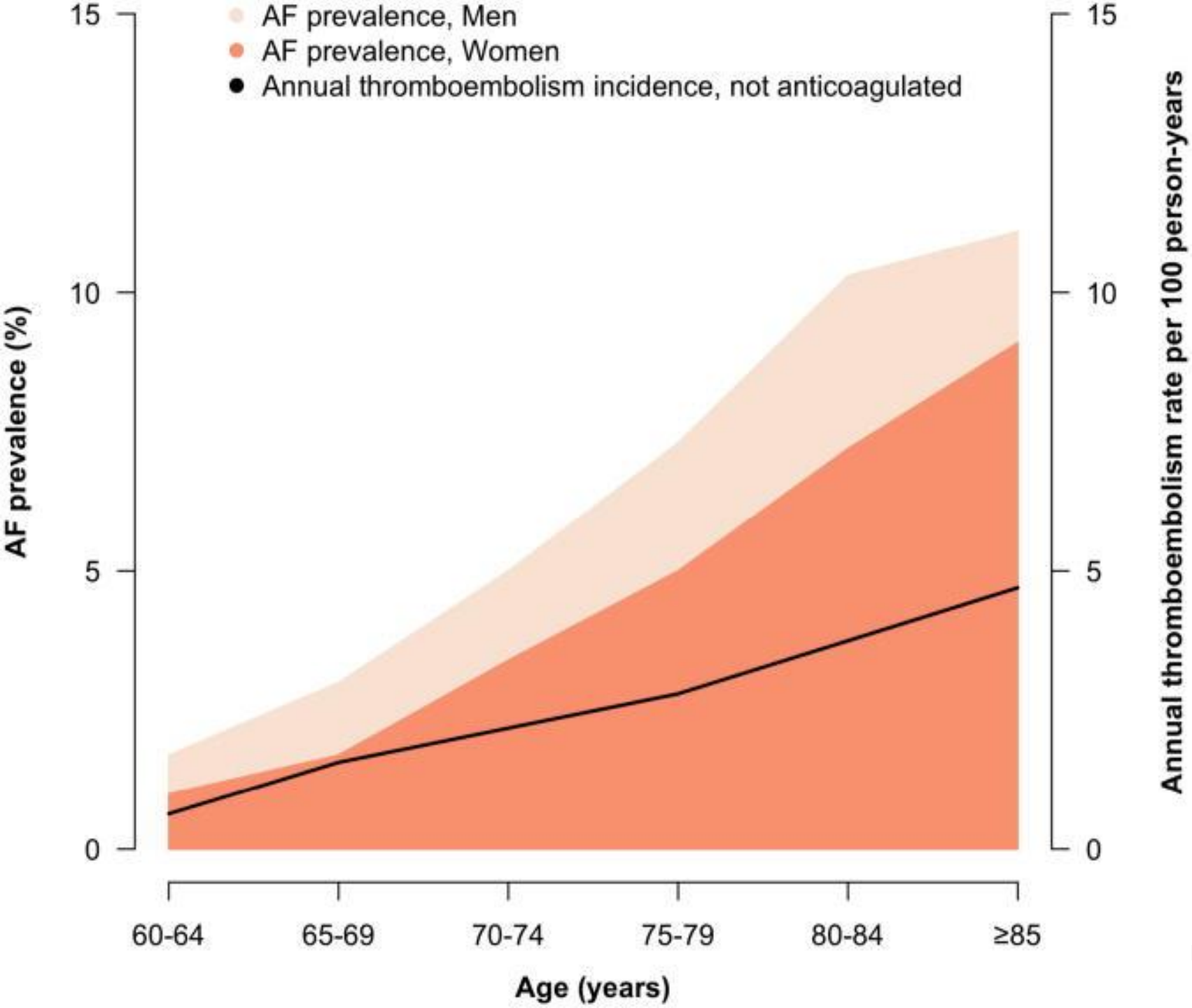
ÚJ TÍPUSÚ ORÁLIS ANTIGOAGULÁNSOK (NOAC, DOAC) A STROKE MEGELŐZÉSÉBEN

Dr. Fehér Gergely

Szigetvári Kórház

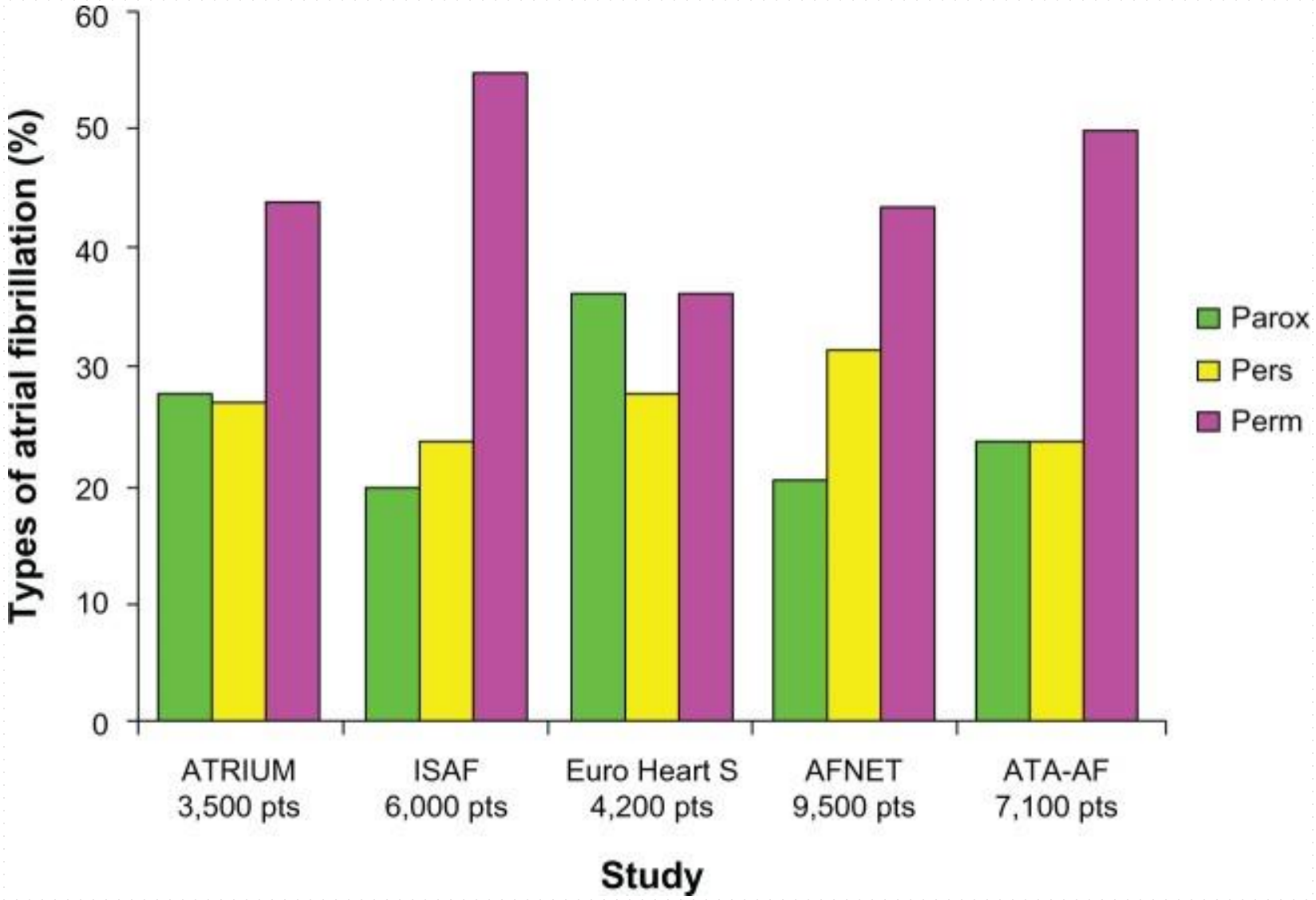
Neurológiai Osztály



PITVAR-FIBRILLÁCIÓ JELENTŐSÉGE

Lubitz SA. Et al. J Am Geriatr Soc. 2013;61(10):1798-803

PITVARFIBRILLÁCIÓ TÍPUSAI



Massimo Z. et al. Clin Epidemiol. 2014; 6: 213–220.

Prolonged Ambulatory Cardiac Monitoring Improves the Detection and Treatment of Atrial Fibrillation in Patients with Cryptogenic Stroke: Primary Results from the EMBRACE Multicenter Randomized Trial

Background: **Detecting** atrial fibrillation (AF) in stroke/TIA patients can result in therapy to prevent recurrent strokes. However, standard short duration monitoring (24-48 h) for atrial fibrillation may not detect AF.

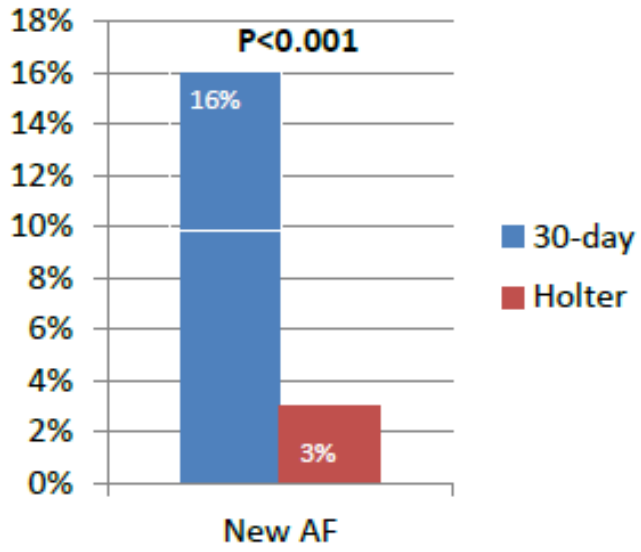
Purpose: This study is the first randomized trial to evaluate whether longer non-invasive ECG monitoring after stroke/TIA would produce beneficial results.

Methods: n=572 (age 73±9yrs;); recent ischemic stroke/TIA, no known AF; 16 stroke centers; Randomized to wear either an event-triggered cardiac monitor up to 30 days or a repeat 24 h Holter. AF events automatically recorded.

Primary Outcome: ≥1 episodes of AF of at least 30 seconds within 90 days of randomization

Secondary Outcomes: monitoring adherence ; anticoagulation status

Results: New AF detected among 16% of 30-day monitoring group, vs. 3% in the Holter group (p<0.001). In the 30 day group three quarters of AF events occurred within the first 2 weeks. 71% of all patients were anticoagulated; anticoagulant use at 90 days > 30 day group (49/280; 18%) vs. Holter group (28/279; 10%; p=0.01).



Conclusion: Paroxysmal AF is undiagnosed and untreated in many stroke/TIA patients ; in the post-stroke setting it is under-detected by the Holter monitor. Prolonged continuous monitoring for 30 days is "feasible, more effective, and leads to clinically meaningful changes in patient management. "

Presented by: Gladstone DJ, International Stroke Conference, Honolulu, HI

A CHA_2DS_2-VASc sémát a $CHADS_2$ pontozási rendszer kiegészítésére az Európai Kardiológiai Társaság is átvette

$CHADS_2$	*Pontszám*	*CHA_2DS_2-VASc*	*Pontszám*
Pangásos szívelégtelenség	1	Pangásos szívelégtelenség/balkamra dysfunctio	1
Hypertonia	1	Hypertonia	1
Életkor ≥75 év	**1**	**Életkor ≥75 év**	**2**
Diabetes mellitus	1	Diabetes mellitus	1
Stroke/TIA/TE	2	Stroke/TIA/TE	2
Maximális pontszám	**6**	**Érbetegség (korábbi MI, PAD vagy aorta plakk)**	**1**
		Életkor 65-74 év	**1**
		Nemi hovatartozás (azaz női nem)	**1**
		Maximális pontszám	**9**

CHA_2DS_2-VASc

- Azok a betegek, akiknél a $CHADS_2$-pontszám 0-1, vagy
- ha részletesebb stroke kockázatfelmérés indokolt

Camm et al. Eur Heart J 2010;31:2369-429.

