

THE BURDEN OF ATRIAL FIBRILLATION

2018 Full Report

**Understanding the Impact of the New Millennium
Epidemic across Europe**



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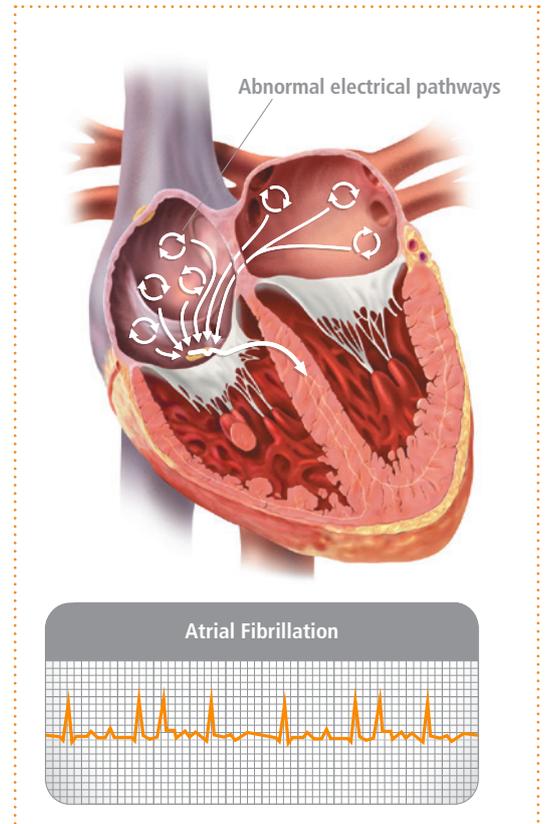
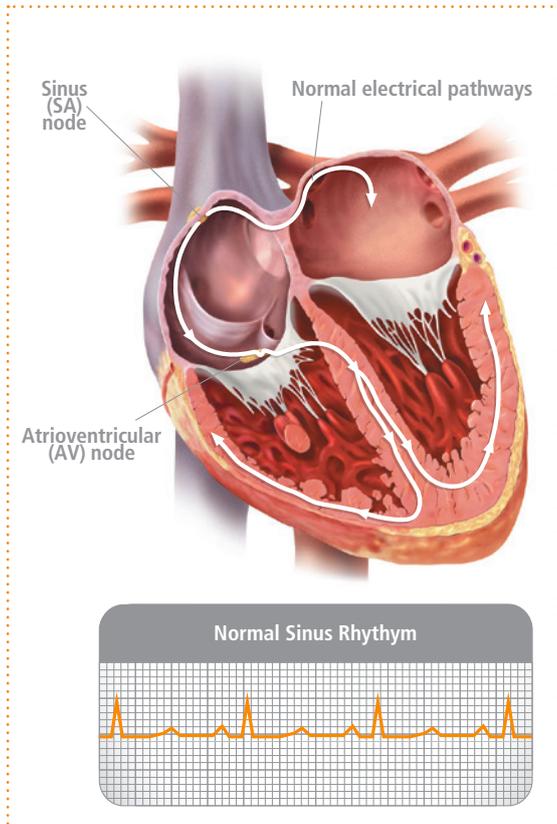
Atrial Fibrillation is fast becoming one of the world's most significant health issues that places a critical burden on healthcare systems

