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**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)*

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**Keywords** Guidelines • Atrial fibrillation • AF-CARE • Comorbidity • Risk factors • Anticoagulation • Rate control • Rhythm control • Cardioversion • Antiarrhythmic drugs • Catheter ablation • AF surgery • Evaluation • Stroke • Thromboembolism

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# Abbreviations and acronyms

| | |
|---|---|
| AAD | Antiarrhythmic drugs |
| ACE | Angiotensin-converting enzyme |
| ACEi | Angiotensin-converting enzyme inhibitor |
| ACS | Acute coronary syndromes |
| ACTIVE W | Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (trial) |
| AF | Atrial fibrillation |
| AF-CARE | Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment |
| AFEQT | Atrial Fibrillation Effect on QualiTy-of-Life (questionnaire) |
| AFFIRM | Atrial Fibrillation Follow-up Investigation of Rhythm Management (trial) |
| AFL | Atrial flutter |
| AFQLQ | Atrial Fibrillation Quality of Life Questionnaire |
| AF-QoL | Atrial Fibrillation Quality of Life (questionnaire) |
| AFSS | Atrial Fibrillation Severity Scale |
| AI | Artificial intelligence |
| APACHE-AF | Apixaban After Anticoagulation-associated Intracerebral Haemorrhage in Patients With Atrial Fibrillation (trial) |
| APAF-CRT | Ablate and Pace for Atrial Fibrillation—cardiac resynchronization therapy |
| ARB | Angiotensin receptor blocker |
| ARTESiA | Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (trial) |
| AT | Atrial tachycardia |
| ATHENA | A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg twice daily for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter (trial) |
| AUGUSTUS | An open-label, 2 × 2 factorial, randomized controlled, clinical trial to evaluate the safety of apixaban vs. vitamin k antagonist and aspirin vs. aspirin placebo in patients with atrial fibrillation and acute coronary syndrome or percutaneous coronary intervention |
| AVERROES | Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment (trial) |
| AVN | Atrioventricular node |
| b.p.m. | Beats per minute |
| BMI | Body mass index |
| BNP | B-type natriuretic peptide |
| BP | Blood pressure |
| $C_2$HEST | Coronary artery disease or chronic obstructive pulmonary disease (1 point each); hypertension (1 point); elderly (age ≥75 years, 2 points); systolic heart failure (2 points); thyroid disease (hyperthyroidism, 1 point) |
| CABANA | Catheter Ablation versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (trial) |
| CAD | Coronary artery disease |
| CASTLE-AF | Catheter Ablation versus Standard Conventional Treatment in Patients With Left Ventricle (LV) Dysfunction and AF (trial) |
| CASTLE-HTx | Catheter Ablation for Atrial Fibrillation in Patients With End-Stage Heart Failure and Eligibility for Heart Transplantation (trial) |
| CCS | Chronic coronary syndrome |
| $CHADS_2$ | Congestive heart failure, hypertension, age >75 years, diabetes; previous stroke (2 points) |
| $CHA_2DS_2$-VA | Congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years (score) |
| $CHA_2DS_2$-VASc | Congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke or TIA or thromboembolism (2 points), vascular disease, age 65–74 years, sex category |
| CKD | Chronic kidney disease |
| CMR | Cardiac magnetic resonance |
| COMPASS | Cardiovascular Outcomes for People Using Anticoagulation Strategies (trial) |
| CPAP | Continuous positive airway pressure |
| CrCl | Creatinine clearance |
| CRT | Cardiac resynchronization therapy |
| CT | Computed tomography |
| CTA | Computed tomography angiography |
| CTI | Cavo-tricuspid isthmus |
| DAPT | Dual antiplatelet therapy |
| DOAC | Direct oral anticoagulant |
| EAST-AFNET 4 | Early treatment of Atrial fibrillation for Stroke prevention Trial |
| ECG | Electrocardiogram |
| ECV | Electrical cardioversion |
| EHRA | European Heart Rhythm Association |
| ELAN | Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillatioN (trial) |
| ESUS | Embolic stroke of undetermined source |
| FFP | Fresh frozen plasma |
| GI | Gastrointestinal |
| GWAS | Genome-wide association studies |
| HAS-BLED | Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years), Drugs/alcohol concomitantly (score) |
| HAVOC | Hypertension, age, valvular heart disease, peripheral vascular disease, obesity, congestive heart failure, and coronary artery disease |
| HbA1c | Haemoglobin A1c (glycated or glycosylated haemoglobin) |
| HCM | Hypertrophic cardiomyopathy |
| HF | Heart failure |
| HFmrEF | Heart failure with mildly reduced ejection fraction |
| HFpEF | Heart failure with preserved ejection fraction |
| HFrEF | Heart failure with reduced ejection fraction |
| HR | Hazard ratio |
| i.v. | Intravenous |

| | |
|---|---|
| ICH | Intracranial haemorrhage |
| ICHOM | International Consortium for Health Outcomes Measurement |
| IMT | Intima-media thickness |
| INR | International normalized ratio (of prothrombin time) |
| LA | Left atrium |
| LAA | Left atrial appendage |
| LAAO | Left atrial appendage occlusion |
| LAAOS III | Left Atrial Appendage Occlusion Study |
| LEGACY | Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: a 5 Year follow-up study |
| LMWH | Low molecular weight heparin |
| LOOP | Atrial Fibrillation Detected by Continuous ECG Monitoring (trial) |
| LV | Left ventricle |
| LVEF | Left ventricular ejection fraction |
| LVH | Left ventricular hypertrophy |
| mEHRA | Modified European Heart Rhythm Association score |
| MI | Myocardial infarction |
| MRI | Magnetic resonance imaging |
| NOAH | Non-vitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes (trial) |
| NSAID | Non-steroidal anti-inflammatory drug |
| NT-proBNP | N-terminal pro-B-type natriuretic peptide |
| NYHA | New York Heart Association |
| OAC | Oral anticoagulant(s) |
| OR | Odds ratio |
| OSA | Obstructive sleep apnoea |
| PAD | Peripheral arterial disease |
| PCC | Prothrombin complex concentrate |
| PCI | Percutaneous intervention |
| PFO | Patent foramen ovale |
| POAF | Post-operative atrial fibrillation |
| PPG | Photoplethysmography |
| PROM | Patient-reported outcome measure |
| PVD | Peripheral vascular disease |
| PVI | Pulmonary vein isolation |
| QLAF | Quality of Life in Atrial Fibrillation (questionnaire) |
| QRS | Q wave, R wave, and S wave, the 'QRS complex' represents ventricular depolarization |
| RACE 7 ACWAS | Rate Control versus Electrical Cardioversion Trial 7—Acute Cardioversion versus Wait and See (trial) |
| RACE I | RAte Control versus Electrical cardioversion study |
| RACE II | Rate Control Efficacy in Permanent Atrial Fibrillation (trial) |
| RACE 3 | Routine versus Aggressive upstream rhythm Control for prevention of Early AF in heart failure (trial) |
| RACE 4 | IntegRAted Chronic Care Program at Specialized AF Clinic Versus Usual CarE in Patients with Atrial Fibrillation (trial) |
| RATE-AF | RAte control Therapy Evaluation in permanent Atrial Fibrillation (trial) |
| RCT | Randomized controlled trial |
| RR | Relative risk |
| SAVE | Sleep Apnea cardioVascular Endpoints (trial) |
| SBP | Systolic blood pressure |
| SGLT2 | Sodium-glucose cotransporter-2 |
| SIC-AF | Successful Intravenous Cardioversion for Atrial Fibrillation |
| SORT-AF | Supervised Obesity Reduction Trial for AF Ablation Patients (trial) |
| SoSTART | Start or STop Anticoagulants Randomised Trial |
| SR | Sinus rhythm |
| STEEER-AF | Stroke prevention and rhythm control Therapy: Evaluation of an Educational programme of the European Society of Cardiology in a cluster-Randomised trial in patients with Atrial Fibrillation (trial) |
| STEMI | ST-segment elevation myocardial infarction |
| STROKESTOP | Systematic ECG Screening for Atrial Fibrillation Among 75 Year Old Subjects in the Region of Stockholm and Halland, Sweden (trial) |
| TE | Thromboembolism |
| TIA | Transient ischaemic attack |
| TIMING | Timing of Oral Anticoagulant Therapy in Acute Ischemic Stroke With Atrial Fibrillation (trial) |
| TOE | Transoesophageal echocardiography |
| TSH | Thyroid-stimulating hormone |
| TTE | Transthoracic echocardiogram |
| TTR | Time in therapeutic range |
| UFH | Unfractionated heparin |
| VKA | Vitamin K antagonist |

# 1. Preamble

Guidelines evaluate and summarize available evidence with the aim of assisting health professionals in proposing the best diagnostic or therapeutic approach for an individual patient with a given condition. Guidelines are intended for use by health professionals and the European Society of Cardiology (ESC) makes its Guidelines freely available.

ESC Guidelines do not override the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable in each country to drugs and devices at the time of prescription and to respect the ethical rules of their profession.

ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated when warranted by new evidence. ESC Policies and Procedures for formulating and issuing ESC Guidelines can be found on the ESC website (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Guidelines-development/Writing-ESC-Guidelines). This guideline updates and replaces the previous version from 2020.

The Members of this task force were selected by the ESC to include professionals involved with the medical care of patients with this pathology as well as patient representatives and methodologists. The selection procedure included an open call for authors and aimed to include members from across the whole of the ESC region and from relevant ESC Subspecialty Communities. Consideration was given to diversity

and inclusion, notably with respect to gender and country of origin. The task force performed a critical review and evaluation of the published literature on diagnostic and therapeutic approaches including assessment of the risk–benefit ratio. The strength of every recommendation and the level of evidence supporting them were weighed and scored according to predefined scales as outlined in *Tables 1 and 2* below. Patient-reported outcome measures (PROMs) and patient-reported experience measures were also evaluated as the basis for recommendations and/or discussion in these guidelines. The task force followed ESC voting procedures and all approved recommendations were subject to a vote and achieved at least 75% agreement among voting members. Members of the task force with declared interests on specific topics were asked to abstain from voting on related recommendations.

**Table 1** **Classes of recommendations**

| Classes of recommendations | Definition | Wording to use |
|---|---|---|
| Class I | Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective. | Is recommended or is indicated |
| Class II | Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure. | |
| Class IIa | Weight of evidence/opinion is in favour of usefulness/efficacy. | Should be considered |
| Class IIb | Usefulness/efficacy is less well established by evidence/opinion. | May be considered |
| Class III | Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful. | Is not recommended |



**Table 2** **Levels of evidence**

| | |
|---|---|
| Level of evidence A | Data derived from multiple randomized clinical trials or meta-analyses. |
| Level of evidence B | Data derived from a single randomized clinical trial or large non-randomized studies. |
| Level of evidence C | Consensus of opinion of the experts and/or small studies, retrospective studies, registries. |

The experts of the writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. Their declarations of interest were reviewed according to the ESC declaration of interest rules which can be found on the ESC website (http://www.escardio.org/guidelines) and have been compiled in a report published in a supplementary document with the guidelines. Funding for the development of ESC Guidelines is derived entirely from the ESC with no involvement of the healthcare industry.

The ESC Clinical Practice Guidelines (CPG) Committee supervises and co-ordinates the preparation of new guidelines and is responsible for the approval process. In addition to review by the CPG Committee, ESC Guidelines undergo multiple rounds of double-blind peer review by external experts, including members from across the whole of the ESC region, all National Cardiac Societies of the ESC and from relevant ESC Subspecialty Communities. After appropriate revisions, the guidelines are signed off by all the experts in the task force. The finalized document is signed off by the CPG Committee for publication in the *European Heart Journal*.

ESC Guidelines are based on analyses of published evidence, chiefly on clinical trials and meta-analyses of trials, but potentially including other types of studies. Evidence tables summarizing key information from relevant studies are generated early in the guideline development process to facilitate the formulation of recommendations, to enhance comprehension of recommendations after publication, and reinforce transparency in the guidelines development process. The tables are published in their own section of ESC Guidelines and reference specific recommendation tables.

Off-label use of medication may be presented in this guideline if a sufficient level of evidence shows that it can be considered medically appropriate for a given condition. However, the final decisions concerning an individual patient must be made by the responsible health professional giving special consideration to:

- The specific situation of the patient. Unless otherwise provided for by national regulations, off-label use of medication should be limited to situations where it is in the patient's interest with regard to the quality, safety, and efficacy of care, and only after the patient has been informed and has provided consent.
- Country-specific health regulations, indications by governmental drug regulatory agencies, and the ethical rules to which health professionals are subject, where applicable.

# 2. Introduction

Atrial fibrillation (AF) is one of the most commonly encountered heart conditions, with a broad impact on all health services across primary and secondary care. The prevalence of AF is expected to double in the next few decades as a consequence of the ageing population, an increasing burden of comorbidities, improved awareness, and new technologies for detection.

The effects of AF are variable across individual patients; however, morbidity from AF remains highly concerning. Patients with AF can suffer from a variety of symptoms and poor quality of life. Stroke and heart failure as consequences of AF are now well appreciated by healthcare professionals, but AF is also linked to a range of other thromboembolic outcomes. These include subclinical cerebral damage (potentially leading to vascular dementia), and thromboembolism to every other organ, all of which contribute to the higher risk of mortality associated with AF.

The typical drivers of AF onset and progression are a range of comorbidities and associated risk factors. To achieve optimal care for patients with AF, it is now widely accepted that these comorbidities and risk factors must be managed early and in a dynamic way. Failure to do so contributes to recurrent cycles of AF, treatment failure, poor patient outcomes, and a waste of healthcare resources. In this iteration of the European Society of Cardiology (ESC) practice guidelines on AF, the task force has consolidated and evolved past approaches to develop the AF-CARE framework (Atrial Fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment). Comorbidities and risk factors is placed as the initial and central component of patient management. This should be considered first as it applies to all patients with AF, regardless of their thromboembolic risk factors or any symptoms that might warrant intervention. This is followed by considering how best to [A] avoid stroke and thromboembolism, and then the options available to reduce symptoms, and in some cases improve prognosis, through [R] rate and rhythm control. [E] Evaluation and reassessment should be individualized for every patient, with a dynamic approach that accounts for how AF and its associated conditions change over time.

Patient empowerment is critical in any long-term medical problem to achieve better outcomes, encourage adherence, and to seek timely guidance on changes in clinical status. A patient-centred, shared decision-making approach will facilitate the choice of management that suits each individual patient, particularly in AF where some therapies and interventions improve clinical outcomes, and others are focused on addressing symptoms and quality of life. Education and awareness are essential, not only for patients but also healthcare professionals in order to constrain the impact of AF on patients and healthcare services.

With this in mind, the task force have created a range of patient pathways that cover the major aspects of AF-CARE. At present, these remain based on the time-orientated classification of AF (first-diagnosed, paroxysmal, persistent, and permanent), but ongoing research may allow for pathology-based classifications and a future of personalized medicine. Clinical practice guidelines can only cover common scenarios with an evidence base, and so there remains a need for healthcare professionals to care for patients within a local multidisciplinary team. While guideline-adherent care has repeatedly been shown to improve patient outcomes, the actual implementation of guidelines is often poor in many healthcare settings. This has been demonstrated in the ESC's first randomized controlled trial (RCT), STEEER-AF (Stroke prevention and rhythm control Therapy: Evaluation of an Educational programme of the European Society of Cardiology in a cluster-Randomised trial in patients with Atrial Fibrillation), which has sought to improve guideline adherence in parallel to guideline production. The task force developing the 2024 AF Guidelines have made implementation a key goal by focusing on the underpinning evidence and using a consistent writing style for each recommendation (the intervention proposed, the population it should be applied to, and the potential value to the patient, followed by any exceptions). *Tables 3* and *4* below outline new recommendations and those with important revisions. These initiatives have been designed to make the *2024 ESC Guidelines for the management of AF* easier to read, follow, and implement, with the aim of improving the lives of patients with AF. A patient version of these guidelines is also available at http://www.escardio.org/Guidelines/guidelines-for-patients.

## 2.1. What is new

**Table 3** New recommendations

| | Class[a] | Level[b] |
|---|---|---|
| **Diagnostic evaluation of new AF—*Section 3.4*** | | |
| A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions. | I | C |
| **Principles of AF-CARE—*Section 4.2*** | | |
| Education directed to patients, family members, caregivers, and healthcare professionals is recommended to optimize shared decision-making, facilitating open discussion of both the benefit and risk associated with each treatment option. | I | C |
| Access to patient-centred management according to the AF-CARE principles is recommended in all patients with AF, regardless of gender, ethnicity, and socioeconomic status, to ensure equality in healthcare provision and improve outcomes. | I | C |
| Patient-centred AF management with a multidisciplinary approach should be considered in all patients with AF to optimize management and improve outcomes. | IIa | B |
| **[C] Comorbidity and risk factor management—*Section 5*** | | |
| Diuretics are recommended in patients with AF, HF, and congestion to alleviate symptoms and facilitate better AF management. | I | C |
| Appropriate medical therapy for HF is recommended in AF patients with HF and impaired LVEF to reduce symptoms and/or HF hospitalization and prevent AF recurrence. | I | B |
| Sodium-glucose cotransporter-2 inhibitors are recommended for patients with HF and AF regardless of left ventricular ejection fraction to reduce the risk of HF hospitalization and cardiovascular death. | I | A |
| Effective glycaemic control is recommended as part of comprehensive risk factor management in individuals with diabetes mellitus and AF, to reduce burden, recurrence, and progression of AF. | I | C |
| Bariatric surgery may be considered in conjunction with lifestyle changes and medical management in individuals with AF and body mass index ≥40 kg/m$^2$ [c] where a rhythm control strategy is planned, to reduce recurrence and progression of AF. | IIb | C |
| Management of obstructive sleep apnoea may be considered as part of a comprehensive management of risk factors in individuals with AF to reduce recurrence and progression. | IIb | B |
| When screening for obstructive sleep apnoea in individuals with AF, using only symptom-based questionnaires is not recommended. | III | B |
| **Initiating oral anticoagulation—*Section 6.1*** | | |
| Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. | I | A |
| A $CHA_2DS_2$-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | I | C |
| A $CHA_2DS_2$-VA score of 1 should be considered an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | IIa | C |
| Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of $CHA_2DS_2$-VA score, to prevent ischaemic stroke and thromboembolism. | I | B |
| Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients. | I | B |
| Direct oral anticoagulant therapy may be considered in patients with asymptomatic device-detected subclinical AF and elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism, excluding patients at high risk of bleeding. | IIb | B |
| **Oral anticoagulants—*Section 6.2*** | | |
| A reduced dose of DOAC therapy is not recommended, unless patients meet DOAC-specific criteria, to prevent underdosing and avoidable thromboembolic events. | III | B |
| Maintaining VKA treatment rather than switching to a DOAC may be considered in patients aged ≥75 years on clinically stable therapeutic VKA with polypharmacy to prevent excess bleeding risk. | IIb | B |
| **Antiplatelet drugs and combinations with anticoagulants—*Section 6.3*** | | |
| Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism. | III | B |

*Continued*

| | | |
|---|---|---|
| **Residual ischaemic stroke risk despite anticoagulation—*Section 6.4*** | | |
| A thorough diagnostic work-up should be considered in patients taking an oral anticoagulant and presenting with ischaemic stroke or thromboembolism to prevent recurrent events, including assessment of non-cardioembolic causes, vascular risk factors, dosage, and adherence. | IIa | B |
| Adding antiplatelet treatment to anticoagulation is not recommended in patients with AF to prevent recurrent embolic stroke. | III | B |
| Switching from one DOAC to another, or from a DOAC to a VKA, without a clear indication is not recommended in patients with AF to prevent recurrent embolic stroke. | III | B |
| **Surgical left atrial appendage occlusion—*Section 6.6*** | | |
| Surgical closure of the left atrial appendage should be considered as an adjunct to oral anticoagulation in patients with AF undergoing endoscopic or hybrid AF ablation to prevent ischaemic stroke and thromboembolism. | IIa | C |
| Stand-alone endoscopic surgical closure of the left atrial appendage may be considered in patients with AF and contraindications for long-term anticoagulant treatment to prevent ischaemic stroke and thromboembolism. | IIb | C |
| **Management of bleeding on anticoagulant therapy—*Section 6.7.2*** | | |
| Specific antidotes should be considered in AF patients on a DOAC who develop a life-threatening bleed, or bleed into a critical site, to reverse the antithrombotic effect. | IIa | B |
| **Management of heart rate in patients with AF—*Section 7.1*** | | |
| Rate control therapy is recommended in patients with AF, as initial therapy in the acute setting, an adjunct to rhythm control therapies, or as a sole treatment strategy to control heart rate and reduce symptoms. | I | B |
| Beta-blockers, diltiazem, verapamil, or digoxin are recommended as first-choice drugs in patients with AF and LVEF >40% to control heart rate and reduce symptoms. | I | B |
| Atrioventricular node ablation combined with cardiac resynchronization therapy should be considered in severely symptomatic patients with permanent AF and at least one hospitalization for HF to reduce symptoms, physical limitations, recurrent HF hospitalization, and mortality. | IIa | B |
| **General principles and anticoagulation—*Section 7.2.1*** | | |
| Direct oral anticoagulants are recommended in preference to VKAs in eligible patients with AF undergoing cardioversion for thromboembolic risk reduction. | I | A |
| Cardioversion of AF (either electrical or pharmacological) should be considered in symptomatic patients with persistent AF as part of a rhythm control approach. | IIa | B |
| A wait-and-see approach for spontaneous conversion to sinus rhythm within 48 h of AF onset should be considered in patients without haemodynamic compromise as an alternative to immediate cardioversion. | IIa | B |
| Implementation of a rhythm control strategy should be considered within 12 months of diagnosis in selected patients with AF at risk of thromboembolic events to reduce the risk of cardiovascular death or hospitalization. | IIa | B |
| Early cardioversion is not recommended without appropriate anticoagulation or transoesophageal echocardiography if AF duration is longer than 24 h, or there is scope to wait for spontaneous cardioversion. | III | C |
| **Electrical cardioversion—*Section 7.2.2*** | | |
| Electrical cardioversion as a diagnostic tool should be considered in patients with persistent AF where there is uncertainty about the value of sinus rhythm restoration on symptoms, or to assess improvement in left ventricular function. | IIa | C |
| **Antiarrhythmic drugs—*Section 7.2.4*** | | |
| Antiarrhythmic drug therapy is not recommended in patients with advanced conduction disturbances unless antibradycardia pacing is provided. | III | C |
| **Catheter ablation—*Section 7.2.5*** | | |
| Sinus node disease/tachycardia–bradycardia syndrome | | |
| Atrial fibrillation catheter ablation should be considered in patients with AF-related bradycardia or sinus pauses on AF termination to improve symptoms and avoid pacemaker implantation. | IIa | C |
| Recurrence after catheter ablation | | |
| Repeat AF catheter ablation should be considered in patients with AF recurrence after initial catheter ablation, provided the patient's symptoms were improved after the initial PVI or after failed initial PVI, to reduce symptoms, recurrence, and progression of AF. | IIa | B |
| **Anticoagulation in patients undergoing catheter ablation—*Section 7.2.6*** | | |
| Uninterrupted oral anticoagulation is recommended in patients undergoing AF catheter ablation to prevent peri-procedural ischaemic stroke and thromboembolism. | I | A |

*Continued*

| | | |
|---|---|---|
| **Endoscopic and hybrid AF ablation—*Section 7.2.7*** | | |
| Continuation of oral anticoagulation is recommended in patients with AF at elevated thromboembolic risk after concomitant, endoscopic, or hybrid AF ablation, independent of rhythm outcome or LAA exclusion, to prevent ischaemic stroke and thromboembolism. | I | C |
| Endoscopic and hybrid ablation procedures should be considered in patients with symptomatic persistent AF refractory to AAD therapy to prevent symptoms, recurrence, and progression of AF, within a shared decision-making rhythm control team of electrophysiologists and surgeons. | IIa | A |
| **AF ablation during cardiac surgery—*Section 7.2.8*** | | |
| Intraprocedural imaging for detection of left atrial thrombus in patients undergoing surgical ablation is recommended to guide surgical strategy, independent of oral anticoagulant use, to prevent peri-procedural ischaemic stroke and thromboembolism. | I | C |
| Concomitant surgical ablation should be considered in patients undergoing non-mitral valve cardiac surgery and AF suitable for a rhythm control strategy to prevent symptoms and recurrence of AF, with shared decision-making supported by an experienced team of electrophysiologists and arrhythmia surgeons. | IIa | B |
| **Patient-reported outcome measures—*Section 8.4*** | | |
| Evaluating quality of care and identifying opportunities for improved treatment of AF should be considered by practitioners and institutions to improve patient experiences. | IIa | B |
| **Acute and chronic coronary syndromes in patients with AF—*Section 9.2*** | | |
| Recommendations for AF patients with chronic coronary or vascular disease | | |
| Antiplatelet therapy beyond 12 months is not recommended in stable patients with chronic coronary or vascular disease treated with oral anticoagulation, due to lack of efficacy and to avoid major bleeding. | III | B |
| **Trigger-induced AF—*Section 9.5*** | | |
| Long-term oral anticoagulation should be considered in suitable patients with trigger-induced AF at elevated thromboembolic risk to prevent ischaemic stroke and systemic thromboembolism. | IIa | C |
| **Post-operative AF—*Section 9.6*** | | |
| Peri-operative amiodarone therapy is recommended where drug therapy is desired to prevent post-operative AF after cardiac surgery. | I | A |
| Concomitant posterior peri-cardiotomy should be considered in patients undergoing cardiac surgery to prevent post-operative AF. | IIa | B |
| **Patients with embolic stroke of unknown source (ESUS)—*Section 9.7*** | | |
| Initiation of oral anticoagulation in ESUS patients without documented AF is not recommended due to lack of efficacy in preventing ischaemic stroke and thromboembolism. | III | A |
| **Atrial flutter—*Section 9.14*** | | |
| Oral anticoagulation is recommended in patients with atrial flutter at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. | I | B |
| **Screening strategies for AF—*Section 10.3*** | | |
| Review of an ECG (12-lead, single, or multiple leads) by a physician is recommended to provide a definite diagnosis of AF and commence appropriate management. | I | B |
| Population-based screening for AF using a prolonged non-invasive ECG-based approach should be considered in individuals aged ≥75 years, or ≥65 years with additional $CHA_2DS_2$-VA risk factors to ensure earlier detection of AF. | IIa | B |
| **Primary prevention of AF—*Section 10.5*** | | |
| Maintaining optimal blood pressure is recommended in the general population to prevent AF, with ACE inhibitors or ARBs as first-line therapy. | I | B |
| Appropriate medical HF therapy is recommended in individuals with HFrEF to prevent AF. | I | B |
| Maintaining normal weight (BMI 20–25 kg/m$^2$) is recommended for the general population to prevent AF. | I | B |
| Maintaining an active lifestyle is recommended to prevent AF, with the equivalent of 150–300 min per week of moderate intensity or 75–150 min per week of vigorous intensity aerobic physical activity. | I | B |
| Avoidance of binge drinking and alcohol excess is recommended in the general population to prevent AF. | I | B |
| Metformin or SGLT2 inhibitors should be considered for individuals needing pharmacological management of diabetes mellitus to prevent AF. | IIa | B |
| Weight reduction should be considered in obese individuals to prevent AF. | IIa | B |

AAD, antiarrhythmic drugs; ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; ARB, angiotensin receptor blocker; BMI, body mass index; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; DOAC, direct oral anticoagulant; ECG, electrocardiogram; ESUS, embolic stroke of undetermined source; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LAA, left atrial appendage; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; SGLT2, sodium-glucose cotransporter-2; VKA, vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

[c]Or body mass index ≥35 kg/m$^2$ with obesity-related complications.

**Table 4 Revised recommendations**

| Recommendations in 2020 version | Class[a] | Level[b] | Recommendations in 2024 version | Class[a] | Level[b] |
|---|---|---|---|---|---|
| ***Section 3.2*—Diagnostic criteria for AF** | | | | | |
| ECG documentation is required to establish the diagnosis of AF. A standard 12-lead ECG recording or a single-lead ECG tracing of ≥30 s 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 | Confirmation by an electrocardiogram (12-lead, multiple, or single leads) is recommended to establish the diagnosis of clinical AF and commence risk stratification and treatment. | I | A |
| In patients with AF, it is recommended to:<br>• Evaluate AF-related symptoms (including fatigue, tiredness, exertional shortness of breath, palpitations, and chest pain) and quantify the patient symptom status using the modified EHRA symptom scale before and after initiation of treatment.<br>• Evaluate AF-related symptoms before and after cardioversion of persistent AF to aid rhythm control treatment decisions. | I | C | Evaluating the impact of AF-related symptoms is recommended before and after major changes in treatment to inform shared decision-making and guide treatment choices. | I | B |
| ***Section 5*—[C] Comorbidity and risk factor management** | | | | | |
| Attention to good BP control is recommended in AF patients with hypertension to reduce AF recurrences and risk of stroke and bleeding. | I | B | Blood pressure lowering treatment is recommended in patients with AF and hypertension to reduce recurrence and progression of AF and prevent adverse cardiovascular events. | I | B |
| In obese patients with AF, weight loss together with management of other risk factors should be considered to reduce AF incidence, AF progression, AF recurrences, and symptoms. | IIa | B | Weight loss is recommended as part of comprehensive risk factor management in overweight and obese individuals with AF to reduce symptoms and AF burden, with a target of 10% or more reduction in body weight. | I | B |
| Physical activity should be considered to help prevent AF incidence or recurrence, with the exception of excessive endurance exercise, which may promote AF. | IIa | C | A tailored exercise programme is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence. | I | B |
| Advice and management to avoid alcohol excess should be considered for AF prevention and in AF patients considered for OAC therapy. | IIa | B | Reducing alcohol consumption to ≤3 standard drinks (≤30 grams of alcohol) per week is recommended as part of comprehensive risk factor management to reduce AF recurrence. | I | B |
| ***Section 6.6*—Surgical left atrial appendage occlusion** | | | | | |
| Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery. | IIb | C | Surgical closure of the left atrial appendage is recommended as an adjunct to oral anticoagulation in patients with AF undergoing cardiac surgery to prevent ischaemic stroke and thromboembolism. | I | B |
| ***Section 6.7*—Bleeding risk** | | | | | |
| For a formal risk-score-based assessment of bleeding risk, the HAS-BLED score should be considered to help address modifiable bleeding risk factors, and to identify patients at high risk of bleeding (HAS-BLED score ≥3) for early and more frequent clinical review and follow-up. | IIa | B | Assessment and management of modifiable bleeding risk factors is recommended in all patients eligible for oral anticoagulation, as part of shared decision-making to ensure safety and prevent bleeding. | I | B |

*Continued*

| | | | | | |
|---|---|---|---|---|---|
| ***Section 7.2*—Rhythm control strategies in patients with AF** | | | | | |
| AF catheter ablation for PVI should/may be considered as first-line rhythm control therapy to improve symptoms in selected patients with symptomatic:<br>• Paroxysmal AF episodes. | IIa | B | Catheter ablation is recommended as a first-line option within a shared decision-making rhythm control strategy in patients with paroxysmal AF, to reduce symptoms, recurrence, and progression of AF. | I | A |
| Thoracoscopic procedures—including hybrid surgical ablation—should be considered in patients who have symptomatic paroxysmal or persistent AF refractory to AAD therapy and have failed percutaneous AF ablation, or with evident risk factors for catheter ablation failure, to maintain long-term sinus rhythm. The decision must be supported by an experienced team of electrophysiologists and surgeons. | IIa | B | Endoscopic and hybrid ablation procedures may be considered in patients with symptomatic paroxysmal AF refractory to AAD therapy and failed percutaneous catheter ablation strategy to prevent symptoms, recurrence, and progression of AF, within a shared decision-making rhythm control team of electrophysiologists and surgeons. | IIb | B |
| Thoracoscopic procedures—including hybrid surgical ablation—may be considered in patients with persistent AF with risk factors for recurrence, who remain symptomatic during AF despite at least one failed AAD and who prefer further rhythm control therapy. | IIb | C | Endoscopic and hybrid ablation procedures should be considered in patients with symptomatic persistent AF refractory to AAD therapy to prevent symptoms, recurrence, and progression of AF, within a shared decision-making rhythm control team of electrophysiologists and surgeons. | IIa | A |
| Concomitant AF ablation should be considered in patients undergoing cardiac surgery, balancing the benefits of freedom from atrial arrhythmias and the risk factors for recurrence (left atrial dilatation, years in AF, age, renal dysfunction, and other cardiovascular risk factors). | IIa | A | Concomitant surgical ablation is recommended in patients undergoing mitral valve surgery and AF suitable for a rhythm control strategy to prevent symptoms and recurrence of AF, with shared decision-making supported by an experienced team of electrophysiologists and arrhythmia surgeons. | I | A |
| ***Section 9.6*—Post-operative AF** | | | | | |
| Long-term OAC therapy to prevent thromboembolic events may be considered in patients at risk for stroke with post-operative AF after cardiac surgery, considering the anticipated net clinical benefit of OAC therapy and informed patient preferences. | IIb | B | Long-term oral anticoagulation should be considered in patients with post-operative AF after cardiac and non-cardiac surgery at elevated thromboembolic risk, to prevent ischaemic stroke and thromboembolism. | IIa | B |

AAD, antiarrhythmic drugs; AF, atrial fibrillation; BP, blood pressure; ECG, electrocardiogram; EHRA, European Heart Rhythm Association; HAS-BLED, Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years), Drugs/alcohol concomitantly; LAA, left atrial appendage; OAC, oral anticoagulant; PVI, pulmonary vein isolation; RR, relative risk.
[a]Class of recommendation.
[b]Level of evidence.

# 3. Definitions and clinical impact

## 3.1. Definition and classification of AF

Atrial fibrillation is one of the most common heart rhythm disorders. A supraventricular arrhythmia with uncoordinated atrial activation, AF results in a loss of effective atrial contraction (see Supplementary data online for pathophysiology). AF is reflected on the surface electrocardiogram (ECG) by the absence of discernible and regular P waves, and irregular activation of the ventricles. This results in no specific pattern to RR intervals, in the absence of an atrioventricular block. The definition of AF by temporal pattern is presented in *Table 5*. It should be noted that these categories reflect observed episodes of AF and do not suggest the underlying pathophysiological process. Some patients may progress consecutively through these categories, while others may need periodic reclassification due to their individual clinical status. Over time, some patients with AF develop atrial and ventricular damage, which can make attempts at rhythm control futile. For this reason, or when patients and physicians make a joint decision for rate control, AF is classified as permanent (the most common 'type' of AF in historical registries).[1] Despite many limitations, this task force have retained this temporal approach because most trials in patients with AF have used these definitions. Classifying AF by underlying drivers could inform management, but the evidence in support of the clinical use of such classification is currently lacking.

Several other classifications have been applied to patients with AF, many of which have limited evidence to support them. The definition of AF is a developing field and ongoing research may allow for pathology-based strategies that could facilitate personalized management in the future. *Table 6* presents some commonly used concepts in current clinical practice. Due to the lack of supporting evidence (particularly for the time periods stated), this task force have edited and updated these definitions by consensus.

**Table 5 Definitions and classifications for the temporal pattern of AF**

| Temporal classification | Definition |
|---|---|
| **First-diagnosed AF** | AF that has not been diagnosed before, regardless of symptom status, temporal pattern, or duration. |
| **Paroxysmal AF** | AF which terminates spontaneously within 7 days or with the assistance of an intervention. Evidence suggests that most self-terminating paroxysms last <48 h.[2] |
| **Persistent AF** | AF episodes which are not self-terminating. Many intervention trials have used 7 days as a cut-off for defining persistent AF.[3,4] Long-standing persistent AF is arbitrarily defined as continuous AF of at least 12 months' duration but where rhythm control is still a treatment option in selected patients, distinguishing it from permanent AF. |
| **Permanent AF** | AF for which no further attempts at restoration of sinus rhythm are planned, after a shared decision between the patient and physician. |

AF, atrial fibrillation.



**Table 6 Other clinical concepts relevant to AF**

| Clinical concept | Definition |
|---|---|
| **Clinical AF** | Symptomatic or asymptomatic AF that is clearly documented by an ECG (12-lead ECG or other ECG devices). The minimum duration to establish the diagnosis of clinical AF for ambulatory ECG is not clear and depends on the clinical context. Periods of 30 s or more may indicate clinical concern, and trigger further monitoring or risk stratification for thromboembolism. |
| **Device-detected subclinical AF** | Device-detected subclinical AF refers to asymptomatic episodes of AF detected on continuous monitoring devices. These devices include implanted cardiac electronic devices, for which most atrial high-rate episodes[a] may be AF, as well as consumer-based wearable monitors. Confirmation is needed by a competent professional reviewing intracardiac electrograms or an ECG-recorded rhythm.[5,6] Device-detected subclinical AF is a predictor of future clinical AF.[7] |
| **AF burden** | The overall time spent in AF during a clearly specified and reported period of monitoring, expressed as a percentage of time. |
| **Recent-onset AF** | There is accumulating data on the value of the term recent-onset AF in decision-making for acute pharmacological or electrical cardioversion of AF. The cut-off time interval to define this entity has not yet been established.[8–10] |
| **Trigger-induced AF** | New AF episode in close proximity to a precipitating and potentially reversible factor.[11–14] |
| **Early AF** | The time since diagnosis that qualifies for early AF is dissociated from any underlying atrial cardiomyopathy and is not well defined, broadly ranging from 3 to 24 months.[15–17] The definition of early AF also does not necessarily determine early timing of intervention. |
| **Self-terminating AF** | Paroxysmal AF which terminates spontaneously.[2] This definition may be of value for decisions on acute rhythm control taken jointly by the patient and healthcare provider. |
| **Non-self-terminating AF** | Atrial fibrillation which does not terminate spontaneously and, if needed, termination can be achieved only with an intervention. |
| **Atrial cardiomyopathy** | A combination of structural, electrical, or functional changes in the atria that leads to clinical impact (e.g. progression/recurrence of AF, limited effectiveness of AF therapy, and/or development of heart failure).[18,19] Atrial cardiomyopathy includes inflammatory and prothrombotic remodelling of the atria, neurohormonal activation (thereby affecting the ventricles), and fibrosis of myocardial tissue.[20] |

AF, atrial fibrillation; b.p.m., beats per minute; ECG, electrocardiogram.
[a]Atrial high-rate episodes are defined as episodes generally lasting more than 5 min with an atrial lead rate ≥170 b.p.m.,[7,21–24] detected by implanted cardiac devices that allow for automated continuous monitoring and storage of atrial rhythm. Atrial high-rate episodes need to be visually inspected because some may be electrical artefacts or false positives.



