

# 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	CABANA	Catheter Ablation versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (trial)
ACE	Angiotensin-converting enzyme	CAD	Coronary artery disease
ACEi	Angiotensin-converting enzyme inhibitor	CASTLE-AF	Catheter Ablation versus Standard Conventional Treatment in Patients With Left Ventricle (LV) Dysfunction and AF (trial)
ACS	Acute coronary syndromes	CASTLE-HTx	Catheter Ablation for Atrial Fibrillation in Patients With End-Stage Heart Failure and Eligibility for Heart Transplantation (trial)
ACTIVE W	Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (trial)	CCS	Chronic coronary syndrome
AF	Atrial fibrillation	CHADS <sub>2</sub>	Congestive heart failure, hypertension, age >75 years, diabetes; previous stroke (2 points)
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 <sub>2</sub> DS <sub>2</sub> -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)
AFEQT	Atrial Fibrillation Effect on QualiTY-of-Life (questionnaire)	CHA <sub>2</sub> DS <sub>2</sub> -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
AFFIRM	Atrial Fibrillation Follow-up Investigation of Rhythm Management (trial)	CKD	Chronic kidney disease
AFL	Atrial flutter	CMR	Cardiac magnetic resonance
AFQLQ	Atrial Fibrillation Quality of Life Questionnaire	COMPASS	Cardiovascular Outcomes for People Using Anticoagulation Strategies (trial)
AF-QoL	Atrial Fibrillation Quality of Life (questionnaire)	CPAP	Continuous positive airway pressure
AFSS	Atrial Fibrillation Severity Scale	CrCl	Creatinine clearance
AI	Artificial intelligence	CRT	Cardiac resynchronization therapy
APACHE-AF	Apixaban After Anticoagulation-associated Intracerebral Haemorrhage in Patients With Atrial Fibrillation (trial)	CT	Computed tomography
APAF-CRT	Ablate and Pace for Atrial Fibrillation—cardiac resynchronization therapy	CTA	Computed tomography angiography
ARB	Angiotensin receptor blocker	CTI	Cavo-tricuspid isthmus
ARTESiA	Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (trial)	DAPT	Dual antiplatelet therapy
AT	Atrial tachycardia	DOAC	Direct oral anticoagulant
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)	EAST-AFNET 4	Early treatment of Atrial fibrillation for Stroke prevention 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	ECG	Electrocardiogram
AVERROES	Apixaban Versus Acetylsalicylic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Are Unsuitable for Vitamin K Antagonist Treatment (trial)	ECV	Electrical cardioversion
AVN	Atrioventricular node	EHRA	European Heart Rhythm Association
b.p.m.	Beats per minute	ELAN	Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillation (trial)
BMI	Body mass index	ESUS	Embolic stroke of undetermined source
BNP	B-type natriuretic peptide	FFP	Fresh frozen plasma
BP	Blood pressure	GI	Gastrointestinal
C <sub>2</sub> HES <sub>T</sub>	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)	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
		HFrfEF	Heart failure with reduced ejection fraction
		HR	Hazard ratio
		i.v.	Intravenous



ICH	Intracranial haemorrhage	SAVE	Sleep Apnea cardioVascular Endpoints (trial)
ICHOM	International Consortium for Health Outcomes Measurement	SBP	Systolic blood pressure
IMT	Intima-media thickness	SGLT2	Sodium-glucose cotransporter-2
INR	International normalized ratio (of prothrombin time)	SIC-AF	Successful Intravenous Cardioversion for Atrial Fibrillation
LA	Left atrium	SORT-AF	Supervised Obesity Reduction Trial for AF Ablation Patients (trial)
LAA	Left atrial appendage	SoSTART	Start or STop Anticoagulants Randomised Trial
LAAO	Left atrial appendage occlusion	SR	Sinus rhythm
LAAOS III	Left Atrial Appendage Occlusion Study	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)
LEGACY	Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: a 5 Year follow-up study	STEMI	ST-segment elevation myocardial infarction
LMWH	Low molecular weight heparin	STROKESTOP	Systematic ECG Screening for Atrial Fibrillation Among 75 Year Old Subjects in the Region of Stockholm and Halland, Sweden (trial)
LOOP	Atrial Fibrillation Detected by Continuous ECG Monitoring (trial)	TE	Thromboembolism
LV	Left ventricle	TIA	Transient ischaemic attack
LVEF	Left ventricular ejection fraction	TIMING	Timing of Oral Anticoagulant Therapy in Acute Ischemic Stroke With Atrial Fibrillation (trial)
LVH	Left ventricular hypertrophy	TOE	Transoesophageal echocardiography
mEHRA	Modified European Heart Rhythm Association score	TSH	Thyroid-stimulating hormone
MI	Myocardial infarction	TTE	Transthoracic echocardiogram
MRI	Magnetic resonance imaging	TTR	Time in therapeutic range
NOAH	Non-vitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes (trial)	UFH	Unfractionated heparin
NSAID	Non-steroidal anti-inflammatory drug	VKA	Vitamin K antagonist
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	Rate Control versus Electrical Cardioversion Trial 7—Acute Cardioversion versus Wait and See (trial)		
ACWAS			
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		

## 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

	Definition	Wording to use	
Classes of recommendations	<b>Class I</b>	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
	<b>Class II</b>	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
	<b>Class III</b>	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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**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.

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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), STEER-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 <sup>a</sup>	Level <sup>b</sup>
<b>Diagnostic evaluation of new AF—Section 3.4</b>		
A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions.	I	C
<b>Principles of AF-CARE—Section 4.2</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.	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
<b>[C] Comorbidity and risk factor management—Section 5</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
Bariatric surgery may be considered in conjunction with lifestyle changes and medical management in individuals with AF and body mass index $\geq 40$ kg/m <sup>2</sup> <sup>c</sup> 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
<b>Initiating oral anticoagulation—Section 6.1</b>		
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.	I	A
A CHA <sub>2</sub> DS <sub>2</sub> -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 <sub>2</sub> DS <sub>2</sub> -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 <sub>2</sub> DS <sub>2</sub> -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
<b>Oral anticoagulants—Section 6.2</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
Maintaining VKA treatment rather than switching to a DOAC may be considered in patients aged $\geq 75$ years on clinically stable therapeutic VKA with polypharmacy to prevent excess bleeding risk.	IIb	B
<b>Antiplatelet drugs and combinations with anticoagulants—Section 6.3</b>		
Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism.	III	B

Continued

<b>Residual ischaemic stroke risk despite anticoagulation—Section 6.4</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.	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
<b>Surgical left atrial appendage occlusion—Section 6.6</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.	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
<b>Management of bleeding on anticoagulant therapy—Section 6.7.2</b>		
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
<b>Management of heart rate in patients with AF—Section 7.1</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.	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
<b>General principles and anticoagulation—Section 7.2.1</b>		
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
<b>Electrical cardioversion—Section 7.2.2</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.	IIa	C
<b>Antiarrhythmic drugs—Section 7.2.4</b>		
Antiarrhythmic drug therapy is not recommended in patients with advanced conduction disturbances unless antibradycardia pacing is provided.	III	C
<b>Catheter ablation—Section 7.2.5</b>		
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
<b>Anticoagulation in patients undergoing catheter ablation—Section 7.2.6</b>		
Uninterrupted oral anticoagulation is recommended in patients undergoing AF catheter ablation to prevent peri-procedural ischaemic stroke and thromboembolism.	I	A

Continued

<b>Endoscopic and hybrid AF ablation—Section 7.2.7</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
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
<b>AF ablation during cardiac surgery—Section 7.2.8</b>		
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
<b>Patient-reported outcome measures—Section 8.4</b>		
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
<b>Acute and chronic coronary syndromes in patients with AF—Section 9.2</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.	III	B
<b>Trigger-induced AF—Section 9.5</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.	IIa	C
<b>Post-operative AF—Section 9.6</b>		
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
<b>Patients with embolic stroke of unknown source (ESUS)—Section 9.7</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
<b>Atrial flutter—Section 9.14</b>		
Oral anticoagulation is recommended in patients with atrial flutter at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.	I	B
<b>Screening strategies for AF—Section 10.3</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.	I	B
Population-based screening for AF using a prolonged non-invasive ECG-based approach should be considered in individuals aged $\geq 75$ years, or $\geq 65$ years with additional CHA <sub>2</sub> DS <sub>2</sub> -VA risk factors to ensure earlier detection of AF.	IIa	B
<b>Primary prevention of AF—Section 10.5</b>		
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 <sup>2</sup> ) 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<sub>2</sub>DS<sub>2</sub>-VA, congestive heart failure, hypertension, age  $\geq 75$  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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>Or body mass index  $\geq 35$  kg/m<sup>2</sup> with obesity-related complications.

**Table 4** Revised recommendations

Recommendations in 2020 version	Class <sup>a</sup>	Level <sup>b</sup>	Recommendations in 2024 version	Class <sup>a</sup>	Level <sup>b</sup>
<b>Section 3.2—Diagnostic criteria for AF</b>					
ECG documentation is required to establish the diagnosis of AF. A standard 12-lead ECG recording or a single-lead ECG tracing of $\geq 30$ 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.	<b>I</b>	<b>B</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.	<b>I</b>	<b>A</b>
In patients with AF, it is recommended to: <ul style="list-style-type: none"> <li>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.</li> <li>Evaluate AF-related symptoms before and after cardioversion of persistent AF to aid rhythm control treatment decisions.</li> </ul>	<b>I</b>	<b>C</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.	<b>I</b>	<b>B</b>
<b>Section 5—[C] Comorbidity and risk factor management</b>					
Attention to good BP control is recommended in AF patients with hypertension to reduce AF recurrences and risk of stroke and bleeding.	<b>I</b>	<b>B</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.	<b>I</b>	<b>B</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.	<b>IIa</b>	<b>B</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.	<b>I</b>	<b>B</b>
Physical activity should be considered to help prevent AF incidence or recurrence, with the exception of excessive endurance exercise, which may promote AF.	<b>IIa</b>	<b>C</b>	A tailored exercise programme is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence.	<b>I</b>	<b>B</b>
Advice and management to avoid alcohol excess should be considered for AF prevention and in AF patients considered for OAC therapy.	<b>IIa</b>	<b>B</b>	Reducing alcohol consumption to $\leq 3$ standard drinks ( $\leq 30$ grams of alcohol) per week is recommended as part of comprehensive risk factor management to reduce AF recurrence.	<b>I</b>	<b>B</b>
<b>Section 6.6—Surgical left atrial appendage occlusion</b>					
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.	<b>IIb</b>	<b>C</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.	<b>I</b>	<b>B</b>
<b>Section 6.7—Bleeding risk</b>					
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 $\geq 3$ ) for early and more frequent clinical review and follow-up.	<b>IIa</b>	<b>B</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.	<b>I</b>	<b>B</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: <ul style="list-style-type: none"> <li>• Paroxysmal AF episodes.</li> </ul>	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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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 atrio-ventricular 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).<sup>1</sup> 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
<b>First-diagnosed AF</b>	AF that has not been diagnosed before, regardless of symptom status, temporal pattern, or duration.
<b>Paroxysmal AF</b>	AF which terminates spontaneously within 7 days or with the assistance of an intervention. Evidence suggests that most self-terminating paroxysms last <48 h. <sup>2</sup>
<b>Persistent AF</b>	AF episodes which are not self-terminating. Many intervention trials have used 7 days as a cut-off for defining persistent AF. <sup>3,4</sup> 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.
<b>Permanent AF</b>	AF for which no further attempts at restoration of sinus rhythm are planned, after a shared decision between the patient and physician.

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AF, atrial fibrillation.

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

Clinical concept	Definition
<b>Clinical AF</b>	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.
<b>Device-detected subclinical AF</b>	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 <sup>a</sup> 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. <sup>5,6</sup> Device-detected subclinical AF is a predictor of future clinical AF. <sup>7</sup>

Continued

<b>AF burden</b>	The overall time spent in AF during a clearly specified and reported period of monitoring, expressed as a percentage of time.
<b>Recent-onset AF</b>	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. <sup>8–10</sup>
<b>Trigger-induced AF</b>	New AF episode in close proximity to a precipitating and potentially reversible factor. <sup>11–14</sup>
<b>Early AF</b>	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. <sup>15–17</sup> The definition of early AF also does not necessarily determine early timing of intervention.
<b>Self-terminating AF</b>	Paroxysmal AF which terminates spontaneously. <sup>2</sup> This definition may be of value for decisions on acute rhythm control taken jointly by the patient and healthcare provider.
<b>Non-self-terminating AF</b>	Atrial fibrillation which does not terminate spontaneously and, if needed, termination can be achieved only with an intervention.
<b>Atrial cardiomyopathy</b>	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). <sup>18,19</sup> Atrial cardiomyopathy includes inflammatory and prothrombotic remodelling of the atria, neurohormonal activation (thereby affecting the ventricles), and fibrosis of myocardial tissue. <sup>20</sup>

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AF, atrial fibrillation; b.p.m., beats per minute; ECG, electrocardiogram.

<sup>a</sup>Atrial high-rate episodes are defined as episodes generally lasting more than 5 min with an atrial lead rate  $\geq 170$  b.p.m.,<sup>7,21–24</sup> 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.<sup>25–29</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>25–29</sup>	I	A

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AF, atrial fibrillation.  
<sup>a</sup>Class of recommendation.  
<sup>b</sup>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,<sup>30</sup> although 90% of patients with AF describe symptoms with variable severity.<sup>31</sup> Even in symptomatic patients, some episodes of AF may remain asymptomatic.<sup>32,33</sup> The presence or absence of symptoms is not related to incident stroke, systemic embolism, or mortality.<sup>34</sup> However, symptoms do impact on patient quality of life.<sup>35,36</sup> Cardiac-specific AF symptoms such as palpitations are less common than non-specific symptoms such as fatigue, but they significantly impair quality of life.<sup>36,37</sup> Although women are often underrepresented in clinical trials of AF,<sup>38–40</sup> the available literature suggests that women with AF appear to be more symptomatic and have poorer quality of life.<sup>41,42</sup> 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,<sup>43,44</sup> with higher prevalence of these symptoms in women with AF.<sup>45</sup>

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.<sup>46–48</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>17,36,46–55</sup>	I	B

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AF, atrial fibrillation.  
<sup>a</sup>Class of recommendation.  
<sup>b</sup>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.<sup>56</sup> 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.<sup>57,58</sup>

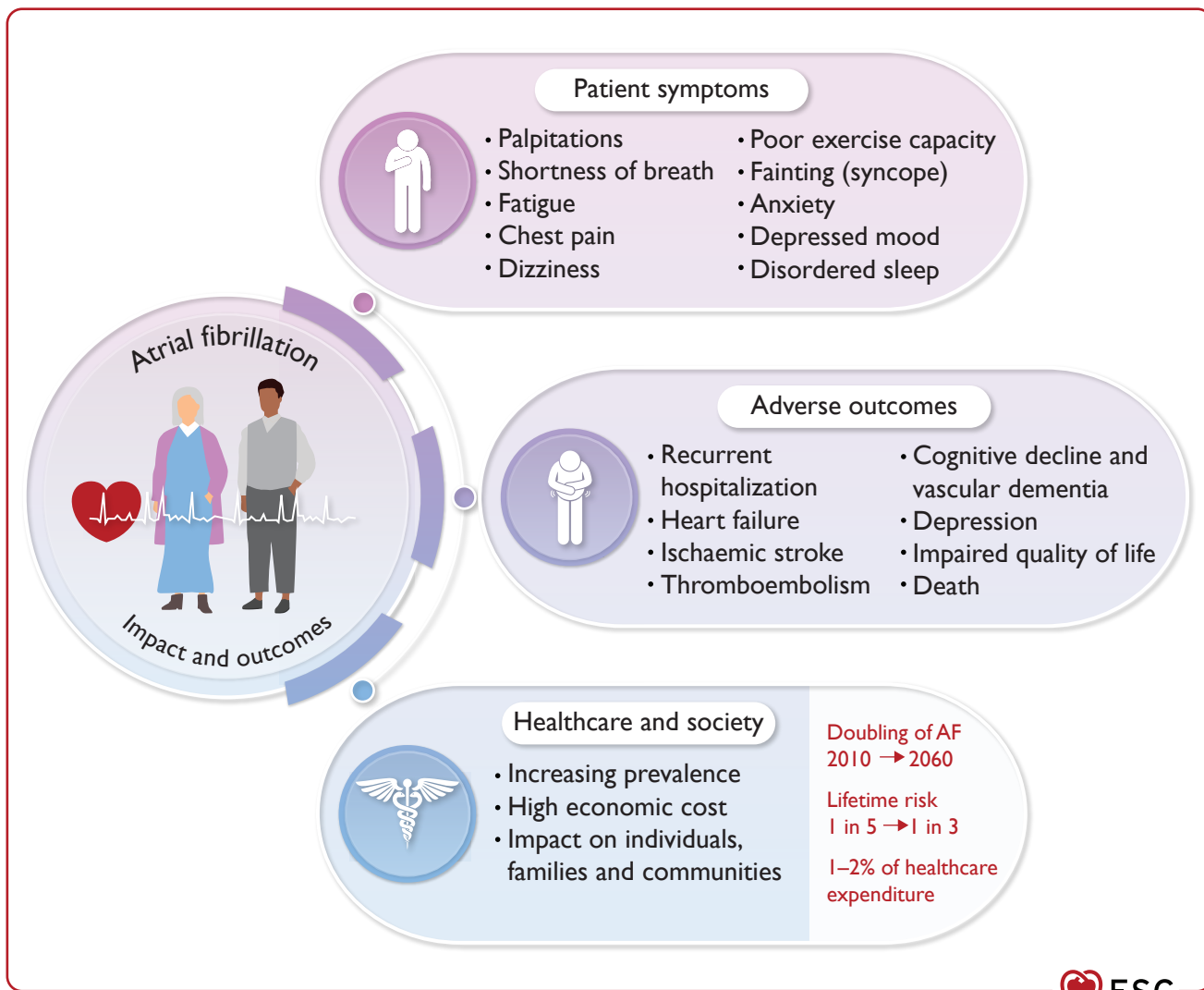
Other investigations will depend on individualized assessment and the planned treatment strategy.<sup>59–65</sup> A transthoracic echocardiogram (TTE) should be carried out in the initial work-up, where this will guide management decisions, or in patients where there is a change in cardiovascular signs 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.<sup>66</sup> Further details on TTE and re-assessment (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 <sup>a</sup>	Level <sup>b</sup>
A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions. <sup>59,65,67</sup>	I	C

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AF, atrial fibrillation.  
<sup>a</sup>Class of recommendation.  
<sup>b</sup>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

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### 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).<sup>68,69</sup> 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.<sup>69–71</sup> The latter typically include arterial thromboembolic events (preferred to the term systemic), although venous thromboembolism is also associated

AF, atrial fibrillation.

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

All patients	Selected patients
<ul style="list-style-type: none"> <li>Medical history to determine AF pattern, relevant family history, and comorbidities, and to assess risk factors for thromboembolism and bleeding</li> </ul>	<ul style="list-style-type: none"> <li>Ambulatory ECG monitoring for assessing AF burden and ventricular rate control</li> <li>Exercise ECG to evaluate rate control or effects of class IC antiarrhythmic drugs</li> </ul>
<ul style="list-style-type: none"> <li>12-lead ECG</li> </ul>	<ul style="list-style-type: none"> <li>Further blood tests for investigation of cardiovascular disease and refinement of stroke/bleeding risk (e.g. NT-proBNP, troponin)</li> </ul>
<ul style="list-style-type: none"> <li>Assess symptoms and functional impairment</li> </ul>	<ul style="list-style-type: none"> <li>Transoesophageal echocardiography for left atrial thrombus and valvular disease assessment</li> </ul>
<ul style="list-style-type: none"> <li>Collect generic or AF-specific patient-reported outcome measures</li> </ul>	<ul style="list-style-type: none"> <li>Coronary CT, angiography, or ischaemia imaging for suspected CAD</li> </ul>
<ul style="list-style-type: none"> <li>Blood tests (full blood count, kidney function, serum electrolytes, liver function, glucose/HbA1c, and thyroid function)</li> </ul>	<ul style="list-style-type: none"> <li>CMR for evaluation of atrial and ventricular cardiomyopathies, and to plan interventional procedures</li> </ul>
<ul style="list-style-type: none"> <li>Transthoracic echocardiography where this will guide AF-CARE management decisions</li> </ul>	<ul style="list-style-type: none"> <li>Brain imaging and cognitive function assessment for cerebrovascular disease and dementia risk</li> </ul>

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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.<sup>72,73</sup> Patients with AF also have an increased risk of cognitive impairment (adjusted hazard ratio [HR], 1.39; 95% CI, 1.25–1.53)<sup>74</sup> and dementia (OR, 1.6; 95% CI, 1.3–2.0).<sup>75–77</sup> 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;  $P = .09$ ).<sup>78</sup>

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.<sup>79</sup> 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.<sup>80</sup>

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).<sup>81</sup> The most frequent cause of death in patients with AF is heart failure related,<sup>70</sup> with complex relationships to cardiovascular and non-cardiovascular disease.<sup>82</sup> There is up to a two-fold increased risk of all-cause mortality (RR, 1.95; 95% CI, 1.50–2.54),<sup>68</sup> and cardiovascular mortality (RR, 2.03; 95% CI, 1.79–2.30)<sup>69</sup> 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;  $P < .001$ ).<sup>78</sup> 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).<sup>83</sup> Despite OAC, patients with AF remain at high residual risk of death, highlighting the importance of attention to concomitant disease.<sup>84</sup>

### 3.6. Atrial flutter

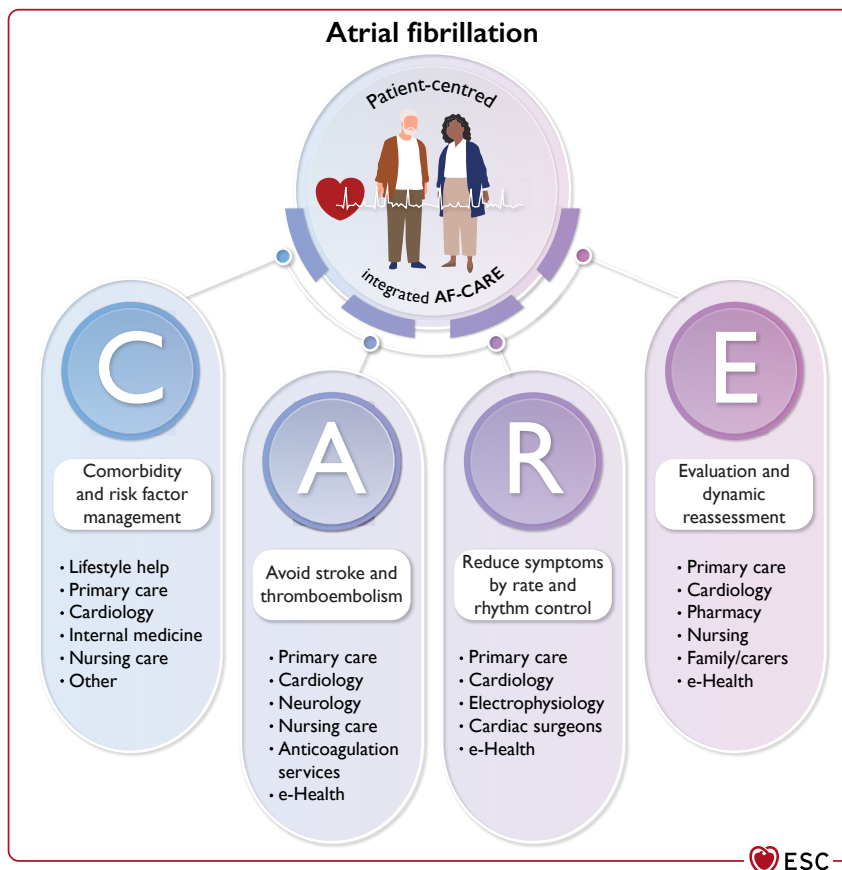
Atrial flutter (AFL) is the among the most common atrial tachyarrhythmias, with an overall incidence rate of 88 per 100 000 person-years, rising to 317 per 100 000 person-years in people over 50 years of age.<sup>85</sup> Risk factors for AFL and AF are similar, and more than half of all patients with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

## 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) <sup>a</sup>

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.

<sup>a</sup>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](#)).<sup>92</sup> 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.<sup>93,94</sup> 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.<sup>95</sup> 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.<sup>93,94</sup> 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.<sup>96–98</sup> Healthcare professionals involved in multidisciplinary AF management should have a knowledge of all available options for diagnosis and treatment.<sup>99–101</sup> In the STEER-AF trial,<sup>99</sup> 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.<sup>102</sup>

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

### 4.1.4. Inclusive management of AF

Evidence is growing on differences in AF incidence, prevalence, risk factors, comorbidities, and outcomes according to gender.<sup>108</sup> 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).<sup>109</sup> Registry studies have reported differences in outcomes, with higher morbidity and mortality in women, although these may be confounded by age and comorbidity burden.<sup>110–112</sup> Women with AF may be more symptomatic, and report a lower quality of life.<sup>41,113</sup> 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.<sup>109</sup> 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.<sup>114</sup>

## 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<sup>115–118</sup> 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,<sup>119</sup> and the AF Better Care (ABC) pathway in the 2020 ESC Guidelines for the diagnosis and management of AF.<sup>120</sup> 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).

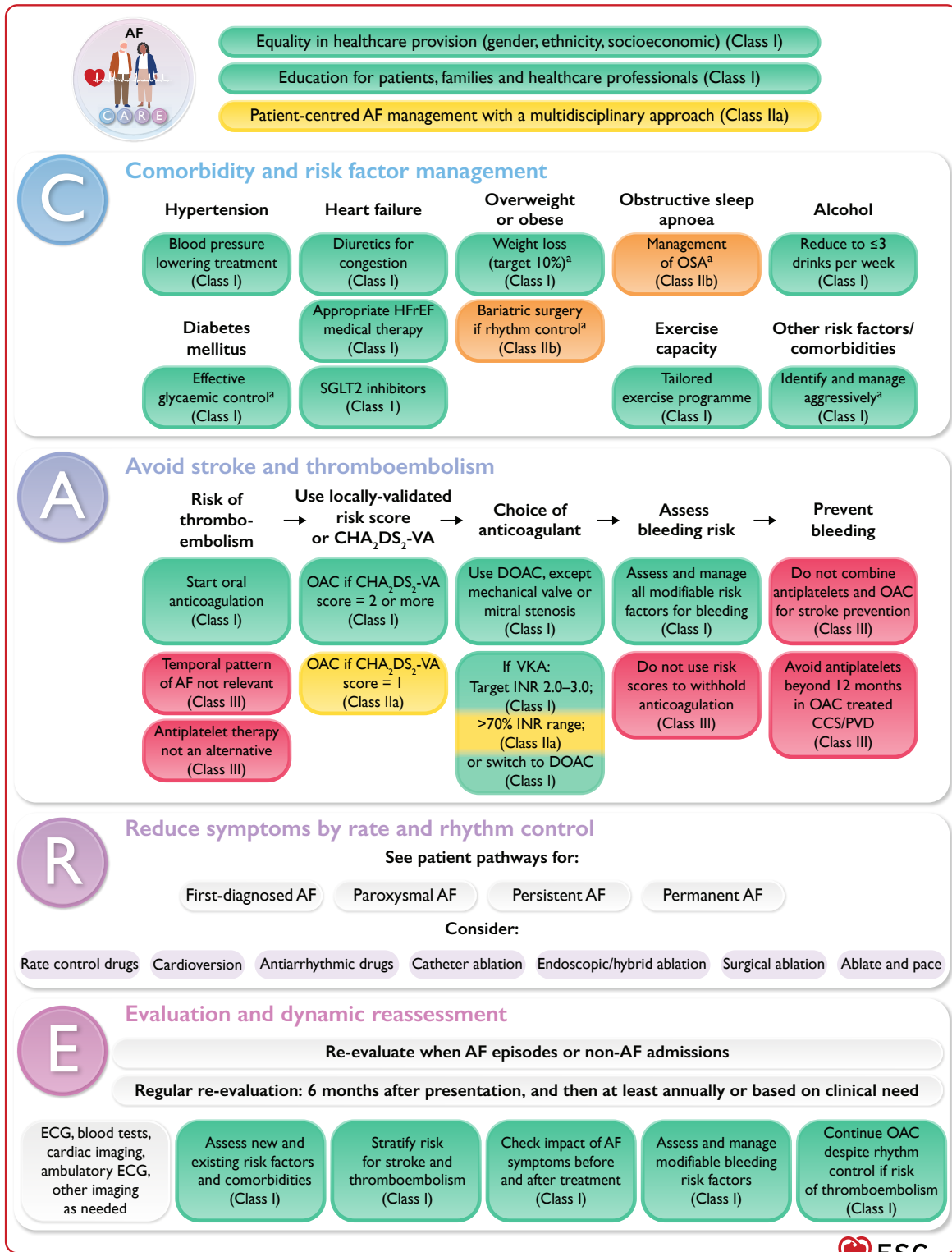
### Recommendation Table 4 — Recommendations for patient-centred care and education (see also Evidence Table 4)

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>94,103</sup>	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. <sup>79,121–124</sup>	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.

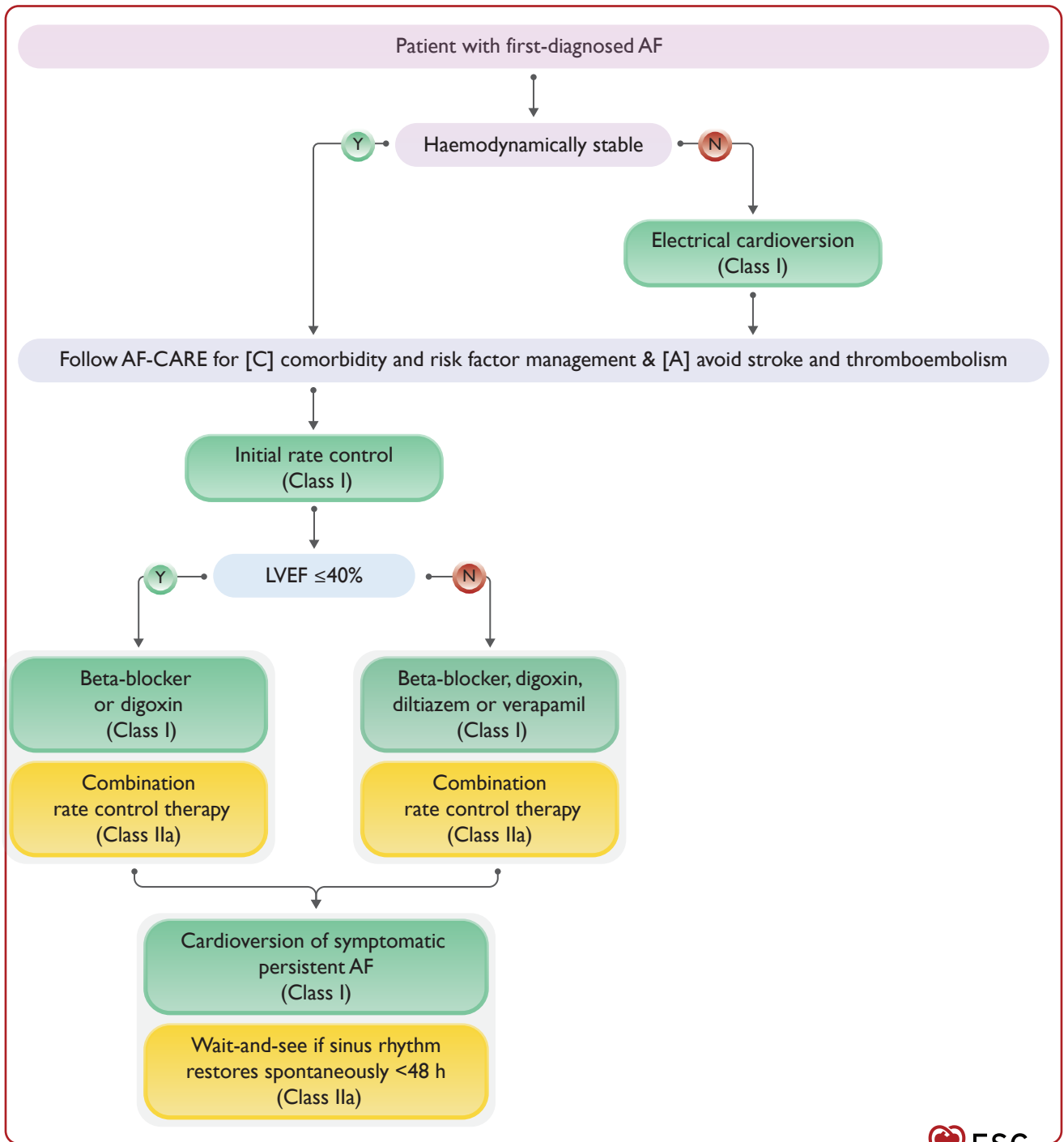
<sup>a</sup>Class of recommendation.

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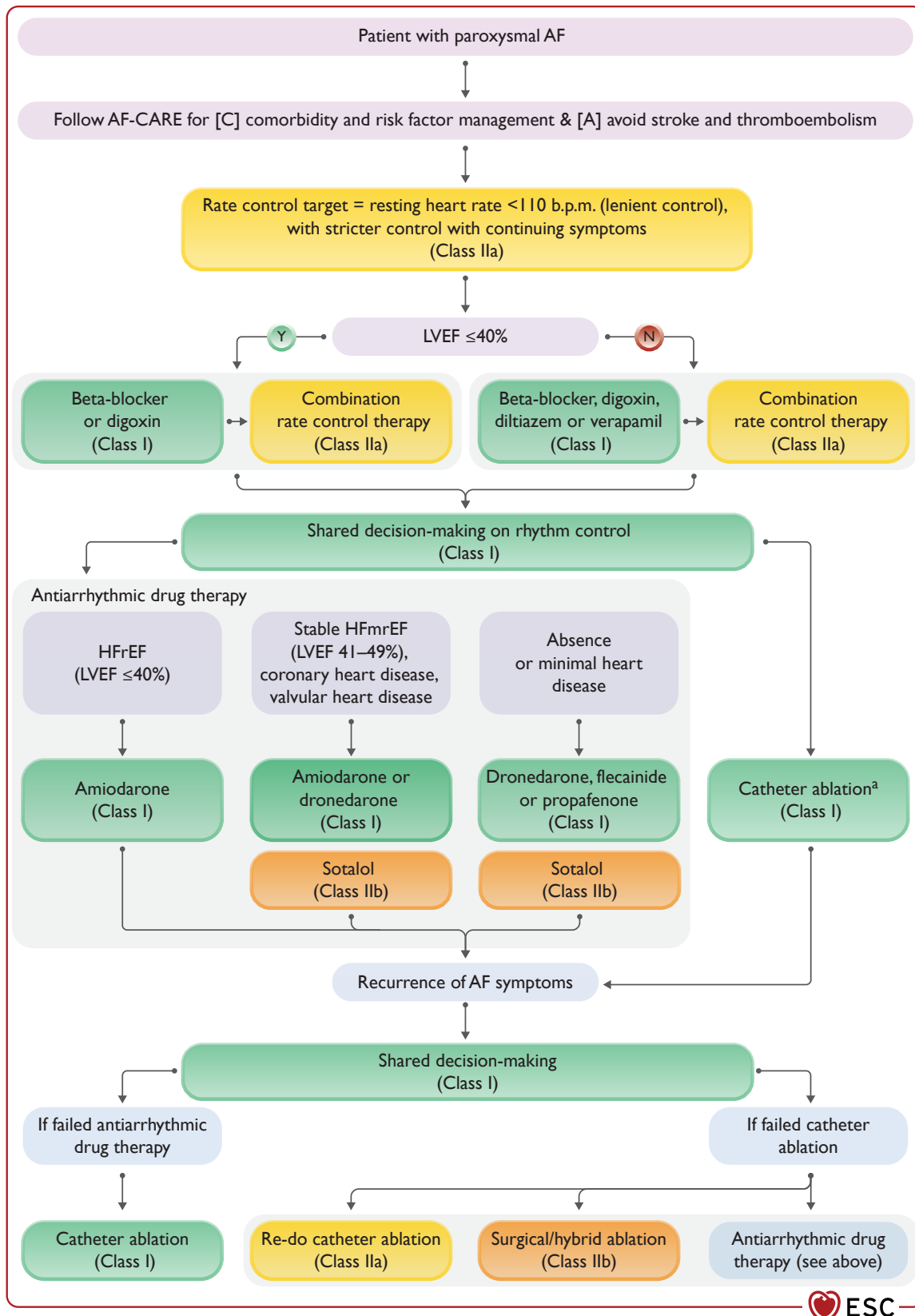


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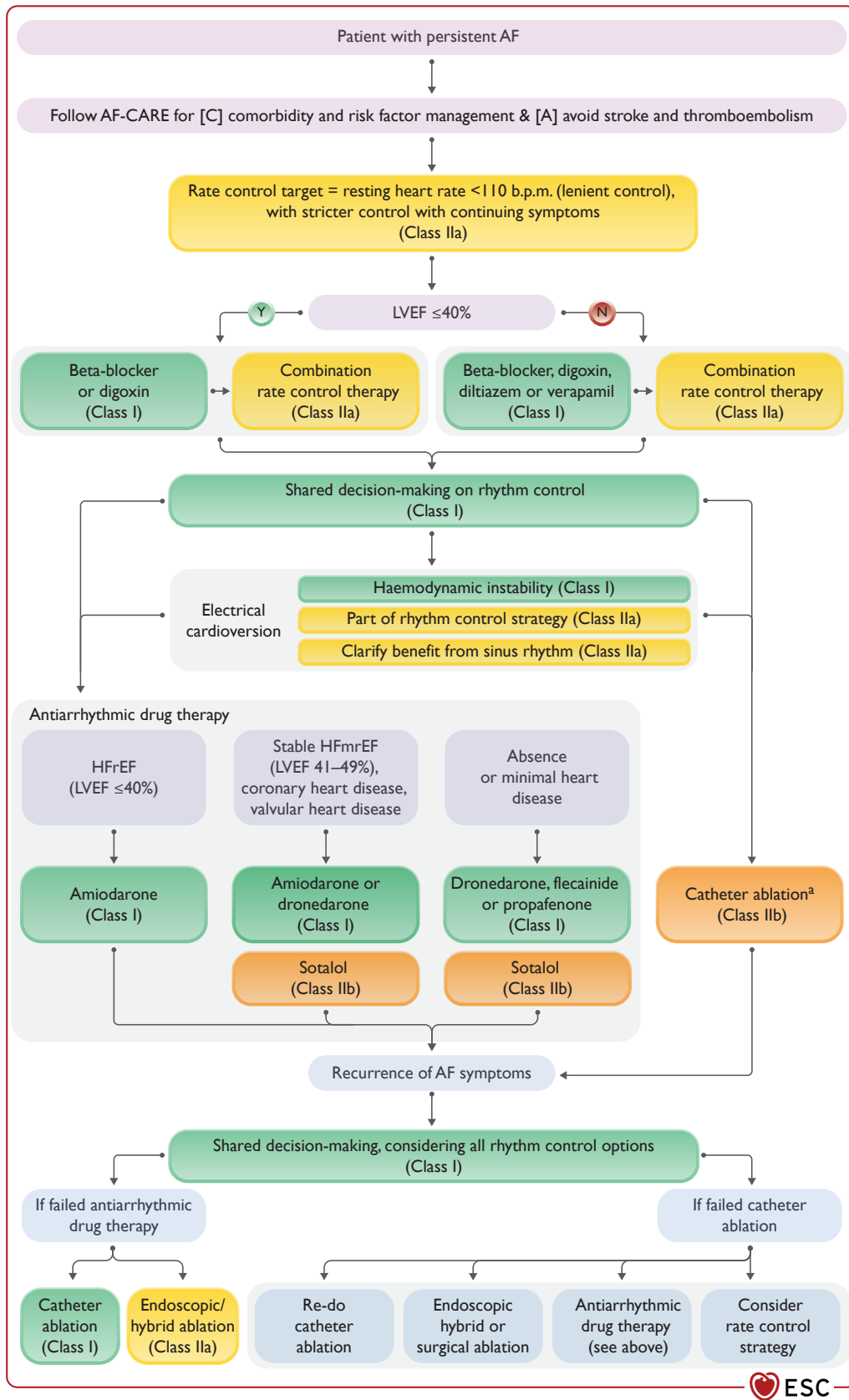
**Figure 3** Central illustration. Patient pathway for AF-CARE (see Figures 4, 5, 6, and 7 for the [R] pathways for first-diagnosed, paroxysmal, persistent and permanent AF). AF, atrial fibrillation; AF-CARE, atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; CCS, chronic coronary syndrome; CHA<sub>2</sub>DS<sub>2</sub>-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. <sup>a</sup>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. <sup>a</sup>In patients with HFrEF: Class I if high probability of tachycardia-induced cardiomyopathy; and Class IIa in selected patients to improve prognosis.

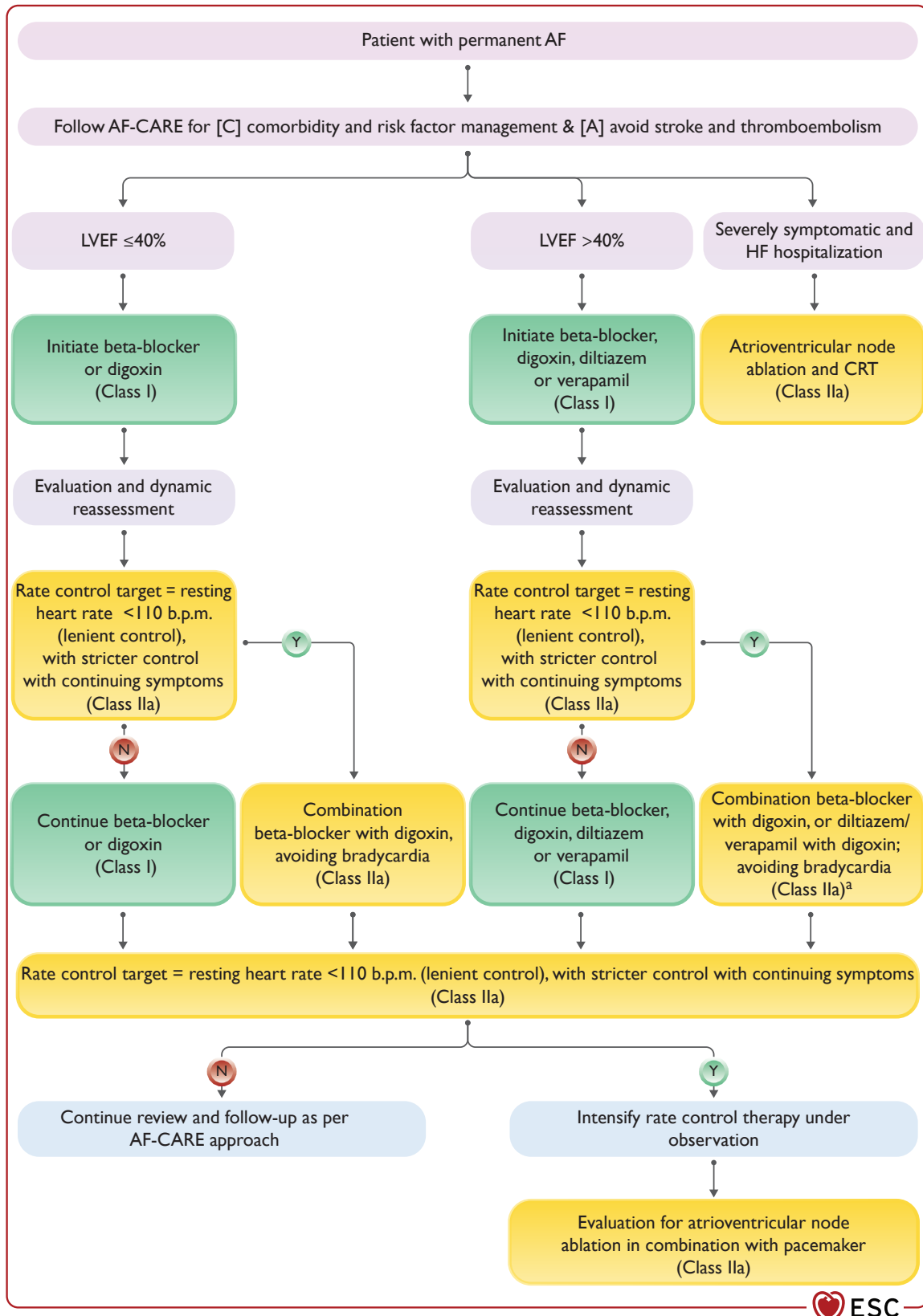


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**Figure 6** [R] Pathway for patients with persistent AF. AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation 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. <sup>a</sup>In patients with HFrEF: Class I if high probability of tachycardia-induced cardiomyopathy; and Class IIa in selected patients to improve prognosis.



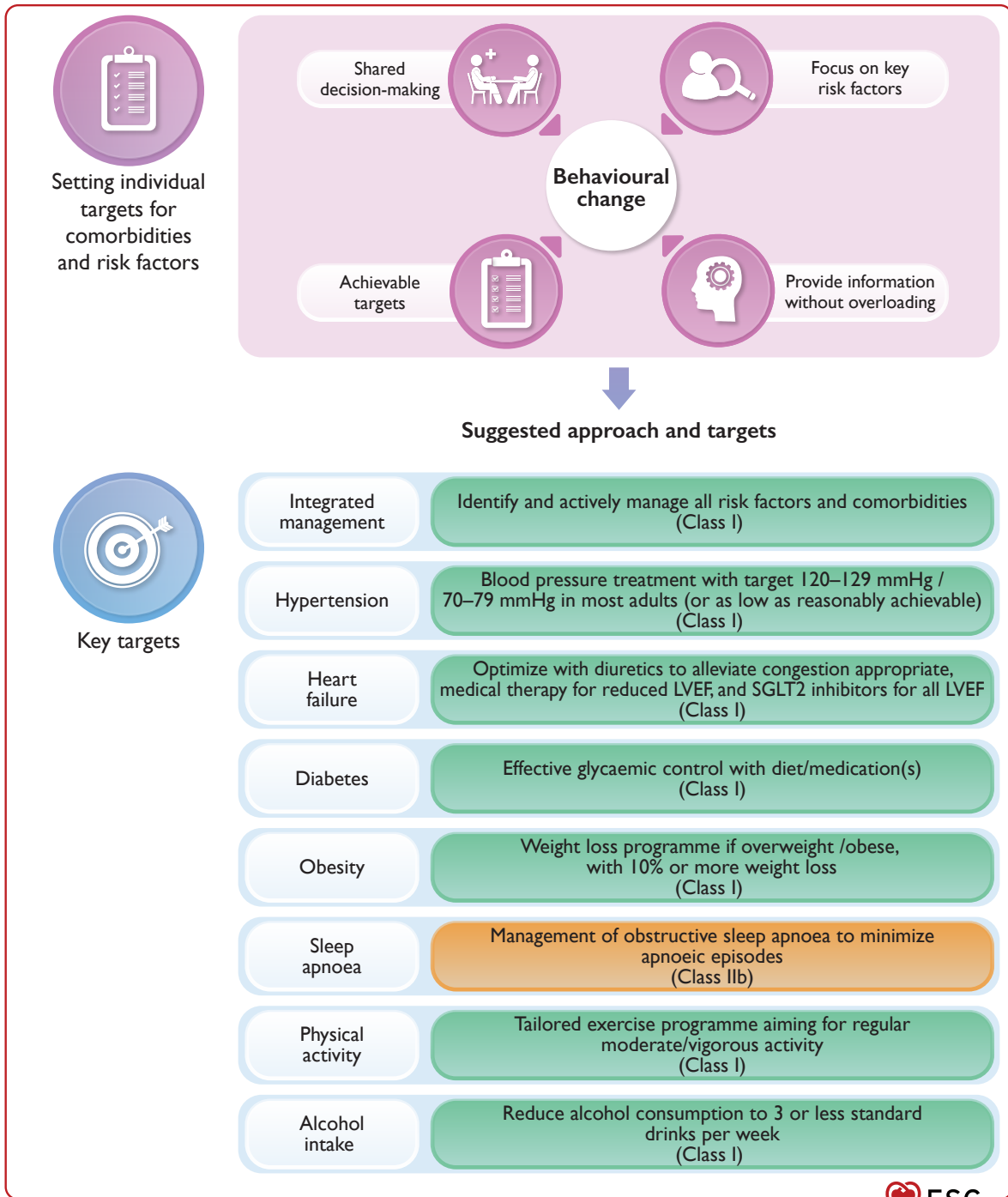


**Figure 7** [R] Pathway for patients with permanent AF. AF, atrial fibrillation; AF-CARE, Atrial fibrillation—[C] Comorbidity and risk factor management, [A] Avoid stroke and thromboembolism, [R] Reduce symptoms by rate and rhythm control, [E] Evaluation and dynamic reassessment; b.p.m., beats per minute; 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. <sup>a</sup>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 <sup>a</sup>	Level <sup>b</sup>
Identification and management of risk factors and comorbidities is recommended as an integral part of AF care. <sup>39,125–127</sup>	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. <sup>126–130</sup>	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. <sup>131–137</sup>	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. <sup>136,138–140</sup>	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. <sup>125–128</sup>	I	B
A tailored exercise programme is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence. <sup>141–146</sup>	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. <sup>126,127,147</sup>	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 <sup>2</sup> <sup>c</sup> 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. <sup>126–128,148–154</sup>	IIb	B
When screening for obstructive sleep apnoea in individuals with AF, using only symptom-based questionnaires is not recommended. <sup>155–157</sup>	III	B

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AF, atrial fibrillation; HF, heart failure; LVEF, left ventricular ejection fraction.

<sup>a</sup>Class of recommendation.<sup>b</sup>Level of evidence.<sup>c</sup>Or body mass index ≥35 kg/m<sup>2</sup> 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.<sup>158–161</sup>

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.<sup>162</sup> 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.<sup>129</sup>

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.<sup>163–171</sup> Optimal control of blood pressure should be considered an essential component of treating AF and undertaken within a strategy of comprehensive risk factor management.<sup>126–128</sup> 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.<sup>172–175</sup>

## 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.<sup>176,177</sup> 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.<sup>178</sup> Numerous cardiovascular and non-cardiovascular conditions impact the development of both AF and heart failure, leading to the common pathway of atrial cardiomyopathy.<sup>18</sup> In patients with acute heart failure attending the emergency department, AF is one of the most prevalent triggering factors of the episode.<sup>179</sup> The development of heart failure in patients with AF is associated with a two-fold increase in stroke and thromboembolism,<sup>180</sup> even after anticoagulation,<sup>181</sup> and 25% higher all-cause mortality.<sup>178</sup> 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.<sup>182</sup> 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<sup>183</sup> of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.<sup>137</sup> Achieving euvoalaemia 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,<sup>132,184</sup> and an individual patient-level analysis of RCTs found no

difference between beta-blockers and placebo for all-cause mortality in HFrEF with AF.<sup>133</sup> 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.<sup>48,185,186</sup> 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.<sup>134–136</sup> 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).<sup>187</sup> 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,<sup>137</sup> albeit with limited evidence to date in AF.<sup>188–190</sup> For treatment of HFpEF and AF,<sup>191</sup> pre-specified subgroup data on AF from multiple large trials show that the SGLT2 inhibitors dapagliflozin, empagliflozin, and sotagliflozin are effective in improving prognosis.<sup>138–140</sup>

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.<sup>39</sup> 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.<sup>192</sup>

### 5.3. Type 2 diabetes mellitus

Diabetes mellitus is present in around 25% of patients with AF.<sup>193–195</sup> Patients with both diabetes and AF have a worse prognosis,<sup>196</sup> 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.<sup>195,197</sup> Moreover, diabetes is a major factor influencing thromboembolic risk.<sup>198,199</sup> Following catheter ablation of AF, diabetes and higher HbA1c are associated with increased length of stay and a greater recurrence of AF.<sup>200–203</sup>

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.<sup>126–128</sup> However, robust evidence is limited, and individual glucose-lowering medications have had variable effects on AF.<sup>204–206</sup> 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.<sup>207</sup>

### 5.4. Obesity

Obesity frequently coexists with other risk factors that have been independently associated with the development of AF.<sup>208,209</sup> Obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>) and being overweight (BMI  $>25$  kg/m<sup>2</sup>) are associated with a greater risk of recurrent atrial arrhythmias after AF ablation (13% increase for every 5 kg/m<sup>2</sup> higher BMI).<sup>210–212</sup> 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<sup>2</sup>).<sup>125</sup> Cohort studies have also shown a graded response to maintenance of sinus rhythm,<sup>126</sup> improved ablation outcomes,<sup>128</sup> and reversal of the type of AF<sup>127</sup> 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.<sup>213</sup> 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.<sup>126</sup> Observational studies have raised the possibility of a point of no return in terms of the benefit of weight loss,<sup>214</sup> but also the possibility that bariatric surgery can improve symptoms and reduce AF recurrence.<sup>215–217</sup>

### 5.5. Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is a highly prevalent condition, particularly in patients with AF.<sup>157,218</sup> 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.<sup>155–157,219</sup> Questionnaires assessing daytime sleepiness are poor predictors of moderate-to-severe OSA.<sup>155</sup> 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.<sup>220,221</sup>

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.<sup>222</sup> Conversely, OSA patients treated with CPAP seem to mitigate their propensity toward developing AF.<sup>148–153,222–224</sup> A small randomized trial of CPAP vs. no therapy demonstrated reversal of atrial remodelling in individuals with moderate OSA.<sup>154</sup> However, other small RCTs have failed to show a benefit of CPAP therapy on ablation outcomes<sup>225</sup> or post-cardioversion.<sup>226</sup> Data on the cardiovascular mortality benefit of CPAP therapy in OSA are inconclusive.<sup>227–230</sup>

### 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.<sup>141</sup> Better cardiorespiratory fitness has a demonstrated inverse relationship to AF burden in both middle-aged and elderly people.<sup>141</sup> 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.<sup>142,143</sup> 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.<sup>141–145</sup>

## 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.<sup>231,232</sup> 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.<sup>233</sup> In patients receiving OAC, alcohol excess is associated with a greater risk of bleeding,<sup>234</sup> 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.<sup>147,235</sup> 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 ( $\leq 30$  grams or 3 standard drinks of alcohol) in the intervention arm, with 61% attaining abstinence.<sup>147</sup> In observational data of patients undergoing catheter ablation, reduction of consumption to  $\leq 7$  standard drinks ( $\leq 70$  grams of alcohol) per week was associated with improved maintenance of sinus rhythm.<sup>128,235</sup>

## 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.<sup>236,237</sup> 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.<sup>238</sup> 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.<sup>239,240</sup> Antiplatelet drugs alone (aspirin, or aspirin in combination with clopidogrel) are not recommended for stroke prevention in AF.<sup>241,242</sup>

#### 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<sub>2</sub> 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](#)).<sup>243–245</sup> 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,<sup>246</sup> and a lack of evidence from clinical trials on the ability of stroke risk scoring to enhance clinical practice.<sup>243</sup> 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.<sup>25–28,245</sup>

Substantive changes have occurred in the decades since these risk scores were developed in regards to population-level risk factor profiles, therapies, and targets.<sup>198</sup> 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,<sup>247–250</sup> and cohort data suggest a two-fold increased risk of ischaemic stroke and mortality in AF patients with CKD vs. without.<sup>251</sup> 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.<sup>70,252,253</sup> 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.<sup>254,255</sup> 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<sub>2</sub>DS<sub>2</sub>–VASc, giving points for congestive heart failure, hypertension, age  $\geq 75$  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.<sup>112,256,257</sup> The inclusion of gender complicates clinical practice both for healthcare professionals and patients.<sup>258</sup> 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<sub>2</sub>DS<sub>2</sub>–VASc; instead providing different score levels for women and men with AF to qualify for OAC. Hence, CHA<sub>2</sub>DS<sub>2</sub>–VA (excluding gender) has effectively been in place ([Table 10](#)).<sup>78</sup> This task force proposes, in the absence of other locally validated alternatives, that clinicians and patients should use the CHA<sub>2</sub>DS<sub>2</sub>–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,<sup>259</sup> NCT02387229<sup>260</sup>), OAC are recommended in those with a CHA<sub>2</sub>DS<sub>2</sub>–VA score of 2 or more and should be considered in those with a CHA<sub>2</sub>DS<sub>2</sub>–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 <sup>a</sup>	Level <sup>b</sup>
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. <sup>239,240</sup>	I	A
A CHA <sub>2</sub> DS <sub>2</sub> -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 <sub>2</sub> DS <sub>2</sub> -VA score, to prevent ischaemic stroke and thromboembolism. <sup>270–276</sup>	I	B
Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients. <sup>277–280</sup>	I	B

Continued

A CHA <sub>2</sub> DS <sub>2</sub> -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. <sup>281,282</sup>	IIb	B
Antiplatelet therapy is not recommended as an alternative to anticoagulation in patients with AF to prevent ischaemic stroke and thromboembolism. <sup>242,283</sup>	III	A
Using the temporal pattern of clinical AF (paroxysmal, persistent, or permanent) is not recommended to determine the need for oral anticoagulation. <sup>284,285</sup>	III	B

AF, atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

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**Table 10 Updated definitions for the CHA<sub>2</sub>DS<sub>2</sub>-VA score**

CHA <sub>2</sub> DS <sub>2</sub> -VA component	Definition and comments	Points awarded <sup>a</sup>
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%. <sup>261–263</sup>	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). <sup>162,264</sup>	1
A	Age 75 years or above Age is an independent determinant of ischaemic stroke risk. <sup>265</sup> 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, <sup>266</sup> 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. <sup>267</sup> OR Peripheral vascular disease, including: intermittent claudication, previous revascularization for PVD, percutaneous or surgical intervention on the abdominal aorta, and complex aortic plaque on imaging (defined as features of mobility, ulceration, pedunculation, or thickness ≥4 mm). <sup>268,269</sup>	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<sub>2</sub>DS<sub>2</sub>-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.

<sup>a</sup>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<sup>286</sup>; however, a phase 3 trial of asundexian was terminated early due to lack of efficacy against apixaban (NCT05643573), despite favourable phase 2 results.<sup>287</sup> 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,<sup>288,289</sup> but there are also some common cardiovascular and non-cardiovascular drugs that interact with DOACs.<sup>290,291</sup> [Figure 9](#) highlights common and major interactions to consider for VKAs and DOACs.

