AF - what should we do?

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Atrial fibrillation

- Commonest chronic heart rhythm disorder
- Prevalence of 1% i.e.: 45,000 patients in New Zealand
- Prevalence is increasing
- In elderly patients 15% of strokes are due to AF
- AF strokes are associated with higher mortality and more disability than other strokes

Atrial fibrillation

- Aspirin reduces stroke risk by 22% compared to placebo
- Warfarin reduces stroke risk by 62% compared to placebo
- Anticoagulation is under used, is sub optimally used and often is inappropriately discontinued
- Time in therapeutic ranges is ~55%

AF - what should we do?

- 84 year old frail female with AF 96/minute
- MI 2 years ago, arthritis
- On aspirin, metformin, indocid
- Creatinine clearance 40mL/min

General management of the AF patient

Clinical management of patients with AF involves the following five objectives:

- Prevention of thromboembolism with aspirin, warfarin or dabigatran with an acceptable rate of bleeding
- Rate control
- Correction of the rhythm disturbance
- ablation
- Optimal management of concomitant cardiovascular disease

AF - what should we do?

- Doctors often overestimates the risk of bleeding and under estimates the risk of stroke

AF - what should we do?

- Doctors fear more adverse results from comission than from omission

$CHA_2DS_2VAS_C$ score

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75	2
Diabetes mellitus	1
Stroke / TIA / thromboembolism	2
Vascular disease[a]	1
Age 65 – 74	1
Sex category (i.e. female sex)	1
Maximum score	9

[a] Prior MI, PAD, aortic plaque

Lip et al., *Chest*. 2010; 137:263

Adjusted stroke rate according to $CHA_2DS_2VAS_C$ score

$CHA_2DS_2VAS_C$ score	Patients (n=7,329)	Adjusted stroke rate (%/year)
0	1	0%
1	422	1.3%
2	1,230	2.2%
3	1,730	3.2%
4	1,718	4.0%
5	1,159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	12	15.2%

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Lip et al., *Chest*. 2010; 137:263

Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristics[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g.: age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Camm et al., *EHJ.* 2010; 31:2369

HAS-BLED bleeding score

HAS-BLED score

	n	Bleeds, n	Bleeds/100 patients*
0	798	9	1.13
1	1286	13	1.02
2	744	14	1.88
3	187	7	3.74
4	46	4	8.70
5	8	1	12.50
Any score	3071	48	1.56

*p for trend of increasing bleeding risk with increasing score = 0.007

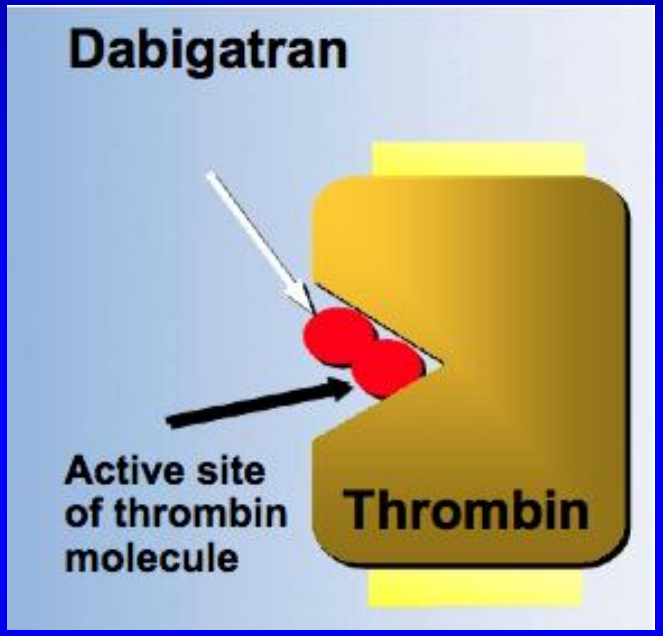
Approach to thromboprophylaxis in patients with AF

$CHA_2DS_2VAS_C$ score	Recommended antithrombotic therapy
≥2	Warfarin/Dabigatran
1	Either OAC[a] or aspirin 75-325 mg daily. Preferred: OAC rather than aspirin.
0	Either aspirin 75-325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

AF = atrial fibrillation
CHA2DS2-VASc = cardiac failure
OAC = oral anticoagulation, such as a vitamin K antagonist adjusted to an intensity range of INR 2.0–3.0 (target 2.5)

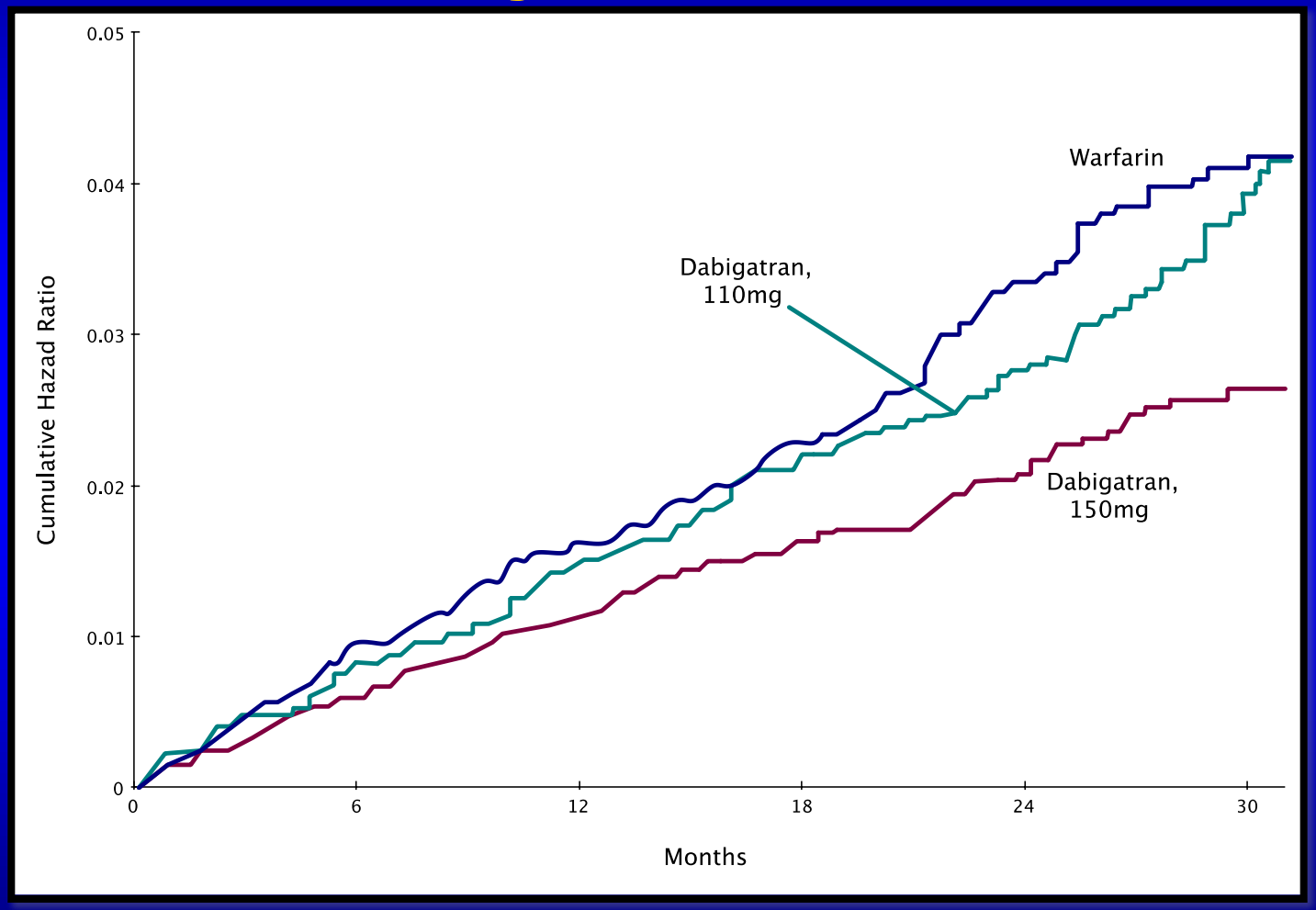
Camm et al., *EHJ.* 2010; 31:2369

Dabigatran



- Oral prodrug
- Potent, direct, competitive inhibitor of thrombin
- 80% excreted by kidneys
- Half life 12 to 17 hours
- Better efficacy and safety than warfarin for stroke prevention in AF (RE-LY)

Dabigatran in AF: stroke or systemic embolism



Connolly et al., *NEJM*. 2009; 361:1139

Dabigatran vs warfarin for AF:RE-LY
trade offs per 1000 patients per year

	Warfarin	110 mg	150 mg
Stroke or embolism	17	15 p=0.34	11 p<0.001
Intracranial haemorrhage	8	2 p<0.001	3 p<0.001
Mortality	41	37 p=0.13	36 p=0.05
Myocardial Infarction	5	7 p=0.07	7 p=0.048
	6*	8* p=0.08*	8* p=0.12*
Major bleeding	36	29 p=0.003	33 p=0.31

p values compared to warfarin, * revised data, NEJM;2010:363,1876

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RE-LY. *NEJM.* 2009; 361:1139

Adverse drug reports with Dabigatran
Medsafe: May 2012; 372 reports

Deaths = 13

- 10 Unrelated
- 1 Unknown cause
- 1 May be contributory
- 1 Due to

"Bleeding" = 150 Reports

- 3 Subdural haemorrhage
- 1 Cerebral haemorrhage
- 1 Intracranial haemorrhage

Dabigatran usage by month

	Estimated patients	Proportion of prescriptions with NHI info	Prescriptions*
Jul 11	5,700	99.5%	6,000
Aug 11	7,500	99.2%	4,100
Sep 11	7,500	99.1%	3,200
Oct 11	6,900	99.3%	3,900
Nov 11	7,100	99.4%	3,300
Dec 11	7,300	99.4%	3,400
Jan 12	7,000	99.1%	3,500
Feb 12	7,000	99.4%	3,200

**** Prescriptions may cover up to 3 months of treatment, so patient numbers per month are expected to be greater than prescriptions***

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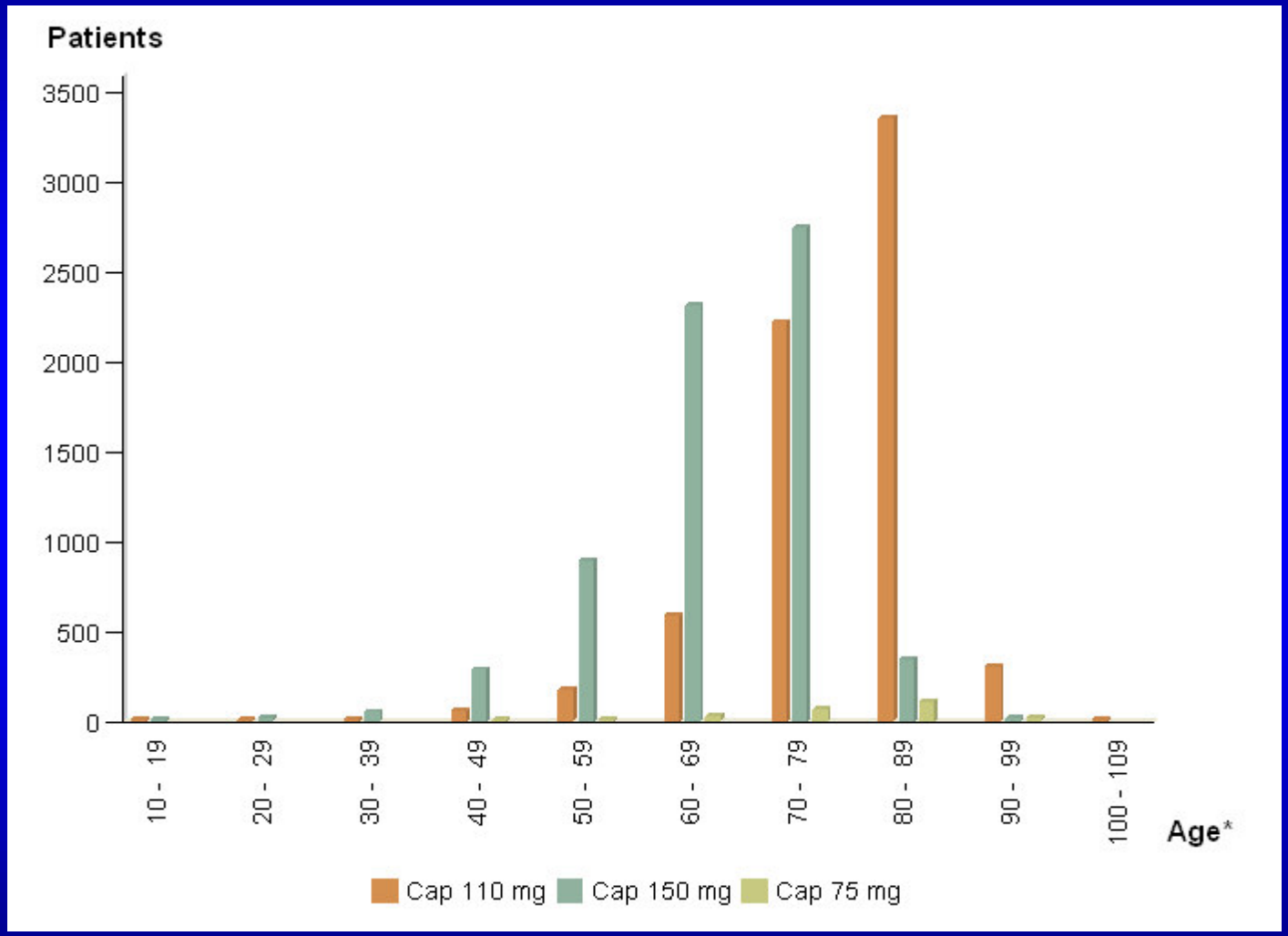
Number of new patients each month

Month	Number of new patients
	5,700
Aug 2011	3,000
Sep 2011	1,300
Oct 2011	700
Nov 2011	700
Dec 2011	600
Jan 2012	400
Feb 2012	500

Dabigatran usage by Age and Formulation - July 2011 to February 2012



**Patient age as of 1/01/2012*

Advantages of dabigatran

- Several advantages of dabigatran particularly decreased intracranial hemorrhage, even compared with warfarin with good INR control (3-4 events per 1000 patients treated)
- Decreased minor bleeding is important because it may lead to non-adherence
- May prescribe warfarin because of concern about increased rate of MI with dabigatran,

Dabigatran or warfarin
Considerations

- Need consideration of adherence (bid vs INR testing)
- Need consideration of patient values and preferences
- Assiduous blood pressure control
- ? Need for aspirin, dose should be ≤100mg/day and consider PPIs

Why would you use warfarin
Considerations

- Good INR control (but would have to accept increased rate of intracranial haemorrhage
- Preference for INR testing rather than bid dosing
- Impaired renal function with creatinine clearance < 30 ml/min
- Concern about lack of reversibility
- Side effects such as gastric discomfort with dabigatran
- Prosthetic heart valve

Which dose of dabigatran ?

Lower-dose regimen (110mg bd)

- Elderly
- Renal impairment
- Lower stroke risk (CHADSvas$_2$ score of 1)
- Increased bleeding risk

Higher-dose regimen (150mg bd)

- Higher stroke risk (CHADSvas$_2$ score ≥ 2)

Avoiding intracranial haemorrhage during antithrombotic therapy

- Elderly patients and those with cerebrovascular disease are at special risk
- Keep INRs <3.0
- Warfarin combined with aspirin should be used with special caution in elderly patients and those with cerebrovascular disease
- Modest blood pressure-lowering profoundly reduces CNS bleeding

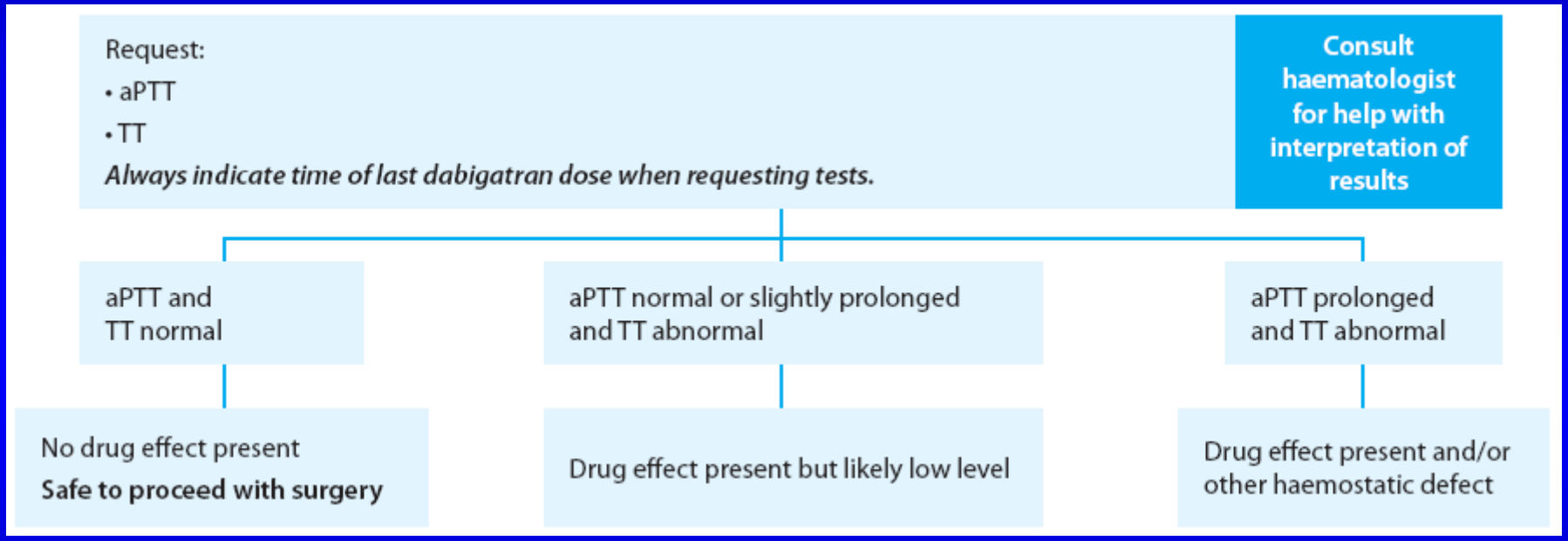
Hart et al., *Stroke*. 2005; 36:1588

Blood pressure control

- Modest reduction in blood pressure profoundly lowers ICH risk
- In the randomized Perindopril Protection Against Recurrent Stroke Study (PROGRESS) trial involving patients with previous stroke or TIA, 72% of participants were receiving antiplatelet therapy and 10% oral anticoagulants
- Haemorrhagic stroke was reduced 50% (95% CI 26 to 67) by a mean 9 mmHg reduction in systolic blood pressure

Chapman et al., *Stroke*. 2004; 35:116

Testing for dabigatran anticoagulant effect



http://www.pharmac.govt.nz/2011/06/13/Dabigatran%20testing%20and%20perioperative%20management.pdf

