# Current Guidelines for the Diagnosis and Management of Atrial Fibrillation

2023.6.23

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# Disclosure

- **Relationships with commercial interests:**
  - **Grants/Research Support:** Abbott, Bayer, BMS/Pfizer, Biosense Webster, Chong Kun Dang, Daewoong Pharmaceutical Co., Daiichi-Sankyo, DeepQure, Dreamtech Co., Ltd., Jeil Pharmaceutical Co. Ltd, Medtronic, Samjinpharm, Seers Technology, and Skylabs.
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ESC GUIDELINES

# 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

**The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)**

**Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC**

**Endorsed by the European Stroke Organisation (ESO)**

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ESC European Society of Cardiology
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ESC GUIDELINES

# 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

**The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)**

**Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC**

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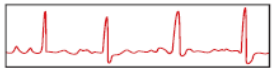
# Update of new ESC 2020 AF guidelines: CC to ABC

## CC To ABC

### Confirm AF



A 12-lead ECG or a rhythm strip showing AF pattern for ≥30 s

### Characterise AF (the 4S-AF scheme)

- **S**troke risk (St) (e.g., $CHA_2DS_2$-VASc score)
- **S**ymptom severity (Sy) (e.g., EHRA symptom score)
- **S**everity of AF burden (Sb) (duration, spontaneous termination)
- **S**ubstrate severity (Su) (age, comorbidities, atrial enlargement/fibrosis)

### Treat AF: The ABC pathway

**A** — Anticoagulation/ Avoid stroke

1. Identify low-risk patients $CHA_2DS_2$-VASc 0(m), 1(f)
2. Offer stroke prevention if $CHA_2DS_2VASc$ ≥1(m), 2(f)

Assess bleeding risk, address modifiable bleeding risk factors

3. Choose OAC (NOAC or VKA with well-managed TTR)

**B** — Better symptom control

Assess symptoms, QoL and patient's preferences

Optimize rate control

Consider a rhythm control strategy (CV, AADs, ablation)

**C** — Comorbidities/ Cardiovascular risk factor management

Comorbidities and cardiovascular risk factors

Lifestyle changes (obesity reduction, regular exercise, reduction of alcohol use, etc.)

# Diagnosis of AF

## Definition of Atrial fibrillation

A supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction.

***Electrocardiographic characteristics of AF include:***

- Irregularly irregular R-R intervals (when atrioventricular conduction is not impaired),
- Absence of distinct repeating P waves, and
- Irregular atrial activations.

| Recommendations | Class | Level |
|---|---|---|
| **ECG documentation is required to establish the diagnosis of AF.**<br><br>• A **standard 12-lead ECG** recording or a **single-lead ECG tracing of ≥30 seconds** showing heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) is diagnostic of clinical AF. | I | B |



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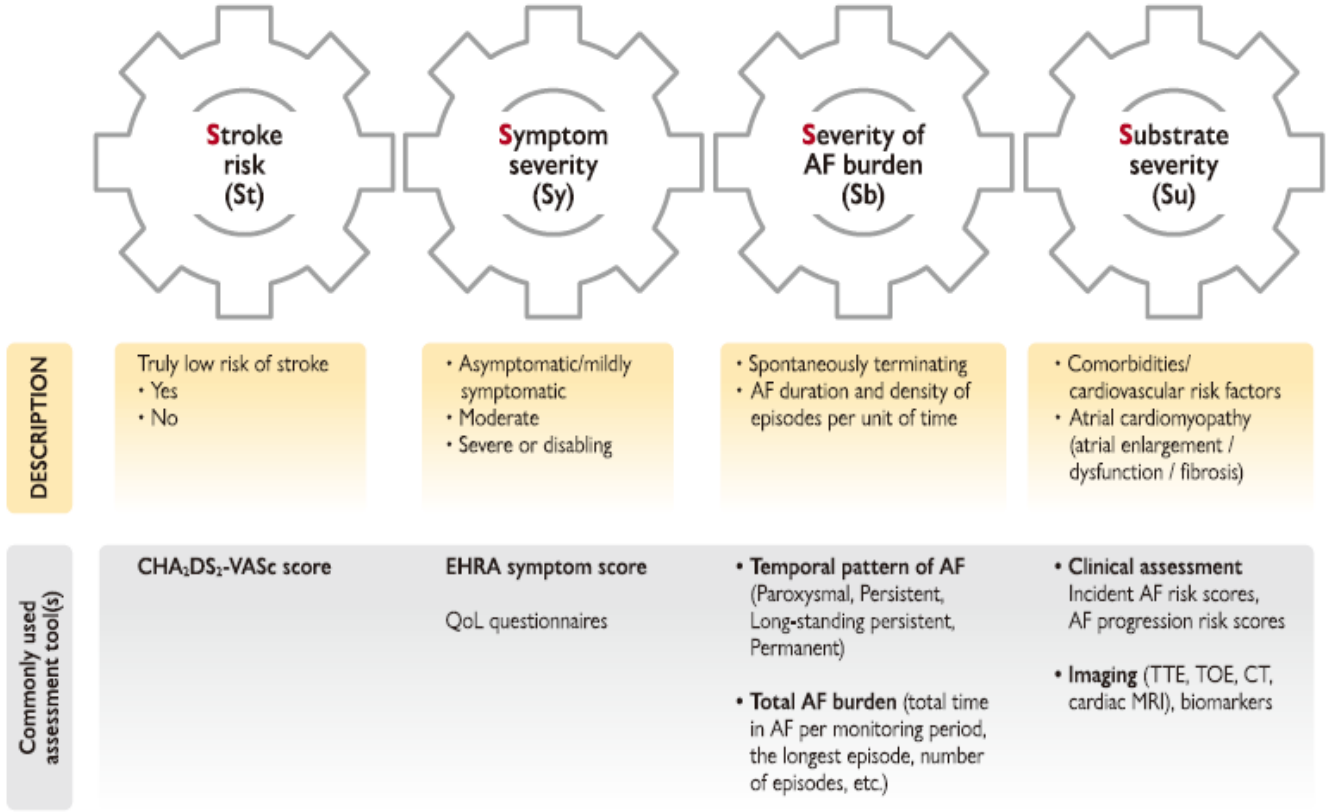
# Classification of AF

| AF pattern | Definition |
|---|---|
| **First diagnosed** | AF not diagnosed before. |
| **Paroxysmal** | AF that terminates spontaneously or with intervention within 7 days of onset. |
| **Persistent** | AF that is continuously sustained beyond 7 days, including episodes that are terminated by cardioversion after 7 days or more. |
| **Long-standing persistent** | Continuous AF of >12 months duration when decided to adopt a rhythm control strategy. |
| **Permanent** | AF that is accepted by the patient and physician, and no further attempts to restore/maintain sinus rhythm will be undertaken. Permanent AF represents a therapeutic attitude of the patient and physician rather than an inherent pathophysiological attribute of AF, and the term should not be used in the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation. |

## 4S-AF scheme as an example of structured characterization of AF



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# A hypothetical treatment decision supporting algorithm using the 4S-AF scheme for structured characterisation of patients with AF in clinical practice

| Stroke | Symptoms | Severity of AF burden | Substrate |
|---|---|---|---|
| | | | (+1 if >75 years old) |
| **Truly low risk** | | **Spontaneously terminating** | **Comorbidity/CV risk factors** |
| **0** = Yes | **0** = No or mild | **0** = Yes | **0** = No |
| **1** = No | **1** = Moderate | **1** = No | **1** = Single |
| | **2** = Severe or disabling | **Duration of AF and density of episodes** | **2** = Multiple (2 or more) |
| | | **0** = Short and infrequent | **LA enlargement/dysfunction** |
| | | **1** = Intermediate and/or frequent | **0** = No |
| | | **2** = Long or very frequent | **1** = Mild-moderate |
| | | | **2** = Severe |
| | | | **LA fibrosis** |
| | | | **0** = No |
| | | | **1** = Mild |
| | | | **2** = Moderate-severe |
| **0 = no antithrombotic therapy** | | | |
| **1 = OAC** | | | |
| | **2** | **0-1** | **0-2** |
| | **1** | **2** | **3-4** |
| | **0** | **3** | **5 or more** |

| Current commonly used tools for assessment of the 4S-AF domains | | | |
|---|---|---|---|
| **CHA2DS2-VASc score** | **EHRA symptom score** | **Temporal pattern of AF** | **Various** |
| Truly low risk: 0 males, 1 females | EHRA 1-2a = 0 | Paroxysmal or first onset = 0 | Clinical assessment |
| OAC: >= 1 males , >=2 females | EHRA 2b = 1 | Persistent = 1 | Transthoracic echocardiography |
| | EHRA 3-4 =2 | Long-standing persistent = 2 | AF progression risk scores |
| | | Permanent = 2 | Advanced imaging |
| | | | Biomarkers |

| |
|---|
| **All green => Rhythm control** |
| **1 Yellow, 2 Green => Rhythm control can be attempted** |
| **Red => Consider rate control** |
| **Consultation or rate control** |



Potpara T, et al. Thromb Haemost 2020; DOI: 10.1055/s-0040-1716408.

# Screening of AF

| Recommendations | Class | Level |
|---|---|---|
| When screening for AF it is recommended that:<br>• The **individuals** undergoing screening are **informed about the significance and treatment implications of detecting AF.**<br>• A **structured referral platform is organized for screen-positive cases** for further physician-led clinical evaluation to confirm the diagnosis of AF and provide optimal management of patients with confirmed AF.<br>• **Definite diagnosis of AF in screen-positive cases is established only after physician reviews the single-lead ECG recording of ≥30 seconds or 12-lead ECG and confirms that it shows AF.** | I | B |
| **Systematic ECG screening** should be considered to detect AF in individuals aged ≥75 years, or those at high risk of stroke. | IIa | B |

## Potential benefits from and risks of screening for AF

**AF SCREENING**

**RISKS**

- Abnormal results may cause anxiety
- ECG misinterpretation results may lead to overdiagnosis and overtreatment
- ECG may detect other abnormalities (true or false positives) that may lead to invasive tests and treatments that have the potential for serious harm (e.g., angiography / revascularisation with bleeding, contrast-induced nephropathy and allergic reactions to the contrast)

**BENEFITS**

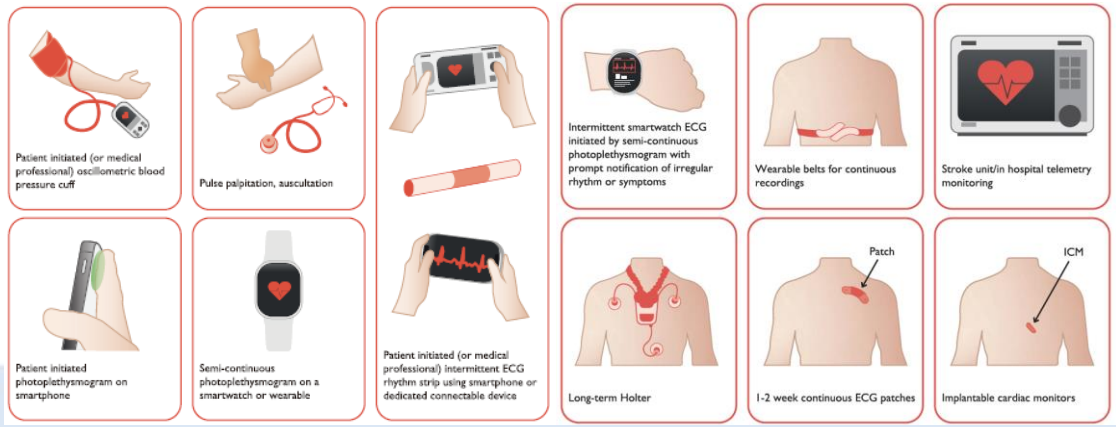
**Prevention of:**
- Stroke/SE using OAC in patients at risk
- Subsequent onset of symptoms

