

**ALPIC 2016**

Advanced Learning on Platelets & Thrombosis International Course

March, 25-26, 2016

Kalavrita Canyon Hotel

KALAVRITA - GREECE

Organized by



Institute for the Study and Education  
on Thrombosis and Antithrombotic Therapy



Atherothrombosis Research Centre,  
University of Ioannina

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[www.alpic2016.gr](http://www.alpic2016.gr)

The course  
will be accredited  
with CME credits  
by the  
Panhellenic Medical  
Association

## Round Table: DOACs and real-world data: What have we learned that the RCTs have not told us?

Chairmen: **John Goudevenos (Greece),  
Spyros Vasdekis (Greece)**

Individualizing oral anticoagulant therapy for stroke prevention in AF. What factors are really important?  
**George Andrikopoulos (Greece)**

*George Andrikopoulos,  
Henry Dunant Hospital Center,  
Athens, Greece*

# ΕΠΙΠΟΛΑΣΜΟΣ ΚΟΛΠΙΚΗΣ ΜΑΡΜΑΡΥΓΗΣ ΣΤΟΝ ΕΛΛΗΝΙΚΟ ΠΛΗΘΥΣΜΟ (>14 ΕΤΩΝ) ΔΕΔΟΜΕΝΑ ΑΠΟ ΤΟ ΠΡΟΓΡΑΜΜΑ ΠΡΟΛΗΨΗΣ ΤΟΥ ΕΛΙΚΑΡ

**Συνολικός αριθμός συμμετεχόντων: 44.956 άτομα > 14 ετών**  
**Δεδομένα για ΚΜ από 2011 ως 2013: 6970 ερωτηματολόγια**  
**πληθυσμός > 14 ετών: 9148309 (84,80%)**

	Αριθμός ασθενών	Κολπική Μαρμαρυγή (>14 ετών)	ΚΜ στο σύνολο του πληθυσμού	Κολπική Μαρμαρυγή (>75 ετών)
2011	3150	3,5%	2,9%	11%
2012	1570	3,9%	3,3%	11,5%
2013	2250	3,4%	2,9%	10,5%

# Clinical Profile and Therapeutic Management of Patients with Atrial Fibrillation in Greece: Results from the Registry of Atrial Fibrillation to Investigate New Guidelines (RAFTING)

DIMITRIOS FARMAKIS<sup>1,2</sup>, ATHANASIOS PIPILIS<sup>3</sup>, ANNA ANTONIOU<sup>4</sup>, SOTIRIOS KALIAMBAKOS<sup>3</sup>, JOHN GOUDEVENOS<sup>5</sup>, MARIA ANASTASIOU-NANA<sup>2</sup>, VLASSIOS PYRGAKIS<sup>6</sup>, GEORGIOS PARCHARIDIS<sup>7</sup>, JOHN LEKAKIS<sup>2</sup>, ON BEHALF OF THE RAFTING INVESTIGATORS.\*

Table 4. Drug therapy at baseline.

Medication	All patients (n=1127)	Non-newly diagnosed patients (n=807)
<b>Anti-thrombotic, %:</b>		
Warfarin	44.1	55.9
Aspirin	26.2	26.3
Clopidogrel	14.6	15.1
Low-molecular-weight heparin	1.0	0.7
Other	0.9	1.1
None	25.2	13.4
<b>Antiarrhythmic, %:</b>		
Propafenone	9.7	12.5
Beta-blocker	44.3	47.9
Amiodarone	9.3	10.6
Sotalol	5.2	6.9
Diltiazem	8.5	10.3
Verapamil	1.6	2.0
Digitalis	17.2	22.0
<b>Other cardioactive, %:</b>		
Angiotensin-converting enzyme inhibitor	28.0	28.1
Angiotensin II antagonist	35.9	38.4
Other calcium channel blocker	17.5	18.0
Statin	36.0	37.5
Diuretic	51.7	56.8
Nitrate	11.1	12.0
<b>Other, %:</b>		
Bronchodilator	12.1	13.8
Thyroid hormone therapy	13.1	13.5
Insulin	5.3	6.1
Oral antidiabetic	18.1	19.0

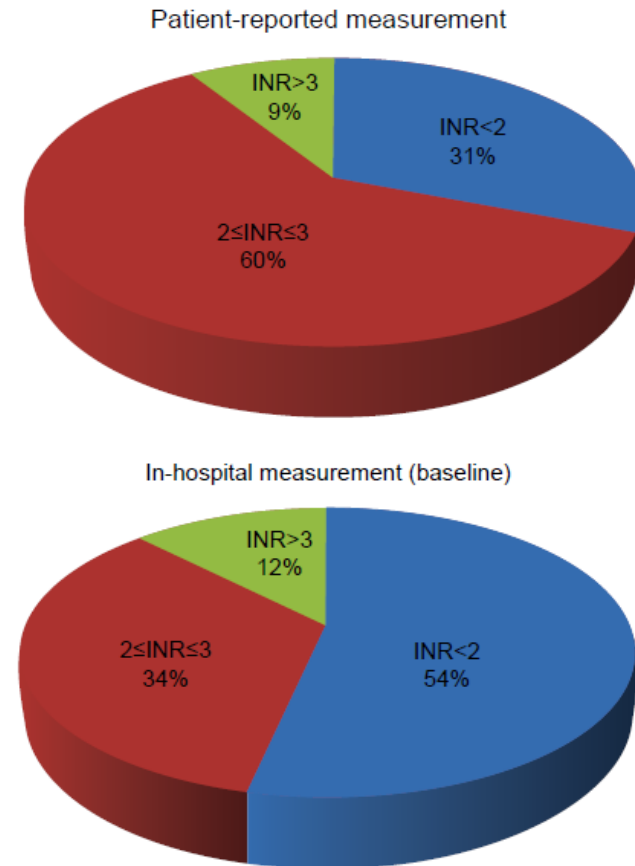


Figure 4. Values of INR in patients on warfarin therapy.

## Anticoagulation therapy in elderly patients with atrial fibrillation: results from the Registry of Atrial Fibrillation To Investigate the Implementation of New Guidelines (RAFTING).

Pipilis A<sup>1</sup>, Farmakis D, Kaliambakos S, Goudevenos J, Lekakis J; RAFTING Investigators.

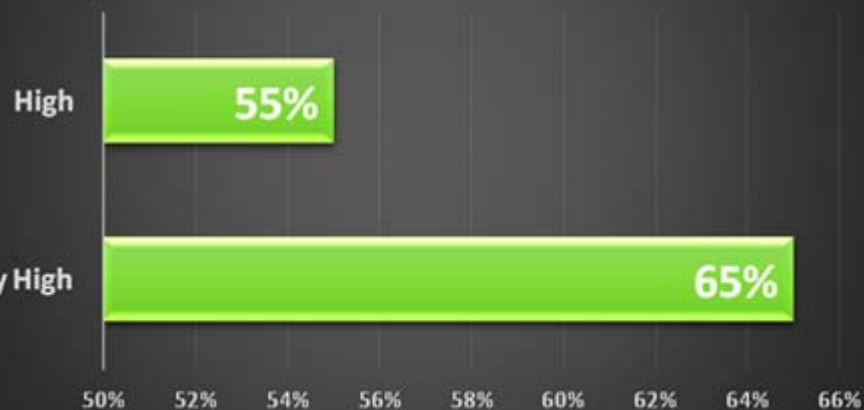
### Author information

#### Abstract

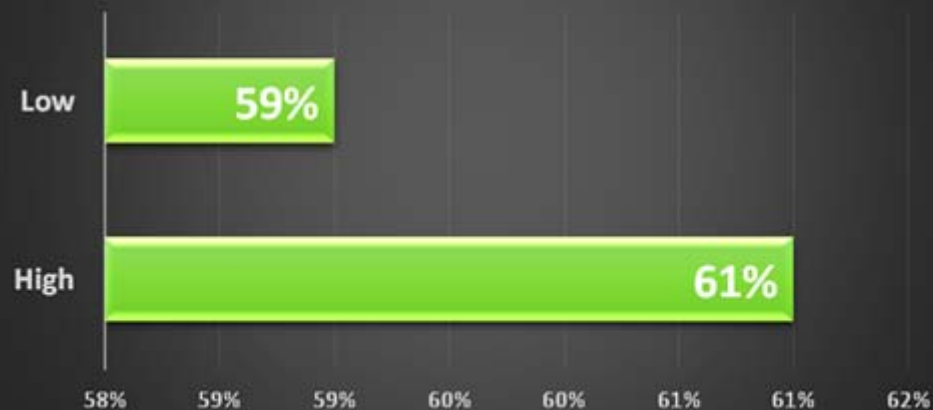
**BACKGROUND:** Patients with atrial fibrillation aged 75 years or older have a CHA<sub>2</sub>DS<sub>2</sub>-VASc score that dictates oral anticoagulants. We recorded physicians' anticoagulation attitudes in elderly patients with atrial fibrillation and assessed the impact of stroke and bleeding risk.

