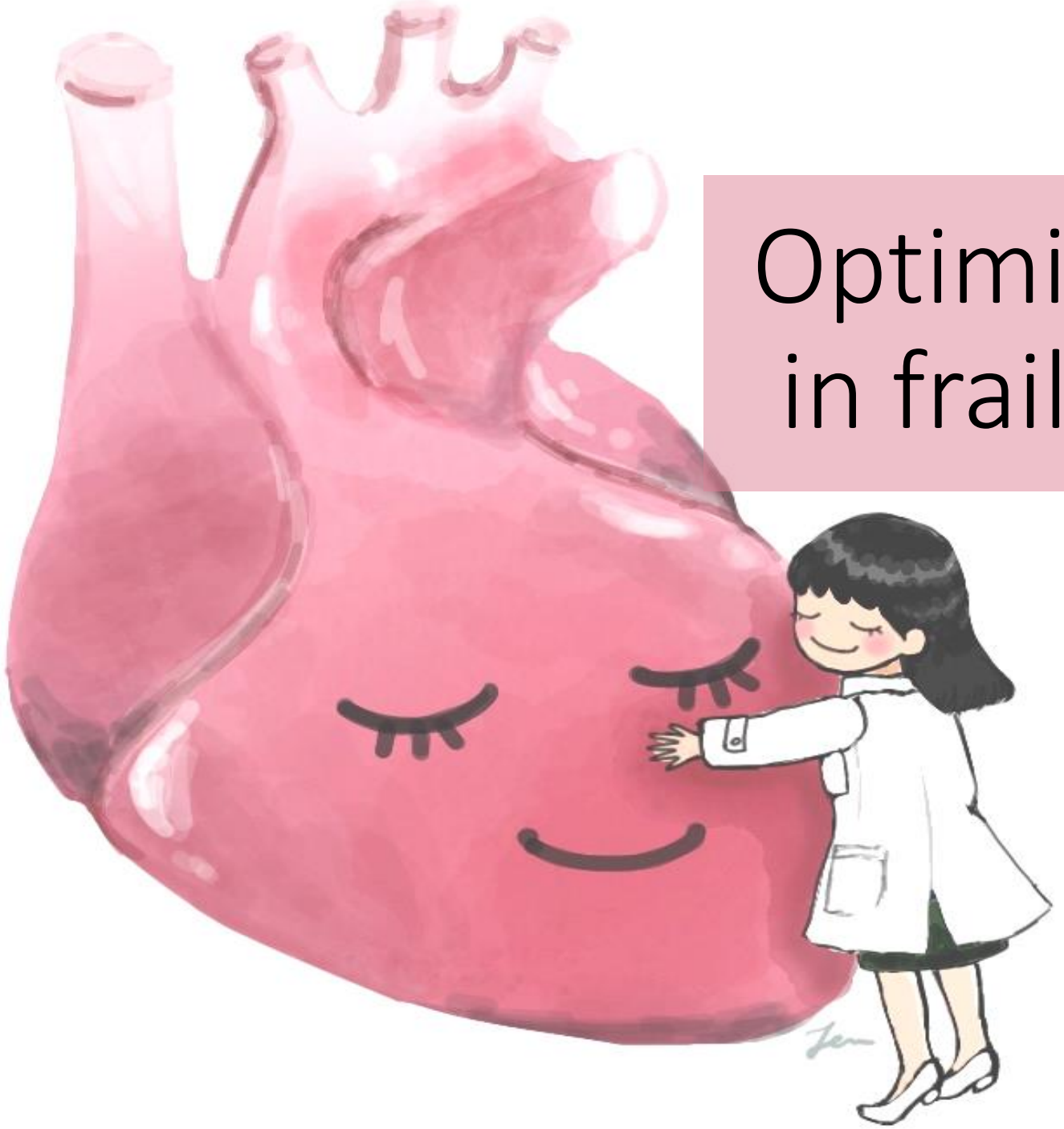


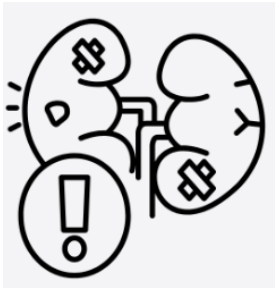
Optimize DOAC treatment in frail patient with NVAF

臺大醫院 吳宜真 藥師

2024.11.17

Case scenario 1

- Antithrombotic agent for 80 yr female, 150 cm, 45 kg, AF, stroke, HTN, CKD (Scr 1.8, eClcr 18 ml/min)
  - (A) Apixaban 2.5 mg bid
  - (B) Edoxaban 30 mg qd
  - (C) Edoxaban 15 mg qd
  - (D) Clopidogrel + Rivaroxaban 2.5 mg bid
  - (E) Dabigatran 110 mg bid
  - (F) Clopidogrel 75 mg qd + edoxaban 15 mg qd
  - (G) Warfarin 2.5 mg hs



Case scenario 2

- Antithrombotic agent for 75 yr male, 165 cm, 70 kg, AF, DM, ACS s/p PCI 2 months ago, Scr 1.1 (eCLcr 57.4 ml/min)
  - (A) Aspirin + clopidogrel + edoxaban 15 mg qd
  - (B) Ticagrelor + rivaroxaban 15 mg qd
  - (C) Prasugrel + dabigatran 110 mg bid
  - (D) Clopidogrel + apixaban 2.5 mg bid
  - (E) Clopidogrel + apixaban 5 mg bid
  - (F) Clopidogrel + edoxaban 30 mg qd

Outline

- 202408 ESC AF guideline updated in pharmaceutical care

- Considerations for DOAC Use in the Elderly AF

ESC
European Society of Cardiology
European Heart Journal (2024) **00**, 1–101
https://doi.org/10.1093/eurheartj/ehae176

ESC GUIDELINES

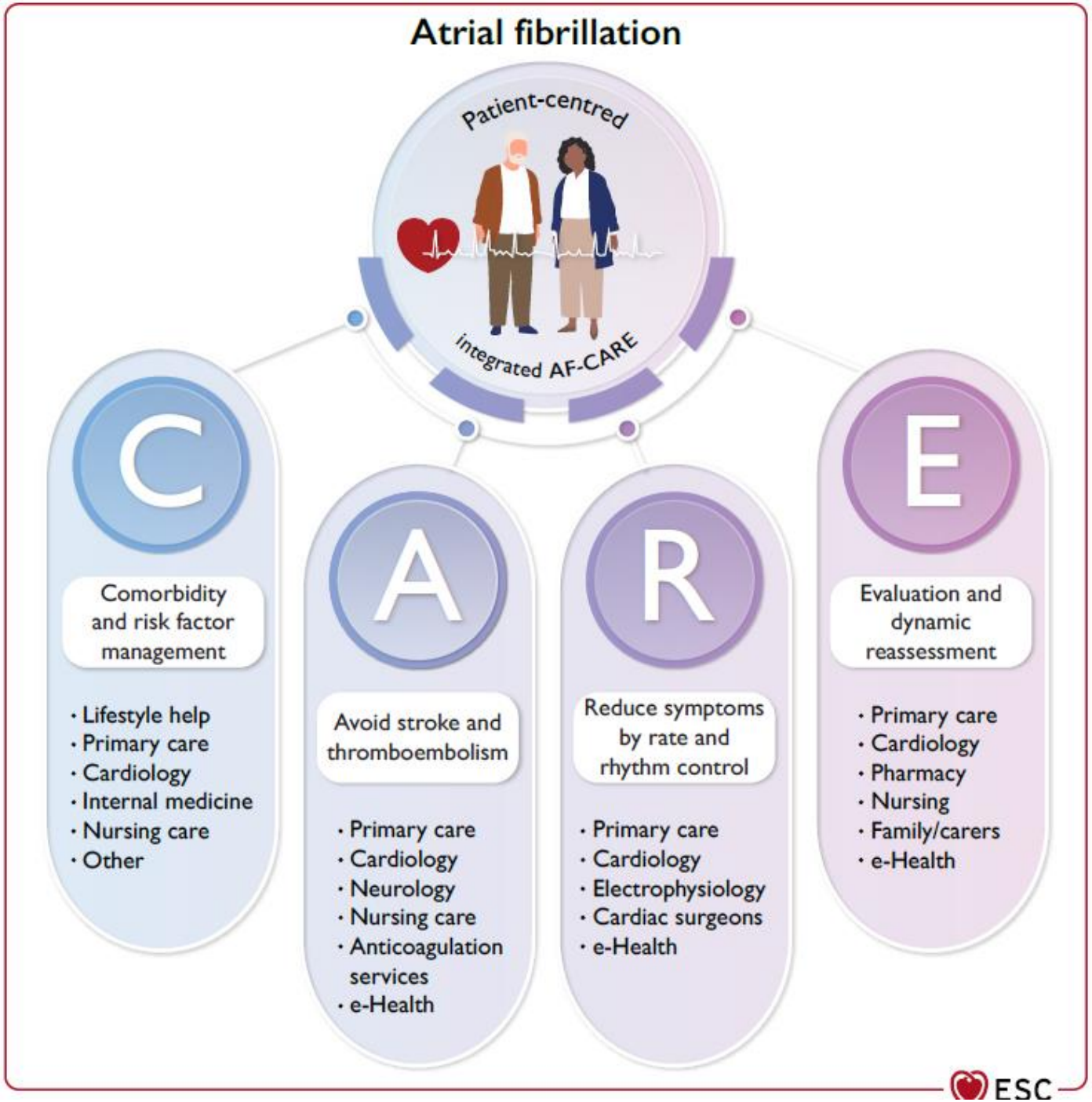
2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

Developed by the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC), with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC.

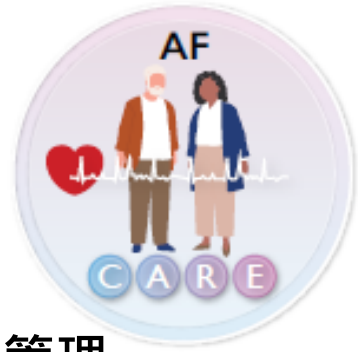
Endorsed by the European Stroke Organisation (ESO)

Multidisciplinary approach to AF management

- C: 處理共病症
- A: 避免中風/血栓
- R: 症狀緩解 (rate/rhythm control)
- E: 評估監測



European Heart Journal (2024) **00**, 1–101



Equality in healthcare provision (gender, ethnicity, socioeconomic) (Class I)

Education for patients, families and healthcare professionals (Class I)

Patient-centred AF management with a multidisciplinary approach (Class IIa)

共病管理

C

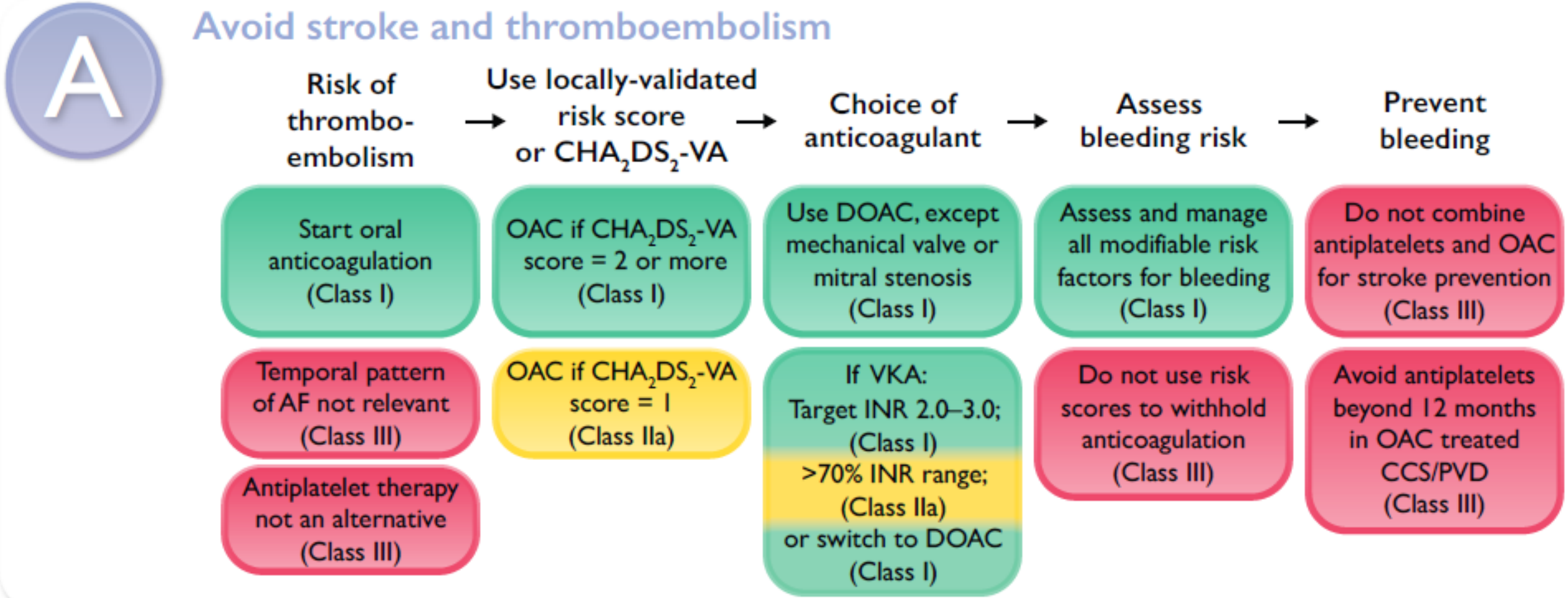
Comorbidity and risk factor management

Target BP 120-129/70-79 mmHg

Hypertension	Heart failure	Overweight or obese	Obstructive sleep apnoea	Alcohol
Blood pressure lowering treatment (Class I)	Diuretics for congestion (Class I)	Weight loss (target 10%)[a] (Class I)	Management of OSA[a] (Class IIb)	Reduce to ≤3 drinks per week (Class I)
	Appropriate HFrEF medical therapy (Class I)	Bariatric surgery if rhythm control[a] (Class IIb)		
Diabetes mellitus			**Exercise capacity**	**Other risk factors/ comorbidities**
Effective glycaemic control[a] (Class I)	SGLT2 inhibitors (Class I)		Tailored exercise programme (Class I)	Identify and manage aggressively[a] (Class I)

