Prevention of Strokes related to Atrial Fibrillation – Appendix 2

European Cardiology Society Guidelines for Atrial Fibrillation 2020 –

Excerpts and Summary for General Practitioners NHS HULL

Full ESC Guidelines are available on line

https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management

Definition of Atrial Fibrillation

A supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction. *Electrocardiographic characteristics of AF include:*

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

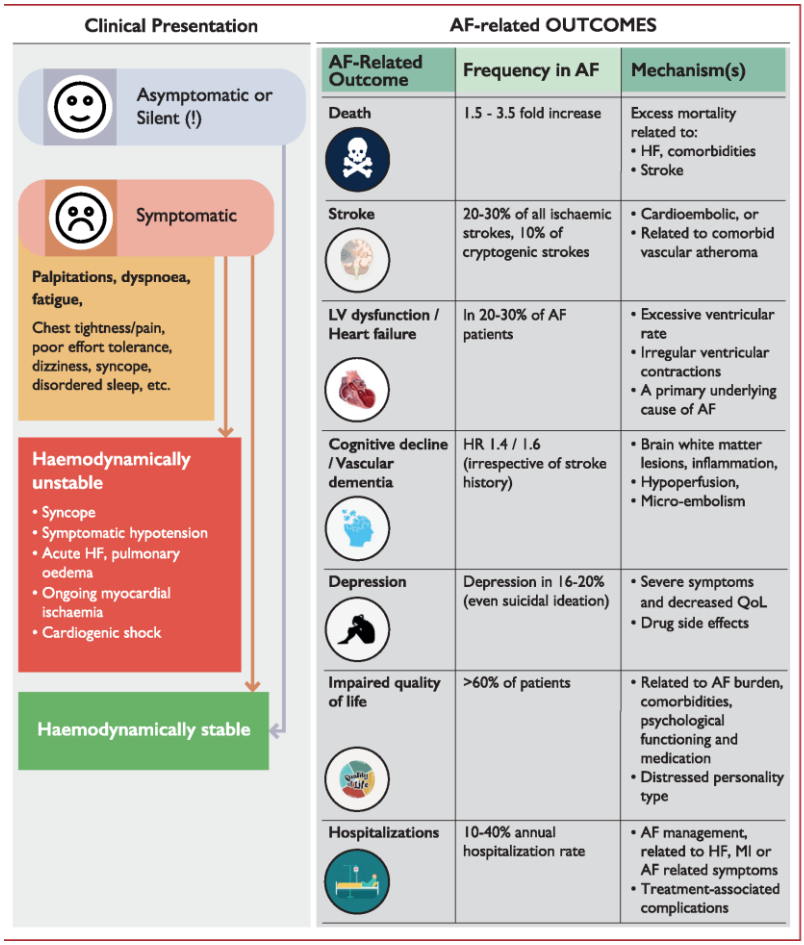
To establish a diagnosis of AF requires either

A standard 12 lead ECG or a 30 second single lead ECG demonstrating irregular RR intervals and absent P waves as above.

Prevalence

The currently estimated prevalence of AF in adults is between 2% and 4% and a 2.3-fold rise is expected in coming years, owing to extended longevity in the general population and intensifying search for undiagnosed AF.

Increasing age is a prominent AF risk factor, but increasing burden of other comorbidities including hypertension, diabetes mellitus, heart failure (HF), coronary artery disease (CAD), chronic kidney disease (CKD),[21] obesity, and obstructive sleep apnoea (OSA) is also important