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



**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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>25–28,292–294</sup>	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. <sup>295–298</sup>	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. <sup>299–303</sup>	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. <sup>304–308</sup>	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. <sup>309</sup>	IIb	B
A reduced dose of DOAC therapy is not recommended, unless patients meet DOAC-specific criteria, <sup>c</sup> to prevent underdosing and avoidable thromboembolic events. <sup>310–312</sup>	III	B

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AF, atrial fibrillation; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; TTR, time in therapeutic range; VKA, vitamin K antagonist.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>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).<sup>25–28</sup> 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.<sup>292</sup> Post-marketing observational data on the effectiveness and safety of dabigatran,<sup>313,314</sup> rivaroxaban,<sup>315,316</sup> apixaban,<sup>317</sup> and edoxaban<sup>318</sup> 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.<sup>319–321</sup> 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.<sup>293</sup>

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,<sup>322</sup> confirmed in large-scale real-world data.<sup>323</sup> 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,<sup>324</sup> 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),<sup>325</sup> although specific dosing adjustments apply.<sup>25–28,326</sup> 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.<sup>327</sup> Dabigatran is more dependent on renal elimination and so is contraindicated with an estimated glomerular filtration rate <30 mL/min/1.73 m<sup>2</sup>. 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,<sup>328,329</sup> and one trial showing that rivaroxaban 10 mg led to significantly lower rates of cardiovascular events and major bleeding compared with VKA.<sup>330</sup> 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](#)).<sup>326</sup>

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.<sup>331</sup> 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.<sup>332</sup> 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.<sup>304,333,334</sup> 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.<sup>294</sup> 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,<sup>311</sup> but need to be avoided as they increase the risk of stroke without decreasing bleeding risk.<sup>310</sup> 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.<sup>335</sup> Drug interactions need to be considered in all patients taking or planned for DOACs (see [Figure 9](#) for common drug interactions).<sup>336</sup> 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.<sup>337,338</sup> Patients should always be involved in decision-making on anticoagulation,<sup>339</sup> 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: (i) age $\geq$ 80 years (ii) body weight $\leq$ 60 kg (iii) serum creatinine $\geq$ 133 mmol/L.	2.5 mg twice daily
Dabigatran	150 mg twice daily	Dose reduction recommended if any apply: (i) age $\geq$ 80 years (ii) receiving concomitant verapamil. Dose reduction considered on an individual basis if any apply: (i) age 75–80 (ii) moderate renal impairment (creatinine clearance 30–50 mL/min) (iii) patients with gastritis, oesophagitis, or gastro-oesophageal reflux (iv) others at increased risk of bleeding.	110 mg twice daily
Edoxaban	60 mg once daily	Dose reduction if any apply: (i) moderate or severe renal impairment (creatinine clearance 15–50 mL/min) (ii) body weight $\leq$ 60 kg (iii) concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole.	30 mg once daily
Rivaroxaban	20 mg once daily	Creatinine clearance 15–49 mL/min.	15 mg once daily

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).<sup>239</sup>

Vitamin K antagonists are still used in many patients worldwide, but prescriptions have declined sharply since the introduction of DOACs.<sup>340,341</sup> Vitamin K antagonists are currently the only treatment option in AF patients with mechanical heart valves or moderate-to-severe mitral valve stenosis.<sup>294,331</sup> 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).<sup>342</sup> 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.<sup>295–297,343</sup> However, VKAs are associated with higher rates of intracranial bleeding,<sup>299,300</sup> and also higher rates of other types of bleeding compared with DOACs.<sup>83</sup>

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 ( $\geq$ 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).<sup>309</sup> 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.<sup>282</sup> 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.<sup>281</sup> 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<sub>2</sub>DS<sub>2</sub>-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.<sup>344</sup> 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).<sup>345–347</sup> 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.<sup>348</sup> 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).<sup>242</sup>

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).<sup>349,350</sup> 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.<sup>349</sup> 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,<sup>351,352</sup> 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 <sup>a</sup>	Level <sup>b</sup>
Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism. <sup>345,347,353</sup>	III	B

AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>252,354</sup> One-third of patients with AF presenting with an ischaemic stroke are already on anticoagulation,<sup>355</sup> with heterogeneous aetiology.<sup>356</sup> 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.<sup>357</sup> 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.<sup>358</sup> 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.<sup>252,356,359</sup> 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.<sup>360,361</sup> Emerging, but observational evidence suggests that switching provides limited reduction in the risk of recurrent ischaemic stroke.<sup>252,356,359</sup> The alternative strategy of adding antiplatelet therapy to OAC may lead to an increased risk of bleeding.<sup>356,359</sup> Aside from thorough attention to underlying risk factors and comorbidities, 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>356,357</sup>	IIa	B
Adding antiplatelet treatment to anticoagulation is not recommended in patients with AF to prevent recurrent embolic stroke. <sup>356,359</sup>	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. <sup>252,356,359</sup>	III	B

AF, atrial fibrillation; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>362,363</sup> 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.<sup>364</sup> With DOACs demonstrating similar rates of major bleeding to aspirin,<sup>242</sup> 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.<sup>365</sup> 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.<sup>366,367</sup> Larger trials<sup>368,369</sup> 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](#)).<sup>370–372</sup> 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.<sup>373</sup> Observational studies have also supported the use of antiplatelet therapy without associated increases in device-related thrombosis or stroke.<sup>374–376</sup> 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.<sup>377</sup> While waiting for solid RCT data (NCT03445949, NCT03568890),<sup>378</sup> pertinent decisions on antithrombotic treatment are usually made on an individualized basis.<sup>379–381</sup> Prevention of recurrent stroke, in addition to OAC, is another potential indication for LAAO. Only limited data are so far available from registries,<sup>382</sup> 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.<sup>362,383–385</sup> Voluntary registries enrolling patients considered ineligible for OAC have reported low peri-procedural risk,<sup>372,376,386,387</sup> 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 ( $P < .001$ ).<sup>388</sup> Registries with new-generation devices report a lower complication rate compared with RCT data.<sup>389,390</sup> Device-related thrombi occur with an incidence of 1.7%–7.2% and are associated with a higher risk of ischaemic stroke.<sup>386,391–397</sup> 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.<sup>391</sup> 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.<sup>398</sup>

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

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

AF, atrial fibrillation; LAA, left atrial appendage.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>399,400</sup> 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;  $P = .001$ ).<sup>401</sup> 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.<sup>402</sup> 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.<sup>403</sup> 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).<sup>404</sup>

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.<sup>405</sup> A multidisciplinary team approach can facilitate the choice between epicardial or percutaneous LAA closure in such patients.<sup>406</sup> The majority of safety data and experience in epicardial LAA closure originate from a single clipping device (AtriClip)<sup>403,407,408</sup> (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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>400,401,408–412</sup>	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. <sup>402,403</sup>	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. <sup>399,405,406,413</sup>	IIb	C

AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

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## 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).<sup>414–418</sup> 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.<sup>419–421</sup> 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.<sup>422,423</sup> 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](#)).<sup>424</sup> Systematic reviews and validation studies in external cohorts have shown contrasting results and only modest predictive ability.<sup>244,425–434</sup> 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<sup>435</sup> or an intracerebral bleed related to cerebral amyloid angiopathy<sup>436</sup> 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,<sup>437</sup> 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).<sup>438</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>439–444</sup>	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. <sup>431,445,446</sup>	III	B

AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

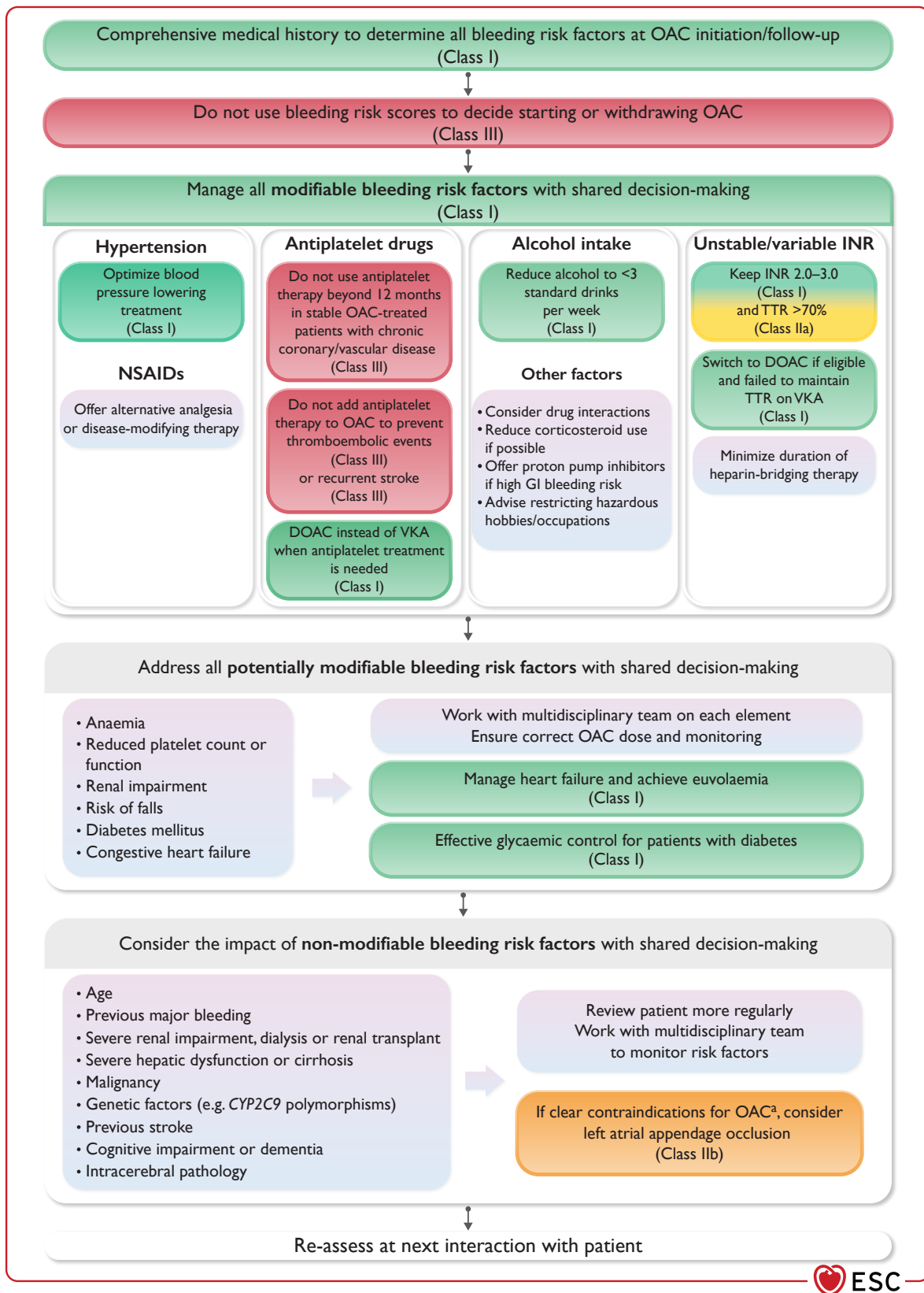
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### 6.7.2. Management of bleeding on anticoagulant therapy

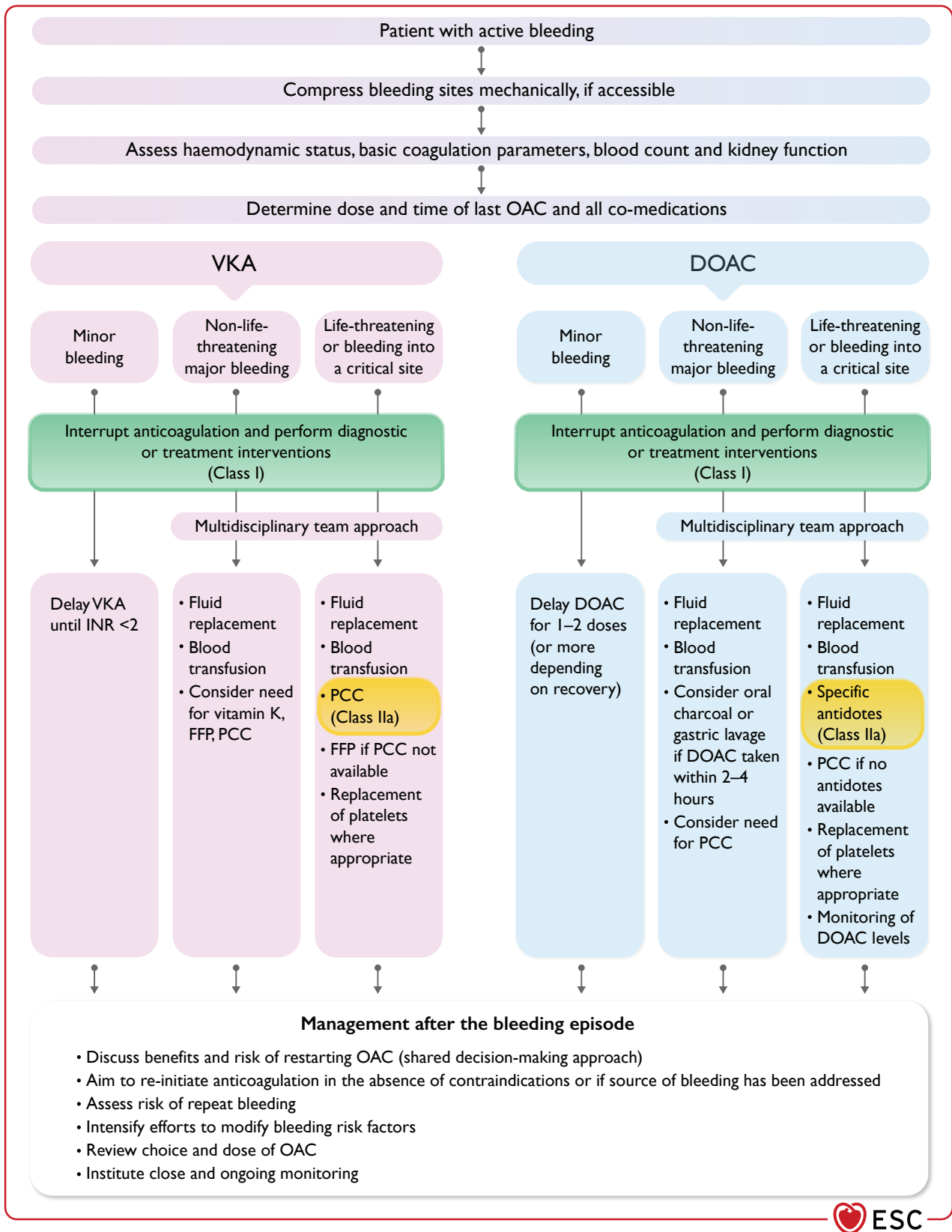
General management of bleeding in patients receiving OAC is outlined in Figure 11. Cause-specific management is beyond the scope of these guidelines, and will depend on the individual circumstances of the patient and the healthcare environment.<sup>447</sup> Assessment of patients with active bleeding 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.<sup>447–449</sup> 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 preferable to achieve haemostasis.<sup>450</sup> 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. <sup>a</sup>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.



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**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.<sup>451</sup> 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.<sup>452</sup> 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.<sup>453</sup>

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.<sup>335</sup>

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.<sup>454</sup> 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.<sup>335</sup>

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>450</sup>	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. <sup>451,455,456</sup>	IIa	B

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AF, atrial fibrillation; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>457</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>458–460</sup>	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. <sup>48,461,462</sup>	I	B
Beta-blockers and/or digoxin are recommended in patients with AF and LVEF ≤40% to control heart rate and reduce symptoms. <sup>40,185,463–465</sup>	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. <sup>459,460,466</sup>	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. <sup>467–469</sup>	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. <sup>470,471</sup>	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. <sup>472,473</sup>	IIb	B

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AF, atrial fibrillation; b.p.m., beats per minute; HF, heart failure; LVEF, left ventricular ejection fraction.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>186,459</sup> 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.<sup>474</sup> 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.<sup>462,475,476</sup> More selective beta-1 receptor blockers have a better efficacy and safety profile than unselective beta-blockers.<sup>477</sup> 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).<sup>177,478</sup> In selected patients who are haemodynamically unstable or with severely impaired LVEF, intravenous amiodarone, landiolol, or digoxin can be used.<sup>472,473,479</sup>

### 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).<sup>480</sup>

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.<sup>459</sup> Some antiarrhythmic drugs (AADs) also have rate-limiting properties (e.g. amiodarone, sotalol), but they should generally be used only for rhythm control. Dronedronarone should not be instituted for rate control since it increases rates of heart failure, stroke, and cardiovascular death in permanent AF.<sup>481</sup>

**Beta-blockers**, specifically beta-1 selective adrenoceptor 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.<sup>133,482</sup>

**Verapamil and diltiazem** are non-dihydropyridine calcium channel blockers. They provide rate control<sup>461</sup> and have a different adverse effect profile, making verapamil or diltiazem useful for those experiencing side effects from beta-blockers.<sup>483</sup> 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.<sup>480</sup>

**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.<sup>185,484</sup> Lower doses of digoxin may be associated with better prognosis.<sup>185</sup> Serum digoxin concentrations can be monitored to avoid toxicity,<sup>485</sup> 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.<sup>48</sup> Two ongoing RCTs are addressing digoxin and digitoxin use in patients with HFrEF with and without AF (EudraCT-2013-005326-38, NCT03783429).<sup>486</sup>

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

Agent <sup>a</sup>	Intravenous administration	Usual range for oral maintenance dose	Contraindicated
<b>Beta-blockers<sup>b</sup></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 <sup>c</sup>	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.
Digitoxin	0.4–0.6 mg	0.05–0.1 mg once daily	Check renal function before starting digoxin and adapt dose in CKD patients.
Other			
Amiodarone <sup>d</sup>	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.

<sup>a</sup>All rate control drugs are contraindicated in Wolff–Parkinson–White syndrome; also intravenous amiodarone.

<sup>b</sup>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).

<sup>c</sup>No data on atenolol; should not be used in heart failure with reduced ejection fraction or in pregnancy.

<sup>d</sup>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.<sup>487</sup>

### 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.<sup>468,488</sup> 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.<sup>489,490</sup> This strategy does not worsen LV function,<sup>491</sup> and may even improve LVEF in selected patients.<sup>492,493</sup> 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.<sup>187,494</sup>

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).<sup>470,471</sup> 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.<sup>495,496</sup> In CRT recipients, the presence (or occurrence) of AF is one of the main reasons for suboptimal biventricular pacing.<sup>187</sup> 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.<sup>187</sup>

## 7.2. Rhythm control strategies in patients with AF

### 7.2.1. General principles and anticoagulation

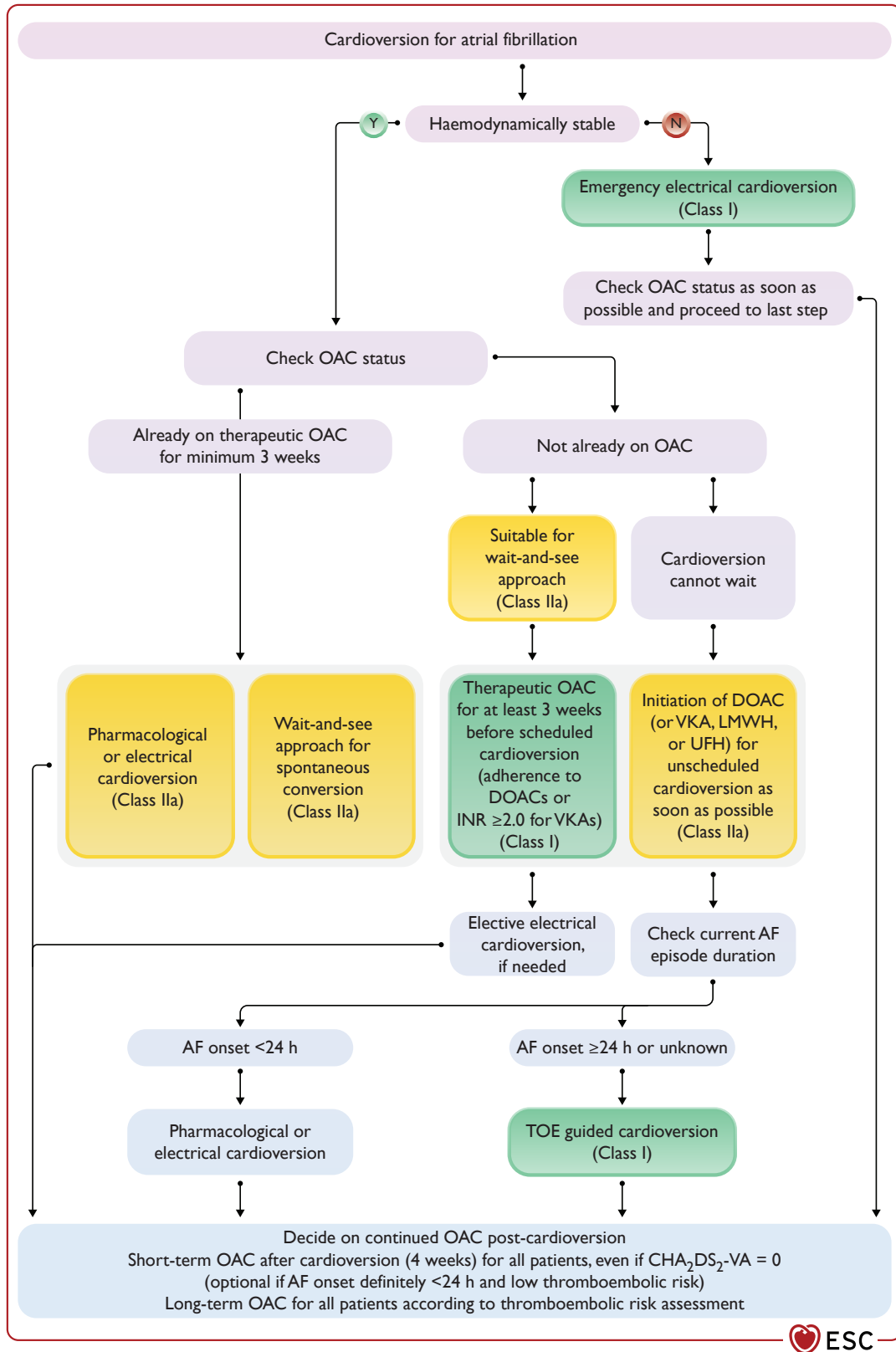
Rhythm control refers to therapies dedicated to restoring and maintaining sinus rhythm. These treatments include cardioversion, AADs, percutaneous catheter ablation, endoscopic and hybrid ablation, and open surgical approaches (see [Supplementary data online, Additional Evidence Table S17](#)). Rhythm 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.<sup>10</sup>

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.<sup>497–500</sup> 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,<sup>497–500</sup> and may increase hospitalization.<sup>457</sup> In contrast, multiple studies have shown that rhythm control strategies have a positive effect on quality of life once sinus rhythm is maintained.<sup>501,502</sup> 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,<sup>17</sup> consistent use of OAC, improvements in ablation technology,<sup>503–509</sup> and identification and management of risk factors and comorbidities.<sup>39,510,511</sup> 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





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**Figure 12** Approaches for cardioversion in patients with AF. AF, atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-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. <sup>a</sup>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.<sup>512</sup> 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.<sup>4</sup> 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.<sup>513</sup> 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.<sup>3</sup> 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.<sup>17</sup> 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.<sup>4,17,502,513,514</sup>

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.<sup>319–321</sup> 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.<sup>515–519</sup> 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 <sup>a</sup>	Level <sup>b</sup>
Electrical cardioversion is recommended in AF patients with acute or worsening haemodynamic instability to improve immediate patient outcomes. <sup>520</sup>	I	C
Direct oral anticoagulants are recommended in preference to VKAs in eligible patients with AF undergoing cardioversion for thromboembolic risk reduction. <sup>293,319–321,521</sup>	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. <sup>319–321</sup>	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. <sup>319–321,522</sup>	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. <sup>239,319,320,523,524</sup>	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. <sup>52,525,526</sup>	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. <sup>10,525</sup>	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. <sup>17,527</sup>	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. <sup>319–321,528</sup>	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. <sup>529</sup>	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. <sup>522</sup>	III	C

AF, atrial fibrillation; DOAC, direct oral anticoagulant; INR, international normalized ratio of prothrombin time; VKA, vitamin K antagonist.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>530</sup> Structured and integrated care for patients with acute-onset AF at the emergency department is associated with better outcomes without compromising safety.<sup>531</sup> Rates of major adverse clinical events after cardioversion are significantly lower with DOACs compared with warfarin.<sup>293</sup>

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.<sup>532–534</sup> 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.<sup>535</sup> 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.<sup>536</sup> A randomized trial showed that maximum fixed-energy shocks were more effective than low-escalating energy for ECV.<sup>537</sup>

Immediate administration of vernakalant,<sup>538</sup> or pre-treatment for 3–4 days with flecainide,<sup>539,540</sup> ibutilide,<sup>541,542</sup> propafenone,<sup>543</sup> or amiodarone<sup>544–546</sup> improves the rate of successful ECV and can facilitate long-term maintenance of sinus rhythm by preventing early recurrent AF.<sup>547</sup> 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.<sup>546</sup>

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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>548</sup>	IIa	C

AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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,<sup>549</sup> with timing of cardioversion being a significant determinant of success.<sup>550</sup> 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).<sup>10,119,445,551–555</sup>

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).<sup>556</sup> Pharmacological cardioversion does not require fasting, sedation, or anaesthesia. Anticoagulation should be started or continued according to a formal (re-)assessment of thromboembolic risk.<sup>554,557–559</sup>

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.<sup>560</sup> 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.<sup>561</sup>

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>562–566</sup>	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. <sup>562–568</sup>	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. <sup>473,569,570</sup>	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. <sup>560,571–573</sup>	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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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)	<ul style="list-style-type: none"> <li>• Should not be used in patients with severe structural or coronary artery disease, Brugada syndrome, or severe renal failure (CrCl &lt;35 mL/min/1.73 m<sup>2</sup>).</li> <li>• Prior documentation of safety and efficacy in an inpatient setting is recommended prior to pill-in-the-pocket use.</li> <li>• An AVN-blocking agent should be administered to avoid 1:1 conduction if transformation to AFL.</li> <li>• Drug infusion should be discontinued in case of QRS widening &gt;25% or bundle branch block occurrence.</li> <li>• Caution is needed in patients with sinus node disease and AVN dysfunction.</li> <li>• Do NOT use for conversion of atrial flutter.</li> </ul>
	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)	<ul style="list-style-type: none"> <li>• May cause phlebitis (use a large peripheral vein, avoid i.v. administration &gt;24 h and use preferably volumetric pump).</li> <li>• May cause hypotension, bradycardia/atrioventricular block, QT prolongation.</li> <li>• Only if no other option in patients with hyperthyroidism (risk of thyrotoxicosis).</li> <li>• Consider the broad range of drug interactions.</li> </ul>
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)	<ul style="list-style-type: none"> <li>• Should be used in the setting of a cardiac care unit as it may cause QT prolongation and torsades de pointes.</li> <li>• ECG monitoring for at least 4 h after administration to detect any proarrhythmic effects.</li> <li>• Should not be used in patients with prolonged QT, severe LVH, or low LVEF.</li> </ul>
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	<ul style="list-style-type: none"> <li>• Should not be used in patients with arterial hypotension (SBP &lt;100 mmHg), recent ACS (within 1 month), NYHA III or IV HF, QT prolongation or severe aortic stenosis.</li> <li>• May cause arterial hypotension, QT prolongation, QRS widening, or non-sustained ventricular tachycardia.</li> </ul>

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 sotalolol 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](#)).<sup>17,445,574,575</sup> 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.<sup>39,128</sup> 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).<sup>39</sup> The selection of an AAD for long-term rhythm control requires careful evaluation that takes into account AF type, patient parameters, and safety profile.<sup>445</sup> 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.<sup>17</sup>

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.<sup>576,577</sup> When one AAD fails to reduce AF recurrences, a clinically acceptable response may be achieved with another drug, particularly if from a different class.<sup>578</sup> 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<sup>574,579,580</sup> and amiodarone.<sup>581</sup> In contrast, use of AADs within a rhythm control strategy can be associated with reduction of morbidity and mortality in selected patients.<sup>582</sup>

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](#).<sup>577,583,584</sup>

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>577,585–587</sup>	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. <sup>512,577,588,589</sup>	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. <sup>526,577,585,590</sup>	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

*Continued*

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. <sup>585,587</sup>	IIb	A
Antiarrhythmic drug therapy is not recommended in patients with advanced conduction disturbances unless antibradycardia pacing is provided.	III	C

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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>503–509</sup> 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](#)).<sup>15,16,591–594</sup> 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.<sup>595–598</sup>

Pulmonary vein isolation (PVI) remains the cornerstone of AF catheter ablation,<sup>503,508,593,599</sup> but the optimal ablation strategy has not been clarified in the non-paroxysmal AF population.<sup>600</sup> 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.<sup>601</sup> 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.<sup>602</sup>

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.<sup>3</sup> 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.<sup>4,603</sup> Randomized trials have shown that AF catheter ablation in patients with HFpEF significantly reduces arrhythmia recurrence and increases ejection fraction, with improvement in clinical outcomes and mortality also observed in selected patients.<sup>4,513,514,604–612</sup> 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.<sup>604,608,613–617</sup> The prognostic value of catheter ablation in patients with HFpEF is less well established than for HFrEF.<sup>617–626</sup>

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.<sup>627–631</sup>

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.<sup>632,633</sup> In addition, implantable loop recorders have been used to quantify AF burden before and after ablation as an additional endpoint beyond binary AF elimination.<sup>634</sup> 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.<sup>635</sup> A short-term AAD treatment (2–3 months) following ablation reduces early recurrences of AF,<sup>554,635–639</sup> but does not affect late recurrences<sup>636,637,640–642</sup> or 1 year clinical outcomes.<sup>642</sup> 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.<sup>643–645</sup>

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Shared decision-making</b>		
Shared decision-making is recommended when considering catheter ablation for AF, taking into account procedural risks, likely benefits, and risk factors for AF recurrence. <sup>128,210,503,646</sup>	I	C
<b>AF patients resistant or intolerant to antiarrhythmic drug therapy</b>		
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. <sup>3,15,503,505,506,508</sup>	I	A
<b>First-line rhythm control therapy</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. <sup>16,591–594</sup>	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

Continued

<b>Patients with heart failure</b>		
AF catheter ablation is recommended in patients with AF and HFrEF with high probability of tachycardia-induced cardiomyopathy to reverse left ventricular dysfunction. <sup>604,611</sup>	I	B
AF catheter ablation should be considered in selected AF patients with HFrEF to reduce HF hospitalization and prolong survival. <sup>4,513,514,604,610,612</sup>	IIa	B
<b>Sinus node disease/tachycardia–bradycardia syndrome</b>		
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. <sup>595–598</sup>	IIa	C
<b>Recurrence after catheter ablation</b>		
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. <sup>643–645</sup>	IIa	B

AF, atrial fibrillation; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; PVI, pulmonary vein isolation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

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**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.<sup>554,647</sup>

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).<sup>554,648</sup> 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.<sup>649,650</sup> 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.<sup>650</sup> 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,<sup>651–653</sup> 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](#)).<sup>654–656</sup> Patients with interrupted OAC showed an increase in silent stroke detected by brain magnetic resonance imaging (MRI) as compared with those with uninterrupted OAC.<sup>657–659</sup> 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.<sup>655</sup>

Anticoagulation with heparin during AF ablation is common practice.<sup>554</sup> Post-ablation DOACs should be continued as per the dosing regimen when haemostasis has been achieved.<sup>335,554,647</sup> 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](#)).<sup>647</sup> 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.<sup>660–663</sup> 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<sub>2</sub>DS<sub>2</sub>-VA score and not the perceived success of the ablation procedure.<sup>554</sup>

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>554,647</sup>	I	C
Uninterrupted oral anticoagulation is recommended in patients undergoing AF catheter ablation to prevent peri-procedural ischaemic stroke and thromboembolism. <sup>664,665</sup>	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 <sub>2</sub> DS <sub>2</sub> -VA score, to reduce the risk of peri-procedural ischaemic stroke and thromboembolism. <sup>554,663</sup>	I	C
Continuation of oral anticoagulation is recommended after AF ablation according to the patient's CHA <sub>2</sub> DS <sub>2</sub> -VA score, and not the perceived success of the ablation procedure, to prevent ischaemic stroke and thromboembolism. <sup>554</sup>	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. <sup>649,650</sup>	Ila	B

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AF, atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>666,667</sup>

For paroxysmal AF, an endoscopic or hybrid ablation approach may be considered after a failed percutaneous catheter ablation strategy.<sup>668–670</sup> 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.<sup>669</sup> For persistent AF, endoscopic or hybrid ablation approaches are suitable as a first procedure to maintain long-term sinus rhythm in selected patients.<sup>667–672</sup> 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).<sup>669</sup> 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.<sup>673</sup> 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.<sup>667,669</sup>

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<sup>670</sup> and two multicentre RCTs.<sup>671,674</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>667–671,674</sup>	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. <sup>668,669</sup>	IIb	B

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AAD, antiarrhythmic drugs; AF, atrial fibrillation; LAA, left atrial appendage.

<sup>a</sup>Class of recommendation.<sup>b</sup>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.<sup>675–677</sup> 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 cryotherapy ablation with LAA amputation (see [Supplementary data online, Additional Evidence Table S25](#)).<sup>678–681</sup> Education and training, close co-operation within a multidisciplinary team, and shared decision-making can improve the quality and outcomes of surgical ablation.<sup>682</sup>

A number of RCTs have shown that surgical AF ablation during cardiac surgery increases freedom from arrhythmia recurrence.<sup>683–688</sup> Performing surgical AF ablation, mainly targeting those patients needing mitral valve surgery, is not associated with increased morbidity or mortality.<sup>678,683–685</sup> Observational data, including large registries, have supported the potential value of surgical AF ablation,<sup>689–700</sup> 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).<sup>701</sup> 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.<sup>702</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>683–685,701</sup>	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. <sup>701,703–707</sup>	IIa	B

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AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.<sup>b</sup>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.<sup>708</sup> 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.<sup>709</sup> 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.<sup>710,711</sup> 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.<sup>712</sup> 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.<sup>713</sup> For co-ordination of care there is a core role for cardiologists, general practitioners, specialized nurses, and pharmacists.<sup>714</sup> 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 coordinates 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,<sup>715,716</sup> while others are nurse-led<sup>79,122,124,717</sup> or cardiologist-led.<sup>79,122,124,717</sup> Several published models used computerized decision support systems or electronic health applications.<sup>79,122,715,718</sup> 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.<sup>121–123</sup> However, the



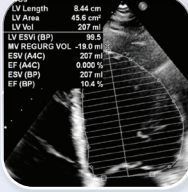

RACE 4 (IntegRATED Chronic Care Program at Specialized AF Clinic Versus Usual CarE in Patients with Atrial Fibrillation) trial, which included 1375 patients, failed to demonstrate superiority of nurse-led over usual care.<sup>79</sup> New studies of the components and optimal models for delivery for 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.<sup>719</sup> 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.<sup>720</sup> 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.<sup>721,722</sup> 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](#)).<sup>723–725</sup> 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.<sup>59,67,726</sup> 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.<sup>723,727</sup> 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](#)).<sup>59,724,725,728</sup> 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.<sup>729–731</sup>

AF-CARE pathway	Objective for imaging	Assessment	Example of pathology
<b>C</b> Comorbidity and risk factor management	To identify comorbidities which are associated with recurrence and progression of AF	Left ventricular ejection fraction, wall motion abnormalities, diastolic indices, right ventricular function and left ventricular hypertrophy to determine subtype and aetiology of heart failure Detection of pericardial fluid or pericardial disease Detection of valvular disease	<b>Cardiac amyloid</b> 
<b>A</b> Avoid stroke and thromboembolism	To determine stroke risk, choice of anticoagulant drug and ensure safety for cardioversion	Detection of heart failure for CHA <sub>2</sub> DS <sub>2</sub> -VA score Detection of moderate-severe mitral stenosis to determine choice of anticoagulation Transoesophageal echocardiogram for left atrial appendage assessment to exclude thrombus prior to cardioversion	<b>Clot in LAA</b> 
<b>R</b> Reduce symptoms by rate and rhythm control	To determine optimal choice of rate and rhythm control strategy and likely success of ablation	Left ventricular ejection fraction to determine choice of rate control Severity of valvular disease to determine choice of rhythm control Left ventricular size and function to determine choice of rhythm control Left atrial size and function to determine risk of arrhythmia recurrence following ablation	<b>Severe LV impairment</b> 
<b>E</b> Evaluation and dynamic reassessment	To detect changes in the patient's heart structure and function which would affect their management plan	Reassess known valve disease for increase in severity Reassess left ventricular size and function if there is a change in the patient's clinical status or symptoms	<b>Mixed mitral valve disease</b> 

**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<sub>2</sub>DS<sub>2</sub>-VA, congestive heart failure, hypertension, age  $\geq 75$  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.<sup>732</sup> 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](#)).<sup>36</sup> Patient-reported outcome measures are valuable to measure quality of life, functional status, symptoms, and treatment burden for patients

with AF over time.<sup>55,733–735</sup> Patient-reported outcome measures are playing an increasing role in clinical trials to assess the success of treatment; however, they remain under-utilized.<sup>736,737</sup> They can be divided into generic or disease-specific tools, with the latter helping to provide insight into AF-related impacts.<sup>738</sup> 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.<sup>48</sup> Intervention studies have demonstrated an association between improvement in PROM scores and reduction in AF burden and symptoms.<sup>48,738</sup>

Atrial fibrillation-specific questionnaires include the AF 6 (AF6),<sup>739</sup> Atrial Fibrillation Effect on Quality-of-Life (AFEQT),<sup>740</sup> the Atrial Fibrillation Quality of Life Questionnaire (AFQLQ),<sup>741</sup> the Atrial Fibrillation Quality of Life (AF-QoL),<sup>742</sup> and the Quality of Life in Atrial Fibrillation (QLAF).<sup>743</sup> The measurement properties of most of these tools lack sufficient validation.<sup>49</sup> 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.<sup>744</sup> 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.<sup>49–55</sup>

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

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

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AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>551,745</sup>

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.<sup>746</sup> Amiodarone is a second-line option because of its delayed activity; however, it may be an appropriate alternative in the acute setting.<sup>747,748</sup> 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.<sup>749</sup> 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.<sup>477,750,751</sup>

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

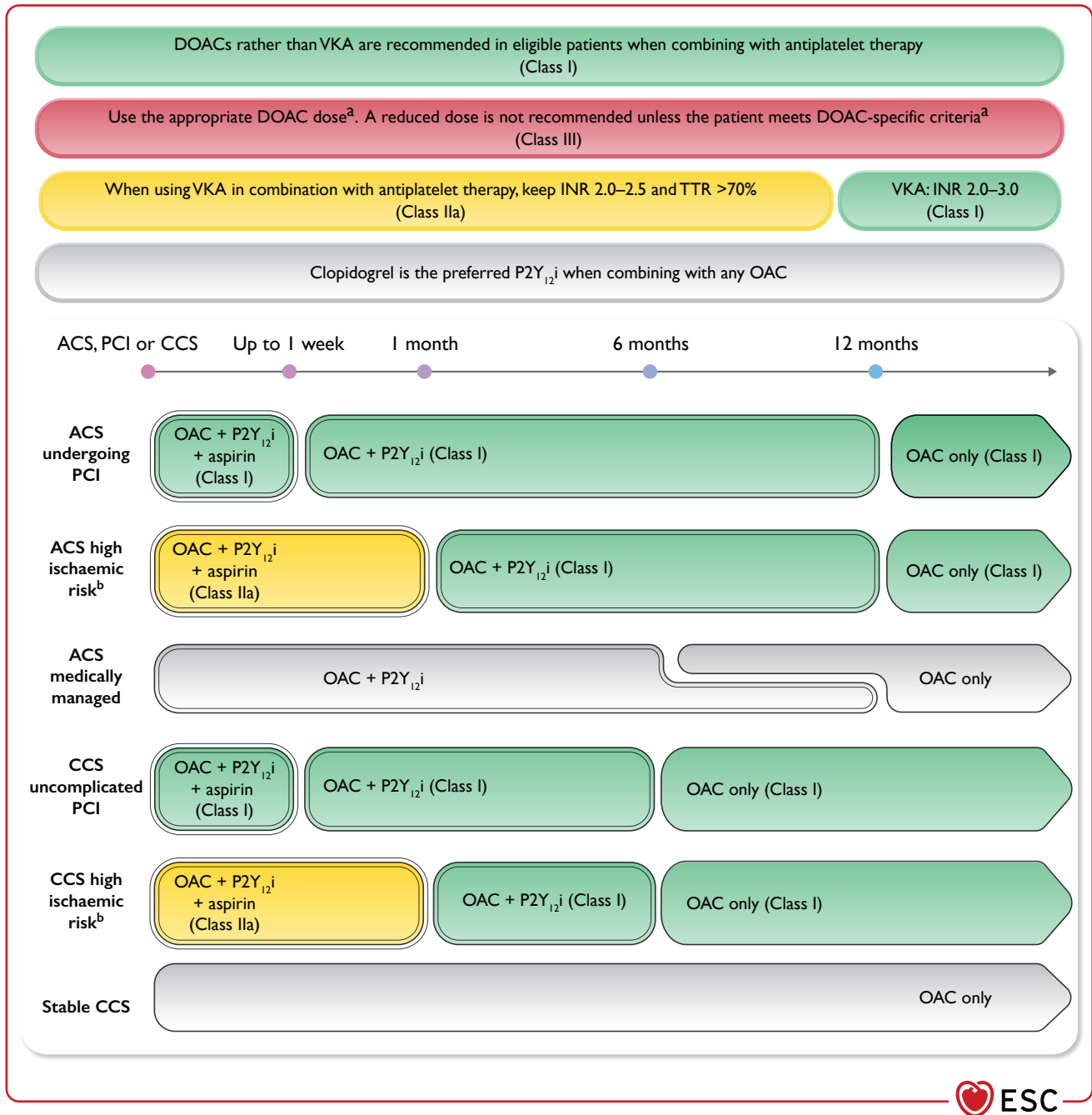
The incidence of AF in acute coronary syndromes (ACS) ranges from 2% to 23%.<sup>752</sup> The risk of new-onset AF is increased by 60%–77% in patients suffering an MI,<sup>753</sup> and AF may be associated with an increased risk of ST-segment elevation myocardial infarction (STEMI) or non-STEMI ACS.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

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.<sup>761,762</sup> 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<sub>12</sub> 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<sub>12</sub> inhibitor results in less major bleeding than triple therapy that includes aspirin. Clopidogrel is the preferred P2Y<sub>12</sub> inhibitor, as the evidence for ticagrelor and prasugrel is less clear with higher bleeding risk.<sup>763–769</sup> 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.<sup>761,762,770–772</sup> 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<sub>12</sub> inhibitor for a median time of 6 days.<sup>773</sup> At the end of the trial, apixaban and a P2Y<sub>12</sub> 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.<sup>774,775</sup>

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.<sup>776</sup> 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.<sup>207</sup>



**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<sub>12</sub>i, P2Y<sub>12</sub>-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. <sup>a</sup>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). <sup>b</sup>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.<sup>760,764,774</sup> 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.<sup>353</sup> 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.<sup>437,777–779</sup> 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 <sup>a</sup>	Level <sup>b</sup>
<b>General recommendations for patients with AF and an indication for concomitant antiplatelet therapy</b>		
For combinations with antiplatelet therapy, a DOAC is recommended in eligible patients in preference to a VKA to mitigate bleeding risk and prevent thromboembolism. <sup>764,766</sup>	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. <sup>765</sup>	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. <sup>766</sup>	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
<b>Recommendations for AF patients with ACS</b>		
Early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant (preferably DOAC) with a P2Y <sub>12</sub> 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. <sup>764–767</sup>	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. <sup>776</sup>	IIa	C

Continued

<b>Recommendations for AF patients undergoing PCI</b>		
After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of an oral anticoagulant and a P2Y <sub>12</sub> inhibitor (preferably clopidogrel) for up to 6 months is recommended to avoid major bleeding, if ischaemic risk is low. <sup>763–766,776,780</sup>	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. <sup>776</sup>	IIa	B
<b>Recommendations for AF patients with chronic coronary or vascular disease</b>		
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. <sup>353,781,782</sup>	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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>783,784</sup> Manifest PAD is associated with incident AF.<sup>785</sup> PAD predicts a higher mortality in patients with AF and is an independent predictor of stroke in those not on OAC.<sup>783,786</sup> Patients with lower extremity artery disease and AF also have a higher overall mortality and risk of major cardiac events.<sup>784,787,788</sup> 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.<sup>784</sup> 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).<sup>789</sup>

Anticoagulation alone is usually sufficient in the chronic disease phase, with DOACs being the preferred agents despite one RCT sub-analysis showing a higher risk of bleeding as compared with warfarin.<sup>790</sup> 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<sup>791</sup> and 90 days for neuro-interventional procedures).<sup>792</sup>

**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.<sup>793</sup>

### 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.<sup>794</sup>

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).<sup>795</sup> 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 ( $\leq 4$  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%).<sup>796</sup> 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;  $P = .90$ ).<sup>797</sup> 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 ( $\geq 1$  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.<sup>798</sup>

Until additional trials report on the clinical challenge of post-ICH anticoagulation (NCT03950076, NCT03996772), an individualized multi-disciplinary 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.<sup>11–14</sup> The degree of inflammation correlates with the incidence of AF,<sup>799</sup> 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.<sup>12,800–807</sup> In addition to other acute triggers which may be causal (such as alcohol<sup>808,809</sup> and illicit drug use<sup>810</sup>), 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.<sup>811,812</sup> In the acute phase of sepsis, patients show an unclear risk–benefit profile with anticoagulation therapy.<sup>813,814</sup> Prospective studies on anticoagulation in patients with triggered AF episodes are lacking.<sup>802,812,815</sup> 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**

<b>Acute conditions</b>
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)
<b>Chronic conditions with inflammation and enhanced AF substrate</b>
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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>13,800,806,807,815</sup>	IIa	C

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AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.<sup>b</sup>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,<sup>816–818</sup> 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.<sup>819</sup> Although POAF episodes may be self-terminating, POAF is associated with 4–5 times increase in recurrent AF during the next 5 years,<sup>820,821</sup> and is a risk factor for stroke, MI, heart failure, and death.<sup>822–827</sup> Other adverse events associated with POAF include haemodynamic instability, prolonged hospital stay, infections, renal complications, bleeding, increased in-hospital death, and greater healthcare cost.<sup>828–830</sup>

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-acetylcysteine in cardiac and non-cardiac surgery is associated with a reduced incidence of POAF,<sup>831–834</sup> but not major adverse events.<sup>835</sup> 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).<sup>836</sup> Prevention of peri-operative AF can also be achieved with amiodarone. In a meta-analysis, amiodarone (oral or intravenous [i.v.]) and beta-blockers were equally effective in reducing post-operative AF,<sup>837</sup> but their combination was better than beta-blockers alone.<sup>838</sup> Lower cumulative doses of amiodarone (<3000 mg during the loading phase) could be effective, with fewer adverse events.<sup>837,839,840</sup> Withdrawal of beta-blockers should be avoided due to increased risk of POAF.<sup>841</sup> Other treatment strategies (steroids, magnesium, sotalol, (bi)atrial pacing, and botulinum injection into the epicardial fat pad) lack scientific evidence for the prevention of peri-operative AF.<sup>842,843</sup> 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;  $P = .0005$ ).<sup>844–846</sup> 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;  $P = .22$ ).<sup>847</sup>

The evidence for prevention of ischaemic stroke in POAF by OAC is limited.<sup>822,827</sup> Oral anticoagulant therapy is associated with a high

bleeding risk soon after cardiac surgery or major non-cardiac interventions.<sup>827</sup> Conversely, meta-analyses of observational cohort studies suggest a possible protective impact of OAC in POAF for all-cause mortality<sup>848</sup> and a lower risk of thromboembolic events following cardiac surgery, accompanied by higher rates of bleeding.<sup>849</sup> 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 <sup>a</sup>	Level <sup>b</sup>
Peri-operative amiodarone therapy is recommended where drug therapy is desired to prevent post-operative AF after cardiac surgery. <sup>838,839,850,851</sup>	I	A
Concomitant posterior peri-cardiotomy should be considered in patients undergoing cardiac surgery to prevent post-operative AF. <sup>845,846</sup>	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. <sup>811,852–854</sup>	IIa	B
Routine use of beta-blockers is not recommended in patients undergoing non-cardiac surgery for the prevention of post-operative AF. <sup>836,855</sup>	III	B

AF, atrial fibrillation.

<sup>a</sup>Class of recommendation.<sup>b</sup>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.<sup>856</sup> Of note, these patients have a recurrent risk of stroke of 4%–5% per year.<sup>856</sup> 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.<sup>856</sup> AF is reported to be the underlying mechanism in 30% of ESUS patients.<sup>857–859</sup> The detection of AF among ESUS patients increases the longer cardiac monitoring is provided (see [Supplementary data online, Additional Evidence Table S29](#)).<sup>857,860–864</sup> 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.<sup>865</sup> In patients with ESUS, factors associated with an increased detection of AF are increasing age,<sup>866,867</sup> left atrial enlargement,<sup>866</sup> cortical location of stroke,<sup>868</sup> large or small vessel disease,<sup>863</sup> an increased number of

atrial premature beats per 24 h,<sup>868</sup> rhythm irregularity,<sup>859</sup> and risk stratification scores (such as CHA<sub>2</sub>DS<sub>2</sub>-VASc,<sup>869</sup> Brown ESUS-AF,<sup>870</sup> HAVOC,<sup>871</sup> and C<sub>2</sub>HEST<sup>872</sup>). This task force recommends prolonged monitoring depending on the presence of the above-mentioned risk markers.<sup>865,873,874</sup>

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.<sup>875–877</sup> 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 <sup>a</sup>	Level <sup>b</sup>
Prolonged monitoring for AF is recommended in patients with ESUS to inform on AF treatment decisions. <sup>861–863</sup>	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. <sup>875,876</sup>	III	A

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AF, atrial fibrillation; ESUS, embolic stroke of undetermined source.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>878–881</sup> 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.<sup>882</sup> A multidisciplinary approach is essential to prevent maternal and foetal complications, bringing together gynaecologists, neonatologists, anaesthesiologists, and cardiologists experienced in maternal medicine.<sup>883</sup>

Pregnancy is associated with a hypercoagulable state and increased thromboembolic risk.<sup>884</sup> 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*.<sup>885</sup> 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.<sup>886</sup> However, an accidental exposure during pregnancy should not lead to a recommendation for termination of the pregnancy.<sup>887</sup> Vaginal delivery should be advised for most women, but is contraindicated during VKA treatment because of the risk of foetal intracranial bleeding.<sup>885</sup>

Intravenous selective beta-1 receptor blockers are recommended as first choice for acute heart rate control of AF.<sup>888</sup> This does not include atenolol, which can lead to intrauterine growth retardation.<sup>889</sup> 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.<sup>885</sup> In haemodynamically stable women without structural heart disease, intravenous ibutilide or flecainide may be considered for termination of AF, but experience is limited.<sup>890</sup> Catheter ablation is normally avoided during pregnancy,<sup>883</sup> but is technically feasible without radiation in refractory symptomatic cases with a minimal/zero fluoroscopy approach.<sup>883</sup>

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 <sup>a</sup>	Level <sup>b</sup>
Immediate electrical cardioversion is recommended in patients with AF during pregnancy and haemodynamic instability or pre-excited AF to improve maternal and foetal outcomes. <sup>885,891–893</sup>	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. <sup>885</sup>	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. <sup>888</sup>	I	C
Electrical cardioversion should be considered for persistent AF in pregnant women with HCM to improve maternal and foetal outcomes. <sup>885,894</sup>	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. <sup>885</sup>	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. <sup>895,896</sup>	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. <sup>885</sup>	IIb	C

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AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; LMWH, low molecular weight heparin; VKA, vitamin K antagonist.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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 anti-coagulants 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.<sup>897</sup> 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<sub>2</sub>DS<sub>2</sub>-VA score). Direct oral anticoagulants are contraindicated in patients with mechanical heart valves,<sup>331</sup> but appear safe in patients with congenital heart disease,<sup>898,899</sup> or those with a valvular bioprosthesis.<sup>900,901</sup>

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.<sup>902,903</sup> 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.<sup>904</sup> Patients with stroke who underwent closure of their PFO may have an increased risk of AF,<sup>905</sup> 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.<sup>906–908</sup> AF catheter ablation of late atrial arrhythmias is likely to be effective after surgical atrial septal closure.<sup>909</sup>

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

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>897</sup>	IIa	C

AF, atrial fibrillation; AFL, atrial flutter.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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.<sup>910,911</sup>

Clinical and subclinical hyperthyroidism, as well as subclinical hypothyroidism, are associated with an increased risk of AF.<sup>912,913</sup> 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,<sup>914,915</sup> as well as cancer patients on immune checkpoint inhibitors.<sup>916,917</sup> In hyperthyroidism, and even in the euthyroid range, the risk of AF increases according to the reduction in TSH and elevated levels of thyroxine.<sup>918,919</sup> Moreover, the risk of stroke is higher in patients with hyperthyroidism, which can be mitigated by treating the thyroid disorder.<sup>920,921</sup> Amiodarone induces thyroid dysfunction in 15%–20% of treated patients, leading to both hypo- and hyperthyroidism,<sup>922,923</sup> 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.<sup>924–926</sup> Primary aldosteronism is related to an increased risk of AF through direct actions and vascular effects,<sup>927,928</sup> with a three-fold higher rate of incident AF compared with patients with essential hypertension.<sup>929</sup> 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.<sup>930,931</sup> 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.<sup>932</sup>

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.<sup>933–937</sup>

## 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.<sup>271,938–970</sup> AF can be the presenting or only clinically overt feature.<sup>969,971–975</sup> AF in these patients is associated with adverse clinical outcomes,<sup>947,954,959,963,965,976–978</sup> 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.<sup>979</sup>

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.<sup>959,966,980,981</sup> Programming a single high-rate ventricular fibrillation zone  $\geq 210$ – $220$  b.p.m. with long detection time is safe,<sup>950,953,982</sup> 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.<sup>983,984</sup> Immediate electrical cardioversion is needed for haemodynamically compromised patients with



pre-excited AF, and atrioventricular node-modulating drugs should be avoided.<sup>985,986</sup> Pharmacological cardioversion can be attempted using ibutilide<sup>987</sup> or flecainide, while propafenone should be used with caution due to effects on the atrioventricular node.<sup>988,989</sup> 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.<sup>990</sup>

## 9.12. AF-CARE in cancer

All types of cancer show an increased risk of AF, with prevalence varying from 2% to 28%.<sup>991–995</sup> 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.<sup>916,994,996</sup> Risk of AF is dependent on, among other factors, the cancer type and stage,<sup>997</sup> and is greater in older patients with pre-existing cardiovascular disease.<sup>991,993,994</sup> 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%).<sup>994</sup>

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.<sup>991,994</sup> On the other hand, the coexistence of cancer increases the risk of all-cause mortality and major bleeding in patients with AF.<sup>998</sup> Bleeding in those receiving OAC can also unmask the presence of cancer.<sup>999</sup>

Stroke risk scores may underestimate thromboembolic risk in cancer patients.<sup>1000</sup> 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.<sup>998</sup> 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.<sup>1001–1010</sup> Low molecular weight heparin is a short-term anticoagulation option, mostly during some cancer treatments, recent active bleeding, or thrombocytopenia.<sup>1011</sup> Decision-making on AF management, including on rhythm control, is best performed within a cardio-oncology multidisciplinary team.<sup>916,1012</sup> 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.<sup>1013–1016</sup> 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.<sup>1016,1017</sup> 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%.<sup>1018</sup> Frailty status is a strong independent risk factor for new-onset AF among older adults with hypertension.<sup>1019</sup>

Atrial fibrillation in frail patients is associated with less use of OAC and lower rates of management with a rhythm control strategy.<sup>1015,1018,1020</sup> 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).<sup>1021</sup> The value of observational data which show potential benefit from OAC (in particular, DOACs) is limited due to prescription biases.<sup>1022–1027</sup> Frail patients aged  $\geq 75$  years with polypharmacy and stable on a VKA may remain on the VKA rather than switching to a DOAC (Section 6.2).<sup>309</sup>

## 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,<sup>983</sup> with small randomized trials showing that cavo-tricuspid isthmus (CTI) ablation is superior to AADs.<sup>1028,1029</sup> 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.<sup>1030,1031</sup> 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.<sup>983</sup>

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

Recommendation	Class <sup>a</sup>	Level <sup>b</sup>
Oral anticoagulation is recommended in patients with atrial flutter at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism. <sup>86,1032</sup>	I	B

AF, atrial fibrillation; AFL, atrial flutter.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

## 10. Screening and prevention of AF

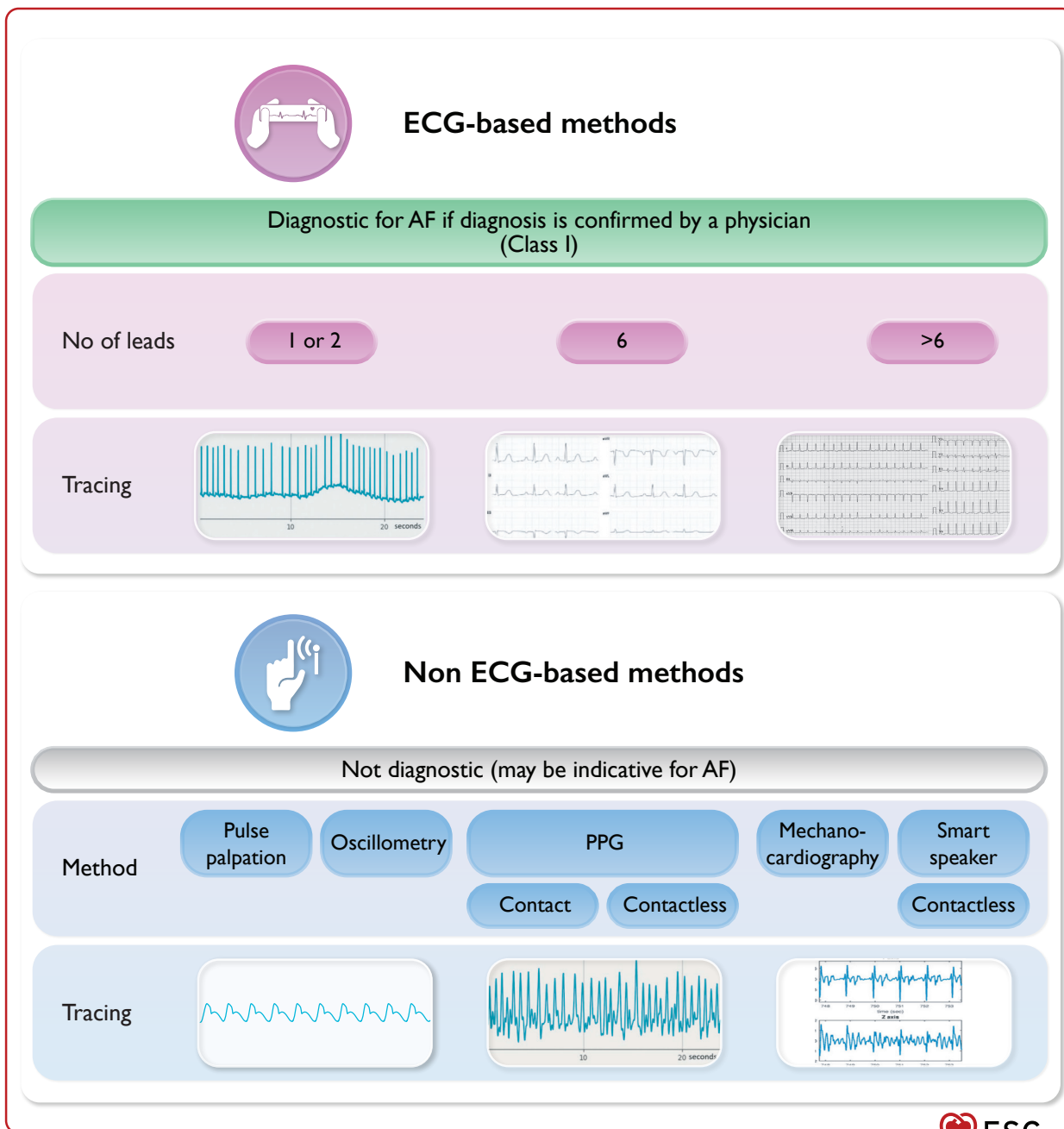
### 10.1. Epidemiology of AF

Atrial fibrillation is the most common sustained arrhythmia worldwide, with an estimated global prevalence in 2019 of 59.7 million persons with AF.<sup>1033</sup> Incident cases of AF are doubling every few decades.<sup>1034</sup> Future increases are anticipated, in particular in middle-income countries.<sup>1034</sup> In community-based individuals, the prevalence of AF in a United States of America cohort was up to 5.9%.<sup>1035</sup> The age-standardized prevalence and incidence rates have remained constant over time.<sup>1033,1036</sup> 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.<sup>1037</sup> The lifetime risk

of AF has been estimated to be as high as 1 in 3 for older individuals,<sup>1038</sup> 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.<sup>1039–1041</sup> 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.<sup>1042</sup>

### 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 smart-watches. 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.<sup>1043,1044</sup> 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<sup>1045</sup>
- (ii) Use of artificial intelligence algorithms to identify patients at risk<sup>1046</sup>
- (iii) ECG-based devices
  - (a) Conventional ECG devices
    - (1) Classic 12-lead ECG<sup>1047</sup>
    - (2) Holter monitoring (from 24 h to a week or more)<sup>1048</sup>
    - (3) Mobile cardiac telemetry (during hospitalization)<sup>1049</sup>
    - (4) Handheld devices<sup>1050–1052</sup>
    - (5) Wearable patches (up to 14 days)<sup>1053–1067</sup>
    - (6) Biotextiles (up to 30 days)<sup>1068–1072</sup>
    - (7) Smart devices (30 s)<sup>1073–1091</sup>
  - (b) Implantable loop recorders (3–5 years)<sup>1092–1099</sup>
- (iv) Non-ECG-based devices
  - (a) Photoplethysmography and automatic algorithms: contact (fingertip, smart device, band) and contactless (video)<sup>1100–1106</sup>
  - (b) Oscillometry (blood pressure monitors that derive heart rhythm regularity algorithmically)<sup>1107–1110</sup>
  - (c) Mechanocardiography (accelerometers and gyroscopes to sense the mechanical activity of the heart)<sup>1111</sup>
  - (d) Contactless video plethysmography (through video monitoring)<sup>1112–1115</sup>
  - (e) Smart speakers (through the identification of abnormal heart rate patterns)<sup>1116</sup>

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ECG, electrocardiogram.

Most consumer-based devices use photoplethysmography, and several large studies have been performed typically in low-risk individuals.<sup>633,1076,1117,1118</sup> 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.<sup>605</sup> 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.<sup>1119</sup> 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.<sup>1120</sup> 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.<sup>1091,1121–1125</sup>

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.<sup>1046</sup> 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.<sup>1126</sup> 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.<sup>1127</sup>

### 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<sup>1128</sup> 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.<sup>1129</sup> 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.<sup>5,857,1130,1131</sup> Pacemaker studies have shown that patients with a low burden of device-detected subclinical AF have a lower risk of ischaemic stroke.<sup>5,24,1131,1132</sup> This has been confirmed in RCTs assessing DOAC use in patients with device-detected subclinical AF (see *Section 6.1.1*).<sup>5,281,282</sup> The burden needed for device-detected subclinical AF to translate into stroke risk is not known, and further studies are clearly needed.<sup>1133,1134</sup> 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 <sup>a</sup>	Level <sup>b</sup>
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. <sup>1091,1121–1123,1125</sup>	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 <sub>2</sub> DS <sub>2</sub> -VA risk factors to ensure earlier detection of AF. <sup>6,1135–1137</sup>	IIa	B

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AF, atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-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.

<sup>a</sup>Class of recommendation.

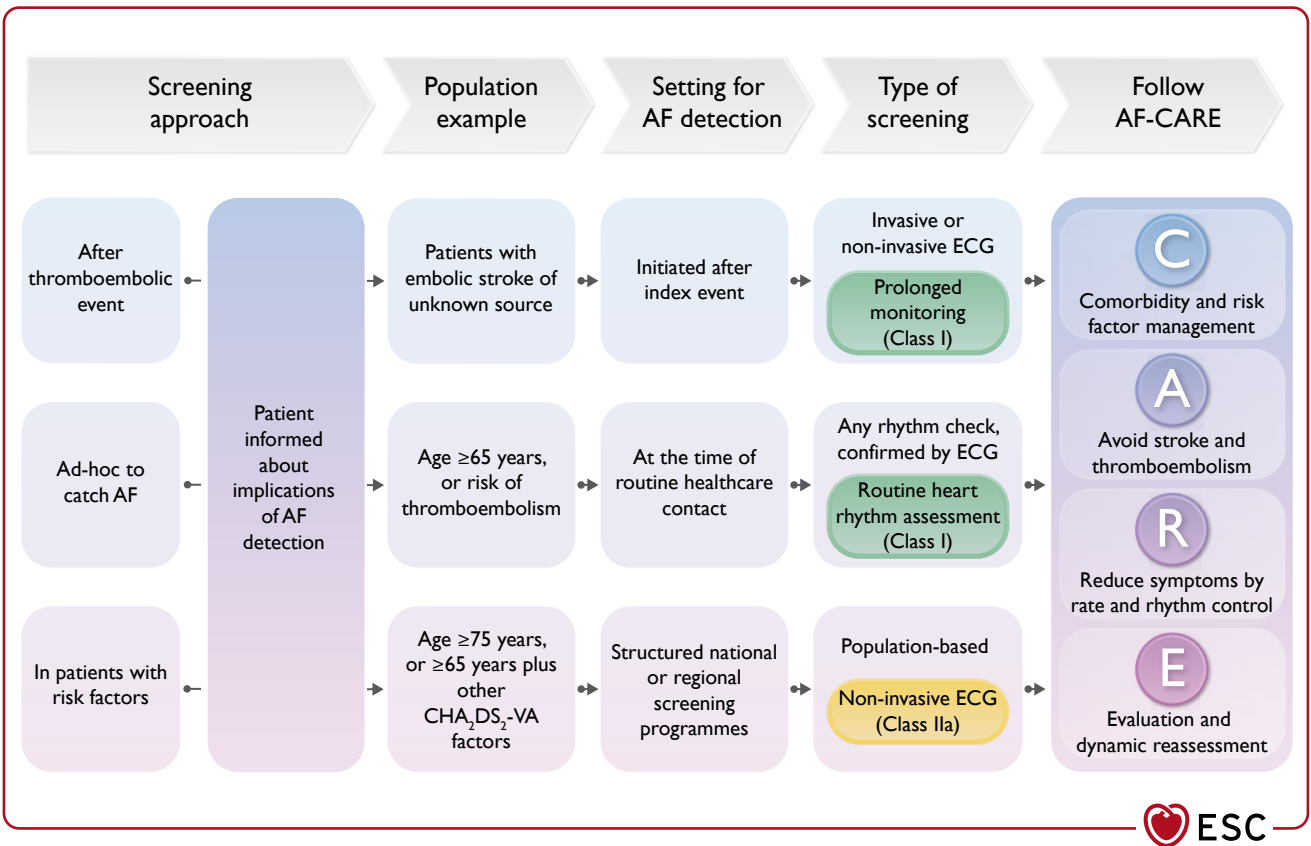
<sup>b</sup>Level of evidence.

