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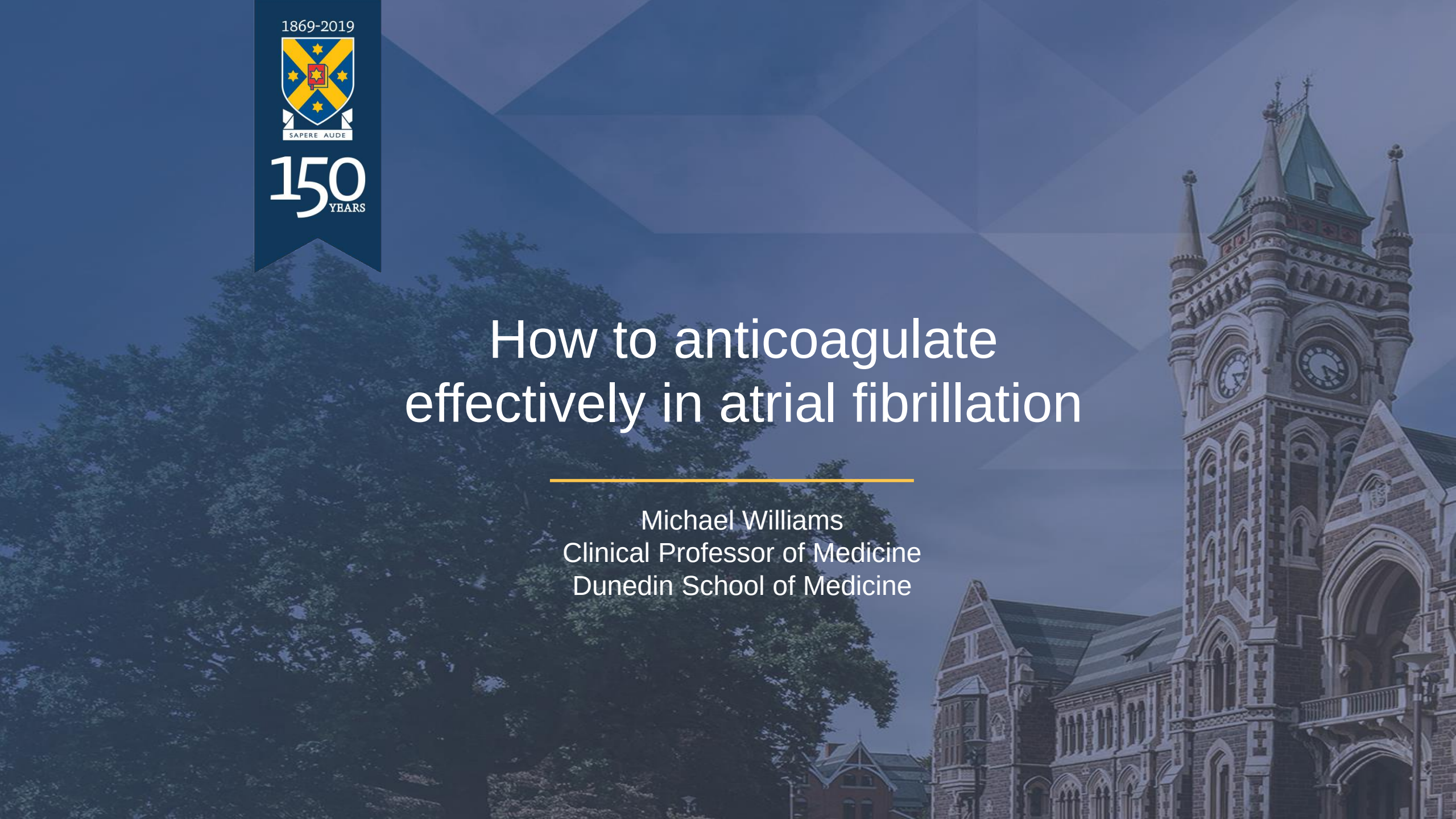
## Friday, August 09, 2019 (Room 3)

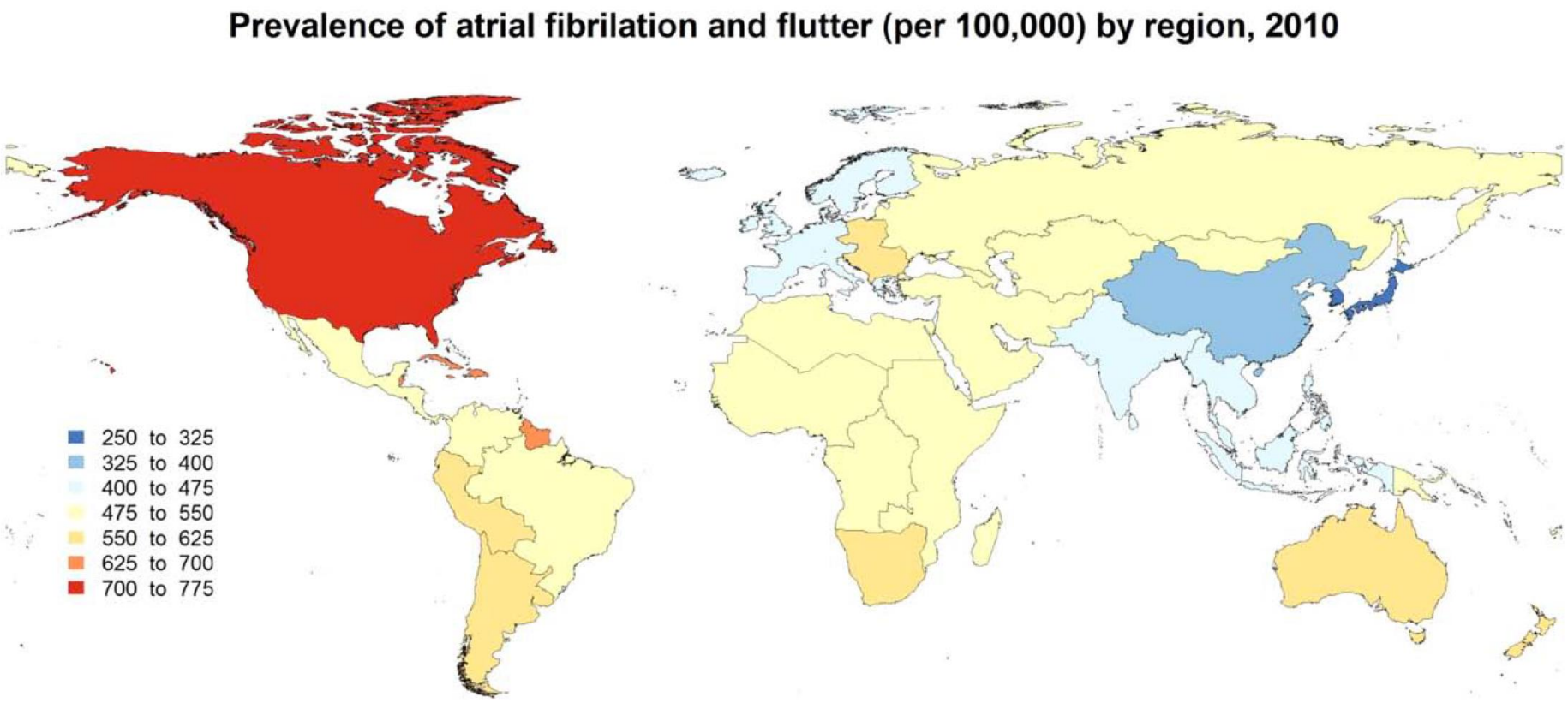
14:00 - 14:55 WS #27: How to Anticoagulate Effectively in AF

15:05 - 16:00 WS #37: How to Anticoagulate Effectively in AF (Repeated)



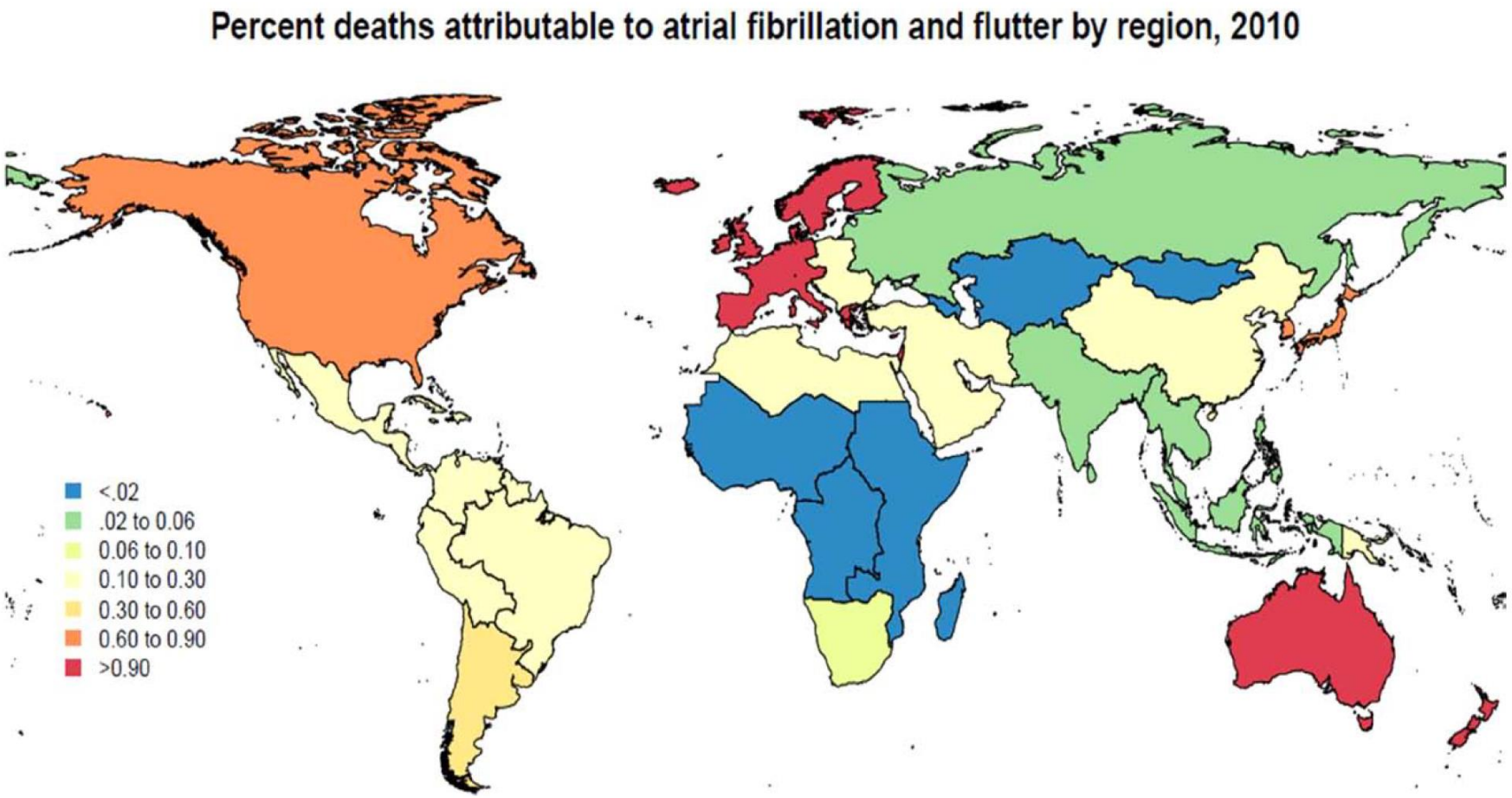

# How to anticoagulate effectively in atrial fibrillation

Michael Williams
Clinical Professor of Medicine
Dunedin School of Medicine




Age-adjusted prevalence rates (per 100 000 population) of atrial fibrillation in the 21 Global Burden of Disease regions, 2010