Clinical Presentation
AF-related OUTCOMES
Asymptomatic or Silent (!)
Symptomatic
Palpitations, dyspnoea, fatigue,
Chest tightness/pain, poor effort tolerance, dizziness, syncope, disordered sleep, etc.
Haemodynamically unstable
• Syncope
• Symptomatic hypotension
• Acute HF, pulmonary oedema
• Ongoing myocardial ischaemia
• Cardiogenic shock
Haemodynamically stable
AF-Related Outcome
Frequency in AF
Mechanism(s)
Death
1.5 - 3.5 fold increase
Excess mortality related to:
• HF, comorbidities
• Stroke
Stroke
20-30% of all ischaemic strokes, 10% of cryptogenic strokes
• Cardioembolic, or
• Related to comorbid vascular atheroma
LV dysfunction / Heart failure
In 20-30% of AF patients
• Excessive ventricular rate
• Irregular ventricular contractions
• A primary underlying cause of AF
Cognitive decline / Vascular dementia
HR 1.4 / 1.6 (irrespective of stroke history)
• Brain white matter lesions, inflammation,
• Hypoperfusion,
• Micro-embolism
Depression
Depression in 16-20% (even suicidal ideation)
• Severe symptoms and decreased QoL
• Drug side effects
Impaired quality of life
>60% of patients
• Related to AF burden, comorbidities, psychological functioning and medication
• Distressed personality type
Hospitalizations
10-40% annual hospitalization rate
• AF management, related to HF, MI or AF related symptoms
• Treatment-associated complications
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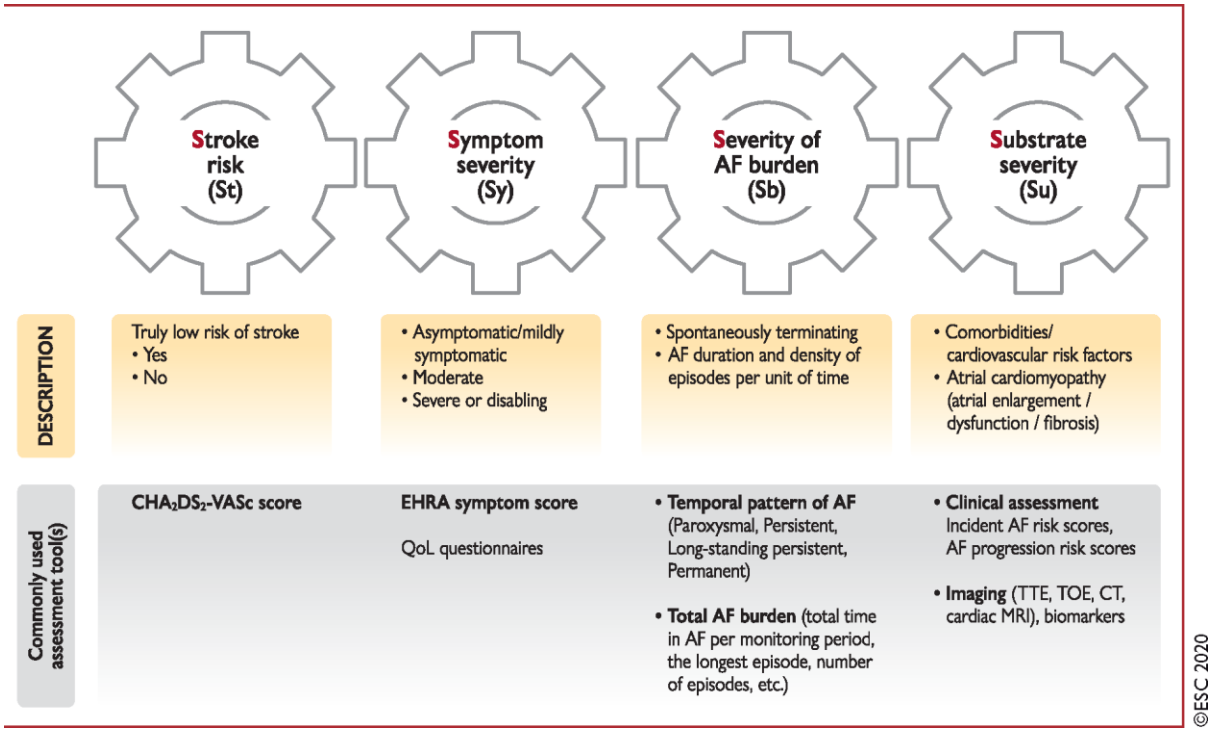
Assessment of AF

4S-AF scheme as an example of structured characterization of AF.[151] AF = atrial fibrillation; ...