European Heart Journal (2024) **00**, 1–101

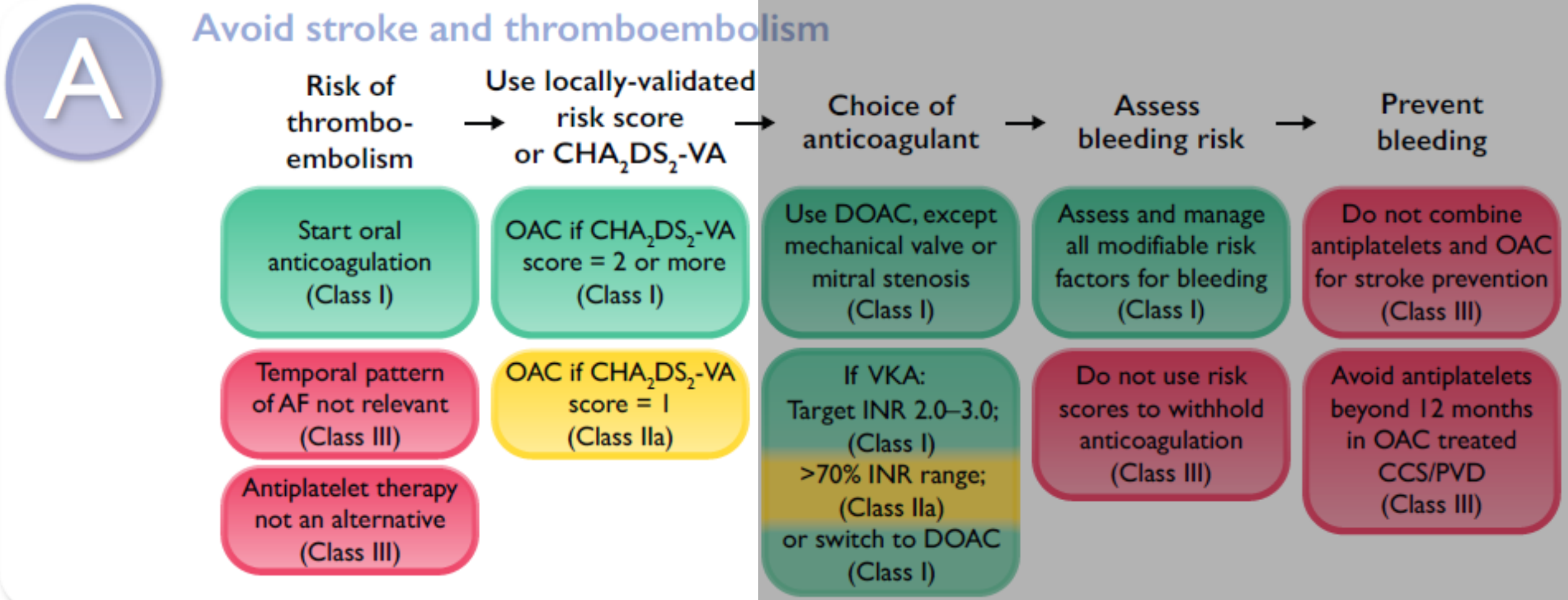
栓塞預防



評估栓塞風險: CHA_2DS_2-VA ≥ 1 考慮用藥　　抗凝藥物選擇　　出血風險評估/減少出血策略

European Heart Journal (2024) **00**, 1–101

栓塞預防



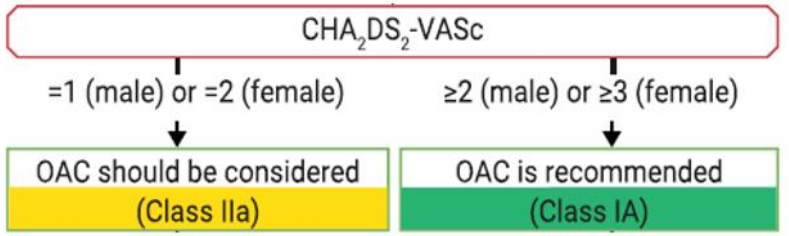
- 用抗凝劑，非抗血小板藥物
- 不依照paroxysmal/persistence/permanent AF來決定是否要抗凝治療
- **CHA_2DS_2-VA ≥ 1 考慮用藥 (2分以上為class I)**

European Heart Journal (2024) **00**, 1–101

CHA_2DS_2-VA score

CHA_2DS_2-VA~~Sc~~ score

2020 ESC AF guideline



CHA_2DS_2-VA component		Definition and comments	
C	Chronic heart failure 有心衰竭症狀,或LVEF≦40%	Symptoms and signs of heart failure (irrespective of LVEF, thus including HFpEF, HFmrEF, and HFrEF), or the presence of asymptomatic LVEF ≤40%.[261–263]	1
H	Hypertension **>140/90 mmHg或有吃血壓藥**	Resting blood pressure >140/90 mmHg on at least two occasions, or current antihypertensive treatment. The optimal BP target associated with lowest risk of major cardiovascular events is 120–129/70–79 mmHg (or keep as low as reasonably achievable).[162,264]	1
A	Age 75 years or above	Age is an independent determinant of ischaemic stroke risk.[265] Age-related risk is a continuum, but for reasons of practicality, two points are given for age ≥75 years.	2
D	Diabetes mellitus	Diabetes mellitus (type 1 or type 2), as defined by currently accepted criteria,[266] or treatment with glucose lowering therapy.	1
S	Prior stroke, TIA, or arterial thromboembolism	Previous thromboembolism is associated with highly elevated risk of recurrence and therefore weighted 2 points. **Peripheral embolism, pulmonary embolism**	2
V	Vascular disease **CAD, PAD**	Coronary artery disease, including prior myocardial infarction, angina, history of coronary revascularization (surgical or percutaneous), and significant CAD on angiography or cardiac imaging.[267] OR Peripheral vascular disease, including: intermittent claudication, previous revascularization for PVD, percutaneous or surgical intervention on the abdominal aorta, and complex aortic plaque on imaging (defined as features of mobility, ulceration, pedunculation, or thickness ≥4 mm).[268,269]	1
A	Age 65–74 years	1 point is given for age between 65 and 74 years.	1

栓塞預防

Avoid stroke and thromboembolism

Risk of thrombo-embolism	Use locally-validated risk score or CHA_2DS_2-VA	Choice of anticoagulant	Assess bleeding risk	Prevent bleeding
Start oral anticoagulation (Class I)	OAC if CHA_2DS_2-VA score = 2 or more (Class I)	Use DOAC, except mechanical valve or mitral stenosis (Class I)	Assess and manage all modifiable risk factors for bleeding (Class I)	Do not combine antiplatelets and OAC for stroke prevention (Class III)
Temporal pattern of AF not relevant (Class III)	OAC if CHA_2DS_2-VA score = 1 (Class IIa)	If VKA: Target INR 2.0–3.0; (Class I) >70% INR range; (Class IIa) or switch to DOAC (Class I)	Do not use risk scores to withhold anticoagulation (Class III)	Avoid antiplatelets beyond 12 months in OAC treated CCS/PVD (Class III)
Antiplatelet therapy not an alternative (Class III)				

抗凝藥物選擇

出血風險評估/減少出血策略

European Heart Journal (2024) **00**, 1–101

Meta-analysis of DOAC vs warfarin in NVAF RCT

Dabigatran 150 mg bid
Rivaroxaban 20 mg qd
Apixaban 5 mg bid
Edoxaban 60 m qd

DOAC 有效**減少栓塞及重大出血風險**

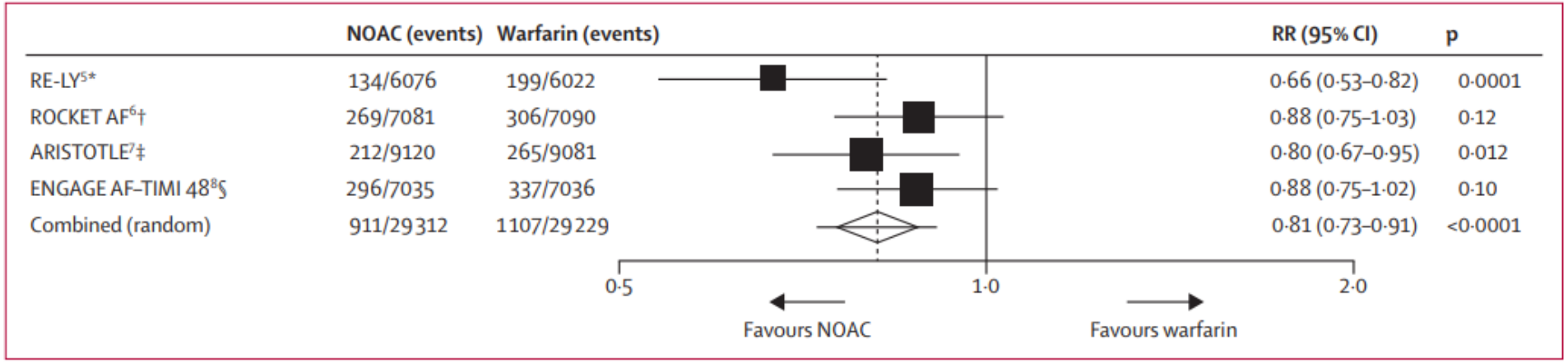


***Figure 1*: Stroke or systemic embolic events**
Data are n/N, unless otherwise indicated. Heterogeneity: I^2=47%; p=0·13. NOAC=new oral anticoagulant. RR=risk ratio. *Dabigatran 150 mg twice daily. †Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. §Edoxaban 60 mg once daily.

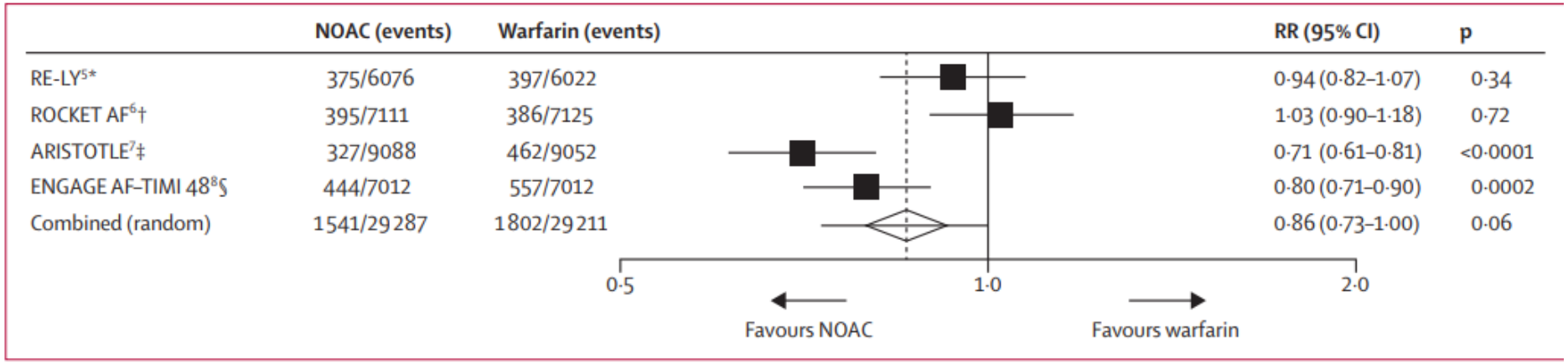


***Figure 3*: Major bleeding**

<u>禁忌:</u>

- **機械性心臟瓣膜置換**
- **中重度的二尖瓣狹窄**
- **懷孕**
- **正在重大出血、嚴重肝(腎)功能不全、APS(抗磷脂質症候群)**

Lancet 2014; 383: 955–62

口服抗凝血藥品(OAC)