**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.<sup>1138–1140</sup> No increased detection of AF was seen in groups randomized to single timepoint screening.<sup>1138–1140</sup> 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.<sup>1135</sup> 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.<sup>1123,1135</sup>

**10.3.2. Prolonged screening**

Studies using prolonged screening have shown an increased detection of AF leading to initiation of OAC.<sup>1129,1135,1141</sup> Two RCTs have investigated the effect on clinical outcomes in prolonged screening for AF.<sup>5,6</sup> 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<sub>2</sub>DS<sub>2</sub>-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;  $P = .045$ ).<sup>6</sup> 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.<sup>5</sup> 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).<sup>1136</sup> This was not repeated in a second meta-analysis including older RCTs, where no risk reduction was seen with regard to mortality or stroke.<sup>1135</sup> 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.<sup>1142</sup>

A high degree of interaction occurs between all factors related to AF development (see [Supplementary data online, Additional Evidence Table S33](#)).<sup>1038,1039,1143–1145</sup> For ease of clinical application, risk prediction tools have combined various factors, and have recently employed machine learning algorithms for prediction.<sup>1146,1147</sup> Classical risk scores are also available with variable predictive ability and model performance (see [Supplementary data online, Table S7](#)).<sup>1148</sup> 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 <sup>1149–1151</sup>
	Male sex <sup>1149–1152</sup>
	European ancestry <sup>1149,1150</sup>
	Lower socioeconomic status <sup>1150</sup>
Lifestyle behaviours	Smoking/tobacco use <sup>1149–1151</sup>
	Alcohol intake <sup>1149,1150</sup>
	Physical inactivity <sup>1149,1150</sup>
	Vigorous exercise <sup>1153–1156</sup>
	Competitive or athlete-level endurance sports <sup>1151,1157</sup>
	Caffeine <sup>1158–1160</sup>

*Continued*

Comorbidities and risk factors	Hypertension <sup>1149–1151</sup>
	Heart failure <sup>178,1149–1151,1161</sup>
	Valvular disease <sup>1149,1151,1162–1164</sup>
	Coronary artery disease <sup>1149,1151,1161,1165</sup>
	Peripheral arterial disease <sup>785</sup>
	Congenital heart disease <sup>1149,1166</sup>
	Heart rate, heart rate variability <sup>1167,1168</sup>
	Total cholesterol <sup>1149,1150</sup>
	Low-density lipoprotein cholesterol <sup>1150</sup>
	High-density lipoprotein cholesterol <sup>1150</sup>
	Triglycerides <sup>1150</sup>
	Impaired glucose tolerance, <sup>1169–1172</sup> diabetes mellitus <sup>1149–1151,1169</sup>
	Renal dysfunction/CKD <sup>1149–1151,1173,1174</sup>
	Obesity <sup>1149–1151,1175,1176</sup>
	Body mass index, weight <sup>1149–1151</sup>
	Height <sup>1150</sup>
	Sleep apnoea <sup>1149,1151,1177,1178</sup>
Chronic obstructive pulmonary disease <sup>1179</sup>	
Subclinical atherosclerosis	Coronary artery calcification <sup>1149,1151,1180</sup>
	Carotid IMT and carotid plaque <sup>1149,1151,1181,1182</sup>
ECG abnormalities	PR interval prolongation <sup>1149,1151,1183</sup>
	Sick sinus syndrome <sup>1149,1184,1185</sup>
	Wolff–Parkinson–White <sup>1149,1186</sup>
Genetic factors	Family history of AF <sup>1149,1151,1187–1190</sup>
	AF-susceptible loci identified by GWAS <sup>1149,1151,1191,1192</sup>
	Short QT syndrome <sup>1149</sup>
	Genetic cardiomyopathies <sup>990,1193</sup>
Biomarkers	C-reactive protein <sup>1150,1151</sup>
	Fibrinogen <sup>1150</sup>
	Growth differentiation factor-15 <sup>1194</sup>
	Natriuretic peptides (atrial and B-type) <sup>1195–1200</sup>
	Cardiac troponins <sup>1199</sup>
Others	Inflammatory biomarkers <sup>1149,1151</sup>
	Thyroid dysfunction <sup>912,1149–1151</sup>
	Autoimmune diseases <sup>1150</sup>
	Air pollution <sup>1149,1201</sup>
	Sepsis <sup>1149,1202</sup>
Psychological factors <sup>1203,1204</sup>	

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 <sup>a</sup>	Level <sup>b</sup>
Maintaining optimal blood pressure is recommended in the general population to prevent AF, with ACE inhibitors or ARBs as first-line therapy. <sup>1205–1207</sup>	I	B
Appropriate medical HF therapy is recommended in individuals with HFrEF to prevent AF. <sup>133,136,1208–1211</sup>	I	B
Maintaining normal weight (BMI 20–25 kg/m <sup>2</sup> ) is recommended for the general population to prevent AF. <sup>208,1212,1213</sup>	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. <sup>1214–1219</sup>	I	B
Avoidance of binge drinking and alcohol excess is recommended in the general population to prevent AF. <sup>1220–1223</sup>	I	B
Metformin or SGLT2 inhibitors should be considered for individuals needing pharmacological management of diabetes mellitus to prevent AF. <sup>1210,1211,1224–1226</sup>	IIa	B
Weight reduction should be considered in obese individuals to prevent AF. <sup>1212,1227–1231</sup>	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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

#### 10.5.1. Hypertension

Management of hypertension has been associated with a reduction in incident AF.<sup>1205–1207,1232</sup> 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.<sup>1207</sup> 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.<sup>1233–1236</sup>

#### 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.<sup>1208</sup> Similarly, beta-blockers in HFrEF led to a 33% reduction in the odds of incident AF.<sup>133</sup> Mineralocorticoid receptor antagonists have also been shown to reduce the risk of new-onset AF by 42% in patients with HFrEF.<sup>1209</sup> 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.<sup>136,1210,1211,1237</sup> 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.<sup>1238</sup> There is some evidence to suggest that effective CRT in eligible patients with HFrEF reduces the risk of incident AF.<sup>1239</sup> 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.<sup>1240</sup> More than glycaemic control *per se*, the class of glucose-lowering agent may influence the risk of AF.<sup>1240</sup> Insulin promotes adipogenesis and cardiac fibrosis, and sulfonylureas have been consistently associated with an increased risk of AF.<sup>193</sup> Observational studies have associated metformin with lower rates of incident AF.<sup>1224,1225,1241–1243</sup> 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.<sup>136,1226,1244–1246</sup> 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.<sup>1210,1211</sup>

#### 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<sup>2</sup> increase of BMI).<sup>208</sup> 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<sup>2</sup>.<sup>1212</sup> Similarly, observational studies in populations using bariatric surgery for weight loss in morbidly obese individuals (BMI ≥40 kg/m<sup>2</sup>) have observed a lower risk of incident AF.<sup>1227–1231</sup>

#### 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.<sup>230</sup> 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.<sup>1247</sup> Moderate aerobic exercise may also reduce the risk of new-onset AF.<sup>1214–1219</sup> 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.<sup>1248</sup>

### 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](#)).<sup>1220–1222</sup> 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.<sup>1223</sup>

## 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 health-care 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<sub>2</sub>DS<sub>2</sub>-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<sub>2</sub>DS<sub>2</sub>-VA = 1 anticoagulation should be considered; CHA<sub>2</sub>DS<sub>2</sub>-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<sub>2</sub>DS<sub>2</sub>-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 <sup>a</sup>	Level <sup>b</sup>
<b>Recommendations for the diagnosis of AF</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
<b>Recommendations for symptom evaluation in patients with AF</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.	I	B
<b>Recommendations for diagnostic evaluation in patients with new AF</b>		
A transthoracic echocardiogram is recommended in patients with an AF diagnosis where this will guide treatment decisions.	I	C
<b>Recommendations for patient-centred care and education</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.	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
<b>Recommendations for comorbidity and risk factor management in AF</b>		
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 $\leq 3$ standard drinks ( $\leq 30$ 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
<b>Recommendations to assess and manage thromboembolic risk in AF</b>		
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.	I	A
A CHA <sub>2</sub> DS <sub>2</sub> -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 <sub>2</sub> DS <sub>2</sub> -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

Continued

<b>Recommendations for oral anticoagulation in AF</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.	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
<b>Recommendations for combining antiplatelet drugs with anticoagulants for stroke prevention</b>		
Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischaemic stroke or thromboembolism.	III	B
<b>Recommendations for thromboembolism despite anticoagulation</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
<b>Recommendations for surgical left atrial appendage occlusion</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.	I	B
<b>Recommendations for assessment of bleeding risk</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
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
<b>Recommendations for management of bleeding in anticoagulated patients</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
<b>Recommendations for heart rate control in patients with AF</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.	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
<b>Recommendations for general concepts in rhythm control</b>		
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
<b>Recommendations for pharmacological cardioversion of AF</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.	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

Continued



<b>Recommendations for antiarrhythmic drugs for long-term maintenance of sinus rhythm</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.	I	A
Dronedaron 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
<b>Recommendations for catheter ablation of AF</b>		
<b>Shared decision-making</b>		
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
<b>Atrial fibrillation patients resistant or intolerant to antiarrhythmic drug therapy</b>		
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
<b>First-line rhythm control therapy</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
<b>Patients with heart failure</b>		
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
<b>Recommendations for anticoagulation in patients undergoing catheter ablation</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.	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 <sub>2</sub> DS <sub>2</sub> -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 <sub>2</sub> DS <sub>2</sub> -VA score, and not the perceived success of the ablation procedure, to prevent ischaemic stroke and thromboembolism.	I	C
<b>Recommendations for endoscopic and hybrid AF ablation</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
<b>Recommendations for AF ablation during cardiac surgery</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.	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
<b>Recommendations for patients with acute coronary syndromes or undergoing percutaneous intervention</b>		
<b>General recommendations for patients with AF and an indication for concomitant antiplatelet therapy</b>		
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
<b>Recommendations for AF patients with ACS</b>		
Early cessation ( $\leq 1$ week) of aspirin and continuation of an oral anticoagulant (preferably DOAC) with a P2Y <sub>12</sub> 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
<b>Recommendations for AF patients undergoing PCI</b>		
After uncomplicated PCI, early cessation ( $\leq 1$ week) of aspirin and continuation of an oral anticoagulant and a P2Y <sub>12</sub> inhibitor (preferably clopidogrel) for up to 6 months is recommended to avoid major bleeding, if ischaemic risk is low.	I	A

Continued

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 $\geq 65$ 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 <sup>2</sup> ) 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<sub>2</sub>DS<sub>2</sub>-VA, congestive heart failure, hypertension, age  $\geq 75$  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.

<sup>a</sup>Class of recommendation.

<sup>b</sup>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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## 18. References

- Alam M, Bhandari SJ, Shahzad SA, Lakkis N. Real-life global survey evaluating patients with atrial fibrillation (REALISE-AF): results of an international observational registry. *Expert Rev Cardiovasc Ther* 2012;**10**:283–91. <https://doi.org/10.1586/erc.12.8>
- De With RR, Erküner Ö, Rienstra M, Nguyen BO, Körver FWJ, Linz D, et al. Temporal patterns and short-term progression of paroxysmal atrial fibrillation: data from RACE V. *Europace* 2020;**22**:1162–72. <https://doi.org/10.1093/europace/eaab123>
- Packer DL, Mark DB, Robb RA, Monahan KH, Bahnsen TD, Poole JE, et al. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: the CABANA randomized clinical trial. *JAMA* 2019;**321**:1261–74. <https://doi.org/10.1001/jama.2019.0693>
- Marrouche NF, Brachmann J, Andersen D, Siebels J, Boersma L, Jordans L, et al. Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med* 2018;**378**:417–27. <https://doi.org/10.1056/NEJMoa1707855>
- Svensen JH, Diederichsen SZ, Højberg S, Krieger DW, Graff C, Kronborg C, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): a randomised controlled trial. *Lancet* 2021;**398**:1507–16. [https://doi.org/10.1016/S0140-6736\(21\)01698-6](https://doi.org/10.1016/S0140-6736(21)01698-6)
- Svensen E, Friberg L, Frykman V, Al-Khalili F, Engdahl J, Rosenqvist M. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. *Lancet* 2021;**398**:1498–506. [https://doi.org/10.1016/S0140-6736\(21\)01637-8](https://doi.org/10.1016/S0140-6736(21)01637-8)
- Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, et al. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012;**366**:120–9. <https://doi.org/10.1056/NEJMoa1105575>
- McIntyre WF, Healey JS, Bhatnagar AK, Wang P, Gordon JA, Baranchuk A, et al. Vernakalant for cardioversion of recent-onset atrial fibrillation: a systematic review and meta-analysis. *Europace* 2019;**21**:1159–66. <https://doi.org/10.1093/europace/euz175>
- Bager JE, Martín A, Carbajosa Dalmau J, Simon A, Merino JL, Ritz B, et al. Vernakalant for cardioversion of recent-onset atrial fibrillation in the emergency department: the SPECTRUM study. *Cardiology* 2022;**147**:566–77. <https://doi.org/10.1159/000526831>
- Pluymaekers N, Dudink E, Luermans J, Meeder JG, Lenderink T, Widdershoven J, et al. Early or delayed cardioversion in recent-onset atrial fibrillation. *N Engl J Med* 2019;**380**:1499–508. <https://doi.org/10.1056/NEJMoa1900353>
- Lubitz SA, Yin X, Rienstra M, Schnabel RB, Walkey AJ, Magnani JW, et al. Long-term outcomes of secondary atrial fibrillation in the community: the Framingham Heart Study. *Circulation* 2015;**131**:1648–55. <https://doi.org/10.1161/CIRCULATIONAHA.114.014058>
- Wang EY, Hulme OL, Khurshid S, Weng LC, Choi SH, Walkey AJ, et al. Initial precipitants and recurrence of atrial fibrillation. *Circ Arrhythm Electrophysiol* 2020;**13**:e007716. <https://doi.org/10.1161/CIRCEP.119.007716>
- Corica B, Romiti GF, Basili S, Proietti M. Prevalence of new-onset atrial fibrillation and associated outcomes in patients with sepsis: a systematic review and meta-analysis. *J Pers Med* 2022;**12**:547. <https://doi.org/10.3390/jpm12040547>
- Bedford JP, Ferrando-Vivas P, Redfern O, Rajappan K, Harrison DA, Watkinson PJ, et al. New-onset atrial fibrillation in intensive care: epidemiology and outcomes. *Eur Heart J Acute Cardiovasc Care* 2022;**11**:620–8. <https://doi.org/10.1093/ehjacc/zuac080>
- Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA* 2005;**293**:2634–40. <https://doi.org/10.1001/jama.293.21.2634>
- Andrade JG, Wells GA, Deyell MW, Bennett M, Essebag V, Champagne J, et al. Cryoablation or drug therapy for initial treatment of atrial fibrillation. *N Engl J Med* 2021;**384**:305–15. <https://doi.org/10.1056/NEJMoa2029980>
- Kirchhof P, Camm AJ, Goette A, Brandes A, Eckardt L, Elvan A, et al. Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med* 2020;**383**:1305–16. <https://doi.org/10.1056/NEJMoa2019422>
- Coats AJS, Heymans S, Farmakis D, Anker SD, Backs J, Bauersachs J, et al. Atrial disease and heart failure: the common soil hypothesis proposed by the heart failure association of the European Society of Cardiology. *Eur Heart J* 2022;**43**:863–7. <https://doi.org/10.1093/eurheartj/ehab834>
- Schnabel RB, Marinelli EA, Arbelo E, Boriani G, Boveda S, Buckley CM, et al. Early diagnosis and better rhythm management to improve outcomes in patients with atrial fibrillation: the 8th AFNET/EHRA consensus conference. *Europace* 2023;**25**:6–27. <https://doi.org/10.1093/europace/eauc062>
- Goette A, Kalman JM, Aguinaga L, Akar J, Cabrera JA, Chen SA, et al. EHRA/HRS/APHRS/SOLAECE expert consensus on atrial cardiomyopathies: definition, characterization, and clinical implication. *Europace* 2016;**18**:1455–90. <https://doi.org/10.1093/europace/euw161>
- Sagris D, Georgiopoulos G, Pateras K, Perlepe K, Korompoki E, Milonis H, et al. Atrial high-rate episode duration thresholds and thromboembolic risk: a systematic review and meta-analysis. *J Am Heart Assoc* 2021;**10**:e022487. <https://doi.org/10.1161/JAHA.121.022487>
- Kaufman ES, Israel CW, Nair GM, Armaganian L, Divakaramenon S, Mairesse GH, et al. Positive predictive value of device-detected atrial high-rate episodes at different rates and durations: an analysis from ASSERT. *Heart Rhythm* 2012;**9**:1241–6. <https://doi.org/10.1016/j.hrthm.2012.03.017>
- Miyazawa K, Pastori D, Martin DT, Choucair WK, Halperin JL, Lip GYH. Characteristics of patients with atrial high rate episodes detected by implanted defibrillator and resynchronization devices. *Europace* 2022;**24**:375–83. <https://doi.org/10.1093/europace/eaab186>
- Vitolo M, Imberti JF, Maisano A, Albini A, Bonini N, Valenti AC, et al. Device-detected atrial high rate episodes and the risk of stroke/thromboembolism and atrial fibrillation incidence: a systematic review and meta-analysis. *Eur J Intern Med* 2021;**92**:100–6. <https://doi.org/10.1016/j.ejim.2021.05.038>
- Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;**361**:1139–51. <https://doi.org/10.1056/NEJMoa0905561>
- Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, et al. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;**369**:2093–104. <https://doi.org/10.1056/NEJMoa1310907>
- Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011;**365**:981–92. <https://doi.org/10.1056/NEJMoa1107039>
- Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;**365**:883–91. <https://doi.org/10.1056/NEJMoa1009638>
- Stroke prevention in atrial fibrillation study. Final results. *Circulation* 1991;**84**:527–39. <https://doi.org/10.1161/01.CIR.84.2.527>
- Mannina C, Jin Z, Matsumoto K, Ito K, Biviano A, Elkind MSV, et al. Frequency of cardiac arrhythmias in older adults: findings from the subclinical atrial fibrillation and risk of ischemic stroke (SAFARIS) study. *Int J Cardiol* 2021;**337**:64–70. <https://doi.org/10.1016/j.ijcard.2021.05.006>
- Schnabel RB, Pecun L, Ojeda FM, Lucerna M, Rzyayeva N, Blankenberg S, et al. Gender differences in clinical presentation and 1-year outcomes in atrial fibrillation. *Heart* 2017;**103**:1024–30. <https://doi.org/10.1136/heartjnl-2016-310406>
- Simantirakis EN, Papakonstantinou PE, Chlouverakis GI, Kanoupakis EM, Mavrakis HE, Kallergis EM, et al. Asymptomatic versus symptomatic episodes in patients with paroxysmal atrial fibrillation via long-term monitoring with implantable loop recorders. *Int J Cardiol* 2017;**231**:125–30. <https://doi.org/10.1016/j.ijcard.2016.12.025>
- Verma A, Champagne J, Sapp J, Essebag V, Novak P, Skanes A, et al. Discerning the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): a prospective, multicenter study. *JAMA Intern Med* 2013;**173**:149–56. <https://doi.org/10.1001/jamainternmed.2013.1561>



34. Sgreccia D, Manicardi M, Malavasi VL, Vitolo M, Valenti AC, Proietti M, et al. Comparing outcomes in asymptomatic and symptomatic atrial fibrillation: a systematic review and meta-analysis of 81,462 patients. *J Clin Med* 2021;**10**:3979. <https://doi.org/10.3390/jcm10173979>
35. Holmes DN, Piccini JP, Allen LA, Fonarow GC, Gersh BJ, Kowey PR, et al. Defining clinically important difference in the atrial fibrillation effect on quality-of-life score. *Circ Cardiovasc Qual Outcomes* 2019;**12**:e005358. <https://doi.org/10.1161/CIRCOUTCOMES.118.005358>
36. Jones J, Stanbury M, Haynes S, Bunting KV, Lobban T, Camm AJ, et al. Importance and assessment of quality of life in symptomatic permanent atrial fibrillation: patient focus groups from the RATE-AF trial. *Cardiology* 2020;**145**:666–75. <https://doi.org/10.1159/000511048>
37. Abu HO, Wang W, Otabil EM, Saczynski JS, Mehawej J, Mishra A, et al. Perception of atrial fibrillation symptoms: impact on quality of life and treatment in older adults. *J Am Geriatr Soc* 2022;**70**:2805–17. <https://doi.org/10.1111/jgs.17954>
38. Rienstra M, Vermond RA, Crijns HJ, Tijssen JG, Van Gelder IC; RACE Investigators. Asymptomatic persistent atrial fibrillation and outcome: results of the RACE study. *Heart Rhythm* 2014;**11**:939–45. <https://doi.org/10.1016/j.hrthm.2014.03.016>
39. Rienstra M, Hobbelt AH, Alings M, Tijssen JGP, Smit MD, Brugemann J, et al. Targeted therapy of underlying conditions improves sinus rhythm maintenance in patients with persistent atrial fibrillation: results of the RACE 3 trial. *Eur Heart J* 2018;**39**:2987–96. <https://doi.org/10.1093/eurheartj/ehx739>
40. Mulder BA, Van Veldhuisen DJ, Crijns HJ, Tijssen JG, Hillege HL, Alings M, et al. Digoxin in patients with permanent atrial fibrillation: data from the RACE II study. *Heart Rhythm* 2014;**11**:1543–50. <https://doi.org/10.1016/j.hrthm.2014.06.007>
41. Kloosterman M, Crijns H, Mulder BA, Groenewald HF, Van Veldhuisen DJ, Rienstra M, et al. Sex-related differences in risk factors, outcome, and quality of life in patients with permanent atrial fibrillation: results from the RACE II study. *Europace* 2020;**22**:1619–27. <https://doi.org/10.1093/eurpace/euz300>
42. Park YJ, Park JW, Yu HT, Kim TH, Uhm JS, Joung B, et al. Sex difference in atrial fibrillation recurrence after catheter ablation and antiarrhythmic drugs. *Heart* 2023;**109**:519–26. <https://doi.org/10.1136/heartjnl-2021-320601>
43. Kupper N, van den Broek KC, Widdershoven J, Denollet J. Subjectively reported symptoms in patients with persistent atrial fibrillation and emotional distress. *Front Psychol* 2013;**4**:192. <https://doi.org/10.3389/fpsyg.2013.00192>
44. Schnabel RB, Michal M, Wilde S, Wiltink J, Wild PS, Sinning CR, et al. Depression in atrial fibrillation in the general population. *PLoS One* 2013;**8**:e79109. <https://doi.org/10.1371/journal.pone.0079109>
45. Gleason KT, Dennison Himmelfarb CR, Ford DE, Lehmann H, Samuel L, Han HR, et al. Association of sex, age and education level with patient reported outcomes in atrial fibrillation. *BMC Cardiovasc Disord* 2019;**19**:85. <https://doi.org/10.1186/s12872-019-1059-6>
46. Schnabel RB, Pecun L, Rzyayeva N, Lucerna M, Purmah Y, Ojeda FM, et al. Symptom burden of atrial fibrillation and its relation to interventions and outcome in Europe. *J Am Heart Assoc* 2018;**7**:e007559. <https://doi.org/10.1161/JAHA.117.007559>
47. Wynn GJ, Todd DM, Webber M, Bonnett L, McShane J, Kirchhof P, et al. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. *Europace* 2014;**16**:965–72. <https://doi.org/10.1093/eurpace/eut395>
48. Kotecha D, Bunting KV, Gill SK, Mehta S, Stanbury M, Jones JC, et al. Effect of digoxin vs bisoprolol for heart rate control in atrial fibrillation on patient-reported quality of life: the RATE-AF randomized clinical trial. *JAMA* 2020;**324**:2497–508. <https://doi.org/10.1001/jama.2020.23138>
49. Kotecha D, Ahmed A, Calvert M, Lencioni M, Terwee CB, Lane DA. Patient-reported outcomes for quality of life assessment in atrial fibrillation: a systematic review of measurement properties. *PLoS One* 2016;**11**:e0165790. <https://doi.org/10.1371/journal.pone.0165790>
50. Mantovan R, Macle L, De Martino G, Chen J, Morillo CA, Novak P, et al. Relationship of quality of life with procedural success of atrial fibrillation (AF) ablation and postablation AF burden: substudy of the STAR AF randomized trial. *Can J Cardiol* 2013;**29**:1211–7. <https://doi.org/10.1016/j.cjca.2013.06.006>
51. Samuel M, Khairy P, Champagne J, Deyell MW, Macle L, Leong-Sit P, et al. Association of atrial fibrillation burden with health-related quality of life after atrial fibrillation ablation: substudy of the cryoballoon vs contact-force atrial fibrillation ablation (CIRCA-DOSE) randomized clinical trial. *JAMA Cardiol* 2021;**6**:1324–8. <https://doi.org/10.1001/jamacardio.2021.3063>
52. Sandhu RK, Smigorowsky M, Lockwood E, Savu A, Kaul P, McAlister FA. Impact of electrical cardioversion on quality of life for the treatment of atrial fibrillation. *Can J Cardiol* 2017;**33**:450–5. <https://doi.org/10.1016/j.cjca.2016.11.013>
53. Terracabras M, Mantovan R, Jiang CY, Betts TR, Chen J, Deisenhofer I, et al. Association between quality of life and procedural outcome after catheter ablation for atrial fibrillation: a secondary analysis of a randomized clinical trial. *JAMA Netw Open* 2020;**3**:e2025473. <https://doi.org/10.1001/jamanetworkopen.2020.25473>
54. Zenger B, Zhang M, Lyons A, Bunch TJ, Fang JC, Freedman RA, et al. Patient-reported outcomes and subsequent management in atrial fibrillation clinical practice: results from the Utah mEVAL AF program. *J Cardiovasc Electrophysiol* 2020;**31**:3187–95. <https://doi.org/10.1111/jce.14795>
55. Arbelo E, Aktaa S, Bollmann A, D'Avila A, Drossart I, Dwight J, et al. Quality indicators for the care and outcomes of adults with atrial fibrillation. *Europace* 2021;**23**:494–5. <https://doi.org/10.1093/eurpace/eaab253>
56. Kvist LM, Vinter N, Urbonaviciene G, Lindholt JS, Diederichsen ACP, Frost L. Diagnostic accuracies of screening for atrial fibrillation by cardiac nurses versus radiographers. *Open Heart* 2019;**6**:e000942. <https://doi.org/10.1136/openhrt-2018-000942>
57. Hijazi Z, Oldgren J, Siegbahn A, Granger CB, Wallentin L. Biomarkers in atrial fibrillation: a clinical review. *Eur Heart J* 2013;**34**:1475–80. <https://doi.org/10.1093/eurheartj/ehs024>
58. Berg DD, Ruff CT, Morrow DA. Biomarkers for risk assessment in atrial fibrillation. *Clin Chem* 2021;**67**:87–95. <https://doi.org/10.1093/clinchem/hvaa298>
59. Tops LF, Schalij MJ, Bax JJ. Imaging and atrial fibrillation: the role of multimodality imaging in patient evaluation and management of atrial fibrillation. *Eur Heart J* 2010;**31**:542–51. <https://doi.org/10.1093/eurheartj/ehq005>
60. Obeng-Gyimah E, Nazarian S. Advancements in imaging for atrial fibrillation ablation: is there a potential to improve procedural outcomes? *J Innov Card Rhythm Manag* 2020;**11**:4172–8. <https://doi.org/10.19102/icrm.2020.110701>
61. Romero J, Husain SA, Kelesidis I, Sanz J, Medina HM, Garcia MJ. Detection of left atrial appendage thrombus by cardiac computed tomography in patients with atrial fibrillation: a meta-analysis. *Circ Cardiovasc Imaging* 2013;**6**:185–94. <https://doi.org/10.1161/CIRCIMAGING.112.000153>
62. Bisbal F, Benito E, Teis A, Alarcón F, Sarrías A, Caixal G, et al. Magnetic resonance imaging-guided fibrosis ablation for the treatment of atrial fibrillation: the ALICIA trial. *Circ Arrhythm Electrophysiol* 2020;**13**:e008707. <https://doi.org/10.1161/CIRCEP.120.008707>
63. Khurram IM, Habibi M, Gucuk Ipek E, Chrispin J, Yang E, Fukumoto K, et al. Left atrial LGE and arrhythmia recurrence following pulmonary vein isolation for paroxysmal and persistent AF. *JACC Cardiovasc Imaging* 2016;**9**:142–8. <https://doi.org/10.1016/j.jcmg.2015.10.015>
64. Marrouche NF, Wilber D, Hindricks G, Jais P, Akoum N, Marchlinski F, et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. *JAMA* 2014;**311**:498–506. <https://doi.org/10.1001/jama.2014.3>
65. Roney CH, Sillett C, Whitaker J, Lemus JAS, Sim I, Kotadia I, et al. Applications of multimodality imaging for left atrial catheter ablation. *Eur Heart J Cardiovasc Imaging* 2021;**23**:31–41. <https://doi.org/10.1093/ehjci/jeab205>
66. Potter A, Augustine DX, Ingram TE. Referring for echocardiography: when not to test. *Br J Gen Pract* 2021;**71**:333–4. <https://doi.org/10.3399/bjgp21X716441>
67. Troughton RV, Asher CR, Klein AL. The role of echocardiography in atrial fibrillation and cardioversion. *Heart* 2003;**89**:1447–54. <https://doi.org/10.1136/heart.89.12.1447>
68. Odutayo A, Wong CX, Hsiao AJ, Hopewell S, Altman DG, Emdin CA. Atrial fibrillation and risks of cardiovascular disease, renal disease, and death: systematic review and meta-analysis. *BMJ* 2016;**354**:i4482. <https://doi.org/10.1136/bmj.i4482>
69. Ruddox V, Sandven I, Munkhaugen J, Skattebu J, Edvardsen T, Otterstad JE. Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2017;**24**:1555–66. <https://doi.org/10.1177/2047487317715769>
70. Bassand JP, Accetta G, Al Mahmeed W, Corbalan R, Eikelboom J, Fitzmaurice DA, et al. Risk factors for death, stroke, and bleeding in 28,628 patients from the GARFIELD-AF registry: rationale for comprehensive management of atrial fibrillation. *PLoS One* 2018;**13**:e0191592. <https://doi.org/10.1371/journal.pone.0191592>
71. Bassand JP, Accetta G, Camm AJ, Cools F, Fitzmaurice DA, Fox KA, et al. Two-year outcomes of patients with newly diagnosed atrial fibrillation: results from GARFIELD-AF. *Eur Heart J* 2016;**37**:2882–9. <https://doi.org/10.1093/eurheartj/ehw233>
72. Hornestam B, Adiels M, Wai Giang K, Hansson PO, Björck L, Rosengren A. Atrial fibrillation and risk of venous thromboembolism: a Swedish nationwide registry study. *Europace* 2021;**23**:1913–21. <https://doi.org/10.1093/eurpace/eaab180>
73. Lutsey PL, Norby FL, Alonso A, Cushman M, Chen LY, Michos ED, et al. Atrial fibrillation and venous thromboembolism: evidence of bidirectionality in the atherosclerosis risk in communities study. *J Thromb Haemost* 2018;**16**:670–9. <https://doi.org/10.1111/jth.13974>
74. Koh YH, Lew LZW, Franke KB, Elliott AD, Lau DH, Thiyagarajah A, et al. Predictive role of atrial fibrillation in cognitive decline: a systematic review and meta-analysis of 2.8 million individuals. *Europace* 2022;**24**:1229–39. <https://doi.org/10.1093/eurpace/eaac003>
75. Papanastasiou CA, Theochari CA, Zareifopoulos N, Arfaras-Melainis A, Giannakoulas G, Karamitsos TD, et al. Atrial fibrillation is associated with cognitive impairment, all-cause dementia, vascular dementia, and Alzheimer's disease: a systematic review and meta-analysis. *J Gen Intern Med* 2021;**36**:3122–35. <https://doi.org/10.1007/s11606-021-06954-8>
76. Giannone ME, Filippini T, Whelton PK, Chiari A, Vitolo M, Boriani G, et al. Atrial fibrillation and the risk of early-onset dementia: a systematic review and meta-analysis. *J Am Heart Assoc* 2022;**11**:e025653. <https://doi.org/10.1161/JAHA.122.025653>



77. Zuin M, Roncon L, Passaro A, Bosi C, Cervellati C, Zuliani G. Risk of dementia in patients with atrial fibrillation: short versus long follow-up. A systematic review and meta-analysis. *Int J Geriatr Psychiatry* 2021;**36**:1488–500. <https://doi.org/10.1002/gps.5582>
78. Mobley AR, Subramanian A, Champai A, Wang X, Myles P, McCreavy P, et al. Thromboembolic events and vascular dementia in patients with atrial fibrillation and low apparent stroke risk. *Nat Med* 2024. <https://doi.org/10.1038/s41591-024-03049-9>.
79. Wijnvliet E, Tieleman RG, van Gelder IC, Pluymaekers N, Rienstra M, Folkeringa RJ, et al. Nurse-led vs. usual-care for atrial fibrillation. *Eur Heart J* 2020;**41**:634–41. <https://doi.org/10.1093/eurheartj/ehz666>
80. Wong CX, Brooks AG, Lau DH, Leong DP, Sun MT, Sullivan T, et al. Factors associated with the epidemic of hospitalizations due to atrial fibrillation. *Am J Cardiol* 2012;**110**:1496–9. <https://doi.org/10.1016/j.amjcard.2012.07.011>
81. Dai H, Zhang Q, Much AA, Maor E, Segev A, Beinart R, et al. Global, regional, and national prevalence, incidence, mortality, and risk factors for atrial fibrillation, 1990–2017: results from the Global Burden of Disease Study 2017. *Eur Heart J Qual Care Clin Outcomes* 2021;**7**:574–82. <https://doi.org/10.1093/ehjqcco/qcaa061>
82. Ťica O, Ťica O, Bunting KV, deBono J, Gkoutos GV, Popescu MI, et al. Post-mortem examination of high mortality in patients with heart failure and atrial fibrillation. *BMC Med* 2022;**20**:331. <https://doi.org/10.1186/s12916-022-02533-8>
83. Bassand JP, Virdone S, Badoz M, Verheugt FWA, Camm AJ, Cools F, et al. Bleeding and related mortality with NOACs and VKAs in newly diagnosed atrial fibrillation: results from the GARFIELD-AF registry. *Blood Adv* 2021;**5**:1081–91. <https://doi.org/10.1182/bloodadvances.2020003560>
84. Pokorney SD, Piccini JP, Stevens SR, Patel MR, Pieper KS, Halperin JL, et al. Cause of death and predictors of all-cause mortality in anticoagulated patients with nonvalvular atrial fibrillation: data from ROCKET AF. *J Am Heart Assoc* 2016;**5**:e002197. <https://doi.org/10.1161/JAHA.115.002197>
85. Granada J, Uribe W, Chyow PH, Maassen K, Vierkant R, Smith PN, et al. Incidence and predictors of atrial flutter in the general population. *J Am Coll Cardiol* 2000;**36**:2242–6. [https://doi.org/10.1016/S0735-1097\(00\)00982-7](https://doi.org/10.1016/S0735-1097(00)00982-7)
86. Vadmann H, Nielsen PB, Hjortshøj SP, Riahi S, Rasmussen LH, Lip GY, et al. Atrial flutter and thromboembolic risk: a systematic review. *Heart* 2015;**101**:1446–55. <https://doi.org/10.1136/heartjnl-2015-307550>
87. Leloirier P, Humphries KH, Krahn A, Connolly SJ, Talajic M, Green M, et al. Prognostic differences between atrial fibrillation and atrial flutter. *Am J Cardiol* 2004;**93**:647–9. <https://doi.org/10.1016/j.amjcard.2003.11.042>
88. Biblo LA, Yuan Z, Quan KJ, Mackall JA, Rimm AA. Risk of stroke in patients with atrial flutter. *Am J Cardiol* 2001;**87**:346–9, A9. [https://doi.org/10.1016/S0002-9149\(00\)01374-6](https://doi.org/10.1016/S0002-9149(00)01374-6)
89. Corrado G, Sgalambro A, Mantero A, Gentile F, Gasparini M, Bufalino R, et al. Thromboembolic risk in atrial flutter. The FLASIEC (Flutter Atriale Società Italiana di Ecografia Cardiovascolare) multicentre study. *Eur Heart J* 2001;**22**:1042–51. <https://doi.org/10.1053/ehj.2000.2427>
90. Lin YS, Chen TH, Chi CC, Lin MS, Tung TH, Liu CH, et al. Different implications of heart failure, ischemic stroke, and mortality between nonvalvular atrial fibrillation and atrial flutter—a view from a national cohort study. *J Am Heart Assoc* 2017;**6**:e006406. <https://doi.org/10.1161/JAHA.117.006406>
91. Giehm-Reese M, Johansen MN, Kronborg MB, Jensen HK, Gerdes C, Kristensen J, et al. Discontinuation of oral anticoagulation and risk of stroke and death after ablation for typical atrial flutter: a nation-wide Danish cohort study. *Int J Cardiol* 2021;**333**:110–6. <https://doi.org/10.1016/j.ijcard.2021.02.057>
92. Gallagher C, Rowett D, Nyfort-Hansen K, Simmons S, Brooks AG, Moss JR, et al. Patient-centered educational resources for atrial fibrillation. *JACC Clin Electrophysiol* 2019;**5**:1101–14. <https://doi.org/10.1016/j.jacep.2019.08.007>
93. Chung MK, Fagerlin A, Wang PJ, Ajayi TB, Allen LA, Baykaner T, et al. Shared decision making in cardiac electrophysiology procedures and arrhythmia management. *Circ Arrhythm Electrophysiol* 2021;**14**:e007958. <https://doi.org/10.1161/CIRCEP.121.007958>
94. Wang PJ, Lu Y, Mahaffey KW, Lin A, Morin DP, Sears SF, et al. A randomized clinical trial to evaluate an atrial fibrillation stroke prevention shared decision-making pathway. *J Am Heart Assoc* 2022;**12**:e028562. <https://doi.org/10.1161/JAHA.122.028562>
95. Seaburg L, Hess EP, Coylewright M, Ting HH, McLeod CJ, Montori VM. Shared decision making in atrial fibrillation: where we are and where we should be going. *Circulation* 2014;**129**:704–10. <https://doi.org/10.1161/CIRCULATIONAHA.113.004498>
96. Zhang J, Lenarczyk R, Marin F, Malaczynska-Rajpold K, Kosiuk J, Doehner W, et al. The interpretation of CHA2DS2-VASc score components in clinical practice: a joint survey by the European Heart Rhythm Association (EHRA) scientific initiatives committee, the EHRA young electrophysiologists, the Association of Cardiovascular Nursing and Allied Professionals, and the European Society of Cardiology council on stroke. *Europace* 2021;**23**:314–22. <https://doi.org/10.1093/eurpace/eaab358>
97. Omoush A, Aloush S, Albashtawy M, Rayan A, Alkhaldeh A, Eshah N, et al. Nurses' knowledge of anticoagulation therapy for atrial fibrillation patients: effectiveness of an educational course. *Nurs Forum* 2022;**57**:825–32. <https://doi.org/10.1111/nuf.12770>
98. Heidbuchel H, Dagnes N, Antz M, Kuck KH, Lazure P, Murray S, et al. Major knowledge gaps and system barriers to guideline implementation among European physicians treating patients with atrial fibrillation: a European Society of Cardiology international educational needs assessment. *Europace* 2018;**20**:1919–28. <https://doi.org/10.1093/eurpace/euy039>
99. Bunting KV, Van Gelder IC, Kotecha D. STEER-AF: a cluster-randomized education trial from the ESC. *Eur Heart J* 2020;**41**:1952–4. <https://doi.org/10.1093/eurheartj/ehaa421>
100. Tanner FC, Brooks N, Fox KF, Gonçalves L, Kearney P, Michalis L, et al. ESC core curriculum for the cardiologist. *Eur Heart J* 2020;**41**:3605–92. <https://doi.org/10.1093/eurheartj/ehaa641>
101. Astin F, Carroll D, De Geest S, Fernandez-Oliver AL, Holt J, Hinterbuchner L, et al. A core curriculum for the continuing professional development of nurses working in cardiovascular settings: developed by the education committee of the Council on Cardiovascular Nursing and Allied Professions (CCNAP) on behalf of the European Society of Cardiology. *Eur J Cardiovasc Nurs* 2015;**14**:S1–17. <https://doi.org/10.1177/1474515115580905>
102. Sterlinski M, Bunting KV, Boriani G, Boveda S, Guasch E, Mont L, et al. STEER-AF Trial Team. Design and deployment of the STEER-AF trial to evaluate and improve guideline adherence: a cluster-randomised trial by the European Society of Cardiology and European Heart Rhythm Association. *Europace* 2024;euaa178. <https://doi.org/10.1093/eurpace/eaee178>
103. Vinereanu D, Lopes RD, Bahit MC, Xavier D, Jiang J, Al-Khalidi HR, et al. A multifaceted intervention to improve treatment with oral anticoagulants in atrial fibrillation (IMPACT-AF): an international, cluster-randomised trial. *Lancet* 2017;**390**:1737–46. [https://doi.org/10.1016/S0140-6736\(17\)32165-7](https://doi.org/10.1016/S0140-6736(17)32165-7)
104. Franchi C, Antoniazzi S, Ardoino I, Proietti M, Marcucci M, Santalucia P, et al. Simulation-based education for physicians to increase oral anticoagulants in hospitalized elderly patients with atrial fibrillation. *Am J Med* 2019;**132**:e634–47. <https://doi.org/10.1016/j.amjmed.2019.03.052>
105. Baicus C, Delcea C, Dima A, Oprisan E, Jurcut C, Dan GA. Influence of decision aids on oral anticoagulant prescribing among physicians: a randomised trial. *Eur J Clin Invest* 2017;**47**:649–58. <https://doi.org/10.1111/eci.12786>
106. Ono F, Akiyama S, Suzuki A, Ikeda Y, Takahashi A, Matsuoka H, et al. Impact of care coordination on oral anticoagulant therapy among patients with atrial fibrillation in routine clinical practice in Japan: a prospective, observational study. *BMC Cardiovasc Disord* 2019;**19**:235. <https://doi.org/10.1186/s12872-019-1216-y>
107. Ferguson C, Hickman LD, Phillips J, Newton PJ, Inglis SC, Lam L, et al. An mHealth intervention to improve nurses' atrial fibrillation and anticoagulation knowledge and practice: the EVICOAG study. *Eur J Cardiovasc Nurs* 2019;**18**:7–15. <https://doi.org/10.1177/1474515118793051>
108. Lip GY, Laroche C, Popescu MI, Rasmussen LH, Vitali-Serdoz L, Dan GA, et al. Improved outcomes with European Society of Cardiology guideline-adherent antithrombotic treatment in high-risk patients with atrial fibrillation: a report from the EORP-AF general pilot registry. *Europace* 2015;**17**:1777–86. <https://doi.org/10.1093/eurpace/euv269>
109. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al. Sex differences in cardiac arrhythmia: a consensus document of the European Heart Rhythm Association, endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. *Europace* 2018;**20**:1565–1565a. <https://doi.org/10.1093/eurpace/euy067>
110. Camm AJ, Accetta G, Al Mahmeed W, Ambrosio G, Goldhaber SZ, Haas S, et al. Impact of gender on event rates at 1 year in patients with newly diagnosed non-valvular atrial fibrillation: contemporary perspective from the GARFIELD-AF registry. *BMJ Open* 2017;**7**:e014579. <https://doi.org/10.1136/bmjopen-2016-014579>
111. Emdin CA, Wong CX, Hsiao AJ, Altman DG, Peters SA, Woodward M, et al. Atrial fibrillation as risk factor for cardiovascular disease and death in women compared with men: systematic review and meta-analysis of cohort studies. *BMJ* 2016;**532**:h7013. <https://doi.org/10.1136/bmj.h7013>
112. Tomasdottir M, Friberg L, Hijazi Z, Lindback J, Oldgren J. Risk of ischemic stroke and utility of CHA2DS2-VASc score in women and men with atrial fibrillation. *Clin Cardiol* 2019;**42**:1003–9. <https://doi.org/10.1002/clc.23257>
113. Kloosterman M, Chua W, Fabritz L, Al-Khalidi HR, Schotten U, Nielsen JC, et al. Sex differences in catheter ablation of atrial fibrillation: results from AXAFA-AFNET 5. *Europace* 2020;**22**:1026–35. <https://doi.org/10.1093/eurpace/eaab015>
114. Benjamin EJ, Thomas KL, Go AS, Desvigne-Nickens P, Albert CM, Alonso A, et al. Transforming atrial fibrillation research to integrate social determinants of health: a national heart, lung, and blood institute workshop report. *JAMA Cardiol* 2023;**8**:182–91. <https://doi.org/10.1001/jamacardio.2022.4091>
115. Karlsson LO, Nilsson S, Bang M, Nilsson L, Charitakis E, Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: a cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). *PLoS Med* 2018;**15**:e1002528. <https://doi.org/10.1371/journal.pmed.1002528>

116. Biersteker TE, Schallij MJ, Treskes RW. Impact of mobile health devices for the detection of atrial fibrillation: systematic review. *JMIR Mhealth Uhealth* 2021;**9**:e26161. <https://doi.org/10.2196/26161>
117. Romiti GF, Pastori D, Rivera-Caravaca JM, Ding WY, Gue YX, Menichelli D, et al. Adherence to the 'atrial fibrillation better care' pathway in patients with atrial fibrillation: impact on clinical outcomes—a systematic review and meta-analysis of 285,000 patients. *Thromb Haemost* 2022;**122**:406–14. <https://doi.org/10.1055/a-1515-9630>
118. Gallagher C, Elliott AD, Wong CX, Rangnekar G, Middeldorp ME, Mahajan R, et al. Integrated care in atrial fibrillation: a systematic review and meta-analysis. *Heart* 2017;**103**:1947–53. <https://doi.org/10.1136/heartjnl-2016-310952>
119. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;**37**:2893–962. <https://doi.org/10.1093/eurheartj/ehw210>
120. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;**42**:373–498. <https://doi.org/10.1093/eurheartj/ehaa612>
121. Qvist I, Hendriks JM, Møller DS, Albertsen AE, Mogensen HM, Oddershede GD, et al. Effectiveness of structured, hospital-based, nurse-led atrial fibrillation clinics: a comparison between a real-world population and a clinical trial population. *Open Heart* 2016;**3**:e000335. <https://doi.org/10.1136/openhrt-2015-000335>
122. Hendriks JM, de Wit R, Crijns HJ, Vrijhoef HJ, Prins MH, Pisters R, et al. Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. *Eur Heart J* 2012;**33**:2692–9. <https://doi.org/10.1093/eurheartj/ehs071>
123. Carter L, Gardner M, Magee K, Fearon A, Morgulis I, Doucette S, et al. An integrated management approach to atrial fibrillation. *J Am Heart Assoc* 2016;**5**:e002950. <https://doi.org/10.1161/JAHA.115.002950>
124. van den Dries CJ, van Doorn S, Rutten FH, Oudega R, van de Leur S, Elvan A, et al. Integrated management of atrial fibrillation in primary care: results of the ALL-IN cluster randomized trial. *Eur Heart J* 2020;**41**:2836–44. <https://doi.org/10.1093/eurheartj/ehaa055>
125. Abed HS, Wittert GA, Leong DP, Shirazi MG, Bahrami B, Middeldorp ME, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. *JAMA* 2013;**310**:2050–60. <https://doi.org/10.1001/jama.2013.280521>
126. Pathak RK, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, Wong CX, et al. Long-term effect of goal-directed weight management in an atrial fibrillation cohort: a long-term follow-up study (LEGACY). *J Am Coll Cardiol* 2015;**65**:2159–69. <https://doi.org/10.1016/j.jacc.2015.03.002>
127. Middeldorp ME, Pathak RK, Meredith M, Mehta AB, Elliott AD, Mahajan R, et al. PREVENTion and regReSSive effect of weight-loss and risk factor modification on atrial fibrillation: the REVERSE-AF study. *Europace* 2018;**20**:1929–35. <https://doi.org/10.1093/europace/euy117>
128. Pathak RK, Middeldorp ME, Lau DH, Mehta AB, Mahajan R, Twomey D, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. *J Am Coll Cardiol* 2014;**64**:2222–31. <https://doi.org/10.1016/j.jacc.2014.09.028>
129. Pinho-Gomes AC, Azevedo L, Copland E, Canoy D, Nazarzadeh M, Ramakrishnan R, et al. Blood pressure-lowering treatment for the prevention of cardiovascular events in patients with atrial fibrillation: an individual participant data meta-analysis. *PLoS Med* 2021;**18**:e1003599. <https://doi.org/10.1371/journal.pmed.1003599>
130. Parkash R, Wells GA, Sapp JL, Healey JS, Tardif J-C, Greiss I, et al. Effect of aggressive blood pressure control on the recurrence of atrial fibrillation after catheter ablation: a randomized, open-label clinical trial (SMAC-AF [Substrate Modification with Aggressive Blood Pressure Control]). *Circulation* 2017;**135**:1788–98. <https://doi.org/10.1161/CIRCULATIONAHA.116.026230>
131. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the task force for the diagnosis and treatment of acute and chronic heart failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2012;**33**:1787–847. <https://doi.org/10.1093/eurheartj/ehs104>
132. Olsson LG, Swedberg K, Ducharme A, Granger CB, Michelson EL, McMurray JJ, et al. Atrial fibrillation and risk of clinical events in chronic heart failure with and without left ventricular systolic dysfunction: results from the Candesartan in Heart failure-Assessment of Reduction in Mortality and morbidity (CHARM) program. *J Am Coll Cardiol* 2006;**47**:1997–2004. <https://doi.org/10.1016/j.jacc.2006.01.060>
133. Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JG, et al. Efficacy of beta blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. *Lancet* 2014;**384**:2235–43. [https://doi.org/10.1016/S0140-6736\(14\)61373-8](https://doi.org/10.1016/S0140-6736(14)61373-8)
134. Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, et al. Eplerenone in patients with systolic heart failure and mild symptoms. *N Engl J Med* 2011;**364**:11–21. <https://doi.org/10.1056/NEJMoa1009492>
135. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 2014;**371**:993–1004. <https://doi.org/10.1056/NEJMoa1409077>
136. Pandey AK, Okaj I, Kaur H, Belley-Cote EP, Wang J, Oraai A, et al. Sodium-glucose cotransporter inhibitors and atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2021;**10**:e022222. <https://doi.org/10.1161/JAHA.121.022222>
137. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumhach A, Bohm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;**42**:3599–726. <https://doi.org/10.1093/eurheartj/ehab368>
138. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med* 2022;**387**:1089–98. <https://doi.org/10.1056/NEJMoa2206286>
139. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Böhm M, et al. Empagliflozin in heart failure with a preserved ejection fraction. *N Engl J Med* 2021;**385**:1451–61. <https://doi.org/10.1056/NEJMoa2107038>
140. Bhatt DL, Szarek M, Steg PG, Cannon CP, Leiter LA, McGuire DK, et al. Sotagliflozin in patients with diabetes and recent worsening heart failure. *N Engl J Med* 2021;**384**:117–28. <https://doi.org/10.1056/NEJMoa2030183>
141. Pathak RK, Elliott A, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, et al. Impact of CARDIOrespiratory FITness on arrhythmia recurrence in obese individuals with atrial fibrillation: the CARDIO-FIT study. *J Am Coll Cardiol* 2015;**66**:985–96. <https://doi.org/10.1016/j.jacc.2015.06.488>
142. Hegbom F, Stavem K, Sire S, Haldal M, Orning OM, Gjesdal K. Effects of short-term exercise training on symptoms and quality of life in patients with chronic atrial fibrillation. *Int J Cardiol* 2007;**116**:86–92. <https://doi.org/10.1016/j.ijcard.2006.03.034>
143. Osbak PS, Mourier M, Kjaer A, Henriksen JH, Kofoed KF, Jensen GB. A randomized study of the effects of exercise training on patients with atrial fibrillation. *Am Heart J* 2011;**162**:1080–7. <https://doi.org/10.1016/j.ahj.2011.09.013>
144. Malmo V, Nes BM, Amundsen BH, Tjonna AE, Stoylen A, Rossvoll O, et al. Aerobic interval training reduces the burden of atrial fibrillation in the short term: a randomized trial. *Circulation* 2016;**133**:466–73. <https://doi.org/10.1161/CIRCULATIONAHA.115.018220>
145. Oesterle A, Giancaterino S, Van Noord MG, Pellegrini CN, Fan D, Srivatsa UN, et al. Effects of supervised exercise training on atrial fibrillation: a meta-analysis of randomized controlled trials. *J Cardiopulm Rehabil Prev* 2022;**42**:258–65. <https://doi.org/10.1097/HCR.0000000000000665>
146. Elliott AD, Verdicchio CV, Mahajan R, Middeldorp ME, Gallagher C, Mishima RS, et al. An exercise and physical activity program in patients with atrial fibrillation: the ACTIVE-AF randomized controlled trial. *JACC Clin Electrophysiol* 2023;**9**:455–65. <https://doi.org/10.1016/j.jacep.2022.12.002>
147. Voskoboinik A, Kalman JM, De Silva A, Nicholls T, Costello B, Nanayakkara S, et al. Alcohol abstinence in drinkers with atrial fibrillation. *N Engl J Med* 2020;**382**:20–8. <https://doi.org/10.1056/NEJMoa1817591>
148. Holmqvist F, Guan N, Zhu Z, Kowey PR, Allen LA, Fonarow GC, et al. Impact of obstructive sleep apnea and continuous positive airway pressure therapy on outcomes in patients with atrial fibrillation—results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Am Heart J* 2015;**169**:647–654.e2. <https://doi.org/10.1016/j.ahj.2014.12.024>
149. Fein AS, Shvilkin A, Shah D, Haffajee CI, Das S, Kumar K, et al. Treatment of obstructive sleep apnea reduces the risk of atrial fibrillation recurrence after catheter ablation. *J Am Coll Cardiol* 2013;**62**:300–5. <https://doi.org/10.1016/j.jacc.2013.03.052>
150. Li L, Wang ZV, Li J, Ge X, Guo LZ, Wang Y, et al. Efficacy of catheter ablation of atrial fibrillation in patients with obstructive sleep apnea with and without continuous positive airway pressure treatment: a meta-analysis of observational studies. *Europace* 2014;**16**:1309–14. <https://doi.org/10.1093/europace/euu066>
151. Naruse Y, Tada H, Satoh M, Yanagihara M, Tsuneoka H, Hirata Y, et al. Concomitant obstructive sleep apnea increases the recurrence of atrial fibrillation following radiofrequency catheter ablation of atrial fibrillation: clinical impact of continuous positive airway pressure therapy. *Heart Rhythm* 2013;**10**:331–7. <https://doi.org/10.1016/j.hrthm.2012.11.015>
152. Qureshi WT, Nasir UB, Alqalyoobi S, O'Neal WT, Mawri S, Sabbagh S, et al. Meta-analysis of continuous positive airway pressure as a therapy of atrial fibrillation in obstructive sleep apnea. *Am J Cardiol* 2015;**116**:1767–73. <https://doi.org/10.1016/j.amjcard.2015.08.046>
153. Shukla A, Aizer A, Holmes D, Fowler S, Park DS, Bernstein S, et al. Effect of obstructive sleep apnea treatment on atrial fibrillation recurrence: a meta-analysis. *JACC Clin Electrophysiol* 2015;**1**:41–51. <https://doi.org/10.1016/j.jacep.2015.02.014>
154. Nalliah CJ, Wong GR, Lee G, Voskoboinik A, Kee K, Goldin J, et al. Impact of CPAP on the atrial fibrillation substrate in obstructive sleep apnea: the SLEEP-AF study. *JACC Clin Electrophysiol* 2022;**8**:869–77. <https://doi.org/10.1016/j.jacep.2022.04.015>
155. Kadhikar M, Middeldorp ME, Elliott AD, Jones D, Hendriks JML, Gallagher C, et al. Self-reported daytime sleepiness and sleep-disordered breathing in patients with atrial

- fibrillation: SNOozE-AF. *Can J Cardiol* 2019;**35**:1457–64. <https://doi.org/10.1016/j.cjca.2019.07.627>
156. Traaen GM, Overland B, Aakeroy L, Hunt TE, Bendz C, Sande L, et al. Prevalence, risk factors, and type of sleep apnea in patients with paroxysmal atrial fibrillation. *Int J Cardiol Heart Vasc* 2020;**26**:100447. <https://doi.org/10.1016/j.ijcha.2019.100447>
  157. Kadhim K, Middeldorp ME, Elliott AD, Agbaedeng T, Gallagher C, Malik V, et al. Prevalence and assessment of sleep-disordered breathing in patients with atrial fibrillation: a systematic review and meta-analysis. *Can J Cardiol* 2021;**37**:1846–56. <https://doi.org/10.1016/j.cjca.2021.09.026>
  158. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish atrial fibrillation cohort study. *Eur Heart J* 2012;**33**:1500–10. <https://doi.org/10.1093/eurheartj/ehr488>
  159. Lopes LC, Spencer FA, Neumann I, Ventresca M, Ebrahim S, Zhou Q, et al. Systematic review of observational studies assessing bleeding risk in patients with atrial fibrillation not using anticoagulants. *PLoS One* 2014;**9**:e88131. <https://doi.org/10.1371/journal.pone.0088131>
  160. Potpara TS, Polovina MM, Licina MM, Marinkovic JM, Lip GY. Predictors and prognostic implications of incident heart failure following the first diagnosis of atrial fibrillation in patients with structurally normal hearts: the Belgrade atrial fibrillation study. *Eur J Heart Fail* 2013;**15**:415–24. <https://doi.org/10.1093/eurjhf/hft004>
  161. Noubiap JJ, Feteih VF, Middeldorp ME, Fitzgerald JL, Thomas G, Kleinig T, et al. A meta-analysis of clinical risk factors for stroke in anticoagulant-naïve patients with atrial fibrillation. *Europace* 2021;**23**:1528–38. <https://doi.org/10.1093/europace/euab087>
  162. McEvoy JW, Touyz RM, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, et al. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J* 2024. <https://doi.org/10.1093/eurheartj/ehae178>
  163. Santoro F, Di Biase L, Trivedi C, Burkhardt JD, Paoletti Perini A, Sanchez J, et al. Impact of uncontrolled hypertension on atrial fibrillation ablation outcome. *JACC Clin Electrophysiol* 2015;**1**:164–73. <https://doi.org/10.1016/j.jacep.2015.04.002>
  164. Trines SA, Stabile G, Arbelo E, Dagnes N, Brugada J, Kautzner J, et al. Influence of risk factors in the ESC-EHRA EORP atrial fibrillation ablation long-term registry. *Pacing Clin Electrophysiol* 2019;**42**:1365–73. <https://doi.org/10.1111/pace.13763>
  165. Shah AN, Mittal S, Sichrovsky TC, Cotiga D, Arshad A, Maleki K, et al. Long-term outcome following successful pulmonary vein isolation: pattern and prediction of very late recurrence. *J Cardiovasc Electrophysiol* 2008;**19**:661–7. <https://doi.org/10.1111/j.1540-8167.2008.01101.x>
  166. Berruezo A, Tamborero D, Mont L, Benito B, Tolosana JM, Sitges M, et al. Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation. *Eur Heart J* 2007;**28**:836–41. <https://doi.org/10.1093/eurheartj/ehm027>
  167. Themistoclakis S, Schweikert RA, Saliba WI, Bonso A, Rossillo A, Bader G, et al. Clinical predictors and relationship between early and late atrial tachyarrhythmias after pulmonary vein antrum isolation. *Heart Rhythm* 2008;**5**:679–85. <https://doi.org/10.1016/j.hrthm.2008.01.031>
  168. Letsas KP, Weber R, Burkle G, Mihos CC, Minners J, Kalusche D, et al. Pre-ablative predictors of atrial fibrillation recurrence following pulmonary vein isolation: the potential role of inflammation. *Europace* 2009;**11**:158–63. <https://doi.org/10.1093/europace/eun309>
  169. Khaykin Y, Oosthuizen R, Zarnett L, Essebag V, Parkash R, Seabrook C, et al. Clinical predictors of arrhythmia recurrences following pulmonary vein antrum isolation for atrial fibrillation: predicting arrhythmia recurrence post-PVAI. *J Cardiovasc Electrophysiol* 2011;**22**:1206–14. <https://doi.org/10.1111/j.1540-8167.2011.02108.x>
  170. Kamioka M, Hijioka N, Matsumoto Y, Nodera M, Kaneshiro T, Suzuki H, et al. Uncontrolled blood pressure affects atrial remodeling and adverse clinical outcome in paroxysmal atrial fibrillation. *Pacing Clin Electrophysiol* 2018;**41**:402–10. <https://doi.org/10.1111/pace.13311>
  171. Zylla MM, Hochadel M, Andresen D, Brachmann J, Eckardt L, Hoffmann E, et al. Ablation of atrial fibrillation in patients with hypertension—an analysis from the German ablation registry. *J Clin Med* 2020;**9**:1–14. <https://doi.org/10.3390/jcm9082402>
  172. Galzerano D, Di Michele S, Paolisso G, Tuccillo B, Lama D, Carbotta S, et al. A multicentre, randomized study of telmisartan versus carvedilol for prevention of atrial fibrillation recurrence in hypertensive patients. *J Renin Angiotensin Aldosterone Syst* 2012;**13**:496–503. <https://doi.org/10.1177/1470320312443909>
  173. Du H, Fan J, Ling Z, Woo K, Su L, Chen S, et al. Effect of nifedipine versus telmisartan on prevention of atrial fibrillation recurrence in hypertensive patients. *Hypertension* 2013;**61**:786–92. <https://doi.org/10.1161/HYPERTENSIONAHA.111.202309>
  174. Giannopoulos G, Kossyvakis C, Efreimidis M, Katsivas A, Panagopoulou V, Doudoumis K, et al. Central sympathetic inhibition to reduce postablation atrial fibrillation recurrences in hypertensive patients: a randomized, controlled study. *Circulation* 2014;**130**:1346–52. <https://doi.org/10.1161/CIRCULATIONAHA.114.010999>
  175. Schneider MP, Hua TA, Bohm M, Wachtell K, Kjeldsen SE, Schmieder RE. Prevention of atrial fibrillation by renin-angiotensin system inhibition: a meta-analysis. *J Am Coll Cardiol* 2010;**55**:2299–307. <https://doi.org/10.1016/j.jacc.2010.01.043>
  176. Blum S, Aeschbacher S, Meyre P, Zwimpfer L, Reichlin T, Beer JH, et al. Incidence and predictors of atrial fibrillation progression. *J Am Heart Assoc* 2019;**8**:e012554. <https://doi.org/10.1161/JAHA.119.012554>
  177. Kotecha D, Piccini JP. Atrial fibrillation in heart failure: what should we do? *Eur Heart J* 2015;**36**:3250–7. <https://doi.org/10.1093/eurheartj/ehv513>
  178. Santhanakrishnan R, Wang N, Larson MG, Magnani JW, McManus DD, Lubitz SA, et al. Atrial fibrillation begets heart failure and vice versa: temporal associations and differences in preserved versus reduced ejection fraction. *Circulation* 2016;**133**:484–92. <https://doi.org/10.1161/CIRCULATIONAHA.115.018614>
  179. Rossello X, Gil V, Escoda R, Jacob J, Aguirre A, Martín-Sánchez FJ, et al. Editor's choice – impact of identifying precipitating factors on 30-day mortality in acute heart failure patients. *Eur Heart J Acute Cardiovasc Care* 2019;**8**:667–80. <https://doi.org/10.1177/2048872619869328>
  180. Atrial Fibrillation Investigators. Echocardiographic predictors of stroke in patients with atrial fibrillation: a prospective study of 1066 patients from 3 clinical trials. *Arch Intern Med* 1998;**158**:1316–20. <https://doi.org/10.1001/archinte.158.12.1316>
  181. Rohla M, Weiss TW, Pecan L, Patti G, Siller-Matula JM, Schnabel RB, et al. Risk factors for thromboembolic and bleeding events in anticoagulated patients with atrial fibrillation: the prospective, multicentre observational PREvention of thromboembolic events—European Registry in Atrial Fibrillation (PREFER in AF). *BMJ Open* 2019;**9**:e022478. <https://doi.org/10.1136/bmjopen-2018-022478>
  182. Kotecha D, Chudasama R, Lane DA, Kirchhof P, Lip GY. Atrial fibrillation and heart failure due to reduced versus preserved ejection fraction: a systematic review and meta-analysis of death and adverse outcomes. *Int J Cardiol* 2016;**203**:660–6. <https://doi.org/10.1016/j.ijcard.2015.10.220>
  183. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 focused update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2023;**44**:3627–39. <https://doi.org/10.1093/eurheartj/ehad195>
  184. ACTIVE I Investigators; Yusuf S, Healey JS, Pogue J, Chrolavicius S, Flather M, et al. Irbesartan in patients with atrial fibrillation. *N Engl J Med* 2011;**364**:928–38. <https://doi.org/10.1056/NEJMoa1008816>
  185. Ziff OJ, Lane DA, Samra M, Griffith M, Kirchhof P, Lip GY, et al. Safety and efficacy of digoxin: systematic review and meta-analysis of observational and controlled trial data. *BMJ* 2015;**351**:h4451. <https://doi.org/10.1136/bmj.h4451>
  186. Groeneweld HF, Crijns HJ, Van den Berg MP, Van Sonderen E, Alings AM, Tijssen JG, et al. The effect of rate control on quality of life in patients with permanent atrial fibrillation: data from the RACE II (Rate Control Efficacy in Permanent Atrial Fibrillation II) study. *J Am Coll Cardiol* 2011;**58**:1795–803. <https://doi.org/10.1016/j.jacc.2011.06.055>
  187. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J* 2021;**42**:3427–520. <https://doi.org/10.1093/eurheartj/ehab364>
  188. Solomon SD, Claggett B, Lewis EF, Desai A, Anand I, Sweitzer NK, et al. Influence of ejection fraction on outcomes and efficacy of spironolactone in patients with heart failure with preserved ejection fraction. *Eur Heart J* 2016;**37**:455–62. <https://doi.org/10.1093/eurheartj/ehv464>
  189. Lund LH, Claggett B, Liu J, Lam CS, Jhund PS, Rosano GM, et al. Heart failure with mid-range ejection fraction in CHARM: characteristics, outcomes and effect of candesartan across the entire ejection fraction spectrum. *Eur J Heart Fail* 2018;**20**:1230–9. <https://doi.org/10.1002/ejhf.1149>
  190. Cleland JGF, Bunting KV, Flather MD, Altman DG, Holmes J, Coats AJS, et al. Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction: an individual patient-level analysis of double-blind randomized trials. *Eur Heart J* 2018;**39**:26–35. <https://doi.org/10.1093/eurheartj/ehx564>
  191. Tica O, Khamboo W, Kotecha D. Breaking the cycle of heart failure with preserved ejection fraction and atrial fibrillation. *Card Fail Rev* 2022;**8**:e32. <https://doi.org/10.15420/cfr.2022.03>
  192. Nguyen BO, Crijns H, Tijssen JGP, Geelhoed B, Hobbelt AH, Hemels MEW, et al. Long-term outcome of targeted therapy of underlying conditions in patients with early persistent atrial fibrillation and heart failure: data of the RACE 3 trial. *Europace* 2022;**24**:910–20. <https://doi.org/10.1093/europace/euab270>
  193. Wang A, Green JB, Halperin JL, Piccini JP, Sr. Atrial fibrillation and diabetes mellitus: JACC review topic of the week. *J Am Coll Cardiol* 2019;**74**:1107–15. <https://doi.org/10.1016/j.jacc.2019.07.020>
  194. Aljila F, Buttia C, Reichlin T, Razvi S, Minder B, Wilhelm M, et al. Association of diabetes with atrial fibrillation types: a systematic review and meta-analysis. *Cardiovasc Diabetol* 2021;**20**:230. <https://doi.org/10.1186/s12933-021-01423-2>
  195. Ding WY, Kotalczyk A, Boriani G, Marin F, Blomstrom-Lundqvist C, Potpara TS, et al. Impact of diabetes on the management and outcomes in atrial fibrillation: an analysis from the ESC-EHRA EORP-AF long-term general registry. *Eur J Intern Med* 2022;**103**:41–9. <https://doi.org/10.1016/j.ejim.2022.04.026>
  196. Proietti M, Romiti GF, Basili S. The case of diabetes mellitus and atrial fibrillation: underlining the importance of non-cardiovascular comorbidities. *Eur J Intern Med* 2022;**103**:38–40. <https://doi.org/10.1016/j.ejim.2022.06.017>