## 3.2. Diagnostic criteria for AF

In many patients, the diagnosis of AF is straightforward, e.g. typical symptoms associated with characteristic features on a standard 12-lead ECG that indicate the need for AF management. Diagnosis becomes more challenging in the context of asymptomatic episodes or AF detected on longer-term monitoring devices, particularly those that do

not provide an ECG (see *Section 10*). To guard against inappropriate diagnosis of AF, this task force continues to recommend that ECG documentation is required to initiate risk stratification and AF management. In current practice, ECG confirmation can include multiple options: not only where AF persists across a standard 12-lead ECG, but also single- and multiple-lead devices that provide an ECG (see Supplementary data online, Additional Evidence *Table S1*). This does not include non-ECG wearables and other devices that typically use photoplethysmography. Note that many pivotal AF trials required two or more ECGs documenting AF, or an established AF diagnosis before randomization.[25–29] The time period of AF required for diagnosis on monitoring devices is not clear cut. A standard 12-lead ECG measures 10 s, while 30 s or more on single-lead or multiple-lead ECG devices has generally been the consensus opinion, albeit with limited evidence.

**Recommendation Table 1 — Recommendations for the diagnosis of AF (see also Evidence Table 1)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Confirmation by an electrocardiogram (12-lead, multiple, or single leads) is recommended to establish the diagnosis of clinical AF and commence risk stratification and treatment.[25–29] | I | A |

AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.



## 3.3. Symptoms attributable to AF

Symptoms related to episodes of AF are variable and broad, and not just typical palpitations (*Figure 1*). Asymptomatic episodes of AF can occur,[30] although 90% of patients with AF describe symptoms with variable severity.[31] Even in symptomatic patients, some episodes of AF may remain asymptomatic.[32,33] The presence or absence of symptoms is not related to incident stroke, systemic embolism, or mortality.[34] However, symptoms do impact on patient quality of life.[35,36] Cardiac-specific AF symptoms such as palpitations are less common than non-specific symptoms such as fatigue, but they significantly impair quality of life.[36,37] Although women are often underrepresented in clinical trials of AF,[38–40] the available literature suggests that women with AF appear to be more symptomatic and have poorer quality of life.[41,42] Patients with AF report a higher burden of anxiety and severity of depression (odds ratio [OR], 1.08; 95% confidence interval [CI], 1.02–1.15; $P = .009$) as compared with the general population,[43,44] with higher prevalence of these symptoms in women with AF.[45]

Assessment of AF-related symptoms should be recorded initially, after a change in treatment, or before and after intervention. The modified European Heart Rhythm Association score (mEHRA) symptom classification (*Table 7*) is similar to the New York Heart Association (NYHA) functional class for heart failure. It correlates with quality of life scores in clinical trials, is associated with clinical progress and events, and may be a valuable starting point in routine practice to assess the burden and impact of symptoms together with the patient.[46–48] Note that symptoms may also relate to associated comorbidities and not just the AF component. The patient-related effects of symptoms from AF over time can alternatively be evaluated using patient-reported outcome measures (see *Section 8.4*).

**Recommendation Table 2 — Recommendations for symptom evaluation in patients with AF (see also Evidence Table 2)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Evaluating the impact of AF-related symptoms is recommended before and after major changes in treatment to inform shared decision-making and guide treatment choices.[17,36,46–55] | I | B |

AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.



## 3.4. Diagnostic evaluation of new AF

All patients with AF should be offered a comprehensive diagnostic assessment and review of medical history to identify risk factors and/or comorbidities needing active treatment. *Table 8* displays the essential diagnostic work-up for a patient with AF.

A 12-lead ECG is warranted in all AF patients to confirm rhythm, determine ventricular rate, and look for signs of structural heart disease, conduction defects, or ischaemia.[56] Blood tests should be carried out (kidney function, serum electrolytes, liver function, full blood count, glucose/glycated haemoglobin [HbA1c], and thyroid tests) to detect any concomitant conditions that may exacerbate AF or increase the risk of bleeding and/or thromboembolism.[57,58]

Other investigations will depend on individualized assessment and the planned treatment strategy.[59–65] A transthoracic echocardiogram (TTE) should be carried out in the initial work-up, where this will guide management decisions, or in patients where there is a change in cardiovascular signs or symptoms. The task force recognizes that accessibility to TTE might be limited or delayed in the primary care setting, but this should not delay initiation of oral anticoagulation (OAC) or other components of AF-CARE where indicated.[66] Further details on TTE and reassessment (e.g. if elevated heart rate limits diagnostic imaging, or where there is a change in clinical status) are presented in *Section 8.3*. Additional imaging using different modalities may be required to assist with comorbidity and AF-related management (see Supplementary data online, *Figure S1*).

**Recommendation Table 3 — Recommendations for diagnostic evaluation in patients with new AF (see also Evidence Table 3)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions.[59,65,67] | I | C |

AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

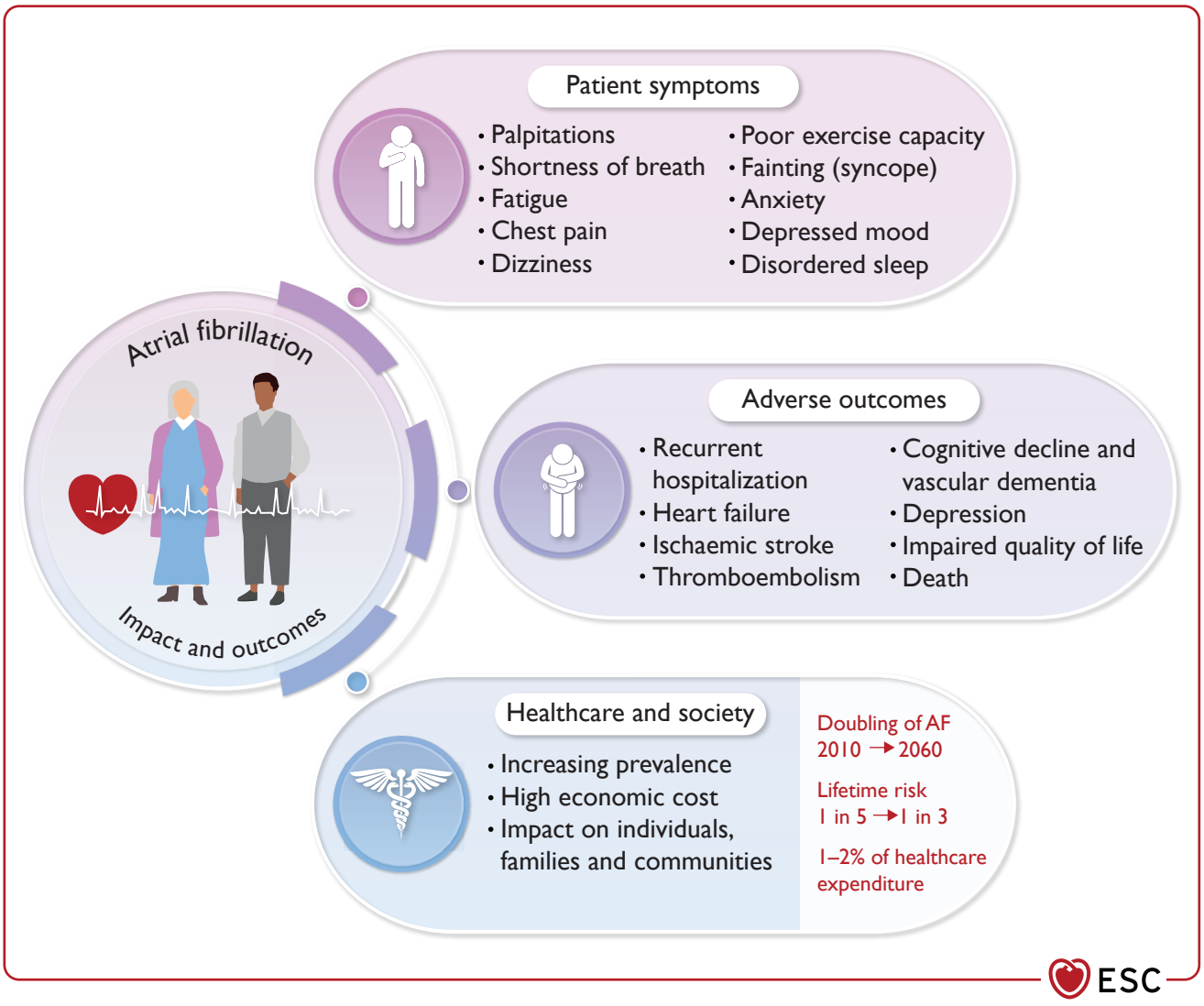


**Figure 1** Impacts and outcomes associated with clinical AF. AF, atrial fibrillation.

**Table 7 The modified European Heart Rhythm Association (mEHRA) symptom classification**

| Score | Symptoms | Description |
|---|---|---|
| 1 | None | AF does not cause any symptoms |
| 2a | Mild | Normal daily activity not affected by symptoms related to AF |
| 2b | Moderate | Normal daily activity not affected by symptoms related to AF, but patient troubled by symptoms |
| 3 | Severe | Normal daily activity affected by symptoms related to AF |
| 4 | Disabling | Normal daily activity discontinued |

AF, atrial fibrillation.



## 3.5. Adverse events associated with AF

Atrial fibrillation is associated with a range of serious adverse events (*Figure 1*) (see Supplementary data online, *Additional Evidence Table S2*). Patients with AF also have high rates of hospitalization and complications from coexisting medical conditions. The most common non-fatal outcome in those with AF is heart failure, occurring in around half of patients over time. Patients with AF have a four- to five-fold increase in the relative risk (RR) of heart failure compared with those without AF, as demonstrated in two meta-analyses (RR, 4.62; 95% CI, 3.13–6.83 and RR, 4.99; 95% CI, 3.0–8.22).[68,69] The next most common adverse impacts from AF are ischaemic stroke (RR, 2.3; 95% CI, 1.84–2.94), ischaemic heart disease (RR, 1.61; 95% CI, 1.38–1.87), and other thromboembolic events.[69–71] The latter typically include arterial thromboembolic events (preferred to the term systemic), although venous thromboembolism is also associated

**Table 8 Diagnostic work-up for patients with AF**

| All patients | Selected patients |
|---|---|
| • Medical history to determine AF pattern, relevant family history, and comorbidities, and to assess risk factors for thromboembolism and bleeding | • Ambulatory ECG monitoring for assessing AF burden and ventricular rate control<br>• Exercise ECG to evaluate rate control or effects of class IC antiarrhythmic drugs |
| • 12-lead ECG | • Further blood tests for investigation of cardiovascular disease and refinement of stroke/bleeding risk (e.g. NT-proBNP, troponin) |
| • Assess symptoms and functional impairment | • Transoesophageal echocardiography for left atrial thrombus and valvular disease assessment |
| • Collect generic or AF-specific patient-reported outcome measures | • Coronary CT, angiography, or ischaemia imaging for suspected CAD |
| • Blood tests (full blood count, kidney function, serum electrolytes, liver function, glucose/HbA1c, and thyroid function) | • CMR for evaluation of atrial and ventricular cardiomyopathies, and to plan interventional procedures |
| • Transthoracic echocardiography where this will guide AF-CARE management decisions | • Brain imaging and cognitive function assessment for cerebrovascular disease and dementia risk |

AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; CAD, coronary artery disease; CMR, cardiac magnetic resonance; CT, computed tomography; CTA, computed tomography angiography; ECG, electrocardiogram; HbA1c, glycated haemoglobin; NT-proBNP, N-terminal pro-B-type natriuretic peptide.



with AF.[72,73] Patients with AF also have an increased risk of cognitive impairment (adjusted hazard ratio [HR], 1.39; 95% CI, 1.25–1.53)[74] and dementia (OR, 1.6; 95% CI, 1.3–2.0).[75–77] It should be noted that most of the observational studies on adverse events have a mix of patients taking and not taking OAC. When carefully controlling for the confounding effects of stroke, comorbidities, and OAC, AF exposure was still significantly associated with vascular dementia (HR, 1.68; 95% CI, 1.33–2.12; $P < .001$), but not Alzheimer's disease (HR, 0.85; 95% CI, 0.70–1.03; $P = .09$).[78]

Hospital admission rates due to AF vary widely depending on the population studied, and may be skewed by selection bias. In a Dutch RCT including first-diagnosed AF patients (mean age 64 years), cardiovascular hospitalization rates were 7.0% to 9.4% per year.[79] An Australian study identified 473 501 hospitalizations for AF during 15 years of follow-up (300 million person-years), with a relative increase in AF hospitalizations of 203% over the study period, in contrast to an increase for all hospitalizations of 71%. The age-specific incidence of hospital admission increased particularly in the older age groups.[80]

Atrial fibrillation is also associated with increased mortality. In 2017, AF contributed to over 250 000 deaths globally, with an age-standardized mortality rate of 4.0 per 100 000 people (95% uncertainty interval 3.9–4.2).[81] The most frequent cause of death in patients with AF is heart failure related,[70] with complex relationships to cardiovascular and non-cardiovascular disease.[82] There is up to a two-fold increased risk of all-cause mortality (RR, 1.95; 95% CI, 1.50–2.54),[68] and cardiovascular mortality (RR, 2.03; 95% CI, 1.79–2.30)[69] in AF compared with sinus rhythm. Even in the absence of major thromboembolic risk factors, the incidence of death is 15.5 per 1000 person-years in those with AF exposure, compared with 9.4 per 1000 person-years without (adjusted HR, 1.44; 95% CI, 1.38–1.50; $P < .001$).[78] Patients with OAC-related bleeding have higher mortality, including both minor and major bleeding (as defined by the International Society on Thrombosis and Haemostasis scale).[83] Despite OAC, patients with AF remain at high residual risk of death, highlighting the importance of attention to concomitant disease.[84]

## 3.6. Atrial flutter

Atrial flutter (AFL) is the among the most common atrial tachyarrhythmias, with an overall incidence rate of 88 per 100 000 person-years, rising to 317 per 100 000 person-years in people over 50 years of age.[85] Risk factors for AFL and AF are similar, and more than half of all patients with AFL will develop AF.[85] Observational studies suggest that thromboembolic risk is elevated in AFL.[86] In direct comparison of AFL with AF, some studies suggest a similar risk of stroke and others a lower risk in AFL,[87–90] possibly due to different comorbidity burdens and the impact of confounders such as AFL/AF ablation and anticoagulation (more frequently stopped in AFL).[91]

# 4. Patient pathways and management of AF

## 4.1. Patient-centred, multidisciplinary AF management

### 4.1.1. The patient at the heart of care

A patient-centred and integrated approach to AF management means working with a model of care that respects the patient's experience, values, needs, and preferences for planning, co-ordination, and delivery of care. A central component of this model is the therapeutic relationship between the patient and the multidisciplinary team of healthcare professionals (*Figure 2*). In patient-centred AF management, patients are seen not as passive recipients of health services, but as active participants who work as partners alongside healthcare professionals. Patient-centred AF management requires integration of all aspects of AF management. This includes symptom control, lifestyle recommendations, psychosocial support, and management of comorbidities, alongside optimal medical treatment consisting of pharmacotherapy, cardioversion, and interventional or surgical ablation (*Table 9*). Services should be designed to ensure that all patients have access to an organized model of AF management, including tertiary care specialist services when indicated (see Supplementary data online, *Table S1, Evidence Table 4 and Additional Evidence Table S3*). It is equally important to maintain pathways for patients to promptly re-engage with specialist services when their condition alters.

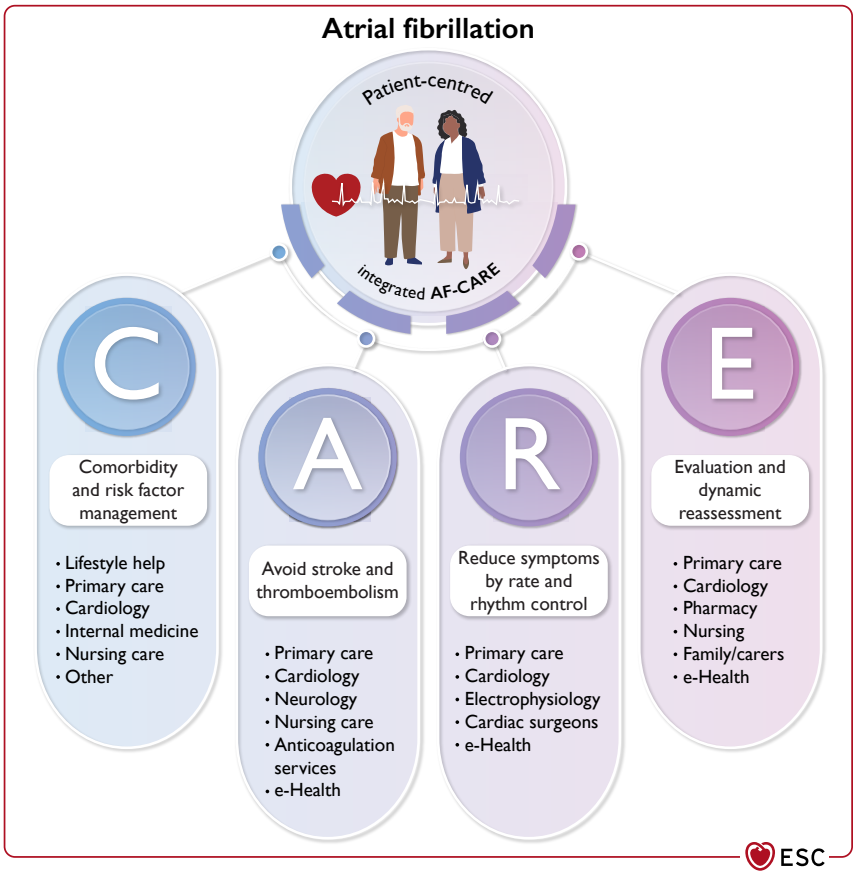


**Figure 2** Multidisciplinary approach to AF management. Principal caregivers are involved in the community and hospital settings to provide optimal, patient-centred care for patients living with AF. AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment.

**Table 9 Achieving patient-centred AF management**

| **Components of patient-centred AF management:** |
|---|
| • Optimal treatment according to the AF-CARE pathway, which includes: |
| ◦ [C] Comorbidity and risk factor management |
| ◦ [A] Avoid stroke and thromboembolism |
| ◦ [R] Reduce symptoms by rate and rhythm control |
| ◦ [E] Evaluation and dynamic reassessment |
| • Lifestyle recommendations |
| • Psychosocial support |
| • Education and awareness for patients, family members, and caregivers |
| • Seamless co-ordination between primary care and specialized AF care |
| **How to implement patient-centred AF management:** |
| • Shared decision-making |
| • Multidisciplinary team approach |
| • Patient education and empowerment, with emphasis on self-care |
| • Structured educational programmes for healthcare professionals |
| • Technology support (e-Health, m-Health, telemedicine)[a] |

AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment.
[a]e-Health refers to healthcare services provided using electronic methods; m-Health, refers to healthcare services supported by mobile devices; and telemedicine refers to remote diagnosis or treatment supported by telecommunications technology.



### 4.1.2. Education and shared decision-making

Clear advice about the rationale for treatments, the possibility of treatment modification, and shared decision-making can help patients live with AF (see Supplementary data online, *Table S2*).[92] An open and effective relationship between the patient and the healthcare professional is critical, with shared decision-making found to improve outcomes for OAC and arrhythmia management.[93,94] In using a shared approach, both the clinician and patient are involved in the decision-making process (to the extent that the patient prefers). Information is shared in both directions. Furthermore, both the clinician and the patient express their preferences and discuss the options. Of the potential treatment decisions, no treatment is also a possibility.[95] There are several toolkits available to facilitate this, although most are focused on anticoagulation decisions. For example, the Shared Decision-Making Toolkit (http://afibguide.com, http://afibguide.com/clinician) and the Successful Intravenous Cardioversion for Atrial Fibrillation (SIC-AF) score have been shown to reduce decisional conflict compared with usual care in patients with AF.[93,94] Patient-support organizations can also make an important contribution to providing understandable and actionable knowledge about AF and its treatments (e.g. local support groups and international charities, such as http://afa-international.org). As AF is a chronic or recurrent disease in most patients, education is central to empower patients, their families, and caregivers.

### 4.1.3. Education of healthcare professionals

Gaps in knowledge and skills across all domains of AF care are consistently described among cardiologists, neurologists, internal medicine specialists, emergency physicians, general practitioners, nurses, and allied health practitioners.[96–98] Healthcare professionals involved in multidisciplinary AF management should have a knowledge of all available options for diagnosis and treatment.[99–101] In the STEEER-AF trial,[99] real-world adherence to clinical practice guidelines for AF across six ESC countries was poor. These findings highlight the critical need for appropriate training and education of healthcare professionals.[102]

Specifically targeted education for healthcare professionals can increase knowledge and lead to more appropriate use of OAC for prevention of thromboembolism.[103] However, educational interventions for healthcare providers are often not enough to sustainably impact behaviour.[104] Other tools may be needed, such as active feedback,[103] clinical decision support tools,[105] expert consultation,[106] or e-Health learning.[107]

### 4.1.4. Inclusive management of AF

Evidence is growing on differences in AF incidence, prevalence, risk factors, comorbidities, and outcomes according to gender.[108] Women diagnosed with AF are generally older, have more hypertension and heart failure with preserved ejection fraction (HFpEF), and have less diagnosed coronary artery disease (CAD).[109] Registry studies have reported differences in outcomes, with higher morbidity and mortality in women, although these may be confounded by age and comorbidity burden.[110–112] Women with AF may be more symptomatic, and report a lower quality of life.[41,113] It is unclear whether this is related to delayed medical assessment in women, or whether there are genuine sex differences. Despite a higher symptom load, women are less likely to undergo AF ablation than men, even though antiarrhythmic drug therapy seems to be associated with more proarrhythmic events in women.[109] These observations call for more research on gender differences in order to prevent disparities and inequality in care. Other diversity aspects such as age, race, ethnicity, and transgender issues, as well as social determinants (including socioeconomic status, disability, education level, health literacy, and rural/urban location) are important contributors to inequality that should be actively considered to improve patient outcomes.[114]

## 4.2. Principles of AF-CARE

The *2024 ESC Guidelines for the management of AF* have compiled and evolved past approaches to create principles of management to aid implementation of these guidelines, and hence improve patient care and outcomes. There is growing evidence that clinical support tools[115–118] can aid best-practice management, with the caveat that any tool is a guide only, and that all patients require personalized attention. The AF-CARE approach covers many established principles in the management of AF, but does so in a systematic, time-orientated format with four essential treatment pillars (*Figure 3*; central illustration). Joint management with each patient forms the starting point of the AF-CARE approach. Notably, it takes account of the growing evidence base that therapies for AF are most effective when associated health conditions are addressed. A careful search for these comorbidities and risk factors [C] is critical and should be applied in all patients with a diagnosis of AF. Avoidance of stroke and thromboembolism [A] in patients with risk factors is considered next, focused on appropriate use of anticoagulant therapy. Reducing AF-related symptoms and morbidity by effective use of heart rate and rhythm control [R] is then applied, which in selected patients may also reduce hospitalization or improve prognosis. The potential benefit of rhythm control, accompanied by consideration of all risks involved, should be considered in all patients at each contact point with healthcare professionals. As AF, and its related comorbidities, changes over time, different levels of evaluation [E] and re-evaluation are required in each patient, and these approaches should be dynamic. Due to the wide variability in response to therapy, and the changing pathophysiology of AF as age and comorbidities advance, reassessment should be built into the standard care pathway to prevent adverse outcomes for patients and improve population health.

AF-CARE builds upon prior ESC Guidelines, e.g. the five-step outcome-focused integrated approach in the *2016 ESC Guidelines for the management of AF*,[119] and the AF Better Care (ABC) pathway in the *2020 ESC Guidelines for the diagnosis and management of AF*.[120] The reorganization into AF-CARE was based on the parallel developments in new approaches and technologies (in particular for rhythm control), with new evidence consistently suggesting that all aspects of AF management are more effective when comorbidities and risk factors have been considered. This includes management relating to symptom benefit, improving prognosis, prevention of thromboembolism, and the response to rate and rhythm control strategies. AF-CARE makes explicit the need for individualized evaluation and follow-up in every patient, with an active approach that accounts for how patients, their AF, and associated comorbidities change over time. The AF-CARE principles have been applied to different patient pathways for ease of implementation into routine clinical care. This includes the management of first-diagnosed AF (*Figure 4*), paroxysmal AF (*Figure 5*), persistent AF (*Figure 6*), and permanent AF (*Figure 7*).

**Recommendation Table 4 — Recommendations for patient-centred care and education (see also Evidence Table 4)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Education directed to patients, family members, caregivers, and healthcare professionals is recommended to optimize shared decision-making, facilitating open discussion of both the benefit and risk associated with each treatment option.[94,103] | I | C |
| Access to patient-centred management according to the AF-CARE principles is recommended in all patients with AF, regardless of gender, ethnicity, and socioeconomic status, to ensure equality in healthcare provision and improve outcomes. | I | C |
| Patient-centred AF management with a multidisciplinary approach should be considered in all patients with AF to optimize management and improve outcomes.[79,121–124] | IIa | B |

AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment.
[a]Class of recommendation.
[b]Level of evidence.

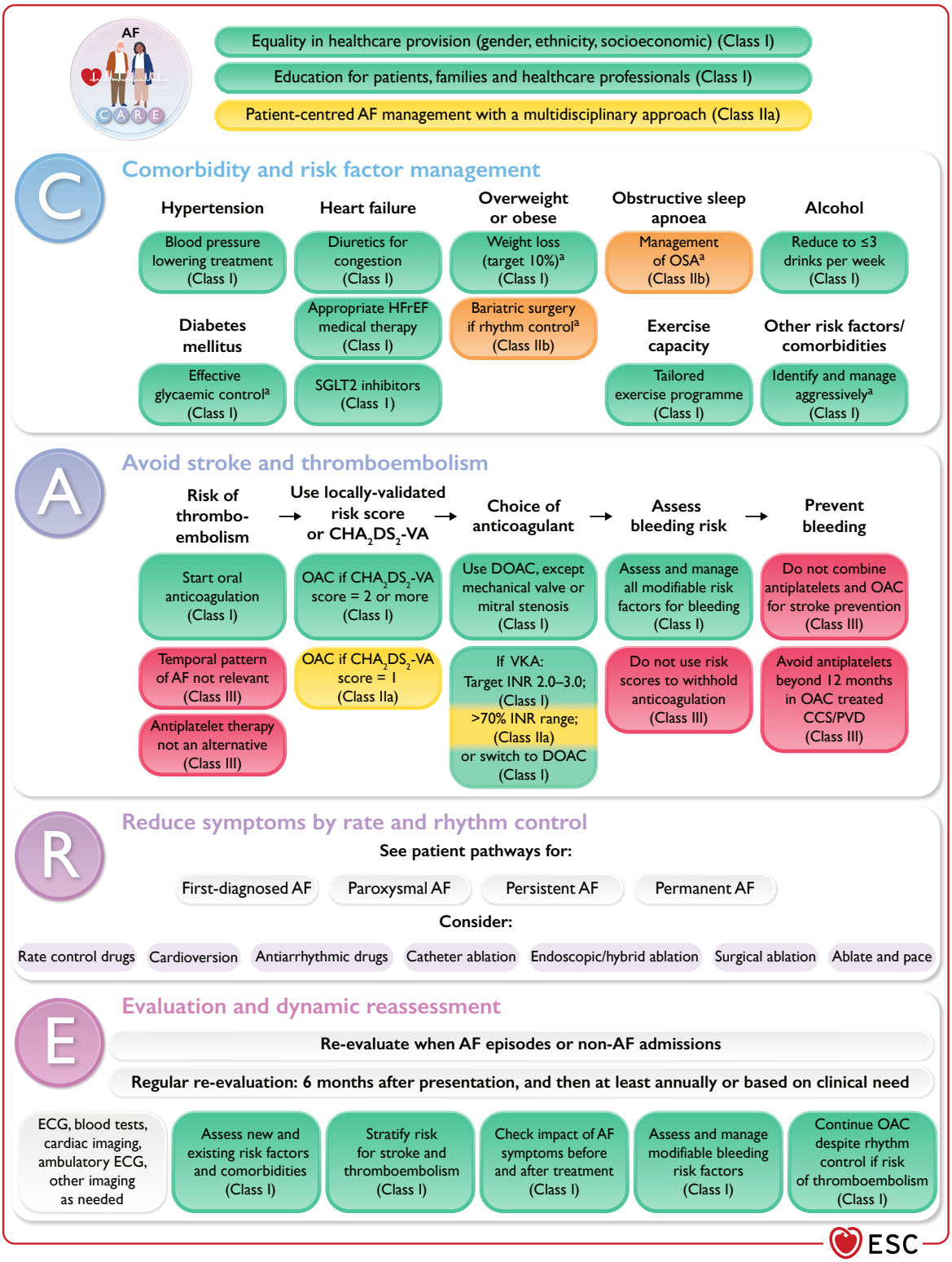


**Figure 3** Central illustration. Patient pathway for AF-CARE (see *Figures 4*, *5*, *6*, and *7* for the [R] pathways for first-diagnosed, paroxysmal, persistent and permanent AF). AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; CCS, chronic coronary syndrome; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; DOAC, direct oral anticoagulant; ECG, electrocardiogram; HFrEF, heart failure with reduced ejection fraction; INR, international normalized ratio of prothrombin time; OAC, oral anticoagulant; OSA, obstructive sleep apnoea; PVD, peripheral vascular disease; SGLT2, sodium-glucose cotransporter-2; VKA, vitamin K antagonist. [a]As part of a comprehensive management of cardiometabolic risk factors.

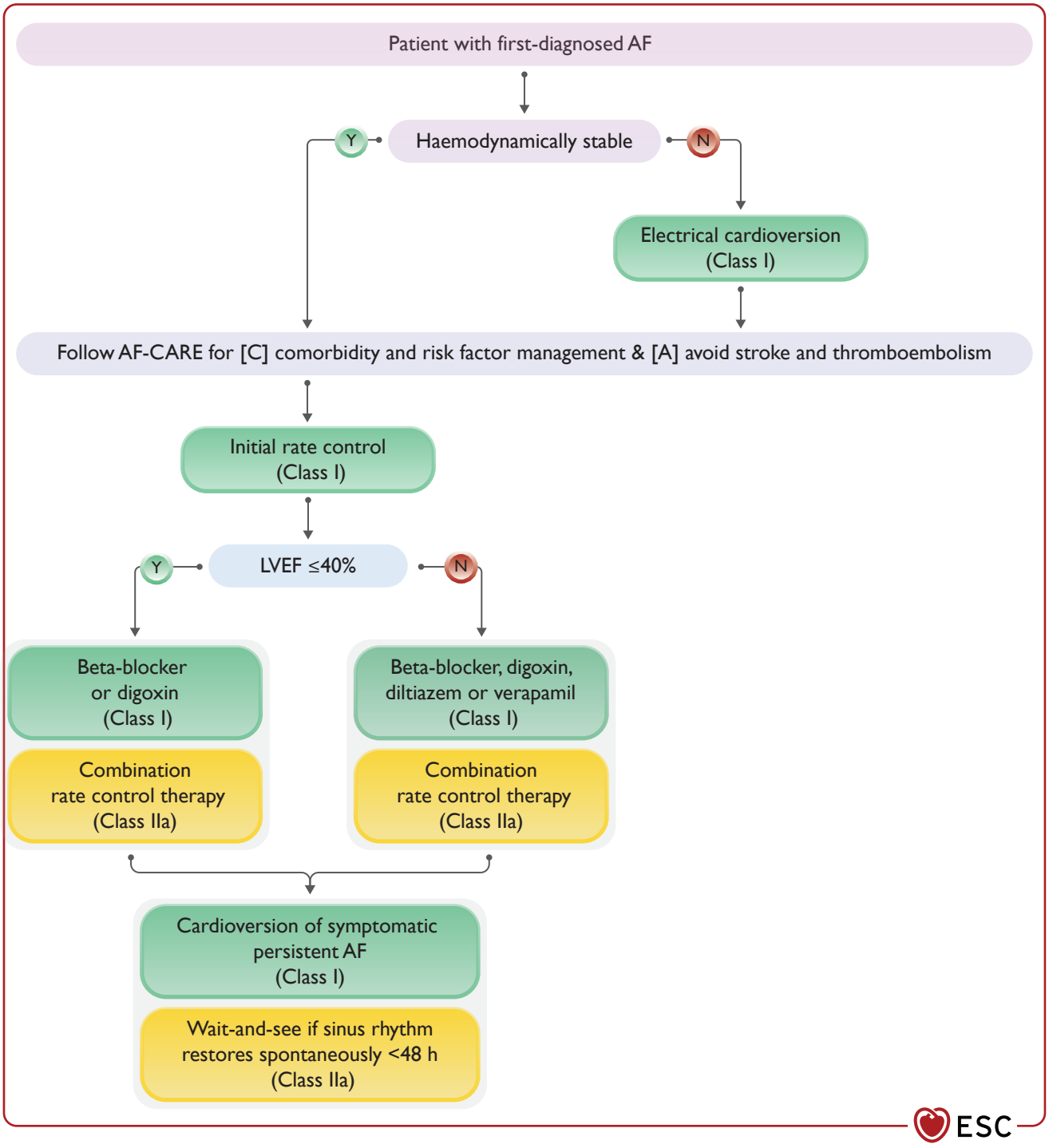


**Figure 4** [R] Pathway for patients with first-diagnosed AF. AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; LVEF, left ventricular ejection fraction. After following the pathway for first-diagnosed AF, patients with recurrent AF should enter the AF-CARE [R] pathway for paroxysmal, persistent, or permanent AF, depending on the type of their AF.

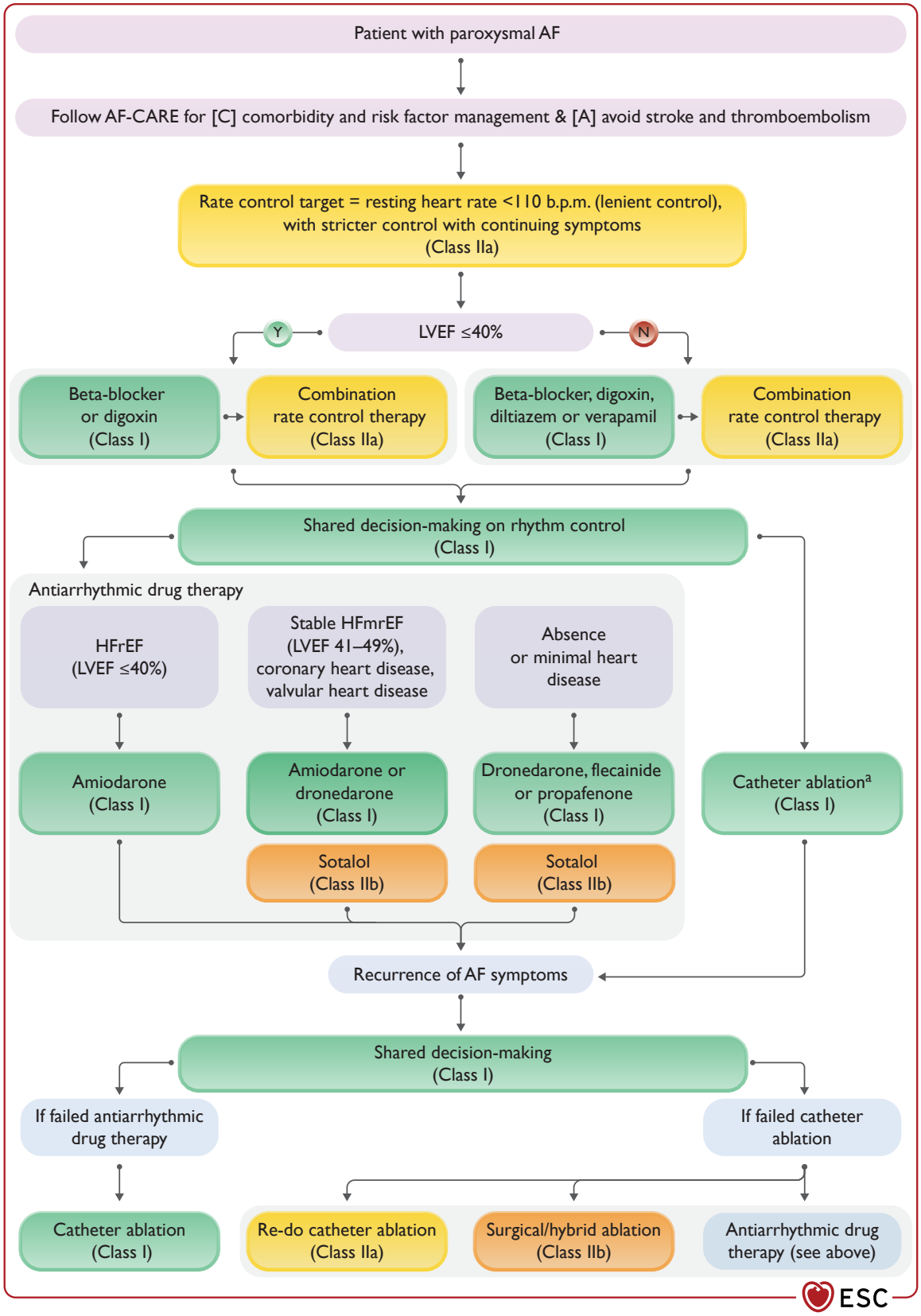


**Figure 5** [R] Pathway for patients with paroxysmal AF. AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; b.p.m., beats per minute; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, Heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction. [a]In patients with HFrEF: Class I if high probability of tachycardia-induced cardiomyopathy; and Class IIa in selected patients to improve prognosis.

