Anticoagulation for Arrhythmia

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Atrial Arrhythmia – Lightening the Burden

Queenstown, New Zealand
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SeaWorld
PHOTO SPOT
Presented by
FUJIFILM

ANTICOAGULATION FOR ARRHYTHMIA

1. Introduction

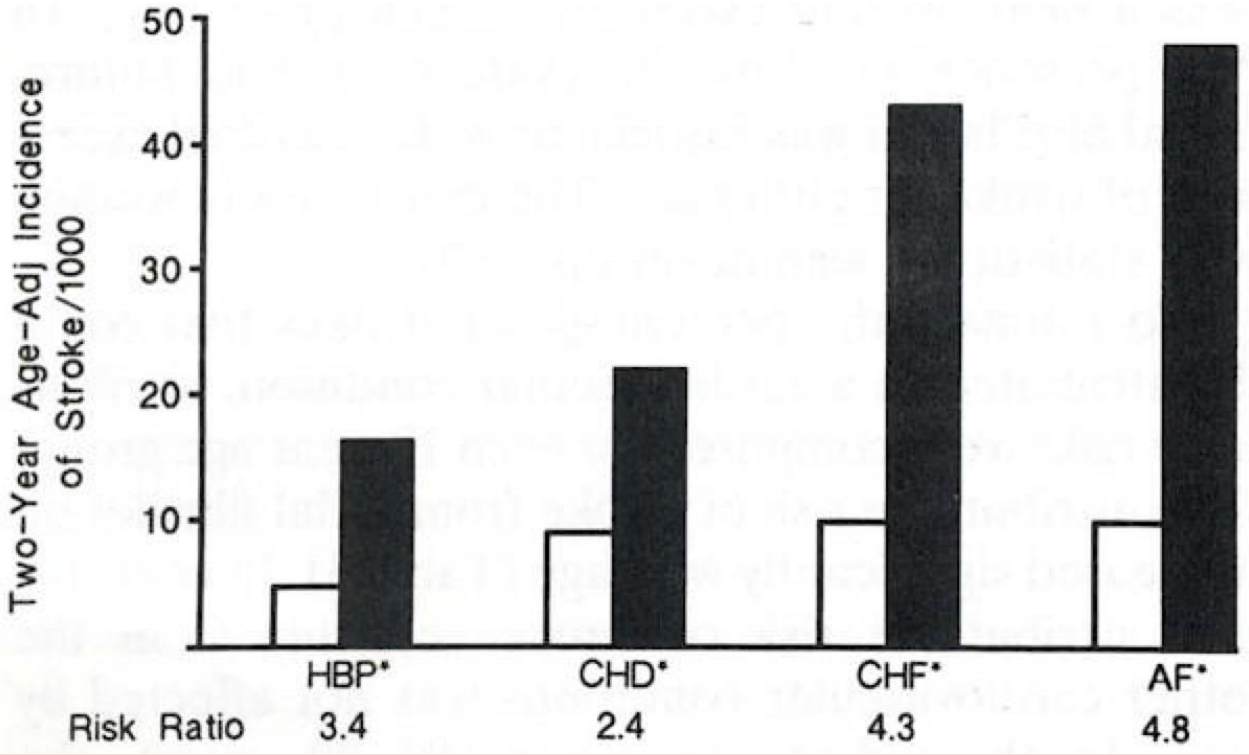
2. Who to anticoagulate?

3. Which agents to use?

INTRODUCTION

The single most important issue in managing atrial arrhythmias is risk assessment and prevention of thromboembolic complications

POWERFUL RISK FACTOR FOR STROKE



Wolf PA et al. *Stroke* 1991;22:983-8

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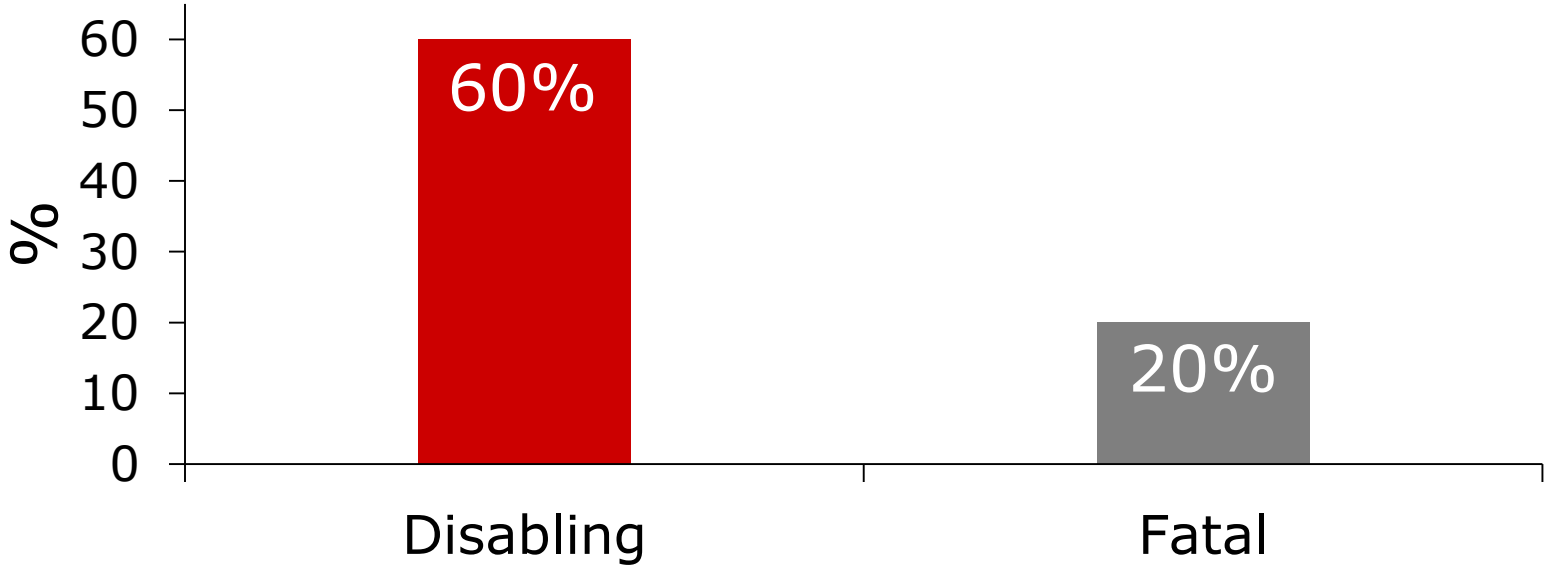
NOT ALL ISCHEMIC STROKES ARE THE SAME

- 597 consecutive patients with a first stroke and AF
- Stroke outcomes are worse with AF vs no AF



Gladstone DJ et al. *Stroke* 2009;40:235-40
Dulli D et al. *Neurepidemiology* 1998;17:80-9

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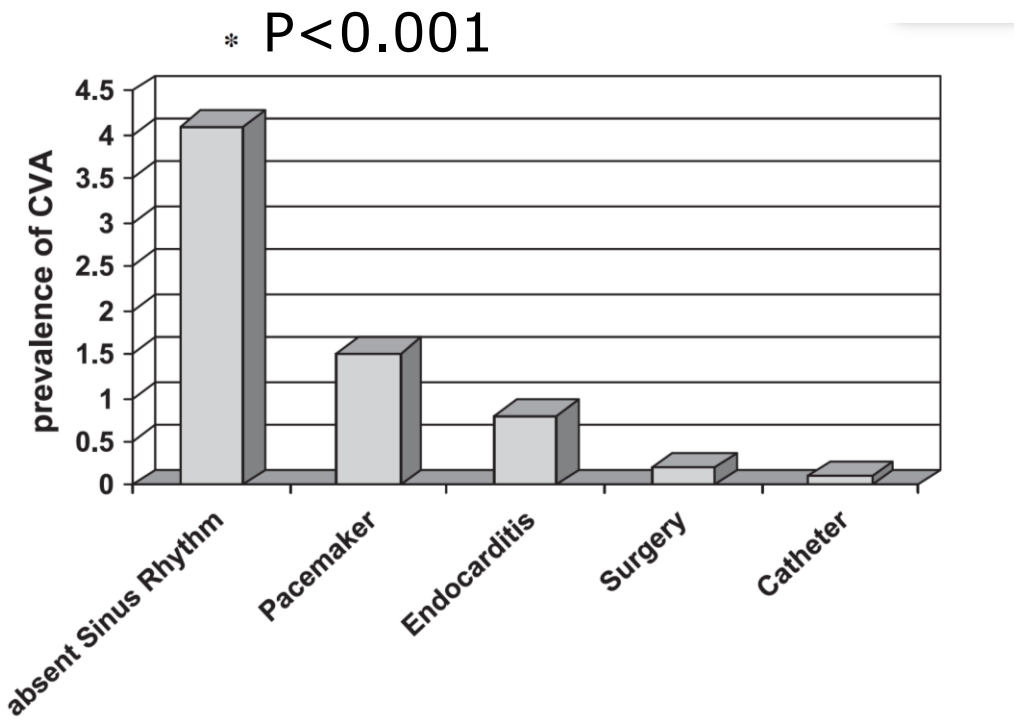
CVA IN ACHD