**Circulation 2014;129:837-847**




Proportion of global deaths associated with atrial fibrillation in 2010

**Circulation 2014;129:837-847**

*Original scientific paper*

European Journal of Preventive Cardiology

European Journal of Preventive Cardiology
2017, Vol. 24(3) 311–319

DOI: 10.1177/2047487316674830
ejpc.sagepub.com

SAGE

# Atrial fibrillation in New Zealand primary care: Prevalence, risk factors for stroke and the management of thromboembolic risk

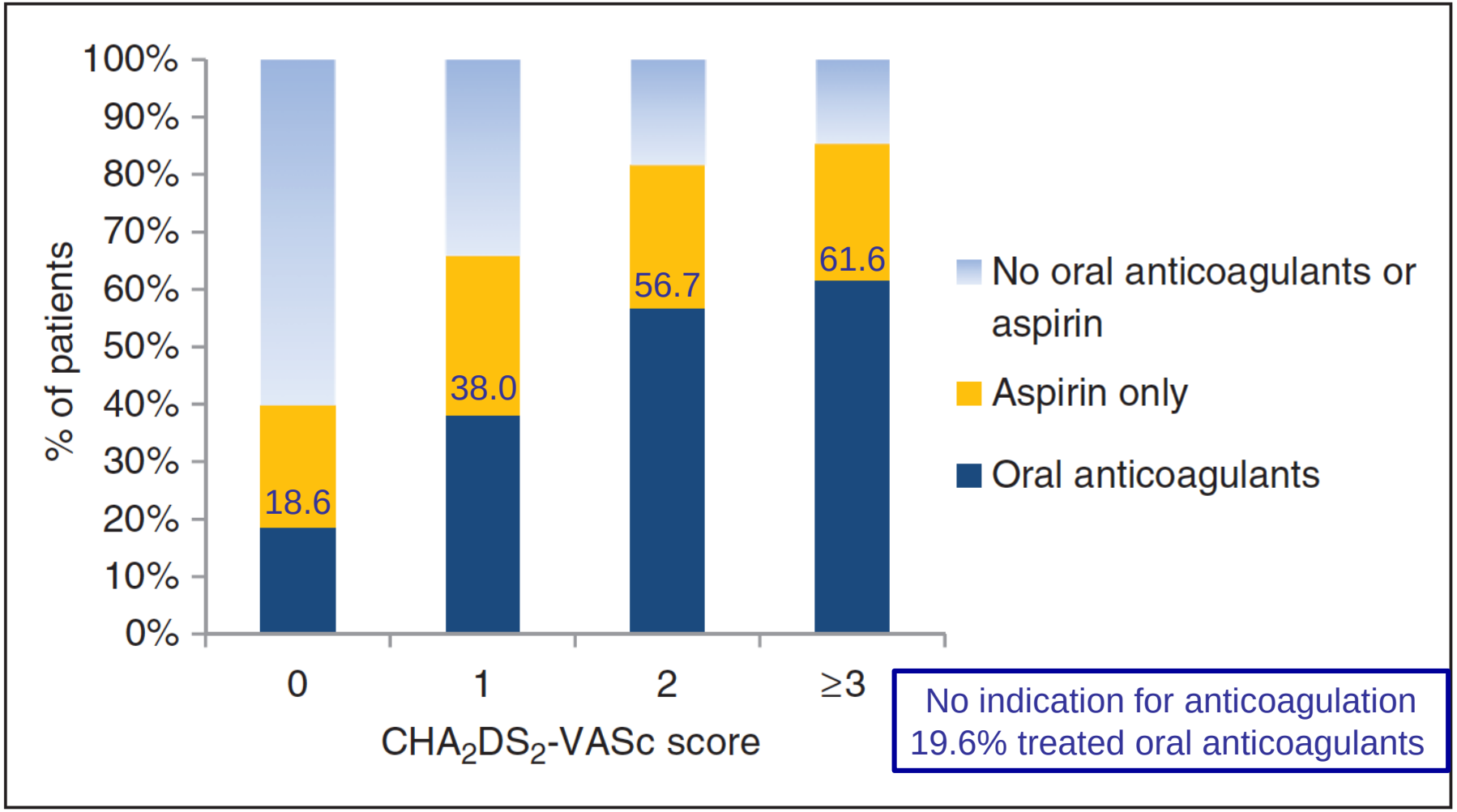
**Andrew M Tomlin[1], Hywel S Lloyd[1,2] and Murray W Tilyard[1,2]**

**Design:** A retrospective cohort study utilising electronic medical records for 739,000 patients registered with 170 general practices in 2014.

**Methods:** Patient diagnoses and prescriptions from 2010–2014 were analysed to identify patients with atrial fibrillation in 2014 and co-morbidities included in the $CHA_2DS_2$-VASc algorithm. Adjusted prevalence of atrial fibrillation by patient demographic group and the proportion of patients following recommended antithrombotic therapy were calculated.

**Results:** 12,712 patients were identified with AF (1.72%, 95% confidence interval 1.69%–1.75%). Prevalence was significantly higher for Maori (odds ratio 1.91, 95% confidence interval 1.80–2.03) than Europeans after adjusting for age, sex, deprivation and clinical risk factors. Stroke risk for Maori and Pacific Island patients was higher than for Europeans across all age groups. Of the 10,406 patients (81.9%) at high risk for thromboembolism, 60.5% were using anticoagulants, 24.1% aspirin monotherapy and 15.4% neither anticoagulants nor aspirin. Oral anticoagulants were used by 31.5% of patients at low risk ($CHA_2DS_2$-VASc <2).

# Medicine use by $CHA_2DS_2$-VASc score in patients with AF




European Journal of Preventive Cardiology 2017;24:311–319

# Key points in $CHA_2DS_2$-VASc ≥ 2

- Elderly (> 75yrs)
  - Less likely to be anticoagulated (58% vs 65%)
  - Highest rate of Aspirin prescription (25%)
- Gender
  - Females less likely to be anticoagulated (58% vs 63%)
- Ethnicity
  - Maori patients more likely to be anticoagulated (67% vs 60%)

European Journal of Preventive Cardiology 2017;24:311–319

# Stroke prevention in atrial fibrillation patients

- Vitamin K antagonists – Warfarin vs control (Aspirin or no therapy)
  - Reduce the risk of stroke by two thirds
  - Mortality reduced by one quarter
- Limitations
  - Limited therapeutic window
  - Frequent monitoring and dose adjustment
- Advantages
  - Only effective therapy in AF patients with rheumatic mitral valve disease and/or a mechanical heart valve prosthesis
  - Effective with adequate time in therapeutic range

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# Stroke prevention in atrial fibrillation patients