Warfarin

Direct oral anticoagulant (DOAC)
Non-vitamin K antagonist (NOAC)

warfarin

dabigatran

apixaban

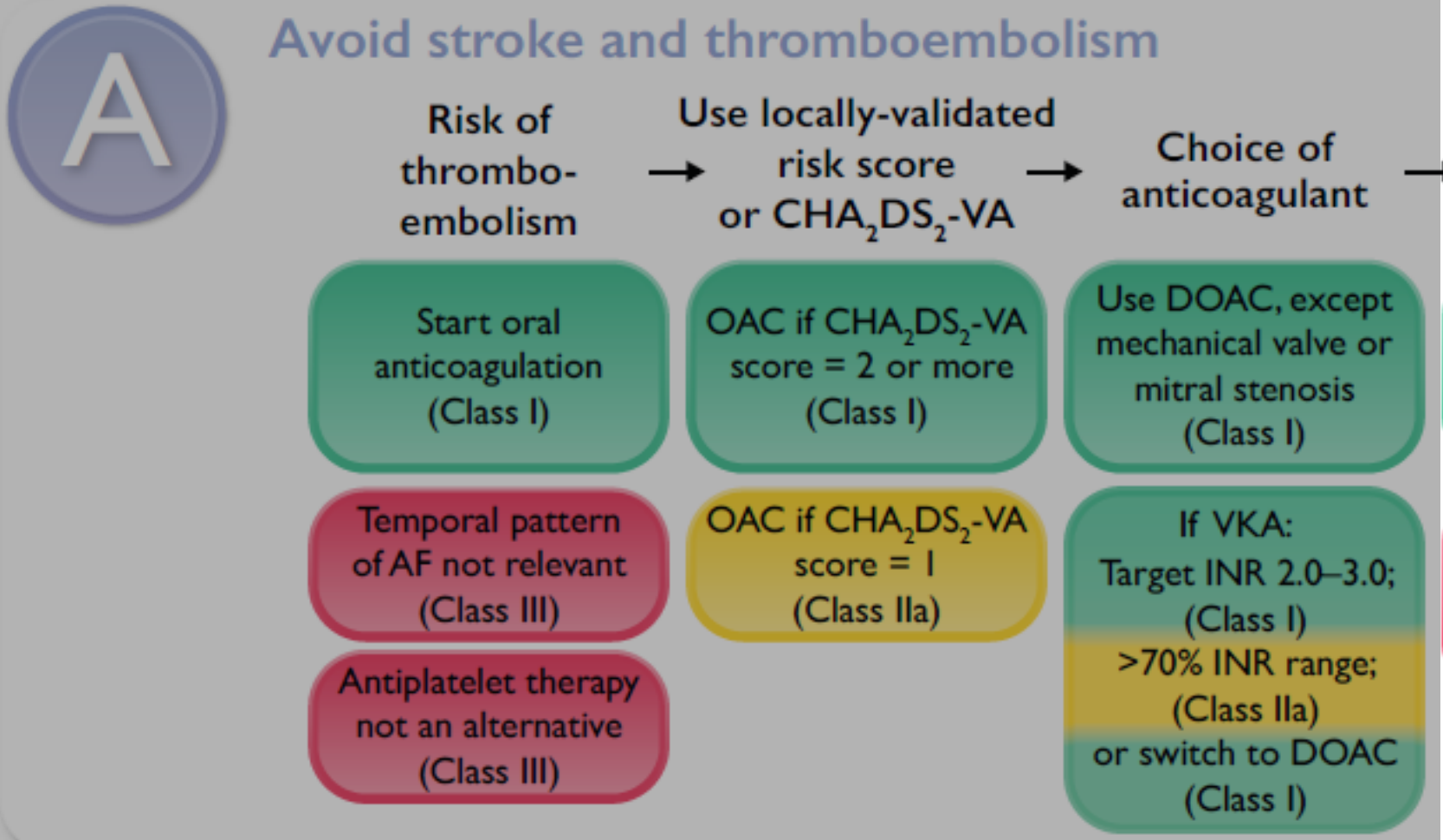
- INR目標為2-3 (ESC)，須維持TTR (Time in therapeutic range)>70%並規則追蹤INR
- 如果TTR<70%，建議換成DOAC (如沒有禁忌症)
- 年紀≥ 75歲且服用多種藥物的臨床穩定使用VKA者(TTR~70%)可以考慮維持治療避免過度出血風險 (class IIb) (Circulation 2024 FRAIL-AF)

rivaroxaban

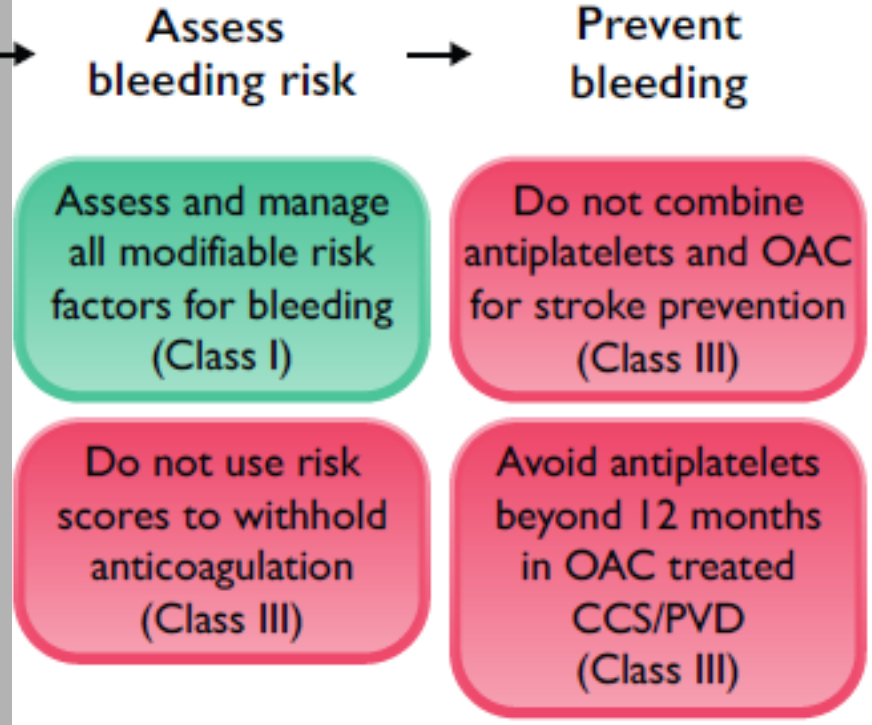
edoxaban

European Heart Journal (2024) **00**, 1–101

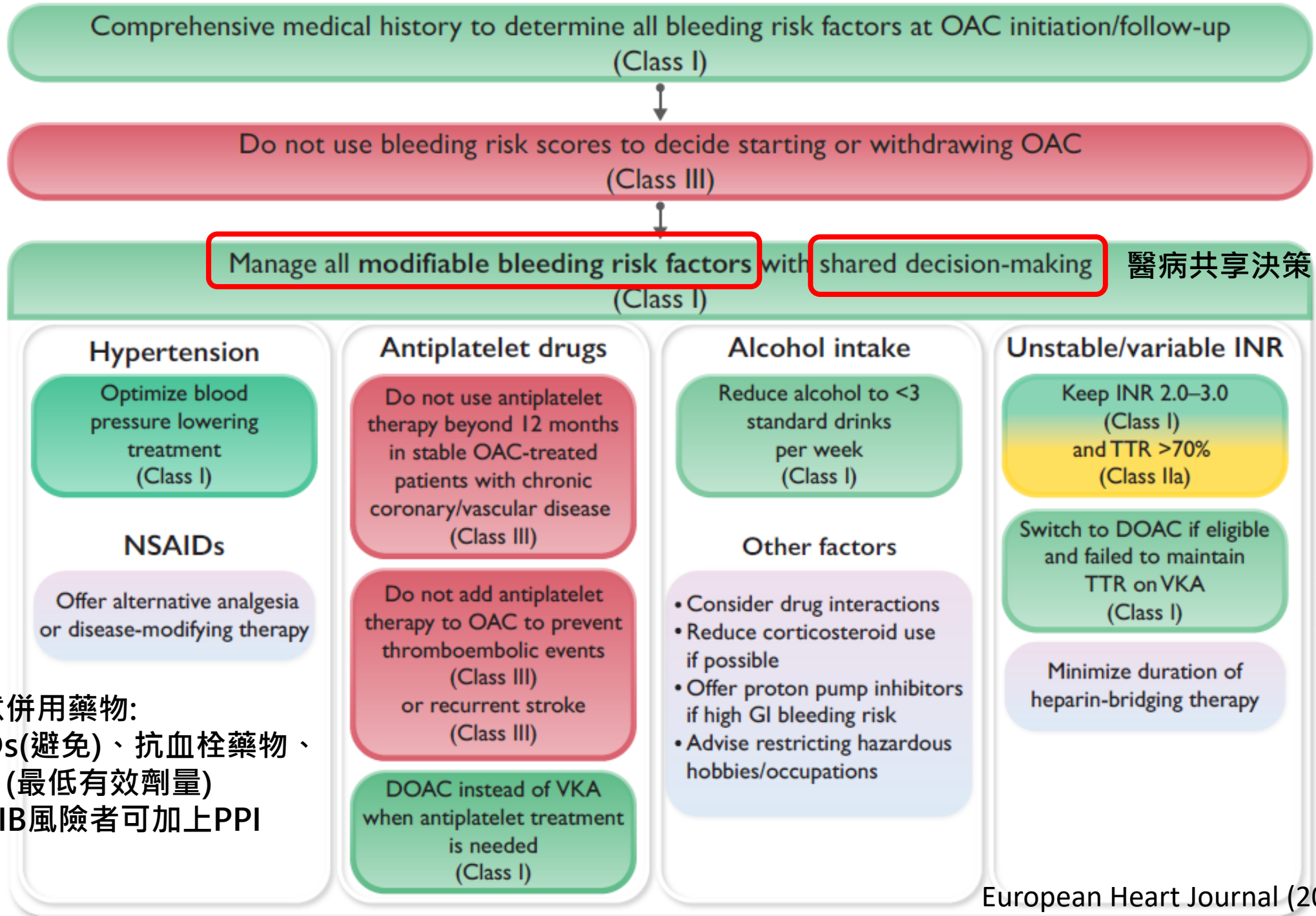
栓塞預防



出血風險評估/減少出血策略



European Heart Journal (2024) **00**, 1–101



醫病共享決策 (SDM)

控壓
限酒

控制INR, TTR

如果TTR控制不佳則考慮換成DOAC

- 留意併用藥物:
NSAIDs(避免)、抗血栓藥物、類固醇 (最低有效劑量)
- 高GIB風險者可加上PPI

European Heart Journal (2024) **00**, 1–101

症狀緩解

R Reduce symptoms by rate and rhythm control

See patient pathways for:

First-diagnosed AF | Paroxysmal AF | Persistent AF | Permanent AF

Consider:

Rate control drugs | Cardioversion | Antiarrhythmic drugs | Catheter ablation | Endoscopic/hybrid ablation | Surgical ablation | Ablate and pace

評估監測

E Evaluation and dynamic reassessment

Re-evaluate when AF episodes or non-AF admissions

Regular re-evaluation: 6 months after presentation, and then at least annually or based on clinical need

ECG, blood tests, cardiac imaging, ambulatory ECG, other imaging as needed

Assess new and existing risk factors and comorbidities (Class I)

危險因子共病症

Stratify risk for stroke and thromboembolism (Class I)

中風/栓塞預防

Check impact of AF symptoms before and after treatment (Class I)

症狀評估

Assess and manage modifiable bleeding risk factors (Class I)

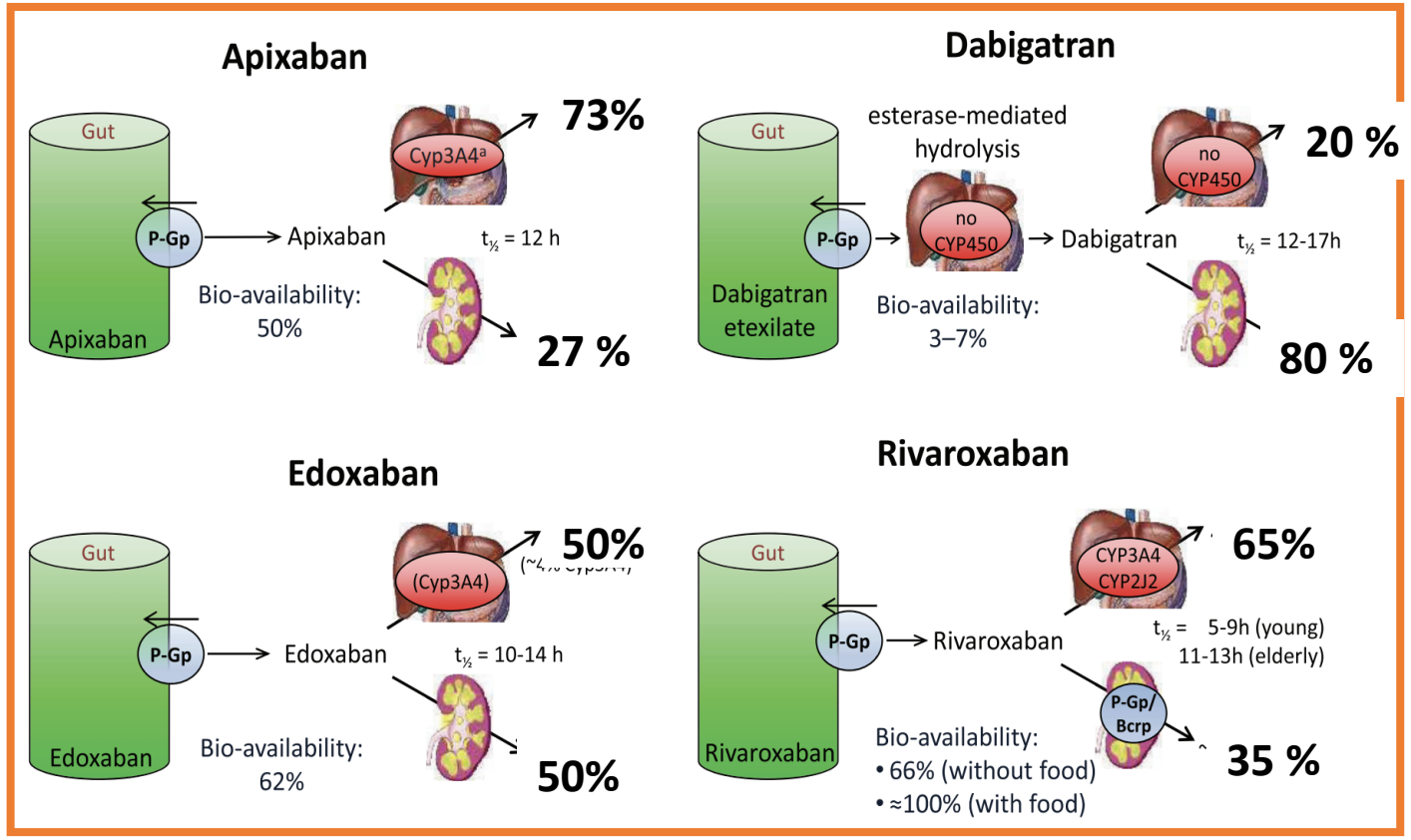
減少出血危險因子

Continue OAC despite rhythm control if risk of thromboembolism (Class I)