- N=23,153
- Retrospective
- Europe and Canada
- Age last follow-up:
  - 36.4 (16-91) years
- F-up: 842,769 pt-yrs
- Incidence of CVA:
  - Overall: 0.05%/year



Hoffman A et al. *Heart* 2010;96:1223-6

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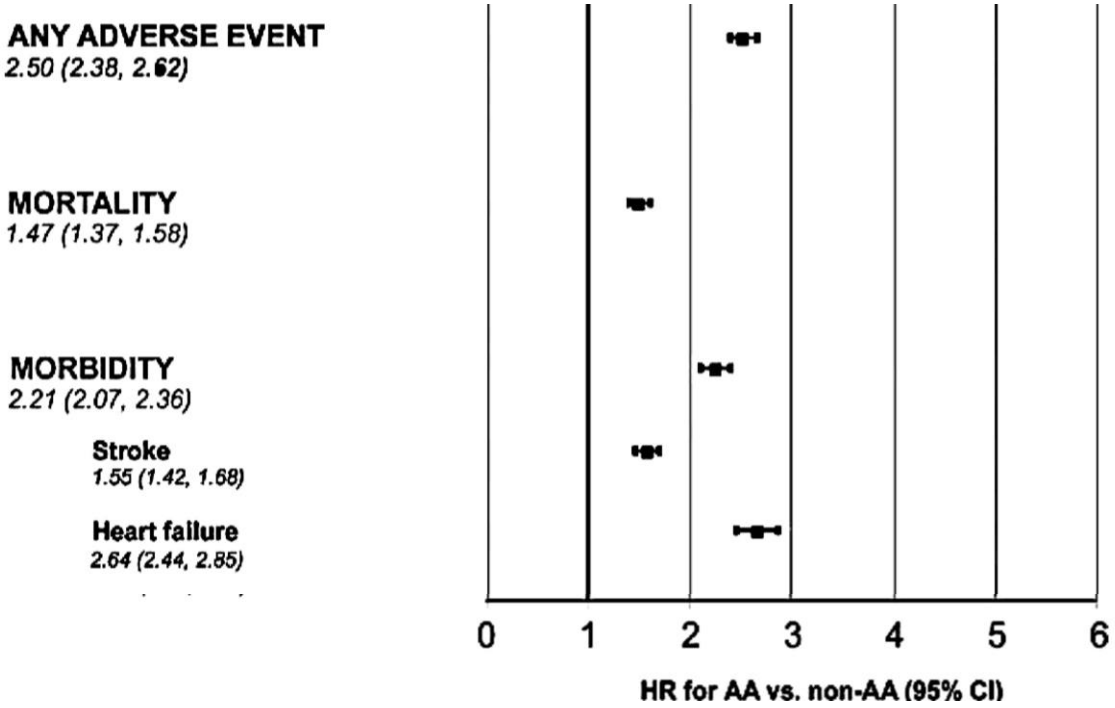
ATRIAL ARRHYTHMIAS AND STROKE

- Quebec CHD administrative database
- N=38,428
- ICD-9 codes
- Atrial arrhythmias: 15%



Bouchardy J et al. *Circulation* 2009;120:1679-86

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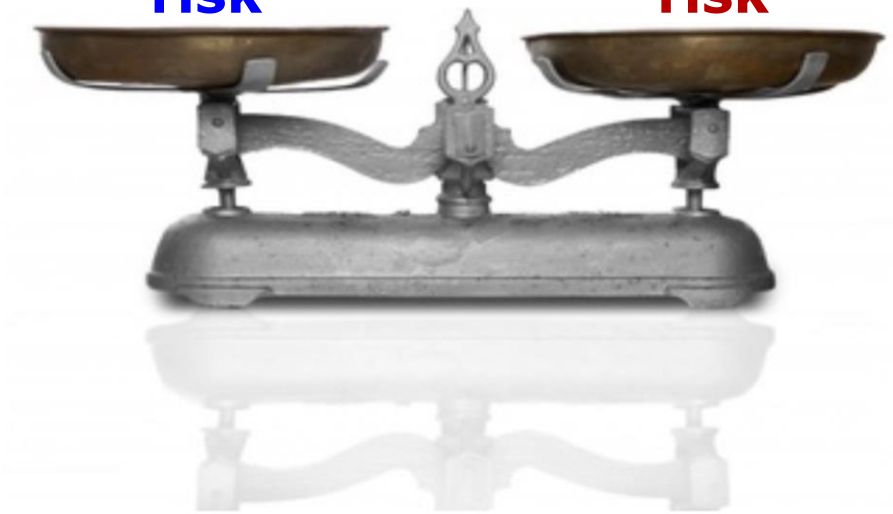
WHO TO ANTICOAGULATE?

Thromboembolic risk

Bleeding risk



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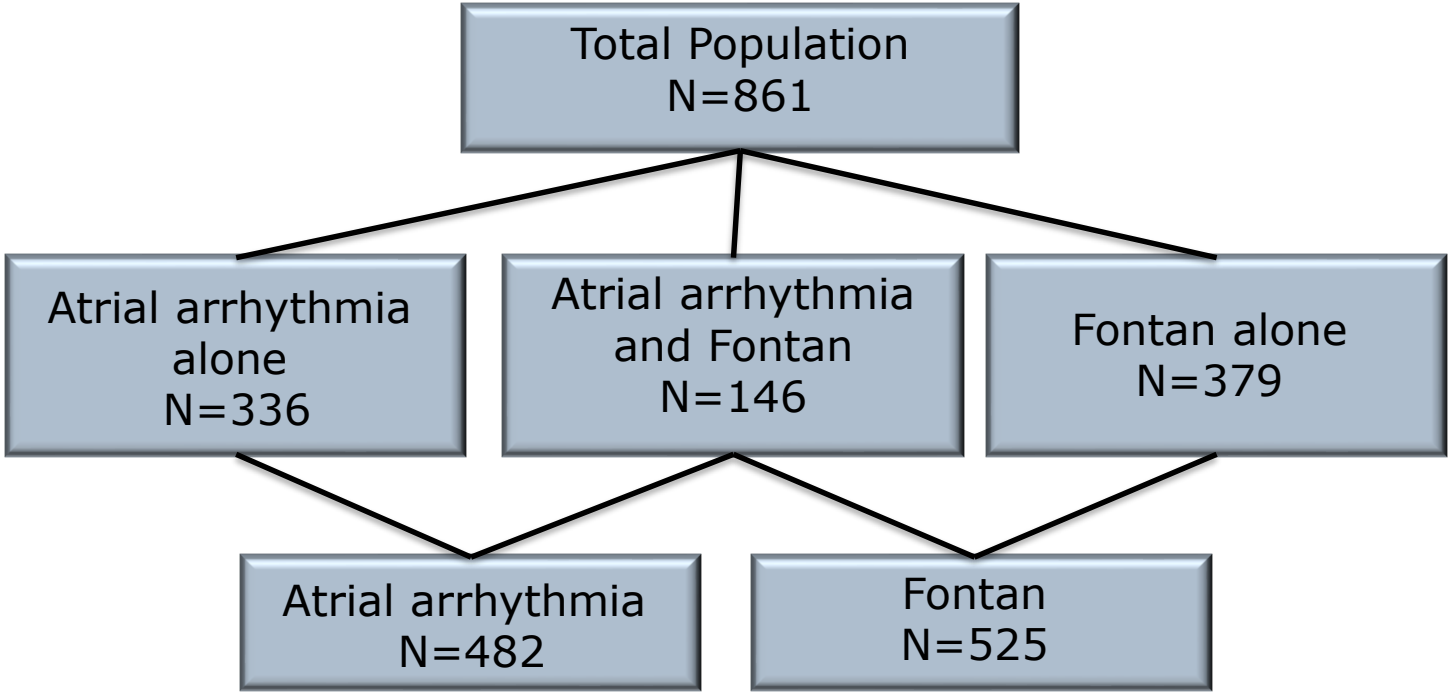
TACTIC

The Anti-Coagulation Therapy Study In Congenital Heart Disease

Khairy P et al. *Int J Cardiol* 2016;120:1679-86

PATIENT POPULATION

TACTIC



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INDEPENDENT ADJUDICATION

TACTIC

Atrial arrhythmias

- IART
- Focal atrial tachycardia
- Atrial fibrillation

Thromboembolic event

- Systemic
- Pulmonary
- Intracardiac thrombus
- Other

Bleeding complications

- *Major bleed:* at least 1
  - ≥20 g reduction in Hgb
  - Transfusion of ≥2 units of blood
  - Symptomatic bleeding in a critical area or organ
- *Minor: other*