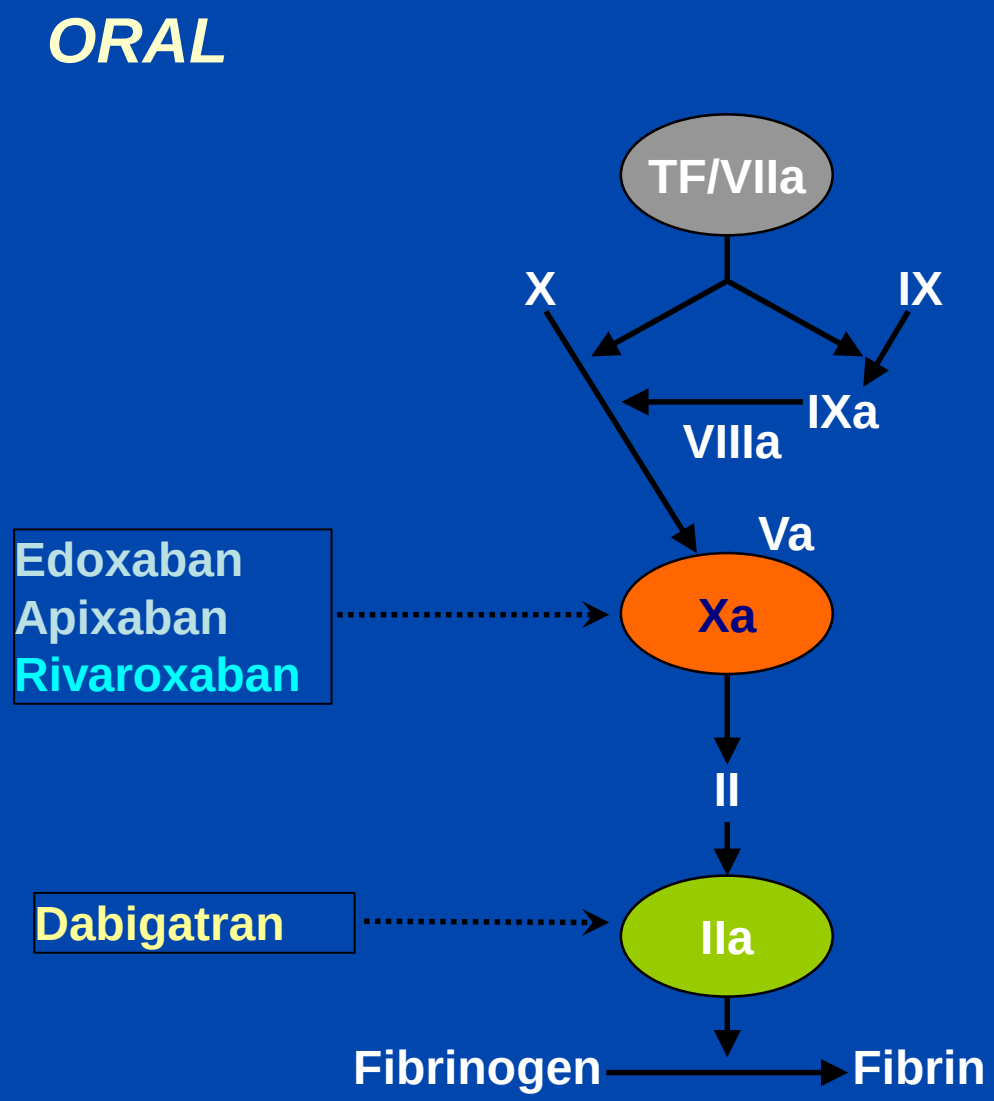
## Antiplatelet Agents

- Aspirin
  - Limited evidence for benefit
  - Stroke reduced by up to 20% - meta-analysis randomised trials
  - No benefit compared to no treatment – several large cohort series
  - Bleeding risk similar to Warfarin and DOACs in the elderly
- Aspirin and Clopidogrel
  - Inferior to oral anticoagulation, annual stroke rate 5.6% for aspirin and clopidogrel vs. 3.9% with Warfarin therapy
  - Bleeding rates higher than antiplatelet monotherapy (2.0% vs. 1.3%)
  - Bleeding rates similar to Warfarin with less benefit

## Not recommended for stroke prevention

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

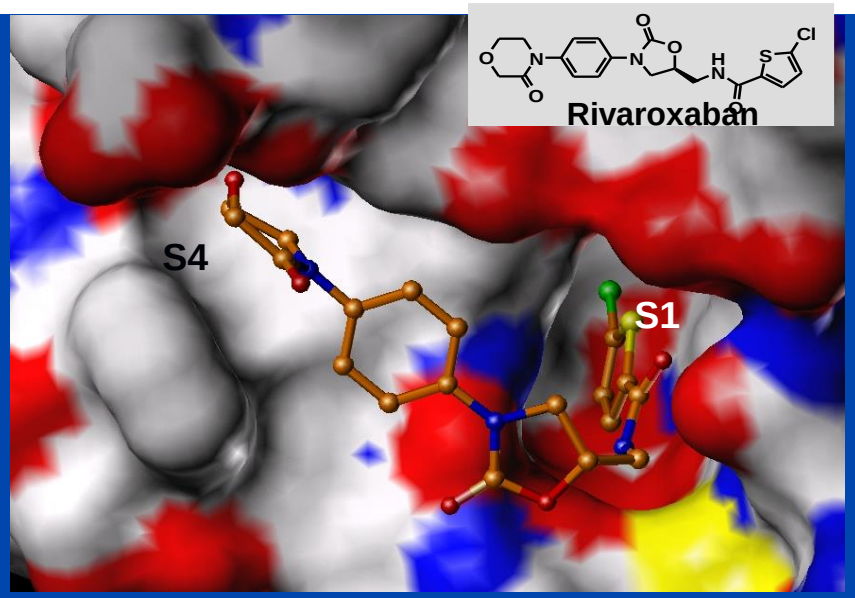
# Direct Oral Anticoagulants – DOAC




Adapted from Weitz & Bates, *J Thromb Haemost* 2007

# Rivaroxaban: Human Factor Xa/rivaroxaban complex

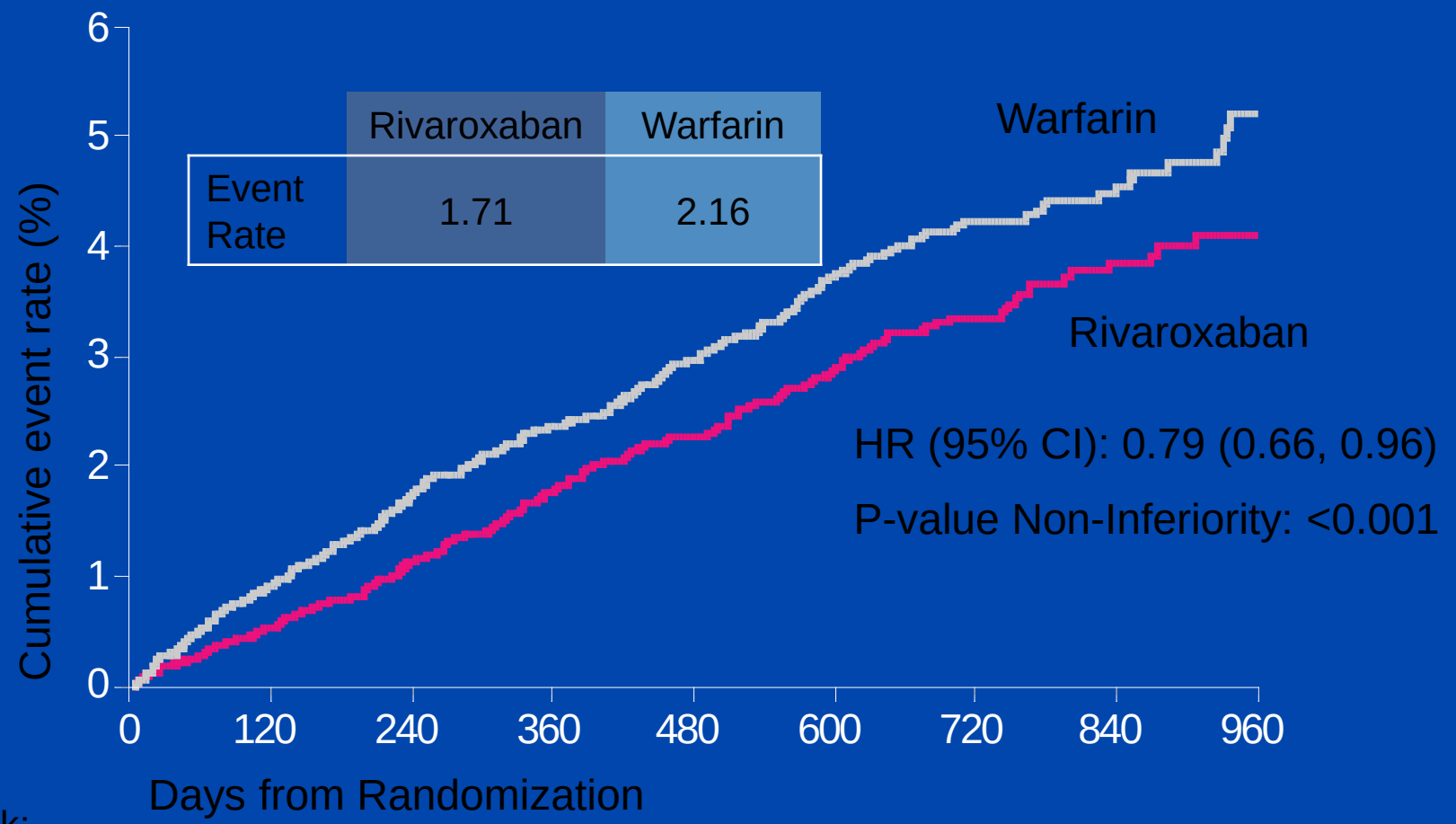
- Should be taken with food to aid absorption
- Peak plasma levels in 2 – 4 hours
- Half life of 5 – 13 hours
- Excretion: 66% liver, 33% renal
- Contraindicated with moderate to severe hepatic dysfunction with coagulopathy
- Requires adjustment for renal impairment (CrCl 30–49 mL/min by Cockroft–Gault formula)
- No requirement for routine coagulation monitoring




Roehrig *et al., J Med Chem* 2005; Perzborn *et al.*, *J Thromb Haemost* 2005

# ROCKET AF STUDY: NEJM 2011; 365:883-891

## Primary Efficacy Outcome: Stroke and non-CNS Embolism




| No. at risk: | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Rivaroxaban | 6958 | 6211 | 5786 | 5468 | 4406 | 3407 | 2472 | 1496 | 634 |
| Warfarin | 7004 | 6327 | 5911 | 5542 | 4461 | 3478 | 2539 | 1538 | 655 |

Event Rates are per 100 patient-years
Based on Protocol Compliant on Treatment Population

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# ROCKET AF STUDY: NEJM 2011; 365:883-891