持續OAC的使用

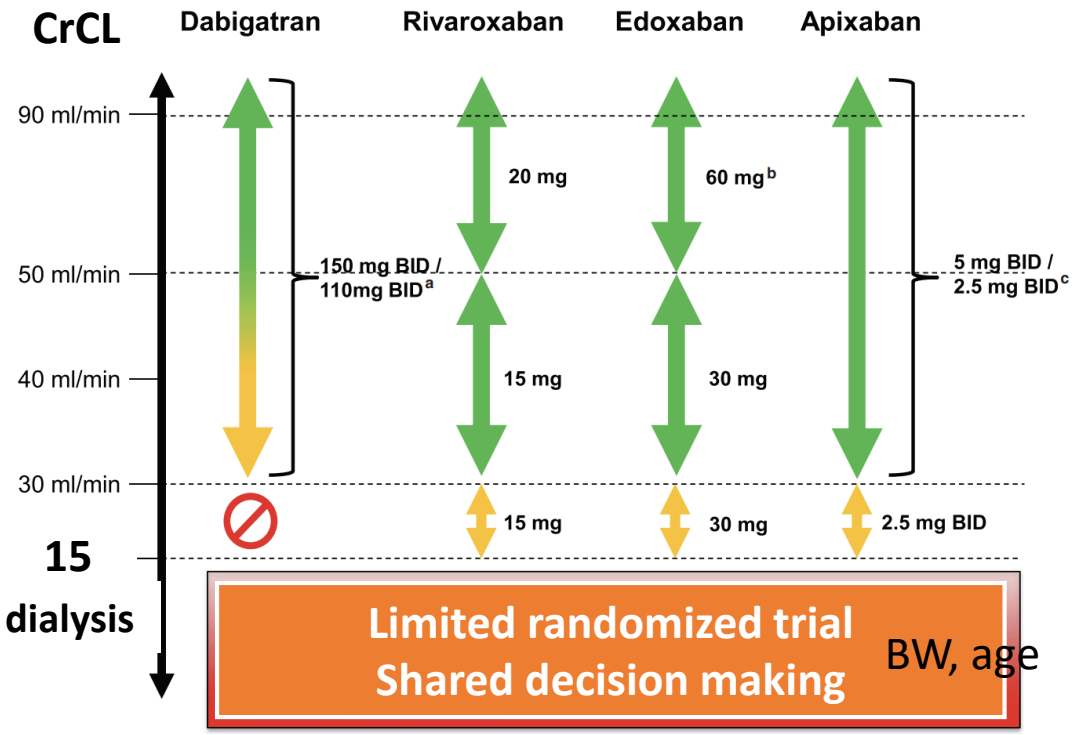
European Heart Journal (2024) **00**, 1–101

DOAC: pharmacokinetics



Europace (2021) 23, 1612–1676

Dose adjustment



NOAC Use recommendations in liver disease

	A (<7 pts)	B (7-9 pts)	C (>9 pts)
Dabigatran	Normal dose	Use with caution	Not recommended
Apixaban			
Edoxaban			
Rivaroxaban		Not recommended	

Table 11 Recommended doses for direct oral anticoagulant therapy

DOAC	Standard full dose	Criteria for dose reduction	Reduced dose only if criteria met
Apixaban	5 mg twice daily	Two out of three needed for dose reduction: (i) age ≥80 years (ii) body weight ≤60 kg (iii) serum creatinine ≥133 mmol/L. (Scr ≥ 1.5)	2.5 mg twice daily
Dabigatran	150 mg twice daily	Dose reduction recommended if any apply: (i) age ≥80 years (ii) receiving concomitant verapamil. Dose reduction considered on an individual basis if any apply: (i) age 75–80 (ii) moderate renal impairment (creatinine clearance 30–50 mL/min) (iii) patients with gastritis, oesophagitis, or gastro-oesophageal reflux (iv) others at increased risk of bleeding.	110 mg twice daily
Edoxaban	60 mg once daily	Dose reduction if any apply: (i) moderate or severe renal impairment (creatinine clearance 15–50 mL/min) (ii) body weight ≤60 kg (iii) concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole.	30 mg once daily
Rivaroxaban	20 mg once daily	Creatinine clearance 15–49 mL/min.	15 mg once daily

三項符合兩項則調整劑量(ABC)

Europe: 年紀≥80歲或與verapamil並用則降低劑量

高流血風險者考慮降低劑量

Taiwan:
BW<50 kg

BCD criteria

Clcr 15-49 則降低劑量

Taiwan: 10-15 mg qd for
Clcr 15-49 ml/min

Vitamin K antagonist oral anticoagulants	Direct oral anticoagulants			
	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Avoid where possible NSAIDs Fluconazole Voriconazole Fluoxetine	**Avoid where possible** Carbamazepine Phenytoin Phenobarbital Rifampicin Ritonavir Itraconazole Ketoconazole	**Avoid where possible** Dronedarone Carbamazepine Phenytoin Rifampicin Ritonavir Itraconazole Ketoconazole Cyclosporin Glecaprevir/pibrentasvir Tacrolimus	**Avoid where possible** Carbamazepine Phenytoin Phenobarbital Rifampicin Ritonavir	**Avoid where possible** Dronedarone Carbamazepine Phenytoin Phenobarbital Itraconazole Ketoconazole Posaconazole Voriconazole Rifampicin Ritonavir
Reduce warfarin dose Amiodarone Metronidazole Sulphonamides Allopurinol Fluvastatin Gemfibrozil Fluorouracil	**Avoid or reduce apixaban dose if another interacting drug therapy** Posaconazole Voriconazole Protease inhibitors Apalutamide Enzalutamide Tyrosine kinase inhibitors	**Delay timing of drugs and/or adjust dose** Amiodarone Ticagrelor Verapamil Quinidine Clarithromycin Posaconazole	**Avoid or reduce edoxaban dose** Dronedarone **Avoid or reduce edoxaban dose if another interacting drug therapy** Cyclosporin Itraconazole Ketoconazole Erythromycin	**Avoid if another interacting drug therapy** Protease inhibitors Tyrosine kinase inhibitors **Caution if renal function impaired** Verapamil Cyclosporin Clarithromycin Erythromycin Fluconazole
Increase warfarin dose Carbamazepine				
Monitor INR carefully Dronedarone Statins Penicillin antibiotics Macrolide antibiotics Quinolone antibiotics Rifampicin Methotrexate Ritonavir Phenytoin Sodium valproate Tamoxifen Chemotherapies	**Limit consumption** Grapefruit juice St John's wort	**Limit consumption** Grapefruit juice St John's wort	**Limit consumption** Grapefruit juice St John's wort	**Limit consumption** Grapefruit juice St John's wort
Limit consumption Alcohol Grapefruit/cranberry juice St John's wort				

	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
p-gp 受質	Yes	Yes	Yes	Yes
CYP3A4 受質	Yes (~25%)	No	No (<4%)	Yes (~18%)

ESC

ESC European Society of Cardiology
Europace (2021) **00**, 1–65
doi:10.1093/europace/euab065

POSITION PAPER
EHRA PRACTICAL GUIDE

2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation

Merative **Micromedex**®

Home | Drug Interactions | IV Compatibility | Drug ID | Drug Comparison | CareNotes | NeoFax Pediatric

Drug Interactions

Type the drug name (brand or generic) in the search field. Select the drug and click the (Add) button.

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Back — **Drug Interactions**

Item(s)

Enter Item Name — Add

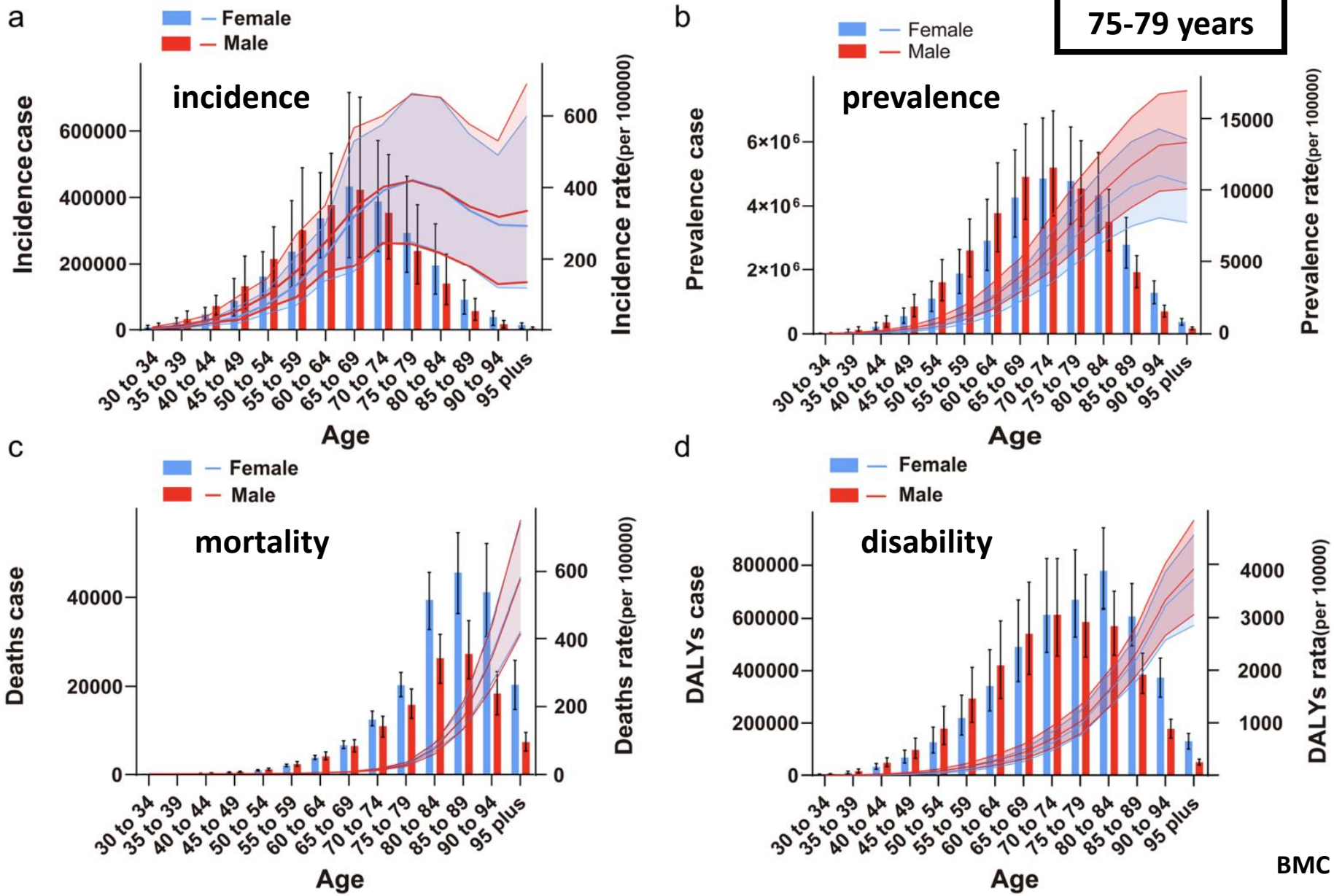
- DOAC level monitoring:
  - severe bleeding, the need for urgent surgery, or thromboembolic events despite apparent DOAC compliance
  - insufficient evidence

