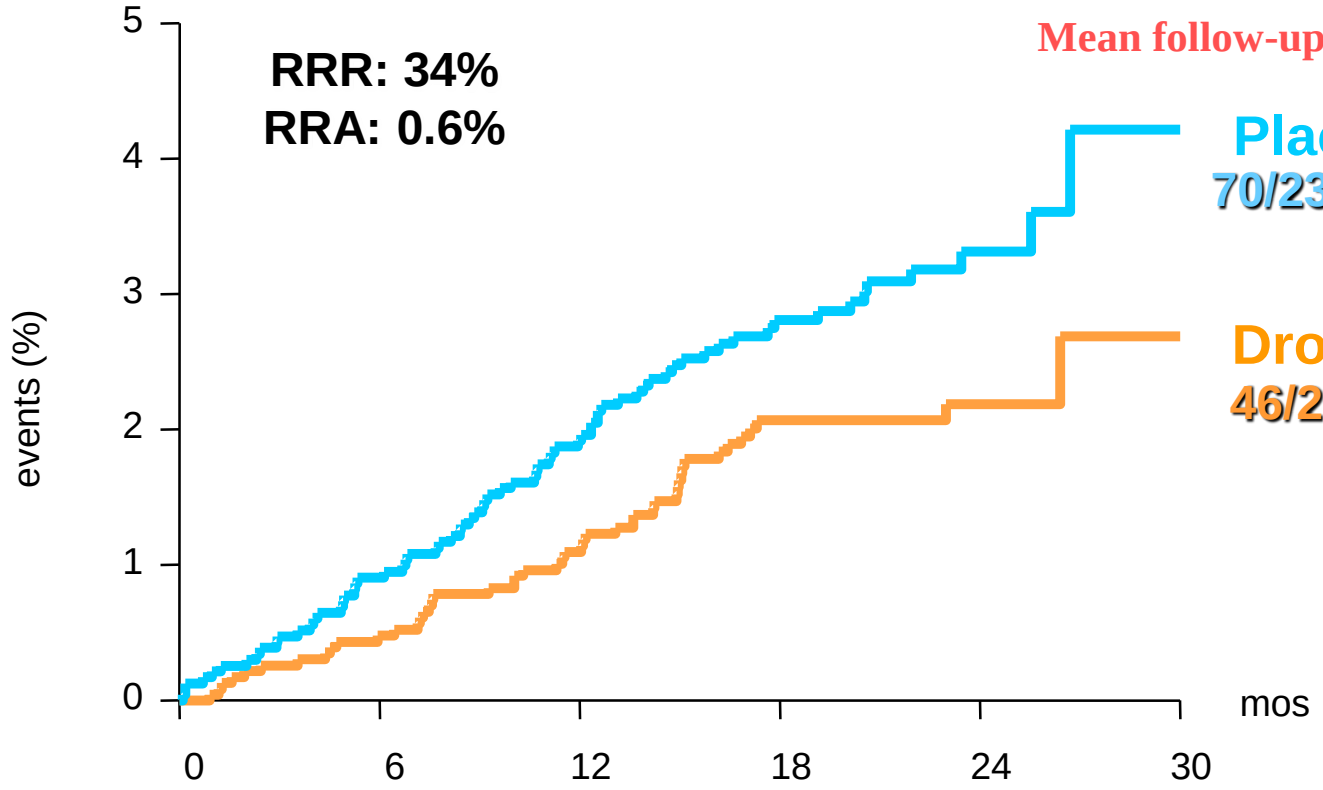
(*OAT 59 %,* beta blockers 57 %)

16325 pts

Rhythm control tx. Only AADs

(*OAT 59 %,* class III 82%, Ic 15 %)

Reduction of Stroke with antiarrhythmic drugs



Pz a rischio						
Placebo	2327	2275	2220	1598	618	6
Dronedarone	2301	2266	2223	1572	608	4