## Primary Safety Outcomes

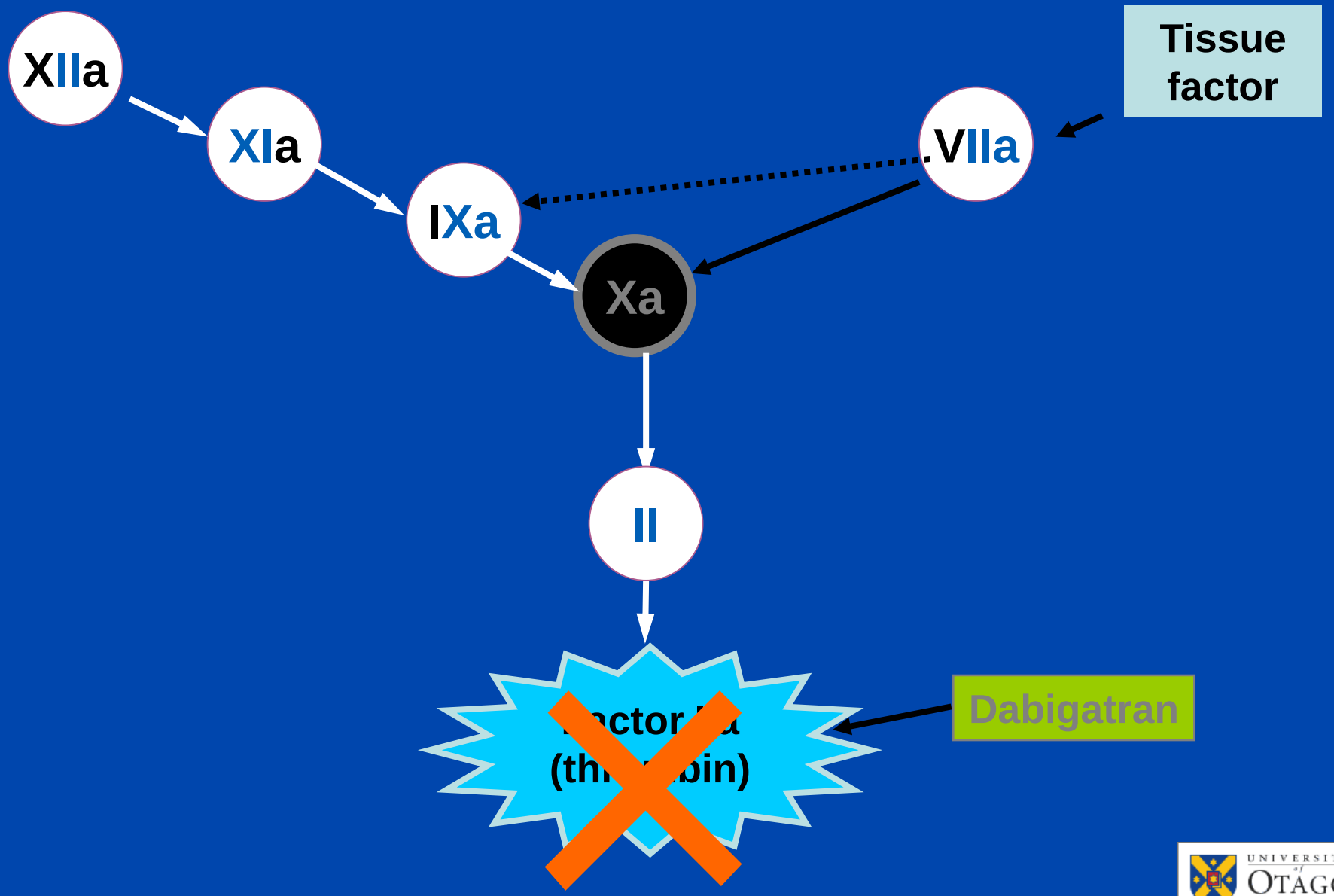
| | Rivaroxaban | Warfarin | | |
|---|---|---|---|---|
| | Event Rate or N (Rate) | Event Rate or N (Rate) | HR (95% CI) | P-value |
| Major | 3.60 | 3.45 | 1.04 (0.90, 1.20) | 0.576 |
| ≥2 g/dL Hgb drop | 2.77 | 2.26 | 1.22 (1.03, 1.44) | 0.019 |
| Transfusion (> 2 units) | 1.65 | 1.32 | 1.25 (1.01, 1.55) | 0.044 |
| Critical organ bleeding | 0.82 | 1.18 | 0.69 (0.53, 0.91) | 0.007 |
| Bleeding causing death | 0.24 | 0.48 | 0.50 (0.31, 0.79) | 0.003 |
| Intracranial Hemorrhage | 55 (0.49) | 84 (0.74) | 0.67 (0.47, 0.94) | 0.019 |
| Intraparenchymal | 37 (0.33) | 56 (0.49) | 0.67 (0.44, 1.02) | 0.060 |
| Intraventricular | 2 (0.02) | 4 (0.04) | | |
| Subdural | 14 (0.13) | 27 (0.27) | 0.53 (0.28, 1.00) | 0.051 |
| Subarachnoid | 4 (0.04) | 1 (0.01) | | |

Event Rates are per 100 patient-years
Based on Safety on Treatment Population

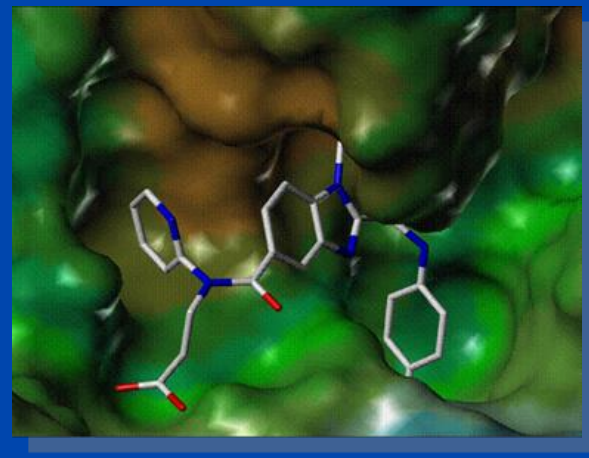
# Summary Rivaroxaban

- **Dose:**
  - 20 mg once daily
  - 15 mg once daily (CrCl 30–49 mL/min by Cockroft–Gault formula)
- **Efficacy**:
  - Rivaroxaban was non-inferior to warfarin
  - Rivaroxaban was superior to warfarin while patients were taking study drug.
- **Safety**:
  - Similar rates of bleeding and adverse events.
  - Less ICH and fatal bleeding with rivaroxaban.
- **Conclusion**:
  - Rivaroxaban is a proven alternative to warfarin for moderate or high risk patients with AF.

# Direct Thrombin inhibition



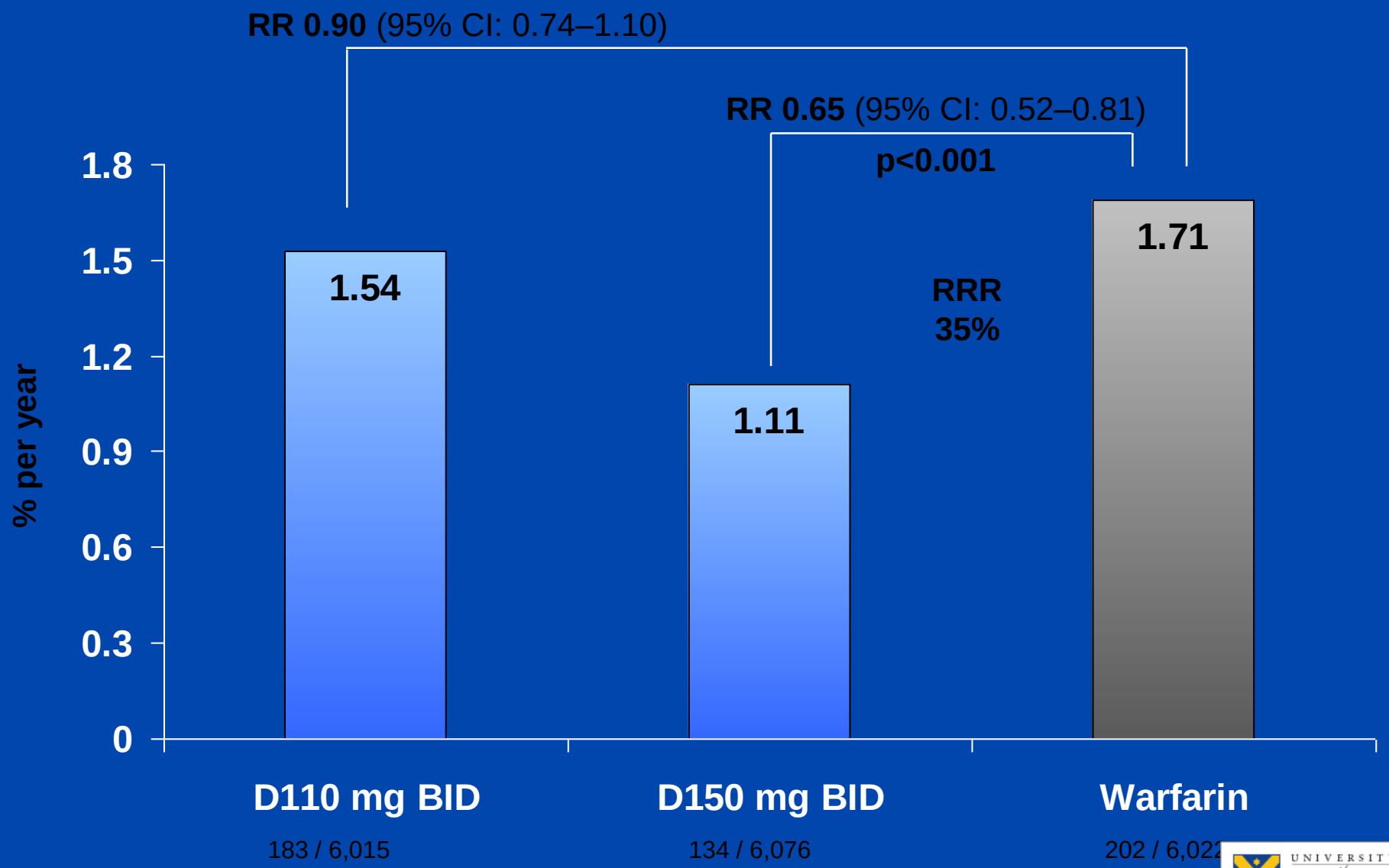
# Dabigatran etexilate: a novel direct thrombin inhibitor



- Oral prodrug, converted to dabigatran
- Peak plasma levels in 2 hours
- Half life of 12 – 17 hours
- ~ 80% renally excreted
- 2 to 3 days treatment for steady state levels
- Predictable and consistent anticoagulant effects
- Low potential for drug-drug interactions, no drug-food interactions
- No requirement for routine coagulation monitoring
- Potent antithrombotic effects are achieved with direct thrombin inhibitors by specifically blocking the activity of thrombin (both free and clot-bound),

Stangier J et al *British Journal of Clinical Pharmacology* 2007, DOI:10.1111/j.1365-2125.2007.02899.
Sorbera LA et al Dabigatran/Dabigatran Etexilate Drugs of the Future 2005; 30 (9): 877-885. Belch S et al. *DMB* 2007; doi:10.1124/dmb.107.019083

# Stroke / Systemic embolism – RELY Trial




Connolly SJ., et al. *N Engl J Med* 2009; 361:1139-1151.

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# Major bleeding and components

Data represents %/year

| Characteristic | D 110 mg | D 150 mg | Warfarin | P-value 110 vs. W | P-value 150 vs. W |
|---|---|---|---|---|---|
| Number of patients (n) | 6015 | 6076 | 6022 | | |
| Major bleeding | | | 3.57 | | |
| - Life threatening | 1.24 | 1.49 | 1.85 | <0.001 | 0.03 |
| - Non-life threatening | 1.83 | 2.06 | 1.92 | 0.65 | 0.39 |
| - Gastrointestinal | | | 1.07 | | |

| Moderate renal impairment GFR 30-50ml/min | D 110 mg | D 150 mg | Elderly ≥ 75 yr | D 110 mg | D 150 mg |
|---|---|---|---|---|---|
| Stroke/SSE rate | 2.4 | 1.3 | | 1.9 | 1.4 |
| Major bleeding | 5.7 | 5.3 | | 4.4 | 5.1 |

Connolly SJ., et al. *N Engl J Med* 2009; 361:1139-1151.