Outline

- 202408 ESC AF guideline updated in pharmaceutical care

- Considerations for DOAC Use in the Elderly AF

AF risk in different age groups



Peaking at 75-79 years

After 75Y: Female is more prevalent

Higher mortality and disability in female

Global Burden of Disease study 2019 (GBD2019) China

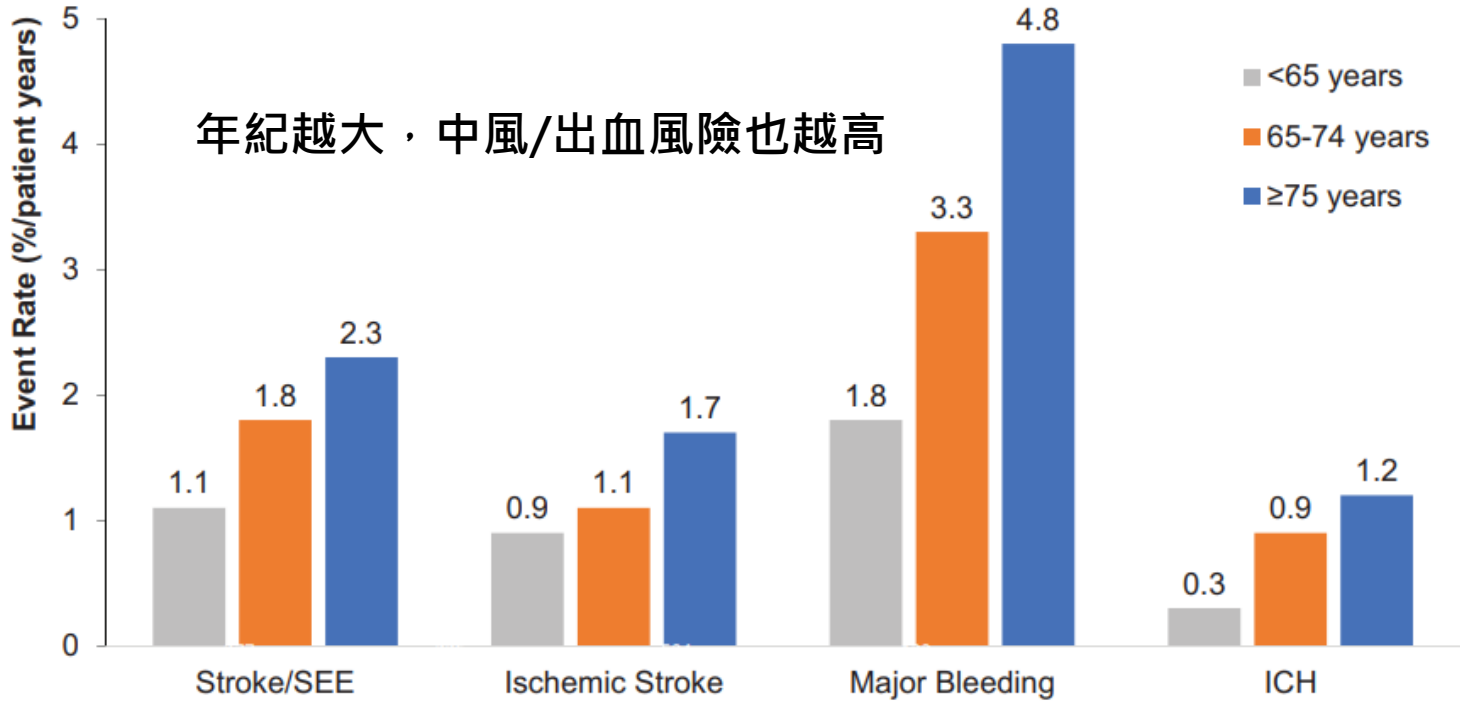
BMC Public Health (2022) 22:2015

DOAC in older non-valvular AF

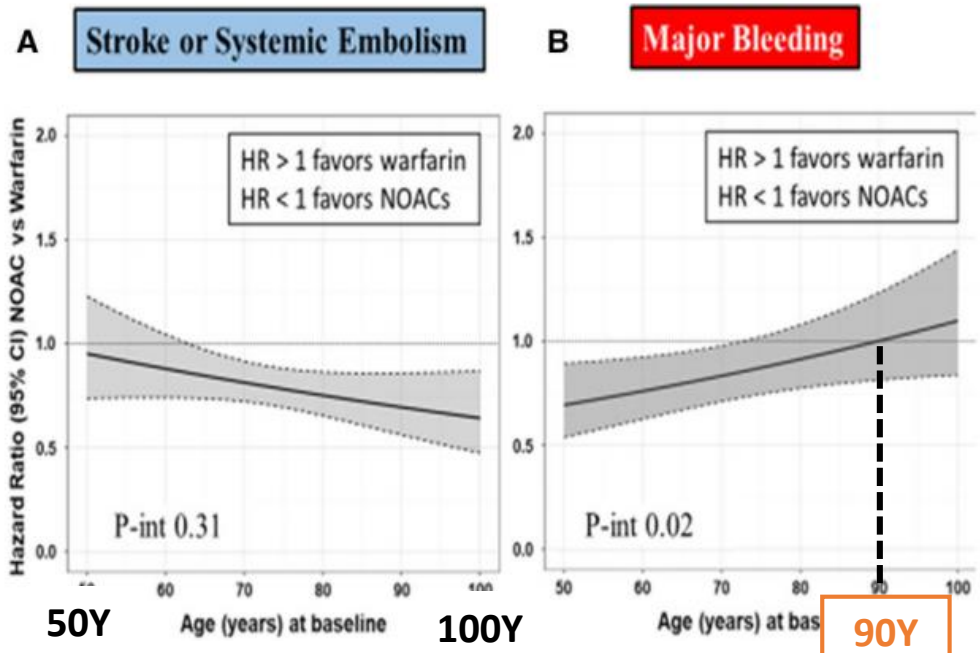
	RE-LY[10]	ROCKET-AF[8]	ARISTOTLE[9]	ENGAGE AF-TIMI 48[4]	AVERROES[11]	ELDERCARE[12]
NOAC	Dabigatran	Rivaroxaban	Apixaban	Edoxaban	5/2.5 mg	15 mg
Dose(s)	150 mg, 110 mg	20/15 mg	5/2.5 mg	60/30 mg, 30/15 mg		
≥75 years, *N* (%)	7258 (40)	6229 (44)	5678 (31)	8474 (40)	1898 (34)	984 (100[a])

老人約佔31-40%

Adjusted HR (95% CI)				
65-74 vs <65 years	1.45 (1.04-2.00)	1.13 (0.77-1.67)	1.83 (1.40-2.39)	3.30 (1.72-6.31)
≥75 vs <65 years	1.83 (1.32-2.54)	1.81 (1.24-2.63)	2.68 (2.04-3.52)	3.77 (1.94-7.30)



年紀越大，中風/出血風險也越高



從50-100歲使用DOAC都能有效減少栓塞風險
90歲以下使用DOAC重大出血風險比VKA少

EHJ supl. (2022) 24. A1–A10,

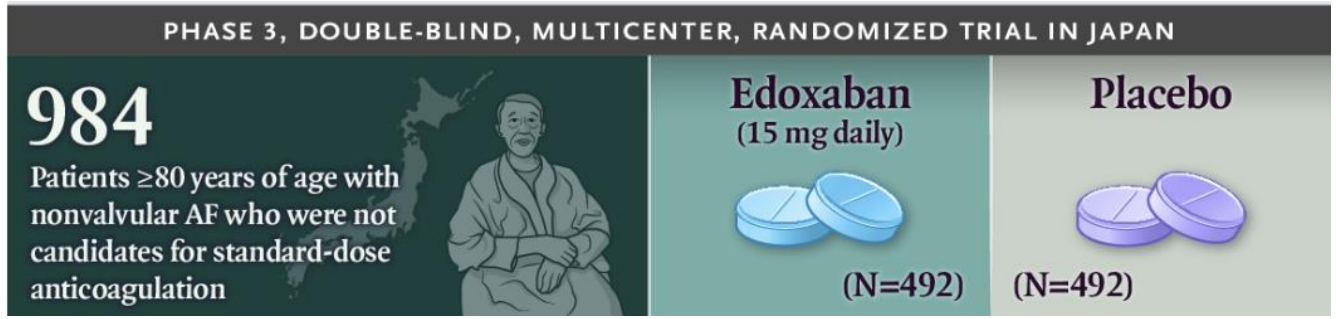
Comparisons of DOAC in age≥ 75

		DABIGATRAN		RIVAROXABAN	APIXABAN	EDOXABAN
≥75 YEARS OLD		150 mg	110 mg			
Stroke/systemic embolism (SE)	*RCT*	↘	=	=	↘	=
	Obs.	= to ↘		= to ↘	= to ↘	NR
Major bleeding	*RCT*	=	=	=	↘	↘
	Obs.	= to ↘		= to ↗	↘	NR
Intracranial hemorrhage (ICH)	*RCT*	↘	↘	=	↘	↘
	Obs.	↘		= to ↘	↘	NR
Gastrointestinal bleeding (GIB)	*RCT*	↗	↗	↗	NR	↗
	Obs.	= to ↗		= to ↗	= to ↘	NR
Mortality	*RCT*	=	=	NR	NR	NR
	Obs.	↘		= to ↘	↘	NR

- In RCT:
  - **Apixaban, dabigatran 150 mg** reduce stroke/systemic embolism
  - **Apixaban ,edoxaban** reduce major bleeding and ICH
  - Dabigatran, rivaroxaban, edoxaban increase GIB

Front Pharmacol . 2020 Sep 9:11:583311.

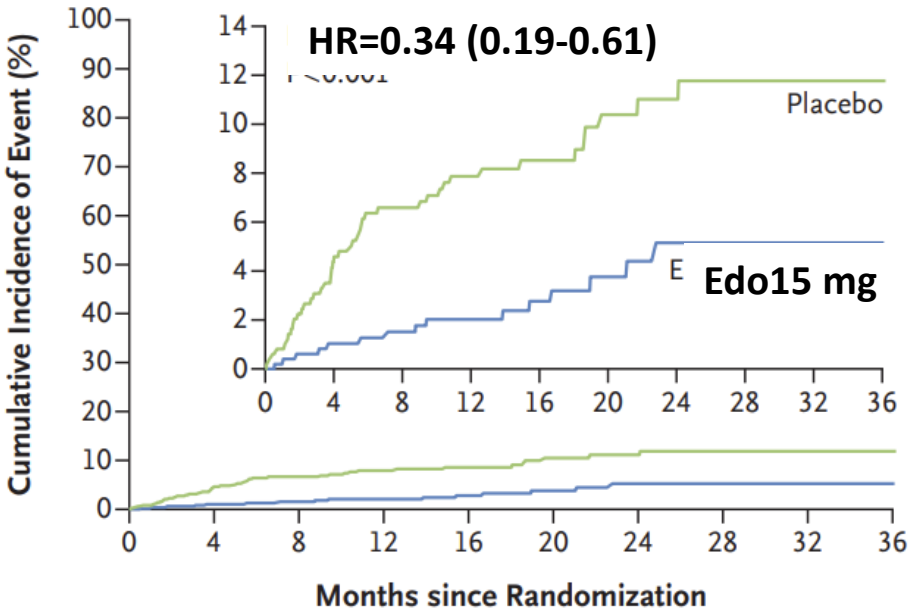
2020 NEJM ELDERCARE-AF



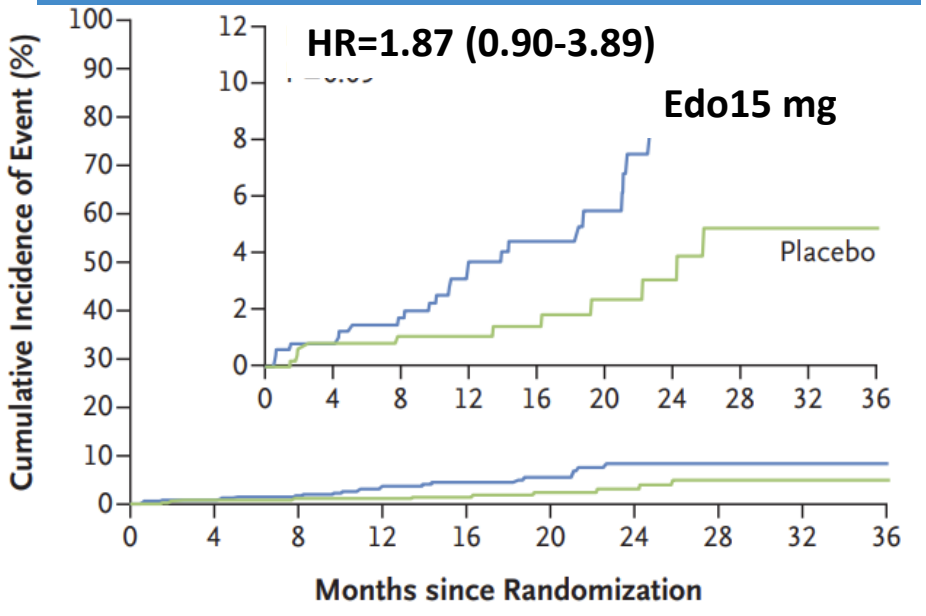
- Age ≥ 80 with NVAF who are not candidates for standard dose OAC
  - CrCL 15-30 mL/min or
  - BW≤ 45 kg or
  - Bleeding history or
  - NSAID/APT use

- Mean age: 86.6±4.2 years
- CrCL: 36.3±14.4 mL/min
- CHA_2DS_2-VASc score: 3.1±1.1
- HAS-BLED: 2.3±0.9