ATHENA. Circulation 2009;120:1174-1180

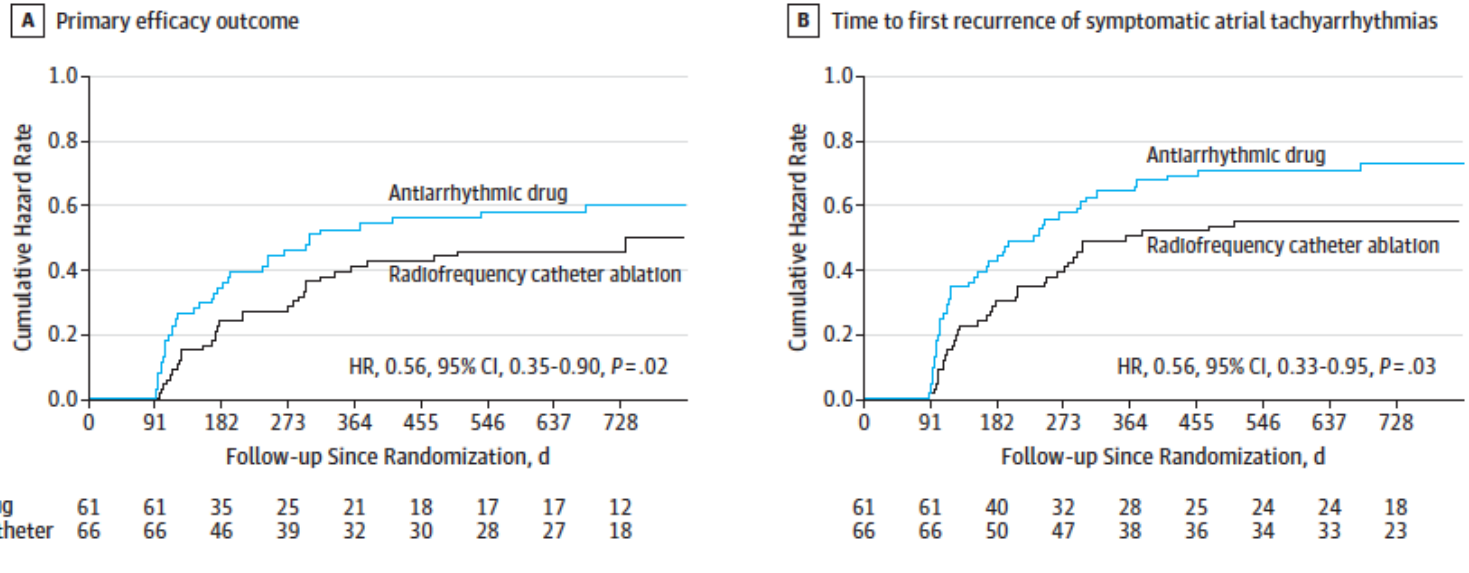
What is the thromboembolic risk after AF ablation?

Original Investigation

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.