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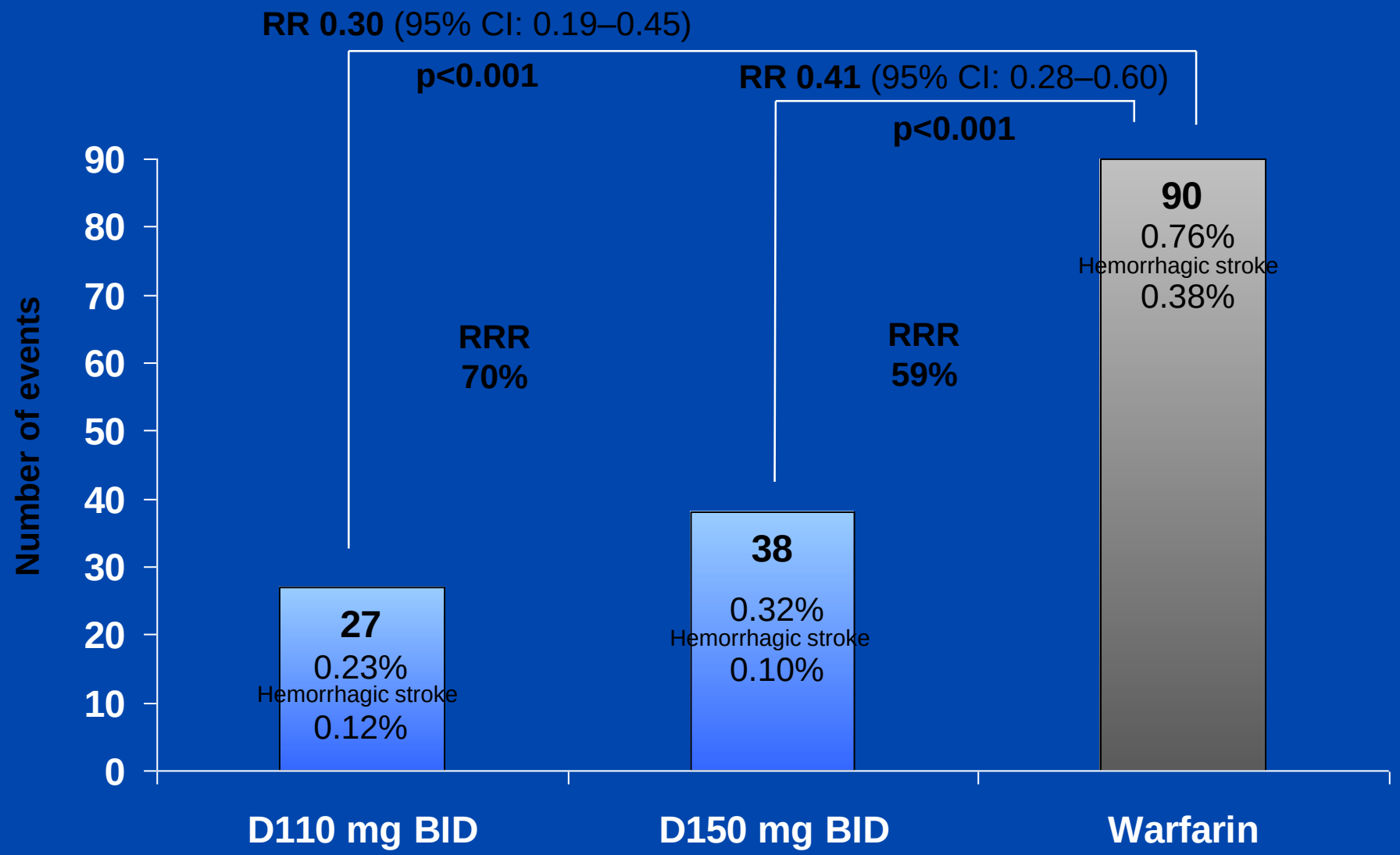
# Intra-cranial bleeding rates



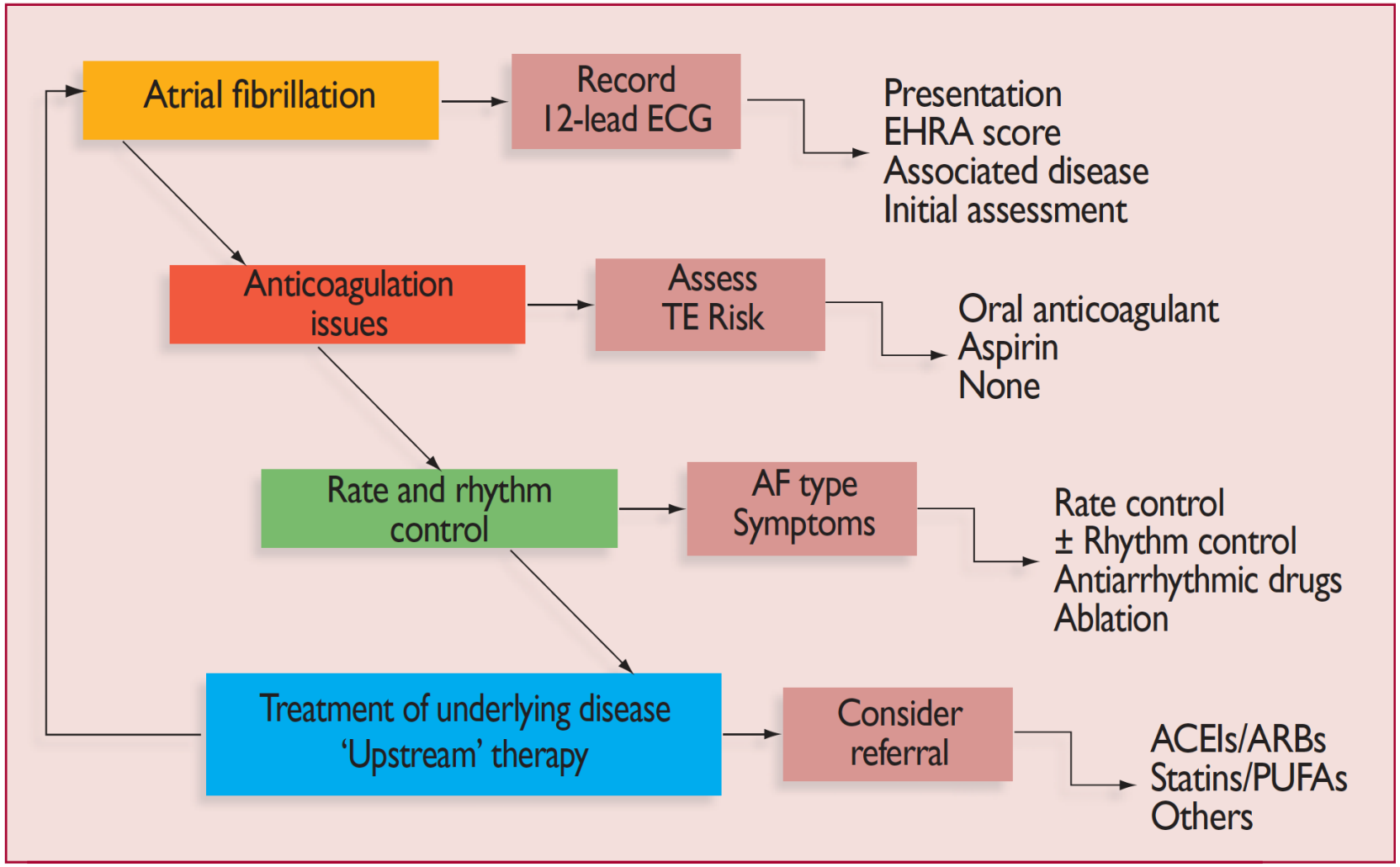

Connolly SJ., et al. *N Engl J Med* 2009; 361:1139-1151.

# Conclusions

- Both doses of dabigatran provide different and complementary advantages over warfarin
  - 150 mg BD has superior efficacy with similar bleeding
  - 110 mg BD has significantly less bleeding with similar efficacy
  - Similar net clinical benefit was seen between the two dabigatran doses

Connolly SJ., et al. *N Engl J Med* 2009; 361:1139-1151.

