

ATRIAL FIBRILLATION MANAGEMENT

2019 Executive Summary

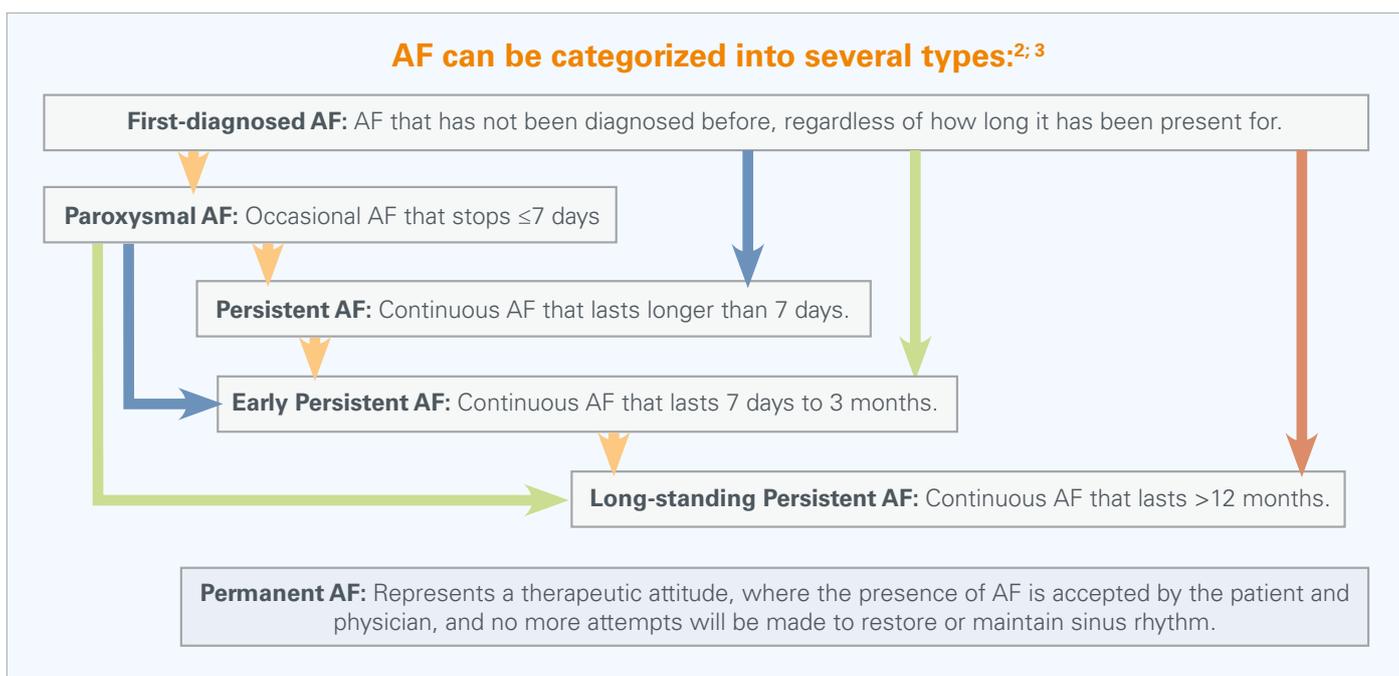
**Overview of Atrial Fibrillation Management
and Treatment Outcomes**



The management of atrial fibrillation focuses on effectively and safely controlling the irregular heart rhythm, improving symptoms, and reducing key complications based on shared decision-making between healthcare professionals and patients.

WHAT IS ATRIAL FIBRILLATION AND WHY IS IT IMPORTANT?

Atrial fibrillation (AF) is characterized by an irregular and often fast heartbeat that results in uncoordinated contraction of the top 2 chambers of the heart (ie, atria).¹



■ Risk factors for AF include:



LIFESTYLE FACTORS

Obesity⁴⁻⁷, smoking², alcohol consumption^{2, 7-8}



OTHER CONDITIONS

High blood pressure⁷, Heart failure⁹⁻¹⁴, History of heart attack^{9,15}, Coronary artery or other heart disease^{5,9}



NON-MODIFIABLE FACTORS

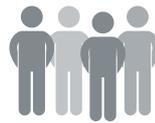
Older age^{2,16}, Family history or other genetic factors^{9, 17-18}, Male sex^{2, 9, 16}

Early detection and diagnosis of AF may help improve patient outcomes, since a long history and duration of AF have been associated with recurrence.¹⁹⁻²²



15%-30%

OF PATIENTS EXPERIENCE
NO SYMPTOMS (i.e. silent AF)²³



PAROXYSMAL
AF

1 in 5
PATIENTS PROGRESS
IN 1 YEAR²⁴⁻²⁷



PERSISTENT
AF

Patients with AF have an increased risk for life-threatening complications and other diseases:²⁸

5x Increase heart failure 

2.4x Increase stroke 

2x Increase cardiovascular mortality 

- AF worsens quality of life for patients and caregivers.²⁹⁻³⁴
- AF increasingly places a **critical financial burden** on the healthcare system, costing **€660-€3,286 million annually across European countries**.³⁵⁻³⁹

The 2016 (ESC)/ (EACTS) guidelines on the management of AF and the 2017(HRS)/ (EHRA)/(ECAS)/ (APHRS)/ (SOLAECE) expert consensus statement on catheter and surgical ablation of AF recommend an integrated management strategy to reduce mortality, tailor management to patient preferences, and reduce hospitalizations.

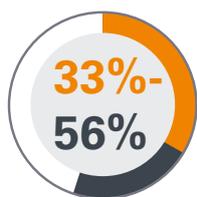
AF patient care pathway management includes:²

- MANAGEMENT of underlying cardiovascular risk factors and REDUCING STROKE RISK** → to improve life expectancy and quality of life
- ELECTRICAL OR PHARMACEUTICAL CARIOVERSION** → when a patient is experiencing an AF episode
- RATE CONTROL THERAPIES** → to control heart rate
- RHYTHM CONTROL THERAPIES** → including antiarrhythmic drugs and catheter ablation, to maintain normal sinus rhythm

- Education and screening programs aimed at **increasing awareness and diagnosis of AF are critical to reducing the risk of stroke and death** in patients with undiagnosed AF.⁴⁰⁻⁴¹
 - Ideally, patients will recognize AF symptoms and contact their clinicians when symptoms arise.⁴²
- **Early treatment of AF is important**, as it may improve patient life expectancy and quality of life.²

Antiarrhythmic drug (AAD) therapy is moderately effective. It is commonly associated with treatment withdrawals, however, it has been shown to improve quality of life, and is affordable in the short term.

