NOAC'S For Stroke Prevention in Atrial Fibrillation

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- New
- Oral
- Anti
- Coagulant

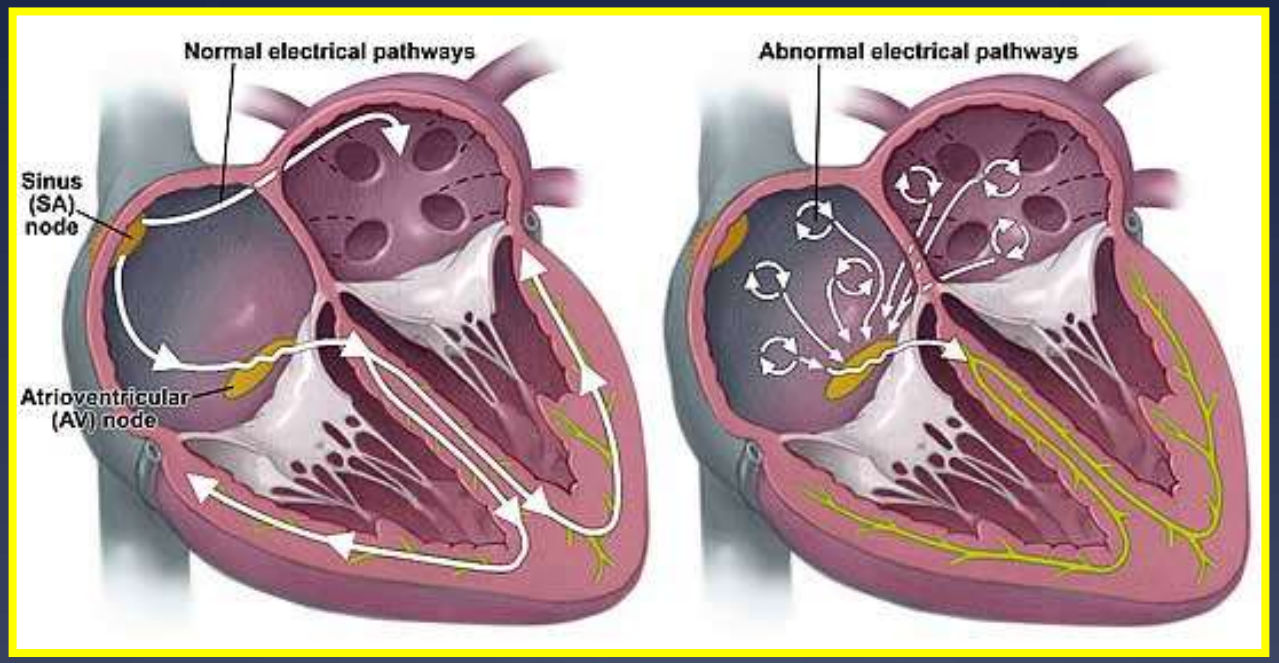
Formal Definition: Atrial Fibrillation

AF is an arrhythmia characterized by uncoordinated atrial activation, with consequent deterioration of atrial mechanical function

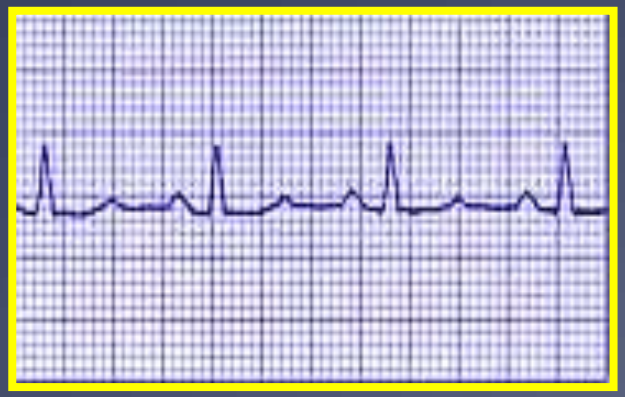
Circulation 2011; 121: e269-e367

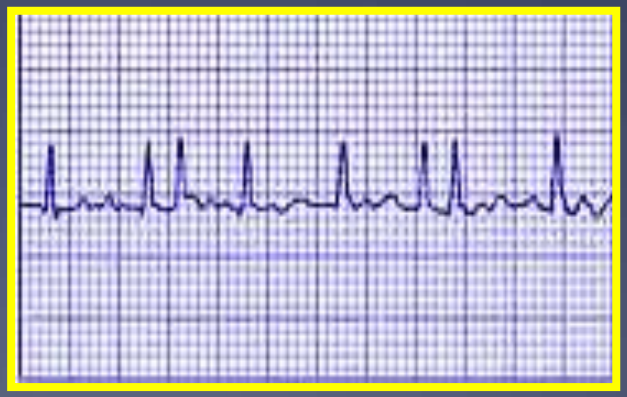
The ECG of Atrial Fibrillation

Normal sinus rhythm



Atrial fibrillation





Definitions of AF: A Simplified Scheme

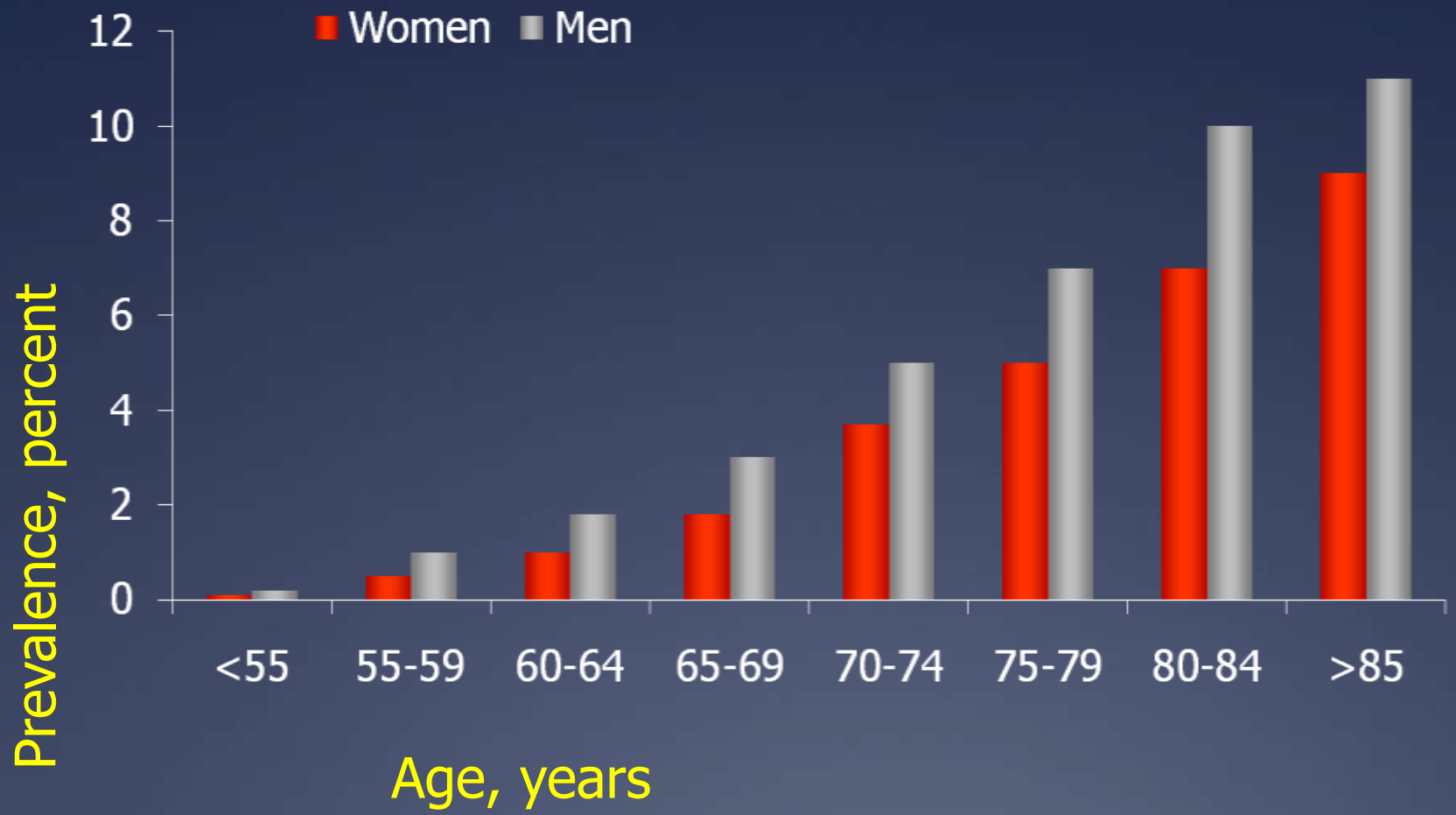
Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Long-standing persistent AF	• Continuous AF >12 mo in duration.
Permanent AF	• The term “permanent AF” is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF. • Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

AF indicates atrial fibrillation.