**METHODS:** Atrial Fibrillation To Investigate the Implementation of New Guidelines, a countrywide prospective registry performed in Greece during 2010, a period when only vitamin-K antagonists (VKA) were available, enrolled

Proportion of Elderly patients on VKAs in relation to CHA<sub>2</sub>DS<sub>2</sub>-VASc



Proportion of Elderly patients on VKAs in relation to HASBLED



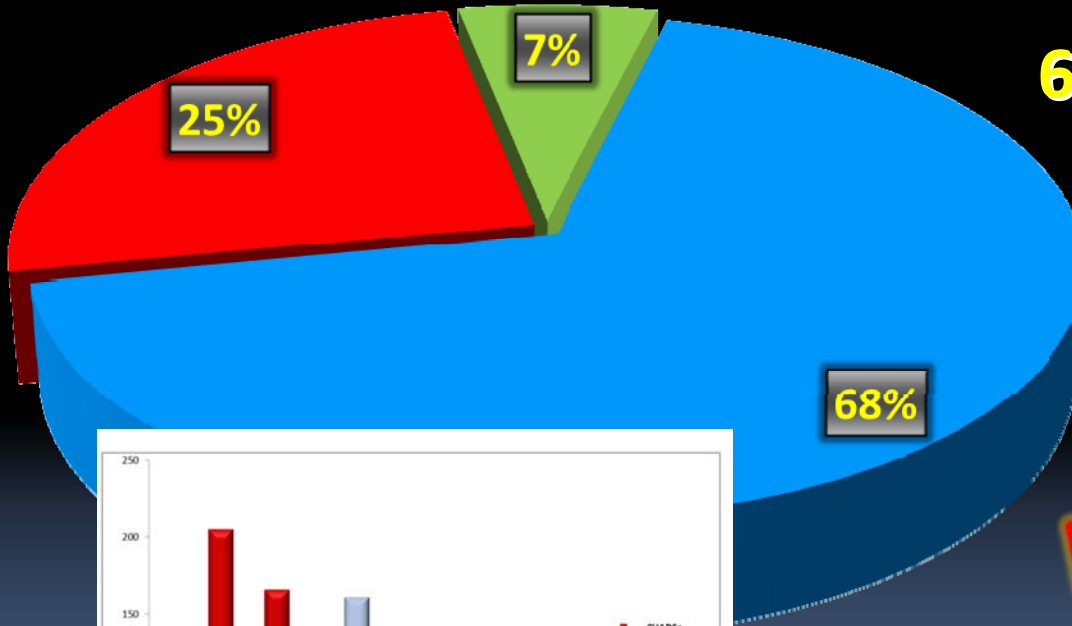
**CONCLUSION:** In this countrywide atrial fibrillation registry, 61% of elderly patients received VKA, a decision driven mainly by stroke risk. VKA use was not higher in patients with low bleeding risk.

Original Research

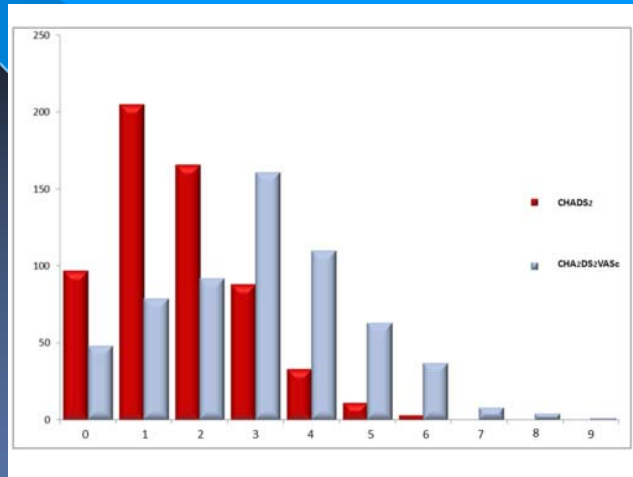
# Management of Atrial Fibrillation in Greece: the MANAGE-AF Study

GEORGE ANDRIKOPOULOS<sup>1</sup>, SOKRATIS PASTROMAS<sup>1</sup>, IOANNIS MANTAS<sup>2</sup>,  
 DIMITRIS SAKELLARIOU<sup>3</sup>, CHRISTOS KYRPIZIDIS<sup>4</sup>, PANTELIS MAKRIDIS<sup>5</sup>, GEORGIOS GOUMAS<sup>3</sup>,  
 DIMITRIS STAKOS<sup>6</sup>, ALEXANDROS GOTSIS<sup>7</sup>, ATHANASIOS KARTALIS<sup>8</sup>, GEORGIOS KAZIANIS<sup>9</sup>,  
 DIMITRIOS BABALIS<sup>10</sup>, KONSTANTINA TOLI<sup>2</sup>, MARIA PAPAVALSILEIOU<sup>11</sup>, PETROS KALOGEROPOULOS<sup>9</sup>,  
 PANOS VARDAS<sup>12</sup>; ON BEHALF OF THE MANAGE-AF INVESTIGATORS\*

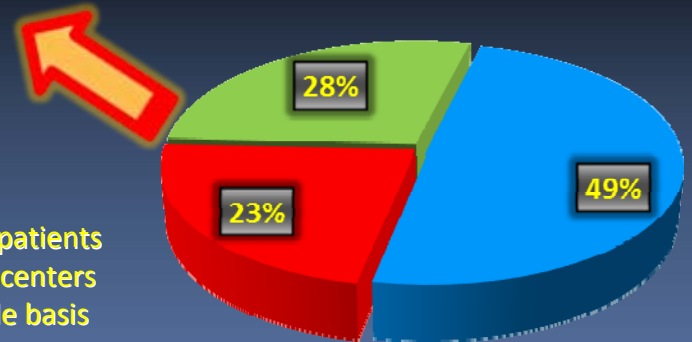
## 6-month follow-up



- AOC\*
- APL
- No Drug



603 consecutive patients with AF from 27 centers on a countrywide basis



## Baseline status

## Original Research

# A Greek Prospective Observational Study of Cardiovascular Morbidity and Mortality in Patients with Atrial Fibrillation

PANOS VARDAS<sup>1</sup>, GEORGE ANDRIKOPOULOS<sup>2</sup>, BARBARA BAROUTSOU<sup>3</sup>; THE ODYSSEY INVESTIGATORS\*

## Cardiovascular Morbidity and Mortality of AF

Table 1. Baseline and clinical characteristics of patients according to treatment strategy (n=1545)

Characteristics	Overall (N=1545)	Rhythm control Treatment (N=679) (43%)	Rate control Treatment (N=820) (57%)	p
Age mean (years)	68.8 ± 10.6	65.4 ± 11.4%	71.3 ± 9.0%	<0.001
Female sex (%)	67 (4.3%)	282 (48.1%)	352 (45.4%)	0.322
Height (cm)	168.1 ± 9.3	168.3 ± 9.6	168.0 ± 9.0	0.4550
Weight (kg) (SD)	80.9 ± 15.7	80.0 ± 14.2	81.4 ± 16.2	0.1854
Waist circumference (cm)	98.7 ± 15.2	98.4 ± 15.0	99.2 ± 15.3	0.2087
Blood pressure: Systolic (mmHg)	132.0 ± 16.7	132.0 ± 18.3	132.0 ± 15.2	0.8231
Blood pressure: Diastolic (mmHg)	80.4 ± 25.7	80.5 ± 26.1	79.4 ± 9.7	0.1956
Resting heart rate (bpm)	75.7 ± 20.8	73.4 ± 18.6	77.4 ± 22.4	<0.0001
Smoking status:				0.4335
Never	730 (53.4%)	306 (53.3%)	424 (55.7%)	
Active	191 (14.1%)	90 (15.7%)	101 (13.3%)	
No smoking Now- Previous	414 (30.3%)	178 (31.0%)	236 (31.0%)	
Hypertension	967 (67.7%)	399 (68.0%)	568 (73.4%)	
Diabetes mellitus	239 (17.2%)	77 (13.1%)	162 (20.9%)	
Dyslipidaemia	722 (52.1%)	317 (54.0%)	405 (52.3%)	
Abdominal obesity	614 (45.0%)	265 (45.1%)	349 (45.1%)	
Family history of coronary heart disease	270 (19.6%)	123 (21.0%)	147 (19.0%)	
Coronary heart disease	267 (19.7%)	96 (16.4%)	171 (22.0%)	
Myocardial infarction	102 (7.4%)	31 (5.3%)	71 (9.2%)	
Stroke	96 (7.1%)	24 (4.1%)	72 (9.3%)	
Transient ischaemic attack	93 (6.5%)	35 (6.0%)	58 (7.5%)	
Peripheral artery disease	68 (4.7%)	23 (3.9%)	45 (5.8%)	
Carotid stenosis	103 (7.3%)	34 (5.8%)	69 (8.9%)	
Heart failure	321 (22.6%)	84 (14.3%)	237 (30.5%)	
Valvular heart disease	553 (38.9%)	173 (29.5%)	380 (49%)	
Peripheral embolic episodes	8 (0.8%)	2 (0.3%)	6 (0.8%)	
History of supraventricular or ventricular arrhythmia	73 (5.0%)	38 (6.5%)	35 (4.5%)	0.1122
History of cardiovascular interventions	246 (17.6%)	83 (14.1%)	163 (21.0%)	0.0011
Type of AF:				0.0001
First episode	104 (8.6%)	64 (11.3%)	40 (5.3%)	
Paroxysmal	445 (35.7%)	401 (70.6%)	44 (5.9%)	
Persistent	144 (10.7%)	85 (15.0%)	59 (7.9%)	
Permanent	625 (45.0%)	18 (3.2%)	607 (80.9%)	
ECG at visit:				
Atrial fibrillation	59.6%	144 (24.5%)	707 (91.2%)	<0.0001
Sinus rhythm	33.4%	404 (68.8%)	33 (4.3%)	<0.0001

## Cardiovascular Morbidity and Mortality of AF

Table 2. Anticoagulation therapy at V0.