Khairy P et al. *Int J Cardiol* 2016;120:1679-86

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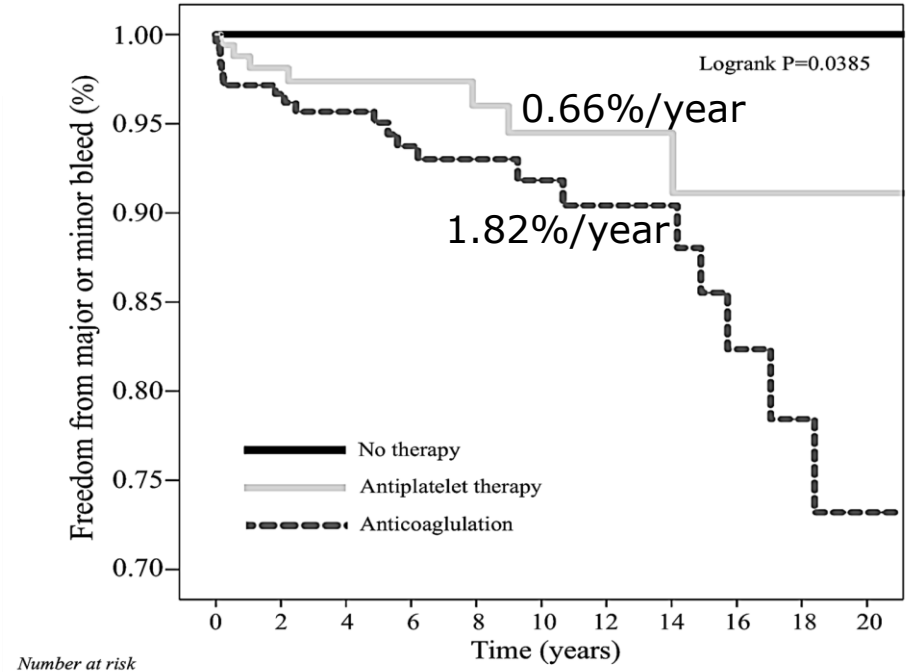
BLEEDING EVENTS

TACTIC



Number at risk

No therapy	38	23	14	11	7	3
Antiplatelet therapy	182	111	70	33	22	7
Anticoagulation	262	171	94	54	25	10

- 44 bleeding events in 40 (8.3%) patients
- Multivariable analysis:
  - *Anticoagulation:*
    - HR 4.8, 95% CI (1.1, 21.6), P=0.043
  - *HAS-BLED score*:
    - HR 3.2, 95% CI (1.02, 9.78), P=0.047

Khairy P et al. *Int J Cardiol* 2016;120:1679-86

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THROMBOEMBOLIC EVENTS

TACTIC

- Rate: 1.14%/year
- Event-free survival
  - 89.3±1.8% at 10 years
  - 84.7±2.7% at 15 years

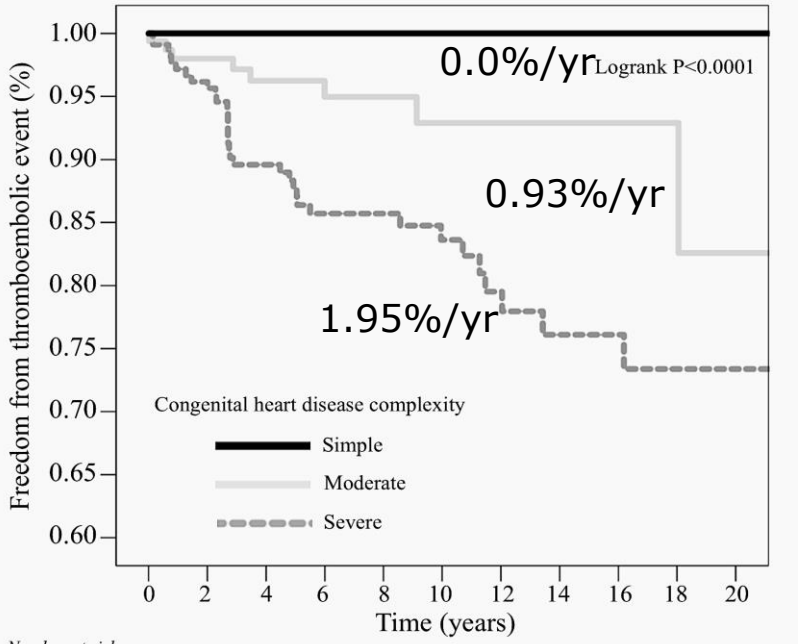
Thromboembolic events, N (%)	
Number of patients with events	42 (8.7)
Stroke or transient ischemic attack	14 (2.9)
Renal emboli	1 (0.2)
Peripheral arterial	2 (0.4)
Intracardiac thrombosis	20 (4.1)
Pulmonary	5 (1.0)

- Multivariable analysis
  - Complexity of CHD: HR 3.5, 95% CI (1.8, 6.9), P<0.001

- No association: arrhythmia type, $CHADS_2$, CHA_2DS_2-VASc

COMPLEXITY OF CHD

TACTIC



Number at risk

Simple	89	47	31	14	10	4
Moderate	166	103	52	27	14	7
Severe	227	154	94	51	28	8

COMPLEXITY	TYPE OF CHD
SIMPLE	Isolated aortic, mitral valve disease
	Small ASD
	Isolated small VSD
	Mild pulmonary stenosis
	Repaired PDA, ASD, VSD no residua
MODERATE	Aortic coarcation
	Ebstein anomaly
	AVSD
	Anomalous pulmonary venous return
	Sinus venous ASD
	Tetralogy of Fallot
SEVERE	Conduits
	Cyanotic congenital heart disease
	Single ventricle, Fontan
	Transposition of the great arteries
	Eisenmenger syndrome

Khairy P et al. *Int J Cardiol* 2016;120:1679-86

Warnes CA et al. *Circulation* 2008;118:e714-833

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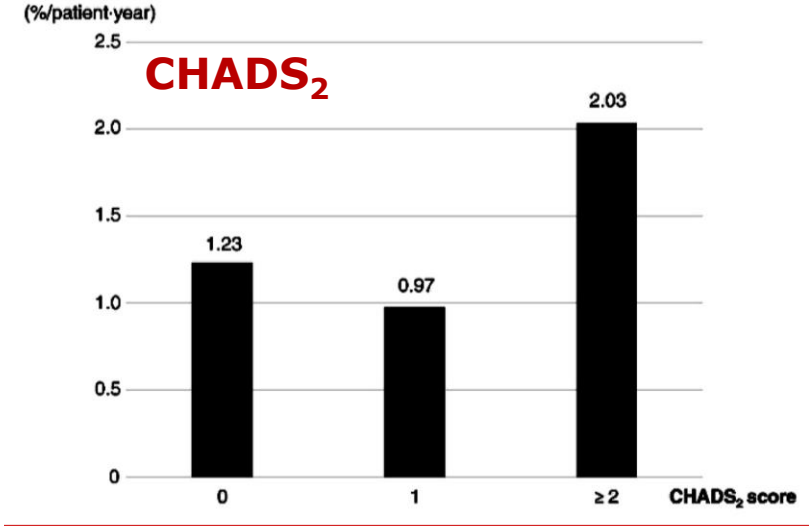
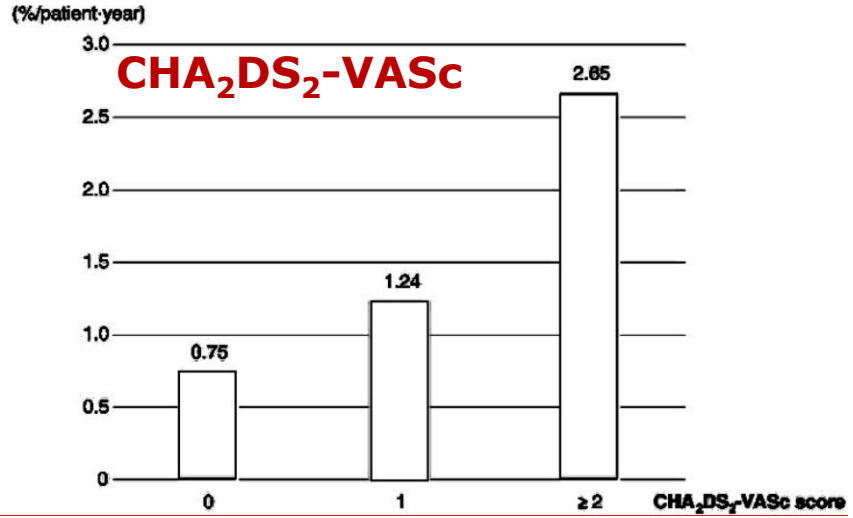
NON-ANTICOAGULATED ACHD POPULATION

- 157 adults with CHD, atrial arrhythmia, no anticoagulant
- 14 (8.9%) thromboembolic events
  - Associated factors: age, vascular disease, persistent AF





Masuda K et al. *Int J Cardiol* 2017;234:69-75

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2014 PACES/HRS Expert Consensus Statement

Recognition and Management of Arrhythmias in Adults with Congenital Heart Disease

Paul Khairy, George Van Hare, Seshadri Balaji, Charles I Berul, Frank Cecchin, Mitchell I Cohen, Curt J Daniels, Barbara J Deal, Joseph A Dearani, Natasja de Groot, Anne M Dubin, Louise Harris, Jan Janousek, Ronald K Kanter, Peter P Karpawich, James C Perry, Stephen P Seslar, Maully J Shah, Michael J Silka, John K Triedman, Edward P Walsh, Carole A Warnes

Ideas | People | Technology

www.HRSonline.org

WHO TO TREAT?

