ACC Latin America Conference 2017

MEXICO CITY

JUNE 22 – 24, 2017

GLOBAL EXPERTS, LOCAL LEARNING

Disclosures:

ACC Latin America Conference 2017

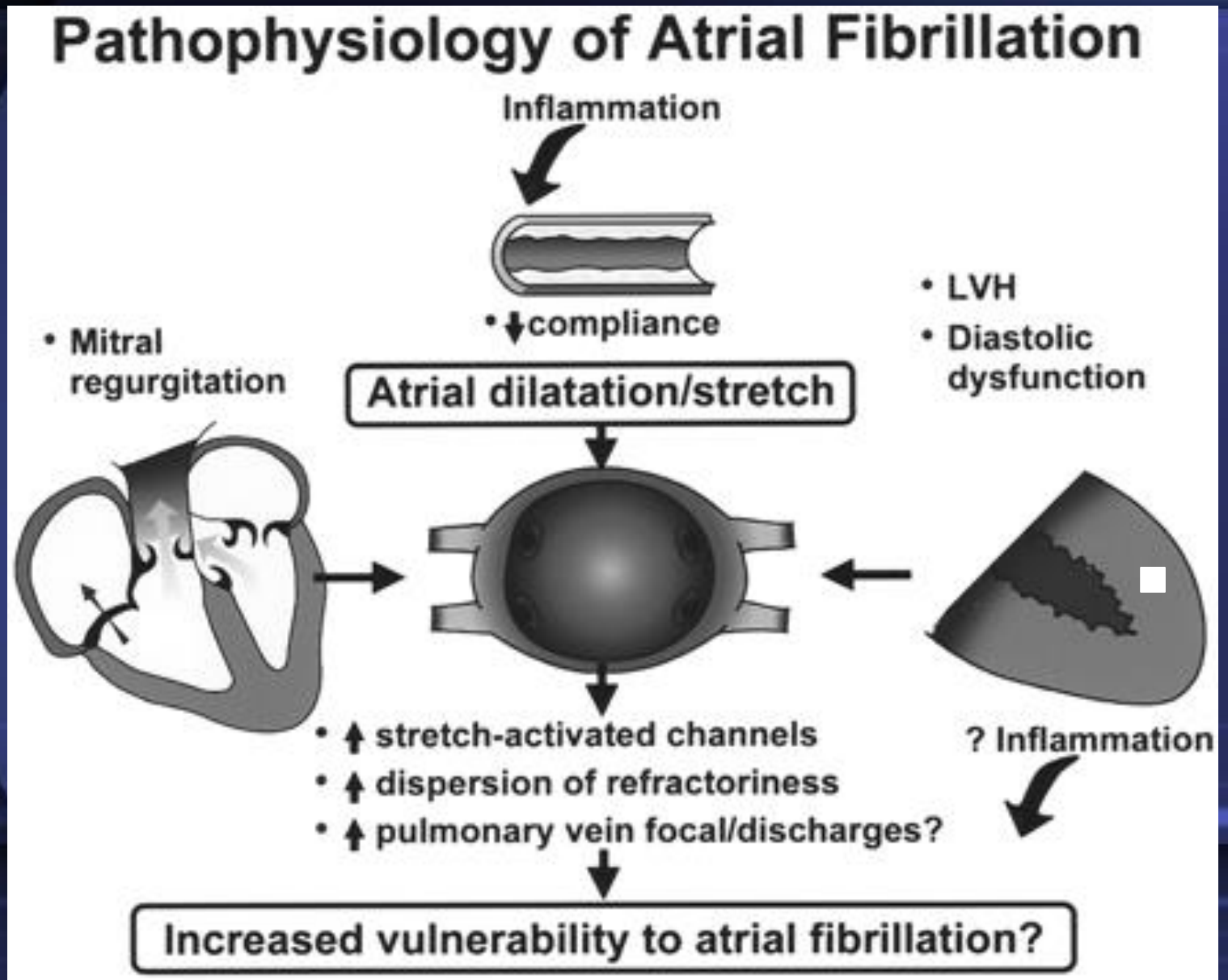
Advisor and Spekaer: Abbott, Boheinger, MSD,Pfizer, Menarini, Bayer, AstraZeneca, Merck, Servier.

No Diclosures for this presentation.

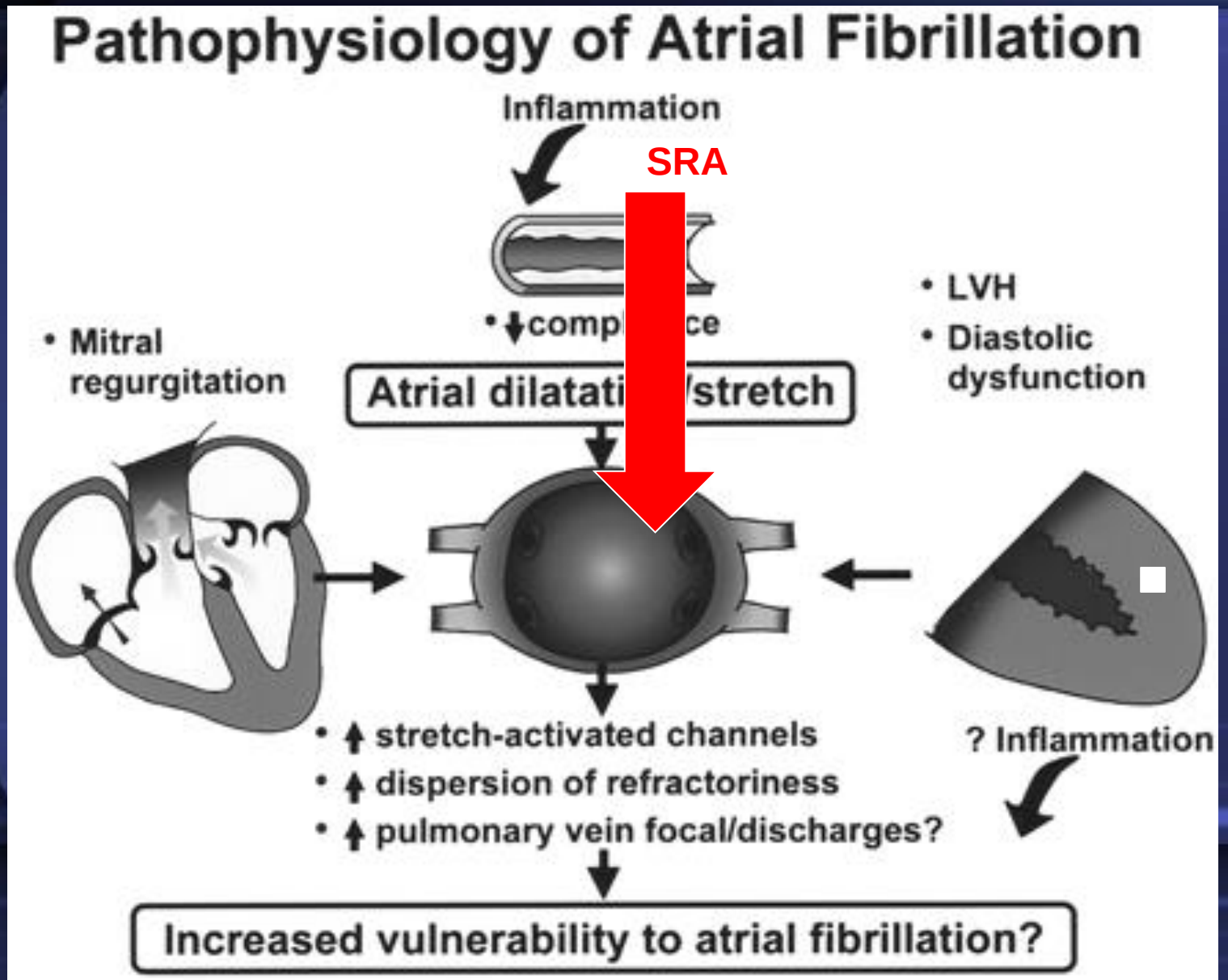
ATRIAL FIBRILATION

- Globally Atrial Fib. varies from 30-35 millions in the planet.
- Is the most common Arrhythmia in the world: increasingly aging population, more Hypertension, more HF, more diabetics…..
- Stroke is a devastating cosequence