RE-LY:
Risk of major bleeding

	Warfarin (n=6022)	Dabigatran 110 mg BID (n=6015)	Dabigatran 150 mg BID (n=6076)	Dabigatran 110 mg BID vs Warfarin (n=12 037)		Dabigatran 150 mg BID vs Warfarin (n=12 098)	
	%/y	%/y	%/y	RR (95% CI)	*P*	RR (95% CI)	*P*
Major bleeding	3.57	2.87	3.31	0.80 (0.70–0.93)	0.002	0.93 (0.81–1.07)	0.32
Intracranial	0.76	0.23	0.32	0.30 (0.19–0.45)	<0.001	0.42 (0.29–0.62)	<0.001
Intracerebral	0.41	0.13	0.13	0.31 (0.17–0.55)	<0.001	0.33 (0.19–0.57)	<0.001
Subdural	0.34	0.10	0.19	0.30 (0.16–0.57)	<0.001	0.56 (0.34–0.94)	0.028
Extracranial	2.84	2.66	3.02	0.94 (0.81–1.09)	0.42	1.07 (0.92–1.24)	0.36
Gastrointestinal	1.25	1.36	1.85	1.09 (0.87–1.36)	0.44	1.49 (1.21–1.84)	<0.001
Nongastrointestinal	1.71	1.41	1.38	0.82 (0.67–1.01)	0.06	0.80 (0.65–0.99)	0.038
Life-threatening bleeding	1.85	1.24	1.49	0.67 (0.54–0.82)	<0.001	0.80 (0.66–0.98)	0.030
Fatal bleeding	0.33	0.19	0.23	0.58 (0.35–0.97)	0.039	0.70 (0.43–1.14)	0.15
Minor bleeding	16.37	13.16	14.84	0.79 (0.74–0.84)	<0.001	0.91 (0.85–0.97)	0.005
Red cell transfusion	1.93	1.74	2.10	0.90 (0.75–1.09)	0.29	1.10 (0.92–1.31)	0.30

•RR, relative risk; and CI, confidence interval

Eikelboom et al., *Circulation.* 2011; 123:2363

RE-LY:

Risk of major, intracranial and extracranial bleeding

	Warfarin	Dabigatran 110 mg BID	Dabigatran 150 mg BID	Dabigatran 110 mg BID vs Warfarin (n=12 037)		Dabigatran 150 mg BID vs Warfarin (n=12 098)	
	%/y	%/y	%/y	RR	*P**	RR	*P**
Stroke/systemic embolism							
Age <75 y	1.43	1.32	0.90	0.93 (0.70–1.22)		0.63 (0.46–0.86)	
Age ≥75 y	2.14	1.89	1.43	0.88 (0.66–1.17)	0.81	0.67 (0.49–0.90)	0.81
Major bleeding							
Age <75 y	3.04	1.89	2.12	0.62 (0.50–0.77)		0.70 (0.57–0.86)	
Age ≥75 y	4.37	4.43	5.10	1.01 (0.83–1.23)	<0.001	1.18 (0.98–1.42)	<0.001
Intracranial bleeding							
Age <75 y	0.61	0.14	0.26	0.22 (0.11–0.45)		0.43 (0.25–0.74)	
Age ≥75 y	1.00	0.37	0.41	0.37 (0.21–0.64)	0.28	0.42 (0.25–0.70)	0.91

- RR, relative risk; and CI, confidence interval
- *P for interaction

Eikelboom et al., *Circulation.* 2011; 123:2363

RE-LY:

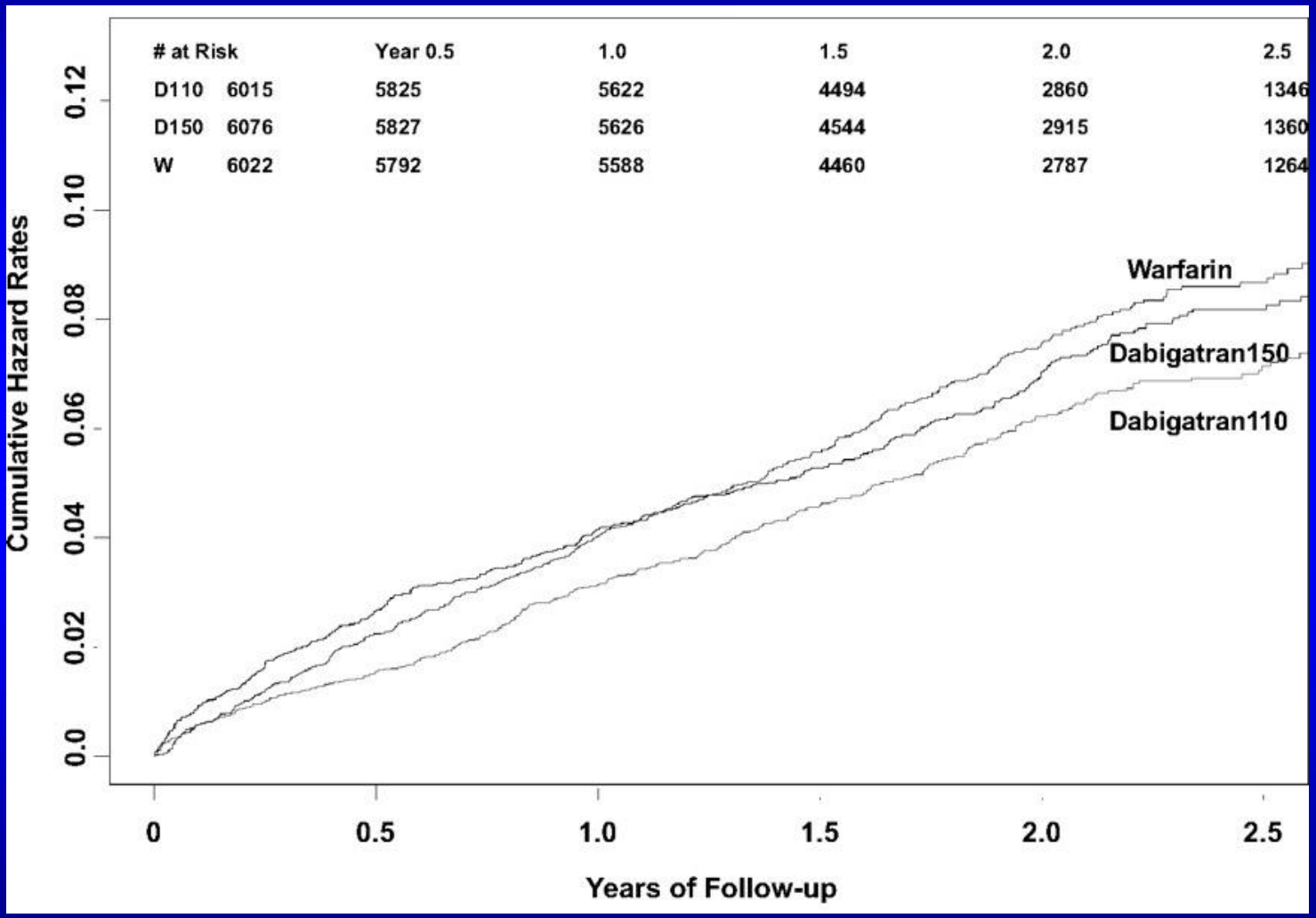
Risk of major, intracranial and extracranial bleeding

	Warfarin	Dabigatran 110 mg BID	Dabigatran 150 mg BID	Dabigatran 110 mg BID vs Warfarin (n=12 037)		Dabigatran 150 mg BID vs Warfarin (n=12 098)	
	%/y	%/y	%/y	RR	*P**	RR	*P**
Extracranial bleeding							
Age <75 y	2.44	1.76	1.91	0.72 (0.57–0.90)		0.78 (0.63–0.98)	
Age ≥75 y	3.44	4.10	4.68	1.20 (0.97–1.48)	0.001	1.39 (1.13–1.70)	<0.001
Gastrointestinal bleeding							
Age <75 y	1.03	0.84	1.22	0.82 (0.58–1.15)		1.19 (0.87–1.63)	
Age ≥75 y	1.59	2.19	2.80	1.39 (1.03–1.98)	0.02	1.79 (1.35–2.37)	0.06

- RR, relative risk; and CI, confidence interval
- *P for interaction

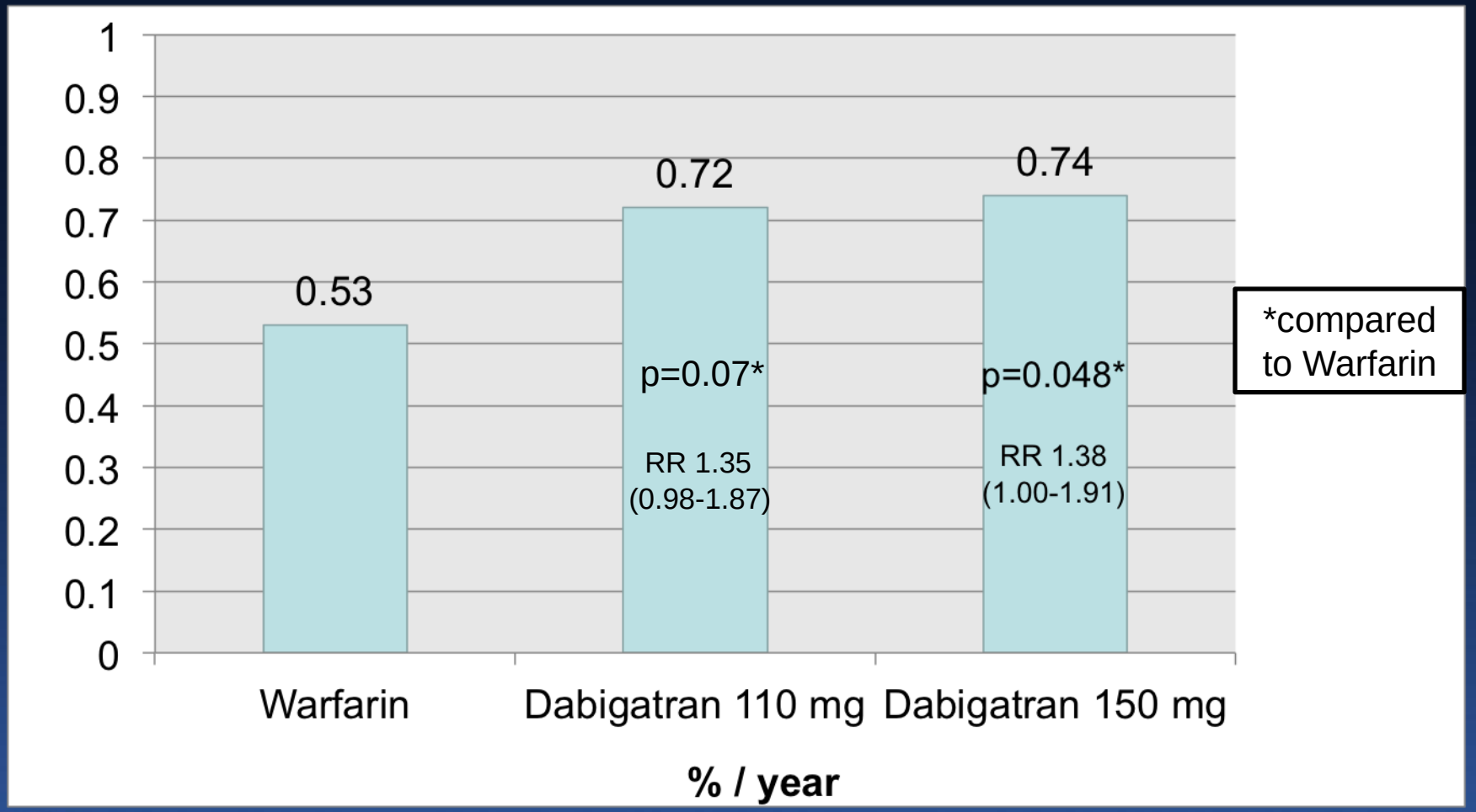
Eikelboom et al., *Circulation.* 2011; 123:2363

RE-LY:
Time to major bleed



Eikelboom et al., *Circulation.* 2011; 123:2363

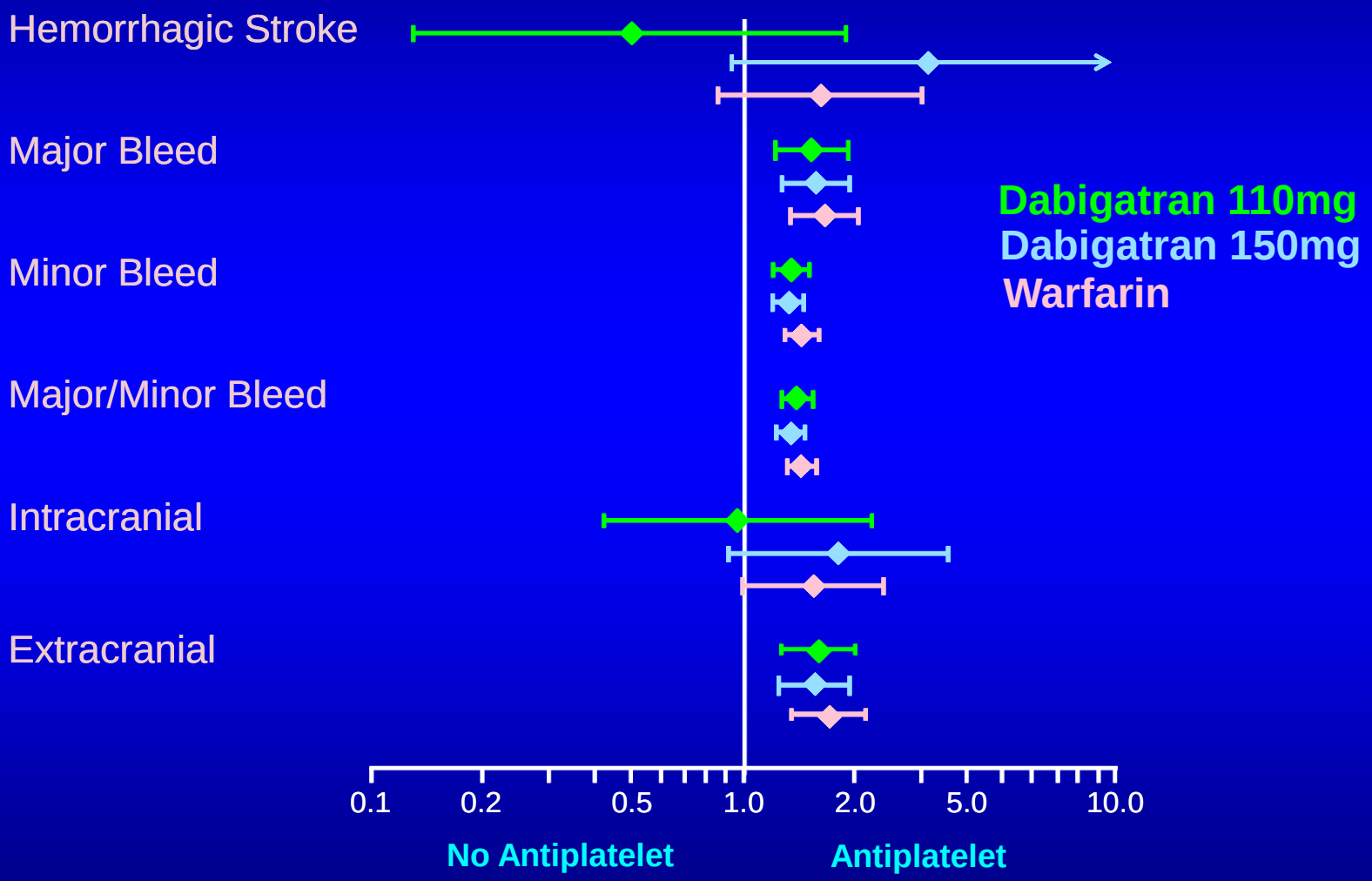
Dabigatran vs warfarin: effect on myocardial infarction