197. Karayiannides S, Norhammar A, Landstedt-Hallin L, Friberg L, Lundman P. Prognostic impact of type 1 and type 2 diabetes mellitus in atrial fibrillation and the effect of severe hypoglycaemia: a nationwide cohort study. *Eur J Prev Cardiol* 2022;**29**:1759–69. <https://doi.org/10.1093/eurjpc/zwac093>
198. Lip GY, Nieuwlaet R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. *Chest* 2010;**137**:263–72. <https://doi.org/10.1378/chest.09-1584>
199. Abdel-Qadir H, Gunn M, Lega IC, Pang A, Austin PC, Singh SM, et al. Association of diabetes duration and glycemic control with stroke rate in patients with atrial fibrillation and diabetes: a population-based cohort study. *J Am Heart Assoc* 2022;**11**:e023643. <https://doi.org/10.1161/JAHA.121.023643>
200. Donnellan E, Aagaard P, Kanj M, Jaber W, Elshazly M, Hoosien M, et al. Association between pre-ablation glycemic control and outcomes among patients with diabetes undergoing atrial fibrillation ablation. *JACC Clin Electrophysiol* 2019;**5**:897–903. <https://doi.org/10.1016/j.jacep.2019.05.018>
201. D'Souza S, Elshazly MB, Dargham SR, Donnellan E, Asaad N, Hayat S, et al. Atrial fibrillation catheter ablation complications in obese and diabetic patients: insights from the US nationwide inpatient sample 2005–2013. *Clin Cardiol* 2021;**44**:1151–60. <https://doi.org/10.1002/clc.23667>
202. Creta A, Providencia R, Adragao P, de Asmundis C, Chun J, Chierchia G, et al. Impact of type-2 diabetes mellitus on the outcomes of catheter ablation of atrial fibrillation (European Observational Multicentre Study). *Am J Cardiol* 2020;**125**:901–6. <https://doi.org/10.1016/j.amjcard.2019.12.037>
203. Wang Z, Wang YJ, Liu ZY, Li Q, Kong YW, Chen YW, et al. Effect of insulin resistance on recurrence after radiofrequency catheter ablation in patients with atrial fibrillation. *Cardiovasc Drugs Ther* 2023;**37**:705–13. <https://doi.org/10.1007/s10557-022-07317-z>
204. Papazoglou AS, Kartas A, Moysidis DV, Tsagkaris C, Papadakos SP, Bekiaridou A, et al. Glycemic control and atrial fibrillation: an intricate relationship, yet under investigation. *Cardiovasc Diabetol* 2022;**21**:39. <https://doi.org/10.1186/s12933-022-01473-0>
205. Zhang Z, Zhang X, Korantzopoulos P, Letsas KP, Tse G, Gong M, et al. Thiazolidinedione use and atrial fibrillation in diabetic patients: a meta-analysis. *BMC Cardiovasc Disord* 2017;**17**:96. <https://doi.org/10.1186/s12872-017-0531-4>
206. Bell DSH, Goncalves E. Atrial fibrillation and type 2 diabetes: prevalence, etiology, pathophysiology and effect of anti-diabetic therapies. *Diabetes Obes Metab* 2019;**21**:210–7. <https://doi.org/10.1111/dom.13512>
207. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J* 2023;**44**:4043–140. <https://doi.org/10.1093/eurheartj/ehad192>
208. Di Benedetto L, Michels G, Luben R, Khaw KT, Pfister R. Individual and combined impact of lifestyle factors on atrial fibrillation in apparently healthy men and women: the EPIC-Norfolk prospective population study. *Eur J Prev Cardiol* 2018;**25**:1374–83. <https://doi.org/10.1177/2047487318782379>
209. Grundvold I, Bodegard J, Nilsson PM, Svennblad B, Johansson G, Ostgren CJ, et al. Body weight and risk of atrial fibrillation in 7,169 patients with newly diagnosed type 2 diabetes: an observational study. *Cardiovasc Diabetol* 2015;**14**:5. <https://doi.org/10.1186/s12933-014-0170-3>
210. Wong CX, Sullivan T, Sun MT, Mahajan R, Pathak RK, Middeldorp M, et al. Obesity and the risk of incident, post-operative, and post-ablation atrial fibrillation: a meta-analysis of 626,603 individuals in 51 studies. *JACC Clin Electrophysiol* 2015;**1**:139–52. <https://doi.org/10.1016/j.jacep.2015.04.004>
211. Providencia R, Adragao P, de Asmundis C, Chun J, Chierchia G, Defaye P, et al. Impact of body mass index on the outcomes of catheter ablation of atrial fibrillation: a European observational multicenter study. *J Am Heart Assoc* 2019;**8**:e012253. <https://doi.org/10.1161/JAHA.119.012253>
212. Glover BM, Hong KL, Dagues N, Arbelo E, Laroche C, Riahi S, et al. Impact of body mass index on the outcome of catheter ablation of atrial fibrillation. *Heart* 2019;**105**:244–50. <https://doi.org/10.1136/heartjnl-2018-313490>
213. Gessler N, Willems S, Steven D, Aberle J, Akbulak RO, Gosau N, et al. Supervised obesity reduction trial for AF ablation patients: results from the SORT-AF trial. *Europace* 2021;**23**:1548–58. <https://doi.org/10.1093/europace/euab122>
214. Mohanty S, Mohanty P, Natale V, Trivedi C, Gianni C, Burkhardt JD, et al. Impact of weight loss on ablation outcome in obese patients with longstanding persistent atrial fibrillation. *J Cardiovasc Electrophysiol* 2018;**29**:246–53. <https://doi.org/10.1111/jce.13394>
215. Donnellan E, Wazni OM, Kanj M, Elshazly M, Hussein AA, Patel DR, et al. Impact of risk-factor modification on arrhythmia recurrence among morbidly obese patients undergoing atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2020;**31**:1979–86. <https://doi.org/10.1111/jce.14607>
216. Donnellan E, Wazni OM, Kanj M, Baranowski B, Cremer P, Harb S, et al. Association between pre-ablation bariatric surgery and atrial fibrillation recurrence in morbidly obese patients undergoing atrial fibrillation ablation. *Europace* 2019;**21**:1476–83. <https://doi.org/10.1093/europace/euz183>
217. Donnellan E, Wazni O, Kanj M, Hussein A, Baranowski B, Lindsay B, et al. Outcomes of atrial fibrillation ablation in morbidly obese patients following bariatric surgery compared with a nonobese cohort. *Circ Arrhythm Electrophysiol* 2019;**12**:e007598. <https://doi.org/10.1161/CIRCEP.119.007598>
218. Moola AI, Parrini I, Tetta C, Lucà F, Parise G, Rao CM, et al. Obstructive sleep apnea and atrial fibrillation. *J Clin Med* 2022;**11**:1242. <https://doi.org/10.3390/jcm11051242>
219. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline. *J Clin Sleep Med* 2017;**13**:479–504. <https://doi.org/10.5664/jcsm.6506>
220. Linz D, Brooks AG, Elliott AD, Nalliah CJ, Hendriks JML, Middeldorp ME, et al. Variability of sleep apnea severity and risk of atrial fibrillation: the VARIO-SA-AF study. *JACC Clin Electrophysiol* 2019;**5**:692–701. <https://doi.org/10.1016/j.jacep.2019.03.005>
221. Linz D, Linz B, Dobrev D, Baumert M, Hendriks JM, Pepin JL, et al. Personalized management of sleep apnea in patients with atrial fibrillation: an interdisciplinary and translational challenge. *Int J Cardiol Heart Vasc* 2021;**35**:100843. <https://doi.org/10.1016/j.ijcha.2021.100843>
222. Kanagala R, Murali NS, Friedman PA, Ammash NM, Gersh BJ, Ballman KV, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. *Circulation* 2003;**107**:2589–94. <https://doi.org/10.1161/01.CIR.0000068337.25994.21>
223. Abumumar AM, Newman D, Dorian P, Shapiro CM. Cardiac effects of CPAP treatment in patients with obstructive sleep apnea and atrial fibrillation. *J Interv Card Electrophysiol* 2019;**54**:289–97. <https://doi.org/10.1007/s10840-018-0482-4>
224. Mittal S, Golombek D, Pimienta J. Sleep apnoea and AF: where do we stand? Practical advice for clinicians. *Arrhythm Electrophysiol Rev* 2021;**10**:140–6. <https://doi.org/10.15420/aer.2021.05>
225. Hunt TE, Traaen GM, Aakeroy L, Bendz C, Overland B, Akre H, et al. Effect of continuous positive airway pressure therapy on recurrence of atrial fibrillation after pulmonary vein isolation in patients with obstructive sleep apnea: a randomized controlled trial. *Heart Rhythm* 2022;**19**:1433–41. <https://doi.org/10.1016/j.hrthm.2022.06.016>
226. Caples SM, Mansukhani MP, Friedman PA, Somers VK. The impact of continuous positive airway pressure treatment on the recurrence of atrial fibrillation post cardioversion: a randomized controlled trial. *Int J Cardiol* 2019;**278**:133–6. <https://doi.org/10.1016/j.ijcard.2018.11.100>
227. Labarca G, Dreyse J, Drake L, Jorquera J, Barbe F. Efficacy of continuous positive airway pressure (CPAP) in the prevention of cardiovascular events in patients with obstructive sleep apnea: systematic review and meta-analysis. *Sleep Med Rev* 2020;**52**:101312. <https://doi.org/10.1016/j.smrv.2020.101312>
228. Abuzaid AS, Al Ashry HS, Elbadawi A, Ld H, Saad M, Elgendy IY, et al. Meta-analysis of cardiovascular outcomes with continuous positive airway pressure therapy in patients with obstructive sleep apnea. *Am J Cardiol* 2017;**120**:693–9. <https://doi.org/10.1016/j.amjcard.2017.05.042>
229. Yu J, Zhou Z, McEvoy RD, Anderson CS, Rodgers A, Perkovic V, et al. Association of positive airway pressure with cardiovascular events and death in adults with sleep apnea: a systematic review and meta-analysis. *JAMA* 2017;**318**:156–66. <https://doi.org/10.1001/jama.2017.7967>
230. McEvoy RD, Antic NA, Heeley E, Luo Y, Ou Q, Zhang X, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016;**375**:919–31. <https://doi.org/10.1056/NEJMoa1606599>
231. Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Albersen IE, Lane DA, et al. Alcohol intake and prognosis of atrial fibrillation. *Heart* 2013;**99**:1093–9. <https://doi.org/10.1136/heartjnl-2013-304036>
232. Lim C, Kim T-H, Yu HT, Lee S-R, Cha M-J, Lee J-M, et al. Effect of alcohol consumption on the risk of adverse events in atrial fibrillation: from the COMparison study of Drugs for symptom control and complication pREvention of Atrial Fibrillation (CODE-AF) registry. *EP Europace* 2021;**23**:548–56. <https://doi.org/10.1093/europace/euaa340>
233. Lee SR, Choi EK, Jung JH, Han KD, Oh S, Lip GYH. Lower risk of stroke after alcohol abstinence in patients with incident atrial fibrillation: a nationwide population-based cohort study. *Eur Heart J* 2021;**42**:4759–68. <https://doi.org/10.1093/eurheartj/ehab315>
234. Pisters R, Lane DA, Nieuwlaet R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest* 2010;**138**:1093–100. <https://doi.org/10.1378/chest.10-0134>
235. Takahashi Y, Nitta J, Kobori A, Sakamoto Y, Nagata Y, Tanimoto K, et al. Alcohol consumption reduction and clinical outcomes of catheter ablation for atrial fibrillation. *Circ Arrhythm Electrophysiol* 2021;**14**:e009770. <https://doi.org/10.1161/CIRCEP.121.009770>
236. Friberg L, Hammar N, Rosenqvist M. Stroke in paroxysmal atrial fibrillation: report from the Stockholm cohort of atrial fibrillation. *Eur Heart J* 2010;**31**:967–75. <https://doi.org/10.1093/eurheartj/ehn599>
237. Banerjee A, Taillandier S, Olesen JB, Lane DA, Lallemand B, Lip GY, et al. Pattern of atrial fibrillation and risk of outcomes: the Loire valley atrial fibrillation project. *Int J Cardiol* 2013;**167**:2682–7. <https://doi.org/10.1016/j.ijcard.2012.06.118>
238. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 1991;**22**:983–8. <https://doi.org/10.1161/01.STR.22.8.983>

239. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med* 2007;**146**: 857–67. <https://doi.org/10.7326/0000-4819-146-12-200706190-00007>
240. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;**383**: 955–62. [https://doi.org/10.1016/S0140-6736\(13\)62343-0](https://doi.org/10.1016/S0140-6736(13)62343-0)
241. Sjalander S, Sjalander A, Svensson PJ, Friberg L. Atrial fibrillation patients do not benefit from acetylsalicylic acid. *Europace* 2014;**16**:631–8. <https://doi.org/10.1093/eurpace/eut333>
242. Connolly SJ, Eikelboom J, Joyner C, Diener HC, Hart R, Golitsyn S, et al. Apixaban in patients with atrial fibrillation. *N Engl J Med* 2011;**364**:806–17. <https://doi.org/10.1056/NEJMoa1007432>
243. van Doorn S, Rutten FH, O'Flynn CM, Oudega R, Hoes AW, Moons KGM, et al. Effectiveness of CHA2DS2-VASc based decision support on stroke prevention in atrial fibrillation: a cluster randomised trial in general practice. *Int J Cardiol* 2018;**273**:123–9. <https://doi.org/10.1016/j.ijcard.2018.08.096>
244. Borre ED, Goode A, Raitz G, Shah B, Lowenstern A, Chatterjee R, et al. Predicting thromboembolic and bleeding event risk in patients with non-valvular atrial fibrillation: a systematic review. *Thromb Haemost* 2018;**118**:2171–87. <https://doi.org/10.1055/s-0038-1675400>
245. van der Endt VHW, Milders J, de Vries BBLP, Trines SA, Groenwold RHH, Dekkers OM, et al. Comprehensive comparison of stroke risk score performance: a systematic review and meta-analysis among 6 267 728 patients with atrial fibrillation. *Europace* 2022;**24**:1739–53. <https://doi.org/10.1093/eurpace/eauc096>
246. Quinn GR, Severdija ON, Chang Y, Singer DE. Wide variation in reported rates of stroke across cohorts of patients with atrial fibrillation. *Circulation* 2017;**135**: 208–19. <https://doi.org/10.1161/CIRCULATIONAHA.116.024057>
247. Pisters R, Lane DA, Marin F, Camm AJ, Lip GY. Stroke and thromboembolism in atrial fibrillation. *Circ J* 2012;**76**:2289–304. <https://doi.org/10.1253/circj.CJ-12-1036>
248. Hohnloser SH, Hijazi Z, Thomas L, Alexander JH, Amerena J, Hanna M, et al. Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial. *Eur Heart J* 2012;**33**:2821–30. <https://doi.org/10.1093/eurheartj/ehs274>
249. Fox KA, Piccini JP, Wojdyla D, Becker RC, Halperin JL, Nessel CC, et al. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. *Eur Heart J* 2011;**32**:2387–94. <https://doi.org/10.1093/eurheartj/ehr342>
250. Yaghi S, Henninger N, Giles JA, Leon Guerrero C, Mistry E, Liberman AL, et al. Ischaemic stroke on anticoagulation therapy and early recurrence in acute cardioembolic stroke: the IAC study. *J Neurol Neurosurg Psychiatry* 2021;**92**:1062–7. <https://doi.org/10.1136/jnnp-2021-326166>
251. Ocak G, Khairoun M, Khairoun O, Bos WJW, Fu EL, Cramer MJ, et al. Chronic kidney disease and atrial fibrillation: a dangerous combination. *PLoS One* 2022;**17**:e0266046. <https://doi.org/10.1371/journal.pone.0266046>
252. Seiffge DJ, De Marchis GM, Koga M, Paciaroni M, Wilson D, Cappellari M, et al. Ischemic stroke despite oral anticoagulant therapy in patients with atrial fibrillation. *Ann Neurol* 2020;**87**:677–87. <https://doi.org/10.1002/ana.25700>
253. Paciaroni M, Agnelli G, Falocci N, Caso V, Becattini C, Marcheselli S, et al. Prognostic value of trans-thoracic echocardiography in patients with acute stroke and atrial fibrillation: findings from the RAF study. *J Neurol* 2016;**263**:231–7. <https://doi.org/10.1007/s00415-015-7957-3>
254. Hijazi Z, Oldgren J, Siegbahn A, Wallentin L. Application of biomarkers for risk stratification in patients with atrial fibrillation. *Clin Chem* 2017;**63**:152–64. <https://doi.org/10.1137/clinchem.2016.255182>
255. Singleton MJ, Yuan Y, Dawood FZ, Howard G, Judd SE, Zakai NA, et al. Multiple blood biomarkers and stroke risk in atrial fibrillation: the REGARDs study. *J Am Heart Assoc* 2021;**10**:e020157. <https://doi.org/10.1161/JAHA.120.020157>
256. Wu VC, Wu M, Aboyans V, Chang SH, Chen SW, Chen MC, et al. Female sex as a risk factor for ischaemic stroke varies with age in patients with atrial fibrillation. *Heart* 2020;**106**:534–40. <https://doi.org/10.1136/heartjnl-2019-315065>
257. Mikkelsen AP, Lindhardtsen J, Lip GY, Gislason GH, Torp-Pedersen C, Olesen JB. Female sex as a risk factor for stroke in atrial fibrillation: a nationwide cohort study. *J Thromb Haemost* 2012;**10**:1745–51. <https://doi.org/10.1111/j.1538-7836.2012.04853.x>
258. Antonenko K, Paciaroni M, Agnelli G, Falocci N, Becattini C, Marcheselli S, et al. Sex-related differences in risk factors, type of treatment received and outcomes in patients with atrial fibrillation and acute stroke: results from the RAF study (early recurrence and cerebral bleeding in patients with acute ischemic stroke and atrial fibrillation). *Eur Stroke J* 2017;**2**:46–53. <https://doi.org/10.1177/2396987316679577>
259. Wang X, Mobley AR, Tica O, Okoth K, Ghosh RE, Myles P, et al. Systematic approach to outcome assessment from coded electronic healthcare records in the DaRe2THINK NHS-embedded randomized trial. *Eur Heart J - Dig Health* 2022;**3**: 426–36. <https://doi.org/10.1093/ehjdh/ztac046>
260. Rivard L, Khairy P, Talajic M, Tardif JC, Nattel S, Bherer L, et al. Blinded randomized trial of anticoagulation to prevent ischemic stroke and neurocognitive impairment in atrial fibrillation (BRAIN-AF): methods and design. *Can J Cardiol* 2019;**35**:1069–77. <https://doi.org/10.1016/j.cjca.2019.04.022>
261. Chung S, Kim TH, Uhm JS, Cha MJ, Lee JM, Park J, et al. Stroke and systemic embolism and other adverse outcomes of heart failure with preserved and reduced ejection fraction in patients with atrial fibrillation (from the COmparison study of Drugs for symptom control and complication prEvention of Atrial Fibrillation [CODE-AF]). *Am J Cardiol* 2020;**125**:68–75. <https://doi.org/10.1016/j.amjcard.2019.09.035>
262. Uhm JS, Kim J, Yu HT, Kim TH, Lee SR, Cha MJ, et al. Stroke and systemic embolism in patients with atrial fibrillation and heart failure according to heart failure type. *ESC Heart Fail* 2021;**8**:1582–9. <https://doi.org/10.1002/ehf2.13264>
263. McMurray JJ, Ezekowitz JA, Lewis BS, Gersh BJ, van Diepen S, Amerena J, et al. Left ventricular systolic dysfunction, heart failure, and the risk of stroke and systemic embolism in patients with atrial fibrillation: insights from the ARISTOTLE trial. *Circ Heart Fail* 2013;**6**:451–60. <https://doi.org/10.1161/CIRCHEARTFAILURE.112.000143>
264. Kim D, Yang PS, Kim TH, Jang E, Shin H, Kim HY, et al. Ideal blood pressure in patients with atrial fibrillation. *J Am Coll Cardiol* 2018;**72**:1233–45. <https://doi.org/10.1016/j.jacc.2018.05.076>
265. Lip GY, Clementy N, Pericart L, Banerjee A, Fauchier L. Stroke and major bleeding risk in elderly patients aged  $\geq 75$  years with atrial fibrillation: the Loire valley atrial fibrillation project. *Stroke* 2015;**46**:143–50. <https://doi.org/10.1161/STROKEAHA.114.007199>
266. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2022. *Diabetes Care* 2022;**45**:S17–38. <https://doi.org/10.2337/medc22-s002>
267. Steensig K, Olesen KKW, Thim T, Nielsen JC, Jensen SE, Jensen LO, et al. Should the presence or extent of coronary artery disease be quantified in the CHA2DS2-VASc score in atrial fibrillation? A report from the western Denmark heart registry. *Thromb Haemost* 2018;**118**:2162–70. <https://doi.org/10.1055/s-0038-1675401>
268. Zabalgoitia M, Halperin JL, Pearce LA, Blackshear JL, Asinger RV, Hart RG. Transesophageal echocardiographic correlates of clinical risk of thromboembolism in nonvalvular atrial fibrillation. Stroke prevention in atrial fibrillation III investigators. *J Am Coll Cardiol* 1998;**31**:1622–6. [https://doi.org/10.1016/S0735-1097\(98\)00146-6](https://doi.org/10.1016/S0735-1097(98)00146-6)
269. Stroke Prevention in Atrial Fibrillation Investigators Committee on Echocardiography. Transesophageal echocardiography in atrial fibrillation: standards for acquisition and interpretation and assessment of interobserver variability. Stroke prevention in atrial fibrillation investigators committee on echocardiography. *J Am Soc Echocardiogr* 1996;**9**:556–66. [https://doi.org/10.1016/S0894-7317\(96\)90127-3](https://doi.org/10.1016/S0894-7317(96)90127-3)
270. Lozier MR, Sanchez AM, Lee JJ, Donath EM, Font VE, Escobar E. Thromboembolic outcomes of different anticoagulation strategies for patients with atrial fibrillation in the setting of hypertrophic cardiomyopathy: a systematic review. *J Atr Fibrillation* 2019;**12**:2207. <https://doi.org/10.4022/jafb.2207>
271. Guttman OP, Rahman MS, O'Mahony C, Anastakis A, Elliott PM. Atrial fibrillation and thromboembolism in patients with hypertrophic cardiomyopathy: systematic review. *Heart* 2014;**100**:465–72. <https://doi.org/10.1136/heartjnl-2013-304276>
272. Guttman OP, Pavlou M, O'Mahony C, Monserrat L, Anastakis A, Rapezzi C, et al. Prediction of thromboembolic risk in patients with hypertrophic cardiomyopathy (HCM risk-CVA). *Eur J Heart Fail* 2015;**17**:837–45. <https://doi.org/10.1002/ehf.316>
273. Vilches S, Fontana M, Gonzalez-Lopez E, Mitrani L, Satrio G, Renju M, et al. Systemic embolism in amyloid transthyretin cardiomyopathy. *Eur J Heart Fail* 2022;**24**: 1387–96. <https://doi.org/10.1002/ehf.2566>
274. Lee SE, Park JK, Uhm JS, Kim JY, Pak HN, Lee MH, et al. Impact of atrial fibrillation on the clinical course of apical hypertrophic cardiomyopathy. *Heart* 2017;**103**:1496–501. <https://doi.org/10.1136/heartjnl-2016-310720>
275. Hirota T, Kubo T, Baba Y, Ochi Y, Takahashi A, Yamasaki N, et al. Clinical profile of thromboembolic events in patients with hypertrophic cardiomyopathy in a regional Japanese cohort—results from Kochi RYOMA study. *Circ J* 2019;**83**:1747–54. <https://doi.org/10.1253/circj.CJ-19-0186>
276. Hsu JC, Huang YT, Lin LY. Stroke risk in hypertrophic cardiomyopathy patients with atrial fibrillation: a nationwide database study. *Aging (Albany NY)* 2020;**12**:24219–27. <https://doi.org/10.18632/aging.104133>
277. Chao TF, Lip GYH, Liu CJ, Lin YJ, Chang SL, Lo LW, et al. Relationship of aging and incident comorbidities to stroke risk in patients with atrial fibrillation. *J Am Coll Cardiol* 2018;**71**:122–32. <https://doi.org/10.1016/j.jacc.2017.10.085>
278. Weijs B, Dudink E, de Vos CB, Limantoro I, Tieleman RG, Pisters R, et al. Idiopathic atrial fibrillation patients rapidly outgrow their low thromboembolic risk: a 10-year follow-up study. *Neth Heart J* 2019;**27**:487–97. <https://doi.org/10.1007/s12471-019-1272-z>
279. Bezabhe WM, Bereznicki LR, Radford J, Wimmer BC, Salahudeen MS, Garrahy E, et al. Stroke risk reassessment and oral anticoagulant initiation in primary care patients with atrial fibrillation: A ten-year follow-up. *Eur J Clin Invest* 2021;**51**:e13489. <https://doi.org/10.1111/eci.13489>
280. Fauchier L, Bodin A, Bisson A, Herbert J, Spiesser P, Clementy N, et al. Incident comorbidities, aging and the risk of stroke in 608,108 patients with atrial fibrillation: a nationwide analysis. *J Clin Med* 2020;**9**:1234. <https://doi.org/10.3390/jcm9041234>



281. Kirchhof P, Poennis T, Goette A, Camm AJ, Diener HC, Becher N, et al. Anticoagulation with edoxaban in patients with atrial high-rate episodes. *N Engl J Med* 2023;**389**:1167–79. <https://doi.org/10.1056/NEJMoa2303062>
282. Healey JS, Lopes RD, Granger CB, Alings M, Rivard L, McIntyre VF, et al. Apixaban for stroke prevention in subclinical atrial fibrillation. *N Engl J Med* 2024;**390**:107–17. <https://doi.org/10.1056/NEJMoa2310234>
283. van Walraven C, Hart RG, Singer DE, Laupacis A, Connolly S, Petersen P, et al. Oral anticoagulants vs aspirin in nonvalvular atrial fibrillation: an individual patient meta-analysis. *JAMA* 2002;**288**:2441–8. <https://doi.org/10.1001/jama.288.19.2441>
284. Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. Stroke prevention in atrial fibrillation investigators. *J Am Coll Cardiol* 2000;**35**:183–7. [https://doi.org/10.1016/S0735-1097\(99\)00489-1](https://doi.org/10.1016/S0735-1097(99)00489-1)
285. Nieuwlaat R, Dinh T, Olsson SB, Camm AJ, Capucci A, Tieleman RG, et al. Should we abandon the common practice of withholding oral anticoagulation in paroxysmal atrial fibrillation? *Eur Heart J* 2008;**29**:915–22. <https://doi.org/10.1093/eurheartj/ehh101>
286. Ruff CT. AZALEA-TIMI 71 Steering Committee. Abela-cimab, a novel factor XI/XIIa inhibitor, vs rivaroxaban in patients with atrial fibrillation: primary results of the AZALEA-TIMI 71 randomized trial. *Circulation* 2024;**148**:e282–317. <https://doi.org/10.1161/CIR.0000000000001200>
287. Piccini JP, Caso V, Connolly SJ, Fox KAA, Oldgren J, Jones WS, et al. Safety of the oral factor XIa inhibitor asundexian compared with apixaban in patients with atrial fibrillation (PACIFIC-AF): a multicentre, randomised, double-blind, double-dummy, dose-finding phase 2 study. *Lancet* 2022;**399**:1383–90. [https://doi.org/10.1016/S0140-6736\(22\)00456-1](https://doi.org/10.1016/S0140-6736(22)00456-1)
288. Tan CSS, Lee SWH. Warfarin and food, herbal or dietary supplement interactions: a systematic review. *Br J Clin Pharmacol* 2021;**87**:352–74. <https://doi.org/10.1111/bcp.14404>
289. Holbrook AM, Pereira JA, Labiris R, McDonald H, Douketis JD, Crowther M, et al. Systematic overview of warfarin and its drug and food interactions. *Arch Intern Med* 2005;**165**:1095–106. <https://doi.org/10.1001/archinte.165.10.1095>
290. Ferri N, Colombo E, Tenconi M, Baldessin L, Corsini A. Drug-drug interactions of direct oral anticoagulants (DOACs): from pharmacological to clinical practice. *Pharmaceutics* 2022;**14**:1120. <https://doi.org/10.3390/pharmaceutics14061120>
291. Mar PL, Gopinathannair R, Gengler BE, Chung MK, Perez A, Dukes J, et al. Drug interactions affecting oral anticoagulant use. *Circ Arrhythm Electrophysiol* 2022;**15**:e007956. <https://doi.org/10.1161/CIRCEP.121.007956>
292. Carnicelli AP, Hong H, Connolly SJ, Eikelboom J, Giugliano RP, Morrow DA, et al. Direct oral anticoagulants versus warfarin in patients with atrial fibrillation: patient-level network meta-analyses of randomized clinical trials with interaction testing by age and sex. *Circulation* 2022;**145**:242–55. <https://doi.org/10.1161/CIRCULATIONAHA.121.056355>
293. Kotecha D, Pollack CV, Jr, De Caterina R, Renda G, Kirchhof P. Direct oral anticoagulants halve thromboembolic events after cardioversion of AF compared with warfarin. *J Am Coll Cardiol* 2018;**72**:1984–6. <https://doi.org/10.1016/j.jacc.2018.07.083>
294. Connolly SJ, Karthikeyan G, Ntsekhe M, Haileamlak A, El Sayed A, El Ghamrawy A, et al. Rivaroxaban in rheumatic heart disease-associated atrial fibrillation. *N Engl J Med* 2022;**387**:978–88. <https://doi.org/10.1056/NEJMoa2209051>
295. Halperin JL, Hart RG, Kronmal RA, McBride R. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: stroke prevention in atrial fibrillation II study. *Lancet* 1994;**343**:687–91. [https://doi.org/10.1016/S0140-6736\(94\)91577-6](https://doi.org/10.1016/S0140-6736(94)91577-6)
296. Singer DE, Hughes RA, Gress DR, Sheehan MA, Oertel LB, Maraventano SV, et al. The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1990;**323**:1505–11. <https://doi.org/10.1056/NEJM199011293232201>
297. Gulløv AL, Koefoed BG, Petersen P, Pedersen TS, Andersen ED, Godtfredsen J, et al. Fixed minidose warfarin and aspirin alone and in combination vs adjusted-dose warfarin for stroke prevention in atrial fibrillation: second Copenhagen atrial fibrillation, aspirin, and anticoagulation study. *Arch Intern Med* 1998;**158**:1513–21. <https://doi.org/10.1001/archinte.158.14.1513>
298. Blackshear JL, Halperin JL, Hart RG, Laupacis A. Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: stroke prevention in atrial fibrillation III randomised clinical trial. *Lancet* 1996;**348**:633–8. [https://doi.org/10.1016/S0140-6736\(96\)03487-3](https://doi.org/10.1016/S0140-6736(96)03487-3)
299. Amin A, Deitelzweig S, Jing Y, Makenbaeva D, Wiederkehr D, Lin J, et al. Estimation of the impact of warfarin's time-in-therapeutic range on stroke and major bleeding rates and its influence on the medical cost avoidance associated with novel oral anticoagulant use—learnings from ARISTOTLE, ROCKET-AF, and RE-LY trials. *J Thromb Thrombolysis* 2014;**38**:150–9. <https://doi.org/10.1007/s11239-013-1048-z>
300. Sjalander S, Sjögren V, Renlund H, Norrving B, Sjalander A. Dabigatran, rivaroxaban and apixaban vs. high TTR warfarin in atrial fibrillation. *Thromb Res* 2018;**167**:113–8. <https://doi.org/10.1016/j.thromres.2018.05.022>
301. van Miert JHA, Kooistra HAM, Veeger N, Westerterp A, Piersma-Wichers M, Meijer K. Choosing between continuing vitamin K antagonists (VKA) or switching to a direct oral anticoagulant in currently well-controlled patients on VKA for atrial fibrillation: a randomised controlled trial (GAIN). *Br J Haematol* 2019;**186**:e21–3. <https://doi.org/10.1111/bjh.15856>
302. Krittayaphong R, Chantrarat T, Rojarekumpai R, Jittham P, Sairat P, Lip GYH. Poor time in therapeutic range control is associated with adverse clinical outcomes in patients with non-valvular atrial fibrillation: a report from the nationwide COOL-AF registry. *J Clin Med* 2020;**9**:1698. <https://doi.org/10.3390/jcm9061698>
303. Szummer K, Gasparini A, Eliasson S, Årnlöv J, Qureshi AR, Bárány P, et al. Time in therapeutic range and outcomes after warfarin initiation in newly diagnosed atrial fibrillation patients with renal dysfunction. *J Am Heart Assoc* 2017;**6**:e004925. <https://doi.org/10.1161/JAHA.116.004925>
304. Cardoso R, Ternes CMP, Justino GB, Fernandes A, Rocha AV, Knijnik L, et al. Non-vitamin K antagonists versus warfarin in patients with atrial fibrillation and bioprosthetic valves: a systematic review and meta-analysis. *Am J Med* 2022;**135**:228–234.e1. <https://doi.org/10.1016/j.amjmed.2021.08.026>
305. Wan Y, Heneghan C, Perera R, Roberts N, Hallowell J, Glasziou P, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. *Circ Cardiovasc Qual Outcomes* 2008;**1**:84–91. <https://doi.org/10.1161/CIRCOUTCOMES.108.796185>
306. Vestergaard AS, Skjøth F, Larsen TB, Ehlers LH. The importance of mean time in therapeutic range for complication rates in warfarin therapy of patients with atrial fibrillation: a systematic review and meta-regression analysis. *PLoS One* 2017;**12**:e0188482. <https://doi.org/10.1371/journal.pone.0188482>
307. Macaluso GP, Pagani FD, Slaughter MS, Milano CA, Feller ED, Tatoes AJ, et al. Time in therapeutic range significantly impacts survival and adverse events in destination therapy patients. *ASAIO J* 2022;**68**:14–20. <https://doi.org/10.1097/MAT.0000000000001572>
308. Heneghan C, Ward A, Perera R, Bankhead C, Fuller A, Stevens R, et al. Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data. *Lancet* 2012;**379**:322–34. [https://doi.org/10.1016/S0140-6736\(11\)61294-4](https://doi.org/10.1016/S0140-6736(11)61294-4)
309. Joosten LPT, van Doorn S, van de Ven PM, Köhler BTG, Nierman MC, Koek HL, et al. Safety of switching from a vitamin K antagonist to a non-vitamin K antagonist oral anticoagulant in frail older patients with atrial fibrillation: results of the FRAIL-AF randomized controlled trial. *Circulation* 2024;**149**:279–89. <https://doi.org/10.1161/CIRCULATIONAHA.123.066485>
310. Yao X, Shah ND, Sangaralingham LR, Gersh BJ, Noseworthy PA. Non-vitamin K antagonist oral anticoagulant dosing in patients with atrial fibrillation and renal dysfunction. *J Am Coll Cardiol* 2017;**69**:2779–90. <https://doi.org/10.1016/j.jacc.2017.03.600>
311. Steinberg BA, Shrader P, Thomas L, Ansell J, Fonarow GC, Gersh BJ, et al. Off-label dosing of non-vitamin K antagonist oral anticoagulants and adverse outcomes: the ORBIT-AF II registry. *J Am Coll Cardiol* 2016;**68**:2597–604. <https://doi.org/10.1016/j.jacc.2016.09.966>
312. Alexander JH, Andersson U, Lopes RD, Hijazi Z, Hohnloser SH, Ezekowitz JA, et al. Apixaban 5 mg twice daily and clinical outcomes in patients with atrial fibrillation and advanced age, low body weight, or high creatinine: a secondary analysis of a randomized clinical trial. *JAMA Cardiol* 2016;**1**:673–81. <https://doi.org/10.1001/jamacardio.2016.1829>
313. Carmo J, Moscoso Costa F, Ferreira J, Mendes M. Dabigatran in real-world atrial fibrillation. Meta-analysis of observational comparison studies with vitamin K antagonists. *Thromb Haemost* 2016;**116**:754–63. <https://doi.org/10.1160/TH16-03-0203>
314. Huisman MV, Rothman KJ, Paquette M, Teutsch C, Diener HC, Dubner SJ, et al. Two-year follow-up of patients treated with dabigatran for stroke prevention in atrial fibrillation: global registry on long-term antithrombotic treatment in patients with atrial fibrillation (GLORIA-AF) registry. *Am Heart J* 2018;**198**:55–63. <https://doi.org/10.1016/j.ahj.2017.08.018>
315. Camm AJ, Amarenco P, Haas S, Hess S, Kirchhof P, Kuhls S, et al. XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation. *Eur Heart J* 2016;**37**:1145–53. <https://doi.org/10.1093/eurheartj/ehv466>
316. Martinez CAA, Lanás F, Radaideh G, Kharabsheh SM, Lambelet M, Viaud MAL, et al. XANTUS-EL: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation in Eastern Europe, Middle East, Africa and Latin America. *Egypt Heart J* 2018;**70**:307–13. <https://doi.org/10.1016/j.ehj.2018.09.002>
317. Li XS, Deitelzweig S, Keshishian A, Hamilton M, Horblyuk R, Gupta K, et al. Effectiveness and safety of apixaban versus warfarin in non-valvular atrial fibrillation patients in “real-world” clinical practice. A propensity-matched analysis of 76,940 patients. *Thromb Haemost* 2017;**117**:1072–82. <https://doi.org/10.1160/TH17-01-0068>
318. Lee SR, Choi EK, Han KD, Jung JH, Oh S, Lip GYH. Edoxaban in Asian patients with atrial fibrillation: effectiveness and safety. *J Am Coll Cardiol* 2018;**72**:838–53. <https://doi.org/10.1016/j.jacc.2018.05.066>
319. Cappato R, Ezekowitz MD, Klein AL, Camm AJ, Ma CS, Le Heuzey JY, et al. Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation. *Eur Heart J* 2014;**35**:3346–55. <https://doi.org/10.1093/eurheartj/ehu367>
320. Goette A, Merino JL, Ezekowitz MD, Zamoryakhin D, Melino M, Jin J, et al. Edoxaban versus enoxaparin-warfarin in patients undergoing cardioversion of atrial fibrillation (ENSURE-AF): a randomised, open-label, phase 3b trial. *Lancet* 2016;**388**:1995–2003. [https://doi.org/10.1016/S0140-6736\(16\)31474-X](https://doi.org/10.1016/S0140-6736(16)31474-X)

321. Ezekowitz MD, Pollack CV, Jr, Halperin JL, England RD, VanPelt Nguyen S, Spahr J, et al. Apixaban compared to heparin/vitamin K antagonist in patients with atrial fibrillation scheduled for cardioversion: the EMANATE trial. *Eur Heart J* 2018;**39**:2959–71. <https://doi.org/10.1093/eurheartj/ehy148>
322. Savarese G, Giugliano RP, Rosano GM, McMurray J, Magnani G, Filippatos G, et al. Efficacy and safety of novel oral anticoagulants in patients with atrial fibrillation and heart failure: a meta-analysis. *JACC Heart Fail* 2016;**4**:870–80. <https://doi.org/10.1016/j.jchf.2016.07.012>
323. von Lueder TG, Atar D, Agewall S, Jensen JK, Hopper I, Kotecha D, et al. All-cause mortality and cardiovascular outcomes with non-vitamin K oral anticoagulants versus warfarin in patients with heart failure in the food and drug administration adverse event reporting system. *Am J Ther* 2019;**26**:e671–8. <https://doi.org/10.1097/MJT.0000000000000883>
324. Harrison SL, Buckley BJR, Proietti R, Underhill P, Lane DA, et al. Oral anticoagulants and outcomes in adults >=80 years with atrial fibrillation: a global federated health network analysis. *J Am Geriatr Soc* 2022;**70**:2386–92. <https://doi.org/10.1111/jgs.17884>
325. Malhotra K, Ishaq MF, Goyal N, Katsanos AH, Parissis J, Alexandrov AW, et al. Oral anticoagulation in patients with chronic kidney disease: a systematic review and meta-analysis. *Neurology* 2019;**92**:e2421–31. <https://doi.org/10.1212/WNL.00000000000007534>
326. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European heart rhythm association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J* 2018;**39**:1330–93. <https://doi.org/10.1093/eurheartj/ehy136>
327. Rhee TM, Lee SR, Choi EK, Oh S, Lip GYH. Efficacy and safety of oral anticoagulants for atrial fibrillation patients with chronic kidney disease: a systematic review and meta-analysis. *Front Cardiovasc Med* 2022;**9**:885548. <https://doi.org/10.3389/fcvm.2022.885548>
328. Reinecke H, Engelbertz C, Bauersachs R, Breithardt G, Echterhoff HH, Gerß J, et al. A randomized controlled trial comparing apixaban with the vitamin K antagonist phenprocoumon in patients on chronic hemodialysis: the AXADIA-AFNET 8 study. *Circulation* 2023;**147**:296–309. <https://doi.org/10.1161/CIRCULATIONAHA.122.062779>
329. Pokorney SD, Chertow GM, Al-Khalidi HR, Gallup D, Dignacco P, Mussina K, et al. Apixaban for patients with atrial fibrillation on hemodialysis: a multicenter randomized controlled trial. *Circulation* 2022;**146**:1735–45. <https://doi.org/10.1161/CIRCULATIONAHA.121.054990>
330. De Vriese AS, Caluwé R, Van Der Meersch H, De Boeck K, De Bacquer D. Safety and efficacy of vitamin K antagonists versus rivaroxaban in hemodialysis patients with atrial fibrillation: a multicenter randomized controlled trial. *J Am Soc Nephrol* 2021;**32**:1474–83. <https://doi.org/10.1681/ASN.2020111566>
331. Eikelboom JW, Connolly SJ, Brueckmann M, Granger CB, Kappetein AP, Mack MJ, et al. Dabigatran versus warfarin in patients with mechanical heart valves. *N Engl J Med* 2013;**369**:1206–14. <https://doi.org/10.1056/NEJMoa1300615>
332. Wang TY, Svensson LG, Wen J, Vekstein A, Gerdisch M, Rao VU, et al. Apixaban or warfarin in patients with an on-X mechanical aortic valve. *NEJM Evid* 2023;**2**:EVID0a2300067. <https://doi.org/10.1056/EVID0a2300067>
333. Guimarães HP, Lopes RD, de Barros ESPGM, Liporace IL, Sampaio RO, Tarasoutchi F, et al. Rivaroxaban in patients with atrial fibrillation and a bioprosthetic mitral valve. *N Engl J Med* 2020;**383**:2117–26. <https://doi.org/10.1056/NEJMoa2029603>
334. Collet JP, Van Belle E, Thiele H, Berti S, Lhermusier T, Mangold T, et al. Apixaban vs. standard of care after transcatheter aortic valve implantation: the ATLANTIS trial. *Eur Heart J* 2022;**43**:2783–97. <https://doi.org/10.1093/eurheartj/ehac242>
335. Steffel J, Collins R, Antz M, Cornu P, Desteghe L, Haeusler KG, et al. 2021 European heart rhythm association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Europace* 2021;**23**:1612–76. <https://doi.org/10.1093/eurpace/ebab065>
336. Grymonprez M, Carnoy L, Capiou A, Boussery K, Mehuis E, De Backer TL, et al. Impact of P-glycoprotein and CYP3A4-interacting drugs on clinical outcomes in patients with atrial fibrillation using non-vitamin K antagonist oral anticoagulants: a nationwide cohort study. *Eur Heart J Cardiovasc Pharmacother* 2023;**9**:722–30. <https://doi.org/10.1093/ehjcvp/pvad070>
337. Testa S, Legnani C, Antonucci E, Paoletti O, Dellanoce C, Cosmi B, et al. Drug levels and bleeding complications in atrial fibrillation patients treated with direct oral anticoagulants. *J Thromb Haemost* 2019;**17**:1064–72. <https://doi.org/10.1111/jth.14457>
338. Suwa M, Nohara Y, Morii I, Kino M. Safety and efficacy re-evaluation of edoxaban and rivaroxaban dosing with plasma concentration monitoring in non-valvular atrial fibrillation: with observations of on-label and off-label dosing. *Circ Rep* 2023;**5**:80–9. <https://doi.org/10.1253/circrep.CR-22-0076>
339. Song D, Zhou J, Fan T, Chang J, Qiu Y, Zhuang Z, et al. Decision aids for shared decision-making and appropriate anticoagulation therapy in patients with atrial fibrillation: a systematic review and meta-analysis. *Eur J Cardiovasc Nurs* 2022;**21**:97–106. <https://doi.org/10.1093/eurjcn/zvab085>
340. Vora P, Morgan Stewart H, Russell B, Asimwe A, Brobert G. Time trends and treatment pathways in prescribing individual oral anticoagulants in patients with nonvalvular atrial fibrillation: an observational study of more than three million patients from Europe and the United States. *Int J Clin Pract* 2022;**2022**:6707985. <https://doi.org/10.1155/2022/6707985>
341. Grymonprez M, Simoens C, Steurbaut S, De Backer TL, Lahousse L. Worldwide trends in oral anticoagulant use in patients with atrial fibrillation from 2010 to 2018: a systematic review and meta-analysis. *Europace* 2022;**24**:887–98. <https://doi.org/10.1093/eurpace/ebab303>
342. De Caterina R, Husted S, Wallentin L, Andreotti F, Arnesen H, Bachmann F, et al. Vitamin K antagonists in heart disease: current status and perspectives (section III). Position paper of the ESC working group on thrombosis—task force on anticoagulants in heart disease. *Thromb Haemost* 2013;**110**:1087–107. <https://doi.org/10.1160/TH13-06-0443>
343. Pandey AK, Xu K, Zhang L, Gupta S, Eikelboom J, Cook O, et al. Lower versus standard INR targets in atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials. *Thromb Haemost* 2020;**120**:484–94. <https://doi.org/10.1055/s-0039-3401823>
344. Sanders P, Svennberg E, Diederichsen SZ, Crijns HJGM, Lambiase PD, Boriani G, et al. Great debate: device-detected subclinical atrial fibrillation should be treated like clinical atrial fibrillation. *Eur Heart J* 2024;ehae365. <https://doi.org/10.1093/eurheartj/ehae365>
345. ACTIVE Investigators; Connolly SJ, Pogue J, Hart RG, Hohnloser SH, Pfeffer M, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. *N Engl J Med* 2009;**360**:2066–78. <https://doi.org/10.1056/NEJMoa0901301>
346. Mant J, Hobbs FD, Fletcher K, Roaloe A, Fitzmaurice D, Lip GY, et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 2007;**370**:493–503. [https://doi.org/10.1016/S0140-6736\(07\)61233-1](https://doi.org/10.1016/S0140-6736(07)61233-1)
347. Lip GY. The role of aspirin for stroke prevention in atrial fibrillation. *Nat Rev Cardiol* 2011;**8**:602–6. <https://doi.org/10.1038/nrcardio.2011.112>
348. ACTIVE Writing Group of the ACTIVE Investigators; Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. *Lancet* 2006;**367**:1903–12. [https://doi.org/10.1016/S0140-6736\(06\)68845-4](https://doi.org/10.1016/S0140-6736(06)68845-4)
349. Fox KAA, Velentgas P, Camm AJ, Bassand JP, Fitzmaurice DA, Gersh BJ, et al. Outcomes associated with oral anticoagulants plus antiplatelets in patients with newly diagnosed atrial fibrillation. *JAMA Netw Open* 2020;**3**:e200107. <https://doi.org/10.1001/jamanetworkopen.2020.0107>
350. Verheugt FWA, Gao H, Al Mahmeed W, Ambrosio G, Angchaisuksiri P, Atar D, et al. Characteristics of patients with atrial fibrillation prescribed antiplatelet monotherapy compared with those on anticoagulants: insights from the GARFIELD-AF registry. *Eur Heart J* 2018;**39**:464–73. <https://doi.org/10.1093/eurheartj/ehx730>
351. Steffel J, Eikelboom JW, Anand SS, Shestakovska O, Yusuf S, Fox KAA. The COMPASS trial: net clinical benefit of low-dose rivaroxaban plus aspirin as compared with aspirin in patients with chronic vascular disease. *Circulation* 2020;**142**:40–8. <https://doi.org/10.1161/CIRCULATIONAHA.120.046048>
352. Sharma M, Hart RG, Connolly SJ, Bosch J, Shestakovska O, Ng KKH, et al. Stroke outcomes in the COMPASS trial. *Circulation* 2019;**139**:1134–45. <https://doi.org/10.1161/CIRCULATIONAHA.118.035864>
353. Yasuda S, Kaikita K, Akao M, Aka J, Matoba T, Nakamura M, et al. Antithrombotic therapy for atrial fibrillation with stable coronary disease. *N Engl J Med* 2019;**381**:1103–13. <https://doi.org/10.1056/NEJMoa1904143>
354. Senoo K, Lip GY, Lane DA, Büller HR, Kotecha D. Residual risk of stroke and death in anticoagulated patients according to the type of atrial fibrillation: AMADEUS trial. *Stroke* 2015;**46**:2523–8. <https://doi.org/10.1161/STROKEAHA.115.009487>
355. Meinel TR, Branca M, De Marchis GM, Nedeltchev K, Kahles T, Bonati L, et al. Prior anticoagulation in patients with ischemic stroke and atrial fibrillation. *Ann Neurol* 2021;**89**:42–53. <https://doi.org/10.1002/ana.25917>
356. Polymeris AA, Meinel TR, Oehler H, Hölscher K, Zietz A, Scheitz JF, et al. Aetiology, secondary prevention strategies and outcomes of ischaemic stroke despite oral anticoagulant therapy in patients with atrial fibrillation. *J Neurol Neurosurg Psychiatry* 2022;**93**:588–98. <https://doi.org/10.1136/jnnp-2021-328391>
357. Paciaroni M, Agnelli G, Caso V, Silvestrelli G, Seiffge DJ, Engelter S, et al. Causes and risk factors of cerebral ischemic events in patients with atrial fibrillation treated with non-vitamin K antagonist oral anticoagulants for stroke prevention. *Stroke* 2019;**50**:2168–74. <https://doi.org/10.1161/STROKEAHA.119.025350>
358. Purrucker JC, Hölscher K, Kollmer J, Ringleb PA. Etiology of ischemic strokes of patients with atrial fibrillation and therapy with anticoagulants. *J Clin Med* 2020;**9**:2938. <https://doi.org/10.3390/jcm9092938>
359. Paciaroni M, Caso V, Agnelli G, Mosconi MG, Giustozzi M, Seiffge DJ, et al. Recurrent ischemic stroke and bleeding in patients with atrial fibrillation who suffered an acute stroke while on treatment with nonvitamin K antagonist oral anticoagulants: the RENO-EXTEND study. *Stroke* 2022;**53**:2620–7. <https://doi.org/10.1161/STROKEAHA.121.038239>
360. Smits E, Andreotti F, Houben E, Crijns H, Haas S, Spentzouris G, et al. Adherence and persistence with once-daily vs twice-daily direct oral anticoagulants among patients

- with atrial fibrillation: real-world analyses from The Netherlands, Italy and Germany. *Drugs Real World Outcomes* 2022;**9**:199–209. <https://doi.org/10.1007/s40801-021-00289-w>
361. Polymeris AA, Zietz A, Schaub F, Meya L, Traenka C, Thilemann S, et al. Once versus twice daily direct oral anticoagulants in patients with recent stroke and atrial fibrillation. *Eur Stroke J* 2022;**7**:221–9. <https://doi.org/10.1177/23969873221099477>
  362. Glikson M, Wolff R, Hindricks G, Mandrolia J, Camm AJ, Lip GYH, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion—an update. *Europace* 2020;**22**:184. <https://doi.org/10.1093/eurpace/euz258>
  363. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. *Ann Thorac Surg* 1996;**61**:755–9. [https://doi.org/10.1016/0003-4975\(95\)00887-X](https://doi.org/10.1016/0003-4975(95)00887-X)
  364. Reddy VY, Doshi SK, Kar S, Gibson DN, Price MJ, Huber K, et al. 5-Year outcomes after left atrial appendage closure: from the PREVAIL and PROTECT AF trials. *J Am Coll Cardiol* 2017;**70**:2964–75. <https://doi.org/10.1016/j.jacc.2017.10.021>
  365. Lakkireddy D, Thaler D, Ellis CR, Swarup V, Sondergaard L, Carroll J, et al. Amplatzer amulet left atrial appendage occluder versus watchman device for stroke prophylaxis (amulet IDE): a randomized, controlled trial. *Circulation* 2021;**144**:1543–52. <https://doi.org/10.1161/CIRCULATIONAHA.121.057063>
  366. Osmancik P, Herman D, Neuzil P, Hala P, Taborsky M, Kala P, et al. Left atrial appendage closure versus direct oral anticoagulants in high-risk patients with atrial fibrillation. *J Am Coll Cardiol* 2020;**75**:3122–35. <https://doi.org/10.1016/j.jacc.2020.04.067>
  367. Osmancik P, Herman D, Neuzil P, Hala P, Taborsky M, Kala P, et al. 4-Year outcomes after left atrial appendage closure versus nonwarfarin oral anticoagulation for atrial fibrillation. *J Am Coll Cardiol* 2022;**79**:1–14. <https://doi.org/10.1016/j.jacc.2021.10.023>
  368. Korsholm K, Damgaard D, Valentin JB, Packer EJS, Odenstedt J, Sinisalo J, et al. Left atrial appendage occlusion vs novel oral anticoagulation for stroke prevention in atrial fibrillation: rationale and design of the multicenter randomized occlusion-AF trial. *Am Heart J* 2022;**243**:28–38. <https://doi.org/10.1016/j.ahj.2021.08.020>
  369. Huijboom M, Maarse M, Aarnink E, van Dijk V, Swaans M, van der Heijden J, et al. COMPARE LAEO: rationale and design of the randomized controlled trial “COMPARing Effectiveness and safety of Left Atrial Appendage Occlusion to standard of care for atrial fibrillation patients at high stroke risk and ineligible to use oral anticoagulation therapy”. *Am Heart J* 2022;**250**:45–56. <https://doi.org/10.1016/j.ahj.2022.05.001>
  370. Freeman JV, Higgins AY, Wang Y, Du C, Friedman DJ, Daimee UA, et al. Antithrombotic therapy after left atrial appendage occlusion in patients with atrial fibrillation. *J Am Coll Cardiol* 2022;**79**:1785–98. <https://doi.org/10.1016/j.jacc.2022.02.047>
  371. Patti G, Sticchi A, Verolino G, Pasceri V, Vizzi V, Brcsic E, et al. Safety and efficacy of single versus dual antiplatelet therapy after left atrial appendage occlusion. *Am J Cardiol* 2020;**134**:83–90. <https://doi.org/10.1016/j.amjcard.2020.08.013>
  372. Boersma LV, Schmidt B, Betts TR, Sievert H, Tamburino C, Teiger E, et al. Implant success and safety of left atrial appendage closure with the WATCHMAN device: periprocedural outcomes from the EWOLUTION registry. *Eur Heart J* 2016;**37**:2465–74. <https://doi.org/10.1093/eurheartj/ehv730>
  373. Garg J, Shah S, Shah K, Turagam MK, Tzou W, Natale A, et al. Direct oral anticoagulant versus warfarin for watchman left atrial appendage occlusion—systematic review. *JACC Clin Electrophysiol* 2020;**6**:1735–7. <https://doi.org/10.1016/j.jacep.2020.08.020>
  374. Osman M, Busu T, Osman K, Khan SU, Daniels M, Holmes DR, et al. Short-term antiplatelet versus anticoagulant therapy after left atrial appendage occlusion: a systematic review and meta-analysis. *JACC Clin Electrophysiol* 2020;**6**:494–506. <https://doi.org/10.1016/j.jacep.2019.11.009>
  375. Hildick-Smith D, Landmesser U, Camm AJ, Diener HC, Paul V, Schmidt B, et al. Left atrial appendage occlusion with the Amplatzer Amulet device: full results of the prospective global observational study. *Eur Heart J* 2020;**41**:2894–901. <https://doi.org/10.1093/eurheartj/ehaa169>
  376. Reddy VY, Mobius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiebe J, et al. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study with Watchman Left Atrial Appendage Closure Technology). *J Am Coll Cardiol* 2013;**61**:2551–6. <https://doi.org/10.1016/j.jacc.2013.03.035>
  377. Sondergaard L, Wong YH, Reddy VY, Boersma LVA, Bergmann MW, Doshi S, et al. Propensity-matched comparison of oral anticoagulation versus antiplatelet therapy after left atrial appendage closure with Watchman. *JACC Cardiovasc Interv* 2019;**12**:1055–63. <https://doi.org/10.1016/j.jcin.2019.04.004>
  378. Flores-Umanzor EJ, Cepas-Guillen PL, Arzamendi D, Cruz-Gonzalez I, Regueiro A, Freixa X. Rationale and design of a randomized clinical trial to compare two antithrombotic strategies after left atrial appendage occlusion: double antiplatelet therapy vs. apixaban (ADALA study). *J Interv Card Electrophysiol* 2020;**59**:471–7. <https://doi.org/10.1007/s10840-020-00884-x>
  379. Aminian A, Schmidt B, Mazzone P, Berti S, Fischer S, Montorfano M, et al. Incidence, characterization, and clinical impact of device-related thrombus following left atrial appendage occlusion in the prospective global AMPLATZER amulet observational study. *JACC Cardiovasc Interv* 2019;**12**:1003–14. <https://doi.org/10.1016/j.jcin.2019.02.003>
  380. Kany S, Metzner A, Lubos E, Kirchhof P. The atrial fibrillation heart team-guiding therapy in left atrial appendage occlusion with increasingly complex patients and little evidence. *Eur Heart J* 2022;**43**:1691–2. <https://doi.org/10.1093/eurheartj/ehab744>
  381. Saw J, Holmes DR, Cavalcante JL, Freeman JV, Goldsweig AM, Kavinsky CJ, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. *Heart Rhythm* 2023;**20**:e1–16. <https://doi.org/10.1016/j.hrthm.2023.01.007>
  382. Cruz-González I, González-Ferreiro R, Freixa X, Gafoor S, Shakir S, Omran H, et al. Left atrial appendage occlusion for stroke despite oral anticoagulation (resistant stroke). Results from the Amplatzer Cardiac Plug registry. *Rev Esp Cardiol (Engl Ed)* 2020;**73**:28–34. <https://doi.org/10.1016/j.rec.2019.02.013>
  383. Willits I, Keltie K, Linker N, de Belder M, Henderson R, Patrick H, et al. Left atrial appendage occlusion in the UK: prospective registry and data linkage to hospital episode statistics. *Eur Heart J Qual Care Clin Outcomes* 2021;**7**:468–75. <https://doi.org/10.1093/ehjqcco/qcab042>
  384. Price MJ, Valderrabano M, Zimmerman S, Friedman DJ, Kar S, Curtis JP, et al. Periprocedural pericardial effusion complicating transcatheter left atrial appendage occlusion: a report from the NCDR LAEO registry. *Circ Cardiovasc Interv* 2022;**15**:e011718. <https://doi.org/10.1161/CIRCINTERVENTIONS.121.011718>
  385. Aminian A, De Backer O, Nielsen-Kudsk JE, Mazzone P, Berti S, Fischer S, et al. Incidence and clinical impact of major bleeding following left atrial appendage occlusion: insights from the amplatzer amulet observational post-market study. *EuroIntervention* 2021;**17**:774–82. <https://doi.org/10.4244/EIJ-D-20-01309>
  386. Boersma LV, Ince H, Kische S, Pokushalov E, Schmitz T, Schmidt B, et al. Evaluating real-world clinical outcomes in atrial fibrillation patients receiving the WATCHMAN left atrial appendage closure technology: final 2-year outcome data of the EWOLUTION trial focusing on history of stroke and hemorrhage. *Circ Arrhythm Electrophysiol* 2019;**12**:e006841. <https://doi.org/10.1161/CIRCEP.118.006841>
  387. Tzikas A, Shakir S, Gafoor S, Omran H, Berti S, Santoro G, et al. Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER cardiac plug. *EuroIntervention* 2016;**11**:1170–9. [https://doi.org/10.4244/EIJY15M01\\_06](https://doi.org/10.4244/EIJY15M01_06)
  388. Nazir S, Ahuja KR, Kolte D, Isogai T, Michihata N, Saad AM, et al. Association of hospital procedural volume with outcomes of percutaneous left atrial appendage occlusion. *JACC Cardiovasc Interv* 2021;**14**:554–61. <https://doi.org/10.1016/j.jcin.2020.11.029>
  389. Freeman JV, Varosy P, Price MJ, Slotwiner D, Kusumoto FM, Rammohan C, et al. The NCDR left atrial appendage occlusion registry. *J Am Coll Cardiol* 2020;**75**:1503–18. <https://doi.org/10.1016/j.jacc.2019.12.040>
  390. Cruz-Gonzalez I, Korsholm K, Trejo-Velasco B, Thambo JB, Mazzone P, Rioufol G, et al. Procedural and short-term results with the new watchman FLX left atrial appendage occlusion device. *JACC Cardiovasc Interv* 2020;**13**:2732–41. <https://doi.org/10.1016/j.jcin.2020.06.056>
  391. Simard T, Jung RG, Lehenbauer K, Piayda K, Pracon R, Jackson GG, et al. Predictors of device-related thrombus following percutaneous left atrial appendage occlusion. *J Am Coll Cardiol* 2021;**78**:297–313. <https://doi.org/10.1016/j.jacc.2021.04.098>
  392. Simard TJ, Hibbert B, Alkhouli MA, Abraham NS, Holmes DR, Jr. Device-related thrombus following left atrial appendage occlusion. *EuroIntervention* 2022;**18**:224–32. <https://doi.org/10.4244/EIJ-D-21-01010>
  393. Lempereur M, Aminian A, Freixa X, Gafoor S, Kefer J, Tzikas A, et al. Device-associated thrombus formation after left atrial appendage occlusion: a systematic review of events reported with the Watchman, the Amplatzer Cardiac Plug and the Amulet. *Catheter Cardiovasc Interv* 2017;**90**:E111–21. <https://doi.org/10.1002/ccd.26903>
  394. Saw J, Tzikas A, Shakir S, Gafoor S, Omran H, Nielsen-Kudsk JE, et al. Incidence and clinical impact of device-associated thrombus and peri-device leak following left atrial appendage closure with the amplatzer cardiac plug. *JACC Cardiovasc Interv* 2017;**10**:391–9. <https://doi.org/10.1016/j.jcin.2016.11.029>
  395. Fauchier L, Cinaud A, Brigadeau F, Lepillier A, Pierre B, Abbey S, et al. Device-related thrombosis after percutaneous left atrial appendage occlusion for atrial fibrillation. *J Am Coll Cardiol* 2018;**71**:1528–36. <https://doi.org/10.1016/j.jacc.2018.01.076>
  396. Dukkkipati SR, Kar S, Holmes DR, Doshi SK, Swarup V, Gibson DN, et al. Device-related thrombus after left atrial appendage closure: incidence, predictors, and outcomes. *Circulation* 2018;**138**:874–85. <https://doi.org/10.1161/CIRCULATIONAHA.118.035090>
  397. Kar S, Doshi SK, Sadhu A, Horton R, Osorio J, Ellis C, et al. Primary outcome evaluation of a next-generation left atrial appendage closure device: results from the PINNACLE FLX trial. *Circulation* 2021;**143**:1754–62. <https://doi.org/10.1161/CIRCULATIONAHA.120.050117>
  398. Alkhouli M, Du C, Killu A, Simard T, Noseworthy PA, Friedman PA, et al. Clinical impact of residual leaks following left atrial appendage occlusion: insights from the NCDR LAEO registry. *JACC Clin Electrophysiol* 2022;**8**:766–78. <https://doi.org/10.1016/j.jacep.2022.03.001>
  399. Tsai YC, Phan K, Munkholm-Larsen S, Tian DH, La Meir M, Yan TD. Surgical left atrial appendage occlusion during cardiac surgery for patients with atrial fibrillation: a meta-analysis. *Eur J Cardiothorac Surg* 2015;**47**:847–54. <https://doi.org/10.1093/ejcts/ezu291>