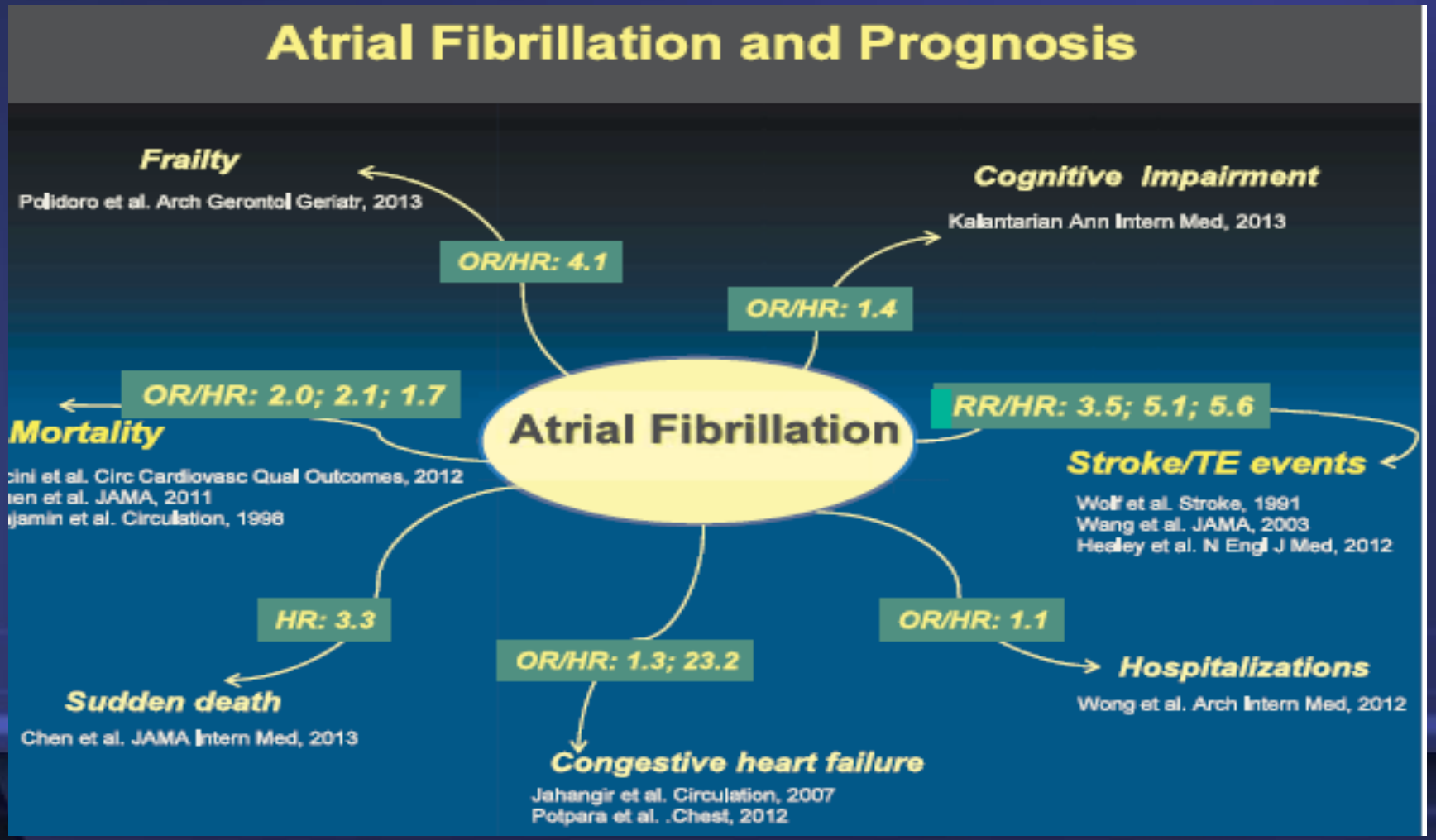
The new concept in AFib



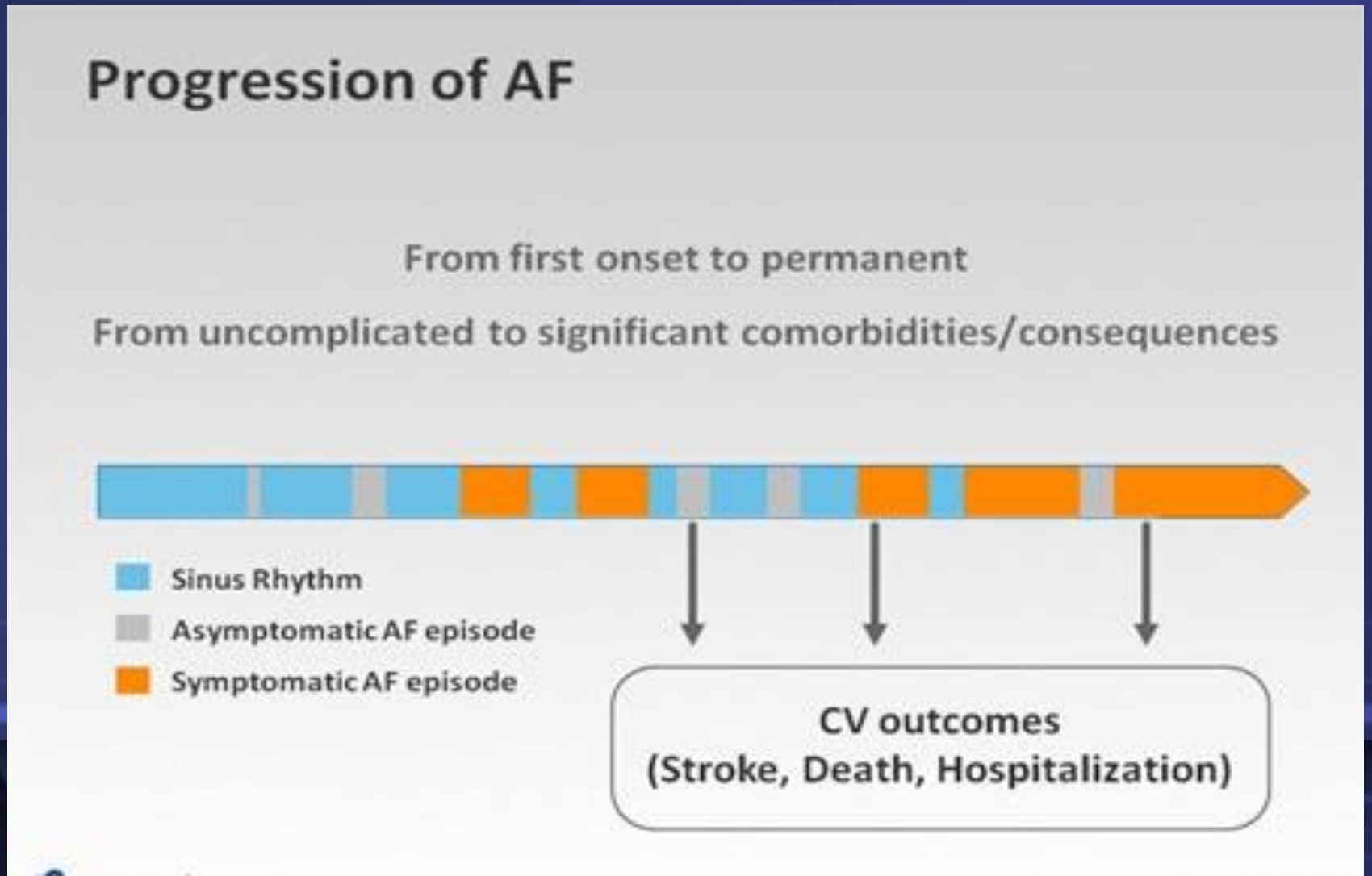
The new concept in AFib



ATRIAL FIB. IS A SISTEMIC DISEASE WITH SISTEMIC CONSEQUENCES



ATRIAL FIB. IS A PROGRESSIVE DISEASE



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ATRIAL FIBRILATION:CONTEMPORARY MANAGEMENT STRATEGIES

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Member HRA.

Sody Award Jackso Memorial Hospital, U of Miami

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QUESTIONS DILEMMAS AND PROBLEMS IN MANEGMENT OF ATRIAL FIB 2017

STILL WE DON´T HAVE ANSWERS FOR THOSE…

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Member HRA,

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ADVANCES

First question: Which is the meaning of “Non Valvular Atrial Fibrilation?

- Valvular AF refers to AF that occurs in the presence of mechanical prosthetic heart valves or moderate to severe mitral stenosis (ussualy of rehumatic origin).
- These patients were excluded from NOACs trials.

SECOND QUESTION:
IS IT POSSIBLE TO USE NOACS IN:

	Eligible	Contra-indicated
Mechanical prosthetic valve		✓
Moderate to severe mitral stenosis (usually of rheumatic origin)		✓
Mild to moderate other native valvular disease	✓	
Severe aortic stenosis	✓ Limited data. Most will undergo intervention	
Bioprosthetic valve[a]	✓ (except for the first 3 months post-operatively)	
Mitral valve repair[a]	✓ (except for the first 3–6 months post-operatively)	