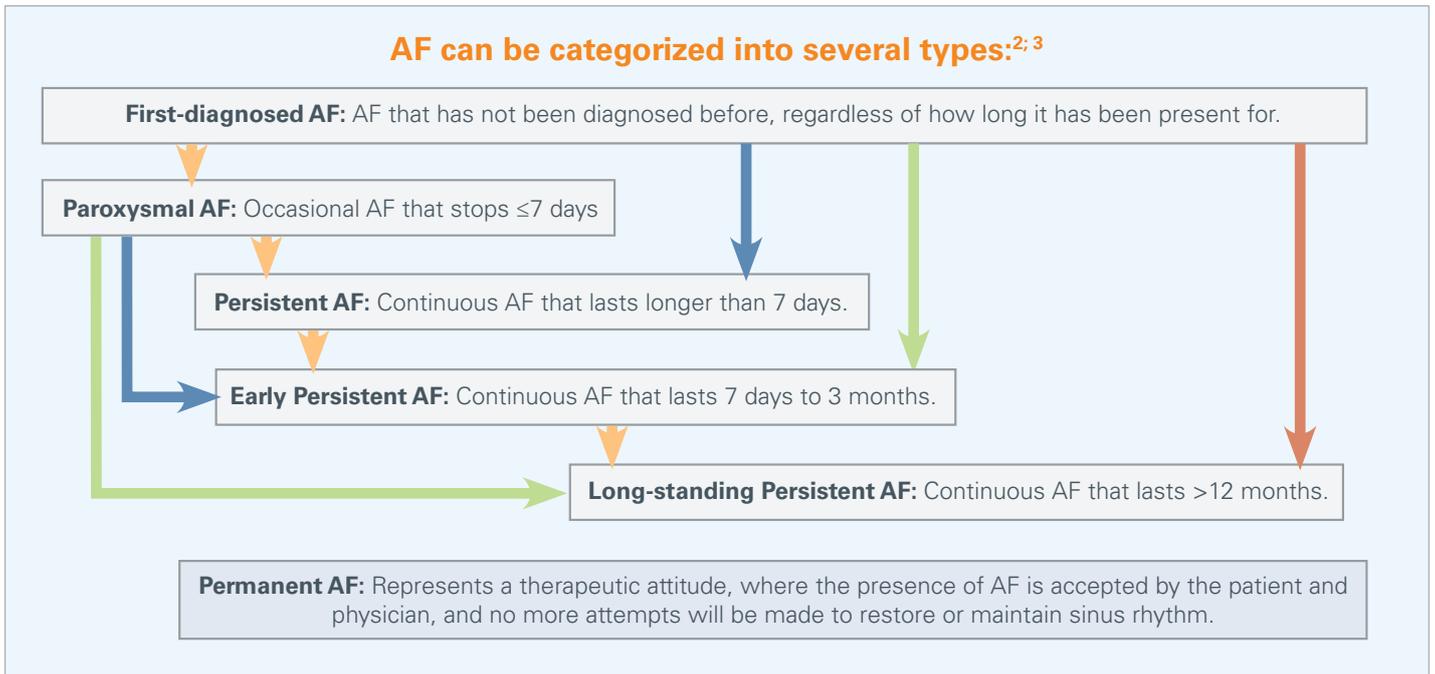
ATRIAL FIBRILLATION

What is Atrial Fibrillation and why is it important?

■ The heart normally contracts in a coordinated manner, with a steady beat (i.e., rhythm) and at a consistent speed (i.e., rate).¹

■ 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 (i.e., atria).¹



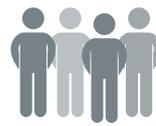


■ Patients may have episodes of AF that fall into one or more of the above categories; patients are categorized based on their most frequent pattern of AF.^{2,3}

■ Early detection and diagnosis of AF may help improve patient outcomes, since long history and duration of AF have been associated with recurrence.⁴⁻⁷



15%-30%
OF PATIENTS
EXPERIENCE
NO SYMPTOMS
(ie, silent AF)⁸



PAROXYSMAL AF

1 in 5
PATIENTS
PROGRESS
IN 1 YEAR⁹⁻¹²



PERSISTENT AF

Patients with AF have an increased risk for life-threatening complications and other diseases:¹³

5x Increase heart failure 

2.4x Increase stroke 

2x Increase cardiovascular mortality 

■ AF worsens quality of life for patients, which can be burdensome to caregivers.¹⁴⁻¹⁹

■ AF increasingly places a **critical financial burden** on the healthcare system, costing **€660-€3,286 million** annually across European countries.²⁰⁻²⁴

AF is a new millennium epidemic that affects millions of lives, mostly affecting the middle-aged and elderly.

OVER 11M PEOPLE AFFECTED IN EUROPE

How common is AF?