Atrial Fibrillation: Epidemiology

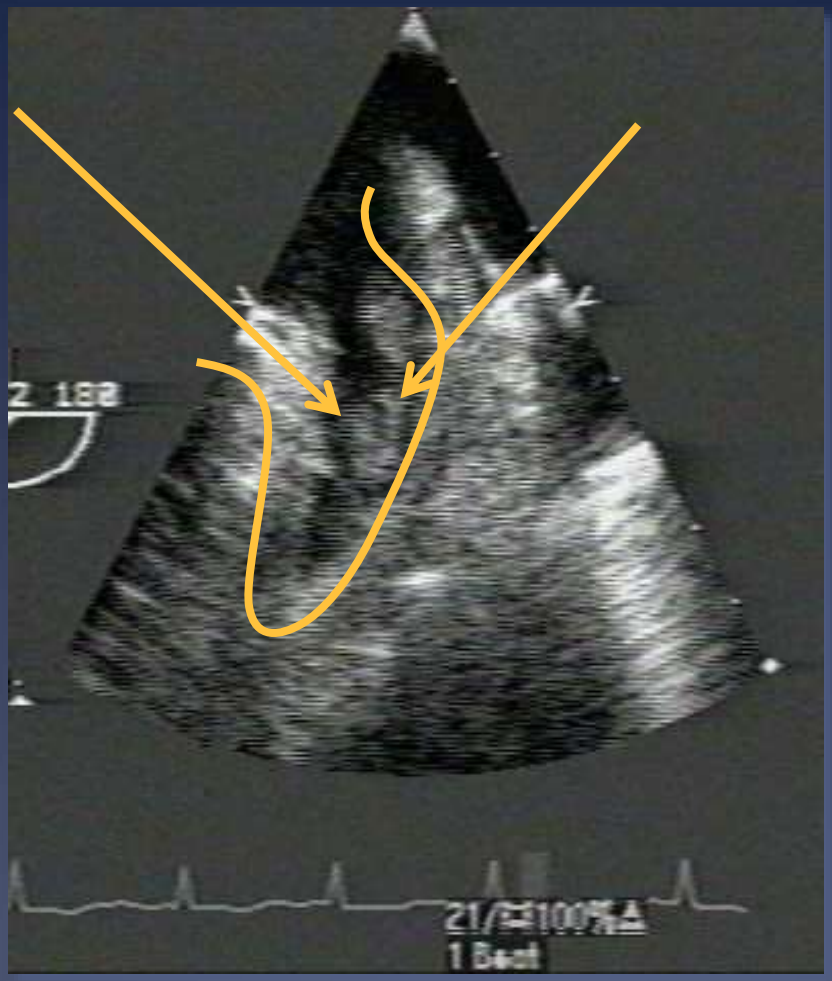
- The No. 1 preventable cause of stroke
- In the United States, up to 16 million individuals will be affected by the year 2050
- Increasing survival from heart attack and increasing age ("the 'graying' of America") help explain rise in incidence of AF

Relationship Between Atrial Fibrillation and Age



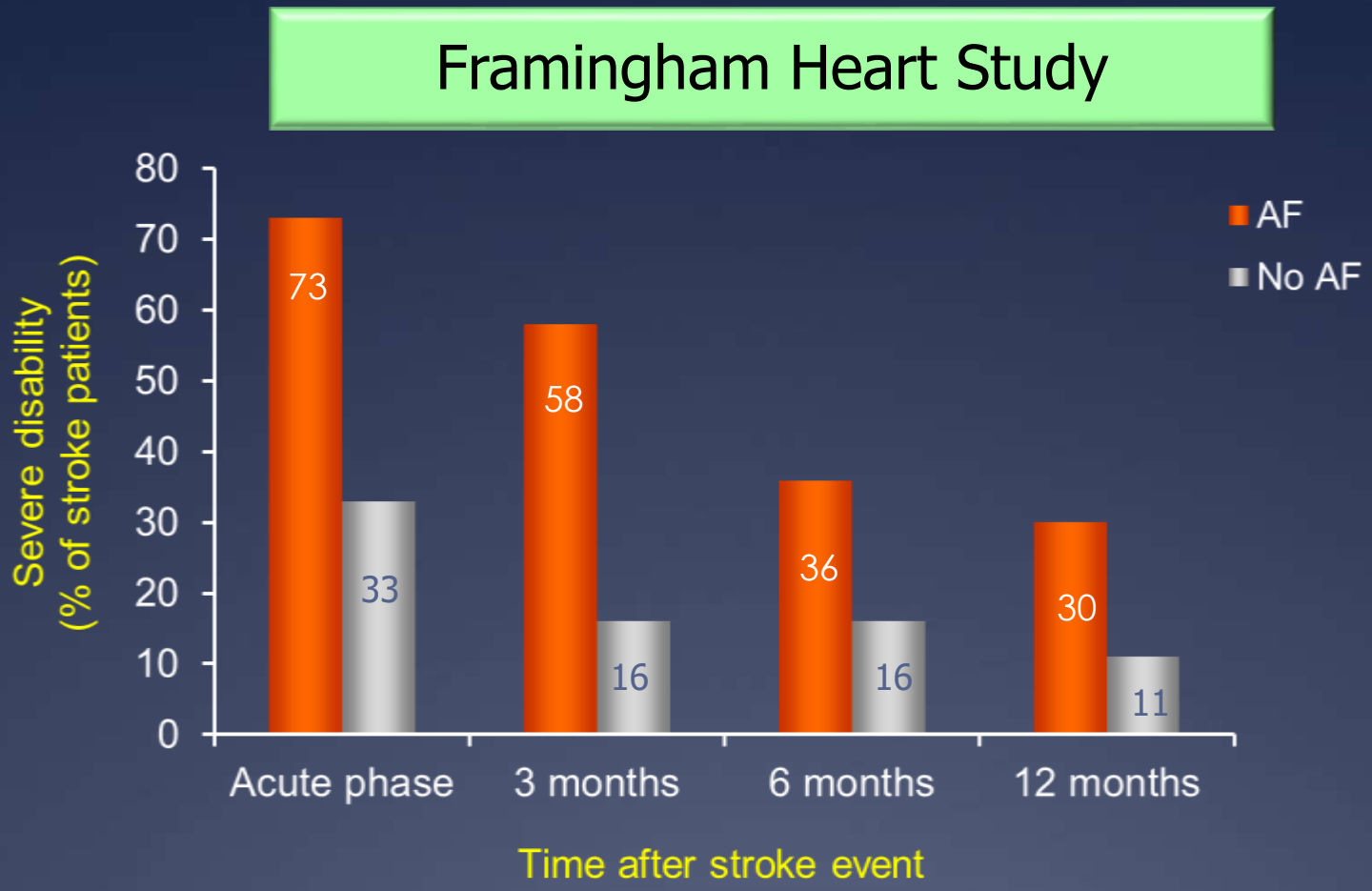
Go AS, et al. JAMA. 2001; 285:2370-2375.

Atrial Fibrillation Causes Stroke
Left Atrial Appendage Thrombus



Chimowitz. *Stroke* 1993; 24: 1015
Zabalgoitia. *J Am Coll Cardiol* 1998; 31: 1622

Ischemic Strokes in Atrial Fibrillation More Likely to be Severely Disabling



Lin HJ, et al. *Stroke*. 1996;27:1760-1764.

The CHA_2DS_2-VASc Score
Stroke Risk Score for Atrial Fibrillation

	Weight (points)
Congestive heart failure or LVEF ≤ 35%	1
Hypertension	1
Age > 75 years	2
Diabetes mellitus	1
Stroke/TIA/systemic embolism	2
Vascular Disease (MI/PAD/Aortic plaque)	1
Age 65-74 years	1
Sex **c**ategory (female)	1

Moderate-High risk ≥ 2

Low risk 0-1

Lip GYH, Halperin JL. *Am J Med* 2010; 123: 484.

CHA_2DS_2-VASc

Stroke or Other TE at One Year

CHA_2DS_2-VASc Score	#	#TE Events	TE Rate During 1 yr (95% CI)	TE Rate During 1 yr, Adjusted for Aspirin RX
0	103	0	0% (0-0)	0%
1	162	1	0.6% (0.0-3.4)	0.7%
2	184	3	1.6% (0.3-4.7)	1.9%
3	203	8	3.9% (1.7-7.6)	4.7%
4	208	4	1.9% (0.5-4.9)	2.3%
5	95	3	3.2% (0.7-9.0)	3.9%
6	57	2	3.6% (0.4-12.3)	4.5%
7	25	2	8.0% (1.0-26.0)	10.1%
8	9	1	11.1% (0.3-48.3)	14.2%
9	1	1	100% (2.5-100)	100%
Total	1,084	25	*P Value for trend 0.003*	

Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Chest. 2010 Feb;137(2):263-72. Pub Med PMID: 19762550.