**Prevention/reversal of:**
- Electrical/mechanical atrial remodelling
- AF-related haemodynamic derangements
- Atrial and ventricular tachycardia-induced cardiopmyopathy

**Prevention/reduction of:**
- AF-related morbidity; hospitalization; mortality

**Reduction of:**
- The outcomes associated with conditions / diseases associated with AF that are discovered and treated as a consequence of the examinations prompted by AF detection

## Systems used for AF screening

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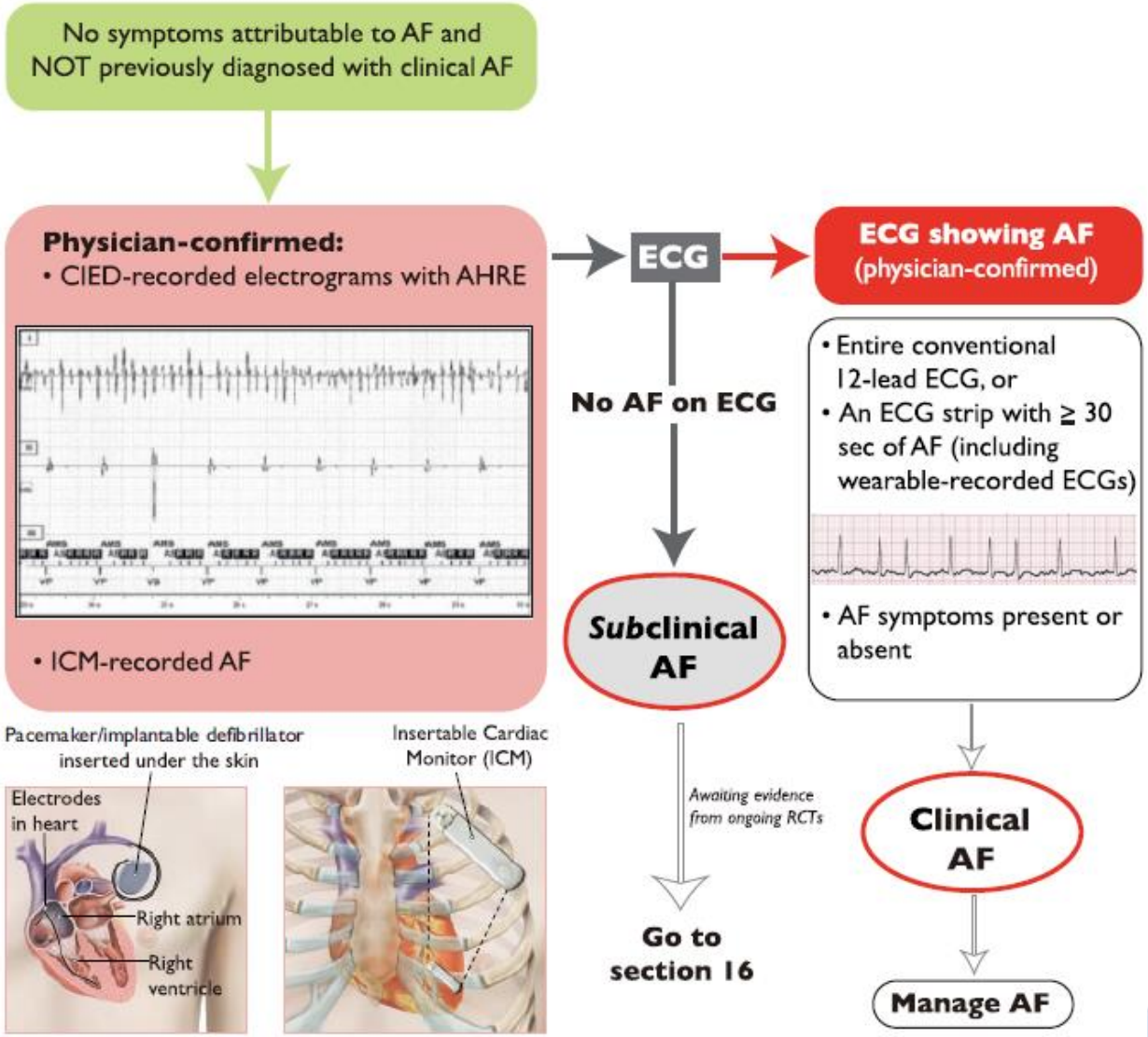
# Diagnosis of AHRE/subclinical AF




| Currently used terms | |
|---|---|
| **Clinical AF** | ***Symptomatic* or *asymptomatic*** AF that is documented by surface ECG. |
| **Atrial High Rate Episodes (AHRE)** | Refers to individuals ***without symptoms*** *attributable to AF,* in whom ***clinical AF is NOT previously detected*** *(that is, there is no surface ECG tracing of AF)*<br><br>***AHRE*** – events fulfilling programmed or specified criteria for AHRE that are detected by ***CIEDs with an atrial lead allowing automated continuous monitoring of atrial rhythm and tracings storage.*** CIED-recorded AHRE need to be visually inspected because some AHRE may be electrical artefacts/false positives. |
| **Subclinical AF** | ***Subclinical AF*** includes<br>• ***AHRE confirmed to be AF, AFL, or an AT, or***<br>• ***AF episodes detected by insertable cardiac monitor***<br>• ***or wearable monitor and confirmed*** by visually reviewed intracardiac electrograms or ECG-recorded rhythm. |



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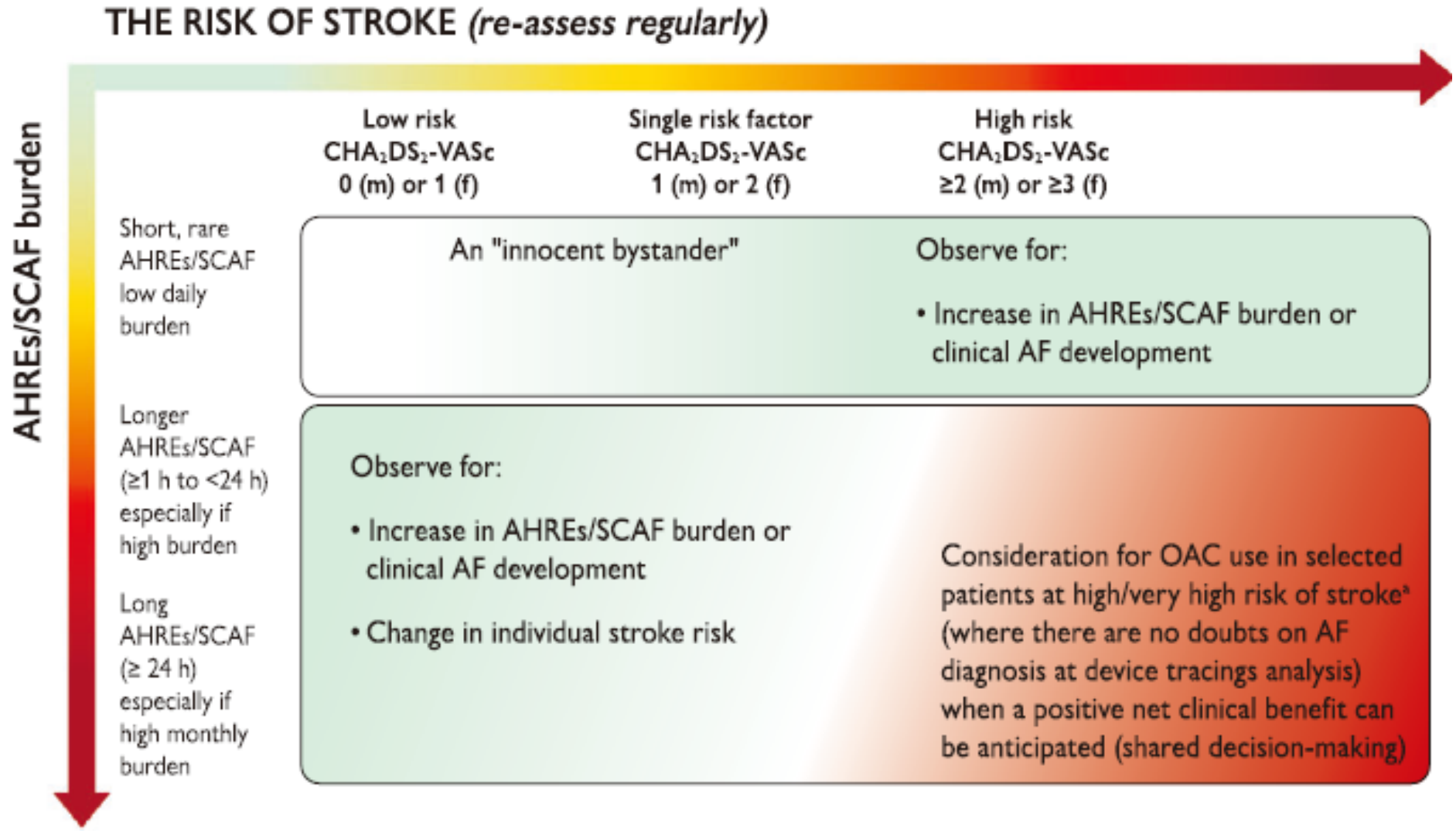
# Proposed management of AHRE/subclinical AF



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# Changes in the recommendations (2020 vs. 2016)

| 2020 | Class[a] | 2016 | Class[a] |
|---|---|---|---|
| **Recommendations for the prevention of thrombo-embolic events in AF** | | | |
| For bleeding risk assessment, a formal structured risk-score-based bleeding risk assessment is recommended to help identify non-modifiable and address modifiable bleeding risk factors in all AF patients, and to identify patients potentially at high risk of bleeding who should be scheduled for early and more frequent clinical review and follow-up. | I | Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding. | IIa |
| In patients on VKAs with low time in INR therapeutic range (e.g. TTR<70%), recommended options are:<br>• Switching to a NOAC but ensuring good adherence and persistence with therapy; or<br>• Efforts to improve TTR (e.g. education/counselling and more frequent INR checks). | I<br>IIa | AF patients already on treatment with a VKAs may be considered for NOAC treatment if TTR is not well controlled despite good adherence, or if patient preference without contraindications to NOAC (e.g. prosthetic valve). | IIb |



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# Recommendations for rhythm control/catheter ablation of AF

| 2020 | Class[a] | 2016 | Class[a] |
|---|---|---|---|
| *AF catheter ablation after drug therapy failure* | | | |
| AF catheter ablation for PVI is recommended for rhythm control after one failed or intolerant class I or III AAD, to improve symptoms of AF recurrences in patients with:<br>• Paroxysmal AF, or<br>• Persistent AF without major risk factors for AF recurrence, or<br>• Persistent AF with major risk factors for AF recurrence. | I | Catheter or surgical ablation should be considered in patients with symptomatic persistent or long-standing persistent AF refractory to AAD therapy to improve symptoms, considering patient choice, benefit and risk, supported by an AF Heart Team. | IIa |