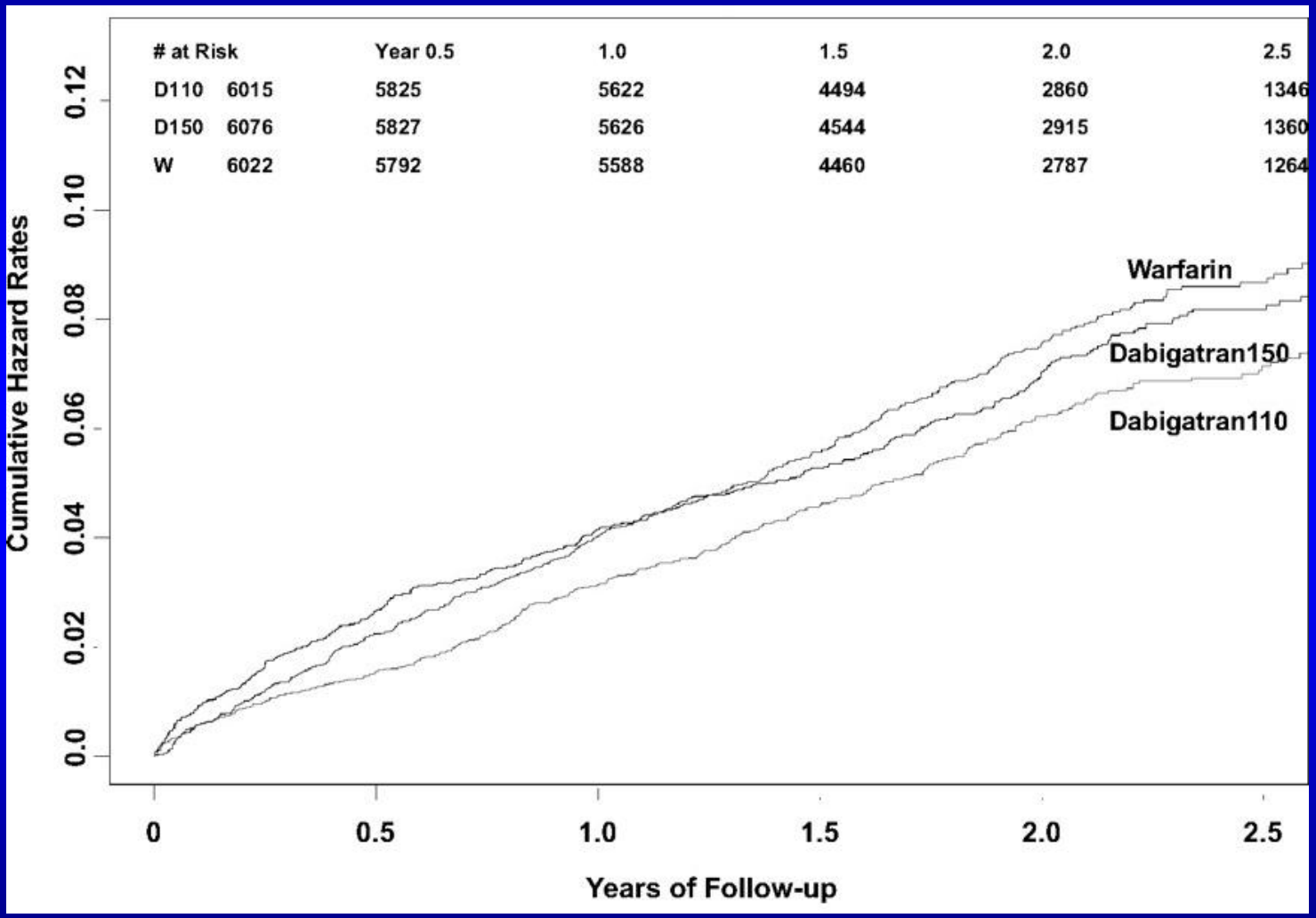
RE-LY, *NEJM*, 2009;361:1139

RE-LY Substudy

Antiplatelet vs No antiplatelet: Bleeding



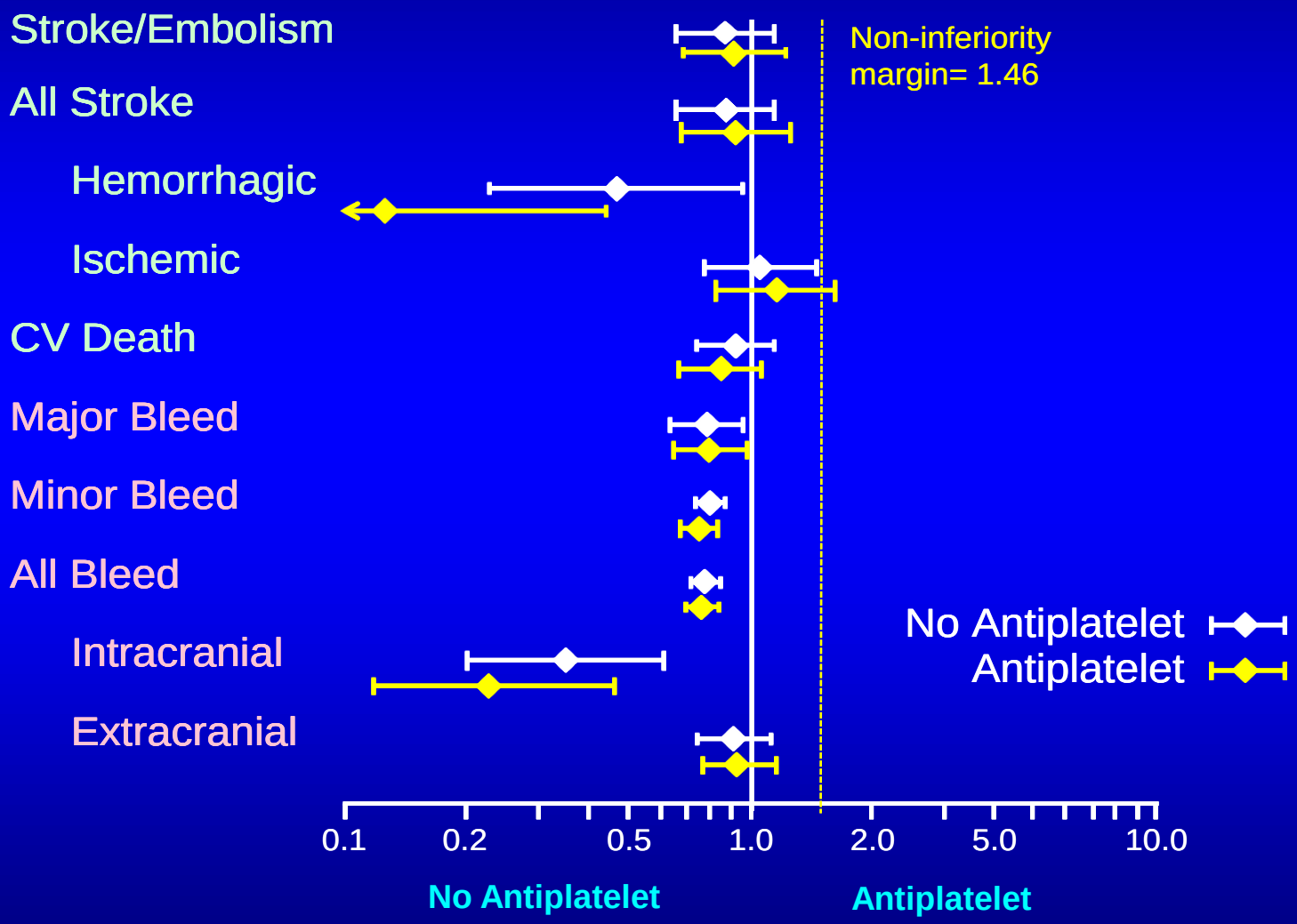
RE-LY:
Time to major bleed



Eikelboom et al., *Circulation.* 2011; 123:2363

RE-LY Substudy

Dabigatran 110mg vs Warfarin



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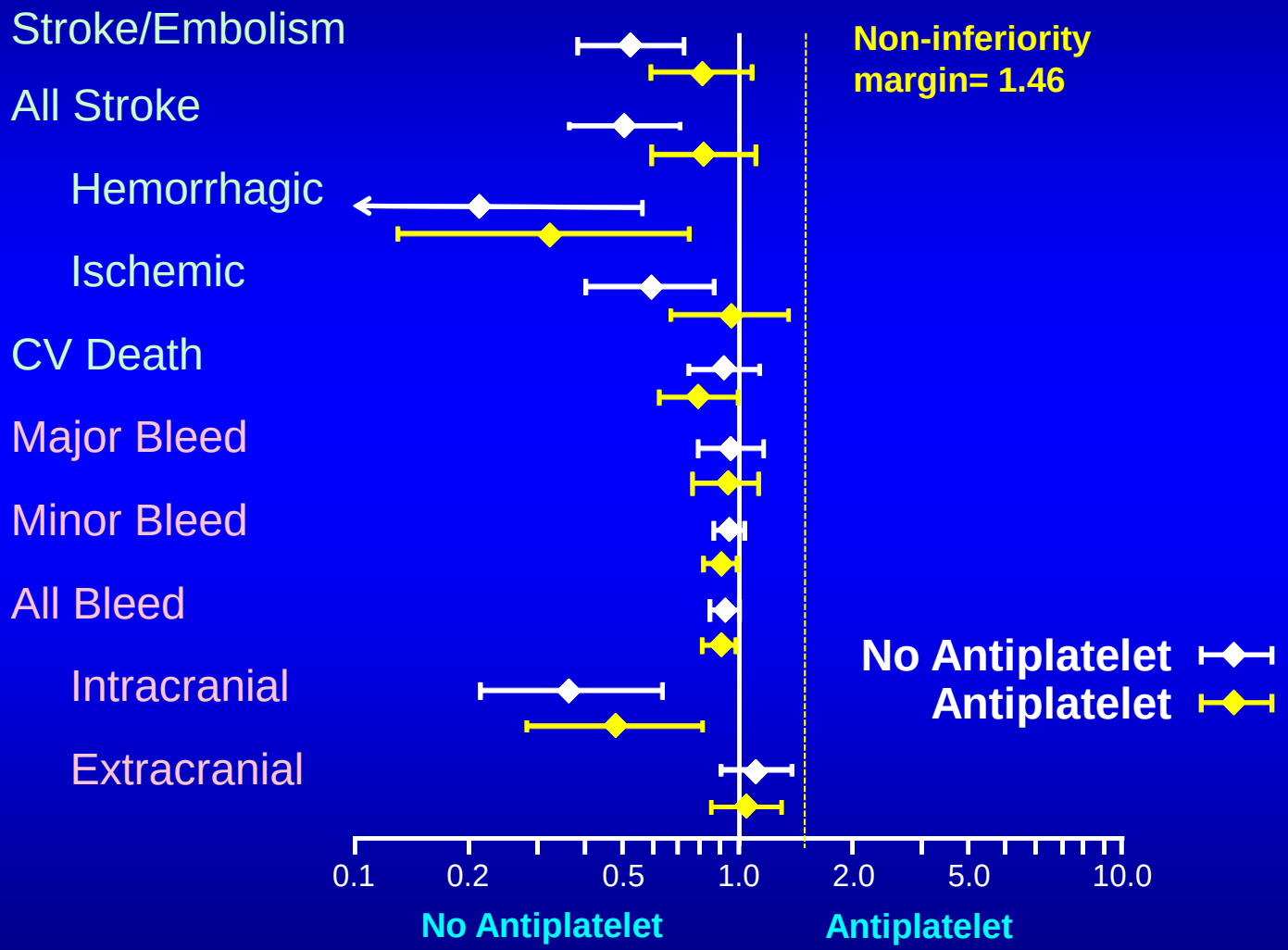
RE-LY Substudy

Dabigatran 150mg vs Warfarin



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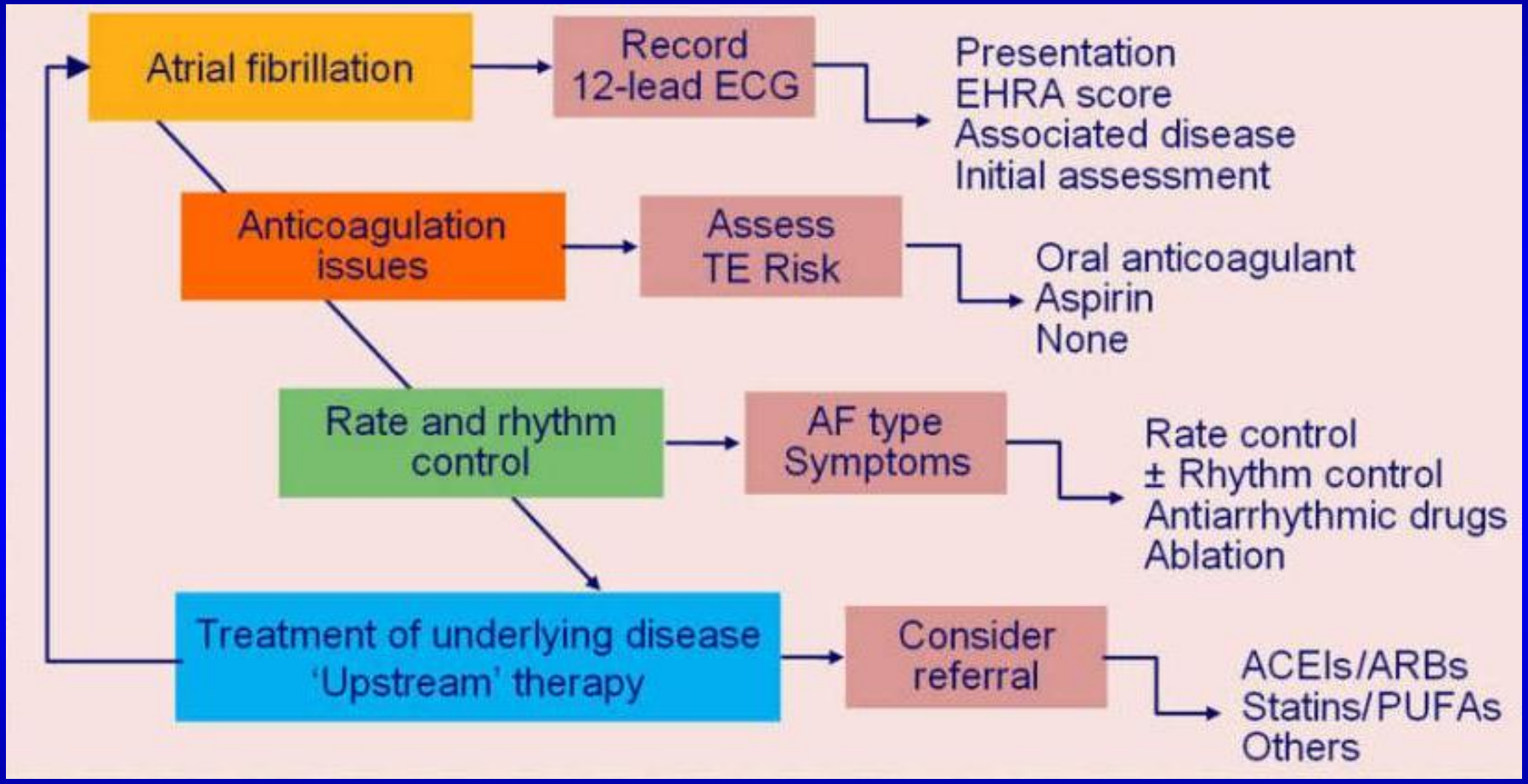
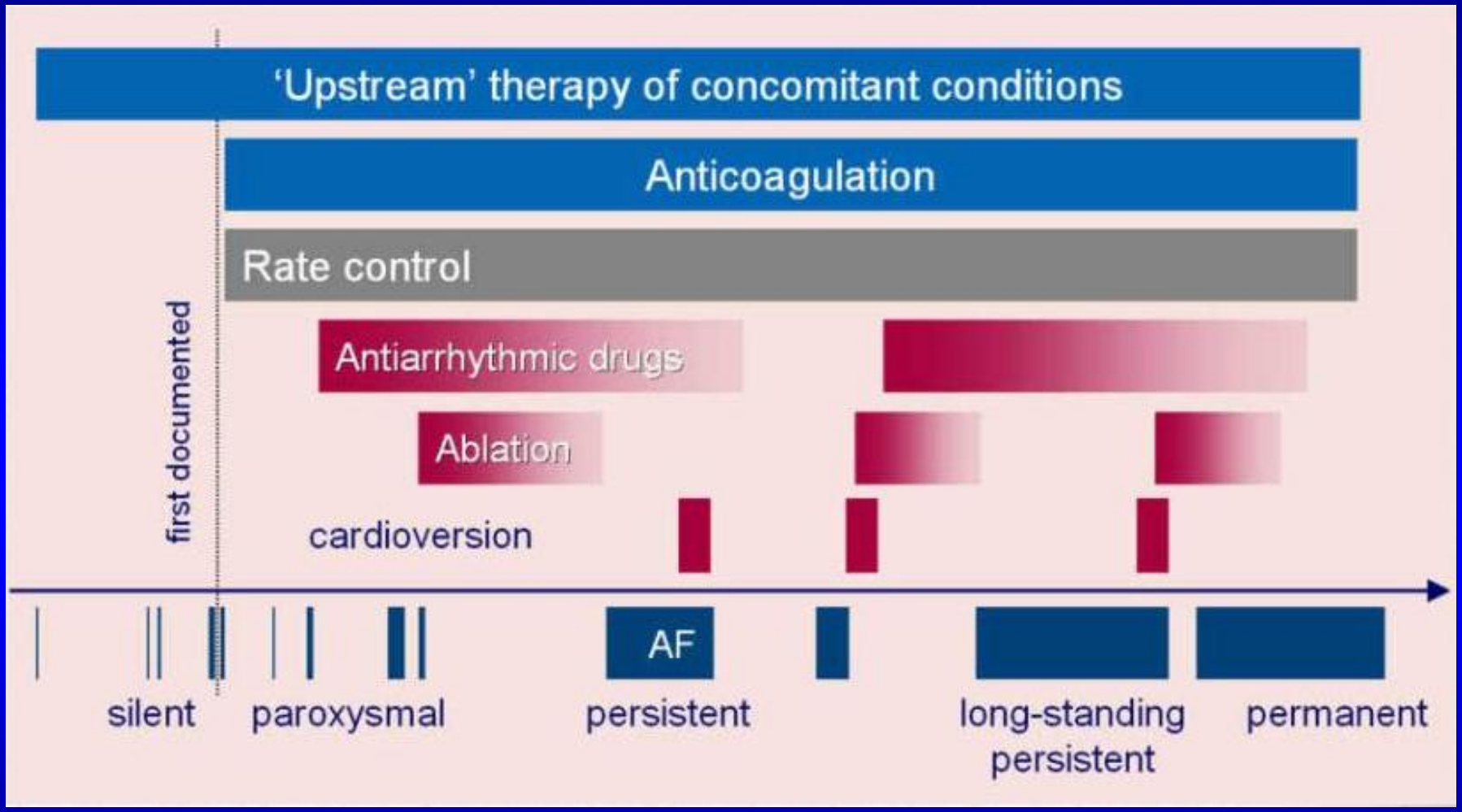
The management cascade for patients with AF



AECI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin-receptor blocker; PUFA = polyunsaturated fatty acid; TE = thrombo-embolism

Natural time course of AF



AF = atrial fibrillation

Atrial fibrillation

A substantial threat to the brain

- 2-5% per year stroke rate
- 12%per year for those with prior stroke
- AF-related strokes have worse outcomes than other ischaemic strokes

Risk of stroke in AF

High-Risk Factors

- Mitral stenosis
- Prosthetic heart valve
- History of stroke or TIA

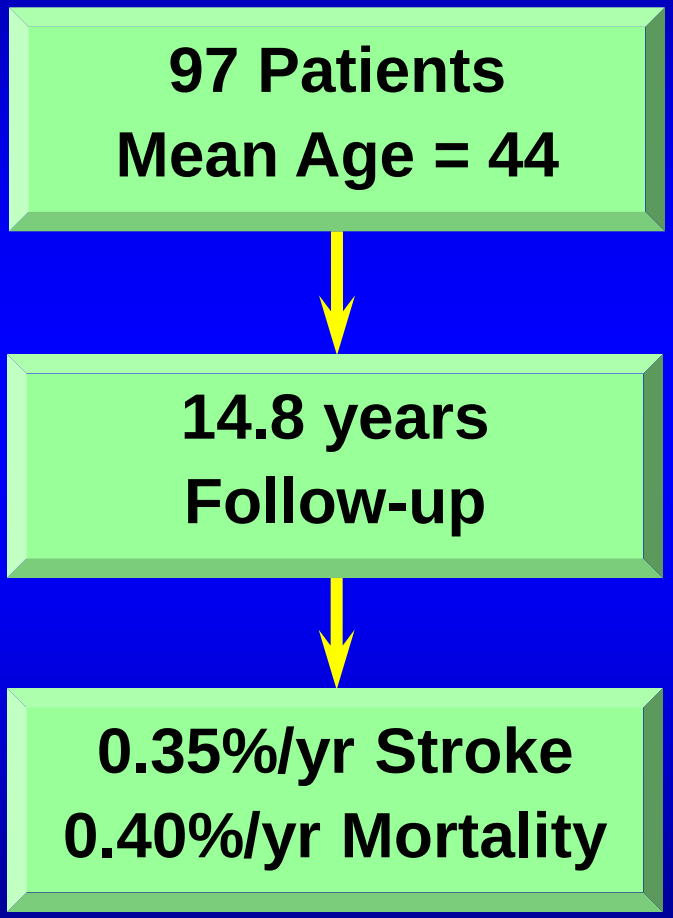
Moderate-Risk Factors

- Age >75 years
- Hypertension
- Diabetes mellitus
- Heart failure or ↓ LV function

Singer DE, et al. *Chest* 2004;126:429S.
Fang MC, et al. *Circulation* 2005; 112: 1687.