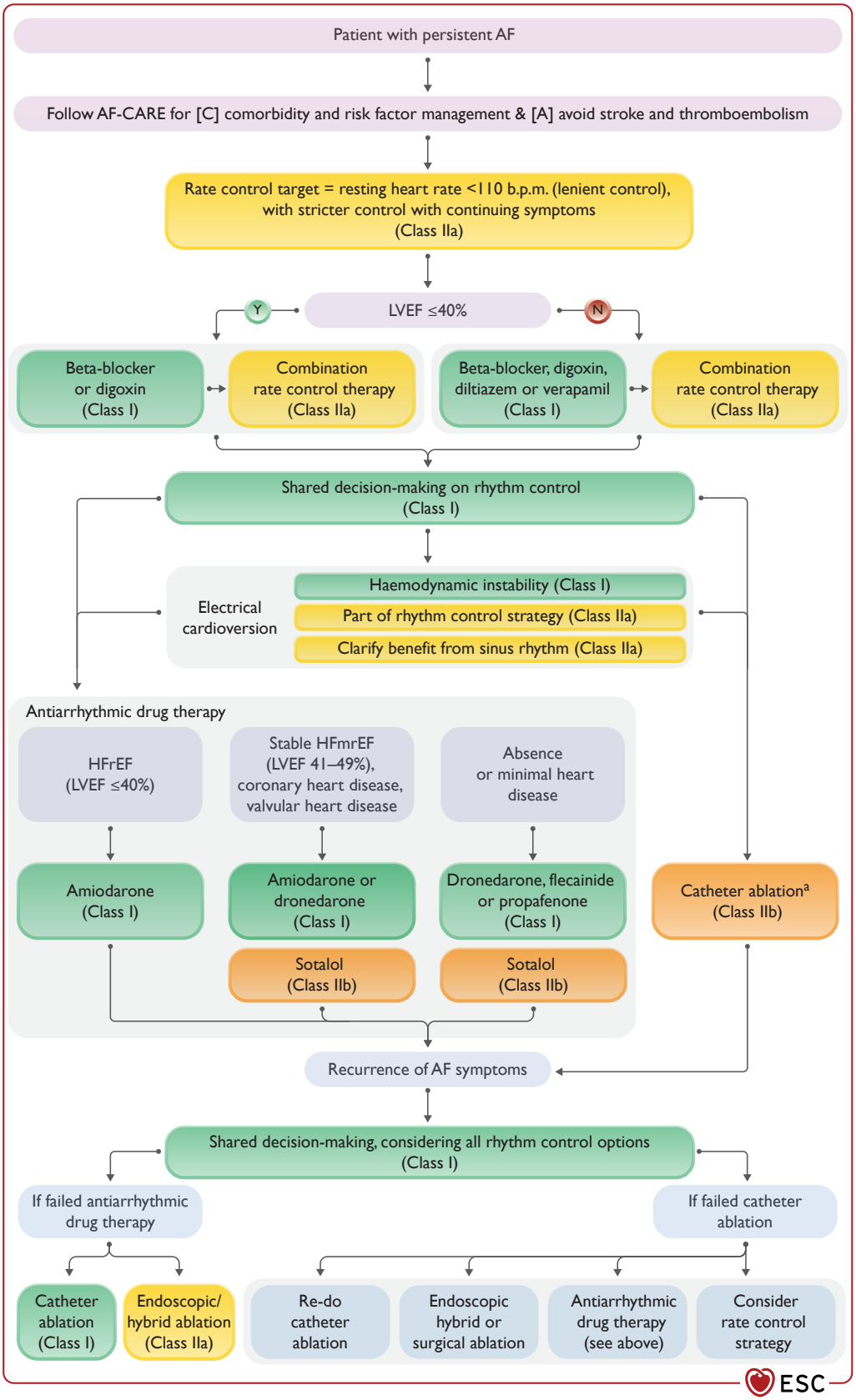


**Figure 6** [R] Pathway for patients with persistent AF. AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; b.p.m., beats per minute; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction. [a]In patients with HFrEF: Class I if high probability of tachycardia-induced cardiomyopathy; and Class IIa in selected patients to improve prognosis.

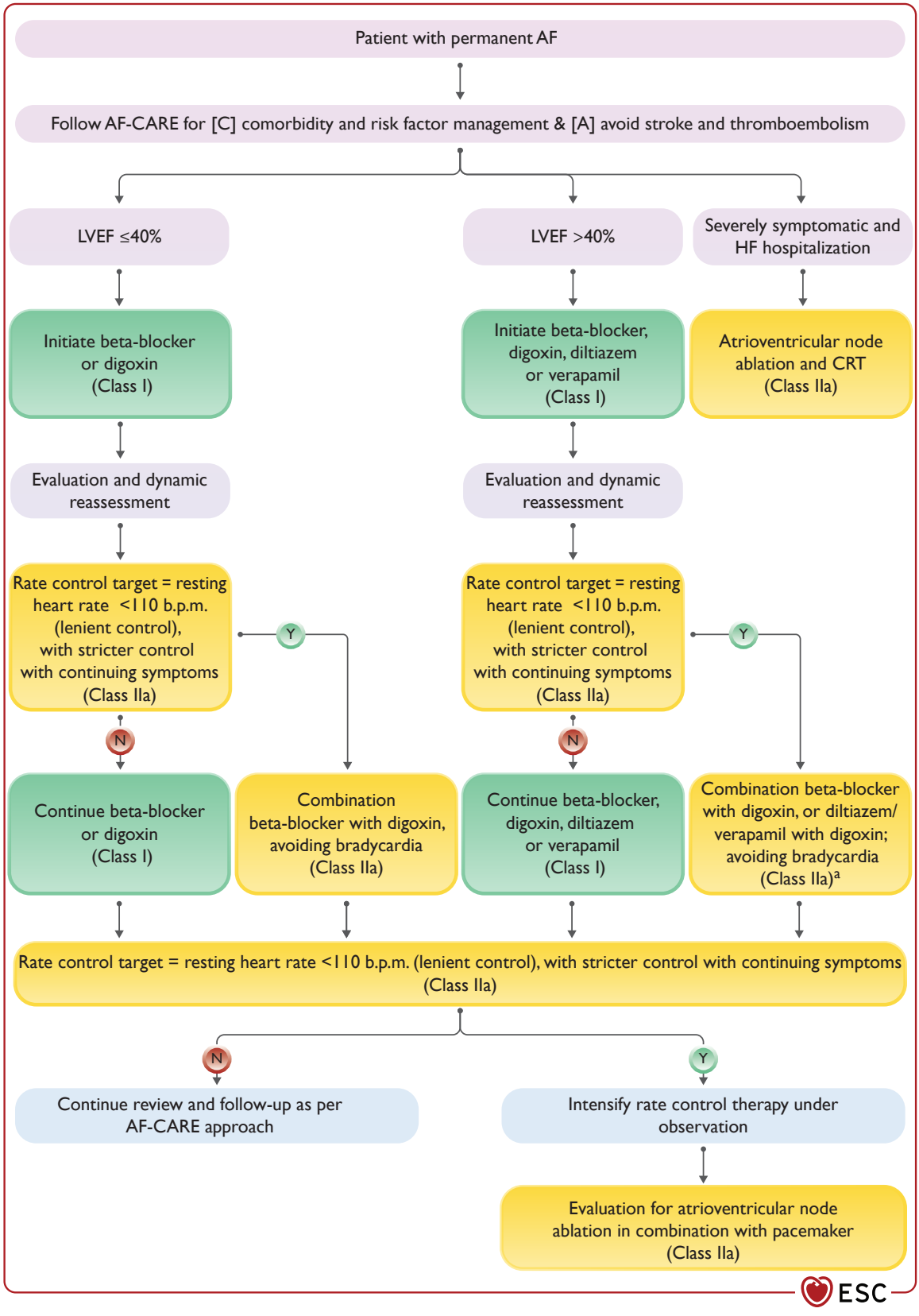


**Figure 7** [R] Pathway for patients with permanent AF. AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; b.p.m., beats per minute; CRT, cardiac resynchronization therapy; HF, heart failure; LVEF, left ventricular ejection fraction. Permanent AF is a shared decision made between the patient and physician that no further attempts at restoration of sinus rhythm are planned. [a]Note that the combination of beta-blockers with diltiazem or verapamil should only be used under specialist advice, and monitored with an ambulatory ECG to check for bradycardia.

## 5. [C] Comorbidity and risk factor management

A broad array of comorbidities are associated with the recurrence and progression of AF. Managing comorbidities is also central to the success of other aspects of care for patients with AF, with evidence available for hypertension, heart failure, diabetes mellitus, obesity, and sleep apnoea, along with lifestyle changes that improve physical activity and reduce alcohol intake (see Supplementary data online, *Additional Evidence Table S4*). Identification and treatment of these comorbidities and clusters of risk factors form an important part of effective AF-CARE (*Figure 8*), with the evidence outlined in the rest of this section highlighting where management can improve patient outcomes or prevent AF recurrence. Many of these factors (and more) are also associated with incident AF (see *Section 10*).

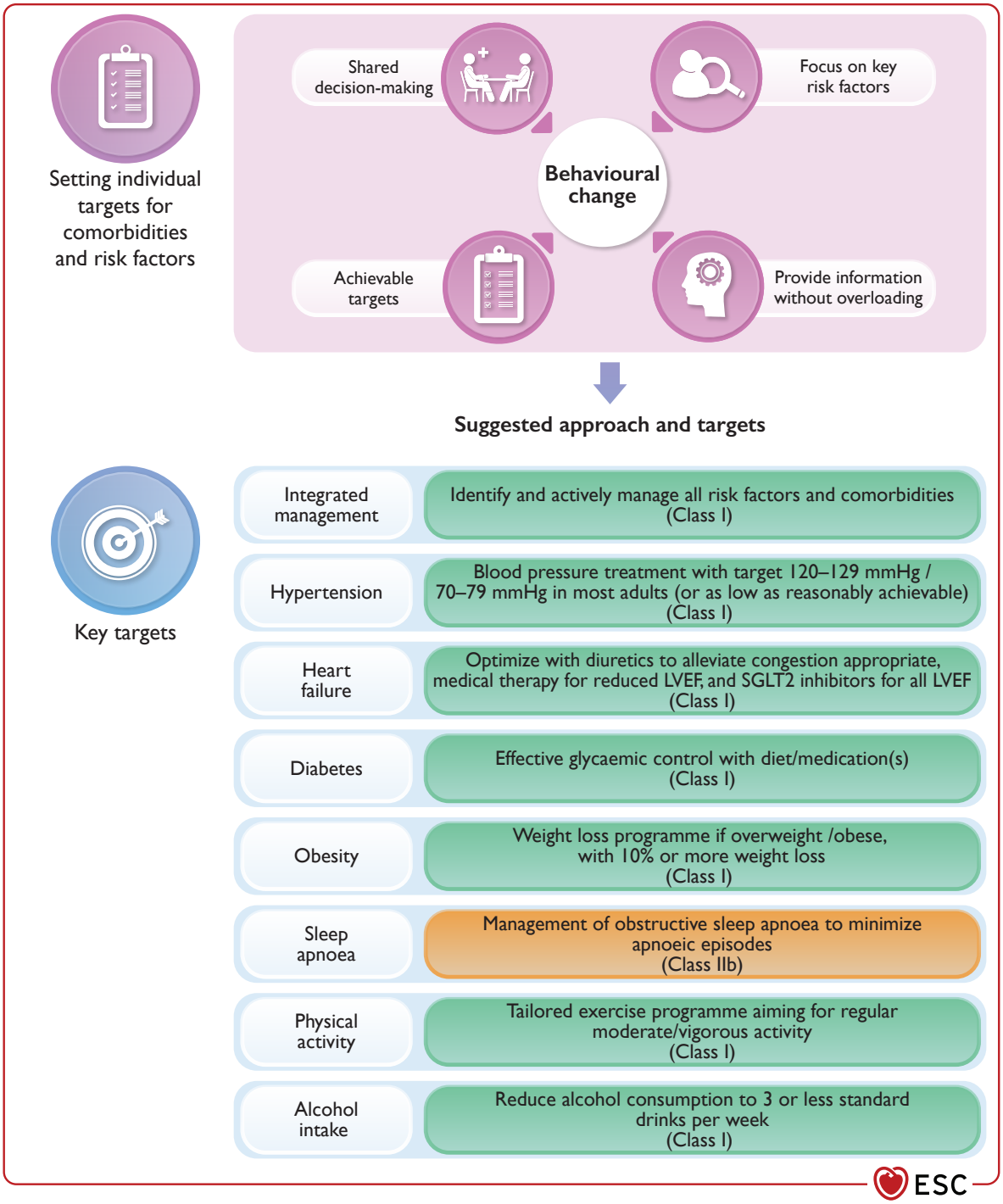


**Figure 8** Management of key comorbidities to reduce AF recurrence. LVEF, left ventricular ejection fraction; SGLT2, sodium-glucose cotransporter-2.

**Recommendation Table 5 — Recommendations for comorbidity and risk factor management in AF (see also Evidence Table 5)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Identification and management of risk factors and comorbidities is recommended as an integral part of AF care.[39,125–127] | I | B |
| Blood pressure lowering treatment is recommended in patients with AF and hypertension to reduce recurrence and progression of AF and prevent adverse cardiovascular events.[126–130] | I | B |
| Diuretics are recommended in patients with AF, HF, and congestion to alleviate symptoms and facilitate better AF management. | I | C |
| Appropriate medical therapy for HF is recommended in AF patients with HF and impaired LVEF to reduce symptoms and/or HF hospitalization and prevent AF recurrence.[131–137] | I | B |
| Sodium-glucose cotransporter-2 inhibitors are recommended for patients with HF and AF regardless of left ventricular ejection fraction to reduce the risk of HF hospitalization and cardiovascular death.[136,138–140] | I | A |
| Effective glycaemic control is recommended as part of comprehensive risk factor management in individuals with diabetes mellitus and AF, to reduce burden, recurrence, and progression of AF. | I | C |
| Weight loss is recommended as part of comprehensive risk factor management in overweight and obese individuals with AF to reduce symptoms and AF burden, with a target of 10% or more reduction in body weight.[125–128] | I | B |
| A tailored exercise programme is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence.[141–146] | I | B |
| Reducing alcohol consumption to ≤3 standard drinks (≤30 grams of alcohol) per week is recommended as part of comprehensive risk factor management to reduce AF recurrence.[126,127,147] | I | B |
| Bariatric surgery may be considered in conjunction with lifestyle changes and medical management in individuals with AF and body mass index ≥40 kg/m$^2$ [c] where a rhythm control strategy is planned, to reduce recurrence and progression of AF. | IIb | C |
| Management of obstructive sleep apnoea may be considered as part of a comprehensive management of risk factors in individuals with AF to reduce recurrence and progression.[126–128,148–154] | IIb | B |
| When screening for obstructive sleep apnoea in individuals with AF, using only symptom-based questionnaires is not recommended.[155–157] | III | B |



AF, atrial fibrillation; HF, heart failure; LVEF, left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.
[c]Or body mass index ≥35 kg/m$^2$ with obesity-related complications.

## 5.1. Hypertension

Hypertension in patients with AF is associated with an increased risk of stroke, heart failure, major bleeding, and cardiovascular mortality.[158–161] The target for treated systolic blood pressure (BP) in most adults is 120–129 mmHg. Where BP-lowering treatment is poorly tolerated, clinically significant frailty exists or the patient's age is 85 years or older, a more lenient target of <140 mmHg is acceptable or 'as low as reasonably achievable'. On-treatment diastolic BP should ideally be 70–79 mmHg.[162] In an individual participant data meta-analysis of 22 randomized trials reporting baseline AF, a 5 mmHg reduction in systolic BP reduced the risk of major cardiovascular events by 9% (HR, 0.91; 95% CI, 0.83–1.00), with identical effect in patients with AF or sinus rhythm.[129]

In individuals with AF, hypertension often coexists with other modifiable and non-modifiable risk factors that all contribute to recurrence of AF, readmission to hospital, and ongoing symptoms after rhythm control.[163–171] Optimal control of blood pressure should be considered an essential component of treating AF and undertaken within a strategy of comprehensive risk factor management.[126–128] Although the majority of research has focused on clinical outcomes, limited comparative data on hypertension medication suggests that use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) may be superior for prevention of recurrent AF.[172–175]

## 5.2. Heart failure

Heart failure is a key determinant of prognosis in patients with AF, as well as an important factor associated with recurrence and progression of AF.[176,177] During 30 years of follow-up in the Framingham cohort, 57% of those with new heart failure had concomitant AF, and 37% of those with new AF had heart failure.[178] Numerous cardiovascular and non-cardiovascular conditions impact the development of both AF and heart failure, leading to the common pathway of atrial cardiomyopathy.[18] In patients with acute heart failure attending the emergency department, AF is one of the most prevalent triggering factors of the episode.[179] The development of heart failure in patients with AF is associated with a two-fold increase in stroke and thromboembolism,[180] even after anticoagulation,[181] and 25% higher all-cause mortality.[178] Prognosis may be affected by left ventricular ejection fraction (LVEF), with the rate of death highest with the combination of AF and heart failure with reduced ejection fraction (HFrEF) (LVEF ≤ 40%), as compared with AF and HFpEF (LVEF ≥ 50%). However, rates of stroke and incident heart failure hospitalization are similar regardless of LVEF.[182] Due to how common concomitant AF and heart failure are in clinical practice, strategies to improve outcomes in these patients are detailed within each component of the AF-CARE pathway. However, it is also critical that heart failure itself is managed appropriately in patients with AF to prevent avoidable adverse events.

Optimization of heart failure management should follow current ESC Guidelines: 2023 Focused Update[183] of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.[137] Achieving euvolaemia with diuretics is an important first step that not only manages the heart failure component, but can also facilitate better control of heart rate in AF. For HFrEF, it should be highlighted that many older guideline-recommended therapies lack specific evidence for benefit in patients with coexisting AF. No trial data are available in this context for ACE inhibitors, there are conflicting data on ARBs,[132,184] and an individual patient-level analysis of RCTs found no

difference between beta-blockers and placebo for all-cause mortality in HFrEF with AF.[133] However, these drugs have clear proof of safety and there may be other indications for these therapies beyond prognosis, including comorbidity management and symptom improvement. These and other therapies may also have dual functions, for example, beta-blockers or digoxin for rate control of AF, in addition to improving heart failure metrics and reducing hospitalization.[48,185,186] More recent additions to HFrEF management, such as eplerenone, sacubitril-valsartan, and sodium-glucose cotransporter-2 (SGLT2) inhibitors, had substantial numbers of patients with AF enrolled in RCTs, with no evidence that AF status affected their ability to reduce cardiovascular mortality/heart failure hospitalization.[134–136] Cardiac resynchronization therapy (CRT) in the context of HFrEF and AF is discussed in detail in the 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy, with an important focus on ensuring effective biventricular pacing (with a low threshold for considering atrioventricular node ablation).[187] Patients who have heart failure with mildly reduced ejection fraction (HFmrEF) (LVEF 41%–49%) and AF should generally be treated according to guidance for HFrEF,[137] albeit with limited evidence to date in AF.[188–190] For treatment of HFpEF and AF,[191] pre-specified subgroup data on AF from multiple large trials show that the SGLT2 inhibitors dapagliflozin, empaglifozin, and sotagliflozin are effective in improving prognosis.[138–140]

Appropriate management of heart failure has the potential to reduce recurrence of AF, e.g. by reducing adverse atrial and ventricular myocardial remodelling, but there are limited data for specific therapies. In the Routine versus Aggressive upstream rhythm Control for prevention of Early AF in heart failure (RACE 3) trial, combined management of mild-to-moderate heart failure with ACE inhibitors/ARBs, mineralocorticoid receptor antagonists, statins, and cardiac rehabilitation increased the maintenance of sinus rhythm on ambulatory monitoring at 12 months.[39] This benefit was not preserved at the 5 year follow-up, although this may have been confounded by the lack of ongoing intervention beyond the initial 12 months.[192]

## 5.3. Type 2 diabetes mellitus

Diabetes mellitus is present in around 25% of patients with AF.[193–195] Patients with both diabetes and AF have a worse prognosis,[196] with increased healthcare utilization and excess mortality and cardiovascular events. The prevalence and incidence of AF and type 2 diabetes are widely increasing, thus making the association of these two conditions a public health challenge.[195,197] Moreover, diabetes is a major factor influencing thromboembolic risk.[198,199] Following catheter ablation of AF, diabetes and higher HbA1c are associated with increased length of stay and a greater recurrence of AF.[200–203]

In cohort studies, the management of diabetes mellitus as part of comprehensive risk factor management has been associated with reduced AF symptoms, burden, reversal of the type of AF (from persistent to paroxysmal or no AF), and improved maintenance of sinus rhythm.[126–128] However, robust evidence is limited, and individual glucose-lowering medications have had variable effects on AF.[204–206] There are emerging data of the use of SGLT2 and glucagon-like peptide-1 antagonists in patients with diabetes and AF that may impact on treatment choice in the near future. Importantly, diabetes frequently coexists with multiple risk factors in patients with AF, and a comprehensive approach to management is required. Further details are provided in the 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes.[207]

## 5.4. Obesity

Obesity frequently coexists with other risk factors that have been independently associated with the development of AF.[208,209] Obesity (body mass index [BMI] $\geq$30 kg/m$^2$) and being overweight (BMI >25 kg/m$^2$) are associated with a greater risk of recurrent atrial arrhythmias after AF ablation (13% increase for every 5 kg/m$^2$ higher BMI).[210–212] In the setting of comprehensive risk factor management, weight loss of $\geq$10% in overweight and obese individuals with AF has been associated with reduced AF symptoms and AF burden in an RCT (aiming for BMI <27 kg/m$^2$).[125] Cohort studies have also shown a graded response to maintenance of sinus rhythm,[126] improved ablation outcomes,[128] and reversal of the type of AF[127] commensurate with the degree of weight loss and risk factor management. However, in the Supervised Obesity Reduction Trial for AF Ablation Patients (SORT-AF) randomized trial in AF ablation patients, a sole weight loss intervention that achieved 4% loss in weight over 12 months did not impact ablation outcomes.[213] This is consistent with the findings in LEGACY (Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: a 5 Year follow-up study) that showed that weight loss of $\leq$3% had no impact on AF recurrence.[126] Observational studies have raised the possibility of a point of no return in terms of the benefit of weight loss,[214] but also the possibility that bariatric surgery can improve symptoms and reduce AF recurrence.[215–217]

## 5.5. Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is a highly prevalent condition, particularly in patients with AF.[157,218] Optimal screening tools in the AF population are still under evaluation, although it may be reasonable to screen for OSA in patients where a rhythm control strategy is being pursued. Polysomnography or home sleep apnoea testing are suggested in preference to screening questionnaires.[155–157,219] Questionnaires assessing daytime sleepiness are poor predictors of moderate-to-severe OSA.[155] Which parameter should be used to focus on risk of AF in patients with OSA, and to guide OSA treatment in patients with AF, is still unclear.[220,221]

Observational studies have suggested that individuals with OSA not treated with continuous positive airway pressure (CPAP) respond poorly to treatments for AF, with an increased risk of recurrence after cardioversion or ablation.[222] Conversely, OSA patients treated with CPAP seem to mitigate their propensity toward developing AF.[148–153,222–224] A small randomized trial of CPAP vs. no therapy demonstrated reversal of atrial remodelling in individuals with moderate OSA.[154] However, other small RCTs have failed to show a benefit of CPAP therapy on ablation outcomes[225] or post-cardioversion.[226] Data on the cardiovascular mortality benefit of CPAP therapy in OSA are inconclusive.[227–230]

## 5.6. Physical inactivity

Reduced cardiorespiratory fitness frequently coexists with other modifiable risk factors and has been associated with a greater recurrence of AF after catheter ablation.[141] Better cardiorespiratory fitness has a demonstrated inverse relationship to AF burden in both middle-aged and elderly people.[141] Small RCTs, meta-analyses, and observational

cohorts have shown that regular aerobic exercise may also improve AF-related symptoms, quality of life, and exercise capacity.[142,143] Better cardiorespiratory fitness and a gain in cardiorespiratory fitness over time are associated with a greater reduction in AF burden and improved maintenance of sinus rhythm.[141–145]

## 5.7. Alcohol excess

Alcohol consumption can increase the risk of adverse events in patients with AF, such as thromboembolism, death, or AF-related hospitalization.[231,232] Alcohol is associated with an increased risk of ischaemic stroke in patients with newly diagnosed AF, and alcohol abstinence after AF diagnosis can reduce the risk of ischaemic stroke.[233] In patients receiving OAC, alcohol excess is associated with a greater risk of bleeding,[234] mediated by poor adherence, alcohol–drug interactions, liver disease, and variceal bleeding.

Alcohol consumption is associated with a dose-dependent increase in the recurrence of AF after catheter ablation.[147,235] In an RCT among regular non-binge drinkers with AF, the goal of abstinence led to a significant reduction in AF recurrence and burden; alcohol intake was reduced from 16.8 to 2.1 standard drinks per week (≤30 grams or 3 standard drinks of alcohol) in the intervention arm, with 61% attaining abstinence.[147] In observational data of patients undergoing catheter ablation, reduction of consumption to ≤7 standard drinks (≤70 grams of alcohol) per week was associated with improved maintenance of sinus rhythm.[128,235]

# 6. [A] Avoid stroke and thromboembolism

## 6.1. Initiating oral anticoagulation

Atrial fibrillation is a major risk factor for thromboembolism, irrespective of whether it is paroxysmal, persistent, or permanent.[236,237] Left untreated, and dependent on other patient-specific factors, the risk of ischaemic stroke in AF is increased five-fold, and one in every five strokes is associated with AF.[238] The default approach should therefore be to provide OAC to all eligible patients, except those at low risk of incident stroke or thromboembolism. The effectiveness of OAC to prevent ischaemic stroke in patients with AF is well established.[239,240] Antiplatelet drugs alone (aspirin, or aspirin in combination with clopidogrel) are not recommended for stroke prevention in AF.[241,242]

### 6.1.1. Decision support for anticoagulation in AF

Tools have been developed to enable easier implementation of OAC in patients with clinical AF. The majority of OAC clinical trials have used variations of the $CHADS_2$ score to indicate those at risk (with points for chronic heart failure, hypertension, age, diabetes, and 2 points for prior stroke/transient ischaemic attack [TIA]). Although most available stroke risk scores are simple and practical, the predictive value of scores is generally modest (see Supplementary data online, *Table S3*).[243–245] Classification and discrimination of adverse events is relatively poor for all scores and hence the benefit of using them to select patients for OAC is unclear. There is also considerable variation in the definition of risk factors across countries,[246] and a lack of evidence from clinical trials on the ability of stroke risk scoring to enhance clinical practice.[243] This guideline continues to provide a Class IA recommendation for the use of OAC in patients at risk of thromboembolism. However, in the absence of strong evidence for how to apply risk scores in real-world patients, this has been separated from the use of any particular risk score. This is also in line with regulatory approvals for direct oral anticoagulants (DOACs), which do not stipulate risk scores or numerical thresholds.[25–28,245]

Substantive changes have occurred in the decades since these risk scores were developed in regards to population-level risk factor profiles, therapies, and targets.[198] Historical scores do not take into account parameters that have been associated with thromboembolism in contemporary cohorts, such as cancer, chronic kidney disease (CKD), ethnicity, and a range of circulating biomarkers (including troponin and B-type natriuretic peptide [BNP]). As an example, for CKD there is a correlation between decreasing glomerular filtration rate and proteinuria with stroke risk,[247–250] and cohort data suggest a two-fold increased risk of ischaemic stroke and mortality in AF patients with CKD vs. without.[251] Other factors, such as atrial enlargement, hyperlipidaemia, smoking, and obesity, have been identified in specific cohort studies as additional risk factors for ischaemic stroke in AF.[70,252,253] Biomarkers, such as troponin, natriuretic peptides, growth differentiation factor-15, cystatin C, and interleukin-6, can also indicate residual stroke risk among anticoagulated AF patients.[254,255] Biomarker-guided stroke prevention is currently being evaluated in an ongoing RCT (NCT03753490). Until further validation within RCTs is available, this task force continues to support using simple clinical classification for implementation of OAC. Clinicians should use tools that have been validated in their local population and take an individualized approach to thromboembolic risk stratification that considers the full range of each patient's specific risk factors. The absolute risk level at which to start OAC in individual patients cannot be estimated from population-level studies. It will vary depending on how those factors interact with other medical issues, and the degree of risk acceptable or tolerated by that person. In general, most of the available risk scores have a threshold of 0.6%–1.0% per annum of thromboembolic events for clinical AF to warrant OAC prescription.

Across Europe, the most popular risk score is $CHA_2DS_2$–VASc, giving points for congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/TIA/thromboembolism (2 points), vascular disease, age 65–74 years and female sex. However, implementation has varied in terms of gender. Female sex is an age-dependent stroke risk modifier rather than a risk factor per se.[112,256,257] The inclusion of gender complicates clinical practice both for healthcare professionals and patients.[258] It also omits individuals who identify as non-binary, transgender, or are undergoing sex hormone therapy. Previous guidelines from the ESC (and globally) have not actually used $CHA_2DS_2$-VASc; instead providing different score levels for women and men with AF to qualify for OAC. Hence, $CHA_2DS_2$-VA (excluding gender) has effectively been in place (*Table 10*).[78] This task force proposes, in the absence of other locally validated alternatives, that clinicians and patients should use the $CHA_2DS_2$-VA score to assist in decisions on OAC therapy (i.e. without a criterion for birth sex or gender). Pending further trials in lower risk patients (NCT04700826,[259] NCT02387229[260]), OAC are recommended in those with a $CHA_2DS_2$-VA score of 2 or more and should be considered in those with a $CHA_2DS_2$-VA score of 1, following a patient-centred and shared care approach. Healthcare professionals should take care to assess for other thromboembolic risk factors that may also indicate the need for OAC prescription.

**Recommendation Table 6 — Recommendations to assess and manage thromboembolic risk in AF (see also Evidence Table 6)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.[239,240] | I | A |
| A $CHA_2DS_2$-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | I | C |
| Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of $CHA_2DS_2$-VA score, to prevent ischaemic stroke and thromboembolism.[270–276] | I | B |
| Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients.[277–280] | I | B |
| A $CHA_2DS_2$-VA score of 1 should be considered an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | IIa | C |
| Direct oral anticoagulant therapy may be considered in patients with asymptomatic device-detected subclinical AF and elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism, excluding patients at high risk of bleeding.[281,282] | IIb | B |
| Antiplatelet therapy is not recommended as an alternative to anticoagulation in patients with AF to prevent ischaemic stroke and thromboembolism.[242,283] | III | A |
| Using the temporal pattern of clinical AF (paroxysmal, persistent, or permanent) is not recommended to determine the need for oral anticoagulation.[284,285] | III | B |

*Continued*

AF, atrial fibrillation; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; DOAC, direct oral anticoagulant.
[a]Class of recommendation.
[b]Level of evidence.

**Table 10 Updated definitions for the $CHA_2DS_2$-VA score**

| $CHA_2DS_2$-VA component | | Definition and comments | Points awarded[a] |
|---|---|---|---|
| C | Chronic heart failure | 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 | 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. | 2 |
| V | Vascular disease | Coronary artery disease, including prior myocardial infarction, angina, history of coronary revascularization (surgical or percutaneous), and significant CAD on angiography or cardiac imaging.[267]<br>OR<br>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 |

BP, blood pressure; CAD, coronary artery disease; $CHA_2DS_2$-VA, chronic heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; PVD, peripheral vascular disease.
[a]In addition to these factors, other markers that modify an individual's risk for stroke and thromboembolism should be considered, including cancer, chronic kidney disease, ethnicity (black, Hispanic, Asian), biomarkers (troponin and BNP), and in specific groups, atrial enlargement, hyperlipidaemia, smoking, and obesity.

## 6.2. Oral anticoagulants

Vitamin K antagonists (VKA), predominantly warfarin but also other coumarin and indandione derivatives, have been the principal drugs to prevent thromboembolic events in the context of AF. As with any anticoagulant, a balance must be reached between preventing thromboembolism and preserving physiological haemostasis, with VKA-associated intracranial and other major haemorrhage the most critical limitation for acceptance of OAC. The global switch to DOACs as first-line therapy has changed this risk–benefit balance, allowing more widespread prescription with no need for routine monitoring (see Supplementary data online, *Additional Evidence Tables S5–S7*). This component of AF management may see substantive changes in the coming years, with a number of factor XI inhibitors in various stages of clinical evaluation. A phase 2 trial of abelacimab in patients with AF has shown lower rates of bleeding compared with rivaroxaban[286]; however, a phase 3 trial of asundexian was terminated early due to lack of efficacy against apixaban (NCT05643573), despite favourable phase 2 results.[287] Regardless of the type of OAC prescribed, healthcare teams should be aware of the potential for interactions with other drugs, foods, and supplements, and incorporate this information into the education provided to patients and their carers. The list of potential interactions with VKA is broad,[288,289] but there are also some common cardiovascular and non-cardiovascular drugs that interact with DOACs.[290,291] *Figure 9* highlights common and major interactions to consider for VKAs and DOACs.

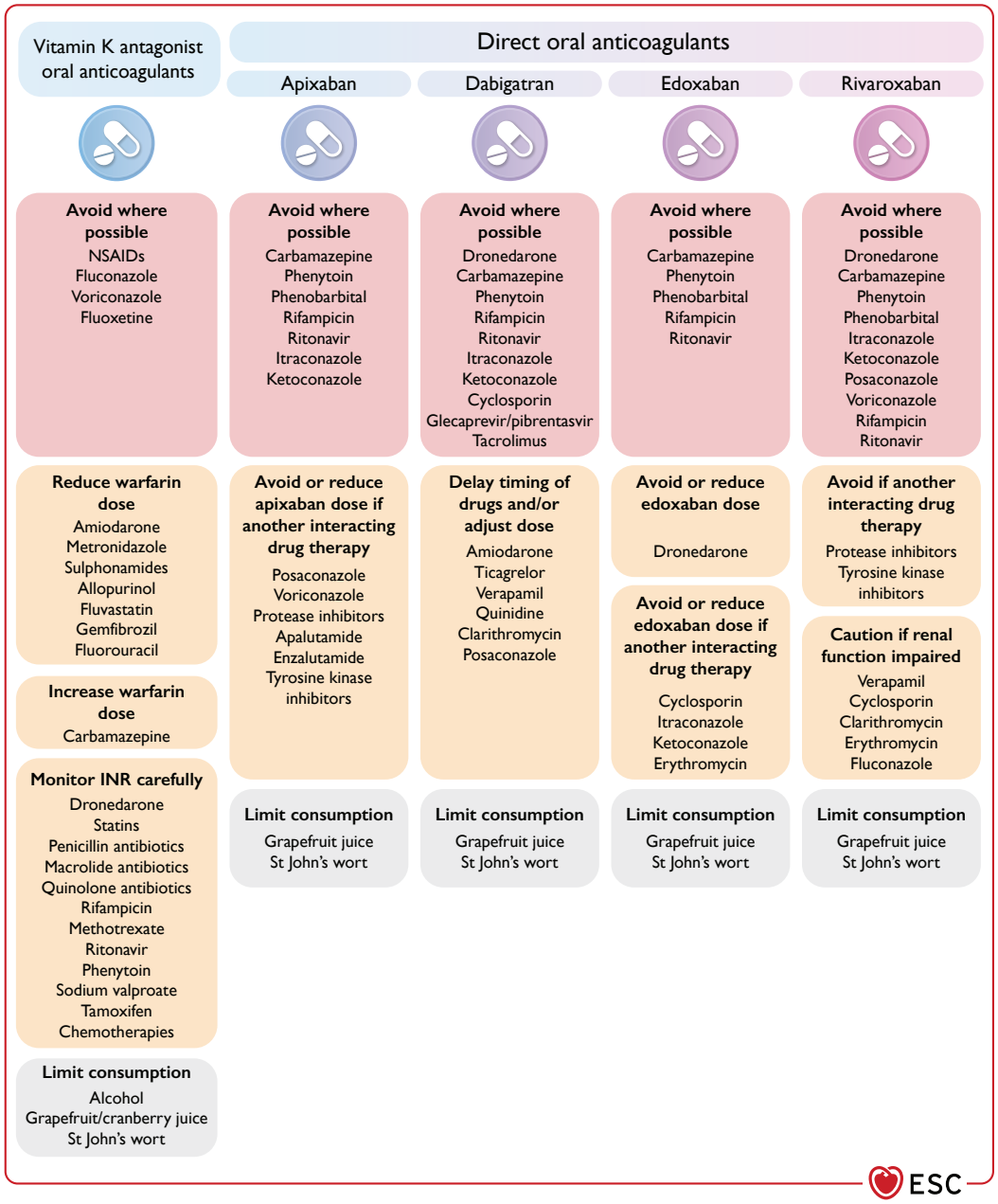


**Figure 9** Common drug interactions with oral anticoagulants. INR, international normalized ratio of prothrombin time; NSAID, non-steroidal anti-inflammatory drug. This figure depicts only common or major interactions and is not an exhaustive list of all potential interactions. Please see the European Medicines Agency website or your local formulary for more information.

**Recommendation Table 7 — Recommendations for oral anticoagulation in AF (see also Evidence Table 7)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Direct oral anticoagulants are recommended in preference to VKAs to prevent ischaemic stroke and thromboembolism, except in patients with mechanical heart valves or moderate-to-severe mitral stenosis.[25–28,292–294] | I | A |
| A target INR of 2.0–3.0 is recommended for patients with AF prescribed a VKA for stroke prevention to ensure safety and effectiveness.[295–298] | I | B |
| Switching to a DOAC is recommended for eligible patients that have failed to maintain an adequate time in therapeutic range on a VKA (TTR <70%) to prevent thromboembolism and intracranial haemorrhage.[299–303] | I | B |
| Keeping the time in therapeutic range above 70% should be considered in patients taking a VKA to ensure safety and effectiveness, with INR checks at appropriate frequency and patient-directed education and counselling.[304–308] | IIa | A |
| Maintaining VKA treatment rather than switching to a DOAC may be considered in patients aged ≥75 years on clinically stable therapeutic VKA with polypharmacy to prevent excess bleeding risk.[309] | IIb | B |
| A reduced dose of DOAC therapy is not recommended, unless patients meet DOAC-specific criteria,[c] to prevent underdosing and avoidable thromboembolic events.[310–312] | III | B |



AF, atrial fibrillation; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; TTR, time in therapeutic range; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.
[c]See *Table 11*.

### 6.2.1. Direct oral anticoagulants

The DOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) have all demonstrated at least non-inferior efficacy compared with warfarin for the prevention of thromboembolism, but with the added benefit of a 50% reduction in intracranial haemorrhage (ICH).[25–28] Meta-analyses of individual data from 71 683 RCT patients showed that standard, full-dose DOAC treatment compared with warfarin reduces the risk of stroke or systemic embolism (HR, 0.81; 95% CI, 0.73–0.91), all-cause mortality (HR, 0.90; 95% CI, 0.85–0.95), and intracranial bleeding (HR, 0.48; 95% CI, 0.39–0.59), with no significant difference in other major bleeding (HR, 0.86; 95% CI, 0.73–1.00) and little or no between-trial heterogeneity.[292] Post-marketing observational data on the effectiveness and safety of dabigatran,[313,314] rivaroxaban,[315,316] apixaban,[317] and edoxaban[318] vs. warfarin show general consistency with the respective phase 3 RCTs.

For patients undergoing cardioversion, three underpowered trials showed non-significantly lower rates of cardiovascular events with DOACs compared with warfarin.[319–321] In meta-analysis of these 5203 patients predominantly undergoing electrical cardioversion, the composite of stroke, systemic embolism, myocardial infarction (MI), and cardiovascular death was significantly lower at 0.42% in patients randomized to a DOAC vs. 0.98% in those allocated VKA (risk ratio, 0.42; 95% CI, 0.21–0.86; $P = .017$), with no heterogeneity between trials and no significant difference in major bleeding.[293]

Specific patient subgroups show consistent benefit with DOACs vs. VKAs. For heart failure, major thromboembolic events were lower in DOAC-treated patients vs. warfarin in subgroup analysis of landmark RCTs,[322] confirmed in large-scale real-world data.[323] In a retrospective cohort of patients aged over 80 years, DOAC use was associated with a lower risk of ischaemic stroke, dementia, mortality, and major bleeding than warfarin,[324] but this may be confounded by prescription bias.