Receiving oral anticoagulant therapy (OACs)		Treatment		p
		Rhythm control	Rate control	
No	Frequency	285	127	<0.0001
	Col Pct	48.6%	16.4%	
Yes	Frequency	302	649	
	Col Pct	51.5%	83.6%	

# Baseline characteristics in AF patients enrolled in different settings

	<b>MANAGE AF (n=603)</b>	<b>MANAGE AF OACs (n=297)</b>	<b>ROCKET AF (n=7133)</b>	<b>RECORD AF (n=5604)</b>	<b>Euro Heart Survey (n=5333)</b>	<b>AFNET (n=9582)</b>
Age (years)	68.5	70.1	73	66	(66)	68.4
Gender (male), n (%)	52.5	55.2	60.3	57	59	63.7
OAC treated	49.3	100	100	52.0	64.2	50.7
<b>Stroke Risk Factors</b>						
Hypertension, n (%)	70.3	72.7	90.8	68	62.2	69.2
Heart Failure, n (%)	23.3	28.6	62.3	26	32.8	29.0
Diabetes, n (%)	21.8	25.5	39.5	16	18	21.7
<b>CAD (%)</b>	<b>20.5</b>	<b>21.9</b>	<b>18</b>	<b>18</b>	<b>32</b>	<b>28.1</b>
Stroke/TIA, n (%)	9.2	14.1	54.6	10	12	12.4

*N Engl J Med* 2011;365(10):883-91

*Am J Cardiol* 2010;105(5):687-93

*Eur Heart J* 26 (22): 2422-2434

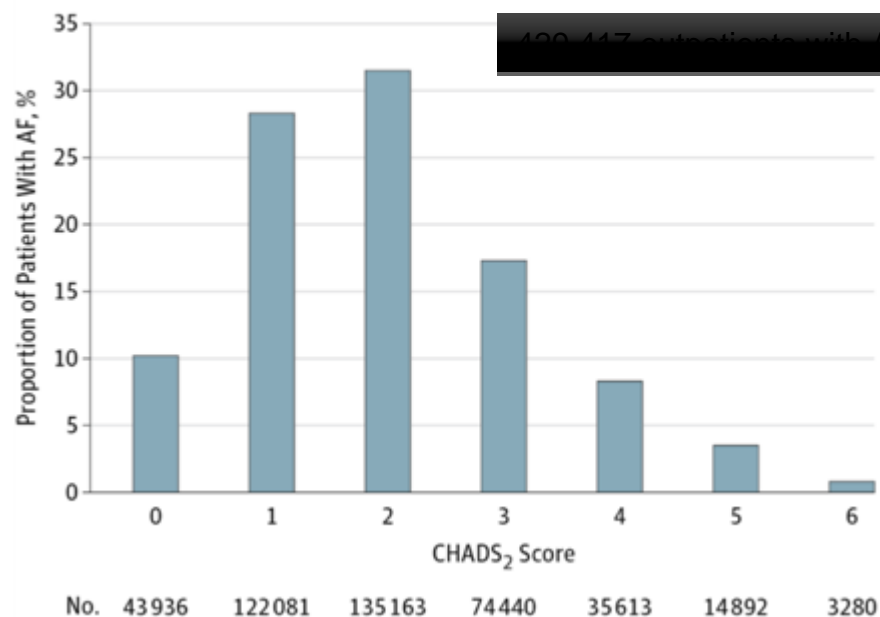
*Europace* 2009 Apr;11(4):423-34

**From: Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk: Insights From the NCDR PINNACLE Registry**

JAMA Cardiol. Published online March 16, 2016. doi:10.1001/jamacardio.2015.0374

**DESIGN, SETTING, AND PARTICIPANTS** Cross-sectional registry study of outpatients with AF enrolled in the American College of Cardiology National Cardiovascular Data Registry's PINNACLE (Practice Innovation and Clinical Excellence) Registry between January 1, 2008, and December 30, 2012. As a measure of stroke risk, we calculated the CHADS<sub>2</sub> score and the

**A** Distribution of CHADS<sub>2</sub> scores within the cohort



**B** Distribution of CHA<sub>2</sub>DS<sub>2</sub>-VASc scores within the cohort

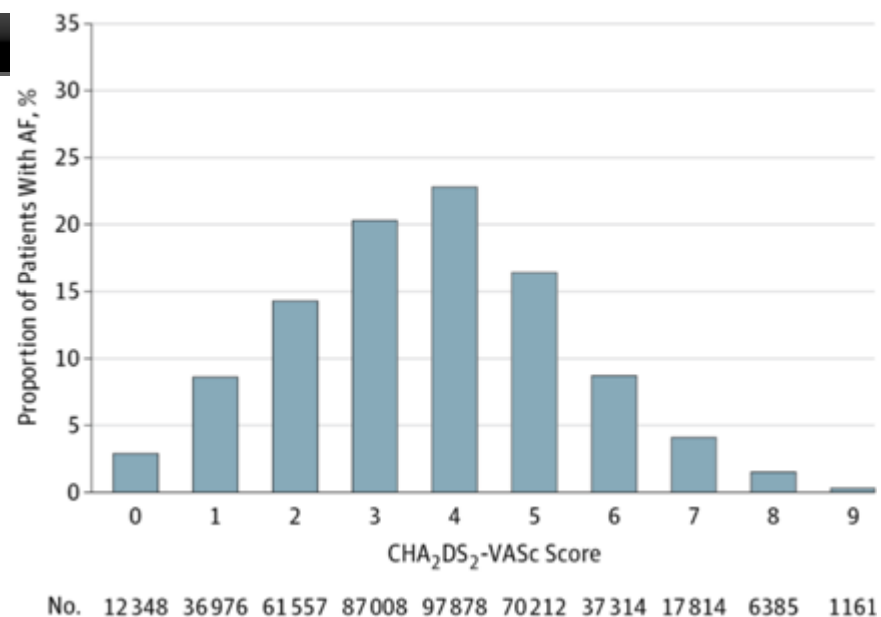


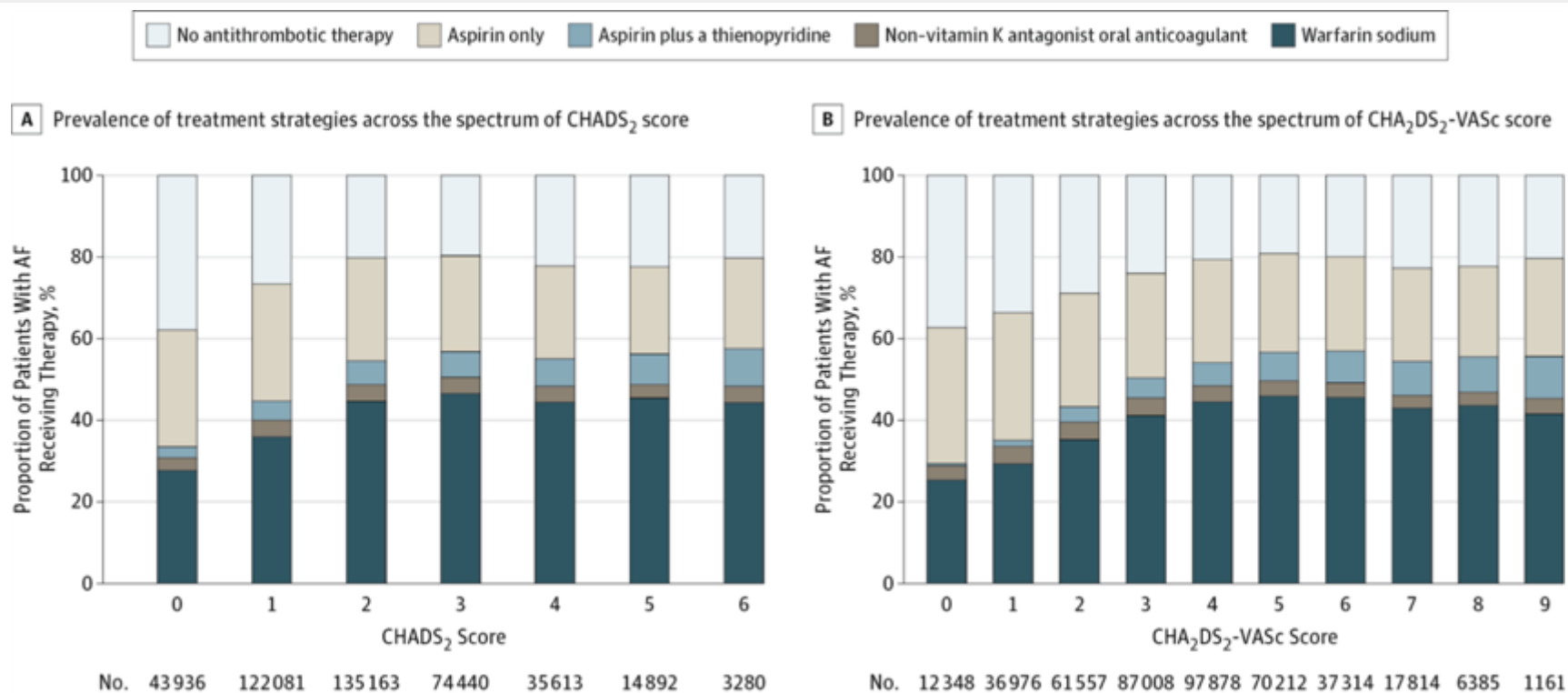
Figure Legend:

Prevalence of Patients With Atrial Fibrillation (AF) Across the Spectrum of the CHADS<sub>2</sub> Score and the CHA<sub>2</sub>DS<sub>2</sub>-VASc Score Shown is the distribution of patients with AF in the cohort characterized by the CHADS<sub>2</sub> score (A) and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (B).



## From: Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk: Insights From the NCDR PINNACLE Registry

JAMA Cardiol. Published online March 16, 2016. doi:10.1001/jamacardio.2015.0374



### Figure Legend:

Prevalence of Antithrombotic Therapies in Patients With Atrial Fibrillation (AF) Across the Spectrum of Stroke Risk by the CHADS<sub>2</sub> Score and the CHA<sub>2</sub>DS<sub>2</sub>-VASc Score. Shown is the proportion of patients treated with different antithrombotic therapies based on the CHADS<sub>2</sub> score (A) and the CHA<sub>2</sub>DS<sub>2</sub>-VASc score (B). Oral anticoagulant therapy was defined as prescription of either warfarin sodium, dabigatran, or rivaroxaban, further stratified by warfarin (dark blue) vs dabigatran or rivaroxaban (dark brown). Other treatment strategies included prescription of aspirin only (light brown), aspirin plus a thienopyridine (light blue), or no antithrombotic therapy (light grey). Treatment with a thienopyridine was defined as prescription of clopidogrel bisulfate, ticlopidine hydrochloride, or prasugrel.