With drug therapy treatment:



of patients are in **NORMAL SINUS RHYTHM AT 1 YEAR⁴³**



of patients **WITHDRAW FROM TREATMENT DUE TO ADVERSE EVENTS⁴³**



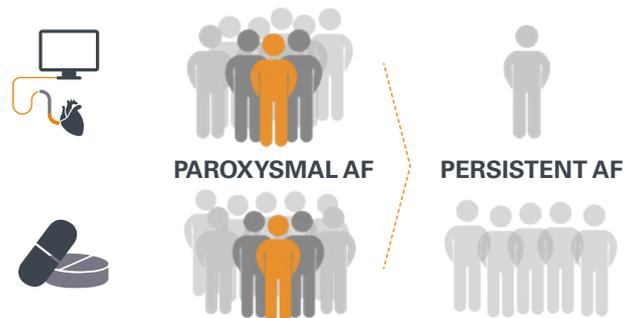
of patients **IMPROVEMENT IN QUALITY OF LIFE⁴⁴**

Catheter ablation is highly effective, associated with a low rate of ablation-related adverse events, and has been shown to reduce the rate of AF-related complications. It has also been shown to improve quality of life, and reduce resource utilization.

With catheter ablation treatment:



Catheter ablation is more effective than drug therapy, has a low chance of AF-related complications, has significantly greater improvement in quality of life, and is less costly over the long term:



Patients with **paroxysmal AF** who undergo catheter ablation are **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs**^{*59}

Similarly **LOW RATES OF AF-RELATED COMPLICATIONS**^{55, 57-58}

- Death
- Stroke
- Cardiac arrest
- Cardiovascular hospitalization

*(HR 0.11; 95% CI 0.025-0.483; p=0.0034.)

Guidance on the delivery of good care to patients with AF and on the use of catheter and surgical ablation to treat AF are available from the 2016 ESC/EACTS guidelines² & 2017 HRS/EHRA/ECAS/APHRs/SOLAECE expert consensus statement on catheter and surgical ablation³

WHAT ARE THE RECOMMENDATIONS FOR MANAGING A PATIENT WITH AF?

The ESC/EACTS guidelines and the HRS/EHRA/ECAS/APHRs/SOLAECE consensus statement recommend an integrated approach to AF management that involves patients and multidisciplinary teams of healthcare professionals to improve access to care and patient compliance. The use of anticoagulants, cardioversion, rate control therapies, and rhythm control therapies are recommended to manage AF.²⁻³

1 Integrated Management of AF & Collaborative Decision Making

Following the diagnosis of AF, guidelines recommend an integrated and structured approach to patient care and AF management that involves multidisciplinary teams of cardiologists and electrophysiologists, non-specialist healthcare professionals, and allied health professionals, and places patients in a central role in decision-making.²

■ Key aims are to:



REDUCE MORTALITY



TAILOR MANAGEMENT TO PATIENT PREFERENCES



REDUCE HOSPITALIZATIONS



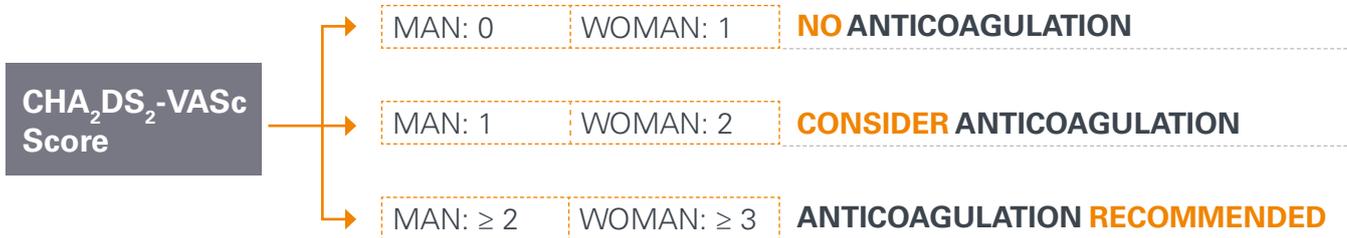
IMPROVE ADHERENCE TO LONG-TERM THERAPY



IMPROVE ADHERENCE TO GUIDELINES

MANAGEMENT OF AF PATIENTS

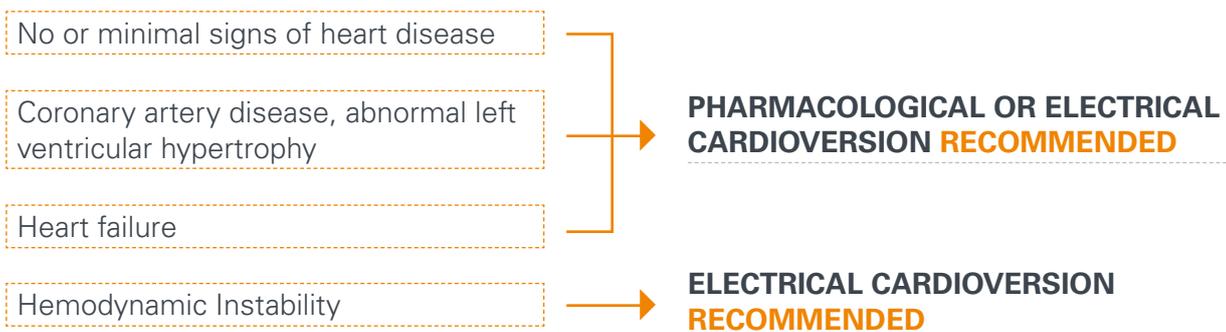
2 Oral Anticoagulation Therapy for Stroke Prevention in Patients with AF²