JAMA 2014

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

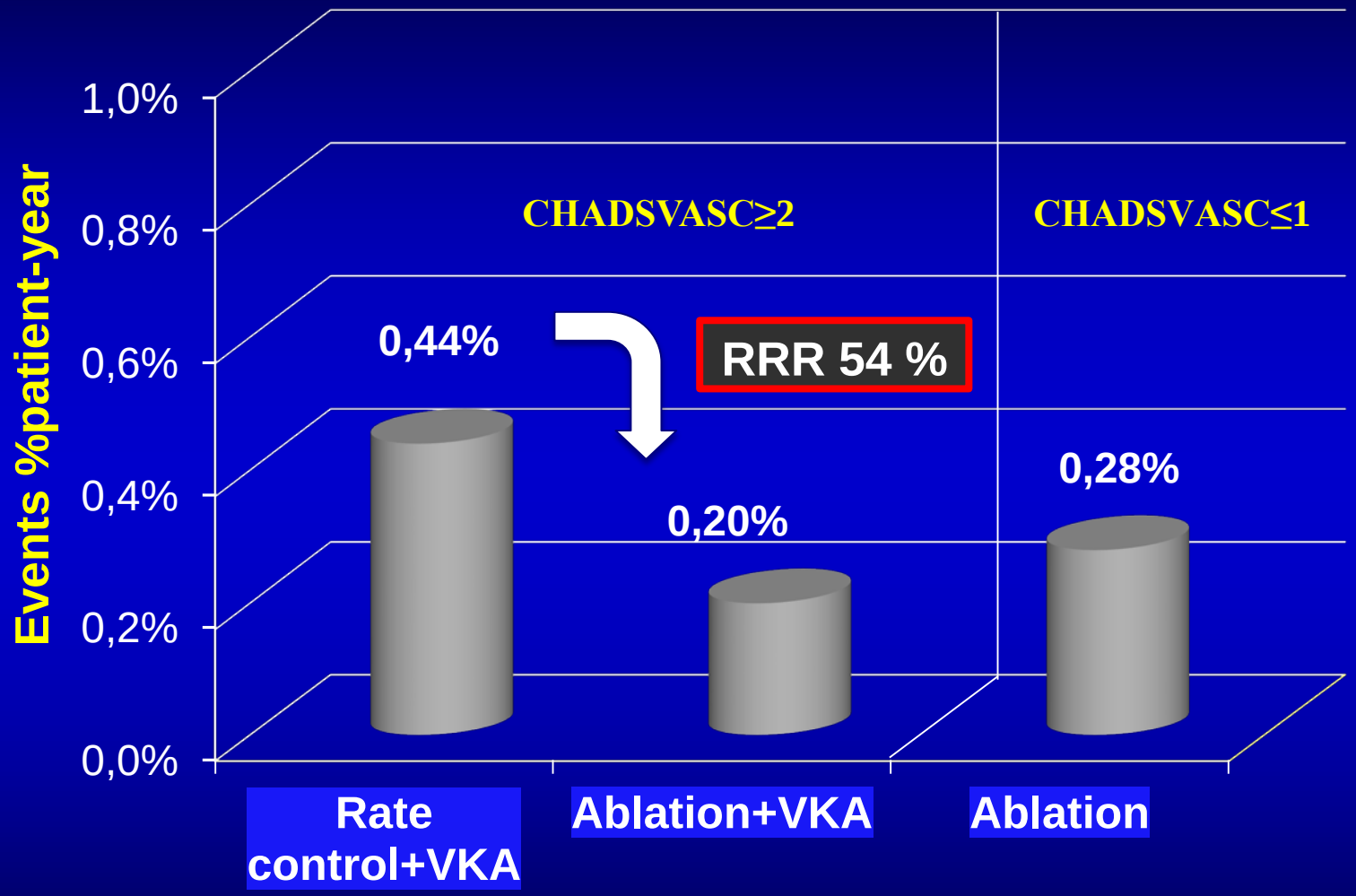
Thromboembolic and Haemorragic events in 1500 patients (5 years of follow up)