AF is the most common type of cardiac arrhythmia, affecting over 886,000 new people each year in Europe.²⁵

■ Over **1 Million people suffer with AF** in each of France, Germany, Italy, and the UK.²⁵

■ The number of **new people each year with AF varies by region**, from nearly 78,000 in France to over 116,000 in Germany.²⁵



Prevalence and Incidence of AF & Atrial Flutter in Europe

Total number of people with AF & AFL (Prevalence)

Region	Total number of people with AF & AFL (Prevalence)	Rate* for AF & AFL per 100,000 of the population
EUROPE**	11,062,761	788
FRANCE	1,001,409	814
GERMANY	1,453,541	833
ITALY	1,014,483	753
UNITED KINGDOM	1,232,144	1094

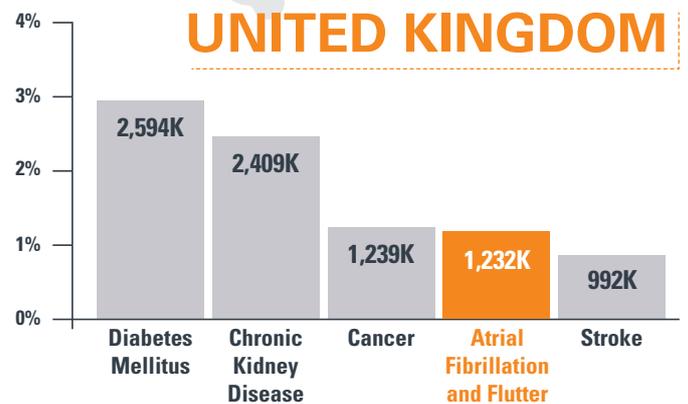
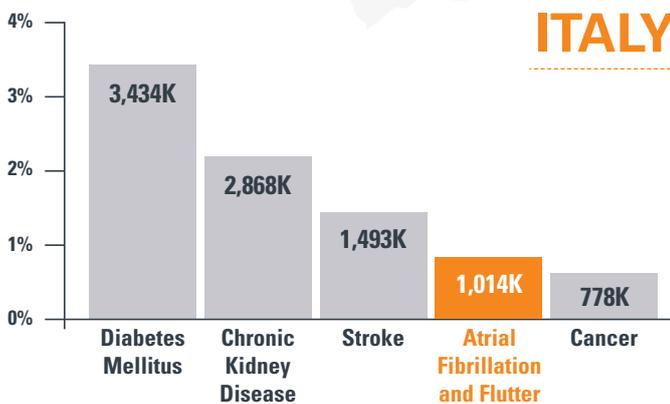
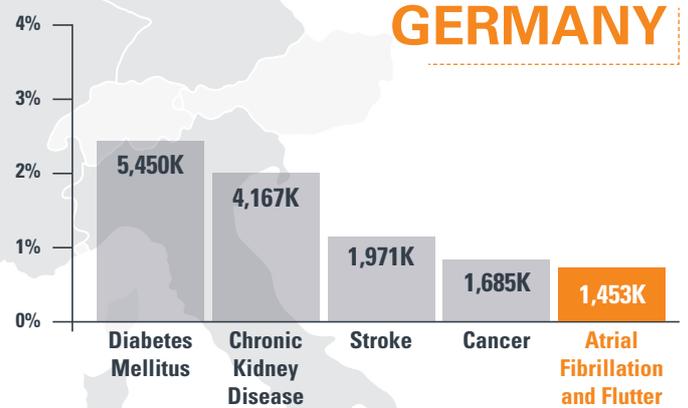
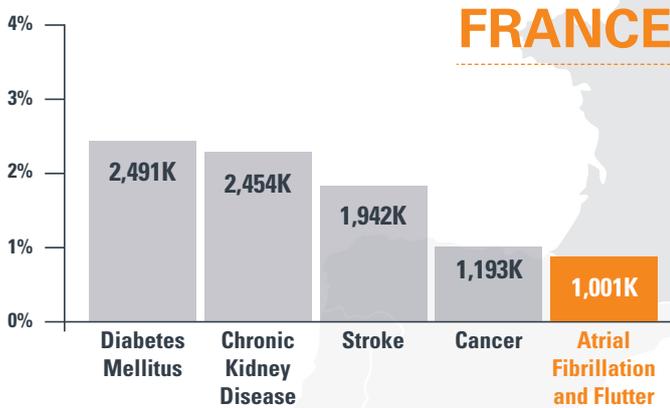
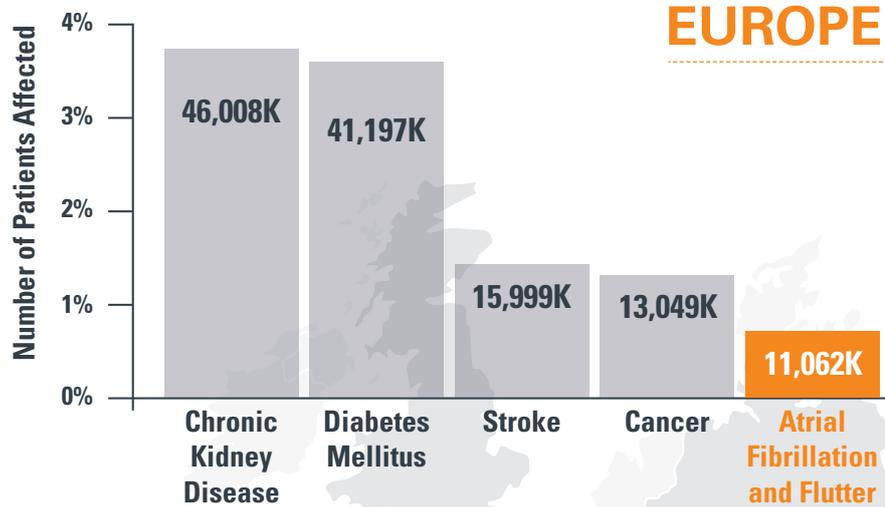
Number of new people diagnosed with AF & AFL per year (Incidence)