COR	LOE	Recommendation
I	B	Adults with **complex CHD** and sustained or recurrent IART or AF should receive **long-term oral anticoagulation** for the prevention of thromboembolic complications
IIa	C	**Long-term oral anticoagulation** therapy is reasonable in adults with **CHD of moderate complexity** and sustained or recurrent IART or AF
IIb	B	It may be reasonable for adults with IART or AF and **simple non-valvular forms of CHD** to receive either an oral anticoagulant, aspirin, or no therapy for the prevention of thromboembolic complications on the basis of established scores for stroke risk (e.g., CHA_2DS_2-VASc) and bleeding risk (e.g., HAS-BLED)

Khairy P et al. *Heart Rhythm* 2014;11:e102-65

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FIRST ANTICOAGULANT

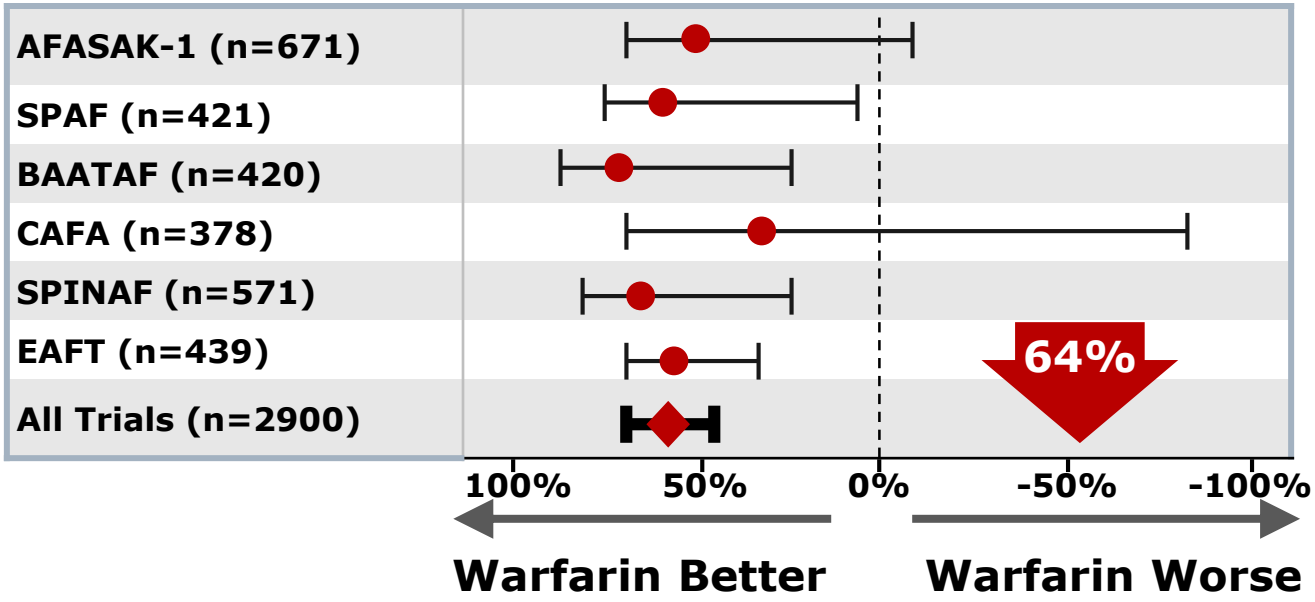
- *Heparin*: serendipitously discovered in 1916
- Originally isolated from canine liver cells

McLean J. The thromboplastic action of cephalin. *Am J Physiol* 1916;41:250–257

> "The heparphosphatid…when purified by many precipitations in alcohol at 60°…shows a marked power to inhibit the coagulation."

WARFARIN AND STROKE RISK

- Meta-analysis of 6 RCTs, N=2900
- Warfarin reduced stroke risk by 64% in patients with AF



Hart RG et al. *Ann Intern Med* 2007;146:857-67

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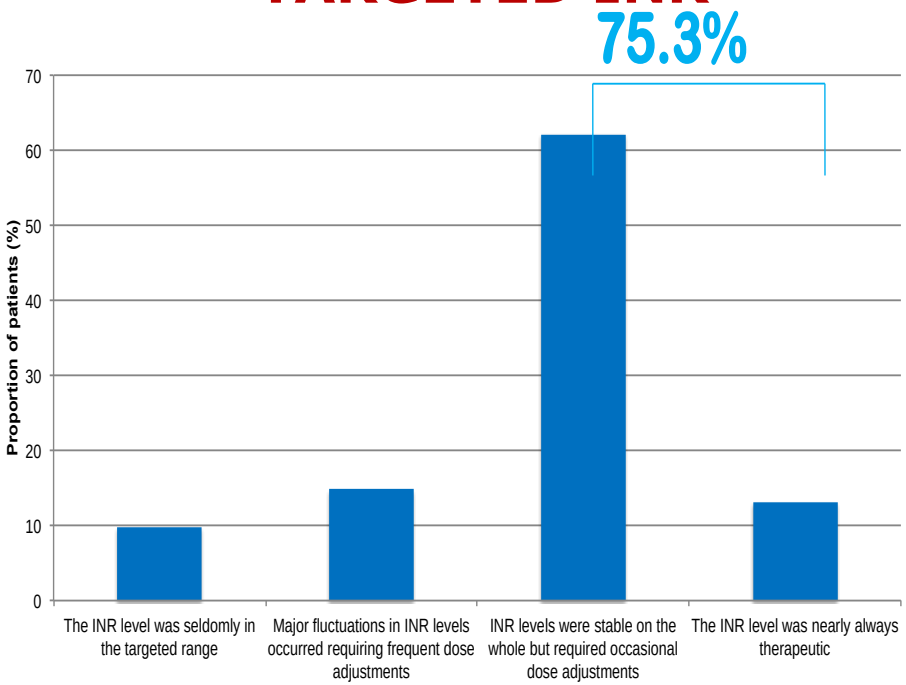
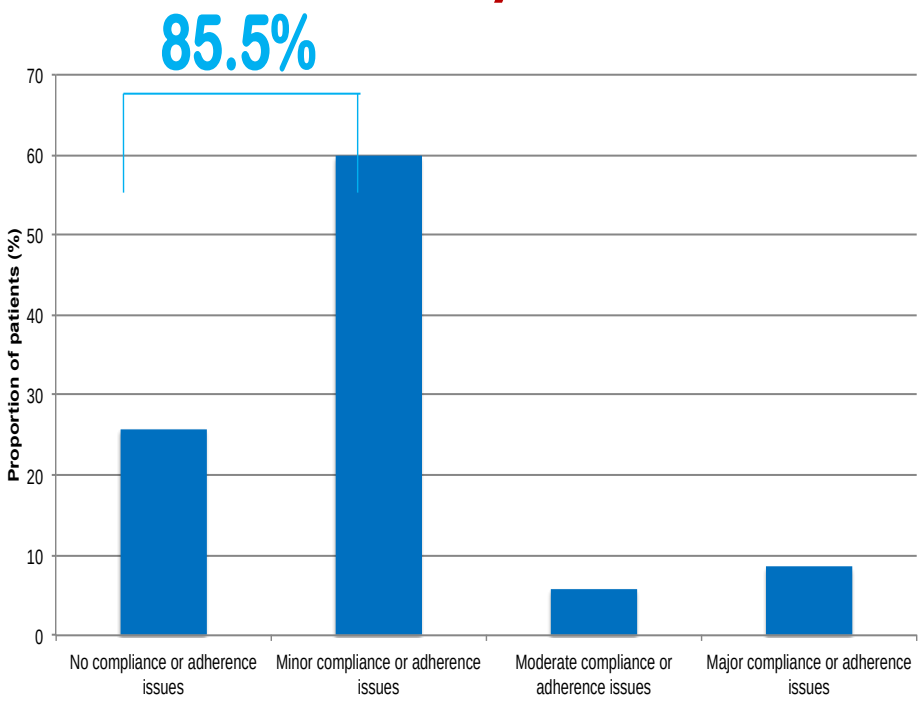
PHYSICIAN ASSESSMENT

TACTIC

TARGETED INR



COMPLIANCE/ADHERENCE



Basmaji S et al. *Unpublished*

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TTR

- *What would you guess is the proportion of TTR?*

A. >85%

B. 70-85%

C. 50-70%

D. <50%

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TTR

TACTIC

	Mean (%)	95% CI
Time in therapeutic range	41.9	39.0, 44.8
Time below therapeutic range	37.3	34.0, 40.5
Time above therapeutic range	20.8	18.0, 23.7