A structured assessment of AF which includes symptom assessment, a structured assessment of stroke risk , burden of AF and evaluation of 'substrate' -see table below

At Specialist level the substrate for AF relates to LA dilation and fibrosis with subsequent LA dysfunction and delay in electromechanical conduction. Non-invasive, multimodality imaging can provide all needed information.

AF burden refers to the time spent in AF as detected during monitoring and the heart rate – higher burden defines the need for rate limiting medication and should be reviewed at least annually due to the impact on quality of life and the risk of Heart Failure.

The 'standard package' for diagnostic evaluation of AF patients should include complete medical history and assessment of concomitant conditions, AF pattern, stroke risk, AF-related symptoms, thrombo-embolism, and LV dysfunction. A 12-lead ECG is recommended in all AF patients, to establish the diagnosis of AF, assess ventricular rate during AF, and check for the presence of conduction defects, ischaemia, or signs of structural heart disease.

Laboratory tests (thyroid and kidney function, serum electrolytes, full blood count) and transthoracic echocardiography (LV size and function, LA size, valvular disease, and right

heart size and systolic function) are needed to guide treatment. Based on the patient's characteristics, specific additional information can be obtained.

Clinical Review

AF patients need regular follow-up initially at 3-6 months after diagnosis and annually thereafter as part of the QOF process in Primary Care to ensure continued optimal management.

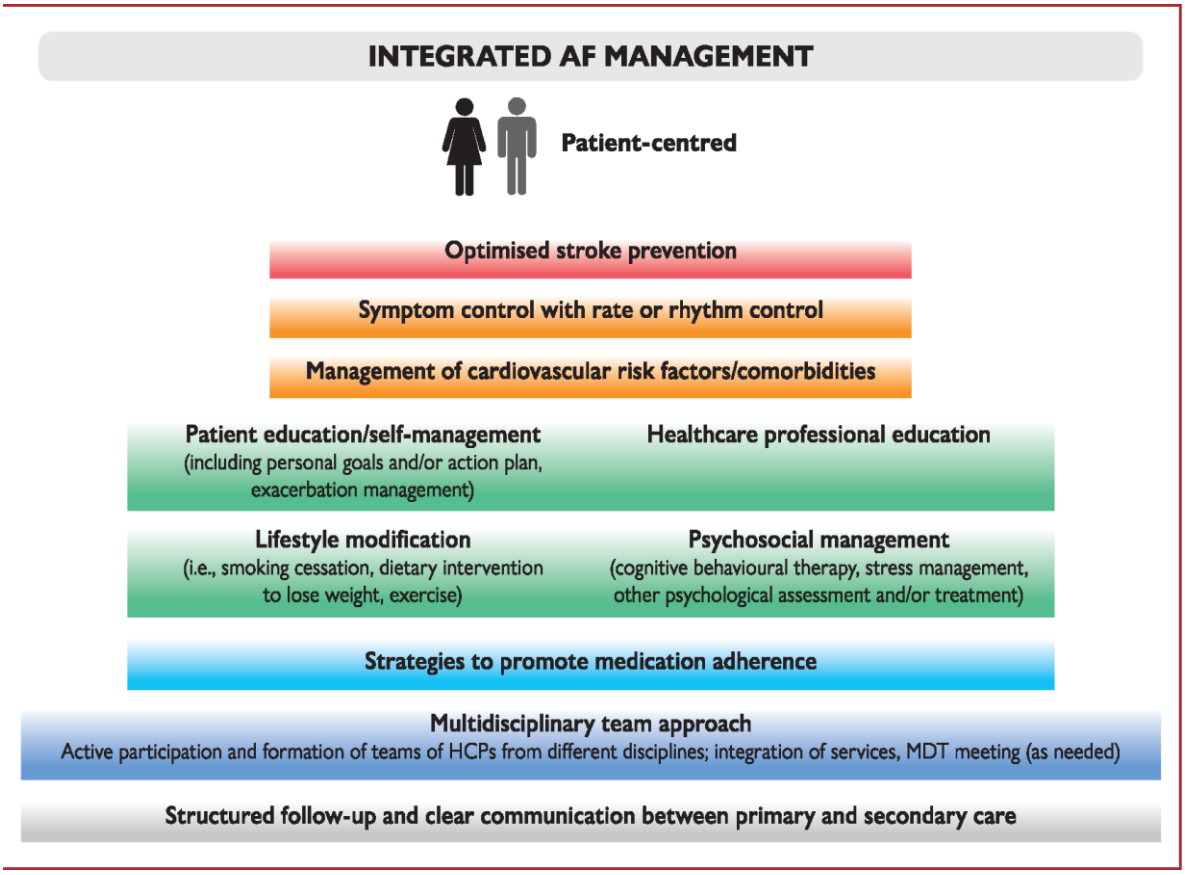
Annual review of medication choices and doses should be guided by assessment of renal and hepatic function as well as any change in the CHA2DS2-Vasc and HASBLED scores.