K-VITAMIN ANTAGONISTA KEZELÉS PITVARFIBRILLÁCIÓBAN

- 28044 beteg utánkövetéses meta-analízise
- **Warfarin** adása **64%-kal** csökkentette az ischaemiás stroke előfordulását
- **Thrombocyta aggregáció gátló** terápia esetén **22%-os** csökkenés érhető el
- Vérzéses szövődmények száma kevés (cca. 0.3% évente)

Hart RG et al. Ann Intern Med. 2007;146(12):857-67

VÉRZÉSES SZÖVŐDMÉNYEK ASPIRIN VS WARFARIN MELLETT

TABLE 3. ADVERSE EVENTS ACCORDING TO TREATMENT ASSIGNMENT.*

EVENT	WARFARIN (N=1103)	ASPIRIN (N=1103)	ODDS RATIO (95% CI)	P VALUE†
	no. (%)			
Death	47 (4.3)	53 (4.8)	0.88 (0.58–1.32)	0.61
Related to hemorrhage	7 (0.6)	5 (0.4)	1.40 (0.42–5.13)	0.77
First hemorrhage‡				
Major	38 (3.4)	30 (2.7)	1.28 (0.78–2.10)	0.39
Minor	261 (23.7)	188 (17.0)	1.51 (1.22–1.87)	<0.001
			RATE RATIO (95% CI)	P VALUE§
	no. of events (rate/100 patient-yr)			
All hemorrhages¶				
Major	44 (2.2)	30 (1.5)	1.48 (0.93–2.44)	0.10
Minor	413 (20.8)	259 (12.9)	1.61 (1.38–1.89)	<0.001

*Maximal follow-up was 25 months. Hemorrhages occurring on the day of the primary event (death or recurrent ischemic stroke) are included. CI denotes confidence interval.

†P values were calculated by the exact test of two independent proportions.

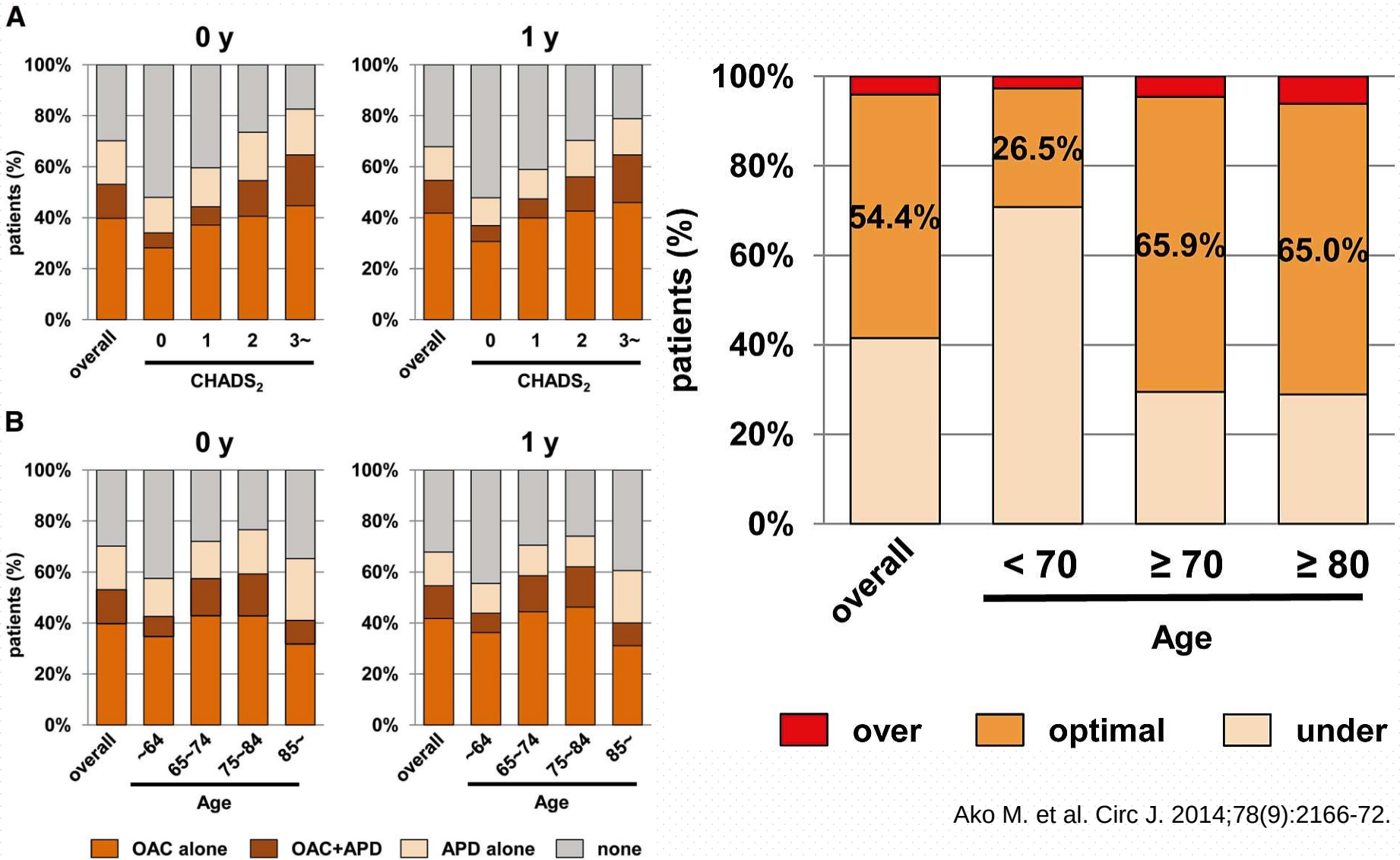
‡The first hemorrhage is the first or only hemorrhage for each patient.

§P values were calculated by the exact conditional binomial test for two independent Poisson processes.

¶All hemorrhages include all hemorrhages in any patient.

Mohr JP et al. N Engl J Med. 2001;345(20):1444-51

EVIDENCIÁK ÉS A VALÓSÁG



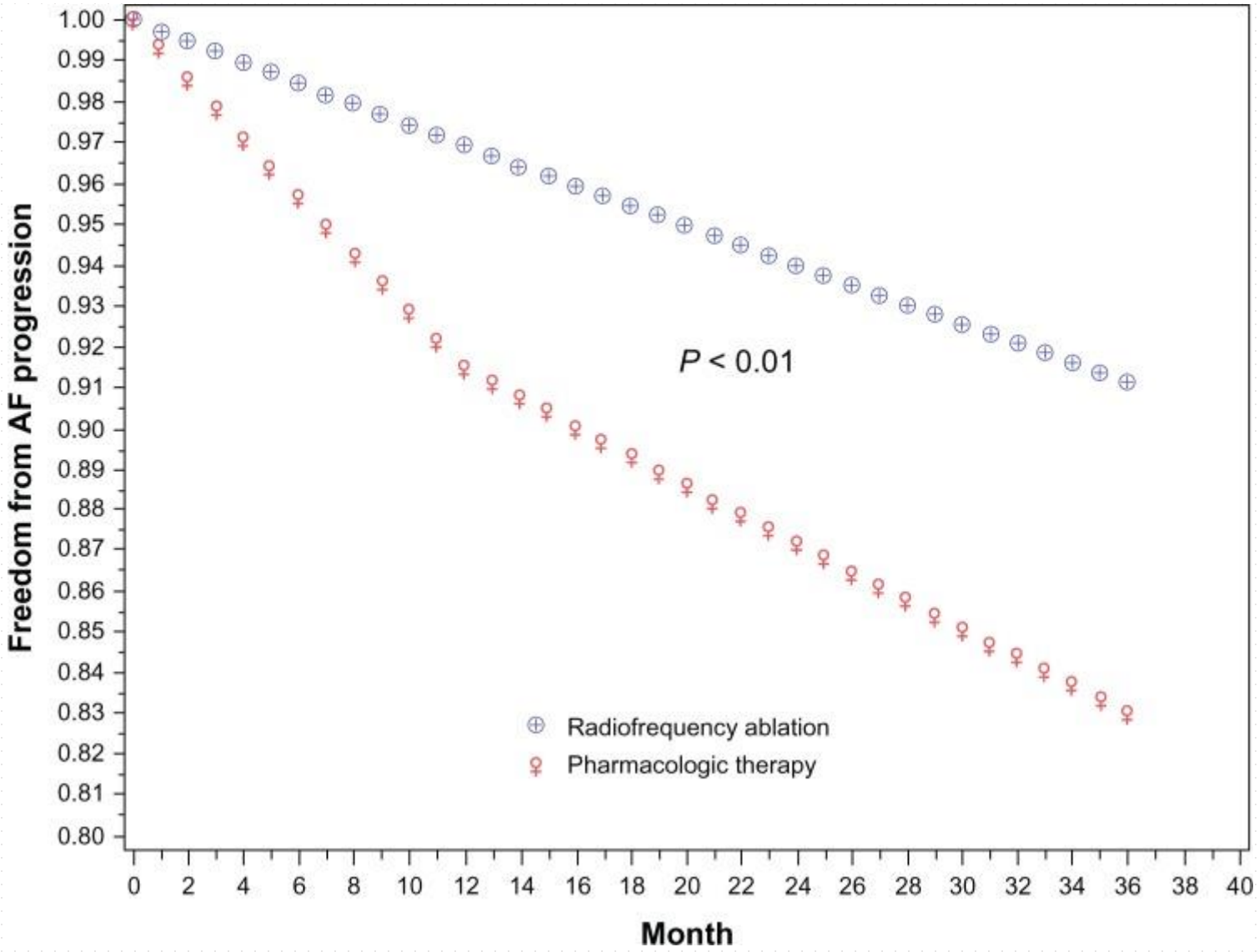
Ako M. et al. Circ J. 2014;78(9):2166-72.

MIÉRT HASZNÁLUNK ACENOCOUMAROLT?

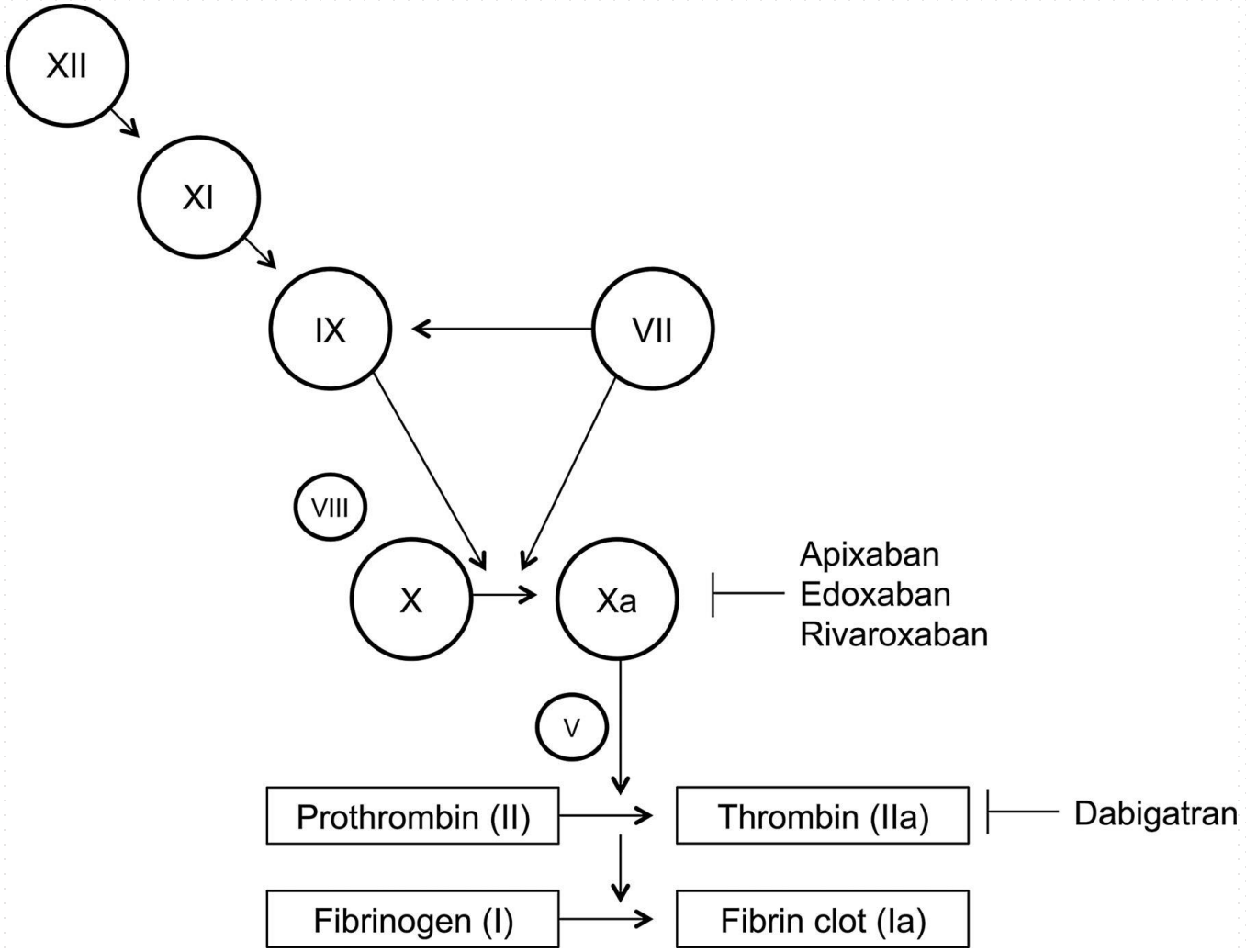
- The percentage of visits within the intended range of INR (2 to 3) was 65.5% with warfarin and 63.4% with acenocoumarol. *Thirty percent of patients on warfarin had 75% or more of their controls within range, while for those treated with acenocoumarol this percentage was 22.5%*. In the acenocoumarol group, 0.3 visits/patient/year presented an INR > or = 6 versus 0.07 in the warfarin group (p = 0.003).