PTAV and TAVI	✓ (but no prospective data; may require combination with single or double antiplatelets: consider bleeding risk)	
Hypertrophic cardiomyopathy	✓ (but no prospective data)	

THIRD QUESTION:
IS ATRIAL FIB. A PREVENTIVE DISEASE?

YES!

BECAUSE THERE ARE RISK FACTORS!

Cardiovascular and other conditions independently associated with atrial fibrillation (1)

Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF)	HR range 0.4–3.2
Older age 50-59 years 60-69 years 70-79 years 80-89 years	HR: 1.00 (reference) 4.98 (95% CI 3.49–7.10) 7.35 (95% CI 5.28–10.2) 9.33 (95% CI 6.68–13.0)
Hypertension (treated) vs. none	HR 1.32 (95% CI 1.08–1.60)
Heart failure vs. none	HR 1.43 (95% CI 0.85–2.40)
Valvular heart disease vs. none	RR 2.42 (95% CI 1.62–3.60)
Myocardial infarction vs. none	HR 1.46 (95% CI 1.07–1.98)
Thyroid dysfunction Hypothyroidism Subclinical hyperthyroidism Overt hyperthyroidism	(reference: euthyroid) HR 1.23 (95% CI 0.77–1.97) RR 1.31 (95% CI 1.19–1.44) RR 1.42 (95% CI 1.22–1.63)
Obesity (body mass index) None (<25 kg/m²) Overweight (25–30 kg/m²) Obese (≥31 kg/m²)	HR: 1.00 (reference) 1.13 (95% CI 0.87–1.46) 1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none	HR 1.25 (95% CI 0.98–1.60)

HR = hazard ratio; RR = risk ratio

Continued on next slide

European Heart Journal - doi:10.1093/eurheartj/ehw210

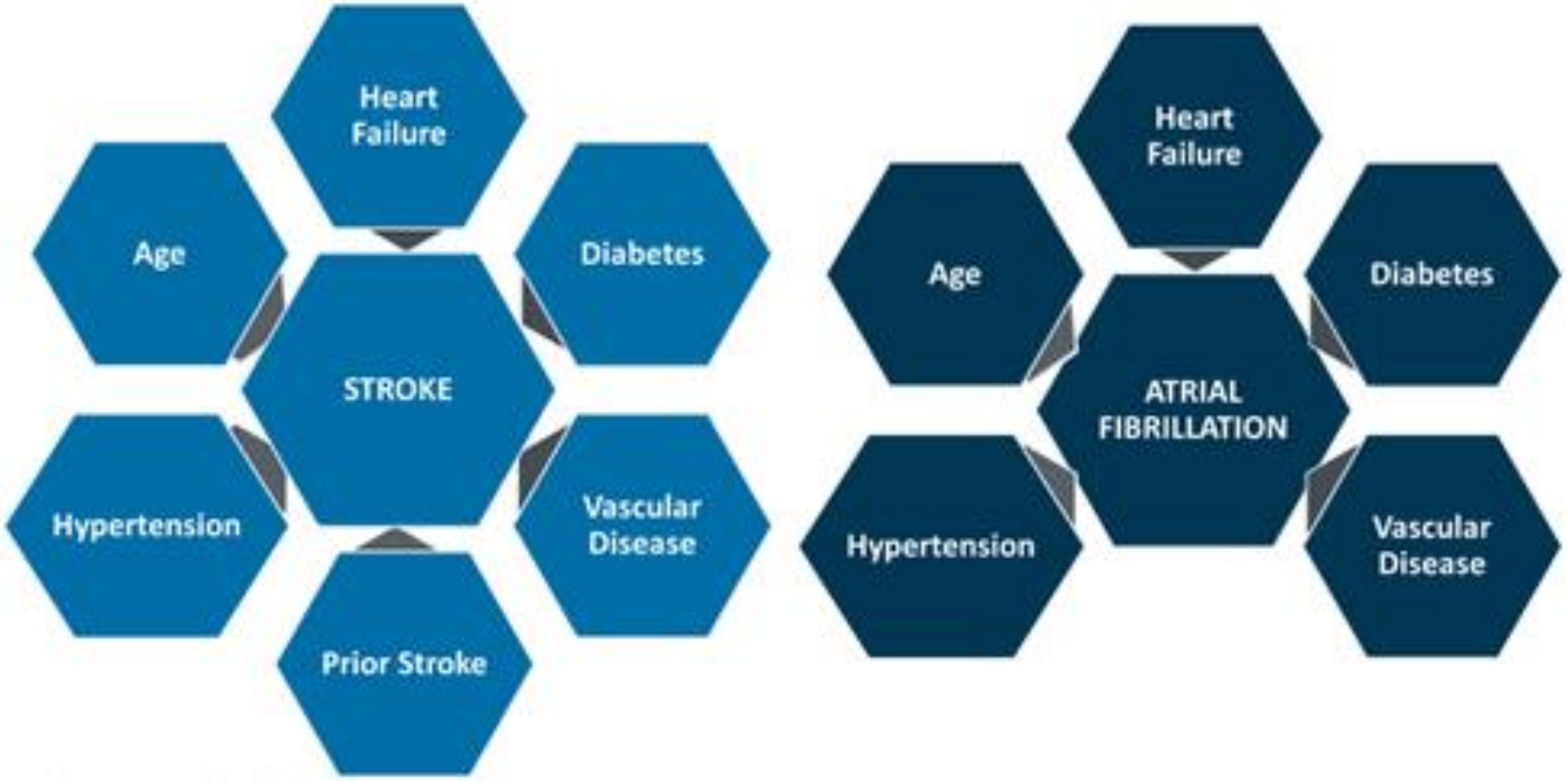
Cardiovascular and other conditions independently associated with atrial fibrillation (2)