減少 Stroke and systemic thromboembolism



Major bleeding 無顯著差異



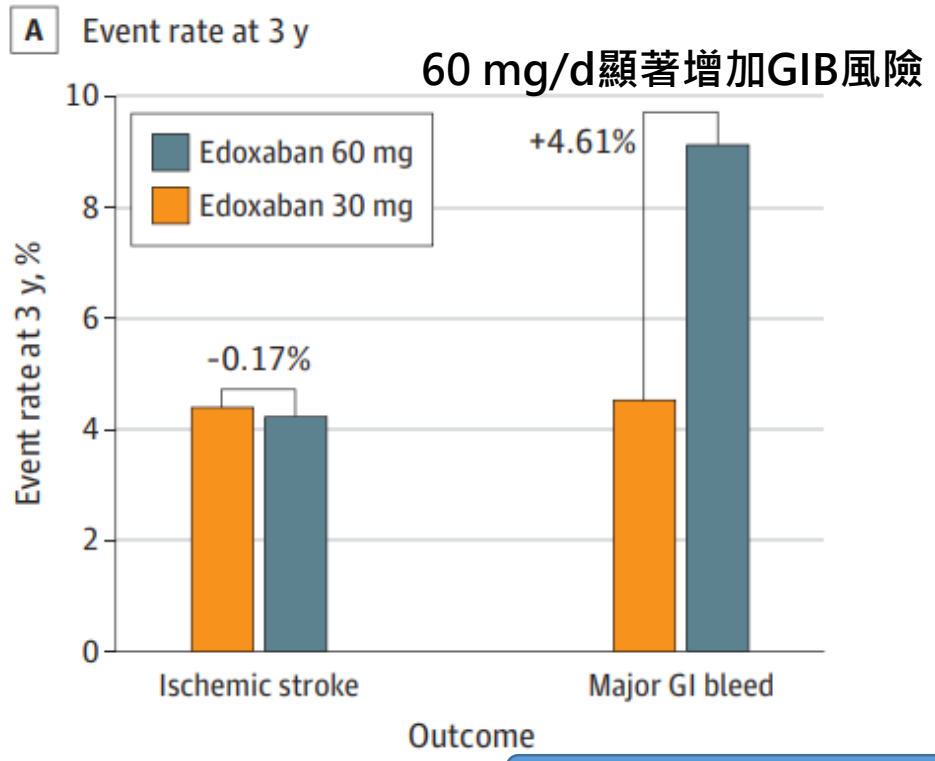
NEJM. 2020;383:1735-45

JAMA Cardiology | Original Investigation

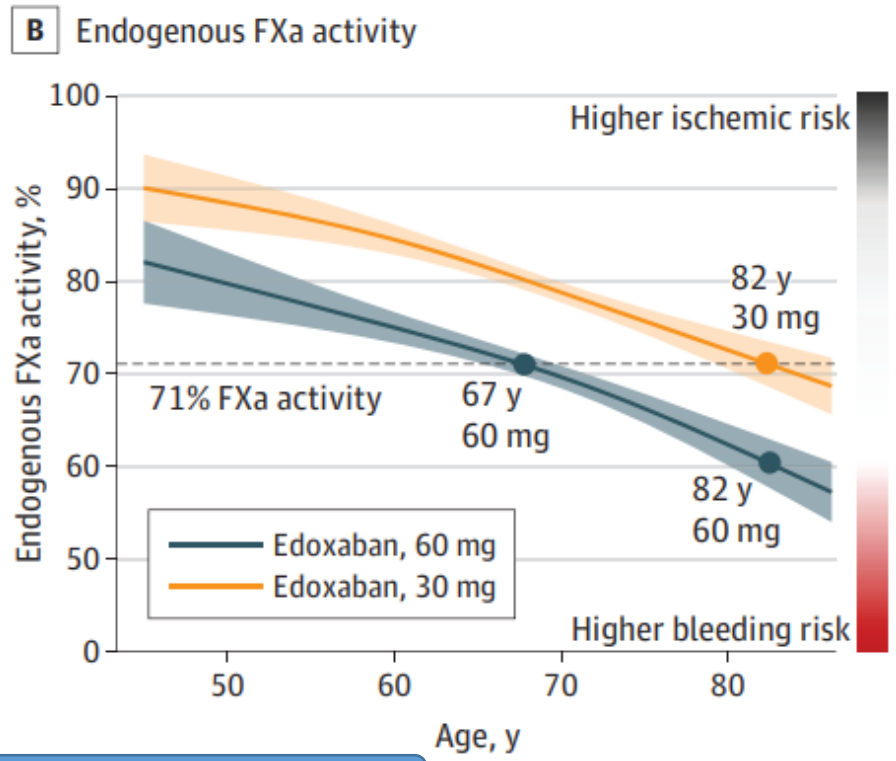
Dose Reduction of Edoxaban in Patients 80 Years and Older With Atrial Fibrillation

Post Hoc Analysis of the ENGAGE AF-TIMI 48 Randomized Clinical Trial

- Dose-reduction criteria for edoxaban (BW ≦ 60 kg or CrCl 15 to 50 mL/min or DDI)
- Dose-reduction criteria(n=1891)/ No dose-reduction criteria (n=1700)



60 mg/d顯著增加GIB風險



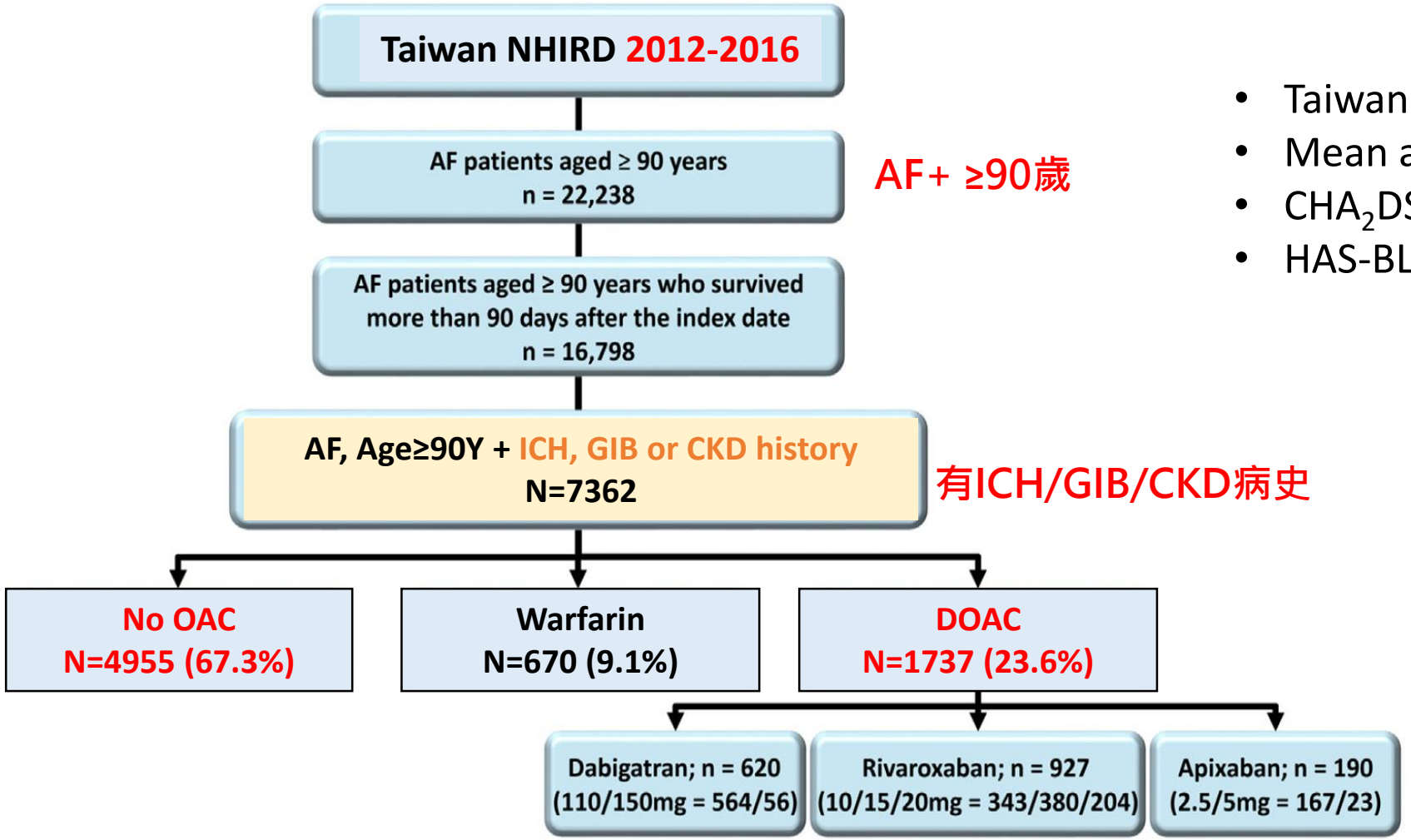
>80 yr 使用60 mg 內生性Fa Xa活性較低，出血風險上升

兩組缺血性中風發生率類似

Patients with No Dose-Reduction Criteria

JAMA Cardiol . 2024 Jul 10:e241793.

DOAC in very elderly (>90yr) AF with high risk for bleeding



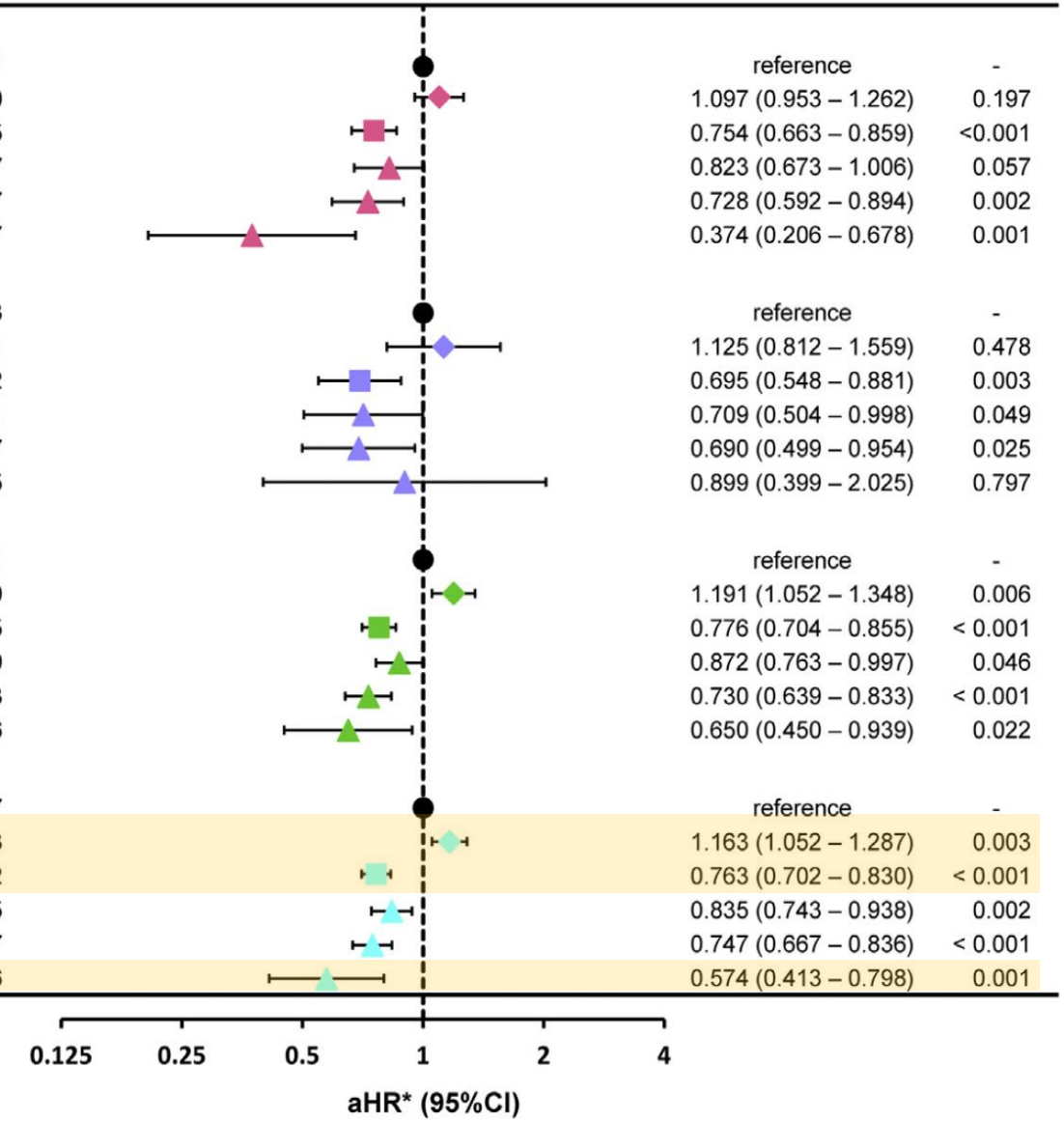
- Taiwan NHIRD
- Mean age: 92.5±2.8 years
- CHA_2DS_2-VASc score: 5.8±1.5
- HAS-BLED: 4.3±1.1

Heart Rhythm . 2021 Jun;18(6):871-877

Composite risk of 中風(出血或缺血)、嚴重出血、死亡

- Reference:沒用OAC
- Warfarin 增加風險
- DOAC 減少風險

	Number of patients	Number of event	Incidence+	aHR* (95%CI)	P value
History of CKD (n = 3,151)					
Without OACs	2,058	1,287	46.51	reference	-
Warfarin	356	234	49.50	1.097 (0.953 – 1.262)	0.197
NOACs	737	286	33.95	0.754 (0.663 – 0.859)	<0.001
Dabigatran	262	138	37.67	0.823 (0.673 – 1.006)	0.057
Rivaroxaban	384	132	33.27	0.728 (0.592 – 0.894)	0.002
Apixaban	91	16	20.17	0.374 (0.206 – 0.678)	0.001
History of ICH (n = 950)					
Without OACs	689	447	45.53	reference	-
Warfarin	58	40	53.11	1.125 (0.812 – 1.559)	0.478
NOACs	203	83	33.42	0.695 (0.548 – 0.881)	0.003
Dabigatran	67	36	33.91	0.709 (0.504 – 0.998)	0.049
Rivaroxaban	110	41	32.17	0.690 (0.499 – 0.954)	0.025
Apixaban	26	6	40.75	0.899 (0.399 – 2.025)	0.797
History of GI bleeding (n = 5,370)					
Without OACs	3,683	2,336	43.91	reference	-
Warfarin	440	283	51.09	1.191 (1.052 – 1.348)	0.006
NOACs	1,247	520	33.35	0.776 (0.704 – 0.855)	< 0.001
Dabigatran	452	242	36.19	0.872 (0.763 – 0.997)	0.046
Rivaroxaban	658	249	31.73	0.730 (0.639 – 0.833)	< 0.001
Apixaban	137	29	27.36	0.650 (0.450 – 0.939)	0.022
One of above risk factors (n = 7,362)					
Without OACs	4,955	3,084	42.77	reference	-
Warfarin	670	435	49.53	1.163 (1.052 – 1.287)	0.003
NOACs	1,737	695	32.22	0.763 (0.702 – 0.830)	< 0.001
Dabigatran	620	319	34.15	0.835 (0.743 – 0.938)	0.002
Rivaroxaban	927	340	31.77	0.747 (0.667 – 0.836)	< 0.001
Apixaban	190	36	23.56	0.574 (0.413 – 0.798)	0.001



Heart Rhythm . 2021 Jun;18(6):871-877

Elderly ≥ 75 yrs or frail patient with AF

Eligible for oral anticoagulation?