Region	Number of new people diagnosed with AF & AFL per year (Incidence)	Rate* for AF & AFL per 100,000 of the population
EUROPE**	886,500	66
FRANCE	77,837	69
GERMANY	116,468	71
ITALY	81,907	68
UNITED KINGDOM	97,555	92

*Age-standardized values.

**Obtained for Europe, part of the Four World Regions category in the Online GBD Tool.
Source: Global Burden of Disease Collaborative Network (2016).

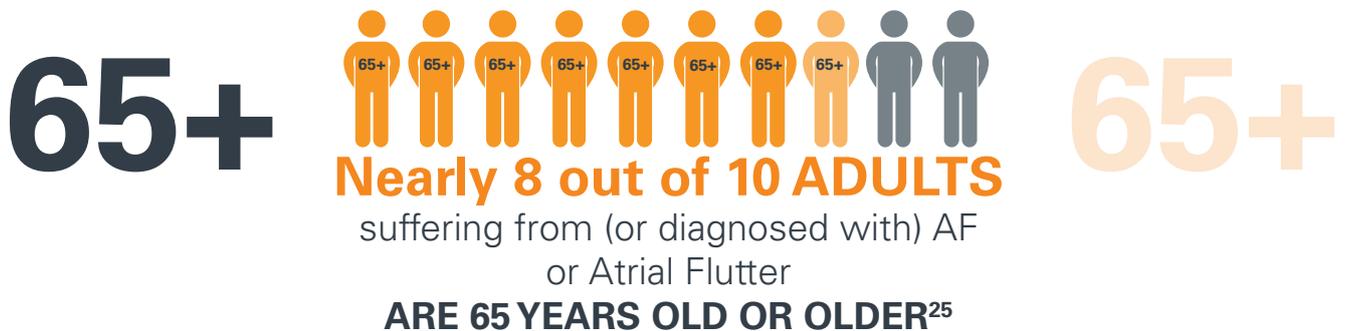
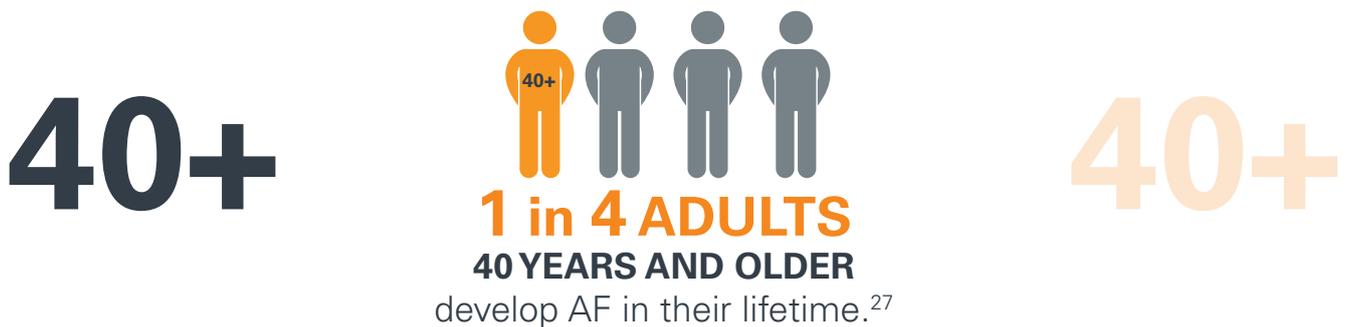
AF is almost as common as stroke and cancer in Europe, France, Germany, Italy, and the United Kingdom.²⁵