Characteristic/comorbidity	Association with AF
Chronic obstructive pulmonary disease FEV1 ≥80% FEV1 60–80% FEV1 <60%	RR: 1.00 (reference) 1.28 (95% CI 0.79–2.06) 2.53 (95% CI 1.45–4.42)
Obstructive sleep apnoea vs. none	HR 2.18 (95% CI 1.34–3.54)
Chronic kidney disease None Stage 1 or 2 Stage 3 Stage 4 or 5	OR: 1.00 (reference) 2.67 (95% CI 2.04–3.48) 1.68 (95% CI 1.26–2.24) 3.52 (95% CI 1.73–7.15)
Smoking Never Former Current	HR: 1.00 (reference) 1.32 (95% CI 1.10–1.57) 2.05 (95% CI 1.71–2.47)
Alcohol consumption None 1– 6 drinks/week 7–14 drinks/week 15–21 drinks/week >21 drinks/week	RR: 1.00 (reference) 1.01 (95% CI 0.94–1.09) 1.07 (95% CI 0.98–1.17) 1.14 (95% CI 1.01–1.28) 1.39 (95% CI 1.22–1.58)
Habitual vigorous exercise Non-exercisers <1 day/week 1–2 days/week 3–4 days/week 5–7 days/week	RR: 1.00 (reference) 0.90 (95% CI 0.68–1.20) 1.09 (95% CI 0.95–1.26) 1.04 (95% CI 0.91–1.19) 1.20 (95% CI 1.02–1.41)

European Heart Journal - doi:10.1093/eurheartj/ehw210

Risk Factors for Stroke and AF

- The risk factors for stroke in AF are very similar to the risk factors that lead to the development of AF

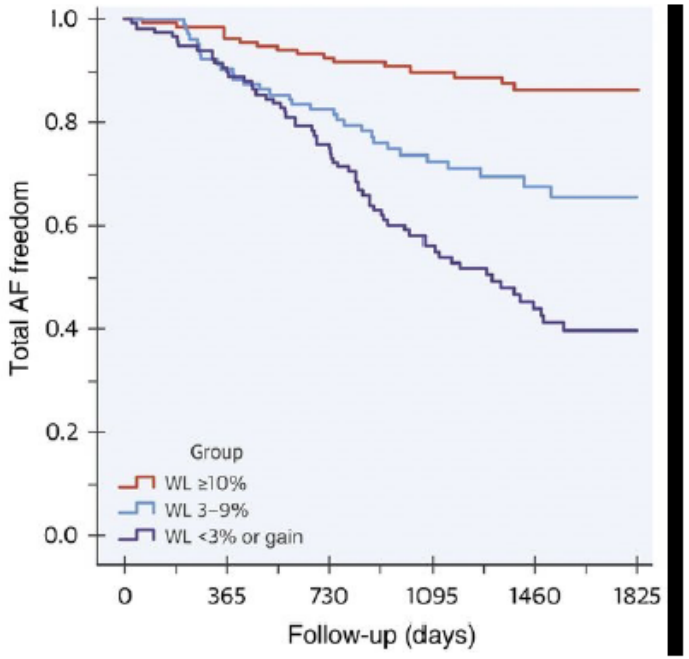


CDC website: Atrial Fibrillation Fact Sheet

IT IS CRUCIAL TO CONTROL THE RISK FACTORS.

NOT ONLY ABLATION AND DRUGS!

Benefits of Weight Loss, Fitness, and Intensive Risk Factors Management in AF



Pathak et al. *J Am Coll Cardiol* 2015

LEGACY - Sustained weight loss in obese patients with symptomatic AF is associated with:

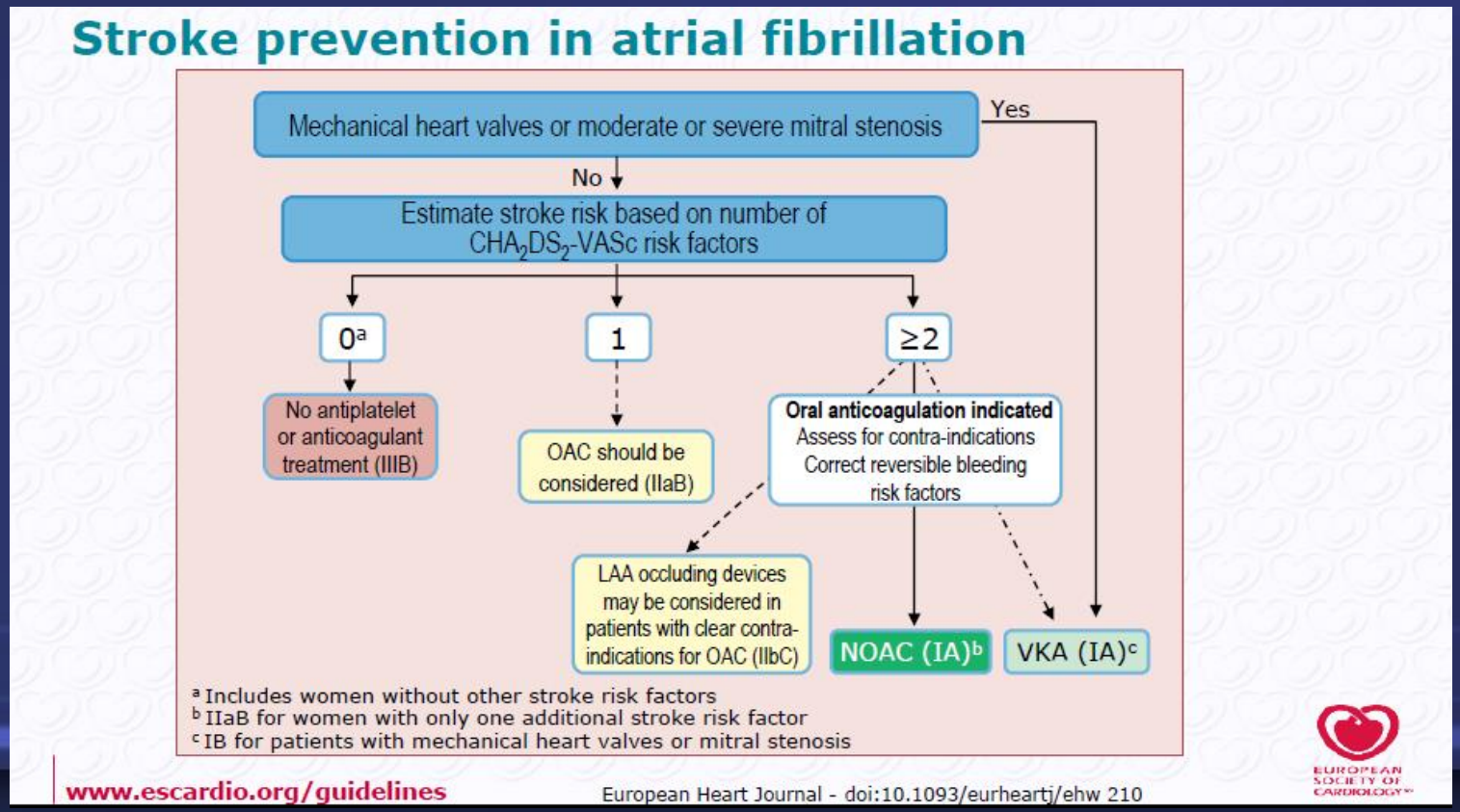
1. **A dose-dependent effect on long-term freedom from AF (6-fold)**
2. A reduction in LA volume and LVH
3. Lower BP & lipids
4. Improved glycaemic control
5. A reduction in *hs*CRP