# Distribution of NOAC doses studied in their respective Phase III studies in patients with NVAF

Dabigatran RE-LY <sup>1</sup>		Rivaroxaban ROCKET AF <sup>2</sup>		Apixaban ARISTOTLE <sup>3</sup>		Edoxaban ENGAGE-AF (high-dose arm) <sup>4</sup>	
150 mg	50% (n=6076)	20 mg	79% (n=5637)	5 mg	95% (n=8692)	60 mg	75% (n=5251)
110 mg	50% (n=6015)	15 mg	21% (n=1474)	2.5 mg	5% (n=428)	30 mg	25% (n=1784)

**Τι ποσοστό των ασθενών στις μεγάλες μελέτες έπαιρνε τη μειωμένη δόση του αντιπηκτικού;**

1. Connolly SC et al. N Engl J Med 2009;361:1139–51;
2. Fox KAA et al. Eur Heart J 2011;32:2387–94;
3. Granger CB et al. N Engl J Med 2011;365:981–92;
4. Giugliano RP et al. N Engl J Med. 2013;369:2093–104;

# What do prescription data show us about how NOACs are prescribed across all indications?

UK prescription data (all indications; IMS data June 2014–June 2015)

Dabigatran		Rivaroxaban*		Apixaban		Edoxaban
150 mg	40%	20 mg	75%	5 mg	59%	
110 mg	58%	15 mg	23%	2.5 mg	41%	Not available
75 mg	2%	10 mg	3%	–		

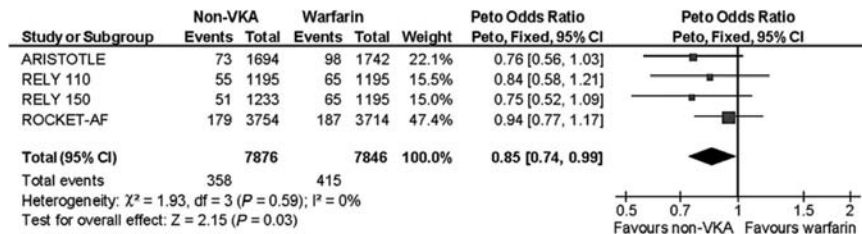
Dabigatran RE-LY <sup>1</sup>		Rivaroxaban ROCKET AF <sup>2</sup>		Apixaban ARISTOTLE <sup>3</sup>		Edoxaban ENGAGE-AF (high-dose arm) <sup>4</sup>	
150 mg	50% (n=6076)	20 mg	79% (n=5637)	5 mg	95% (n=8692)	60 mg	75% (n=5251)
110 mg	50% (n=6015)	15 mg	21% (n=1474)	2.5 mg	5% (n=428)	30 mg	25% (n=1784)

# Which NOAC to Choose?

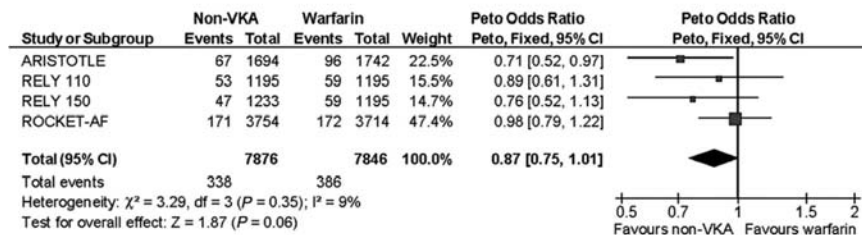
<b>Specific Patient Characteristics</b>	<b>NOAC</b>
Previous stroke (secondary prevention)	<ul style="list-style-type: none"><li>• Rivaroxaban</li><li>• Apixaban</li></ul>
Previous GI bleeding or high risk	<ul style="list-style-type: none"><li>• Apixaban</li><li>• Edoxaban</li></ul>
High risk of ischemic stroke, low bleeding risk	<ul style="list-style-type: none"><li>• Dabigatran 150 mg</li></ul>
High risk of bleeding (eg, HAS-BLED $\geq 3$ )	<ul style="list-style-type: none"><li>• Dabigatran 110 mg</li><li>• Apixaban</li><li>• Edoxaban</li></ul>
CAD, previous MI or high-risk for ACS/MI	<ul style="list-style-type: none"><li>• Rivaroxaban</li></ul>
Renal impairment	<ul style="list-style-type: none"><li>• Apixaban</li><li>• Rivaroxaban</li></ul>
GI upset/disorders	<ul style="list-style-type: none"><li>• Apixaban</li><li>• Rivaroxaban</li><li>• Edoxaban</li></ul>
Patient preference	<ul style="list-style-type: none"><li>• Rivaroxaban</li><li>• Edoxaban</li></ul>

# Forest plot of the effects of nonvitamin-K-antagonists (non-VKAs) vs warfarin on efficacy outcomes (stroke or systemic embolism; stroke; ischemic or unknown stroke; disabling or fatal stroke) in patients with atrial fibrillation (AF) and previous stroke or transient ischemic attack.

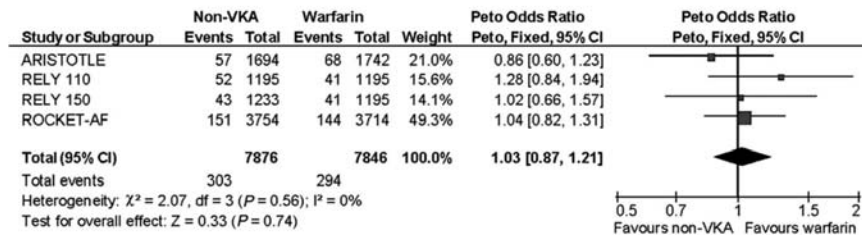
## Stroke or systemic embolism



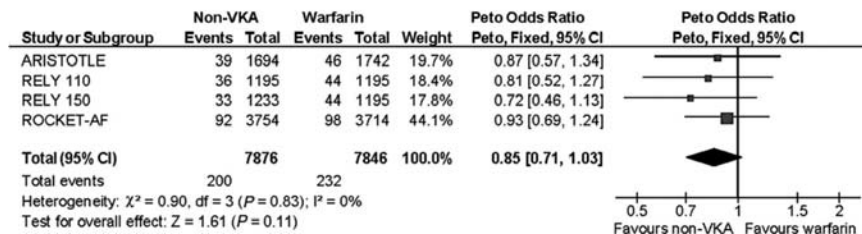
## Stroke



## Ischemic or unknown stroke



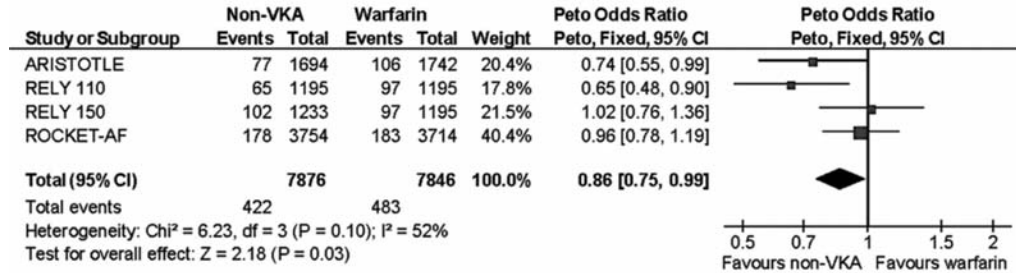
## Disabling or fatal stroke



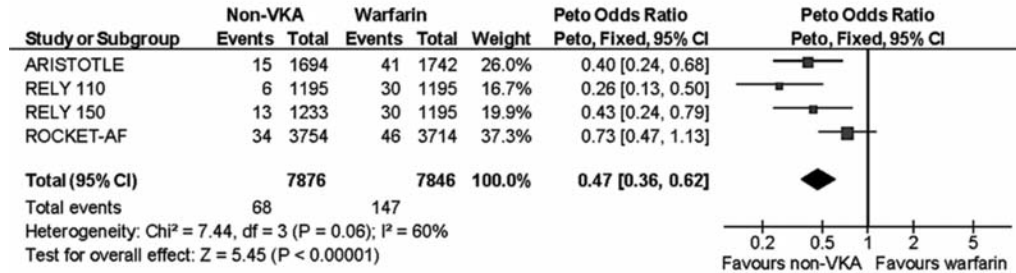


# Forest plot of the effects of nonvitamin-K-antagonists (non-VKA) vs warfarin on safety outcomes in patients with atrial fibrillation (AF) and previous stroke or transient ischemic attack.

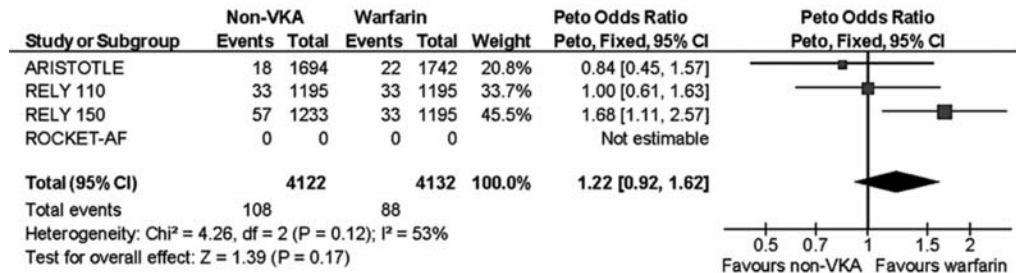
## Major bleeding



## Intracranial bleeding



## Gastrointestinal major bleeding



George Ntaios et al. Stroke. 2012;43:3298-3304



*Prevention*

## Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 2

Hans-Christoph Diener<sup>1\*</sup>, James Aisenberg<sup>2</sup>, Jack Ansell<sup>3</sup>, Dan Atar<sup>4</sup>,  
Günter Breithardt<sup>5</sup>, John Eikelboom<sup>6</sup>, Michael D. Ezekowitz<sup>7,8,9</sup>,  
Christopher B. Granger<sup>10</sup>, Jonathan L. Halperin<sup>11</sup>, Stefan H. Hohnloser<sup>12</sup>,  
Elaine M. Hylek<sup>13</sup>, Paulus Kirchhof<sup>14,15</sup>, Deirdre A. Lane<sup>16</sup>, Freek W.A. Verheugt<sup>17</sup>,  
Roland Veltkamp<sup>18</sup>, and Gregory Y.H. Lip<sup>19,20</sup>