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# Recommendations for rhythm control/catheter ablation of AF

| 2020 | Class[a] | 2016 | Class[a] |
|---|---|---|---|
| *First-line therapy* | | | |
| AF catheter ablation:<br>• Is recommended to reverse LV dysfunction in AF patients when tachycardia-induced cardiomyopathy is highly probable, independent of their symptom status. | I | AF ablation should be considered in symptomatic patients with AF and HFrEF to improve symptoms and cardiac function when tachy-cardiomyopathy is suspected. | IIa |
| • Should be considered in selected AF patients with HFrEF to improve survival and reduce HF hospitalization. | IIa | | |
| *Techniques and technologies* | | | |
| Complete electrical isolation of the pulmonary veins is recom-mended during all AF catheter-ablation procedures. | I | Catheter ablation should target isolation of the pulmonary veins using radiofrequency ablation or cryothermy balloon catheters. | IIa |
| If patient has a history of CTI-dependent atrial flutter or if typical atrial flutter is induced at the time of AF ablation, delivery of a CTI lesion may be considered. | IIb | Ablation of common atrial flutter should be considered to prevent recurrent flutter as part of an AF ablation procedure if docu-mented or occurring during the AF ablation | IIa |
| *Lifestyle modification and other strategies to improve outcomes of ablation* | | | |
| Weight loss is recommended in obese patients with AF, particu-larly those who are being evaluated to undergo AF ablation. | I | In obese patients with AF, weight loss together with management of other risk factors should be considered to reduce AF burden and symptoms. | IIa |



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# Recommendations for long-term antiarrhythmic drugs

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Amiodarone is recommended for long-term rhythm control in all AF patients, including those with HFrEF. However, owing to its extracardiac toxicity, other AADs should be considered first whenever possible.[233,570,884,942,983,985] | I | A |
| Dronedarone is recommended for long-term rhythm control in AF patients with:<br>• Normal or mildly impaired (but stable) LV function, or<br>• HFpEF, ischaemic, or VHD.[884,923,925,985] | I | A |
| Flecainide or propafenone is recommended for long-term rhythm control in AF patients with normal LV function and without structural heart disease, including significant LVH and myocardial ischaemia.[594,884,910,942,983,984] | I | A |
| In AF patients treated with sotalol, close monitoring of QT interval, serum potassium levels, CrCl, and other proarrhythmia risk factors is recommended.[884,942] | I | B |



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# Recommendations for long-term antiarrhythmic drugs

| | | |
|---|---|---|
| In AF patients treated with flecainide for long-term rhythm control, concomitant use of an atrioventricular nodal-blocking drug (if tolerated) should be considered. | IIa | C |
| Sotalol may be considered for long-term rhythm control in patients with normal LV function or with ischaemic heart disease if close monitoring of QT interval, serum potassium levels, CrCl, and other proarrhythmia risk factors is provided.[233,983] | IIb | A |
| AAD therapy is not recommended in patients with permanent AF under rate control and in patients with advanced conduction disturbances unless antibradycardia pacing is provided. | III | C |



AAD = antiarrhythmic drug; AF = atrial fibrillation; CrCl = Creatinine clearance; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular; LVH = LV hypertrophy; VHD = Valvular heart disease.

[a]Class of recommendation.

[b]Level of evidence.



2020 ESC Guidelines for the diagnosis and management of atrial fibrillation. Eur Heart J 2020

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Society Guidelines

# The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation

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CLINICAL PRACTICE GUIDELINE: FOCUSED UPDATE

# 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

*Developed in Collaboration With the Society of Thoracic Surgeons*

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Canadian Journal of Cardiology 37 (2021) 1607–1618

Review

# Management of Atrial Fibrillation in 2021: An Updated Comparison of the Current CCS/CHRS, ESC, and AHA/ACC/HRS Guidelines

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# Risk factor modification

| | 2020 CCS/CHRS | 2020 ESC | 2019 AHA/ACC/HRS |
|---|---|---|---|
| Identification and management for general risk reduction | • Systematic approach to identification of traditional modifiable cardiovascular risk factors or conditions associated with AF recommended, with guideline-adherent management to reduce major cardiovascular events (**Strong Recommendation**) | • Identification and management of risk factors and concomitant diseases recommended (**Class I**) | • "Taken together, these studies support a treatment approach that addresses the risk factors for AF."<br>• No specific recommendation |
| For management of AF | • Identification and management of traditional modifiable cardiovascular risk factors or conditions associated with AF recommended, with strict guideline-adherent management to prevent recurrence of arrhythmia or decrease symptom burden (**Strong Recommendation**) | • Modification of unhealthy lifestyle and targeted therapy of intercurrent conditions, recommended to reduce AF burden and severity of symptoms (**Class I**) | |

# Anti-arrhythmic drugs for long-term rhythm control and contraindications according to presence of structural heart disease

| Anti-arrhythmic | 2020 CCS/CHRS | 2020 ESC | 2019 AHA/ACC/HRS |
|---|---|---|---|
| Amiodarone | • Can be used in all populations, including HF and CAD<br>• Consider alternative AADs or ablation rather than long-term amiodarone | • Recommended in all patients, including HFrEF, but other AADs should be considered first whenever possible (**Class I**) | • Caution if sinus or AV node dysfunction, infranodal disease, lung disease, or prolonged QT interval<br>• Consider amiodarone after other agents failed or contraindicated (**Class I**) |
| Dronedarone | • Can be used in CAD or in absence of HF<br>• Should be used with caution in combination with digoxin | • Recommended in patients with normal or mildly impaired LVEF, or HFpEF, ischemic, or VHD (**Class I**) | • Caution if prolonged QT interval or QT drugs, renal disease, hypoK or hypoMg, or diuretic therapy<br>• Avoid in NYHA III to IV patients or recent decompensated HF (**Class III**) |
| Flecainide and propafenone (Class 1C agents) | • Can be used in the absence of HF or CAD<br>• Class 1C agents should be combined with AV-nodal blocking agent; use caution in patients with LVH | • Recommended in patients with normal LV function and without structural heart disease (LVH, ischemia) (**Class I**)<br>• If flecainide, concomitant AV nodal blocking drug (**Class IIa**) | • Caution if sinus or AV node dysfunction, HF, CAD, atrial flutter, infranodal disease, Brugada syndrome, liver disease, renal disease (flecainide), asthma (propafenone) |
| Sotalol | • Can be used in all populations, except HF with LVEF ≤ 40% or LVH<br>• Use caution in patients with high-risk features for Torsade de pointes* | • May be considered in patients with normal LV function or ischemic heart disease, if QT interval, potassium, CrCl, and other pro-arrhythmia risk factors closely monitored (**Class IIb**) | • Caution if prolonged QT interval or QT drugs, renal disease, hypoK, hypoMg, diuretic therapy, sinus or AV nodal dysfunction, HF, or asthma |

# Indications for catheter ablation

| Indication | 2020 CCS/CHRS | 2020 ESC | 2019 AHA/ACC/HRS |
|---|---|---|---|
| **Percutaneous catheter ablation** | | | |
| Paroxysmal AF | • In symptomatic patients after adequate trial of AAD (**Strong Recommendation**) | • In symptomatic patients after failed drug therapy (**Class I**) | • In symptomatic patients refractory or intolerant to at least 1 class I or III AAD (**Class I; 2014**) |
| Persistent AF | • Same as above | • If no major risk factors for recurrence (**Class I**) and if major risk factors (**Class IIa**) | • In symptomatic patients refractory or intolerant to at least 1 class I or II AAD (**Class IIa; 2014**) |
| Longstanding, persistent AF | • Same as above | • Not specifically discussed | • In symptomatic patients refractory or intolerant to at least 1 class I or III AAD (**Class IIb; 2014**) |
| First line | • In selected patients with symptomatic AF (**Weak Recommendation**) | • Depending on patient preference (**Class IIa** for paroxysmal AF, **Class IIb** for persistent AF without risk factors) | • Reasonable when a rhythm control strategy is desired (**Class IIa** for paroxysmal AF, **Class IIb** for persistent AF; 2014) |
| LV dysfunction | • No specific recommendation; supporting evidence highlighted in text | • First line depending on patient preference (**Class I**) or after failed AAD therapy (**Class IIa**) | • In select patients with symptomatic AF and HFrEF (**Class IIb; 2019**) |
| Atrial flutter | • A reasonable alternative to pharmacologic rhythm or rate control (**Strong Recommendation**) | • Consider ablation of CTI-dependent atrial flutter at the time of AF ablation (**Class IIb**) | • No specific recommendation |
| CHD | • No specific recommendation | • Catheter ablation of atrial arrhythmias associated with CHD in experienced centres (**Class IIb**) | • No specific recommendation |

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Review Article

# 2021 Focused Update Consensus Guidelines of the Asia Pacific Heart Rhythm Society on Stroke Prevention in Atrial Fibrillation: Executive Summary*

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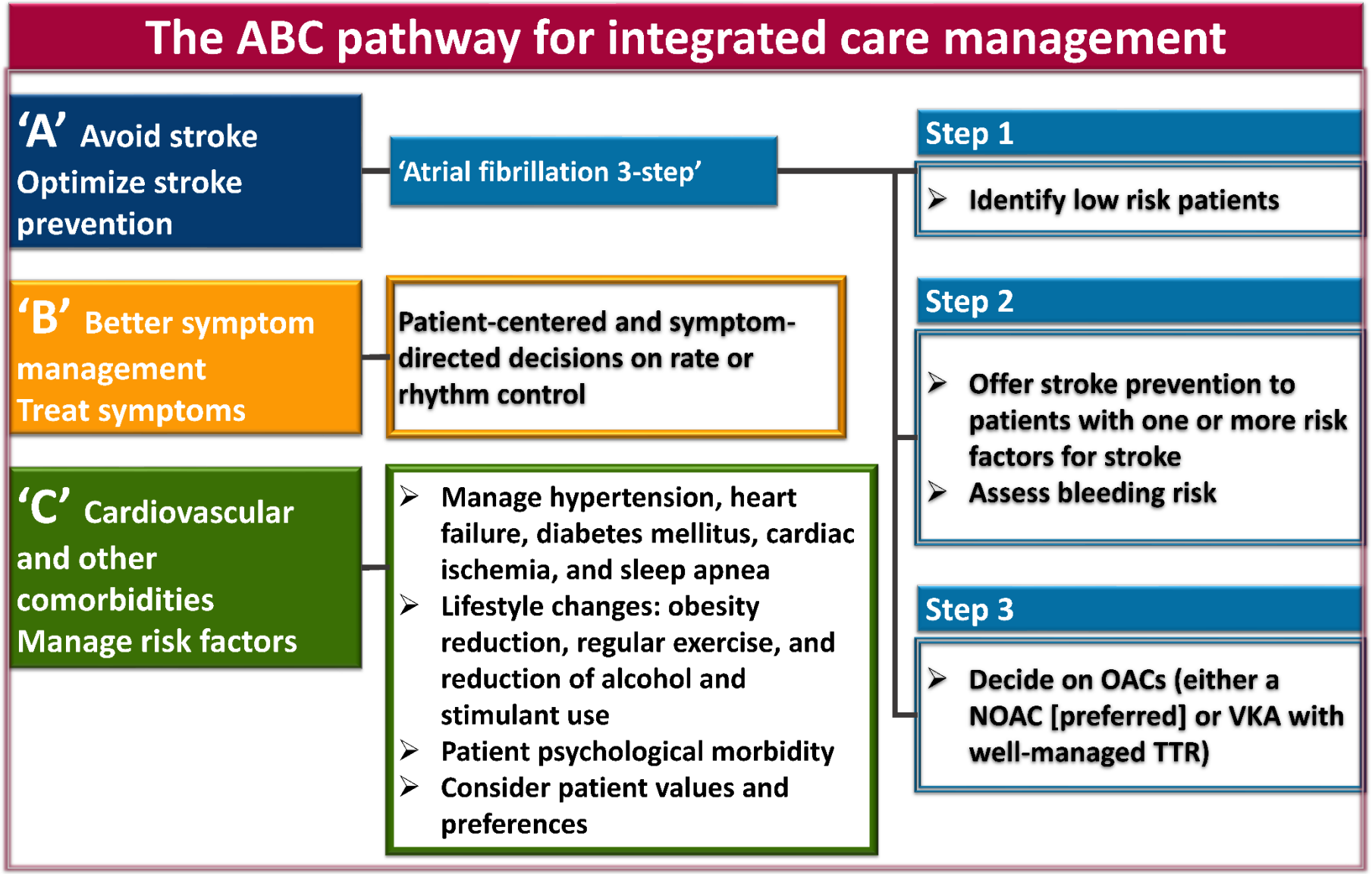
Thromb Haemost