European Heart Journal - doi:10.1093/eurheartj/ehw 210

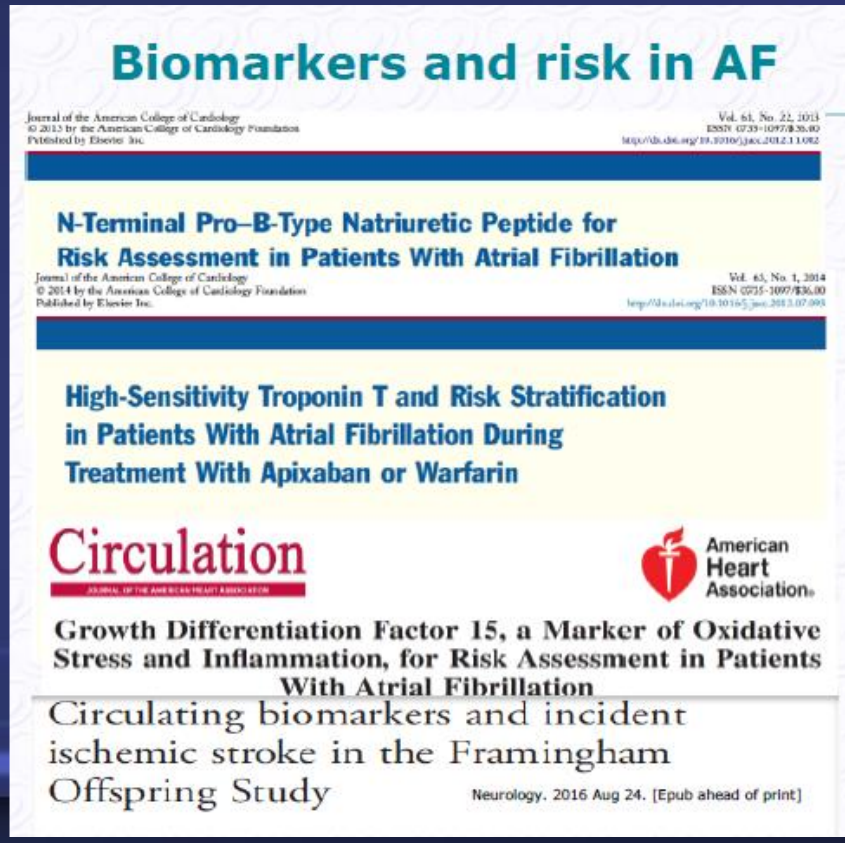
FIRST DILEMMA

Trombosis vs. hemorragia.

DILEMMA


Stroke prevention in atrial fibrillation
Mechanical heart valves or moderate or severe mitral stenosis
Yes
No
Estimate stroke risk based on number of CHA2DS2-VASc risk factors
0a
1
≥2
No antiplatelet or anticoagulant treatment (IIIB)
OAC should be considered (IIaB)
Oral anticoagulation indicated
Assess for contra-indications
Correct reversible bleeding risk factors
LAA occluding devices may be considered in patients with clear contra-indications for OAC (IIbC)
NOAC (IA)b
VKA (IA)c
a Includes women without other stroke risk factors
b IIaB for women with only one additional stroke risk factor
c IB for patients with mechanical heart valves or mitral stenosis
www.escardio.org/guidelines
European Heart Journal - doi:10.1093/eurheartj/ehw 210
EUROPEAN SOCIETY OF CARDIOLOGY

Biomarkers and risk in AF



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http://dx.doi.org/10.1016/j.jacc.2012.11.082

N-Terminal Pro–B-Type Natriuretic Peptide for Risk Assessment in Patients With Atrial Fibrillation

Journal of the American College of Cardiology
© 2014 by the American College of Cardiology Foundation
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Vol. 63, No. 1, 2014
ISSN 0735-1097/$36.00

High-Sensitivity Troponin T and Risk Stratification in Patients With Atrial Fibrillation During Treatment With Apixaban or Warfarin

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

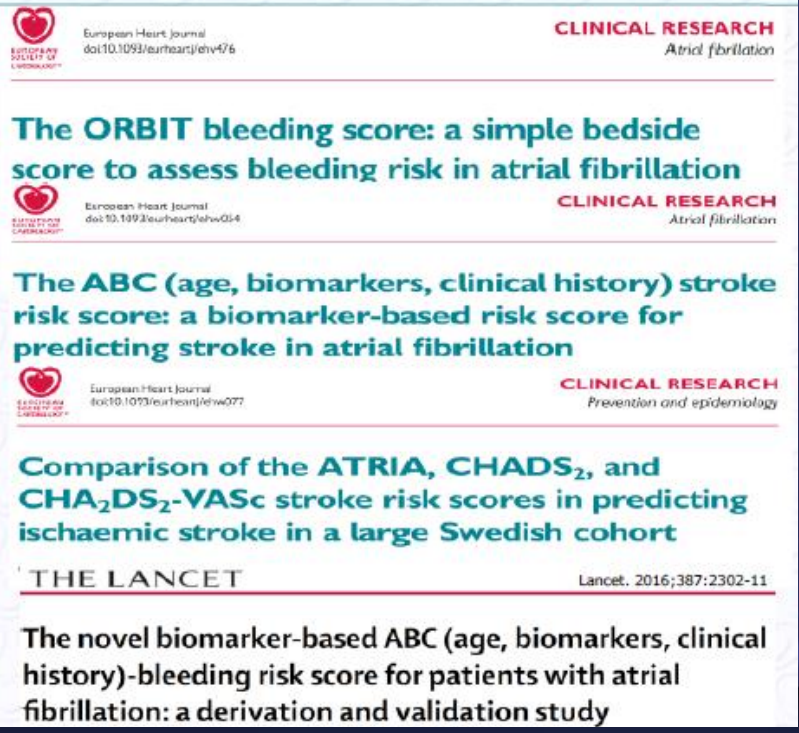
American Heart Association.