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First choice	NOACs as a group are superior to warfarin for secondary stroke prevention in patients with AF
Comment	Aspirin should not be used for secondary stroke prevention in patients with AF. The combination of antiplatelet therapy plus OAC in patients with AF does not prevent major ischaemic events better than does OAC monotherapy and should be restricted to specific high-risk periods

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**Είναι τα NOACs κατάλληλα για ασθενείς με νεφρική δυσλειτουργία;**



**Άντρας 65 ετών με χρόνια κοιλιακή  
μαρμαρυγή, βρίσκεται υπό αγωγή με ABK  
(GFR=40 ml/min)**

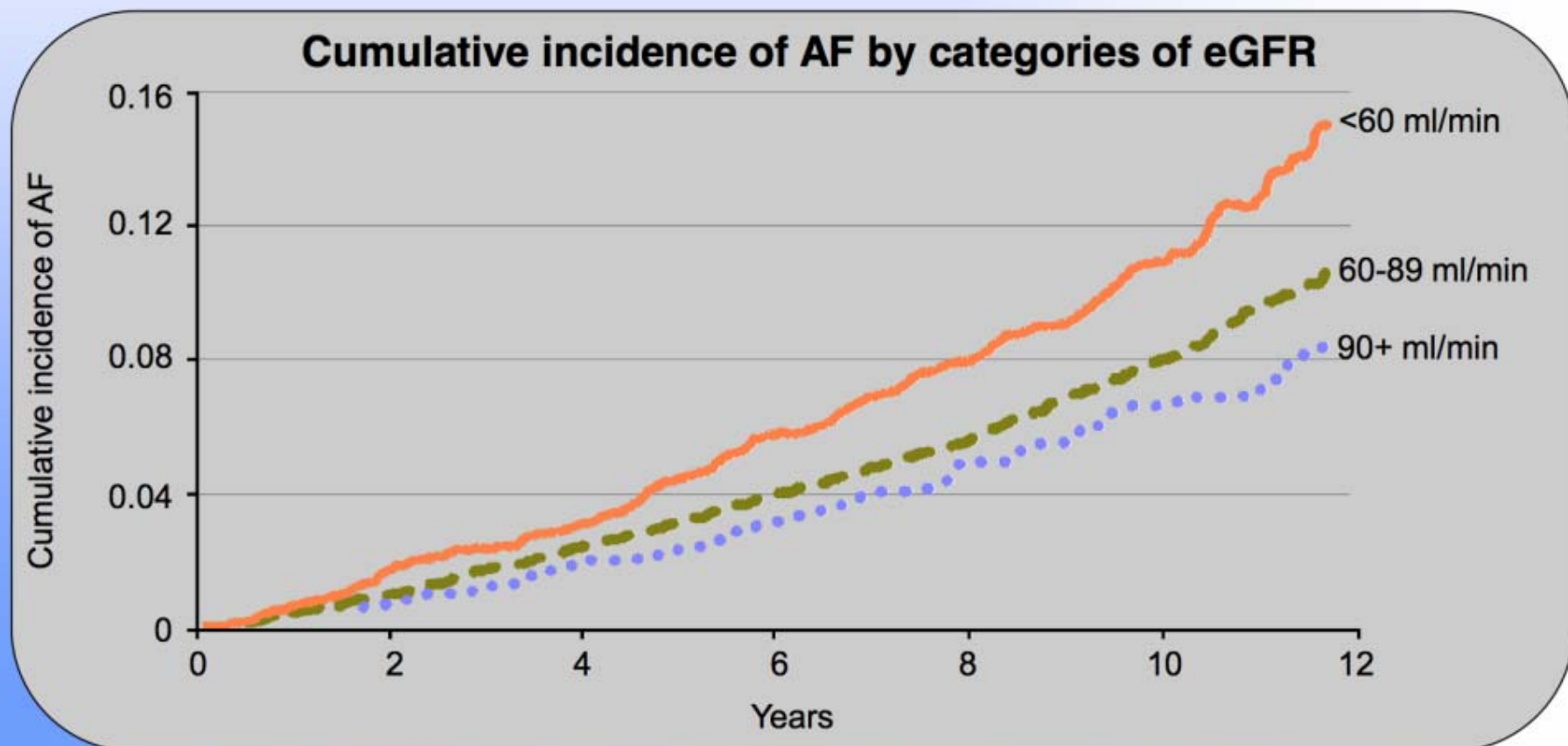
- 1. Dabigatran**
- 2. Rivaroxaban**
- 3. Apixaban**
- 4. Edoxaban**
- 5. Keep on VKAs**



# Chronic Kidney Disease and Atrial Fibrillation

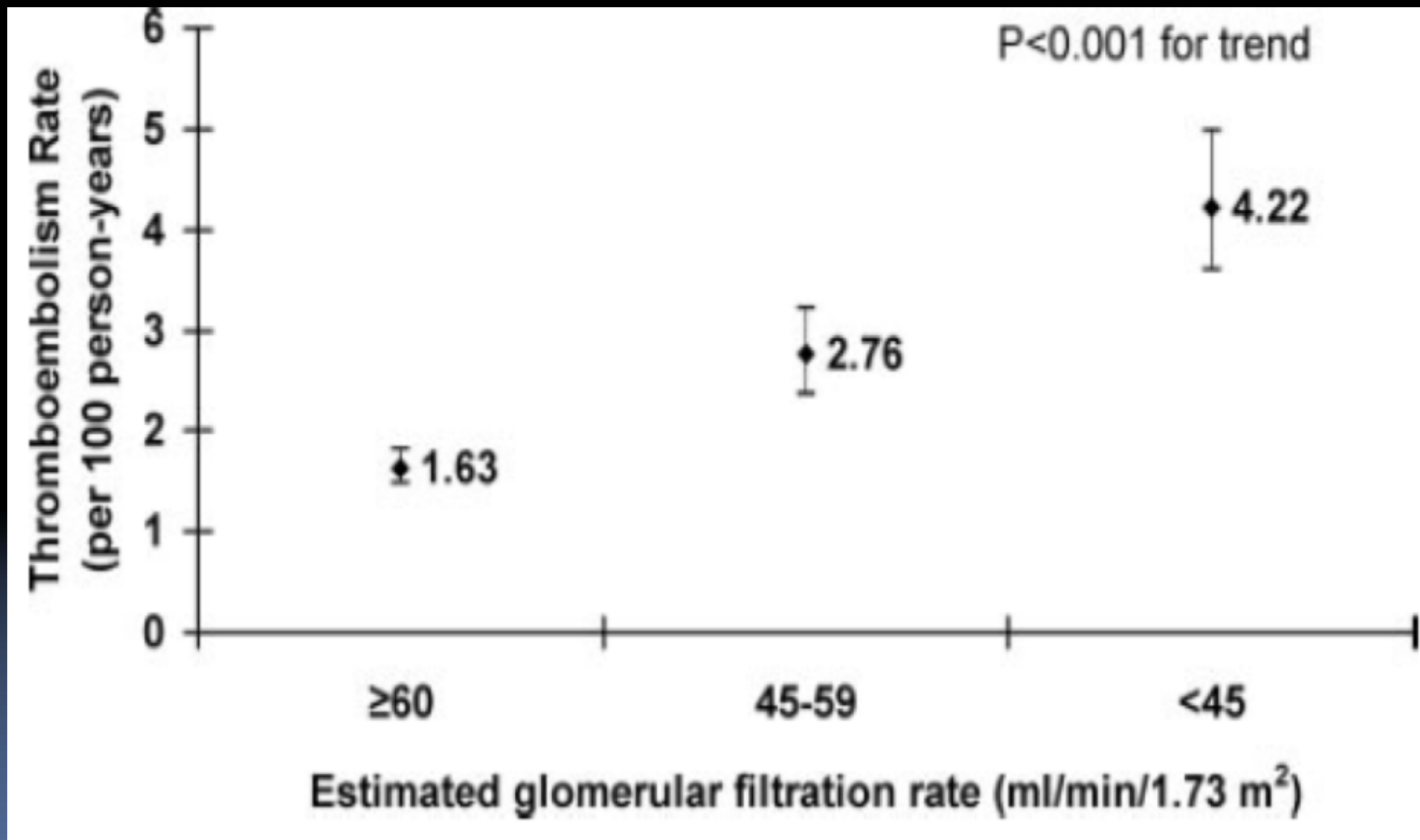
- Atherosclerosis Risk in Communities (ARIC) Study
- 10,328 subjects free of AF
- eGFR determined in all subjects at baseline
- median follow-up 10.1 years
- 788 incident AF cases