Natural history of "Lone" Atrial Fibrillation

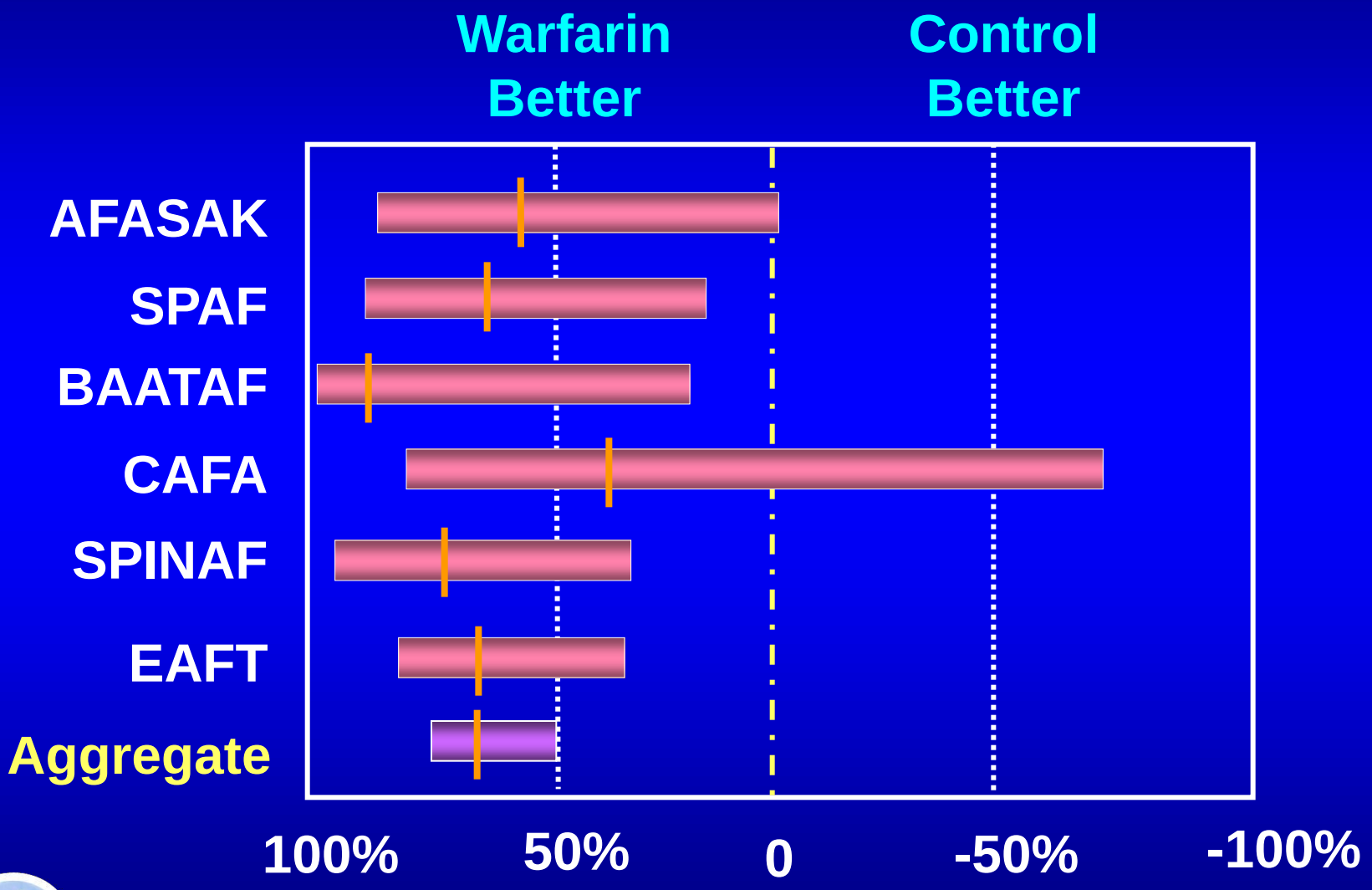
No Cardiopulmonary Disease; <60 Years Old



Kopecky S, et al. *N Engl J Med* 1987; 317:669.

Anticoagulation in Atrial Fibrillation

Stroke Risk Reductions



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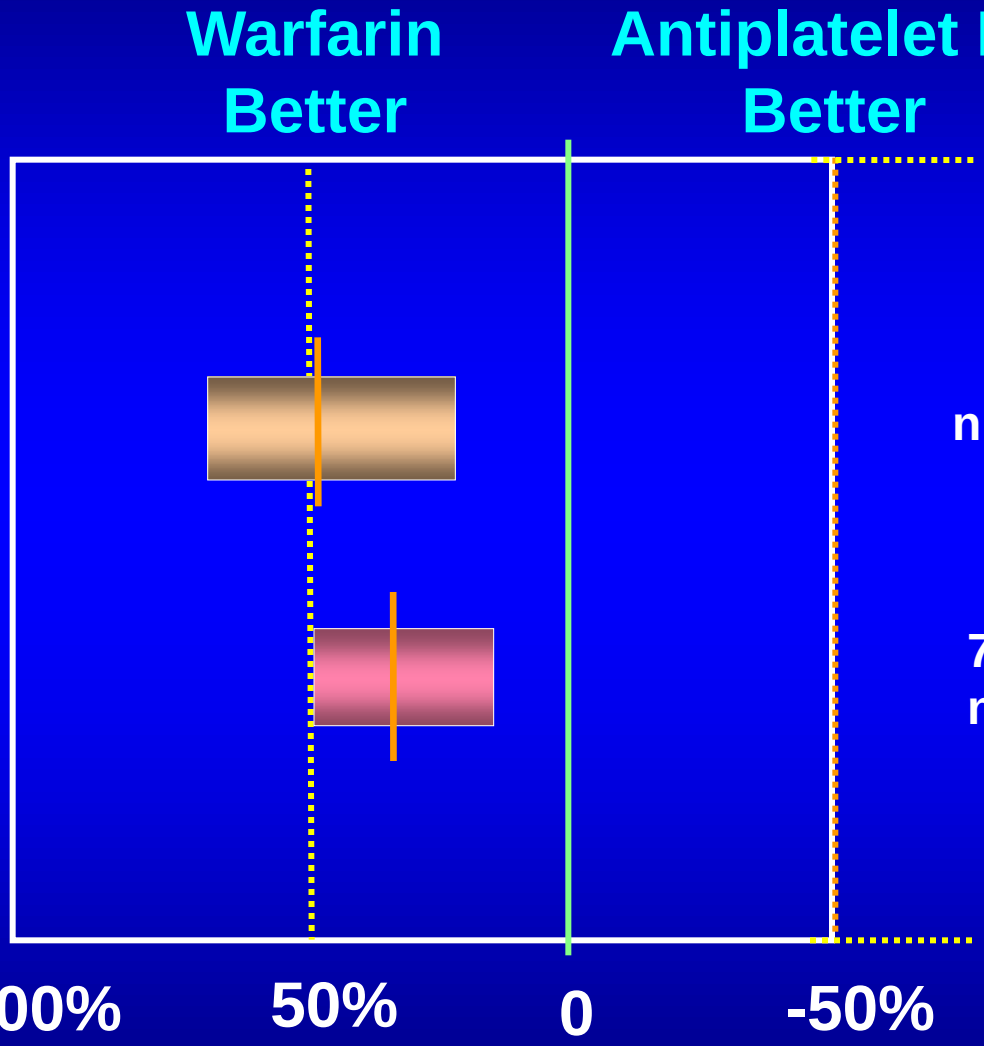
Hart R, et al. *Ann Intern Med* 2007;146:857.

Reduction in risk of stroke with different anti-thrombotic therapy for Atrial Fibrillation

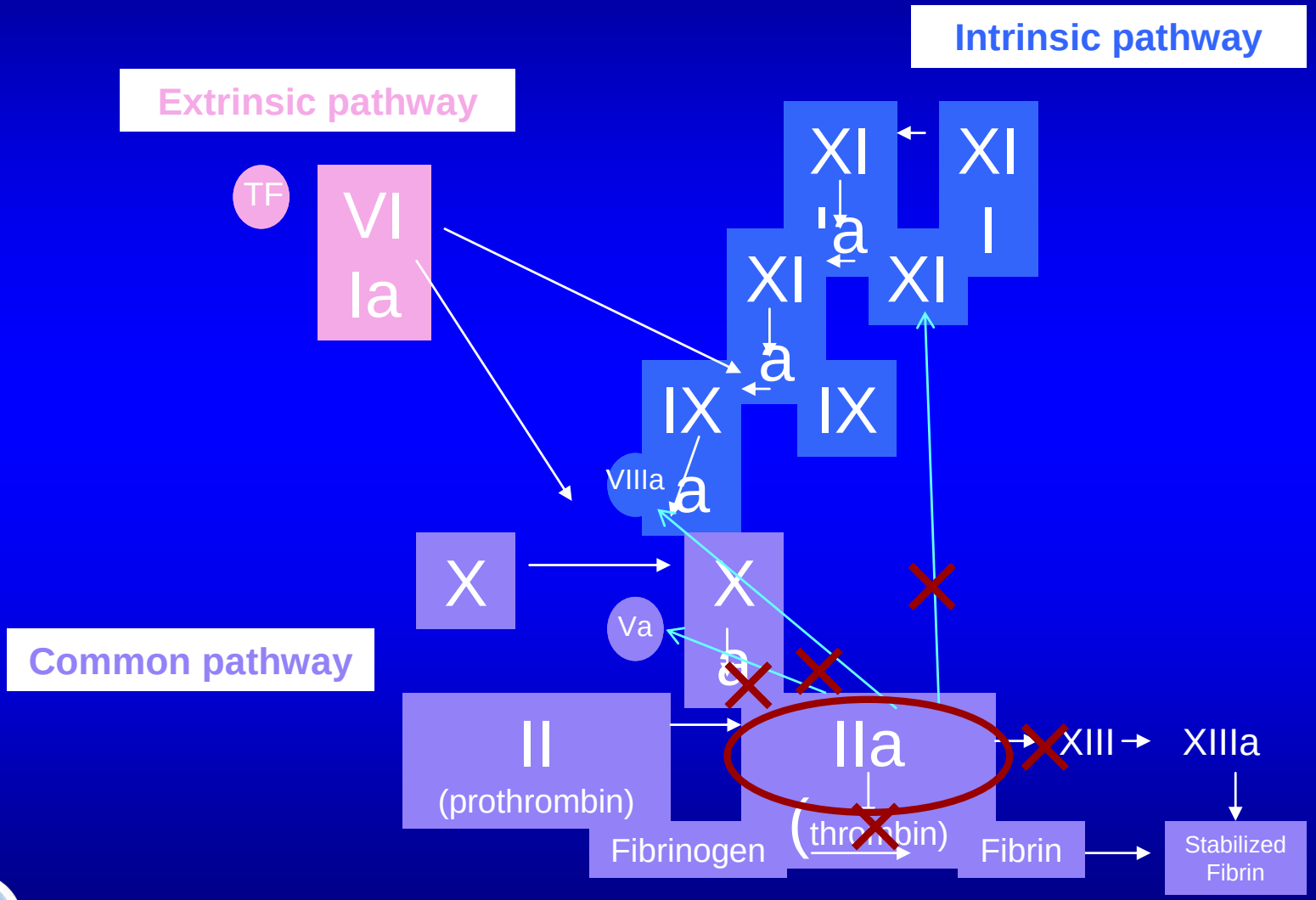


Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, NZ

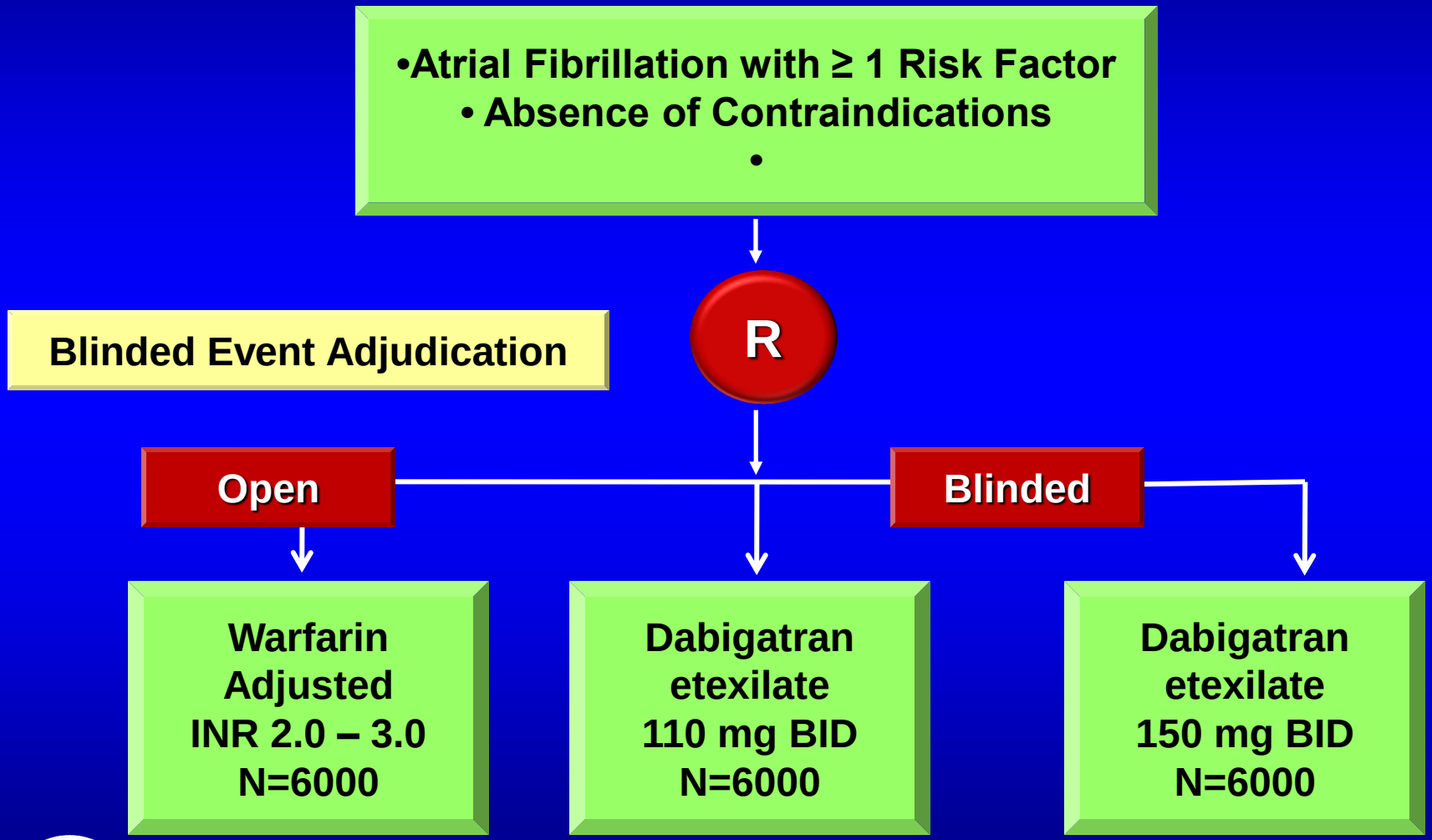
Connolly S, et al. *Lancet* 2006; 367:1903.
Hart R, et al. *Ann Intern Med* 2007;146:857.

Dabigatran/Pradaxa

Oral Direct Thrombin Inhibitor



The RE-LY Trial
Warfarin vs Dabigatran in high risk AF

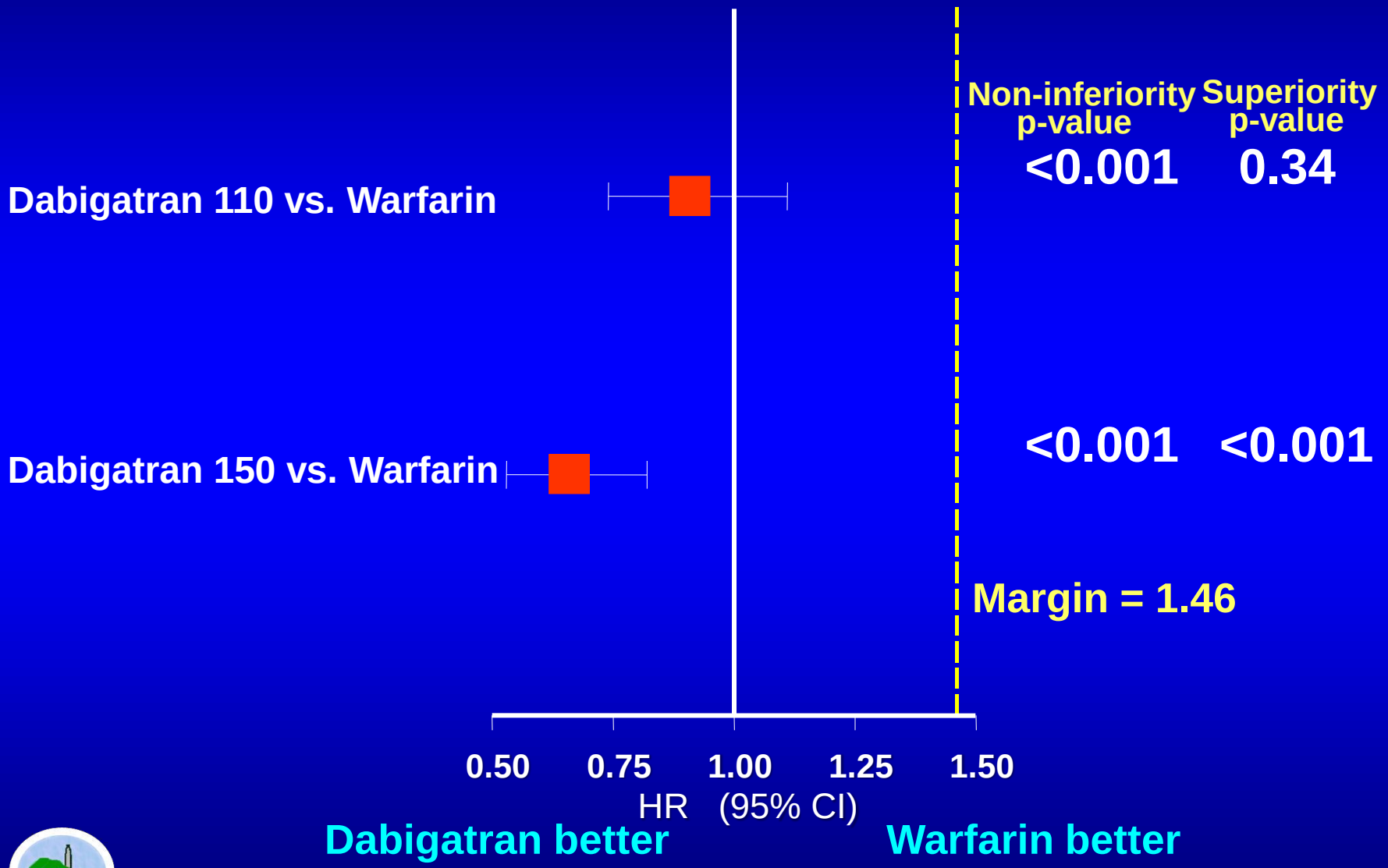


RE-LY: Baseline characteristics

Characteristic	Dabigatran 110 mg	Dabigatran 150 mg	Warfarin
Randomized	6015	6076	6022
Mean age (years)	71.4	71.5	71.6
Male (%)	64.3	63.2	63.3
CHADS2 score (mean)	2.1	2.2	2.1
0-1 (%)	32.6	32.2	30.9
2 (%)	34.7	35.2	37.0
3+ (%)	32.7	32.6	32.1
Prior stroke/TIA (%)	19.9	20.3	19.8
Prior MI (%)	16.8	16.9	16.1
CHF (%)	32.2	31.8	31.9
Baseline ASA (%)	40.0	38.7	40.6
Warfarin Naïve (%)	49.9	49.8	51.4