Growth Differentiation Factor 15, a Marker of Oxidative Stress and Inflammation, for Risk Assessment in Patients With Atrial Fibrillation

Circulating biomarkers and incident ischemic stroke in the Framingham Offspring Study

Neurology. 2016 Aug 24. [Epub ahead of print]

Biomarker risk scores in AF



European Heart Journal
doi:10.1093/eurheartj/ehv476

CLINICAL RESEARCH
Atrial fibrillation

The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation

European Heart Journal
doi:10.1093/eurheartj/ehv014

CLINICAL RESEARCH
Atrial fibrillation

The ABC (age, biomarkers, clinical history) stroke risk score: a biomarker-based risk score for predicting stroke in atrial fibrillation

European Heart Journal
doi:10.1093/eurheartj/ehw077

CLINICAL RESEARCH
Prevention and epidemiology

Comparison of the ATRIA, $CHADS_2$, and CHA_2DS_2-VASc stroke risk scores in predicting ischaemic stroke in a large Swedish cohort

THE LANCET

Lancet. 2016;387:2302-11

The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study

Performance and Validation of a Novel Biomarker-Based Stroke Risk Score for Atrial Fibrillation

- 8356 patients with 16,137 person-years of follow-up in anticoagulated patients with AF in the RE-LY study.
- ABC risk score. which incorporates age. biomarkers (hs-cTn and NT-proBNP), and clinical history of prior stroke.
- The biomarker-based ABC stroke score is an improved decision-making tool for patients with AF, specially for CHA_2DS_2VASc score ≥ 2

http://dx.doi.org/10.1161/CIRCULATIONAHA.116.022802
Published Ahead of Print: August 28, 2016

JAMA Cardiology | Original Investigation

Effectiveness and Safety of Standard-Dose Nonvitamin K Antagonist Oral Anticoagulants and Warfarin Among Patients With Atrial Fibrillation With a Single Stroke Risk Factor
A Nationwide Cohort Study

Gregory Y. H. Lip, MD; Flemming Skjøth, MSc, PhD; Peter Brønnum Nielsen, MSc, PhD; Jette Nordstrøm Kjældgaard, BSc; Torben Bjerregaard Larsen, MD, PhD

SULTS Of 14 020 participants, 5151 (36.7%) were women, and the median age for rticipants was 66.5 years. For the principal effectiveness end point of ischemic oke/systemic embolism, no significant differences of the NOACs compared with treatment th warfarin across strata were evident. For the end point of "any bleeding," this was gnificantly lower for treatment with apixaban (hazard ratio [HR], 0.35; 95% CI, 0.17-0.72) d dabigatran (HR, 0.48; 95% CI, 0.30-0.77) compared with warfarin in the main analysis, d was not significantly different for treatment with rivaroxaban vs warfarin (HR, 0.84; 95% 0.49-1.44). There was broad consistency across most subgroups in the sensitivity analyses d whether 1- or 2.5-year follow-up periods were analyzed. However, falsification end points nerally did not falsify, indicating the possible presence of residual confounding across these mparisons, presumably related to selective prescribing and unobserved covariates.

CONCLUSIONS AND RELEVANCE In this Danish cohort study of patients with atrial fibrillation and a single stroke risk factor, there was no difference between NOACs compared with treatment with warfarin in terms of the risk of having an ischemic stroke/systemic embolism. For "any bleeding," this was lower for treatment with apixaban and dabigatran compared with warfarin. These data do not allow for a definitive statement of the comparative effectiveness or safety of NOACs because of the possible residual confounding that was unmasked with falsification outcomes.

JAMA on line 14 Jun 2017

PROBLEMS in AF 2017

- There is evidence of underuse of anticoagulants for AF after 10 years of DOACs.
- Inconsistent approach to cardiovascular risk factors
- Inadecuate teatment for concomitant commorbidities.
- In Real Life studies, DOACs are used in sub-therapeutic dosis
- **Anticoagulation is used thinking in preventing bleeding complications more than in preventing tromboembolism.** Stroke is “God´s design”; bleeding is a medical complication”!

Fear to anticoagulation persist!

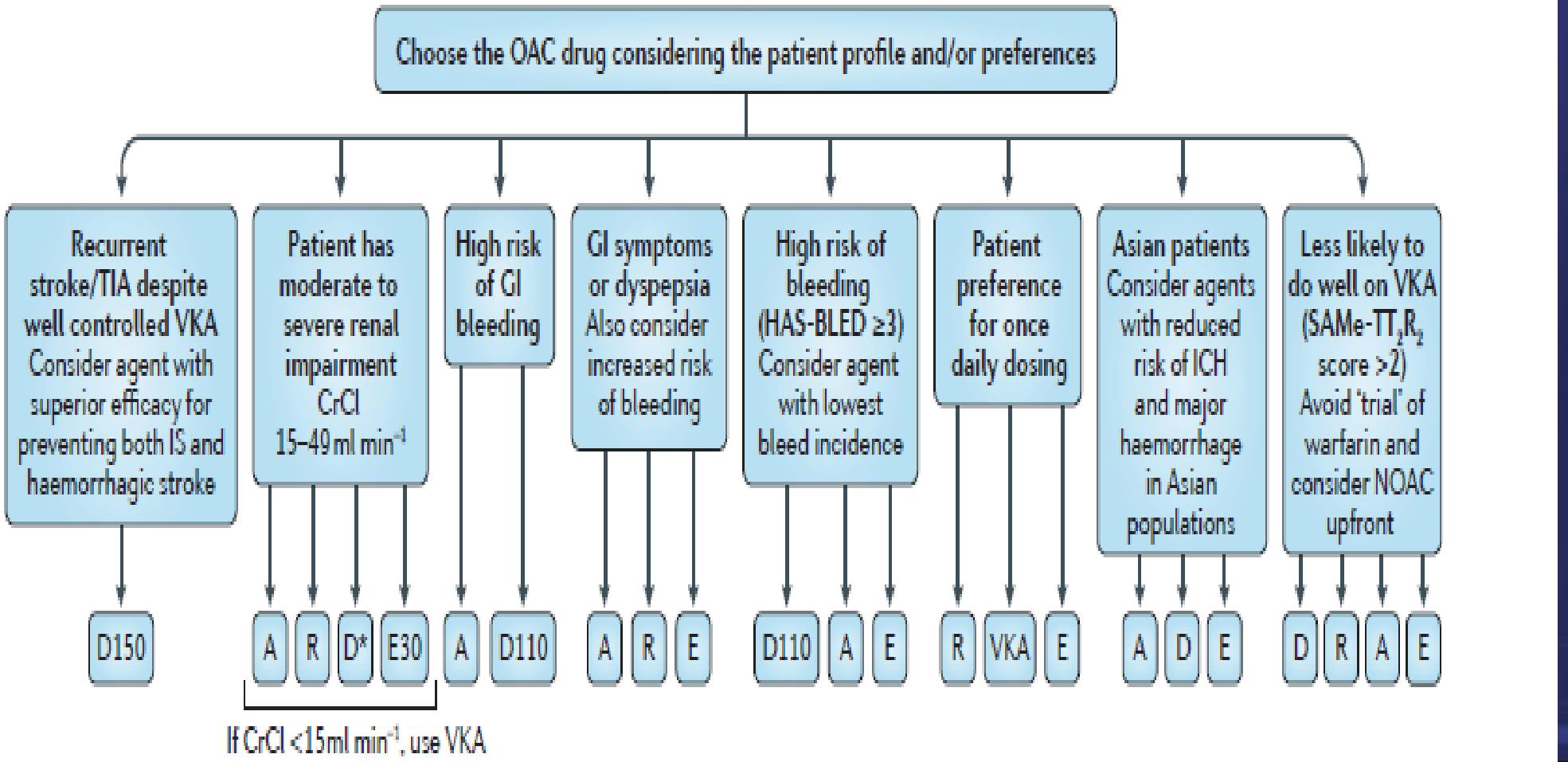
ANOTHER PROBLEM:
ARE ALL NOACS THE SAME?

All NOACs are equal, but some are more equal than others….