Alonso et al, Circulation 2011;123:2946



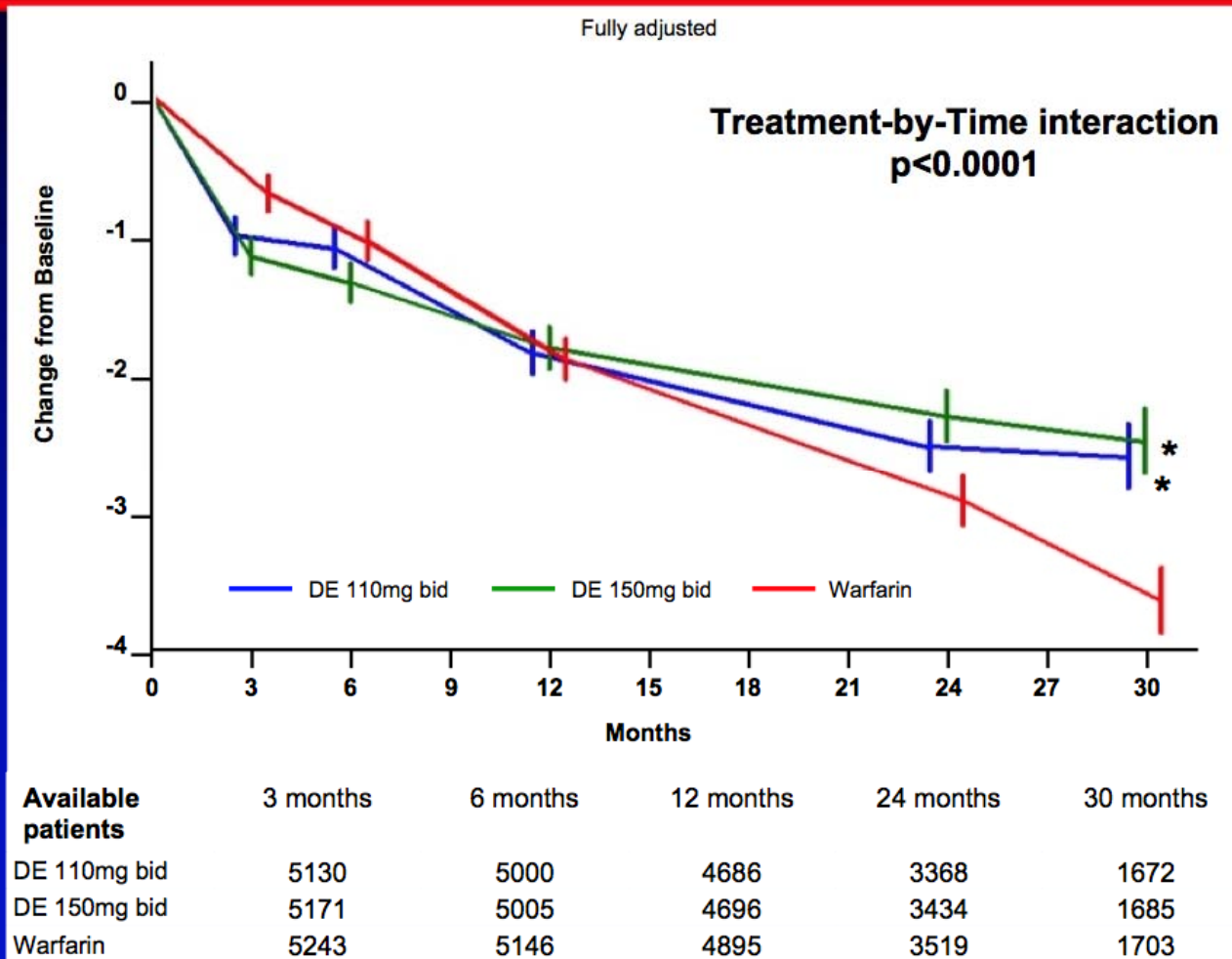
# THROMBOEMBOLIC RISK IS HIGHER IN PATIENTS WITH CKD

10,908 patients - 33,165 person-years of follow-up



# DABIGATRAN VS WARFARIN

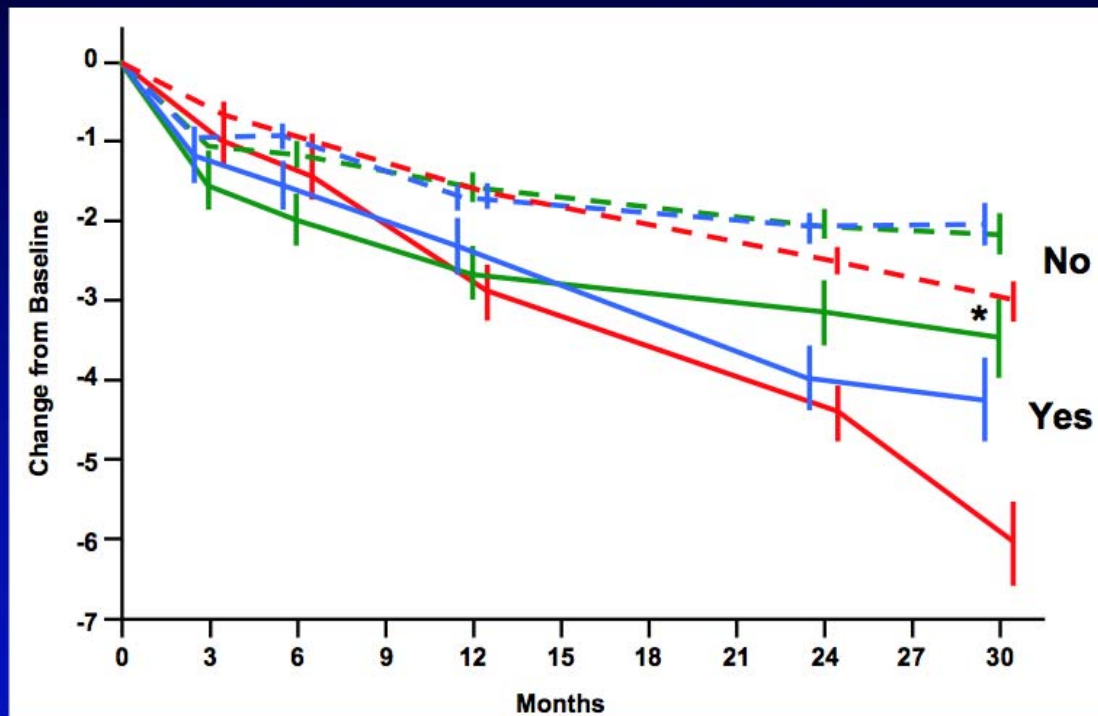
## Change in GFR (CKD-EPI) Assigned to D110, D150 or Warfarin



# DABIGATRAN VS WARFARIN

## Change in GFR (CKD-EPI)

### Diabetes Subgroup Analysis



..... DE 110mg - No      ..... DE 150mg - No      ..... Warfarin - No  
—— DE 110mg - Yes      —— DE 150mg - Yes      —— Warfarin - Yes

\*p < 0.0025 vs warfarin

# RIVAROXABAN VS WARFARIN

## Efficacy endpoints on treatment

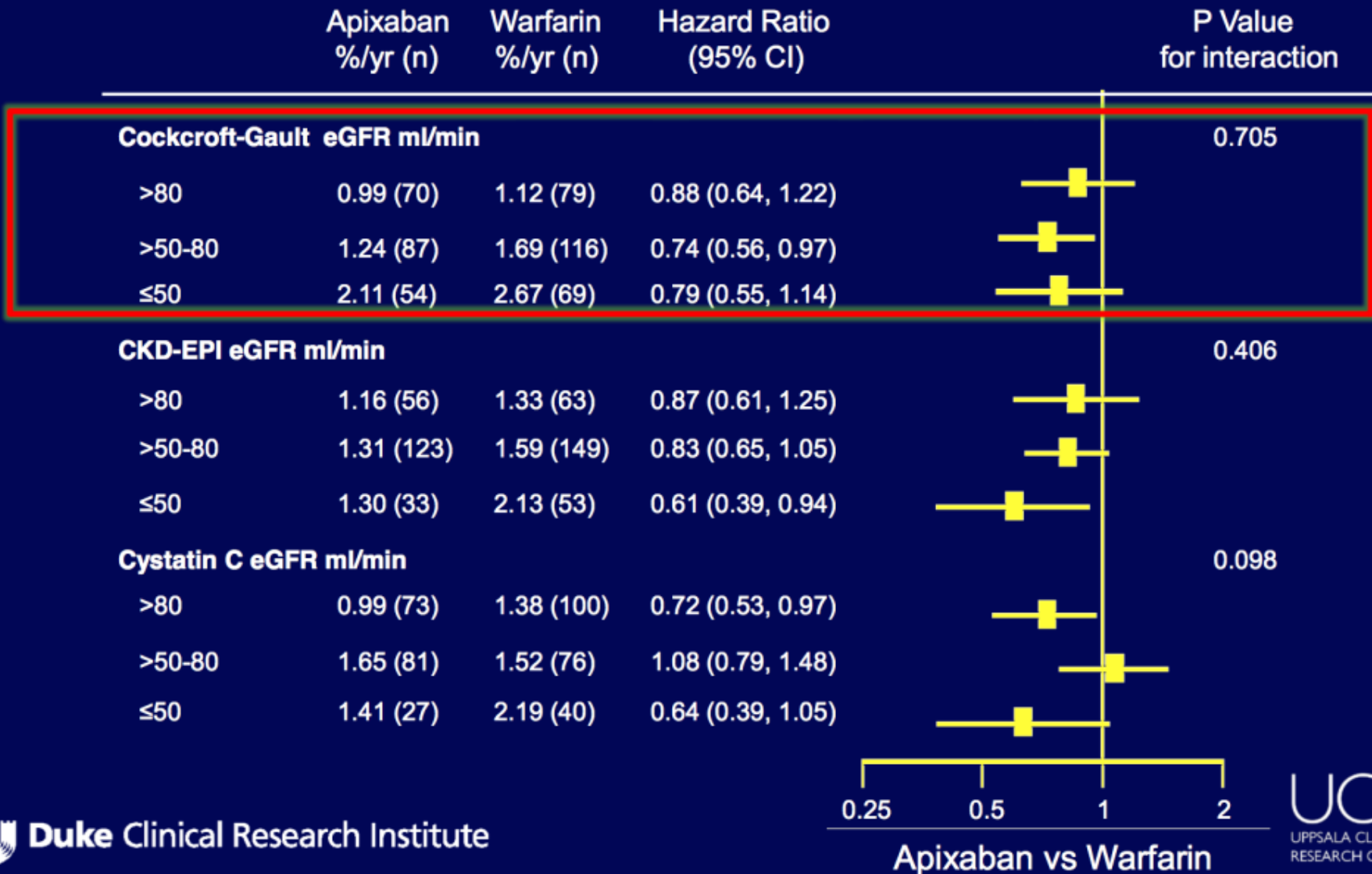
Clinical endpoint (% per year)	Rivaroxaban (N=7111)	Warfarin (N=7116)	◆ CrCl ≥50 ml/min <sup>†</sup> ◆ CrCl 30–49 ml/min <sup>‡</sup>	HR (95% CI) Rivaroxaban vs warfarin	P (interaction)
Primary efficacy endpoint*	1.57	2.00	◆	0.78 (0.63–0.98)	0.76
	2.32	2.77	◆	0.84 (0.57–1.23)	
PE + vascular death	2.76	3.32	◆	0.83 (0.70–0.98)	0.38
	4.64	4.83	◆	0.96 (0.73–1.27)	
PE + MI, vascular death	3.55	4.16	◆	0.85 (0.73–0.99)	0.98
	5.58	6.54	◆	0.85 (0.67–1.09)	
Stroke					
Ischaemic	1.20	1.34	◆	0.90 (0.69–1.16)	0.41
	1.98	1.78	◆	1.11 (0.71–1.73)	
Haemorrhagic	0.26	0.42	◆	0.62 (0.37–1.03)	0.88
	0.29	0.52	◆	0.56 (0.21–1.51)	
Undetermined	0.07	0.10	◆	0.68 (0.24–1.90)	0.84
	0.05	0.09	◆	0.51 (0.05–5.67)	