DEMOGRAPHICS OF AF

Who is at risk for AF?

AF is a common age-related arrhythmia:^{3; 26; 27} it mostly affects people **40 years old and older** and is more **common in men**.



■ In adults of European descent older than 40 years, men are 13% more likely to develop AF than women during their lifetime.²⁷

TYPES OF AF

Which type of AF is most common?

In Europe, 75% of patients have paroxysmal or persistent AF.

■ PERSISTENT AF IS

2X MORE COMMON

in patients with symptoms than in patients without.²⁸

■ PERMANENT AF IS

3X MORE COMMON

in patients without symptoms than in those with, primarily due to lower use of therapeutic management strategies and treatments.²⁸

Distribution* of AF Types Among European Patients

Type of AF	Patients WITH symptoms	Patients WITHOUT symptoms
PAROXYSMAL	40%	34%
PERSISTENT	46%	24%
PERMANENT**	14%	42%

*Based on reported distribution of AF type in symptomatic patients. proportions were redistributed to include paroxysmal, persistent and permanent.

**Permanent AF reflects a decision regarding the patient's treatment strategy, and does not physiologically differ from other types of AF.

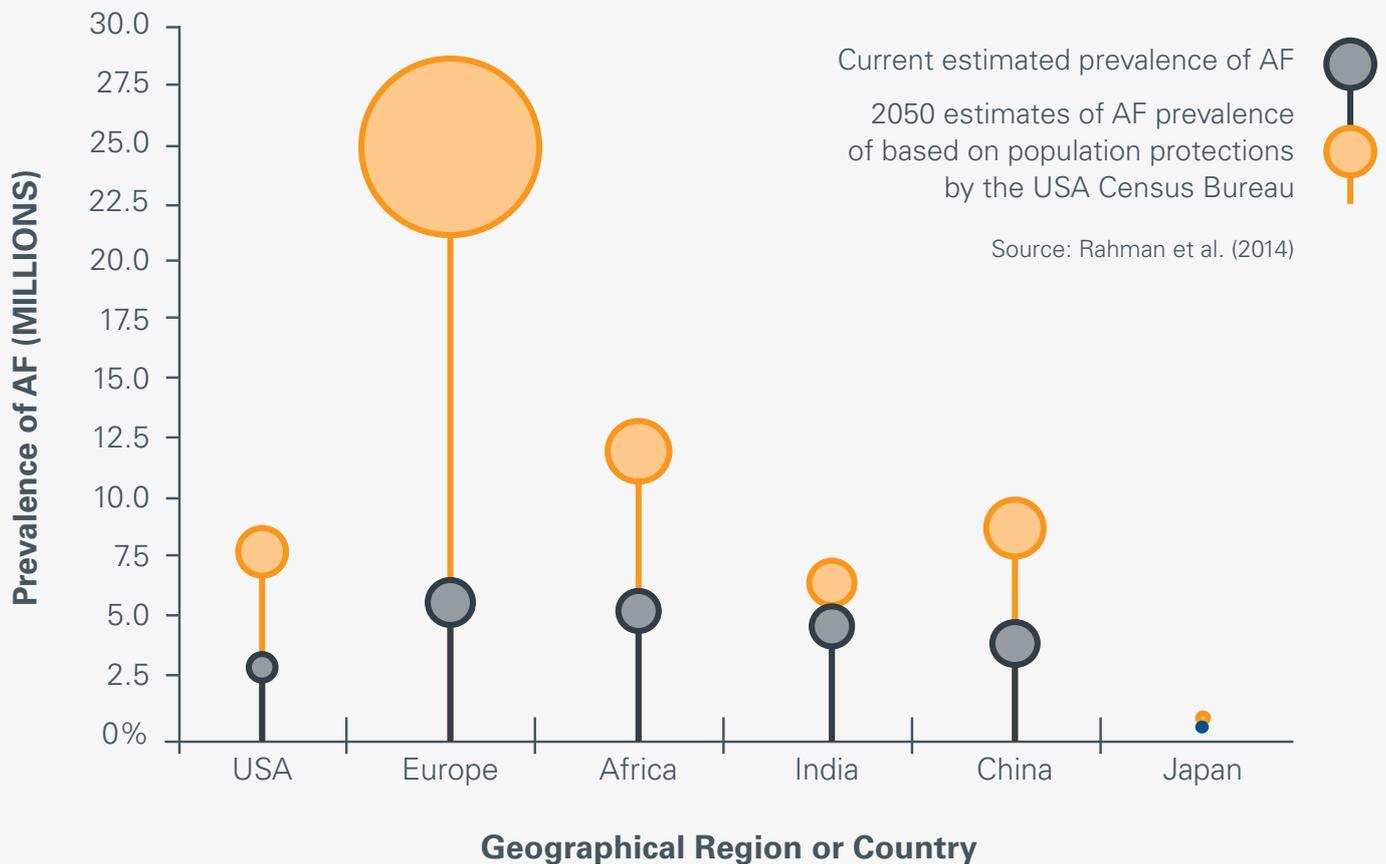
Source: adapted from Boriani et al. (2015)

HOW WILL AF AFFECT EUROPE IN THE FUTURE?

By 2050, Europe is expected to have the most patients with AF compared to other regions.²⁹

BY 2030 THE NUMBER PEOPLE WITH AF IS EXPECTED TO INCREASE UP TO **70%**³¹

- European countries have an aging population that is growing rapidly.³⁰
- By 2030, the number people with AF is expected to increase up to 70%.³¹
- By 2050, Europe is projected to have the **greatest increase in AF** compared to other regions globally.²⁹



With more patients suffering with atrial fibrillation, rate of stroke, hospitalizations, and doctor visits are expected to rise.

- Estimates suggest that over the next 12 years, there will be a 70% increase in the number of people affected by Atrial Fibrillation, **the number of stroke events and medical visits is expected to increase by:**³¹