400. Whitlock RP, Vincent J, Blackall MH, Hirsh J, Frenes S, Novick R, et al. Left atrial appendage occlusion study II (LAAOS II). *Can J Cardiol* 2013;**29**:1443–7. <https://doi.org/10.1016/j.cjca.2013.06.015>
401. Whitlock RP, Belley-Cote EP, Paparella D, Healey JS, Brady K, Sharma M, et al. Left atrial appendage occlusion during cardiac surgery to prevent stroke. *N Engl J Med* 2021;**384**:2081–91. <https://doi.org/10.1056/NEJMoa2101897>
402. Zhang S, Cui Y, Li J, Tian H, Yun Y, Zhou X, et al. Concomitant transcatheter occlusion versus thoracoscopic surgical clipping for left atrial appendage in patients undergoing ablation for atrial fibrillation: a meta-analysis. *Front Cardiovasc Med* 2022;**9**:970847. <https://doi.org/10.3389/fcvm.2022.970847>
403. van Laar C, Verberkmoes NJ, van Es HW, Lewalter T, Dunnington G, Stark S, et al. Thoracoscopic left atrial appendage clipping: a multicenter cohort analysis. *JACC Clin Electrophysiol* 2018;**4**:893–901. <https://doi.org/10.1016/j.jacep.2018.03.009>
404. Kiviniemi T, Bustamante-Munguira J, Olsson C, Jeppsson A, Halfwerk FR, Hartikainen J, et al. A randomized prospective multicenter trial for stroke prevention by prophylactic surgical closure of the left atrial appendage in patients undergoing bioprosthetic aortic valve surgery—LAA-CLOSURE trial protocol. *Am Heart J* 2021;**237**:127–34. <https://doi.org/10.1016/j.ahj.2021.03.014>
405. Cartledge R, Suwalski G, Witkowska A, Gottlieb G, Cioci A, Chidiac G, et al. Standalone epicardial left atrial appendage exclusion for thromboembolism prevention in atrial fibrillation. *Interact Cardiovasc Thorac Surg* 2022;**34**:548–55. <https://doi.org/10.1093/icvts/ivab334>
406. Branzoli S, Guarracini F, Marini M, D'Onghia G, Penzo D, Piffer S, et al. Heart team for left atrial appendage occlusion: a patient-tailored approach. *J Clin Med* 2022;**11**:176. <https://doi.org/10.3390/jcm11010176>
407. Toale C, Fitzmaurice GJ, Eaton D, Lyne J, Redmond KC. Outcomes of left atrial appendage occlusion using the AtriClip device: a systematic review. *Interact Cardiovasc Thorac Surg* 2019;**29**:655–62. <https://doi.org/10.1093/icvts/ivz156>
408. Caliskan E, Sahin A, Yilmaz M, Seifert B, Hinzpeter R, Alkadhhi H, et al. Epicardial left atrial appendage AtriClip occlusion reduces the incidence of stroke in patients with atrial fibrillation undergoing cardiac surgery. *Eurpace* 2018;**20**:e105–14. <https://doi.org/10.1093/europace/eux211>
409. Nso N, Nassar M, Zirkiyeva M, Lakhdar S, Shaukat T, Guzman L, et al. Outcomes of cardiac surgery with left atrial appendage occlusion versus no occlusion, direct oral anticoagulants, and vitamin K antagonists: a systematic review with meta-analysis. *Int J Cardiol Heart Vasc* 2022;**40**:100998. <https://doi.org/10.1016/j.ijcha.2022.100998>
410. Ibrahim AM, Tandan N, Koester C, Al-Akchar M, Bhandari B, Botchway A, et al. Meta-analysis evaluating outcomes of surgical left atrial appendage occlusion during cardiac surgery. *Am J Cardiol* 2019;**124**:1218–25. <https://doi.org/10.1016/j.amjcard.2019.07.032>
411. Park-Hansen J, Holme SJV, Irmukhamedov A, Carranza CL, Greve AM, Al-Farra G, et al. Adding left atrial appendage closure to open heart surgery provides protection from ischemic brain injury six years after surgery independently of atrial fibrillation history: the LAACS randomized study. *J Cardiothorac Surg* 2018;**13**:53. <https://doi.org/10.1186/s13019-018-0740-7>
412. Soltész EG, Dewan KC, Anderson LH, Ferguson MA, Gillinov AM. Improved outcomes in CABG patients with atrial fibrillation associated with surgical left atrial appendage exclusion. *J Card Surg* 2021;**36**:1201–8. <https://doi.org/10.1111/jocs.15335>
413. Fu M, Qin Z, Zheng S, Li Y, Yang S, Zhao Y, et al. Thoracoscopic left atrial appendage occlusion for stroke prevention compared with long-term warfarin therapy in patients with nonvalvular atrial fibrillation. *Am J Cardiol* 2019;**123**:50–6. <https://doi.org/10.1016/j.amjcard.2018.09.025>
414. Peterson D, Geison E. Pharmacist interventions to reduce modifiable bleeding risk factors using HAS-BLED in patients taking warfarin. *Fed Pract* 2017;**34**:S16–20.
415. Chao TF, Lip GYH, Lin YJ, Chang SL, Lo LW, Hu YF, et al. Incident risk factors and major bleeding in patients with atrial fibrillation treated with oral anticoagulants: a comparison of baseline, follow-up and Delta HAS-BLED scores with an approach focused on modifiable bleeding risk factors. *Thromb Haemost* 2018;**47**:768–77. <https://doi.org/10.1055/s-0038-1636534>
416. Linkins LA, Choi PT, Douketis JD. Clinical impact of bleeding in patients taking oral anticoagulant therapy for venous thromboembolism: a meta-analysis. *Ann Intern Med* 2003;**139**:893–900. <https://doi.org/10.7326/0003-4819-139-11-200312020-00007>
417. Kirchhof P, Haas S, Amarencu P, Hoss S, Lambalet M, van Eickels M, et al. Impact of modifiable bleeding risk factors on major bleeding in patients with atrial fibrillation anticoagulated with rivaroxaban. *J Am Heart Assoc* 2020;**9**:e009530. <https://doi.org/10.1161/JAHA.118.009530>
418. Guo Y, Lane DA, Chen Y, Lip GYH; mAF-App II Trial investigators. Regular bleeding risk assessment associated with reduction in bleeding outcomes: the mAFA-II randomized trial. *Am J Med* 2020;**133**:1195–1202.e2. <https://doi.org/10.1016/j.amjmed.2020.03.019>
419. Lane DA, Lip GYH. Stroke and bleeding risk stratification in atrial fibrillation: a critical appraisal. *Eur Heart J Suppl* 2020;**22**:O14–27. <https://doi.org/10.1093/eurheartj/suaa178>
420. Lip GYH, Lane DA. Bleeding risk assessment in atrial fibrillation: observations on the use and misuse of bleeding risk scores. *J Thromb Haemost* 2016;**14**:1711–4. <https://doi.org/10.1111/jth.13386>
421. Gorog DA, Gue YX, Chao TF, Fauchier L, Ferreiro JL, Huber K, et al. Assessment and mitigation of bleeding risk in atrial fibrillation and venous thromboembolism: a position paper from the ESC working group on thrombosis, in collaboration with the European Heart Rhythm Association, the Association for Acute Cardiovascular Care and the Asia-Pacific Heart Rhythm Society. *Eurpace* 2022;**24**:1844–71. <https://doi.org/10.1093/europace/eauc020>
422. Nelson WW, Laliberté F, Patel AA, Germain G, Pilon D, McCormick N, et al. Stroke risk reduction outweighed bleeding risk increase from vitamin K antagonist treatment among nonvalvular atrial fibrillation patients with high stroke risk and low bleeding risk. *Curr Med Res Opin* 2017;**33**:631–8. <https://doi.org/10.1080/03007995.2016.1275936>
423. Hijazi Z, Lindbäck J, Oldgren J, Benz AP, Alexander JH, Connolly SJ, et al. Individual net clinical outcome with oral anticoagulation in atrial fibrillation using the ABC-AF risk scores. *Am Heart J* 2023;**261**:55–63. <https://doi.org/10.1016/j.ahj.2023.03.012>
424. Hijazi Z, Lindbäck J, Alexander JH, Hanna M, Held C, Hylek EM, et al. The ABC (age, biomarkers, clinical history) stroke risk score: a biomarker-based risk score for predicting stroke in atrial fibrillation. *Eur Heart J* 2016;**37**:1582–90. <https://doi.org/10.1093/eurheartj/ehw054>
425. Gao X, Cai X, Yang Y, Zhou Y, Zhu W. Diagnostic accuracy of the HAS-BLED bleeding score in VKA- or DOAC-treated patients with atrial fibrillation: a systematic review and meta-analysis. *Front Cardiovasc Med* 2021;**8**:757087. <https://doi.org/10.3389/fcvm.2021.757087>
426. Zhu W, He W, Guo L, Wang X, Hong K. The HAS-BLED score for predicting major bleeding risk in anticoagulated patients with atrial fibrillation: a systematic review and meta-analysis. *Clin Cardiol* 2015;**38**:555–61. <https://doi.org/10.1002/clc.22435>
427. Caldeira D, Costa J, Fernandes RM, Pinto FJ, Ferreira JJ. Performance of the HAS-BLED high bleeding-risk category, compared to ATRIA and HEMORR2HAGES in patients with atrial fibrillation: a systematic review and meta-analysis. *J Interv Card Electrophysiol* 2014;**40**:277–84. <https://doi.org/10.1007/s10840-014-9930-y>
428. Zeng J, Yu P, Cui W, Wang X, Ma J, Zeng C. Comparison of HAS-BLED with other risk models for predicting the bleeding risk in anticoagulated patients with atrial fibrillation: a PRISMA-compliant article. *Medicine (Baltimore)* 2020;**99**:e20782. <https://doi.org/10.1097/MD.00000000000020782>
429. Wang C, Yu Y, Zhu W, Yu J, Lip GYH, Hong K. Comparing the ORBIT and HAS-BLED bleeding risk scores in anticoagulated atrial fibrillation patients: a systematic review and meta-analysis. *Oncotarget* 2017;**8**:109703–11. <https://doi.org/10.18632/oncotarget.19858>
430. Loewen P, Dahri K. Risk of bleeding with oral anticoagulants: an updated systematic review and performance analysis of clinical prediction rules. *Ann Hematol* 2011;**90**:1191–200. <https://doi.org/10.1007/s00277-011-1267-3>
431. Hilken NA, Algra A, Greving JP. Predicting major bleeding in ischemic stroke patients with atrial fibrillation. *Stroke* 2017;**48**:3142–4. <https://doi.org/10.1161/STROKEAHA.117.019183>
432. Dalggaard F, Pieper K, Verheugt F, Camm AJ, Fox KA, Kakkar AK, et al. GARFIELD-AF model for prediction of stroke and major bleeding in atrial fibrillation: a Danish nationwide validation study. *BMJ Open* 2019;**9**:e033283. <https://doi.org/10.1136/bmjopen-2019-033283>
433. Mori N, Sotomi Y, Hirata A, Hirayama A, Sakata Y, Higuchi Y. External validation of the ORBIT bleeding score and the HAS-BLED score in nonvalvular atrial fibrillation patients using direct oral anticoagulants (Asian Data from the DIRECT Registry). *Am J Cardiol* 2019;**124**:1044–8. <https://doi.org/10.1016/j.amjcard.2019.07.005>
434. Yao X, Gersh BJ, Sangaralingham LR, Kent DM, Shah ND, Abraham NS, et al. Comparison of the CHA2DS2-VASc, CHADS2, HAS-BLED, ORBIT, and ATRIA risk scores in predicting non-vitamin K antagonist oral anticoagulants-associated bleeding in patients with atrial fibrillation. *Am J Cardiol* 2017;**120**:1549–56. <https://doi.org/10.1016/j.amjcard.2017.07.051>
435. Giustozzi M, Proietti G, Becattini C, Roila F, Agnelli G, Mandalà M. ICH in primary or metastatic brain cancer patients with or without anticoagulant treatment: a systematic review and meta-analysis. *Blood Adv* 2022;**6**:4873–83. <https://doi.org/10.1182/bloodadvances.2022008086>
436. Shoamanesh A. Anticoagulation in patients with cerebral amyloid angiopathy. *Lancet* 2023;**402**:1418–9. [https://doi.org/10.1016/S0140-6736\(23\)02025-1](https://doi.org/10.1016/S0140-6736(23)02025-1)
437. Kurlander JE, Barnes GD, Fisher A, Gonzalez JJ, Helminski D, Saini SD, et al. Association of antisecretory drugs with upper gastrointestinal bleeding in patients using oral anticoagulants: a systematic review and meta-analysis. *Am J Med* 2022;**135**:1231–1243.e8. <https://doi.org/10.1016/j.amjmed.2022.05.031>
438. Moayyedi P, Eikelboom JW, Bosch J, Connolly SJ, Dyal L, Shestakovska O, et al. Pantoprazole to prevent gastroduodenal events in patients receiving rivaroxaban and/or aspirin in a randomized, double-blind, placebo-controlled trial. *Gastroenterology* 2019;**157**:403–412.e5. <https://doi.org/10.1053/j.gastro.2019.04.041>
439. DiMarco JP, Flaker G, Waldo AL, Corley SD, Greene HL, Safford RE, et al. Factors affecting bleeding risk during anticoagulant therapy in patients with atrial fibrillation: observations from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;**149**:650–6. <https://doi.org/10.1016/j.ahj.2004.11.015>
440. Harskamp RE, Lucassen WAM, Lopes RD, Himmelreich JCL, Parati G, Weert H. Risk of stroke and bleeding in relation to hypertension in anticoagulated patients with atrial

- fibrillation: a meta-analysis of randomised controlled trials. *Acta Cardiol* 2022;**77**:191–5. <https://doi.org/10.1080/00015385.2021.1882111>
441. Schulman S, Beyth RJ, Kearon C, Levine MN. Hemorrhagic complications of anticoagulant and thrombolytic treatment: American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). *Chest* 2008;**133**:257s–98s. <https://doi.org/10.1378/chest.08-0674>
  442. Gallego P, Roldán V, Torregrosa JM, Gálvez J, Valdés M, Vicente V, et al. Relation of the HAS-BLED bleeding risk score to major bleeding, cardiovascular events, and mortality in anticoagulated patients with atrial fibrillation. *Circ Arrhythm Electrophysiol* 2012;**5**:312–8. <https://doi.org/10.1161/CIRCEP.111.967000>
  443. Bouillon K, Bertrand M, Boudali L, Ducimetière P, Dray-Spira R, Zureik M. Short-term risk of bleeding during heparin bridging at initiation of vitamin K antagonist therapy in more than 90 000 patients with nonvalvular atrial fibrillation managed in outpatient care. *J Am Heart Assoc* 2016;**5**:e004065. <https://doi.org/10.1161/JAHA.116.004065>
  444. White HD, Gruber M, Feysi J, Kaatz S, Tse HF, Husted S, et al. Comparison of outcomes among patients randomized to warfarin therapy according to anticoagulant control: results from SPORTIF III and V. *Arch Intern Med* 2007;**167**:239–45. <https://doi.org/10.1001/archinte.167.3.239>
  445. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Jr, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation* 2014;**130**:2071–104. <https://doi.org/10.1161/CIR.0000000000000040>
  446. Olesen JB, Lip GY, Lindhardsen J, Lane DA, Ahlehoj O, Hansen ML, et al. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with atrial fibrillation: a net clinical benefit analysis using a 'real world' nationwide cohort study. *Thromb Haemost* 2011;**106**:739–49. <https://doi.org/10.1160/TH11-05-0364>
  447. Tomaselli GF, Mahaffey KW, Cuker A, Dobesh PP, Doherty JU, Eikelboom JW, et al. 2020 ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol* 2020;**76**:594–622. <https://doi.org/10.1016/j.jacc.2020.04.053>
  448. Cuker A. Laboratory measurement of the non-vitamin K antagonist oral anticoagulants: selecting the optimal assay based on drug, assay availability, and clinical indication. *J Thromb Thrombolysis* 2016;**41**:241–7. <https://doi.org/10.1007/s11239-015-1282-7>
  449. Douxfils J, Ageno W, Samama CM, Lessire S, Ten Cate H, Verhamme P, et al. Laboratory testing in patients treated with direct oral anticoagulants: a practical guide for clinicians. *J Thromb Haemost* 2018;**16**:209–19. <https://doi.org/10.1111/jth.13912>
  450. Milling TJ, Jr, Refaai MA, Sarode R, Lewis B, Mangione A, Durn BL, et al. Safety of a four-factor prothrombin complex concentrate versus plasma for vitamin K antagonist reversal: an integrated analysis of two phase IIIb clinical trials. *Acad Emerg Med* 2016;**23**:466–75. <https://doi.org/10.1111/acem.12911>
  451. Pollack CV, Jr, Reilly PA, van Ryn J, Eikelboom JW, Glund S, Bernstein RA, et al. Idarucizumab for dabigatran reversal—full cohort analysis. *N Engl J Med* 2017;**377**:431–41. <https://doi.org/10.1056/NEJMoa1707278>
  452. Connolly SJ, Sharma M, Cohen AT, Demchuk AM, Członkowska A, Lindgren AG, et al. ANNEX-A investigators. Andexanet for factor Xa inhibitor-associated acute intracerebral hemorrhage. *N Engl J Med* 2024;**390**:1745–55. <https://doi.org/10.1056/NEJMoa2313040>
  453. Milioglu I, Farmakis I, Neudeker M, Hussain Z, Guha A, Giannakoulas G, et al. Prothrombin complex concentrate in major bleeding associated with DOACs: an updated systematic review and meta-analysis. *J Thromb Thrombolysis* 2021;**52**:1137–50. <https://doi.org/10.1007/s11239-021-02480-w>
  454. Meyre PB, Blum S, Hennings E, Aeschbacher S, Reichlin T, Rodondi N, et al. Bleeding and ischaemic events after first bleed in anticoagulated atrial fibrillation patients: risk and timing. *Eur Heart J* 2022;**43**:4899–908. <https://doi.org/10.1093/eurheartj/ehac587>
  455. Connolly SJ, Crowther M, Eikelboom JW, Gibson CM, Curnutte JT, Lawrence JH, et al. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. *N Engl J Med* 2019;**380**:1326–35. <https://doi.org/10.1056/NEJMoa1814051>
  456. Fanikos J, Murwin D, Gruenenfelder F, Tartakovsky I, França LR, Reilly PA, et al. Global use of idarucizumab in clinical practice: outcomes of the RE-VECTO surveillance program. *Thromb Haemost* 2020;**120**:27–35. <https://doi.org/10.1055/s-0039-1695771>
  457. Kotecha D, Calvert M, Deeks JJ, Griffith M, Kirchhof P, Lip GY, et al. A review of rate control in atrial fibrillation, and the rationale and protocol for the RATE-AF trial. *BMJ Open* 2017;**7**:e015099. <https://doi.org/10.1136/bmjopen-2016-015099>
  458. Hess PL, Sheng S, Matsouaka R, DeVore AD, Heidenreich PA, Yancy CW, et al. Strict versus lenient versus poor rate control among patients with atrial fibrillation and heart failure (from the get with the guidelines—heart failure program). *Am J Cardiol* 2020;**125**:894–900. <https://doi.org/10.1016/j.amjcard.2019.12.025>
  459. Van Gelder IC, Groenveld HF, Crijns HJ, Tuininga YS, Tijssen JG, Alings AM, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med* 2010;**362**:1363–73. <https://doi.org/10.1056/NEJMoa1001337>
  460. Olshansky B, Rosenfeld LE, Warner AL, Solomon AJ, O'Neill G, Sharma A, et al. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study: approaches to control rate in atrial fibrillation. *J Am Coll Cardiol* 2004;**43**:1201–8. <https://doi.org/10.1016/j.jacc.2003.11.032>
  461. Ulimoen SR, Enger S, Carlson J, Platonov PG, Pripp AH, Abdelnoor M, et al. Comparison of four single-drug regimens on ventricular rate and arrhythmia-related symptoms in patients with permanent atrial fibrillation. *Am J Cardiol* 2013;**111**:225–30. <https://doi.org/10.1016/j.amjcard.2012.09.020>
  462. Tisdale JE, Padhi ID, Goldberg AD, Silverman NA, Webb CR, Higgins RS, et al. A randomized, double-blind comparison of intravenous diltiazem and digoxin for atrial fibrillation after coronary artery bypass surgery. *Am Heart J* 1998;**135**:739–47. [https://doi.org/10.1016/S0002-8703\(98\)70031-6](https://doi.org/10.1016/S0002-8703(98)70031-6)
  463. Khand AU, Rankin AC, Martin VW, Taylor J, Gemmell I, Cleland JG. Carvedilol alone or in combination with digoxin for the management of atrial fibrillation in patients with heart failure? *J Am Coll Cardiol* 2003;**42**:1944–51. <https://doi.org/10.1016/j.jacc.2003.07.020>
  464. Nikolaidou T, Channer KS. Chronic atrial fibrillation: a systematic review of medical heart rate control management. *Postgrad Med J* 2009;**85**:303–12. <https://doi.org/10.1136/pgmj.2008.068908>
  465. Figulla HR, Gietzen F, Zeymer U, Raiber M, Heggemann J, Soballa R, et al. Diltiazem improves cardiac function and exercise capacity in patients with idiopathic dilated cardiomyopathy. Results of the Diltiazem in Dilated Cardiomyopathy Trial. *Circulation* 1996;**94**:346–52. <https://doi.org/10.1161/01.CIR.94.3.346>
  466. Andrade JG, Roy D, Wyse DG, Tardif JC, Talajic M, Leduc H, et al. Heart rate and adverse outcomes in patients with atrial fibrillation: a combined AFFIRM and AF-CHF substudy. *Heart Rhythm* 2016;**13**:54–61. <https://doi.org/10.1016/j.hrthm.2015.08.028>
  467. Weerasooriya R, Davis M, Powell A, Szili-Torok T, Shah C, Whalley D, et al. The Australian Intervention Randomized Control of Rate in Atrial Fibrillation Trial (AIRCRAFT). *J Am Coll Cardiol* 2003;**41**:1697–702. [https://doi.org/10.1016/S0735-1097\(03\)00338-3](https://doi.org/10.1016/S0735-1097(03)00338-3)
  468. Lim KT, Davis MJ, Powell A, Arnold A, Moulden K, Bulsara M, et al. Ablate and pace strategy for atrial fibrillation: long-term outcome of AIRCRAFT trial. *Europace* 2007;**9**:498–505. <https://doi.org/10.1093/europace/eum091>
  469. Vijayaraman P, Subzposh FA, Naperkowski A. Atrioventricular node ablation and His bundle pacing. *Europace* 2017;**19**:iv10–6. <https://doi.org/10.1093/europace/eux263>
  470. Brignole M, Pokushalov E, Pentimalli F, Palmisano P, Chieffo E, Occhetta E, et al. A randomized controlled trial of atrioventricular junction ablation and cardiac resynchronization therapy in patients with permanent atrial fibrillation and narrow QRS. *Eur Heart J* 2018;**39**:3999–4008. <https://doi.org/10.1093/eurheartj/ehy555>
  471. Brignole M, Pentimalli F, Palmisano P, Landolina M, Quartieri F, Occhetta E, et al. AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial. *Eur Heart J* 2021;**42**:4731–9. <https://doi.org/10.1093/eurheartj/ehab569>
  472. Delle Karth G, Geppert A, Neunteufl T, Priglinger U, Haumer M, Gschwandner M, et al. Amiodarone versus diltiazem for rate control in critically ill patients with atrial tachyarrhythmias. *Crit Care Med* 2001;**29**:1149–53. <https://doi.org/10.1097/00003246-200106000-00011>
  473. Hou ZY, Chang MS, Chen CY, Tu MS, Lin SL, Chiang HT, et al. Acute treatment of recent-onset atrial fibrillation and flutter with a tailored dosing regimen of intravenous amiodarone. A randomized, digoxin-controlled study. *Eur Heart J* 1995;**16**:521–8. <https://doi.org/10.1093/oxfordjournals.eurheartj.a060945>
  474. Van Gelder IC, Wyse DG, Chandler ML, Cooper HA, Olshansky B, Hagens VE, et al. Does intensity of rate-control influence outcome in atrial fibrillation? An analysis of pooled data from the RACE and AFFIRM studies. *Europace* 2006;**8**:935–42. <https://doi.org/10.1093/europace/eul106>
  475. Scheuermeyer FX, Grafstein E, Stenstrom R, Christenson J, Heslop C, Heilbron B, et al. Safety and efficiency of calcium channel blockers versus beta-blockers for rate control in patients with atrial fibrillation and no acute underlying medical illness. *Acad Emerg Med* 2013;**20**:222–30. <https://doi.org/10.1111/acem.12091>
  476. Siu CW, Lau CP, Lee WL, Lam KF, Tse HF. Intravenous diltiazem is superior to intravenous amiodarone or digoxin for achieving ventricular rate control in patients with acute uncomplicated atrial fibrillation. *Crit Care Med* 2009;**37**:2174–9, quiz 2180. <https://doi.org/10.1097/CCM.0b013e3181a02f56>
  477. Perrett M, Gohil N, Tica O, Bunting KV, Kotecha D. Efficacy and safety of intravenous beta-blockers in acute atrial fibrillation and flutter is dependent on beta-1 selectivity: a systematic review and meta-analysis of randomised trials. *Clin Res Cardiol* 2023;**113**:831–41. <https://doi.org/10.1007/s00392-023-02295-0>
  478. Darby AE, Dimarco JP. Management of atrial fibrillation in patients with structural heart disease. *Circulation* 2012;**125**:945–57. <https://doi.org/10.1161/CIRCULATIONAHA.111.019935>
  479. Imamura T, Kinugawa K. Novel rate control strategy with landiolol in patients with cardiac dysfunction and atrial fibrillation. *ESC Heart Fail* 2020;**7**:2208–13. <https://doi.org/10.1002/ehf2.12879>
  480. Ulimoen SR, Enger S, Pripp AH, Abdelnoor M, Arnesen H, Gjesdal K, et al. Calcium channel blockers improve exercise capacity and reduce N-terminal Pro-B-type natriuretic peptide levels compared with beta-blockers in patients with permanent atrial fibrillation. *Eur Heart J* 2014;**35**:517–24. <https://doi.org/10.1093/eurheartj/ehz429>
  481. Connolly SJ, Camm AJ, Halperin JL, Joyner C, Alings M, Amerena J, et al. Dronedarone in high-risk permanent atrial fibrillation. *N Engl J Med* 2011;**365**:2268–76. <https://doi.org/10.1056/NEJMoa1109867>



482. Karwath A, Bunting KV, Gill SK, Tica O, Pendleton S, Aziz F, et al. Redefining beta-blocker response in heart failure patients with sinus rhythm and atrial fibrillation: a machine learning cluster analysis. *Lancet* 2021;**398**:1427–35. [https://doi.org/10.1016/S0140-6736\(21\)01638-X](https://doi.org/10.1016/S0140-6736(21)01638-X)
483. Koldenhof T, Wijtvielt P, Pluymaekers N, Rienstra M, Folkeringa RJ, Bronzwaer P, et al. Rate control drugs differ in the prevention of progression of atrial fibrillation. *Europace* 2022;**24**:384–9. <https://doi.org/10.1093/europace/euab191>
484. Champs A, Mitchell C, Tica O, Ziff OJ, Bunting KV, Mobley AR, et al. Digoxin in patients with heart failure and/or atrial fibrillation: a systematic review and meta-analysis of 5.9 million patient years of follow-up. SSRN preprint. 2023. <https://doi.org/10.2139/ssrn.4544769>.
485. Andrews P, Anseeuw K, Kotecha D, Lapostolle F, Thanacoody R. Diagnosis and practical management of digoxin toxicity: a narrative review and consensus. *Eur J Emerg Med* 2023;**30**:395–401. <https://doi.org/10.1097/MEJ.0000000000001065>
486. Bavendiek U, Berliner D, Dávila LA, Schwab J, Maier L, Philipp SA, et al. Rationale and design of the DIGIT-HF trial (DIGitoxin to Improve ouTcomes in patients with advanced chronic Heart Failure): a randomized, double-blind, placebo-controlled study. *Eur J Heart Fail* 2019;**21**:676–84. <https://doi.org/10.1002/ehf.1452>
487. Clempo HF, Wood MA, Gilligan DM, Ellenbogen KA. Intravenous amiodarone for acute heart rate control in the critically ill patient with atrial tachyarrhythmias. *Am J Cardiol* 1998;**81**:594–8. [https://doi.org/10.1016/S0002-9149\(97\)00962-4](https://doi.org/10.1016/S0002-9149(97)00962-4)
488. Queiroga A, Marshall HJ, Clune M, Gammage MD. Ablate and pace revisited: long term survival and predictors of permanent atrial fibrillation. *Heart* 2003;**89**:1035–8. <https://doi.org/10.1136/heart.89.9.1035>
489. Geelen P, Brugada J, Andries E, Brugada P. Ventricular fibrillation and sudden death after radiofrequency catheter ablation of the atrioventricular junction. *Pacing Clin Electrophysiol* 1997;**20**:343–8. <https://doi.org/10.1111/j.1540-8159.1997.tb06179.x>
490. Wang RX, Lee HC, Hodge DO, Cha YM, Friedman PA, Rea RF, et al. Effect of pacing method on risk of sudden death after atrioventricular node ablation and pacemaker implantation in patients with atrial fibrillation. *Heart Rhythm* 2013;**10**:696–701. <https://doi.org/10.1016/j.hrthm.2013.01.021>
491. Chatterjee NA, Upadhyay GA, Ellenbogen KA, McAlister FA, Choudhry NK, Singh JP. Atrioventricular nodal ablation in atrial fibrillation: a meta-analysis and systematic review. *Circ Arrhythm Electrophysiol* 2012;**5**:68–76. <https://doi.org/10.1161/CIRCEP.111.967810>
492. Bradley DJ, Shen WK. Overview of management of atrial fibrillation in symptomatic elderly patients: pharmacologic therapy versus AV node ablation. *Clin Pharmacol Ther* 2007;**81**:284–7. <https://doi.org/10.1038/sj.cpt.6100062>
493. Ozcan C, Jahangir A, Friedman PA, Patel PJ, Munger TM, Rea RF, et al. Long-term survival after ablation of the atrioventricular node and implantation of a permanent pacemaker in patients with atrial fibrillation. *N Engl J Med* 2001;**344**:1043–51. <https://doi.org/10.1056/NEJM200104053441403>
494. Chatterjee NA, Upadhyay GA, Ellenbogen KA, Hayes DL, Singh JP. Atrioventricular nodal ablation in atrial fibrillation: a meta-analysis of biventricular vs. right ventricular pacing mode. *Eur J Heart Fail* 2012;**14**:661–7. <https://doi.org/10.1093/eurjhf/hfs036>
495. Huang W, Su L, Wu S. Pacing treatment of atrial fibrillation patients with heart failure: His bundle pacing combined with atrioventricular node ablation. *Card Electrophysiol Clin* 2018;**10**:519–35. <https://doi.org/10.1016/j.jcep.2018.05.016>
496. Huang W, Su L, Wu S, Xu L, Xiao F, Zhou X, et al. Benefits of permanent His bundle pacing combined with atrioventricular node ablation in atrial fibrillation patients with heart failure with both preserved and reduced left ventricular ejection fraction. *J Am Heart Assoc* 2017;**6**:e005309. <https://doi.org/10.1161/JAHA.116.005309>
497. Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, Kamp O, Kingma T, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002;**347**:1834–40. <https://doi.org/10.1056/NEJMoa021375>
498. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;**347**:1825–33. <https://doi.org/10.1056/NEJMoa021328>
499. Hohnloser SH, Kuck KH, Lillenthal J. Rhythm or rate control in atrial fibrillation—pharmacological intervention in atrial fibrillation (PIAF): a randomised trial. *Lancet* 2000;**356**:1789–94. [https://doi.org/10.1016/S0140-6736\(00\)03230-X](https://doi.org/10.1016/S0140-6736(00)03230-X)
500. Roy D, Talajic M, Nattel S, Wyse DG, Dorian P, Lee KL, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. *N Engl J Med* 2008;**358**:2667–77. <https://doi.org/10.1056/NEJMoa0708789>
501. Blomström-Lundqvist C, Gizurarson S, Schwieler J, Jensen SM, Bergfeldt L, Kennebäck G, et al. Effect of catheter ablation vs antiarrhythmic medication on quality of life in patients with atrial fibrillation: the CAPTAF randomized clinical trial. *JAMA* 2019;**321**:1059–68. <https://doi.org/10.1001/jama.2019.0335>
502. Mark DB, Anstrom KJ, Sheng S, Piccini JP, Baloch KN, Monahan KH, et al. Effect of catheter ablation vs medical therapy on quality of life among patients with atrial fibrillation: the CABANA randomized clinical trial. *JAMA* 2019;**321**:1275–85. <https://doi.org/10.1001/jama.2019.0692>
503. Wilber DJ, Pappone C, Neuzil P, De Paola A, Marchlinski F, Natale A, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *JAMA* 2010;**303**:333–40. <https://doi.org/10.1001/jama.2009.2029>
504. Calkins H, Reynolds MR, Spector P, Sondhi M, Xu Y, Martin A, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ Arrhythm Electrophysiol* 2009;**2**:349–61. <https://doi.org/10.1161/CIRCEP.108.824789>
505. Jais P, Cauchemez B, Macle L, Daoud E, Khairy P, Subbiah R, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation* 2008;**118**:2498–505. <https://doi.org/10.1161/CIRCULATIONAHA.108.772582>
506. Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG, et al. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. *J Am Coll Cardiol* 2013;**61**:1713–23. <https://doi.org/10.1016/j.jacc.2012.11.064>
507. Poole JE, Bahnon TD, Monahan KH, Johnson G, Rostami H, Silverstein AP, et al. Recurrence of atrial fibrillation after catheter ablation or antiarrhythmic drug therapy in the CABANA trial. *J Am Coll Cardiol* 2020;**75**:3105–18. <https://doi.org/10.1016/j.jacc.2020.04.065>
508. Mont L, Bisbal F, Hernandez-Madrid A, Perez-Castellano N, Vinolas X, Arenal A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). *Eur Heart J* 2014;**35**:501–7. <https://doi.org/10.1093/eurheartj/ehf457>
509. Scherr D, Khairy P, Miyazaki S, Aurillac-Lavignolle V, Pascale P, Wilton SB, et al. Five-year outcome of catheter ablation of persistent atrial fibrillation using termination of atrial fibrillation as a procedural endpoint. *Circ Arrhythm Electrophysiol* 2015;**8**:18–24. <https://doi.org/10.1161/CIRCEP.114.001943>
510. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. *Circulation* 2017;**136**:583–96. <https://doi.org/10.1161/CIRCULATIONAHA.116.023163>
511. Sanders P, Elliott AD, Linz D. Upstream targets to treat atrial fibrillation. *J Am Coll Cardiol* 2017;**70**:2906–8. <https://doi.org/10.1016/j.jacc.2017.10.043>
512. Hohnloser SH, Crijns HJ, van Eickels M, Gaudin C, Page RL, Torp-Pedersen C, et al. Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med* 2009;**360**:668–78. <https://doi.org/10.1056/NEJMoa0803778>
513. Sohns C, Fox H, Marrouche NF, Crijns H, Costard-Jaeckle A, Bergau L, et al. Catheter ablation in end-stage heart failure with atrial fibrillation. *N Engl J Med* 2023;**389**:1380–9. <https://doi.org/10.1056/NEJMoa2306037>
514. Di Biase L, Mohanty P, Mohanty S, Santangeli P, Trivedi C, Lakkireddy D, et al. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial. *Circulation* 2016;**133**:1637–44. <https://doi.org/10.1161/CIRCULATIONAHA.115.019406>
515. Nuotio I, Hartikainen JE, Gronberg T, Biancari F, Airaksinen KE. Time to cardioversion for acute atrial fibrillation and thromboembolic complications. *JAMA* 2014;**312**:647–9. <https://doi.org/10.1001/jama.2014.3824>
516. Garg A, Khunger M, Seicean S, Chung MK, Tchou PJ. Incidence of thromboembolic complications within 30 days of electrical cardioversion performed within 48 hours of atrial fibrillation onset. *JACC Clin Electrophysiol* 2016;**2**:487–94. <https://doi.org/10.1016/j.jacep.2016.01.018>
517. Tampieri A, Cipriano V, Mucci F, Rusconi AM, Lenzi T, Cenni P. Safety of cardioversion in atrial fibrillation lasting less than 48 h without post-procedural anticoagulation in patients at low cardioembolic risk. *Intern Emerg Med* 2018;**13**:87–93. <https://doi.org/10.1007/s11739-016-1589-1>
518. Airaksinen KE, Gronberg T, Nuotio I, Nikkinen M, Ylitalo A, Biancari F, et al. Thromboembolic complications after cardioversion of acute atrial fibrillation: the FinCV (Finnish CardioVersion) study. *J Am Coll Cardiol* 2013;**62**:1187–92. <https://doi.org/10.1016/j.jacc.2013.04.089>
519. Hansen ML, Jepsen RM, Olesen JB, Ruwald MH, Karasoy D, Gislason GH, et al. Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy. *Europace* 2015;**17**:18–23. <https://doi.org/10.1093/europace/euu189>
520. Bonfanti L, Annovi A, Sanchis-Gomar F, Saccenti C, Meschi T, Ticinesi A, et al. Effectiveness and safety of electrical cardioversion for acute-onset atrial fibrillation in the emergency department: a real-world 10-year single center experience. *Clin Exp Emerg Med* 2019;**6**:64–9. <https://doi.org/10.15441/ceem.17.286>
521. Telles-Garcia N, Dahal K, Kocherla C, Lip GYH, Reddy P, Dominic P. Non-vitamin K antagonists oral anticoagulants are as safe and effective as warfarin for cardioversion of atrial fibrillation: a systematic review and meta-analysis. *Int J Cardiol* 2018;**268**:143–8. <https://doi.org/10.1016/j.ijcard.2018.04.034>
522. Klein AL, Grimm RA, Murray RD, Apperson-Hansen C, Asinger RW, Black IW, et al. Use of transthoracic echocardiography to guide cardioversion in patients with atrial fibrillation. *N Engl J Med* 2001;**344**:1411–20. <https://doi.org/10.1056/NEJM200105103441901>
523. Brunetti ND, Tarantino N, De Gennaro L, Correale M, Santoro F, Di Biase M. Direct oral anti-coagulants compared to vitamin-K antagonists in cardioversion of atrial fibrillation: an updated meta-analysis. *J Thromb Thrombolysis* 2018;**45**:550–6. <https://doi.org/10.1007/s11239-018-1622-5>
524. Steinberg JS, Sadaniantz A, Kron J, Krahn A, Denny DM, Daubert J, et al. Analysis of cause-specific mortality in the Atrial Fibrillation Follow-up Investigation of Rhythm

- Management (AFFIRM) study. *Circulation* 2004;**109**:1973–80. <https://doi.org/10.1161/01.CIR.0000118472.77237.FA>
525. Crijs HJ, Weijls B, Fairley AM, Lewalter T, Maggioni AP, Martín A, et al. Contemporary real life cardioversion of atrial fibrillation: results from the multinational RHYTHM-AF study. *Int J Cardiol* 2014;**172**:588–94. <https://doi.org/10.1016/j.ijcard.2014.01.099>
  526. Kirchhof P, Andresen D, Bosch R, Borggrefe M, Meinertz T, Parade U, et al. Short-term versus long-term antiarrhythmic drug treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial. *Lancet* 2012;**380**:238–46. [https://doi.org/10.1016/S0140-6736\(12\)60570-4](https://doi.org/10.1016/S0140-6736(12)60570-4)
  527. Zhu W, Wu Z, Dong Y, Lip GYH, Liu C. Effectiveness of early rhythm control in improving clinical outcomes in patients with atrial fibrillation: a systematic review and meta-analysis. *BMC Med* 2022;**20**:340. <https://doi.org/10.1186/s12916-022-02545-4>
  528. Stellbrink C, Nixdorff U, Hofmann T, Lehmacher W, Daniel WG, Hanrath P, et al. Safety and efficacy of enoxaparin compared with unfractionated heparin and oral anticoagulants for prevention of thromboembolic complications in cardioversion of non-valvular atrial fibrillation: the Anticoagulation in Cardioversion using Enoxaparin (ACE) trial. *Circulation* 2004;**109**:997–1003. <https://doi.org/10.1161/01.CIR.0000120509.64740.DC>
  529. Lip GY, Hammerstingl C, Marin F, Cappato R, Meng IL, Kirsch B, et al. Left atrial thrombus resolution in atrial fibrillation or flutter: results of a prospective study with rivaroxaban (X-TRA) and a retrospective observational registry providing baseline data (CLOT-AF). *Am Heart J* 2016;**178**:126–34. <https://doi.org/10.1016/j.ahj.2016.05.007>
  530. Stiell IG, Eagles D, Nemnom MJ, Brown E, Taljaard M, Archambault PM, et al. Adverse events associated with electrical cardioversion in patients with acute atrial fibrillation and atrial flutter. *Can J Cardiol* 2021;**37**:1775–82. <https://doi.org/10.1016/j.cjca.2021.08.018>
  531. Stiell IG, Archambault PM, Morris J, Mercier E, Eagles D, Perry JJ, et al. RAFF-3 Trial: a stepped-wedge cluster randomised trial to improve care of acute atrial fibrillation and flutter in the emergency department. *Can J Cardiol* 2021;**37**:1569–77. <https://doi.org/10.1016/j.cjca.2021.06.016>
  532. Gurevitz OT, Ammash NM, Malouf JF, Chandrasekaran K, Rosales AG, Ballman KV, et al. Comparative efficacy of monophasic and biphasic waveforms for transthoracic cardioversion of atrial fibrillation and atrial flutter. *Am Heart J* 2005;**149**:316–21. <https://doi.org/10.1016/j.ahj.2004.07.007>
  533. Mortensen K, Risius T, Schwemer TF, Aydin MA, Köster R, Klemm HU, et al. Biphasic versus monophasic shock for external cardioversion of atrial flutter: a prospective, randomized trial. *Cardiology* 2008;**111**:57–62. <https://doi.org/10.1159/000113429>
  534. Inácio JF, da Rosa Mdos S, Shah J, Rosário J, Vissoci JR, Manica AL, et al. Monophasic and biphasic shock for transthoracic conversion of atrial fibrillation: systematic review and network meta-analysis. *Resuscitation* 2016;**100**:66–75. <https://doi.org/10.1016/j.resuscitation.2015.12.009>
  535. Eid M, Abu Jazar D, Medhekar A, Khalife W, Javid A, Ahsan C, et al. Anterior-posterior versus anterior-lateral electrodes position for electrical cardioversion of atrial fibrillation: a meta-analysis of randomized controlled trials. *Int J Cardiol Heart Vasc* 2022;**43**:101129. <https://doi.org/10.1016/j.ijcha.2022.101129>
  536. Squara F, Elbaum C, Garret G, Liprandi L, Scarlatti D, Bun SS, et al. Active compression versus standard anterior-posterior defibrillation for external cardioversion of atrial fibrillation: a prospective randomized study. *Heart Rhythm* 2021;**18**:360–5. <https://doi.org/10.1016/j.hrthm.2020.11.005>
  537. Schmidt AS, Lauridsen KG, Torp P, Bach LF, Rickers H, Løfgren B. Maximum-fixed energy shocks for cardioverting atrial fibrillation. *Eur Heart J* 2020;**41**:626–31. <https://doi.org/10.1093/eurheartj/ehz585>
  538. Müssigbrodt A, John S, Kosiuk J, Richter S, Hindricks G, Bollmann A. Vernakalant-facilitated electrical cardioversion: comparison of intravenous vernakalant and amiodarone for drug-enhanced electrical cardioversion of atrial fibrillation after failed electrical cardioversion. *Europace* 2016;**18**:51–6. <https://doi.org/10.1093/europace/euv194>
  539. Climent VE, Marin F, Mainar L, Gomez-Aldaravi R, Martinez JG, Chorro FJ, et al. Effects of pretreatment with intravenous flecainide on efficacy of external cardioversion of persistent atrial fibrillation. *Pacing Clin Electrophysiol* 2004;**27**:368–72. <https://doi.org/10.1111/j.1540-8159.2004.00444.x>
  540. Tieleman RG, Van Gelder IC, Bosker HA, Kingma T, Wilde AA, Kirchhof CJ, et al. Does flecainide regain its antiarrhythmic activity after electrical cardioversion of persistent atrial fibrillation? *Heart Rhythm* 2005;**2**:223–30. <https://doi.org/10.1016/j.hrthm.2004.11.014>
  541. Oral H, Souza JJ, Michaud GF, Knight BP, Goyal R, Strickberger SA, et al. Facilitating transthoracic cardioversion of atrial fibrillation with ibutilide pretreatment. *N Engl J Med* 1999;**340**:1849–54. <https://doi.org/10.1056/NEJM199906173402401>
  542. Nair M, George LK, Koshy SK. Safety and efficacy of ibutilide in cardioversion of atrial flutter and fibrillation. *J Am Board Fam Med* 2011;**24**:86–92. <https://doi.org/10.3122/jabfm.2011.01.080096>
  543. Bianconi L, Mennuni M, Lukic V, Castro A, Chieffi M, Santini M. Effects of oral propafenone administration before electrical cardioversion of chronic atrial fibrillation: a placebo-controlled study. *J Am Coll Cardiol* 1996;**28**:700–6. [https://doi.org/10.1016/S0735-1097\(96\)00230-6](https://doi.org/10.1016/S0735-1097(96)00230-6)
  544. Channer KS, Birchall A, Steeds RP, Walters SJ, Yeo WW, West JN, et al. A randomized placebo-controlled trial of pre-treatment and short- or long-term maintenance therapy with amiodarone supporting DC cardioversion for persistent atrial fibrillation. *Eur Heart J* 2004;**25**:144–50. <https://doi.org/10.1016/j.ehj.2003.10.020>
  545. Capucci A, Villani GQ, Aschieri D, Rosi A, Piepoli MF. Oral amiodarone increases the efficacy of direct-current cardioversion in restoration of sinus rhythm in patients with chronic atrial fibrillation. *Eur Heart J* 2000;**21**:66–73. <https://doi.org/10.1053/ehj.1999.1734>
  546. Um KJ, McIntyre WF, Healey JS, Mendoza PA, Koziarz A, Amit G, et al. Pre- and post-treatment with amiodarone for elective electrical cardioversion of atrial fibrillation: a systematic review and meta-analysis. *Europace* 2019;**21**:856–63. <https://doi.org/10.1093/europace/euy310>
  547. Toso E, Iannaccone M, Caponi D, Rotondi F, Santoro A, Gallo C, et al. Does antiarrhythmic drugs premedication improve electrical cardioversion success in persistent atrial fibrillation? *J Electrocardiol* 2017;**50**:294–300. <https://doi.org/10.1016/j.jelectrocard.2016.12.004>
  548. Ganapathy AV, Monjabez S, Ganapathy KS, Shanon F, Razavi M. “Asymptomatic” persistent or permanent atrial fibrillation: a misnomer in selected patients. *Int J Cardiol* 2015;**185**:112–3. <https://doi.org/10.1016/j.ijcard.2015.03.122>
  549. Voskoboinik A, Kalman E, Plunkett G, Knott J, Moskovitch J, Sanders P, et al. A comparison of early versus delayed elective electrical cardioversion for recurrent episodes of persistent atrial fibrillation: a multi-center study. *Int J Cardiol* 2019;**284**:33–7. <https://doi.org/10.1016/j.ijcard.2018.10.068>
  550. Airaksinen KEJ. Early versus delayed cardioversion: why should we wait? *Expert Rev Cardiovasc Ther* 2020;**18**:149–54. <https://doi.org/10.1080/14779072.2020.1736563>
  551. Boriani G, Diemberger I, Biffi M, Martignani C, Branzi A. Pharmacological cardioversion of atrial fibrillation: current management and treatment options. *Drugs* 2004;**64**:2741–62. <https://doi.org/10.2165/00003495-200464240-00003>
  552. Dan GA, Martinez-Rubio A, Agewall S, Boriani G, Borggrefe M, Gaita F, et al. Antiarrhythmic drugs—clinical use and clinical decision making: a consensus document from the European Heart Rhythm Association (EHRA) and European Society of Cardiology (ESC) Working Group on Cardiovascular Pharmacology, endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS) and International Society of Cardiovascular Pharmacotherapy (ISCP). *Europace* 2018;**20**:731–732an. <https://doi.org/10.1093/europace/eux373>
  553. Gitt AK, Smolka W, Michailov G, Bernhardt A, Pittrow D, Lewalter T. Types and outcomes of cardioversion in patients admitted to hospital for atrial fibrillation: results of the German RHYTHM-AF study. *Clin Res Cardiol* 2013;**102**:713–23. <https://doi.org/10.1007/s00392-013-0586-x>
  554. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. *Europace* 2018;**20**:157–208. <https://doi.org/10.1093/europace/eux275>
  555. Danias PG, Caulfield TA, Weigner MJ, Silverman DI, Manning WJ. Likelihood of spontaneous conversion of atrial fibrillation to sinus rhythm. *J Am Coll Cardiol* 1998;**31**:588–92. [https://doi.org/10.1016/S0735-1097\(97\)00534-2](https://doi.org/10.1016/S0735-1097(97)00534-2)
  556. Tsiachris D, Doundoulakis I, Pagkalidou E, Kordalis A, Deftereos S, Gatzoulis KA, et al. Pharmacologic cardioversion in patients with paroxysmal atrial fibrillation: a network meta-analysis. *Cardiovasc Drugs Ther* 2021;**35**:293–308. <https://doi.org/10.1007/s10557-020-07127-1>
  557. Grönberg T, Nuotio I, Nikkinen M, Ylitalo A, Vasankari T, Hartikainen JE, et al. Arrhythmic complications after electrical cardioversion of acute atrial fibrillation: the FinCV study. *Europace* 2013;**15**:1432–5. <https://doi.org/10.1093/europace/eut106>
  558. Brandes A, Crijs H, Rienstra M, Kirchhof P, Grove EL, Pedersen KB, et al. Cardioversion of atrial fibrillation and atrial flutter revisited: current evidence and practical guidance for a common procedure. *Europace* 2020;**22**:1149–61. <https://doi.org/10.1093/europace/euaa057>
  559. Stiell IG, Sivilotti MLA, Taljaard M, Bernie D, Vadeboncoeur A, Hohl CM, et al. Electrical versus pharmacological cardioversion for emergency department patients with acute atrial fibrillation (RAFF2): a partial factorial randomised trial. *Lancet* 2020;**395**:339–49. [https://doi.org/10.1016/S0140-6736\(19\)32994-0](https://doi.org/10.1016/S0140-6736(19)32994-0)
  560. Alboni P, Botto GL, Baldi N, Luzi M, Russo V, Gianfranchi L, et al. Outpatient treatment of recent-onset atrial fibrillation with the “pill-in-the-pocket” approach. *N Engl J Med* 2004;**351**:2384–91. <https://doi.org/10.1056/NEJMoa041233>
  561. Brembilla-Perrot B, Houriez P, Beurrier D, Claudon O, Terrier de la Chaise A, Louis P. Predictors of atrial flutter with 1:1 conduction in patients treated with class I antiarrhythmic drugs for atrial tachyarrhythmias. *Int J Cardiol* 2001;**80**:7–15. [https://doi.org/10.1016/S0167-5273\(01\)00459-4](https://doi.org/10.1016/S0167-5273(01)00459-4)
  562. Conde D, Costabel JP, Caro M, Ferro A, Lambardi F, Corrales Barboza A, et al. Flecainide versus vernakalant for conversion of recent-onset atrial fibrillation. *Int J Cardiol* 2013;**168**:2423–5. <https://doi.org/10.1016/j.ijcard.2013.02.006>
  563. Markey GC, Salter N, Ryan J. Intravenous flecainide for emergency department management of acute atrial fibrillation. *J Emerg Med* 2018;**54**:320–7. <https://doi.org/10.1016/j.jemermed.2017.11.016>
  564. Martinez-Marcos FJ, Garcia-Garmendia JL, Ortega-Carpio A, Fernandez-Gomez JM, Santos JM, Camacho C. Comparison of intravenous flecainide, propafenone, and

- amiodarone for conversion of acute atrial fibrillation to sinus rhythm. *Am J Cardiol* 2000;**86**:950–3. [https://doi.org/10.1016/S0002-9149\(00\)01128-0](https://doi.org/10.1016/S0002-9149(00)01128-0)
565. Reisinger J, Gatterer E, Lang W, Vanicek T, Eisserer G, Bachleitner T, et al. Flecainide versus ibutilide for immediate cardioversion of atrial fibrillation of recent onset. *Eur Heart J* 2004;**25**:1318–24. <https://doi.org/10.1016/j.ehj.2004.04.030>
566. Zhang N, Guo JH, Zhang H, Li XB, Zhang P, Xu Y. Comparison of intravenous ibutilide vs. propafenone for rapid termination of recent onset atrial fibrillation. *Int J Clin Pract* 2005;**59**:1395–400. <https://doi.org/10.1111/j.1368-5031.2005.00705.x>
567. Camm AJ, Capucci A, Hohnloser SH, Torp-Pedersen C, Van Gelder IC, Mangal B, et al. A randomized active-controlled study comparing the efficacy and safety of vernakalant to amiodarone in recent-onset atrial fibrillation. *J Am Coll Cardiol* 2011;**57**:313–21. <https://doi.org/10.1016/j.jacc.2010.07.046>
568. Roy D, Pratt CM, Torp-Pedersen C, Wyse DG, Toft E, Juul-Moller S, et al. Vernakalant hydrochloride for rapid conversion of atrial fibrillation: a phase 3, randomized, placebo-controlled trial. *Circulation* 2008;**117**:1518–25. <https://doi.org/10.1161/CIRCULATIONAHA.107.723866>
569. Deedwania PC, Singh BN, Ellenbogen K, Fisher S, Fletcher R, Singh SN. Spontaneous conversion and maintenance of sinus rhythm by amiodarone in patients with heart failure and atrial fibrillation: observations from the veterans affairs congestive heart failure survival trial of antiarrhythmic therapy (CHF-STAT). The Department of Veterans Affairs CHF-STAT Investigators. *Circulation* 1998;**98**:2574–9. <https://doi.org/10.1161/01.cir.98.23.2574>
570. Hofmann R, Steinwender C, Kammler J, Kypka A, Wimmer G, Leisch F. Intravenous amiodarone bolus for treatment of atrial fibrillation in patients with advanced congestive heart failure or cardiogenic shock. *Wien Klin Wochenschr* 2004;**116**:744–9. <https://doi.org/10.1007/s00508-004-0264-0>
571. Alboni P, Botto GL, Boriani G, Russo G, Pacchioni F, Iori M, et al. Intravenous administration of flecainide or propafenone in patients with recent-onset atrial fibrillation does not predict adverse effects during 'pill-in-the-pocket' treatment. *Heart* 2010;**96**:546–9. <https://doi.org/10.1136/hrt.2009.187963>
572. Khan IA. Single oral loading dose of propafenone for pharmacological cardioversion of recent-onset atrial fibrillation. *J Am Coll Cardiol* 2001;**37**:542–7. [https://doi.org/10.1016/S0735-1097\(00\)01116-5](https://doi.org/10.1016/S0735-1097(00)01116-5)
573. Khan IA. Oral loading single dose flecainide for pharmacological cardioversion of recent-onset atrial fibrillation. *Int J Cardiol* 2003;**87**:121–8. [https://doi.org/10.1016/S0167-5273\(02\)00467-9](https://doi.org/10.1016/S0167-5273(02)00467-9)
574. Al-Khatib SM, Allen LaPointe NM, Chatterjee R, Crowley MJ, Dupre ME, Kong DF, et al. Rate- and rhythm-control therapies in patients with atrial fibrillation: a systematic review. *Ann Intern Med* 2014;**160**:760–73. <https://doi.org/10.7326/M13-1467>
575. Andrade JG, Aguilar M, Atzema C, Bell A, Cairns JA, Cheung CC, et al. The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation. *Can J Cardiol* 2020;**36**:1847–948. <https://doi.org/10.1016/j.cjca.2020.09.001>
576. Lafuente-Lafuente C, Valembos L, Bergmann JF, Belmin J. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. *Cochrane Database Syst Rev* 2015;**3**:CD005049. <https://doi.org/10.1002/14651858.CD005049.pub4>
577. Valembos L, Audureau E, Takeda A, Jarzebowski W, Belmin J, Lafuente-Lafuente C. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. *Cochrane Database Syst Rev* 2019;**2019**:Cd005049. <https://doi.org/10.1002/14651858.CD005049.pub5>
578. Crijns HJ, Van Gelder IC, Van Gilst WH, Hillege H, Gosselink AM, Lie KI. Serial antiarrhythmic drug treatment to maintain sinus rhythm after electrical cardioversion for chronic atrial fibrillation or atrial flutter. *Am J Cardiol* 1991;**68**:335–41. [https://doi.org/10.1016/0002-9149\(91\)90828-9](https://doi.org/10.1016/0002-9149(91)90828-9)
579. Chatterjee S, Sardar P, Lichstein E, Mukherjee D, Aikat S. Pharmacologic rate versus rhythm-control strategies in atrial fibrillation: an updated comprehensive review and meta-analysis. *Pacing Clin Electrophysiol* 2013;**36**:122–33. <https://doi.org/10.1111/j.1540-8159.2012.03513.x>
580. Kotecha D, Kirchhof P. Rate and rhythm control have comparable effects on mortality and stroke in atrial fibrillation but better data are needed. *Evid Based Med* 2014;**19**:222–3. <https://doi.org/10.1136/ebmed-2014-110062>
581. Piccini JP, Hasselblad V, Peterson ED, Washam JB, Califf RM, Kong DF. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. *J Am Coll Cardiol* 2009;**54**:1089–95. <https://doi.org/10.1016/j.jacc.2009.04.085>
582. Eckardt L, Sehner S, Suling A, Borof K, Breithardt G, Crijns H, et al. Attaining sinus rhythm mediates improved outcome with early rhythm control therapy of atrial fibrillation: the EAST-AFNET 4 trial. *Eur Heart J* 2022;**43**:4127–44. <https://doi.org/10.1093/eurheartj/ehac471>
583. Freemantle N, Lafuente-Lafuente C, Mitchell S, Eckert L, Reynolds M. Mixed treatment comparison of dronedarone, amiodarone, sotalol, flecainide, and propafenone, for the management of atrial fibrillation. *Europace* 2011;**13**:329–45. <https://doi.org/10.1093/europace/euq450>
584. Frommeyer G, Eckardt L. Drug-induced proarrhythmia: risk factors and electrophysiological mechanisms. *Nat Rev Cardiol* 2016;**13**:36–47. <https://doi.org/10.1038/nrcardio.2015.110>
585. Kochiadakis GE, Marketou ME, Igoumenidis NE, Chrysostomakis SI, Mavrakis HE, Kaleboubas MD, et al. Amiodarone, sotalol, or propafenone in atrial fibrillation: which is preferred to maintain normal sinus rhythm? *Pacing Clin Electrophysiol* 2000;**23**:1883–7. <https://doi.org/10.1111/j.1540-8159.2000.tb07044.x>
586. Roy D, Talajic M, Dorian P, Connolly S, Eisenberg MJ, Green M, et al. Amiodarone to prevent recurrence of atrial fibrillation. Canadian Trial of Atrial Fibrillation Investigators. *N Engl J Med* 2000;**342**:913–20. <https://doi.org/10.1056/NEJM200003303421302>
587. Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, et al. Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;**352**:1861–72. <https://doi.org/10.1056/NEJMoa041705>
588. Ehrlich JR, Look C, Kostev K, Israel CVV, Goette A. Impact of dronedarone on the risk of myocardial infarction and stroke in atrial fibrillation patients followed in general practices in Germany. *Int J Cardiol* 2019;**278**:126–32. <https://doi.org/10.1016/j.ijcard.2018.11.133>
589. Singh BN, Connolly SJ, Crijns HJ, Roy D, Kowey PR, Capucci A, et al. Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. *N Engl J Med* 2007;**357**:987–99. <https://doi.org/10.1056/NEJMoa054686>
590. Stroobandt R, Stiels B, Hoebrechts R. Propafenone for conversion and prophylaxis of atrial fibrillation. Propafenone Atrial Fibrillation Trial Investigators. *Am J Cardiol* 1997;**79**:418–23. [https://doi.org/10.1016/S0002-9149\(96\)00779-5](https://doi.org/10.1016/S0002-9149(96)00779-5)
591. Wazni OM, Dandamudi G, Sood N, Hoyt R, Tyler J, Durran S, et al. Cryoballoon ablation as initial therapy for atrial fibrillation. *N Engl J Med* 2021;**384**:316–24. <https://doi.org/10.1056/NEJMoa2029554>
592. Cosedis Nielsen J, Johannessen A, Raatikainen P, Hindricks G, Walfridsson H, Kongstad O, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. *N Engl J Med* 2012;**367**:1587–95. <https://doi.org/10.1056/NEJMoa1113566>
593. Morillo CA, Verma A, Connolly SJ, Kuck KH, Nair GM, Champagne J, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. *JAMA* 2014;**311**:692–700. <https://doi.org/10.1001/jama.2014.467>
594. Kuniss M, Pavlovic N, Velagic V, Hermida JS, Healey S, Arena G, et al. Cryoballoon ablation vs. antiarrhythmic drugs: first-line therapy for patients with paroxysmal atrial fibrillation. *Europace* 2021;**23**:1033–41. <https://doi.org/10.1093/europace/euab029>
595. Hocini M, Sanders P, Deisenhofer I, Jais P, Hsu LF, Scavee C, et al. Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses. *Circulation* 2003;**108**:1172–5. <https://doi.org/10.1161/01.CIR.0000090685.13169.07>
596. Inada K, Yamane T, Tokutake K, Yokoyama K, Mishima T, Hioki M, et al. The role of successful catheter ablation in patients with paroxysmal atrial fibrillation and prolonged sinus pauses: outcome during a 5-year follow-up. *Europace* 2014;**16**:208–13. <https://doi.org/10.1093/europace/eut159>
597. Chen YW, Bai R, Lin T, Salim M, Sang CH, Long DY, et al. Pacing or ablation: which is better for paroxysmal atrial fibrillation-related tachycardia-bradycardia syndrome? *Pacing Clin Electrophysiol* 2014;**37**:403–11. <https://doi.org/10.1111/pace.12340>
598. Zhang R, Wang Y, Yang M, Yang Y, Wang Z, Yin X, et al. Risk stratification for atrial fibrillation and outcomes in tachycardia-bradycardia syndrome: ablation vs. pacing. *Front Cardiovasc Med* 2021;**8**:674471. <https://doi.org/10.3389/fcvm.2021.674471>
599. Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F, Jr, et al. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;**354**:934–41. <https://doi.org/10.1056/NEJMoa050955>
600. Yan Huo TG, Schönbauer R, Wójcik M, Fiedler L, Roithinger FX, Martinek M, et al. Low-voltage myocardium-guided ablation trial of persistent atrial fibrillation. *NEJM Evid* 2022;**1**:EVIDo2200141. <https://doi.org/10.1056/EVIDo2200141>
601. Reddy VY, Gerstenfeld EP, Natale A, Whang W, Cuoco FA, Patel C, et al. Pulsed field or conventional thermal ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2023;**389**:1660–71. <https://doi.org/10.1056/NEJMoa2307291>
602. Kalman JM, Al-Kaisey AM, Parameswaran R, Hawson J, Anderson RD, Lim M, et al. Impact of early vs. delayed atrial fibrillation catheter ablation on atrial arrhythmia recurrences. *Eur Heart J* 2023;**44**:2447–54. <https://doi.org/10.1093/eurheartj/ehad247>
603. Kalman JM, Sanders P, Rosso R, Calkins H. Should we perform catheter ablation for asymptomatic atrial fibrillation? *Circulation* 2017;**136**:490–9. <https://doi.org/10.1161/CIRCULATIONAHA.116.024926>
604. Hunter RJ, Berriman TJ, Diab I, Kamdar R, Richmond L, Baker V, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). *Circ Arrhythm Electrophysiol* 2014;**7**:31–8. <https://doi.org/10.1161/CIRCEP.113.000806>
605. Jones DG, Haldar SK, Hussain W, Sharma R, Francis DP, Rahman-Haley SL, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. *J Am Coll Cardiol* 2013;**61**:1894–903. <https://doi.org/10.1016/j.jacc.2013.01.069>
606. Kuck KH, Merkely B, Zahn R, Arentz T, Seidl K, Schluter M, et al. Catheter ablation versus best medical therapy in patients with persistent atrial fibrillation and congestive heart failure: the randomized AMICA trial. *Circ Arrhythm Electrophysiol* 2019;**12**:e007731. <https://doi.org/10.1161/CIRCEP.119.007731>