Dr Puneet Kakar MRCP LLM MSc

Consultant Stroke physician

Epsom general hospital


Choose the OAC drug considering the patient profile and/or preferences
Recurrent stroke/TIA despite well controlled VKA Consider agent with superior efficacy for preventing both IS and haemorrhagic stroke
Patient has moderate to severe renal impairment CrCl 15–49 ml min⁻¹
High risk of GI bleeding
GI symptoms or dyspepsia Also consider increased risk of bleeding
High risk of bleeding (HAS-BLED ≥3) Consider agent with lowest bleed incidence
Patient preference for once daily dosing
Asian patients Consider agents with reduced risk of ICH and major haemorrhage in Asian populations
Less likely to do well on VKA (SAMe-TT2R2 score >2) Avoid 'trial' of warfarin and consider NOAC upfront
D150
A
R
D*
E30
A
D110
A
R
E
D110
A
E
R
VKA
E
A
D
E
D
R
A
E
If CrCl <15ml min⁻¹, use VKA

Question: how to adjust the dosis of DOACS in CKD?

Drug Name	Study	Excretion	Dosages and renal adjustment
Dabigatran	RE-LY 75	**Mostly renal**	**CrCl > 30 ml/min : 150 mg orally twice daily CrCl 15- 30 ml/min : 110 mg orally twice daily CrCl < 15 ml/min : Avoid**
Rivaroxaban	ROCKET AF[57]	**Partially renal**	**CrCl > 50 ml/min : 20 mg orally once daily CrCl 15 - 50 ml/min : 15 mg orally once daily CrCl < 15 ml/min : Avoid**
Apixaban	ARISTOTLE[59] AVERROES[58]	**Partially renal**	**Recommended dose: 5 mg orally twice daily No dose adjustment required in patients with mild, moderate, or severe renal impairment alone In patients with at least 2 of the following: - age ≥80 years - body weight ≤60 kg - serum creatinine ≥1.5 mg/dL The recommended dose is 2.5 mg orally twice daily CrCl < 15 ml/min : Avoid**

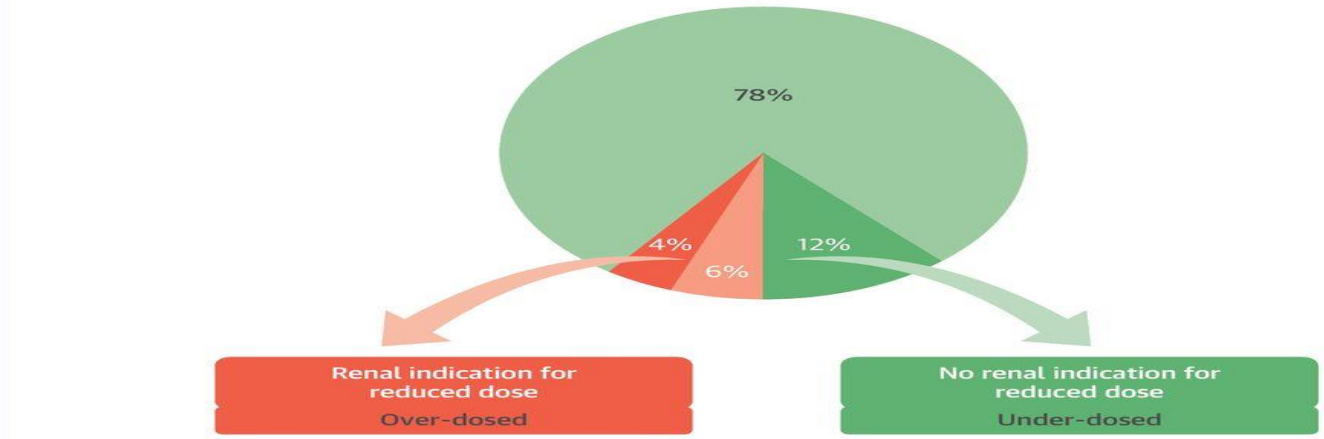
J Atr Fibrillation. 2015 Apr-May; 7(6): 1069.

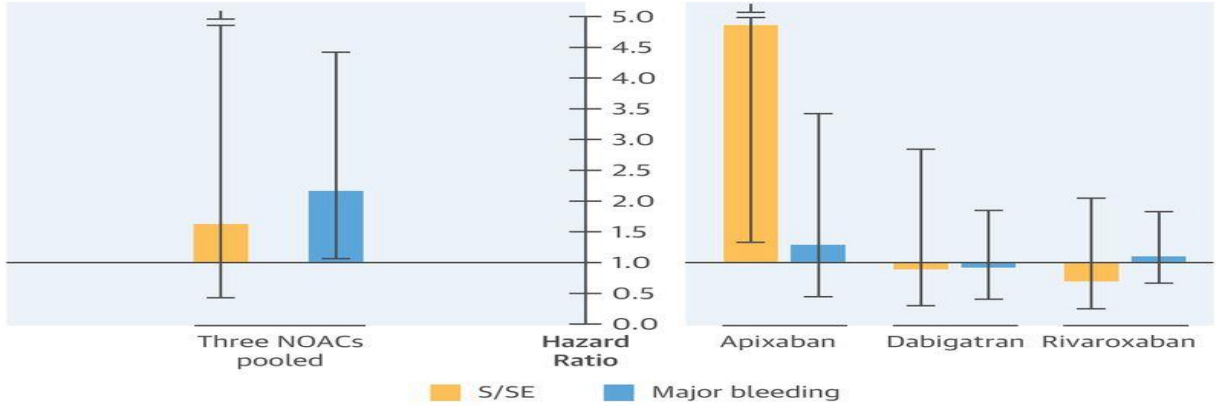
PROBLEM: AF, RENAL FUNCTION AND DOSIS ADJUSTMENT FOR DOACS

- **Among the 1,473 patients with a renal indication for dose reduction, 43.0% were potentially overdosed. These patients were associated with a higher risk of major bleeding** (hazard ratio [HR], 2.19; 95% confidence interval [CI], 1.07-4.46), **but no significant difference in stroke. Among the 13,392 patients without a renal indication for dose reduction, 13.3% were potentially underdosed**.
- **The apixaban underdosed patients were associated with a higher risk of stroke** (HR, 4.87; 95% CI, 1.30-18.26), **but no significant difference in bleeding**. **The rivaroxaban and dabigatran underdosed patients were not associated with any stroke.**

JACC 69, Issue 23, June 2017

CENTRAL ILLUSTRATION: Prevalence and Impact of Inappropriate NOAC Dosing





Yao, X. et al. J Am Coll Cardiol. 2017;69(23):2779–90.

WHETHER TO INTERRUPT DOAC THERAPY

1 **Assess patient bleed risk checklist**
Bleed risk considered increased if any 1 of the following: major bleed or ICH <3 months; quantitative or qualitative platelet abnormality, including aspirin use; prior bleed during previous bridging.

CONSIDERATIONS

1 Increased patient bleed risk?

- **No** → Procedural bleed risk?
  - No clinically important risk → Perform the procedure uninterrupted, but time it at DOAC interval trough.
  - Low → **INTERRUPT**
  - Uncertain, intermediate, or high → **INTERRUPT**
- **Yes** → **INTERRUPT**

CONSIDERATIONS

WHEN TO INTERRUPT

Type of DOAC: DTI | FXa inhibitor

Measure CrCl

GUIDANCE

CrCl	Discontinue
<15	No data; consider dTT and/or ≥96 hrs.
15-29	≥72 hrs
30-49	≥48 hrs
50-79	≥36 hrs
≥80	≥24 hrs

CrCl	Discontinue
<15	No data; consider anti Xa level and/or≥48 hrs.
15-29	≥36 hrs
≥30	≥24 hrs

CrCl	Discontinue
<15	No data; consider dTT.
15-29	≥ 120
30-49	≥ 96 hrs
50-79	≥ 72 hrs
≥ 80	≥ 48 hrs

CrCl	Discontinue
<30	No data; consider anti Xa level and/or ≥72 hrs.
≥30	≥48 hrs

Insufficient data on best practices. Interrupt at least as long as determined by CrCl (Table 2) and possibly longer.