Oliva Berini E. et al. Med Clin (Barc). 2008 ;131(3):96-7

CARDIOVERSIO HATÉKONYSÁGA



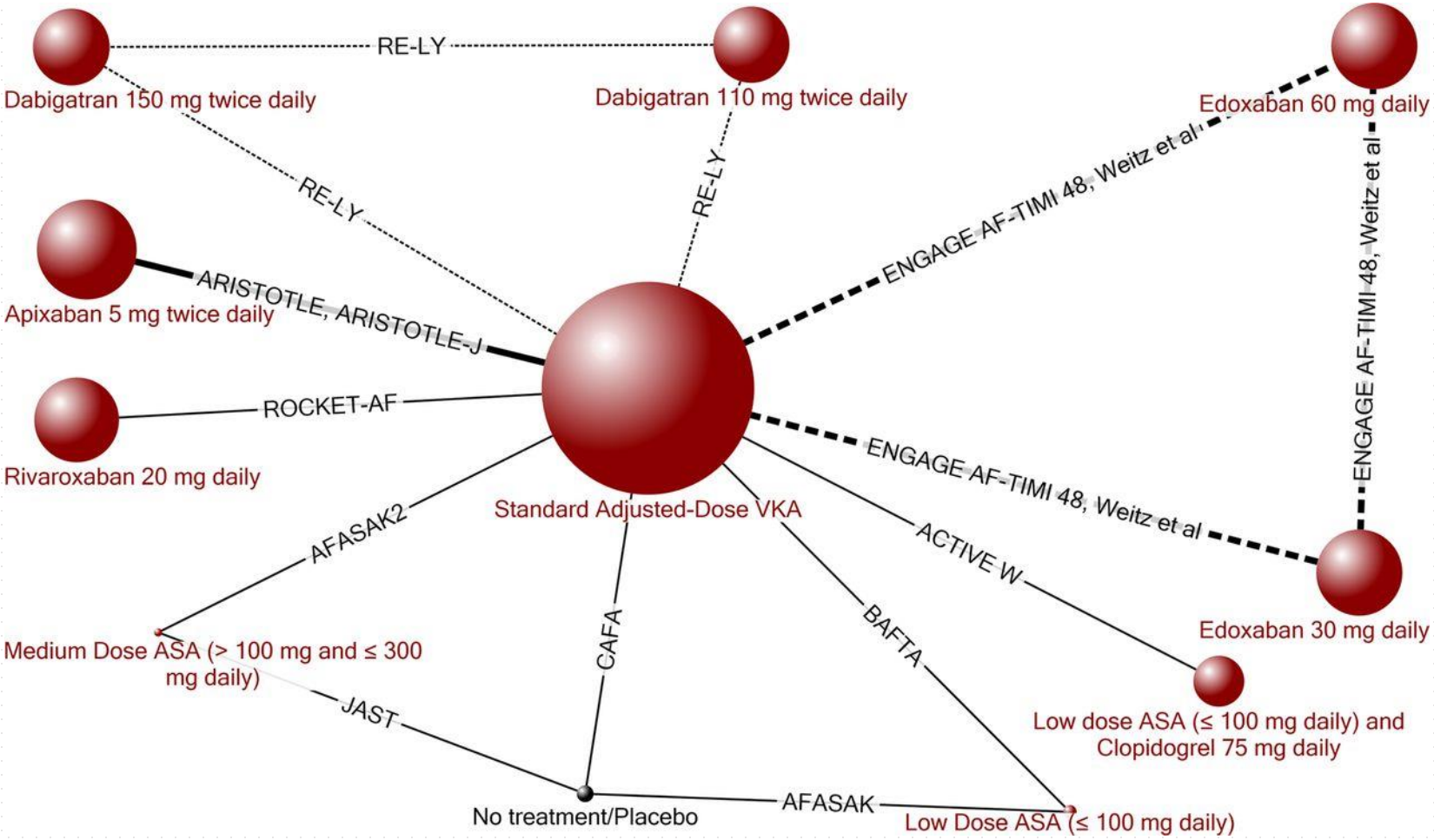
Key targets of the direct oral anticoagulants in the coagulation cascade.



Richard P W Cowell Postgrad Med J 2014;90:529-539

PMJ

PREVENCIÓS TANULMÁNYOK



Chris Cameron et al. BMJ Open 2014;4:e004301

BMJ Open

LEGFONTOSABB TANULMÁNYOK

	Dabigatran (RE-LY)	Apixaban (ARISTOTLE)	Rivaroxaban (ROCKET AF)	Edoxaban (ENGAGE AF TIMI)
betegszám	18 113	18201	14264	21105
beválasztás	egyszeres vak	kettős vak	kettős vak	kettős vak
életkor	71 év	70 év	73 év	72 év
nemi megoszlás	63,6 % férfi	64,7% férfi	60,3% férfi	62 % férfi
CHADS2 score	2,1	2,1	3,5	2,8
diabetes	23 %	25 %	40 %	36,2 %
vesebetegség	30 alatti GFR kizárási kritérium	25 alatti GFR kizárási kritérium	30 alatti GFR kizárási kritérium	30 alatti GFR kizárási kritérium

EREDMÉNYEK: DABIGATRAN

	Warfarin (n=6022)	Dabigatran 110 mg (n=6015)	p érték	Dabigatran 150 mg (n=6076)	p érték
ISCHAEMIÁS STROKE	142	159	**0,35**	111	**0,03**
SYSTEMAS EMBOLISATIO (ÉS STROKE)	199	182	**0,34**	134	**<0,001**
MAJOR VÉRZÉS	397	322	**0,003**	350	**0,31**
VÉRZÉSES STROKE	45	14	**<0,001**	12	**<0,001**
GI VÉRZÉS	120	133	**0,43**	182	**<0,001**
VASCULARIS HALÁLOZÁS	317	289	**0,21**	274	**0,04**
HALÁLOZÁS	487	446	**0,13**	438	**0,051**

EREDMÉNYEK: APIXABAN

	Warfarin (n=9081)	Apixaban 2,5 mg (n=428) Apixaban 5 mg (n=8692	p érték
ISCHAEMIÁS STROKE	175	162	**0,42**
SYSTEMAS EMBOLISATIO	17	115	**0,1**
MAJOR VÉRZÉS	877	613	**<0,001**
VÉRZÉSES STROKE	122	52	**<0,001**
GI VÉRZÉS	119	105	**0,37**
VASCULARIS HALÁLOZÁS (+ÖSSZHALÁLOZÁS)	906	810	**0,01**
HALÁLOZÁS	669	603	**0,047**

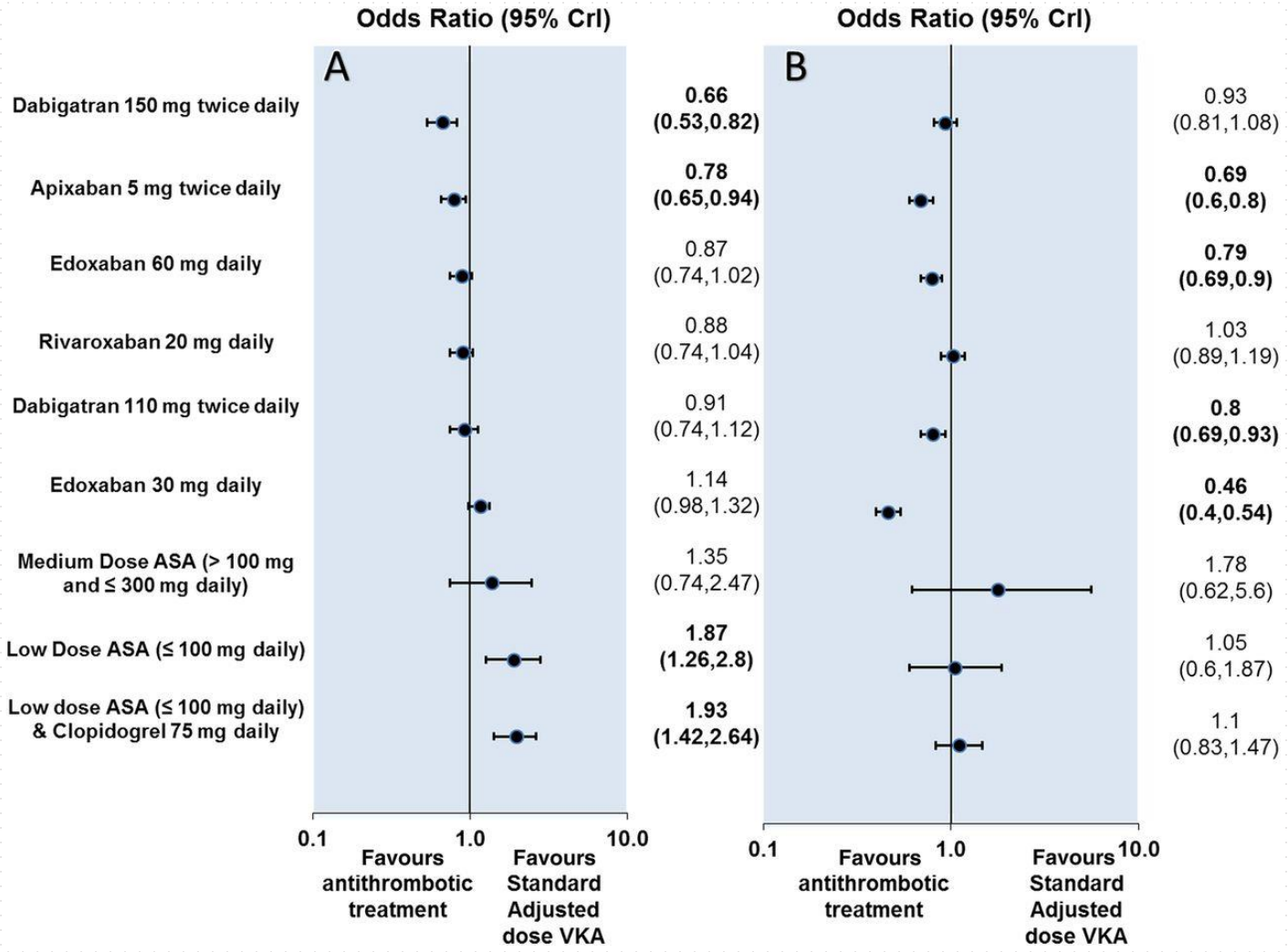
EREDMÉNYEK: RIVAROXABAN

	Warfarin (n=7133)	Rivaroxaban 20 és 15 mg (n=7131)	p érték
STROKE ÉS SYSTEMAS EMBOLISATIO	241	188	**0,02**
ISCHAEMIAS STROKE	161	149	**0,51**
MAJOR VÉRZÉS	386	395	**0,58**
VÉRZÉSES STROKE	84	55	**0,02**
GI VÉRZÉS	154	224	**<0,001**
VASCULARIS HALÁLOZÁS	193	170	**0,289**
HALÁLOZÁS	250	208	**0,071**