**Abstract**

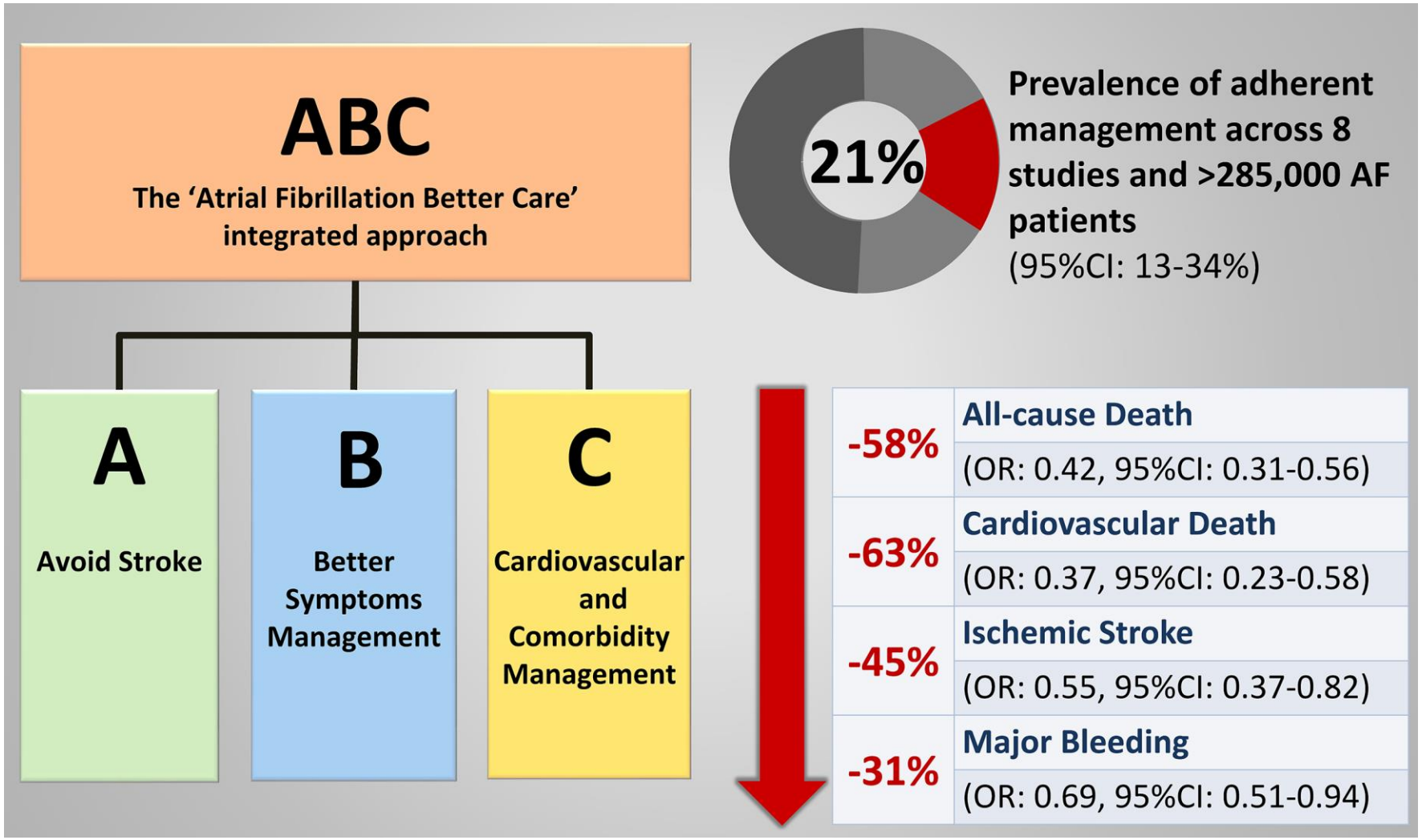
The consensus of the Asia Pacific Heart Rhythm Society (APHRS) on stroke prevention in atrial fibrillation (AF) has been published in 2017 which provided useful clinical

# The ABC pathway of integrated care management




2021 Focused update of the 2017 consensus guidelines of the Asia Pacific Heart Rhythm Society (APHRS) on stroke prevention in atrial fibrillation. Journal of Arrhythmia 2021 doi/10.1002/joa3.12652; Thromb Haemost. 2021 doi: 10.1055/s-0041-1739411

# Impacts of adherence to the ABC pathway on clinical outcomes in patients with AF

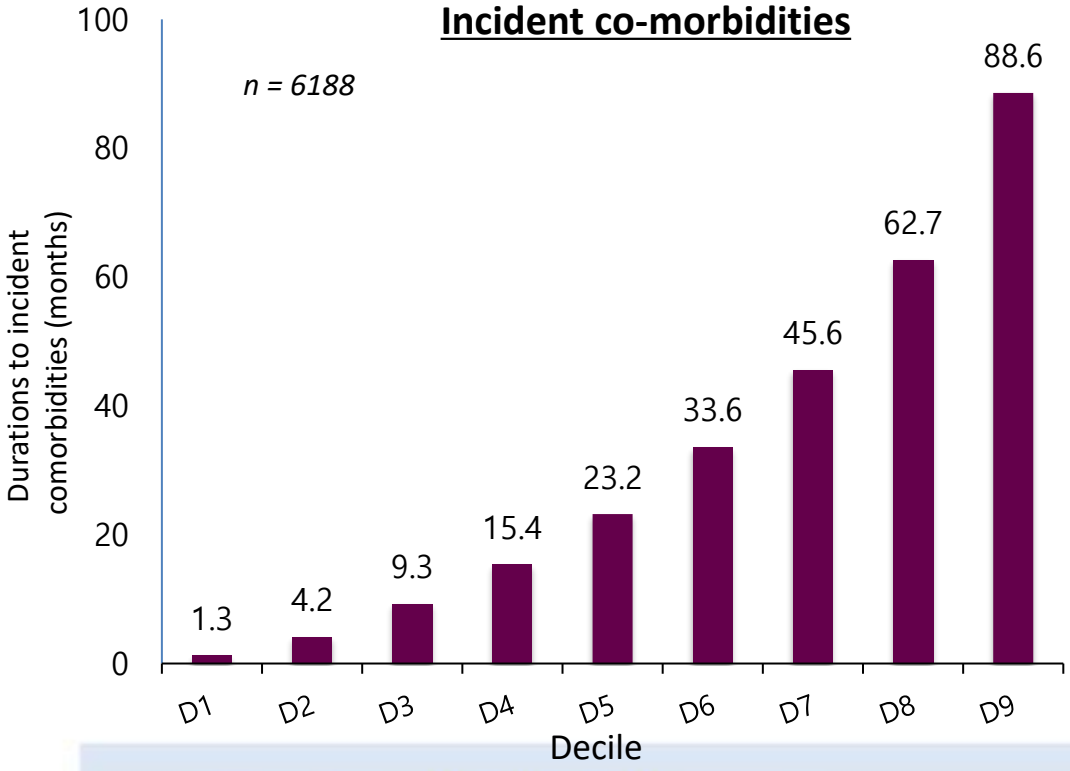


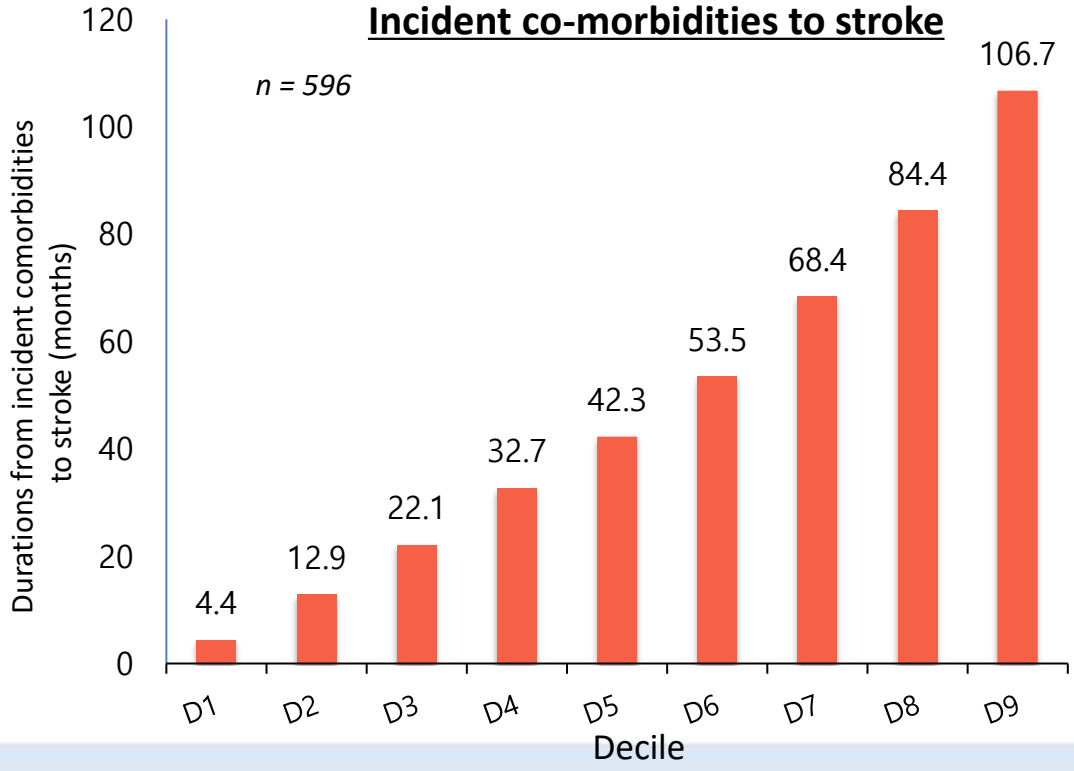



2021 Focused update of the 2017 consensus guidelines of the Asia Pacific Heart Rhythm Society (APHRS) on stroke prevention in atrial fibrillation. Journal of Arrhythmia 2021 doi/10.1002/joa3.12652; Thromb Haemost. 2021 doi: 10.1055/s-0041-1739411

# 4 Months may be a Reasonable Timing Interval at which the Stroke Risk of Patients with AF should be Reassessed.

- In the study by Chao et al. which studied 14,606 patients with AF with a baseline $CHA_2DS_2$-VASc score of 0 (males) or 1 (females), 6188 patients acquired new risk factors with the acquisition of 1 or more new comorbidities approx 4–5 months after their initial AF diagnosis.
- The most common incident comorbidity was hypertension, followed by heart failure, diabetes mellitus, and vascular disease; indeed, the onset of new comorbidities would depend on the type of comorbidity. Importantly, 596 of these original experienced ischemic stroke, and the duration from the acquirement of incident comorbidities to the occurrence of ischemic stroke was an average of 4.4 months for 90% of the patients.




SEOUL NATIONAL UNIVERSITY HOSPITAL

Adapted from: Chao TF, et al. Thromb Haemost. 2019;119(7):1162-1170.

1. Chao TF, et al. Incident co-morbidities in patients with atrial fibrillation initially with a CHA2DS2-VASc score of 0 (males) or 1 (females): implications for reassessment of stroke risk in initially 'low-risk'patients. Thromb Haemost. 2019;119(7):1162-1170.