N=567

	Event	No Event	P-value
Proportion of time above therapeutic range (%)			
Bleeding event (N=34)	32.5 (19.6, 45.4)	19.5 (16.7, 22.3)	0.0060
Proportion of time below therapeutic range (%)			
Thromboembolic event (N=47)	31.3 (21.4, 41.1)	19.1 (16.2, 22.0)	0.0032

Basmaji S et al. *Unpublished*

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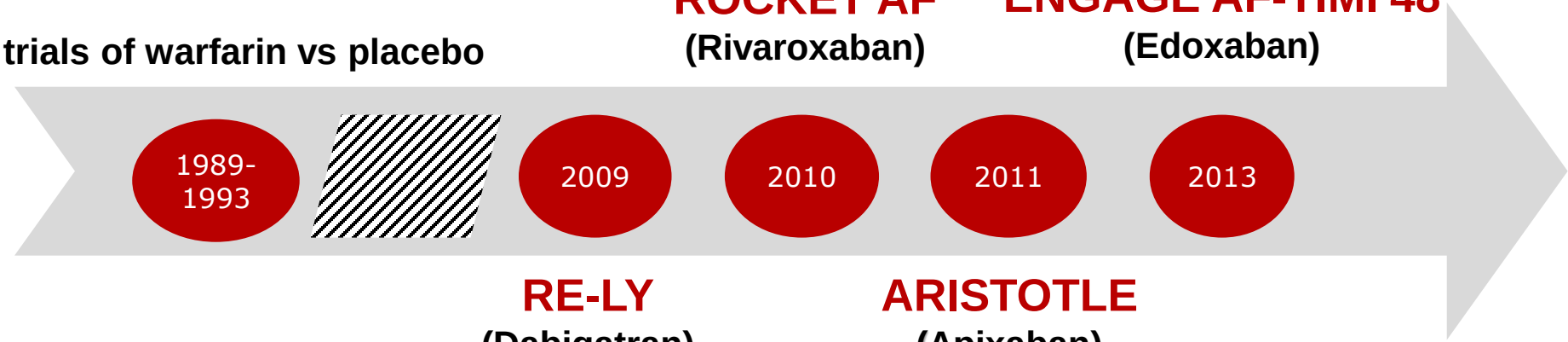
PIVOTAL WARFARIN-CONTROLLED TRIALS

Warfarin vs placebo
N=2,900

DOACs vs warfarin
N=71,683

6 trials of warfarin vs placebo



ROCKET AF
(Rivaroxaban)

ENGAGE AF-TIMI 48
(Edoxaban)

RE-LY
(Dabigatran)

ARISTOTLE
(Apixaban)

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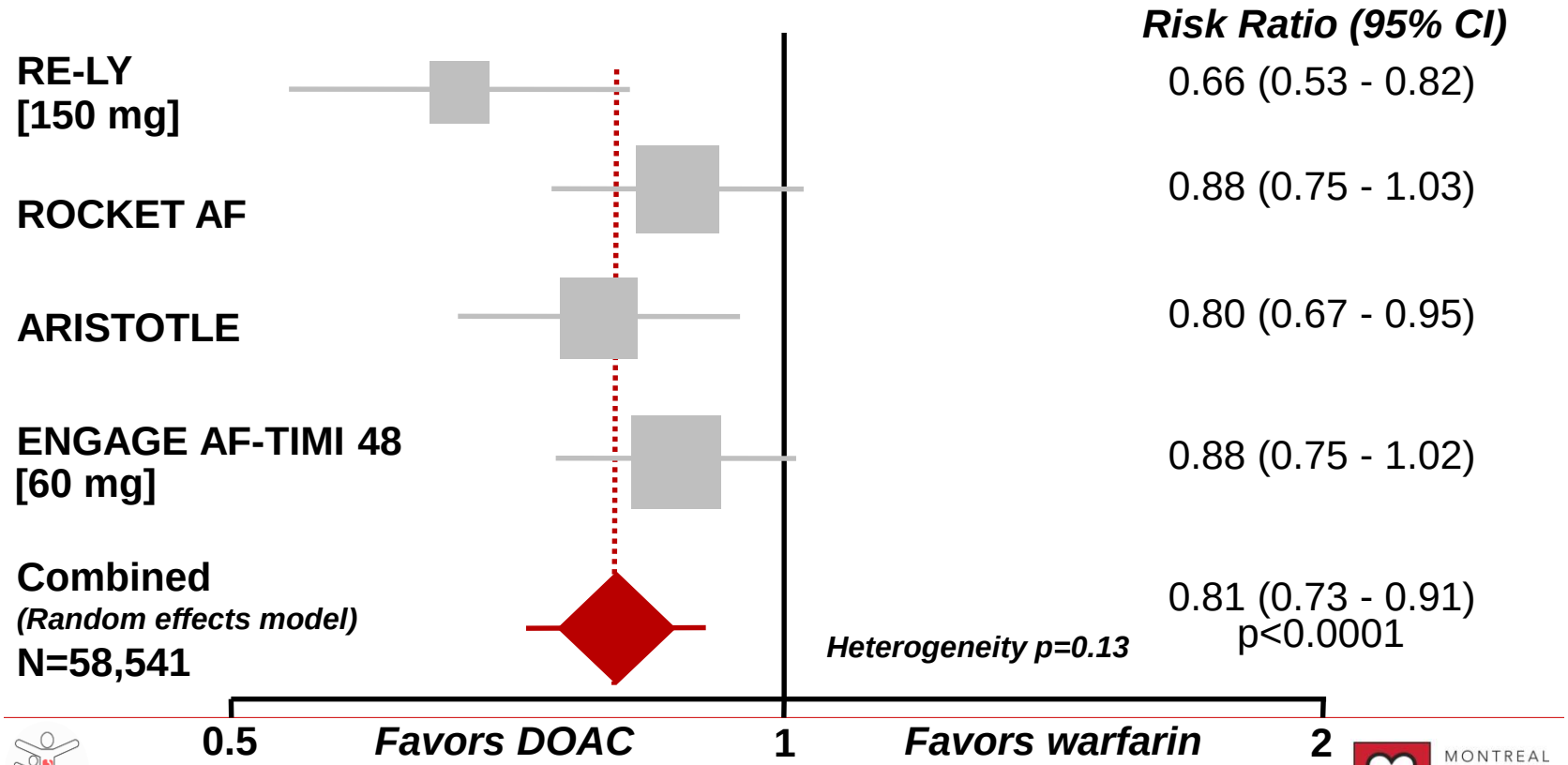
SYSTEMIC THROMBOEMBOLIC EVENTS



Ruff CT et al. *Lancet* 2014;383:955-62

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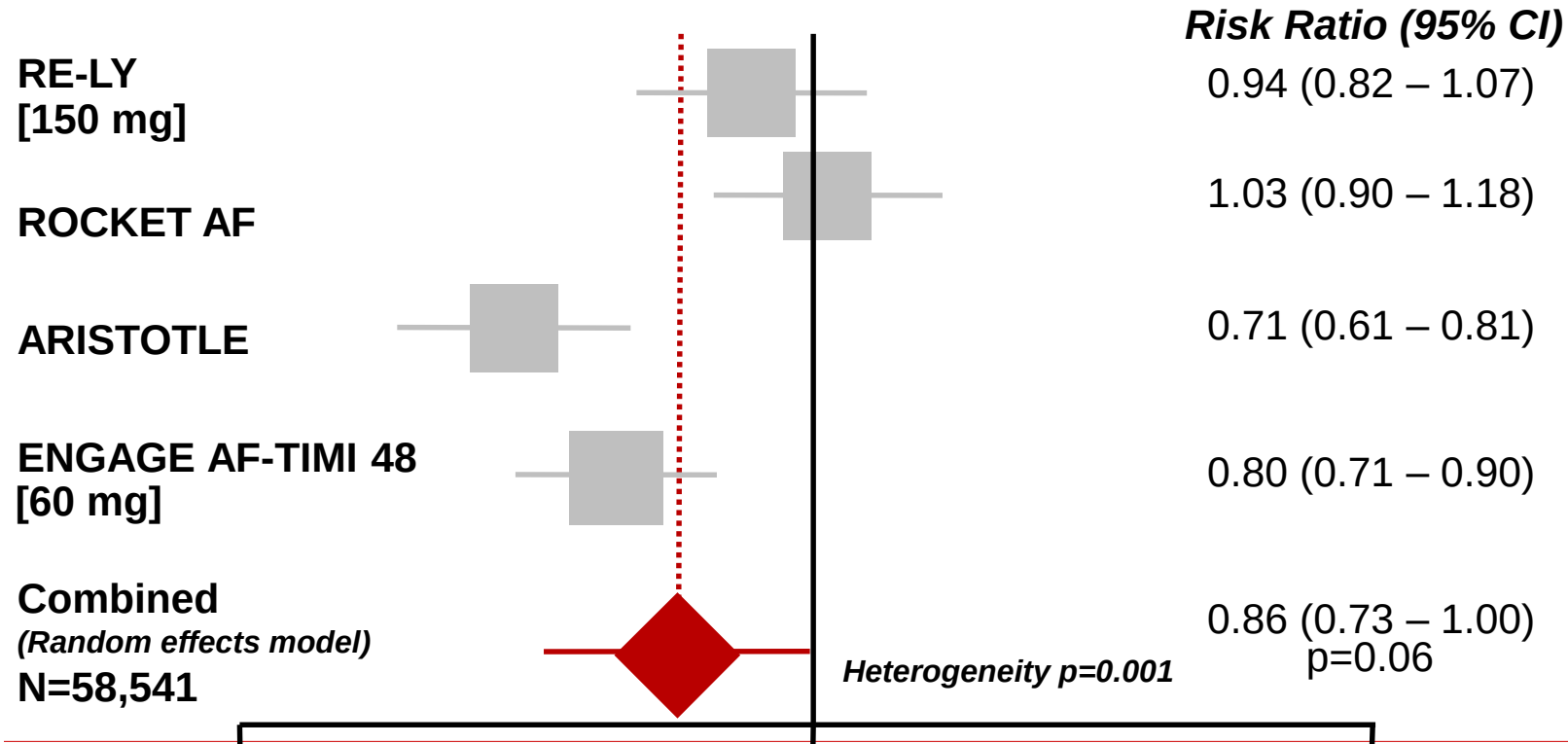
MAJOR BLEEDING