Direct oral anticoagulants retain their efficacy and safety over VKAs in patients with mild-to-moderate CKD (creatinine clearance [CrCl] >30 mL/min),[325] although specific dosing adjustments apply.[25–28,326] In Europe, reduced doses of rivaroxaban, apixaban, and edoxaban are approved in patients with severe CKD (CrCl 15–29 mL/min), although limited numbers of patients were included in the major RCTs against VKA.[327] Dabigatran is more dependent on renal elimination and so is contraindicated with an estimated glomerular filtration rate <30 mL/min/1.73 $m^2$. Small trials have been performed in patients on haemodialysis, with two finding no difference between apixaban 2.5 mg twice daily and VKA for efficacy or safety outcomes,[328,329] and one trial showing that rivaroxaban 10 mg led to significantly lower rates of cardiovascular events and major bleeding compared with VKA.[330] Careful institution and regular follow-up are advised when instituting anticoagulants in any patient with impaired renal function (See Supplementary data online, *Additional Evidence Table 8*).[326]

Direct oral anticoagulants as a class should be avoided in specific patient groups, such as those with mechanical heart valves or moderate-to-severe mitral stenosis. In patients with mechanical heart valves, an excess of thromboembolic and major bleeding events among patients on dabigatran therapy vs. VKA was observed, with an RCT terminated prematurely.[331] A trial of apixaban vs. VKA after implantation of a mechanical aortic valve was also stopped due to excess thromboembolic events in the apixaban group.[332] The restriction on DOAC use does not apply to bioprosthetic heart valves (including mitral) or after transcatheter aortic valve implantation, where DOACs can be used and trial data show non-inferiority for clinical events compared with VKAs.[304,333,334] With regards to mitral stenosis, the DOAC vs. VKA trials excluded patients with moderate-to-severe disease. In 4531 randomized patients with rheumatic heart disease and AF, VKAs led to a lower rate of composite cardiovascular events and death than rivaroxaban, without a higher rate of bleeding.[294] Eighty-two per cent of the patients included had a mitral valve area ≤2 cm, supporting the restriction of DOAC use in patients with moderate-to-severe mitral stenosis. Note that patients with other types of valve disease (mitral regurgitation and others) should preferentially be prescribed a DOAC, and the term 'valvular' AF is obsolete and should be avoided.

Inappropriate dose reductions for DOACs are frequent in clinical practice,[311] but need to be avoided as they increase the risk of stroke without decreasing bleeding risk.[310] Hence, DOAC therapy should be instituted according to the standard full dose as tested in phase 3 RCTs and approved by regulators (*Table 11*). The prescribed dosage should consider the individual patient's profile.[335] Drug interactions need to be considered in all patients taking or planned for DOACs (see *Figure 9* for common drug interactions).[336] There is insufficient evidence currently to advise on routine laboratory testing for DOAC levels. However, in certain situations, measurement of DOAC levels (where available) may be helpful, such as severe bleeding, the need for urgent surgery, or thromboembolic events despite apparent DOAC compliance.[337,338] Patients should always be involved in decision-making on anticoagulation,[339] leading to better alignment with personal preferences that can help to increase understanding and adherence.

**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:<br>(i) age ≥80 years<br>(ii) body weight ≤60 kg<br>(iii) serum creatinine ≥133 mmol/L. | 2.5 mg twice daily |
| Dabigatran | 150 mg twice daily | Dose reduction recommended if any apply:<br>(i) age ≥80 years<br>(ii) receiving concomitant verapamil.<br>Dose reduction considered on an individual basis if any apply:<br>(i) age 75–80<br>(ii) moderate renal impairment (creatinine clearance 30–50 mL/min)<br>(iii) patients with gastritis, oesophagitis, or gastro-oesophageal reflux<br>(iv) others at increased risk of bleeding. | 110 mg twice daily |
| Edoxaban | 60 mg once daily | Dose reduction if any apply:<br>(i) moderate or severe renal impairment (creatinine clearance 15–50 mL/min)<br>(ii) body weight ≤60 kg<br>(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 |

DOAC, direct oral anticoagulant.
Dose and dose adjustments are taken from the European Medicines Association Summary of Product Characteristics for each DOAC. There may be other patient-specific reasons for providing a reduced dose, but, in general, the standard full dose should be used to provide optimal prevention of thromboembolism related to AF. Note that antiplatelet agents should be stopped in most patients when commencing a DOAC (see *Section 6.3*). A number of drug interactions exist with each DOAC and should be taken into consideration (see *Figure 9*).

### 6.2.2. Vitamin K antagonists

Vitamin K antagonist therapy reduces stroke risk by 64% and mortality by 26% in patients with AF at elevated thromboembolic risk (mostly warfarin in trials, compared with placebo or no treatment).[239] Vitamin K antagonists are still used in many patients worldwide, but prescriptions have declined sharply since the introduction of DOACs.[340,341] Vitamin K antagonists are currently the only treatment option in AF patients with mechanical heart valves or moderate-to-severe mitral valve stenosis.[294,331] The use of VKAs is not only limited by numerous drug and food interactions (*Figure 9*), but also a narrow therapeutic range. This requires frequent monitoring and dose adjustment according to the prothrombin time expressed as the international normalized ratio (INR).[342] If the time in therapeutic range (TTR) is maintained for long periods (e.g. >70% with INR 2.0–3.0), then VKA can be effective for thromboembolic protection with an acceptable safety profile.[295–297,343] However, VKAs are associated with higher rates of intracranial bleeding,[299,300] and also higher rates of other types of bleeding compared with DOACs.[83]

In view of the potential safety benefits, switching from VKAs to a DOAC is justified where there are concerns about intracranial bleeding or for patient-choice reasons, and a switch is recommended where patients have failed to maintain an adequate TTR (<70%). This depends on patients fulfilling eligibility criteria for DOACs and should take into account other correctable reasons for poor INR control. There is limited data on switching OAC in older patients (≥75 years) with polypharmacy or other markers of frailty. A recent trial in this patient group prematurely stopped for futility showed that switching from VKAs to DOACs led to a higher primary outcome rate of major or clinically relevant non-major bleeding events compared with continuing with INR-guided VKA (17.8 vs. 10.5 per 100 patient-years, driven by non-major bleeds).[309] Hence, in such patients who are clinically stable with good TTR, VKAs may be continued rather than switching to a DOAC after an open discussion with the patient and shared decision-making.

### 6.2.3. Clinical vs. device-detected subclinical AF

The known benefit of anticoagulation applies to clinical AF. Two RCTs have been published assessing the value of DOAC therapy in device-detected subclinical AF. The ARTESiA trial (Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation) was completed with 4012 patients with device-detected subclinical AF and a mean follow-up of 3.5 years.[282] The primary efficacy outcome of stroke or systemic embolism was significantly less in those randomized to apixaban compared with aspirin (HR, 0.63; 95% CI, 0.45–0.88; $P = .007$). In the intention-to-treat analysis, the primary safety outcome of major bleeding was higher with apixaban (HR, 1.36; 95% CI, 1.01–1.82; $P = .04$). The NOAH trial (Non-vitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes) was stopped prematurely due to safety concerns and futility for the efficacy of edoxaban, and hence provides limited information.[281] The analysis of 2536 patients with device-detected atrial high-rate episodes and a median follow-up of 21 months identified no difference in a composite of cardiovascular death, stroke, or embolism comparing edoxaban and placebo (HR, 0.81; 95% CI, 0.60–1.08; $P = .15$). Those randomized to edoxaban had a higher rate of the composite of death or major bleeding than placebo (HR, 1.31; 95% CI, 1.02–1.67; $P = .03$). Patients had a low burden of device-detected subclinical AF in both trials (median duration 1.5 h and

2.8 h, respectively), with lower rates of thromboembolism (around 1% per patient-year) than would be expected for an equivalent cohort of patients with clinical AF and a $CHA_2DS_2$-VASc score of 4.

Considering the trade-off between potential benefit and the risk of major bleeding, this task force concludes that DOAC therapy may be considered in subgroups of patients with asymptomatic device-detected subclinical AF who have high estimated stroke risk and an absence of major bleeding risk factors (see *Section 6.7*). The duration and burden of subclinical AF that could indicate potential benefit from OAC remains uncertain.[344] Regardless of the initial decision on OAC, patients with subclinical AF should receive management and follow-up for all aspects of AF-CARE as the risk of developing clinical AF is high (6%–9% per year).

## 6.3. Antiplatelet drugs and combinations with anticoagulants

Antiplatelet drugs, such as aspirin and clopidogrel, are not an alternative to OAC. They should not be used for stroke prevention, and can lead to potential harm (especially among elderly patients with AF).[345–347] In ACTIVE W (Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events), dual antiplatelet therapy (DAPT) with aspirin and clopidogrel was less effective than warfarin for the prevention of stroke, systemic embolism, MI, or vascular death (annual risk of events 5.6% vs. 3.9%, respectively; $P = .0003$), with similar rates of major bleeding.[348] The AVERROES (Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment) trial demonstrated a lower rate of stroke or systemic embolism with apixaban compared with aspirin (HR, 0.45; 95% CI, 0.32–0.62; $P < .001$), with no significant difference in major bleeding (there were 11 cases of intracranial bleeding with apixaban and 13 with aspirin).[242]

The combination of OAC with antiplatelet agents (especially aspirin) without an adequate indication occurs frequently in clinical practice (see Supplementary data online, *Additional Evidence Table S9*).[349,350] Bleeding events are more common when antithrombotic agents are combined, and no clear benefit has been observed in terms of prevention of stroke or death.[349] In general, combining antiplatelet drugs with anticoagulants (DOACs or VKAs) should only occur in selected patients with acute vascular disease (e.g. acute coronary syndromes; see *Section 9.2*). The combination of low-dose rivaroxaban (2.5 mg) with aspirin reduced the risk of stroke in patients with chronic vascular disease in a subanalysis of the COMPASS (Cardiovascular Outcomes for People Using Anticoagulation Strategies) trial,[351,352] but this cannot be generalized to AF patients because those with an indication for full-dose anticoagulants were excluded.

**Recommendation Table 8 — Recommendations for combining antiplatelet drugs with anticoagulants for stroke prevention (see also Evidence Table 8)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism.[345,347,353] | III | B |

AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.



## 6.4. Residual ischaemic stroke risk despite anticoagulation

Although OAC significantly reduces the risk of ischaemic stroke in patients with AF, there remains a residual risk.[252,354] One-third of patients with AF presenting with an ischaemic stroke are already on anticoagulation,[355] with heterogeneous aetiology.[356] This may include non-AF-related competing stroke mechanisms (such as large artery and small vessel diseases), non-adherence to therapy, an inappropriately low dose of anticoagulant, or thromboembolism despite sufficient anticoagulation.[357] Laboratory measurement of INR or DOAC levels may contribute to revealing an amenable cause of the stroke. Regardless of anticoagulation status, patients with ischaemic stroke are more likely to have cardiovascular risk factors.[358] Many clinicians managing patients with an incident stroke despite taking anticoagulation will be tempted to switch their anticoagulant regimen. While there may be some advantage in switching from VKAs to DOACs for protection against future recurrent ischaemic or haemorrhagic stroke, this task force does not recommend routinely switching from one DOAC to another, or from a DOAC to a VKA, since this has no proven efficacy.[252,356,359] There may be individual reasons for switching, including potential interactions with new drugs; however, there is no consistent data across countries that adherence or efficacy differs between once- and twice-daily approaches.[360,361] Emerging, but observational evidence suggests that switching provides limited reduction in the risk of recurrent ischaemic stroke.[252,356,359] The alternative strategy of adding antiplatelet therapy to OAC may lead to an increased risk of bleeding.[356,359] Aside from thorough attention to underlying risk factors and co-morbidities, the approach to management of patients with a stroke despite OAC remains a distinct challenge.

**Recommendation Table 9 — Recommendations for thromboembolism despite anticoagulation (see also Evidence Table 9)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| A thorough diagnostic work-up should be considered in patients taking an oral anticoagulant and presenting with ischaemic stroke or thromboembolism to prevent recurrent events, including assessment of non-cardioembolic causes, vascular risk factors, dosage, and adherence.[356,357] | IIa | B |
| Adding antiplatelet treatment to anticoagulation is not recommended in patients with AF to prevent recurrent embolic stroke.[356,359] | III | B |
| Switching from one DOAC to another, or from a DOAC to a VKA, without a clear indication is not recommended in patients with AF to prevent recurrent embolic stroke.[252,356,359] | III | B |

AF, atrial fibrillation; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.



## 6.5. Percutaneous left atrial appendage occlusion

Percutaneous left atrial appendage occlusion (LAAO) is a device-based therapy that aims to prevent ischaemic stroke in patients with AF.[362,363] In the VKA era, two RCTs compared warfarin with LAAO using the

Watchman device. The 5-year pooled outcomes demonstrated a similar rate of the composite endpoint (cardiovascular or unexplained death, systemic embolism, and stroke) between the LAAO and warfarin arms. Those randomized to LAAO had significantly lower rates of haemorrhagic stroke and all-cause death, but also a 71% non-significant increase in ischaemic stroke and systemic embolism.[364] With DOACs demonstrating similar rates of major bleeding to aspirin,[242] warfarin in the control arms in these trials is no longer standard of care and hence the place of LAAO in current practice is unclear. The Amulet occluder is an alternative LAAO device which was non-inferior in an RCT to the Watchman device for safety events (procedure-related complications, death, or major bleeding) and thromboembolism.[365] In the PRAGUE-17 trial, 402 AF patients were randomized to DOAC or LAAO (Watchman or Amulet), with non-inferiority reported for a broad composite primary endpoint of stroke, TIA, systemic embolism, cardiovascular death, major or non-major clinically relevant bleeding, and procedure/device-related complications.[366,367] Larger trials[368,369] are expected to provide more comprehensive data that can add to the current evidence base (see Supplementary data online, *Additional Evidence Table S10*).

Pending further RCTs (see Supplementary data online, *Table S4*), patients with a contraindication to all of the OAC options (the four DOACs and VKAs) have the most appropriate rationale for LAAO implantation, despite the paradox that the need for post-procedure antithrombotic treatment exposes the patient to a bleeding risk that may be equivalent to that of DOACs. Regulatory approvals based on RCT protocols suggest the need for 45 days of VKA plus aspirin after implantation, followed by 6 months of DAPT in patients with no major peri-device leaks, and then ongoing aspirin (see Supplementary data online, *Figure S2*).[370–372] However, real-world practice is markedly different and also varied. Direct oral anticoagulant administration at full or reduced dose has been proposed as a treatment alternative to warfarin.[373] Observational studies have also supported the use of antiplatelet therapy without associated increases in device-related thrombosis or stroke.[374–376] In a propensity-matched comparison of patients receiving limited early OAC vs. antiplatelet treatment post-Watchman implantation, thromboembolic event rates and bleeding complications were similar.[377] While waiting for solid RCT data (NCT03445949, NCT03568890),[378] pertinent decisions on antithrombotic treatment are usually made on an individualized basis.[379–381] Prevention of recurrent stroke, in addition to OAC, is another potential indication for LAAO. Only limited data are so far available from registries,[382] with ongoing trials expected to provide more insight (NCT03642509, NCT05963698).

Left atrial appendage occlusion device implantation is associated with procedural risk including stroke, major bleeding, device-related thrombus, pericardial effusion, vascular complications, and death.[362,383–385] Voluntary registries enrolling patients considered ineligible for OAC have reported low peri-procedural risk,[372,376,386,387] although national registries report in-hospital major adverse event rates of 9.5% in centres performing 5–15 LAAO cases per year, and 5.6% performing 32–211 cases per year ($P < .001$).[388] Registries with new-generation devices report a lower complication rate compared with RCT data.[389,390] Device-related thrombi occur with an incidence of 1.7%–7.2% and are associated with a higher risk of ischaemic stroke.[386,391–397] Their detection can be documented as late as 1 year post-implantation in one-fifth of patients, thus mandating a late 'rule-out' imaging approach.[391] Likewise, follow-up screening for peri-device leaks is relevant, as small leaks (0–5 mm) are present in ~25% and have been associated with higher thromboembolic and bleeding events during 1 year follow-up in a large observational registry of one particular device.[398]

**Recommendation Table 10 — Recommendations for percutaneous left atrial appendage occlusion (see also Evidence Table 10)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Percutaneous LAA occlusion may be considered in patients with AF and contraindications for long-term anticoagulant treatment to prevent ischaemic stroke and thromboembolism.[372,376,386,387] | IIb | C |

AF, atrial fibrillation; LAA, left atrial appendage.
[a]Class of recommendation.
[b]Level of evidence.



## 6.6. Surgical left atrial appendage occlusion

Surgical occlusion or exclusion of the left atrial appendage (LAA) can contribute to stroke prevention in patients with AF undergoing cardiac surgery.[399,400] The Left Atrial Appendage Occlusion Study (LAAOS III) randomized 4811 patients with AF to undergo or not undergo LAAO at the time of cardiac surgery for another indication. During a mean of 3.8 years follow-up, ischaemic stroke or systemic embolism occurred in 114 patients (4.8%) in the occlusion group and 168 (7.0%) in the control arm (HR, 0.67; 95% CI, 0.53–0.85; $P = .001$).[401] The LAAOS III trial did not compare appendage occlusion with anticoagulation (77% of participants continued to receive OAC), and therefore, surgical LAA closure should be considered as an adjunct therapy to prevent thromboembolism in addition to anticoagulation in patients with AF.

There are no RCT data showing a beneficial effect on ischaemic stroke or systemic embolism in patients with AF undergoing LAAO during endoscopic or hybrid AF ablation. A meta-analysis of RCT and observational data showed no differences in stroke prevention or all-cause mortality when comparing LAA clipping during thoracoscopic AF ablation with percutaneous LAAO and catheter ablation.[402] While the percutaneous LAAO/catheter ablation group showed a higher acute success rate, it was also associated with a higher risk of haemorrhage during the peri-operative period. In an observational study evaluating 222 AF patients undergoing LAA closure using a clipping device as a part of endoscopic or hybrid AF ablation, complete closure was achieved in 95% of patients.[403] There were no intra-operative complications, and freedom from a combined endpoint of ischaemic stroke, haemorrhagic stroke, or TIA was 99.1% over 369 patient-years of follow-up. Trials evaluating the beneficial effect of surgical LAA closure in patients undergoing cardiac surgery but without a known history of AF are ongoing (NCT03724318, NCT02701062).[404]

There is a potential advantage for stand-alone epicardial over percutaneous LAA closure in patients with a contraindication for OAC, as there is no need for post-procedure anticoagulation after epicardial closure. Observational data show that stand-alone LAA closure using an epicardial clip is feasible and safe.[405] A multidisciplinary team approach can facilitate the choice between epicardial or percutaneous LAA closure in such patients.[406] The majority of safety data and experience in epicardial LAA closure originate from a single clipping device (AtriClip)[403,407,408] (see Supplementary data online, *Additional Evidence Table S11*).

**Recommendation Table 11 — Recommendations for surgical left atrial appendage occlusion (see also Evidence Table 11)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Surgical closure of the left atrial appendage is recommended as an adjunct to oral anticoagulation in patients with AF undergoing cardiac surgery to prevent ischaemic stroke and thromboembolism.[400,401,408–412] | I | B |
| Surgical closure of the left atrial appendage should be considered as an adjunct to oral anticoagulation in patients with AF undergoing endoscopic or hybrid AF ablation to prevent ischaemic stroke and thromboembolism.[402,403] | IIa | C |
| Stand-alone endoscopic surgical closure of the left atrial appendage may be considered in patients with AF and contraindications for long-term anticoagulant treatment to prevent ischaemic stroke and thromboembolism.[399,405,406,413] | IIb | C |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

## 6.7. Bleeding risk

### 6.7.1. Assessment of bleeding risk

When initiating antithrombotic therapy, modifiable bleeding risk factors should be managed to improve safety (*Figure 10*).[414–418] This includes strict control of hypertension, advice to reduce excess alcohol intake, avoidance of unnecessary antiplatelet or anti-inflammatory agents, and attention to OAC therapy (adherence, control of TTR if on VKAs, and review of interacting medications). Clinicians should consider the balance between stroke and bleeding risk—as factors for both are dynamic and overlapping, they should be re-assessed at each review depending on the individual patient.[419–421] Bleeding risk factors are rarely a reason to withdraw or withhold OAC in eligible patients, as the risk of stroke without anticoagulation often outweighs the risk of major bleeding.[422,423] Patients with non-modifiable risk factors should be reviewed more often, and where appropriate, a multidisciplinary team approach should be instituted to guide management.

Several bleeding risk scores have been developed to account for a wide range of clinical factors (see Supplementary data online, *Table S5* and *Additional Evidence Tables S12* and *S13*).[424] Systematic reviews and validation studies in external cohorts have shown contrasting results and only modest predictive ability.[244,425–434] This task force does not recommend a specific bleeding risk score given the uncertainty in accuracy and potential adverse implications of not providing appropriate OAC to those at thromboembolic risk. There are very few absolute contraindications to OAC (especially DOAC therapy). Whereas primary intracranial tumours[435] or an intracerebral bleed related to cerebral amyloid angiopathy[436] are examples where OAC should be avoided, many other contraindications are relative or temporary. For example, a DOAC can often be safely initiated or re-initiated after acute bleeding has stopped, as long as the source has been fully investigated and managed. Co-prescription of proton pump inhibitors is common in clinical practice for patients receiving OAC that are at high risk of gastrointestinal bleeding. However, the evidence base is limited and not specifically in patients with AF. Whereas observational studies have shown potential benefit from proton pump inhibitors,[437] a large RCT in patients receiving low-dose anticoagulation and/or aspirin for stable cardiovascular disease found that pantoprazole had no significant impact on upper gastrointestinal bleeding events compared with placebo (HR, 0.88; 95% CI, 0.67–1.15).[438] Hence, the use of gastric protection should be individualized for each patient according to the totality of their perceived bleeding risk.

**Recommendation Table 12 — Recommendations for assessment of bleeding risk (see also Evidence Table 12)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Assessment and management of modifiable bleeding risk factors is recommended in all patients eligible for oral anticoagulation, as part of shared decision-making to ensure safety and prevent bleeding.[439–444] | I | B |
| Use of bleeding risk scores to decide on starting or withdrawing oral anticoagulation is not recommended in patients with AF to avoid under-use of anticoagulation.[431,445,446] | III | B |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

### 6.7.2. Management of bleeding on anticoagulant therapy

General management of bleeding in patients receiving OAC is outlined in *Figure 11*. Cause-specific management is beyond the scope of these guidelines, and will depend on the individual circumstances of the patient and the healthcare environment.[447] Assessment of patients with active bleeding should include confirmation of the bleeding site, bleeding severity, type/dose/timepoint of last anticoagulant intake, concomitant use of other antithrombotic agents, and other factors influencing bleeding risk (renal function, platelet count, and medications such as non-steroidal anti-inflammatories). INR testing and information on recent results are invaluable for patients taking VKAs. Specific coagulation tests for DOACs include diluted thrombin time, ecarin clotting time, ecarin chromogenic assay for dabigatran, and chromogenic anti-factor Xa assay for rivaroxaban, apixaban, and edoxaban.[447–449] Diagnostic and treatment interventions to identify and manage the cause of bleeding (e.g. gastroscopy) should be performed promptly.

In cases of minor bleeding, temporary withdrawal of OAC while the cause is managed is usually sufficient, noting that the reduction in anticoagulant effect is dependent on the INR level for VKAs or the half-life of the particular DOAC.

For major bleeding events in patients taking VKAs, administration of fresh frozen plasma restores coagulation more rapidly than vitamin K, but prothrombin complex concentrates achieve even faster blood coagulation with fewer complications, and so are preferrable to achieve haemostasis.[450] In DOAC-treated patients where the last DOAC dose was taken within 2–4 h, charcoal administration and/or gastric lavage may reduce further exposure. If the patient is taking dabigatran, idarucizumab can fully reverse its anticoagulant effect and help to achieve haemostasis within 2–4 h in

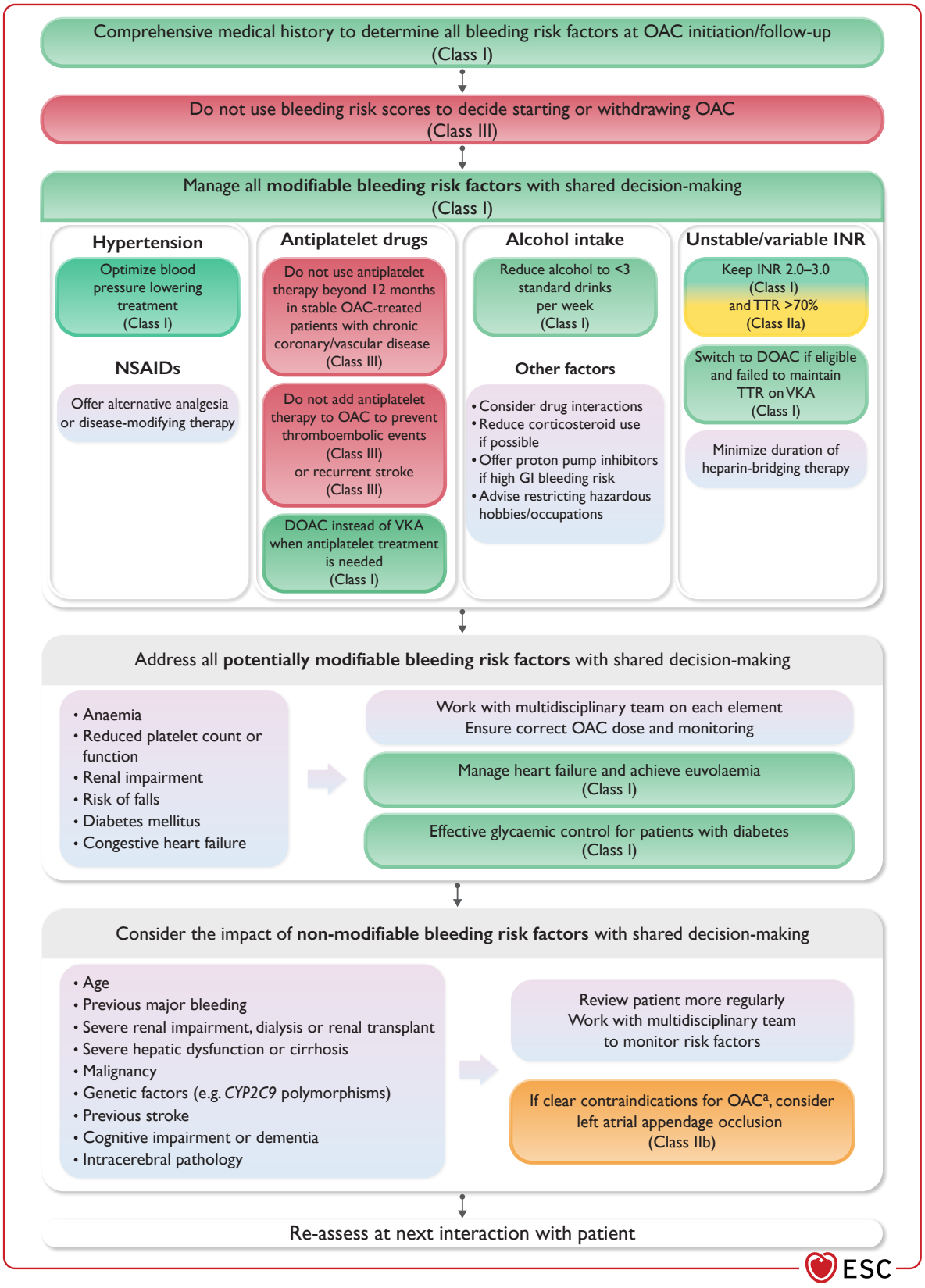


**Figure 10** Modifying the risk of bleeding associated with OAC. DOAC, direct oral anticoagulant; GI, gastrointestinal; INR, international normalized ratio of prothrombin time; NSAID, non-steroidal anti-inflammatory drug; OAC, oral anticoagulant; TTR, time in therapeutic range; VKA, vitamin K antagonist. [a]Absolute contraindications for OAC therapy are rare, and include primary intracranial tumours and intracerebral bleeds related to amyloid angiopathy. In most cases, contraindications may be relative or temporary. Left atrial appendage occlusion can be performed through a percutaneous or endoscopic approach.

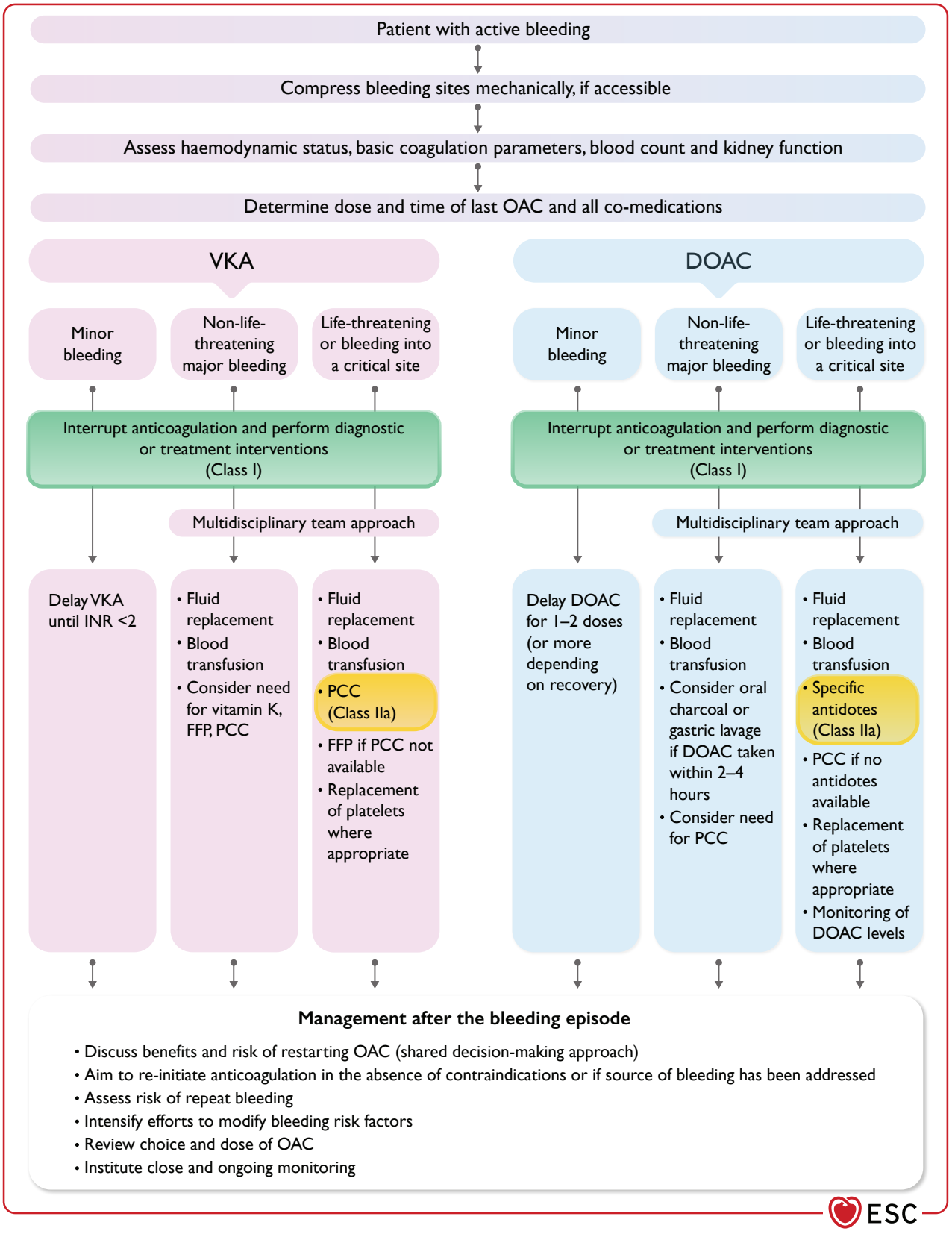


**Figure 11** Management of oral anticoagulant-related bleeding in patients with AF. DOAC, direct oral anticoagulant; FFP, fresh frozen plasma; INR, international normalized ratio of prothrombin time; OAC, oral anticoagulant; PCC, prothrombin complex concentrate; VKA, vitamin K antagonist.

uncontrolled bleeding.[451] Dialysis can also be effective in reducing dabigatran concentration. Andexanet alfa rapidly reverses the activity of factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) (see Supplementary data online, *Additional evidence Table S14*). An open-label RCT comparing andexanet alfa to usual care in patients presenting with acute ICH within 6 h of symptom onset was stopped early due to improved control of bleeding after 450 patients had been randomized.[452] As DOAC-specific antidotes are not yet available in all institutions, prothrombin complex concentrates are often used in cases of serious bleeding on factor Xa inhibitors, with evidence limited to observational studies.[453]

Due to the complexities of managing bleeding in patients taking OAC, it is advisable that each institution develop specific policies involving a multidisciplinary team that includes cardiologists, haematologists, emergency physicians/intensive care specialists, surgeons, and others. It is also important to educate patients taking anticoagulants on the signs and symptoms of bleeding events and to alert their healthcare provider when such events occur.[335]

The decision to reinstate OAC will be determined by the severity, cause, and subsequent management of bleeding, preferably by a multidisciplinary team and with close monitoring. Failure to reinstitute OAC after a bleed significantly increases the risk of MI, stroke, and death.[454] However, if the cause of severe or life-threatening bleeds cannot be treated or reversed, the risk of ongoing bleeding may outweigh the benefit of thromboembolic protection.[335]

**Recommendation Table 13 — Recommendations for management of bleeding in anticoagulated patients (see also Evidence Table 13)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Interrupting anticoagulation and performing diagnostic or treatment interventions is recommended in AF patients with active bleeding until the cause of bleeding is identified and resolved. | I | C |
| Prothrombin complex concentrates should be considered in AF patients on VKAs who develop a life-threatening bleed, or bleed into a critical site, to reverse the antithrombotic effect.[450] | IIa | C |
| Specific antidotes should be considered in AF patients on a DOAC who develop a life-threatening bleed, or bleed into a critical site, to reverse the antithrombotic effect.[451,455,456] | IIa | B |



AF, atrial fibrillation; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

# 7. [R] Reduce symptoms by rate and rhythm control

Most patients diagnosed with AF will need therapies and/or interventions to control heart rate, revert to sinus rhythm, or maintain sinus rhythm to limit symptoms or improve outcomes. While the concept of choosing between rate and rhythm control is often discussed, in reality most patients require a combination approach which should be consciously re-evaluated during follow-up. Within a patient-centred and shared-management approach, rhythm control should be a consideration in all suitable AF patients, with explicit discussion of benefits and risks.

## 7.1. Management of heart rate in patients with AF

Limiting tachycardia is an integral part of AF management and is often sufficient to improve AF-related symptoms. Rate control is indicated as initial therapy in the acute setting, in combination with rhythm control therapies, or as the sole treatment strategy to control heart rate and reduce symptoms. Limited evidence exists to inform the best type and intensity of rate control treatment.[457] The approach to heart rate control presented in *Figure 7* can be used for all types of AF, including paroxysmal, persistent, and permanent AF.

**Recommendation Table 14 — Recommendations for heart rate control in patients with AF (see also Evidence Table 14)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Rate control therapy is recommended in patients with AF, as initial therapy in the acute setting, an adjunct to rhythm control therapies, or as a sole treatment strategy to control heart rate and reduce symptoms.[458–460] | I | B |
| Beta-blockers, diltiazem, verapamil, or digoxin are recommended as first-choice drugs in patients with AF and LVEF >40% to control heart rate and reduce symptoms.[48,461,462] | I | B |
| Beta-blockers and/or digoxin are recommended in patients with AF and LVEF ≤40% to control heart rate and reduce symptoms.[40,185,463–465] | I | B |
| Combination rate control therapy should be considered if a single drug does not control symptoms or heart rate in patients with AF, providing that bradycardia can be avoided, to control heart rate and reduce symptoms. | IIa | C |
| Lenient rate control with a resting heart rate of < 110 b.p.m. should be considered as the initial target for patients with AF, with stricter control reserved for those with continuing AF-related symptoms.[459,460,466] | IIa | B |
| Atrioventricular node ablation in combination with pacemaker implantation should be considered in patients unresponsive to, or ineligible for, intensive rate and rhythm control therapy to control heart rate and reduce symptoms.[467–469] | IIa | B |
| Atrioventricular node ablation combined with cardiac resynchronization therapy should be considered in severely symptomatic patients with permanent AF and at least one hospitalization for HF to reduce symptoms, physical limitations, recurrent HF hospitalization, and mortality.[470,471] | IIa | B |
| Intravenous amiodarone, digoxin, esmolol, or landiolol may be considered in patients with AF who have haemodynamic instability or severely depressed LVEF to achieve acute control of heart rate.[472,473] | IIb | B |



AF, atrial fibrillation; b.p.m., beats per minute; HF, heart failure; LVEF, left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.

### 7.1.1. Indications and target heart rate

The optimal heart rate target in AF patients depends on the setting, symptom burden, presence of heart failure, and whether rate control is combined with a rhythm control strategy. In the RACE II (Rate Control Efficacy in Permanent Atrial Fibrillation) RCT of patients with permanent AF, lenient rate control (target heart rate <110 [beats per minute] b.p.m.) was non-inferior to a strict approach (<80 b.p.m. at rest; <110 b.p.m. during exercise; Holter for safety) for a composite of clinical events, NYHA class, or hospitalization.[186,459] Similar results were found in a post-hoc combined analysis from the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) and the RACE (Rate Control versus Electrical cardioversion) studies.[474] Therefore, lenient rate control is an acceptable initial approach, unless there are ongoing symptoms or suspicion of tachycardia-induced cardiomyopathy, where stricter targets may be indicated.