3 Rate Control Therapy to Lower and Control Heart Rate and Improve Symptoms of AF²

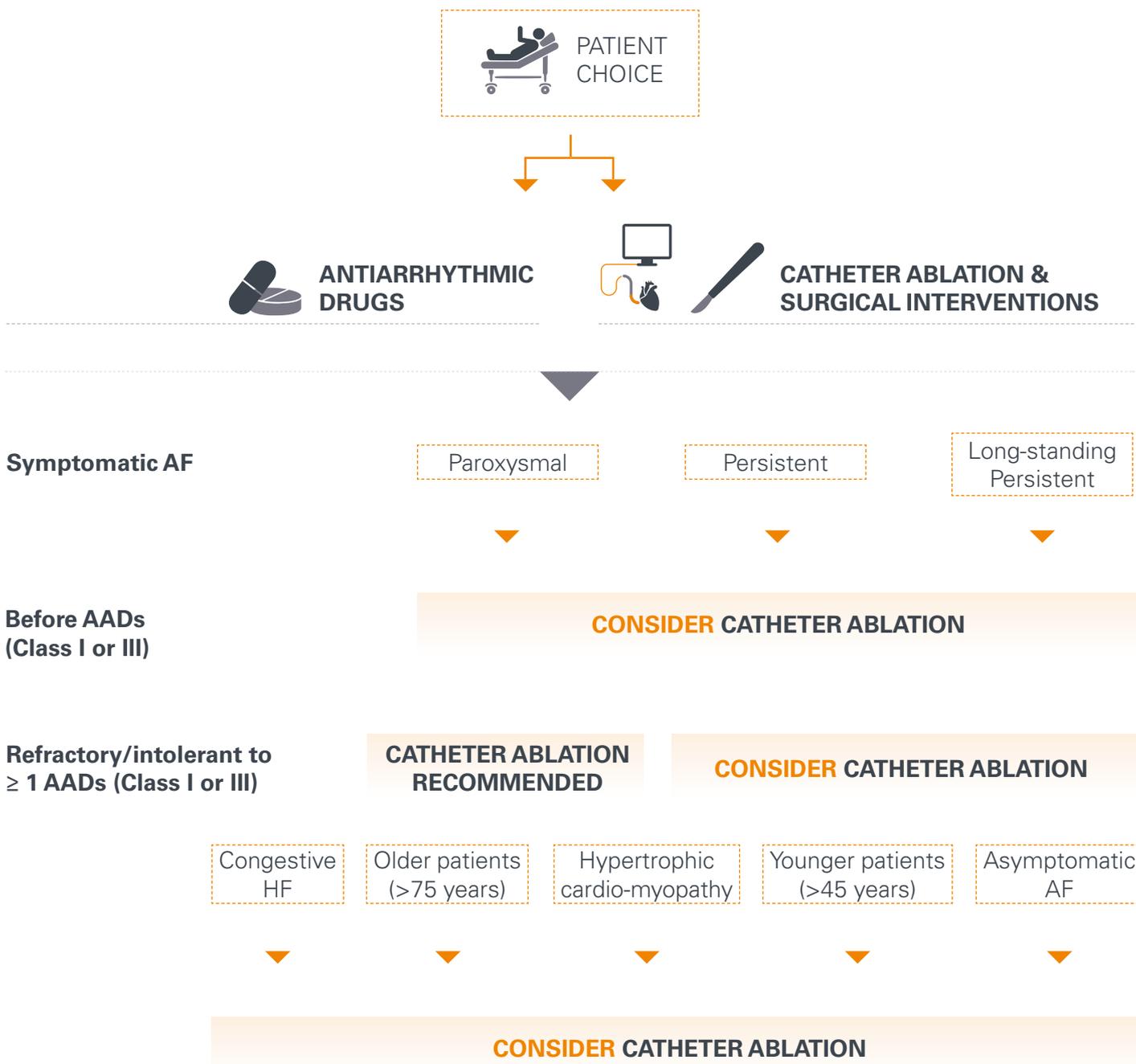


4 Acute Rhythm Control Therapy to Restore Normal Sinus Rhythm²

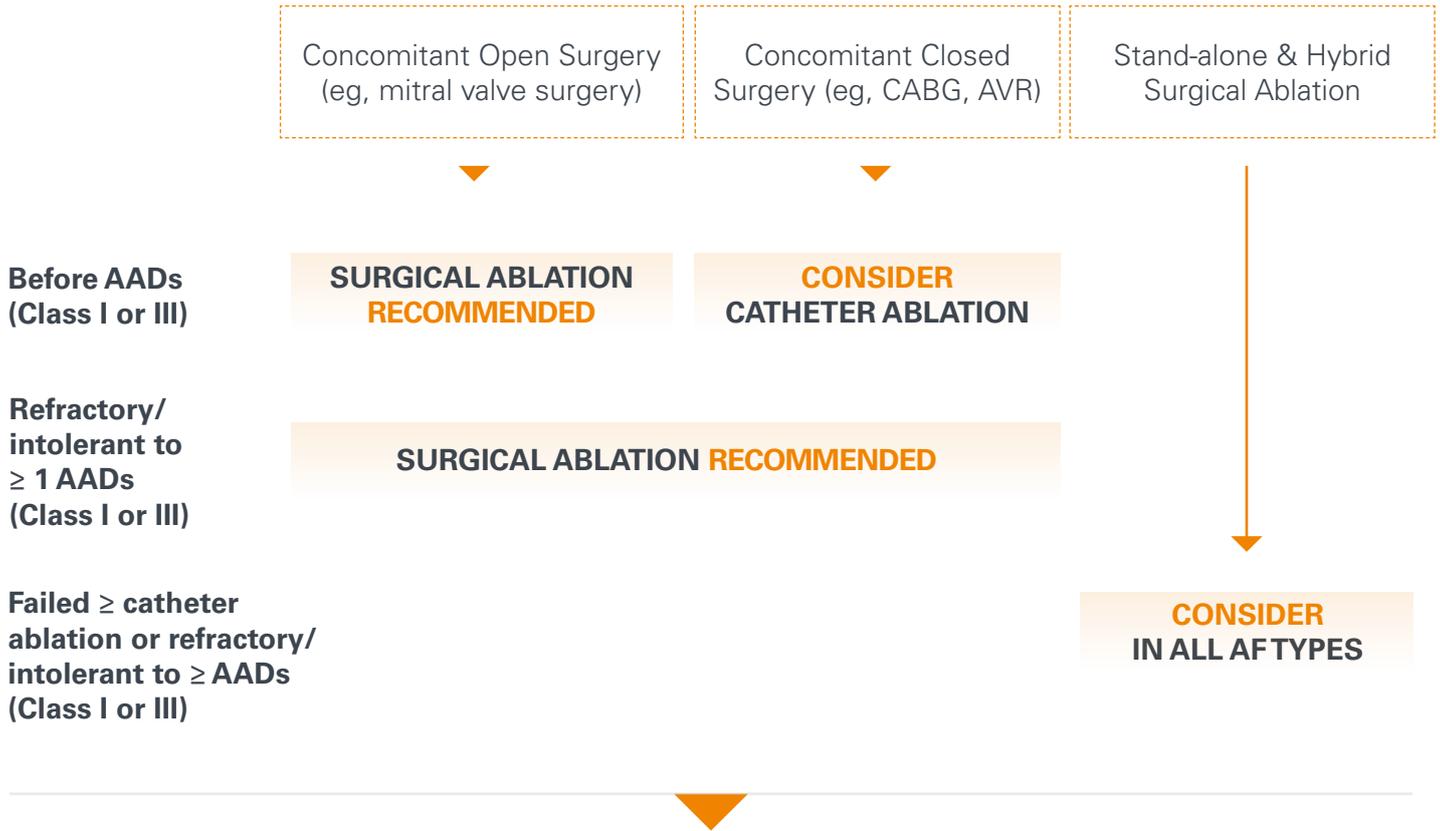


5 Rhythm Control Therapy to Maintain Normal Sinus Rhythm and Improve Symptoms of AF^{2,3}

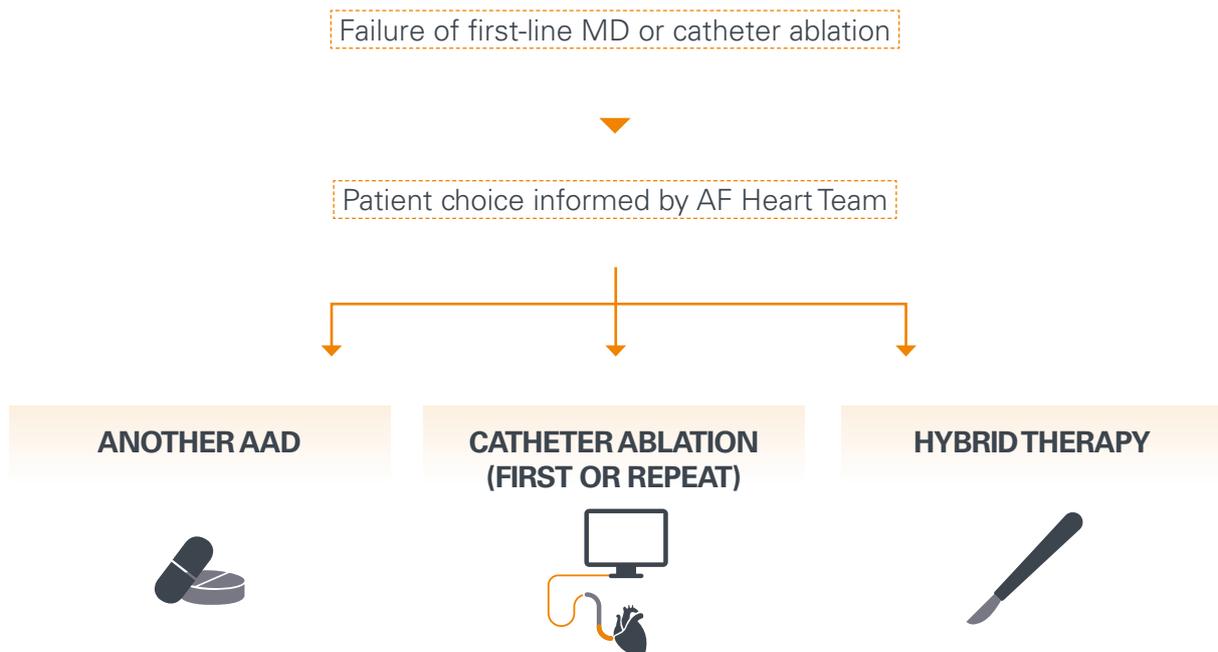
- Guidelines recommend that treatment with AADs, catheter ablation, and/or surgical ablation be dependent on patient choice.^{2,3}
- The choice of AADs needs to consider the presence of comorbidities, cardiovascular risk, potential for proarrhythmia, toxic effects, symptom burden, and patient preference.²



MANAGEMENT OF AF PATIENTS



6 Selection of 2nd rhythm control therapy after failure of 1st rhythm control therapy²



Abbreviations: AAD = antiarrhythmic drug; AF = atrial fibrillation; AVR = aortic valve replacement; CABG = coronary artery bypass graft; CHA2DS2-VASc = Congestive Heart failure, hypertension, Age ≥ 75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female); HF = heart failure; LVEF = left ventricular ejection fraction
 Source: 2016 ESC Guidelines², and 2017 HRS/EHRA Consensus Statement³

The goal of AF patient care pathway management includes detection and management of key complications and cardiovascular risk factors, including stroke and heart failure.

HOW IS THE PATIENT WITH AF TREATED?