500 pts- Rate control + VKA *FOR CHADSVASC ≥ 2*

500 pts- AF ablation + VKA *FOR CHADSVASC ≥ 2*

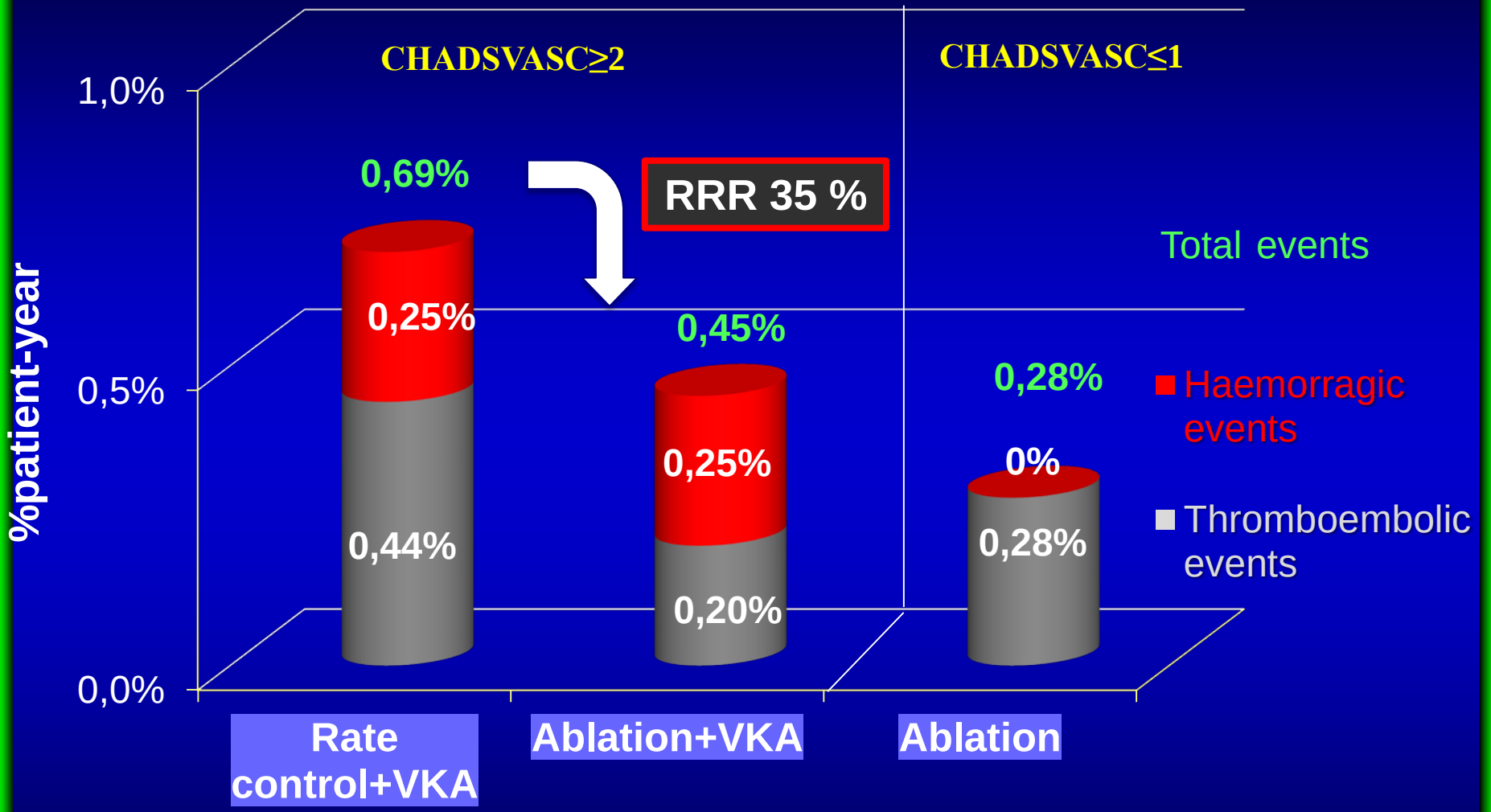
500 pts- AF ablation *FOR CHADSVASC ≤ 1*