Assessment of Bleeding Risk: The HAS-BLED Score

	Clinical characteristic	Points
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding tendency or predisposition	1
L	Labile INRs (< 60% of time in therapeutic range)	1
E	Elderly (age ≥ 65)	1
D	Drugs (concomitant aspirin, NSAID) or alcohol (1 point each)	1 or 2

Maximum: 9 points

INR = international normalized ratio; NSAID = nonsteroidal anti-inflammatory drug

Pisters R, et al. *Chest*. 2010;138(5):1093-1100.

ESC 2012 AF Update Guidelines

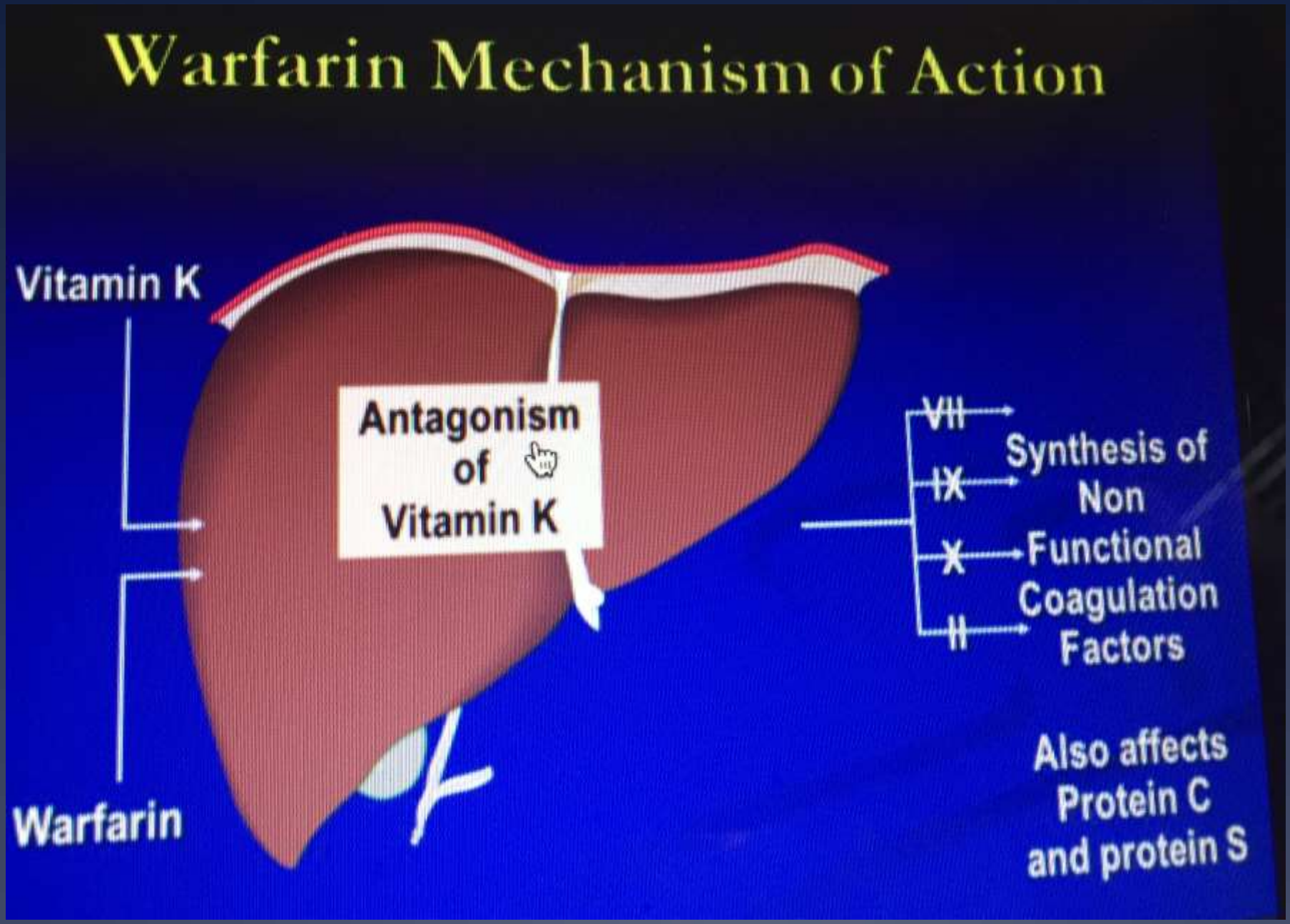
Important New Developments

- Assess stroke risk exclusively with CHA_2DS_2-VASc and no longer use $CHADS_2$
- ESC Guidelines recommend anticoagulation for stroke prevention with CHA_2DS_2-VASc score of 1 or greater
- Preference given to novel, non-monitored anticoagulants: apixaban, rivaroxaban, and dabigatran

Key points ACC 2014 guidelines SPAF

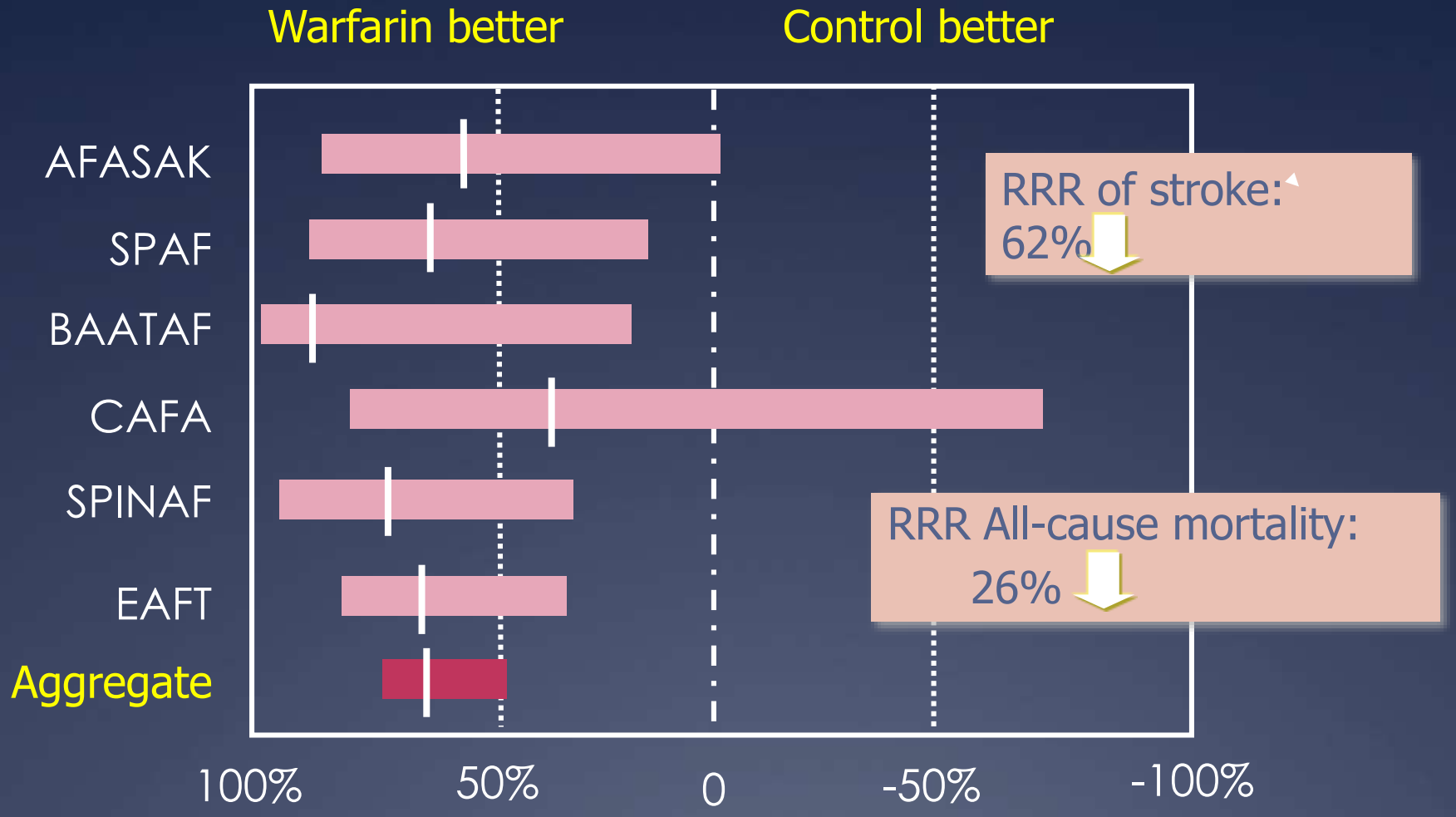
1. CHA_2DS_2VASc Score used as thromboembolic risk assessment
2. Decision on anticoagulation based on risk not classification of AFIB
3. Decision must balance thromboembolic risk vs bleed risk and patient choice
4. CHA_2DS_2VASc score 2 or greater with non valvular AFIB anticoagulation either Coumadin (INR 2-3) or NOAC
5. CHA_2DS_2VASc 0 non-valvular afib, reasonable no anticoagulation
6. CHA_2DS_2VASc 1 (dealers choice) asa or anticoagulant or nothing
7. Patient who cannot maintain therapeutic INR with non-valvular AFIB, NOAC indicated
8. Mechanical valve with AFIB Coumadin INR 2-3 (aortic) 2.5-3.5 (mitral)

Warfarin Mechanism of Action



Anticoagulation in Atrial Fibrillation

Effects on Stroke Risk Reduction



RRR, relative risk reduction.