EREDMÉNYEK: EDOXABAN

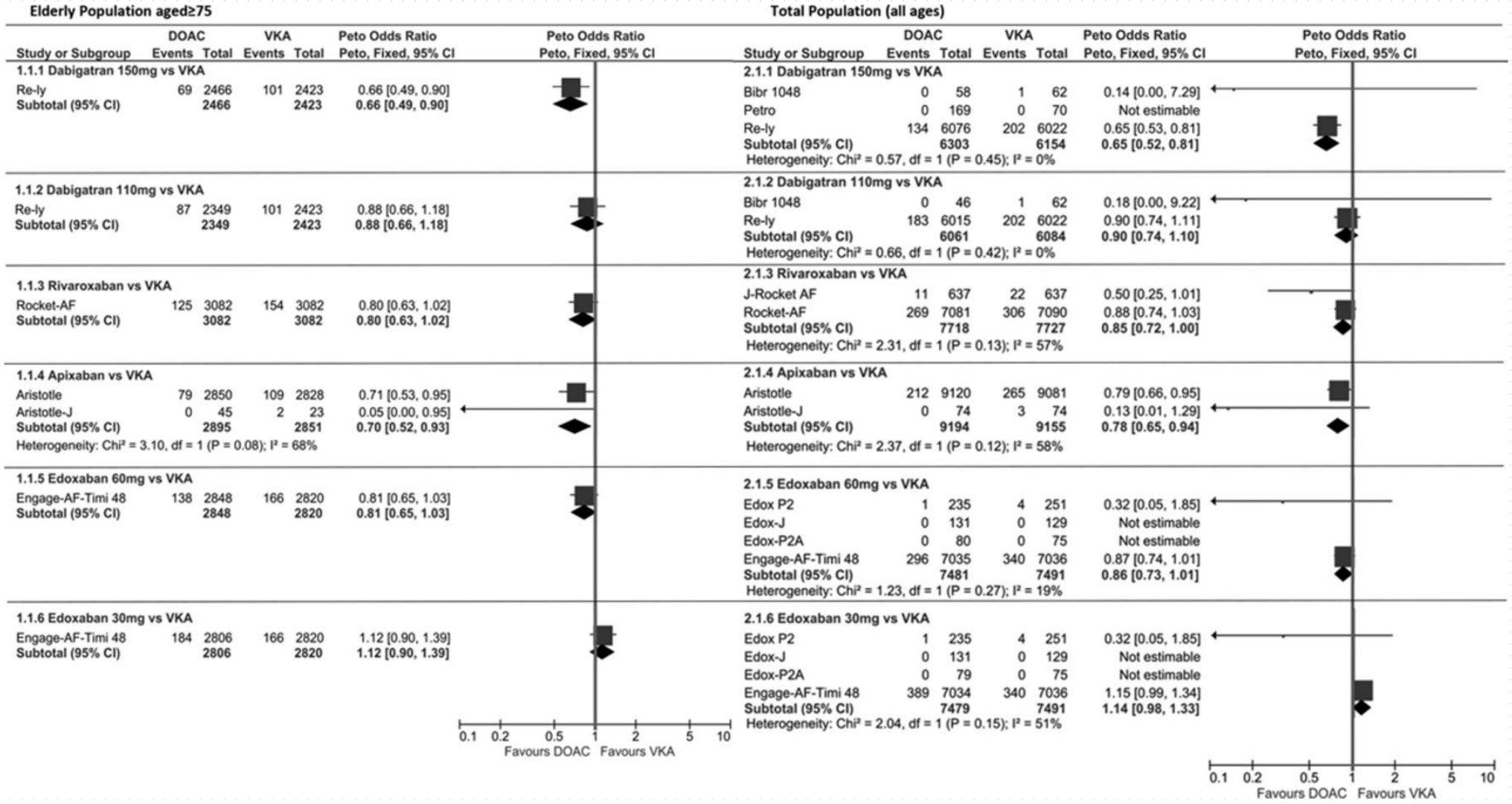
	Warfarin (n=7036)	Edoxaban 30 mg (n=7034)	p érték	Edoxaban 60 mg (n=7035)	p érték
ISCHAEMIÁS STROKE	235	333	**< 0,001**	236	**0,97**
SYSTEMAS EMBOLISATIO	23	29	**0,43**	15	**0,19**
MAJOR VÉRZÉS	524	254	**< 0,001**	418	**< 0,001**
VÉRZÉSES STROKE	90	30	**< 0,001**	49	**< 0,001**
GI VÉRZÉS	190	129	**< 0,001**	232	**0,03**
VASCULARIS HALÁLOZÁS	611	527	**0,008**	530	**0,08**
HALÁLOZÁS	839	737	**0,08**	773	**0,006**

EMBOLISATIO VS VÉRZÉS A FELSOROLT TANULMÁNYOKBAN



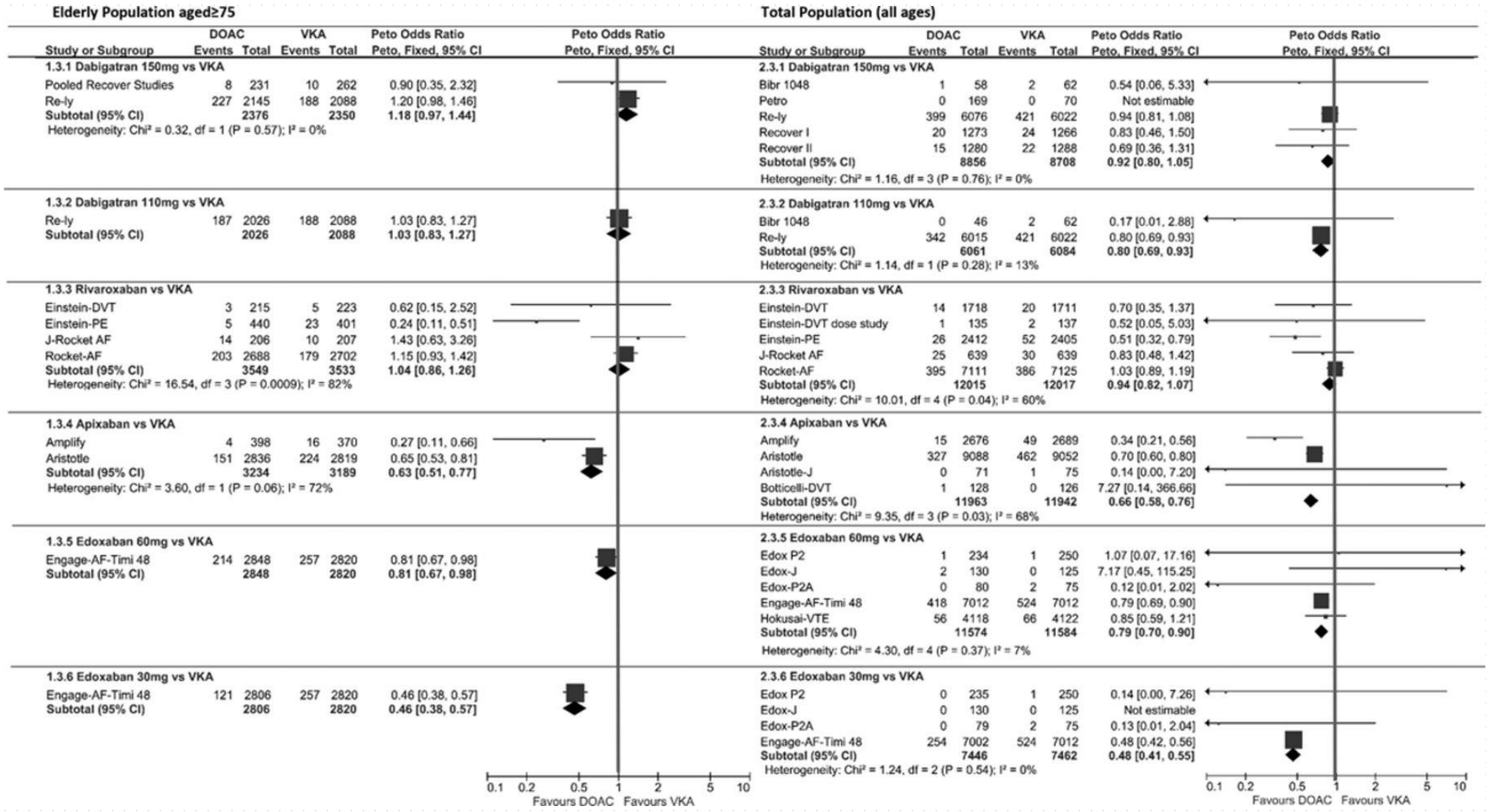
Chris Cameron et al. BMJ Open 2014;4:e004301

NOAC HASZNÁLATA >75 ÉV FELETT : ISCHAEMIA



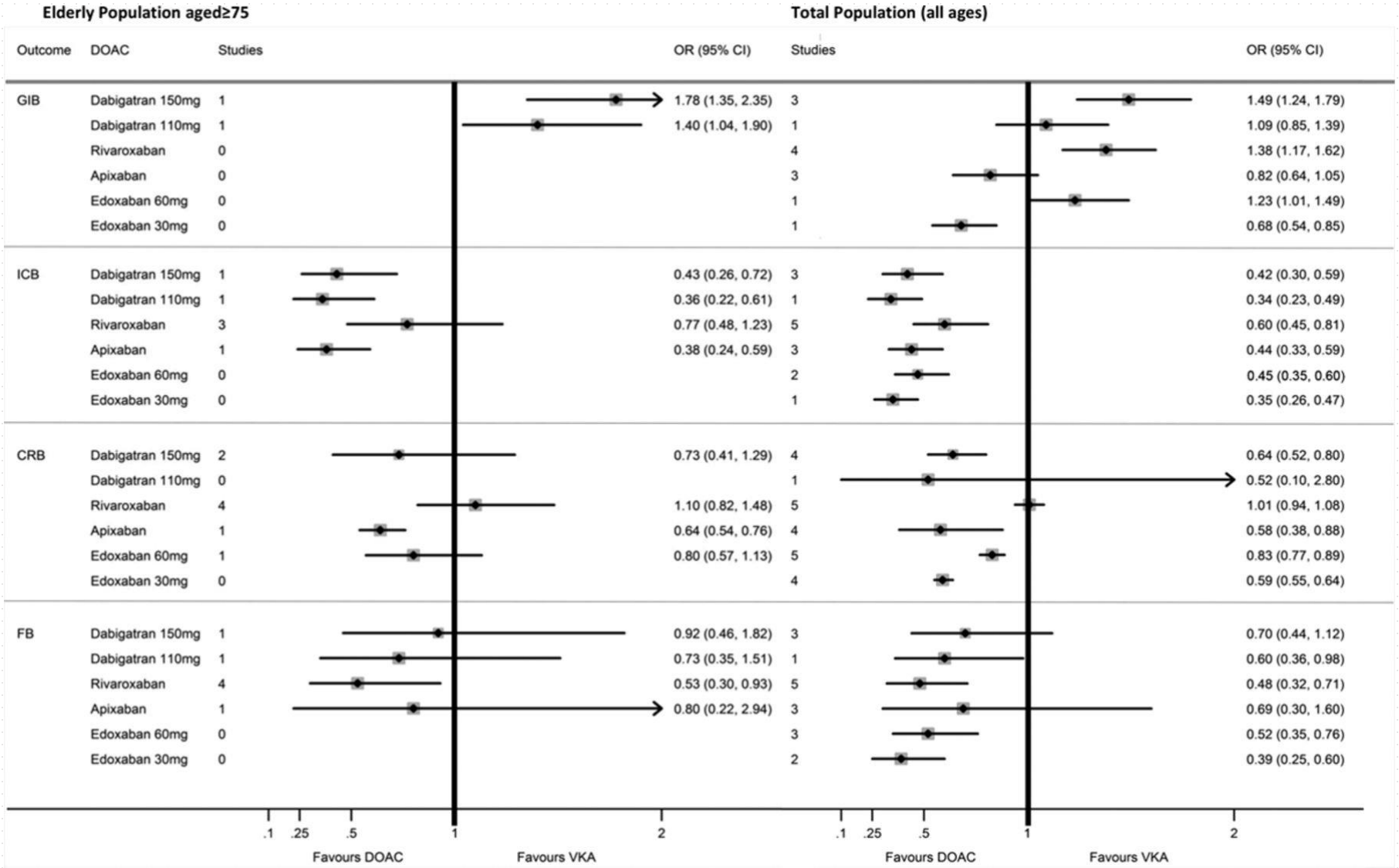
Manuj Sharma et al. Circulation. 2015;132:194-204