Use clinical judgment.

PARENTERAL BRIDGING *NOT* INDICATED FOR DOACS.
Perform the procedure

CrCl — creatinine clearance
DTI — direct thrombin inhibitor (dabigatran)
dTT — dilute thrombin time assay
FXa inhibitor — Factor Xa inhibitor (apixaban, edoxaban, rivaroxaban)
ICH — intracranial hemorrhage

ABLATION: A SOLUTION FOR ANTIARRHYTHMIC USE?

Pulmonary Vein Isolation With Versus Without Continued Antiarrhythmic Drug Treatment in Subjects With Recurrent Atrial Fibrillation (POWDER-AF)

Arrhythmias occurred in 2.7% (n=2) patients who continued antiarrhythmic drug therapy, compared with 21.9% (n=16) of those who discontinued therapy (P<0.001).

The freedom from atrial fibrillation in the patients after PVI without drugs was 78%, which confirms a good outcome with cardiac ablation, but by adding drugs, you can reach up to 97% freedom from atrial fibrillation.

In addition, patients who continued AAD had a lower occurrence of repeat ablation (1.3%) vs those who stopped therapy (17.1%; odds ratio [OR] 0.06, 95% CI 0.001–0.46)

Heart Rhythm Society (HRS) Scientific Sessions 2017
5 Jun

Anticoagulation, atrial fibrillation, and chronic kidney disease—whose side are you on?

Gunnar Henrik Heine Correspondence information about the author Gunnar Henrik Heine
,

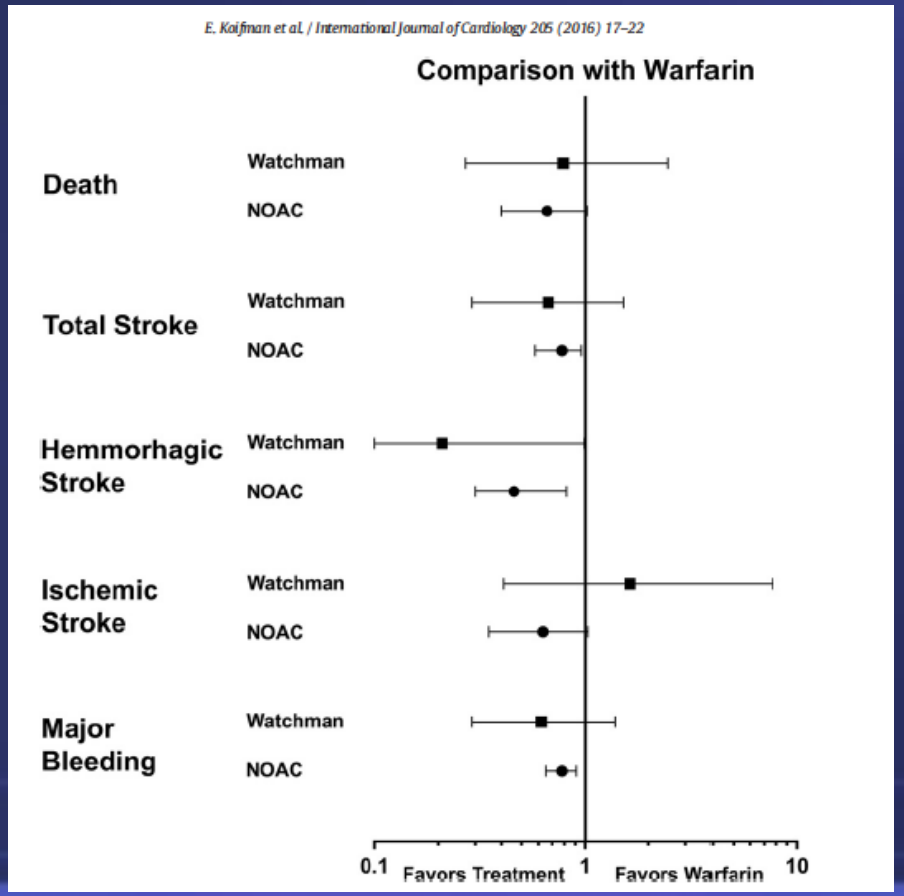
- Whether to initiate oral anticoagulant therapy in advanced chronic kidney disease patients with atrial fibrillation remains debatable. Although randomized trial data are lacking, observational studies yield controversial results. Keskar and colleagues analyzed data from a Canadian health care system and found that in **elderly chronic kidney disease patients with atrial fibrillation, oral anticoagulant therapy did not prevent ischemic strokes, induced hemorrhages, but prolonged life. These paradoxical findings emphasize the dire need for an adequately powered randomized trial.**

Kidney April 2017Volume 91, Issue 4, Pages 778–780

Does Left Atrial Appendage (LAA) occlusion prevent stroke?

- Left atrial thrombus on echo always in the LAA
- Results with device closure of the LAA mixed

Comparison of Watchman device with new oral anti-coagulants in patients with atrial fibrillation: A network meta-analysis☆



McMaster University
DIVISION OF CARDIOLOGY

Do NOACs Prevent Stroke in Rheumatic AF?

- Rheumatic disease common in low-middle income countries
- ‘Global’ trials excluded rheumatic patients

THE PROBLEM WITH EVIDENCE: DELAYED OR NO ANTICOGULATION… RESULT: DEMENTIA!

- **Patients prescribed aspirin and clopidogrel 3 years or more after their initial diagnosis had a more than threefold increase in the risk of dementia (hazard ratio [HR] 3.39, 95% CI 2.4–4.65; P<0.0001).**
- **Similarly, delays in warfarin therapy were associated with a two-and-a-half times greater risk of developing dementia (HR 2.55, 95% CI 1.59–4.09; P<0.0001).**

Dementia rates increase with delays in initiation of anticoagulation treatment for atrial fibrillation. Heart Rhythm Society 2017 Scientific Sessions. May 12, 2017; Chicago, IL. Abstract C-AB30-03

Implications of AF

- How to manage patients with HF, valvular disease, hypertension?
  - AF is present in up to 90% of participants in hypertension trials[a]
  - In patients with hypertension, ACEis and ARBs may reduce AF or its progression
  - If you knew the patient already had AF, is may change how hypertension is treated
- Patients may present with HF and silent AF
  - Treatment with ß-blocker

a. Manolis AJ, et al. *J Hypertens*. 2012;30:239-252

Conclusions

- 1) All Risk Factors for CAD and Stroke are the same for AF corresponding to >85%
- 2) Focus on primary prevention and management of traditional cardiovascular risk factors.
- 3) The importance for detect AF as early as possible
- 4) Sub-use and sub-dosis:a problem of Real World.
- 5)CKD and DOACs need attention,
- 6) Anticoagulation in Afib. is the hallmark regardless of other manegment.
- 7) Atrial fib. induces stroke, HF, dementia and detrimental quality of life..

A Fibrilation

- Requieres apply all known and developing

MANAGEMENT STRATEGIES


MEN WERE NOT BORN TO DIE,
BUT TO INNOVATE
A ARENDT