Ruff CT et al. *Lancet* 2014;383:955-62

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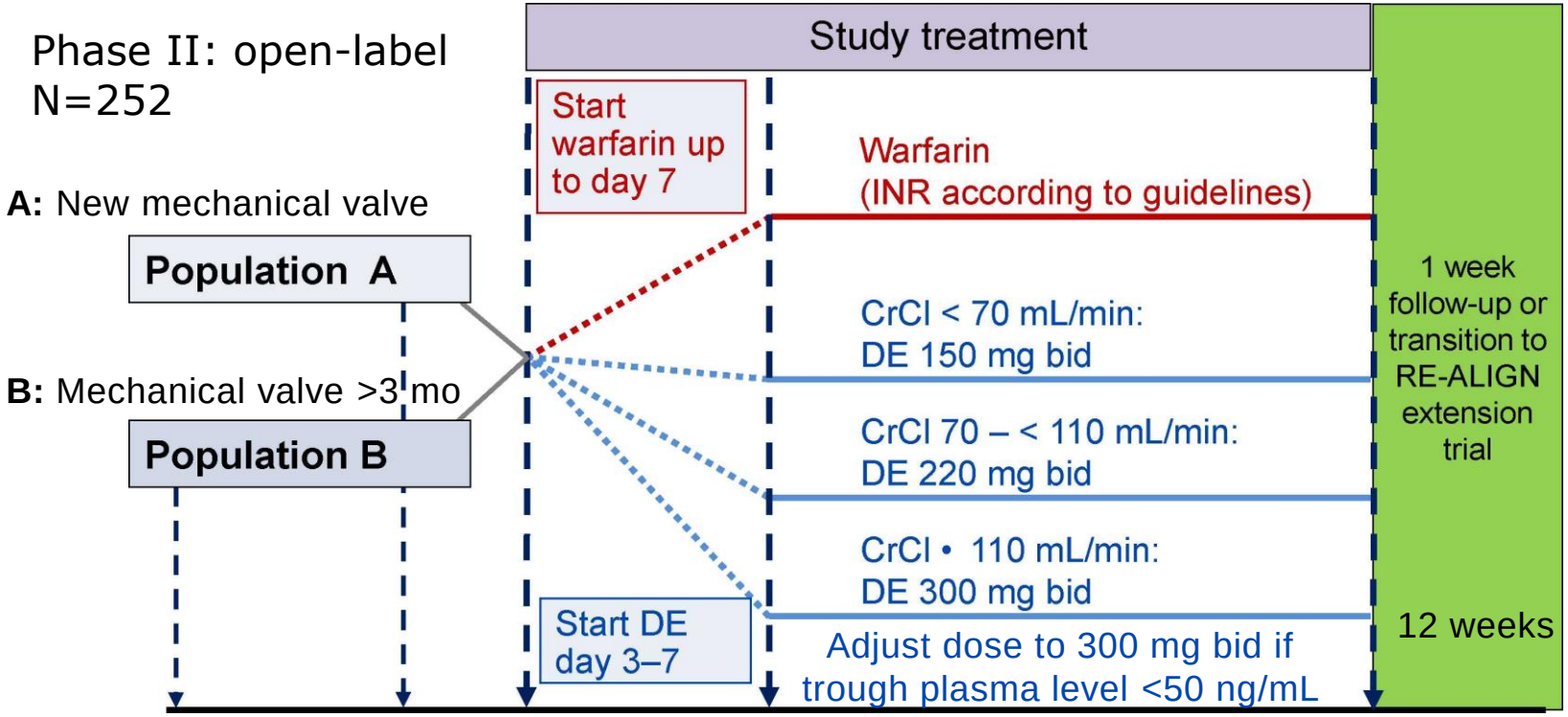
RE-ALIGN: DABIGATRAN AND MECHANICAL VALVES

- Phase II: open-label
- N=252



Eikelboom JW et al. *NEJM* 2013;369:1206-14

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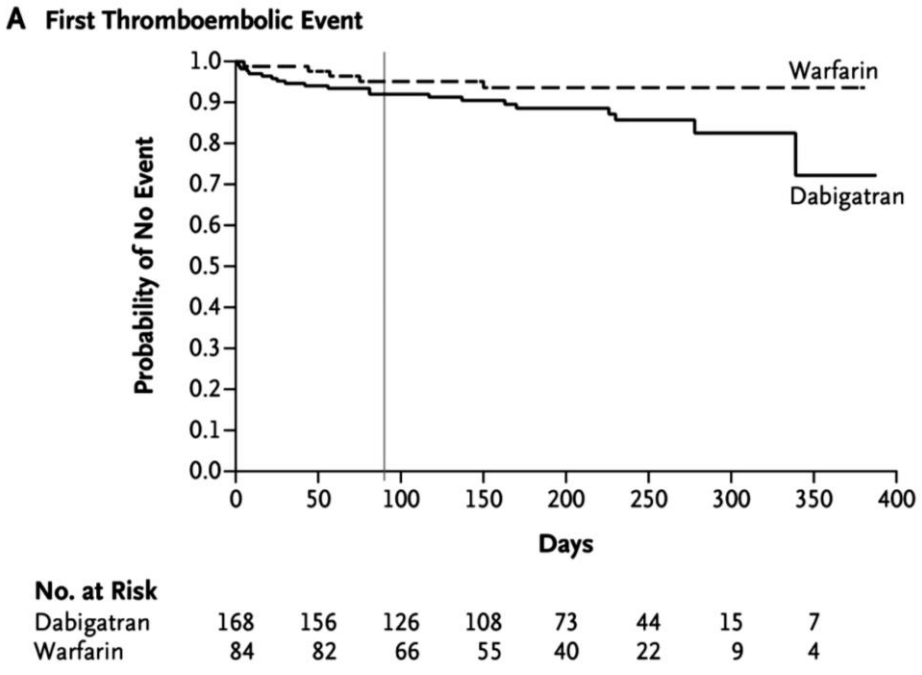