Based on per-protocol population on treatment

\*Stroke and systemic embolism

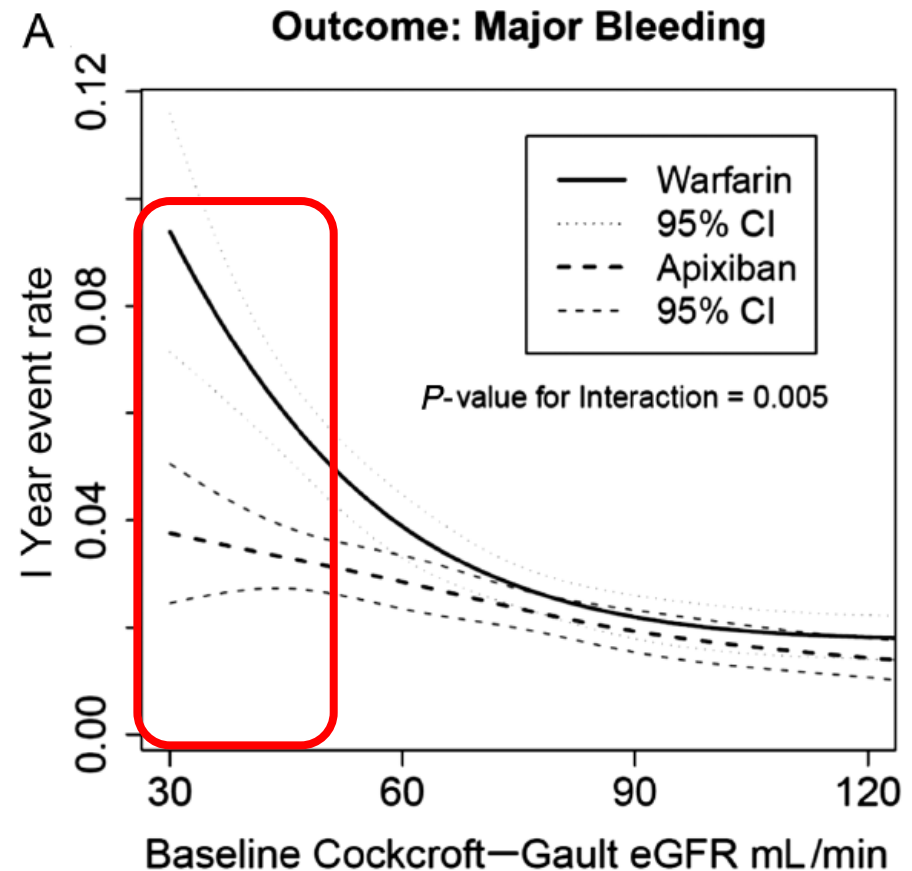
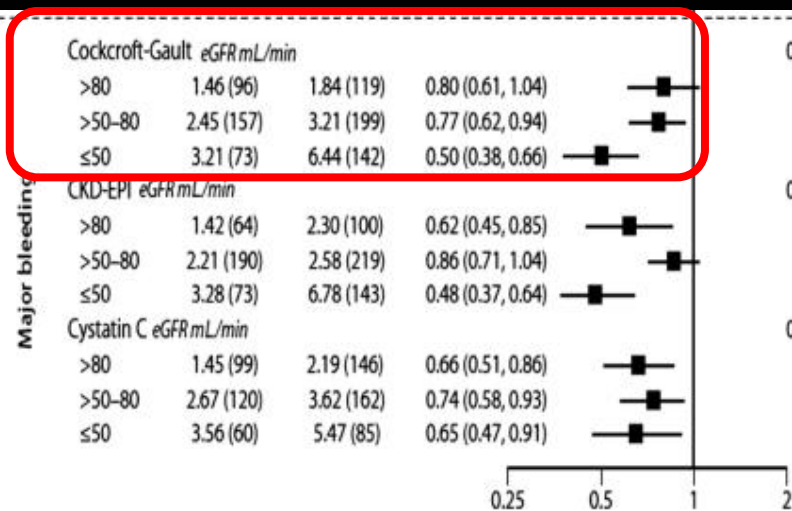
<sup>†</sup>Rivaroxaban 20 mg od. <sup>‡</sup>Rivaroxaban 15 mg od

# Apixaban versus Warfarin: Effect on Stroke/SEE According to Kidney Function



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

Stefan H. Hohnloser., et al. Eur Heart J 2012



**Figure 1** Forrest plot for effect of apixaban vs. warfarin for outcomes of stroke or systemic embolism, mortality, and to renal function estimated with the Cockcroft-Gault, CKD-EPI, and cystatin C. Interaction *P*-values are based on categorical renal function rates.





## Prevention

**Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 2****Table 1** Dose reduction of non-vitamin K oral anticoagulants for reduced creatinine clearance

Drug	Dose reduction criteria	Reduced dose
Dabigatran	Creatinine clearance <50 mL/min	110 mg twice a day is recommended in ESC guidelines
Rivaroxaban	Creatinine clearance <50 mL/min	Use 15 mg once a day
Apixaban	2 of three criteria: age $\geq$ 80 years, weight $\leq$ 60 kg, creatinine $\geq$ 1.5 mg/dL	Use 2.5 mg twice a day
Edoxaban	Creatinine clearance $\leq$ 50 mL/min	Use 30 mg once a day

First choice	Patients with AF and stage III CKD (creatinine clearance 30–49 mL/min) may be treated with apixaban 5 mg twice daily (apixaban 2.5 mg twice a day if $\geq$ 1 additional criteria: age $\geq$ 80 years, body weight $\leq$ 60 kg, serum creatinine $\geq$ 1.5 mg/dL (133 $\mu$ mol/L are present), rivaroxaban 15 mg daily, or edoxaban 30 mg once daily
Second choice	Dabigatran 110 mg twice daily
Not recommended	Dabigatran 150 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily
First choice	For patients with AF on haemodialysis, no anticoagulation or VKA therapy is appropriate
Not recommended	Dabigatran, rivaroxaban, apixaban*, or edoxaban
First choice	Patients with AF and creatinine clearance of >95 mL/min may be treated with dabigatran 150 twice daily, rivaroxaban 20 mg once daily or apixaban 5 mg twice daily. No preference for NOACS over VKAs
Second choice	Edoxaban 60 mg once daily (not recommended in USA based on FDA indication approval)

**Μπορούμε να χρησιμοποιούμε τα  
NOACs στους ηλικιωμένους ασθενείς;**

# New Oral Anticoagulants in Elderly Adults: Evidence from a Meta-Analysis of Randomized Trials

Partha Sardar, MD,\* Saurav Chatterjee, MD,<sup>†</sup> Shobhana Chaudhari, MD,\*  
and Gregory Y. H. Lip, MD<sup>‡</sup>

10 RCTs included 25,031 elderly ( $\geq 75$ ) participants

Risk of major or clinically relevant **bleeding** was not significantly different between NOACs and conventional therapy in elderly adults (**OR = 1.02**, 95% confidence interval = **0.73-1.43**)