AF patient care pathway management includes rhythm control therapy to restore sinus rhythm during an episode of AF and rate and rhythm control therapies over the long-term.²⁻³

- The therapeutic goal of the initial management strategy for AF is to **treat any underlying cardiovascular conditions and reduce the risk of stroke.**²



THE PRESENCE OF CARDIOVASCULAR RISK FACTORS often exacerbates AF²



AF IS ASSOCIATED WITH AN INCREASED RISK OF STROKE compared to patients in sinus rhythm⁶⁰

Current treatment options available for managing AF include:

RATE CONTROL THERAPIES



PHARMACOLOGICAL

Beta blockers or non-dihydropyridine calcium channel antagonists, digitalis glycosides, or amiodarone



SURGICAL

AV node ablation with pacemaker implantation

ACUTE RHYTHM CONTROL THERAPIES

RHYTHM CONTROL THERAPIES FOR AN EPISODE OF AF

Electrical and pharmacological cardioversion

NON- EPISODIC RHYTHM CONTROL THERAPIES



PHARMACOLOGICAL



INTERVENTIONAL



SURGICAL

Over the long-term:

RATE CONTROL THERAPIES

are indicated to lower and control the heart rate in patients with AF

may also be sufficient **TO CONTROL SYMPTOMS OF AF**



of patients being in **SINUS RHYTHM AT 1-YEAR FOLLOWUP**⁶¹

RHYTHM CONTROL THERAPIES

that include AADs and catheter ablation are

the most common methods for **CONTROLLING AF**, effectively preventing recurrence in



as many as **94%** of patients **OVER 1-YEAR**^{2, 45-50}

Antiarrhythmic drug therapy is an integral part of maintaining sinus rhythm after cardioversion; antiarrhythmic drugs act to suppress the firing of or depress the transmission of abnormal electrical signals.²

WHAT IS THE IMPACT OF ANTIARRHYTHMIC DRUG THERAPY IN MANAGING AF?

Antiarrhythmic drug therapy is fairly safe, cost effective and affordable in the short term but can be costly over the long term. Although moderately effective at maintaining normal sinus rhythm, it is effective at controlling symptoms of AF and improving patient quality of life.

- Choice of AAD is primarily guided by safety considerations, including:²

ABSOLUTE or **RELATIVE** CONTRAINDICATIONS

RISK FACTORS for adverse events

such as onset of **new arrhythmia** or **exacerbation of existing arrhythmia** and **effects outside the heart**

FACTORS that influence **DRUG DISPOSITION**

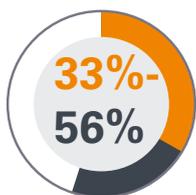
such as patient age and **renal or hepatic function**

PATIENT PREFERENCE

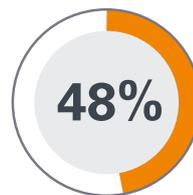
CLINICAL IMPACT

Antiarrhythmic drug therapy is fairly safe and moderately effective at maintaining normal sinus rhythm; its impact on consequences such as stroke, heart failure and mortality have been demonstrated in a limited number of studies.

AADs are moderately effective:



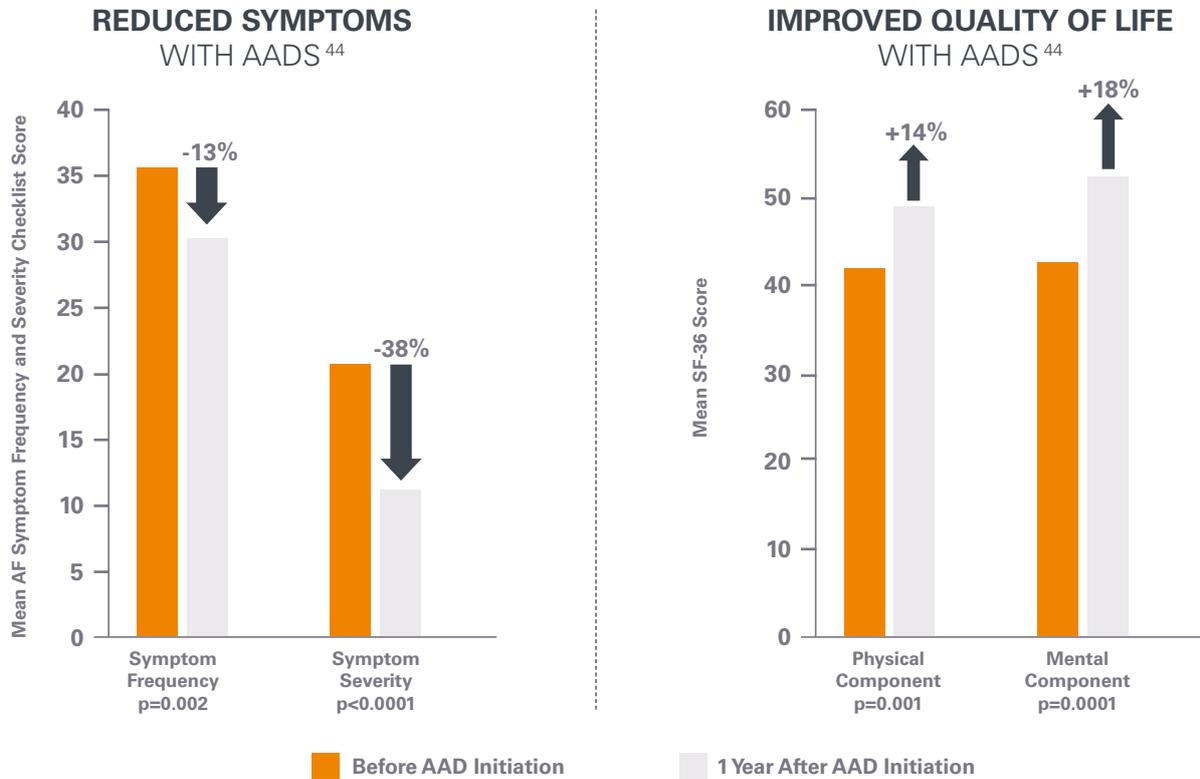
rate for **maintaining normal sinus rhythm** at 1 year.⁴³



of patients with AF are **not well managed on AADs**.⁶²

PATIENT IMPACT

Antiarrhythmic drug therapy is effective at controlling symptoms of AF and significantly improves patient quality of life.



Abbreviations: AAD = antiarrhythmic drug; AF = atrial fibrillation; SF-36 = Short Form 36 questionnaire. Source: Jais et al. (2008)

ECONOMIC IMPACT

Antiarrhythmic drug therapy is cost effective and affordable in the short term, but can be costly over the long term.

- Several studies show that AADs are cost effective, with key drivers including reduced adverse events, stroke, heart failure and mortality.⁶³⁻⁶⁵

Initial cost of AAD treatment is **LOW**

however

LENGTH of treatment is **INDEFINITE** and the **cumulative cost** of AADs

INCREASES 28% ANNUALLY over 9 years*⁶⁶

- Cost of AAD therapy is influenced by its **toxicity level** and **effectiveness** in restoring sinus rhythm and **reducing the risk of AF-related consequences**.^{65, 67-72}

*From one study performed in France; data were limited for other European countries.