是否耐受
評估功能狀態、
出血風險、共病等

Yes

No

Absolute contraindication to NOAC?

如要使用OAC且沒有DOAC
禁忌，優先選DOAC

Yes

No

VKA
(target INR 2.0-3.0)

NOAC

注意劑量調整
優先選擇apixaban, edoxaban

Assess criteria for dose reduction

Yes

No

Apixaban 2.5 mg BID
Or
Edoxaban 30 mg OD

Apixaban 5 mg BID
Or
Edoxaban 60 mg OD

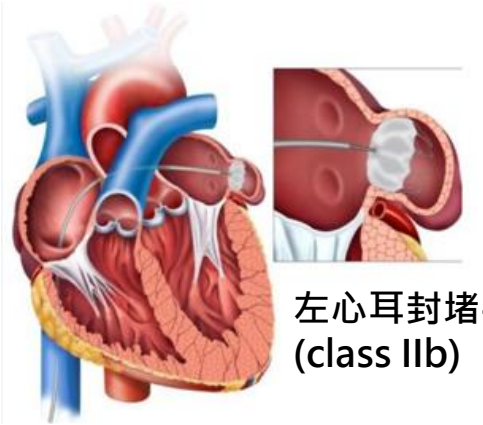
留意>80yr 使用標準edoxaban 60 mg/d 的GI出血風險

Non-pharmacologic therapy
(e.g., left atrial appendage exclusion)

or

Edoxaban 15 mg OD

低劑量的edoxaban 15 mg/d ，有吃藥比沒吃藥好



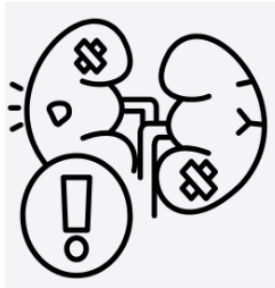
左心耳封堵手術
(class IIb)

EHJ supl. (2022) 24. A1–A10,
Int J Cardiol Heart Vasc. 2024 Feb; 50: 101333.
JAMA Cardiol . 2024 Jul 10:e241793.

Case scenario 1

- Antithrombotic agent for 80 yr female, 150 cm, 45 kg, AF, stroke, HTN, CKD (Scr 1.8, eClcr 18 ml/min)
  - (A) Apixaban 2.5 mg bid
  - (B) Edoxaban 30 mg qd
  - (C) Edoxaban 15 mg qd
  - (D) Clopidogrel + Rivaroxaban 2.5 mg bid
  - (E) Dabigatran 110 mg bid
  - (F) Clopidogrel 75 mg qd + edoxaban 15 mg qd
  - (G) Warfarin 2.5 mg hs

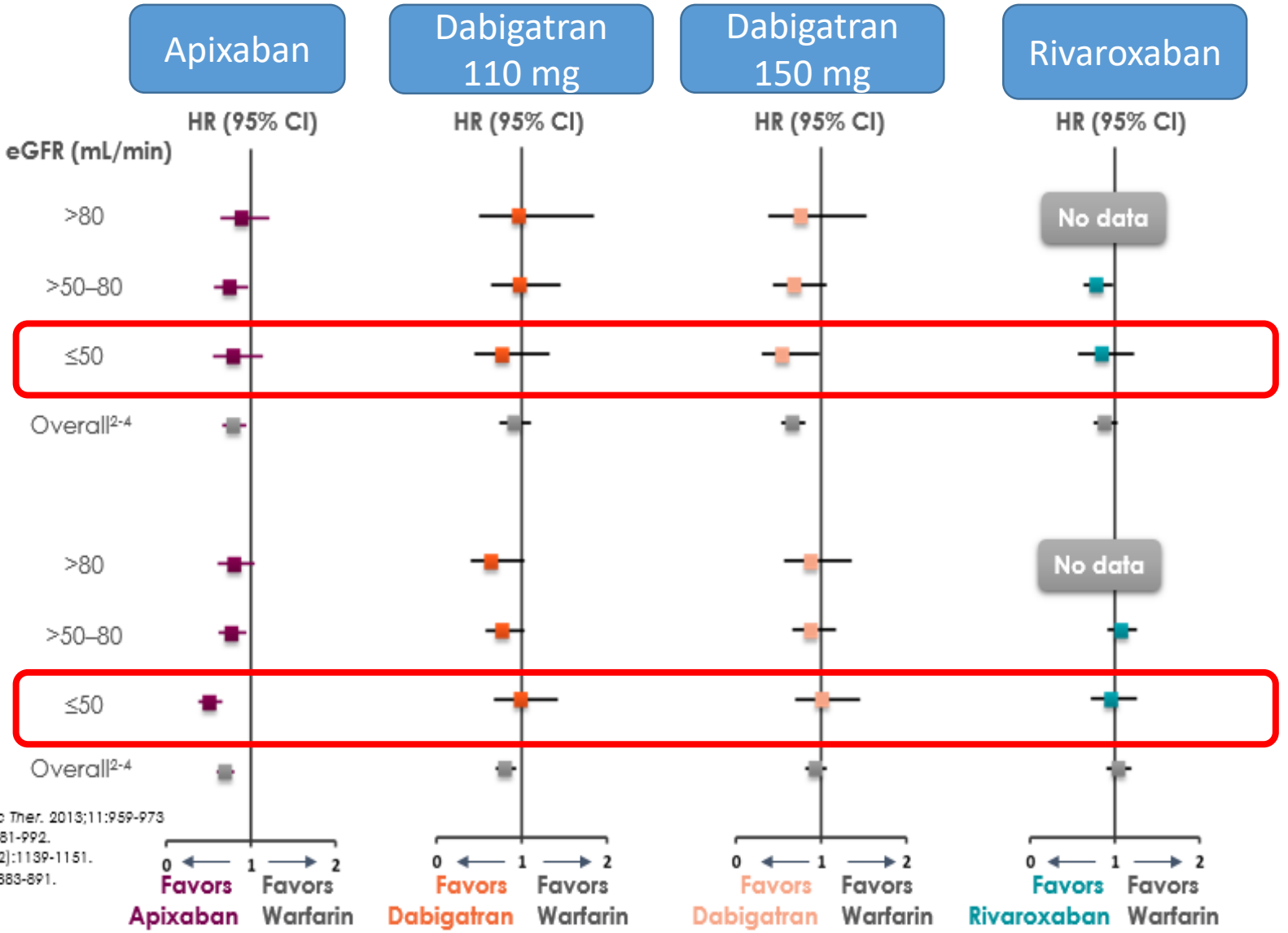
CHA_2DS_2-VA = 5 (Age, stroke, HTN)



DOACs efficacy and safety in renal impairment

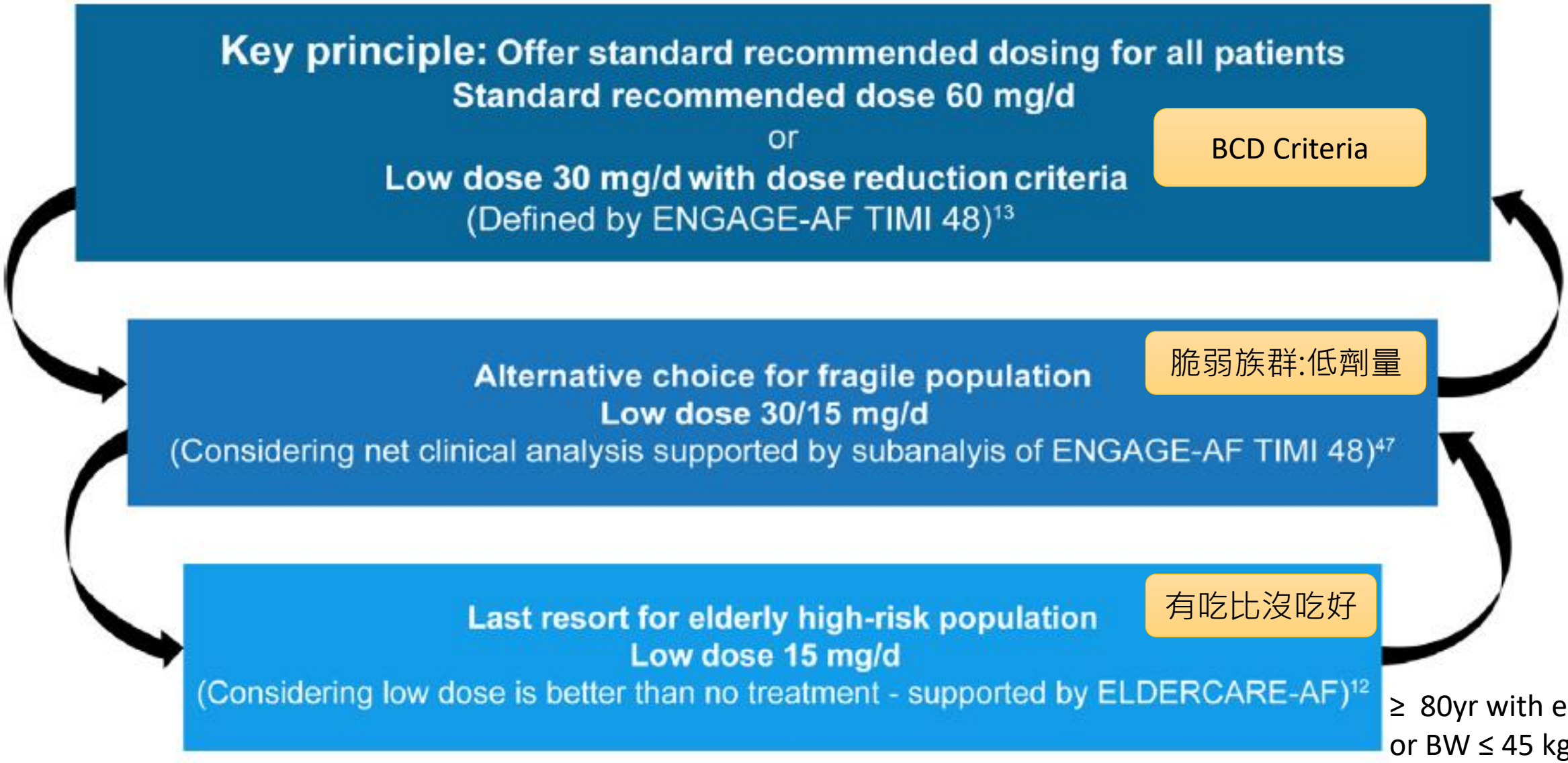
Apixaban:

- 腎排除比率最低(~27%)
- RCT in ESRD under KRT
  (RENAL-AF, AXADIA–AFNET 8)



1. Capranzano P et al. *Expert Rev Cardiovasc Ther.* 2013;11:959-973
2. Granger CB et al. *N Engl J Med.* 2011;365:981-992.
3. Connolly SJ et al. *N Engl J Med.* 2009;361(12):1139-1151.
4. Patel MR et al. *N Engl J Med.* 2011;365(10):883-891.

FIGURE 3 Practical Considerations for Dosing in a Real-World Setting (e.g., Edoxaban)



≥ 80yr with eClr 15-30, or BW ≤ 45 kg, or bleeding history, or NSAID/APT user

JACC: Asia. 2023 Oct, 3 (5) 707–723

2023 American Geriatrics Society Beers Criteria (老人潛在不適當用藥)

Drugs	Rationale	Recommendation	Quality of evidence	Strength of recommendation
Warfarin (VKA)	Higher major bleeding risks(esp. ICH), similar or lower effectiveness than warfarin. DOACs are preferred choice for most people	Avoid unless contraindicated to DOAC If long term warfarin use with TTR>70% and no ADR, may keep VKA	High	Strong
Rivaroxaban	Higher risk of major bleeding and GIB than other DOACs, particularly apixaban. Reasonable when once daily dosing is necessary for better compliance All DOACs confer lower risk of ICH than warfarin	Avoid if safer anticoagulant alternatives	Moderate	Strong
Dabigatran	Increase GIB risk compared with VKA, Increase GIB/major bleeding compared with apixaban.	Use with caution	Moderate	Strong

J Am Geriatr Soc. 2023;71:2052–2081. *Ther Adv Chronic Dis* 2019, Vol. 10: 1–21

Case scenario 1

- Antithrombotic agent for 80 yr female, 150 cm, 45 kg, AF, stroke, HTN, CKD (Scr 1.8, eClcr 18 ml/min)

  CHA_2DS_2-VA = 5 (Age, stroke, HTN)