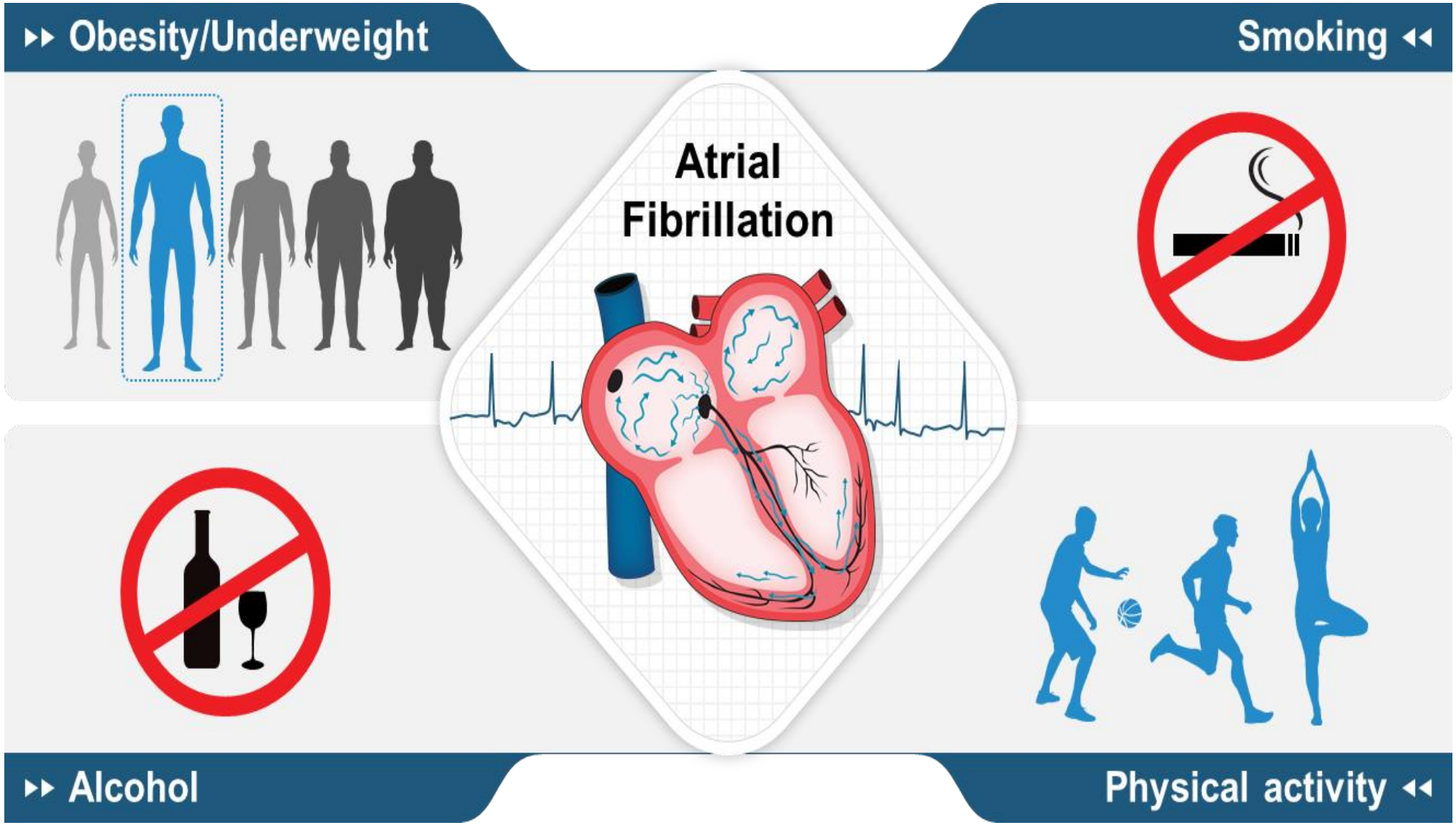
# 2021 APHRS Recommendations

| | |
|---|---|
| 1 | The $CHA_2DS_2$-VASc score is recommended for stroke risk assessment for Asian patients with AF. |
| 2 | The stroke risk of patients with AF is not static and should be re-assessed regularly (at least annually and every 4 months if possible). |
| 3 | In patients with AF initially at low risk of stroke ($CHA_2DS_2$-VASc= 0 in men or 1 in women), a reassessment of stroke risk should ideally be made at 4 months after the index evaluation and OACs should be prescribed timely once their $CHA_2DS_2$-VASc scores increase. |

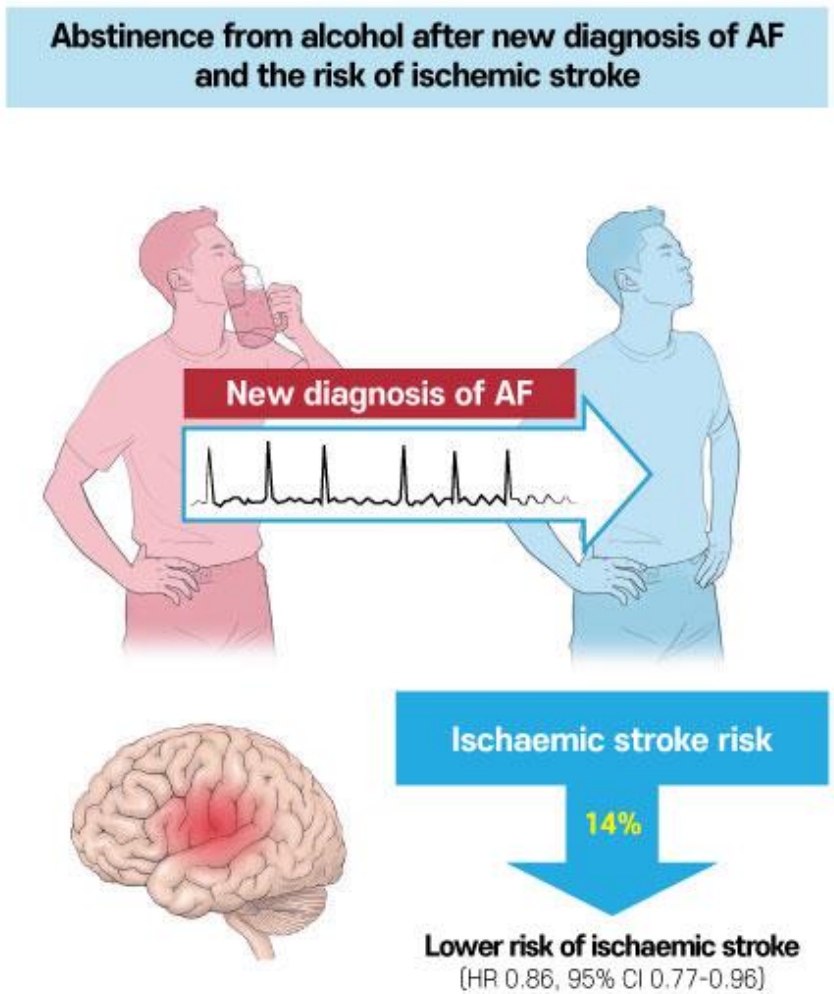


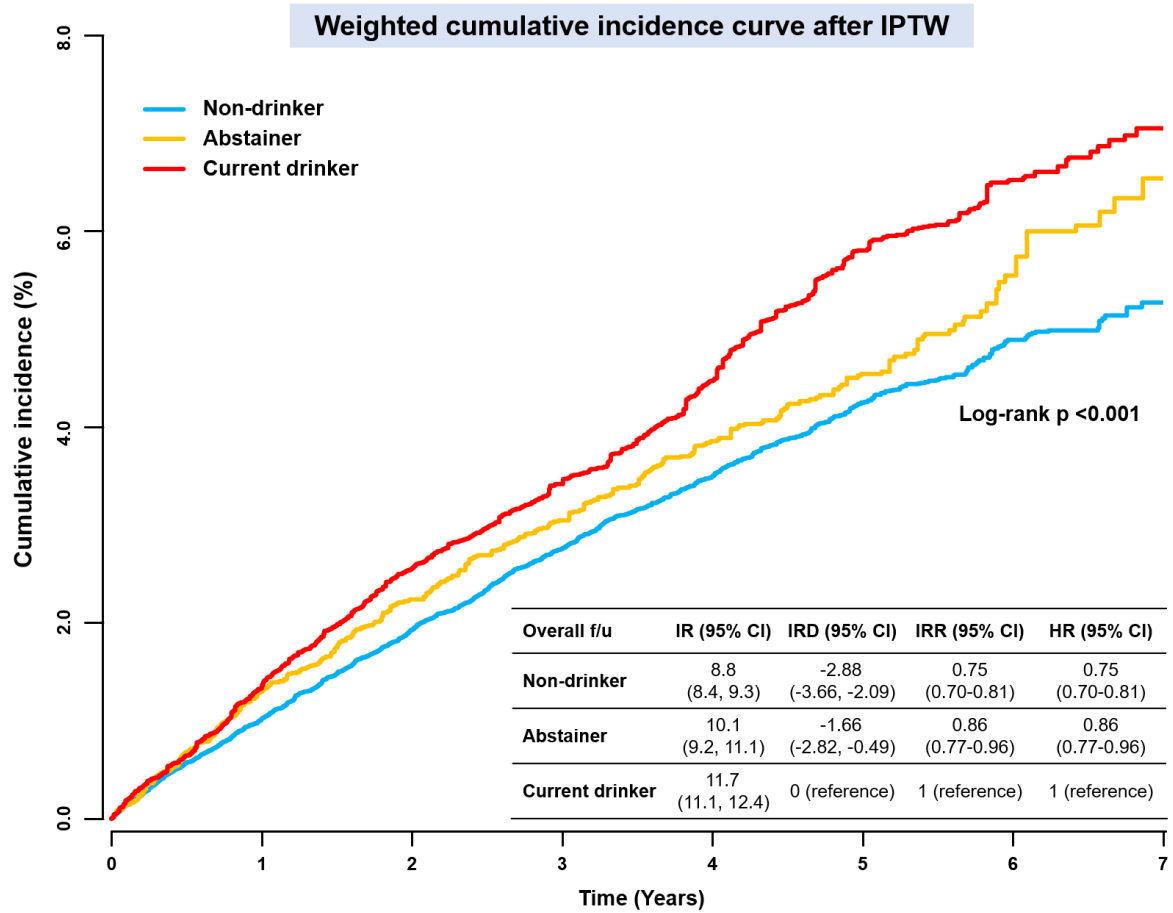
1. Chao TF, et al. 2021 Focused update of the 2017 consensus guidelines of the Asia Pacific Heart Rhythm Society (APHRS) on stroke prevention in atrial fibrillation. Journal of Arrhythmia. 2021;37(6):1389-1426.