Signs of Heart Failure, Review of Medication Compliance and evidence of overt cognitive decline should be checked, Routine Bloods FBC, Bioprofile and if indicated NT Pro BNP.

As symptoms related to AF may range from none to disabling, and rhythm control treatment decisions (including catheter ablation) are influenced by symptom severity, symptom status should be characterized using the European Heart Rhythm Association (EHRA) symptom scale

EHRA symptom scale

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



Patient Treatment Choices and Management

CHA2DS2-VASc and HASBLED scores are central to therapeutic choices and are detailed below

A high bleeding risk score should not lead to withholding OAC, as the net clinical benefit of OAC is even greater amongst such patients. However, the formal assessment of bleeding risk informs management of patients taking OAC, focusing attention on modifiable bleeding risk factors that should be managed and (re)assessed at every patient contact, and identifying high-risk patients with non-modifiable bleeding risk factors who should be reviewed earlier.

Absolute contraindications to oral anticoagulants

The few absolute contraindications to OAC include active serious bleeding (where the source should be identified and treated), associated comorbidities (e.g. severe thrombocytopenia <50 platelets/μL, severe anaemia under investigation, etc.), or a recent high-risk bleeding event such as intracranial haemorrhage (ICH). Non-drug options may be considered in such cases

Vitamin K Antagonist (Warfarin)

Compared with control or placebo, vitamin K antagonist (VKA) therapy (mostly warfarin) reduces stroke risk by 64% and mortality by 26%,[412] and is still used in many AF patients worldwide. VKAs are currently the only treatment with established safety in AF patients with rheumatic mitral valve disease and/or an artificial heart valve.

At high TTR (Time in the Therapeutic Range) values, the efficacy of VKAs in stroke prevention may be similar to NOACs, whereas the relative safety benefit with NOACs is less affected by TTR, with consistently lower serious bleeding rates (e.g. ICH) seen with NOACs compared with warfarin, notwithstanding that the absolute difference is small.

Non-vitamin K antagonist oral anticoagulants

In four pivotal RCTs, apixaban, dabigatran, edoxaban, and rivaroxaban have shown non-inferiority to warfarin in the prevention of stroke/systemic embolism. In a meta-analysis of these RCTs, NOACs were associated with a 19% significant stroke/systemic embolism risk reduction, a 51% reduction in haemorrhagic stroke, and similar ischaemic stroke risk reduction compared with VKAs, but NOACs were associated with a significant 10% reduction in all-cause mortality (. There was a non-significant 14% reduction in major bleeding risk, significant 52% reduction in ICH, and 25% increase in gastrointestinal bleeding with NOACs vs. warfarin.