Thromboembolic events / 100 pts/ year



Gallo et al JCM 2016; 17: 187

Thromboembolic and Haemorragic events/ 100 pts/ year



Gallo et al JCM 2016; 17: 187

Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries

2496 ablated pts matched with **2496** non-ablated pts

Follow up 4.4 years

78 TE events (0,7 %pts/y) in ablated pts
112 TE events (1.01%pts/y) in non-ablated pts

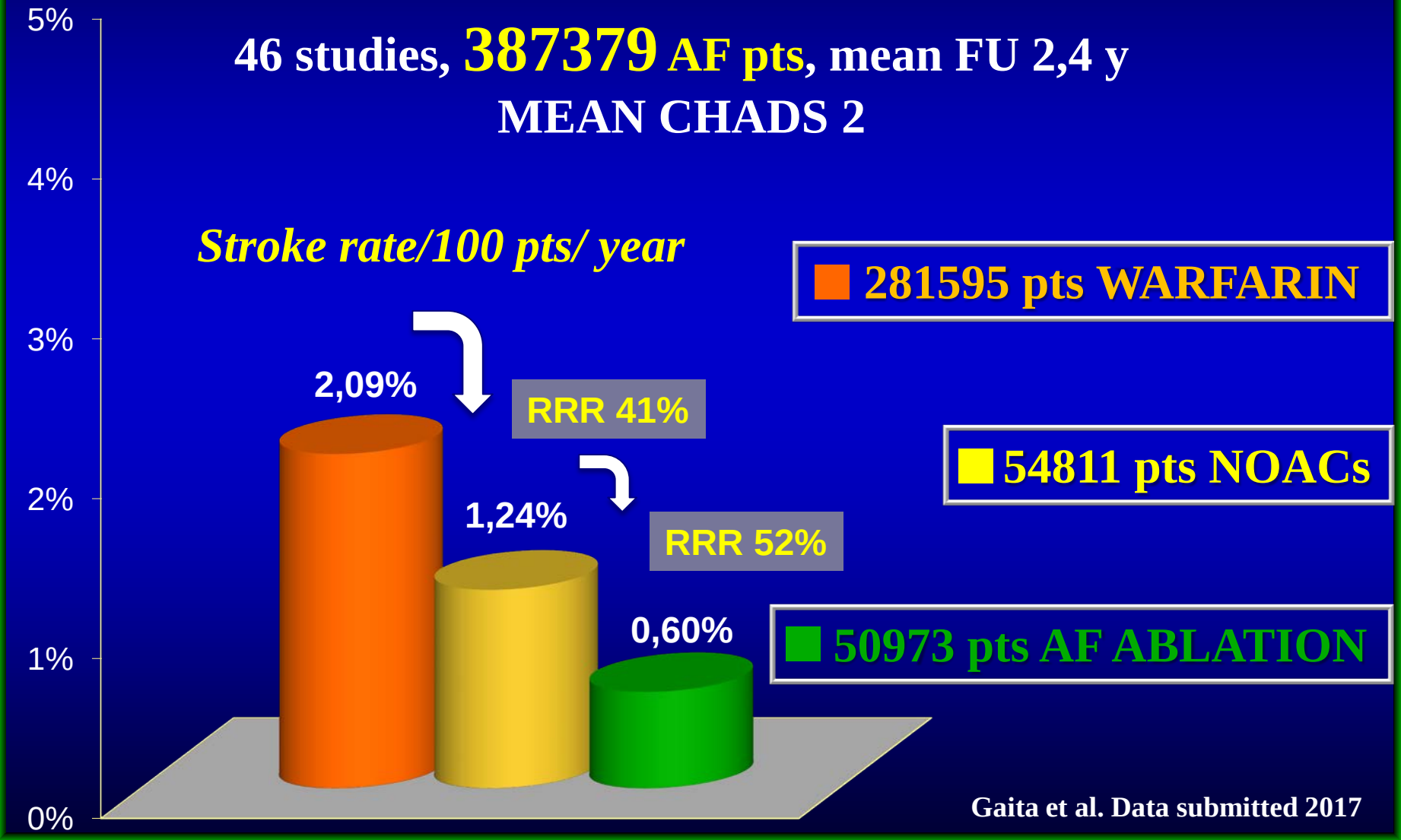
Stroke reduction with ablation 31%

Friberg L et al. Eur Heart Journal 2016; 37:2478

TE events in AF pts (metanalysis)
warfarin vs. NOACs vs. AF Ablation

46 studies, 387379 AF pts, mean FU 2,4 y

MEAN CHADS 2



Gaita et al. Data submitted 2017

Conclusions

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

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

Conclusions

In pts with $CHADS_2 \geq 2$
the best therapy to reduce TE risk could be
AF ablation associated with OAT

In pts with $CHADS_2$ 0-1
the best therapy to reduce TE risk is
AF ablation without OAT
(haemorrhagic risk > TE risk)

Thank you for your attention !