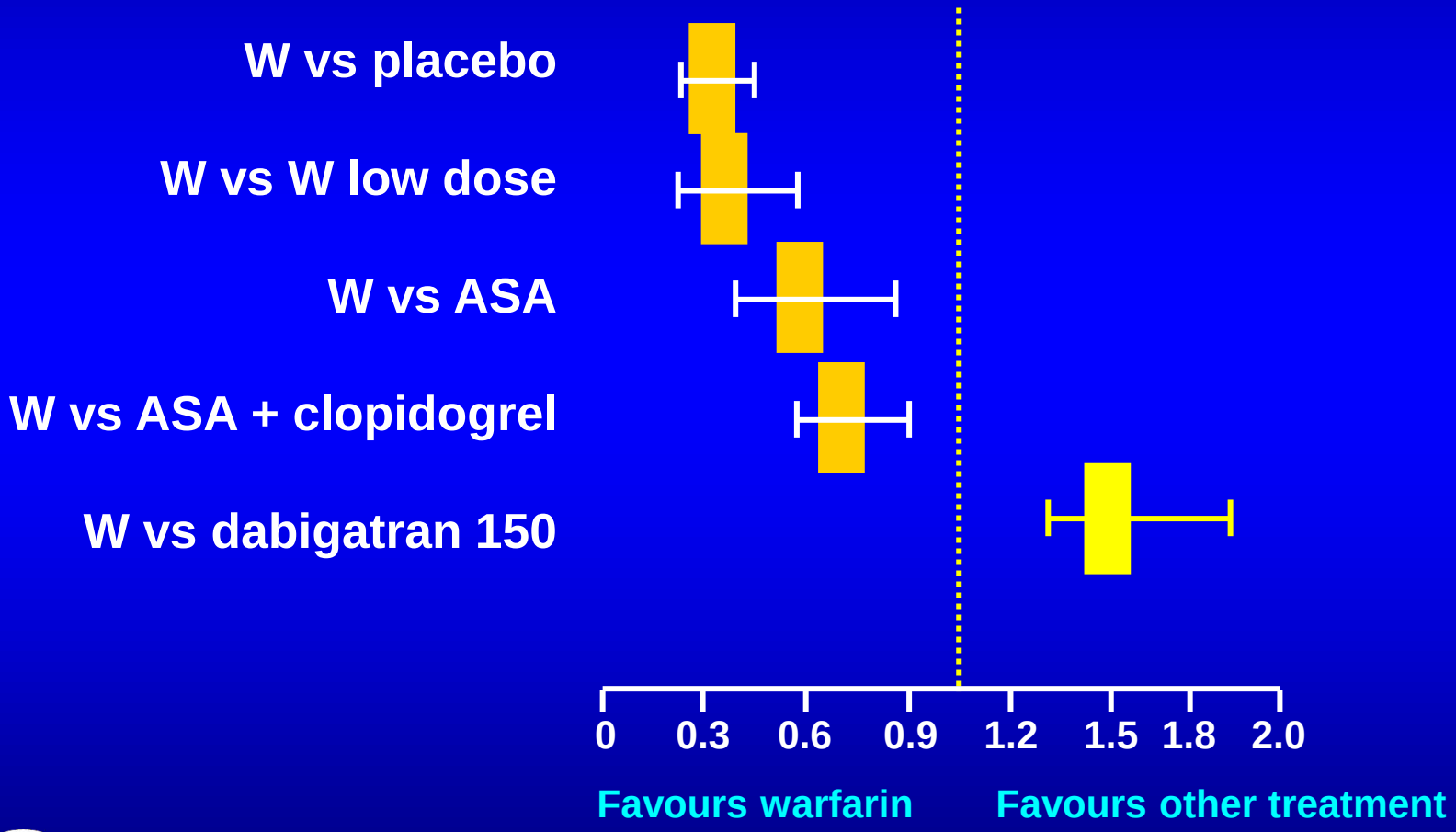
Connolly et al., *NEJM*, 2009

RE-LY: Stroke or systemic embolism



Connolly et al., *NEJM*, 2009

Clinical trials of anti-thrombotic treatments for prevention of ischemic stroke in AF



RE-LY: Outcomes in secondary-prevention patients with AF by treatment assignment

End point	Warfarin	Dabigatran 110 mg twice daily	RR (95% CI) vs warfarin	p	Dabigatran 150 mg twice daily	RR (95% CI) vs warfarin	p
Stroke/ systemic embolism (%/year)	2.74	2.32	0.85 (0.59–1.22)	0.37	2.07	0.76 (0.53–1.10)	0.14
Hemorrhagic stroke (n)	18	2	0.11 (0.03–0.47)	0.003	5	0.27 (0.10–0.72)	0.009
ICH (n)	30	6	0.20 (0.08–0.47)	0.001	13	0.41 (0.21–0.79)	0.007

Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, NZ

Diener HC et al. American Stroke Association International Stroke Conference 2010; February 26, 2010; San Antonio, TX.

RE-LY: Secondary efficacy outcomes according to treatment group

Event	Dabigatran 110 mg	Dabigatran 150 mg	Warfarin
Myocardial infarction	0.7%	0.7%	0.5%
Vascular death	2.4%	2.3%	2.7%
All-cause mortality	3.8%	3.6%	4.1%

Connolly, et al. *N Engl J Med* 2009;361:1139-51

RE-LY: Annual rates of bleeding

	Dabigatran 110mg	Dabigatran 150mg	Warfarin	Dabigatran 110mg vs. Warfarin		Dabigatran 150mg vs. Warfarin	
n	6015	6078	6022	RR 95% CI	p	RR 95% CI	p
Total	14.6%	16.4%	18.2%	0.78 0.74-0.83	<0.001	0.91 0.86-0.97	0.002
Major	2.7 %	3.1 %	3.4 %	0.80 0.69-0.93	0.003	0.93 0.81-1.07	0.31
Life-threatening	1.2 %	1.5 %	1.8 %	0.68 0.55-0.83	<0.001	0.81 0.66-0.99	0.04
Gastro-intestinal	1.1 %	1.5 %	1.0 %	1.10 0.86-1.41	0.43	1.50 1.19-1.89	<0.001

Connolly, et al. *N Engl J Med* 2009;361:1139-51

Key bleeding risk factors

Age > 75 years, frailty, co-morbidity

On anti-platelet

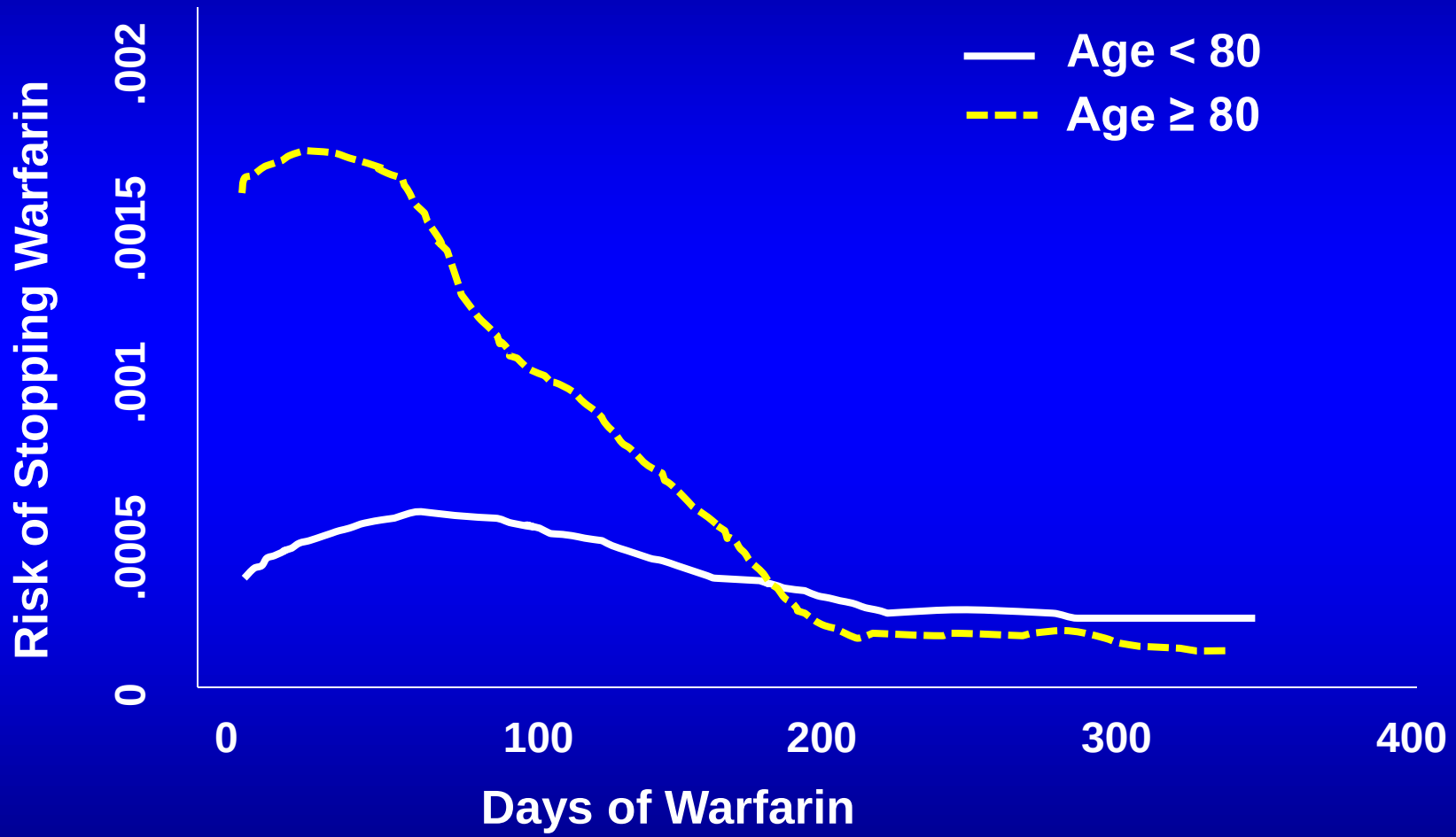
Renal impairment

Use of NSAID

Clinically important bleeding history (eg GI haemorrhage)

Labile INR's on warfarin

Risk of stopping therapy in the first year among patients newly starting warfarin by age



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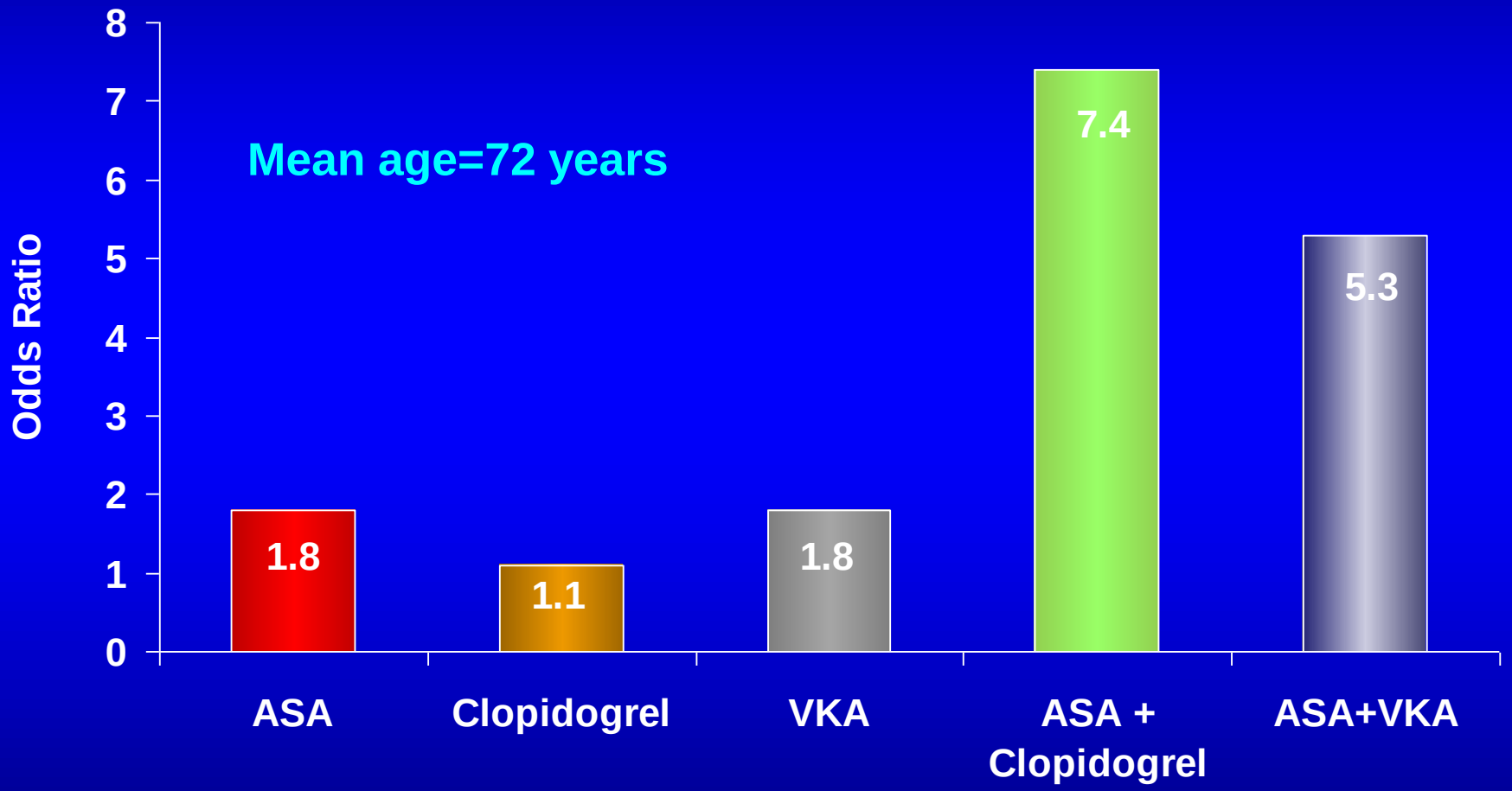
Hylek EM et al, *Circulation* 2007;115(21):2689.

Risk of GI bleeding with different anti-thrombotic agents



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Hallas J, et al. BMJ
doi:10.1136/bmj.38947.697558.AE

Low does aspirin compared to placebo for primary prevention of vascular disease

Absolute reduction = 0·06% per year
(12%PR = 0.06%AR)

Primary prevention trials with 95000 individuals & 3554 serious vascular events

Anti-Thrombotic Trialist Collaboration
Lancet 2009

Anti-coagulation and anti-platetet treatment:
Consider strength of indication and bleeding risk

	Anti-coagulation	Anti-platelet
Weak indication	Atrial fibrillation but no risk factors for stroke	CV risk factors but no clinical evidence of CVD
Usually indicated	Atrial fibrillation and risk factors for stroke	Stable coronary artery or cerebro-vascular disease
Strong indication	Atrial fibrillation and previous stroke / TIA. Mechanical heart valve	Coronary stent < 6 months Drug eluting stent <12 months Acute coronary syndrome or carotid territory stroke/TIA < 6mths Advanced CVD / history of multiple events

Phase III AF trials

	RE-LY		ROCKET-AF	ARISTOTLE
Drug	Dabigatran (inhibits thrombin)		Rivaroxaban (inhibits Xa)	Apixaban (inhibits Factor Xa)
	110 mg BID	150 mg BID	20 mg QD	5 mg BID
Stroke + SEE	non-inferior	superior	ITT cohort: non-infer. On Rx cohort: superior	superior
Bleeding	lower	similar	similar	lower
Mortality	similar	p=0.051	similar	superior: p=0.047
Ischemic stroke	similar	lower	similar	similar

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Connolly, et al. *N Engl J Med* 2009;361:1139
Patel, et al. *N Engl J Med* 2011; 365(10):883
Granger, et al. *N Engl J Med* 2011; 365(11): 981

Issues/limitations of dabigatran reported in clinical practice

Potential risks of major bleeding in elderly[1,2]

- Low body weight and decreased renal function increase drug exposure

Increased risk of bleeding with AF ablation[3]

- Compared with warfarin, periprocedural use increases risk of bleeding

Poor outcomes following trauma[4]

- No method readily available to determine degree of anticoagulation & no reversal agent

Possible increased risk of ACS or MI (Factor IIa inhibitor)[5]

High rates of early discontinuation[6]

Higher cost

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1 Legrand M, et al. Arch Intern Med 2011; 171(14):1285
2 Harper P, et al. N Engl J Med 2012; 366(9): 864
3 Lakkireddy D, et al. J Am Coll Cardiol 2012; 59(13): 1168
4 Cotton BA, et al. N Engl J Med 2011; 365(21): 2039
5 Uchino K, et al. Arch Intern Med 2012; 172(5): 397
6 Stanek E. Circulation 2011; 124: A16675

Perioperative management of dabigatran

Renal function (CrCl, mL/min)	Half life of dabigatran (hours)[d]	Timing of discontinuation after last dose of dabigatran before surgery	
		Standard risk of bleeding	High risk of bleeding[e]
>80	13 (11-22)	24 hours	2 days
>50 to ≤80	15 (12-34)	24 hours	3 days
>30 to ≤50	18 (13-23)	At least 2 days (48 hours)	4 days
≤30[f]	27 (22-35)	2-5 days	>5 days

d. Stangier et al. Clin Pharmacokinet 2010; 49: 259-268, geometric mean (range).
e. Types of surgery associated with a high risk of bleeding (or in major surgery where complete haemostasis may be required) including but not limited to cardiac surgery, neurosurgery, abdominal surgery, or surgeries involving a major organ. Other procedures such as spinal anaesthsia may also require complete haemostatic function. Other important determinants of bleeding risk include advancing age, co-morbidities (eg, major cardiac, respiratory, or liver disease) and concomitant use of anti-platelet therapy.
f. Dabigatran is contraindicated for use in patients with CrCl ≤30 ml/min. CrCl = creatinine clearance.