CHA_2DS_2-VASc score			
Risk factors and definitions		**Points awarded**	**Comment**
C	**Congestive heart failure** • Clinical HF, or objective evidence of moderate to severe LV dysfunction, or HCM	1	Recent decompensated HF irrespective of LVEF (thus incorporating HFrEF or HFpEF), or the presence (even if asymptomatic) of moderate-severe LV systolic impairment on cardiac imaging[335]; HCM confers a high stroke risk[336] and OAC is beneficial for stroke reduction.[337]
H	**Hypertension** • or on antihypertensive therapy	1	History of hypertension may result in vascular changes that predispose to stroke, and a well-controlled BP today may not be well-controlled over time.[324] Uncontrolled BP – the optimal BP target associated with the lowest risk of ischaemic stroke, death, and other cardiovascular outcomes is 120 – 129/<80 mmHg.[338]
A	**Age 75 years or older**	2	Age is a powerful driver of stroke risk, and most population cohorts show that the risk rises from age 65 years upwards.[339] Age-related risk is a continuum, but for reasons of simplicity and practicality, 1 point is given for age 65 – 74 years and 2 points for age ≥75 years.
D	**Diabetes mellitus** • Treatment with oral hypoglycaemic drugs and/or insulin or fasting blood glucose >125 mg/dL (7 mmol/L)	1	Diabetes mellitus is a well-established risk factor for stroke, and more recently stroke risk has been related to duration of diabetes mellitus (the longer the duration of diabetes mellitus, the higher the risk of thromboembolism[340]) and presence

CHA_2DS_2-VASc score			
Risk factors and definitions		**Points awarded**	**Comment**
			of diabetic target organ damage, e.g. retinopathy.[341] Both type 1 and type 2 diabetes mellitus confer broadly similar thromboembolic risk in AF, although the risk may be slightly higher in patients aged <65 years with type 2 diabetes mellitus compared to patients with type 1 diabetes mellitus.[342]
S	**Stroke**Previous stroke, TIA, or thromboembolism	2	Previous stroke, systemic embolism, or TIA confers a particularly high risk of ischaemic stroke, hence weighted 2 points. Although excluded from RCTs, AF patients with ICH (including haemorrhagic stroke) are at very high risk of subsequent ischaemic stroke, and recent observational studies suggest that such patients would benefit from oral anticoagulation.[343–345]
V	**Vascular disease** • Angiographically significant CAD, previous myocardial infarction, PAD, or aortic plaque	1	Vascular disease (PAD or myocardial infarction) confers a 17 – 22% excess risk, particularly in Asian patients.[346–348] Angiographically significant CAD is also an independent risk factor for ischaemic stroke among AF patients (adjusted incidence rate ratio 1.29, 95% CI 1.08 – 1.53).[349] Complex aortic plaque on the descending aorta, as an indicator of significant vascular disease, is also a strong predictor of ischaemic stroke.[350]

CHA_2DS_2-VASc score			
Risk factors and definitions		**Points awarded**	**Comment**
A	**Age 65 – 74 years**	1	See above. Recent data from Asia suggest that the risk of stroke may rise from age 50 – 55 years upwards and that a modified CHA_2DS_2-VASc score may be used in Asian patients.[351,352]
Sc	**Sex category (female)**	1	A stroke risk modifier rather than a risk factor.[353]
Maximum score		**9**	

AF = atrial fibrillation; BP = blood pressure; CAD = coronary artery disease; CHA_2DS_2-VASc = Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65-74 years, Sex category (female); CI = confidence interval; EF = ejection fraction; HCM = hypertrophic cardiomyopathy; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; ICH = intracranial haemorrhage; LV = left ventricular; LVEF = left ventricular ejection fraction; OAC = oral anticoagulant; PAD = peripheral artery disease; RCT = randomized controlled trial; TIA = transient ischaemic attack.