Hart RG, et al. *Ann Intern Med.* 1999;131:492-501.

Known Problems With Warfarin

1) Delayed onset/offset
2) Unpredictable dose response
3) Narrow therapeutic index
4) Drug-drug, drug-food interactions
5) Problematic monitoring
6) High bleeding rate
7) Slow reversibility

National assessment of warfarin Anticoagulation Therapy for Stroke prevention in AFIB
Circulation 2014

Time in Therapeutic range (TTR)

All patients :53.7%
On therapy < 6 months: 47.6%
On therapy > 6 months: 57.5%

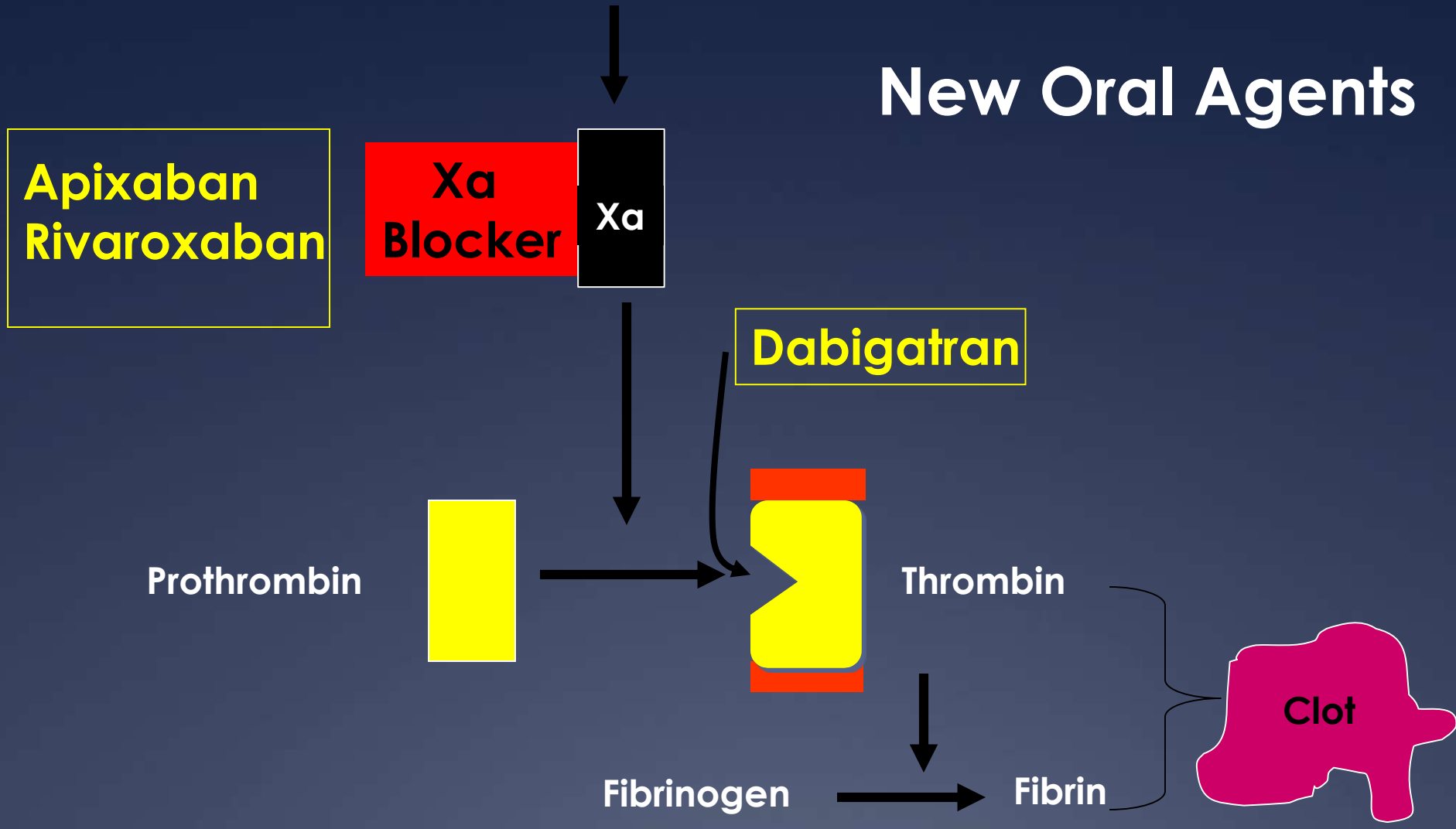
Note: clinical Trials vs NOAC's 64% TTR

Properties of an Ideal Anticoagulant

Properties	Benefit
Oral, once-daily dosing	Ease of administration
Rapid onset of action	No need for overlapping parenteral anticoagulant
Minimal food or drug interactions	Simplified dosing
Predictable anticoagulant effect	No coagulation monitoring
Extra renal clearance	Safe in patients with renal disease
Rapid offset in action	Simplifies management in case of bleeding or intervention
Antidote	For emergencies

Common Pathway

New Oral Agents



Advantages of new oral anticoagulants (NOACs) over vitamin K antagonists (VKAs) for thromboembolic prevention in patients with non-valvular AF

* predictable effect without need for monitoring
* fewer food and drug interactions
* more predictable half-life/elimination
* improved efficacy/safety ratio

Comparison Overview of New Anticoagulants with Warfarin

Features	Warfarin	New Agents
Onset	Slow	Rapid
Dosing	Variable	Fixed
Food effect	Yes	No
Drug interactions	Many	Few
Monitoring	Yes	No
Half-life	Long	Short
Antidote	Yes	No

NOACs approved or under evaluation for prevention of systemic embolism or stroke in patients with non-valvular AF

	Dabigatran	Apixaban	Edoxaban *	Rivaroxaban
Action	Direct thrombin inhibitor	Activated factor Xa (FXa) inhibitor	Activated factor Xa (FXa) inhibitor	Activated factor Xa (FXa) inhibitor
Dose	150 mg BID 110 mg BID	5 mg BID 2.5 mg BID	60 mg QD 30 mg QD 15 mg QD	20 mg QD 15 mg QD
Phase III clinical trial	RE-LY [1]	ARISTOTLE [2] AVERROES [3]	ENGAGE-AF [4]	ROCKET-AF [5]

* not yet approved by EMA

1. Connolly et al, N Engl J Med 2009; 361:1139-51
2. Granger et al, N Engl J Med 2011; 365:981-92
3. Connolly et al, N Engl J Med 2011; 364:806-17
4. Ruff et al, Am Heart J 2010; 160:635-41
5. Patel et al, N Engl J Med 2011;365:883-91

Novel Oral Anticoagulants

Important Comparative Features

Dabigatran	• Oral direct thrombin inhibitor • Twice daily dosing • Renal clearance
Rivaroxaban	• Direct factor Xa inhibitor • Once daily (maintenance), twice daily (loading) • Renal clearance
Apixaban	• Direct factor Xa inhibitor • Twice daily dosing • Hepatic clearance
Edoxaban	• Direct factor Xa inhibitor • Once daily dosing • Hepatic clearance