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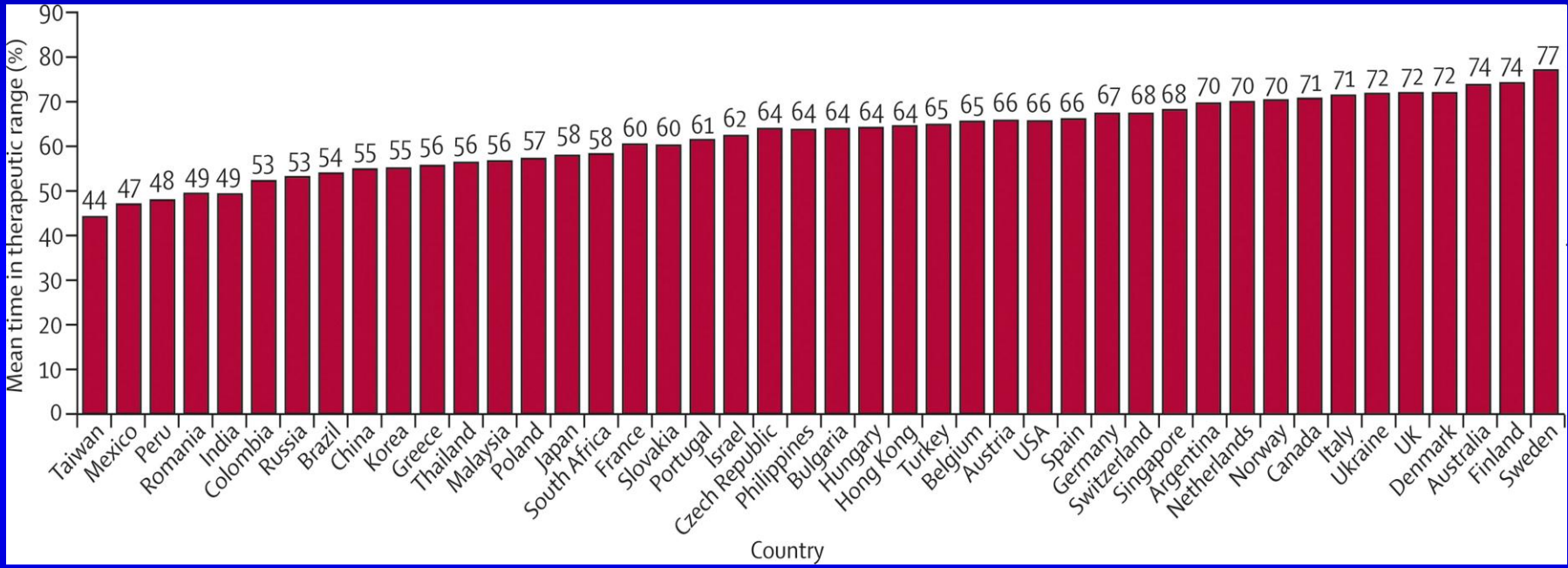
http://www.pharmac.govt.nz/2011/06/13/Dabigatran%20testing%20and%20perioperative%20management.pdf

Country distribution of mean time in therapeutic range – RE-LY trial



Wallentin L, et al. *Lancet* 2010; 376: 975

RE-LY: intracranial bleeding compared to warfarin according to INR control

Mean time in therapeutic range	110 mg dabigatran	150 mg dabigatran	Warfarin	110 mg dabigatran vs warfarin		150 mg dabigatran vs warfarin	
	Rates per 100 person-years	Rates per 100 person-years	Rates per 100 person-years	HR (95% CI)	P	HR (95% CI)	P
<57.1%	0.28	0.34	0.64	0.43 (0.19 – 1.00)		0.53 (0.25 – 1.15)	
57.1-65.5%	0.30	0.42	0.93	0.31 (0.15 – 0.66)		0.45 (0.24 – 0.88)	
65.5-72.6%	0.13	0.24	0.67	0.20 (0.07 – 0.58)		0.35 (0.15 – 0.82)	
>72.6%	0.21	0.30	0.77	0.27 (0.11 – 0.66)	0.71	0.39 (0.18 – 0.84)	0.89

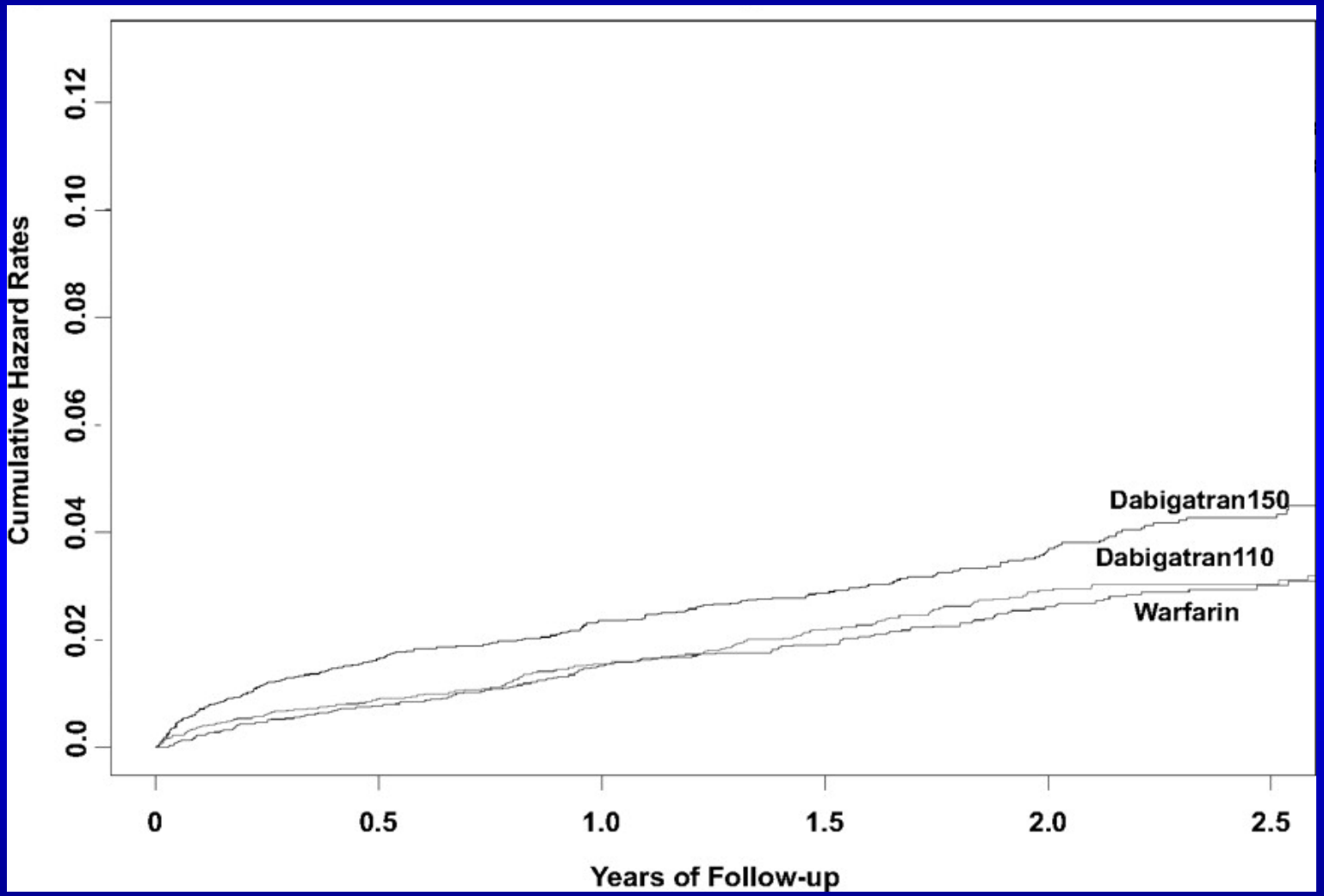
Wallentin L, et al. *Lancet* 2010; 376: 975

RE-LY: intracranial bleeding compared to warfarin according to INR control

- Even with excellent INR control ie in therapeutic range > 72.6% there are 5 more intracranial haemorrhages per 1000 patients treated for a year with warfarin compared to dabigatran150mg bid and 6 per 1000 patients treated for a year compared with dabigatran 110mg bid, p< 0.05

Wallentin L, et al. *Lancet* 2010; 376: 975

RE-LY:
Time to GI major bleed



Eikelboom J W et al. Circulation 2011;123:2363-2372

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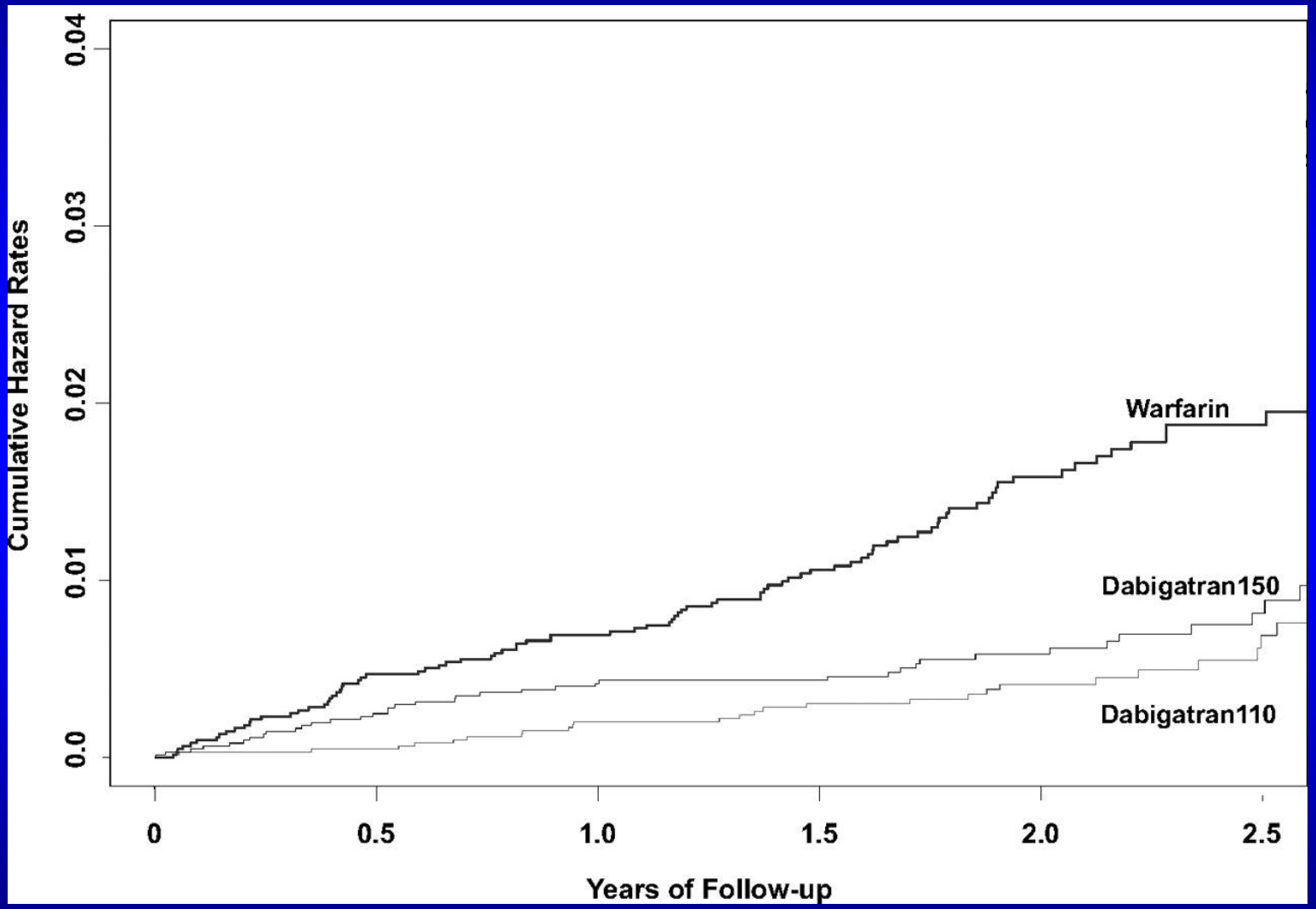
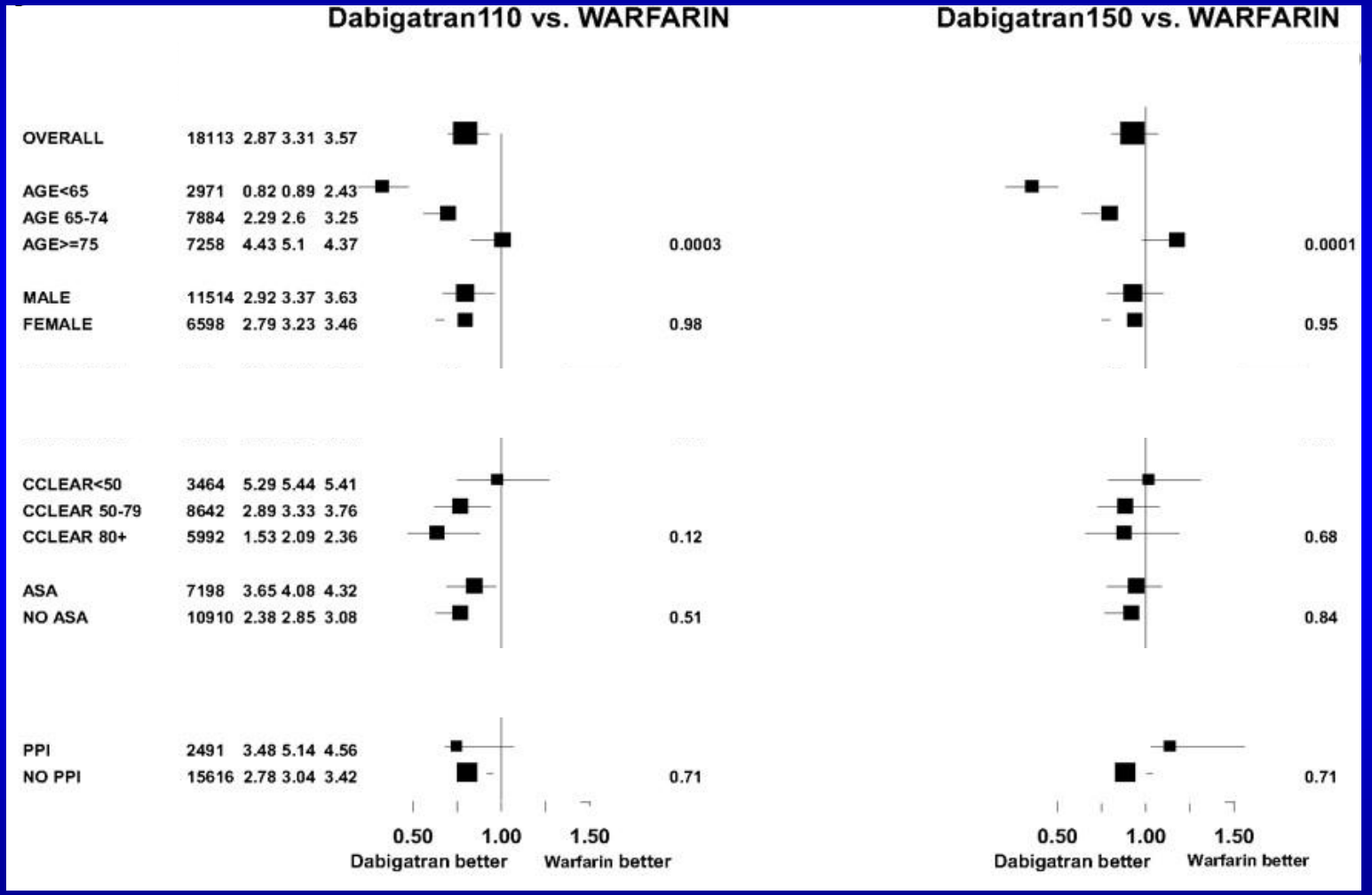
RE-LY:
Time to All intracranial bleeds



Eikelboom J W et al. Circulation 2011;123:2363-2372

RE-LY:
Major bleeding dabigatran vs warfarin



Eikelboom J W et al. Circulation 2011;123:2363-2372

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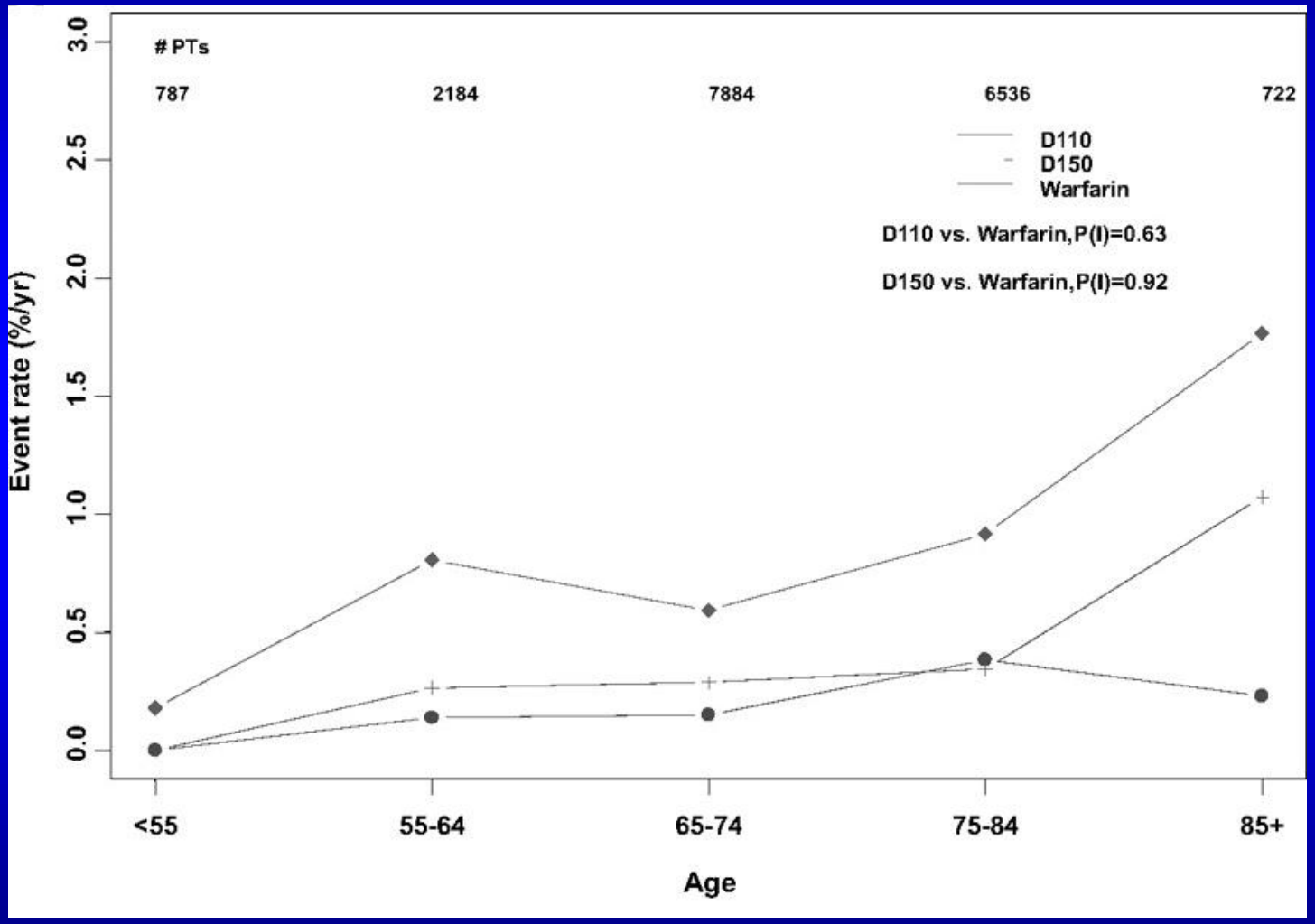
RE-LY:
Intracranial bleeding rate