607. MacDonald MR, Connelly DT, Hawkins NM, Steedman T, Payne J, Shaw M, et al. Radiofrequency ablation for persistent atrial fibrillation in patients with advanced heart failure and severe left ventricular systolic dysfunction: a randomised controlled trial. *Heart* 2011;**97**:740–7. <https://doi.org/10.1136/hrt.2010.207340>
608. Parkash R, Wells GA, Rouleau J, Talajic M, Essebag V, Skanes A, et al. Randomized ablation-based rhythm-control versus rate-control trial in patients with heart failure and atrial fibrillation: results from the RAFT-AF trial. *Circulation* 2022;**145**:1693–704. <https://doi.org/10.1161/CIRCULATIONAHA.121.057095>
609. Romero J, Gabr M, Alviz I, Briceno D, Diaz JC, Rodriguez D, et al. Improved survival in patients with atrial fibrillation and heart failure undergoing catheter ablation compared to medical treatment: a systematic review and meta-analysis of randomized controlled trials. *J Cardiovasc Electrophysiol* 2022;**33**:2356–66. <https://doi.org/10.1111/jce.15622>
610. Chen S, Purerfellner H, Meyer C, Acou VJ, Schratzer A, Ling Z, et al. Rhythm control for patients with atrial fibrillation complicated with heart failure in the contemporary era of catheter ablation: a stratified pooled analysis of randomized data. *Eur Heart J* 2020;**41**:2863–73. <https://doi.org/10.1093/eurheartj/ehz443>
611. Prabhu S, Taylor AJ, Costello BT, Kaye DM, McLellan AJA, Voskoboinik A, et al. Catheter ablation versus medical rate control in atrial fibrillation and systolic dysfunction: the CAMERA-MRI study. *J Am Coll Cardiol* 2017;**70**:1949–61. <https://doi.org/10.1016/j.jacc.2017.08.041>
612. Packer DL, Piccini JP, Monahan KH, Al-Khalidi HR, Silverstein AP, Noseworthy PA, et al. Ablation versus drug therapy for atrial fibrillation in heart failure: results from the CABANA trial. *Circulation* 2021;**143**:1377–90. <https://doi.org/10.1161/CIRCULATIONAHA.120.050991>
613. Smit MD, Moes ML, Maass AH, Achekar ID, Van Geel PP, Hillege HL, et al. The importance of whether atrial fibrillation or heart failure develops first. *Eur J Heart Fail* 2012;**14**:1030–40. <https://doi.org/10.1093/eurjhf/hfs097>
614. Sohns C, Zintl K, Zhao Y, Dagher L, Andresen D, Siebels J, et al. Impact of left ventricular function and heart failure symptoms on outcomes post ablation of atrial fibrillation in heart failure: CASTLE-AF trial. *Circ Arrhythm Electrophysiol* 2020;**13**:e008461. <https://doi.org/10.1161/CIRCEP.120.008461>
615. Sugumar H, Prabhu S, Costello B, Chieng D, Azzopardi S, Voskoboinik A, et al. Catheter ablation versus medication in atrial fibrillation and systolic dysfunction: late outcomes of CAMERA-MRI study. *JACC Clin Electrophysiol* 2020;**6**:1721–31. <https://doi.org/10.1016/j.jacep.2020.08.019>
616. Kirstein B, Neudeck S, Gaspar T, Piorkowski J, Wechselberger S, Kronborg MB, et al. Left atrial fibrosis predicts left ventricular ejection fraction response after atrial fibrillation ablation in heart failure patients: the fibrosis-HF study. *Europace* 2020;**22**:1812–21. <https://doi.org/10.1093/europace/eaab179>
617. Ishiguchi H, Yoshiga Y, Shimizu A, Ueyama T, Fukuda M, Kato T, et al. Long-term events following catheter-ablation for atrial fibrillation in heart failure with preserved ejection fraction. *ESC Heart Fail* 2022;**9**:3505–18. <https://doi.org/10.1002/ehf2.14079>
618. Gu G, Wu J, Gao X, Liu M, Jin C, Xu Y. Catheter ablation of atrial fibrillation in patients with heart failure and preserved ejection fraction: a meta-analysis. *Clin Cardiol* 2022;**45**:786–93. <https://doi.org/10.1002/clc.23841>
619. Yamauchi R, Morishima I, Okumura K, Kanzaki Y, Morita Y, Takagi K, et al. Catheter ablation for non-paroxysmal atrial fibrillation accompanied by heart failure with preserved ejection fraction: feasibility and benefits in functions and B-type natriuretic peptide. *Europace* 2021;**23**:1252–61. <https://doi.org/10.1093/europace/eaab420>
620. Rordorf R, Scuzzoso F, Chun KRJ, Khelae SK, Kueffer FJ, Braegelmann KM, et al. Cryoballoon ablation for the treatment of atrial fibrillation in patients with concomitant heart failure and either reduced or preserved left ventricular ejection fraction: results from the Cryo AF global registry. *J Am Heart Assoc* 2021;**10**:e021323. <https://doi.org/10.1161/JAHA.121.021323>
621. Cha YM, Wokhlu A, Asirvatham SJ, Shen VK, Friedman PA, Munger TM, et al. Success of ablation for atrial fibrillation in isolated left ventricular diastolic dysfunction: a comparison to systolic dysfunction and normal ventricular function. *Circ Arrhythm Electrophysiol* 2011;**4**:724–32. <https://doi.org/10.1161/CIRCEP.110.960690>
622. Machino-Ohtsuka T, Seo Y, Ishizu T, Sugano A, Atsumi A, Yamamoto M, et al. Efficacy, safety, and outcomes of catheter ablation of atrial fibrillation in patients with heart failure with preserved ejection fraction. *J Am Coll Cardiol* 2013;**62**:1857–65. <https://doi.org/10.1016/j.jacc.2013.07.020>
623. Aldaas OM, Lupercio F, Darden D, Mylavarapu PS, Malladi CL, Han FT, et al. Meta-analysis of the usefulness of catheter ablation of atrial fibrillation in patients with heart failure with preserved ejection fraction. *Am J Cardiol* 2021;**142**:66–73. <https://doi.org/10.1016/j.amjcard.2020.11.039>
624. Black-Maier E, Ren X, Steinberg BA, Green CL, Barnett AS, Rosa NS, et al. Catheter ablation of atrial fibrillation in patients with heart failure and preserved ejection fraction. *Heart Rhythm* 2018;**15**:651–7. <https://doi.org/10.1016/j.hrthm.2017.12.001>
625. von Olshausen G, Benson L, Dahlström U, Lund LH, Savarese G, Braunschweig F. Catheter ablation for patients with atrial fibrillation and heart failure: insights from the Swedish Heart Failure Registry. *Eur J Heart Fail* 2022;**24**:1636–46. <https://doi.org/10.1002/ehf2.2604>
626. Shiraishi Y, Kohsaka S, Ikemura N, Kimura T, Katsumata Y, Tanimoto K, et al. Catheter ablation for patients with atrial fibrillation and heart failure with reduced and preserved ejection fraction: insights from the KiCS-AF multicentre cohort study. *Europace* 2023;**25**:83–91. <https://doi.org/10.1093/europace/eauc108>
627. Wu L, Narasimhan B, Ho KS, Zheng Y, Shah AN, Kantharia BK. Safety and complications of catheter ablation for atrial fibrillation: predictors of complications from an updated analysis the national inpatient database. *J Cardiovasc Electrophysiol* 2021;**32**:1024–34. <https://doi.org/10.1111/jce.14979>
628. Tripathi B, Arora S, Kumar V, Abdelrahman M, Lahewala S, Dave M, et al. Temporal trends of in-hospital complications associated with catheter ablation of atrial fibrillation in the United States: an update from nationwide inpatient sample database (2011–2014). *J Cardiovasc Electrophysiol* 2018;**29**:715–24. <https://doi.org/10.1111/jce.13471>
629. Steinbeck G, Sinner MF, Lutz M, Muller-Nurasyid M, Kaab S, Reinecke H. Incidence of complications related to catheter ablation of atrial fibrillation and atrial flutter: a nationwide in-hospital analysis of administrative data for Germany in 2014. *Eur Heart J* 2018;**39**:4020–9. <https://doi.org/10.1093/eurheartj/ehy452>
630. Deshmukh A, Patel NJ, Pant S, Shah N, Chothani A, Mehta K, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: analysis of 93 801 procedures. *Circulation* 2013;**128**:2104–12. <https://doi.org/10.1161/CIRCULATIONAHA.113.003862>
631. Cheng EP, Liu CF, Yeo I, Markowitz SM, Thomas G, Ip JE, et al. Risk of mortality following catheter ablation of atrial fibrillation. *J Am Coll Cardiol* 2019;**74**:2254–64. <https://doi.org/10.1016/j.jacc.2019.08.1036>
632. Gawalko M, Duncker D, Manning M, van der Velden RMJ, Hermans ANL, Verhaert DVM, et al. The European TeleCheck-AF project on remote app-based management of atrial fibrillation during the COVID-19 pandemic: centre and patient experiences. *Europace* 2021;**23**:1003–15. <https://doi.org/10.1093/europace/eaab050>
633. Rizas KD, Freyer L, Sappler N, von Stülpnagel L, Spielbichler P, Krasniqi A, et al. Smartphone-based screening for atrial fibrillation: a pragmatic randomized clinical trial. *Nat Med* 2022;**28**:1823–30. <https://doi.org/10.1038/s41591-022-01979-w>
634. Andrade JG, Champagne J, Dubuc M, Deyell MW, Verma A, Macle L, et al. Cryoballoon or radiofrequency ablation for atrial fibrillation assessed by continuous monitoring: a randomized clinical trial. *Circulation* 2019;**140**:1779–88. <https://doi.org/10.1161/CIRCULATIONAHA.119.042622>
635. Duytschaever M, Demolder A, Philips T, Sarkozy A, El Haddad M, Taghji P, et al. Pulmonary vein isolation with vs. without continued antiarrhythmic drug treatment in subjects with Recurrent Atrial Fibrillation (POWDER AF): results from a multicentre randomized trial. *Eur Heart J* 2018;**39**:1429–37. <https://doi.org/10.1093/eurheartj/ehx666>
636. Darkner S, Chen X, Hansen J, Pehron S, Johannessen A, Nielsen JB, et al. Recurrence of arrhythmia following short-term oral AMIOdarone after Catheter ablation for atrial fibrillation: a double-blind, randomized, placebo-controlled study (AMIO-CAT trial). *Eur Heart J* 2014;**35**:3356–64. <https://doi.org/10.1093/eurheartj/ehu354>
637. Leong-Sit P, Roux JF, Zado E, Callans DJ, Garcia F, Lin D, et al. Antiarrhythmics after ablation of atrial fibrillation (5A study): six-month follow-up study. *Circ Arrhythm Electrophysiol* 2011;**4**:11–4. <https://doi.org/10.1161/CIRCEP.110.955393>
638. Kaitani K, Inoue K, Kobori A, Nakazawa Y, Ozawa T, Kurotobi T, et al. Efficacy of antiarrhythmic drugs short-term use after catheter ablation for atrial fibrillation (EAST-AF) trial. *Eur Heart J* 2016;**37**:610–8. <https://doi.org/10.1093/eurheartj/ehv501>
639. Noseworthy PA, Van Houten HK, Sangaralingham LR, Deshmukh AJ, Kapa S, Mulpuru SK, et al. Effect of antiarrhythmic drug initiation on readmission after catheter ablation for atrial fibrillation. *JACC Clin Electrophysiol* 2015;**1**:238–44. <https://doi.org/10.1016/j.jacep.2015.04.016>
640. Xu X, Alida CT, Yu B. Administration of antiarrhythmic drugs to maintain sinus rhythm after catheter ablation for atrial fibrillation: a meta-analysis. *Cardiovasc Ther* 2015;**33**:242–6. <https://doi.org/10.1111/1755-5922.12133>
641. Chen W, Liu H, Ling Z, Xu Y, Fan J, Du H, et al. Efficacy of short-term antiarrhythmic drugs use after catheter ablation of atrial fibrillation—a systematic review with meta-analyses and trial sequential analyses of randomized controlled trials. *PLoS One* 2016;**11**:e0156121. <https://doi.org/10.1371/journal.pone.0156121>
642. Schleberger R, Metzner A, Kuck KH, Andresen D, Willems S, Hoffmann E, et al. Antiarrhythmic drug therapy after catheter ablation for atrial fibrillation—insights from the German Ablation Registry. *Pharmacol Res Perspect* 2021;**9**:e00880. <https://doi.org/10.1002/prp2.880>
643. Zhang XD, Gu J, Jiang WF, Zhao L, Zhou L, Wang YL, et al. Optimal rhythm-control strategy for recurrent atrial tachycardia after catheter ablation of persistent atrial fibrillation: a randomized clinical trial. *Eur Heart J* 2014;**35**:1327–34. <https://doi.org/10.1093/eurheartj/ehu017>
644. Zhou L, He L, Wang W, Li C, Li S, Tang R, et al. Effect of repeat catheter ablation vs. antiarrhythmic drug therapy among patients with recurrent atrial tachycardia/atrial fibrillation after atrial fibrillation catheter ablation: data from CHINA-AF registry. *Europace* 2023;**25**:382–9. <https://doi.org/10.1093/europace/eauc169>
645. Fink T, Metzner A, Willems S, Eckardt L, Ince H, Brachmann J, et al. Procedural success, safety and patients satisfaction after second ablation of atrial fibrillation in the elderly: results from the German ablation registry. *Clin Res Cardiol* 2019;**108**:1354–63. <https://doi.org/10.1007/s00392-019-01471-5>

646. Winkle RA, Mead RH, Engel G, Kong MH, Fleming W, Salcedo J, et al. Impact of obesity on atrial fibrillation ablation: patient characteristics, long-term outcomes, and complications. *Heart Rhythm* 2017;**14**:819–27. <https://doi.org/10.1016/j.hrthm.2017.02.023>
647. Sticherling C, Marin F, Birnie D, Boriani G, Calkins H, Dan G-A, et al. Antithrombotic management in patients undergoing electrophysiological procedures: a European Heart Rhythm Association (EHRA) position document endorsed by the ESC Working Group Thrombosis, Heart Rhythm Society (HRS), and Asia Pacific Heart Rhythm Society (APHRS). *EP Europace* 2015;**17**:1197–214. <https://doi.org/10.1093/europace/euv190>
648. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *J Interv Card Electrophysiol* 2012;**33**:171–257. <https://doi.org/10.1007/s10840-012-9672-7>
649. Noubiap JJ, Agbaedeng TA, Ndooudoungue AL, Nyaga UF, Kengne AP. Atrial thrombus detection on transoesophageal echocardiography in patients with atrial fibrillation undergoing cardioversion or catheter ablation: a pooled analysis of rates and predictors. *J Cardiovasc Electrophysiol* 2021;**32**:2179–88. <https://doi.org/10.1111/jce.15082>
650. Lurie A, Wang J, Hinnegan KJ, McIntyre WF, Belle-Côté EP, Amit G, et al. Prevalence of left atrial thrombus in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol* 2021;**77**:2875–86. <https://doi.org/10.1016/j.jacc.2021.04.036>
651. Efremidis M, Bazoukis G, Vlachos K, Prappa E, Megasiotou A, Dragasis S, et al. Safety of catheter ablation of atrial fibrillation without pre- or peri-procedural imaging for the detection of left atrial thrombus in the era of uninterrupted anticoagulation. *J Arrhythm* 2021;**37**:28–32. <https://doi.org/10.1002/joa3.12466>
652. Diab M, Wazni OM, Saliba WJ, Tarakji KG, Ballout JA, Hutt E, et al. Ablation of atrial fibrillation without left atrial appendage imaging in patients treated with direct oral anticoagulants. *Circ Arrhythm Electrophysiol* 2020;**13**:e008301. <https://doi.org/10.1161/CIRCEP.119.008301>
653. Patel K, Natale A, Yang R, Trivedi C, Romero J, Briceno D, et al. Is transesophageal echocardiography necessary in patients undergoing ablation of atrial fibrillation on an uninterrupted direct oral anticoagulant regimen? Results from a prospective multicenter registry. *Heart Rhythm* 2020;**17**:2093–9. <https://doi.org/10.1016/j.hrthm.2020.07.017>
654. Mao YJ, Wang H, Huang PF. Meta-analysis of the safety and efficacy of using minimally interrupted novel oral anticoagulants in patients undergoing catheter ablation for atrial fibrillation. *J Interv Card Electrophysiol* 2021;**60**:407–17. <https://doi.org/10.1007/s10840-020-00754-6>
655. van Vugt SPG, Westra SW, Volleberg R, Hannink G, Nakamura R, de Asmundis C, et al. Meta-analysis of controlled studies on minimally interrupted vs. continuous use of non-vitamin K antagonist oral anticoagulants in catheter ablation for atrial fibrillation. *Europace* 2021;**23**:1961–9. <https://doi.org/10.1093/europace/euab175>
656. Ge Z, Faggioni M, Baber U, Sartori S, Sorrentino S, Farhan S, et al. Safety and efficacy of nonvitamin K antagonist oral anticoagulants during catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *Cardiovasc Ther* 2018;**36**:e12457. <https://doi.org/10.1111/1755-5922.12457>
657. Asad ZUA, Akhtar KH, Jafray AH, Khan MH, Khan MS, Munir MB, et al. Uninterrupted versus interrupted direct oral anticoagulation for catheter ablation of atrial fibrillation: a systematic review and meta-analysis. *J Cardiovasc Electrophysiol* 2021;**32**:1995–2004. <https://doi.org/10.1111/jce.15043>
658. Mao YJ, Wang H, Huang PF. Peri-procedural novel oral anticoagulants dosing strategy during atrial fibrillation ablation: a meta-analysis. *Pacing Clin Electrophysiol* 2020;**43**:1104–14. <https://doi.org/10.1111/pace.14040>
659. Basu-Ray I, Khanra D, Kupó P, Bunch J, Theus SA, Mukherjee A, et al. Outcomes of uninterrupted vs interrupted periprocedural direct oral anticoagulants in atrial fibrillation ablation: a meta-analysis. *J Arrhythm* 2021;**37**:384–93. <https://doi.org/10.1002/joa3.12507>
660. Romero J, Cerrud-Rodriguez RC, Diaz JC, Rodriguez D, Arshad S, Alviz I, et al. Oral anticoagulation after catheter ablation of atrial fibrillation and the associated risk of thromboembolic events and intracranial hemorrhage: a systematic review and meta-analysis. *J Cardiovasc Electrophysiol* 2019;**30**:1250–7. <https://doi.org/10.1111/jce.14052>
661. Liu XH, Xu Q, Luo T, Zhang L, Liu HJ. Discontinuation of oral anticoagulation therapy after successful atrial fibrillation ablation: a systematic review and meta-analysis of prospective studies. *PLoS One* 2021;**16**:e0253709. <https://doi.org/10.1371/journal.pone.0253709>
662. Proietti R, Alturki A, Di Biase L, China P, Forleo G, Corrado A, et al. Anticoagulation after catheter ablation of atrial fibrillation: an unnecessary evil? A systematic review and meta-analysis. *J Cardiovasc Electrophysiol* 2019;**30**:468–78. <https://doi.org/10.1111/jce.13822>
663. Maduray K, Moneruzzaman M, Changwe GJ, Zhong J. Benefits and risks associated with long-term oral anticoagulation after successful atrial fibrillation catheter ablation: systematic review and meta-analysis. *Clin Appl Thromb Hemost* 2022;**28**:10760296221118480. <https://doi.org/10.1177/10760296221118480>
664. Brockmeyer M, Lin Y, Parco C, Karathanos A, Krieger T, Schulze V, et al. Uninterrupted anticoagulation during catheter ablation for atrial fibrillation: no difference in major bleeding and stroke between direct oral anticoagulants and vitamin K antagonists in an updated meta-analysis of randomised controlled trials. *Acta Cardiol* 2021;**76**:288–95. <https://doi.org/10.1080/00015385.2020.1724689>
665. Di Monaco A, Guida P, Vitulano N, Quadrini F, Troisi F, Langialonga T, et al. Catheter ablation of atrial fibrillation with uninterrupted anticoagulation: a meta-analysis of six randomized controlled trials. *J Cardiovasc Med (Hagerstown)* 2020;**21**:483–90. <https://doi.org/10.2459/JCM.0000000000000939>
666. Maesen B, Luermans J, Bidar E, Chaldoupi SM, Gelsomino S, Maessen JG, et al. A hybrid approach to complex arrhythmias. *Europace* 2021;**23**:ii28–33. <https://doi.org/10.1093/europace/euab027>
667. van der Heijden CAJ, Vroomen M, Luermans JG, Vos R, Crijns H, Gelsomino S, et al. Hybrid versus catheter ablation in patients with persistent and longstanding persistent atrial fibrillation: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2019;**56**:433–43. <https://doi.org/10.1093/ejcts/ezy475>
668. Boersma LV, Castella M, van Boven WV, Berruezo A, Yilmaz A, Nadal M, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. *Circulation* 2012;**125**:23–30. <https://doi.org/10.1161/CIRCULATIONAHA.111.074047>
669. Castella M, Kotecha D, van Laar C, Wintgens L, Castillo Y, Kelder J, et al. Thoracoscopic vs. catheter ablation for atrial fibrillation: long-term follow-up of the FAST randomized trial. *Europace* 2019;**21**:746–53. <https://doi.org/10.1093/europace/euy325>
670. van der Heijden CAJ, Weberndörfer V, Vroomen M, Luermans JG, Chaldoupi SM, Bidar E, et al. Hybrid ablation versus repeated catheter ablation in persistent atrial fibrillation: a randomized controlled trial. *JACC Clin Electrophysiol* 2023;**9**:1013–23. <https://doi.org/10.1016/j.jacep.2022.12.011>
671. DeLurgio DB, Crossen KJ, Gill J, Blauth C, Oza SR, Magnano AR, et al. Hybrid convergent procedure for the treatment of persistent and long-standing persistent atrial fibrillation: results of CONVERGE clinical trial. *Circ Arrhythm Electrophysiol* 2020;**13**:e009288. <https://doi.org/10.1161/CIRCEP.120.009288>
672. Pokushalov E, Romanov A, Elesin D, Bogachev-Prokophiev A, Losik D, Bairamova S, et al. Catheter versus surgical ablation of atrial fibrillation after a failed initial pulmonary vein isolation procedure: a randomized controlled trial. *J Cardiovasc Electrophysiol* 2013;**24**:1338–43. <https://doi.org/10.1111/jce.12245>
673. Haldar S, Khan HR, Boyalla V, Kralj-Hans I, Jones S, Lord J, et al. Catheter ablation vs. thoracoscopic surgical ablation in long-standing persistent atrial fibrillation: CASA-AF randomized controlled trial. *Eur Heart J* 2020;**41**:4471–80. <https://doi.org/10.1093/eurheartj/ehaa658>
674. Doll N, Weimar T, Kosior DA, Bulava A, Mokracek A, Mönnig G, et al. Efficacy and safety of hybrid epicardial and endocardial ablation versus endocardial ablation in patients with persistent and longstanding persistent atrial fibrillation: a randomised, controlled trial. *EClinicalMedicine* 2023;**61**:102052. <https://doi.org/10.1016/j.eclinm.2023.102052>
675. Malaisrie SC, McCarthy PM, Kruse J, Matsouka R, Andrei AC, Grau-Sepulveda MV, et al. Burden of preoperative atrial fibrillation in patients undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2018;**155**:2358–2367 e1. <https://doi.org/10.1016/j.jtcvs.2018.01.069>
676. Saxena A, Dinh DT, Reid CM, Smith JA, Shardey GC, Newcomb AE. Does preoperative atrial fibrillation portend a poorer prognosis in patients undergoing isolated aortic valve replacement? A multicentre Australian study. *Can J Cardiol* 2013;**29**:697–703. <https://doi.org/10.1016/j.cjca.2012.08.016>
677. Quader MA, McCarthy PM, Gillinov AM, Alster JM, Cosgrove DM, 3rd, Lytle BW, et al. Does preoperative atrial fibrillation reduce survival after coronary artery bypass grafting? *Ann Thorac Surg* 2004;**77**:1514–22; discussion 1522–4. <https://doi.org/10.1016/j.athoracsur.2003.09.069>
678. Damiano RJ, Jr, Schwartz FH, Bailey MS, Maniar HS, Munfakh NA, Moon MR, et al. The Cox Maze IV procedure: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2011;**141**:113–21. <https://doi.org/10.1016/j.jtcvs.2010.08.067>
679. Cox JL, Schuessler RB, Boineau JP. The development of the Maze procedure for the treatment of atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2000;**12**:2–14. [https://doi.org/10.1016/S1043-0679\(00\)70010-4](https://doi.org/10.1016/S1043-0679(00)70010-4)
680. Melby SJ, Zierer A, Bailey MS, Cox JL, Lawton JS, Munfakh N, et al. A new era in the surgical treatment of atrial fibrillation: the impact of ablation technology and lesion set on procedural efficacy. *Ann Surg* 2006;**244**:583–92. <https://doi.org/10.1097/01.sla.0000237654.00841.26>
681. Badhwar V, Rankin JS, Damiano RJ, Jr, Gillinov AM, Bakaeen FG, Edgerton JR, et al. The Society of Thoracic Surgeons 2017 clinical practice guidelines for the surgical treatment of atrial fibrillation. *Ann Thorac Surg* 2017;**103**:329–41. <https://doi.org/10.1016/j.athoracsur.2016.10.076>
682. Ad N, Henry L, Hunt S, Holmes SD. Impact of clinical presentation and surgeon experience on the decision to perform surgical ablation. *Ann Thorac Surg* 2013;**96**:763–8; discussion 768–9. <https://doi.org/10.1016/j.athoracsur.2013.03.066>
683. Cheng DC, Ad N, Martin J, Berglin EE, Chang BC, Doukas G, et al. Surgical ablation for atrial fibrillation in cardiac surgery: a meta-analysis and systematic review. *Innovations (Phila)* 2010;**5**:84–96. <https://doi.org/10.1177/155698451000500204>



684. McClure GR, Belley-Cote EP, Jaffer IH, Dvirnik N, An KR, Fortin G, et al. Surgical ablation of atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials. *Europace* 2018;**20**:1442–50. <https://doi.org/10.1093/europace/eux336>
685. Phan K, Xie A, La Meir M, Black D, Yan TD. Surgical ablation for treatment of atrial fibrillation in cardiac surgery: a cumulative meta-analysis of randomised controlled trials. *Heart* 2014;**100**:722–30. <https://doi.org/10.1136/heartjnl-2013-305351>
686. Barnett SD, Ad N. Surgical ablation as treatment for the elimination of atrial fibrillation: a meta-analysis. *J Thorac Cardiovasc Surg* 2006;**131**:1029–35. <https://doi.org/10.1016/j.jtcvs.2005.10.020>
687. Gillinov AM, Gelijns AC, Parides MK, DeRose JJ, Jr, Moskowitz AJ, Voisine P, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med* 2015;**372**:1399–409. <https://doi.org/10.1056/NEJMoa1500528>
688. MacGregor RM, Bakir NH, Pedamallu H, Sinn LA, Maniar HS, Melby SJ, et al. Late results after stand-alone surgical ablation for atrial fibrillation. *J Thorac Cardiovasc Surg* 2022;**164**:1515–1528.e8. <https://doi.org/10.1016/j.jtcvs.2021.03.109>
689. Musharbash FN, Schill MR, Sinn LA, Schuessler RB, Maniar HS, Moon MR, et al. Performance of the Cox-Maze IV procedure is associated with improved long-term survival in patients with atrial fibrillation undergoing cardiac surgery. *J Thorac Cardiovasc Surg* 2018;**155**:159–70. <https://doi.org/10.1016/j.jtcvs.2017.09.095>
690. Rankin JS, Lerner DJ, Braid-Forbes MJ, McCrea MM, Badhwar V. Surgical ablation of atrial fibrillation concomitant to coronary-artery bypass grafting provides cost-effective mortality reduction. *J Thorac Cardiovasc Surg* 2020;**160**:675–686 e13. <https://doi.org/10.1016/j.jtcvs.2019.07.131>
691. Suwalski P, Kowalewski M, Jasinski M, Staromlynski J, Zembala M, Widenka K, et al. Survival after surgical ablation for atrial fibrillation in mitral valve surgery: analysis from the Polish National Registry of Cardiac Surgery Procedures (KROK). *J Thorac Cardiovasc Surg* 2019;**157**:1007–1018 e4. <https://doi.org/10.1016/j.jtcvs.2018.07.099>
692. Suwalski P, Kowalewski M, Jasinski M, Staromlynski J, Zembala M, Widenka K, et al. Surgical ablation for atrial fibrillation during isolated coronary artery bypass surgery. *Eur J Cardiothorac Surg* 2020;**57**:691–700. <https://doi.org/10.1093/ejcts/ezz298>
693. Wehbe M, Albert M, Lewalter T, Ouarrak T, Senges J, Hanke T, et al. The German cardiosurgery atrial fibrillation registry: 1-year follow-up outcomes. *Thorac Cardiovasc Surg* 2023;**71**:255–63. <https://doi.org/10.1055/s-0042-1750311>
694. Kim HJ, Kim YJ, Kim M, Yoo JS, Kim DH, Park DW, et al. Surgical ablation for atrial fibrillation during aortic and mitral valve surgery: a nationwide population-based cohort study. *J Thorac Cardiovasc Surg* 2024;**167**:981–93. <https://doi.org/10.1016/j.jtcvs.2022.08.038>
695. Ad N, Henry L, Hunt S, Holmes SD. Do we increase the operative risk by adding the Cox Maze III procedure to aortic valve replacement and coronary artery bypass surgery? *J Thorac Cardiovasc Surg* 2012;**143**:936–44. <https://doi.org/10.1016/j.jtcvs.2011.12.018>
696. Maesen B, van der Heijden CAJ, Bidar E, Vos R, Athanasiou T, Maessen JG. Patient-reported quality of life after stand-alone and concomitant arrhythmia surgery: a systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg* 2022;**34**:339–48. <https://doi.org/10.1093/icvts/ivab282>
697. Osmancik P, Budera P, Talavera D, Hlavicka J, Herman D, Holy J, et al. Five-year outcomes in cardiac surgery patients with atrial fibrillation undergoing concomitant surgical ablation versus no ablation. The long-term follow-up of the PRAGUE-12 study. *Heart Rhythm* 2019;**16**:1334–40. <https://doi.org/10.1016/j.hrthm.2019.05.001>
698. Lee R, Jivan A, Kruse J, McGee EC, Jr, Malaisrie SC, Bernstein R, et al. Late neurologic events after surgery for atrial fibrillation: rare but relevant. *Ann Thorac Surg* 2013;**95**:126–31; discussion 131–2. <https://doi.org/10.1016/j.athoracsur.2012.08.048>
699. Kowalewski M, Pasierski M, Kołodziejczak M, Litwinowicz R, Kowalówka A, Wańha W, et al. Atrial fibrillation ablation improves late survival after concomitant cardiac surgery. *J Thorac Cardiovasc Surg* 2023;**166**:1656–1668.e8. <https://doi.org/10.1016/j.jtcvs.2022.04.035>
700. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. *J Thorac Cardiovasc Surg* 1999;**118**:833–40. [https://doi.org/10.1016/S0022-5223\(99\)70052-8](https://doi.org/10.1016/S0022-5223(99)70052-8)
701. Huffman MD, Karmali KN, Berendsen MA, Andrei AC, Kruse J, McCarthy PM, et al. Concomitant atrial fibrillation surgery for people undergoing cardiac surgery. *Cochrane Database Syst Rev* 2016;**8**:CD011814. <https://doi.org/10.1002/14651858.CD011814.pub2>
702. Kowalewski M, Pasierski M, Finke J, Kołodziejczak M, Staromlynski J, Litwinowicz R, et al. Permanent pacemaker implantation after valve and arrhythmia surgery in patients with preoperative atrial fibrillation. *Heart Rhythm* 2022;**19**:1442–9. <https://doi.org/10.1016/j.hrthm.2022.04.007>
703. Pokushalov E, Romanov A, Corbucci G, Cherniavsky A, Karaskov A. Benefit of ablation of first diagnosed paroxysmal atrial fibrillation during coronary artery bypass grafting: a pilot study. *Eur J Cardiothorac Surg* 2012;**41**:556–60. <https://doi.org/10.1093/ejcts/ezr101>
704. Yoo JS, Kim JB, Ro SK, Jung Y, Jung SH, Choo SJ, et al. Impact of concomitant surgical atrial fibrillation ablation in patients undergoing aortic valve replacement. *Circ J* 2014;**78**:1364–71. <https://doi.org/10.1253/circj.CJ-13-1533>
705. Malaisrie SC, Lee R, Kruse J, Lapin B, Wang EC, Bonow RO, et al. Atrial fibrillation ablation in patients undergoing aortic valve replacement. *J Heart Valve Dis* 2012;**21**:350–7.
706. Rankin JS, Lerner DJ, Braid-Forbes MJ, Ferguson MA, Badhwar V. One-year mortality and costs associated with surgical ablation for atrial fibrillation concomitant to coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2017;**52**:471–7. <https://doi.org/10.1093/ejcts/ezx126>
707. Schill MR, Musharbash FN, Hansalia V, Greenberg JW, Melby SJ, Maniar HS, et al. Late results of the Cox-Maze IV procedure in patients undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2017;**153**:1087–94. <https://doi.org/10.1016/j.jtcvs.2016.12.034>
708. Gupta D, Ding WY, Calvert P, Williams E, Das M, Tovmassian L, et al. Cryoballoon pulmonary vein isolation as first-line treatment for typical atrial flutter. *Heart* 2023;**109**:364–71. <https://doi.org/10.1136/heartjnl-2022-321729>
709. Steinberg C, Champagne J, Deyell MV, Dubuc M, Leong-Sit P, Calkins H, et al. Prevalence and outcome of early recurrence of atrial tachyarrhythmias in the cryoballoon vs irrigated radiofrequency catheter ablation (CIRCA-DOSE) study. *Heart Rhythm* 2021;**18**:1463–70. <https://doi.org/10.1016/j.hrthm.2021.06.1172>
710. Heijman J, Linz D, Schotten U. Dynamics of atrial fibrillation mechanisms and comorbidities. *Annu Rev Physiol* 2021;**83**:83–106. <https://doi.org/10.1146/annurev-physiol-031720-085307>
711. Fabritz L, Crijns H, Guasch E, Goette A, Hausler KG, Kotecha D, et al. Dynamic risk assessment to improve quality of care in patients with atrial fibrillation: the 7th AFNET/EHRA consensus conference. *Europace* 2021;**23**:329–44. <https://doi.org/10.1093/europace/eaab279>
712. Brandes A, Smit MD, Nguyen BO, Rienstra M, Van Gelder IC. Risk factor management in atrial fibrillation. *Arrhythm Electrophysiol Rev* 2018;**7**:118–27. <https://doi.org/10.15420/aer.2018.18.2>
713. Pokorney SD, Cocoros N, Al-Khalidi HR, Haynes K, Li S, Al-Khatib SM, et al. Effect of mailing educational material to patients with atrial fibrillation and their clinicians on use of oral anticoagulants: a randomized clinical trial. *JAMA Netw Open* 2022;**5**:e2214321. <https://doi.org/10.1001/jamanetworkopen.2022.14321>
714. Ritchie LA, Penson PE, Akpan A, Lip GYH, Lane DA. Integrated care for atrial fibrillation management: the role of the pharmacist. *Am J Med* 2022;**135**:1410–26. <https://doi.org/10.1016/j.amjmed.2022.07.014>
715. Guo Y, Guo J, Shi X, Yao Y, Sun Y, Xia Y, et al. Mobile health technology-supported atrial fibrillation screening and integrated care: a report from the mAFA-II trial long-term extension cohort. *Eur J Intern Med* 2020;**82**:105–11. <https://doi.org/10.1016/j.ejim.2020.09.024>
716. Yan H, Du YX, Wu FQ, Lu XY, Chen RM, Zhang Y. Effects of nurse-led multidisciplinary team management on cardiovascular hospitalization and quality of life in patients with atrial fibrillation: randomized controlled trial. *Int J Nurs Stud* 2022;**127**:104159. <https://doi.org/10.1016/j.ijnurstu.2021.104159>
717. Stewart S, Ball J, Horowitz JD, Marwick TH, Mahadevan G, Wong C, et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. *Lancet* 2015;**385**:775–84. [https://doi.org/10.1016/S0140-6736\(14\)61992-9](https://doi.org/10.1016/S0140-6736(14)61992-9)
718. Cox JL, Parkash R, Foster GA, Xie F, MacKillop JH, Ciaccia A, et al. Integrated management program advancing community treatment of atrial fibrillation (IMPACT-AF): a cluster randomized trial of a computerized clinical decision support tool. *Am Heart J* 2020;**224**:35–46. <https://doi.org/10.1016/j.ahj.2020.02.019>
719. Sposato LA, Stirling D, Saposnik G. Therapeutic decisions in atrial fibrillation for stroke prevention: the role of aversion to ambiguity and physicians' risk preferences. *J Stroke Cerebrovasc Dis* 2018;**27**:2088–95. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.03.005>
720. Noseworthy PA, Brito JP, Kunneman M, Hargraves IG, Zeballos-Palacios C, Montori VM, et al. Shared decision-making in atrial fibrillation: navigating complex issues in partnership with the patient. *J Interv Card Electrophysiol* 2019;**56**:159–63. <https://doi.org/10.1007/s10840-018-0465-5>
721. Poorcheraghi H, Negarandeh R, Pashaepoor S, Jorian J. Effect of using a mobile drug management application on medication adherence and hospital readmission among elderly patients with polypharmacy: a randomized controlled trial. *BMC Health Serv Res* 2023;**23**:1192. <https://doi.org/10.1186/s12913-023-10177-4>
722. Kotecha D, Chua WWL, Fabritz L, Hendriks J, Casadei B, Schotten U, et al. European Society of Cardiology (ESC) Atrial Fibrillation Guidelines Taskforce, the CATCH ME consortium, and the European Heart Rhythm Association (EHRA). European Society of Cardiology smartphone and tablet applications for patients with atrial fibrillation and their health care providers. *Europace* 2018;**20**:225–33. <https://doi.org/10.1093/europace/eux299>
723. Bunting KV, Gill SK, Sitch A, Mehta S, O'Connor K, Lip GY, et al. Improving the diagnosis of heart failure in patients with atrial fibrillation. *Heart* 2021;**107**:902–8. <https://doi.org/10.1136/heartjnl-2020-318557>
724. Donal E, Lip GY, Galderisi M, Goette A, Shah D, Marwan M, et al. EACVI/EHRA expert consensus document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation. *Eur Heart J Cardiovasc Imaging* 2016;**17**:355–83. <https://doi.org/10.1093/ehjci/jev354>

725. Bunting KV, O'Connor K, Steeds RP, Kotecha D. Cardiac imaging to assess left ventricular systolic function in atrial fibrillation. *Am J Cardiol* 2021;**139**:40–9. <https://doi.org/10.1016/j.amjcard.2020.10.012>
726. Timperley J, Mitchell AR, Becher H. Contrast echocardiography for left ventricular opacification. *Heart* 2003;**89**:1394–7. <https://doi.org/10.1136/heart.89.12.1394>
727. Kotecha D, Mohamed M, Shantsila E, Popescu BA, Steeds RP. Is echocardiography valid and reproducible in patients with atrial fibrillation? A systematic review. *Europace* 2017;**19**:1427–38. <https://doi.org/10.1093/europace/eux027>
728. Quintana RA, Dong T, Vajapey R, Reyalden R, Kwon DH, Harb S, et al. Preprocedural multimodality imaging in atrial fibrillation. *Circ Cardiovasc Imaging* 2022;**15**:e014386. <https://doi.org/10.1161/CIRCIMAGING.122.014386>
729. Laubrock K, von Loesch T, Steinmetz M, Lotz J, Frahm J, Uecker M, et al. Imaging of arrhythmia: real-time cardiac magnetic resonance imaging in atrial fibrillation. *Eur J Radiol Open* 2022;**9**:100404. <https://doi.org/10.1016/j.ejro.2022.100404>
730. Sciarà R, Sotgia B, Boni N, Pupi A. Assessment of the influence of atrial fibrillation on gated SPECT perfusion data by comparison with simultaneously acquired nongated SPECT data. *J Nucl Med* 2008;**49**:1283–7. <https://doi.org/10.2967/jnumed.108.051797>
731. Clayton B, Roobottom C, Morgan-Hughes G. CT coronary angiography in atrial fibrillation: a comparison of radiation dose and diagnostic confidence with retrospective gating vs prospective gating with systolic acquisition. *Br J Radiol* 2015;**88**:20150533. <https://doi.org/10.1259/bjr.20150533>
732. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: a systematic review. *Am J Med* 2006;**119**:448.e1–19. <https://doi.org/10.1016/j.amjmed.2005.10.057>
733. Steinberg BA, Dorian P, Anstrom KJ, Hess R, Mark DB, Noseworthy PA, et al. Patient-reported outcomes in atrial fibrillation research: results of a ClinicalTrials.gov analysis. *JACC Clin Electrophysiol* 2019;**5**:599–605. <https://doi.org/10.1016/j.jacep.2019.03.008>
734. Potpara TS, Mihajlovic M, Zec N, Marinkovic M, Kovacevic V, Simic J, et al. Self-reported treatment burden in patients with atrial fibrillation: quantification, major determinants, and implications for integrated holistic management of the arrhythmia. *Europace* 2020;**22**:1788–97. <https://doi.org/10.1093/europace/ea210>
735. Moons P, Norekvål TM, Arbelo E, Borregaard B, Casadei B, Cosyns B, et al. Placing patient-reported outcomes at the centre of cardiovascular clinical practice: implications for quality of care and management. *Eur Heart J* 2023;**44**:3405–22. <https://doi.org/10.1093/eurheartj/ehad514>
736. Allan KS, Aves T, Henry S, Banfield L, Victor JC, Dorian P, et al. Health-related quality of life in patients with atrial fibrillation treated with catheter ablation or antiarrhythmic drug therapy: a systematic review and meta-analysis. *CJC Open* 2020;**2**:286–95. <https://doi.org/10.1016/j.cjco.2020.03.013>
737. Vanderhout S, Fergusson DA, Cook JA, Taljaard M. Patient-reported outcomes and target effect sizes in pragmatic randomized trials in ClinicalTrials.gov: a cross-sectional analysis. *PLoS Med* 2022;**19**:e1003896. <https://doi.org/10.1371/journal.pmed.1003896>
738. Steinberg BA, Piccini JP, Sr. Tackling patient-reported outcomes in atrial fibrillation and heart failure: identifying disease-specific symptoms? *Cardiol Clin* 2019;**37**:139–46. <https://doi.org/10.1016/j.ccl.2019.01.013>
739. Hårdén M, Nyström B, Bengtson A, Medin J, Frison L, Edvardsson N. Responsiveness of AF6, a new, short, validated, atrial fibrillation-specific questionnaire—symptomatic benefit of direct current cardioversion. *J Interv Card Electrophysiol* 2010;**28**:185–91. <https://doi.org/10.1007/s10840-010-9487-3>
740. Tailachidis P, Tsimtsiou Z, Galanis P, Theodorou M, Kouvelas D, Athanasakis K. The atrial fibrillation effect on Quality-of-Life (AFEQT) questionnaire: cultural adaptation and validation of the Greek version. *Hippokratia* 2016;**20**:264–7.
741. Moreira RS, Bassolli L, Coutinho E, Ferrer P, Bragança ÉO, Carvalho AC, et al. Reproducibility and reliability of the quality of life questionnaire in patients with atrial fibrillation. *Arq Bras Cardiol* 2016;**106**:171–81. <https://doi.org/10.5935/abc.20160026>
742. Arribas F, Ormaetxe JM, Peinado R, Perulero N, Ramírez P, Badia X. Validation of the AF-QoL, a disease-specific quality of life questionnaire for patients with atrial fibrillation. *Europace* 2010;**12**:364–70. <https://doi.org/10.1093/europace/eup421>
743. Braganca EO, Filho BL, Maria VH, Levy D, de Paola AA. Validating a new quality of life questionnaire for atrial fibrillation patients. *Int J Cardiol* 2010;**143**:391–8. <https://doi.org/10.1016/j.ijcard.2009.03.087>
744. International Consortium for Health Outcomes Measurement. *Atrial fibrillation data collection reference guide Version 5.0.1*. <https://connect.ichom.org/wp-content/uploads/2023/02/03-Atrial-Fibrillation-Reference-Guide-2023.5.0.1.pdf>
745. Dan GA, Dan AR, Ivanescu A, Buzea AC. Acute rate control in atrial fibrillation: an urgent need for the clinician. *Eur Heart J Suppl* 2022;**24**:D3–D10. <https://doi.org/10.1093/eurheartjsupp/suac022>
746. Shima N, Miyamoto K, Kato S, Yoshida T, Uchino S; AFTER-ICU study group. Primary success of electrical cardioversion for new-onset atrial fibrillation and its association with clinical course in non-cardiac critically ill patients: sub-analysis of a multicenter observational study. *J Intensive Care* 2021;**9**:46. <https://doi.org/10.1186/s40560-021-00562-8>
747. Betthauser KD, Gibson GA, Piche SL, Pope HE. Evaluation of amiodarone use for new-onset atrial fibrillation in critically ill patients with septic shock. *Hosp Pharm* 2021;**56**:116–23. <https://doi.org/10.1177/0018578719868405>
748. Drikite L, Bedford JP, O'Bryan L, Petrinic T, Rajappan K, Doidge J, et al. Treatment strategies for new onset atrial fibrillation in patients treated on an intensive care unit: a systematic scoping review. *Crit Care* 2021;**25**:257. <https://doi.org/10.1186/s13054-021-03684-5>
749. Bedford JP, Johnson A, Redfern O, Gerry S, Doidge J, Harrison D, et al. Comparative effectiveness of common treatments for new-onset atrial fibrillation within the ICU: accounting for physiological status. *J Crit Care* 2022;**67**:149–56. <https://doi.org/10.1016/j.jccr.2021.11.005>
750. Iwahashi N, Takahashi H, Abe T, Okada K, Akiyama E, Matsuzawa Y, et al. Urgent control of rapid atrial fibrillation by landiolol in patients with acute decompensated heart failure with severely reduced ejection fraction. *Circ Rep* 2019;**1**:422–30. <https://doi.org/10.1253/circrep.CR-19-0076>
751. Unger M, Morelli A, Singer M, Radermacher P, Rehberg S, Trimmel H, et al. Landiolol in patients with septic shock resident in an intensive care unit (LANDI-SEP): study protocol for a randomized controlled trial. *Trials* 2018;**19**:637. <https://doi.org/10.1186/s13063-018-3024-6>
752. Gonzalez-Pacheco H, Marquez MF, Arias-Mendoza A, Alvarez-Sangabriel A, Eid-Lidt G, Gonzalez-Hermosillo A, et al. Clinical features and in-hospital mortality associated with different types of atrial fibrillation in patients with acute coronary syndrome with and without ST elevation. *J Cardiol* 2015;**66**:148–54. <https://doi.org/10.1016/j.jicc.2014.11.001>
753. Krijthe BP, Leening MJ, Heeringa J, Kors JA, Hofman A, Franco OH, et al. Unrecognized myocardial infarction and risk of atrial fibrillation: the Rotterdam Study. *Int J Cardiol* 2013;**168**:1453–7. <https://doi.org/10.1016/j.ijcard.2012.12.057>
754. Soliman EZ, Safford MM, Muntner P, Khodneva Y, Dawood FZ, Zakai NA, et al. Atrial fibrillation and the risk of myocardial infarction. *JAMA Intern Med* 2014;**174**:107–14. <https://doi.org/10.1001/jamainternmed.2013.11912>
755. Kraleš S, Schneider K, Lang S, Suselbeck T, Borggreffe M. Incidence and severity of coronary artery disease in patients with atrial fibrillation undergoing first-time coronary angiography. *PLoS One* 2011;**6**:e24964. <https://doi.org/10.1371/journal.pone.0024964>
756. Coscia T, Nestelberger T, Boeddinghaus J, Lopez-Ayala P, Koehlin L, Miró Ò, et al. Characteristics and outcomes of type 2 myocardial infarction. *JAMA Cardiol* 2022;**7**:427–34. <https://doi.org/10.1001/jamacardio.2022.0043>
757. Guimaraes PO, Zakrojsky P, Goyal A, Lopes RD, Kaltenbach LA, Wang TY. Usefulness of antithrombotic therapy in patients with atrial fibrillation and acute myocardial infarction. *Am J Cardiol* 2019;**123**:12–8. <https://doi.org/10.1016/j.amjcard.2018.09.031>
758. Erez A, Goldenberg I, Sabbag A, Nof E, Zahger D, Atar S, et al. Temporal trends and outcomes associated with atrial fibrillation observed during acute coronary syndrome: real-world data from the Acute Coronary Syndrome Israeli Survey (ACSIS), 2000–2013. *Clin Cardiol* 2017;**40**:275–80. <https://doi.org/10.1002/clc.22654>
759. Vrints C, Andreotti F, Koskinas K, Rossell X, Adamo M, Ainslie J, et al. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J* 2024. <https://doi.org/10.1093/eurheartj/ehae177>
760. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J* 2023;**44**:3720–826. <https://doi.org/10.1093/eurheartj/ehad191>
761. Park DY, Wang P, An S, Grimshaw AA, Frampton J, Ohman EM, et al. Shortening the duration of dual antiplatelet therapy after percutaneous coronary intervention for acute coronary syndrome: a systematic review and meta-analysis. *Am Heart J* 2022;**251**:101–14. <https://doi.org/10.1016/j.ahj.2022.05.019>
762. Gargiulo G, Goette A, Tijssen J, Eckardt L, Lewalter T, Vranckx P, et al. Safety and efficacy outcomes of double vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant-based randomized clinical trials. *Eur Heart J* 2019;**40**:3757–67. <https://doi.org/10.1093/eurheartj/ehz732>
763. Dewilde WJ, Oirbans T, Verheugt FW, Kelder JC, De Smet BJ, Herrman JP, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. *Lancet* 2013;**381**:1107–15. [https://doi.org/10.1016/S0140-6736\(12\)62177-1](https://doi.org/10.1016/S0140-6736(12)62177-1)
764. Lopes RD, Heizer G, Aronson R, Vora AN, Massaro T, Mehran R, et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation. *N Engl J Med* 2019;**380**:1509–24. <https://doi.org/10.1056/NEJMoa1817083>
765. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P, et al. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med* 2016;**375**:2423–34. <https://doi.org/10.1056/NEJMoa1611594>
766. Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T, et al. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. *N Engl J Med* 2017;**377**:1513–24. <https://doi.org/10.1056/NEJMoa1708454>
767. Vranckx P, Valgimigli M, Eckardt L, Tijssen J, Lewalter T, Gargiulo G, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. *Lancet* 2019;**394**:1335–43. [https://doi.org/10.1016/S0140-6736\(19\)31872-0](https://doi.org/10.1016/S0140-6736(19)31872-0)
768. Lopes RD, Hong H, Harskamp RE, Bhatt DL, Mehran R, Cannon CP, et al. Safety and efficacy of antithrombotic strategies in patients with atrial fibrillation undergoing

- percutaneous coronary intervention: a network meta-analysis of randomized controlled trials. *JAMA Cardiol* 2019;**4**:747–55. <https://doi.org/10.1001/jamacardio.2019.1880>
769. Oldgren J, Steg PG, Hohnloser SH, Lip GYH, Kimura T, Nordaby M, et al. Dabigatran dual therapy with ticagrelor or clopidogrel after percutaneous coronary intervention in atrial fibrillation patients with or without acute coronary syndrome: a subgroup analysis from the RE-DUAL PCI trial. *Eur Heart J* 2019;**40**:1553–62. <https://doi.org/10.1093/eurheartj/ehz059>
770. Potpara TS, Mujovic N, Proietti M, Dagres N, Hindricks G, Collet JP, et al. Revisiting the effects of omitting aspirin in combined antithrombotic therapies for atrial fibrillation and acute coronary syndromes or percutaneous coronary interventions: meta-analysis of pooled data from the PIONEER AF-PCI, RE-DUAL PCI, and AUGUSTUS trials. *Europace* 2020;**22**:33–46. <https://doi.org/10.1093/eurpace/euz259>
771. Haller PM, Sulzgruber P, Kaufmann C, Geelhood B, Tamargo J, Wassmann S, et al. Bleeding and ischaemic outcomes in patients treated with dual or triple antithrombotic therapy: systematic review and meta-analysis. *Eur Heart J Cardiovasc Pharmacother* 2019;**5**:226–36. <https://doi.org/10.1093/ehjcvp/pvz021>
772. Lopes RD, Hong H, Harskamp RE, Bhatt DL, Mehran R, Cannon CP, et al. Optimal antithrombotic regimens for patients with atrial fibrillation undergoing percutaneous coronary intervention: an updated network meta-analysis. *JAMA Cardiol* 2020;**5**:582–9. <https://doi.org/10.1001/jamacardio.2019.6175>
773. Lopes RD, Vora AN, Liaw D, Granger CB, Darius H, Goodman SG, et al. An open-label, 2 × 2 factorial, randomized controlled trial to evaluate the safety of apixaban vs. vitamin K antagonist and aspirin vs. placebo in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention: rationale and design of the AUGUSTUS trial. *Am Heart J* 2018;**200**:17–23. <https://doi.org/10.1016/j.jahj.2018.03.001>
774. Windecker S, Lopes RD, Massaro T, Jones-Burton C, Granger CB, Aronson R, et al. Antithrombotic therapy in patients with atrial fibrillation and acute coronary syndrome treated medically or with percutaneous coronary intervention or undergoing elective percutaneous coronary intervention: insights from the AUGUSTUS trial. *Circulation* 2019;**140**:1921–32. <https://doi.org/10.1161/CIRCULATIONAHA.119.043308>
775. Harskamp RE, Fanaroff AC, Lopes RD, Wojdyla DM, Goodman SG, Thomas LE, et al. Antithrombotic therapy in patients with atrial fibrillation after acute coronary syndromes or percutaneous intervention. *J Am Coll Cardiol* 2022;**79**:417–27. <https://doi.org/10.1016/j.jacc.2021.11.035>
776. Alexander JH, Wojdyla D, Vora AN, Thomas L, Granger CB, Goodman SG, et al. Risk/benefit tradeoff of antithrombotic therapy in patients with atrial fibrillation early and late after an acute coronary syndrome or percutaneous coronary intervention: insights from AUGUSTUS. *Circulation* 2020;**141**:1618–27. <https://doi.org/10.1161/CIRCULATIONAHA.120.046534>
777. Moayyedi P, Eikelboom JW, Bosch J, Connolly SJ, Dyal L, Shestakovska O, et al. Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin. *Gastroenterology* 2019;**157**:682–691.e2. <https://doi.org/10.1053/j.gastro.2019.05.056>
778. Jeridi D, Pellat A, Ginestet C, Assaf A, Hallit R, Corre F, et al. The safety of long-term proton pump inhibitor use on cardiovascular health: a meta-analysis. *J Clin Med* 2022;**11**:4096. <https://doi.org/10.3390/jcm11144096>
779. Scally B, Emberson JR, Spata E, Reith C, Davies K, Halls H, et al. Effects of gastroprotectant drugs for the prevention and treatment of peptic ulcer disease and its complications: a meta-analysis of randomised trials. *Lancet Gastroenterol Hepatol* 2018;**3**:231–41. [https://doi.org/10.1016/S2468-1253\(18\)30037-2](https://doi.org/10.1016/S2468-1253(18)30037-2)
780. Fiedler KA, Maeng M, Mehilli J, Schulz-Schupke S, Byrne RA, Sibbing D, et al. Duration of triple therapy in patients requiring oral anticoagulation after drug-eluting stent implantation: the ISAR-TRIPLÉ trial. *J Am Coll Cardiol* 2015;**65**:1619–29. <https://doi.org/10.1016/j.jacc.2015.02.050>
781. Matsumura-Nakano Y, Shizuta S, Komasa A, Morimoto T, Masuda H, Shiomi H, et al. Open-label randomized trial comparing oral anticoagulation with and without single antiplatelet therapy in patients with atrial fibrillation and stable coronary artery disease beyond 1 year after coronary stent implantation. *Circulation* 2019;**139**:604–16. <https://doi.org/10.1161/CIRCULATIONAHA.118.036768>
782. Jensen T, Thrane PG, Olesen KKW, Würtz M, Mortensen MB, Gyldenkerne C, et al. Antithrombotic treatment beyond 1 year after percutaneous coronary intervention in patients with atrial fibrillation. *Eur Heart J Cardiovasc Pharmacother* 2023;**9**:208–19. <https://doi.org/10.1093/ehjcvp/pvac058>
783. Vitalis A, Shantsila A, Proietti M, Vohra RK, Kay M, Olshansky B, et al. Peripheral arterial disease in patients with atrial fibrillation: the AFFIRM study. *Am J Med* 2021;**134**:514–8. <https://doi.org/10.1016/j.amjmed.2020.08.026>
784. Wasmer K, Unrath M, Köbe J, Malyar NM, Freisinger E, Meyborg M, et al. Atrial fibrillation is a risk marker for worse in-hospital and long-term outcome in patients with peripheral artery disease. *Int J Cardiol* 2015;**199**:223–8. <https://doi.org/10.1016/j.ijcard.2015.06.094>
785. Griffin WF, Salahuddin T, O'Neal WT, Soliman EZ. Peripheral arterial disease is associated with an increased risk of atrial fibrillation in the elderly. *Europace* 2016;**18**:794–8. <https://doi.org/10.1093/eurpace/euv369>
786. Lin LY, Lee CH, Yu CC, Tsai CT, Lai LP, Hwang JJ, et al. Risk factors and incidence of ischemic stroke in Taiwanese with nonvalvular atrial fibrillation—a nation wide database analysis. *Atherosclerosis* 2011;**217**:292–5. <https://doi.org/10.1016/j.atherosclerosis.2011.03.033>
787. Su MI, Cheng YC, Huang YC, Liu CW. The impact of atrial fibrillation on one-year mortality in patients with severe lower extremity arterial disease. *J Clin Med* 2022;**11**:1936. <https://doi.org/10.3390/jcm11071936>
788. Winkel TA, Hoeks SE, Schouten O, Zeymer U, Limbourg T, Baumgartner I, et al. Prognosis of atrial fibrillation in patients with symptomatic peripheral arterial disease: data from the REduction of Atherothrombosis for Continued Health (REACH) Registry. *Eur J Vasc Endovasc Surg* 2010;**40**:9–16. <https://doi.org/10.1016/j.ejvs.2010.03.003>
789. Nejim B, Mathlouthi A, Weaver L, Faateh M, Arhuidese I, Malas MB. Safety of carotid artery revascularization procedures in patients with atrial fibrillation. *J Vasc Surg* 2020;**72**:2069–18.e4. <https://doi.org/10.1016/j.jvs.2020.01.074>
790. Jones WS, Hellkamp AS, Halperin J, Piccini JP, Breithardt G, Singer DE, et al. Efficacy and safety of rivaroxaban compared with warfarin in patients with peripheral artery disease and non-valvular atrial fibrillation: insights from ROCKET AF. *Eur Heart J* 2014;**35**:242–9. <https://doi.org/10.1093/eurheartj/ehz492>
791. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018;**39**:763–816. <https://doi.org/10.1093/eurheartj/ehx095>
792. Schirmer CM, Bulsara KR, Al-Mufti F, Haranahalli N, Thibault L, Hetsch SW. Antiplatelets and antithrombotics in neurointerventional procedures: guideline update. *J Neurointerv Surg* 2023;**15**:1155–62. <https://doi.org/10.1136/jnis-2022-019844>
793. Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C, et al. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J* 2021;**6**:1–LXII. <https://doi.org/10.1177/2396987321989865>
794. Caso V, Masuhr F. A narrative review of nonvitamin K antagonist oral anticoagulant use in secondary stroke prevention. *J Stroke Cerebrovasc Dis* 2019;**28**:2363–75. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.05.017>
795. Fischer U, Koga M, Strbian D, Branca M, Abend S, Trelle S, et al. Early versus later anticoagulation for stroke with atrial fibrillation. *N Engl J Med* 2023;**388**:2411–21. <https://doi.org/10.1056/NEJMoa2303048>
796. Oldgren J, Åsberg S, Hijazi Z, Wester P, Bertilsson M, Norrving B. Early versus delayed non-vitamin K antagonist oral anticoagulant therapy after acute ischemic stroke in atrial fibrillation (TIMING): a registry-based randomized controlled noninferiority study. *Circulation* 2022;**146**:1056–66. <https://doi.org/10.1161/CIRCULATIONAHA.122.060666>
797. Schreuder F, van Nieuwenhuizen KM, Hofmeijer J, Vermeer SE, Kerkhoff H, Zock E, et al. Apixaban versus no anticoagulation after anticoagulation-associated intracerebral haemorrhage in patients with atrial fibrillation in The Netherlands (APACHE-AF): a randomised, open-label, phase 2 trial. *Lancet Neurol* 2021;**20**:907–16. [https://doi.org/10.1016/S1474-4422\(21\)00298-2](https://doi.org/10.1016/S1474-4422(21)00298-2)
798. SoSTART Collaboration. Effects of oral anticoagulation for atrial fibrillation after spontaneous intracranial haemorrhage in the UK: a randomised, open-label, assessor-masked, pilot-phase, non-inferiority trial. *Lancet Neurol* 2021;**20**:842–53. [https://doi.org/10.1016/S1474-4422\(21\)00264-7](https://doi.org/10.1016/S1474-4422(21)00264-7)
799. Klein Klouwenberg PM, Frencken JF, Kuipers S, Ong DS, Peelen LM, van Vught LA, et al. Incidence, predictors, and outcomes of new-onset atrial fibrillation in critically ill patients with sepsis. A cohort study. *Am J Respir Crit Care Med* 2017;**195**:205–11. <https://doi.org/10.1164/rccm.201603-0618OC>
800. Gundlund A, Olesen JB, Butt JH, Christensen MA, Gislason GH, Torp-Pedersen C, et al. One-year outcomes in atrial fibrillation presenting during infections: a nationwide registry-based study. *Eur Heart J* 2020;**41**:1112–9. <https://doi.org/10.1093/eurheartj/ehz873>
801. Induruwa I, Hennebry E, Hennebry J, Thakur M, Warburton EA, Khadjooi K. Sepsis-driven atrial fibrillation and ischaemic stroke. Is there enough evidence to recommend anticoagulation? *Eur J Intern Med* 2022;**98**:32–6. <https://doi.org/10.1016/j.ejim.2021.10.022>
802. Ko D, Saleeba C, Sadiq H, Crawford S, Paul T, Shi Q, et al. Secondary precipitants of atrial fibrillation and anticoagulation therapy. *J Am Heart Assoc* 2021;**10**:e021746. <https://doi.org/10.1161/JAHA.121.021746>
803. Li YG, Borgi M, Lip GY. Atrial fibrillation occurring initially during acute medical illness: the heterogeneous nature of disease, outcomes and management strategies. *Eur Heart J Acute Cardiovasc Care* 2018;**10**:2048872618801763. <https://doi.org/10.1177/2048872618801763>
804. Lowres N, Hillis GS, Gladman MA, Kol M, Rogers J, Chow V, et al. Self-monitoring for recurrence of secondary atrial fibrillation following non-cardiac surgery or acute