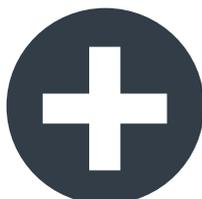
**280K-
340K**

**ADDITIONAL
ISCHEMIC
STROKES**



**3.5-4
MILLION**

**HOSPITALIZATIONS
FOR AF**



**100-120
MILLION**

**OUTPATIENT
VISITS**

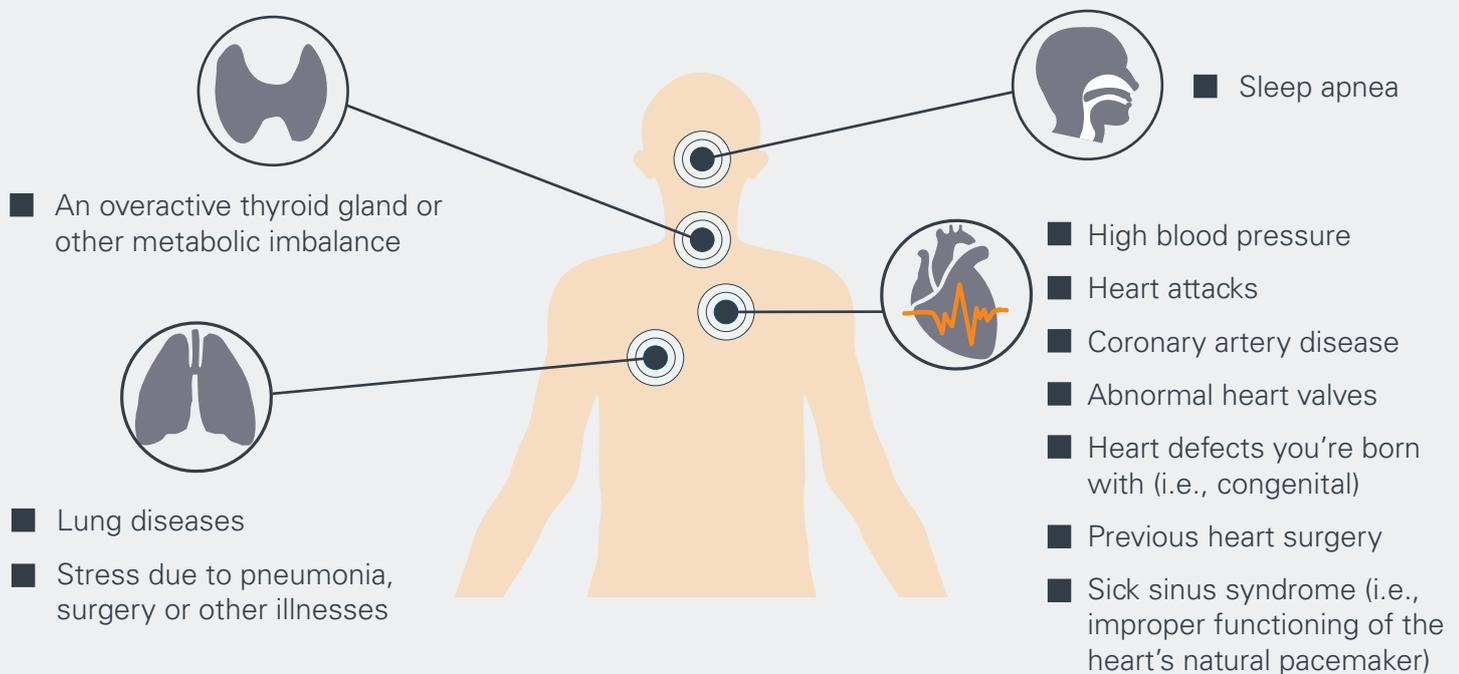
AF develops from structural changes to the heart due to lifestyle, other chronic conditions, and non-modifiable factors.

WHAT CAUSES AF?

- AF is an **irregular and often rapid heartbeat** that occurs when there are extra, uncoordinated electrical signals in the atria.¹

Common causes of AF

Abnormalities or damage to the heart's structure are the most common cause of AF, and this can be caused by:^{2,3,27,32}



Other factors that cause AF:



- Exposure to stimulants, such as medications, caffeine, tobacco or alcohol

WHAT FACTORS LEAD TO AF?

Lifestyle factors, other conditions, and non-modifiable factors increase the risk of developing AF.



LIFESTYLE FACTORS

- Obesity³²⁻³⁵
- Alcohol consumption^{3; 35; 36}
- Risks for cardiovascular disease: smoking, stress, caffeine and other stimulants³
- Activity level^{2; 3; 35}

OTHER CONDITIONS

- High blood pressure³⁵
- Heart failure^{27; 31; 37-40}
- History of heart attack^{27; 41}
- Coronary artery and other heart disease^{27; 33}
- Previous surgery^{42; 43}
- Sleep-disordered breathing (eg, obstructive sleep apnea)^{35; 44}
- Diabetes^{35; 45}

NON-MODIFIABLE FACTORS

- Older age^{3; 46}
- Congenital heart defects⁴⁵
- Family history or other genetic factors^{27; 47; 48}
- Male sex^{3; 27; 46}

The symptoms and clinical consequences of AF negatively impact patient quality of life and increase the risk of mortality.