Eikelboom J W et al. Circulation 2011;123:2363-2372

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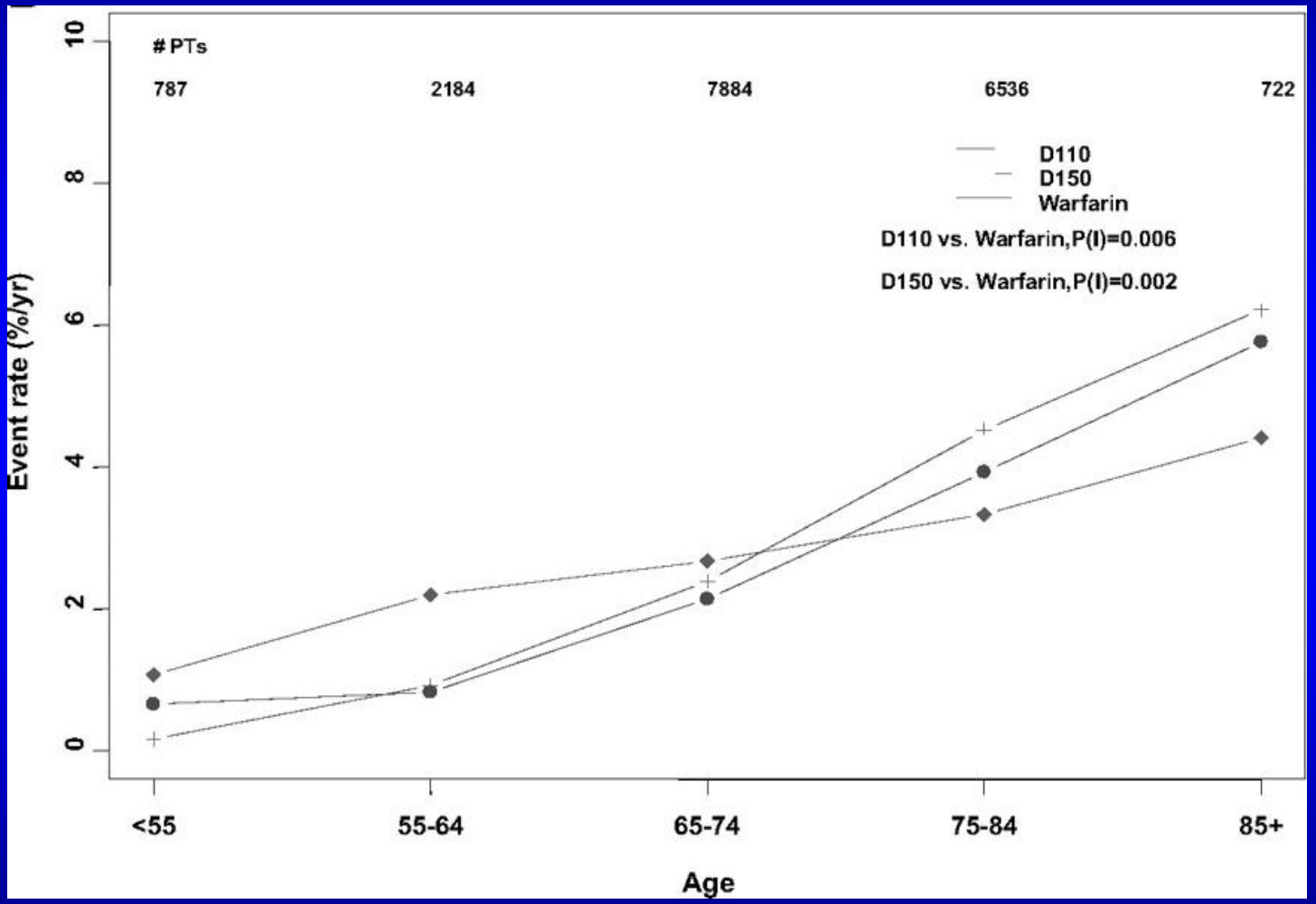
RE-LY:
Extracranial major bleeding rate



Eikelboom J W et al. Circulation 2011;123:2363-2372

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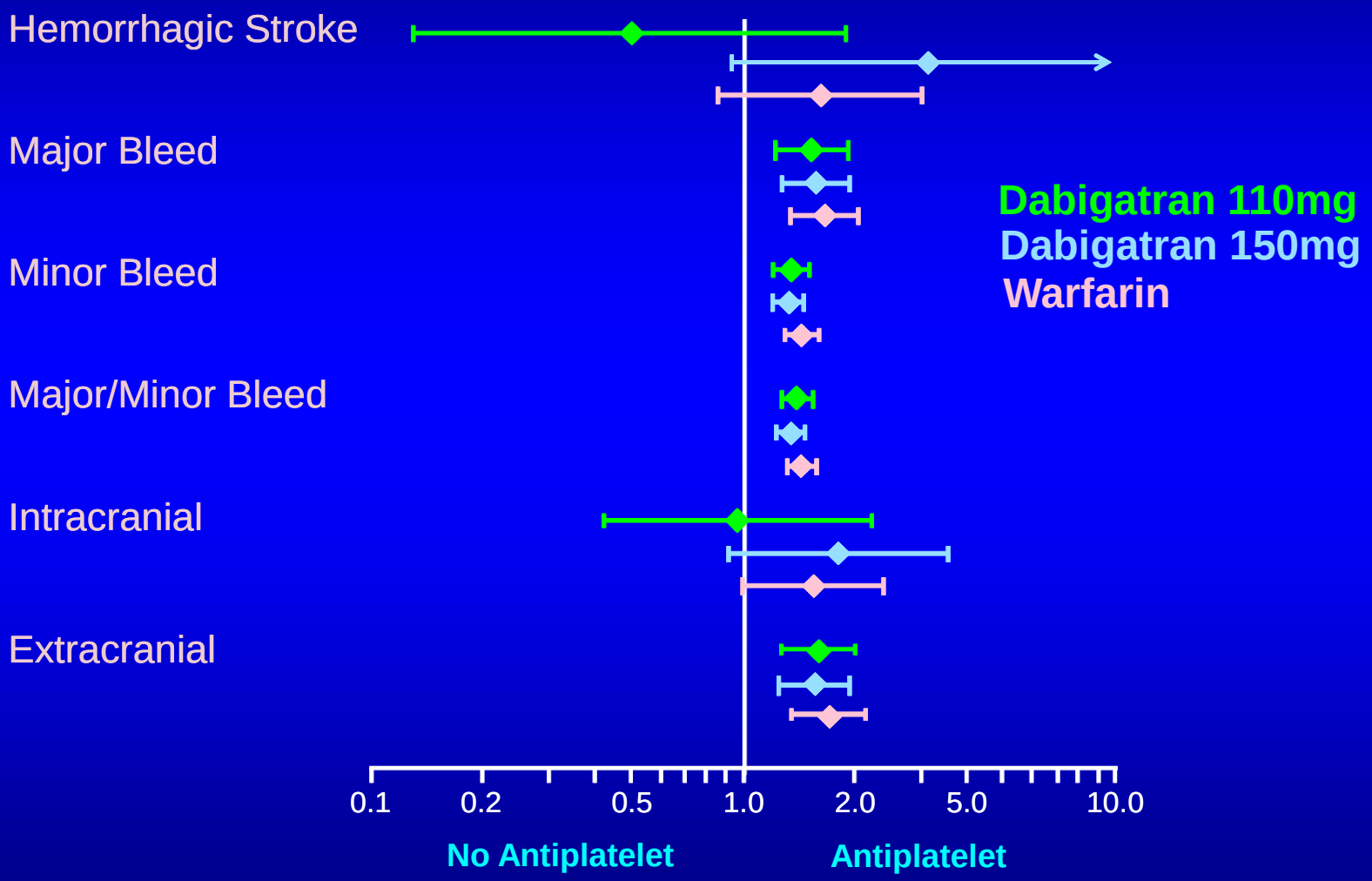
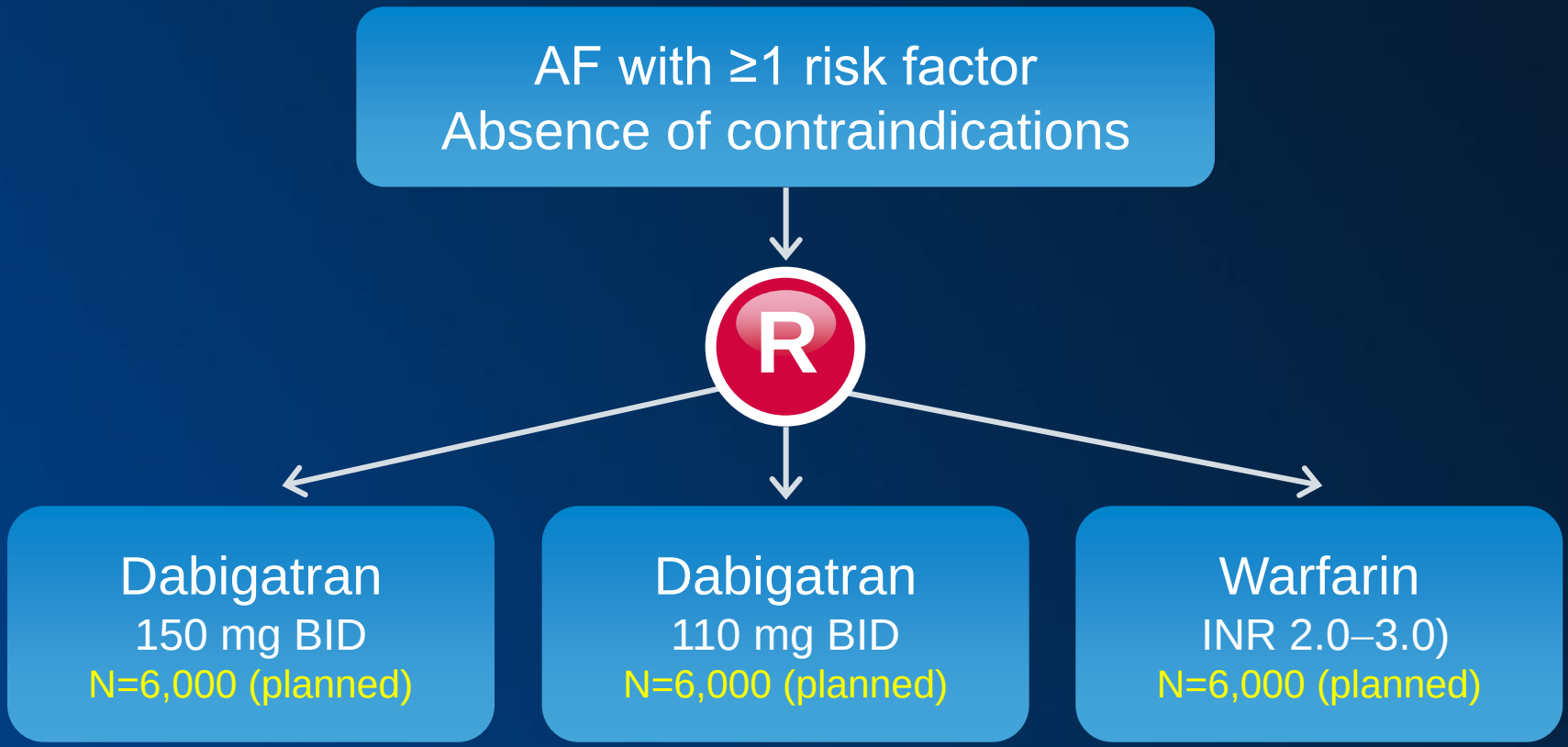
RE-LY Substudy

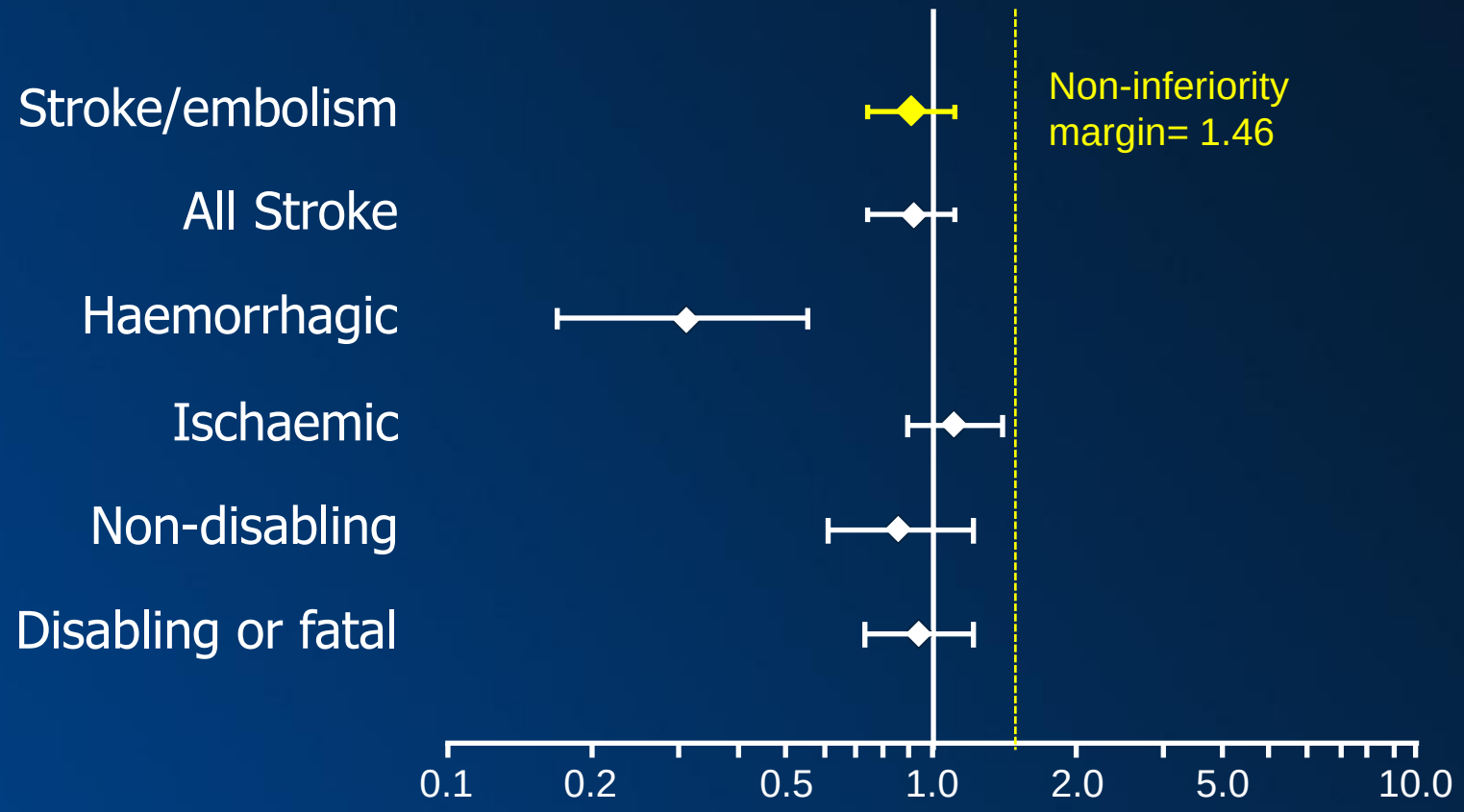
Antiplatelet vs No antiplatelet: Bleeding



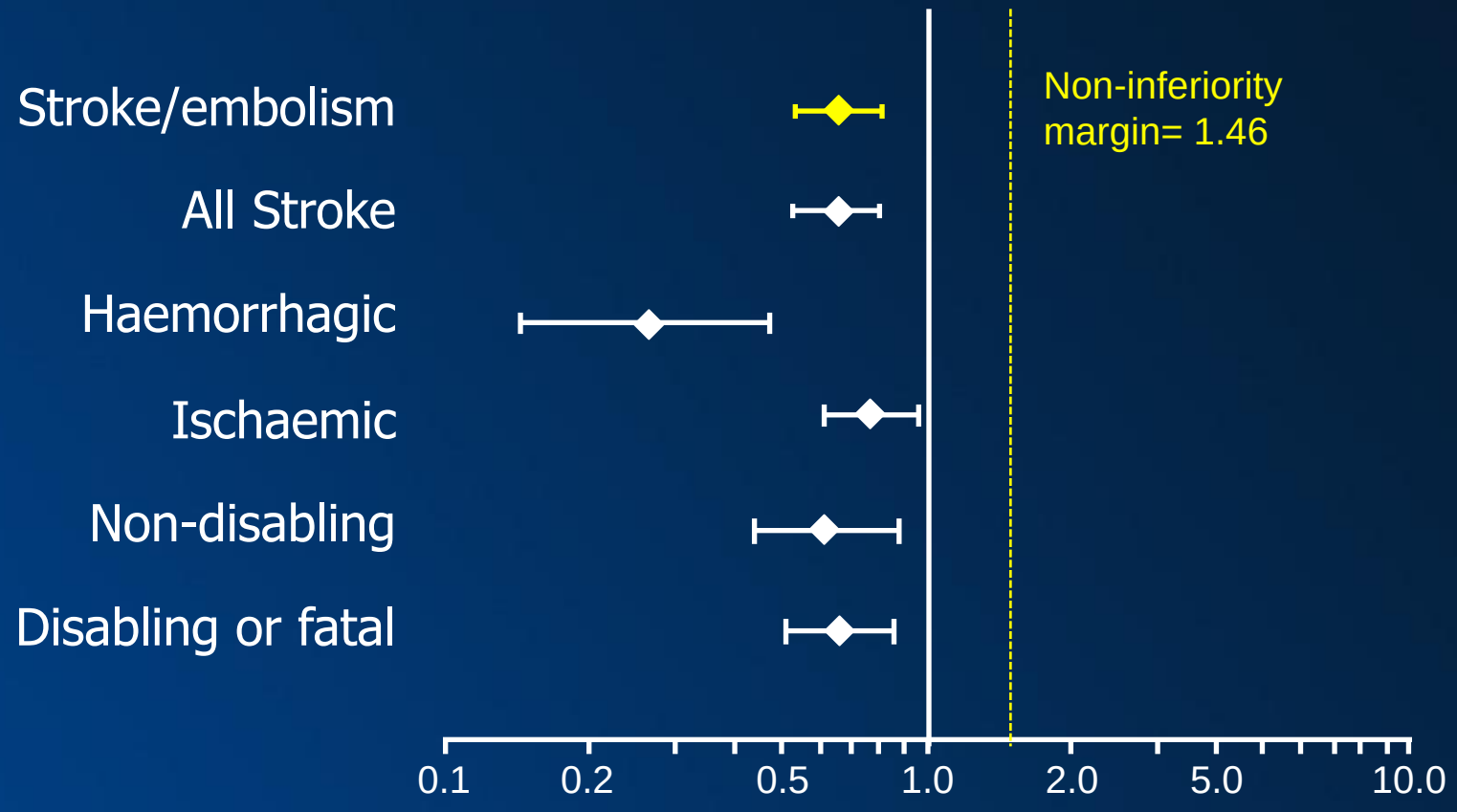
RE-LY® : Study Design



RE-LY®: DE 150 vs warfarin



RE-LY®: DE 150 vs warfarin



The patient on warfarin:
Non ST elevation ACS

My best judgement

- Patient with $CHADS_2$ Score of 3 on aspirin plus dabigatran and presents with non-STEACS – continue or withhold dabigatran 12 hours before radial angiography and PCI: clopidogrel 600 mg, bivalirudin full dose, BMS
- Consider watchman, pulmonary vein ablation, stop dabigatran after 6 weeks