# The integration of lifestyle management in patients with AF



# Lower risk of stroke after alcohol abstinence in patients with incident atrial fibrillation: a nationwide population-based cohort study




| Overall f/u | IR (95% CI) | IRD (95% CI) | IRR (95% CI) | HR (95% CI) |
|---|---|---|---|---|
| Non-drinker | 8.8 (8.4, 9.3) | -2.88 (-3.66, -2.09) | 0.75 (0.70-0.81) | 0.75 (0.70-0.81) |
| Abstainer | 10.1 (9.2, 11.1) | -1.66 (-2.82, -0.49) | 0.86 (0.77-0.96) | 0.86 (0.77-0.96) |
| Current drinker | 11.7 (11.1, 12.4) | 0 (reference) | 1 (reference) | 1 (reference) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Percent at risk (IR)** | | | | | | | |
| Non-drinker | 84.9 (10.3) | 65.4 (9.8) | 48.8 (9.5) | 33.7 (9.2) | 20.2 (9.1) | 7.0 (8.9) | 1.6 (8.8) |
| Abstainer | 84.3 (13.1) | 64.7 (11.5) | 49.2 (10.7) | 33.9 (10.3) | 19.4 (10.0) | 6.6 (10.0) | 1.6 (10.0) |
| Current drinker | 84.5 (13.5) | 64.9 (13.0) | 47.6 (12.0) | 32.6 (11.8) | 18.8 (12.0) | 6.7 (11.8) | 1.6 (11.7) |
| **Absolute difference in IR (95% CI)** | | | | | | | |
| Non-drinker | -3.20 (-4.77, -1.64) | -3.21 (-4.35, -2.07) | -2.52 (-3.47, -1.57) | -2.60 (-3.47, -1.74) | -2.98 (-3.81, -2.15) | -2.89 (-3.69, -2.09) | -2.89 (-3.68, -2.10) |
| Abstainer | -0.42 (-2.84, 1.99) | -1.51 (-3.23, 0.19) | -1.29 (-2.71, 0.13) | -1.46 (-2.75, -0.18) | -2.03 (-3.25, -0.82) | -1.82 (-3.00, -0.64) | -1.70 (-2.87, -0.53) |
| Current drinker | 0 (reference) | 0 (reference) | 0 (reference) | 0 (reference) | 0 (reference) | 0 (reference) | 0 (reference) |
| **IRR (95% CI)** | | | | | | | |
| Non-drinker | 0.76 (0.67, 0.86) | 0.75 (0.68, 0.83) | 0.79 (0.72, 0.86) | 0.75 (0.70, 0.82) | 0.75 (0.70, 0.81) | 0.75 (0.70, 0.81) | 0.75 (0.70, 0.81) |
| Abstainer | 0.96 (0.81, 1.16) | 0.88 (0.76, 1.02) | 0.89 (0.78, 1.01) | 0.84 (0.75, 0.95) | 0.83 (0.74, 0.93) | 0.85 (0.76, 0.95) | 0.86 (0.76, 0.96) |
| Current drinker | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) | 1 (reference) |

Lee SR, Choi EK, Lip GYH et al. Eur Heart J. 2021 Jun 7:ehab315

ESC European Society of Cardiology
European Heart Journal (2018) **00**, 1–64
doi:10.1093/eurheartj/ehy136

SPECIAL ARTICLE

# The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Jan Steffel[1]*, Peter Verhamme[2], Tatjana S. Potpara[3], Pierre Albaladejo[4], Matthias Antz[5], Lien Desteghe[6], Karl Georg Haeusler[7], Jonas Oldgren[8], Holger Reinecke[9], Vanessa Roldan-Schilling[10], Nigel Rowell[11], Peter Sinnaeve[2], Ronan Collins[12], A. John Camm[13], and Hein Heidbüchel[6,14]

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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

Jan Steffel[1]*, Ronan Collins[2], Matthias Antz[3], Pieter Cornu[4], Lien Desteghe[5,6], Karl Georg Haeusler[7], Jonas Oldgren[8], Holger Reinecke[9], Vanessa Roldan-Schilling[10], Nigel Rowell[11], Peter Sinnaeve[12], Thomas Vanassche[12], Tatjana Potpara[13], A. John Camm[14], and Hein Heidbüchel[5,6]

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## 2021 EHRA Practical Guide

# Selected DOAC indications and contra-indications

| Condition | Eligibility for DOAC | Comment |
|---|---|---|
| **Mechanical prosthetic valve** | Contraindicated | Excluded from pivotal RCTs<br>Data indicating worse outcome |
| **Moderate to severe mitral stenosis (usually rheumatic)*** | Contraindicated | Excluded from pivotal RCTs<br>Little rationale for less efficacy and safety vs. VKA |
| **Percutaneous transluminal aortic valvuloplasty** | With caution | No prospective data<br>May require combination with APT |
| **Severe aortic stenosis** | Limited data<br>(excluded in RE-LY) | No pathophysiological rationale for less efficacy / safety<br>Most will undergo intervention |

*Hatched indicates Limited data

Safety and efficacy of apixaban have not been studied in patients with prosthetic heart valves, with or without atrial fibrillation. Therefore, the use of apixaban is not recommended in this setting.[2]

APT, antiplatelet therapy; DOAC, direct-acting oral anticoagulant; RCT, randomised controlled trial; VKA, vitamin K antagonist.

1. Steffel J, et al. Europace 2021;00:1–6; 2. Apixaban SmPC. Available at: www. https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf. Accessed May 2021.

# Practical considerations for initiation and follow-up

## Structured Follow-up for NOAC treated patients

**Initiator of anticoagulant treatment**

- Indication (contraindication?) for anticoagulation
- Baseline blood works, incl. hemoglobin, renal / liver function, full coagulation panel
- Choice of anticoagulant and correct dose
- Education and handover of anticoagulation card
- Organization of follow-up (when, where, by whom, what?)

**Regular follow-up: GP; cardiologist, anticoagulation / AF clinic, ...**
(may be performed via phone / video call, particularly if in-person visit is not possible or deemed risky, e.g., during Covid-19 pandemic)

- Thromboembolic / bleeding events?
- Side effects?
- Adherence (discussion, explanation, remaining pills, NOAC card, ...)?
- Change in co-medication (incl. over-the-counter drugs)?
- Need for blood sampling? Hemoglobin, renal function, coagulation panel etc.
- Re-assessment of $CHA_2DS_2$-VASc and HAS-BLED score
- Modifiable stroke- and bleeding risk factor assessment and -improvement
- Re-assessment of optimal NOAC and correct dosing

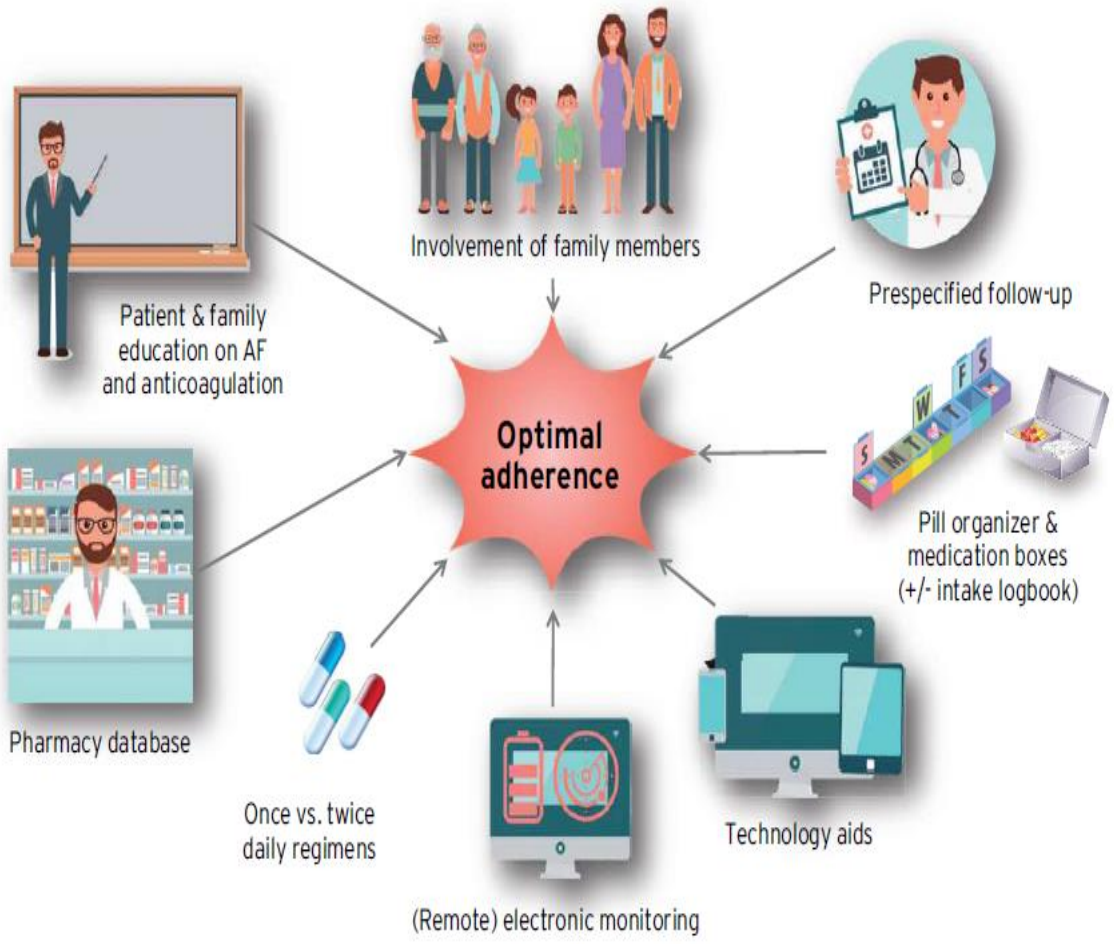
**Interval "quick check" / blood sampling**
- 4-monthly: ≥75y (especially if on dabigatran), or frail.
- Every "CrCl/10" months if CrCl ≤60 ml/min
- Immediately in case of intercurrent conditions, esp. with potential impact on renal or hepatic function (e.g., infection, NSAID use, dehydration etc.).

No severe problems or challenges

Severe problems or challenges → Consultation with specialist / multi-disciplinary team

- Filling of anticoagulation card
- Reinforcement of key educational aspects
- Schedule of date/place for next follow-up

## Measures to optimize adherence to NOACs




1. Steffel J, et al. Europace 2021;00:1–6; 2. Apixaban SmPC. Available at: www. https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf. Accessed May 2021.

# 2021 EHRA Practical Guide
## Interactions of commonly used drugs with DOACs

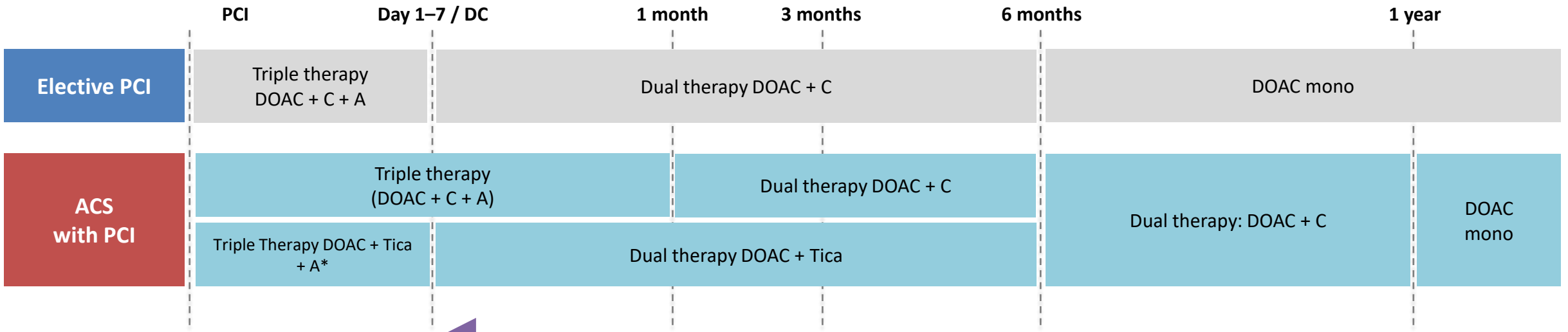
| | Via | Dabigatran | Apixaban | Edoxaban | Rivaroxaban |
|---|---|---|---|---|---|
| **P-gp substrate** | | Yes | Yes | Yes | Yes |
| **CYP3A4 substrate** | | No | Yes (≈25%) | No (<4%) | Yes (≈18%) |
| **Anti-arrhythmic drugs** | | | | | |
| **Amiodarone** | Moderate P-gp inhibition | +12 to 60% | No PK data[a] | +40% | Minor effect[a] |
| **Digoxin** | P-gp competition | No effect | No effect | No effect | No effect |
| **Diltiazem** | Weak P-gp and CYP3A4 inhibition | No effect | +40% | No data yet | No effect |
| **Dronedarone** | P-gp and CYP3A4 inhibition | +70 to 100% | With caution | +85% (dose reduction to 30 mg) | Moderate effect; should be avoided |
| **Quinidine** | P-gp inhibition | +53% | No data yet | +77% (No dose reduction required by label) | Extent of increase unknown |
| **Verapamil** | P-gp inhibition and weak CYP3A4 inhibition | +12 to 180% (if taken simultaneously) | No PK data | +53% (SR) (no dose reduction required by label) | +40% (probably not relevant) |

[a]Based on in vitro investigations, comparing the IC50 for P-gp inhibition to maximal plasma levels at therapeutic dose, and/or on interaction analysis of efficacy and safety endpoints in the Phase-3 clinical trials.