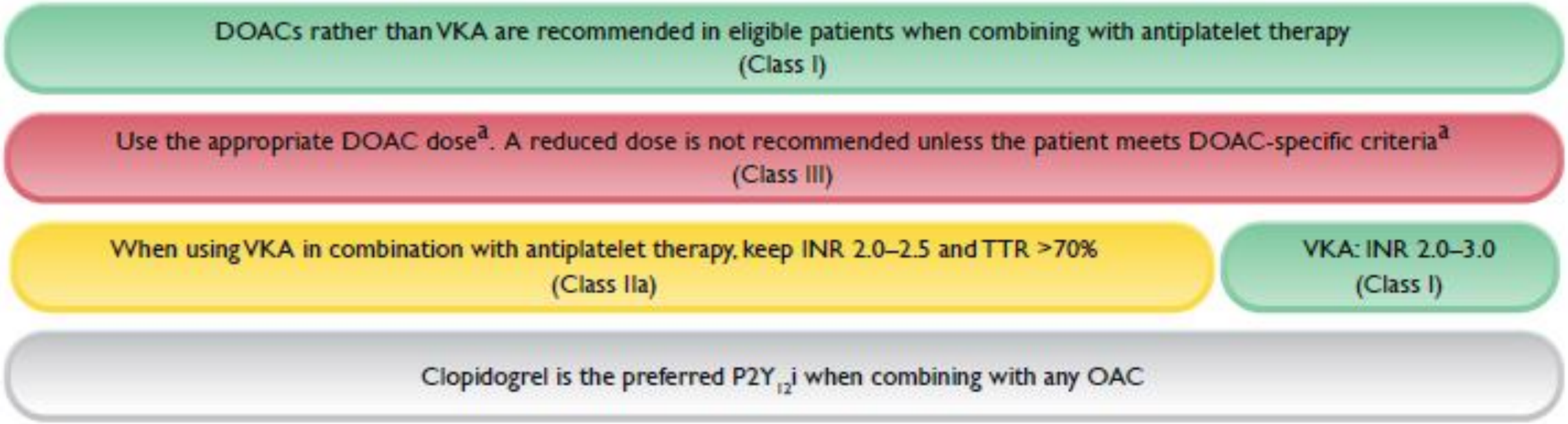
  - (A) Apixaban 2.5 mg bid (Age ≥ 80 yr, BW ≤ 60 kg, Scr ≥ 1.5)
  - (B) Edoxaban 30 mg qd (BW ≤ 60 kg, eClcr 15-50 ml/min)
  - (C) Edoxaban 15 mg qd (Age ≥ 80 yr with BW ≤ 45 kg and eClcr 15-30 ml/min, Eldercare-AF)
  - (D) Clopidogrel + Rivaroxaban 2.5 mg bid
  - (E) Dabigatran 110 mg bid
  - (F) Clopidogrel 75 mg qd + edoxaban 15 mg qd
  - (G) Warfarin 2.5 mg hs

Case scenario 2

- Antithrombotic agent for 75 yr male, 165 cm, 70 kg, AF, DM, ACS s/p PCI 2 months ago, Scr 1.1 (eCLcr 57.4 ml/min)
  - (A) Aspirin + clopidogrel + edoxaban 15 mg qd
  - (B) Ticagrelor + rivaroxaban 15 mg qd
  - (C) Prasugrel + dabigatran 110 mg bid
  - (D) Clopidogrel + apixaban 2.5 mg bid
  - (E) Clopidogrel + apixaban 5 mg bid
  - (F) Clopidogrel + edoxaban 30 mg qd

CHA_2DS_2-VA = 4 (Age, DM, Vascular disease)

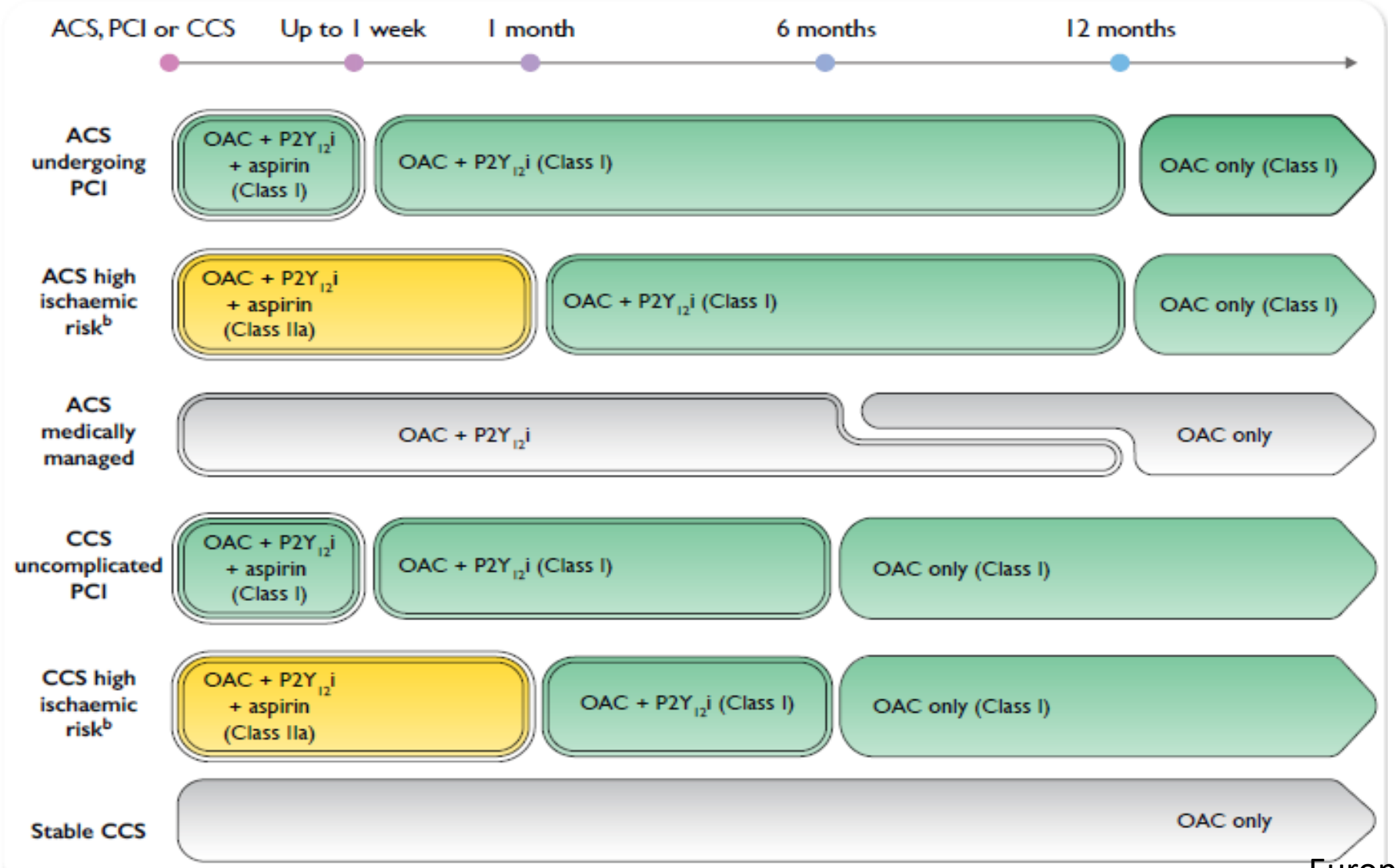
Antithrombotic regimen in AF + PCI (ACS/CCS)



- DOAC優於VKA，勿隨意減低DOAC劑量 (use appropriate DOAC use)
- 如果使用VKA則維持INR 2-2.5 (下修) 及TTR>70%
- 合併DOAC時，P2Y12抑制劑優先選擇clopidogrel

European Heart Journal (2024) **00**, 1–101

Antithrombotic regimen in AF + PCI (ACS/CCS)



- 短期使用TAT (Triple anti-thrombotic agents)，早期停用aspirin(≤1 week) (Class I)
- 高缺血風險者使用TAT 最長一個月(class IIa)
- 半年後(CCS)、一年後(ACS)穩定者單用OAC即可 (class I)

European Heart Journal (2024) **00**, 1–101

Use appropriate DOAC dose

Rivaroxaban 15 mg once daily should be considered in preference to rivaroxaban 20 mg once daily when combined with antiplatelet therapy in patients where concerns about bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke.[765]	IIa	B
Dabigatran 110 mg twice daily should be considered in preference to dabigatran 150 mg twice daily when combined with antiplatelet therapy in patients where concerns about bleeding risk prevail over concerns about stent thrombosis or ischaemic stroke.[766]	IIa	B

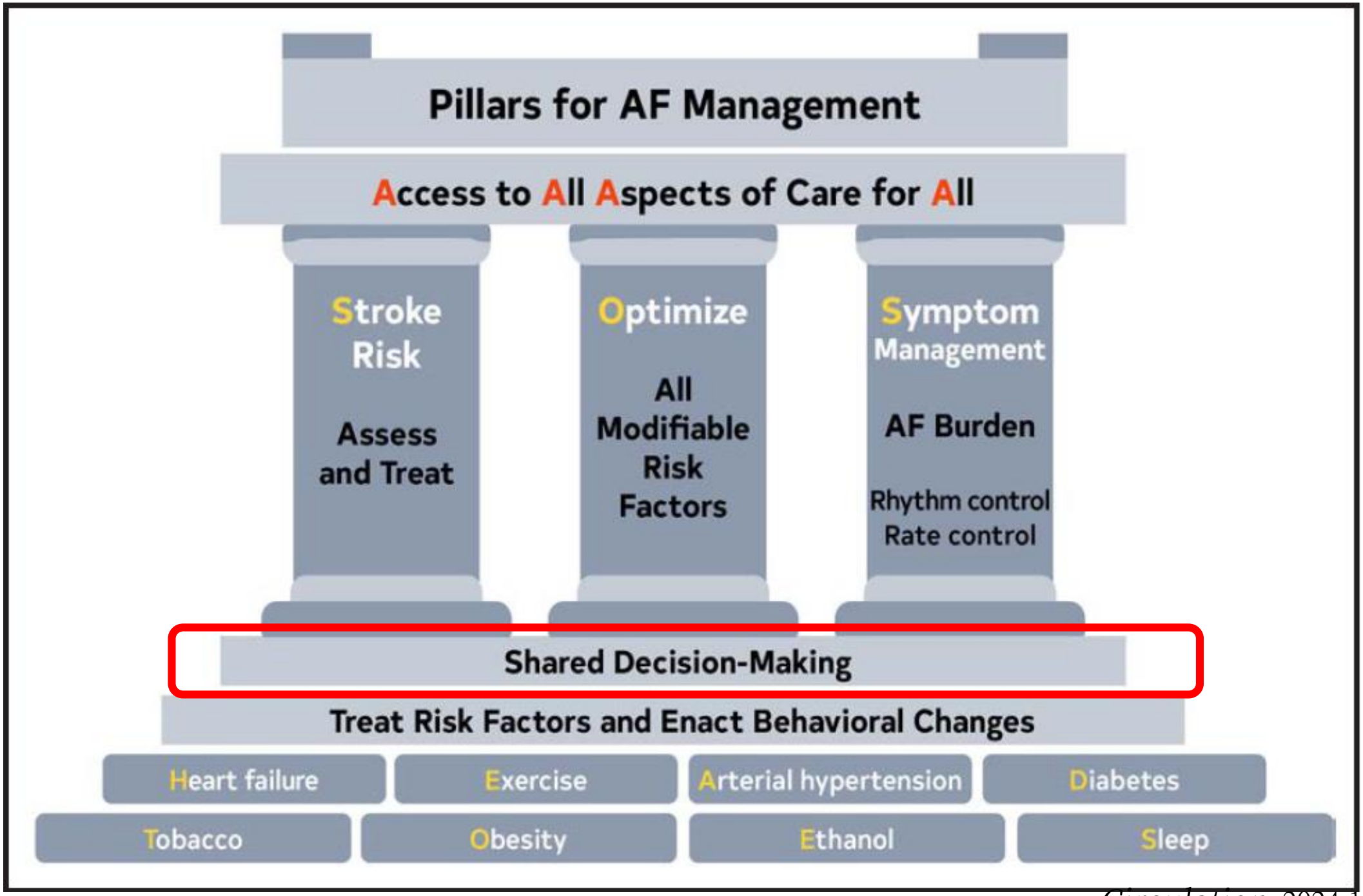
- 避免不適當減用藥量，如果考量流血風險大於缺血風險(ex. 支架再栓塞、中風) 則可考慮減量 rivaroxaban (15mg/d)或 dabigatran (110 mg bid)
- 其他狀況沒有符合劑量調整原則不建議劑量調整

2020 ESC AF

In patients at high bleeding risk (HAS-BLED ≥3), rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1080]	IIa	B
In patients at high bleeding risk (HAS-BLED ≥3), dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1079]	IIa	B

Case scenario 2

- Antithrombotic agent for 75 yr male, 165 cm, 70 kg, AF, DM, ACS s/p PCI 2 months ago, Scr 1.1 (eCLcr 57.4 ml/min)
  - (A) Aspirin + clopidogrel + edoxaban 15 mg qd
  - (B) Ticagrelor + rivaroxaban 15 mg qd
  - (C) Prasugrel + dabigatran 110 mg bid
  - (D) Clopidogrel + apixaban 2.5 mg bid (off label under dose)
  - (E) Clopidogrel + apixaban 5 mg bid (Age ≤80 kg, BW ≥60 kg, Scr ≤ 1.5)
  - (F) Clopidogrel + edoxaban 30 mg qd (eClcr >15-50 ml/min)



Circulation. 2024;149:e1 – e156.

Summary

- 2024 ESC AF guideline update
  - CARE: 共病管理、避免中風/血栓、症狀緩解、評估監測
  - CHA_2DS_2-VA score (取消sex issue)
  - Use appropriate DOAC dosing, drug compliance!
- DOAC use in the elderly
  - Frail, fragile, East-Asia population
  - DOAC > warfarin unless contraindication, apixaban/edoxaban preferred
  - Dose adjustment criteria
    - Apixaban (Age, BW, Clcr), edoxaban (BW, Clcr, DDI), Rivaroxaban (Clcr), Dabigatran (Clcr)
  - Antithrombotic regimen when AF+ACS/CCS: short aspirin duration, clopidogrel as P2Y12 inhibitor when combine DOAC use
  - Shared Decision Making (SDM)