### 7.1.2. Heart rate control in the acute setting

In acute settings, physicians should always evaluate and manage underlying causes for the initiation of AF prior to, or in parallel to, instituting acute rate and/or rhythm control. These include treating sepsis, addressing fluid overload, or managing cardiogenic shock. The choice of drug (*Table 12*) will depend on the patient's characteristics, presence of heart failure and LVEF, and haemodynamic profile (*Figure 7*). In general for acute rate control, beta-blockers (for all LVEF) and diltiazem/verapamil (for LVEF >40%) are preferred over digoxin because of their more rapid onset of action and dose-dependent effects.[462,475,476] More selective beta-1 receptor blockers have a better efficacy and safety profile than unselective beta-blockers.[477] Combination therapy with digoxin may be required in acute settings (combination of beta-blockers with diltiazem/verapamil should be avoided except in closely monitored situations).[177,478] In selected patients who are haemodynamically unstable or with severely impaired LVEF, intravenous amiodarone, landiolol, or digoxin can be used.[472,473,479]

### 7.1.3. Long-term heart rate control

Pharmacological rate control can be achieved with beta-blockers, diltiazem, verapamil, digoxin, or combination therapy (*Table 12*) (see Supplementary data online, *Additional Evidence Table S15*).[480]

The choice of rate control drugs depends on symptoms, comorbidities, and the potential for side effects and interactions. Combination therapy of different rate-controlling drugs should be considered only when needed to achieve the target heart rate, and careful follow-up to avoid bradycardia is advised. Combining beta-blockers with verapamil or diltiazem should only be performed in secondary care with regular monitoring of heart rate by 24 h ECG to check for bradycardia.[459] Some antiarrhythmic drugs (AADs) also have rate-limiting properties (e.g. amiodarone, sotalol), but they should generally be used only for rhythm control. Dronedarone should not be instituted for rate control since it increases rates of heart failure, stroke, and cardiovascular death in permanent AF.[481]

**Beta-blockers**, specifically beta-1 selective adrenoreceptor antagonists, are often first-line rate-controlling agents largely based on their acute effect on heart rate and the beneficial effects demonstrated in patients with chronic HFrEF. However, the prognostic benefit of beta-blockers seen in HFrEF patients with sinus rhythm may not be present in patients with AF.[133,482]

**Verapamil** and **diltiazem** are non-dihydropyridine calcium channel blockers. They provide rate control[461] and have a different adverse effect profile, making verapamil or diltiazem useful for those experiencing side effects from beta-blockers.[483] In a 60 patient crossover RCT, verapamil and diltiazem did not lead to the same reduction in exercise capacity as seen with beta-blockers, and had a beneficial impact on BNP.[480]

**Digoxin** and **digitoxin** are cardiac glycosides that inhibit the sodium–potassium adenosine triphosphatase and augment parasympathetic tone. In RCTs, there is no association between the use of digoxin and any increase in all-cause mortality.[185,484] Lower doses of digoxin may be associated with better prognosis.[185] Serum digoxin concentrations can be monitored to avoid toxicity,[485] especially in patients at higher risk due to older age, renal dysfunction, or use of interacting medications. In RATE-AF (RAte control Therapy Evaluation in permanent Atrial Fibrillation), a trial in patients with symptomatic permanent AF, there was no difference between low-dose digoxin and bisoprolol for patient-reported quality of life outcomes at 6 months. However, those randomized to digoxin demonstrated fewer adverse effects, a greater improvement in mEHRA and NYHA scores, and a reduction in BNP.[48] Two ongoing RCTs are addressing digoxin and digitoxin use in patients with HFrEF with and without AF (EudraCT-2013-005326-38, NCT03783429).[486]

**Table 12 Drugs for rate control in AF**

| Agent[a] | Intravenous administration | Usual range for oral maintenance dose | Contraindicated |
|---|---|---|---|
| **Beta-blockers**[b] | | | |
| Metoprolol tartrate | 2.5–5 mg bolus over 2 mins; up to 15 mg maximal cumulative dose | 25–100 mg twice daily | In case of asthma, non-selective beta-blockers should be avoided. Contraindicated in acute HF and history of severe bronchospasm. |
| Metoprolol XL (succinate) | N/A | 50–200 mg once daily | |
| Bisoprolol | N/A | 1.25–20 mg once daily | |
| Atenolol[c] | N/A | 25–100 mg once daily | |
| Esmolol | 500 µg/kg i.v. bolus over 1 min; followed by 50–300 µg/kg/min | N/A | |
| Landiolol | 100 µg/kg i.v. bolus over 1 min; followed by 10–40 µg/kg/min | N/A | |
| Nebivolol | N/A | 2.5–10 mg once daily | |
| Carvedilol | N/A | 3.125–50 mg twice daily | |

*Continued*

| | | | |
|---|---|---|---|
| **Non-dihydropyridine calcium channel antagonists** | | | |
| Verapamil | 2.5–10 mg i.v. bolus over 5 min | 40 mg twice daily to 480 mg (extended release) once daily | Contraindicated if LVEF ≤40%. Adapt doses in hepatic and renal impairment. |
| Diltiazem | 0.25 mg/kg i.v. bolus over 5 min, then 5–15 mg/h | 60 mg three times daily to 360 mg (extended release) once daily | |
| **Digitalis glycosides** | | | |
| Digoxin | 0.5 mg i.v. bolus (0.75–1.5 mg over 24 h in divided doses) | 0.0625–0.25 mg once daily | High plasma levels associated with adverse events. Check renal function before starting digoxin and adapt dose in CKD patients. |
| Digitoxin | 0.4–0.6 mg | 0.05–0.1 mg once daily | |
| **Other** | | | |
| Amiodarone[d] | 300 mg i.v. diluted in 250 mL 5% dextrose over 30–60 min (preferably via central venous cannula), followed by 900–1200 mg i.v. over 24 h diluted in 500–1000 mL via a central venous cannula | 200 mg once daily after loading Loading: 200 mg three times daily for 4 weeks, then 200 mg daily or less as appropriate (reduce other rate control drugs according to heart rate) | Contraindicated in iodine sensitivity. Serious potential adverse effects (including pulmonary, ophthalmic, hepatic, and thyroid). Consider numerous drug interactions. |

AF, atrial fibrillation; CKD, chronic kidney disease; HF, heart failure; i.v., intravenous; min, minutes; N/A, not available or not widely available. Maximum doses have been defined based on the summary of product characteristic of each drug.
[a]All rate control drugs are contraindicated in Wolff–Parkinson–White syndrome; also intravenous amiodarone.
[b]Other beta-blockers are available but not recommended as specific rate control therapy in AF and therefore not mentioned here (e.g. propranolol and labetalol).
[c]No data on atenolol; should not be used in heart failure with reduced ejection fraction or in pregnancy.
[d]Loading regimen may vary; i.v. dosage should be considered when calculating total load.

Due to its broad extracardiac adverse effect profile, **amiodarone** is reserved as a last option when heart rate cannot be controlled even with maximal tolerated combination therapy, or in patients who do not qualify for atrioventricular node ablation and pacing. Many of the adverse effects from amiodarone have a direct relationship with cumulative dose, restricting the long-term value of amiodarone for rate control.[487]

### 7.1.4. Atrioventricular node ablation and pacemaker implantation

Ablation of the atrioventricular node and pacemaker implantation ('ablate and pace') can lower and regularize heart rate in patients with AF (see Supplementary data online, *Additional Evidence Table S16*). The procedure has a low complication rate and a low long-term mortality risk.[468,488] The pacemaker should be implanted a few weeks before the atrioventricular node ablation, with the initial pacing rate after ablation set at 70–90 b.p.m.[489,490] This strategy does not worsen LV function,[491] and may even improve LVEF in selected patients.[492,493] The evidence base has typically included older patients. For younger patients, ablate and pace should only be considered if heart rate remains uncontrolled despite consideration of other pharmacological and non-pharmacological treatment options. The choice of pacing therapy (right ventricular or biventricular pacing) depends on patient characteristics, presence of heart failure, and LVEF.[187,494]

In severely symptomatic patients with permanent AF and at least one hospitalization for heart failure, atrioventricular node ablation combined with CRT should be considered. In the APAF-CRT (Ablate and Pace for Atrial Fibrillation-cardiac resynchronization therapy) trial in a population with narrow QRS complexes, atrioventricular node ablation combined with CRT was superior to rate control drugs for the primary outcomes (all-cause mortality, and death or hospitalization for heart failure), and secondary outcomes (symptom burden and physical limitation).[470,471] Conduction system pacing may become a potentially useful alternate pacing mode when implementing a pace and ablate strategy, once safety and efficacy have been confirmed in larger RCTs.[495,496] In CRT recipients, the presence (or occurrence) of AF is one of the main reasons for suboptimal biventricular pacing.[187] Improvement of biventricular pacing is indicated and can be reached by intensification of rate control drug regimens, atrioventricular node ablation, or rhythm control, depending on patient and AF characteristics.[187]

## 7.2. Rhythm control strategies in patients with AF

### 7.2.1. General principles and anticoagulation

Rhythm control refers to therapies dedicated to restoring and maintaining sinus rhythm. These treatments include cardioversion, AADs, percutaneous catheter ablation, endoscopic and hybrid ablation, and open surgical approaches (see Supplementary data online, *Additional Evidence Table S17*). Rhythm control is never a strategy on its own; instead, it should always be part of the AF-CARE approach.

In patients with acute or worsening haemodynamic instability thought to be caused by AF, rapid electrical cardioversion is recommended. For other patients, a wait-and-see approach should be considered as an alternative to immediate cardioversion (*Figure 12*). The Rate Control versus Electrical Cardioversion Trial 7–Acute Cardioversion versus Wait and See (RACE 7 ACWAS) trial in patients with recent-onset symptomatic AF without haemodynamic compromise showed a wait-and-see approach for spontaneous conversion until 48 h after the onset of AF symptoms was non-inferior as compared with immediate cardioversion at 4 weeks follow-up.[10]

Since the publication of landmark trials more than 20 years ago, the main reason to consider longer-term rhythm control therapy has been the reduction in symptoms from AF.[497–500] Older studies have shown that the institution of a rhythm control strategy using AADs does not reduce mortality and morbidity when compared with a rate control-only strategy,[497–500] and may increase hospitalization.[457] In contrast, multiple studies have shown that rhythm control strategies have a positive effect on quality of life once sinus rhythm is maintained.[501,502] Therefore, in the case of uncertainty of the presence of symptoms associated with AF, an attempt to restore sinus rhythm is a rational first step. In patients with symptoms, patient factors that favour an attempt at rhythm control should be considered, including suspected tachycardiomyopathy, a brief AF history, non-dilated left atrium, or patient preference.

Rhythm control strategies have significantly evolved due to an increasing experience in the safe use of antiarrhythmic drugs,[17] consistent use of OAC, improvements in ablation technology,[503–509] and identification and management of risk factors and comorbidities.[39,510,511] In the ATHENA trial (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg twice daily for the Prevention of

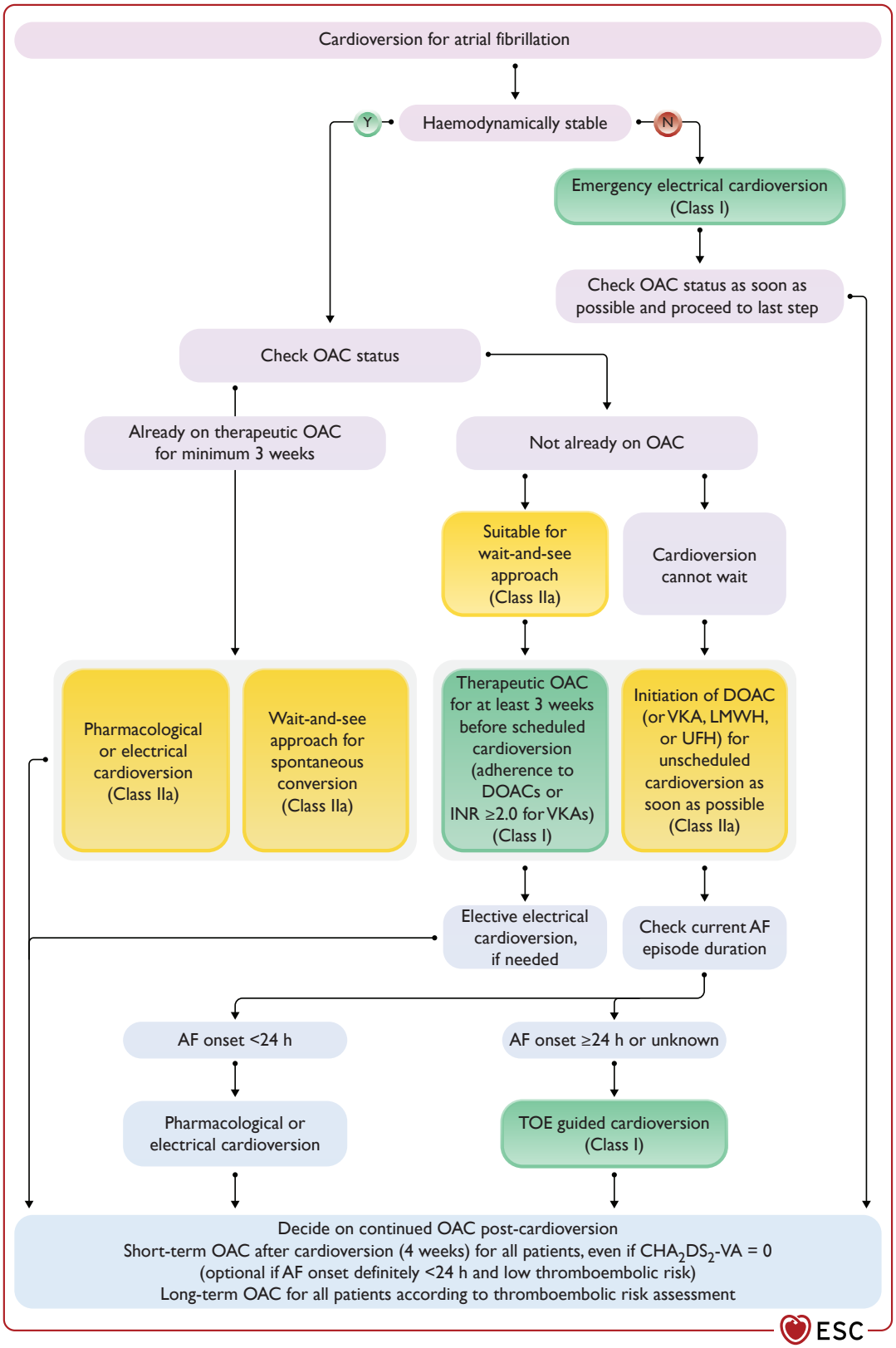


**Figure 12** Approaches for cardioversion in patients with AF. AF, atrial fibrillation; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; h, hour; LMWH, low molecular weight heparin; DOAC, direct oral anticoagulant; OAC, oral anticoagulant; TOE, transoesophageal echocardiography; UFH, unfractionated heparin; VKA, vitamin K antagonist. Flowchart for decision-making on cardioversion of AF depending on clinical presentation, AF onset, oral anticoagulation intake, and risk factors for stroke. [a]See *Section 6*.

Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter), dronedarone significantly reduced the risk of hospitalization due to cardiovascular events or death as compared with placebo in patients with paroxysmal or persistent AF.[512] The CASTLE-AF trial (Catheter Ablation versus Standard Conventional Treatment in Patients With Left Ventricle Dysfunction and AF) demonstrated that a rhythm control strategy with catheter ablation can improve mortality and morbidity in selected patients with HFrEF and an implanted cardiac device.[4] In end-stage HFrEF, the CASTLE-HTx trial (Catheter Ablation for Atrial Fibrillation in Patients With End-Stage Heart Failure and Eligibility for Heart Transplantation) found, in a single centre, that catheter ablation combined with guideline-directed medical therapy significantly reduced the composite of death from any cause, implantation of left ventricular assist device, or urgent heart transplantation compared with medical treatment.[513] At the same time, however, the CABANA trial (Catheter Ablation versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation) could not demonstrate a significant difference in mortality and morbidity between catheter ablation and standard rhythm and/or rate control drugs in symptomatic AF patients older than 64 years, or younger than 65 years with risk factors for stroke.[3] EAST-AFNET 4 (Early treatment of Atrial fibrillation for Stroke prevention Trial) reported that implementation of a rhythm control strategy within 1 year compared with usual care significantly reduced the risk of cardiovascular death, stroke, or hospitalization for heart failure or acute coronary syndrome in patients older than 75 years or with cardiovascular conditions.[17] Of note, rhythm control was predominantly pursued with antiarrhythmic drugs (80% of patients in the intervention arm). Usual care consisted of rate control therapy; only when uncontrolled AF-related symptoms occurred was rhythm control considered. Patients in the EAST-AFNET 4 trial all had cardiovascular risk factors but were at an early stage of AF, with more than 50% being in sinus rhythm and 30% being asymptomatic at the start of the study.

Based on all of these studies, this task force concludes that implementation of a rhythm control strategy can be safely instituted and confers amelioration of AF-related symptoms. Beyond control of symptoms, sinus rhythm maintenance should also be pursued to reduce morbidity and mortality in selected groups of patients.[4,17,502,513,514]

Any rhythm control procedure has an inherent risk of thromboembolism. Patients undergoing cardioversion require at least 3 weeks of therapeutic anticoagulation (adherence to DOACs or INR >2 if VKA) prior to the electrical or pharmacological procedure. In acute settings or when early cardioversion is needed, transoesophageal echocardiography (TOE) can be performed to exclude cardiac thrombus prior to cardioversion. These approaches have been tested in multiple RCTs.[319–321] In the case of thrombus detection, therapeutic anticoagulation should be instituted for a minimum of 4 weeks followed by repeat TOE to ensure thrombus resolution. When the definite duration of AF is less than 48 hours, cardioversion has typically been considered without the need for pre-procedure OAC or TOE for thrombus exclusion. However, the 'definite' onset of AF is often not known, and observational data suggest that stroke/thromboembolism risk is lowest within a much shorter time period.[515–519] This task force reached consensus that safety should come first. Cardioversion is not recommended if AF duration is longer than 24 hours, unless the patient has already received at least 3 weeks of therapeutic anticoagulation or a TOE is performed to exclude intracardiac thrombus. Most patients should continue OAC for at least 4 weeks post-cardioversion. Only for those without thromboembolic risk factors and sinus rhythm restoration within 24 h of AF onset is post-cardioversion OAC optional. In the presence of any thromboembolic risk factors, long-term OAC should be instituted irrespective of the rhythm outcome.

**Recommendation Table 15 — Recommendations for general concepts in rhythm control (see also Evidence Table 15)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Electrical cardioversion is recommended in AF patients with acute or worsening haemodynamic instability to improve immediate patient outcomes.[520] | I | C |
| Direct oral anticoagulants are recommended in preference to VKAs in eligible patients with AF undergoing cardioversion for thromboembolic risk reduction.[293,319–321,521] | I | A |
| Therapeutic oral anticoagulation for at least 3 weeks (adherence to DOACs or INR ≥2.0 for VKAs) is recommended before scheduled cardioversion of AF and atrial flutter to prevent procedure-related thromboembolism.[319–321] | I | B |
| Transoesophageal echocardiography is recommended if 3 weeks of therapeutic oral anticoagulation has not been provided, for exclusion of cardiac thrombus to enable early cardioversion.[319–321,522] | I | B |
| Oral anticoagulation is recommended to continue for at least 4 weeks in all patients after cardioversion and long-term in patients with thromboembolic risk factor(s) irrespective of whether sinus rhythm is achieved, to prevent thromboembolism.[239,319,320,523,524] | I | B |
| Cardioversion of AF (either electrical or pharmacological) should be considered in symptomatic patients with persistent AF as part of a rhythm control approach.[52,525,526] | IIa | B |
| A wait-and-see approach for spontaneous conversion to sinus rhythm within 48 h of AF onset should be considered in patients without haemodynamic compromise as an alternative to immediate cardioversion.[10,525] | IIa | B |
| Implementation of a rhythm control strategy should be considered within 12 months of diagnosis in selected patients with AF at risk of thromboembolic events to reduce the risk of cardiovascular death or hospitalization.[17,527] | IIa | B |
| Initiation of therapeutic anticoagulation should be considered as soon as possible in the setting of unscheduled cardioversion for AF or atrial flutter to prevent procedure-related thromboembolism.[319–321,528] | IIa | B |
| Repeat transoesophageal echocardiography should be considered before cardioversion if thrombus has been identified on initial imaging to ensure thrombus resolution and prevent peri-procedural thromboembolism.[529] | IIa | C |
| Early cardioversion is not recommended without appropriate anticoagulation or transoesophageal echocardiography if AF duration is longer than 24 h, or there is scope to wait for spontaneous cardioversion.[522] | III | C |

AF, atrial fibrillation; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.2. Electrical cardioversion

Electrical cardioversion (ECV) can be safely applied in the elective and acute setting (see Supplementary data online, *Additional Evidence Table S18*) with sedation by intravenous midazolam, propofol, or etomidate.[530] Structured and integrated care for patients with acute-onset AF at the emergency department is associated with better outcomes without compromising safety.[531] Rates of major adverse clinical events after cardioversion are significantly lower with DOACs compared with warfarin.[293]

Blood pressure monitoring and oximetry should be used routinely. Intravenous atropine or isoproterenol, or temporary transcutaneous pacing, should be available in case of post-cardioversion bradycardia. Biphasic defibrillators are standard because of their superior efficacy compared with monophasic defibrillators.[532–534] There is no single optimal position for electrodes, with a meta-analysis of 10 RCTs showing no difference in sinus rhythm restoration comparing anterior-posterior with antero-lateral electrode positioning.[535] Applying active compression to the defibrillation pads is associated with lower defibrillation thresholds, lower total energy delivery, fewer shocks for successful ECV, and higher success rates.[536] A randomized trial showed that maximum fixed-energy shocks were more effective than low-escalating energy for ECV.[537]

Immediate administration of vernakalant,[538] or pre-treatment for 3–4 days with flecainide,[539,540] ibutilide,[541,542] propafenone,[543] or amiodarone[544–546] improves the rate of successful ECV and can facilitate long-term maintenance of sinus rhythm by preventing early recurrent AF.[547] A meta-analysis demonstrated that pre-treatment with amiodarone (200–800 mg/day for 1–6 weeks pre-cardioversion) and post-treatment (200 mg/day) significantly improved the restoration and maintenance of sinus rhythm after ECV of AF.[546]

In some cases of persistent AF there is no clear relationship between the arrhythmia and symptoms. In these cases, restoring sinus rhythm by ECV might serve to confirm the impact of arrhythmia on symptoms and/or on heart failure symptoms and signs. Such an approach might be useful to identify truly asymptomatic individuals, to assess the impact of AF on LV function in patients with HFrEF, and to distinguish AF-related symptoms from heart failure symptoms.

**Recommendation Table 16 — Recommendations for electrical cardioversion of AF (see also Evidence Table 16)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Electrical cardioversion as a diagnostic tool should be considered in patients with persistent AF where there is uncertainty about the value of sinus rhythm restoration on symptoms, or to assess improvement in left ventricular function.[548] | IIa | C |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.3. Pharmacological cardioversion

Pharmacological cardioversion to sinus rhythm is an elective procedure in haemodynamically stable patients. It is less effective than electrical cardioversion for restoration of sinus rhythm,[549] with timing of cardioversion being a significant determinant of success.[550] There are limited contemporary data on the true efficacy of pharmacological cardioversion, which are likely biased by the spontaneous restoration of sinus rhythm in 76%–83% of patients with recent-onset AF (10%–18% within the first 3 h, 55%–66% within 24 h, and 69% within 48 h).[10,119,445,551–555]

The choice of a specific drug is based on the type and severity of concomitant heart disease (*Table 13*). A meta-analysis demonstrated that intravenous vernakalant and flecainide have the highest conversion rate within 4 h, possibly allowing discharge from the emergency department and reducing hospital admissions. Intravenous and oral formulations of Class IC antiarrhythmics (flecainide more so than propafenone) are superior regarding conversion rates within 12 h, while amiodarone efficacy is exhibited in a delayed fashion (within 24 h).[556] Pharmacological cardioversion does not require fasting, sedation, or anaesthesia. Anticoagulation should be started or continued according to a formal (re-)assessment of thromboembolic risk.[554,557–559]

A single self-administered oral dose of flecainide or propafenone (pill-in-the-pocket) is effective in symptomatic patients with infrequent and recent-onset paroxysmal AF. Safe implementation of this strategy requires patient screening to exclude sinus node dysfunction, atrioventricular conduction defects, or Brugada syndrome, as well as prior in-hospital validation of its efficacy and safety.[560] An atrioventricular node-blocking drug should be instituted in patients treated with Class IC AADs to avoid 1:1 conduction if the rhythm transforms to AFL.[561]

**Recommendation Table 17 — Recommendations for pharmacological cardioversion of AF (see also Evidence Table 17)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Intravenous flecainide or propafenone is recommended when pharmacological cardioversion of recent-onset AF is desired, excluding patients with severe left ventricular hypertrophy, HFrEF, or coronary artery disease.[562–566] | I | A |
| Intravenous vernakalant is recommended when pharmacological cardioversion of recent-onset AF is desired, excluding patients with recent ACS, HFrEF, or severe aortic stenosis.[562–568] | I | A |
| Intravenous amiodarone is recommended when cardioversion of AF in patients with severe left ventricular hypertrophy, HFrEF, or coronary artery disease is desired, accepting there may be a delay in cardioversion.[473,569,570] | I | A |
| A single self-administered oral dose of flecainide or propafenone (pill-in-the-pocket) should be considered for patient-led cardioversion in selected patients with infrequent paroxysmal AF, after efficacy and safety assessment and excluding those with severe left ventricular hypertrophy, HFrEF, or coronary artery disease.[560,571–573] | IIa | B |
| Pharmacological cardioversion is not recommended for patients with sinus node dysfunction, atrioventricular conduction disturbances, or prolonged QTc (>500 ms), unless risks for proarrhythmia and bradycardia have been considered. | III | C |



ACS, acute coronary syndromes; AF, atrial fibrillation; HFrEF, heart failure with reduced ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.

**Table 13 Antiarrhythmic drugs for sinus rhythm restoration**

| Drug | Administration route | Initial dosing | Subsequent dosing [long-term approach] | Acute success rate and time to sinus rhythm | Contraindications and precautions |
|---|---|---|---|---|---|
| Flecainide | Oral | 200–300 mg | [long-term 50–150 mg twice daily] | 50%–60% at 3 h and 75%–85% at 6–8 h (3–8 h) | • Should not be used in patients with severe structural or coronary artery disease, Brugada syndrome, or severe renal failure (CrCl <35 mL/min/1.73 $m^2$).<br>• Prior documentation of safety and efficacy in an inpatient setting is recommended prior to pill-in-the-pocket use.<br>• An AVN-blocking agent should be administered to avoid 1:1 conduction if transformation to AFL.<br>• Drug infusion should be discontinued in case of QRS widening >25% or bundle branch block occurrence.<br>• Caution is needed in patients with sinus node disease and AVN dysfunction.<br>• Do NOT use for conversion of atrial flutter. |
| | Intravenous | 1–2 mg/kg over 10 min | | 52%–95% (Up to 6 h) | |
| Propafenone | Oral | 450–600 mg | [long-term 150-300 mg three times daily] | 45%–55% at 3 h, 69%–78% at 8 h (3–8 h) | |
| | Intravenous | 1.5–2 mg/kg over 10 min | | 43%–89% (Up to 6 h) | |
| Amiodarone | Intravenous (/oral) | 300 mg intravenous over 30–60 min | 900-1200 mg intravenous over 24 hours (or 200 mg oral three times daily for 4 weeks). [long-term 200 mg oral daily] | 44% (8–12 h to several days) | • May cause phlebitis (use a large peripheral vein, avoid i.v. administration >24 h and use preferably volumetric pump).<br>• May cause hypotension, bradycardia/ atrioventricular block, QT prolongation.<br>• Only if no other option in patients with hyperthyroidism (risk of thyrotoxicosis).<br>• Consider the broad range of drug interactions. |
| Ibutilide | Intravenous | 1 mg over 10 min (0.01 mg/kg if body weight <60 kg) | 1 mg over 10 min (10–20 min after the initial dose) | 31%–51% (30–90 min) in AF 60–75% in AFL (60 min) | • Should be used in the setting of a cardiac care unit as it may cause QT prolongation and torsades de pointes.<br>• ECG monitoring for at least 4 h after administration to detect any proarrhythmic effects.<br>• Should not be used in patients with prolonged QT, severe LVH, or low LVEF. |
| Vernakalant | Intravenous | 3 mg/kg over 10 min (maximum 339 mg) | 2 mg/kg over 10 min (10–15 min after the initial dose) (maximum 226 mg) | 50% within 10 min | • Should not be used in patients with arterial hypotension (SBP <100 mmHg), recent ACS (within 1 month), NYHA III or IV HF, QT prolongation or severe aortic stenosis.<br>• May cause arterial hypotension, QT prolongation, QRS widening, or non-sustained ventricular tachycardia. |

ACS, acute coronary syndromes; AF, atrial fibrillation; AFL, atrial flutter; AVN, atrioventricular node; CrCl, creatinine clearance; ECG, electrocardiogram; HF, heart failure; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; NYHA, New York Heart Association; QT, QT interval; SBP, systolic blood pressure. Long-term dosage for maintenance of sinus rhythm is indicated in [square brackets]. Long-term oral dosing for dronedarone is 400 mg twice daily, and for sotalol 80-160 mg twice daily.

### 7.2.4. Antiarrhythmic drugs

The aims of long-term rhythm control are to maintain sinus rhythm, improve quality of life, slow the progression of AF, and potentially reduce morbidity related to AF episodes (see Supplementary data online, Additional Evidence *Table S19*).[17,445,574,575] Antiarrhythmic drugs do not eliminate recurrences of AF, but in patients with paroxysmal or persistent AF, a recurrence is not equivalent to treatment failure if episodes are less frequent, briefer, or less symptomatic. Antiarrhythmic drugs also have a role for long-term rhythm control in AF patients that are considered ineligible or unwilling to undergo catheter or surgical ablation.

Before starting AAD treatment, reversible triggers should be identified and underlying comorbidities treated to reduce the arrhythmogenic substrate, prevent progression of AF, and facilitate maintenance of sinus

rhythm.[39,128] The RACE 3 trial, including patients with early persistent AF and mild-to-moderate heart failure (predominantly HFpEF and HFmrEF), showed that targeted therapy of underlying conditions improved sinus rhythm maintenance at 1 year (75% vs. 63% as compared with standard care).[39] The selection of an AAD for long-term rhythm control requires careful evaluation that takes into account AF type, patient parameters, and safety profile.[445] It also includes shared decision-making, balancing the benefit/risk ratio of AADs in comparison with other strategies. Notably, recent evidence has shown that careful institution of AADs can be performed safely.[17]

The long-term effectiveness of AADs is limited. In a meta-analysis of 59 RCTs, AADs reduced AF recurrences by 20%–50% compared with no treatment, placebo, or drugs for rate control.[576,577] When one AAD fails to reduce AF recurrences, a clinically acceptable response may be achieved with another drug, particularly if from a different class.[578] Combinations of AADs are not recommended. The data available suggest that AADs do not produce an appreciable effect on mortality or other cardiovascular complications with the exception of increased mortality signals for sotalol[574,579,580] and amiodarone.[581] In contrast, use of AADs within a rhythm control strategy can be associated with reduction of morbidity and mortality in selected patients.[582]

All AADs may produce serious cardiac (proarrhythmia, negative inotropism, hypotension) and extracardiac adverse effects (organ toxicity, predominantly amiodarone). Drug safety, rather than efficacy, should determine the choice of drug. The risk of proarrhythmia increases in patients with structural heart disease. Suggested doses for long-term oral AAD are presented in *Table 13*.[577,583,584]

**Recommendation Table 18 — Recommendations for antiarrhythmic drugs for long-term maintenance of sinus rhythm (see also Evidence Table 18)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Amiodarone is recommended in patients with AF and HFrEF requiring long-term antiarrhythmic drug therapy to prevent recurrence and progression of AF, with careful consideration and monitoring for extracardiac toxicity.[577,585–587] | I | A |
| Dronedarone is recommended in patients with AF requiring long-term rhythm control, including those with HFmrEF, HFpEF, ischaemic heart disease, or valvular disease to prevent recurrence and progression of AF.[512,577,588,589] | I | A |
| Flecainide or propafenone is recommended in patients with AF requiring long-term rhythm control to prevent recurrence and progression of AF, excluding those with impaired left ventricular systolic function, severe left ventricular hypertrophy, or coronary artery disease.[526,577,585,590] | I | A |
| Concomitant use of a beta-blocker, diltiazem, or verapamil should be considered in AF patients treated with flecainide or propafenone, to prevent 1:1 conduction if their rhythm is transformed to atrial flutter. | IIa | C |
| Sotalol may be considered in patients with AF requiring long-term rhythm control with normal LVEF or coronary artery disease to prevent recurrence and progression of AF, but requires close monitoring of QT interval, serum potassium levels, renal function, and other proarrhythmia risk factors.[585,587] | IIb | A |
| Antiarrhythmic drug therapy is not recommended in patients with advanced conduction disturbances unless antibradycardia pacing is provided. | III | C |

*Continued*

AF, atrial fibrillation; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.5. Catheter ablation

Catheter ablation prevents AF recurrences, reduces AF burden, and improves quality of life in symptomatic paroxysmal or persistent AF where the patient is intolerant or does not respond to AAD.[503–509] Multiple RCTs have provided evidence in favour of catheter ablation as a first-line approach for rhythm control in patients with paroxysmal AF, with a similar risk of adverse events as compared with initial AAD treatment (see Supplementary data online, Additional Evidence *Table S20*).[15,16,591–594] In contrast, it is not clear whether first-line ablation is superior to drug therapy in persistent AF. Catheter ablation may also have a role in patients with symptoms due to prolonged pauses upon AF termination, where non-randomized data have shown improved symptoms, and avoidance of pacemaker implantation.[595–598]

Pulmonary vein isolation (PVI) remains the cornerstone of AF catheter ablation,[503,508,593,599] but the optimal ablation strategy has not been clarified in the non-paroxysmal AF population.[600] New technologies are emerging, such as pulsed field ablation, in which high-amplitude electrical pulses are used to ablate the myocardium by electroporation with high tissue specificity. In a single-blind RCT of 607 patients, pulsed field ablation was non-inferior for efficacy and safety endpoints compared with conventional radiofrequency or cryoballoon ablation.[601] Regarding timing of ablation, a small RCT found that delaying catheter ablation in patients with paroxysmal or persistent AF by 12 months (while on optimized medical therapy) did not impact on arrhythmia-free survival compared with ablation within 1 month.[602]

As with any type of rhythm control, many patients in clinical practice will not be suitable for catheter ablation due to factors that reduce the likelihood of a positive response, such as left atrial dilatation. Definitive evidence that supports the prognostic benefit of catheter ablation is needed before this invasive treatment can be considered for truly asymptomatic patients. As previously noted, the CABANA trial did not confirm a benefit of catheter ablation compared with medical therapy, although high crossover rates and low event rates may have diluted the treatment effect.[3] Therefore, only highly selected asymptomatic patients could be candidates for catheter ablation, and only after detailed discussion of associated risks and potential benefit of delaying AF progression.[4,603] Randomized trials have shown that AF catheter ablation in patients with HFrEF significantly reduces arrhythmia recurrence and increases ejection fraction, with improvement in clinical outcomes and mortality also observed in selected patients.[4,513,514,604–612] Several

characteristics, including but not limited to AF type, left atrial dilatation, and the presence of atrial and/or ventricular fibrosis, could refine patient selection to maximize outcome benefit from AF catheter ablation in patients with HFrEF.[604,608,613–617] The prognostic value of catheter ablation in patients with HFpEF is less well established than for HFrEF.[617–626]

Recent registries and trials report varying rates of peri-procedural serious adverse events associated with catheter ablation (2.9%–7.2%) with a very low 30 day mortality rate (<0.1%). Operator experience and procedural volume at the ablation centre are critical, since they are associated with complication rates and 30 day mortality.[627–631]

Intermittent rhythm monitoring has typically been used to detect AF relapses following catheter ablation. Recent technology developments such as smartwatch or smartphone photoplethysmography and wearable patches may have an emerging role in post-ablation monitoring.[632,633] In addition, implantable loop recorders have been used to quantify AF burden before and after ablation as an additional endpoint beyond binary AF elimination.[634] Management of arrhythmia recurrence post-ablation is an informed, shared decision-making process driven by available options for symptom control. In the post-AF ablation context, there is data supporting a role for AAD continuation or re-initiation, even for previously ineffective drugs.[635] A short-term AAD treatment (2–3 months) following ablation reduces early recurrences of AF,[554,635–639] but does not affect late recurrences[636,637,640–642] or 1 year clinical outcomes.[642] Repeat PVI should be offered in patients with AF recurrence if symptom improvement was demonstrated after the first ablation, with shared decision-making and clear goals of treatment.[643–645]

**Recommendation Table 19 — Recommendations for catheter ablation of AF (see also Evidence Table 19)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **Shared decision-making** | | |
| Shared decision-making is recommended when considering catheter ablation for AF, taking into account procedural risks, likely benefits, and risk factors for AF recurrence.[128,210,503,646] | I | C |
| **AF patients resistant or intolerant to antiarrhythmic drug therapy** | | |
| Catheter ablation is recommended in patients with paroxysmal or persistent AF resistant or intolerant to antiarrhythmic drug therapy to reduce symptoms, recurrence, and progression of AF.[3,15,503,505,506,508] | I | A |
| **First-line rhythm control therapy** | | |
| Catheter ablation is recommended as a first-line option within a shared decision-making rhythm control strategy in patients with paroxysmal AF, to reduce symptoms, recurrence, and progression of AF.[16,591–594] | I | A |
| Catheter ablation may be considered as a first-line option within a shared decision-making rhythm control strategy in selected patients with persistent AF to reduce symptoms, recurrence, and progression of AF. | IIb | C |
| **Patients with heart failure** | | |
| AF catheter ablation is recommended in patients with AF and HFrEF with high probability of tachycardia-induced cardiomyopathy to reverse left ventricular dysfunction.[604,611] | I | B |
| AF catheter ablation should be considered in selected AF patients with HFrEF to reduce HF hospitalization and prolong survival.[4,513,514,604,610,612] | IIa | B |
| **Sinus node disease/tachycardia–bradycardia syndrome** | | |
| AF catheter ablation should be considered in patients with AF-related bradycardia or sinus pauses on AF termination to improve symptoms and avoid pacemaker implantation.[595–598] | IIa | C |
| **Recurrence after catheter ablation** | | |
| Repeat AF catheter ablation should be considered in patients with AF recurrence after initial catheter ablation, provided the patient's symptoms were improved after the initial PVI or after failed initial PVI, to reduce symptoms, recurrence, and progression of AF.[643–645] | IIa | B |

*Continued*

AF, atrial fibrillation; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; PVI, pulmonary vein isolation.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.6. Anticoagulation in patients undergoing catheter ablation

The presence of left atrial thrombus is a contraindication to catheter-based AF ablation due to the risk of thrombus dislodgement leading to ischaemic stroke. Patients planned for catheter ablation of AF with an increased risk of thromboembolism should be on OAC for at least 3 full weeks prior to the procedure.[554,647]

There is a wide range in practice for visualization of intra-atrial thrombi prior to catheter ablation, including TOE, intracardiac echocardiography, or delayed phase cardiac computed tomography (CT).[554,648] The prevalence of left atrial thrombus was 1.3% and 2.7% in two meta-analyses of observational studies in patients planned for catheter ablation of AF on adequate OAC.[649,650] The prevalence of left atrial thrombus was higher in patients with elevated stroke risk scores, and in patients with non-paroxysmal compared with paroxysmal AF.[650] In addition, several patient subgroups with AF have increased risk of ischaemic stroke and intracardiac thrombus even if treated with adequate anticoagulation, including those with cardiac amyloidosis, rheumatic heart disease, and hypertrophic cardiomyopathy (HCM). Cardiac imaging before catheter ablation should be considered in these high-risk patient groups regardless of preceding effective OAC. Observational studies suggest that patients with a low thromboembolic risk profile may be managed without visualization of the LAA,[651–653] but no RCTs have been performed (see Supplementary data online, *Additional Evidence Table S21*).