Catheter ablation is used to create small scars on targeted parts of heart tissue that block the abnormal electrical signals causing the arrhythmia.^{2, 3}

WHAT IS THE IMPACT OF CATHETER ABLATION IN MANAGING AF?

Catheter ablation is highly effective at maintaining sinus rhythm, has a low rate of complications, reduces patient risk of AF-related complications, controls symptoms and significantly improves patient quality of life. It has been proven to be cost effective by reducing the need for unplanned medical visits and overall healthcare cost.

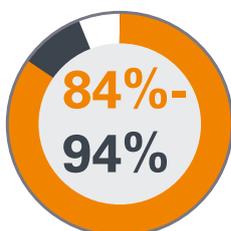
Key considerations for treating patients with catheter ablation include:³

- Type of AF
- Presence of structural heart disease and other comorbidities
- Risk of complications
- Patient preference
- Degree of symptoms
- Candidacy for alternative therapies (eg, rate control, AADs)
- Patient age and frailty

CLINICAL IMPACT

Catheter ablation is highly effective at maintaining sinus rhythm, is associated with a low rate of adverse events and reduced patient risk of AF-related complications, including stroke, dementia, heart failure, and mortality.

- Catheter ablation is highly effective in eligible patients with AF, with recent studies reporting high rates of freedom from atrial arrhythmias at one year after a single procedure with advanced catheter ablation technology:



PAROXYSMAL
AF⁴⁵⁻⁵⁰

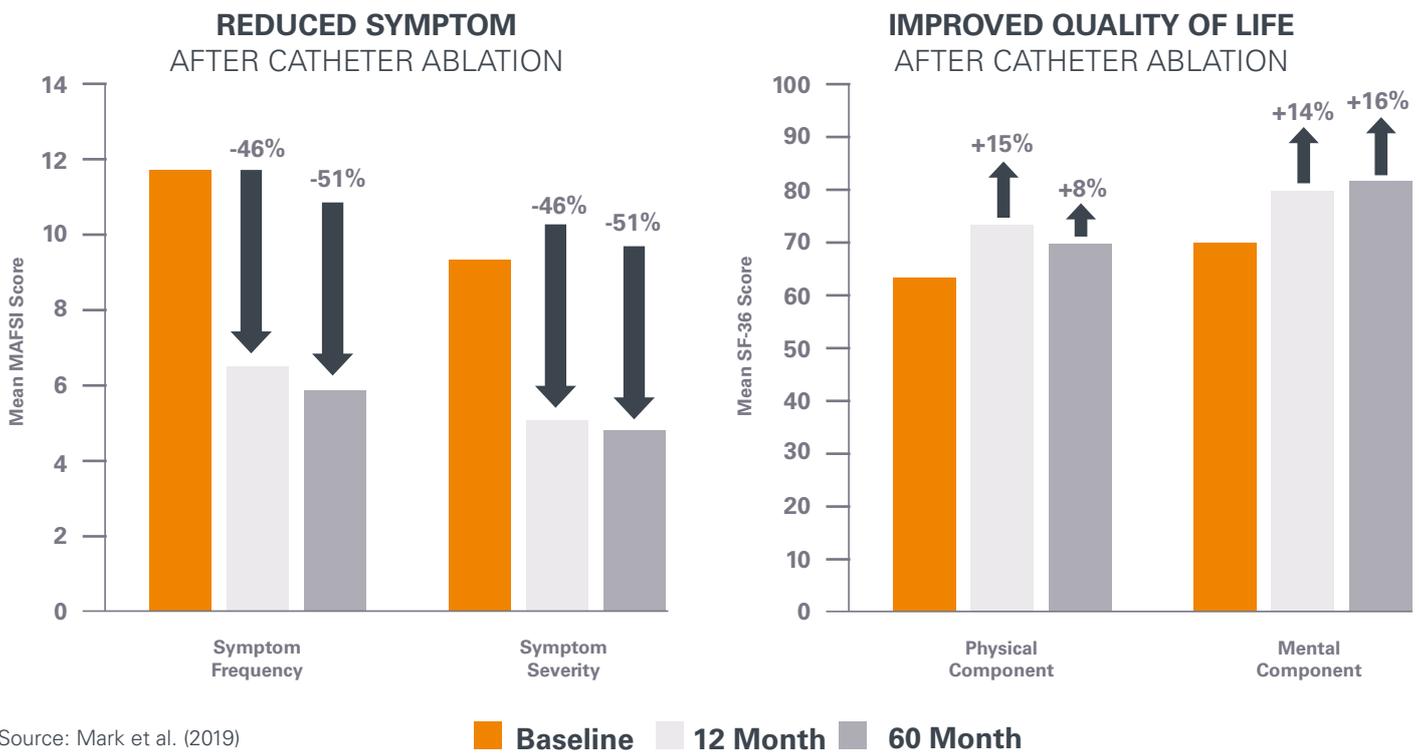


PERSISTENT
AF^{45, 48, 51-54}

PATIENT IMPACT

Catheter ablation is highly effective at controlling symptoms of AF and significantly improves patient quality of life.

- Reductions in symptom severity and improvements in quality of life after catheter ablation of AF are maintained over long-term follow-up.⁵⁶



Source: Mark et al. (2019)

ECONOMIC IMPACT

Catheter ablation is cost effective: it reduces the need for unplanned medical visits, additional treatments to control AF, and subsequent treatment for long-term consequences of AF, in turn, reducing overall healthcare cost.

CATHETER ABLATION reduces the need for unplanned ER visits and hospitalizations

by up to **80%**

as compared to before ablation*⁷³

*at 2 years based on evidence outside of Europe

Recent studies have examined the comparative clinical and cost effectiveness of catheter ablation and drug therapy, including rate and rhythm control drugs, over long-term follow-up.

WHAT IS THE IMPACT OF CATHETER ABLATION COMPARED TO DRUG THERAPY IN MANAGING AF?