- illness: a pilot study. *Int J Cardiol Heart Vasc* 2020;**29**:100566. <https://doi.org/10.1016/j.ijcha.2020.100566>
805. Søgaard M, Skjøth F, Nielsen PB, Smit J, Dalager-Pedersen M, Larsen TB, et al. Thromboembolic risk in patients with pneumonia and new-onset atrial fibrillation not receiving anticoagulation therapy. *JAMA Netw Open* 2022;**5**:e2213945. <https://doi.org/10.1001/jamanetworkopen.2022.13945>
  806. Walkey AJ, Hammill BG, Curtis LH, Benjamin EJ. Long-term outcomes following development of new-onset atrial fibrillation during sepsis. *Chest* 2014;**146**:1187–95. <https://doi.org/10.1378/chest.14-0003>
  807. McIntyre WF, Um KJ, Cheung CC, Belle-Côté EP, Dingwall O, Devereaux PJ, et al. Atrial fibrillation detected initially during acute medical illness: a systematic review. *Eur Heart J Acute Cardiovasc Care* 2019;**8**:130–41. <https://doi.org/10.1177/2048872618799748>
  808. Marcus GM, Vittinghoff E, Whitman IR, Joyce S, Yang V, Nah G, et al. Acute consumption of alcohol and discrete atrial fibrillation events. *Ann Intern Med* 2021;**174**:1503–9. <https://doi.org/10.7326/M21-0228>
  809. Marcus GM, Modrow MF, Schmid CH, Sigona K, Nah G, Yang J, et al. Individualized studies of triggers of paroxysmal atrial fibrillation: the I-STOP-AFib randomized clinical trial. *JAMA Cardiol* 2022;**7**:167–74. <https://doi.org/10.1001/jamacardio.2021.5010>
  810. Lin AL, Nah G, Tang JJ, Vittinghoff E, Dewland TA, Marcus GM. Cannabis, cocaine, methamphetamine, and opiates increase the risk of incident atrial fibrillation. *Eur Heart J* 2022;**43**:4933–42. <https://doi.org/10.1093/eurheartj/ehac558>
  811. Butt JH, Olesen JB, Havers-Borgersen E, Gundlund A, Andersson C, Gislason GH, et al. Risk of thromboembolism associated with atrial fibrillation following noncardiac surgery. *J Am Coll Cardiol* 2018;**72**:2027–36. <https://doi.org/10.1016/j.jacc.2018.07.088>
  812. Gundlund A, Kümler T, Bonde AN, Butt JH, Gislason GH, Torp-Pedersen C, et al. Comparative thromboembolic risk in atrial fibrillation with and without a secondary precipitant—Danish nationwide cohort study. *BMJ Open* 2019;**9**:e028468. <https://doi.org/10.1136/bmjopen-2018-028468>
  813. Walkey AJ, Quinn EK, Winter MR, McManus DD, Benjamin EJ. Practice patterns and outcomes associated with use of anticoagulation among patients with atrial fibrillation during sepsis. *JAMA Cardiol* 2016;**1**:682–90. <https://doi.org/10.1001/jamacardio.2016.2181>
  814. Darwish OS, Strube S, Nguyen HM, Tanios MA. Challenges of anticoagulation for atrial fibrillation in patients with severe sepsis. *Ann Pharmacother* 2013;**47**:1266–71. <https://doi.org/10.1177/1060028013500938>
  815. Quon MJ, Behloul H, Pilote L. Anticoagulant use and risk of ischemic stroke and bleeding in patients with secondary atrial fibrillation associated with acute coronary syndromes, acute pulmonary disease, or sepsis. *JACC Clin Electrophysiol* 2018;**4**:386–93. <https://doi.org/10.1016/j.jacep.2017.08.003>
  816. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. *J Am Coll Cardiol* 2008;**51**:793–801. <https://doi.org/10.1016/j.jacc.2007.10.043>
  817. Gillinov AM, Bagiella E, Moskowitz AJ, Raiten JM, Groh MA, Bowdish ME, et al. Rate control versus rhythm control for atrial fibrillation after cardiac surgery. *N Engl J Med* 2016;**374**:1911–21. <https://doi.org/10.1056/NEJMoa1602002>
  818. Gaudino M, Di Franco A, Rong LQ, Piccini J, Mack M. Postoperative atrial fibrillation: from mechanisms to treatment. *Eur Heart J* 2023;**44**:1020–39. <https://doi.org/10.1093/eurheartj/ehad019>
  819. Kotecha D, Castella M. Is it time to treat post-operative atrial fibrillation just like regular atrial fibrillation? *Eur Heart J* 2020;**41**:652–654a. <https://doi.org/10.1093/eurheartj/ehz412>
  820. Konstantino Y, Zelnik Yovel D, Friger MD, Sahar G, Knyazer B, Amit G. Postoperative atrial fibrillation following coronary artery bypass graft surgery predicts long-term atrial fibrillation and stroke. *Isr Med Assoc J* 2016;**18**:744–8.
  821. Lee SH, Kang DR, Uhm JS, Shim J, Sung JH, Kim JY, et al. New-onset atrial fibrillation predicts long-term newly developed atrial fibrillation after coronary artery bypass graft. *Am Heart J* 2014;**167**:593–600.e1. <https://doi.org/10.1016/j.ahj.2013.12.010>
  822. Lin MH, Kamel H, Singer DE, Wu YL, Lee M, Ovbiagele B. Perioperative/postoperative atrial fibrillation and risk of subsequent stroke and/or mortality. *Stroke* 2019;**50**:1364–71. <https://doi.org/10.1161/STROKEAHA.118.023921>
  823. Alturki A, Marafi M, Proietti R, Cardinale D, Blackwell R, Dorian P, et al. Major adverse cardiovascular events associated with postoperative atrial fibrillation after noncardiac surgery: a systematic review and meta-analysis. *Circ Arrhythm Electrophysiol* 2020;**13**:e007437. <https://doi.org/10.1161/CIRCEP.119.007437>
  824. Goyal P, Kim M, Krishnan U, McCullough SA, Cheung JW, Kim LK, et al. Post-operative atrial fibrillation and risk of heart failure hospitalization. *Eur Heart J* 2022;**43**:2971–80. <https://doi.org/10.1093/eurheartj/ehac285>
  825. Eikelboom R, Sanjanwala R, Le ML, Yamashita MH, Arora RC. Postoperative atrial fibrillation after cardiac surgery: a systematic review and meta-analysis. *Ann Thorac Surg* 2021;**111**:544–54. <https://doi.org/10.1016/j.athoracsur.2020.05.104>
  826. Benedetto U, Gaudino MF, Dimagli A, Gerry S, Gray A, Lees B, et al. Postoperative atrial fibrillation and long-term risk of stroke after isolated coronary artery bypass graft surgery. *Circulation* 2020;**142**:1320–9. <https://doi.org/10.1161/CIRCULATIONAHA.120.046940>
  827. Taha A, Nielsen SJ, Bergfeldt L, Ahlsson A, Friberg L, Björck S, et al. New-onset atrial fibrillation after coronary artery bypass grafting and long-term outcome: a population-based nationwide study from the SWEDEHEART registry. *J Am Heart Assoc* 2021;**10**:e017966. <https://doi.org/10.1161/JAHA.120.017966>
  828. Dobrev D, Aguilar M, Heijman J, Guichard JB, Nattel S. Postoperative atrial fibrillation: mechanisms, manifestations and management. *Nat Rev Cardiol* 2019;**16**:417–36. <https://doi.org/10.1038/s41569-019-0166-5>
  829. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA* 2004;**291**:1720–9. <https://doi.org/10.1001/jama.291.14.1720>
  830. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elyada M, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. *J Am Coll Cardiol* 2004;**43**:742–8. <https://doi.org/10.1016/j.jacc.2003.11.023>
  831. Cardinale D, Sandri MT, Colombo A, Salviati M, Tedeschi I, Bacchiani G, et al. Prevention of atrial fibrillation in high-risk patients undergoing lung cancer surgery: the PRESAGE trial. *Ann Surg* 2016;**264**:244–51. <https://doi.org/10.1097/SLA.0000000000001626>
  832. Ojima T, Nakamori M, Nakamura M, Katsuda M, Hayata K, Kato T, et al. Randomized clinical trial of landiolol hydrochloride for the prevention of atrial fibrillation and post-operative complications after oesophagectomy for cancer. *Br J Surg* 2017;**104**:1003–9. <https://doi.org/10.1002/bjs.10548>
  833. Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database Syst Rev* 2013;**1**:CD003611. <https://doi.org/10.1002/14651858.CD003611.pub3>
  834. Ozyaydin M, Icli A, Yucel H, Akcay S, Peker O, Erdogan D, et al. Metoprolol vs. carvedilol or carvedilol plus N-acetyl cysteine on post-operative atrial fibrillation: a randomized, double-blind, placebo-controlled study. *Eur Heart J* 2013;**34**:597–604. <https://doi.org/10.1093/eurheartj/ehs423>
  835. O'Neal JB, Billings F, Liu X, Shotwell MS, Liang Y, Shah AS, et al. Effect of preoperative beta-blocker use on outcomes following cardiac surgery. *Am J Cardiol* 2017;**120**:1293–7. <https://doi.org/10.1016/j.amjcard.2017.07.012>
  836. Ziff OJ, Samra M, Howard JP, Bromage DI, Ruschitzka F, Francis DP, et al. Beta-blocker efficacy across different cardiovascular indications: an umbrella review and meta-analytic assessment. *BMC Med* 2020;**18**:103. <https://doi.org/10.1186/s12916-020-01564-3>
  837. Tisdale JE, Wroblewski HA, Wall DS, Rieger KM, Hammoud ZT, Young JV, et al. A randomized trial evaluating amiodarone for prevention of atrial fibrillation after pulmonary resection. *Ann Thorac Surg* 2009;**88**:886–93; discussion 894–5. <https://doi.org/10.1016/j.athoracsur.2009.04.074>
  838. Auer J, Weber T, Berent R, Puschmann R, Hartl P, Ng CK, et al. A comparison between oral antiarrhythmic drugs in the prevention of atrial fibrillation after cardiac surgery: the pilot Study of Prevention of Postoperative Atrial Fibrillation (SPPAF), a randomized, placebo-controlled trial. *Am Heart J* 2004;**147**:636–43. <https://doi.org/10.1016/j.ahj.2003.10.041>
  839. Buckley MS, Nolan PE, Jr, Slack MK, Tisdale JE, Hilleman DE, Copeland JG. Amiodarone prophylaxis for atrial fibrillation after cardiac surgery: meta-analysis of dose response and timing of initiation. *Pharmacotherapy* 2007;**27**:360–8. <https://doi.org/10.1592/phco.27.3.360>
  840. Riber LP, Christensen TD, Jensen HK, Høejsgaard A, Pilegaard HK. Amiodarone significantly decreases atrial fibrillation in patients undergoing surgery for lung cancer. *Ann Thorac Surg* 2012;**94**:339–44; discussion 345–6. <https://doi.org/10.1016/j.athoracsur.2011.12.096>
  841. Couffignal C, Amour J, Ait-Hamou N, Cholley B, Fellahi JL, Duval X, et al. Timing of  $\beta$ -blocker reintroduction and the occurrence of postoperative atrial fibrillation after cardiac surgery: a prospective cohort study. *Anesthesiology* 2020;**132**:267–79. <https://doi.org/10.1097/ALN.0000000000003064>
  842. Piccini JP, Ahlsson A, Dorian P, Gillinov MA, Kowey PR, Mack MJ, et al. Design and rationale of a phase 2 study of Neurotoxin (Botulinum Toxin Type A) for the PreVent of post-operative atrial fibrillation—the NOVA study. *Am Heart J* 2022;**245**:51–9. <https://doi.org/10.1016/j.ahj.2021.10.114>
  843. O'Brien B, Burrage PS, Ngai JY, Prutkin JM, Huang CC, Xu X, et al. Society of Cardiovascular Anesthesiologists/European Association of Cardiothoracic Anaesthetists Practice Advisory for the management of perioperative atrial fibrillation in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 2019;**33**:12–26. <https://doi.org/10.1053/j.jvca.2018.09.039>
  844. Gaudino M, Sanna T, Ballman KV, Robinson NB, Hameed I, Audisio K, et al. Posterior left pericardiectomy for the prevention of atrial fibrillation after cardiac surgery: an adaptive, single-centre, single-blind, randomised, controlled trial. *Lancet* 2021;**398**:2075–83. [https://doi.org/10.1016/S0140-6736\(21\)02490-9](https://doi.org/10.1016/S0140-6736(21)02490-9)
  845. Abdelaziz A, Hafez AH, Elaraby A, Roshdy MR, Abdelaziz M, Eltohy MA, et al. Posterior pericardiectomy for the prevention of atrial fibrillation after cardiac surgery: a systematic review and meta-analysis of 25 randomised controlled trials. *EuroIntervention* 2023;**19**:e305–17. <https://doi.org/10.4244/EIJ-D-22-00948>
  846. Soletti GJ, Perezgrovas-Olaria R, Harik L, Rahouma M, Dimagli A, Alzhari T, et al. Effect of posterior pericardiectomy in cardiac surgery: a systematic review and



- meta-analysis of randomized controlled trials. *Front Cardiovasc Med* 2022;**9**:1090102. <https://doi.org/10.3389/fcvm.2022.1090102>
847. Conen D, Ke Wang M, Popova E, Chan MTV, Landoni G, Cata JP, et al. Effect of colchicine on perioperative atrial fibrillation and myocardial injury after non-cardiac surgery in patients undergoing major thoracic surgery (COP-AF): an international randomised trial. *Lancet* 2023;**402**:1627–35. [https://doi.org/10.1016/S0140-6736\(23\)01689-6](https://doi.org/10.1016/S0140-6736(23)01689-6)
848. Fragão-Marques M, Teixeira F, Mancio J, Seixas N, Rocha-Neves J, Falcão-Pires I, et al. Impact of oral anticoagulation therapy on postoperative atrial fibrillation outcomes: a systematic review and meta-analysis. *Thromb J* 2021;**19**:89. <https://doi.org/10.1186/s12959-021-00342-2>
849. Neves IA, Magalhães A, Lima da Silva G, Almeida AG, Borges M, Costa J, et al. Anticoagulation therapy in patients with post-operative atrial fibrillation: systematic review with meta-analysis. *Vascu Pharmacol* 2022;**142**:106929. <https://doi.org/10.1016/j.vph.2021.106929>
850. Daoud EG, Strickberger SA, Man KC, Goyal R, Deeb GM, Bolling SF, et al. Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. *N Engl J Med* 1997;**337**:1785–91. <https://doi.org/10.1056/NEJM199712183372501>
851. Yagdi T, Nalbantgil S, Ayik F, Apaydin A, Islamoglu F, Posacioglu H, et al. Amiodarone reduces the incidence of atrial fibrillation after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003;**125**:1420–5. [https://doi.org/10.1016/S0022-5223\(02\)73292-3](https://doi.org/10.1016/S0022-5223(02)73292-3)
852. Butt JH, Xian Y, Peterson ED, Olsen PS, Rorth R, Gundlund A, et al. Long-term thromboembolic risk in patients with postoperative atrial fibrillation after coronary artery bypass graft surgery and patients with nonvalvular atrial fibrillation. *JAMA Cardiol* 2018;**3**:417–24. <https://doi.org/10.1001/jamacardio.2018.0405>
853. Gialdini G, Nearing K, Bhavne PD, Bonuccelli U, Iadecola C, Healey JS, et al. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. *JAMA* 2014;**312**:616–22. <https://doi.org/10.1001/jama.2014.9143>
854. Horwich P, Buth KJ, Legare JF. New onset postoperative atrial fibrillation is associated with a long-term risk for stroke and death following cardiac surgery. *J Card Surg* 2013;**28**:8–13. <https://doi.org/10.1111/jocs.12033>
855. Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008;**371**:1839–47. [https://doi.org/10.1016/S0140-6736\(08\)60601-7](https://doi.org/10.1016/S0140-6736(08)60601-7)
856. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol* 2014;**13**:429–38. [https://doi.org/10.1016/S1474-4422\(13\)70310-7](https://doi.org/10.1016/S1474-4422(13)70310-7)
857. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014;**370**:2478–86. <https://doi.org/10.1056/NEJMoa1313600>
858. Rubiera M, Aires A, Antonenko K, Lémeret S, Nolte CH, Putaala J, et al. European Stroke Organisation (ESO) guideline on screening for subclinical atrial fibrillation after stroke or transient ischaemic attack of undetermined origin. *Eur Stroke J* 2022;**7**:VI. <https://doi.org/10.1177/23969873221099478>
859. von Falkenhausen AS, Feil K, Sinner MF, Schönecker S, Müller J, Wischmann J, et al. Atrial fibrillation risk assessment after embolic stroke of undetermined source. *Ann Neurol* 2023;**93**:479–88. <https://doi.org/10.1002/ana.26545>
860. Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, et al. Atrial fibrillation in patients with cryptogenic stroke. *N Engl J Med* 2014;**370**:2467–77. <https://doi.org/10.1056/NEJMoa1311376>
861. Wächter R, Gröschel K, Gelbrich G, Hamann GF, Kermer P, Liman J, et al. Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-AF(RANDOMISED)): an open-label randomised controlled trial. *Lancet Neurol* 2017;**16**:282–90. [https://doi.org/10.1016/S1474-4422\(17\)30002-9](https://doi.org/10.1016/S1474-4422(17)30002-9)
862. Buck BH, Hill MD, Quinn FR, Butcher KS, Menon BK, Gulamhusein S, et al. Effect of implantable vs prolonged external electrocardiographic monitoring on atrial fibrillation detection in patients with ischemic stroke: the PER DIEM randomized clinical trial. *JAMA* 2021;**325**:2160–8. <https://doi.org/10.1001/jama.2021.6128>
863. Bernstein RA, Kamel H, Granger CB, Piccini JP, Sethi PP, Katz JM, et al. Effect of long-term continuous cardiac monitoring vs usual care on detection of atrial fibrillation in patients with stroke attributed to large- or small-vessel disease: the STROKE-AF randomized clinical trial. *JAMA* 2021;**325**:2169–77. <https://doi.org/10.1001/jama.2021.6470>
864. Tsigoulis G, Katsanos AH, Köhrmann M, Caso V, Perren F, Palaiodimos L, et al. Duration of implantable cardiac monitoring and detection of atrial fibrillation in ischemic stroke patients: a systematic review and meta-analysis. *J Stroke* 2019;**21**:302–11. <https://doi.org/10.5853/jos.2019.01067>
865. Sagris D, Harrison SL, Buckley BJR, Ntaios G, Lip GYH. Long-term cardiac monitoring after embolic stroke of undetermined source: search longer, look harder. *Am J Med* 2022;**135**:e311–7. <https://doi.org/10.1016/j.amjmed.2022.04.030>
866. Liantinioti C, Palaiodimos L, Tympas K, Parissis J, Theodorou A, Ikonomidis I, et al. Potential utility of neurosonology in paroxysmal atrial fibrillation detection in patients with cryptogenic stroke. *J Clin Med* 2019;**8**:2002. <https://doi.org/10.3390/jcm8112002>
867. Tsigoulis G, Katsanos AH, Grory BM, Köhrmann M, Ricci BA, Tsioufis K, et al. Prolonged cardiac rhythm monitoring and secondary stroke prevention in patients with cryptogenic cerebral ischemia. *Stroke* 2019;**50**:2175–80. <https://doi.org/10.1161/STROKEAHA.119.025169>
868. Favilla CG, Ingala E, Jara J, Fessler E, Cucchiara B, Messé SR, et al. Predictors of finding occult atrial fibrillation after cryptogenic stroke. *Stroke* 2015;**46**:1210–5. <https://doi.org/10.1161/STROKEAHA.114.007763>
869. Lip GY, Nielsen PB. Should patients with atrial fibrillation and 1 stroke risk factor (CHA2DS2-VASc score 1 in men, 2 in women) be anticoagulated? Yes: even 1 stroke risk factor confers a real risk of stroke. *Circulation* 2016;**133**:1498–503; discussion 1503. <https://doi.org/10.1161/CIRCULATIONAHA.115.016713>
870. Ricci B, Chang AD, Hemendinger M, Dakay K, Cutting S, Burton T, et al. A simple score that predicts paroxysmal atrial fibrillation on outpatient cardiac monitoring after embolic stroke of unknown source. *J Stroke Cerebrovasc Dis* 2018;**27**:1692–6. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.01.028>
871. Kwong C, Ling AY, Crawford MH, Zhao SX, Shah NH. A clinical score for predicting atrial fibrillation in patients with cryptogenic stroke or transient ischemic attack. *Cardiology* 2017;**138**:133–40. <https://doi.org/10.1159/000476030>
872. Li YG, Bisson A, Bodin A, Herbert J, Grammatico-Guillon L, Joung B, et al. C(2) HEST score and prediction of incident atrial fibrillation in poststroke patients: a French nationwide study. *J Am Heart Assoc* 2019;**8**:e012546. <https://doi.org/10.1161/JAHA.119.012546>
873. Haeusler KG, Gröschel K, Köhrmann M, Anker SD, Brachmann J, Böhm M, et al. Expert opinion paper on atrial fibrillation detection after ischemic stroke. *Clin Res Cardiol* 2018;**107**:871–80. <https://doi.org/10.1007/s00392-018-1256-9>
874. Dilaveris PE, Antoniou CK, Caiani EG, Casado-Arroyo R, Climent A, Cluitmans M, et al. ESC working group on e-cardiology position paper: accuracy and reliability of electrocardiogram monitoring in the detection of atrial fibrillation in cryptogenic stroke patients: in collaboration with the Council on Stroke, the European Heart Rhythm Association, and the Digital Health Committee. *Eur Heart J Digit Health* 2022;**3**:341–58. <https://doi.org/10.1093/ehjdh/ztac026>
875. Diener HC, Sacco RL, Easton JD, Granger CB, Bernstein RA, Uchiyama S, et al. Dabigatran for prevention of stroke after embolic stroke of undetermined source. *N Engl J Med* 2019;**380**:1906–17. <https://doi.org/10.1056/NEJMoa1813959>
876. Hart RG, Sharma M, Mundl H, Kasner SE, Bangdiwala SI, Berkowitz SD, et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. *N Engl J Med* 2018;**378**:2191–201. <https://doi.org/10.1056/NEJMoa1802686>
877. Poli S, Meissner C, Baezner HJ, Kraft A, Hillenbrand F, Hobohm C, et al. Apixaban for treatment of embolic stroke of undetermined source (ATTICUS) randomized trial—update of patient characteristics and study timeline after interim analysis. *Eur Heart J* 2021;**42**:ehab724.2070. <https://doi.org/10.1093/eurheartj/ehab724.2070>
878. Vaidya VR, Arora S, Patel N, Badheka AO, Patel N, Agnihotri K, et al. Burden of arrhythmia in pregnancy. *Circulation* 2017;**135**:619–21. <https://doi.org/10.1161/CIRCULATIONAHA.116.026681>
879. Lee MS, Chen W, Zhang Z, Duan L, Ng A, Spencer HT, et al. Atrial fibrillation and atrial flutter in pregnant women—a population-based study. *J Am Heart Assoc* 2016;**5**:e003182. <https://doi.org/10.1161/JAHA.115.003182>
880. Tamirisa KP, Elkayam U, Briller JE, Mason PK, Pillarisetti J, Merchant FM, et al. Arrhythmias in pregnancy. *JACC Clin Electrophysiol* 2022;**8**:120–35. <https://doi.org/10.1016/j.jacep.2021.10.004>
881. Salam AM, Ertekin E, van Hagen IM, Al Suwaidi J, Ruys TPE, Johnson MR, et al. Atrial fibrillation or flutter during pregnancy in patients with structural heart disease: data from the ROPAC (Registry on Pregnancy and Cardiac Disease). *JACC Clin Electrophysiol* 2015;**1**:284–92. <https://doi.org/10.1016/j.jacep.2015.04.013>
882. Chokesuwattanakul R, Thongprayoon C, Bathini T, O'Corragain OA, Sharma K, Prechawat S, et al. Incidence of atrial fibrillation in pregnancy and clinical significance: a meta-analysis. *Adv Med Sci* 2019;**64**:415–22. <https://doi.org/10.1016/j.advm.2019.07.003>
883. Tamirisa KP, Dye C, Bond RM, Hollier LM, Marinescu K, Vaseghi M, et al. Arrhythmias and heart failure in pregnancy: a dialogue on multidisciplinary collaboration. *J Cardiovasc Dev Dis* 2022;**9**:199. <https://doi.org/10.3390/jcdd9070199>
884. Al Bahhawi T, Aqeeli A, Harrison SL, Lane DA, Skjøth F, Buchan I, et al. Pregnancy-related complications and incidence of atrial fibrillation: a systematic review. *J Clin Med* 2023;**12**:1316. <https://doi.org/10.3390/jcm12041316>
885. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomstrom-Lundqvist C, Cifkova R, De Bonis M, et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 2018;**39**:3165–241. <https://doi.org/10.1093/eurheartj/ehy340>
886. Areia AL, Mota-Pinto A. Experience with direct oral anticoagulants in pregnancy—a systematic review. *J Perinat Med* 2022;**50**:457–61. <https://doi.org/10.1515/jpm-2021-0457>
887. Ueberham L, Hindricks G. Anticoagulation in special patient populations with atrial fibrillation. *Herz* 2021;**46**:323–8. <https://doi.org/10.1007/s00059-021-05042-1>
888. Bateman BT, Heide-Jørgensen U, Einarsdóttir K, Engeland A, Furu K, Gissler M, et al. β-Blocker use in pregnancy and the risk for congenital malformations: an international cohort study. *Ann Intern Med* 2018;**169**:665–73. <https://doi.org/10.7326/M18-0338>
889. Butters L, Kennedy S, Rubin PC. Atenolol in essential hypertension during pregnancy. *BMJ* 1990;**301**:587–9. <https://doi.org/10.1136/bmj.301.6752.587>

890. Ramlakhan KP, Kauling RM, Schenkelaars N, Segers D, Yap SC, Post MC, et al. Supraventricular arrhythmia in pregnancy. *Heart* 2022;**108**:1674–81. <https://doi.org/10.1136/heartjnl-2021-320451>
891. Katritsis DG, Boriani G, Cosio FG, Hindricks G, Jais P, Josephson ME, et al. European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardíaca y Electrofisiología (SOLAECE). *Eur Heart J* 2017;**19**:465–511. <https://doi.org/10.1093/eurheartj/ehw301>
892. Moore JS, Teefey P, Rao K, Berlowitz MS, Chae SH, Yankowitz J. Maternal arrhythmia: a case report and review of the literature. *Obstet Gynecol Surv* 2012;**67**:298–312. <https://doi.org/10.1097/OGX.0b013e318253a76e>
893. Wang YC, Chen CH, Su HY, Yu MH. The impact of maternal cardioversion on fetal haemodynamics. *Eur J Obstet Gynecol Reprod Biol* 2006;**126**:268–9. <https://doi.org/10.1016/j.ejogrb.2005.11.021>
894. European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery; Camm AJ, Kirchhof P, Lip GY, Schotten U, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010;**31**:2369–429. <https://doi.org/10.1093/eurheartj/ehq278>
895. Kockova R, Kocka V, Kiernan T, Fahy GJ. Ibutilide-induced cardioversion of atrial fibrillation during pregnancy. *J Cardiovasc Electrophysiol* 2007;**18**:545–7. <https://doi.org/10.1111/j.1540-8167.2006.00752.x>
896. Georgiopoulos G, Tsiachris D, Kordalis A, Kontogiannis C, Spartalis M, Pietri P, et al. Pharmacotherapeutic strategies for atrial fibrillation in pregnancy. *Expert Opin Pharmacother* 2019;**20**:1625–36. <https://doi.org/10.1080/14656566.2019.1621290>
897. Jensen AS, Idorn L, Nørgaard B, Vejstrup N, Sondergaard L. Anticoagulation in adults with congenital heart disease: the who, the when and the how? *Heart* 2015;**101**:424–9. <https://doi.org/10.1136/heartjnl-2014-305576>
898. Pujol C, Niesert AC, Engelhardt A, Schoen P, Kusmenkov E, Pittrow D, et al. Usefulness of direct oral anticoagulants in adult congenital heart disease. *Am J Cardiol* 2016;**117**:450–5. <https://doi.org/10.1016/j.amjcard.2015.10.062>
899. Yang H, Bouma BJ, Dimopoulos K, Khairy P, Ladouceur M, Niwa K, et al. Non-vitamin K antagonist oral anticoagulants (NOACs) for thromboembolic prevention, are they safe in congenital heart disease? Results of a worldwide study. *Int J Cardiol* 2020;**299**:123–30. <https://doi.org/10.1016/j.ijcard.2019.06.014>
900. Renda G, Ricci F, Giugliano RP, De Caterina R. Non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation and valvular heart disease. *J Am Coll Cardiol* 2017;**69**:1363–71. <https://doi.org/10.1016/j.jacc.2016.12.038>
901. Caldeira D, David C, Costa J, Ferreira JJ, Pinto FJ. Non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation and valvular heart disease: systematic review and meta-analysis. *Eur Heart J Cardiovasc Pharmacother* 2018;**4**:111–8. <https://doi.org/10.1093/ehjcvp/pvx028>
902. Ammass NM, Phillips SD, Hodge DO, Connolly HM, Grogan MA, Friedman PA, et al. Outcome of direct current cardioversion for atrial arrhythmias in adults with congenital heart disease. *Int J Cardiol* 2012;**154**:270–4. <https://doi.org/10.1016/j.ijcard.2010.09.028>
903. Feltes TF, Friedman RA. Transesophageal echocardiographic detection of atrial thrombi in patients with nonfibrillation atrial tachyarrhythmias and congenital heart disease. *J Am Coll Cardiol* 1994;**24**:1365–70. [https://doi.org/10.1016/0735-1097\(94\)90121-X](https://doi.org/10.1016/0735-1097(94)90121-X)
904. Roos-Hesselink JW, Meijboom FJ, Spitaels SE, van Domburg R, van Rijen EH, Utens EM, et al. Excellent survival and low incidence of arrhythmias, stroke and heart failure long-term after surgical ASD closure at young age. A prospective follow-up study of 21–33 years. *Eur Heart J* 2003;**24**:190–7. [https://doi.org/10.1016/S0195-668X\(02\)00383-4](https://doi.org/10.1016/S0195-668X(02)00383-4)
905. Mas JL, Derumeaux G, Guillon B, Massardier E, Hosseini H, Mechtouff L, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. *N Engl J Med* 2017;**377**:1011–21. <https://doi.org/10.1056/NEJMoa1705915>
906. Gutierrez SD, Earing MG, Singh AK, Tweddell JS, Bartz PJ. Atrial tachyarrhythmias and the Cox-Maze procedure in congenital heart disease. *Congenit Heart Dis* 2013;**8**:434–9. <https://doi.org/10.1111/chd.12031>
907. Kobayashi J, Yamamoto F, Nakano K, Sasako Y, Kitamura S, Kosakai Y. Maze procedure for atrial fibrillation associated with atrial septal defect. *Circulation* 1998;**98**:I399–402.
908. Shim H, Yang JH, Park PW, Jeong DS, Jun TG. Efficacy of the Maze procedure for atrial fibrillation associated with atrial septal defect. *Korean J Thorac Cardiovasc Surg* 2013;**46**:98–103. <https://doi.org/10.5090/kjctcs.2013.46.2.98>
909. Sherwin ED, Triedman JK, Walsh EP. Update on interventional electrophysiology in congenital heart disease: evolving solutions for complex hearts. *Circ Arrhythm Electrophysiol* 2013;**6**:1032–40. <https://doi.org/10.1161/CIRCEP.113.000313>
910. Chiha M, Samarasinghe S, Kabaker AS. Thyroid storm: an updated review. *J Intensive Care Med* 2015;**30**:131–40. <https://doi.org/10.1177/0885066613498053>
911. Y-Hassan S, Falhammar H. Cardiovascular manifestations and complications of pheochromocytomas and paragangliomas. *J Clin Med* 2020;**9**:2435. <https://doi.org/10.3390/jcm9082435>
912. Baumgartner C, da Costa BR, Collet TH, Feller M, Floriani C, Bauer DC, et al. Thyroid function within the normal range, subclinical hypothyroidism, and the risk of atrial fibrillation. *Circulation* 2017;**136**:2100–16. <https://doi.org/10.1161/CIRCULATIONAHA.117.028753>
913. Huang M, Yang S, Ge G, Zhi H, Wang L. Effects of thyroid dysfunction and the thyroid-stimulating hormone levels on the risk of atrial fibrillation: a systematic review and dose-response meta-analysis from cohort studies. *Endocr Pract* 2022;**28**:822–31. <https://doi.org/10.1016/j.eprac.2022.05.008>
914. Shin DG, Kang MK, Han D, Choi S, Cho JR, Lee N. Enlarged left atrium and decreased left atrial strain are associated with atrial fibrillation in patients with hyperthyroidism irrespective of conventional risk factors. *Int J Cardiovasc Imaging* 2022;**38**:613–20. <https://doi.org/10.1007/s10554-021-02450-6>
915. Sawin CT, Geller A, Wolf PA, Belanger AJ, Baker E, Bacharach P, et al. Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons. *N Engl J Med* 1994;**331**:1249–52. <https://doi.org/10.1056/NEJM199411103311901>
916. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J* 2022;**43**:4229–361. <https://doi.org/10.1093/eurheartj/ehac244>
917. El Sabbagh R, Azar NS, Eid AA, Azar ST. Thyroid dysfunctions due to immune checkpoint inhibitors: a review. *Int J Gen Med* 2020;**13**:1003–9. <https://doi.org/10.2147/IJGM.S261433>
918. Gammage MD, Parle JV, Holder RL, Roberts LM, Hobbs FD, Wilson S, et al. Association between serum free thyroxine concentration and atrial fibrillation. *Arch Intern Med* 2007;**167**:928–34. <https://doi.org/10.1001/archinte.167.9.928>
919. Selmer C, Olesen JB, Hansen ML, Lindhardsen J, Olsen AM, Madsen JC, et al. The spectrum of thyroid disease and risk of new onset atrial fibrillation: a large population cohort study. *BMJ* 2012;**345**:e7895. <https://doi.org/10.1136/bmj.e7895>
920. Kim K, Yang PS, Jang E, Yu HT, Kim TH, Uhm JS, et al. Increased risk of ischemic stroke and systemic embolism in hyperthyroidism-related atrial fibrillation: a nationwide cohort study. *Am Heart J* 2021;**242**:123–31. <https://doi.org/10.1016/j.ahj.2021.08.018>
921. Zhang J, Bisson A, Fauchier G, Bodin A, Herbert J, Ducluzeau PH, et al. Yearly incidence of stroke and bleeding in atrial fibrillation with concomitant hyperthyroidism: a national discharge database study. *J Clin Med* 2022;**11**:1342. <https://doi.org/10.3390/jcm11051342>
922. Bartalena L, Bogazzi F, Chiovato L, Hubalewska-Dydejczyk A, Links TP, Vanderpump M. 2018 European Thyroid Association (ETA) guidelines for the management of amiodarone-associated thyroid dysfunction. *Eur Thyroid J* 2018;**7**:55–66. <https://doi.org/10.1159/000486957>
923. Cappellani D, Papini P, Di Certo AM, Morganti R, Urbani C, Manetti L, et al. Duration of exposure to thyrotoxicosis increases mortality of compromised AIT patients: the role of early thyrotoxicity. *J Clin Endocrinol Metab* 2020;**105**:dgaa464. <https://doi.org/10.1210/clinem/dgaa464>
924. Trevisan C, Piovesan F, Lucato P, Zanforlini BM, De Rui M, Maggi S, et al. Parathormone, vitamin D and the risk of atrial fibrillation in older adults: a prospective study. *Nutr Metab Cardiovasc Dis* 2019;**29**:939–45. <https://doi.org/10.1016/j.numecd.2019.05.064>
925. Pepe J, Cipriani C, Curione M, Biamonte F, Colangelo L, Danese V, et al. Reduction of arrhythmias in primary hyperparathyroidism, by parathyroidectomy, evaluated with 24-h ECG monitoring. *Eur J Endocrinol* 2018;**179**:117–24. <https://doi.org/10.1530/EJE-17-0948>
926. Pepe J, Cipriani C, Sonato C, Raimo O, Biamonte F, Minisola S. Cardiovascular manifestations of primary hyperparathyroidism: a narrative review. *Eur J Endocrinol* 2017;**177**:R297–308. <https://doi.org/10.1530/EJE-17-0485>
927. Monticone S, D'Ascenzo F, Moretti C, Williams TA, Veglio F, Gaita F, et al. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* 2018;**6**:41–50. [https://doi.org/10.1016/S2213-8587\(17\)30319-4](https://doi.org/10.1016/S2213-8587(17)30319-4)
928. Bollati M, Lopez C, Bioletto F, Ponzetto F, Ghigo E, Maccario M, et al. Atrial fibrillation and aortic ectasia as complications of primary aldosteronism: focus on pathophysiological aspects. *Int J Mol Sci* 2022;**23**:2111. <https://doi.org/10.3390/ijms23042111>
929. Kim KJ, Hong N, Yu MH, Lee H, Lee S, Lim JS, et al. Time-dependent risk of atrial fibrillation in patients with primary aldosteronism after medical or surgical treatment initiation. *Hypertension* 2021;**77**:1964–73. <https://doi.org/10.1161/HYPERTENSIONAHA.120.16909>
930. Larsson SC, Lee WH, Burgess S, Allara E. Plasma cortisol and risk of atrial fibrillation: a Mendelian randomization study. *J Clin Endocrinol Metab* 2021;**106**:e2521–6. <https://doi.org/10.1210/clinem/dgab219>
931. Di Dalmazi G, Vicennati V, Pizzi C, Mosconi C, Tucci L, Balacchi C, et al. Prevalence and incidence of atrial fibrillation in a large cohort of adrenal incidentalomas: a long-term study. *J Clin Endocrinol Metab* 2020;**105**:dgaa270. <https://doi.org/10.1210/clinem/dgaa270>
932. Hong S, Kim KS, Han K, Park CY. Acromegaly and cardiovascular outcomes: a cohort study. *Eur Heart J* 2022;**43**:1491–9. <https://doi.org/10.1093/eurheartj/ehab822>
933. Polina I, Jansen HJ, Li T, Moghtadaei M, Bohne LJ, Liu Y, et al. Loss of insulin signaling may contribute to atrial fibrillation and atrial electrical remodeling in type 1 diabetes.

- Proc Natl Acad Sci USA* 2020;**117**:7990–8000. <https://doi.org/10.1073/pnas.1914853117>
934. Lee YB, Han K, Kim B, Lee SE, Jun JE, Ahn J, et al. Risk of early mortality and cardiovascular disease in type 1 diabetes: a comparison with type 2 diabetes, a nationwide study. *Cardiovasc Diabetol* 2019;**18**:157. <https://doi.org/10.1186/s12933-019-0953-7>
935. Bisson A, Bodin A, Fauchier G, Herbert J, Angoulvant D, Ducluzeau PH, et al. Sex, age, type of diabetes and incidence of atrial fibrillation in patients with diabetes mellitus: a nationwide analysis. *Cardiovasc Diabetol* 2021;**20**:24. <https://doi.org/10.1186/s12933-021-01216-7>
936. Dahlqvist S, Rosengren A, Gudbjörnsdóttir S, Pivodic A, Wedel H, Kosiborod M, et al. Risk of atrial fibrillation in people with type 1 diabetes compared with matched controls from the general population: a prospective case-control study. *Lancet Diabetes Endocrinol* 2017;**5**:799–807. [https://doi.org/10.1016/S2213-8587\(17\)30262-0](https://doi.org/10.1016/S2213-8587(17)30262-0)
937. Cai X, Li J, Cai W, Chen C, Ma J, Xie Z, et al. Meta-analysis of type 1 diabetes mellitus and risk of cardiovascular disease. *J Diabetes Complications* 2021;**35**:107833. <https://doi.org/10.1016/j.jdiacomp.2020.107833>
938. Zellerhoff S, Pistulli R, Monnig G, Hinterseer M, Beckmann BM, Kobe J, et al. Atrial arrhythmias in long-QT syndrome under daily life conditions: a nested case control study. *J Cardiovasc Electrophysiol* 2009;**20**:401–7. <https://doi.org/10.1111/j.1540-8167.2008.01339.x>
939. Johnson JN, Tester DJ, Perry J, Salisbury BA, Reed CR, Ackerman MJ. Prevalence of early-onset atrial fibrillation in congenital long QT syndrome. *Heart Rhythm* 2008;**5**:704–9. <https://doi.org/10.1016/j.hrthm.2008.02.007>
940. Gaita F, Giustetto C, Bianchi F, Wolpert C, Schimpf R, Riccardi R, et al. Short QT syndrome: a familial cause of sudden death. *Circulation* 2003;**108**:965–70. <https://doi.org/10.1161/01.CIR.0000085071.28695.C4>
941. Borggrefe M, Wolpert C, Antzelevitch C, Veltmann C, Giustetto C, Gaita F, et al. Short QT syndrome genotype-phenotype correlations. *J Electrocardiol* 2005;**38**:75–80. <https://doi.org/10.1016/j.jelectrocard.2005.06.009>
942. Giustetto C, Di Monte F, Wolpert C, Borggrefe M, Schimpf R, Sbragia P, et al. Short QT syndrome: clinical findings and diagnostic-therapeutic implications. *Eur Heart J* 2006;**27**:2440–7. <https://doi.org/10.1093/eurheartj/ehl185>
943. Bordachar P, Reuter S, Garrigue S, Cai X, Hocini M, Jais P, et al. Incidence, clinical implications and prognosis of atrial arrhythmias in Brugada syndrome. *Eur Heart J* 2004;**25**:879–84. <https://doi.org/10.1016/j.ehj.2004.01.004>
944. Francis J, Antzelevitch C. Atrial fibrillation and Brugada syndrome. *J Am Coll Cardiol* 2008;**51**:1149–53. <https://doi.org/10.1016/j.jacc.2007.10.062>
945. Giustetto C, Schimpf R, Mazzanti A, Scrocco C, Maury P, Anttonen O, et al. Long-term follow-up of patients with short QT syndrome. *J Am Coll Cardiol* 2011;**58**:587–95. <https://doi.org/10.1016/j.jacc.2011.03.038>
946. Gollob MH, Redpath CJ, Roberts JD. The short QT syndrome: proposed diagnostic criteria. *J Am Coll Cardiol* 2011;**57**:802–12. <https://doi.org/10.1016/j.jacc.2010.09.048>
947. Kusano KF, Taniyama M, Nakamura K, Miura D, Banba K, Nagase S, et al. Atrial fibrillation in patients with Brugada syndrome relationships of gene mutation, electrophysiology, and clinical backgrounds. *J Am Coll Cardiol* 2008;**51**:1169–75. <https://doi.org/10.1016/j.jacc.2007.10.060>
948. Rodriguez-Manero M, Namdar M, Sarkozy A, Casado-Arroyo R, Ricciardi D, de Asmundis C, et al. Prevalence, clinical characteristics and management of atrial fibrillation in patients with Brugada syndrome. *Am J Cardiol* 2013;**111**:362–7. <https://doi.org/10.1016/j.amjcard.2012.10.012>
949. Choi YJ, Choi EK, Han KD, Jung JH, Park J, Lee E, et al. Temporal trends of the prevalence and incidence of atrial fibrillation and stroke among Asian patients with hypertrophic cardiomyopathy: a nationwide population-based study. *Int J Cardiol* 2018;**273**:130–5. <https://doi.org/10.1016/j.ijcard.2018.08.038>
950. Hernandez-Ojeda J, Arbelo E, Borrás R, Berne P, Tolosana JM, Gomez-Juanatey A, et al. Patients with Brugada syndrome and implanted cardioverter-defibrillators: long-term follow-up. *J Am Coll Cardiol* 2017;**70**:1991–2002. <https://doi.org/10.1016/j.jacc.2017.08.029>
951. Klopotoski M, Kwapiszewska A, Kukula K, Kamiolkowski J, Dabrowski M, Derejko P, et al. Clinical and echocardiographic parameters as risk factors for atrial fibrillation in patients with hypertrophic cardiomyopathy. *Clin Cardiol* 2018;**41**:1336–40. <https://doi.org/10.1002/clc.23050>
952. Rowin EJ, Orfanos A, Estes NAM, Wang W, Link MS, Maron MS, et al. Occurrence and natural history of clinically silent episodes of atrial fibrillation in hypertrophic cardiomyopathy. *Am J Cardiol* 2017;**119**:1862–5. <https://doi.org/10.1016/j.amjcard.2017.02.040>
953. Sacher F, Probst V, Maury P, Babuty D, Mansourati J, Komatsu Y, et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study-part 2. *Circulation* 2013;**128**:1739–47. <https://doi.org/10.1161/CIRCULATIONAHA.113.001941>
954. Siontis KC, Geske JB, Ong K, Nishimura RA, Ommen SR, Gersh BJ. Atrial fibrillation in hypertrophic cardiomyopathy: prevalence, clinical correlations, and mortality in a large high-risk population. *J Am Heart Assoc* 2014;**3**:e001002. <https://doi.org/10.1161/JAHA.114.001002>
955. Sumitomo N, Sakurada H, Taniguchi K, Matsumura M, Abe O, Miyashita M, et al. Association of atrial arrhythmia and sinus node dysfunction in patients with catecholaminergic polymorphic ventricular tachycardia. *Circ J* 2007;**71**:1606–9. <https://doi.org/10.1253/circj.71.1606>
956. Sy RW, Gollob MH, Klein GJ, Yee R, Skanes AC, Gula LJ, et al. Arrhythmia characterization and long-term outcomes in catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2011;**8**:864–71. <https://doi.org/10.1016/j.hrthm.2011.01.048>
957. van Velzen HG, Theuns DA, Yap SC, Michels M, Schinkel AF. Incidence of device-detected atrial fibrillation and long-term outcomes in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 2017;**119**:100–5. <https://doi.org/10.1016/j.amjcard.2016.08.092>
958. Bourfiss M, Te Riele AS, Mast TP, Cramer MJ, Van Der Heijden J, Van Veen TAB, et al. Influence of genotype on structural atrial abnormalities and atrial fibrillation or flutter in arrhythmogenic right ventricular dysplasia/cardiomyopathy. *J Cardiovasc Electrophysiol* 2016;**27**:1420–8. <https://doi.org/10.1111/jce.13094>
959. Camm CF, James CA, Tichnell C, Murray B, Bhonsale A, te Riele AS, et al. Prevalence of atrial arrhythmias in arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Heart Rhythm* 2013;**10**:1661–8. <https://doi.org/10.1016/j.hrthm.2013.08.032>
960. Chu AF, Zado E, Marchlinski FE. Atrial arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and ventricular tachycardia. *Am J Cardiol* 2010;**106**:720–2. <https://doi.org/10.1016/j.amjcard.2010.04.031>
961. Hasselberg NE, Haland TF, Saberniak J, Brekke PH, Berge KE, Leren TP, et al. Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation. *Eur Heart J* 2018;**39**:853–60. <https://doi.org/10.1093/eurheartj/ehx596>
962. Kumar S, Baldinger SH, Gandjbakhch E, Maury P, Sellal JM, Androulakis AF, et al. Long-term arrhythmic and nonarrhythmic outcomes of lamin A/C mutation carriers. *J Am Coll Cardiol* 2016;**68**:2299–307. <https://doi.org/10.1016/j.jacc.2016.08.058>
963. Mussigbrodt A, Knopp H, Efimova E, Weber A, Bertagnoli L, Hilbert S, et al. Supraventricular arrhythmias in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy associate with long-term outcome after catheter ablation of ventricular tachycardias. *Europace* 2018;**20**:1182–7. <https://doi.org/10.1093/europace/eux179>
964. Pasotti M, Klersy C, Pilotto A, Marziliano N, Rapezzi C, Serio A, et al. Long-term outcome and risk stratification in dilated cardiomyopathies. *J Am Coll Cardiol* 2008;**52**:1250–60. <https://doi.org/10.1016/j.jacc.2008.06.044>
965. Saguner AM, Ganahl S, Kraus A, Baldinger SH, Medeiros-Domingo A, Saguner AR, et al. Clinical role of atrial arrhythmias in patients with arrhythmogenic right ventricular dysplasia. *Circ J* 2014;**78**:2854–61. <https://doi.org/10.1253/circj.CJ-14-0474>
966. Tonet JL, Castro-Miranda R, Iwa T, Poulain F, Frank R, Fontaine GH. Frequency of supraventricular tachyarrhythmias in arrhythmogenic right ventricular dysplasia. *Am J Cardiol* 1991;**67**:1153. [https://doi.org/10.1016/0002-9149\(91\)90886-P](https://doi.org/10.1016/0002-9149(91)90886-P)
967. van Rijsingen IA, Nannenberg EA, Arbustini E, Elliott PM, Mogensen J, Hermans-van Ast JF, et al. Gender-specific differences in major cardiac events and mortality in lamin A/C mutation carriers. *Eur J Heart Fail* 2013;**15**:376–84. <https://doi.org/10.1093/eurjhf/hfs191>
968. Aras D, Tufekcioglu O, Ergun K, Ozeke O, Yildiz A, Topaloglu S, et al. Clinical features of isolated ventricular noncompaction in adults long-term clinical course, echocardiographic properties, and predictors of left ventricular failure. *J Card Fail* 2006;**12**:726–33. <https://doi.org/10.1016/j.cardfail.2006.08.002>
969. Li S, Zhang C, Liu N, Bai H, Hou C, Wang J, et al. Genotype-positive status is associated with poor prognoses in patients with left ventricular noncompaction cardiomyopathy. *J Am Heart Assoc* 2018;**7**:e009910. <https://doi.org/10.1161/JAHA.118.009910>
970. Stollberger C, Blazek G, Winkler-Dworak M, Finsterer J. Atrial fibrillation in left ventricular noncompaction with and without neuromuscular disorders is associated with a poor prognosis. *Int J Cardiol* 2009;**133**:41–5. <https://doi.org/10.1016/j.ijcard.2007.11.099>
971. Fatkin D, MacRae C, Sasaki T, Wolff MR, Porcu M, Frenneaux M, et al. Missense mutations in the rod domain of the lamin A/C gene as causes of dilated cardiomyopathy and conduction-system disease. *N Engl J Med* 1999;**341**:1715–24. <https://doi.org/10.1056/NEJM199912033412302>
972. Hong K, Bjerregaard P, Gussak I, Brugada R. Short QT syndrome and atrial fibrillation caused by mutation in KCNH2. *J Cardiovasc Electrophysiol* 2005;**16**:394–6. <https://doi.org/10.1046/j.1540-8167.2005.40621.x>
973. Olesen MS, Yuan L, Liang B, Holst AG, Nielsen N, Nielsen JB, et al. High prevalence of long QT syndrome-associated SCN5A variants in patients with early-onset lone atrial fibrillation. *Circ Cardiovasc Genet* 2012;**5**:450–9. <https://doi.org/10.1161/CIRCGENETICS.111.962597>
974. Pappone C, Radinovic A, Manguso F, Vicedomini G, Sala S, Sacco FM, et al. New-onset atrial fibrillation as first clinical manifestation of latent Brugada syndrome: prevalence and clinical significance. *Eur Heart J* 2009;**30**:2985–92. <https://doi.org/10.1093/eurheartj/ehp326>
975. Peters S. Atrial arrhythmias in arrhythmogenic cardiomyopathy: at the beginning or at the end of the disease story? *Circ J* 2015;**79**:446. <https://doi.org/10.1253/circj.CJ-14-1193>
976. Rowin EJ, Hausvater A, Link MS, Abt P, Gionfriddo W, Wang W, et al. Clinical profile and consequences of atrial fibrillation in hypertrophic cardiomyopathy. *Circulation* 2017;**136**:2420–36. <https://doi.org/10.1161/CIRCULATIONAHA.117.029267>



977. Mazzanti A, Ng K, Faragli A, Maragna R, Chiodaroli E, Orphanou N, et al. Arrhythmic right ventricular cardiomyopathy: clinical course and predictors of arrhythmic risk. *J Am Coll Cardiol* 2016;**68**:2540–50. <https://doi.org/10.1016/j.jacc.2016.09.951>
978. Giustetto C, Cerrato N, Gribaudo E, Scrocco C, Castagno D, Richiardi E, et al. Atrial fibrillation in a large population with Brugada electrocardiographic pattern: prevalence, management, and correlation with prognosis. *Heart Rhythm* 2014;**11**:259–65. <https://doi.org/10.1016/j.hrthm.2013.10.043>
979. Beckmann BM, Holinski-Feder E, Walter MC, Haserück N, Reithmann C, Hinterseer M, et al. Laminopathy presenting as familial atrial fibrillation. *Int J Cardiol* 2010;**145**:394–6. <https://doi.org/10.1016/j.ijcard.2010.04.024>
980. Pizzale S, Gollub MH, Gow R, Birnie DH. Sudden death in a young man with catecholaminergic polymorphic ventricular tachycardia and paroxysmal atrial fibrillation. *J Cardiovasc Electrophysiol* 2008;**19**:1319–21. <https://doi.org/10.1111/j.1540-8167.2008.01211.x>
981. Sugiyasu A, Oginosawa Y, Nogami A, Hata Y. A case with catecholaminergic polymorphic ventricular tachycardia unmasked after successful ablation of atrial tachycardias from pulmonary veins. *Pacing Clin Electrophysiol* 2009;**32**:e21–4. <https://doi.org/10.1111/j.1540-8159.2009.02519.x>
982. Veltmann C, Kuschyk J, Schimpf R, Streitner F, Schoene N, Borggrefe M, et al. Prevention of inappropriate ICD shocks in patients with Brugada syndrome. *Clin Res Cardiol* 2010;**99**:37–44. <https://doi.org/10.1007/s00392-009-0075-4>
983. Brugada J, Katritsis DG, Arbelo E, Arribas F, Baj JJ, Blomstrom-Lundqvist C, et al. 2019 ESC Guidelines for the management of patients with supraventricular tachycardia. The Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). *Eur Heart J* 2020;**41**:655–720. <https://doi.org/10.1093/eurheartj/ehz467>
984. Klein GJ, Bashore TM, Sellers TD, Pritchett EL, Smith WM, Gallagher JJ. Ventricular fibrillation in the Wolff–Parkinson–White syndrome. *N Engl J Med* 1979;**301**:1080–5. <https://doi.org/10.1056/NEJM197911153012003>
985. Morady F, DiCarlo LA, Jr, Baerman JM, De Buitler M. Effect of propranolol on ventricular rate during atrial fibrillation in the Wolff–Parkinson–White syndrome. *Pacing Clin Electrophysiol* 1987;**10**:492–6. <https://doi.org/10.1111/j.1540-8159.1987.tb04511.x>
986. Sellers TD, Jr, Bashore TM, Gallagher JJ. Digitalis in the pre-excitation syndrome. Analysis during atrial fibrillation. *Circulation* 1977;**56**:260–7. <https://doi.org/10.1161/01.CIR.56.2.260>
987. Glatter KA, Dorostkar PC, Yang Y, Lee RJ, Van Hare GF, Keung E, et al. Electrophysiological effects of ibutilide in patients with accessory pathways. *Circulation* 2001;**104**:1933–9. <https://doi.org/10.1161/hc4101.097538>
988. Ludmer PL, McGowan NE, Antman EM, Friedman PL. Efficacy of propafenone in Wolff–Parkinson–White syndrome: electrophysiologic findings and long-term follow-up. *J Am Coll Cardiol* 1987;**9**:1357–63. [https://doi.org/10.1016/S0735-1097\(87\)80478-3](https://doi.org/10.1016/S0735-1097(87)80478-3)
989. Simonian SM, Lotfipour S, Wall C, Langdorf MI. Challenging the superiority of amiodarone for rate control in Wolff–Parkinson–White and atrial fibrillation. *Intern Emerg Med* 2010;**5**:421–6. <https://doi.org/10.1007/s11739-010-0385-6>
990. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, et al. 2023 ESC Guidelines for the management of cardiomyopathies. *Eur Heart J* 2023;**44**:3503–626. <https://doi.org/10.1093/eurheartj/ehad194>
991. Hu YF, Liu CJ, Chang PM, Tsao HM, Lin YJ, Chang SL, et al. Incident thromboembolism and heart failure associated with new-onset atrial fibrillation in cancer patients. *Int J Cardiol* 2013;**165**:355–7. <https://doi.org/10.1016/j.ijcard.2012.08.036>
992. Mosarla RC, Vaduganathan M, Qamar A, Moslehi J, Piazza G, Giugliano RP. Anticoagulation strategies in patients with cancer: JACC review topic of the week. *J Am Coll Cardiol* 2019;**73**:1336–49. <https://doi.org/10.1016/j.jacc.2019.01.017>
993. Malavasi VL, Fantecchi E, Gianolio L, Pesce F, Longo G, Marietta M, et al. Atrial fibrillation in patients with active malignancy and use of anticoagulants: under-prescription but no adverse impact on all-cause mortality. *Eur J Intern Med* 2019;**59**:27–33. <https://doi.org/10.1016/j.ejim.2018.10.012>
994. Farmakis D, Parissis J, Filippatos G. Insights into onco-cardiology: atrial fibrillation in cancer. *J Am Coll Cardiol* 2014;**63**:945–53. <https://doi.org/10.1016/j.jacc.2013.11.026>
995. Yun JP, Choi EK, Han KD, Park SH, Jung JH, Ahn HJ, et al. Risk of atrial fibrillation according to cancer type: a nationwide population-based study. *JACC CardioOncol* 2021;**3**:221–32. <https://doi.org/10.1016/j.jacc.2021.03.006>
996. Alexandre J, Salem JE, Moslehi J, Sasser M, Ropert C, Cautela J, et al. Identification of anticancer drugs associated with atrial fibrillation: analysis of the WHO pharmacovigilance database. *Eur Heart J Cardiovasc Pharmacother* 2021;**7**:312–20. <https://doi.org/10.1093/ehjcvp/pvaa037>
997. Guha A, Fradley MG, Dent SF, Weintraub NL, Lustberg MB, Alonso A, et al. Incidence, risk factors, and mortality of atrial fibrillation in breast cancer: a SEER-medicare analysis. *Eur Heart J* 2022;**43**:300–12. <https://doi.org/10.1093/eurheartj/ehab745>
998. Pastori D, Marang A, Bisson A, Menichelli D, Herbert J, Lip GYH, et al. Thromboembolism, mortality, and bleeding in 2,435,541 atrial fibrillation patients with and without cancer: a nationwide cohort study. *Cancer* 2021;**127**:2122–9. <https://doi.org/10.1002/cncr.33470>
999. Aspberg S, Yu L, Gigante B, Smedby KE, Singer DE. Risk of ischemic stroke and major bleeding in patients with atrial fibrillation and cancer. *J Stroke Cerebrovasc Dis* 2020;**29**:104560. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104560>
1000. D'Souza M, Carlson N, Fosbøl E, Lamberts M, Smedegaard L, Nielsen D, et al. CHA(2)DS(2)-VASc score and risk of thromboembolism and bleeding in patients with atrial fibrillation and recent cancer. *Eur J Prev Cardiol* 2018;**25**:651–8. <https://doi.org/10.1177/2047487318759858>
1001. Chen ST, Hellkamp AS, Becker RC, Berkowitz SD, Breithardt G, Fox KAA, et al. Efficacy and safety of rivaroxaban vs. warfarin in patients with non-valvular atrial fibrillation and a history of cancer: observations from ROCKET AF. *Eur Heart J Qual Care Clin Outcomes* 2019;**5**:145–52. <https://doi.org/10.1093/ehjqcco/qcy040>
1002. Melloni C, Dunning A, Granger CB, Thomas L, Khouri MG, Garcia DA, et al. Efficacy and safety of apixaban versus warfarin in patients with atrial fibrillation and a history of cancer: insights from the ARISTOTLE trial. *Am J Med* 2017;**130**:1440–8.e1. <https://doi.org/10.1016/j.amjmed.2017.06.026>
1003. Fanola CL, Ruff CT, Murphy SA, Jin J, Duggal A, Babilonia NA, et al. Efficacy and safety of edoxaban in patients with active malignancy and atrial fibrillation: analysis of the ENGAGE AF-TIMI 48 trial. *J Am Heart Assoc* 2018;**7**:e008987. <https://doi.org/10.1161/JAHA.118.008987>
1004. Sawant AC, Kumar A, McCray W, Tetewsky S, Parone L, Sridhara S, et al. Superior safety of direct oral anticoagulants compared to warfarin in patients with atrial fibrillation and underlying cancer: a national veterans affairs database study. *J Geriatr Cardiol* 2019;**16**:706–9. <https://doi.org/10.11909/j.issn.1671-5411.2019.09.006>
1005. Shah S, Norby FL, Datta YH, Lutsey PL, MacLehose RF, Chen LY, et al. Comparative effectiveness of direct oral anticoagulants and warfarin in patients with cancer and atrial fibrillation. *Blood Adv* 2018;**2**:200–9. <https://doi.org/10.1182/bloodadvances.2017010694>
1006. Mariani MV, Magnocavallo M, Straito M, Piro A, Severino P, Iannucci G, et al. Direct oral anticoagulants versus vitamin K antagonists in patients with atrial fibrillation and cancer: a meta-analysis. *J Thromb Thrombolysis* 2021;**51**:419–29. <https://doi.org/10.1007/s11239-020-02304-3>
1007. Deitelzweig S, Keshishian AV, Zhang Y, Kang A, Dhamane AD, Luo X, et al. Effectiveness and safety of oral anticoagulants among nonvalvular atrial fibrillation patients with active cancer. *JACC CardioOncol* 2021;**3**:411–24. <https://doi.org/10.1016/j.jacc.2021.06.004>
1008. Lin YS, Kuan FC, Chao TF, Wu M, Chen SW, Chen MC, et al. Mortality associated with the use of non-vitamin K antagonist oral anticoagulants in cancer patients: dabigatran versus rivaroxaban. *Cancer Med* 2021;**10**:7079–88. <https://doi.org/10.1002/cam4.4241>
1009. Atterman A, Asplund K, Friberg L, Engdahl J. Use of oral anticoagulants after ischaemic stroke in patients with atrial fibrillation and cancer. *J Intern Med* 2020;**288**:457–68. <https://doi.org/10.1111/joim.13092>
1010. Atterman A, Friberg L, Asplund K, Engdahl J. Net benefit of oral anticoagulants in patients with atrial fibrillation and active cancer: a nationwide cohort study. *Europace* 2020;**22**:58–65. <https://doi.org/10.1093/eurpace/euz306>
1011. Falanga A, Leader A, Ambaglio C, Bagoly Z, Castaman G, Elalamy I, et al. EHA guidelines on management of antithrombotic treatments in thrombocytopenic patients with cancer. *Hemisphere* 2022;**6**:e750. <https://doi.org/10.1097/HS9.0000000000000750>
1012. Lancellotti P, Suter TM, López-Fernández T, Galderisi M, Lyon AR, Van der Meer P, et al. Cardio-oncology services: rationale, organization, and implementation. *Eur Heart J* 2019;**40**:1756–63. <https://doi.org/10.1093/eurheartj/ehy453>
1013. Richter D, Guasti L, Walker D, Lambrinou E, Lionis C, Abreu A, et al. Frailty in cardiology: definition, assessment and clinical implications for general cardiology. A consensus document of the Council for Cardiology Practice (CCP), Association for Acute Cardio Vascular Care (ACVC), Association of Cardiovascular Nursing and Allied Professions (ACNAP), European Association of Preventive Cardiology (EAPC), European Heart Rhythm Association (EHRA), Council on Valvular Heart Diseases (VHD), Council on Hypertension (CHT), Council of Cardio-Oncology (CCO), Working Group (WG) aorta and peripheral vascular diseases, WG e-cardiology, WG thrombosis, of the European Society of Cardiology, European Primary Care Cardiology Society (EPPCCS). *Eur J Prev Cardiol* 2022;**29**:216–27. <https://doi.org/10.1093/eurjpc/zwaa167>
1014. Proietti M, Vitolo M, Harrison SL, Lane DA, Fauchier L, Marin F, et al. Impact of clinical phenotypes on management and outcomes in European atrial fibrillation patients: a report from the ESC-EHRA EURObservational Research Programme in AF (EORP-AF) general long-term registry. *BMC Med* 2021;**19**:256. <https://doi.org/10.1186/s12916-021-02120-3>
1015. Proietti M, Romiti GF, Vitolo M, Harrison SL, Lane DA, Fauchier L, et al. Epidemiology and impact of frailty in patients with atrial fibrillation in Europe. *Age Ageing* 2022;**51**:afac192. <https://doi.org/10.1093/ageing/afac192>
1016. Savelieva I, Fumagalli S, Kenny RA, Anker S, Benetos A, Boriani G, et al. EHRA expert consensus document on the management of arrhythmias in frailty syndrome, endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia



- Society of Southern Africa (CASSA). *Europace* 2023;**25**:1249–76. <https://doi.org/10.1093/europace/euac123>
1017. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* 2013;**381**:752–62. [https://doi.org/10.1016/S0140-6736\(12\)62167-9](https://doi.org/10.1016/S0140-6736(12)62167-9)
  1018. Villani ER, Tummolo AM, Palmer K, Gravina EM, Vetrano DL, Bernabei R, et al. Frailty and atrial fibrillation: a systematic review. *Eur J Intern Med* 2018;**56**:33–8. <https://doi.org/10.1016/j.ejim.2018.04.018>
  1019. Hang F, Chen J, Wang Z, Yan J, Wu Y. Association between the frailty and new-onset atrial fibrillation/flutter among elderly hypertensive patients. *Front Cardiovasc Med* 2022;**9**:881946. <https://doi.org/10.3389/fcvm.2022.881946>
  1020. Steinberg BA, Holmes DN, Ezekowitz MD, Fonarow GC, Kowey PR, Mahaffey KW, et al. Rate versus rhythm control for management of atrial fibrillation in clinical practice: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) registry. *Am Heart J* 2013;**165**:622–9. <https://doi.org/10.1016/j.ahj.2012.12.019>
  1021. Ko D, Lin KJ, Bessette LG, Lee SB, Walkey AJ, Cheng S, et al. Trends in use of oral anticoagulants in older adults with newly diagnosed atrial fibrillation, 2010–2020. *JAMA Netw Open* 2022;**5**:e2242964. <https://doi.org/10.1001/jamanetworkopen.2022.42964>
  1022. Bul M, Shaikh F, McDonagh J, Ferguson C. Frailty and oral anticoagulant prescription in adults with atrial fibrillation: a systematic review. *Aging Med (Milton)* 2023;**6**:195–206. <https://doi.org/10.1002/agm2.12214>
  1023. Hu J, Zhou Y, Cai Z. Outcome of novel oral anticoagulant versus warfarin in frail elderly patients with atrial fibrillation: a systematic review and meta-analysis of retrospective studies. *Acta Clin Belg* 2023;**78**:367–77. <https://doi.org/10.1080/17843286.2023.2179908>
  1024. Zeng S, Zheng Y, Jiang J, Ma J, Zhu W, Cai X. Effectiveness and safety of DOACs vs. warfarin in patients with atrial fibrillation and frailty: a systematic review and meta-analysis. *Front Cardiovasc Med* 2022;**9**:907197. <https://doi.org/10.3389/fcvm.2022.907197>
  1025. Grymonprez M, Petrovic M, De Backer TL, Steurbaut S, Lahousse L. Impact of frailty on the effectiveness and safety of non-vitamin K antagonist oral anticoagulants (NOACs) in patients with atrial fibrillation: a nationwide cohort study. *Eur Heart J Qual Care Clin Outcomes* 2024;**10**:55–65. <https://doi.org/10.1093/ehjqcc/qcad019>
  1026. Kim D, Yang PS, Sung JH, Jang E, Yu HT, Kim TH, et al. Effectiveness and safety of anticoagulation therapy in frail patients with atrial fibrillation. *Stroke* 2022;**53**:1873–82. <https://doi.org/10.1161/STROKEAHA.121.036757>
  1027. Chao TF, Liu CJ, Lin YJ, Chang SL, Lo WW, Hu YF, et al. Oral anticoagulation in very elderly patients with atrial fibrillation: a nationwide cohort study. *Circulation* 2018;**138**:37–47. <https://doi.org/10.1161/CIRCULATIONAHA.117.031658>
  1028. Da Costa A, Thévenin J, Roche F, Romeyer-Bouchard C, Abdellaoui L, Messier M, et al. Results from the Loire-Ardèche-Drôme-Isère-Puy-de-Dôme (LADIP) trial on atrial flutter, a multicentric prospective randomized study comparing amiodarone and radiofrequency ablation after the first episode of symptomatic atrial flutter. *Circulation* 2006;**114**:1676–81. <https://doi.org/10.1161/CIRCULATIONAHA.106.638395>
  1029. Natale A, Newby KH, Pisano E, Leonelli F, Fanelli R, Potenza D, et al. Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. *J Am Coll Cardiol* 2000;**35**:1898–904. [https://doi.org/10.1016/S0735-1097\(00\)00635-5](https://doi.org/10.1016/S0735-1097(00)00635-5)
  1030. Chinitz JS, Gerstenfeld EP, Marchlinski FE, Callans DJ. Atrial fibrillation is common after ablation of isolated atrial flutter during long-term follow-up. *Heart Rhythm* 2007;**4**:1029–33. <https://doi.org/10.1016/j.hrthm.2007.04.002>
  1031. De Bortoli A, Shi LB, Ohm OJ, Hoff PI, Schuster P, Solheim E, et al. Incidence and clinical predictors of subsequent atrial fibrillation requiring additional ablation after cavotricuspid isthmus ablation for typical atrial flutter. *Scand Cardiovasc J* 2017;**51**:123–8. <https://doi.org/10.1080/14017431.2017.1304570>
  1032. Rahman F, Wang N, Yin X, Ellinor PT, Lubitz SA, LeLorier PA, et al. Atrial flutter: clinical risk factors and adverse outcomes in the Framingham Heart Study. *Heart Rhythm* 2016;**13**:233–40. <https://doi.org/10.1016/j.hrthm.2015.07.031>
  1033. Roth GA, Mensah GA, Johnson CO, Adolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *J Am Coll Cardiol* 2020;**76**:2982–3021. <https://doi.org/10.1016/j.jacc.2020.11.010>
  1034. Lippi G, Sanchis-Gomar F, Cervellin G. Global epidemiology of atrial fibrillation: an increasing epidemic and public health challenge. *Int J Stroke* 2021;**16**:217–21. <https://doi.org/10.1177/1747493019897870>
  1035. Alonso A, Alam AB, Kamel H, Subbian V, Qian J, Boerwinkle E, et al. Epidemiology of atrial fibrillation in the all of US research program. *PLoS One* 2022;**17**:e0265498. <https://doi.org/10.1371/journal.pone.0265498>
  1036. Ghelani KP, Chen LY, Norby FL, Soliman EZ, Koton S, Alonso A. Thirty-year trends in the incidence of atrial fibrillation: the ARIC study. *J Am Heart Assoc* 2022;**11**:e023583. <https://doi.org/10.1161/JAHA.121.023583>
  1037. Williams BA, Chamberlain AM, Blankenship JC, Hylek EM, Voyce S. Trends in atrial fibrillation incidence rates within an integrated health care delivery system, 2006 to 2018. *JAMA Netw Open* 2020;**3**:e2014874. <https://doi.org/10.1001/jamanetworkopen.2020.14874>
  1038. Magnussen C, Niiranen TJ, Ojeda FM, Gianfagna F, Blankenberg S, Njølstad I, et al. Sex differences and similarities in atrial fibrillation epidemiology, risk factors, and mortality in community cohorts: results from the Biomarker Consortium (Biomarker for Cardiovascular Risk Assessment in Europe). *Circulation* 2017;**136**:1588–97. <https://doi.org/10.1161/CIRCULATIONAHA.117.028981>
  1039. Rodriguez CJ, Soliman EZ, Alonso A, Swett K, Okin PM, Goff DC, Jr, et al. Atrial fibrillation incidence and risk factors in relation to race-ethnicity and the population attributable fraction of atrial fibrillation risk factors: the multi-ethnic study of atherosclerosis. *Ann Epidemiol* 2015;**25**:71–6. <https://doi.org/10.1016/j.annepidem.2014.11.024>
  1040. Ugowe FE, Jackson LR, 2nd, Thomas KL. Racial and ethnic differences in the prevalence, management, and outcomes in patients with atrial fibrillation: a systematic review. *Heart Rhythm* 2018;**15**:1337–45. <https://doi.org/10.1016/j.hrthm.2018.05.019>
  1041. Volgman AS, Bairey Merz CN, Benjamin EJ, Curtis AB, Fang MC, Lindley KJ, et al. Sex and race/ethnicity differences in atrial fibrillation. *J Am Coll Cardiol* 2019;**74**:2812–5. <https://doi.org/10.1016/j.jacc.2019.09.045>
  1042. Chung SC, Sofat R, Acosta-Mena D, Taylor JA, Lambiasi PD, Casas JP, et al. Atrial fibrillation epidemiology, disparity and healthcare contacts: a population-wide study of 5.6 million individuals. *Lancet Reg Health Eur* 2021;**7**:100157. <https://doi.org/10.1016/j.lanep.2021.100157>
  1043. Svennberg E, Tjong F, Goette A, Akoum N, Di Biase L, Bordachar P, et al. How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace* 2022;**24**:979–1005. <https://doi.org/10.1093/europace/euac038>
  1044. Spatz ES, Ginsburg GS, Rumsfeld JS, Turakhia MP. Wearable digital health technologies for monitoring in cardiovascular medicine. *N Engl J Med* 2024;**390**:346–56. <https://doi.org/10.1056/NEJMra2301903>
  1045. Cooke G, Doust J, Sanders S. Is pulse palpation helpful in detecting atrial fibrillation? A systematic review. *J Fam Pract* 2006;**55**:130–4.
  1046. Attia ZI, Noseworthy PA, Lopez-Jimenez F, Asirvatham SJ, Deshmukh AJ, Gersh BJ, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *Lancet* 2019;**394**:861–7. [https://doi.org/10.1016/S0140-6736\(19\)31721-0](https://doi.org/10.1016/S0140-6736(19)31721-0)
  1047. Hobbs FD, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. *Health Technol Assess* 2005;**9**:iii–iv, ix–x, 1–74. <https://doi.org/10.3310/hta9400>
  1048. Grond M, Jauss M, Hamann G, Stark E, Veltkamp R, Nabavi D, et al. Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study. *Stroke* 2013;**44**:3357–64. <https://doi.org/10.1161/STROKEAHA.113.001884>
  1049. Rizos T, Guntner J, Jenetzky E, Marquardt L, Reichardt C, Becker R, et al. Continuous stroke unit electrocardiographic monitoring versus 24-hour Holter electrocardiography for detection of paroxysmal atrial fibrillation after stroke. *Stroke* 2012;**43**:2689–94. <https://doi.org/10.1161/STROKEAHA.112.654954>
  1050. Doliwa PS, Frykman V, Rosenqvist M. Short-term ECG for out of hospital detection of silent atrial fibrillation episodes. *Scand Cardiovasc J* 2009;**43**:163–8. <https://doi.org/10.1080/14017430802593435>
  1051. Tieleman RG, Plantinga Y, Rinkes D, Bartels GL, Posma JL, Cator R, et al. Validation and clinical use of a novel diagnostic device for screening of atrial fibrillation. *Europace* 2014;**16**:1291–5. <https://doi.org/10.1093/europace/euu057>
  1052. Kearley K, Selwood M, Van den Bruel A, Thompson M, Mant D, Hobbs FR, et al. Triage tests for identifying atrial fibrillation in primary care: a diagnostic accuracy study comparing single-lead ECG and modified BP monitors. *BMJ Open* 2014;**4**:e004565. <https://doi.org/10.1136/bmjopen-2013-004565>
  1053. Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, Encinas J, et al. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. *Am J Med* 2014;**127**:95.e11–7. <https://doi.org/10.1016/j.amjmed.2013.10.003>
  1054. Turakhia MP, Hoang DD, Zimetbaum P, Miller JD, Froelicher VF, Kumar UN, et al. Diagnostic utility of a novel leadless arrhythmia monitoring device. *Am J Cardiol* 2013;**112**:520–4. <https://doi.org/10.1016/j.amjcard.2013.04.017>
  1055. Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. *Pacing Clin Electrophysiol* 2013;**36**:328–33. <https://doi.org/10.1111/pace.12053>
  1056. Turakhia MP, Ullal AJ, Hoang DD, Than CT, Miller JD, Friday KJ, et al. Feasibility of extended ambulatory electrocardiogram monitoring to identify silent atrial fibrillation in high-risk patients: the Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). *Clin Cardiol* 2015;**38**:285–92. <https://doi.org/10.1002/clc.22387>
  1057. Rooney MR, Soliman EZ, Lutsey PL, Norby FL, Loehr LR, Mosley TH, et al. Prevalence and characteristics of subclinical atrial fibrillation in a community-dwelling elderly population: the ARIC study. *Circ Arrhythm Electrophysiol* 2019;**12**:e007390. <https://doi.org/10.1161/CIRCEP.119.007390>