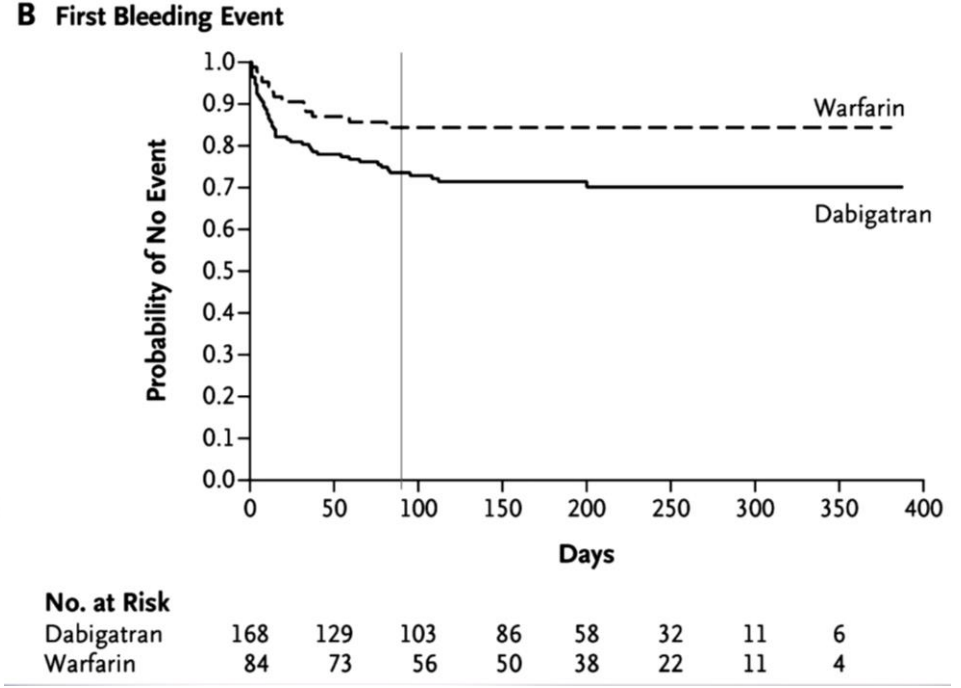

Eikelboom JW et al. *NEJM* 2013;369:1206-14

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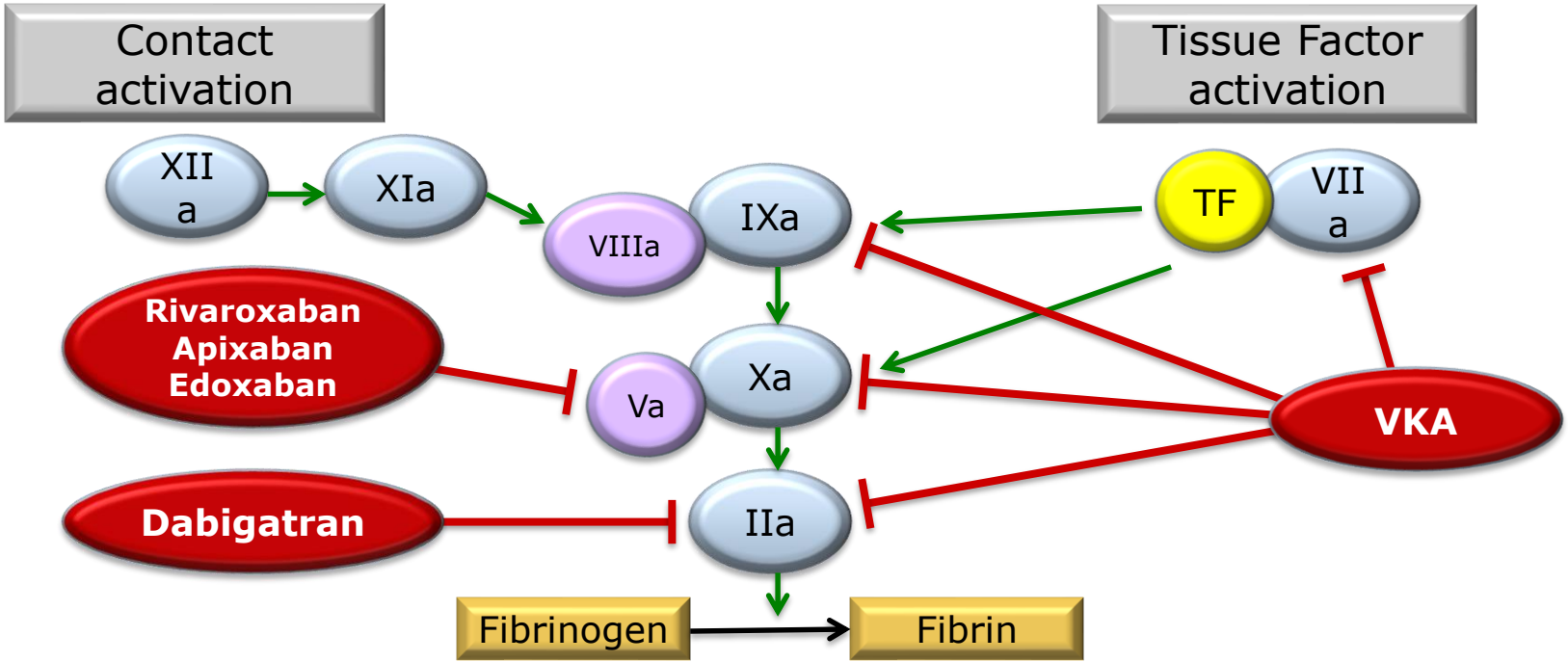
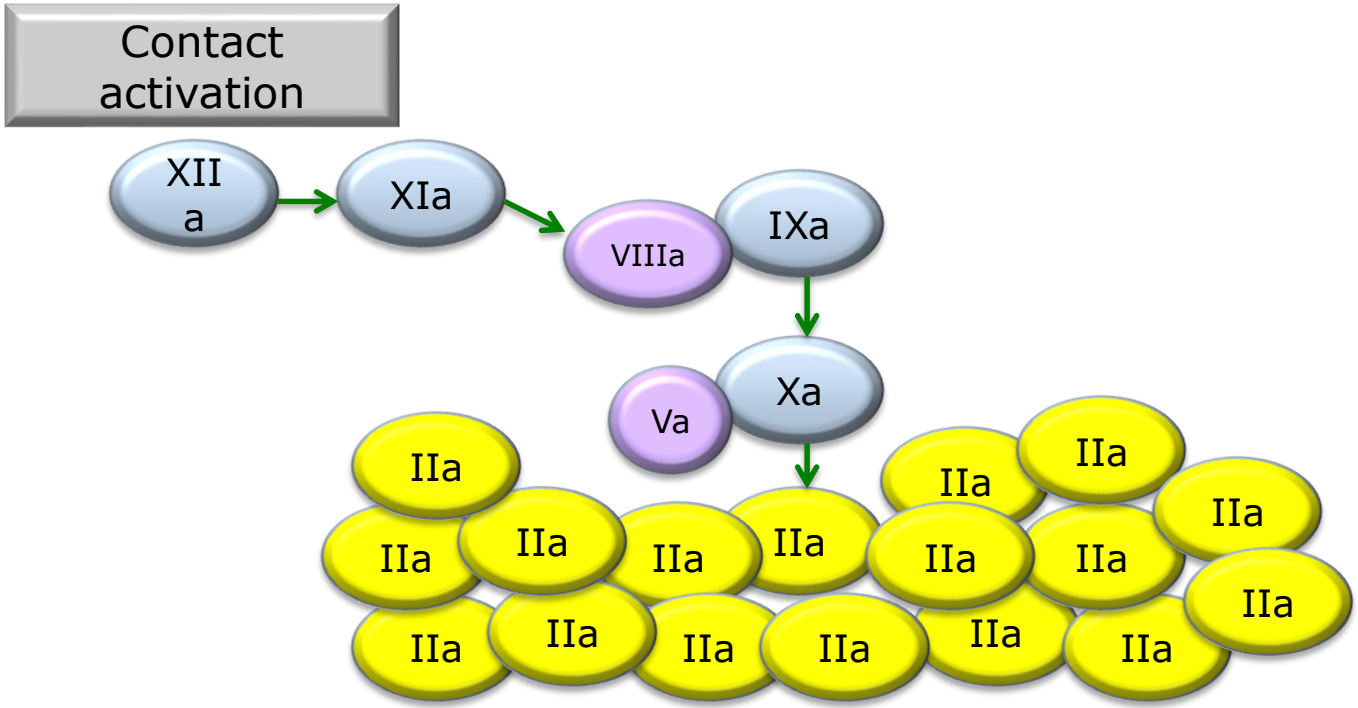
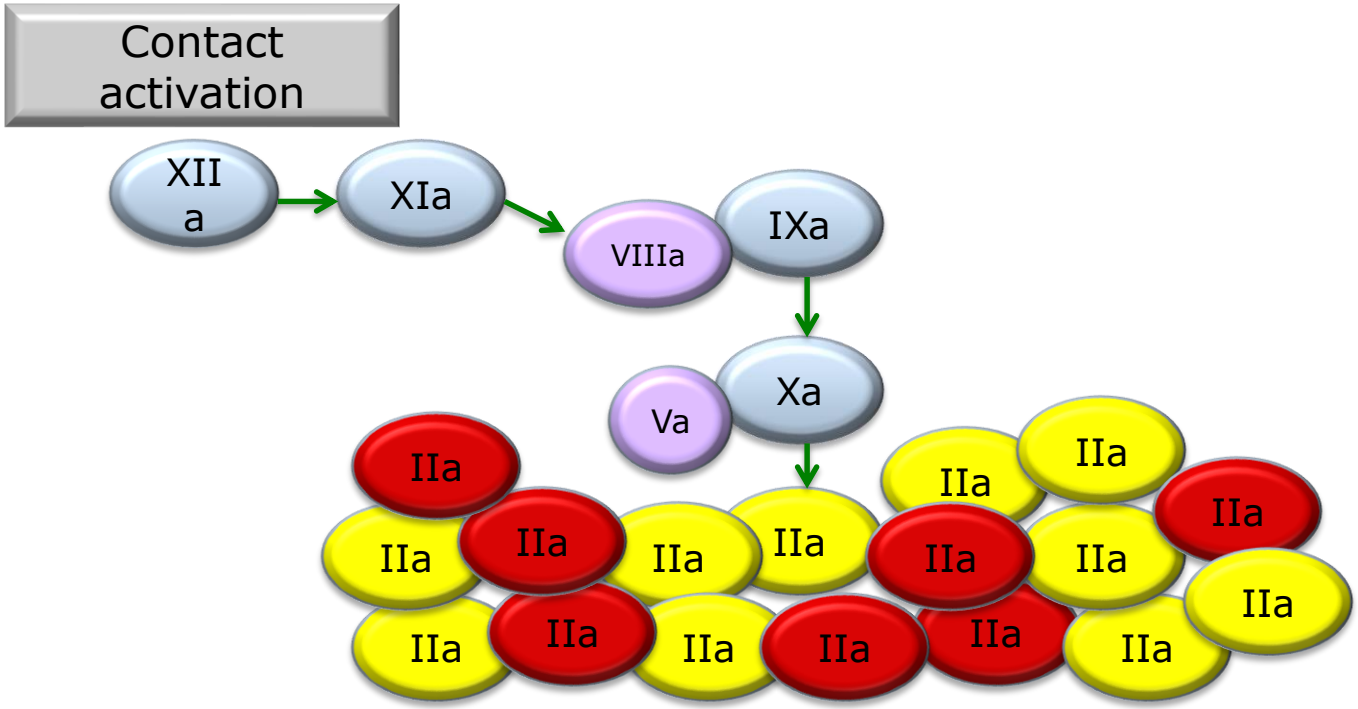
COAGULATION PATHWAYS