DOAC, direct-acting oral anticoagulant; P-gp, p-glycoprotein, PK, pharmacokinetic; PPI, proton pump inhibitor.

Steffel J, et al. Europace 2021;00:1–6.

# 2021 EHRA Practical Guide
## Anticoagulation post PCI/ACS




**In all patients:**

- Avoid use of BMS / first generation DES
- Use PPI if on triple / dual therapy
- Minimize bleeding risk by assessing and treating modifiable bleeding risk factors (e.g., hypertension, etc.)
- Close follow-up; check for signs of (occult) bleeding

**Factors to shorten / de-intensify combination therapy**

- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE < 140 if ACS)

**Factors to lengthen / intensify combination therapy**

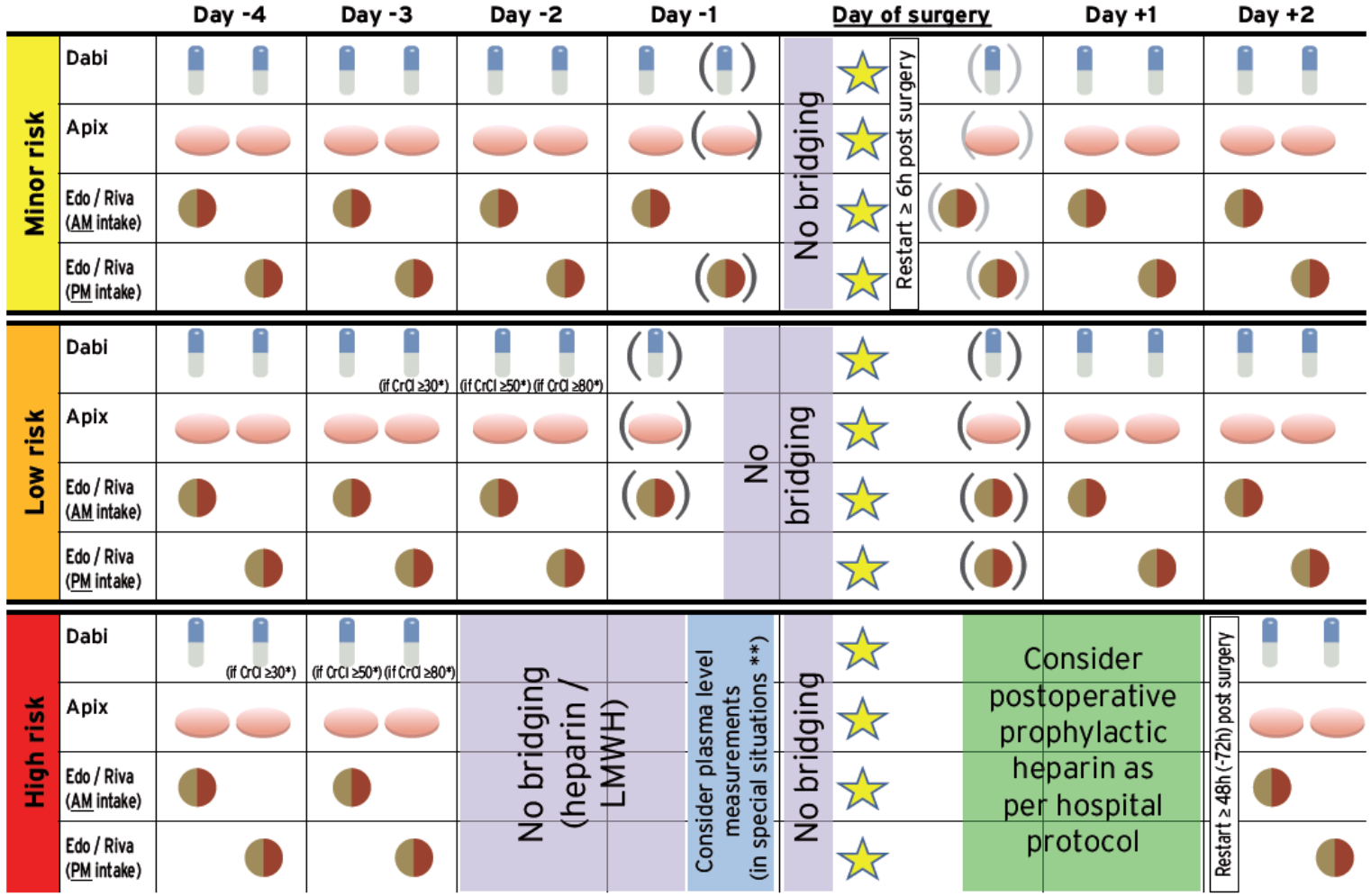
- High atherothrombotic risk (scores as above; stenting of left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

*If triple therapy needs to be continued after discharge clopidogrel is preferred over ticagrelor (due to lack of data)
The concomitant use of apixaban with antiplatelet agents increases the risk of bleeding. Apixaban should be used with caution when coadministered with ASS and/or $P2Y_{12}$ inhibitors because these medicinal products typically increase the bleeding risk.[2]

A, aspirin; ACS, acute coronary syndrome; BMS, bare metal stent; C, clopidogrel; DES, drug-eluting stents; DOAC, direct-acting oral anticoagulant; LAD, left anterior descending; MI, myocardial infraction; mono, monotherapy; PCI, percutaneous coronary intervention; PPI, proton pump inhibitor; Tica, ticagrelor.

1. Steffel J, et al. Europace 2021;00:1–6; 2. Apixaban SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf. Accessed May 2021.

# Perioperative management on NOACs



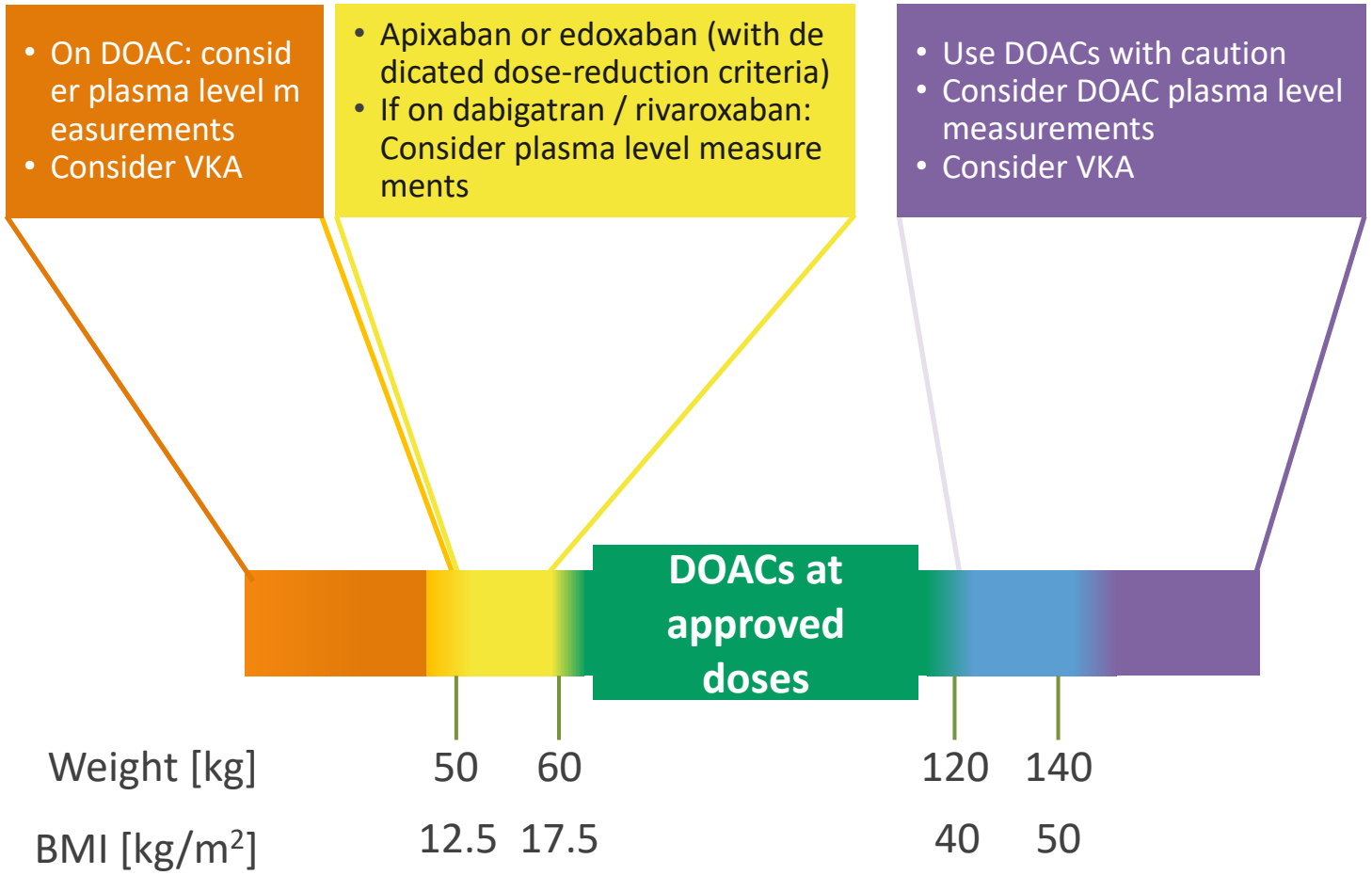

| Minor risk interventions (i.e., infrequent bleeding and with low clinical impact) |
|---|
| Dental extractions (1-3 teeth), paradontal surgery, implant positioning, subgingival scalling / cleaning |
| Cataract or glaucoma intervention |
| Endoscopy without biopsy or resection |
| Superficial surgery (e.g., abscess incision; small dermatologic excisions, skin biopsy) |
| Pacemaker or ICD implantation (except complex procedures) |
| Electrophysiological study or catheter ablation (except complex procedures), see also page 47 |
| Routine elective coronary / peripheral artery intervention (except complex procedures), see also page 48 |
| Intramuscular injection (e.g., vaccination) |
| **Low risk interventions (i.e., infrequent bleeding or with non-severe clinical impact)** |
| Complex dental procedures |
| Endoscopy with simple biopsy |
| Small orthopedic surgery (foot, hand, arthroscopy, ...) |

| High risk interventions (i.e., frequent bleeding and / or with important clinical impact) (continued) |
|---|
| Cardiac surgery |
| Peripheral arterial revascularization surgery (e.g., aortic aneurysm repair, vascular bypass) |
| Complex invasive cardiological interventions, including lead extraction, (epicardial) VT ablation, chronic total occlusion PCI etc. |
| Neurosurgery |
| Spinal or epidural anaesthesia; lumbar diagnostic puncture |
| Complex endoscopy (e.g., multiple / large polypectomy, ERCP with sphincterotomy etc.) |
| Abdominal surgery (incl. liver biopsy) |
| Thoracic surgery |
| Major urologic surgery / biopsy (incl. kidney) |
| Extracorporeal shockwave lithotripsy |
| Major orthopedic surgery |



2021 EHRA Practical Guide on the Use of NOAC in Patients with AF

# 2021 EHRA Practical Guide
## DOACs in high and low body weights[1]




### NOACs in patients with low body weight

There is no universal definition of low body weight although a BMI <18.5 kg/m$^2$ is considered by many western agencies as indicative of being underweight.[408] Low body weight may increase exposure to any NOAC and as such increase the risk of bleeding compared to normal weight patients.[409,410] Bleeding may also be increased with VKA therapy in underweight patients.[410,411] Importantly, patients with low body weight frequently present with other conditions and co-morbidities which may increase the risk of stroke as well as bleeding, including old age, frailty, cancer, and CKD. Of note, renal function may be overestimated in underweight patients due to their reduced muscle mass (especially with the MDRD formula).