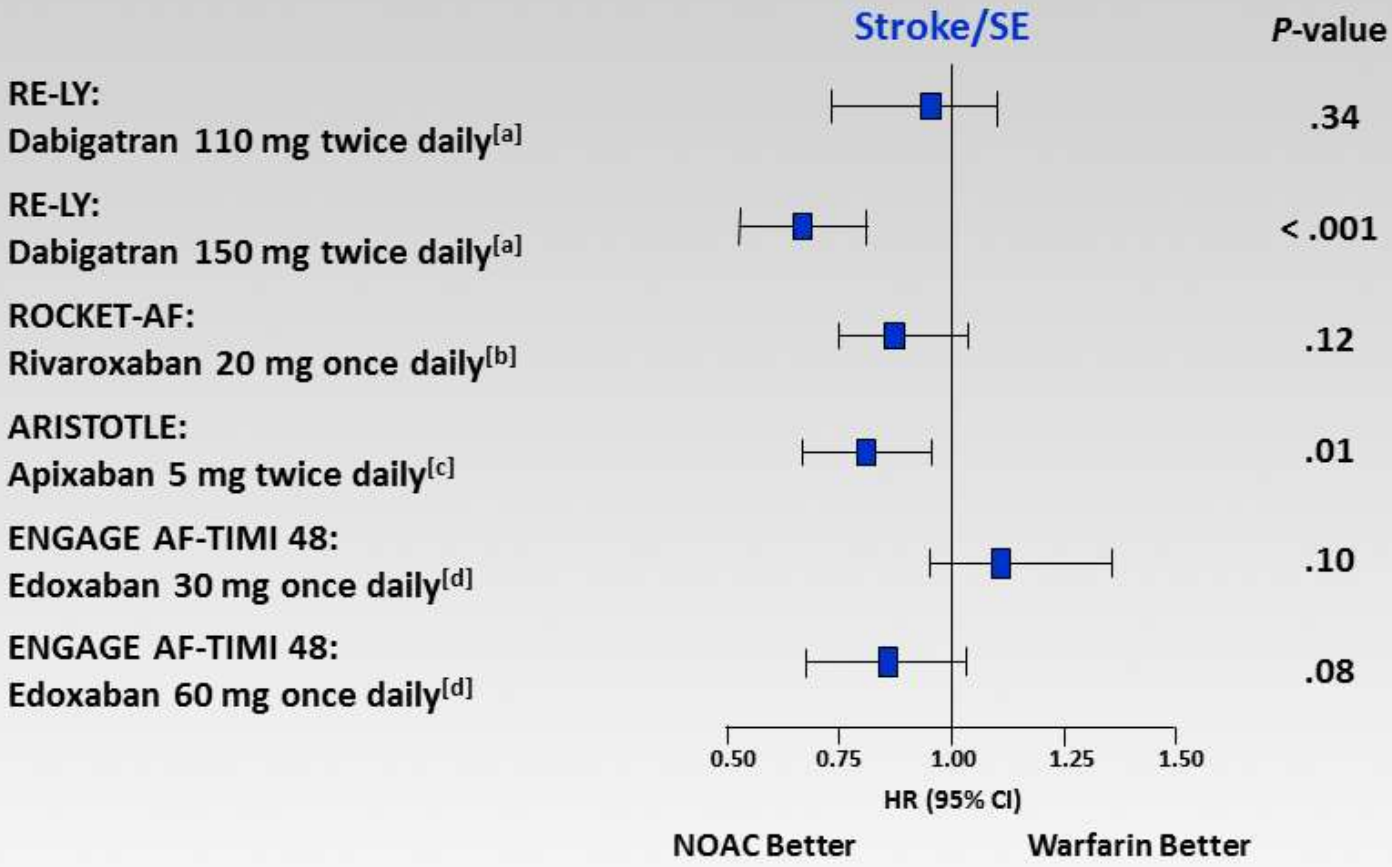
Circulation 2010;121:1523

Pivotal Atrial Fibrillation Trials
Results to Date

Drug Dose (mg)	RE-LY		ROCKET-AF	ARISTOTLE
	Dabigatran 110 bid	150 BID	Rivaroxaban 20 mg qd	Apixaban 5 mg bid
Stroke + SEE	non-infer	Superior	ITT cohort: non-infer. On Rx cohort: Superior	Superior
ICH	Superior	Superior	Superior	Superior
Bleeding	Lower	similar	similar	Lower
Mortality	similar	*P* = 0.051	similar	Superior: *P* = 0.047
Ischemic stroke	similar	Lower	similar	similar
Mean TTR	64%		55%	62%
Stopped drug	21%		23%	23%
WD consent	2.3%		8.7%	1.1%

TTR = time in therapeutic range
WD consent = withdrawal of consent, no further data available

Landmark Oral Anticoagulation Trials: Prevention of Stroke/SE



ARISTOTLE = Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; CI = confidence interval; ENGAGE AF-TIMI 48 = Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation—Thrombolysis in Myocardial Infarction 48; HR = hazard ratio; RE-LY = Randomized Evaluation of Long-Term Anticoagulation Therapy; ROCKET-AF = Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation

a. Connolly SJ, et al. *N Engl J Med*. 2009;361(12):1139-1151.
b. Patel MR, et al. *N Engl J Med*. 2011;365(10):883-891.
c. Granger C, et al. *N Eng J Med*. 2011;365(11):981-992.
d. Giugliano RP, et al. *N Engl J Med*. 2013; 369(22):2093-2104.

Clinical Perspective Regarding RCT Data: Efficacy of Different NOACs

- In the landmark RCTs, NOACs administered twice daily demonstrated superior efficacy compared with warfarin for stroke/SE prevention in AF patients
  - Dabigatran 150 mg twice daily: 34% reduction in stroke/SE[a]
  - Apixaban 5 mg twice daily: 21% reduction in stroke/SE[b]
- NOACs administered once daily demonstrated similar efficacy (noninferiority) compared with warfarin
  - Rivaroxaban 20 mg once daily: 12% reduction in stroke/SE[c]
  - Edoxaban 60 mg once daily: 13% reduction in stroke/SE[d]

RCT = randomized clinical trial

a. Connolly SJ, et al. *N Engl J Med*. 2009;361(12):1139-1151.
b. Granger C, et al. *N Eng J Med*. 2011;365(11):981-992.
c. Patel MR, et al. *N Engl J Med*. 2011;365(10):883-891.
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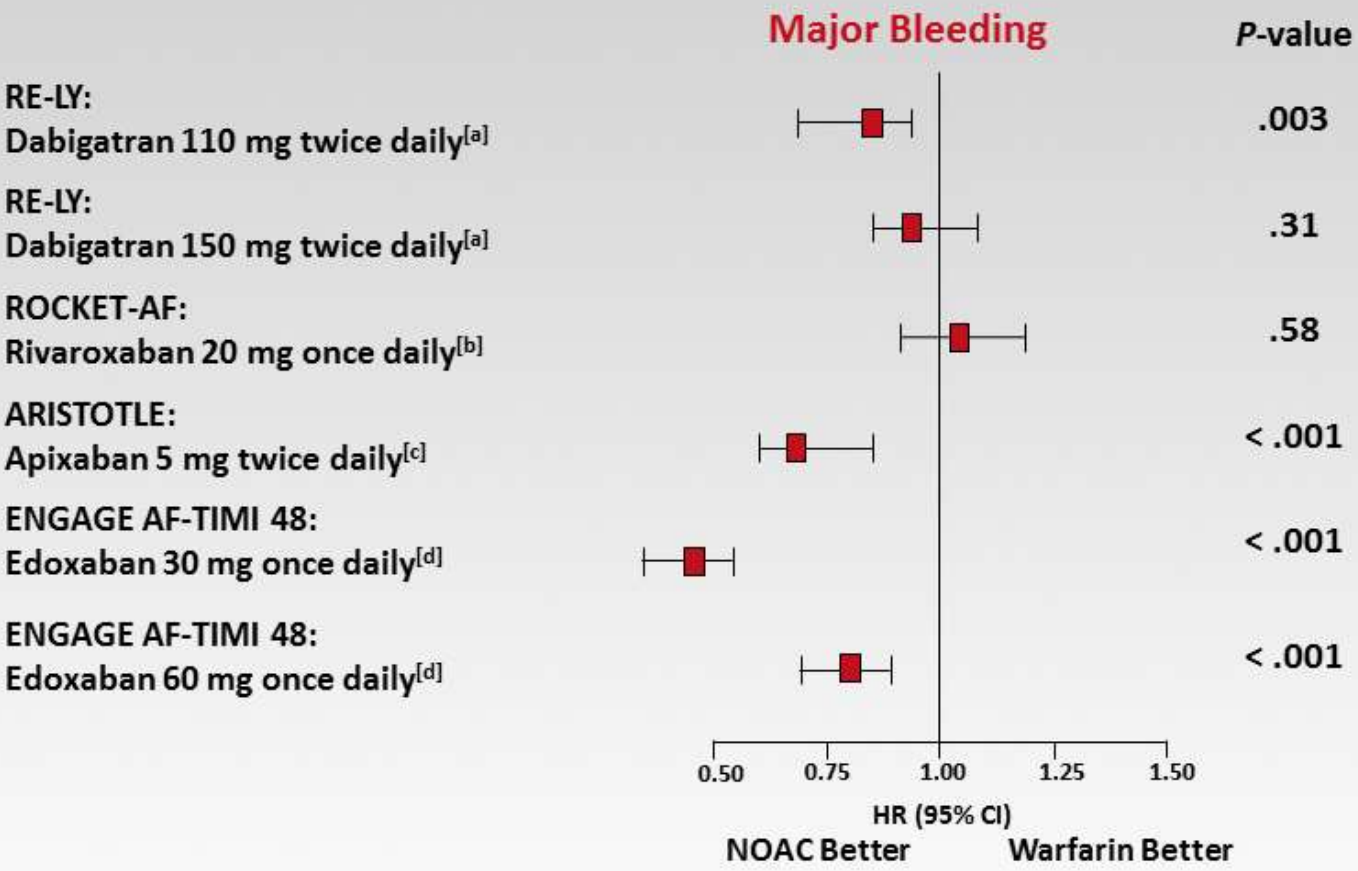
Landmark Oral Anticoagulation Trials: Major Bleeding Risk