Warfarin in STEMI

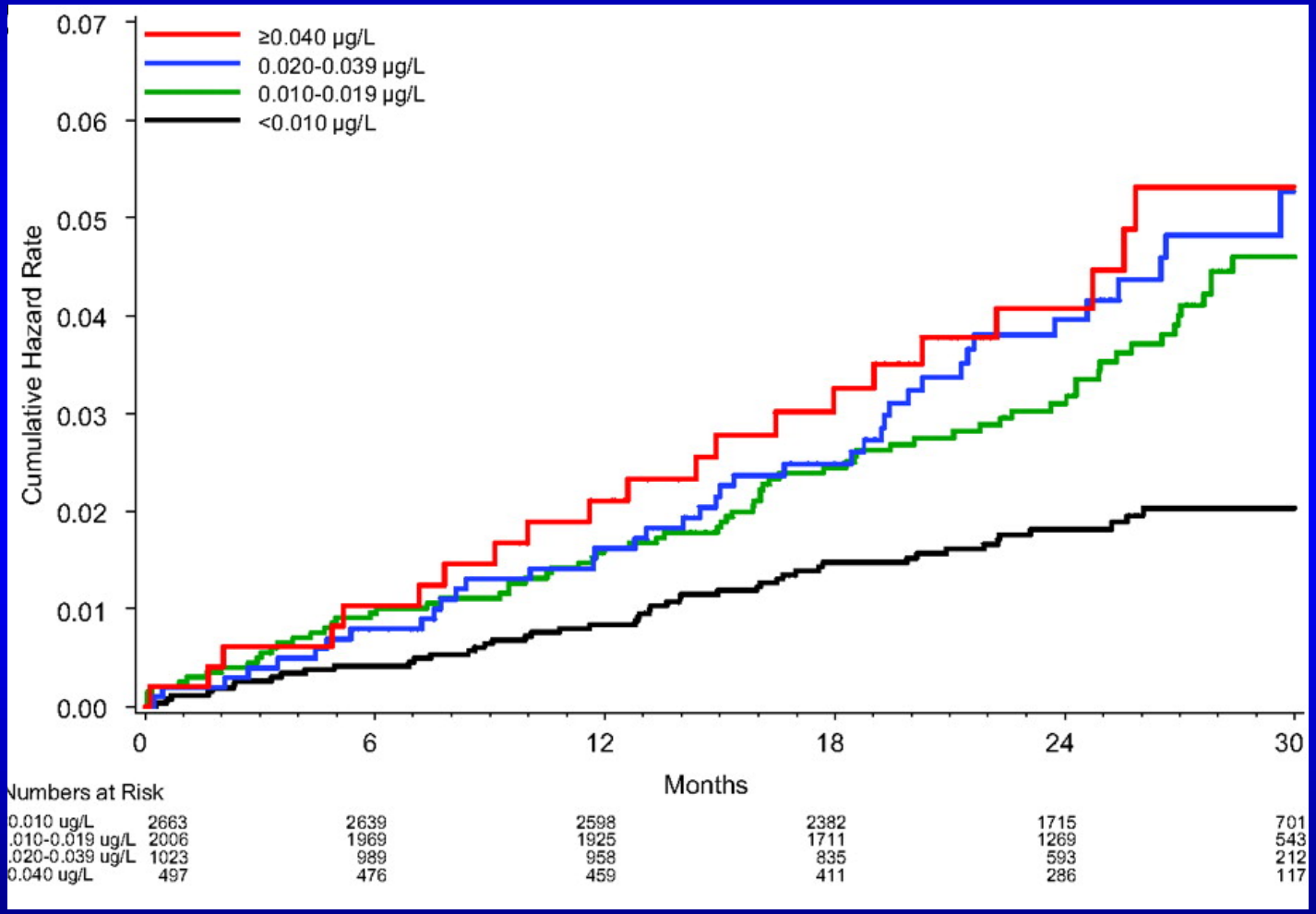
My best judgement

- Radial approach
- Aspirin and clopidogrel (prasugrel/ticlopidine)
- INR is frequently not known
- Use bivalirudin in full dose (Add UFH 30 – 50 U/kg)
- Restricted use of drug-eluting stents

- Triple therapy for 1 month

Troponins in atrial fibrillation

Troponin I and risk for stroke or systemic embolism: RE-LY



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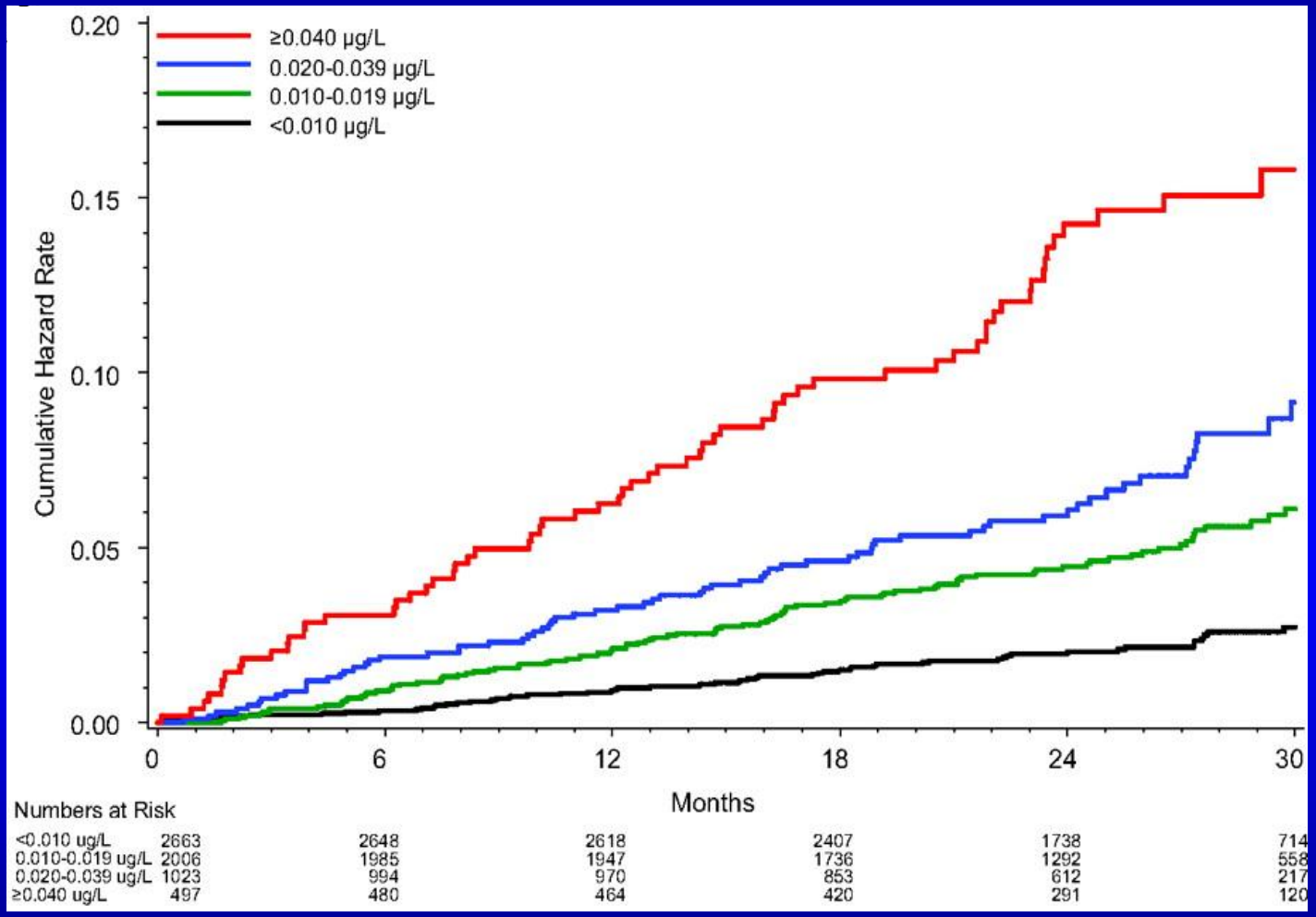
Hijazi, Z., et al. *Circulation*. 2012; 125:1605

Troponin I and vascular death: RE-LY



Hijazi, Z., et al. *Circulation*. 2012; 125:1605

Myocardial Infarction: RE-LY

- There were 103 myocardial infarctions during follow-up
- The annual rates were 0.49% in the group with undetectable troponin I and 1.69% (HR 3.04; 95% CI 1.64–5.64) in the highest troponin I group (P=0.0052)
- The association of troponin I and myocardial infarctions remained significant after adding NT-proBNP to the model
- There was no significant relation between NT-proBNP levels and myocardial infarctions

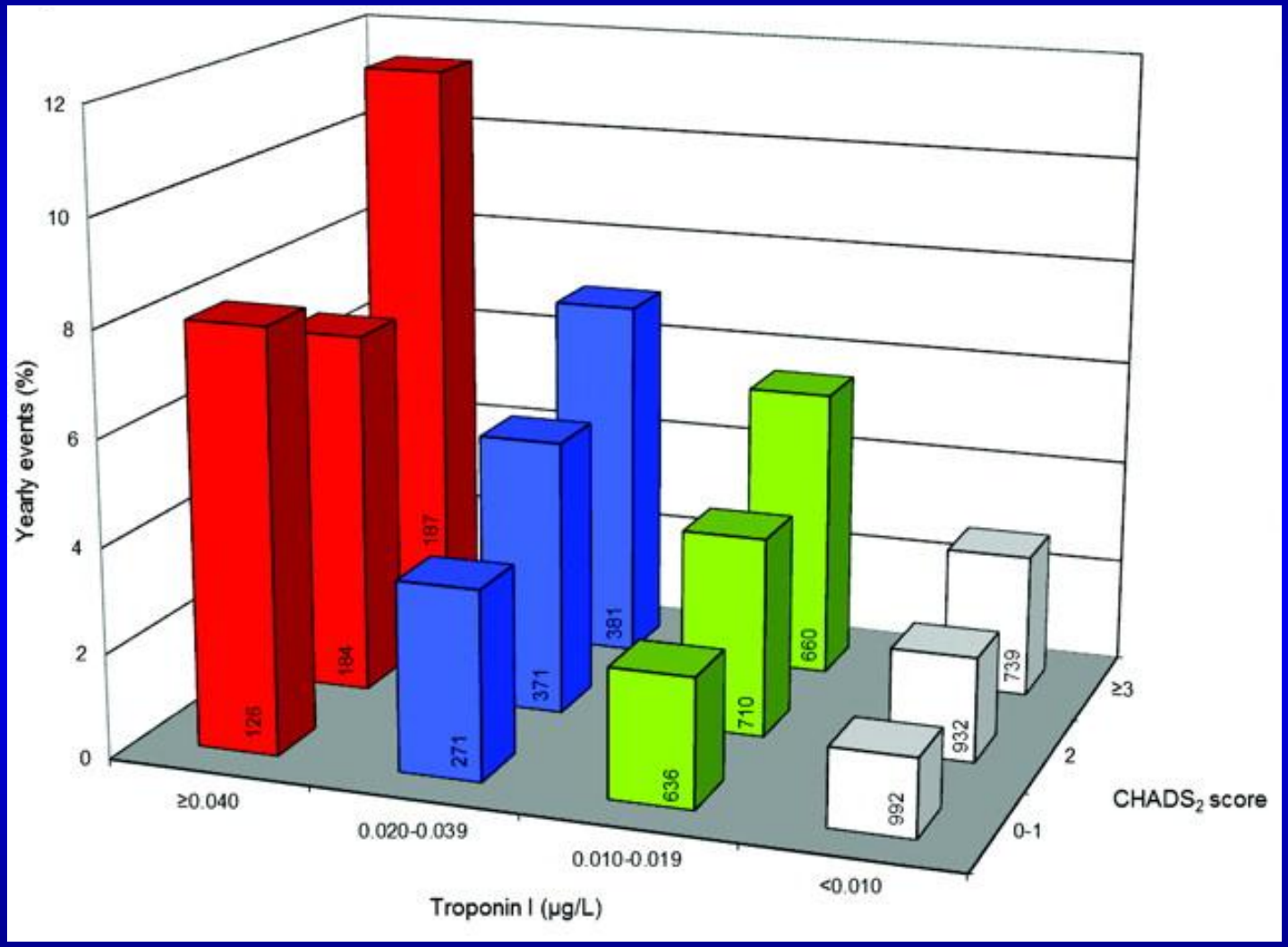
Hijazi, Z., et al. *Circulation*. 2012; 125:1605

Troponin I in relation to major bleeding: RE-LY

Biomarkers	Group	Total number of events, n (%/y)	HR (95% CI)	P value effect of biomarker level
Troponin I group (µg/L)	<0.010	98 (1.72)		0.0009
	0.010 – 0.019	1.25 (2.94)	1.48 (1.13 – 1.93)	
	0.020 – 0.039	67 (3.25)	1.50 (1.09 – 2.07)	
	≥0.040	44 (4.38)	2.01 (1.39 – 2.90)	

Hijazi, Z., et al. *Circulation*. 2012; 125:1605

Troponin I and stroke, systemic embolism, pulmonary embolism, myocardial infarction, vascular death: RE-LY



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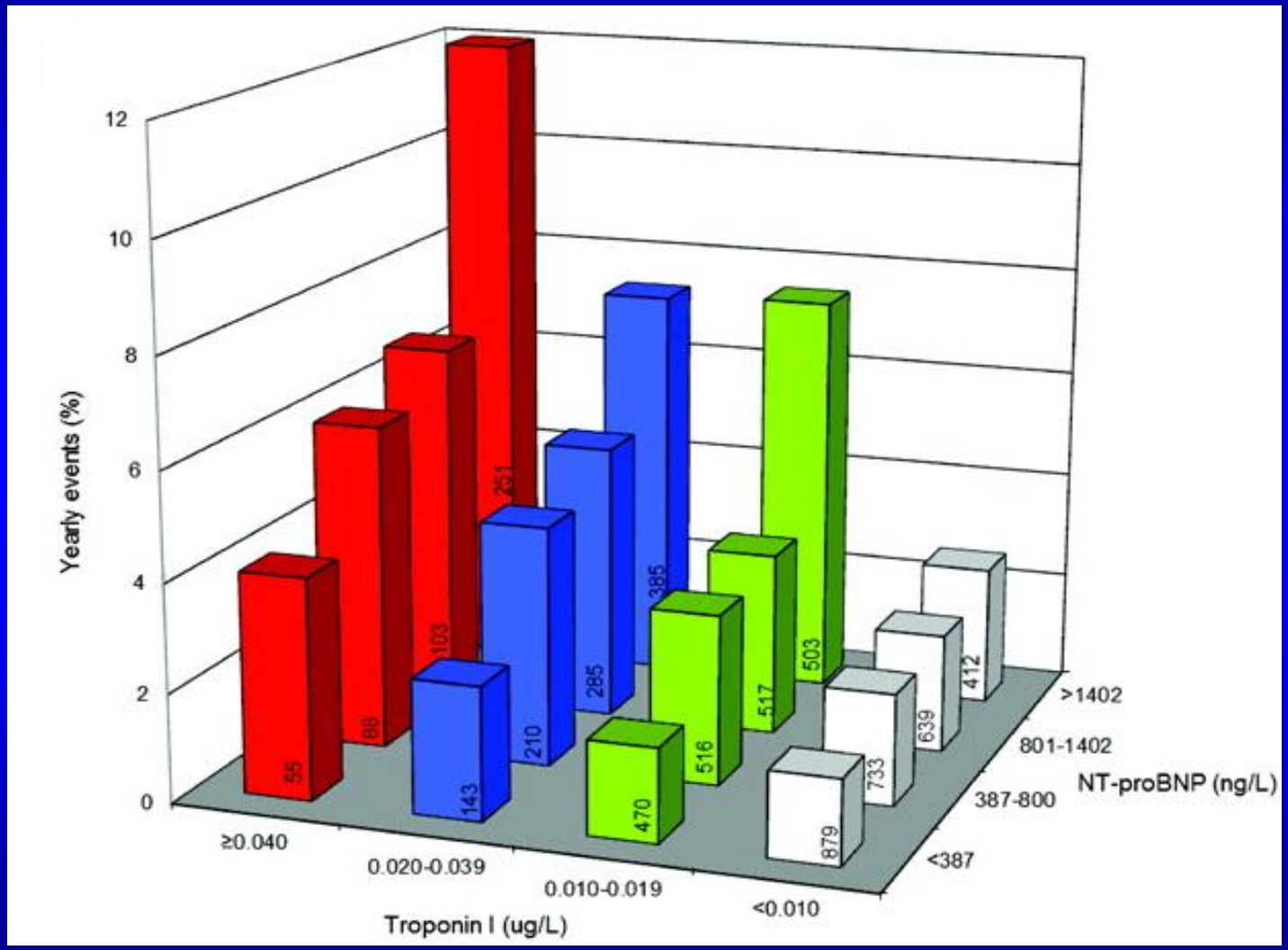
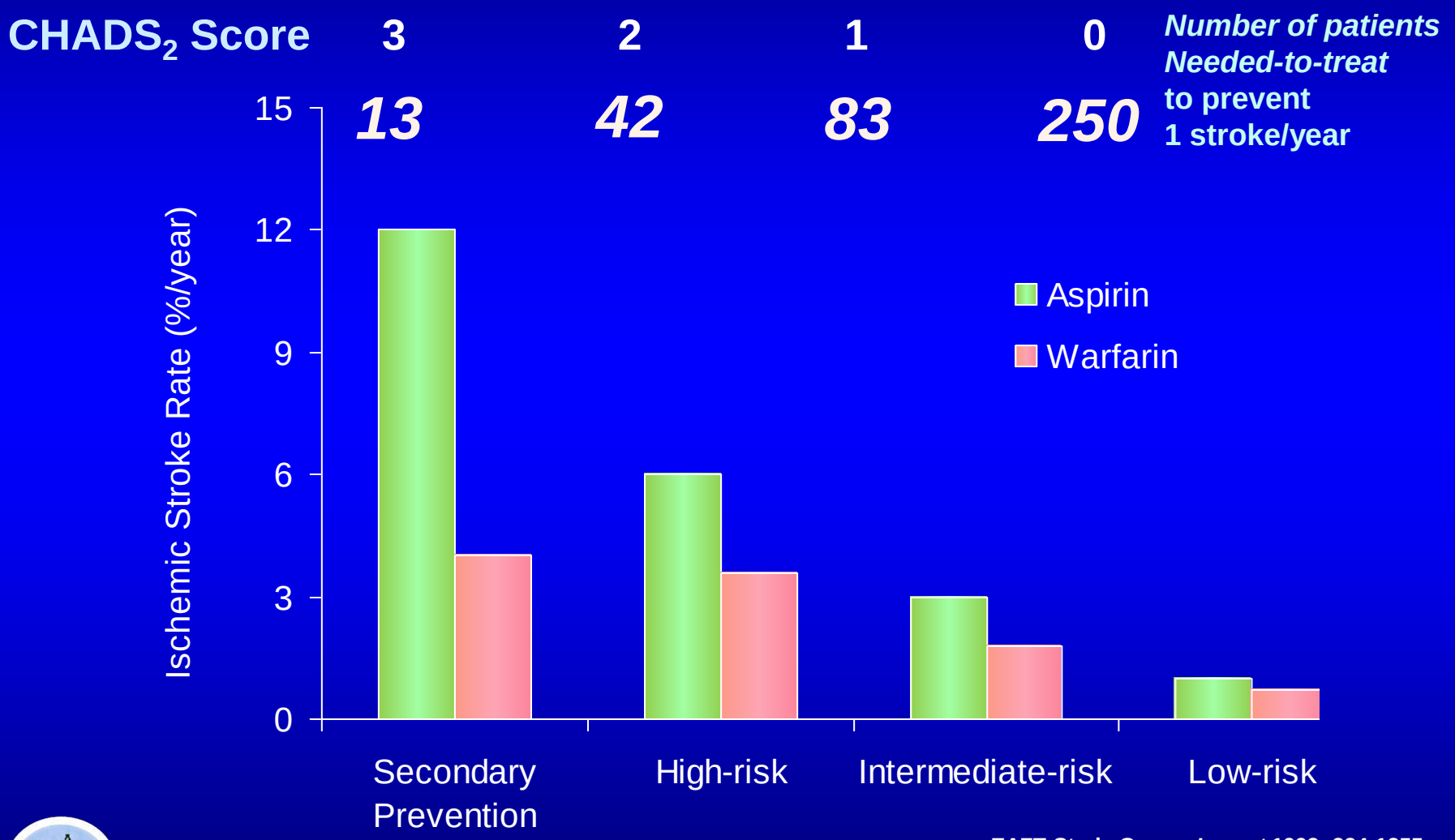
Troponin I and NT-proBNP levels: RE-LY



Hijazi, Z., et al. *Circulation*. 2012; 125:1605

Risk Stratification and Anticoagulation

Stroke Reduction with Warfarin Instead of Aspirin



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EAFT Study Group. *Lancet* 1993; 324:1255.
Zabalgoitia M, et al. *JACC* 1998; 31:1622.