For patients who have been anticoagulated prior to the ablation procedure it is recommended to avoid interruption of OAC (see Supplementary data online, *Additional Evidence Table S22*).[654–656] Patients with interrupted OAC showed an increase in silent stroke detected by brain magnetic resonance imaging (MRI) as compared with those with uninterrupted OAC.[657–659] In a true uninterrupted

DOAC strategy for once-daily dosing, a pre-procedural shift to evening intake might be considered to mitigate bleeding risk. Randomized trials show comparable safety and efficacy with minimally interrupted OAC (withholding the morning DOAC dose on the day of the procedure) and a totally uninterrupted peri-ablation OAC strategy.[655]

Anticoagulation with heparin during AF ablation is common practice.[554] Post-ablation DOACs should be continued as per the dosing regimen when haemostasis has been achieved.[335,554,647] All patients should be kept on an OAC for at least 2 months after an AF ablation procedure irrespective of estimated thromboembolic risk (see Supplementary data online, *Additional Evidence Table S23*).[647] Meta-analyses of observational studies have tried to assess the safety of stopping OAC treatment after catheter ablation for AF, but the results have been heterogenous.[660–663] Until the completion of relevant RCTs (e.g. NCT02168829), it is recommended to continue OAC therapy post-AF ablation according to the patient's $CHA_2DS_2$-VA score and not the perceived success of the ablation procedure.[554]

**Recommendation Table 20 — Recommendations for anticoagulation in patients undergoing catheter ablation (see also Evidence Table 20)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Initiation of oral anticoagulation is recommended at least 3 weeks prior to catheter-based ablation in AF patients at elevated thromboembolic risk, to prevent peri-procedural ischaemic stroke and thromboembolism.[554,647] | I | C |
| Uninterrupted oral anticoagulation is recommended in patients undergoing AF catheter ablation to prevent peri-procedural ischaemic stroke and thromboembolism.[664,665] | I | A |
| Continuation of oral anticoagulation is recommended for at least 2 months after AF ablation in all patients, irrespective of rhythm outcome or $CHA_2DS_2$-VA score, to reduce the risk of peri-procedural ischaemic stroke and thromboembolism.[554,663] | I | C |
| Continuation of oral anticoagulation is recommended after AF ablation according to the patient's $CHA_2DS_2$-VA score, and not the perceived success of the ablation procedure, to prevent ischaemic stroke and thromboembolism.[554] | I | C |
| Cardiac imaging should be considered prior to catheter ablation of AF in patients at high risk of ischaemic stroke and thromboembolism despite taking oral anticoagulation to exclude thrombus.[649,650] | IIa | B |



AF, atrial fibrillation; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.7. Endoscopic and hybrid AF ablation

Minimally invasive surgical AF ablation can be performed via a thoracoscopic approach or a subxiphoid approach. The term endoscopic covers both strategies. Hybrid ablation approaches have been developed where endoscopic epicardial ablation on the beating heart is performed in combination with endocardial catheter ablation, either in a simultaneous or sequential procedure. The rationale for combining an endocardial with an epicardial approach is that a more effective transmural ablation strategy can be pursued.[666,667]

For paroxysmal AF, an endoscopic or hybrid ablation approach may be considered after a failed percutaneous catheter ablation strategy.[668–670] Long-term follow-up of the FAST RCT (mean of 7.0 years), which included patients with paroxysmal and persistent AF, found arrhythmia recurrence was common but substantially lower with thoracoscopic ablation than catheter ablation: 34/61 patients (56%) compared with 55/63 patients (87%), with $P < .001$ for the comparison.[669] For persistent AF, endoscopic or hybrid ablation approaches are suitable as a first procedure to maintain long-term sinus rhythm in selected patients.[667–672] A meta-analysis of three RCTs confirmed a lower rate of atrial arrhythmia recurrence after thoracoscopic vs. catheter ablation (incidence rate ratio, 0.55; 95% CI, 0.38–0.78; with no heterogeneity between trials).[669] An RCT with 12 month follow-up published after the meta-analysis in patients with long-standing persistent AF found no difference in arrhythmia freedom comparing thoracoscopic with catheter ablation.[673] Although overall morbidity and mortality of both techniques is low, endoscopic and hybrid ablation have higher complication rates than catheter ablation, but similar long-term rates of the composite of mortality, MI, or stroke.[667,669]

More recent trials have assessed the efficacy and safety of the hybrid epicardial-plus-endocardial approach in persistent AF refractory to AAD therapy, including a single-centre RCT[670] and two multicentre RCTs.[671,674] Across these trials, hybrid ablation was consistently superior to catheter ablation alone for maintaining long-term sinus rhythm, without significant differences in major adverse events. Notably, these studies were typically performed in highly experienced centres (see Supplementary data online, *Additional Evidence Table S24*).

Similar to other rhythm control approaches, this task force recommends that OAC are continued in all patients who have a risk of thromboembolism, irrespective of rhythm outcome, and regardless of LAA exclusion performed as part of the surgical procedure.

**Recommendation Table 21 — Recommendations for endoscopic and hybrid AF ablation (see also Evidence Table 21)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Continuation of oral anticoagulation is recommended in patients with AF at elevated thromboembolic risk after concomitant, endoscopic, or hybrid AF ablation, independent of rhythm outcome or LAA exclusion, to prevent ischaemic stroke and thromboembolism. | I | C |

*Continued*

| | | |
|---|---|---|
| Endoscopic and hybrid ablation procedures should be considered in patients with symptomatic persistent AF refractory to AAD therapy to prevent symptoms, recurrence, and progression of AF, within a shared decision-making rhythm control team of electrophysiologists and surgeons.[667–671,674] | IIa | A |
| Endoscopic and hybrid ablation procedures may be considered in patients with symptomatic paroxysmal AF refractory to AAD therapy and failed percutaneous catheter ablation strategy to prevent symptoms, recurrence, and progression of AF, within a shared decision-making rhythm control team of electrophysiologists and surgeons.[668,669] | IIb | B |



AAD, antiarrhythmic drugs; AF, atrial fibrillation; LAA, left atrial appendage.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.8. AF ablation during cardiac surgery

Atrial fibrillation is a significant risk factor for early mortality, late mortality, and stroke in patients referred for cardiac surgery.[675–677] The best validated method of surgical ablation is the Maze procedure, consisting of a pattern of transmural lesions including PVI, with subsequent modifications using bipolar radiofrequency and/or cryothermy ablation with LAA amputation (see Supplementary data online, Additional Evidence *Table S25*).[678–681] Education and training, close co-operation within a multidisciplinary team, and shared decision-making can improve the quality and outcomes of surgical ablation.[682]

A number of RCTs have shown that surgical AF ablation during cardiac surgery increases freedom from arrhythmia recurrence.[683–688] Performing surgical AF ablation, mainly targeting those patients needing mitral valve surgery, is not associated with increased morbidity or mortality.[678,683–685] Observational data, including large registries, have supported the potential value of surgical AF ablation,[689–700] but further RCTs are needed to evaluate which patients should be selected, and whether this approach contributes to the prevention of stroke, thromboembolism, and death.

Data on pacemaker implantation rates after surgical AF ablation are variable and are likely influenced by centre experience and the patients treated (e.g. underlying sinus node disease). In a systematic review of 22 RCTs (1726 patients), permanent pacemaker implantation rates were higher with surgical AF ablation than without concomitant AF surgery (6.0% vs. 4.1%; RR, 1.69; 95% CI, 1.12–2.54).[701] Observational registry data from contemporary cohorts (2011–2020) suggest an overall pacemaker rate post-operatively of 2.1% in patients selected for surgical AF ablation, with no discernible impact of surgical ablation on the need for a pacemaker, but higher rates in those needing multivalve surgery.[702] With a safety-first approach in mind, imaging is advised during surgical AF ablation to exclude thrombus and help to plan the surgical approach (e.g. with TOE), regardless of effective pre-procedural anticoagulant use.

**Recommendation Table 22 — Recommendations for AF ablation during cardiac surgery (see also Evidence Table 22)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Concomitant surgical ablation is recommended in patients undergoing mitral valve surgery and AF suitable for a rhythm control strategy to prevent symptoms and recurrence of AF, with shared decision-making supported by an experienced team of electrophysiologists and arrhythmia surgeons.[683–685,701] | I | A |
| Intraprocedural imaging for detection of left atrial thrombus in patients undergoing surgical ablation is recommended to guide surgical strategy, independent of oral anticoagulant use, to prevent peri-procedural ischaemic stroke and thromboembolism. | I | C |
| Concomitant surgical ablation should be considered in patients undergoing non-mitral valve cardiac surgery and AF suitable for a rhythm control strategy to prevent symptoms and recurrence of AF, with shared decision-making supported by an experienced team of electrophysiologists and arrhythmia surgeons.[701,703–707] | IIa | B |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

### 7.2.9. Atrial tachycardia after pulmonary vein isolation

After any ablation for AF, recurrent arrhythmias may manifest as AF, but also as atrial tachycardia (AT). Although AT may be perceived as a step in the right direction by the treating physician, this view is often not shared by the patient because AT can be equally or more symptomatic than the original AF. Conventionally, an early arrhythmia recurrence post-PVI (whether AT, AF, or flutter) is considered potentially transitory.[708] Recent trials using continuous implantable loop recorders for peri-procedural monitoring have provided insight into the incidence and significance of early arrhythmia recurrences, and have confirmed a link between early and later recurrence.[709] Discussion of management options for AT post-ablation should ideally involve a multidisciplinary team with experience in interventional management of complex arrhythmias, considering technical challenges, procedural efficacy, and safety, in the context of patient preferences.

## 8. [E] Evaluation and dynamic reassessment

The development and progression of AF results from continuous interactions between underlying mechanisms (electrical, cellular, neurohormonal, and haemodynamic), coupled with a broad range of clinical factors and associated comorbidities. Each individual factor

has considerable variability over time, affecting its contribution to the AF-promoting substrate. The risk profile of each patient is also far from static, and requires a dynamic mode of care to ensure optimal AF management.[710,711] Patients with AF require periodic reassessment of therapy based on this changing risk status if we are to improve the overall quality of care. Timely attention to modifiable factors and underpinning comorbidities has the potential to slow or reverse the progression of AF, increase quality of life, and prevent adverse outcomes such as heart failure, thromboembolism, and major bleeding.

The [E] in AF-CARE encompasses the range of activity needed by healthcare professionals and patients to: (i) thoroughly evaluate associated comorbidities and risk factors that can guide treatment; and (ii) provide the dynamic assessment needed to ensure that treatment plans remain suited to that particular patient. This task force recommends an adaptive strategy that not only reacts to changes notified by a patient, but also proactively seeks out issues where altering management could impact on patient wellbeing. Avoidance of unnecessary and costly follow-up is also inherent in this framework, with educated and empowered patients contributing to identifying the need for access to specialist care or an escalation of management. The patient-centred, shared decision philosophy is embedded to improve efficiency in models of care and to address the needs of patients with AF.

Medical history and the results of any tests should be regularly re-evaluated to address the dynamic nature of comorbidities and risk factors.[712] This may have impact on therapeutic decisions; e.g. resumption of full-dose DOAC therapy after improvement in the patient's renal function. The timing of review of the AF-CARE pathway is patient specific and should respond to changes in clinical status. In most cases, this task force advises re-evaluation 6 months after initial presentation, and then at least annually by a healthcare professional in primary or secondary care (see *Figure 3*).

## 8.1. Implementation of dynamic care

A multidisciplinary-based approach is advocated to improve implementation of dynamic AF-CARE (see *Figure 2*); although potentially resource intensive, this is preferred to more simplistic or opportunistic methods. For example, in a pragmatic trial of 47 333 AF patients identified through health insurance claims, there was no difference in OAC initiation at 1 year in those randomized to a single mailout of patient and clinician education, compared with those in the usual care group.[713] For co-ordination of care there is a core role for cardiologists, general practitioners, specialized nurses, and pharmacists.[714] If needed, and depending on local resources, others may also be involved (cardiac surgeons, physiotherapists, neurologists, psychologists, and other allied health professionals). It is strongly advocated that one core team member co-ordinates care, and that additional team members become involved according to the needs of the individual patient throughout their AF trajectory.

Several organizational models of integrated care for AF have been evaluated, but which components are most useful remains unclear. Some models include a multidisciplinary team,[715,716] while others are nurse-led[79,122,124,717] or cardiologist-led.[79,122,124,717] Several published models used computerized decision support systems or electronic health applications.[79,122,715,718] Evaluation within RCTs has demonstrated mixed results due to the variety of methods tested and differences in regional care. Several studies report significant improvements with respect to adherence to anticoagulation, cardiovascular mortality, and hospitalization relative to standard of care.[121–123] However, the RACE 4 (IntegRAted Chronic Care Program at Specialized AF Clinic Versus Usual CarE in Patients with Atrial Fibrillation) trial, which included 1375 patients, failed to demonstrate superiority of nurse-led over usual care.[79] New studies of the components and optimal models for delivery for integrated care approaches in routine practice are ongoing (ACTRN12616001109493, NCT03924739).

## 8.2. Improving treatment adherence

Advances in the care of patients with AF can only be effective if appropriate tools are available to support the implementation of the treatment regimen.[719] A number of factors are related to the optimal implementation of care at the level of: (i) the individual patient (culture, cognitive impairment, and psychological status); (ii) the treatment (complexity, side effects, polypharmacy, impact on daily life, and cost); (iii) the healthcare system (access to treatment and multidisciplinary approach); and (iv) the healthcare professional (knowledge, awareness of guidelines, expertise, and communication skills). A collaborative approach to patient care, based upon shared decision-making and goals tailored to individual patient needs, is crucial in promoting ongoing patient adherence to the agreed treatment regimen.[720] Even when treatment seems feasible for the individual, patients often lack access to reliable and up-to-date information about risks and benefits of various treatment options, and consequently are not empowered to engage in their own management. A sense of ownership that promotes the achievement of joint goals can be encouraged through the use of educational programmes, websites (such as https://afibmatters.org), app-based tools, and individually tailored treatment protocols which take into account gender, ethnic, socioeconomic, environmental, and work factors. In addition, practical tools (e.g. schedules, apps, brochures, reminders, pillboxes) can help to implement treatment in daily life.[721,722] Regular review by members of the multidisciplinary team enables the evolution of a flexible and responsive management regimen that the patient will find easier to follow.

## 8.3. Cardiac imaging

A TTE is a valuable asset across all four AF-CARE domains when there are changes in the clinical status of an individual patient (*Figure 13*).[723–725] The key findings to consider from an echocardiogram are any structural heart disease (e.g. valvular disease or left ventricular hypertrophy), impairment of left ventricular function (systolic and/or diastolic to classify heart failure subtype), left atrial dilatation, and right heart dysfunction.[59,67,726] To counter irregularity when in AF, obtaining measurements in cardiac cycles that follow two similar RR intervals can improve the value of parameters compared with sequential averaging of cardiac cycles.[723,727] Contrast TTE or alternative imaging modalities may be required where image quality is poor, and quantification of left ventricular systolic function is needed for decisions on rate or rhythm control. Other cardiac imaging techniques, such as cardiac magnetic resonance (CMR), CT, TOE, and nuclear imaging can be valuable when: (i) TTE quality is suboptimal for diagnostic purposes; (ii) additional information is needed on structure, substrate, or function; and (iii) to support decisions on interventional procedures (see Supplementary data online, *Figure S1*).[59,724,725,728] As with TTE, other types of cardiac imaging can be challenging in the context of AF irregularity or with rapid heart rate, requiring technique-specific modifications when acquiring ECG-gated sequences.[729–731]

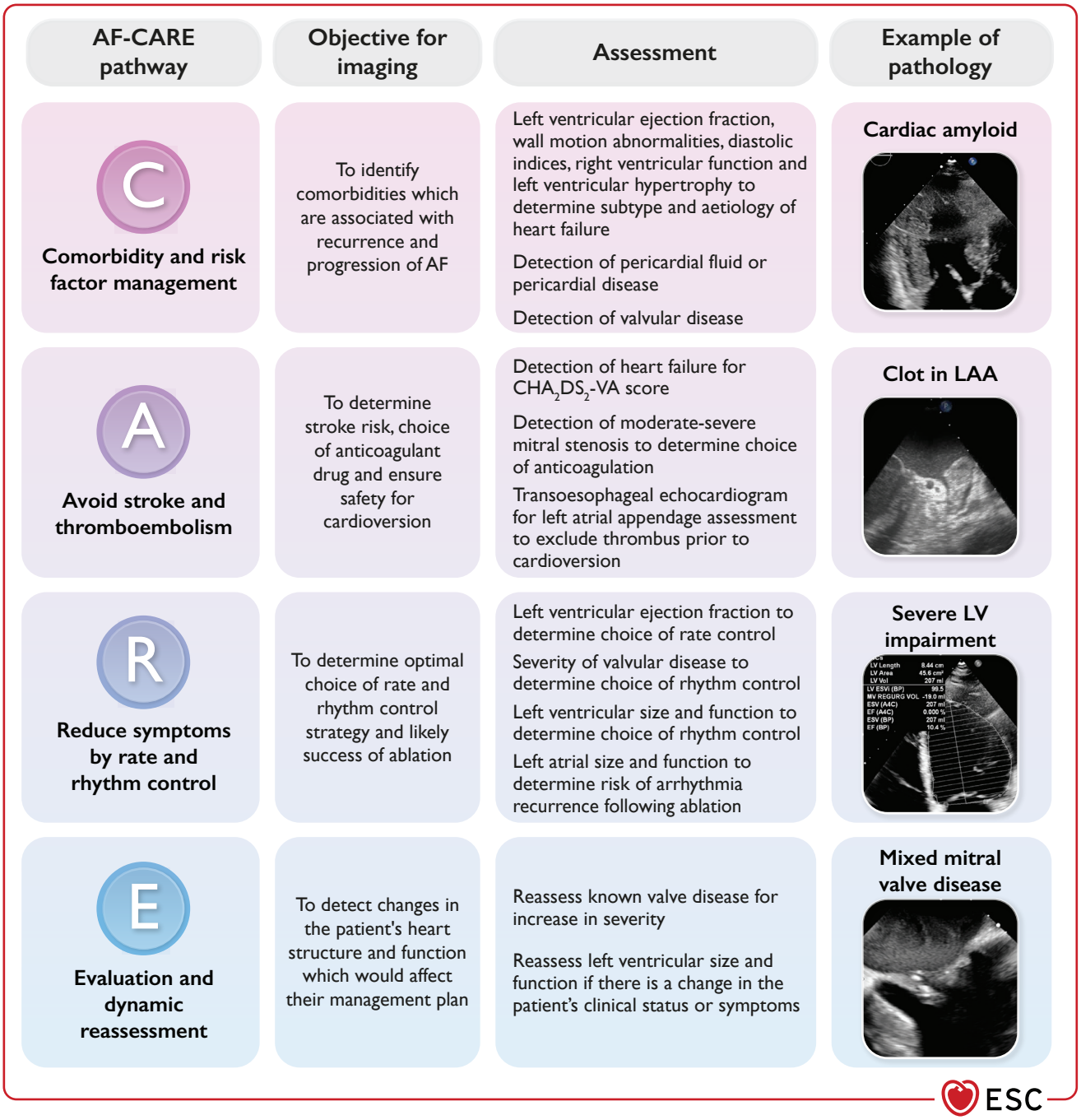


**Figure 13** Relevance of echocardiography in the AF-CARE pathway. AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; LAA, left atrial appendage; LV, left ventricle.

## 8.4. Patient-reported outcome measures

Patients with AF have a lower quality of life compared with the general population.[732] Improvement in quality of life and functional status should play a key role in assessing and reassessing treatment decisions (see Supplementary data online, Additional Evidence *Table S26*).[36] Patient-reported outcome measures are valuable to measure quality of life, functional status, symptoms, and treatment burden for patients with AF over time.[55,733–735] Patient-reported outcome measures are playing an increasing role in clinical trials to assess the success of treatment; however, they remain under-utilized.[736,737] They can be divided into generic or disease-specific tools, with the latter helping to provide insight into AF-related impacts.[738] However, multimorbidity can still confound the sensitivity of all PROMs, impacting on association with other established metrics of treatment performance such as mEHRA symptom

class and natriuretic peptides.[48] Intervention studies have demonstrated an association between improvement in PROM scores and reduction in AF burden and symptoms.[48,738]

Atrial fibrillation-specific questionnaires include the AF 6 (AF6),[739] Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT),[740] the Atrial Fibrillation Quality of Life Questionnaire (AFQLQ),[741] the Atrial Fibrillation Quality of Life (AF-QoL),[742] and the Quality of Life in Atrial Fibrillation (QLAF).[743] The measurement properties of most of these tools lack sufficient validation.[49] The International Consortium for Health Outcomes Measurement (ICHOM) working group recommends the use of the AFEQT PROM or a symptom questionnaire called the Atrial Fibrillation Severity Scale (AFSS) for measuring exercise tolerance and the impact of symptoms in AF.[744] Through wider use of patient experience measures, there is an opportunity at the institutional level to improve the quality of care delivered to patients with AF.[49–55]

**Recommendation Table 23 — Recommendations to improve patient experience (see also Evidence Table 23)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Evaluating quality of care and identifying opportunities for improved treatment of AF should be considered by practitioners and institutions to improve patient experiences.[49–55] | IIa | B |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

# 9. The AF-CARE pathway in specific clinical settings

The following sections detail specific clinical settings where approaches to AF-CARE may vary. Unless specially discussed, measures for [C] comorbidity and risk factor management, [A] avoidance of stroke and thromboembolism, [R] rate and rhythm control, and [E] evaluation and dynamic reassessment should follow the standard pathways introduced in *Section 4*.

## 9.1. AF-CARE in unstable patients

Unstable patients with AF include those with haemodynamic instability caused by the arrhythmia or acute cardiac conditions, and severely ill patients who develop AF (sepsis, trauma, surgery, and particularly cancer-related surgery). Conditions such as sepsis, adrenergic overstimulation, and electrolyte disturbances contribute to onset and recurrence of AF in these patients. Spontaneous restoration of sinus rhythm has been reported in up to 83% during the first 48 h after appropriate treatment of the underlying cause.[551,745]

Emergency electrical cardioversion is still considered the first-choice treatment if sinus rhythm is thought to be beneficial, despite the limitation of having a high rate of immediate relapse.[746] Amiodarone is a second-line option because of its delayed activity; however, it may be an appropriate alternative in the acute setting.[747,748] In a multicentre cohort study carried out in the United Kingdom and the United States of America, amiodarone and beta-blockers were similarly effective for rate control in intensive care patients, and superior to digoxin and calcium channel blockers.[749] The ultra-short acting and highly selective beta-blocker landiolol can safely control rapid AF in patients with low ejection fraction and acutely decompensated heart failure, with a limited impact on myocardial contractility or blood pressure.[477,750,751]

## 9.2. AF-CARE in acute and chronic coronary syndromes

The incidence of AF in acute coronary syndromes (ACS) ranges from 2% to 23%.[752] The risk of new-onset AF is increased by 60%–77% in patients suffering an MI,[753] and AF may be associated with an increased risk of ST-segment elevation myocardial infarction (STEMI) or non-STEMI ACS.[754] Overall, 10%–15% of AF patients undergo percutaneous intervention (PCI) for CAD.[755] In addition, AF is a common precipitant for type 2 MI.[756] Observational studies show that patients with both ACS and AF are less likely to receive appropriate antithrombotic therapy[757] and more likely to experience adverse outcomes.[758] Peri-procedural management of patients with ACS or chronic coronary syndromes (CCS) are detailed in the *2023 ESC Guidelines for the management of acute coronary syndromes* and *2024 ESC Guidelines for the management of chronic coronary syndromes*.[759,760]

The combination of AF with ACS is the area where use of multiple antithrombotic drugs is most frequently indicated, consisting of antiplatelet agents plus OAC (*Figure 14*) (see Supplementary data online, *Additional Evidence Table S27*). There is a general trend to decrease the duration of DAPT to reduce bleeding; however, this may increase ischaemic events and stent thrombosis.[761,762] In ACS there is a high risk of predominantly platelet-driven atherothrombosis and thus of coronary ischaemic events. Acute coronary syndromes treated by PCI require DAPT for improved short- and long-term prognosis. Therefore, a peri-procedural triple antithrombotic regimen including an OAC, aspirin, and a $P2Y_{12}$ inhibitor should be the default strategy for most patients. Major thrombotic events vs. major bleeding risk need to be balanced when prescribing antiplatelet therapy and OAC after the acute phase and/or after PCI. The combination of OAC (preferably a DOAC) and a $P2Y_{12}$ inhibitor results in less major bleeding than triple therapy that includes aspirin. Clopidogrel is the preferred $P2Y_{12}$ inhibitor, as the evidence for ticagrelor and prasugrel is less clear with higher bleeding risk.[763–769] Ongoing trials will add to our knowledge about safely combining DOACs with antiplatelet agents (NCT04981041, NCT04436978). When using VKAs with antiplatelet agents, there is consensus opinion to use an INR range of 2.0–2.5 to mitigate excess bleeding risk.

Short–term triple therapy (≤1 week) is recommended for all patients without diabetes after ACS or PCI. In pooled analyses of RCTs, omitting aspirin in patients with ACS undergoing PCI has the potential for higher rates of ischaemic/stent thrombosis, without impact on incident stroke.[761,762,770–772] None of the trials were powered for ischaemic events. All patients in AUGUSTUS (an open–label, 2 × 2 factorial, randomized controlled clinical trial to evaluate the safety of apixaban vs. vitamin k antagonist and aspirin vs. aspirin placebo in patients with AF and ACS or PCI) received aspirin plus a $P2Y_{12}$ inhibitor for a median time of 6 days.[773] At the end of the trial, apixaban and a $P2Y_{12}$ inhibitor without aspirin was the optimal treatment regimen for most patients with AF and ACS and/or PCI, irrespective of the patient's baseline bleeding and stroke risk.[774,775]

Prolonged triple therapy up to 1 month after ACS/PCI should be considered in patients at high ischaemic risk, e.g. STEMI, prior stent thrombosis, complex coronary procedures, and prolonged cardiac instability, even though these patients were not adequately represented in the RCTs so far available.[776] In AF patients with ACS or CCS and diabetes mellitus undergoing coronary stent implantation, prolonging triple therapy with low-dose aspirin, clopidogrel, and an OAC up to 3 months may be of benefit if thrombotic risk outweighs bleeding risk in the individual patient.[207]

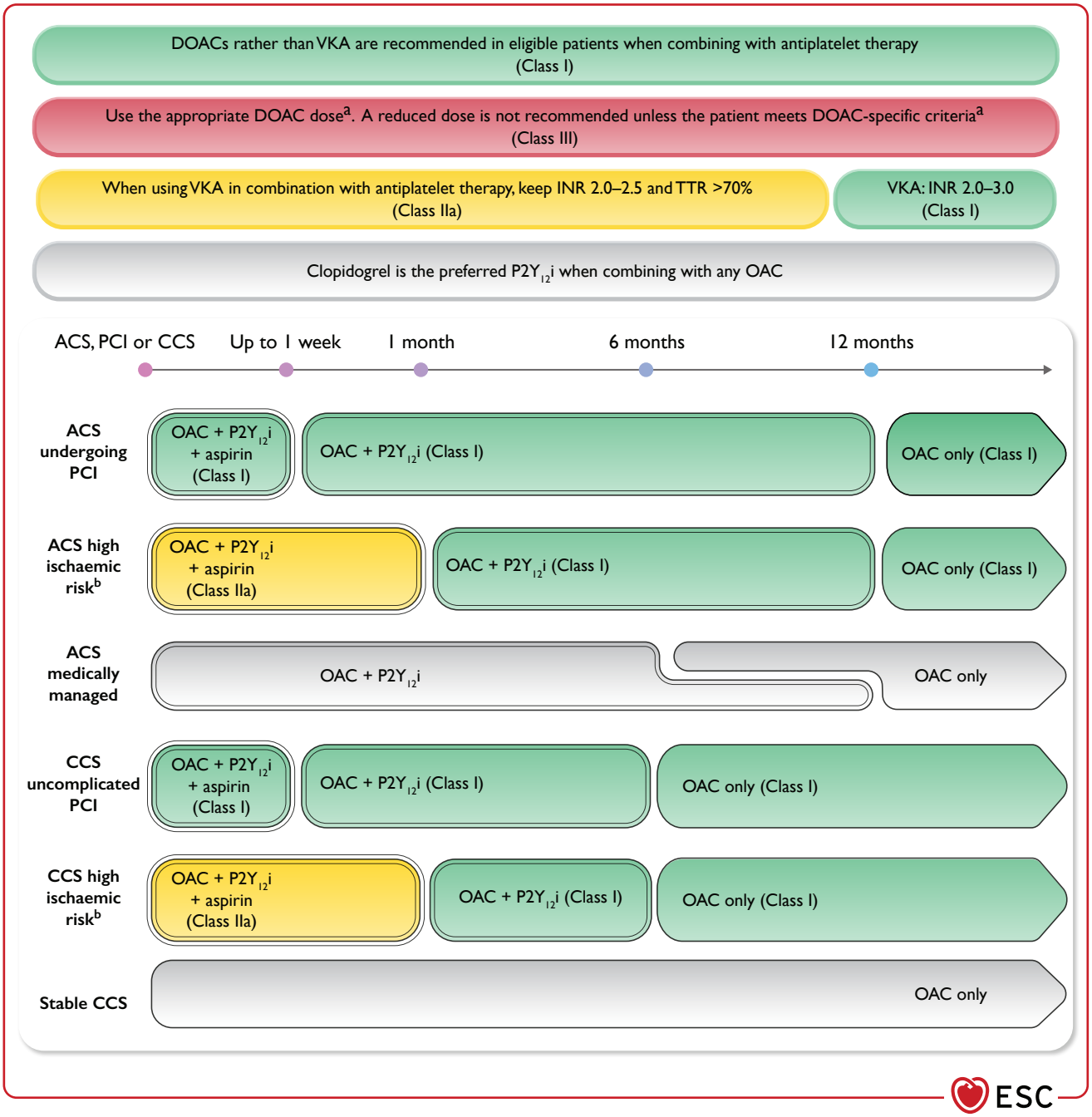


**Figure 14** Antithrombotic therapy in patients with AF and acute or chronic coronary syndromes. ACS, acute coronary syndromes; CCS, chronic coronary syndrome; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; OAC, oral anticoagulant; $P2Y_{12}i$, $P2Y_{12}$-receptor inhibitor antiplatelet agents (clopidogrel, prasugrel, ticagrelor); PCI, percutaneous intervention; TTR, time in therapeutic range; VKA, vitamin K antagonist. The flowchart applies to those patients with an indication for oral anticoagulant therapy. [a]The full standard dose of DOACs should be used unless the patient fulfils dose-reduction criteria (*Table 11*). When rivaroxaban or dabigatran are used as the DOAC and concerns about bleeding risk prevail over stent thrombosis or ischaemic stroke, the reduced dose should be considered (15 mg and 110 mg respectively; Class IIa). [b]In patients with diabetes mellitus undergoing coronary stent implantation, prolonging triple antithrombotic therapy for up to 3 months may be of value if thrombotic risk outweighs the bleeding risk.

The evidence for ACS treated without revascularization is limited. Six to 12 months of a single antiplatelet agent in addition to a long-term DOAC is usually sufficient and can minimize bleeding risk.[760,764,774] Although there are no head-to-head comparisons between aspirin and clopidogrel, studies have typically used clopidogrel. In patients with stable CCS for more than 12 months, sole therapy with a DOAC is sufficient and no additional antiplatelet therapy is required.[353] In patients at potential risk of gastrointestinal bleeding, use of proton pump inhibitors is reasonable during combined antithrombotic therapy, although evidence in AF patients is limited.[437,777–779] Multimorbid patients with ACS or CCS need careful assessment of ischaemic risk and management of modifiable bleeding risk factors, with a comprehensive work-up to individually adapt antithrombotic therapy.

**Recommendation Table 24 — Recommendations for patients with acute coronary syndromes or undergoing percutaneous intervention (see also Evidence Table 24)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **General recommendations for patients with AF and an indication for concomitant antiplatelet therapy** | | |
| For combinations with antiplatelet therapy, a DOAC is recommended in eligible patients in preference to a VKA to mitigate bleeding risk and prevent thromboembolism.[764,766] | I | A |
| 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 |
| Carefully regulated VKA dosing with a target INR of 2.0–2.5 and TTR >70% should be considered when combined with antiplatelet therapy in AF patients to mitigate bleeding risk. | IIa | C |
| **Recommendations for AF patients with ACS** | | |
| Early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant (preferably DOAC) with a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 12 months is recommended in AF patients with ACS undergoing an uncomplicated PCI to avoid major bleeding, if the risk of thrombosis is low or bleeding risk is high.[764–767] | I | A |
| Triple therapy with aspirin, clopidogrel, and oral anticoagulation for longer than 1 week after an ACS should be considered in patients with AF when ischaemic risk outweighs the bleeding risk, with the total duration (≤1 month) decided according to assessment of these risks and clear documentation of the discharge treatment plan.[776] | IIa | C |
| **Recommendations for AF patients undergoing PCI** | | |
| After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant and a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 6 months is recommended to avoid major bleeding, if ischaemic risk is low.[763–766,776,780] | I | A |
| Triple therapy with aspirin, clopidogrel, and an oral anticoagulant for longer than 1 week should be considered after PCI when the risk of stent thrombosis outweighs the bleeding risk, with the total duration (≤1 month) decided according to assessment of these risks and clear documentation.[776] | IIa | B |
| **Recommendations for AF patients with chronic coronary or vascular disease** | | |
| Antiplatelet therapy beyond 12 months is not recommended in stable patients with chronic coronary or vascular disease treated with oral anticoagulation, due to lack of efficacy and to avoid major bleeding.[353,781,782] | III | B |

ACS, acute coronary syndromes; AF, atrial fibrillation; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; PCI, percutaneous intervention; TTR, time in therapeutic range; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

## 9.3. AF-CARE in vascular disease

Peripheral arterial disease (PAD) is common in patients with AF, ranging from 6.7% to 14% of patients.[783,784] Manifest PAD is associated with incident AF.[785] PAD predicts a higher mortality in patients with AF and is an independent predictor of stroke in those not on OAC.[783,786] Patients with lower extremity artery disease and AF also have a higher overall mortality and risk of major cardiac events.[784,787,788] A public health database of >40 000 patients hospitalized for PAD or critical limb ischaemia showed AF to be an independent predictor for mortality (HR, 1.46; 95% CI, 1.39–1.52) and ischaemic stroke (HR, 1.63; 95% CI, 1.44–1.85) as compared with propensity-matched controls.[784] Similarly, in patients undergoing carotid endarterectomy or stenting, the presence of AF is associated with higher mortality (OR, 1.59; 95% CI, 1.11–2.26).[789]

Anticoagulation alone is usually sufficient in the chronic disease phase, with DOACs being the preferred agents despite one RCT subanalysis showing a higher risk of bleeding as compared with warfarin.[790] In the case of recent endovascular revascularization, a period of combination with single antiplatelet therapy should be considered, weighing bleeding and thrombotic risks and keeping the period of combination antithrombotic therapy as brief as possible (ranging between 1 month for peripheral[791] and 90 days for neuro-interventional procedures).[792]

## 9.4. AF-CARE in acute stroke or intracranial haemorrhage

### 9.4.1. Management of acute ischaemic stroke

Management of acute stroke in patients with AF is beyond the scope of these guidelines. In AF patients presenting with acute ischaemic stroke while taking OAC, acute therapy depends on the treatment regimen and intensity of OAC. Management should be co-ordinated by a specialist neurologist team according to relevant guidelines.[793]

### 9.4.2. Introduction or re-introduction of anticoagulation after ischaemic stroke

The optimal time for administering OAC in patients with acute cardioembolic stroke and AF remains unclear. Randomized control trials have been unable to provide any evidence to support the administration of anticoagulants or heparin in patients with acute ischaemic stroke within 48 h from stroke onset. This suggests that low-dose aspirin should be administered to all patients during this timeframe.[794]

Two trials have examined the use of DOAC therapy early after stroke, with no difference in clinical outcomes compared with delayed DOAC prescription. The ELAN (Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillatioN) trial randomized 2013 patients with acute ischaemic stroke and AF to open-label early use of DOACs (<48 h after minor/moderate stroke; day 6–7 after major stroke) vs. later DOAC prescription (day 3–4 after minor stroke; day 6–7 after moderate stroke; day 12–14 after major stroke). There was no significant difference in the composite thromboembolic, bleeding, and vascular death outcome at 30 days (risk difference early vs. late, −1.18%; 95% CI, −2.84 to 0.47).[795] The TIMING (Timing of Oral Anticoagulant Therapy in Acute Ischemic Stroke With Atrial Fibrillation) trial, a registry-based, non-inferiority, open-label, blinded endpoint trial randomized 888 patients within 72 h of ischaemic stroke onset to early (≤4 days) or delayed (5–10 days) DOAC initiation. Early DOAC use was non-inferior to the delayed strategy for the composite of thromboembolism, bleeding and all-cause mortality at 90 days (risk difference, −1.79%; 95% CI, −5.31% to 1.74%).[796] Two ongoing trials will provide further guidance on the most appropriate timing of DOAC therapy after ischaemic stroke (NCT03759938, NCT03021928).

### 9.4.3. Introduction or re-introduction of anticoagulation after haemorrhagic stroke

There is insufficient evidence currently to recommend whether OAC should be started or re-started after ICH to protect against the high risk of ischaemic stroke in these patients (see Supplementary data online, *Additional Evidence Table S28*). Data from two pilot trials are available. The APACHE-AF (Apixaban After Anticoagulation-associated Intracerebral Haemorrhage in Patients With Atrial Fibrillation) trial was a prospective, randomized, open-label trial with masked endpoint assessment; 101 patients who survived 7–90 days after anticoagulation-associated ICH were randomized to apixaban or no OAC. During a median of 1.9 years follow-up (222 person-years), there was no difference in non-fatal stroke or vascular death, with an annual event rate of 12.6% with apixaban and 11.9% with no OAC (adjusted HR, 1.05; 95% CI, 0.48–2.31; $P = .90$).[797] SoSTART (Start or STop Anticoagulants Randomised Trial) was an open-label RCT in 203 patients with AF after symptomatic spontaneous ICH. Starting OAC was not non-inferior to avoiding long-term (≥1 year) OAC, with ICH recurrence in 8/101 (8%) vs. 4/102 (4%) patients (adjusted HR, 2.42; 95% CI, 0.72–8.09). Mortality occurred in 22/101 (22%) patients in the OAC group vs. 11/102 (11%) patients where OAC were avoided.[798]

Until additional trials report on the clinical challenge of post-ICH anticoagulation (NCT03950076, NCT03996772), an individualized multidisciplinary approach is advised led by an expert neurology team.