Several studies have shown that catheter ablation is significantly more effective than AADs at preventing recurrence of atrial arrhythmias with a similar rate of complications.

CLINICAL IMPACT

Catheter ablation is more effective in preventing recurrence, complications, and progression of AF than drug therapy, with a similar rate of adverse events.

The **CABANA** trial found that **CATHETER ABLATION** was more **EFFECTIVE** at preventing recurrence of AF



improvement in survival **FREE FROM ATRIAL ARRHYTHMIA** over **4 years** compared to drug therapy⁵⁵

CATHETER ABLATION was also associated with

up to **46%**

reductions in the probability of **AF-RELATED complications****



Death



Stroke



Cardiac arrest



Cardiovascular hospitalization

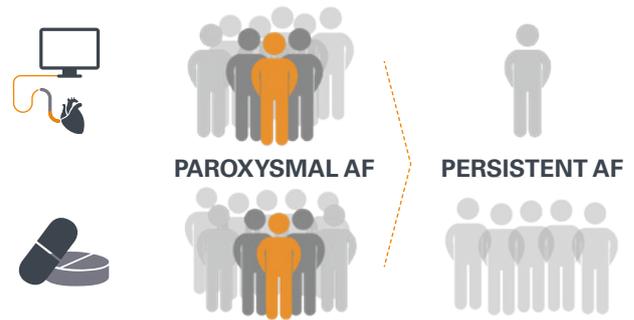
compared to drug therapy over 7-years follow-up.⁷⁴

* (hazard ratio [HR] 0.52; 95% confidence interval [CI] 0.45-0.60; p<0.001)

** 46% cardiac arrest, 41% stroke, 33% death, 17% cardiovascular hospitalization

COMPARISON OF TREATMENTS

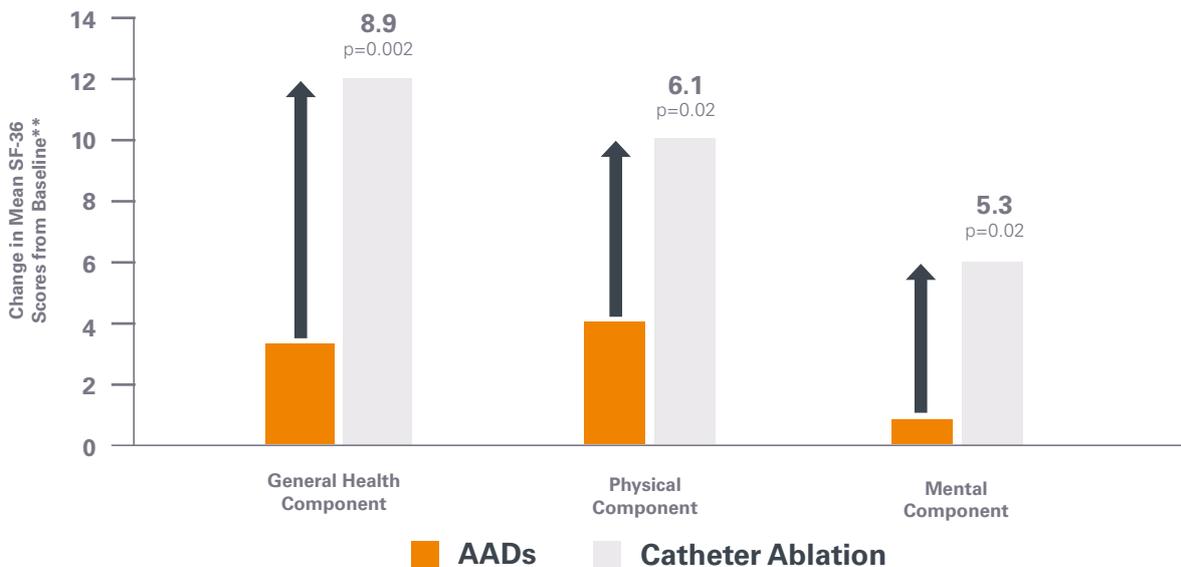
The **ATTEST randomized controlled** trial found that patients receiving ablation, with **paroxysmal AF** are **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs***⁵⁹



PATIENT IMPACT

Catheter ablation of AF results in a significantly greater improvement in patient quality of life than drug therapy.

- The CAPTAF trial reported a **significantly** and **clinically** relevant **greater improvement** from baseline in patient-reported quality of life with catheter ablation than AADs at 1 year.⁵⁸



The CABANA trial reported significantly **GREATER IMPROVEMENT** from baseline in quality of life **WITH CATHETER ABLATION** than with drug therapy at 1 year.



Greater improvement in quality of life from baseline was **MAINTAINED OVER 5 YEARS**.⁵⁶

* (HR 0.11; 95% CI 0.02-0.48; p=0.0034)

**As measured by the SF-36 described in Section 4C.

Abbreviations: AAD = antiarrhythmic drug; CAPTAF = Catheter Ablation compared with Pharmacological Therapy for Atrial Fibrillation; SF-36 = Short Form 36 questionnaire. Source: Blomstrom-Lundqvist et al. (2019)

■ COMPARISON OF TREATMENTS

ECONOMIC IMPACT

Catheter ablation is cost effective compared to antiarrhythmic drugs for the long term treatment of patient with AF.

- A UK database analysis found that catheter ablation treatment was associated with reduced resource utilization compared to drugs over 1 year (excluding the 3 month blanking period).⁷⁶



51% REDUCTION
IN CARDIOVASCULAR-
RELATED OUTPATIENT VISITS
 (p<0.001)



38% REDUCTION
IN INPATIENT ADMISSIONS
FOR HEART FAILURE
 (p=0.0318)

- Despite the initial investment, costs become favorable for catheter ablation at 5 years after the initial ablation procedure when compared to antiarrhythmic drugs.⁶⁶