NOAC HASZNÁLATA >75 ÉV FELETT : VÉRZÉS



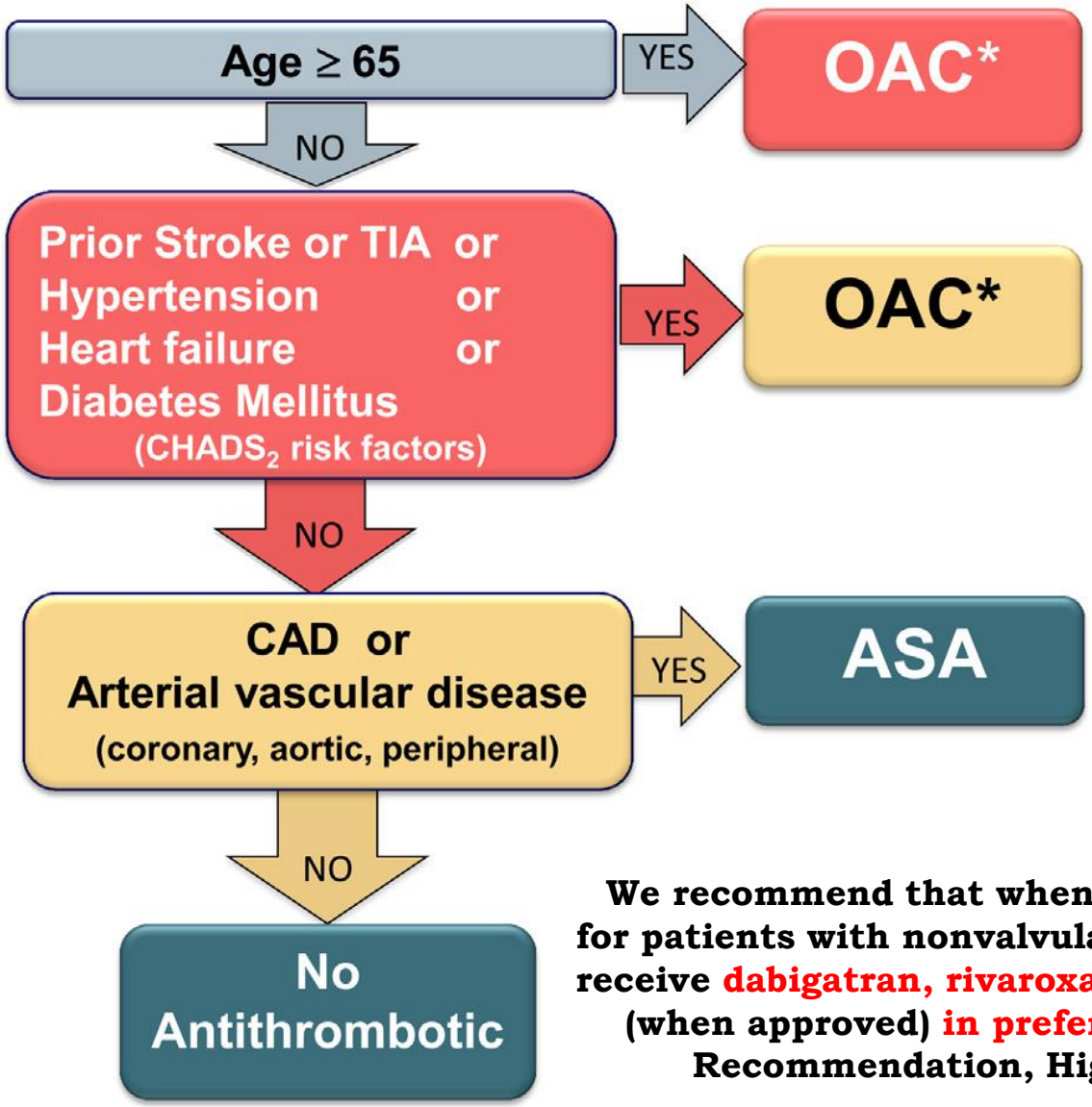
Manuj Sharma et al. Circulation. 2015;132:194-204

NOAC HASZNÁLATA >75 ÉV FELETT : VÉRZÉS



Manuj Sharma et al. Circulation. 2015;132:194-204

The "CCS Algorithm" for OAC Therapy in AF



Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥ 75, low body weight).†

We recommend that when OAC therapy is indicated for patients with nonvalvular AF, most patients should receive dabigatran, rivaroxaban, apixaban, or edoxaban (when approved) in preference to warfarin (Strong Recommendation, High-Quality Evidence).

Verma A et al. Can J Cardiol. 2014;30(10):1114-30.

EVIDENCIÁK ÉS A VALÓSÁG –

KLINIKAI REGISZTEREK

Dabigatran and Postmarketing Reports of Bleeding

Mary Ross Southworth, Pharm.D., Marsha E. Reichman, Ph.D., and Ellis F. Unger, M.D.

Intracranial and Gastrointestinal Bleeding Events in New Users of Dabigatran and Warfarin from the Mini-Sentinel Distributed Database, October 2010 through December 2011.*

Analysis	Dabigatran			Warfarin		
	No. of Patients	No. of Events	Incidence (no. of events/ 100,000 days at risk)	No. of Patients	No. of Events	Incidence (no. of events/ 100,000 days at risk)
Gastrointestinal hemorrhage						
Analysis with required diagnosis of atrial fibrillation	10,599	16	1.6	43,541	160	3.5
Sensitivity analysis without required diagnosis of atrial fibrillation	12,195	19	1.6	119,940	338	3.1
Intracranial hemorrhage						
Analysis with required diagnosis of atrial fibrillation	10,587	8	0.8	43,594	109	2.4
Sensitivity analysis without required diagnosis of atrial fibrillation	12,182	10	0.9	120,020	204	1.9

FDA Drug Safety Communication

Mary Ross Southworth, Pharm.D. N Engl J Med 368;14, 2013

Recent independent FDA data (>134,000 patients) show that benefits of dabigatran are maintained in clinical practice

	Incidence rate per 100 person-years		Adjusted HR (95% CI)
	Dabigatran	Warfarin	
Ischaemic stroke	1.13	1.39	0.80 (0.67–0.96)
Intracranial haemorrhage	0.33	0.96	0.34 (0.26–0.46)
Major GI bleeding	3.42	2.65	1.28 (1.14–1.44)
Acute myocardial infarction	1.57	1.69	0.92 (0.78–1.08)
Mortality	3.26	3.78	0.86 (0.77–0.96)

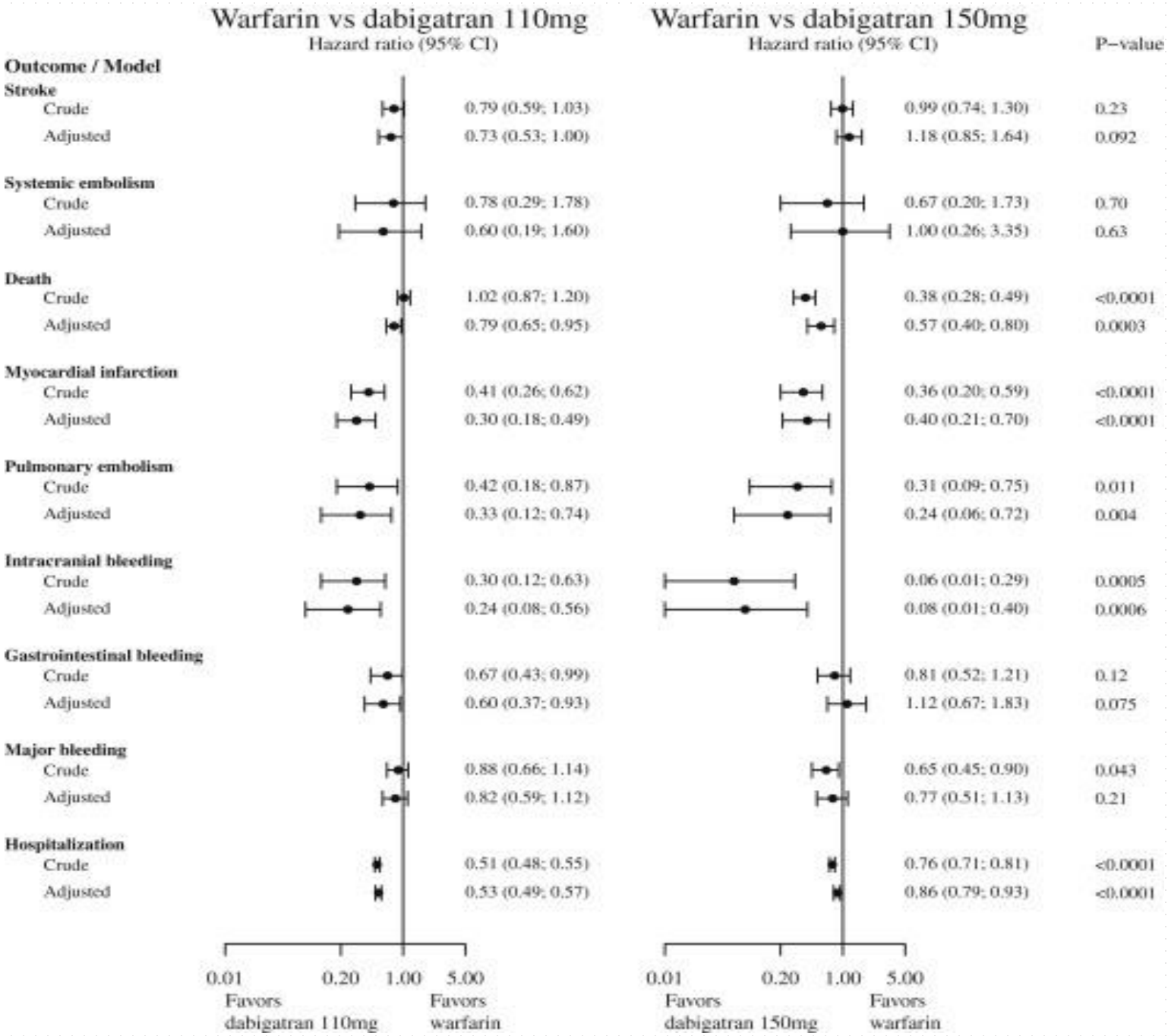
No significant difference identified between dabigatran and warfarin for MI, with fewer ischaemic strokes and ICH, and lower mortality vs warfarin

In the USA, the licensed doses for Pradaxa® are: Pradaxa® 150 mg BID and Pradaxa® 75 mg BID for the prevention of stroke and systemic embolism in adult patients with nonvalvular AF

Primary findings for dabigatran are based on analysis of both 75 mg and 150 mg together without stratification by dose

GI = gastrointestinal

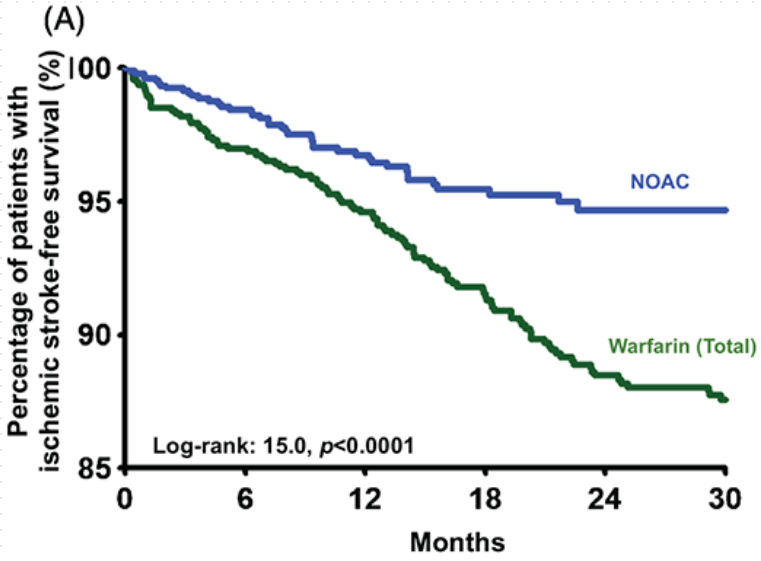
www.fda.gov/Drugs/DrugSafety/ucm396470.htm