Clinical risk factors in the HAS-BLED score[395]

	Risk factors and definitions	Points awarded
H	**Uncontrolled hypertension** • SBP >160 mmHg	1
A	**Abnormal renal and/or hepatic function** Dialysis, transplant, serum creatinine >200 µmol/L, cirrhosis, bilirubin > × 2 upper limit of normal, AST/ALT/ALP >3 × upper limit of normal	1 point for each
S	**Stroke** • Previous ischaemic or haemorrhagic[a] stroke	1
B	**Bleeding history or predisposition** • Previous major haemorrhage or anaemia or severe thrombocytopenia	1
L	**Labile INR**[b] • TTR <60% in patient receiving VKA	1
E	**Elderly** • Aged >65 years or extreme frailty	1
D	**Drugs or excessive alcohol drinking** • Concomitant use of antiplatelet or NSAID; and/or excessive[c] alcohol per week	1 point for each
	Maximum score	**9**

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; SBP = systolic blood pressure; INR = international normalized ratio; NSAID = Non-steroidal anti-inflammatory drug; TTR = time in therapeutic range; VKA = vitamin K antagonist.

a
Haemorrhagic stroke would also score 1 point under the 'B' criterion.

b

Only relevant if patient receiving a VKA.

[c]

Alcohol excess or abuse refers to a high intake (e.g. >14 units per week), where the clinician assesses there would be an impact on health or bleeding risk.

Atrial fibrillation and chronic kidney disease

In patients with mild-to-moderate CKD (CrCl 30 − 49 mL/min), the safety and efficacy of NOACs vs. warfarin was consistent with patients without CKD in landmark NOAC trials, hence the same considerations for stroke risk assessment and choice of OAC may apply. Worsening Creatinine Clearance is a better independent predictor of ischaemic stroke/systemic embolism and bleeding than renal impairment per se.

In patients with CrCl 15 − 29 mL/min, RCT-derived data on the effect of VKA or NOACs are lacking. These patients were essentially excluded from the major RCTs. The evidence for the benefits of OAC in patients with end-stage kidney disease with CrCl≤15 mL/min or on dialysis is even more limited, and to some extent controversial.

Seek specialist advice for these patients

Atrial fibrillation and gastrointestinal disorders

While gastrointestinal lesions can lead to bleeding events in anticoagulated AF patients, some gastrointestinal conditions such as active inflammatory bowel disease increase the risk of AF and stroke. Gastrointestinal bleeding is a well-known complication of OAC. Overall, NOAC use is associated with an increased risk of gastrointestinal bleeding, but in patients treated with apixaban or dabigatran 110 mg the risk is similar to warfarin. Bleeding lesions can be identified in more than 50% of cases of major gastrointestinal bleeding. After correction of the bleeding source, OAC should be restarted, as this strategy has been associated with decreased risks of thrombo-embolism and death.

Management of AF patients with liver disease is challenging, owing to increased bleeding risk, (specialist advice should be sought).

NOACs appear to have a better overall risk–benefit profile compared with warfarin. Prescribing a reduced dose of OAC is less effective in preventing AF adverse outcomes.

The elderly and frail with atrial fibrillation

The prevalence of AF increases progressively with age, and age is an independent risk factor for adverse outcomes in AF. Older people are less likely to receive OAC despite sufficient evidence supporting the use of OAC in this population. Frailty, comorbidities, and increased risk of fall do not outweigh the benefits of OAC given the small absolute risk of bleeding in anticoagulated elderly patients. Evidence from RCTs, meta-analyses and large registries support the use of OAC in this age group. Antiplatelets are neither more effective nor safer than warfarin and may even be harmful, whereas NOACs appear to have a better overall risk–benefit profile compared with warfarin.

Rate control is traditionally the preferred strategy, but evidence informing the choice between rate and rhythm control in the elderly is insufficient. Limited evidence on other AF treatments supports the use of all rate and rhythm control options, including cardioversion, pacemaker implantation, and AF catheter ablation without any age discrimination. AF catheter ablation may be an effective and safe option in selected older individuals with success rates comparable to younger patients and acceptable complication rates. Nevertheless, age was a predictor of complications in AF catheter ablation in some studies and longer follow-up studies suggested an age-related increase in multivariable-adjusted risk for AF/AFL recurrence, death, and major adverse cardiac event.