a. Connolly SJ, et al. *N Engl J Med*. 2009;361(12):1139-1151.
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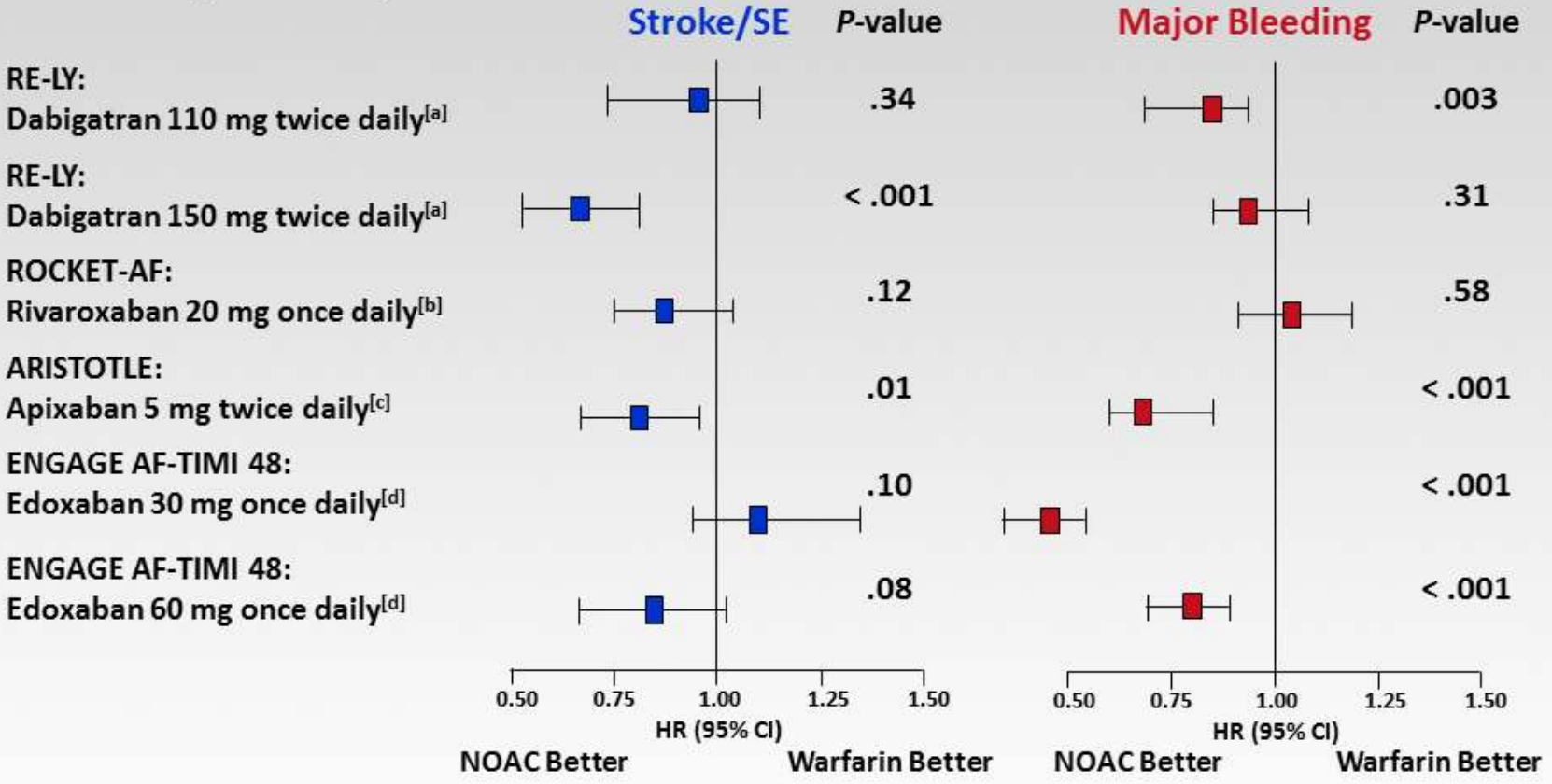
d. Giugliano RP, et al. *N Engl J Med*. 2013; 369(22):2093-2104.

Choice of NOAC Depends on Patient's Risk for Stroke vs Bleeding

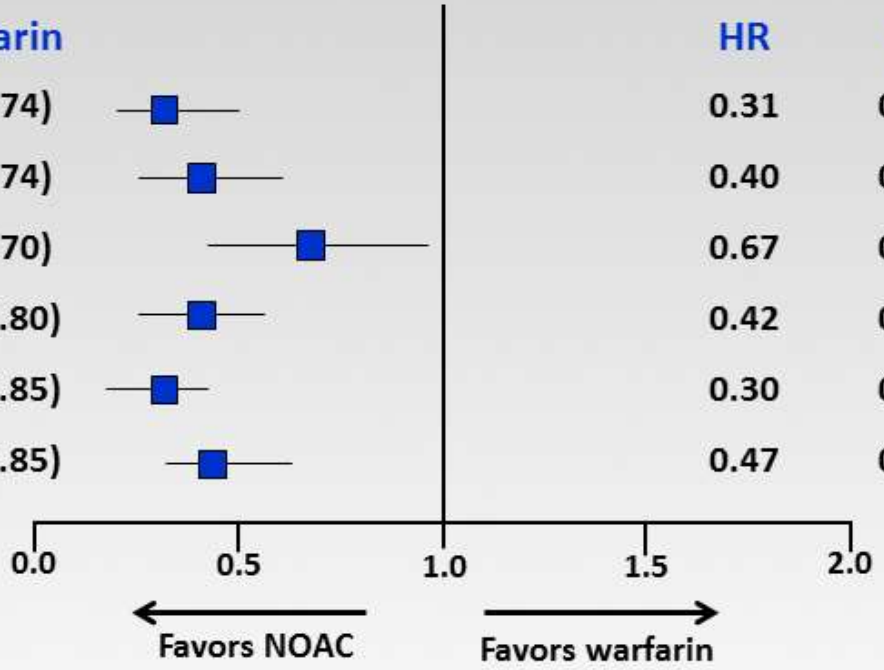
- High stroke risk with moderate risk of bleeding: data less clear; multiple NOACs can be used
- High stroke risk with high bleeding risk: data favors apixaban (decreased risk of stroke/SE and bleeding vs warfarin)



a. Connolly SJ, et al. *N Engl J Med*. 2009;361(12):1139-1151.
b. Patel MR, et al. *N Engl J Med*. 2011;365(10):883-891.
c. Granger C, et al. *N Eng J Med*. 2011;365(11):981-992.
d. Giugliano RP, et al. *N Engl J Med*.2013; 369(22):2093-2104.

Landmark Oral Anticoagulation Trials: ICH

	Pts with events (%/yr)			
	NOAC	Warfarin	HR	95% CI
Dabi 110[a]	27 (0.23)	87 (0.74)	0.31	0.20-0.47
Dabi 150[a]	36 (0.30)	87 (0.74)	0.40	0.27-0.60
Riva 20[b]	55 (0.50)	84 (0.70)	0.67	0.47-0.93
Apix 5[c]	52 (0.33)	122 (0.80)	0.42	0.30-0.58
Edox 30[d]	41 (0.26)	132 (0.85)	0.30	0.21-0.43
Edox 60[d]	61 (0.39)	132 (0.85)	0.47	0.34-0.63