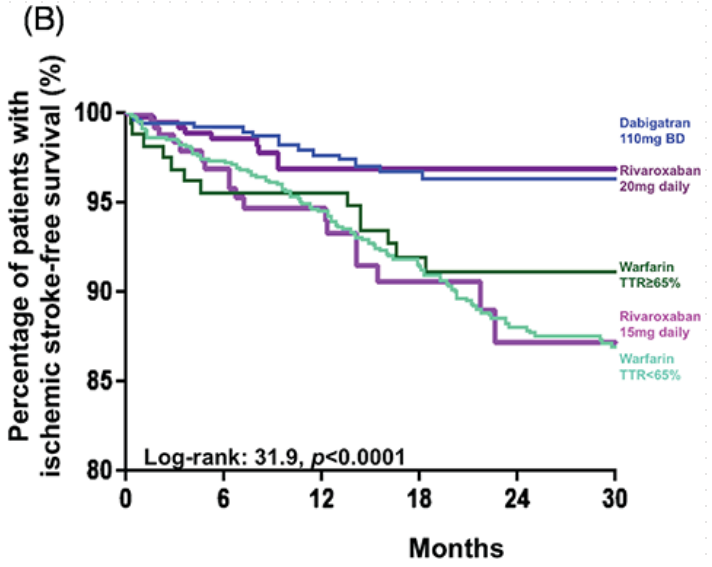


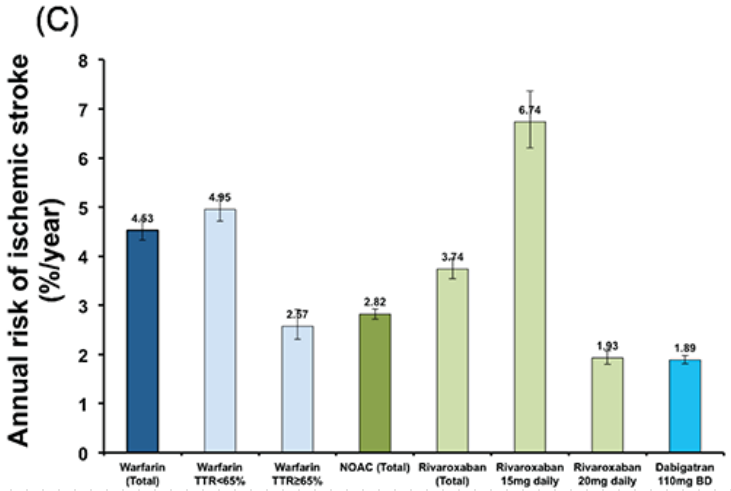
DÁN REGISZTER

Torben BG et al. JACC, 2013;22:2264-2273

HONG KONG ATRIAL FIBRILLATION PROJECT



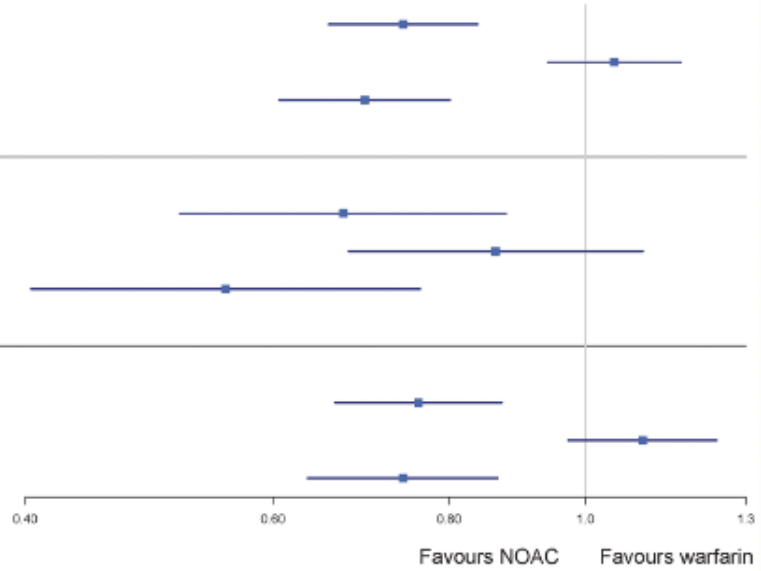




Li WH et al. Clin Cardiol. 2016 Nov 28. doi: 10.1002/clc.22649.

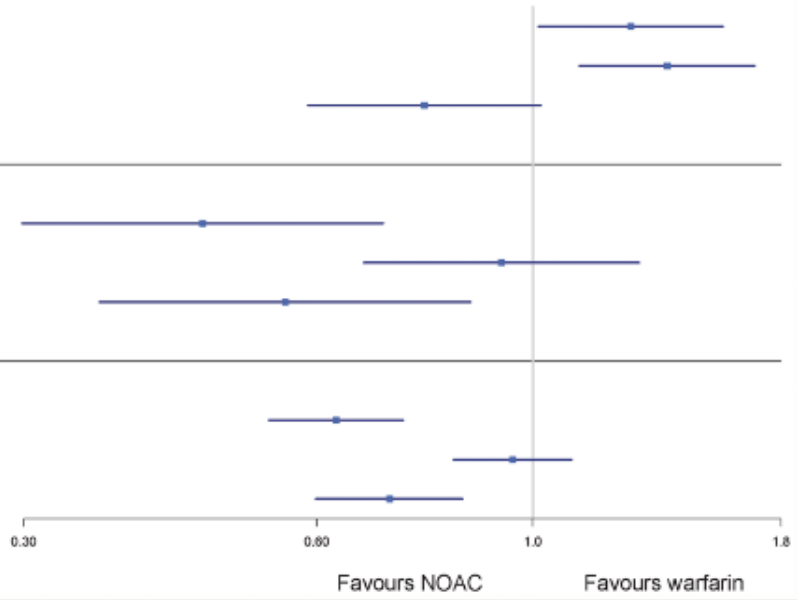
A

OAC	IR	HR (95%CI)	P
Major or CRNM			
Warfarin	11.44	1 (ref.)	
Dabigatran	6.74	0.74 (0.66,0.84)	<0.001
Rivaroxaban	11.43	1.05 (0.94,1.17)	0.400
Apixaban	8.58	0.70 (0.61,0.80)	<0.001
Major			
Warfarin	2.42	1 (ref.)	
Dabigatran	1.29	0.67 (0.52,0.88)	0.004
Rivaroxaban	2.07	0.86 (0.68,1.10)	0.231
Apixaban	1.51	0.56 (0.40,0.76)	0.001
CRNM			
Warfarin	8.85	1 (ref.)	
Dabigatran	5.38	0.76 (0.66,0.87)	<0.001
Rivaroxaban	9.20	1.10 (0.97,1.24)	0.133
Apixaban	7.00	0.74 (0.64,0.87)	<0.001



B

OAC	IR	HR (95% CI)	P
GI			
Warfarin	2.67	1 (ref.)	
Dabigatran	2.43	1.26 (1.01,1.57)	0.037
Rivaroxaban	3.33	1.37 (1.12,1.69)	0.003
Apixaban	2.16	0.77 (0.59,1.02)	0.068
ICH			
Warfarin	1.20	1 (ref.)	
Dabigatran	0.45	0.46 (0.30,0.70)	<0.001
Rivaroxaban	1.19	0.93 (0.67,1.29)	0.656
Apixaban	0.80	0.56 (0.36,0.86)	0.009
Other			
Warfarin	7.33	(1 ref.)	
Dabigatran	3.75	0.63 (0.54,0.74)	<0.001
Rivaroxaban	6.60	0.95 (0.83,1.10)	0.505
Apixaban	5.51	0.71 (0.60,0.85)	<0.001

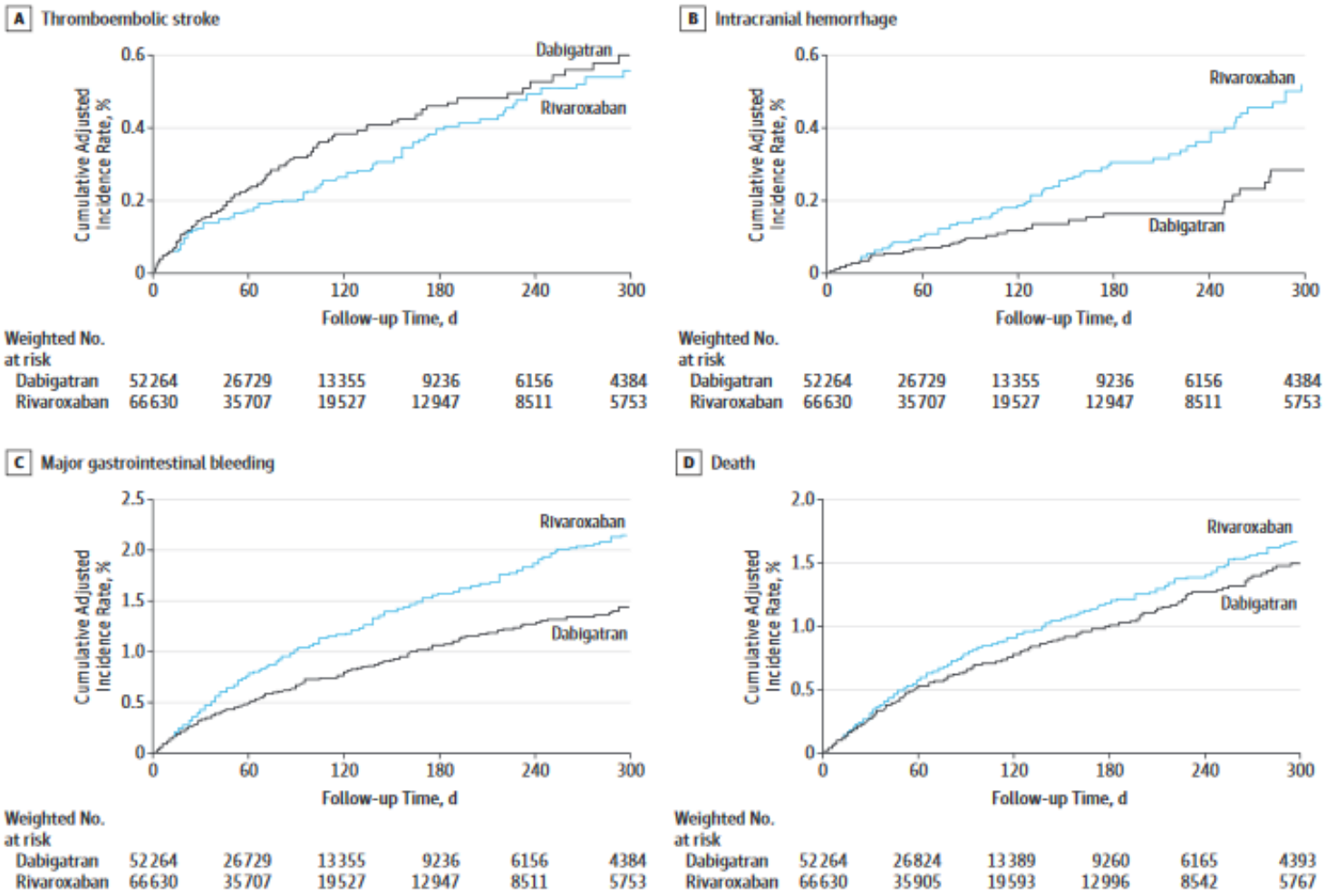


NORVÉG REGISZTER

Halvorsen S. et al.
Eur Heart J Cardiovasc Pharmacother.
2016;3(1):28-36.

MEDICARE ANALÍZIS: DABIGATRAN VS RIVAROXABAN

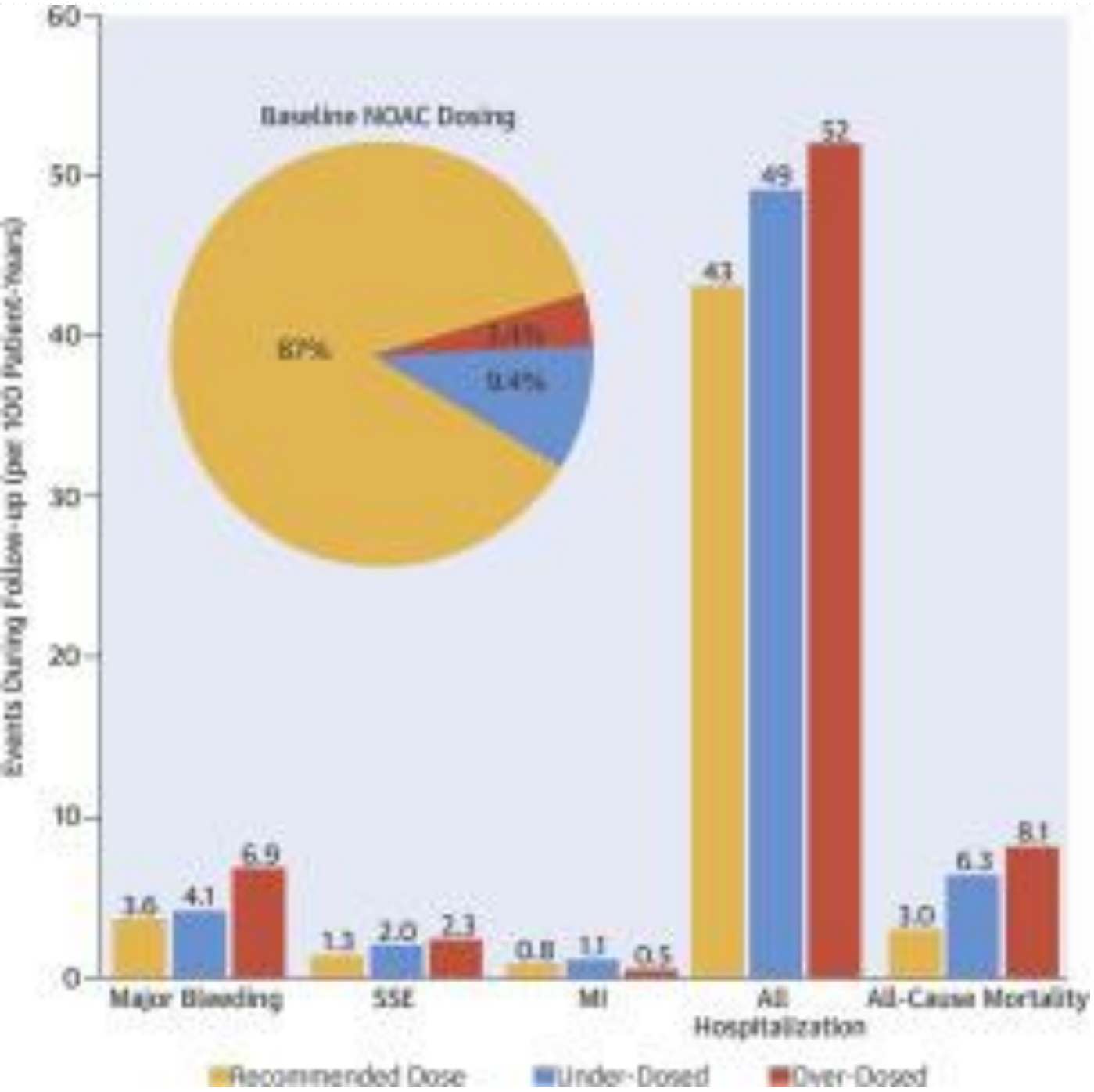
Figure 1. Adjusted Kaplan-Meier Cumulative Incidence Plots of Thromboembolic Stroke, Intracranial Hemorrhage, Major Gastrointestinal Bleeding, and Death in Patients Treated With the Standard Dose of Dabigatran or Rivaroxaban for Stroke Prevention With Atrial Fibrillation



Note that the y-axis scales vary by outcome.