## 9.5. AF-CARE for trigger-induced AF

Trigger-induced AF is defined as new AF in the immediate association of a precipitating and potentially reversible factor. Also known as 'secondary' AF, this task force prefer the term trigger-induced as there are almost always underlying factors in individual patients that can benefit from full consideration of the AF-CARE pathway. The most common precipitant unmasking a tendency to AF is acute sepsis, where AF prevalence is between 9% and 20% and has been associated with a worse prognosis.[11–14] The degree of inflammation correlates with the incidence of AF,[799] which may partly explain the wide variability across studies in prevalence, as well as recurrence of AF. Longer-term data suggest that AF triggered by sepsis recurs after discharge in between a third to a half of patients.[12,800–807] In addition to other acute triggers which may be causal (such as alcohol[808,809] and illicit drug use[810]), numerous conditions are also associated with chronic inflammation leading to subacute stimuli for AF (*Table 14*). The specific trigger of an operative procedure is discussed in *Section 9.6*.

After meeting the diagnostic criteria for AF (see *Section 3.2*), the management of trigger-induced AF is recommended to follow the AF-CARE principles, with critical consideration of underlying risk factors and comorbidities. Based on retrospective and observational data, patients with AF and trigger-induced AF seem to carry the same thromboembolic risk as patients with primary AF.[811,812] In the acute phase of sepsis, patients show an unclear risk–benefit profile with anticoagulation therapy.[813,814] Prospective studies on anticoagulation in patients with triggered AF episodes are lacking.[802,812,815] Acknowledging that there are no RCTs specifically available in this population to assess trigger-induced AF, long-term OAC therapy should be considered in suitable patients with trigger-induced AF who are at elevated risk of thromboembolism, starting OAC after the acute trigger has been corrected and considering the anticipated net clinical benefit and informed patient preferences. As with any decision on OAC, not all patients will be suitable for OAC, depending on relative and absolute contraindications and the risk of major bleeding. The approach to rate and rhythm control will depend on subsequent recurrence of AF or any associated symptoms, and re-evaluation should be individualized to take account of the often high AF recurrence rate.

**Table 14 Non-cardiac conditions associated with trigger-induced AF**

| **Acute conditions** |
|---|
| Infections (bacterial and viral) |
| Pericarditis, myocarditis |
| Emergency conditions (burn injury, severe trauma, shock) |
| Binge alcohol consumption |
| Drug use, including methamphetamines, cocaine, opiates, and cannabis |
| Acute interventions, procedures, and surgery |
| Endocrine disorders (thyroid, adrenal, pituitary, others) |
| **Chronic conditions with inflammation and enhanced AF substrate** |
| Immune-mediated diseases (rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, coeliac disease, psoriasis, others) |
| Obesity |
| Chronic obstructive airways disease |
| Obstructive sleep apnoea |
| Cancer |
| Fatty liver disease |
| Stress |
| Endocrine disorders (see *Section 9.10*) |

**Recommendation Table 25 — Recommendations for trigger-induced AF (see also Evidence Table 25)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Long-term oral anticoagulation should be considered in suitable patients with trigger-induced AF at elevated thromboembolic risk to prevent ischaemic stroke and systemic thromboembolism.[13,800,806,807,815] | IIa | C |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

## 9.6. AF-CARE in post-operative patients

Peri-operative AF describes the onset of the arrhythmia during an ongoing intervention. Post-operative AF (POAF), defined as new-onset AF in the immediate post-operative period, is a common complication with clinical impact that occurs in 30%–50% of patients undergoing cardiac surgery,[816–818] and in 5%–30% of patients undergoing non-cardiac surgery. Intra- and post-operative changes and specific AF triggers (including peri-operative complications) and pre-existing AF-related risk factors and comorbidities increase the susceptibility to POAF.[819] Although POAF episodes may be self-terminating, POAF is associated with 4–5 times increase in recurrent AF during the next 5 years,[820,821] and is a risk factor for stroke, MI, heart failure, and death.[822–827] Other adverse events associated with POAF include haemodynamic instability, prolonged hospital stay, infections, renal complications, bleeding, increased in-hospital death, and greater healthcare cost.[828–830]

While multiple strategies to prevent POAF with pre-treatment or acute drug treatment have been described, there is a lack of evidence from large RCTs. Pre-operative use of propranolol or carvedilol plus *N*-acetyl cysteine in cardiac and non-cardiac surgery is associated with a reduced incidence of POAF,[831–834] but not major adverse events.[835] An umbrella review of 89 RCTs from 23 meta-analyses (19 211 patients, but not necessarily in AF) showed no benefit from beta-blockers in cardiac surgery for mortality, MI, or stroke. In non-cardiac surgery, beta-blockers were associated with reduced rates of MI after surgery (RR range, 0.08–0.92), but higher mortality (RR range, 1.03–1.31), and increased risk of stroke (RR range, 1.33–7.72).[836] Prevention of peri-operative AF can also be achieved with amiodarone. In a meta-analyses, amiodarone (oral or intravenous [i.v.]) and beta-blockers were equally effective in reducing post-operative AF,[837] but their combination was better than beta-blockers alone.[838] Lower cumulative doses of amiodarone (<3000 mg during the loading phase) could be effective, with fewer adverse events.[837,839,840] Withdrawal of beta-blockers should be avoided due to increased risk of POAF.[841] Other treatment strategies (steroids, magnesium, sotalol, (bi)atrial pacing, and botulium injection into the epicardial fat pad) lack scientific evidence for the prevention of peri-operative AF.[842,843] Peri-operative posterior pericardiotomy, due to the reduction of post-operative pericardial effusion, showed a significant decrease in POAF in patients undergoing cardiac surgery (OR, 0.44; 95% CI, 0.27–0.70; $P = .0005$).[844–846] In 3209 patients undergoing non-cardiac thoracic surgery, colchicine did not lead to any significant reduction in AF compared with placebo (HR, 0.85; 95% CI, 0.65–1.10; $P = .22$).[847]

The evidence for prevention of ischaemic stroke in POAF by OAC is limited.[822,827] Oral anticoagulant therapy is associated with a high bleeding risk soon after cardiac surgery or major non-cardiac interventions.[827] Conversely, meta-analyses of observational cohort studies suggest a possible protective impact of OAC in POAF for all-cause mortality[848] and a lower risk of thromboembolic events following cardiac surgery, accompanied by higher rates of bleeding.[849] This task force recommends to treat post-operative AF according to the AF-CARE pathway as discussed for trigger-induced AF (with the [R] pathway the same as for first-diagnosed AF). Ongoing RCTs in cardiac surgery (NCT04045665) and non-cardiac surgery (NCT03968393) will inform optimal long-term OAC use among patients with POAF. While awaiting the results of these trials, this task force recommends that after acute bleeding risk has settled, long-term OAC should be considered in patients with POAF according to their thromboembolic risk factors.

**Recommendation Table 26 — Recommendations for management of post-operative AF (see also Evidence Table 26)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Peri-operative amiodarone therapy is recommended where drug therapy is desired to prevent post-operative AF after cardiac surgery.[838,839,850,851] | I | A |
| Concomitant posterior peri-cardiotomy should be considered in patients undergoing cardiac surgery to prevent post-operative AF.[845,846] | IIa | B |
| Long-term oral anticoagulation should be considered in patients with post-operative AF after cardiac and non-cardiac surgery at elevated thromboembolic risk, to prevent ischaemic stroke and thromboembolism.[811,852–854] | IIa | B |
| Routine use of beta-blockers is not recommended in patients undergoing non-cardiac surgery for the prevention of post-operative AF.[836,855] | III | B |



AF, atrial fibrillation.
[a]Class of recommendation.
[b]Level of evidence.

## 9.7. AF-CARE in embolic stroke of unknown source

The term 'embolic stroke of undetermined source' (ESUS) was introduced to identify non-lacunar strokes whose mechanism is likely to be embolic, but the source remains unidentified.[856] Of note, these patients have a recurrent risk of stroke of 4%–5% per year.[856] The main embolic sources associated with ESUS are concealed AF, atrial cardiomyopathy, left ventricular disease, atherosclerotic plaques, patent foramen ovale (PFO), valvular diseases, and cancer. Atrial cardiomyopathy and left ventricular disease are the most prevalent causes.[856] AF is reported to be the underlying mechanism in 30% of ESUS patients.[857–859] The detection of AF among ESUS patients increases the longer cardiac monitoring is provided (see Supplementary data online, *Additional Evidence Table S29*).[857,860–864] This also holds for the duration of implantable cardiac monitoring, with probability of AF detection ranging from 2% with 1 week to over 20% by 3 years.[865] In patients with ESUS, factors associated with an increased detection of AF are increasing age,[866,867] left atrial enlargement,[866] cortical location of stroke,[868] large or small vessel disease,[863] an increased number of

atrial premature beats per 24 h,[868] rhythm irregularity,[859] and risk stratification scores (such as $CHA_2DS_2$-VASc,[869] Brown ESUS-AF,[870] HAVOC,[871] and $C_2HEST$[872]). This task force recommends prolonged monitoring depending on the presence of the above-mentioned risk markers.[865,873,874]

Currently available evidence, including two completed RCTs and one stopped for futility, do not support the use of DOACs compared with aspirin in patients with acute ESUS without documented AF.[875–877] Ongoing trials will provide further guidance (NCT05134454, NCT05293080, NCT04371055).

**Recommendation Table 27 — Recommendations for patients with embolic stroke of unknown source (see also Evidence Table 27)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Prolonged monitoring for AF is recommended in patients with ESUS to inform on AF treatment decisions.[861–863] | I | B |
| Initiation of oral anticoagulation in ESUS patients without documented AF is not recommended due to lack of efficacy in preventing ischaemic stroke and thromboembolism.[875,876] | III | A |



AF, atrial fibrillation; ESUS, embolic stroke of undetermined source.
[a]Class of recommendation.
[b]Level of evidence.

## 9.8. AF-CARE during pregnancy

Atrial fibrillation is one of the most common arrhythmias during pregnancy, with prevalence increasing due to higher maternal age and changes in lifestyle, and because more women with congenital heart disease survive to childbearing age.[878–881] Rapid atrioventricular conduction of AF may have serious haemodynamic consequences for mother and foetus. AF during pregnancy is associated with an increased risk of death.[882] A multidisciplinary approach is essential to prevent maternal and foetal complications, bringing together gynaecologists, neonatologists, anaesthesiologists, and cardiologists experienced in maternal medicine.[883]

Pregnancy is associated with a hypercoagulable state and increased thromboembolic risk.[884] The same rules for risk assessment of thromboembolism should be used as in non-pregnant women, as detailed in the *2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy*.[885] The preferred agents for anticoagulation of AF during pregnancy are unfractionated or low molecular weight heparins (LMWHs), which do not cross the placenta. Vitamin K antagonists should be avoided in the first trimester (risk of miscarriage, teratogenicity) and from week 36 onwards (risk of foetal intracranial bleeding if early unexpected delivery). Direct oral anticoagulants are not recommended during pregnancy due to concerns about safety.[886] However, an accidental exposure during pregnancy should not lead to a recommendation for termination of the pregnancy.[887] Vaginal delivery should be advised for most women, but is contraindicated during VKA treatment because of the risk of foetal intracranial bleeding.[885]

Intravenous selective beta-1 receptor blockers are recommended as first choice for acute heart rate control of AF.[888] This does not include atenolol, which can lead to intrauterine growth retardation.[889] If beta-blockers fail, digoxin and verapamil can be considered for rate control (verapamil should be avoided in the first trimester). Rhythm control is the preferred strategy during pregnancy. Electrical cardioversion is recommended if there is haemodynamic instability, considerable risk to mother or foetus, or with concomitant HCM. Electrical cardioversion can be performed safely without compromising foetal blood flow, and the consequent risk for foetal arrhythmias or pre-term labour is low. The foetal heart rate should be closely monitored throughout and after cardioversion, which should generally be preceded by anticoagulation.[885] In haemodynamically stable women without structural heart disease, intravenous ibutilide or flecainide may be considered for termination of AF, but experience is limited.[890] Catheter ablation is normally avoided during pregnancy,[883] but is technically feasible without radiation in refractory symptomatic cases with a minimal/zero fluoroscopy approach.[883]

Counselling is important in women of childbearing potential prior to pregnancy, highlighting the potential risks of anticoagulation and rate or rhythm control drugs (including teratogenic risk, where relevant). Contraception and timely switch to safe drugs should be proactively discussed.

**Recommendation Table 28 — Recommendations for patients with AF during pregnancy (see also Evidence Table 28)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Immediate electrical cardioversion is recommended in patients with AF during pregnancy and haemodynamic instability or pre-excited AF to improve maternal and foetal outcomes.[885,891–893] | I | C |
| Therapeutic anticoagulation with LMWHs or VKAs (except VKAs for the first trimester or beyond Week 36) is recommended for pregnant patients with AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.[885] | I | C |
| Beta-1 selective blockers are recommended for heart rate control of AF in pregnancy to reduce symptoms and improve maternal and foetal outcomes, excluding atenolol.[888] | I | C |
| Electrical cardioversion should be considered for persistent AF in pregnant women with HCM to improve maternal and foetal outcomes.[885,894] | IIa | C |
| Digoxin should be considered for heart rate control of AF in pregnancy, if beta-blockers are ineffective or not tolerated, to reduce symptoms and improve maternal and foetal outcomes.[885] | IIa | C |
| Intravenous ibutilide or flecainide may be considered for termination of AF in stable pregnant patients with a structurally normal heart to improve maternal and foetal outcomes.[895,896] | IIb | C |
| Flecainide or propafenone may be considered for longer-term rhythm control in pregnancy, if rate controlling drugs are ineffective or not tolerated, to reduce symptoms and improve maternal and foetal outcomes.[885] | IIb | C |



AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; LMWH, low molecular weight heparin; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

## 9.9. AF-CARE in congenital heart disease

Survival of patients with congenital heart disease has increased over time, but robust data on the management of AF are missing and available evidence is derived mainly from observational studies. Oral anticoagulants are recommended for all patients with AF and intracardiac repair, cyanotic congenital heart disease, Fontan palliation, or systemic right ventricle irrespective of the individuals' thromboembolic risk factors.[897] Patients with AF and other congenital heart diseases should follow the general risk stratification for OAC use in AF (i.e. depending on the thromboembolic risk or $CHA_2DS_2$-VA score). Direct oral anticoagulants are contraindicated in patients with mechanical heart valves,[331] but appear safe in patients with congenital heart disease,[898,899] or those with a valvular bioprosthesis.[900,901]

Rate control drugs such as selective beta-1 receptor blockers, verapamil, diltiazem, and digoxin can be used with caution, with monitoring for bradycardia and hypotension. Rhythm control strategies such as amiodarone may be effective, but warrant monitoring for bradycardia. When cardioversion is planned, both 3 weeks of OAC and TOE should be considered because thrombi are common in patients with congenital heart disease and atrial arrhythmias.[902,903] Ablation approaches can be successful in patients with congenital heart disease, but AF recurrence rates may be high (see Supplementary data online, *Additional Evidence Table S30*).

In patients with atrial septal defect, closure may be performed before the fourth decade of life to decrease the risk of AF or AFL.[904] Patients with stroke who underwent closure of their PFO may have an increased risk of AF,[905] but in patients with PFO and AF, PFO closure is not recommended for stroke prevention. AF surgery or catheter ablation can be considered at the time of closure of the atrial septal defect within a multidisciplinary team.[906–908] AF catheter ablation of late atrial arrhythmias is likely to be effective after surgical atrial septal closure.[909]

**Recommendation Table 29 — Recommendations for patients with AF and congenital heart disease (see also Evidence Table 29)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Oral anticoagulation should be considered in all adult congenital heart disease patients with AF/AFL and intracardiac repair, cyanosis, Fontan palliation, or systemic right ventricle to prevent ischaemic stroke and thromboembolism, regardless of other thromboembolic risk factors.[897] | IIa | C |



AF, atrial fibrillation; AFL, atrial flutter.
[a]Class of recommendation.
[b]Level of evidence.

## 9.10. AF-CARE in endocrine disorders

Endocrine dysfunction is closely related to AF, both as the direct action of endocrine hormones and as a consequence of treatments for endocrine disease. Optimal management of endocrine disorders is therefore part of the AF-CARE pathway.[910,911]

Clinical and subclinical hyperthyroidism, as well as subclinical hypothyroidism, are associated with an increased risk of AF.[912,913] Patients presenting with new-onset or recurrent AF should be tested for thyroid-stimulating hormone (TSH) levels. The risk of AF is enhanced in vulnerable patients, including the elderly and those with structural atrial diseases,[914,915] as well as cancer patients on immune checkpoint inhibitors.[916,917] In hyperthyroidism, and even in the euthyroid range, the risk of AF increases according to the reduction in TSH and elevated levels of thyroxine.[918,919] Moreover, the risk of stroke is higher in patients with hyperthyroidism, which can be mitigated by treating the thyroid disorder.[920,921] Amiodarone induces thyroid dysfunction in 15%–20% of treated patients, leading to both hypo- and hyperthyroidism,[922,923] which warrants referral to an endocrinologist (see Supplementary data online for further details).

Hypercalcaemia may also induce arrhythmias, but the role of primary hyperparathyroidism in incident AF is poorly studied. Surgical parathyroidectomy has been found to reduce both supraventricular and ventricular premature beats.[924–926] Primary aldosteronism is related to an increased risk of AF through direct actions and vascular effects,[927,928] with a three-fold higher rate of incident AF compared with patients with essential hypertension.[929] Increases in genetically predicted plasma cortisol are associated with greater risk of AF, and patients with adrenal incidentalomas with subclinical cortisol secretion have a higher prevalence of AF.[930,931] Acromegaly may predispose to an increased substrate for AF, with incident AF rates significantly higher than controls in long-term follow-up, even after adjusting for AF risk factors.[932]

The association between type 2 diabetes and AF is discussed in *Sections 5.3* (AF recurrence) and *Section 10.5* (incident AF). In addition to insulin-resistance mechanisms typical of type 2 diabetes, the loss of insulin signalling has recently been associated with electrical changes that can lead to AF. Type 1 diabetes is associated with an increased risk of several cardiovascular diseases including AF.[933–937]

## 9.11. AF-CARE in inherited cardiomyopathies and primary arrhythmia syndromes

A higher incidence and prevalence of AF have been described in patients with inherited cardiomyopathies and primary arrhythmia syndromes.[271,938–970] AF can be the presenting or only clinically overt feature.[969,971–975] AF in these patients is associated with adverse clinical outcomes,[947,954,959,963,965,976–978] and has important implications on management (see Supplementary data online, *Additional Evidence Table S31*). When AF presents at a young age, there should be a careful interrogation about family history and a search for underlying disease.[979]

Rhythm control approaches may be challenging in patients with inherited cardiomyopathies and primary arrhythmia syndromes. For example, many drugs have a higher risk of adverse events or may be contraindicated (e.g. amiodarone and sotalol in congenital long QT syndrome, and Class IC AADs in Brugada syndrome) (see Supplementary Data online, *Table S6*). Owing to long-term adverse effects, chronic use of amiodarone is problematic in these typically young individuals. In patients with an implantable cardioverter defibrillator, AF is a common cause of inappropriate shocks.[959,966,980,981] Programming a single high-rate ventricular fibrillation zone ≥210–220 b.p.m. with long detection time is safe,[950,953,982] and is suggested in patients without documented slow monomorphic ventricular tachycardia. Implantation of an atrial lead may be considered in the case of significant bradycardia with beta-blocker treatment.

Patients with Wolff–Parkinson–White syndrome and AF are at risk of fast ventricular rates from rapid conduction of atrial electrical activity to the ventricles via the accessory pathway, potentially leading to ventricular fibrillation and sudden death.[983,984] Immediate electrical cardioversion is needed for haemodynamically compromised patients with

pre-excited AF, and atrioventricular node-modulating drugs should be avoided.[985,986] Pharmacological cardioversion can be attempted using ibutilide[987] or flecainide, while propafenone should be used with caution due to effects on the atrioventricular node.[988,989] Amiodarone should be avoided in pre-excited AF due to its delayed action. Further details on inherited cardiomyopathies can be found in the *2023 ESC Guidelines for the management of cardiomyopathies*.[990]

## 9.12. AF-CARE in cancer

All types of cancer show an increased risk of AF, with prevalence varying from 2% to 28%.[991–995] The occurrence of AF may often be related to a pre-existing atrial substrate with vulnerability to AF. AF may be an indicator of an occult cancer, but also can appear in the context of concomitant surgery, chemotherapy, or radiotherapy.[916,994,996] Risk of AF is dependent on, among other factors, the cancer type and stage,[997] and is greater in older patients with pre-existing cardiovascular disease.[991,993,994] Some procedures are associated with higher incidence of AF, including lung surgery (from 6% to 32%) and non-thoracic surgery such as a colectomy (4%–5%).[994]

Atrial fibrillation in the context of cancer is associated with a two-fold higher risk of systemic thromboembolism and stroke, and six-fold increased risk of heart failure.[991,994] On the other hand, the coexistence of cancer increases the risk of all-cause mortality and major bleeding in patients with AF.[998] Bleeding in those receiving OAC can also unmask the presence of cancer.[999]

Stroke risk scores may underestimate thromboembolic risk in cancer patients.[1000] The association between cancer, AF, and ischaemic stroke also differs between cancer types. In some types of cancer, the risk of bleeding seems to exceed the risk of thromboembolism.[998] Risk stratification is therefore complex in this population, and should be performed on an individual basis considering cancer type, stage, prognosis, bleeding risk, and other risk factors. These aspects can change within a short period of time, requiring dynamic assessment and management.

As with non-cancer patients, DOACs in those with cancer have similar efficacy and better safety compared with VKAs.[1001–1010] Low molecular weight heparin is a short-term anticoagulation option, mostly during some cancer treatments, recent active bleeding, or thrombocytopaenia.[1011] Decision-making on AF management, including on rhythm control, is best performed within a cardio-oncology multidisciplinary team.[916,1012] Attention is required on interactions with cancer treatments, in particular QT-interval prolongation with AADs.

## 9.13. AF-CARE in older, multimorbid, or frail patients

Atrial fibrillation increases with age, and older patients more frequently have multimorbidity and frailty which are associated with worse clinical outcomes.[1013–1016] Multimorbidity is the coexistence of two or more medically diagnosed diseases in the same individual. Frailty is defined as a person more vulnerable and less able to respond to a stressor or acute event, increasing the risk of adverse outcomes.[1016,1017] The prevalence of frailty in AF varies due to different methods of assessment from 4.4% to 75.4%, and AF prevalence in the frail population ranges from 48.2% to 75.4%.[1018] Frailty status is a strong independent risk factor for new-onset AF among older adults with hypertension.[1019]

Atrial fibrillation in frail patients is associated with less use of OAC and lower rates of management with a rhythm control strategy.[1015,1018,1020] Oral anticoagulation initiation in older, frail multimorbid AF patients has improved since the introduction of DOACs, but is still lower in AF patients at older age (OR, 0.98 per year; 95% CI, 0.98–0.98), with dementia (OR, 0.57; 95% CI, 0.55–0.58), or frailty (OR, 0.74; 95% CI, 0.72–0.76).[1021] The value of observational data which show potential benefit from OAC (in particular, DOACs) is limited due to prescription biases.[1022–1027] Frail patients aged ≥75 years with polypharmacy and stable on a VKA may remain on the VKA rather than switching to a DOAC (*Section 6.2*).[309]

## 9.14. AF-CARE in atrial flutter

Due to the association between AFL and thromboembolic outcomes, and the frequent development of AF in patients with AFL, the management of comorbidities and risk factors in AFL should mirror that for AF (see *Section 5*). Similarly, the approach to prevent thromboembolism in AFL includes peri-procedural and long-term OAC (see *Section 6*). Rate control can be difficult to achieve in AFL, despite combination therapy. Rhythm control is often the first-line approach,[983] with small randomized trials showing that cavo-tricuspid isthmus (CTI) ablation is superior to AADs.[1028,1029] Recurrence of AFL is uncommon after achieving and confirming bidirectional block in typical CTI-dependent AFL. However, the majority of patients (50%–70%) have manifested AF during long-term follow-up in observational studies after AFL ablation.[1030,1031] Hence the necessity for long-term dynamic re-evaluation in all patients with AFL in keeping with the AF-CARE approach. More detail on the management of AFL and other atrial arrhythmias is described in the *2019 ESC Guidelines for the management of patients with supraventricular tachycardia*.[983]

**Recommendation Table 30 — Recommendations for prevention of thromboembolism in atrial flutter (see also Evidence Table 30)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Oral anticoagulation is recommended in patients with atrial flutter at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.[86,1032] | I | B |

AF, atrial fibrillation; AFL, atrial flutter.
[a]Class of recommendation.
[b]Level of evidence.



# 10. Screening and prevention of AF

## 10.1. Epidemiology of AF

Atrial fibrillation is the most common sustained arrhythmia worldwide, with an estimated global prevalence in 2019 of 59.7 million persons with AF.[1033] Incident cases of AF are doubling every few decades.[1034] Future increases are anticipated, in particular in middle-income countries.[1034] In community-based individuals, the prevalence of AF in a United States of America cohort was up to 5.9%.[1035] The age-standardized prevalence and incidence rates have remained constant over time.[1033,1036] The increase in overall prevalence is largely attributable to population growth, ageing, and survival from other cardiac conditions. In parallel, increases in risk factor burden, better awareness, and improved detection of AF have been observed.[1037] The lifetime risk

of AF has been estimated to be as high as 1 in 3 for older individuals,[1038] with age-standardized incidence rates higher for men than women. Populations of European ancestry are typically found to have higher AF prevalence, individuals of African ancestry have worse outcomes, and other groups may have less access to interventions.[1039–1041] Socioeconomic and other factors likely play a role in racial and ethnic differences in AF, but studies are also limited due to differences in how groups access healthcare. Greater deprivation in socioeconomic and living status is associated with higher AF incidence.[1042]

## 10.2. Screening tools for AF

In recent years, an abundance of novel devices that can monitor heart rhythm have come to the market, including fitness bands and smartwatches. Although the evidence for clinical effectiveness of digital devices is limited, they may be useful in detecting AF, and their clinical, economic, legal, and policy implications merit further investigation.[1043,1044] Devices for AF detection can broadly be divided into those that provide an ECG, and those with non-ECG approaches such as photoplethysmography (*Figure 15* and *Table 15*).

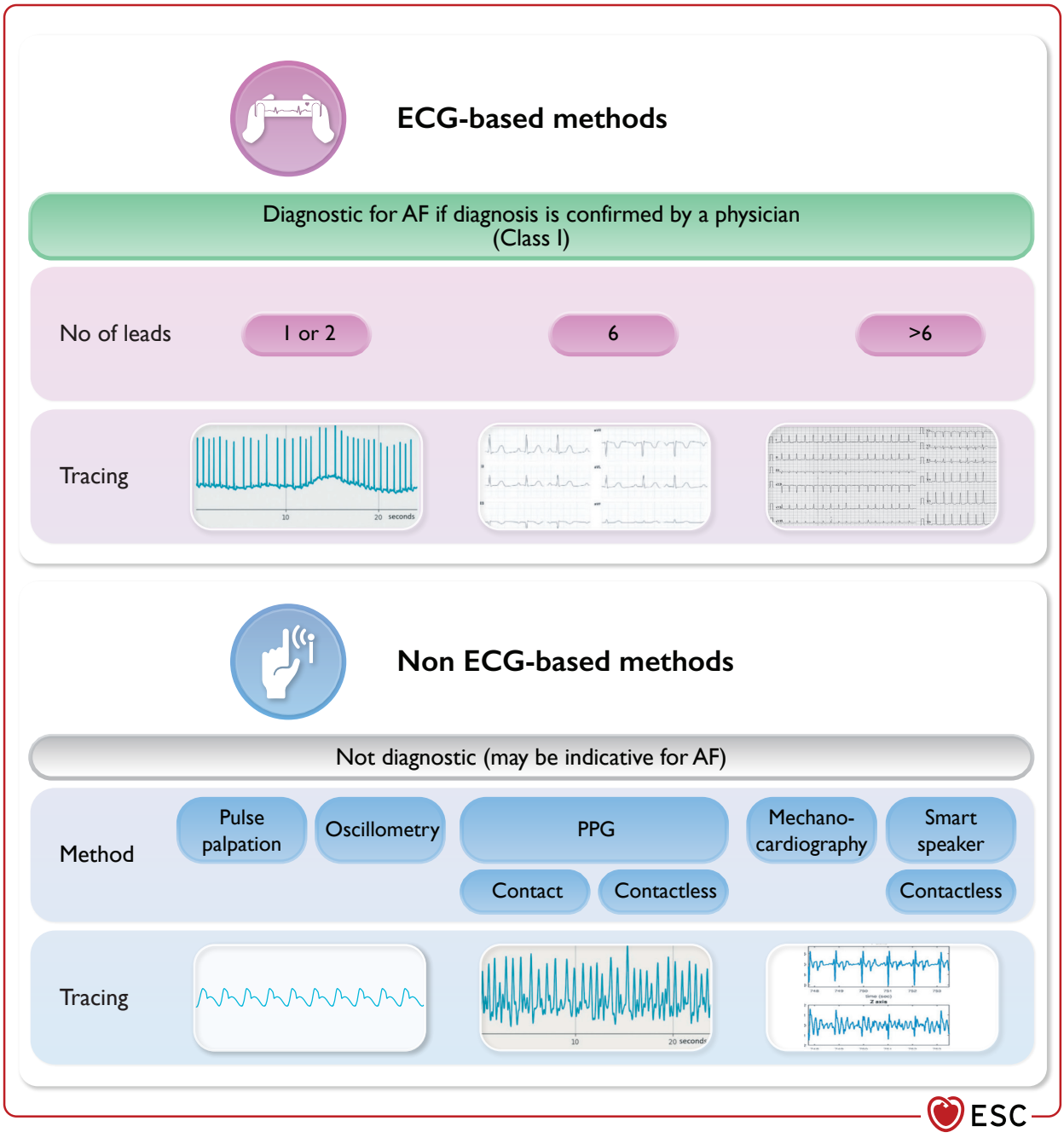


**Figure 15** Non-invasive diagnostic methods for AF screening. AF, atrial fibrillation; BP, blood pressure; ECG, electrocardiogram; PPG, photoplethysmography.

**Table 15 Tools for AF screening**

| Tools for AF screening |
|---|
| (i) Pulse palpation[1045] |
| (ii) Use of artificial intelligence algorithms to identify patients at risk[1046] |
| (iii) ECG-based devices |
| (a) Conventional ECG devices |
| (1) Classic 12-lead ECG [1047] |
| (2) Holter monitoring (from 24 h to a week or more)[1048] |
| (3) Mobile cardiac telemetry (during hospitalization)[1049] |
| (4) Handheld devices[1050–1052] |
| (5) Wearable patches (up to 14 days)[1053–1067] |
| (6) Biotextiles (up to 30 days)[1068–1072] |
| (7) Smart devices (30 s)[1073–1091] |
| (b) Implantable loop recorders (3–5 years)[1092–1099] |
| (iv) Non-ECG-based devices |
| (a) Photoplethysmography and automatic algorithms: contact (fingertip, smart device, band) and contactless (video)[1100–1106] |
| (b) Oscillometry (blood pressure monitors that derive heart rhythm regularity algorithmically)[1107–1110] |
| (c) Mechanocardiography (accelerometers and gyroscopes to sense the mechanical activity of the heart)[1111] |
| (d) Contactless video plethysmography (through video monitoring)[1112–1115] |
| (e) Smart speakers (through the identification of abnormal heart rate patterns)[1116] |

ECG, electrocardiogram.



Most consumer-based devices use photoplethysmography, and several large studies have been performed typically in low-risk individuals.[633,1076,1117,1118] In an RCT of 5551 participants invited by their health insurer, smartphone-based photoplethysmography increased the odds of OAC-treated new AF by 2.12 (95% CI, 1.19–3.76; $P = .01$) compared with usual care.[605] RCTs powered for assessment of clinical outcomes are still lacking for consumer-based AF screening. Further head-to-head comparisons between novel digital devices and those commonly used in healthcare settings are needed to establish their comparative effectiveness in the clinical setting and account for different populations and settings.[1119] In a systematic review of smartphone-based photoplethysmography compared with a reference ECG, unrealistically high sensitivity and specificity were noted, likely due to small, low-quality studies with a high degree of patient selection bias.[1120] Hence, when AF is suggested by a photoplethysmography device or any other screening tool, a single-lead or continuous ECG tracing of >30 s or 12-lead ECG showing AF analysed by a physician with expertise in ECG rhythm interpretation is recommended to establish a definitive diagnosis of AF.[1091,1121–1125]

The combination of big data and artificial intelligence (AI) is having an increasing impact on the field of electrophysiology. Algorithms have been created to improve automated AF diagnosis and several algorithms to aid diagnostics are being investigated.[1046] However, the clinical performance and broad applicability of these solutions are not yet known. The use of AI may enable future treatment changes to be assessed with dynamic and continuous patient-directed monitoring using wearable devices.[1126] There are still challenges in the field that need clarification, such as data acquisition, model performance, external validity, clinical implementation, algorithm interpretation, and confidence, as well as the ethical aspects.[1127]

## 10.3. Screening strategies for AF

Screening can be performed systematically, with an invitation issued to a patient, or opportunistically, at the time of an *ad hoc* meeting with a healthcare professional. Regardless of the mode of invitation, screening should be part of a structured programme[1128] and is not the same as identification of AF during a routine healthcare visit or secondary to arrhythmia symptoms.

Screening can be done at a single timepoint (snapshot of the heart rhythm), e.g. using pulse palpation or a 12-lead ECG. Screening can also be of an extended duration, i.e. prolonged, using either intermittent or continuous monitoring of heart rhythm. Most studies using an opportunistic strategy have screened for AF at a single timepoint with short duration (such as a single timepoint ECG), compared with systematic screening studies that have mainly used prolonged (repeated or continuous) rhythm assessment.[1129] The optimal screening method will vary depending on the population being studied (*Figure 16*) (see Supplementary data online, *Additional Evidence Table S32*). More sensitive methods will detect more AF but may lead to an increased risk of false positives and an increased detection of low burden AF, whereas more specific methods result in less false positives, at the risk of missing AF.

Invasive monitoring of heart rhythm in high-risk populations extended for several years has been shown to result in device-detected AF prevalence of around 30%, albeit most of whom have a low burden of AF.[5,857,1130,1131] Pacemaker studies have shown that patients with a low burden of device-detected subclinical AF have a lower risk of ischaemic stroke.[5,24,1131,1132] This has been confirmed in RCTs assessing DOAC use in patients with device-detected subclinical AF (see *Section 6.1.1*).[5,281,282] The burden needed for device-detected subclinical AF to translate into stroke risk is not known, and further studies are clearly needed.[1133,1134] Benefit and cost-effectiveness of screening are discussed in the Supplementary data online.

**Recommendation Table 31 — Recommendations for screening for AF (see also Evidence Table 31)**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Review of an ECG (12-lead, single, or multiple leads) by a physician is recommended to provide a definite diagnosis of AF and commence appropriate management.[1091,1121–1123,1125] | I | B |
| Routine heart rhythm assessment during healthcare contact is recommended in all individuals aged ≥65 years for earlier detection of AF. | I | C |
| Population-based screening for AF using a prolonged non-invasive ECG-based approach should be considered in individuals aged ≥75 years, or ≥65 years with additional $CHA_2DS_2$-VA risk factors to ensure earlier detection of AF.[6,1135–1137] | IIa | B |



AF, atrial fibrillation; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; ECG, electrocardiogram.
[a]Class of recommendation.
[b]Level of evidence.