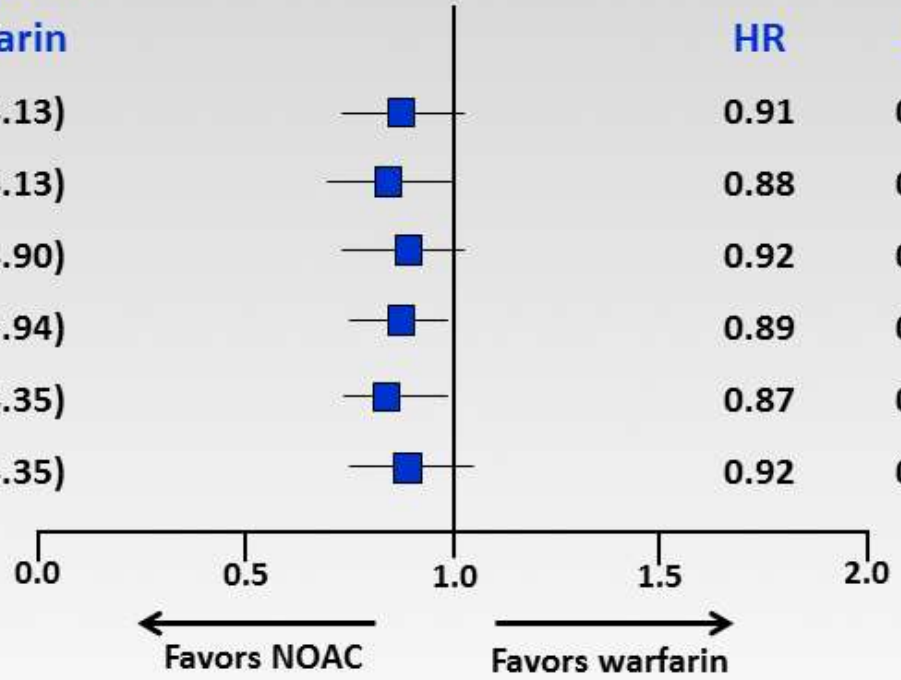


Apix 5 = apixaban 5 mg once daily; dabi 110 = dabigatran 110 mg twice daily; dabi 150 = dabigatran 150 mg twice daily; edox 30 = edoxaban 30 mg once daily; edox 60 = edoxaban 60 mg once daily; ICH = intracranial hemorrhage; riva 20 = rivaroxaban 20 mg once daily

a. Connolly SJ, et al. *N Engl J Med*. 2009;361(12):1139-1151.
b. Patel MR, et al. *N Engl J Med*. 2011;365(10):883-891.
c. Granger C, et al. *N Eng J Med*. 2011;365(11):981-992.
d. Giugliano RP, et al. *N Engl J Med*. 2013; 369(22):2093-2104.

Landmark Oral Anticoagulation Trials: Mortality

	Pts with events (%/yr)		HR	95% CI
	NOAC	Warfarin		
Dabi 110[a]	446 (3.75)	487 (4.13)	0.91	0.80-1.03
Dabi 150[a]	438 (3.64)	487 (4.13)	0.88	0.77-1.00
Riva 20[b]	582 (4.50)	632 (4.90)	0.92	0.82-1.03
Apix 5[c]	603 (3.52)	669 (3.94)	0.89	0.80-0.96
Edox 30[d]	737 (3.80)	839 (4.35)	0.87	0.79-0.96
Edox 60[d]	773 (3.99)	839 (4.35)	0.92	0.83-1.01



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c. Granger C, et al. *N Eng J Med*. 2011;365(11):981-992.
d. Giugliano RP, et al. *N Engl J Med*. 2013; 369(22):2093-2104.

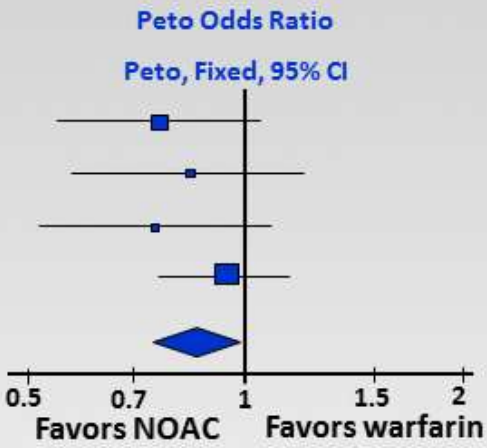
Meta-analysis of NOAC Clinical Trials in AF Patients With Previous Stroke or TIA

Significant Reduction of Stroke/SE Compared With Warfarin Over 1.8-2.0 Years

Stroke or SE

Study of Subgroup	Non-VKA Total	Warfarin Total	Peto Odds Ratio Peto, Fixed, 95% CI
ARISTOTLE	1694	1742	0.76 [0.56-1.03]
RELY 110	1195	1195	0.84 [0.58-1.21]
RELY 150	1233	1195	0.75 [0.52-1.09]
ROCKET-AF	3754	3714	0.94 [0.77-1.17]
Total (95% CI)	7876	7846	0.85 [0.74-0.99]

Heterogeneity: $X^2 = 1.93$, df = 3 ($P = 0.59$); $I^2 = 0\%$
Test for overall effect: Z = 2.15 ($P = 0.03$)

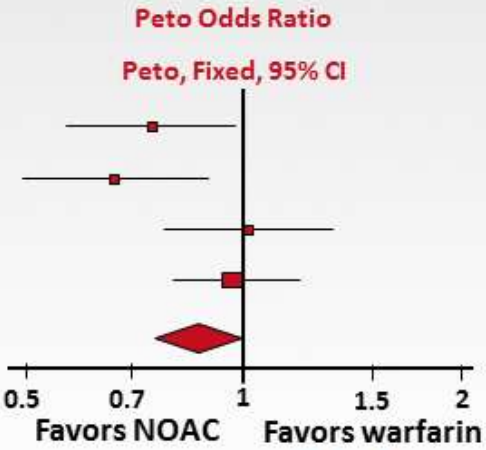


Significant Reduction of Major Bleeding With Warfarin

Major bleeding

Study of Subgroup	Non-VKA Total	Warfarin Total	Peto Odds Ratio Peto, Fixed, 95% CI
ARISTOTLE	1694	1742	0.74 [0.55-0.99]
RELY 110	1195	1195	0.65 [0.48-0.92]
RELY 150	1233	1195	1.02 [0.76-1.36]
ROCKET-AF	3754	3714	0.96 [0.78-1.19]
Total (95% CI)	7876	7846	0.86 [0.75-0.99]

Heterogeneity: $X^2 = 6.23$, df = 3 ($P = 0.10$); $I^2 = 52\%$
Test for overall effect: Z = 2.18 ($P = 0.03$)



Arrhythmia & EP

Ntaios G, et al. *Stroke*. 2012;43(12):3298-3304.

theheart.org from WebMD

Medscape EDUCATION

Compelling RCT Evidence Demonstrate Benefits of NOACs vs Warfarin in AF

- At least as effective as warfarin (ROCKET-AF; ENGAGE AF-TIMI 48)[a,b]
  - Superior efficacy to warfarin in some RCTs (RE-LY, ARISTOTLE)[c,d]
- Similar bleeding risk compared with warfarin
  - Reduced major bleeding risk in ENGAGE AF-TIMI 48 and ARISTOTLE[b,c]
  - Reduced risk of ICH in all RCTs
- Reduced mortality in some RCTs (ENGAGE AF-TIMI 48, ARISTOTLE)[b,c]

a. Patel MR, et al. *N Engl J Med* 2011; 365(10):883-891
b. Giugliano RP, et al. *N Engl J Med* 2013; 369(22):2093-2104
c. Granger CB, et al. *N Engl J Med* 2011;365(11):981-992.
d. Connolly SJ, et al. *N Engl J Med.* 2009;361(12):1139-1151.

Use of OACs With Chronic Aspirin

- Chronic antiplatelet therapy may be indicated in AF patients with CAD or PAD
- Combination OAC (VKA or NOAC) + aspirin:
  - In general, does not enhance efficacy
  - Can place patients at increased risk for bleeding
- In an analysis of the ARISTOTLE study, apixaban had similar beneficial effects on stroke/SE and major bleeding compared with warfarin, irrespective of concomitant aspirin use[a]

CAD = coronary artery disease

a. Alexander JH, et al. *Eur Hear J.* 2014;35(4):224-232.

NOACs in chronic kidney disease – Practical suggestions

- CKD should be considered an additional risk factor for stroke in AF but CKD also increases bleeding risk
- NOACs are a reasonable choice for anticoagulant therapy in AF patients with mild or moderate CKD
- NOACs similar benefit/risk ratio to VKAs with rivaroxaban (15 mg QD) in renal impairment (CrCl <50 ml/min).[1]
  With apixaban, there may be a lower relative bleeding risk [2]

1. Fox et al, Eur Heart J 2011;32:2387-94
2. Hohnloser et al, Eur Heart J 2012;33:2821-30

NOACs in chronic kidney disease – Practical suggestions

- Dabigatran may not be first choice as primarily cleared renally but may be used in stable patients.
- FXa inhibitors have 25-50% renal clearance therefore may be preferred
- Consider dose reductions in patients with CrCl <50 ml/min: apixaban 2.5 mg BID,[1] rivaroxaban 15 mg/day[2]
- Avoid NOACs in AF patients on haemodialysis: consider VKAs

1. Fox et al, Eur Heart J 2011;32:2387-94
2. Connolly et al N Engl J Med 2011; 364:806-17

NOAC Use With Renal Dysfunction

	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Fraction renally excreted	80%	27%	50%	35%
Approved for CrCl	≥30 mL/min	≥15 mL/min	N/A	≥15 mL/min
Dosing recommendation	CrCl ≥50 mL/min: 150 mg twice daily	SCr ≥1.5 mg/dL: 5 mg twice daily	N/A	CrCl ≥50 mL/min: 20 mg once daily
Dosing if CKD	If CrCl 30-49 mL/min: 150 twice daily is possible, but 110 mg twice daily if "high risk of bleeding"	CrCl 15-29 mL/min: 2.5 mg twice daily in combination with age ≥80 yrs or weight ≤60 kg or with other risk factors	N/A	15 mg once daily when CrCl 15-49 mL/min

CKD = chronic kidney disease; CrCl = creatinine clearance; N/A = not available

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

Antithrombotic Agents

A New Era of "Alignment and Flexibility?"