Graham DJ et al. JAMA Intern Med. 2016 ;176(11):1662-1671

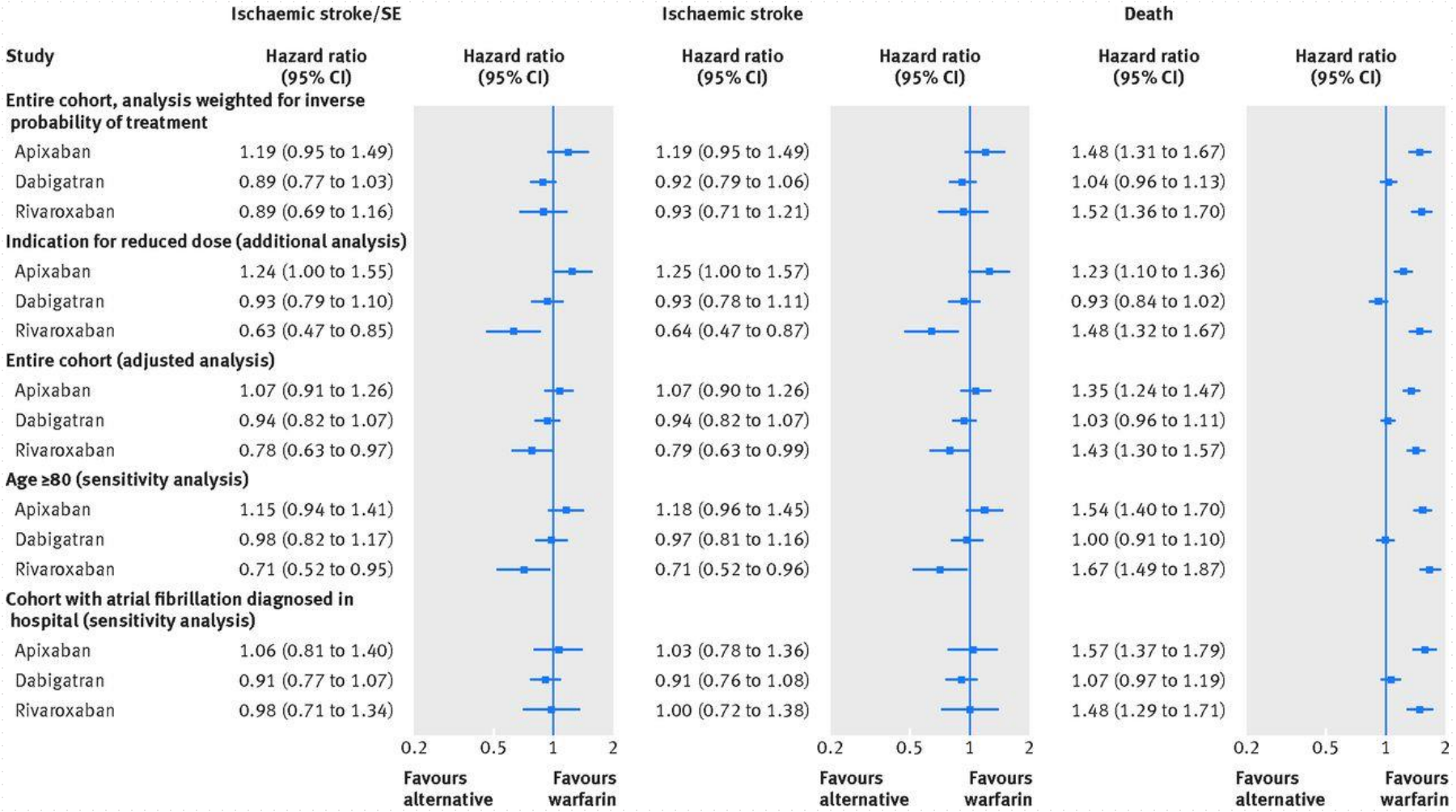
SPECIÁLIS KÉRDÉSEK



FONTOS AZ ADEKVÁT DÓZIS

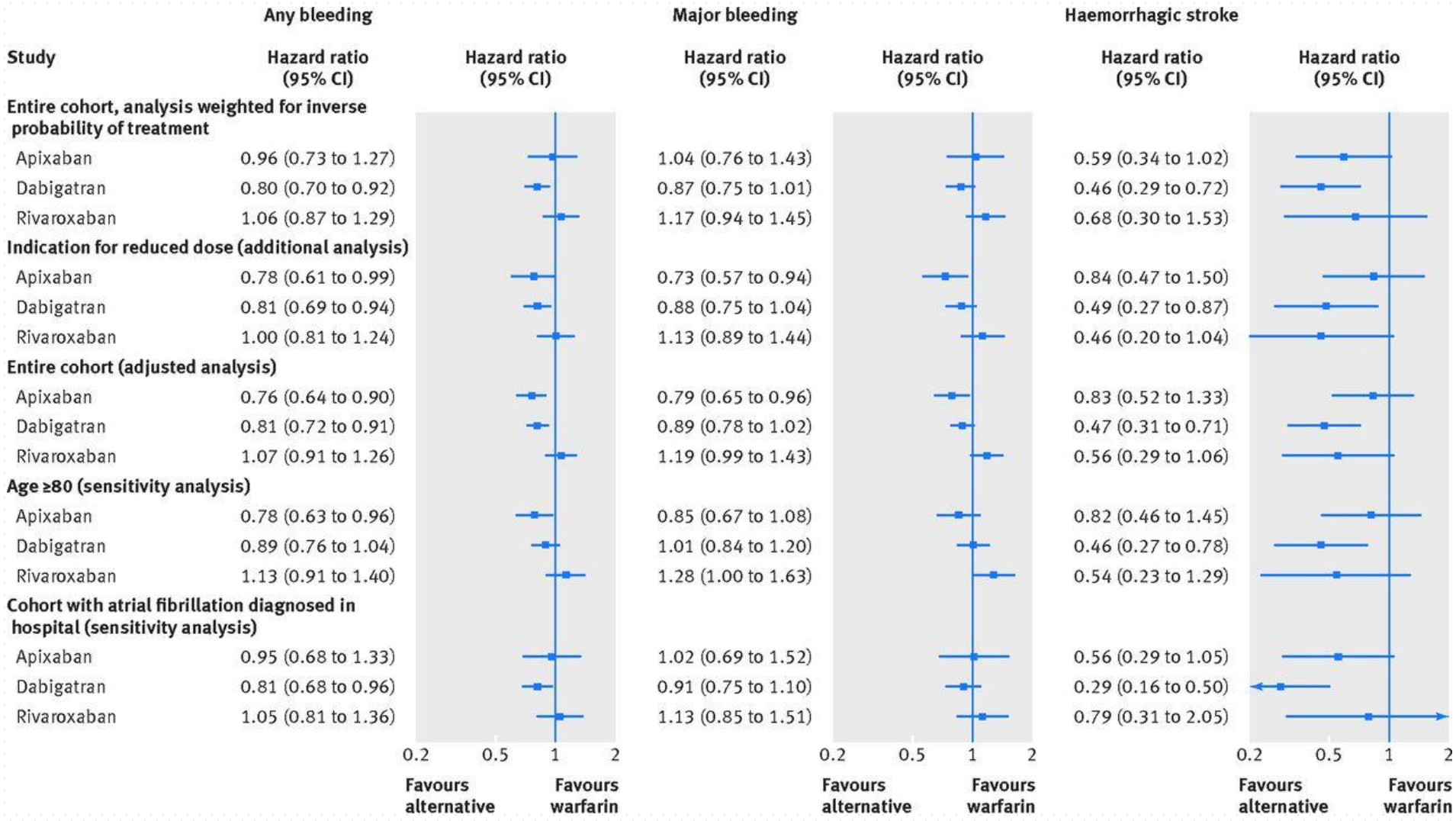
Steinberg BA et al. J Am Coll Cardiol. 2016;68(24):2597-2604.

TAPASZTALATOK ALACSONY DÓZIS ESETÉN - ISCHAEMIA



Peter Brønnum Nielsen et al. BMJ 2017;356:bmj.j510

TAPASZTALATOK ALACSONY DÓZIS ESETÉN - VÉRZÉS



Peter Brønnum Nielsen et al. BMJ 2017;356:bmj.j510

VÉRZÉS NOAC MELLETT

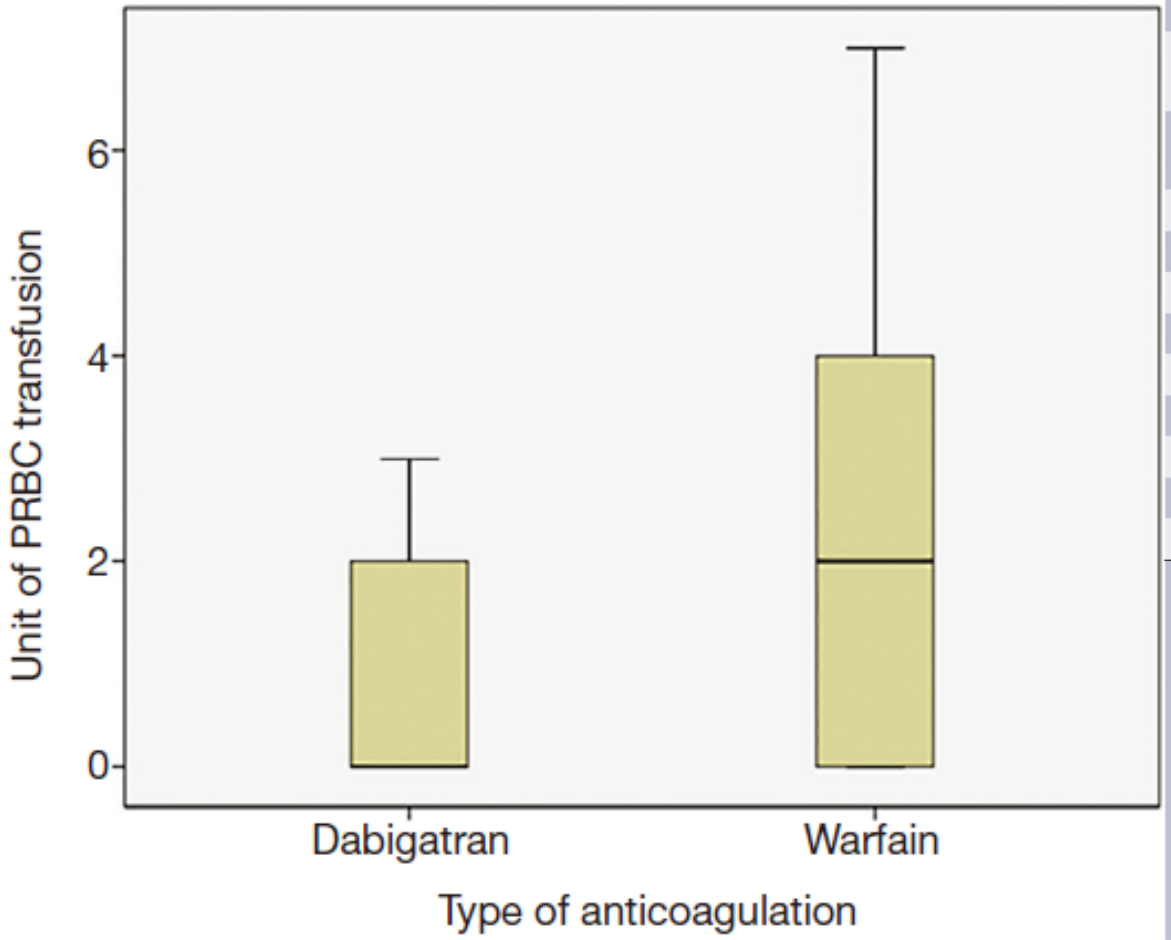


Table 2 Initial clinical presentation, initial laboratory results, and clinical outcomes of patients who presented with GI bleed in both groups