### 10.3.1. Single timepoint screening 'snapshot'

Several cluster RCTs in primary care settings have explored whether screening performed as a snapshot of the heart rhythm at one timepoint can detect more AF compared with usual care in individuals aged ≥65 years.[1138–1140] No increased detection of AF was seen in groups randomized to single timepoint screening.[1138–1140] These findings were confirmed in a meta-analysis of RCTs showing that screening as a one-time event did not increase detection of AF compared with usual care.[1135] Notably, these studies were performed in healthcare settings where the detection of AF in the population might be high, hence the results might not be generalizable to healthcare settings with a lower spontaneous AF detection. There are no RCTs addressing clinical outcomes in patients with AF detected by single timepoint screening.[1123,1135]

### 10.3.2. Prolonged screening

Studies using prolonged screening have shown an increased detection of AF leading to initiation of OAC.[1129,1135,1141] Two RCTs have investigated the effect on clinical outcomes in prolonged screening for AF.[5,6] In the STROKESTOP trial (Systematic ECG Screening for Atrial Fibrillation Among 75 Year Old Subjects in the Region of Stockholm

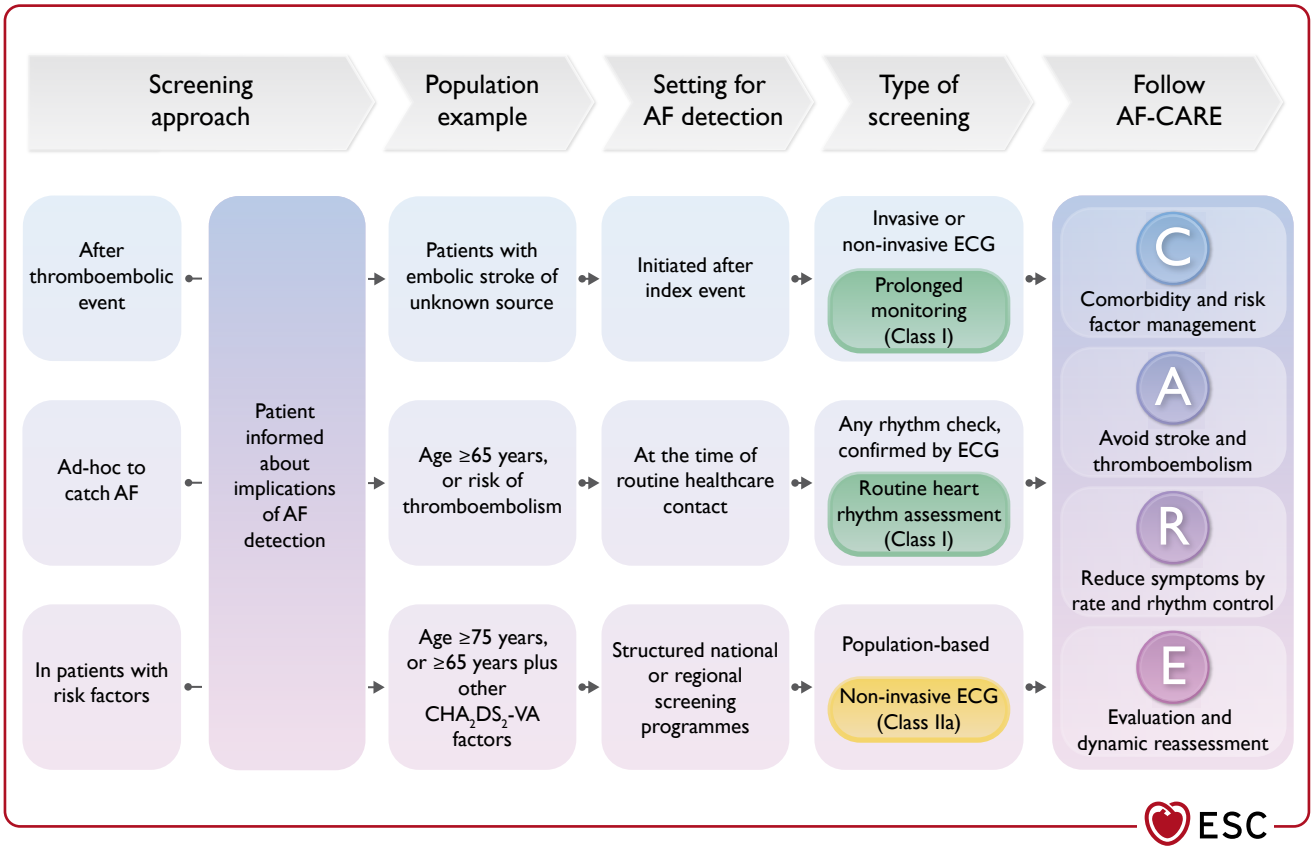


**Figure 16** Approaches to screening for AF. AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/TIA/arterial thromboembolism (2 points), vascular disease, age 65–74 years; ECG, electrocardiogram. See Figure 15 for non-invasive ECG methods.

and Halland, Sweden), 75- and 76-year-olds were randomized to be invited to prolonged screening for AF using single-lead ECGs twice daily for 2 weeks, or to standard of care. After a median of 6.9 years there was a small reduction in the primary combined endpoint of all-cause mortality, stroke, systematic embolism, and severe bleeding in favour of prolonged screening (HR, 0.96; 95% CI, 0.92–1.00; $P = .045$).[6] In the LOOP (Atrial Fibrillation Detected by Continuous ECG Monitoring) trial, individuals at increased risk of stroke were randomized to receive an implantable loop recorder that monitored heart rhythm for an average of 3.3 years, or to a control group receiving standard of care. Although there was a higher detection of AF (31.8%) and subsequent initiation of OAC in the loop recorder group compared with standard of care (12.2%), this was not accompanied by a difference in the primary outcome of stroke or systemic embolism.[5] In a meta-analysis of recent RCTs on the outcome of stroke, a small but significant benefit was seen in favour of prolonged screening (RR, 0.91; 95% CI, 0.84–0.99).[1136] This was not repeated in a second meta-analysis including older RCTs, where no risk reduction was seen with regard to mortality or stroke.[1135] Notably, both these meta-analyses are likely underpowered to assess clinical outcomes.

## 10.4. Factors associated with incident AF

The most common risk predictors for incident (new-onset) AF are shown in *Table 16*. While the factors listed are robustly associated with incident AF in observational studies, it is not known whether the relationships are causal. Studies using Mendelian randomization (genetic proxies for risk factors to estimate causal effects) robustly implicate systolic BP and higher BMI as causal risk factors for incident AF.[1142]

A high degree of interaction occurs between all factors related to AF development (see Supplementary data online, *Additional Evidence Table S33*).[1038,1039,1143–1145] For ease of clinical application, risk prediction tools have combined various factors, and have recently employed machine learning algorithms for prediction.[1146,1147] Classical risk scores are also available with variable predictive ability and model performance (see Supplementary data online, *Table S7*).[1148] Improved outcomes when using these risk scores have yet to be demonstrated. Although knowledge is rapidly increasing about the genetic basis for AF in some patients, the value of genetic screening is limited at the present time (see Supplementary data online).

**Table 16 Factors associated with incident AF**

| | |
|---|---|
| Demographic factors | Age[1149–1151] |
| | Male sex[1149–1152] |
| | European ancestry[1149,1150] |
| | Lower socioeconomic status[1150] |
| Lifestyle behaviours | Smoking/tobacco use[1149–1151] |
| | Alcohol intake[1149,1150] |
| | Physical inactivity[1149,1150] |
| | Vigorous exercise[1153–1156] |
| | Competitive or athlete-level endurance sports[1151,1157] |
| | Caffeine[1158–1160] |
| Comorbidities and risk factors | Hypertension[1149–1151] |
| | Heart failure[178,1149–1151,1161] |
| | Valvular disease[1149,1151,1162–1164] |
| | Coronary artery disease[1149,1151,1161,1165] |
| | Peripheral arterial disease[785] |
| | Congenital heart disease[1149,1166] |
| | Heart rate, heart rate variability[1167,1168] |
| | Total cholesterol[1149,1150] |
| | Low-density lipoprotein cholesterol[1150] |
| | High-density lipoprotein cholesterol[1150] |
| | Triglycerides[1150] |
| | Impaired glucose tolerance,[1169–1172]diabetes mellitus[1149–1151,1169] |
| | Renal dysfunction/CKD[1149–1151,1173,1174] |
| | Obesity[1149–1151,1175,1176] |
| | Body mass index, weight[1149–1151] |
| | Height[1150] |
| | Sleep apnoea[1149,1151,1177,1178] |
| | Chronic obstructive pulmonary disease[1179] |
| Subclinical atherosclerosis | Coronary artery calcification[1149,1151,1180] |
| | Carotid IMT and carotid plaque[1149,1151,1181,1182] |
| ECG abnormalities | PR interval prolongation[1149,1151,1183] |
| | Sick sinus syndrome[1149,1184,1185] |
| | Wolff–Parkinson–White[1149,1186] |
| Genetic factors | Family history of AF[1149,1151,1187–1190] |
| | AF-susceptible loci identified by GWAS[1149,1151,1191,1192] |
| | Short QT syndrome[1149] |
| | Genetic cardiomyopathies[990,1193] |
| Biomarkers | C-reactive protein[1150,1151] |
| | Fibrinogen[1150] |
| | Growth differentiation factor-15[1194] |
| | Natriuretic peptides (atrial and B-type)[1195–1200] |
| | Cardiac troponins[1199] |
| | Inflammatory biomarkers [1149,1151] |
| Others | Thyroid dysfunction[912,1149–1151] |
| | Autoimmune diseases[1150] |
| | Air pollution[1149,1201] |
| | Sepsis[1149,1202] |
| | Psychological factors [1203,1204] |

AF, atrial fibrillation; CKD, chronic kidney disease; GWAS, genome-wide association studies; HF, heart failure; IMT, intima-media thickness.

## 10.5. Primary prevention of AF

Preventing the onset of AF before clinical manifestation has clear potential to improve the lives of the general population and reduce the considerable health and social care costs associated with development of AF. Whereas the [C] in AF-CARE is focused on the effective management of risk factors and comorbidities to limit AF recurrence and progression, there is also evidence they can be targeted to prevent AF. Available data are presented below for hypertension, heart failure, type 2 diabetes mellitus, obesity, sleep apnoea syndrome,

physical activity, and alcohol, although many other risk markers can also be targeted. Further information on each factor's attributable risk for AF is provided in the Supplementary data online (see Supplementary data online, *Evidence Table 32* and *additional Evidence Tables S34–S39*).

**Recommendation Table 32 — Recommendations for primary prevention of AF (see also Evidence Table 32)**

| Recommendation | Class[a] | Level[b] |
|---|---|---|
| Maintaining optimal blood pressure is recommended in the general population to prevent AF, with ACE inhibitors or ARBs as first-line therapy.[1205–1207] | I | B |
| Appropriate medical HF therapy is recommended in individuals with HFrEF to prevent AF.[133,136,1208–1211] | I | B |
| Maintaining normal weight (BMI 20–25 kg/m$^2$) is recommended for the general population to prevent AF.[208,1212,1213] | I | B |
| Maintaining an active lifestyle is recommended to prevent AF, with the equivalent of 150–300 min per week of moderate intensity or 75–150 min per week of vigorous intensity aerobic physical activity.[1214–1219] | I | B |
| Avoidance of binge drinking and alcohol excess is recommended in the general population to prevent AF.[1220–1223] | I | B |
| Metformin or SGLT2 inhibitors should be considered for individuals needing pharmacological management of diabetes mellitus to prevent AF.[1210,1211,1224–1226] | IIa | B |
| Weight reduction should be considered in obese individuals to prevent AF.[1212,1227–1231] | IIa | B |

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; SGLT2, sodium-glucose cotransporter-2.
[a]Class of recommendation.
[b]Level of evidence.



### 10.5.1. Hypertension

Management of hypertension has been associated with a reduction in incident AF.[1205–1207,1232] In the LIFE (Losartan Intervention for End point reduction in hypertension) trial, a 10 mmHg reduction in systolic BP was associated with a 17% reduction in incident AF.[1207] Secondary analysis of RCTs and observational studies suggest that ACE inhibitors or ARBs may be superior to beta-blockers, calcium channel blockers, or diuretics for the prevention of incident AF.[1233–1236]

### 10.5.2. Heart failure

Long-standing established pharmacological treatments for HFrEF have been associated with a reduction in incident AF. The use of ACE inhibitors or ARBs in patients with known HFrEF was associated with a 44% reduction in incidence of AF.[1208] Similarly, beta-blockers in HFrEF led to a 33% reduction in the odds of incident AF.[133] Mineralocorticoid receptor antagonists have also been shown to reduce the risk of new-onset AF by 42% in patients with HFrEF.[1209] Although there have been variable effects of SGLT2 inhibitors on incident AF, several meta-analyses have demonstrated that there is an 18%–37% reduction in incident AF.[136,1210,1211,1237] However, treatment of HFrEF with sacubitril/valsartan has not yet been shown to confer any adjunctive benefit in reducing new-onset AF when compared with ACE inhibitors/ARBs alone.[1238] There is some evidence to suggest that effective CRT in eligible patients with HFrEF reduces the risk of incident AF.[1239] To date, no treatments in HFpEF have been shown to reduce incident AF.

### 10.5.3. Type 2 diabetes mellitus

The integrated care of type 2 diabetes, based on lifestyle and pharmacological treatments for comorbidities such as obesity, hypertension, and dyslipidaemia, are useful steps in preventing atrial remodelling and subsequent AF. Intensive glucose-lowering therapy targeting an HbA1c level of <6.0% (<42 mmol/mol) failed to show a protective effect on incident AF.[1240] More than glycaemic control *per se*, the class of glucose-lowering agent may influence the risk of AF.[1240] Insulin promotes adipogenesis and cardiac fibrosis, and sulfonylureas have been consistently associated with an increased risk of AF.[193] Observational studies have associated metformin with lower rates of incident AF.[1224,1225,1241–1243] Various recent studies and meta-analyses point to the positive role of SGLT2 inhibitors to reduce the risk of incident AF in diabetic and non-diabetic patients.[136,1226,1244–1246] Pooled data from 22 trials including 52 951 patients with type 2 diabetes and heart failure showed that SGLT2 inhibitors compared with placebo can significantly reduce the incidence of AF by 18% in studies on diabetes, and up to 37% in heart failure with or without type 2 diabetes.[1210,1211]

### 10.5.4. Obesity

Management of weight is important in the prevention of AF. In a large population-based cohort study, normal weight was associated with a reduced risk of incident AF compared with those who were obese (4.7% increase in the risk of incident AF for each 1 kg/m$^2$ increase of BMI).[208] In the Women's Health Study, participants who became obese had a 41% increased risk of incident AF compared with those who maintained their BMI <30 kg/m$^2$.[1212] Similarly, observational studies in populations using bariatric surgery for weight loss in morbidly obese individuals (BMI ≥40 kg/m$^2$) have observed a lower risk of incident AF.[1227–1231]

### 10.5.5. Sleep apnoea syndrome

Although it would seem rational to optimize sleep habits, to date there is no conclusive evidence to support this for the primary prevention of AF. The SAVE (Sleep Apnea cardioVascular Endpoints) trial failed to demonstrate a difference in clinical outcomes in those randomized to CPAP therapy or placebo.[230] There was no difference in incident AF, albeit the analysis of AF was not based on systematic screening but rather on clinically documented AF.

### 10.5.6. Physical activity

Several studies have demonstrated beneficial effects of moderate physical activity on cardiovascular health.[1247] Moderate aerobic exercise may also reduce the risk of new-onset AF.[1214–1219] It should be noted that the incidence of AF appears to be increased among athletes, with a meta-analysis of observational studies showing a 2.5-fold increased risk of AF compared with non-athlete controls.[1248]

### 10.5.7. Alcohol intake

The premise that reducing alcohol intake can prevent AF is based on observational studies linking alcohol to an excess risk of incident AF in a dose-dependent manner (see Supplementary data online).[1220–1222] In addition, a population cohort study of those with high alcohol consumption (>60 g/day for men and >40 g/day for women) found that abstinence from alcohol was associated with a lower incidence of AF compared with patients who continued heavy drinking.[1223]

## 11. Key messages

(1) General management: optimal treatment according to the AF-CARE pathway, which includes: [C] Comorbidity and risk factor management; [A] Avoid stroke and thromboembolism; [R] Reduce symptoms by rate and rhythm control; and [E] Evaluation and dynamic reassessment.
(2) Shared care: patient-centred AF management with joint decision-making and a multidisciplinary team.
(3) Equal care: avoid health inequalities based on gender, ethnicity, disability, and socioeconomic factors.
(4) Education: for patients, family members, caregivers, and healthcare professionals to aid shared decision-making.
(5) Diagnosis: clinical AF requires confirmation on an ECG device to initiate risk stratification and AF management.
(6) Initial evaluation: medical history, assessment of symptoms and their impact, blood tests, echocardiography/other imaging, patient-reported outcome measures, and risk factors for thromboembolism and bleeding.
(7) Comorbidities and risk factors: thorough evaluation and management critical to all aspects of care for patients with AF to avoid recurrence and progression of AF, improve success of AF treatments, and prevent AF-related adverse outcomes.
(8) Focus on conditions associated with AF: including hypertension, heart failure, diabetes mellitus, obesity, obstructive sleep apnoea, physical inactivity, and high alcohol intake.
(9) Assessing the risk of thromboembolism: use locally validated risk tools or the $CHA_2DS_2$-VA score and assessment of other risk factors, with reassessment at periodic intervals to assist in decisions on anticoagulant prescription.
(10) Oral anticoagulants: recommended for all eligible patients, except those at low risk of incident stroke or thromboembolism ($CHA_2DS_2$-VA = 1 anticoagulation should be considered; $CHA_2DS_2$-VA ≥2 anticoagulation recommended).
(11) Choice of anticoagulant: DOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are preferred over VKAs (warfarin and others), except in patients with mechanical heart valves and mitral stenosis.
(12) Dose/range of anticoagulant: use full standard doses for DOACs unless the patient meets specific dose-reduction criteria; for VKAs, keep INR generally 2.0–3.0, and in range for >70% of the time.
(13) Switching anticoagulants: switch from a VKA to DOAC if risk of intracranial haemorrhage or poor control of INR levels.
(14) Bleeding risk: modifiable bleeding risk factors should be managed to improve safety; bleeding risk scores should not be used to decide on starting or withdrawing anticoagulants.
(15) Antiplatelet therapy: avoid combining anticoagulants and antiplatelet agents, unless the patient has an acute vascular event or needs interim treatment for procedures.
(16) Rate control therapy: use beta-blockers (any ejection fraction), digoxin (any ejection fraction), or diltiazem/verapamil (LVEF >40%) as initial therapy in the acute setting, an adjunct to rhythm control therapies, or as a sole treatment strategy to control heart rate and symptoms.
(17) Rhythm control: consider in all suitable AF patients, explicitly discussing with patients all potential benefits and risks of cardioversion, antiarrhythmic drugs, and catheter or surgical ablation to reduce symptoms and morbidity.
(18) Safety first: keep safety and anticoagulation in mind when considering rhythm control; e.g. delay cardioversion and provide at least 3 weeks of anticoagulation beforehand if AF duration >24 h, and consider toxicity and drug interactions for antiarrhythmic therapy.
(19) Cardioversion: use electrical cardioversion in cases of haemodynamic instability; otherwise choose electrical or pharmacological cardioversion based on patient characteristics and preferences.
(20) Indication for long-term rhythm control: the primary indication should be reduction in AF-related symptoms and improvement in quality of life; for selected patient groups, sinus rhythm maintenance can be pursued to reduce morbidity and mortality.
(21) Success or failure of rhythm control: continue anticoagulation according to the patient's individual risk of thromboembolism, irrespective of whether they are in AF or sinus rhythm.
(22) Catheter ablation: consider as second-line option if antiarrhythmic drugs fail to control AF, or first-line option in patients with paroxysmal AF.
(23) Endoscopic or hybrid ablation: consider if catheter ablation fails, or an alternative to catheter ablation in persistent AF despite antiarrhythmic drugs.
(24) Atrial fibrillation ablation during cardiac surgery: perform in centres with experienced teams, especially for patients undergoing mitral valve surgery.
(25) Dynamic evaluation: periodically reassess therapy and give attention to new modifiable risk factors that could slow/reverse the progression of AF, increase quality of life, and prevent adverse outcomes.

## 12. Gaps in evidence

The following bullet list gives the most important gaps in evidence where new clinical trials could substantially aid the patient pathway:

**Definition and clinical impact of AF**

- Paroxysmal AF is not one entity, and patterns of AF progression and regression are highly variable. It is uncertain what the relevance is for treatment strategies and management decisions.
- Thirty seconds as definition for clinical AF needs validation and evaluation whether it is related to AF-related outcomes.
- Definition, clinical features, diagnosis, and implementation for treatment choices of atrial cardiomyopathy in patients with AF is unsettled.
- Diversity in AF presentation, underlying pathophysiological mechanisms, and associated comorbidities is incompletely understood with regard to differences in sex, gender, race/ethnicity, socioeconomic state, education, and differences between low-, moderate-, and high-income countries.
- Personalized risk prediction for AF incidence, AF progression, and associated outcomes remains challenging.

- Insights into psychosocial and environmental factors and risk of AF and adverse outcomes in AF are understudied.

### Patient-centred, multidisciplinary AF management

- The benefit of additional education directed to patients, to family members, and to healthcare professionals in order to optimize shared decision-making still needs to be proved.
- Access to patient-centred management according to the AF-CARE principles to ensure equality in healthcare provision and improve outcomes warrants evidence.
- The place of remote monitoring and telemedicine for identification and follow-up of patients with AF, or its subgroups is non-established, though widely applied.

## [C] Comorbidity and risk factor management

- Methods to achieve consistent and reproducible weight loss in patients with AF requires substantial improvement. Despite some evidence demonstrating the benefits of weight loss, widespread adoption has been limited by the need for reproducible strategies.
- The importance of sleep apnoea syndrome and its treatment on AF-related outcomes remains to be elucidated.

## [A] Avoid stroke and thromboembolism

- Data are lacking on how to treat patients with low risk of stroke (with a $CHA_2DS_2$-VA score of 0 or 1), as these patients were excluded from large RCTs.
- Not enough evidence is available for OAC in elderly patients, frail polypharmacy patients, those with cognitive impairment/dementia, recent bleeding, previous ICH, severe end-stage renal failure, liver impairment, cancer, or severe obesity.
- In elderly patients, routinely switching VKAs to DOACs is associated with increased bleeding risk; however, the reasons why this happens are unclear.
- The selection of which patients with asymptomatic device-detected subclinical AF benefit from OAC therapy needs to be defined.
- There is a lack of evidence whether and when to (re)start anticoagulation after intracranial haemorrhage.
- There is lack of evidence about optimal anticoagulation in patients with ischaemic stroke or left atrial thrombus while being treated with OAC.
- There is uncertainty about the place of LAA closure and how to manage antithrombotic post-procedural management when LAAO is performed.
- Balance of thromboembolism and bleeding is unclear in patients with AF and incidental cerebral artery aneurysms identified on brain MRI.

## [R] Reduce symptoms by rate and rhythm control

- In some patients, AF can be benign in terms of symptoms and outcomes. In which patients rhythm control is not needed warrants investigation.
- Application of antiarrhythmic drugs has been hampered by poor effectiveness and side effects; however, new antiarrhythmic drugs are needed to increase the therapeutic arsenal for AF patients.
- The amount of AF reduction obtained by rhythm control to improve outcomes is unknown.
- Large catheter ablation studies showed no improved outcome of patients with AF. Some small studies in specific subpopulations have observed an improved outcome. This warrants further investigation to provide each patient with AF with personalized treatment goals.
- Uncertainty exists on the time of duration of AF and risk of stroke when performing a cardioversion.
- The value of diagnostic cardioversion for persistent AF in steering management of AF is unknown.
- Decisions on continuation of OAC are completely based on stroke risk scores and irrespective of having (episodes) of AF; whether this holds for patients undergoing successful catheter ablation is uncertain.
- Large variability in ablation strategies and techniques exist for patients with persistent AF, or after first failed catheter ablation for paroxysmal AF. The optimal catheter ablation strategy and techniques, however, are unknown.
- Sham-controlled intervention studies are lacking to determine the effects on AF symptoms, quality of life, and PROMS, accounting for the placebo effect that is associated with interventions.

### The AF-CARE pathway in specific clinical settings

- The optimal duration of triple therapy in patients with AF at high risk of recurrent coronary events after acute coronary syndrome is unclear.
- The role of the coronary vessel involved and whether this should impact on the duration of combined OAC and antiplatelet treatment needs further study.
- The role of antiplatelet therapy in patients with AF and peripheral artery disease on OAC is uncertain.
- The use of DOACs in patients with congenital heart disease, particularly in patients with complex corrected congenital defects, is poorly studied.
- Improved risk stratification for stroke in patients with AF and cancer, or with post-operative or trigger-induced AF is needed to inform on OAC treatment decisions.

### Screening and prevention of AF

- There are a lack of adequately powered randomized controlled studies on ischaemic stroke rate in patients screened for AF, both in the primary prevention setting and in secondary prevention (post-stroke), and its cost-effectiveness.
- Population selection that might benefit the most from screening, the optimal duration of screening, and the burden of AF that might increase the risk for patients with screening-detected AF are uncertain.
- Evaluation of strategies to support longer-term use of technologies for AF detection are awaited.
- The role of photoplethysmography technology for AF screening in an effort to assess AF burden and reduce stroke is still unclear.
- How new consumer devices and wearable technology can be used for diagnostic and monitoring purposes in routine clinical practice needs to be clarified.

# 13. 'What to do' and 'What not to do' messages from the guidelines

*Table 17* lists all Class I and Class III recommendations from the text alongside their level of evidence.

**Table 17 'What to do' and 'what not to do'**

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| **Recommendations for the diagnosis of AF** | | |
| Confirmation by an electrocardiogram (12-lead, multiple, or single leads) is recommended to establish the diagnosis of clinical AF and commence risk stratification and treatment. | I | A |
| **Recommendations for symptom evaluation in patients with AF** | | |
| Evaluating the impact of AF-related symptoms is recommended before and after major changes in treatment to inform shared decision-making and guide treatment choices. | I | B |
| **Recommendations for diagnostic evaluation in patients with new AF** | | |
| A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions. | I | C |
| **Recommendations for patient-centred care and education** | | |
| Education directed to patients, family members, caregivers, and healthcare professionals is recommended to optimize shared decision-making, facilitating open discussion of both the benefit and risk associated with each treatment option. | I | C |
| Access to patient-centred management according to the AF-CARE principles is recommended in all patients with AF, regardless of gender, ethnicity, and socioeconomic status, to ensure equality in healthcare provision and improve outcomes. | I | C |
| **Recommendations for comorbidity and risk factor management in AF** | | |
| Identification and management of risk factors and comorbidities is recommended as an integral part of AF care. | I | B |
| Blood pressure lowering treatment is recommended in patients with AF and hypertension to reduce recurrence and progression of AF and prevent adverse cardiovascular events. | I | B |
| Diuretics are recommended in patients with AF, HF, and congestion to alleviate symptoms and facilitate better AF management. | I | C |
| Appropriate medical therapy for HF is recommended in AF patients with HF and impaired LVEF to reduce symptoms and/or HF hospitalization and prevent AF recurrence. | I | B |
| Sodium-glucose cotransporter-2 inhibitors are recommended for patients with HF and AF regardless of left ventricular ejection fraction to reduce the risk of HF hospitalization and cardiovascular death. | I | A |
| Effective glycaemic control is recommended as part of comprehensive risk factor management in individuals with diabetes mellitus and AF, to reduce burden, recurrence, and progression of AF. | I | C |
| Weight loss is recommended as part of comprehensive risk factor management in overweight and obese individuals with AF to reduce symptoms and AF burden, with a target of 10% or more reduction in body weight. | I | B |
| A tailored exercise programme is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence. | I | B |
| Reducing alcohol consumption to ≤3 standard drinks (≤30 grams of alcohol) per week is recommended as part of comprehensive risk factor management to reduce AF recurrence. | I | B |
| When screening for obstructive sleep apnoea in individuals with AF, using only symptom-based questionnaires is not recommended. | III | B |
| **Recommendations to assess and manage thromboembolic risk in AF** | | |
| Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. | I | A |
| A $CHA_2DS_2$-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation. | I | C |
| Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of $CHA_2DS_2$-VA score, to prevent ischaemic stroke and thromboembolism. | I | B |
| Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients. | I | B |
| Antiplatelet therapy is not recommended as an alternative to anticoagulation in patients with AF to prevent ischaemic stroke and thromboembolism. | III | A |
| Using the temporal pattern of clinical AF (paroxysmal, persistent, or permanent) is not recommended to determine the need for oral anticoagulation. | III | B |

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| **Recommendations for oral anticoagulation in AF** | | |
| Direct oral anticoagulants are recommended in preference to VKAs to prevent ischaemic stroke and thromboembolism, except in patients with mechanical heart valves or moderate-to-severe mitral stenosis. | I | A |
| A target INR of 2.0–3.0 is recommended for patients with AF prescribed a VKA for stroke prevention to ensure safety and effectiveness. | I | B |
| Switching to a DOAC is recommended for eligible patients that have failed to maintain an adequate time in therapeutic range on a VKA (TTR <70%) to prevent thromboembolism and intracranial haemorrhage. | I | B |
| A reduced dose of DOAC therapy is not recommended, unless patients meet DOAC-specific criteria, to prevent underdosing and avoidable thromboembolic events. | III | B |
| **Recommendations for combining antiplatelet drugs with anticoagulants for stroke prevention** | | |
| Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism. | III | B |
| **Recommendations for thromboembolism despite anticoagulation** | | |
| Adding antiplatelet treatment to anticoagulation is not recommended in patients with AF to prevent recurrent embolic stroke. | III | B |
| Switching from one DOAC to another, or from a DOAC to a VKA, without a clear indication is not recommended in patients with AF to prevent recurrent embolic stroke. | III | B |
| **Recommendations for surgical left atrial appendage occlusion** | | |
| Surgical closure of the left atrial appendage is recommended as an adjunct to oral anticoagulation in patients with AF undergoing cardiac surgery to prevent ischaemic stroke and thromboembolism. | I | B |
| **Recommendations for assessment of bleeding risk** | | |
| Assessment and management of modifiable bleeding risk factors is recommended in all patients eligible for oral anticoagulation, as part of shared decision-making to ensure safety and prevent bleeding. | I | B |
| Use of bleeding risk scores to decide on starting or withdrawing oral anticoagulation is not recommended in patients with AF to avoid under-use of anticoagulation. | III | B |
| **Recommendations for management of bleeding in anticoagulated patients** | | |
| Interrupting anticoagulation and performing diagnostic or treatment interventions is recommended in AF patients with active bleeding until the cause of bleeding is identified and resolved. | I | C |
| **Recommendations for heart rate control in patients with AF** | | |
| Rate control therapy is recommended in patients with AF, as initial therapy in the acute setting, an adjunct to rhythm control therapies, or as a sole treatment strategy to control heart rate and reduce symptoms. | I | B |
| Beta-blockers, diltiazem, verapamil, or digoxin are recommended as first-choice drugs in patients with AF and LVEF >40% to control heart rate and reduce symptoms. | I | B |
| Beta-blockers and/or digoxin are recommended in patients with AF and LVEF ≤40% to control heart rate and reduce symptoms. | I | B |
| **Recommendations for general concepts in rhythm control** | | |
| Electrical cardioversion is recommended in AF patients with acute or worsening haemodynamic instability to improve immediate patient outcomes. | I | C |
| Direct oral anticoagulants are recommended in preference to VKAs in eligible patients with AF undergoing cardioversion for thromboembolic risk reduction. | I | A |
| Therapeutic oral anticoagulation for at least 3 weeks (adherence to DOACs or INR ≥2.0 for VKAs) is recommended before scheduled cardioversion of AF and atrial flutter to prevent procedure-related thromboembolism. | I | B |
| Transoesophageal echocardiography is recommended if 3 weeks of therapeutic oral anticoagulation has not been provided, for exclusion of cardiac thrombus to enable early cardioversion. | I | B |
| Oral anticoagulation is recommended to continue for at least 4 weeks in all patients after cardioversion and long-term in patients with thromboembolic risk factor(s) irrespective of whether sinus rhythm is achieved, to prevent thromboembolism. | I | B |
| Early cardioversion is not recommended without appropriate anticoagulation or transoesophageal echocardiography if AF duration is longer than 24 h, or there is scope to wait for spontaneous cardioversion. | III | C |
| **Recommendations for pharmacological cardioversion of AF** | | |
| Intravenous flecainide or propafenone is recommended when pharmacological cardioversion of recent-onset AF is desired, excluding patients with severe left ventricular hypertrophy, HFrEF, or coronary artery disease. | I | A |
| Intravenous vernakalant is recommended when pharmacological cardioversion of recent-onset AF is desired, excluding patients with recent ACS, HFrEF, or severe aortic stenosis. | I | A |
| Intravenous amiodarone is recommended when cardioversion of AF in patients with severe left ventricular hypertrophy, HFrEF, or coronary artery disease is desired, accepting there may be a delay in cardioversion. | I | A |
| Pharmacological cardioversion is not recommended for patients with sinus node dysfunction, atrioventricular conduction disturbances, or prolonged QTc (>500 ms), unless risks for proarrhythmia and bradycardia have been considered. | III | C |

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| **Recommendations for antiarrhythmic drugs for long-term maintenance of sinus rhythm** | | |
| Amiodarone is recommended in patients with AF and HFrEF requiring long-term antiarrhythmic drug therapy to prevent recurrence and progression of AF, with careful consideration and monitoring for extracardiac toxicity. | I | A |
| Dronedarone is recommended in patients with AF requiring long-term rhythm control, including those with HFmrEF, HFpEF, ischaemic heart disease, or valvular disease to prevent recurrence and progression of AF. | I | A |
| Flecainide or propafenone is recommended in patients with AF requiring long-term rhythm control to prevent recurrence and progression of AF, excluding those with impaired left ventricular systolic function, severe left ventricular hypertrophy, or coronary artery disease. | I | A |
| Antiarrhythmic drug therapy is not recommended in patients with advanced conduction disturbances unless antibradycardia pacing is provided. | III | C |
| **Recommendations for catheter ablation of AF** | | |
| **Shared decision-making** | | |
| Shared decision-making is recommended when considering catheter ablation for AF, taking into account procedural risks, likely benefits, and risk factors for AF recurrence. | I | C |
| **Atrial fibrillation patients resistant or intolerant to antiarrhythmic drug therapy** | | |
| Catheter ablation is recommended in patients with paroxysmal or persistent AF resistant or intolerant to antiarrhythmic drug therapy to reduce symptoms, recurrence, and progression of AF. | I | A |
| **First-line rhythm control therapy** | | |
| Catheter ablation is recommended as a first-line option within a shared decision-making rhythm control strategy in patients with paroxysmal AF, to reduce symptoms, recurrence, and progression of AF. | I | A |
| **Patients with heart failure** | | |
| Atrial fibrillation catheter ablation is recommended in patients with AF and HFrEF with high probability of tachycardia-induced cardiomyopathy to reverse left ventricular dysfunction. | I | B |
| **Recommendations for anticoagulation in patients undergoing catheter ablation** | | |
| Initiation of oral anticoagulation is recommended at least 3 weeks prior to catheter-based ablation in AF patients at elevated thromboembolic risk, to prevent peri-procedural ischaemic stroke and thromboembolism. | I | C |
| Uninterrupted oral anticoagulation is recommended in patients undergoing AF catheter ablation to prevent peri-procedural ischaemic stroke and thromboembolism. | I | A |
| Continuation of oral anticoagulation is recommended for at least 2 months after AF ablation in all patients, irrespective of rhythm outcome or $CHA_2DS_2$-VA score, to reduce the risk of peri-procedural ischaemic stroke and thromboembolism. | I | C |
| Continuation of oral anticoagulation is recommended after AF ablation according to the patient's $CHA_2DS_2$-VA score, and not the perceived success of the ablation procedure, to prevent ischaemic stroke and thromboembolism. | I | C |
| **Recommendations for endoscopic and hybrid AF ablation** | | |
| Continuation of oral anticoagulation is recommended in patients with AF at elevated thromboembolic risk after concomitant, endoscopic, or hybrid AF ablation, independent of rhythm outcome or LAA exclusion, to prevent ischaemic stroke and thromboembolism. | I | C |
| **Recommendations for AF ablation during cardiac surgery** | | |
| Concomitant surgical ablation is recommended in patients undergoing mitral valve surgery and AF suitable for a rhythm control strategy to prevent symptoms and recurrence of AF, with shared decision-making supported by an experienced team of electrophysiologists and arrhythmia surgeons. | I | A |
| Intraprocedural imaging for detection of left atrial thrombus in patients undergoing surgical ablation is recommended to guide surgical strategy, independent of oral anticoagulant use, to prevent peri-procedural ischaemic stroke and thromboembolism. | I | C |
| **Recommendations for patients with acute coronary syndromes or undergoing percutaneous intervention** | | |
| **General recommendations for patients with AF and an indication for concomitant antiplatelet therapy** | | |
| For combinations with antiplatelet therapy, a DOAC is recommended in eligible patients in preference to a VKA to mitigate bleeding risk and prevent thromboembolism. | I | A |
| **Recommendations for AF patients with ACS** | | |
| Early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant (preferably DOAC) with a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 12 months is recommended in AF patients with ACS undergoing an uncomplicated PCI to avoid major bleeding, if the risk of thrombosis is low or bleeding risk is high. | I | A |
| **Recommendations for AF patients undergoing PCI** | | |
| After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant and a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 6 months is recommended to avoid major bleeding, if ischaemic risk is low. | I | A |

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| **Recommendations for AF patients with chronic coronary or vascular disease** | | |
| Antiplatelet therapy beyond 12 months is not recommended in stable patients with chronic coronary or vascular disease treated with oral anticoagulation, due to lack of efficacy and to avoid major bleeding. | III | B |
| **Recommendations for management of post-operative AF** | | |
| Peri-operative amiodarone therapy is recommended where drug therapy is desired to prevent post-operative AF after cardiac surgery. | I | A |
| Routine use of beta-blockers is not recommended in patients undergoing non-cardiac surgery for the prevention of post-operative AF. | III | B |
| **Recommendations for patients with embolic stroke of unknown source** | | |
| Prolonged monitoring for AF is recommended in patients with ESUS to inform on AF treatment decisions. | I | B |
| Initiation of oral anticoagulation in ESUS patients without documented AF is not recommended due to lack of efficacy in preventing ischaemic stroke and thromboembolism. | III | A |
| **Recommendations for patients with AF during pregnancy** | | |
| Immediate electrical cardioversion is recommended in patients with AF during pregnancy and haemodynamic instability or pre-excited AF to improve maternal and foetal outcomes. | I | C |
| Therapeutic anticoagulation with LMWHs or VKAs (except VKAs for the first trimester or beyond Week 36) is recommended for pregnant patients with AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. | I | C |
| Beta-1 selective blockers are recommended for heart rate control of AF in pregnancy to reduce symptoms and improve maternal and foetal outcomes, excluding atenolol. | I | C |
| **Recommendations for prevention of thromboembolism in atrial flutter** | | |
| Oral anticoagulation is recommended in patients with atrial flutter at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. | I | B |
| **Recommendations for screening for AF** | | |
| Review of an ECG (12-lead, single, or multiple leads) by a physician is recommended to provide a definite diagnosis of AF and commence appropriate management. | I | B |
| Routine heart rhythm assessment during healthcare contact is recommended in all individuals aged ≥65 years for earlier detection of AF. | I | C |
| **Recommendations for primary prevention of AF** | | |
| Maintaining optimal blood pressure is recommended in the general population to prevent AF, with ACE inhibitors or ARBs as first-line therapy. | I | B |
| Appropriate medical HF therapy is recommended in individuals with HFrEF to prevent AF. | I | B |
| Maintaining normal weight (BMI 20–25 kg/m$^2$) is recommended for the general population to prevent AF. | I | B |
| Maintaining an active lifestyle is recommended to prevent AF, with the equivalent of 150–300 min per week of moderate intensity or 75–150 min per week of vigorous intensity aerobic physical activity. | I | B |
| Avoidance of binge drinking and alcohol excess is recommended in the general population to prevent AF. | I | B |

AAD, antiarrhythmic drugs; ACEi, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndromes; AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; AFL, atrial flutter; ARB, angiotensin receptor blocker; BMI, body mass index; $CHA_2DS_2$-VA, congestive heart failure, hypertension, age ≥75 years (2 points), diabetes mellitus, prior stroke/transient ischaemic attack/arterial thromboembolism (2 points), vascular disease, age 65–74 years; DOAC, direct oral anticoagulant; ECG, electrocardiogram; ESUS, embolic stroke of undetermined source; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; INR, international normalized ratio of prothrombin time; LAA, left atrial appendage; LMWH, low molecular weight heparin; LVEF, left ventricular ejection fraction; PCI, percutaneous intervention; SGLT2, sodium-glucose cotransporter-2; TTR, time in therapeutic range; VKA, vitamin K antagonist.
[a]Class of recommendation.
[b]Level of evidence.

# 14. Evidence tables

Evidence tables are available at *European Heart Journal* online.

# 15. Data availability statement

No new data were generated or analysed in support of this research.

# 16. Author information

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# 17. Appendix

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