Special care is needed when anticoagulating low weight patients (*Figure 23*). Body weight ≤60 kg requires dose reduction of apixaban [in patients with age ≥80 years and/or serum Creatinine ≥133 µmol/(1.5 mg/dl)] as well as for edoxaban (see 'NOAC eligibility and dosing' section, *Table 2*), whereas it is in itself not a factor for dose reduction of rivaroxaban or use of lower dose dabigatran.

Both *apixaban* and *edoxaban* showed consistent efficacy and safety compared to warfarin in underweight patients when compared with the overall study population.[98,381,389] Drug concentrations and inhibition of Factor Xa did not differ in patients with low body weight (range 30–55 kg) from patients with middle body weight in an analysis from ENGAGE AF-TIMI 48.[382] As such, both drugs may be a preferred choice for patients ≤60 kg.

Body weight: No dose adjustment for apixaban required, unless criteria for dose reduction are met. Dose reduction to 2.5 mg BD if at least 2 out of 3 fulfilled: age ≥80 years; weight ≤60 kg; creatinine ≥1.5 mg/dl (133 µmol/l).[2]

BD, twice daily; BMI, body mass index; DOAC, direct-acting oral anticoagulant; VKA, vitamin K antagonist.

1. Steffel J, et al. Europace 2021;00:1–6; 2. Apixaban SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf. Accessed May 2021.

# 2021 EHRA Practical Guide
## DOACs in patients with liver disease[1]

**Baseline assessment:**
- H/o thromboembolism or bleeding?
- Relevant co-medications and over-the-counter drugs?
- CBC, liver function test, PT/INR, APTT, renal function
- High bleeding risk (e.g., H/o major bleeding (varices), uncontrolled alcohol intake, etc.)?

Highest risk patients → Consider no anticoagulation / evaluate alternative stroke prevention strategy

All other patients ↓

| Parameter | 1 point | 2 points | 3 points |
|---|---|---|---|
| **Encephalopathy** | No | Grade 1–2 | Grade 3–4 |
| **Ascites** | No | Mild | ≥ Moderate |
| **Bilirubin** | < 2 mg/dL<br>< 34 µmol/L | 2–3 mg/dL<br>34–50 µmol/L | > 3 mg/dL<br>> 50 µmol/L |
| **Albumin** | > 3.5 g/dL<br>> 35 g/L | 2.8–3.5 g/dL<br>28–35 g/L | < 2.8 g/dL<br>< 28 g/dL |
| **INR** | < 1.7 | 1.71–2.30 | >2.30 |

**DOAC 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 | |

- ✓ Assess Child–Pugh score*
- ✓ Check DOAC use recommendations in liver disease
- ✓ Check for drug–drug interactions
- ✓ Discuss in multidisciplinary team

**Close follow-up**
- Signs of (occult) bleeding?
- Adherence? Side effects?
- (New) co-medications, incl. NSAIDs, aspirin, OTC?
- CBC, liver function, PT/INR, aPTT, renal function
- Continue bleeding risk minimization strategies
- Re-enforce education, incl. alcohol abstinence

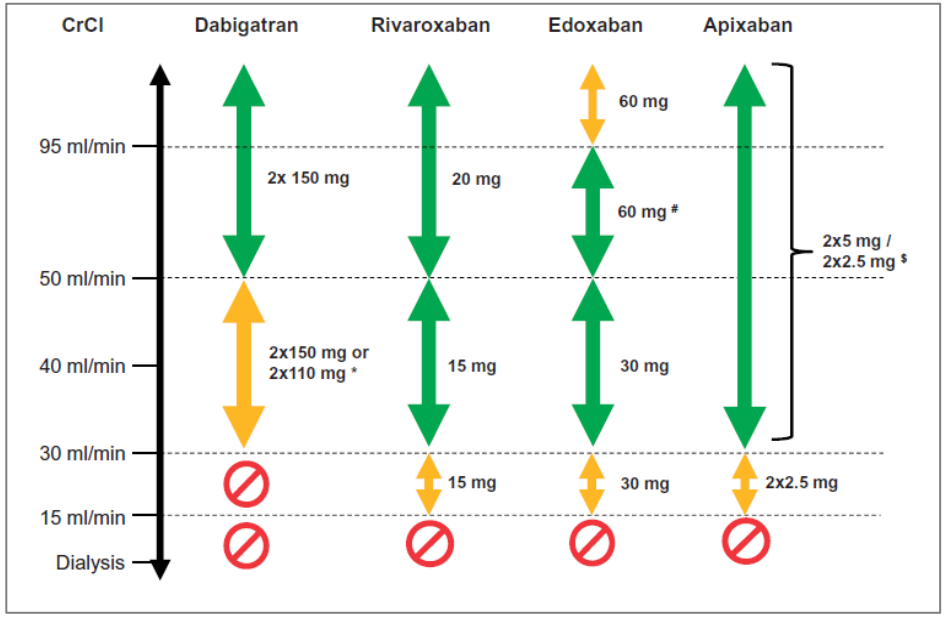
*For patients with mild or moderate hepatic impairment (Child-Pugh A or B) the use of apixaban is recommended with caution. No dose reduction necessary.[2]

aPTT, activated thromboplastin time; CBC, complete blood count; DOAC, direct-acting oral anticoagulant; H/o, however; INR, international normalised ratio; NSAID, non-steroid anti-inflammatory drug; OTC, over the counter; PT, prothrombin time.

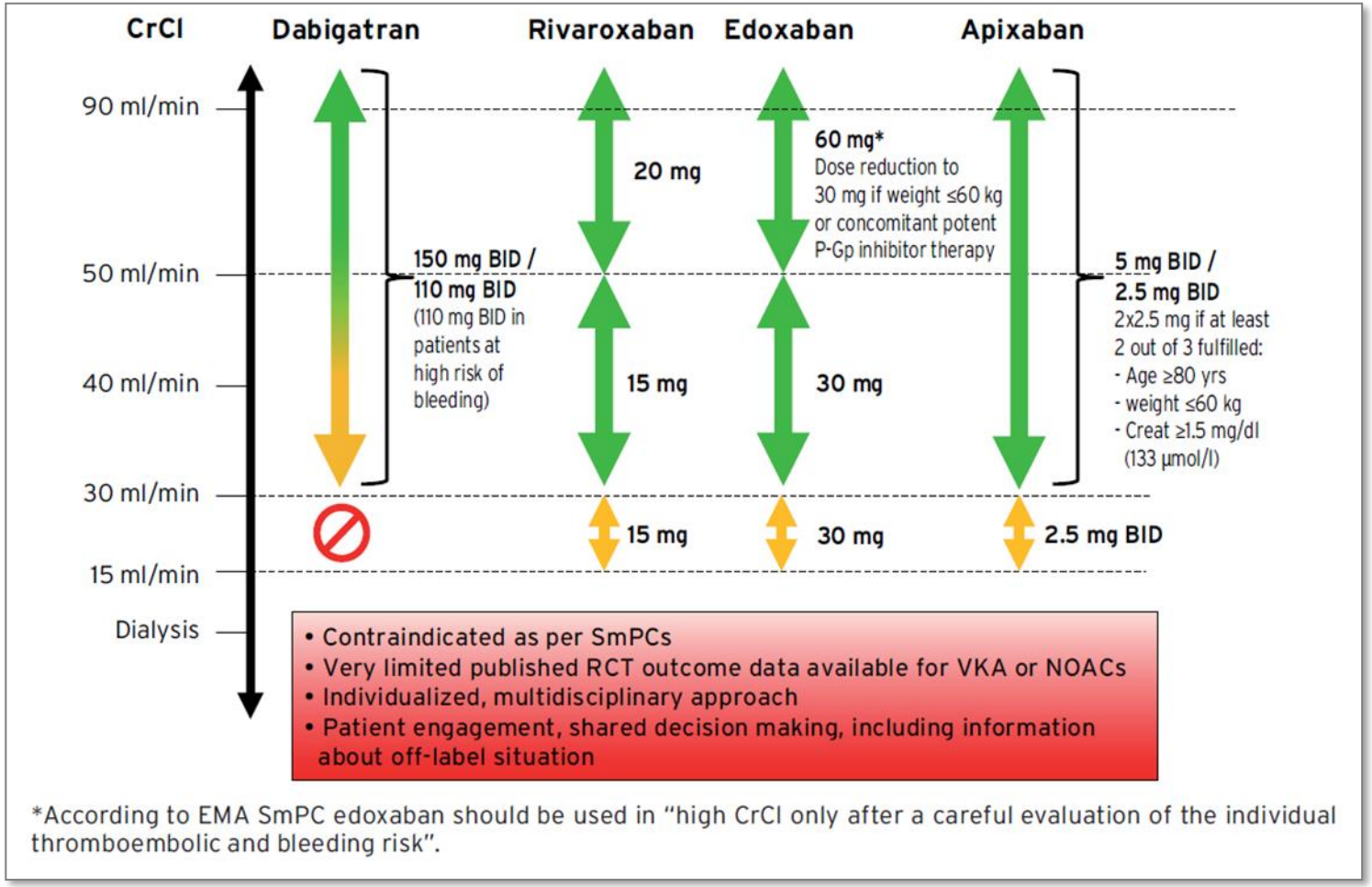
1. Steffel J, et al. Europace 2021;00:1–6; 2. Apixaban SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/eliquis-epar-product-information_en.pdf. Accessed May 2021.

# NOACs in patients with CKD

## 2018 EHRA Practical Guide




## 2021 EHRA Practical Guide




*According to EMA SmPC edoxaban should be used in "high CrCl only after a careful evaluation of the individual thromboembolic and bleeding risk".

# Take Home messages

- Diagnosis of AF: a standard 12-lead ECG recording or a single-lead ECG tracing of ≥ 30 s
- Screening to detect AF & integrated AF management
- Rhythm control/catheter ablation of AF
- Long-term antiarrhythmic drugs
- The ABC pathway of integrated care management
- The integration of lifestyle management in patients with AF
- NOAC practical guideline

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## Thank you for your attention

# NOAC use in frail patients

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|---|---|
| **Very Fit** | Robust, active, energetic and motivated. Commonly exercise regularly. Among the fittest for their age. |
| **Well** | No active disease symptoms but less fit than category 1. Often exercise or very active occasionally, e.g., seasonally. |
| **Managing Well** | Medical problems well controlled, but not regularly active beyond routine walking. |
| **Vulnerable** | Not dependent on others for daily help, but often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day. |
| **Mildly Frail** | Often with more evident slowing; need help in high order with ADLs. Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework. |
| **Moderately Frail** | Need help with all outside activities and with keeping house. Often have problems with stairs and need help with bathing, might need minimal assistance with dressing. |
| **Severely Frail** | Completely dependent for personal care (physical or cognitive). Even so, they seem stable and not at high risk of dying within ~ 6 months. |
| **Very Severely Frail** | Completely dependent, approaching the end of life. Typically can not recover even from a minor illness. |
| **Terminally Ill** | Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail. |

Frailty and terminal illness typically indicate a contraindication to anticoagulation (red).

"Clinical Frailty scale" based on comprehensive geriatric assessment including structured interview
(http://www.csha.ca and Rockwood et al., Lancet 1999; 353: 205-6.)