# Atrial Fibrillation - Management

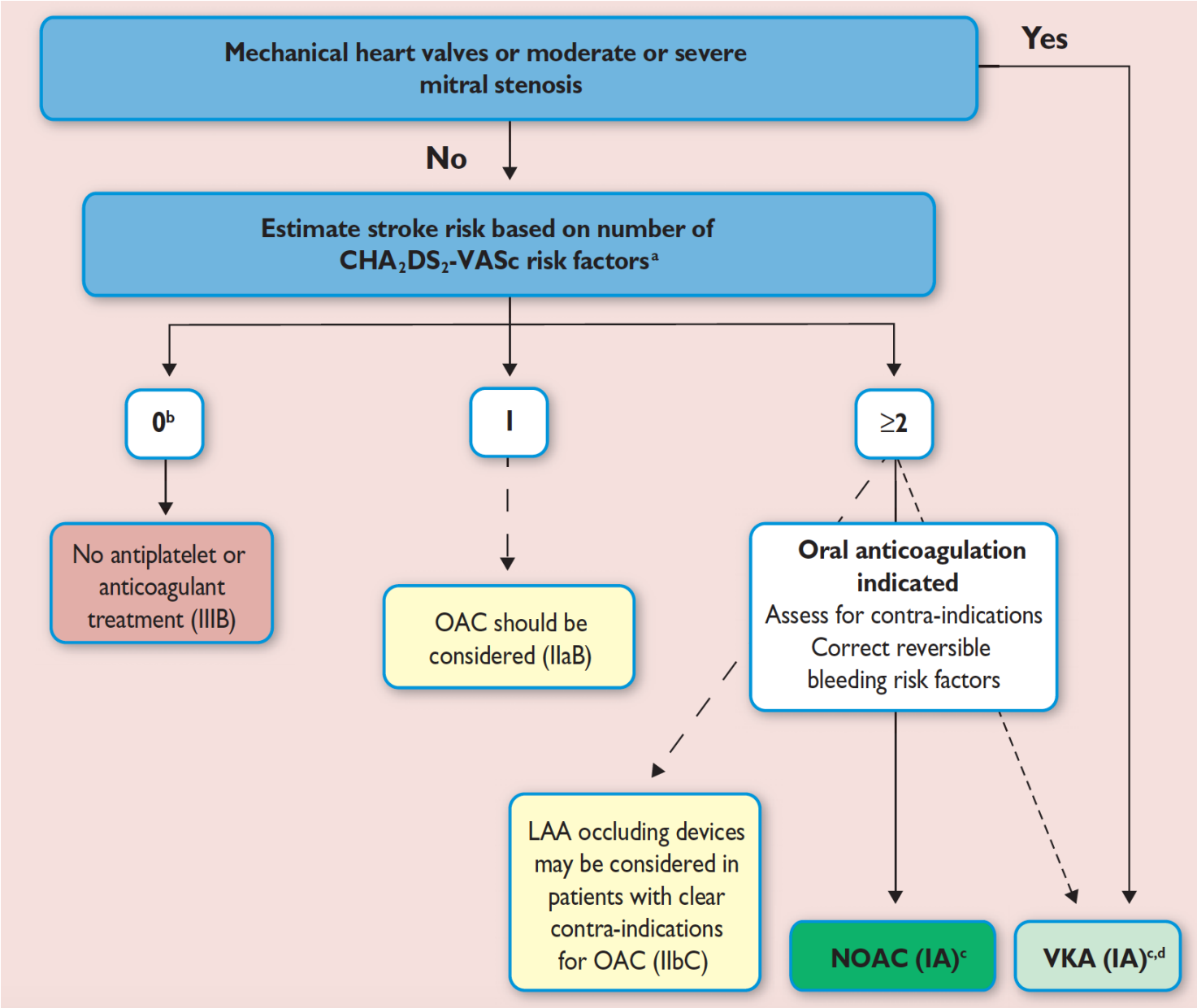



2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism

| $CHA_2DS_2$-VASc risk factor | Points |
|---|---|
| 'C' in $CHA_2DS_2$-VASc refers to moderate-to-severe systolic dysfunction [i.e. heart failure with reduced ejection fraction (HF-REF)] or patients with recent decompensated heart failure requiring hospitalization, irrespective of ejection fraction [i.e. both HF-REF and heart failure with preserved ejection fraction (HF-PEF)] | |
| **Hypertension**<br>Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment | 1 |
| **Age 75 years or older** | 2 |
| **Diabetes mellitus**<br>Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin | 1 |
| **Previous stroke, transient ischaemic attack, or thromboembolism** | 2 |
| **Vascular disease**<br>Previous myocardial infarction, peripheral artery disease, or aortic plaque | 1 |
| **Age 65–74 years** | 1 |
| **Sex category (female)** | 1 |

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962




2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# $CHA_2DS_2$-VASc Score 0 (M) or 1 (F)

- 59 year old male
- Persistent AF
- Normal renal function
- No other risk factors
- $CHA_2DS_2$-VASc score = 0

- 59 year old female
- Persistent AF
- Normal renal function
- No other risk factors
- $CHA_2DS_2$-VASc score = 1

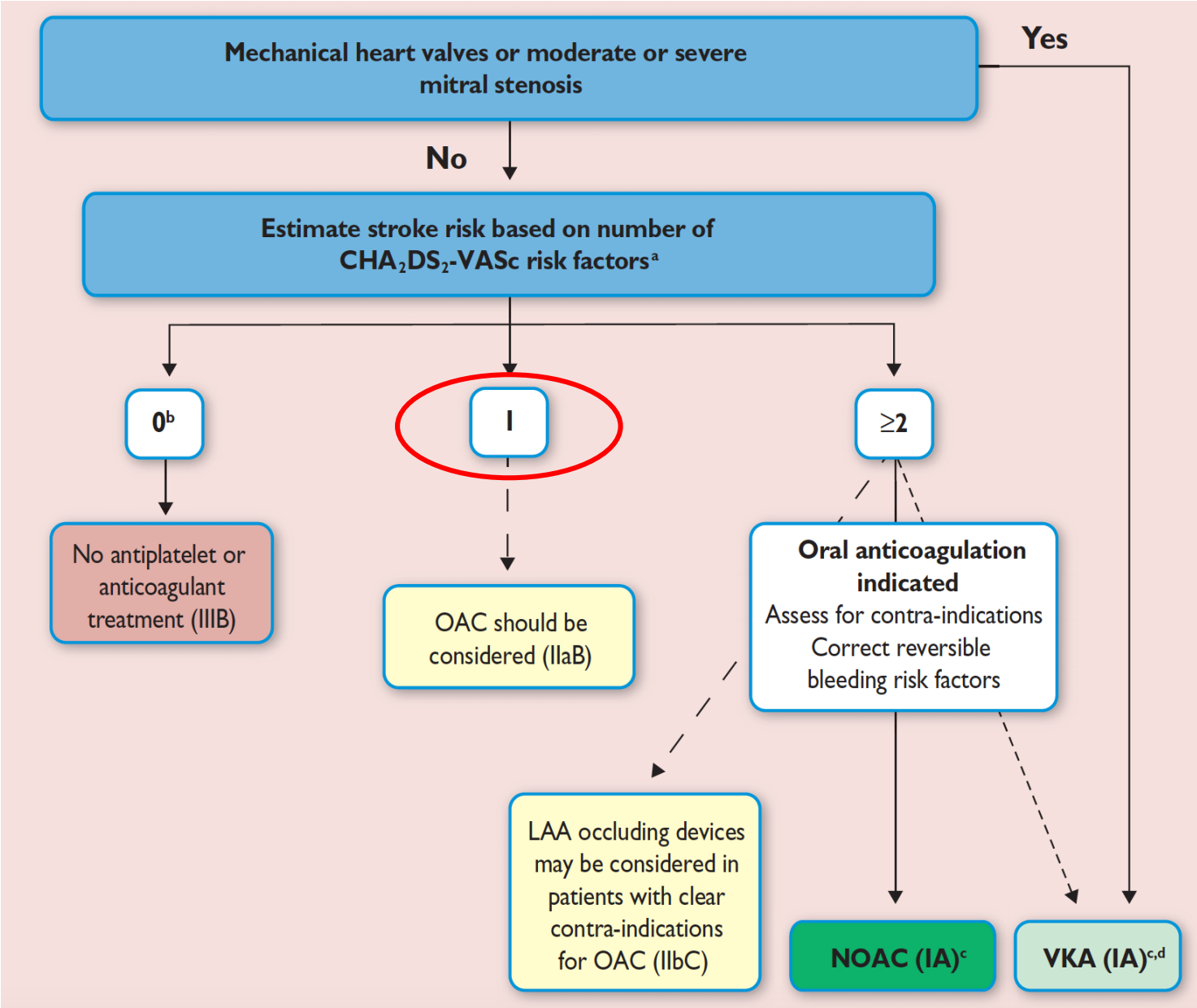
| Recommendations | Class | Level |
|---|---|---|
| In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention. | III (harm) | B |
| Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk. | III (harm) | A |

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# Low to Intermediate Risk
# $CHA_2DS_2$-VASc Score 1 (M) or 2 (F)

- 67 year old male
- Persistent AF
- Normal renal function
- No other risk factors
- $CHA_2DS_2$-VASc score = 1

- 67 year old female
- Persistent AF
- Normal renal function
- No other risk factors
- $CHA_2DS_2$-VASc score = 2

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European Heart Journal 2016; 37: 2893–2962

| Recommendations | Class | Level |
|---|---|---|
| Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a $CHA_2DS_2$-VASc score of 1, considering individual characteristics and patient preferences. | IIa | B |
| Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a $CHA_2DS_2$-VASc score of 2, considering individual characteristics and patient preferences. | IIa | B |

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# Risk factors for ischaemic stroke/TIA/ systemic embolism in patients with AF

| | |
|---|---|
| Age (years)<br><65<br>65–74<br>≥75 | <br>1.0 (Reference)<br>2.97 (2.54–3.48)<br>5.28 (4.57–6.09) |
| Female sex | 1.17 (1.11–1.22) |
| Previous ischaemic stroke | 2.81 (2.68–2.95) |
| Intracranial bleeding | 1.49 (1.33–1.67) |
| Vascular disease (any)<br>• Myocardial infarction<br>• Previous CABG<br>• Peripheral artery disease | 1.14 (1.06–1.23)<br>1.09 (1.03–1.15)<br>1.19 (1.06–1.33)<br>1.22 (1.12–1.32) |
| Hypertension | 1.17 (1.11–1.22) |
| Heart failure (history) | 0.98 (0.93–1.03) |
| Diabetes mellitus | 1.19 (1.13–1.26) |
| Thyroid disease<br>Thyrotoxicosis | 1.00 (0.92–1.09)<br>1.03 (0.83–1.28) |