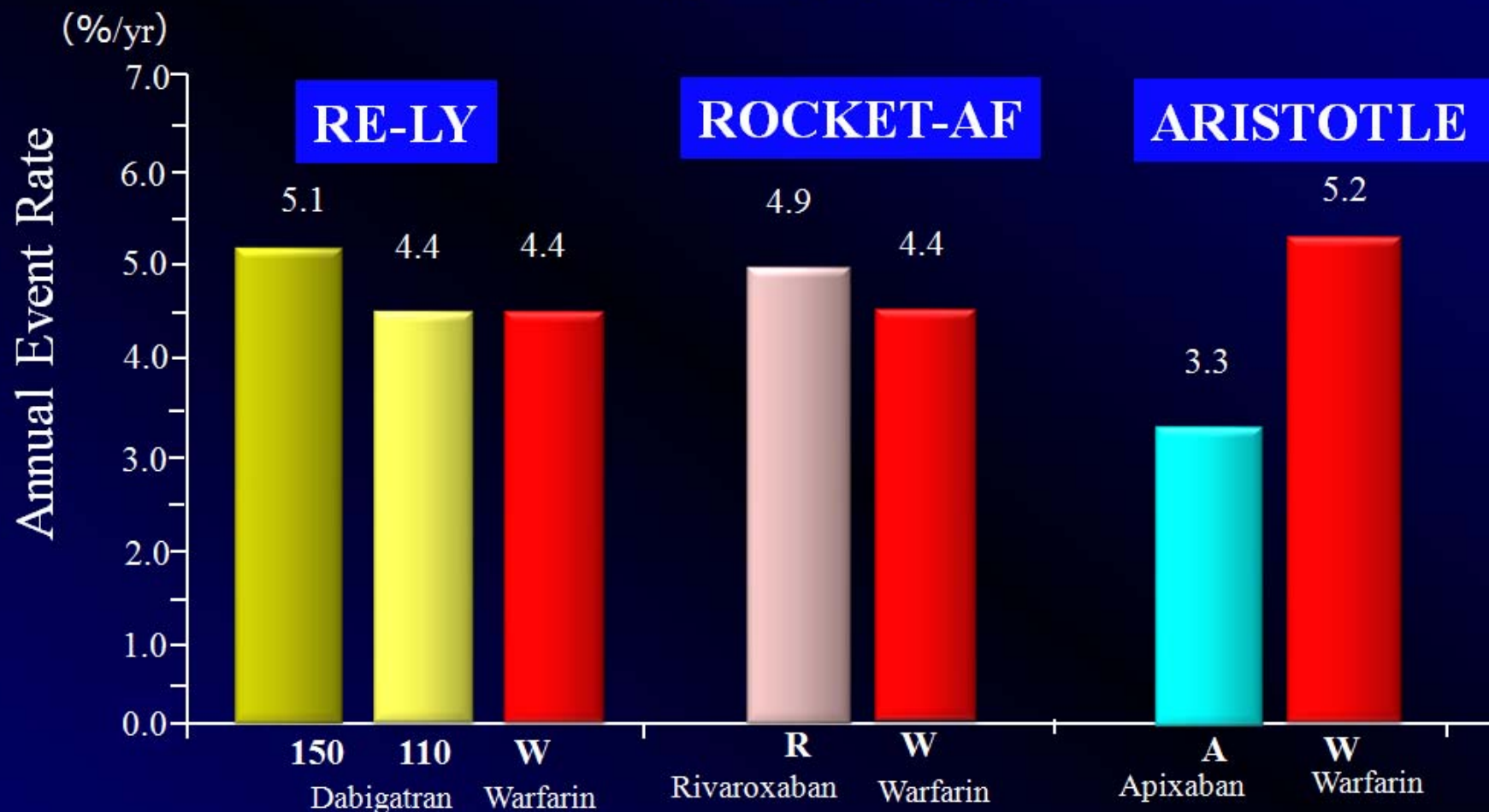
**AF**  
trials

NOACs were more effective than conventional therapy in prevention of stroke or systemic embolism in an elderly population with AF

**Non-  
AF** trials

NOACs had a significantly lower risk of venous thromboembolism (VTE) or VTE-related death than conventional therapy in elderly adults

# Major Bleeding in Patients Aged $\geq 75$ years in NOAC trials



*Connolly SJ, et al.: N Engl J Med 2010; 363, 1875-1876*  
*Pater MR, et al.: N Engl J Med 2011; 365, 883-891*  
*Granger CB, et al.: N Engl J Med 2011; 365: 981-92*

# Are NOACs safe in Adult Congenital Heart Disease?

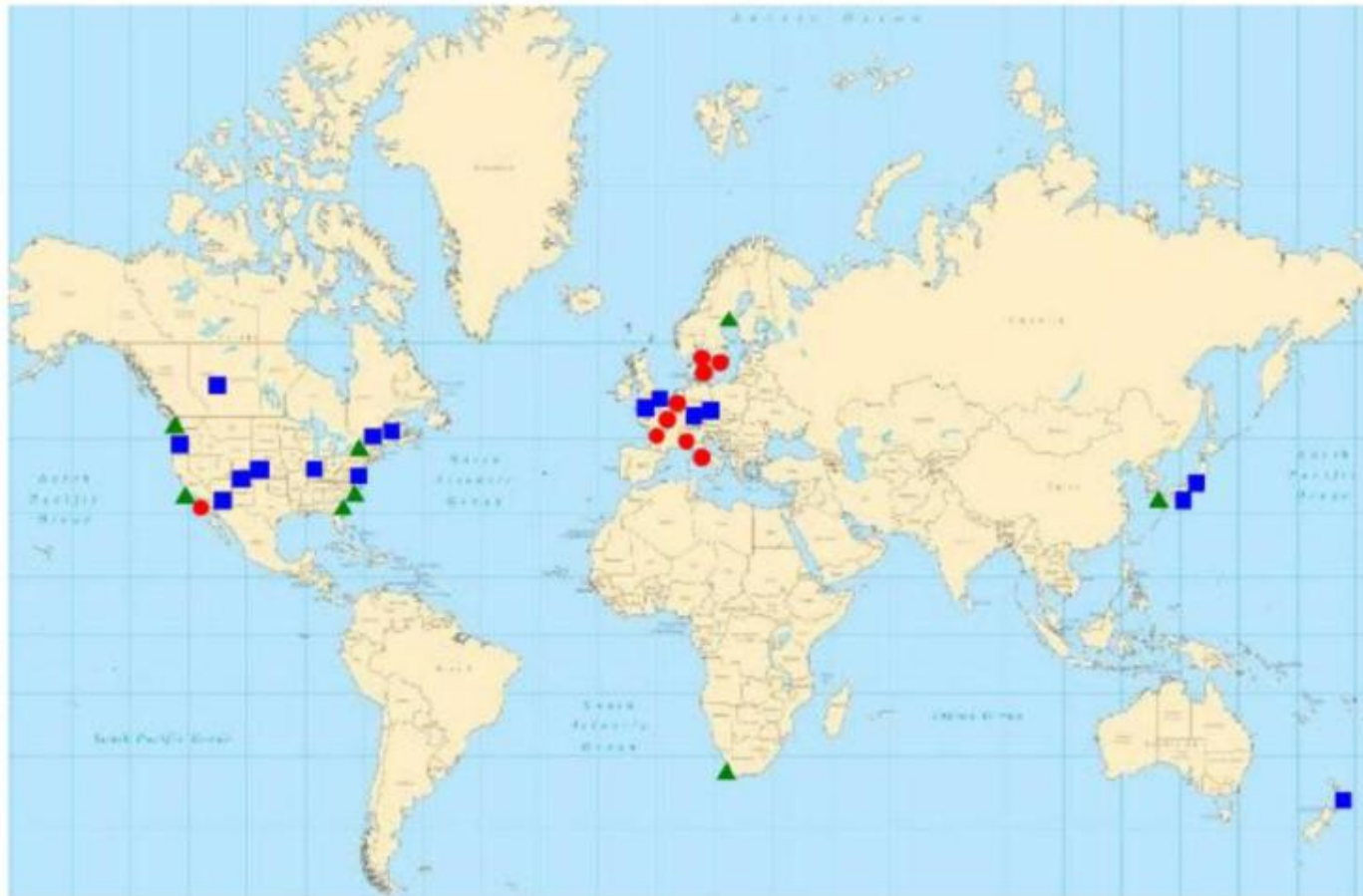
## First results of an International Multicenter Registry

H. Yang, GTJ. Sieswerda, FJ. Meijboom, T. Konings, G. Veen, M. Post, Van Dijk, M. Ladouceur, D. Tobler, M. Schwerzmann, T. Rutz, J. Bouchardy, M. Greutmann, G. Scognamiglio, W. Budts, M. Dellborg, K. Skoglund, T. Kronvall, C. Christersson, J. Aboulhosn, M. Morissens, B. Johansson, H. Schneider, J. Oliver, H. Baumgartner, G. Diller, O. Tutarel, P. Khairy, C. Silversides, G. Webb, G. Veldtman, SAR. Opotowsky, C. Broberg, J. Kay, S. Tsai, T. Moe, T. Akagi, K. Niwa, A. Mizuno, C. O'Donnell, BJ. Bouma, BJM. Mulder



# NOACs are promising alternatives to VKA

**Belgium**  
 Leuven  
 Brussels  
**Canada**  
 Montreal  
 Edmonton  
 Hamilton  
 Toronto  
**France**  
 Paris  
**Germany**  
 Muenster  
 Hannover  
**Italy**  
 Naples  
**Japan**  
 Okayama  
 Tokyo  
**South Korea**  
 Seoul  
**Netherlands**  
 Amsterdam  
 Utrecht  
 Nieuwegein  
 Nijmegen  
**New Zealand**  
 Auckland



**South Africa**  
 Sweden  
 Gothenburg  
 Uppsala  
 Orebro  
 Umea  
**Switzerland**  
 Basel  
 Bern  
 Genève  
 Lausanne  
 Zurich  
**UK**  
 Manchester  
 Leeds  
**USA**  
 Los Angeles  
 Cincinnati  
 Seattle  
 Portland  
 Boston  
 Phoenix  
 Philadelphia  
 Denver  
 Nebraska  
 San Francisco  
 New York

○ = centers with MEC approval   □ = centers in process of obtaining MEC approval   △ = interested centers



# Preliminary results (follow-up)

Cumulative follow-up: **87 patient years (n=133)**

ACHD with AA	Annual events	
	VKA	NOAC
Thromboembolism	1.4%	0%
Major bleeding	4.4%	1.1%

3 Drop outs:

- 1 → major gastro bleeding
- 2 → presumed side-effects

***NOACs seem safe and effective in ACHD patients***



*Prevention*

## Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 1

Hans-Christoph Diener<sup>1\*</sup>, James Aisenberg<sup>2</sup>, Jack Ansell<sup>3</sup>, Dan Atar<sup>4</sup>,  
Günter Breithardt<sup>5</sup>, John Eikelboom<sup>6</sup>, Michael D. Ezekowitz<sup>7,8,9</sup>,  
Christopher B. Granger<sup>10</sup>, Jonathan L. Halperin<sup>11</sup>, Stefan H. Hohnloser<sup>12</sup>,  
Elaine M. Hylek<sup>13</sup>, Paulus Kirchhof<sup>14,15</sup>, Deirdre A. Lane<sup>16</sup>, Freek W.A. Verheugt<sup>17</sup>,  
Roland Veltkamp<sup>18</sup>, and Gregory Y.H. Lip<sup>19,20</sup>

## Patients receiving rhythm- and rate-control therapy

Choice and dose  
of NOAC

The dose of dabigatran or edoxaban should be reduced  
in patients taking verapamil

No dose reduction is needed in patients taking  
rivaroxaban with verapamil

Apixaban does not interact with amiodarone or  
verapamil

Dabigatran is contraindicated in combination with  
dronedrone

Edoxaban 30 mg should be used in patients on  
dronedrone





*Ευχαριστώ για την προσοχή σας*