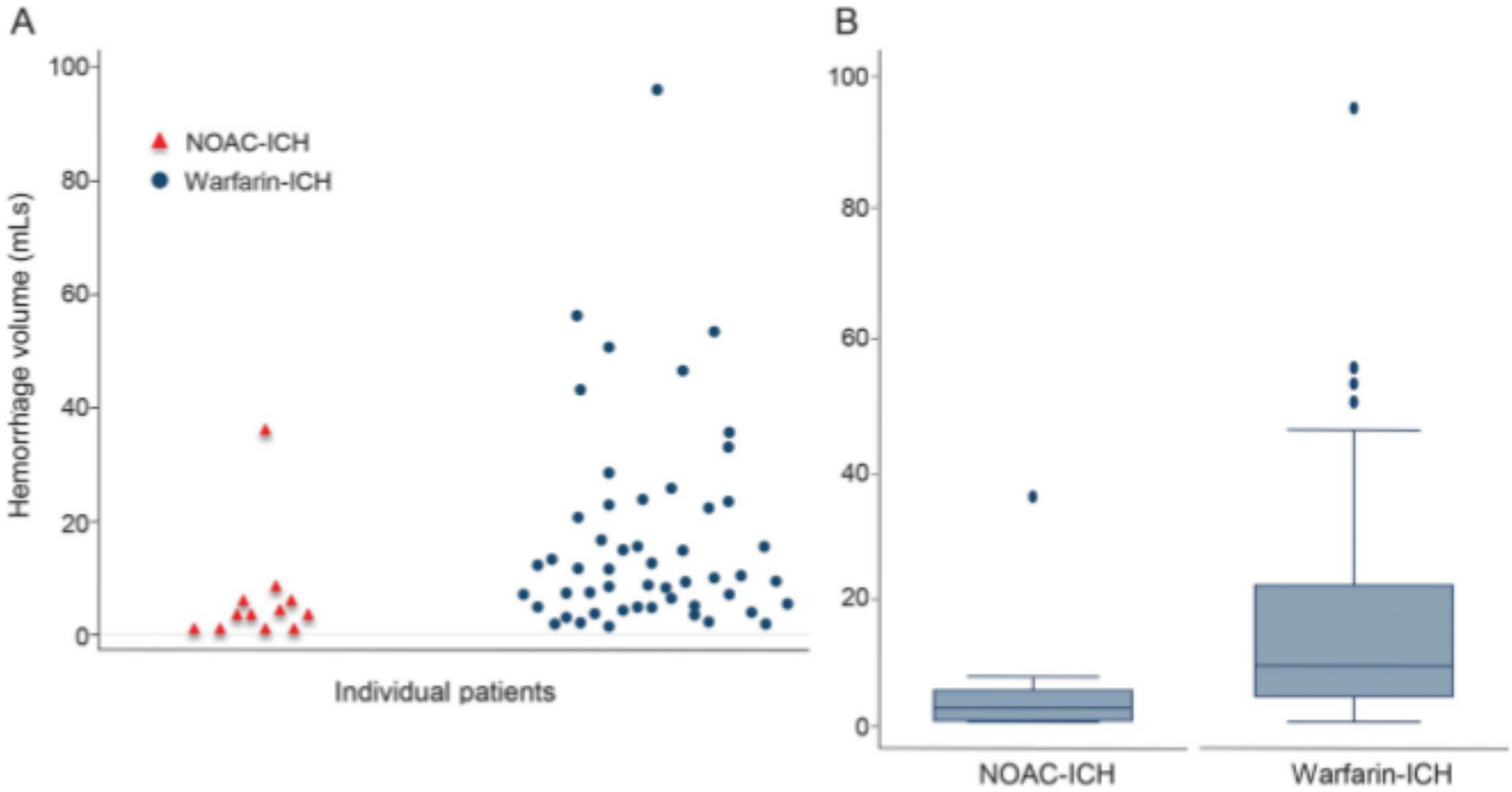
	Dabigatran	Warfarin	P value
Initial presentation			
UGIB n, (%)	0	1 (3.8)	–
LGIB n, (%)	11 (84.6)	20 (76.9)	0.61
Symptomatic anemia n, (%)	2 (15.4)	5 (19.2)	0.81
Hypotension n, (%)	1(7.7)	8(30.8)	0.11
Tachycardia n, (%)	3 (23.0)	5 (19.0)	0.78
Initial Hb at presentation (mg/dL)	10.4±2.1	9.6±2.6	0.34
Second Hb within 24 hr (mg/dL)	9.64±1.3	9.01±2.4	0.31
Platelet count (10^3/mm^3)	189±60	240±89	0.045
Creatinine (mg/dL)	1.35±1	1.35±0.8	0.99
INR	1.81±0.9	2.54±0.3	0.01
AKI n, (%)	4 (31.0)	5 (19.0)	0.42
PRBC transfusion (units)	0.69±1.1	1.92±2.2	0.024*
Length of stay (days)	5.6±4.9	5.9±4	0.86
ICU n, (%)	1 (7.7)	1 (3.8)	0.61
Death n, (%)	1 (7.7)	1 (3.8)	0.61
Endoscopy n, (%)	6 (46.0)	15 (58.0)	0.50

*, after multiple regression analysis correcting for history of CKD, and hemoglobin level at presentation, there is significant association between initial hemoglobin level at presentation, type of anticoagulation, and the quantity of PRBC transfusion with the higher amount of transfused PRBCs in the warfarin group. GI, gastrointestinal; UGIB, upper gastrointestinal bleeding; LGIB, lower gastrointestinal bleeding; Hb, hemoglobin; INR, international normalized ratio; AKI, acute kidney injury; PRBC, packed red blood cell; ICU, intensive care unit; CKD, chronic kidney disease.

Manatsathit W. et al. Cardiovasc Diagn Ther 2014;4(3):224-231

INTRACEREBRALIS VÉRZÉS NOAC MELLETT

Figure 2 Dot plot and box plot



(A) Dot plot of individual participants and their corresponding hemorrhage sizes. Blue dots show warfarin–intracerebral hemorrhage (ICH); red triangles show non–vitamin K oral anticoagulant (NOAC)–ICH. (B) Box plot shows median, lower and upper quartiles, and minimum and maximum values of hematoma volume for NOAC-ICH cases and warfarin-ICH cases.

Wilson D et al. Neurology2016;86:360–366

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Table 2

Practical guide for how to manage bleeding complications in patients on direct oral anticoagulants

Oral thrombin inhibitors (dabigatran)	Oral factor Xa inhibitors (rivaroxaban, apixaban, edoxaban)
None life-threatening bleeding	
Check last intake; restoration of normal coagulation to be expected at 12–24 h (in case of creatinin clearance > 80 ml/min) or 24–36 h (in case of creatinin clearance 50–80 ml/min)	
Local hemostatic interventions, fluid management, transfusion	
Consider tranexamic acid (1000 mg 3dd) or DDAVP (0.3 µg/kg)	
Life-threatening bleeding	
All of the above	All of the above
Idarucizumab	Andexanet alfa
	Ciraparantag (under investigation)
Prothrombin complex concentrate (no evidence)	Prothrombin complex concentrate (healthy volunteer data)
Activated PCC (no evidence)	Activated PCC (no human evidence)
Recombinant factor VIIa (no evidence)	Recombinant factor VIIa (healthy volunteer data)

Suggested management strategy in case of hemorrhagic complications in patients using direct oral anticoagulants, modified from [15]

PCC prothrombin complex concentrate, *dd* daily, *DDAVP* de-amino D-arginine vasopressin

Levi M. Crit Care. 2016; 20: 249

ESC/EHRA-irányelvek

Akut ischemiás stroke NOAC mellett[1]

Ha biztos az utolsó NOAC-dózis időpontja

$4 \times t_{1/2}$ (≈ 48 óra) eltelt:

Thrombolysis mérlegelhető

48 óra nem telt el; spec. teszt* nincs vagy abnormális

Mechanikus rekanalizáció mérlegelhető

Ha nem biztos az utolsó NOAC-dózis időpontja

Thrombolysis általában nem ajánlott

Normális eredményű specifikus tesztek*

Thrombolysis mérlegelhető

Megnyúlt
- **aPTI (dabigatran)**
- **PI (FXa-gátlók)**

Thrombolysis nem végezhető

*** Specifikus koagulációs tesztek:**
- Direkt trombininhibitorok: TI vagy ECT
- FXa-gátlók: X. faktor aktivitása *(kromogén teszt normáltartománya nincs definiálva)*

aPTI = aktivált parciális tromboplasztinidő, **PTI** = protrombinidő, **TI** = trombinidő, **ECT** = ekarin alvadási idő

Forrás: Heidbuchel, H. et al. *Europace* 2013; 15, 625-51.

NOAC ÉS VESEFUNCTIO
MŰTÉTI BEAVATKOZÁS ELŐTT

Table 9 Last intake of drug before elective surgical intervention

	Dabigatran		Apixaban		Edoxaban[a]		Rivaroxaban	
	No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. ≥12 h or 24 h after last intake)							
	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
CrCl ≥80 ml/min	≥24 h	≥48 h	≥24 h	≥48 h	No data	No data	≥24 h	≥48 h
CrCl 50–80 ml/min	**≥36 h**	**≥72 h**	≥24 h	≥48 h	No data	No data	≥24 h	≥48 h
CrCl 30–50 ml/min[b]	**≥48 h**	**≥96 h**	≥24 h	≥48 h	No data	No data	≥24 h	≥48 h
CrCl 15–30 ml/min[b]	Not indicated	Not indicated	**≥36 h**	**≥48 h**	No data	No data	**≥36 h**	**≥48 h**
CrCl <15 ml/min	No official indication for use							

Bold values deviate from the common stopping rule of ≥24 h low risk, ≥48 h high risk.
[a]No EMA approval yet. Needs update after finalisation of SmPC.
[b]Many of these patients may be on the lower dose of dabigatran (i.e. 110 mg BID) or apixaban (i.e. 2.5 mg BID), or have to be on the lower dose of rivaroxaban (15 mg QD).
Low risk = surgery with low risk of bleeding; high risk = surgery with high risk of bleeding. See also Table 10.
CrCl, creatinine clearance.

Heidbuchel, H. et al. Europace 2013; 15, 625-51.

Periprocedural Management of NOACs: EHRA Practical Guide

Procedure	Anticoagulation Management
Dental interventions - Extraction of 1-3 teeth - Periodontal surgery, incision of abscess, implant Ophthalmology - Cataract or glaucoma intervention - Endoscopy without surgery - Superficial surgery (dermatologic excisions)	Very low bleeding risk: Discontinuation of OAC not usually required (perform procedure at concentration)
Endoscopy with biopsy Prostate or bladder biopsy EP study or SVT ablation with transseptal access Angiography PM or ICD implant (uncomplicated)	Low bleeding risk: Discontinue NOAC 24 hours prior to procedure (longer in patients with renal dysfunction)
Complex left-sided ablation (PVI, VT) Spinal or epidural anesthesia, lumbar diagnostic procedures Thoracic and abdominal surgery Liver and kidney biopsy TURP Major orthopedic surgery	High bleeding risk: Discontinue NOAC 48 hours prior to procedure (longer in patients with renal dysfunction)

Heidbuchel H, et al. *Europace*. 2013;15(5):625-651.

LE A WARFARINNAL?

- The use of dabigatran in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications, as compared with warfarin, thus showing no benefit and an excess risk

- Except for low-dose rivaroxaban, the studied dosing regimens, apixaban and dabigatran failed to show a net clinical benefit in addition to dual antiplatelet therapy in acute coronary syndromes.

Ahrens I. et al. Semin Hematol. 2014;51(2):147-5

KÖSZÖNÖM A FIGYELMET!