- Dabigatran: Superior SPAF compared with warfarin
- Rivaroxaban: Once-daily administration and less dependence on kidneys for metabolism; non-inferior in ITT analysis in very high-risk patient population
- Apixaban: Safety equivalent to aspirin in AVERROES, and superior stroke prevention in warfarin intolerant or ineligible
- Apixaban: Superior SPAF, less major bleeding, lower all-cause mortality.

Summary - Stroke Prevention in AF: Which NOAC Should I Use for My Patient?

- NOACs provide superior stroke prevention compared with VKAs in patients with NVAF
- Certain subpopulations may benefit from some NOACs more than others (eg, those with prior stroke)
- There appears to be a difference between the NOACs in the risk for major GI bleeding that may influence treatment choice
- Concomitant disease (eg, renal dysfunction) must be considered when selecting NOACs
- Incorporate strategies that will minimize the need to discontinue OAC therapy; discontinuation increases the risk of thromboembolic event

NOAC Major Concerns

1. LACK OF REVERSIBILITY

2. COST

Clinical Dilemma: Bleeding Risk Correlates With Stroke Risk

- The higher the bleeding risk, as assessed by the HAS-BLED Index, the higher the stroke risk—A "Catch 22" when considering and/or deploying oral anticoagulation.

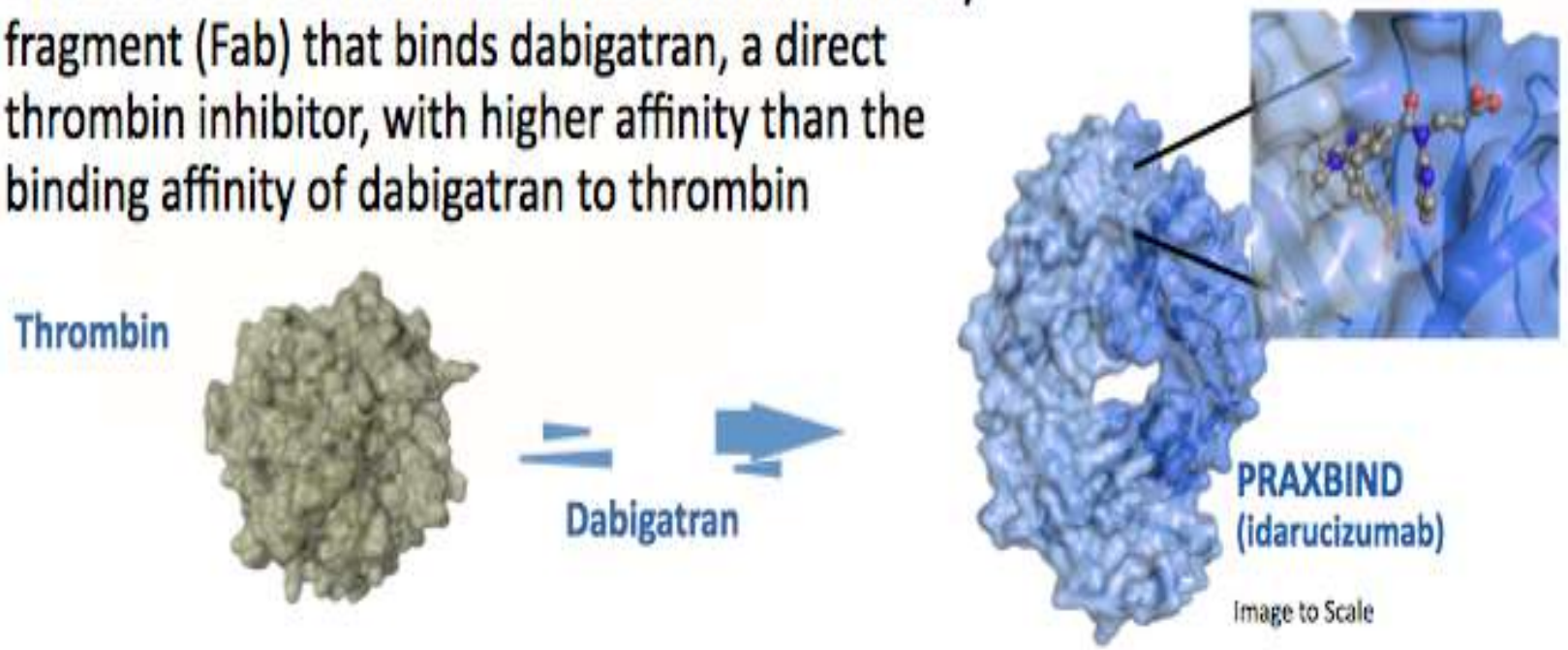
- Based on observational and trial evidence, we must be especially vigilant to prescribe anticoagulation to AF patients at high risk of bleeding, when the thrombosis risk assessment justifies this course of action.

Action Plan When OAC is Indicated and Patient Has High HAS-BLED Index

- Modify bleeding risk factors.
- Intensify surveillance for bleeding and for triggers that cause bleeding.
- Consider "renal dose" for NOAC, especially in the presence of some renal dysfunction or frailty or age ≥ 80 years.
- Monitor renal function with vigilance.
- Prescribe PPI when indicated.
- Consider Left Atrial Appendage Closure (Watchman)

PRAXBIND: Reversal by Design

PRAXBIND is a humanized monoclonal antibody fragment (Fab) that binds dabigatran, a direct thrombin inhibitor, with higher affinity than the binding affinity of dabigatran to thrombin



A specific reversal agent for dabigatran, with no impact on the effect of other anticoagulant or antithrombotic therapies

Please see Important Safety Information throughout this presentation and accompanying full Prescribing Information provided.

Praxbind®
idarucizumab
INJECTION 5g

RE-Verse AD

* RE-VERSE AD found that the effects of dabigatran were completely reversed in 88 to 98% percent of anticoagulated patients receiving idarucizumab. For patients admitted with bleeding, median time to cessation of bleeding was 11.4 hours. For those undergoing urgent procedures, 92% were reported to have normal intraoperative hemostasis after receiving idarucizumab. There were five thrombotic events.

PRAXBIND: Indications and Usage

INDICATIONS AND USAGE

PRAXBIND is indicated in patients treated with Pradaxa® when reversal of the anticoagulant effects of dabigatran is needed:

- For emergency surgery/urgent procedures
- In life-threatening or uncontrolled bleeding

This indication is approved under accelerated approval based on a reduction in unbound dabigatran and normalization of coagulation parameters in healthy volunteers. Continued approval for this indication may be contingent upon the results of an ongoing cohort case series study.

Please see Important Safety Information throughout this presentation and accompanying full Prescribing Information provided.

Praxbind® idarucizumab INJECTION 5g

Anti Xa Reversal

- 1. Andexanet modified human factor Xa molecule
- 2. Binds Xa inhibitors making them unable to bind and inhibit Xa
- 3. ANNEXA-R study ongoing evaluating Safety and efficacy.
- 4. Entering phase 4 clinical evaluation in patients presenting with major bleed taking a Xa inhibitor

COST

* They are expensive
* Cost varies by insurance coverage
* Insurance may drive selection
* Competition Will Drive Down Cost

Deciphering the Pharmaco-economic Maze

"Cost-effectiveness"

Cost: Must take into account the costs of caring long-term for debilitated thromboembolic stroke patients and the costs of caring for intracranial hemorrhage when doing a "cost-effectiveness" analysis of NOACs vs warfarin.

However, we continue to have mostly "silo budgeting."

Current view of Coumadin Clinic

Surgery and Invasive Procedures

* 1. Low risk of bleeding or a location easy to control: Discontinue 24 hours before

* 2. Moderate to high risk of bleed or difficult to control: Discontinue 48 hours

Considerations Before Starting NOAC

- Is The Patient A Candidate (Stroke risk score)
- COMORBIDITIES (bleed risk, renal function)
- COMPLIANCE AND COST
- NOT THE ANSWER FOR A PATIENT WHO IS NON-COMPLIANT WITH COUMADIN
- NO HEAD TO HEAD COMPARISON OF NOAC TO NOAC
- CONTRAINDICATED PATIENTS WITH PROSTHETIC VALVES

NOACs vs Warfarin— In summary

- NOACs generally more effective than warfarin for stroke prevention
- NOACs are generally safer (less bleeding, with some exceptions, but NOACs uniformly cause less intracranial hemorrhage, most devastating and mortality-inducing bleeding complication of OAC)
- NOACs, overall, reduce mortality
- NOACs are more convenient for patient/clinician
- New Reversal agents will increase patient/clinician acceptance
- Cost will come down

Future Coumadin Clinic

THANK YOU