1058. Stehlik J, Schmalfuss C, Bozkurt B, Nativi-Nicolau J, Wohlfahrt P, Wegerich S, et al. Continuous wearable monitoring analytics predict heart failure hospitalization: the LINK-HF multicenter study. *Circ Heart Fail* 2020;**13**:e006513. <https://doi.org/10.1161/CIRCHEARTFAILURE.119.006513>
1059. Ganne C, Talkad SN, Srinivas D, Somanna S. Ruptured blebs and clipping hearts: automatic cardiac changes in neurosurgeons during microsurgical clipping of aneurysms. *Br J Neurosurg* 2016;**30**:450–2. <https://doi.org/10.3109/02688697.2016.1159656>
1060. Smith WM, Riddell F, Madon M, Gleva MJ. Comparison of diagnostic value using a small, single channel, P-wave centric sternal ECG monitoring patch with a standard 3-lead Holter system over 24 hours. *Am Heart J* 2017;**185**:67–73. <https://doi.org/10.1016/j.ahj.2016.11.006>
1061. Olson JA, Fouts AM, Padanilam BJ, Prystowsky EN. Utility of mobile cardiac outpatient telemetry for the diagnosis of palpitations, presyncope, syncope, and the assessment of therapy efficacy. *J Cardiovasc Electrophysiol* 2007;**18**:473–7. <https://doi.org/10.1111/j.1540-8167.2007.00779.x>
1062. Derkac WM, Finkelmeier JR, Horgan DJ, Hutchinson MD. Diagnostic yield of asymptomatic arrhythmias detected by mobile cardiac outpatient telemetry and autotrigger looping event cardiac monitors. *J Cardiovasc Electrophysiol* 2017;**28**:1475–8. <https://doi.org/10.1111/jce.13342>
1063. Teplitzky BA, McRoberts M, Ghanbari H. Deep learning for comprehensive ECG annotation. *Heart Rhythm* 2020;**17**:881–8. <https://doi.org/10.1016/j.hrthm.2020.02.015>
1064. Jeon E, Oh K, Kwon S, Son H, Yun Y, Jung ES, et al. A lightweight deep learning model for fast electrocardiographic beats classification with a wearable cardiac monitor: development and validation study. *JMIR Med Inform* 2020;**8**:e17037. <https://doi.org/10.2196/17037>
1065. Breteler MJMM, Huizinga E, van Loon K, Leenen LPH, Dohmen DAJ, Kalkman CJ, et al. Reliability of wireless monitoring using a wearable patch sensor in high-risk surgical patients at a step-down unit in The Netherlands: a clinical validation study. *BMJ Open* 2018;**8**:e020162. <https://doi.org/10.1136/bmjopen-2017-020162>
1066. Hopkins L, Stacey B, Robinson DBT, James OP, Brown C, Egan RJ, et al. Consumer-grade biosensor validation for examining stress in healthcare professionals. *Physiol Rep* 2020;**8**:e14454. <https://doi.org/10.14814/phy2.14454>
1067. Steinhilber SR, Waalen J, Edwards AM, Ariniello LM, Mehta RR, Ebner GS, et al. Effect of a home-based wearable continuous ECG monitoring patch on detection of undiagnosed atrial fibrillation: the mSToPS randomized clinical trial. *JAMA* 2018;**320**:146–55. <https://doi.org/10.1001/jama.2018.8102>
1068. Elliot CA, Hamlin MJ, Lizamore CA. Validity and reliability of the hexoskin wearable biometric vest during maximal aerobic power testing in elite cyclists. *J Strength Cond Res* 2019;**33**:1437–44. <https://doi.org/10.1519/JSC.0000000000002005>
1069. Eysenck W, Freemantle N, Sulke N. A randomized trial evaluating the accuracy of AF detection by four external ambulatory ECG monitors compared to permanent pacemaker AF detection. *J Interv Card Electrophysiol* 2020;**57**:361–9. <https://doi.org/10.1007/s10840-019-00515-0>
1070. Fabregat-Andres O, Munoz-Macho A, Adell-Beltran G, Ibanez-Catala X, Macia A, Facila L. Evaluation of a new shirt-based electrocardiogram device for cardiac screening in soccer players: comparative study with treadmill ergospirometry. *Cardiol Res* 2014;**5**:101–7. <https://doi.org/10.14740/cr333w>
1071. Feito Y, Moriarty TA, Mangine G, Monahan J. The use of a smart-textile garment during high-intensity functional training: a pilot study. *J Sports Med Phys Fitness* 2019;**59**:947–54. <https://doi.org/10.23736/S0022-4707.18.08689-9>
1072. Pagola J, Juega J, Francisco-Pascual J, Moya A, Sanchis M, Bustamante A, et al. Yield of atrial fibrillation detection with textile wearable Holter from the acute phase of stroke: pilot study of crypto-AF registry. *Int J Cardiol* 2018;**251**:45–50. <https://doi.org/10.1016/j.ijcard.2017.10.063>
1073. Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, Galloway CD, et al. iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke. *Int J Cardiol* 2013;**165**:193–4. <https://doi.org/10.1016/j.ijcard.2013.01.220>
1074. Bumgarner JM, Lambert CT, Hussein AA, Cantillon DJ, Baranowski B, Wolksi K, et al. Smartwatch algorithm for automated detection of atrial fibrillation. *J Am Coll Cardiol* 2018;**71**:2381–8. <https://doi.org/10.1016/j.jacc.2018.03.003>
1075. Lubitz SA, Faranesh AZ, Atlas SJ, McManus DD, Singer DE, Pagoto S, et al. Rationale and design of a large population study to validate software for the assessment of atrial fibrillation from data acquired by a consumer tracker or smartwatch: the Fitbit heart study. *Am Heart J* 2021;**238**:16–26. <https://doi.org/10.1016/j.ahj.2021.04.003>
1076. Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, Ferris T, et al. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019;**381**:1909–17. <https://doi.org/10.1056/NEJMoa1901183>
1077. Saghir N, Aggarwal A, Soneji N, Valencia V, Rodgers G, Kurian T. A comparison of manual electrocardiographic interval and waveform analysis in lead 1 of 12-lead ECG and apple watch ECG: a validation study. *Cardiovasc Digit Health J* 2020;**1**:30–6. <https://doi.org/10.1016/j.cvdhj.2020.07.002>
1078. Seshadri DR, Bittel B, Browsky D, Houghtaling P, Drummond CK, Desai MY, et al. Accuracy of apple watch for detection of atrial fibrillation. *Circulation* 2020;**141**:702–3. <https://doi.org/10.1161/CIRCULATIONAHA.119.044126>
1079. Zhang H, Zhang J, Li HB, Chen YX, Yang B, Guo YT, et al. Validation of single centre pre-mobile atrial fibrillation apps for continuous monitoring of atrial fibrillation in a real-world setting: pilot cohort study. *J Med Internet Res* 2019;**21**:e14909. <https://doi.org/10.2196/14909>
1080. Fan YY, Li YG, Li J, Cheng WK, Shan ZL, Wang YT, et al. Diagnostic performance of a smart device with photoplethysmography technology for atrial fibrillation detection: pilot study (Pre-mAFA II registry). *JMIR Mhealth Uhealth* 2019;**7**:e11437. <https://doi.org/10.2196/11437>
1081. Brito R, Mondouagne LP, Stettler C, Combesure C, Burri H. Automatic atrial fibrillation and flutter detection by a handheld ECG recorder, and utility of sequential finger and precordial recordings. *J Electrocardiol* 2018;**51**:1135–40. <https://doi.org/10.1016/j.jelectrocard.2018.10.093>
1082. Desteghe L, Raymaekers Z, Lutin M, Vijgen J, Dilling-Boer D, Koopman P, et al. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. *Europace* 2017;**19**:29–39. <https://doi.org/10.1093/europace/euw025>
1083. Nigolian A, Dayal N, Nigolian H, Stettler C, Burri H. Diagnostic accuracy of multi-lead ECGs obtained using a pocket-sized bipolar handheld event recorder. *J Electrocardiol* 2018;**51**:278–81. <https://doi.org/10.1016/j.jelectrocard.2017.11.004>
1084. Magnusson P, Lyren A, Mattsson G. Diagnostic yield of chest and thumb ECG after cryptogenic stroke, Transient ECG Assessment in Stroke Evaluation (TEASE): an observational trial. *BMJ Open* 2020;**10**:e037573. <https://doi.org/10.1136/bmjopen-2020-037573>
1085. Carnlöf C, Schenck-Gustafsson K, Jensen-Urstad M, Insulander P. Instant electrocardiogram feedback with a new digital technique reduces symptoms caused by palpitations and increases health-related quality of life (the RedHeart study). *Eur J Cardiovasc Nurs* 2021;**20**:402–10. <https://doi.org/10.1093/eurjcn/zvaa031>
1086. Haverkamp HT, Fosse SO, Schuster P. Accuracy and usability of single-lead ECG from smartphones—a clinical study. *Indian Pacing Electrophysiol J* 2019;**19**:145–9. <https://doi.org/10.1016/j.ijpej.2019.02.006>
1087. Attia ZI, Kapa S, Lopez-Jimenez F, McKie PM, Ladewig DJ, Satam G, et al. Screening for cardiac contractile dysfunction using an artificial intelligence-enabled electrocardiogram. *Nat Med* 2019;**25**:70–4. <https://doi.org/10.1038/s41591-018-0240-2>
1088. Bekker CL, Noordergraaf F, Teerenstra S, Pop G, van den Bemt BJF. Diagnostic accuracy of a single-lead portable ECG device for measuring QTc prolongation. *Ann Noninvasive Electrocardiol* 2020;**25**:e12683. <https://doi.org/10.1111/anec.12683>
1089. Kaleschke G, Hoffmann B, DREWITZ J, Steinbeck G, Naebauer M, Goette A, et al. Prospective, multicentre validation of a simple, patient-operated electrocardiographic system for the detection of arrhythmias and electrocardiographic changes. *Europace* 2009;**11**:1362–8. <https://doi.org/10.1093/europace/eup262>
1090. Guan J, Wang A, Song W, Obore N, He P, Fan S, et al. Screening for arrhythmia with the new portable single-lead electrocardiographic device (SnapECG): an application study in community-based elderly population in Nanjing, China. *Aging Clin Exp Res* 2021;**33**:133–40. <https://doi.org/10.1007/s40520-020-01512-4>
1091. Svennberg E, Stridh M, Engdahl J, Al-Khalili F, Friberg L, Frykman V, et al. Safe automatic one-lead electrocardiogram analysis in screening for atrial fibrillation. *Europace* 2017;**19**:1449–53. <https://doi.org/10.1093/europace/euw286>
1092. Musat DL, Milstein N, Mittal S. Implantable loop recorders for cryptogenic stroke (plus real-world atrial fibrillation detection rate with implantable loop recorders). *Card Electrophysiol Clin* 2018;**10**:111–8. <https://doi.org/10.1016/j.ccep.2017.11.011>
1093. Sakhi R, Theuns D, Szili-Torok T, Yap SC. Insertable cardiac monitors: current indications and devices. *Expert Rev Med Devices* 2019;**16**:45–55. <https://doi.org/10.1080/17434440.2018.1557046>
1094. Tomson TT, Passman R. The reveal LINQ insertable cardiac monitor. *Expert Rev Med Devices* 2015;**12**:7–18. <https://doi.org/10.1586/17434440.2014.953059>
1095. Ciconte G, Saviano M, Giannelli L, Calovic Z, Baldi M, Ciaccio C, et al. Atrial fibrillation detection using a novel three-vector cardiac implantable monitor: the atrial fibrillation detect study. *Europace* 2017;**19**:1101–8. <https://doi.org/10.1093/europace/euw181>
1096. Hindricks G, Pokushalov E, Urban L, Taborsky M, Kuck KH, Lebedev D, et al. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation: results of the XPECT trial. *Circ Arrhythm Electrophysiol* 2010;**3**:141–7. <https://doi.org/10.1161/CIRCEP.109.877852>
1097. Mittal S, Rogers J, Sarkar S, Koehler J, Warman EN, Tomson TT, et al. Real-world performance of an enhanced atrial fibrillation detection algorithm in an insertable cardiac monitor. *Heart Rhythm* 2016;**13**:1624–30. <https://doi.org/10.1016/j.hrthm.2016.05.010>
1098. Nölker G, Mayer J, Boldt LH, Seidl K VVAND, Massa T, Kollum M, et al. Performance of an implantable cardiac monitor to detect atrial fibrillation: results of the DETECT AF study. *J Cardiovasc Electrophysiol* 2016;**27**:1403–10. <https://doi.org/10.1111/jce.13089>
1099. Sanders P, Pürerfellner H, Pokushalov E, Sarkar S, Di Bacco M, Maus B, et al. Performance of a new atrial fibrillation detection algorithm in a miniaturized insertable cardiac monitor: results from the reveal LINQ usability study. *Heart Rhythm* 2016;**13**:1425–30. <https://doi.org/10.1016/j.hrthm.2016.03.005>

1100. Chan PH, Wong CK, Poh YC, Pun L, Leung WW, Wong YF, et al. Diagnostic performance of a smartphone-based photoplethysmographic application for atrial fibrillation screening in a primary care setting. *J Am Heart Assoc* 2016;**5**:e003428. <https://doi.org/10.1161/JAHA.116.003428>
1101. Mc MD, Chong JW, Soni A, Saczynski JS, Esa N, Napolitano C, et al. PULSE-SMART: pulse-based arrhythmia discrimination using a novel smartphone application. *J Cardiovasc Electrophysiol* 2016;**27**:51–7. <https://doi.org/10.1111/jce.12842>
1102. Proesmans T, Mortelmans C, Van Haelst R, Verbrugge F, Vandervoort P, Vaes B. Mobile phone-based use of the photoplethysmography technique to detect atrial fibrillation in primary care: diagnostic accuracy study of the FibriCheck app. *JMIR Mhealth Uhealth* 2019;**7**:e12284. <https://doi.org/10.2196/12284>
1103. Rozen G, Vaid J, Hosseini SM, Kaadan MI, Rafael A, Roka A, et al. Diagnostic accuracy of a novel mobile phone application for the detection and monitoring of atrial fibrillation. *Am J Cardiol* 2018;**121**:1187–91. <https://doi.org/10.1016/j.amjcard.2018.01.035>
1104. O'Sullivan JW, Grigg S, Crawford W, Turakhia MP, Perez M, Ingelsson E, et al. Accuracy of smartphone camera applications for detecting atrial fibrillation: a systematic review and meta-analysis. *JAMA Netw Open* 2020;**3**:e202064. <https://doi.org/10.1001/jamanetworkopen.2020.2064>
1105. Koenig N, Seeck A, Eckstein J, Mainka A, Huebner T, Voss A, et al. Validation of a new heart rate measurement algorithm for fingertip recording of video signals with smartphones. *Telemed J E Health* 2016;**22**:631–6. <https://doi.org/10.1089/tmj.2015.0212>
1106. Krivoshei L, Weber S, Burkard T, Maseli A, Brasier N, Kühne M, et al. Smart detection of atrial fibrillation†. *Europace* 2017;**19**:753–7. <https://doi.org/10.1093/eurpace/euw125>
1107. Wiesel J, Fitzg L, Herschman Y, Messineo FC. Detection of atrial fibrillation using a modified microlife blood pressure monitor. *Am J Hypertens* 2009;**22**:848–52. <https://doi.org/10.1038/ajh.2009.98>
1108. Chen Y, Lei L, Wang JG. Atrial fibrillation screening during automated blood pressure measurement—comment on “diagnostic accuracy of new algorithm to detect atrial fibrillation in a home blood pressure monitor”. *J Clin Hypertens (Greenwich)* 2017;**19**:1148–51. <https://doi.org/10.1111/jch.13081>
1109. Kane SA, Blake JR, McArdle FJ, Langley P, Sims AJ. Opportunistic detection of atrial fibrillation using blood pressure monitors: a systematic review. *Open Heart* 2016;**3**:e000362. <https://doi.org/10.1136/openhrt-2015-000362>
1110. Kario K. Evidence and perspectives on the 24-hour management of hypertension: hemodynamic biomarker-initiated ‘anticipation medicine’ for zero cardiovascular event. *Prog Cardiovasc Dis* 2016;**59**:262–81. <https://doi.org/10.1016/j.pcad.2016.04.001>
1111. Jaakkola J, Jaakkola S, Lahdenoja O, Hurnanen T, Koivisto T, Pänkälä M, et al. Mobile phone detection of atrial fibrillation with mechanocardiography: the MODE-AF study (mobile phone detection of atrial fibrillation). *Circulation* 2018;**137**:1524–7. <https://doi.org/10.1161/CIRCULATIONAHA.117.032804>
1112. Couderc JP, Kyal S, Mestha LK, Xu B, Peterson DR, Xia X, et al. Detection of atrial fibrillation using contactless facial video monitoring. *Heart Rhythm* 2015;**12**:195–201. <https://doi.org/10.1016/j.hrthm.2014.08.035>
1113. Yan BP, Lai WHS, Chan CKY, Au ACK, Freedman B, Poh YC, et al. High-throughput, contact-free detection of atrial fibrillation from video with deep learning. *JAMA Cardiol* 2020;**5**:105–7. <https://doi.org/10.1001/jamacardio.2019.4004>
1114. Yan BP, Lai WHS, Chan CKY, Chan SC, Chan LH, Lam KM, et al. Contact-free screening of atrial fibrillation by a smartphone using facial pulsatile photoplethysmographic signals. *J Am Heart Assoc* 2018;**7**:e008585. <https://doi.org/10.1161/JAHA.118.008585>
1115. Tsouri GR, Li Z. On the benefits of alternative color spaces for noncontact heart rate measurements using standard red-green-blue cameras. *J Biomed Opt* 2015;**20**:048002. <https://doi.org/10.1117/1.JBO.20.4.048002>
1116. Chan J, Rea T, Gollakota S, Sunshine JE. Contactless cardiac arrest detection using smart devices. *NPJ Digit Med* 2019;**2**:52. <https://doi.org/10.1038/s41746-019-0128-7>
1117. Guo Y, Wang H, Zhang H, Liu T, Liang Z, Xia Y, et al. Mobile photoplethysmographic technology to detect atrial fibrillation. *J Am Coll Cardiol* 2019;**74**:2365–75. <https://doi.org/10.1016/j.jacc.2019.08.019>
1118. Lubitz SA, Faranesh AZ, Selvaggi C, Atlas SJ, McManus DD, Singer DE, et al. Detection of atrial fibrillation in a large population using wearable devices: the Fitbit heart study. *Circulation* 2022;**146**:1415–24. <https://doi.org/10.1161/CIRCULATIONAHA.122.060291>
1119. Lopez Perales CR, Van Spall HGC, Maeda S, Jimenez A, Latcu DG, Milman A, et al. Mobile health applications for the detection of atrial fibrillation: a systematic review. *Europace* 2021;**23**:11–28. <https://doi.org/10.1093/eurpace/eaab139>
1120. Gill S, Bunting KV, Sartini C, Cardoso VR, Ghoreishi N, Uh HW, et al. Smartphone detection of atrial fibrillation using photoplethysmography: a systematic review and meta-analysis. *Heart* 2022;**108**:1600–7. <https://doi.org/10.1136/heartjnl-2021-320417>
1121. Mant J, Fitzmaurice DA, Hobbs FD, Jowett S, Murray ET, Holder R, et al. Accuracy of diagnosing atrial fibrillation on electrocardiogram by primary care practitioners and interpretative diagnostic software: analysis of data from screening for atrial fibrillation in the elderly (SAFE) trial. *BMJ* 2007;**335**:380. <https://doi.org/10.1136/bmj.39227.551713.AE>
1122. Halcox J, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, et al. Assessment of remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. *Circulation* 2017;**136**:1784–94. <https://doi.org/10.1161/CIRCULATIONAHA.117.030583>
1123. Duarte R, Stainthorpe A, Greenhalgh J, Richardson M, Nevitt S, Mahon J, et al. Lead-I ECG for detecting atrial fibrillation in patients with an irregular pulse using single time point testing: a systematic review and economic evaluation. *Health Technol Assess* 2020;**24**:1–164. <https://doi.org/10.3310/hta24030>
1124. Mannhart D, Lischer M, Knecht S, du Fay de Lavallaz J, Strebel I, Serban T, et al. Clinical validation of 5 direct-to-consumer wearable smart devices to detect atrial fibrillation: BASEL wearable study. *JACC Clin Electrophysiol* 2023;**9**:232–42. <https://doi.org/10.1016/j.jacep.2022.09.011>
1125. Paul Nordin A, Carlöf C, Insulander P, Mohammad Ali A, Jensen-Urstad M, Saluveer O, et al. Validation of diagnostic accuracy of a handheld, smartphone-based rhythm recording device. *Expert Rev Med Devices* 2023;**20**:55–61. <https://doi.org/10.1080/17434440.2023.2171290>
1126. Gill SK, Barsky A, Guan X, Bunting KV, Karwath A, Tica O, et al. Consumer wearable devices to evaluate dynamic heart rate with digoxin versus beta-blockers: the RATE-AF randomised trial. *Nat Med* 2024;**30**:2030–2036. <https://doi.org/10.1038/s41591-024-03094-4>
1127. Kahwati LC, Asher GN, Kadro ZO, Keen S, Ali R, Coker-Schwimmer E, et al. Screening for atrial fibrillation: updated evidence report and systematic review for the US preventive services task force. *JAMA* 2022;**327**:368–83. <https://doi.org/10.1001/jama.2021.21811>
1128. Strong K, Wald N, Miller A, Alwan A. Current concepts in screening for noncommunicable disease: World Health Organization Consultation Group Report on methodology of noncommunicable disease screening. *J Med Screen* 2005;**12**:12–9. <https://doi.org/10.1258/0969141053279086>
1129. Whitfield R, Ascensão R, da Silva GL, Almeida AG, Pinto FJ, Caldeira D. Screening strategies for atrial fibrillation in the elderly population: a systematic review and network meta-analysis. *Clin Res Cardiol* 2023;**112**:705–15. <https://doi.org/10.1007/s00392-022-02117-9>
1130. Proietti M, Romiti GF, Vitolo M, Borgi M, Rocco AD, Farcomeni A, et al. Epidemiology of subclinical atrial fibrillation in patients with cardiac implantable electronic devices: a systematic review and meta-regression. *Eur J Intern Med* 2022;**103**:84–94. <https://doi.org/10.1016/j.ejim.2022.06.023>
1131. Healey JS, Alings M, Ha A, Leong-Sit P, Birnie DH, de Graaf JJ, et al. Subclinical atrial fibrillation in older patients. *Circulation* 2017;**136**:1276–83. <https://doi.org/10.1161/CIRCULATIONAHA.117.028845>
1132. Van Gelder IC, Healey JS, Crijns H, Wang J, Hohnloser SH, Gold MR, et al. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J* 2017;**38**:1339–44. <https://doi.org/10.1093/eurheartj/ehx042>
1133. Kemp Gudmundsdottir K, Fredriksson T, Svennberg E, Al-Khalili F, Friberg L, Frykman V, et al. Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: the STROKESTOP II study. *Europace* 2020;**22**:24–32. <https://doi.org/10.1093/eurpace/euz255>
1134. Williams K, Modi RN, Dymond A, Hoare S, Powell A, Burt J, et al. Cluster randomised controlled trial of screening for atrial fibrillation in people aged 70 years and over to reduce stroke: protocol for the pilot study for the SAFER trial. *BMJ Open* 2022;**12**:e065066. <https://doi.org/10.1136/bmjopen-2022-065066>
1135. Elbadawi A, Sedhom R, Gad M, Hamed M, Elwagdy A, Barakat AF, et al. Screening for atrial fibrillation in the elderly: a network meta-analysis of randomized trials. *Eur J Intern Med* 2022;**105**:38–45. <https://doi.org/10.1016/j.ejim.2022.07.015>
1136. McIntyre WF, Diederichsen SZ, Freedman B, Schnabel RB, Svennberg E, Healey JS. Screening for atrial fibrillation to prevent stroke: a meta-analysis. *Eur Heart J Open* 2022;**2**:oeac044. <https://doi.org/10.1093/ehjopen/oeac044>
1137. Lyth J, Svennberg E, Bernfort L, Aronsson M, Frykman V, Al-Khalili F, et al. Cost-effectiveness of population screening for atrial fibrillation: the STROKESTOP study. *Eur Heart J* 2023;**44**:196–204. <https://doi.org/10.1093/eurheartj/ehac547>
1138. Lubitz SA, Atlas SJ, Ashburner JM, Lipsanopoulos ATT, Borowsky LH, Guan W, et al. Screening for atrial fibrillation in older adults at primary care visits: VITAL-AF randomized controlled trial. *Circulation* 2022;**145**:946–54. <https://doi.org/10.1161/CIRCULATIONAHA.121.057014>
1139. Uittenbogaart SB, Verbiest-van Gurp N, Lucassen WAM, Winkens B, Nielen M, Erkens PMG, et al. Opportunistic screening versus usual care for detection of atrial fibrillation in primary care: cluster randomised controlled trial. *BMJ* 2020;**370**:m3208. <https://doi.org/10.1136/bmj.m3208>
1140. Kaasenbrood F, Hollander M, de Bruijn SH, Dolmans CP, Tieleman RG, Hoes AW, et al. Opportunistic screening versus usual care for diagnosing atrial fibrillation in general practice: a cluster randomised controlled trial. *Br J Gen Pract* 2020;**70**:e427–33. <https://doi.org/10.3399/bjgp20X708161>
1141. Petryszyn P, Niewinski P, Staniak A, Piotrowski P, Well A, Well M, et al. Effectiveness of screening for atrial fibrillation and its determinants. A meta-analysis. *PLoS One* 2019;**14**:e0213198. <https://doi.org/10.1371/journal.pone.0213198>



1142. Wang Q, Richardson TG, Sanderson E, Tudball MJ, Ala-Korpela M, Davey Smith G, et al. A phenome-wide bidirectional Mendelian randomization analysis of atrial fibrillation. *Int J Epidemiol* 2022;**51**:1153–66. <https://doi.org/10.1093/ije/dyaa041>
1143. Siddiqi HK, Vinayagamoorthy M, Gencer B, Ng C, Pester J, Cook NR, et al. Sex differences in atrial fibrillation risk: the VITAL rhythm study. *JAMA Cardiol* 2022;**7**:1027–35. <https://doi.org/10.1001/jamacardio.2022.2825>
1144. Lu Z, Aribas E, Geurts S, Roeters van Lennep JE, Ikram MA, Bos MM, et al. Association between sex-specific risk factors and risk of new-onset atrial fibrillation among women. *JAMA Netw Open* 2022;**5**:e2229716. <https://doi.org/10.1001/jamanetworkopen.2022.29716>
1145. Wong GR, Nalliah CJ, Lee G, Voskoboinik A, Chieng D, Prabhu S, et al. Sex-related differences in atrial remodeling in patients with atrial fibrillation: relationship to ablation outcomes. *Circ Arrhythm Electrophysiol* 2022;**15**:e009925. <https://doi.org/10.1161/CIRCEP.121.009925>
1146. Mokgokong R, Schnabel R, Witt H, Miller R, Lee TC. Performance of an electronic health record-based predictive model to identify patients with atrial fibrillation across countries. *PLoS One* 2022;**17**:e0269867. <https://doi.org/10.1371/journal.pone.0269867>
1147. Schnabel RB, Witt H, Walker J, Ludwig M, Geelhoed B, Kossack N, et al. Machine learning-based identification of risk-factor signatures for undiagnosed atrial fibrillation in primary prevention and post-stroke in clinical practice. *Eur Heart J Qual Care Clin Outcomes* 2022;**9**:16–23. <https://doi.org/10.1093/ehjqcco/qcac013>
1148. Himmelreich JCL, Veelers L, Lucassen WAM, Schnabel RB, Rienstra M, van Weert H, et al. Prediction models for atrial fibrillation applicable in the community: a systematic review and meta-analysis. *Europace* 2020;**22**:684–94. <https://doi.org/10.1093/europace/eaab005>
1149. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 2019;**139**:e56–528. <https://doi.org/10.1161/CIR.0000000000000659>
1150. Allan V, Honarbakhsh S, Casas JP, Wallace J, Hunter R, Schilling R, et al. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. *Thromb Haemost* 2017;**117**:837–50. <https://doi.org/10.1160/TH16-11-0825>
1151. Kirchhof P, Lip GY, Van Gelder IC, Bax J, Hylek E, Kaab S, et al. Comprehensive risk reduction in patients with atrial fibrillation: emerging diagnostic and therapeutic options—a report from the 3rd Atrial Fibrillation Competence NETwork/European Heart Rhythm Association consensus conference. *Europace* 2012;**14**:8–27. <https://doi.org/10.1093/europace/eur241>
1152. Lu Z, Tilly MJ, Geurts S, Aribas E, Roeters van Lennep J, de Groot NMS, et al. Sex-specific anthropometric and blood pressure trajectories and risk of incident atrial fibrillation: the Rotterdam study. *Eur J Prev Cardiol* 2022;**29**:1744–55. <https://doi.org/10.1093/eurjpc/zwac083>
1153. Giacomantonio NB, Bredin SS, Foulds HJ, Warburton DE. A systematic review of the health benefits of exercise rehabilitation in persons living with atrial fibrillation. *Can J Cardiol* 2013;**29**:483–91. <https://doi.org/10.1016/j.cjca.2012.07.003>
1154. Andersen K, Farahmand B, Ahlbom A, Held C, Ljunghall S, Michaëlsson K, et al. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. *Eur Heart J* 2013;**34**:3624–31. <https://doi.org/10.1093/eurheartj/ehs188>
1155. Qureshi WT, Alirhayim Z, Blaha MJ, Juraschek SP, Keteyian SJ, Brawner CA, et al. Cardiorespiratory fitness and risk of incident atrial fibrillation: results from the Henry Ford exercise testing (FIT) project. *Circulation* 2015;**131**:1827–34. <https://doi.org/10.1161/CIRCULATIONAHA.114.014833>
1156. Kwok CS, Anderson SG, Myint PK, Mamas MA, Loke YK. Physical activity and incidence of atrial fibrillation: a systematic review and meta-analysis. *Int J Cardiol* 2014;**177**:467–76. <https://doi.org/10.1016/j.ijcard.2014.09.104>
1157. Abdulla J, Nielsen JR. Is the risk of atrial fibrillation higher in athletes than in the general population? A systematic review and meta-analysis. *Europace* 2009;**11**:1156–9. <https://doi.org/10.1093/europace/eup197>
1158. Cheng M, Hu Z, Lu X, Huang J, Gu D. Caffeine intake and atrial fibrillation incidence: dose response meta-analysis of prospective cohort studies. *Can J Cardiol* 2014;**30**:448–54. <https://doi.org/10.1016/j.cjca.2013.12.026>
1159. Conen D, Chiuve SE, Everett BM, Zhang SM, Buring JE, Albert CM. Caffeine consumption and incident atrial fibrillation in women. *Am J Clin Nutr* 2010;**92**:509–14. <https://doi.org/10.3945/ajcn.2010.29627>
1160. Shen J, Johnson VM, Sullivan LM, Jacques PF, Magnani JW, Lubitz SA, et al. Dietary factors and incident atrial fibrillation: the Framingham heart study. *Am J Clin Nutr* 2011;**93**:261–6. <https://doi.org/10.3945/ajcn.110.001305>
1161. Schnabel RB, Yin X, Gona P, Larson MG, Beiser AS, McManus DD, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham heart study: a cohort study. *Lancet* 2015;**386**:154–62. [https://doi.org/10.1016/S0140-6736\(14\)61774-8](https://doi.org/10.1016/S0140-6736(14)61774-8)
1162. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the cardiovascular health study). *Am J Cardiol* 1994;**74**:236–41. [https://doi.org/10.1016/0002-9149\(94\)90363-8](https://doi.org/10.1016/0002-9149(94)90363-8)
1163. Lip GYH, Collet JP, de Caterina R, Fauchier L, Lane DA, Larsen TB, et al. Antithrombotic therapy in atrial fibrillation associated with valvular heart disease: executive summary of a joint consensus document from the European Heart Rhythm Association (EHRA) and European Society of Cardiology Working Group on Thrombosis, Endorsed by the ESC Working Group on Valvular Heart Disease, Cardiac Arrhythmia Society of Southern Africa (CASSA), Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), South African Heart (SA Heart) Association and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). *Thromb Haemost* 2017;**117**:2215–36. <https://doi.org/10.1160/TH-17-10-0709>
1164. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham heart study. *JAMA* 1994;**271**:840–4. <https://doi.org/10.1001/jama.1994.03510350050036>
1165. Michniewicz E, Mlodawska E, Lopatowska P, Tomaszuk-Kazberuk A, Malyszko J. Patients with atrial fibrillation and coronary artery disease—double trouble. *Adv Med Sci* 2018;**63**:30–5. <https://doi.org/10.1016/j.advms.2017.06.005>
1166. Loomba RS, Buelow MW, Aggarwal S, Arora RR, Kovach J, Ginde S. Arrhythmias in adults with congenital heart disease: what are risk factors for specific arrhythmias? *Pacing Clin Electrophysiol* 2017;**40**:353–61. <https://doi.org/10.1111/pace.12983>
1167. Siland JE, Geelhoed B, Roselli C, Wang B, Lin HJ, Weiss S, et al. Resting heart rate and incident atrial fibrillation: a stratified Mendelian randomization in the AFGen consortium. *PLoS One* 2022;**17**:e0268768. <https://doi.org/10.1371/journal.pone.0268768>
1168. Geurts S, Tilly MJ, Arshi B, Stricker BHC, Kors JA, Deckers JW, et al. Heart rate variability and atrial fibrillation in the general population: a longitudinal and Mendelian randomization study. *Clin Res Cardiol* 2023;**112**:747–58. <https://doi.org/10.1007/s00392-022-02072-5>
1169. Aune D, Feng T, Schlesinger S, Janszky I, Norat T, Riboli E. Diabetes mellitus, blood glucose and the risk of atrial fibrillation: a systematic review and meta-analysis of cohort studies. *J Diabetes Complications* 2018;**32**:501–11. <https://doi.org/10.1016/j.jdiacomp.2018.02.004>
1170. Nakanishi K, Daimon M, Fujii K, Iwama K, Yoshida Y, Hirose K, et al. Prevalence of glucose metabolism disorders and its association with left atrial remodelling before and after catheter ablation in patients with atrial fibrillation. *Europace* 2023;**25**:eua4119. <https://doi.org/10.1093/europace/ead119>
1171. Kim J, Kim D, Jang E, Kim D, You SC, Yu HT, et al. Associations of high-normal blood pressure and impaired fasting glucose with atrial fibrillation. *Heart* 2023;**109**:929–35. <https://doi.org/10.1136/heartjnl-2022-322094>
1172. Lee SS, Ae Kong K, Kim D, Lim YM, Yang PS, Yi JE, et al. Clinical implication of an impaired fasting glucose and prehypertension related to new onset atrial fibrillation in a healthy Asian population without underlying disease: a nationwide cohort study in Korea. *Eur Heart J* 2017;**38**:2599–607. <https://doi.org/10.1093/eurheartj/ehx316>
1173. Alonso A, Lopez FL, Matsushita K, Loehr LR, Agarwal SK, Chen LY, et al. Chronic kidney disease is associated with the incidence of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study. *Circulation* 2011;**123**:2946–53. <https://doi.org/10.1161/CIRCULATIONAHA.111.020982>
1174. Bansal N, Zelnick LR, Alonso A, Benjamin EJ, de Boer IH, Deo R, et al. eGFR and albuminuria in relation to risk of incident atrial fibrillation: a meta-analysis of the Jackson heart study, the multi-ethnic study of atherosclerosis, and the cardiovascular health study. *Clin J Am Soc Nephrol* 2017;**12**:1386–98. <https://doi.org/10.2215/CJN.01860217>
1175. Asad Z, Abbas M, Javed I, Korantzopoulos P, Stavarakis S. Obesity is associated with incident atrial fibrillation independent of gender: a meta-analysis. *J Cardiovasc Electrophysiol* 2018;**29**:725–32. <https://doi.org/10.1111/jce.13458>
1176. Aune D, Sen A, Schlesinger S, Norat T, Janszky I, Romundstad P, et al. Body mass index, abdominal fatness, fat mass and the risk of atrial fibrillation: a systematic review and dose-response meta-analysis of prospective studies. *Eur J Epidemiol* 2017;**32**:181–92. <https://doi.org/10.1007/s10654-017-0232-4>
1177. May AM, Blackwell T, Stone PH, Stone KL, Cawthon PM, Sauer WH, et al. Central sleep-disordered breathing predicts incident atrial fibrillation in older men. *Am J Respir Crit Care Med* 2016;**193**:783–91. <https://doi.org/10.1164/rccm.201508-1523OC>
1178. Tung P, Levitzky YS, Wang R, Weng J, Quan SF, Gottlieb DJ, et al. Obstructive and central sleep apnea and the risk of incident atrial fibrillation in a community cohort of men and women. *J Am Heart Assoc* 2017;**6**:e004500. <https://doi.org/10.1161/JAHA.116.004500>
1179. Desai R, Patel U, Singh S, Bhuvra R, Fong HK, Nunna P, et al. The burden and impact of arrhythmia in chronic obstructive pulmonary disease: insights from the national inpatient sample. *Int J Cardiol* 2019;**281**:49–55. <https://doi.org/10.1016/j.ijcard.2019.01.074>
1180. O'Neal WT, Eford JT, Qureshi WT, Yeboah J, Alonso A, Heckbert SR, et al. Coronary artery calcium progression and atrial fibrillation: the multi-ethnic study of atherosclerosis. *Circ Cardiovasc Imaging* 2015;**8**:e003786. <https://doi.org/10.1161/CIRCIMAGING.115.003786>
1181. Chen LY, Leening MJ, Norby FL, Roetker NS, Hofman A, Franco OH, et al. Carotid intima-media thickness and arterial stiffness and the risk of atrial fibrillation: the Atherosclerosis Risk in Communities (ARIC) study, Multi-Ethnic Study of



- Atherosclerosis (MESA), and the Rotterdam study. *J Am Heart Assoc* 2016;**5**:e002907. <https://doi.org/10.1161/JAHA.115.002907>
1182. Geurts S, Brunborg C, Papageorgiou G, Ikram MA, Kavousi M. Subclinical measures of peripheral atherosclerosis and the risk of new-onset atrial fibrillation in the general population: the Rotterdam study. *J Am Heart Assoc* 2022;**11**:e023967. <https://doi.org/10.1161/JAHA.121.023967>
  1183. Cheng S, Keyes MJ, Larson MG, McCabe EL, Newton-Cheh C, Levy D, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. *JAMA* 2009;**301**:2571–7. <https://doi.org/10.1001/jama.2009.888>
  1184. Alonso A, Jensen PN, Lopez FL, Chen LY, Psaty BM, Folsom AR, et al. Association of sick sinus syndrome with incident cardiovascular disease and mortality: the atherosclerosis risk in communities study and cardiovascular health study. *PLoS One* 2014;**9**:e109662. <https://doi.org/10.1371/journal.pone.0109662>
  1185. Bodin A, Bisson A, Gaborit C, Herbert J, Clemynt N, Babuty D, et al. Ischemic stroke in patients with sinus node disease, atrial fibrillation, and other cardiac conditions. *Stroke* 2020;**51**:1674–81. <https://doi.org/10.1161/STROKEAHA.120.029048>
  1186. Bunch TJ, May HT, Bair TL, Anderson JL, Crandall BG, Cutler MJ, et al. Long-term natural history of adult Wolff–Parkinson–White syndrome patients treated with and without catheter ablation. *Circ Arrhythm Electrophysiol* 2015;**8**:1465–71. <https://doi.org/10.1161/CIRCEP.115.003013>
  1187. Chang SH, Kuo CF, Chou IJ, See LC, Yu KH, Luo SF, et al. Association of a family history of atrial fibrillation with incidence and outcomes of atrial fibrillation: a population-based family cohort study. *JAMA Cardiol* 2017;**2**:863–70. <https://doi.org/10.1001/jamacardio.2017.1855>
  1188. Fox CS, Parise H, D'Agostino RB, Sr, Lloyd-Jones DM, Vasani RS, Wang TJ, et al. Parental atrial fibrillation as a risk factor for atrial fibrillation in offspring. *JAMA* 2004;**291**:2851–5. <https://doi.org/10.1001/jama.291.23.2851>
  1189. Lubitz SA, Yin X, Fontes JD, Magnani JW, Rienstra M, Pai M, et al. Association between familial atrial fibrillation and risk of new-onset atrial fibrillation. *JAMA* 2010;**304**:2263–9. <https://doi.org/10.1001/jama.2010.1690>
  1190. Zoller B, Ohlsson H, Sundquist J, Sundquist K. High familial risk of atrial fibrillation/atrial flutter in multiplex families: a nationwide family study in Sweden. *J Am Heart Assoc* 2013;**2**:e003384. <https://doi.org/10.1161/JAHA.112.003384>
  1191. Ko D, Benson MD, Ngo D, Yang Q, Larson MG, Wang TJ, et al. Proteomics profiling and risk of new-onset atrial fibrillation: Framingham heart study. *J Am Heart Assoc* 2019;**8**:e010976. <https://doi.org/10.1161/JAHA.118.010976>
  1192. Khera AV, Chaffin M, Aragam KG, Haas ME, Roselli C, Choi SH, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. *Nat Genet* 2018;**50**:1219–24. <https://doi.org/10.1038/s41588-018-0183-z>
  1193. Buckley BJR, Harrison SL, Gupta D, Fazio-Eynullayeva E, Underhill P, Lip GYH. Atrial fibrillation in patients with cardiomyopathy: prevalence and clinical outcomes from real-world data. *J Am Heart Assoc* 2021;**10**:e021970. <https://doi.org/10.1161/JAHA.121.021970>
  1194. Chen M, Ding N, Mok Y, Mathews L, Hoogveen RC, Ballantyne CM, et al. Growth differentiation factor 15 and the subsequent risk of atrial fibrillation: the atherosclerosis risk in communities study. *Clin Chem* 2022;**68**:1084–93. <https://doi.org/10.1093/clinchem/hvac096>
  1195. Chua W, Purmah Y, Cardoso VR, Gkoutos GV, Tull SP, Neculau G, et al. Data-driven discovery and validation of circulating blood-based biomarkers associated with prevalent atrial fibrillation. *Eur Heart J* 2019;**40**:1268–76. <https://doi.org/10.1093/eurheartj/ehy815>
  1196. Brady PF, Chua W, Nehaj F, Connolly DL, Khashaba A, Purmah YJV, et al. Interactions between atrial fibrillation and natriuretic peptide in predicting heart failure hospitalization or cardiovascular death. *J Am Heart Assoc* 2022;**11**:e022833. <https://doi.org/10.1161/JAHA.121.022833>
  1197. Werhahn SM, Becker C, Mende M, Haarmann H, Nolte K, Laufs U, et al. NT-proBNP as a marker for atrial fibrillation and heart failure in four observational outpatient trials. *ESC Heart Fail* 2022;**9**:100–9. <https://doi.org/10.1002/ehf2.13703>
  1198. Geelhoed B, Börschel CS, Niiranen T, Palosaari T, Havulinna AS, Fouodo CJK, et al. Assessment of causality of natriuretic peptides and atrial fibrillation and heart failure: a Mendelian randomization study in the FINRISK cohort. *Europace* 2020;**22**:1463–9. <https://doi.org/10.1093/eurpace/ehaa158>
  1199. Toprak B, Brandt S, Brederecke J, Gianfagna F, Vishram-Nielsen JKK, Ojeda FM, et al. Exploring the incremental utility of circulating biomarkers for robust risk prediction of incident atrial fibrillation in European cohorts using regressions and modern machine learning methods. *Europace* 2023;**25**:812–9. <https://doi.org/10.1093/eurpace/ehac260>
  1200. Benz AP, Hijazi Z, Lindbäck J, Connolly SJ, Eikelboom JW, Oldgren J, et al. Biomarker-based risk prediction with the ABC-AF scores in patients with atrial fibrillation not receiving oral anticoagulation. *Circulation* 2021;**143**:1863–73. <https://doi.org/10.1161/CIRCULATIONAHA.120.053100>
  1201. Monrad M, Sajadieh A, Christensen JS, Ketzler M, Raaschou-Nielsen O, Tjønneland A, et al. Long-term exposure to traffic-related air pollution and risk of incident atrial fibrillation: a cohort study. *Environ Health Perspect* 2017;**125**:422–7. <https://doi.org/10.1289/EHP392>
  1202. Walkey AJ, Greiner MA, Heckbert SR, Jensen PN, Piccini JP, Sinner MF, et al. Atrial fibrillation among medicare beneficiaries hospitalized with sepsis: incidence and risk factors. *Am Heart J* 2013;**165**:949–955.e3. <https://doi.org/10.1016/j.ahj.2013.03.020>
  1203. Svensson T, Kitlinski M, Engstrom G, Melander O. Psychological stress and risk of incident atrial fibrillation in men and women with known atrial fibrillation genetic risk scores. *Sci Rep* 2017;**7**:42613. <https://doi.org/10.1038/srep42613>
  1204. Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB, Sr, Benjamin EJ. Anger and hostility predict the development of atrial fibrillation in men in the Framingham offspring study. *Circulation* 2004;**109**:1267–71. <https://doi.org/10.1161/01.CIR.0000118535.15205.8F>
  1205. Chen LY, Bigger JT, Hickey KT, Chen H, Lopez-Jimenez C, Banerji MA, et al. Effect of intensive blood pressure lowering on incident atrial fibrillation and P-wave indices in the ACCORD blood pressure trial. *Am J Hypertens* 2016;**29**:1276–82. <https://doi.org/10.1093/ajh/hpv172>
  1206. Soliman EZ, Rahman AF, Zhang ZM, Rodriguez CJ, Chang TI, Bates JT, et al. Effect of intensive blood pressure lowering on the risk of atrial fibrillation. *Hypertension* 2020;**75**:1491–6. <https://doi.org/10.1161/HYPERTENSIONAHA.120.14766>
  1207. Larstorp ACK, Stokke IM, Kjeldsen SE, Hecht Olsen M, Okin PM, Devereux RB, et al. Antihypertensive therapy prevents new-onset atrial fibrillation in patients with isolated systolic hypertension: the LIFE study. *Blood Press* 2019;**28**:317–26. <https://doi.org/10.1080/08037051.2019.1633905>
  1208. Healey JS, Baranchuk A, Crystal E, Morillo CA, Garfinkle M, Yusuf S, et al. Prevention of atrial fibrillation with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: a meta-analysis. *J Am Coll Cardiol* 2005;**45**:1832–9. <https://doi.org/10.1016/j.jacc.2004.11.070>
  1209. Swedberg K, Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Shi H, et al. Eplerenone and atrial fibrillation in mild systolic heart failure: results from the EMPHASIS-HF (eplerenone in mild patients hospitalization and Survival study in heart failure) study. *J Am Coll Cardiol* 2012;**59**:1598–603. <https://doi.org/10.1016/j.jacc.2011.11.063>
  1210. Wang M, Zhang Y, Wang Z, Liu D, Mao S, Liang B. The effectiveness of SGLT2 inhibitor in the incidence of atrial fibrillation/atrial flutter in patients with type 2 diabetes mellitus/heart failure: a systematic review and meta-analysis. *J Thorac Dis* 2022;**14**:1620–37. <https://doi.org/10.21037/jtd-22-550>
  1211. Yin Z, Zheng H, Guo Z. Effect of sodium-glucose co-transporter protein 2 inhibitors on arrhythmia in heart failure patients with or without type 2 diabetes: a meta-analysis of randomized controlled trials. *Front Cardiovasc Med* 2022;**9**:902923. <https://doi.org/10.3389/fcvm.2022.902923>
  1212. Tedrow UB, Conen D, Ridker PM, Cook NR, Koplan BA, Manson JE, et al. The long- and short-term impact of elevated body mass index on the risk of new atrial fibrillation in the WHS (Women's Health Study). *J Am Coll Cardiol* 2010;**55**:2319–27. <https://doi.org/10.1016/j.jacc.2010.02.029>
  1213. Chan YH, Chen SW, Chao TF, Kao YW, Huang CY, Chu PH. The impact of weight loss related to risk of new-onset atrial fibrillation in patients with type 2 diabetes mellitus treated with sodium-glucose cotransporter 2 inhibitor. *Cardiovasc Diabetol* 2021;**20**:93. <https://doi.org/10.1186/s12933-021-01285-8>
  1214. Mishima RS, Verdicchio CV, Noubiap JJ, Ariyaratnam JP, Gallagher C, Jones D, et al. Self-reported physical activity and atrial fibrillation risk: a systematic review and meta-analysis. *Heart Rhythm* 2021;**18**:520–8. <https://doi.org/10.1016/j.hrthm.2020.12.017>
  1215. Elliott AD, Linz D, Mishima R, Kadhim K, Gallagher C, Middeldorp ME, et al. Association between physical activity and risk of incident arrhythmias in 402 406 individuals: evidence from the UK Biobank cohort. *Eur Heart J* 2020;**41**:1479–86. <https://doi.org/10.1093/eurheartj/ehz897>
  1216. Jin MN, Yang PS, Song C, Yu HT, Kim TH, Uhm JS, et al. Physical activity and risk of atrial fibrillation: a nationwide cohort study in general population. *Sci Rep* 2019;**9**:13270. <https://doi.org/10.1038/s41598-019-49686-w>
  1217. Khurshid S, Weng LC, Al-Alusi MA, Halford JL, Haimovich JS, Benjamin EJ, et al. Accelerometer-derived physical activity and risk of atrial fibrillation. *Eur Heart J* 2021;**42**:2472–83. <https://doi.org/10.1093/eurheartj/ehab250>
  1218. Tikkanen E, Gustafsson S, Ingelsson E. Associations of fitness, physical activity, strength, and genetic risk with cardiovascular disease: longitudinal analyses in the UK biobank study. *Circulation* 2018;**137**:2583–91. <https://doi.org/10.1161/CIRCULATIONAHA.117.032432>
  1219. Mørseth B, Graff-Iversen S, Jacobsen BK, Jørgensen L, Nyrnes A, Thelle DS, et al. Physical activity, resting heart rate, and atrial fibrillation: the Tromsø study. *Eur Heart J* 2016;**37**:2307–13. <https://doi.org/10.1093/eurheartj/ehw059>
  1220. Csengeri D, Sprünker NA, Di Castelnuovo A, Niiranen T, Vishram-Nielsen JK, Costanzo S, et al. Alcohol consumption, cardiac biomarkers, and risk of atrial fibrillation and adverse outcomes. *Eur Heart J* 2021;**42**:1170–7. <https://doi.org/10.1093/eurheartj/ehaa953>
  1221. Gallagher C, Hendriks JML, Elliott AD, Wong CX, Rangnekar G, Middeldorp ME, et al. Alcohol and incident atrial fibrillation – a systematic review and meta-analysis. *Int J Cardiol* 2017;**246**:46–52. <https://doi.org/10.1016/j.ijcard.2017.05.133>

1222. Tu SJ, Gallagher C, Elliott AD, Linz D, Pitman BM, Hendriks JML, et al. Risk thresholds for total and beverage-specific alcohol consumption and incident atrial fibrillation. *JACC Clin Electrophysiol* 2021;**7**:1561–9. <https://doi.org/10.1016/j.jacep.2021.05.013>
1223. Lee JW, Roh SY, Yoon WS, Kim J, Jo E, Bae DH, et al. Changes in alcohol consumption habits and risk of atrial fibrillation: a nationwide population-based study. *Eur J Prev Cardiol* 2024;**31**:49–58. <https://doi.org/10.1093/eurjpc/zwad270>
1224. Chang SH, Wu LS, Chiou MJ, Liu JR, Yu KH, Kuo CF, et al. Association of metformin with lower atrial fibrillation risk among patients with type 2 diabetes mellitus: a population-based dynamic cohort and *in vitro* studies. *Cardiovasc Diabetol* 2014;**13**:123. <https://doi.org/10.1186/s12933-014-0123-x>
1225. Tseng CH. Metformin use is associated with a lower incidence of hospitalization for atrial fibrillation in patients with type 2 diabetes mellitus. *Front Med (Lausanne)* 2021;**7**:592901. <https://doi.org/10.3389/fmed.2020.592901>
1226. Li WJ, Chen XQ, Xu LL, Li YQ, Luo BH. SGLT2 inhibitors and atrial fibrillation in type 2 diabetes: a systematic review with meta-analysis of 16 randomized controlled trials. *Cardiovasc Diabetol* 2020;**19**:130. <https://doi.org/10.1186/s12933-020-01105-5>
1227. Srivatsa UN, Malhotra P, Zhang XJ, Beri N, Xing G, Brunson A, et al. Bariatric surgery to alleviate occurrence of atrial fibrillation hospitalization—BLOC-AF. *Heart Rhythm O2* 2020;**1**:96–102. <https://doi.org/10.1016/j.hroo.2020.04.004>
1228. Hoskuldottir G, Sattar N, Miftaraj M, Naslund I, Ottosson J, Franzen S, et al. Potential effects of bariatric surgery on the incidence of heart failure and atrial fibrillation in patients with type 2 diabetes mellitus and obesity and on mortality in patients with preexisting heart failure: a nationwide, matched, observational cohort study. *J Am Heart Assoc* 2021;**10**:e019323. <https://doi.org/10.1161/JAHA.120.019323>
1229. Chokesuwattanasakul R, Thongprayoon C, Bathini T, Sharma K, Watthanasantorn K, Lertjitbanjong P, et al. Incident atrial fibrillation in patients undergoing bariatric surgery: a systematic review and meta-analysis. *Intern Med J* 2020;**50**:810–7. <https://doi.org/10.1111/imj.14436>
1230. Lynch KT, Mehaffey JH, Hawkins RB, Hassinger TE, Hallowell PT, Kirby JL. Bariatric surgery reduces incidence of atrial fibrillation: a propensity score-matched analysis. *Surg Obes Relat Dis* 2019;**15**:279–85. <https://doi.org/10.1016/j.soard.2018.11.021>
1231. Jamaly S, Carlsson L, Peltonen M, Jacobson P, Sjostrom L, Karason K. Bariatric surgery and the risk of new-onset atrial fibrillation in Swedish obese subjects. *J Am Coll Cardiol* 2016;**68**:2497–504. <https://doi.org/10.1016/j.jacc.2016.09.940>
1232. Okin PM, Hille DA, Larstorp AC, Wachtell K, Kjeldsen SE, Dahlöf B, et al. Effect of lower on-treatment systolic blood pressure on the risk of atrial fibrillation in hypertensive patients. *Hypertension* 2015;**66**:368–73. <https://doi.org/10.1161/HYPERTENSIONAHA.115.05728>
1233. Wachtell K, Lehto M, Gerds E, Olsen MH, Hornestam B, Dahlöf B, et al. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention for End point reduction in hypertension (LIFE) study. *J Am Coll Cardiol* 2005;**45**:712–9. <https://doi.org/10.1016/j.jacc.2004.10.068>
1234. Schmieder RE, Kjeldsen SE, Julius S, McInnes GT, Zanchetti A, Hua TA, et al. Reduced incidence of new-onset atrial fibrillation with angiotensin II receptor blockade: the VALUE trial. *J Hypertens* 2008;**26**:403–11. <https://doi.org/10.1097/HJH.0b013e3282f35c67>
1235. Schaer BA, Schneider C, Jick SS, Conen D, Osswald S, Meier CR. Risk for incident atrial fibrillation in patients who receive antihypertensive drugs: a nested case-control study. *Ann Intern Med* 2010;**152**:78–84. <https://doi.org/10.7326/0003-4819-152-2-201001190-00005>
1236. Dewland TA, Soliman EZ, Yamal JM, Davis BR, Alonso A, Albert CM, et al. Pharmacologic prevention of incident atrial fibrillation: long-term results from the ALLHAT (antihypertensive and lipid-lowering treatment to prevent heart attack trial). *Circ Arrhythm Electrophysiol* 2017;**10**:e005463. <https://doi.org/10.1161/CIRCEP.117.005463>
1237. Butt JH, Docherty KF, Jhund PS, de Boer RA, Böhm M, Desai AS, et al. Dapagliflozin and atrial fibrillation in heart failure with reduced ejection fraction: insights from DAPA-HF. *Eur J Heart Fail* 2022;**24**:513–25. <https://doi.org/10.1002/ejhf.2381>
1238. Liu X, Liu H, Wang L, Zhang L, Xu Q. Role of sacubitril-valsartan in the prevention of atrial fibrillation occurrence in patients with heart failure: a systematic review and meta-analysis of randomized controlled trials. *PLOS ONE* 2022;**17**:e0263131. <https://doi.org/10.1371/journal.pone.0263131>
1239. Hess PL, Jackson KP, Hasselblad V, Al-Khatib SM. Is cardiac resynchronization therapy an antiarrhythmic therapy for atrial fibrillation? A systematic review and meta-analysis. *Curr Cardiol Rep* 2013;**15**:330. <https://doi.org/10.1007/s11886-012-0330-6>
1240. Fatemi O, Yuriditsky E, Tsioufis C, Tsachris D, Morgan T, Basile J, et al. Impact of intensive glycemic control on the incidence of atrial fibrillation and associated cardiovascular outcomes in patients with type 2 diabetes mellitus (from the action to control cardiovascular risk in diabetes study). *Am J Cardiol* 2014;**114**:1217–22. <https://doi.org/10.1016/j.amjcard.2014.07.045>
1241. Nantsupawat T, Wongcharoen W, Chattipakorn SC, Chattipakorn N. Effects of metformin on atrial and ventricular arrhythmias: evidence from cell to patient. *Cardiovasc Diabetol* 2020;**19**:198. <https://doi.org/10.1186/s12933-020-01176-4>
1242. Chang CY, Yeh YH, Chan YH, Liu JR, Chang SH, Lee HF, et al. Dipeptidyl peptidase-4 inhibitor decreases the risk of atrial fibrillation in patients with type 2 diabetes: a nationwide cohort study in Taiwan. *Cardiovasc Diabetol* 2017;**16**:159. <https://doi.org/10.1186/s12933-017-0640-5>
1243. Ostroplets A, Elias PA, Reyes MV, Wan EY, Pajvani UB, Hripacsak G, et al. Metformin is associated with a lower risk of atrial fibrillation and ventricular arrhythmias compared with sulfonylureas: an observational study. *Circ Arrhythm Electrophysiol* 2021;**14**:e009115. <https://doi.org/10.1161/CIRCEP.120.009115>
1244. Proietti R, Lip GYH. Sodium-glucose cotransporter 2 inhibitors: an additional management option for patients with atrial fibrillation? *Diabetes Obes Metab* 2022;**24**:1897–900. <https://doi.org/10.1111/dom.14818>
1245. Karamichalakis N, Kolovos V, Paraskevaidis I, Tsougos E. A new hope: sodium-glucose cotransporter-2 inhibition to prevent atrial fibrillation. *J Cardiovasc Dev Dis* 2022;**9**:236. <https://doi.org/10.3390/jcdd9080236>
1246. Lee S, Zhou J, Leung KSK, Wai AKC, Jeevaratnam K, King E, et al. Comparison of sodium-glucose cotransporter-2 inhibitor and dipeptidyl peptidase-4 inhibitor on the risks of new-onset atrial fibrillation, stroke and mortality in diabetic patients: a propensity score-matched study in Hong Kong. *Cardiovasc Drugs Ther* 2023;**37**:561–9. <https://doi.org/10.1007/s10557-022-07319-x>
1247. Elliott AD, Maatman B, Emery MS, Sanders P. The role of exercise in atrial fibrillation prevention and promotion: finding optimal ranges for health. *Heart Rhythm* 2017;**14**:1713–20. <https://doi.org/10.1016/j.hrthm.2017.07.001>
1248. Newman W, Parry-Williams G, Wiles J, Edwards J, Hulbert S, Kipourou K, et al. Risk of atrial fibrillation in athletes: a systematic review and meta-analysis. *Br J Sports Med* 2021;**55**:1233–8. <https://doi.org/10.1136/bjsports-2021-103994>