Above are excerpts from the ECS 2020 guidelines for Atrial Fibrillation which are relevant to UK General Practitioners .

The Key Messages are appended below from the ESC 2020 guidelines are appended below

Key messages

1. The diagnosis of AF needs to be confirmed by a conventional 12-lead ECG tracing or rhythm strip showing AF for ≥30 s.
2. Structured characterization of AF, including stroke risk, symptom severity, severity of AF burden, and AF substrate, helps improve personalized treatment of AF patients.
3. Novel tools and technologies for screening and detection of AF such as (micro-)implants and wearables substantially add to the diagnostic opportunities in patients at risk for AF. However, appropriate management pathways based on such tools are still incompletely defined.
4. Integrated holistic management of AF patients is essential to improving their outcomes.
5. Patient values need to be considered in treatment decision making and incorporated into the AF management pathways; the structured assessment of PRO measures is an important element to document and measure treatment success.
6. The ABC pathway streamlines integrated care of AF patients across healthcare levels and among different specialties.
7. Structured, clinical, risk-score–based assessment of individual thrombo-embolic risk, using the CHA_2DS_2-VASc score, should be performed as the first step in optimal thrombo-embolic risk management in AF patients.
8. Patients with AF and risk factors for stroke need to be treated with OAC for stroke prevention. In NOAC-eligible patients, NOACs are preferred over VKAs.
9. A formal structured risk-score–based bleeding risk assessment using, for example, the HAS-BLED score, helps to identify non-modifiable and address modifiable bleeding risk factors in AF patients.
10. An elevated bleeding risk should not automatically lead to withholding OAC in patients with AF and stroke risk. Instead,

modifiable bleeding risk factors should be addressed, and high-risk patients scheduled for a more frequent clinical review and follow-up.

11. Rate control is an integral part of AF management and is often sufficient to improve AF-related symptoms.
12. The primary indication for rhythm control using cardioversion, AADs, and/or catheter ablation is reduction in AF-related symptoms and improvement of QoL.
13. The decision to initiate long-term AAD therapy needs to balance symptom burden, possible adverse drug reactions, particularly drug-induced proarrhythmia or extracardiac side-effects, and patient preferences.
14. Catheter ablation is a well-established treatment for prevention of AF recurrences. When performed by appropriately trained operators, catheter ablation is a safe and superior alternative to AADs for maintenance of sinus rhythm and symptom improvement.
15. Major risk factors for AF recurrence should be assessed and considered in the decision making for interventional therapy.
16. In patients with AF and normal LVEF, catheter ablation has not been shown to reduce total mortality or stroke. In patients with AF and tachycardia-induced cardiomyopathy, catheter ablation reverses LV dysfunction in most cases.
17. Weight loss, strict control of risk factors, and avoidance of triggers for AF are important strategies to improve outcome of rhythm control.
18. Identification and management of risk factors and concomitant diseases is an integral part of the treatment of AF patients.
19. In AF patients with ACS undergoing uncomplicated PCI, an early discontinuation of aspirin and switch to dual antithrombotic therapy with OAC and a $P2Y_{12}$ inhibitor should be considered.
20. Patients with AHRE (Atrial High Rate Episodes)should be regularly monitored for progression to clinical AF and changes in the individual thrombo-embolic risk (i.e. change in CHA_2DS_2-VASc score). In patients with longer AHRE (especially >24 h) and a high CHA_2DS_2-VASc score, it is reasonable to consider the use of OAC when a positive net clinical

benefit from OAC is anticipated in a shared, informed, treatment decision-making process.

Decision Making support is available to NHS Hull GPs through the Advice and Guidance service at Hull Acute Trust , AF related queries should be directed to Dr Hobson or Dr Caldwell our local Electrophysiology Cardiologists.