Eur Heart J 2012;33:2719-47

# Initial Presentation-arrhythmia

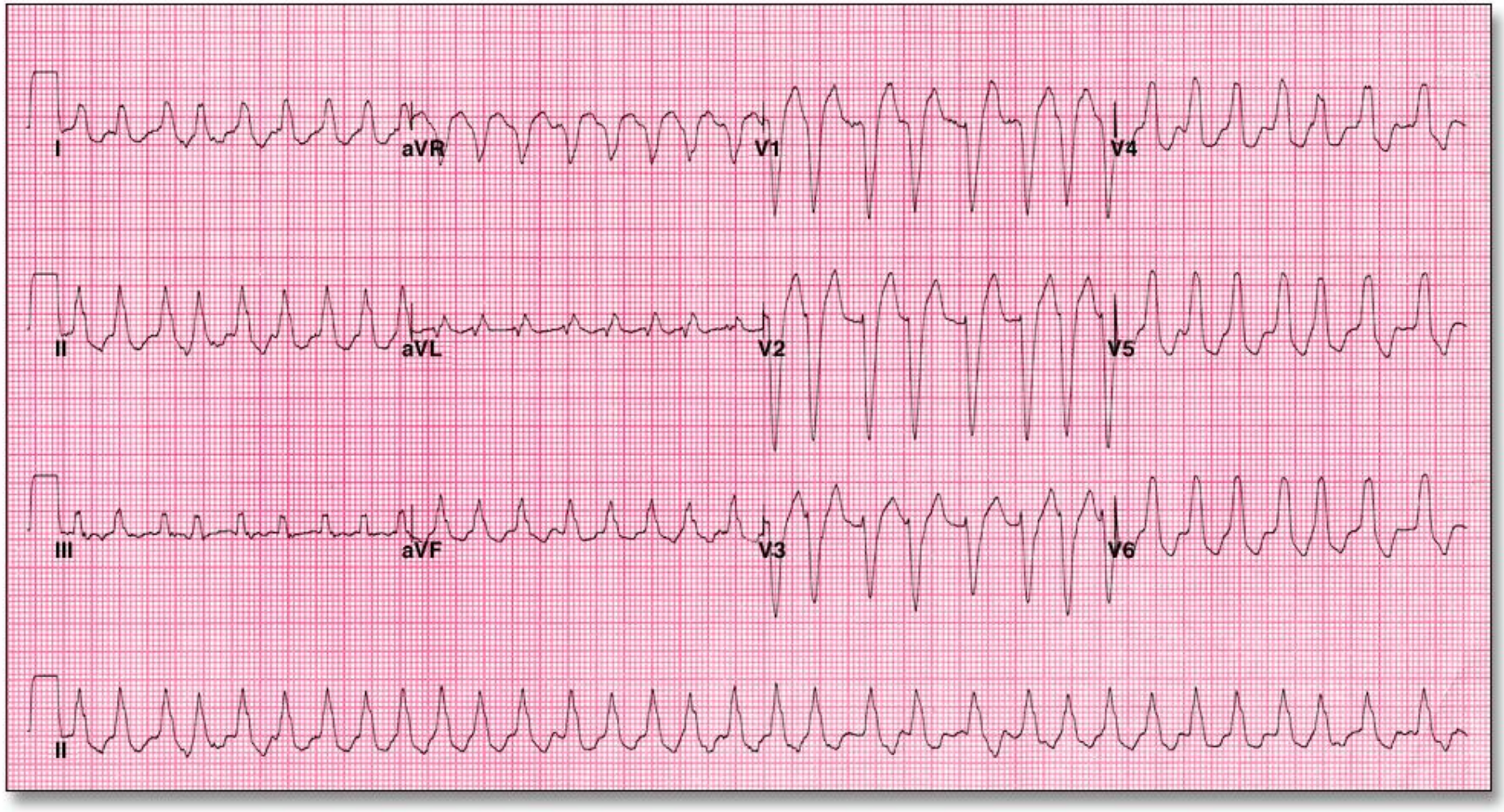
**Chief Complaint:** 69 year old male presents with palpitations, lightheadedness, and dyspnea for 3-4 days

**Past Medical History:** Diabetes mellitus and thyroid nodule

**Blood Pressure:** 117/68 mm Hg
**Pulse:** 155 bpm
**Respiration:** 20
**General Appearance:** No acute distress
**Chest and Lungs:** Clear
**Cardiac Examination:** Irregular tachycardia, S1, S2. No evidence of heart failure

**Test Results:** Normal renal function, GFR 75ml/min

# ECG



# The most appropriate initial treatment is:

A. Cardioversion.

B. Amiodarone.

C. Adenosine.

D. Flecainide.

E. Metoprolol.

# Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism

| $CHA_2DS_2$-VASc risk factor | Points |
|---|---|
| **Congestive heart failure**<br>Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction | 1 |
| **Hypertension**<br>Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment | 1 |
| **Age 75 years or older** | 2 |
| **Diabetes mellitus**<br>Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin | 1 |
| **Previous stroke, transient ischaemic attack, or thromboembolism** | 2 |
| **Vascular disease**<br>Previous myocardial infarction, peripheral artery disease, or aortic plaque | 1 |
| **Age 65–74 years** | 1 |
| **Sex category (female)** | 1 |

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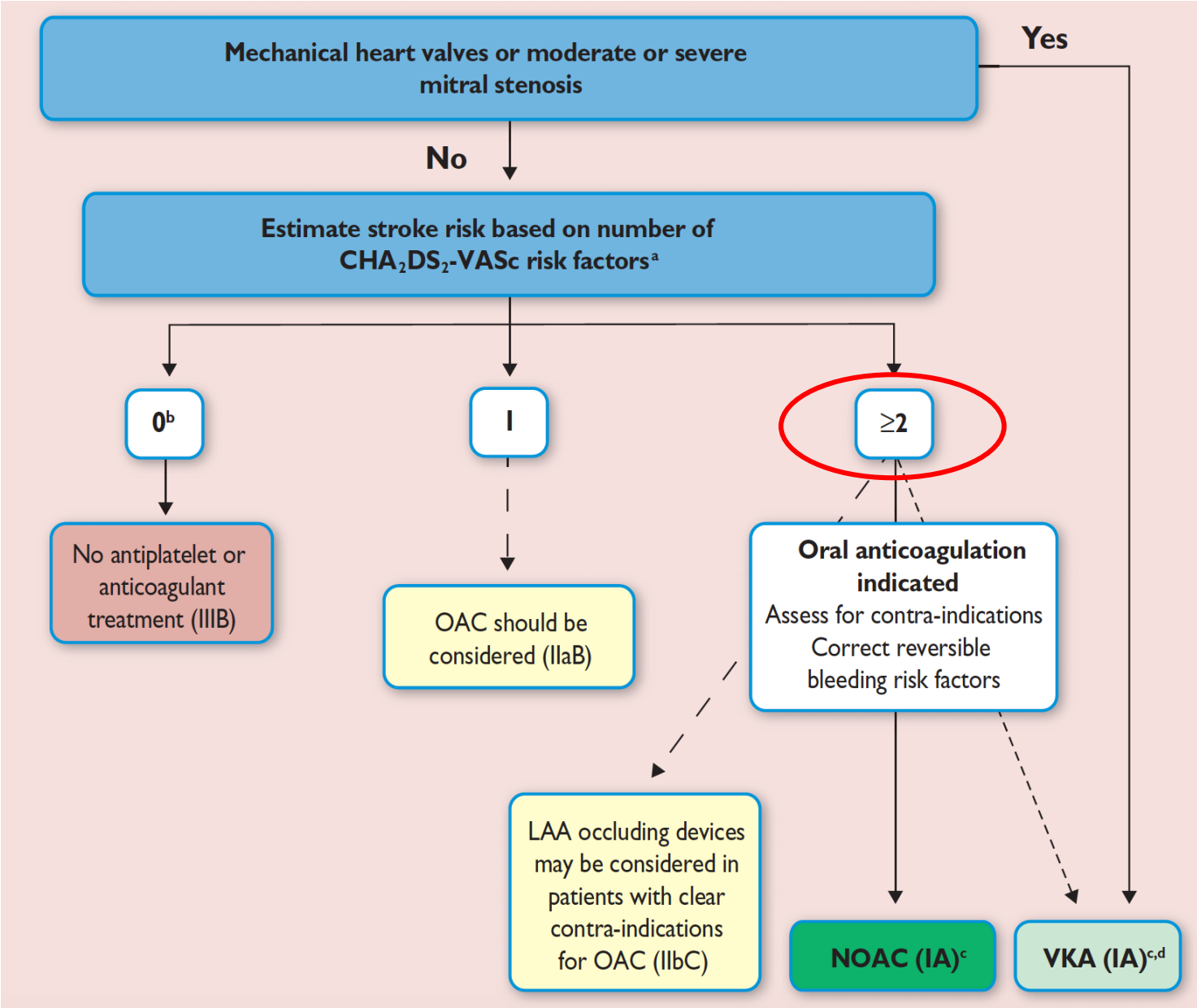


2016 ESC Guidelines for the management of atrial fibrillation
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# HAS-BLED bleeding risk score

| Letter | Clinical characteristic[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 |
| | *Aspirin, Clopidogrel, NSAIDs<br>† > 8 standard units week | Maximum 9 points |

Low risk of bleeding score 0-2. A score of ≥ 3 indicates an increased 1 year bleeding risk indicating caution or more frequent clinical review

# The most appropriate treatment is:

A. Aspirin

B. Warfarin

C. Dabigatran 150mg bd

D. Rivaroxaban 15mg daily

E. Aspirin and Clopidogrel

| Recommendations | Class | Level |
|---|---|---|
| Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a $CHA_2DS_2$-VASc score of 2 or more. | I | A |
| Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a $CHA_2DS_2$-VASc score of 3 or more. | I | A |

## Commentary

The preferred answer is C

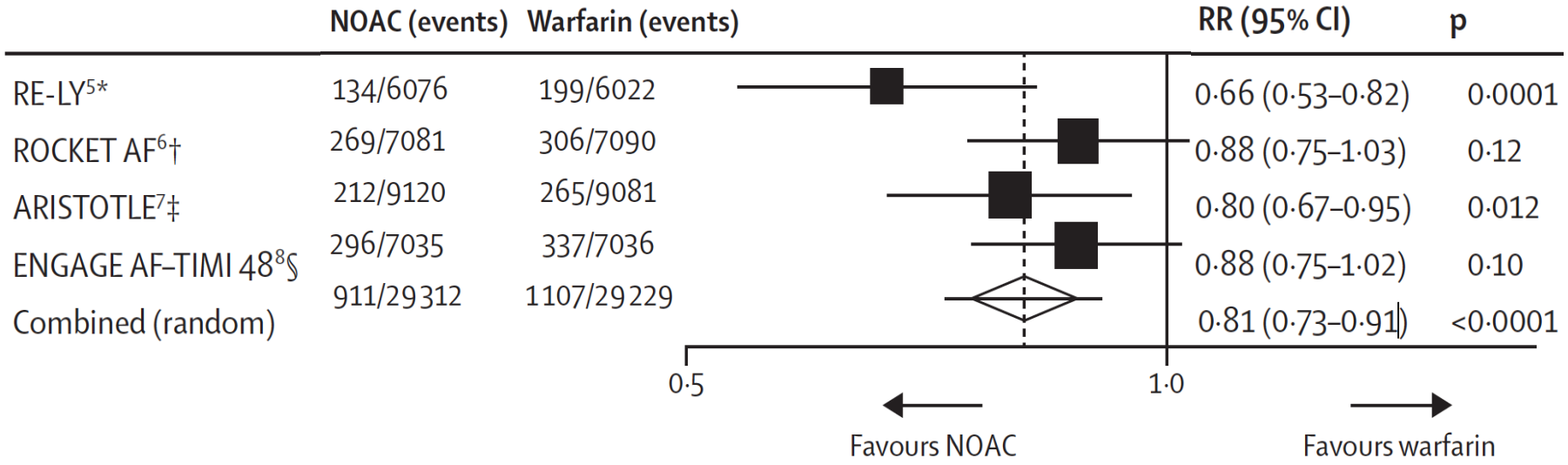
Dabigatran 150mg bd is the recommended dose in the absence of increased bleeding risk or renal impairment