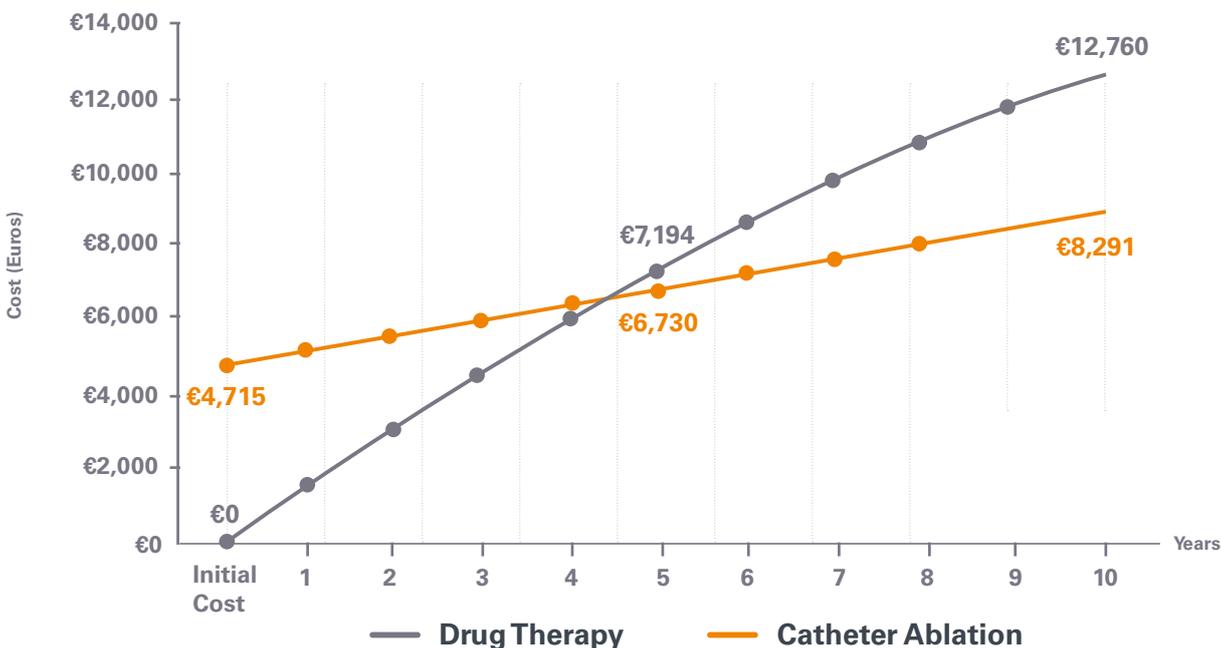


PROJECTING COSTS
TO 10 YEARS AFTER
ABLATION*



catheter ablation was associated with a
35% SAVINGS
IN COSTS COMPARED TO
DRUG THERAPY⁶⁶

CUMULATIVE COSTS OF PAROXYSMAL AF TREATMENT OVER 10 YEARS

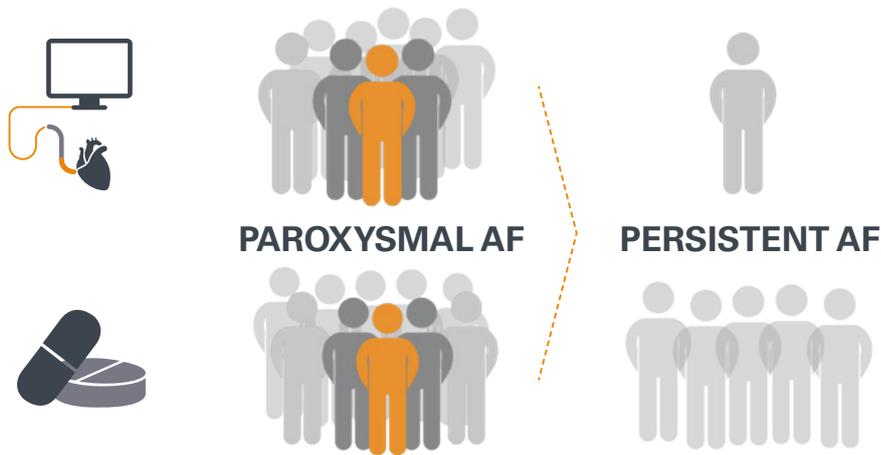


*Study performed in France; data were limited for other European countries.

Catheter ablation is more clinically effective and cost effective compared to drug therapy for the treatment of patients with AF.^{22, 37, 41-44}

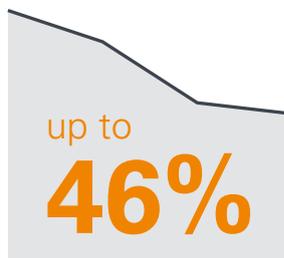


94%
of patients are
FREE FROM ARRHYTHMIA RECURRENCE
AT 1 YEAR⁴⁵⁻⁵⁴



Patients with **paroxysmal AF** who undergo catheter ablation are **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs**^{*59}

CATHETER ABLATION
was also associated with



significant reductions
in the probability of **AF-RELATED complications**



Death



Stroke



Cardiac arrest



Cardiovascular hospitalization

compared to drug therapy over 7-years follow-up.⁷⁴

The 2016 ESC/EACTS guidelines for the management of AF and the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of AF highlight key areas of future research including the following:^{2, 3}

INTEGRATED HEALTHCARE MANAGEMENT TEAM



- Does a **team approach lead to better outcomes** for patients with AF than isolated pillars of care?
- What are the **roles of each member** of the heart team?

RHYTHM CONTROL OUTCOMES



- Does rhythm control therapy have a **prognostic benefit** in patients with AF?
- What are the outcomes of catheter ablation in **high risk patients**?
- What is the **clinical relevance of catheter ablation outcomes** and how do these outcomes relate to quality of life and stroke risk?
- What are the **characteristics of patients** who are most likely to benefit from catheter ablation?

RECURRENCE OF AF AFTER CATHETER ABLATION



- There is limited data on the **optimal treatment strategy** in patients who experience recurrence of AF after catheter ablation. Should patients receive a repeat catheter ablation, surgical ablation, AADs or hybrid therapy (ie, combining AADs with ablation)?

ORAL ANTICOAGULATION THERAPY



- It is unclear if a patient who has subclinical or no AF after successful catheter ablation needs oral anticoagulation. Are there patients who can **safely discontinue oral anticoagulation therapy**?

PROGRESS IN RHYTHM CONTROL THERAPY



- What is the **value of new technologies** for catheter ablation and new AADs in the treatment of patients with AF?

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123104-190912 EMEA
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