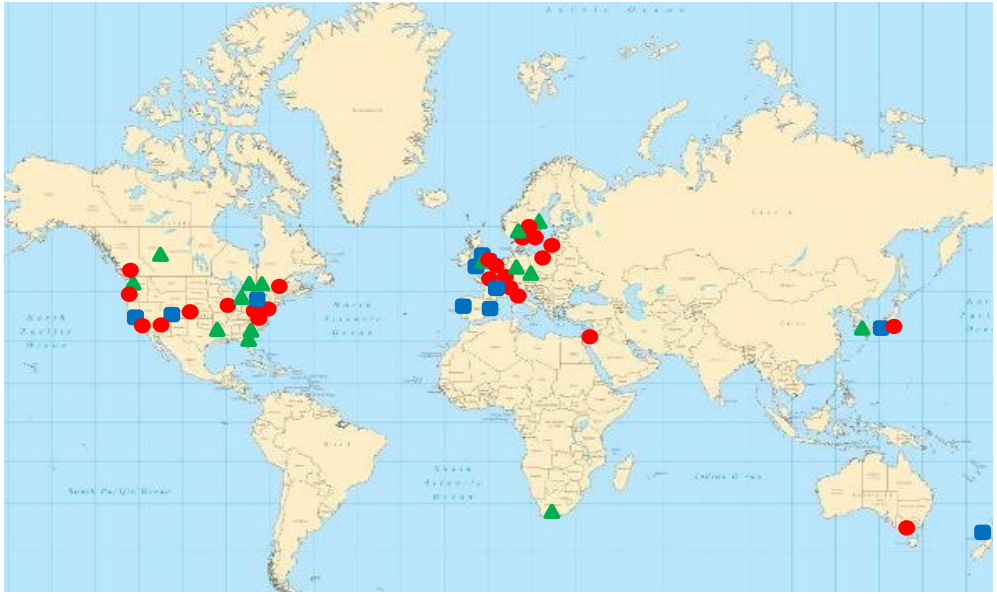
COAGULATION PATHWAYS



COAGULATION PATHWAYS

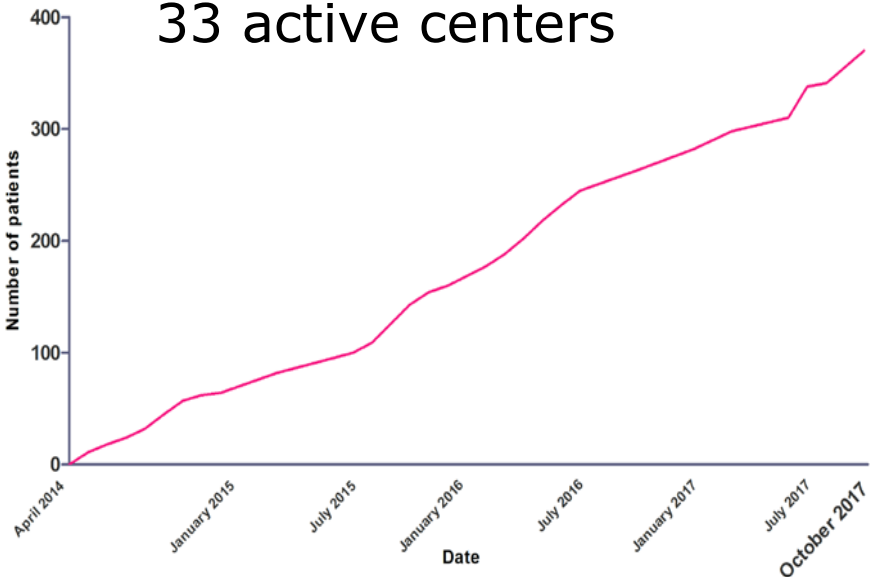


Non-vitamin K antagonist **O**ral anticoagulants for **T**hrombo**E**mbolic prevention



● = centers actively recruiting ■ = centers in process of obtaining MEC approval ▲ = interested centers

N=370
33 active centers



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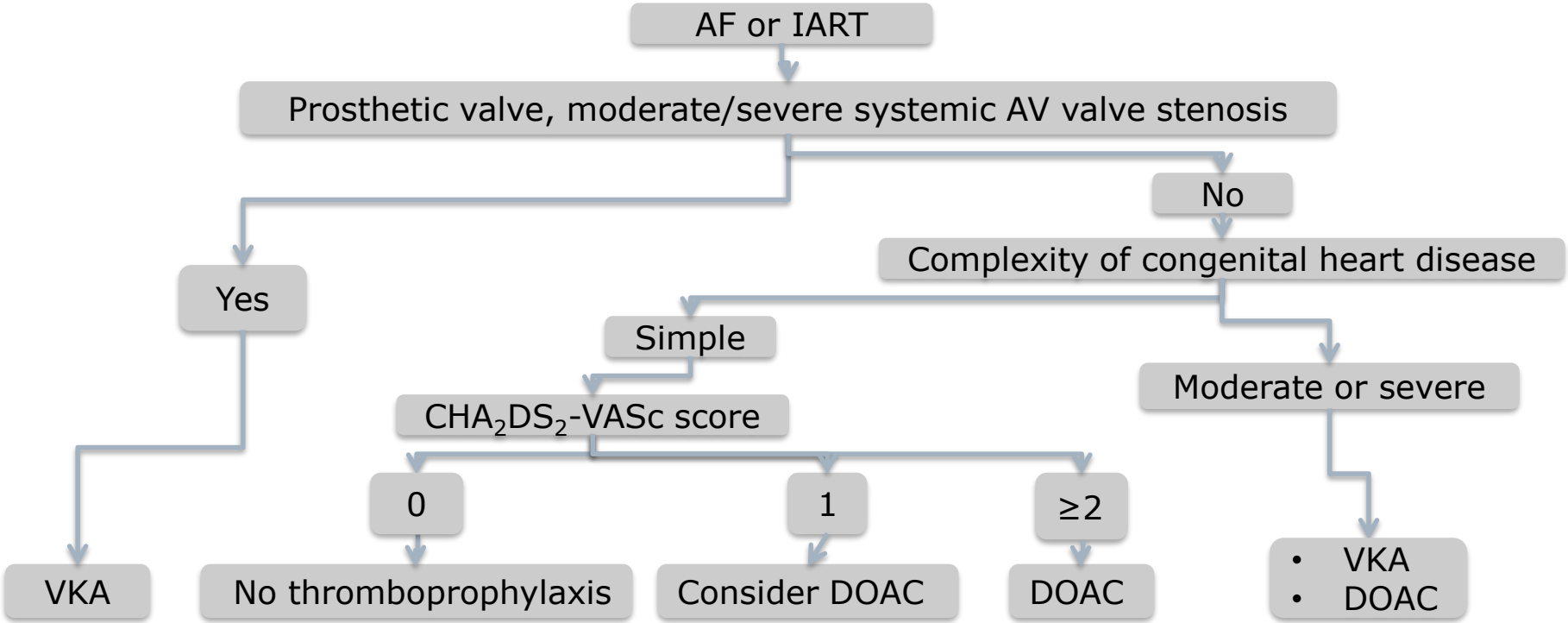
MY CURRENT APPROACH TO ANTICOAGULATION



Adapted from Khairy P et al. *Heart Rhythm* 2014;11:e102-65

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THANK YOU!

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CONCLUSION

- Strong association between atrial arrhythmias (IART and AF) and thromboembolic events in patients with CHD
- Risk increases with complexity of CHD
- Anticoagulation is generally indicated in those with moderate/severe CHD, whereas additional risk stratification tools could help guide therapy in those with simple CHD
- A low %TTR is observed in patients on VKAs, with ramifications regarding bleeding and thromboembolic complications
- Increasing safety data suggest that DOACs are a reasonable alternative to VKAs in patients without prosthetic material or severe systemic AV valve stenosis, although long-term follow-up studies are pending