Recommended Rivaroxaban dose is 20mg rather than 15mg daily

Warfarin may be considered as second line therapy

Aspirin (or Aspirin & Clopidogrel) does not provide adequate reduction in the risk of stroke or systemic embolism

# DOAC vs Warfarin in AF




- All cause mortality (0·90, 0·85–0·95; p=0·0003)
- Haemorrhagic stroke (0·49, 0·38–0·64; p<0·0001)
- Intracranial haemorrhage (0·48, 0·39–0·59; p<0·0001)
- Major bleeding (0·86, 0·73–1·00; 0·06)
- Gastrointestinal bleeding (1·25, 1·01–1·55; p=0·04)

Lancet 2014;383;955-62

# Initiating patients on Dabigatran

- Baseline blood tests recommended for all patients
  - Full blood count – platelets to exclude thrombocytopaenia, haemoglobin to assess for anaemia
  - Coagulation screen – APTT ratio to assess for bleeding or clotting disorders, INR for baseline
  - Creatinine and electrolytes – to assess renal function
  - Liver function tests
- Contraindications
  - Mechanical prosthetic valves, mod-severe mitral stenosis
  - GFR < 30ml/hr
- Regular monitoring renal function
  - Annually, caution in chronic kidney disease
  - Acute illness with acute kidney injury
- Dyspepsia
  - Take with food and water, trial of PPI or H2-receptor antagonist

https://bpac.org.nz/2017/anticoagulants.aspx

# Managing bleeding in patients on Dabigatran

- Minor bleeding, external injury
  - Can be treated in primary care with mechanical compression
  - Oral tranexamic acid 15 mg/kg, four times daily, may be appropriate in some cases to increase clotting and prevent excessive blood loss
  - Adequate fluid intake should be encouraged to ensure continued excretion of dabigatran in the urine
- Spontaneous bleeding
  - Generally requires consultation with a haematology service
- Significant bleeding
  - Idarucizumab (Praxbind) is able to rapidly inhibit dabigatran
  - Indicated in patients who have uncontrolled bleeding or who need to undergo urgent surgery

https://bpac.org.nz/2017/anticoagulants.aspx

# Interruption of Therapy With Dabigatran: Elective Procedure

- Prior to elective surgery with normal renal function (creatinine clearance > 50 mL/min):
  - Skip 2 doses (24 hours) of dabigatran
  - Do the procedure
  - Resume anticoagulation as soon as possible following the procedure
- Prior to elective surgery with a creatinine clearance of 30–50 mL/min:
  - Stop dabigatran 3-5 days before the elective procedure
  - Do the procedure
  - Resume anticoagulation as soon as possible following the procedure

# Initial Presentation - arrhythmia

**Presentation:** 85 year old male is evaluated at the time of a routine review for a repeat prescription. No complaints of palpitations. Breathless on walking uphill.
**Medications:** Bendrofluazide 2.5mg daily, Amlodipine 5mg daily Aspirin 100mg daily (All blister packed)
**Past Medical History:** Hypertension
**Blood Pressure:** 142/90 mmHg
**Pulse:** 75 bpm irregularly irregular
**Chest and Lungs:** Clear
**Cardiac Examination:** Heart sounds S1, S2. No murmurs. No heart failure

**Investigations:** Thyroid function normal
Renal function – GFR 36ml/min
ECG - atrial fibrillation

**$CHA_2DS_2$-VASc score = 3**

# HAS-BLED bleeding risk score

| Letter | Clinical characteristic[a] | Points awarded |
|---|---|---|
| H | Hypertension | 1 |
| A | Abnormal renal and liver function (1 point each) | 1 |
| 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 |
| | *Aspirin, Clopidogrel, NSAIDs<br>† > 8 standard units week | Maximum 9 points |

Low risk of bleeding score 0-2. A score of ≥ 3 indicates an increased 1 year bleeding risk indicating caution or more frequent clinical review

# The most appropriate treatment is:

A. Continue Aspirin

B. Warfarin

C. Dabigatran 150mg bd

D. Rivaroxaban 15mg daily

E. Aspirin and Clopidogrel

# Commentary

The preferred answer is D

The recommended Rivaroxaban dose is 15mg daily adjusting for renal function. Rivaroxaban can also be placed in blister packs

Dabigatran 110mg bd is the recommended dose in patients greater than 80 years

Warfarin may be considered as second line therapy

Aspirin significantly less effective than oral anticoagulation in the elderly with a similar risk of major haemorrhage, intracranial and extracranial bleeding (BAFTA trial, Lancet 2007; 370: 493–503)

# Monitoring patients on Rivaroxaban

- Annual testing of renal function is recommended for all patients taking rivaroxaban, as with all anticoagulants
- Patients with declining renal function
  - Future dose reductions may be required
  - GFR < 30ml/hr change to Warfarin
- Missed doses on once daily therapy
  - Take the missed dose later that day, if remembered
  - Otherwise, normal dosing on the next day
  - Don’t take two doses together

https://bpac.org.nz/2018/rivaroxaban.aspx#1

# Switching anticoagulants

- From Warfarin to Rivaroxaban
  - Warfarin should be stopped, an INR taken daily, and rivaroxaban initiated when INR is ≤ 3.0
- From Rivaroxaban to Warfarin
  - Warfarin and rivaroxaban should be taken concurrently and rivaroxaban withdrawn when the patient's INR is ≥ 2.0
- From Dabigatran to Rivaroxaban
  - Take first dose of rivaroxaban 12 hours after last dose of dabigatran

https://bpac.org.nz/2018/rivaroxaban.aspx#1

# Valvular heart disease and atrial fibrillation

**Presentation:** 74 year old female with know moderate aortic stenosis preserved systolic function. No complaints of palpitations
**Medications:** Amlodipine 2.5mg daily, Cilazapril 2.5mg
**Past Medical History:** Hypertension
**Blood Pressure:** 132/90 mmHg
**Pulse:** 75 bpm irregularly irregular
**Chest and Lungs:** Clear
**Cardiac Examination:** 3/6 ejection systolic murmur
No heart failure

**Investigations:** Renal function – GFR 46ml/min
ECG – new atrial fibrillation

**$CHA_2DS_2$-VASc score = 3**
**HAS-BLED score = 2**

# The most appropriate treatment is:

A. Aspirin

B. Warfarin

C. Dabigatran 150mg bd

D. Rivaroxaban 15mg daily

E. Aspirin and Clopidogrel

# Commentary

Answers B, C or D

Warfarin has previously been considered as first line therapy in valvular heart disease with atrial fibrillation.

Emerging evidence favours DOAC rather than warfarin

Dabigatran 150mg bd is the recommended dose for atrial fibrillation with GFR 30–49 mL/min by Cockroft–Gault formula

The recommended Rivaroxaban dose is 15mg daily adjusting for renal function

# Management of atrial fibrillation in patients with VHD

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **Anticoagulation** | | |
| NOACs should be considered as an alternative to VKAs in patients with aortic stenosis, aortic regurgitation and mitral regurgitation presenting with atrial fibrillation.[38–41] | IIa | B |
| NOACs should be considered as an alternative to VKAs after the third month of implantation in patients who have atrial fibrillation associated with a surgical or transcatheter aortic valve bioprosthesis. | IIa | C |

2017 ESC/EACTS Guidelines for the management of valvular heart disease. European Heart Journal 2017;38:2739-91. doi:10.1093/eurheartj/ehx391

# Evolving definition of Valvular Atrial Fibrillation

- Valvular Atrial Fibrillation
  - Generally refers to AF in the setting of moderate-to-severe mitral stenosis (potentially requiring surgical intervention)
  - Or presence of a mechanical heart valve
- Non valvular Atrial Fibrillation
  - May include patients with mild mitral stenosis, mitral regurgitation, aortic stenosis, aortic regurgitation, and tricuspid regurgitation
- DOACS are preferred in non valvular AF
  - Meta analyses suggest DOACS non inferior or superior to warfarin in reducing risk of stroke or systemic embolism
  - Lower risks of serious bleeding

2019 AHA/ACC/HRS Focused Update of Guideline for the Management of Patients With Atrial Fibrillation. Circulation 2019;140:e125–e151

# Chronic Kidney disease and Atrial Fibrillation

**Presentation:** 68 year old female seen for review. Occasional awareness of palpitations.
**Medications:** Frusemide 40mg, Cilazapril 2.5mg, Felodipine 10mg, Atorvastatin 20mg, Lantus 42 units nocte
**Past Medical History:** Hypertension, Type II diabetes, CKD
**Blood Pressure:** 142/80 mmHg
**Pulse:** 85 bpm irregularly irregular (new finding)
**Chest and Lungs:** Clear
**Cardiac Examination:** Heart sounds S1, S2. No murmurs. No heart failure

**Investigations:** ECG – new atrial fibrillation
Renal function – GFR 19ml/min

**$CHA_2DS_2$-VASc score = 4**
**HAS-BLED score = 3**

# The most appropriate treatment is:

A. Dabigatran 150mg bd

B. Rivaroxaban 15mg daily

C. Warfarin, INR 1.5 – 2.0

D. Wafarin, INR 2.0 – 3.0

# Commentary

Answer D preferred

Warfarin is preferred therapy in chronic kidney disease.

Anticoagulation can be safely used in AF patients with moderate or moderate-to-severe CKD [glomerular filtration rate (GFR) ≥15 mL/min].

No controlled trials of NOACs in patients with severe CKD (CrCl ,25–30 mL/min).

2016 ESC Guidelines for the management of atrial fibrillation
European Heart Journal 2016; 37: 2893–2962

# Managing Warfarin in Primary Care

- Monitoring Warfarin
  - Systematic and practice-wide process to ensure consistent and optimal care
  - INR goal is 2.5, clinically acceptable range of 2.0 – 3.0, or 2.5 – 3.5 for patients with mechanical heart valves
- Initiation of Warfarin in Atrial Fibrillation
  - Begin treatment with warfarin 3 mg, daily, with baseline and then weekly INR testing for the first two weeks, with subsequent dose adjustments as appropriate
- Maintenance Warfarin therapy
  - Dose adjustments at least 4 days apart to allow for changes in steady state
  - Patients with stable results only require testing every four to six weeks

https://bpac.org.nz/2017/anticoagulants.aspx