WHAT ARE THE SYMPTOMS OF AF?

Symptoms of AF disrupt daily life and range from mild to debilitating.^{14; 49-50}
The most common symptoms are:^{8; 31; 51}



65%
PALPITATIONS

50%
FATIGUE

43%
SHORTNESS
OF BREATH

30%
MALAISE



19%
DIZZINESS

12%
ANXIETY

12%
CHEST PAIN

5%
OTHER



OVER
50% of AF PATIENTS
have a reduced ability to exercise⁸

■ The frequency and severity of symptoms varies a lot from patient to patient and, within a patient, symptoms can fluctuate widely over time.⁸

CLINICAL BURDEN

- Patients with AF often experience symptoms that impair functional status, disrupt daily life activities, and impact quality of life.⁴⁹⁻⁵¹



19%
IMPAIRMENT IN
FUNCTIONAL
STATUS^{52*}

25%
DISRUPTION TO
DAILY
ACTIVITIES^{52**}

**UP
TO 47%**
REDUCTION IN
QUALITY
OF LIFE^{52; 53***}

- **Patients who do not** experience symptoms of AF may be at **greater risk** of complications and disease severity due to lack of treatment:



15%-30%
have SILENT AF^{8; 28}



AS MANY AS 1 in 4
PATIENTS are DIAGNOSED
WITH AF AFTER SUFFERING A
STROKE^{3; 8}



**PATIENTS WITH SILENT AF
EXPERIENCE POORER**
general HEALTH and QUALITY OF LIFE
than HEALTHY INDIVIDUALS⁵⁴

With disease progression, patients are more likely to experience:⁵⁵

- **More severe mobility problems**

- **Problems with self-care**

- **Inability to continue regular activities**

- **Increased pain and discomfort**

- **Anxiety and depression**

*Based on functional capacity, as measured using the Goldman Specific Activity Scale, in AF patients (score, 75 [standard deviation (SD) 20]) vs. healthy individuals (score, 93 [SD 11]).

**As measured using the Illness Intrusiveness scale in AF patients (score, 35 [SD 15]) vs. health individuals (score, 28 [SD 19]).

***As measured using the SF-36 QoL scale. Reductions were observed on SF-36 subscales.

HOW DOES AF CHANGE OVER TIME?

AF is typically a progressive disease.



15%-20%
OF PATIENTS WITH
PAROXYSMAL AF

WILL PROGRESS TO

PERSISTENT AF
over 1 year.^{9; 10; 12}

- AF causes remodeling of the heart, making normal heart rhythm more difficult.^{9; 10; 12; 56}
- AF typically progresses from paroxysmal AF, where episodes are intermittent and self-terminating, to long-standing persistent AF, where episodes are continuous and terminate with intervention.³
- At diagnosis, **each decade** of age was associated with **nearly double the risk of disease progression**.⁵⁷
- Patients with silent AF (i.e., without symptoms) may be **more likely to progress or may progress faster** to persistent AF, partly due to a lack of treatment.¹¹
- AF **may also regress** from persistent AF to paroxysmal AF.^{12; 57; 58}

A higher risk of AF progression is associated with:

- | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> ■ Older age⁹ ■ Heart failure⁹ ■ Valvular heart disease^{9; 12; 36} | <ul style="list-style-type: none"> ■ Larger left atrium⁹ ■ Hyperthyroidism¹² | <ul style="list-style-type: none"> ■ Moderate to high alcohol consumption³⁶ ■ Asymptomatic and untreated AF^{11; 59} |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|

- Compared with patients who did not progress, patients who progress from paroxysmal to persistent AF more often experience:⁹

- | | |
|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|
| <ul style="list-style-type: none"> ■ New onset heart failure, or worsening heart failure | <ul style="list-style-type: none"> ■ Thromboembolism |
|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|

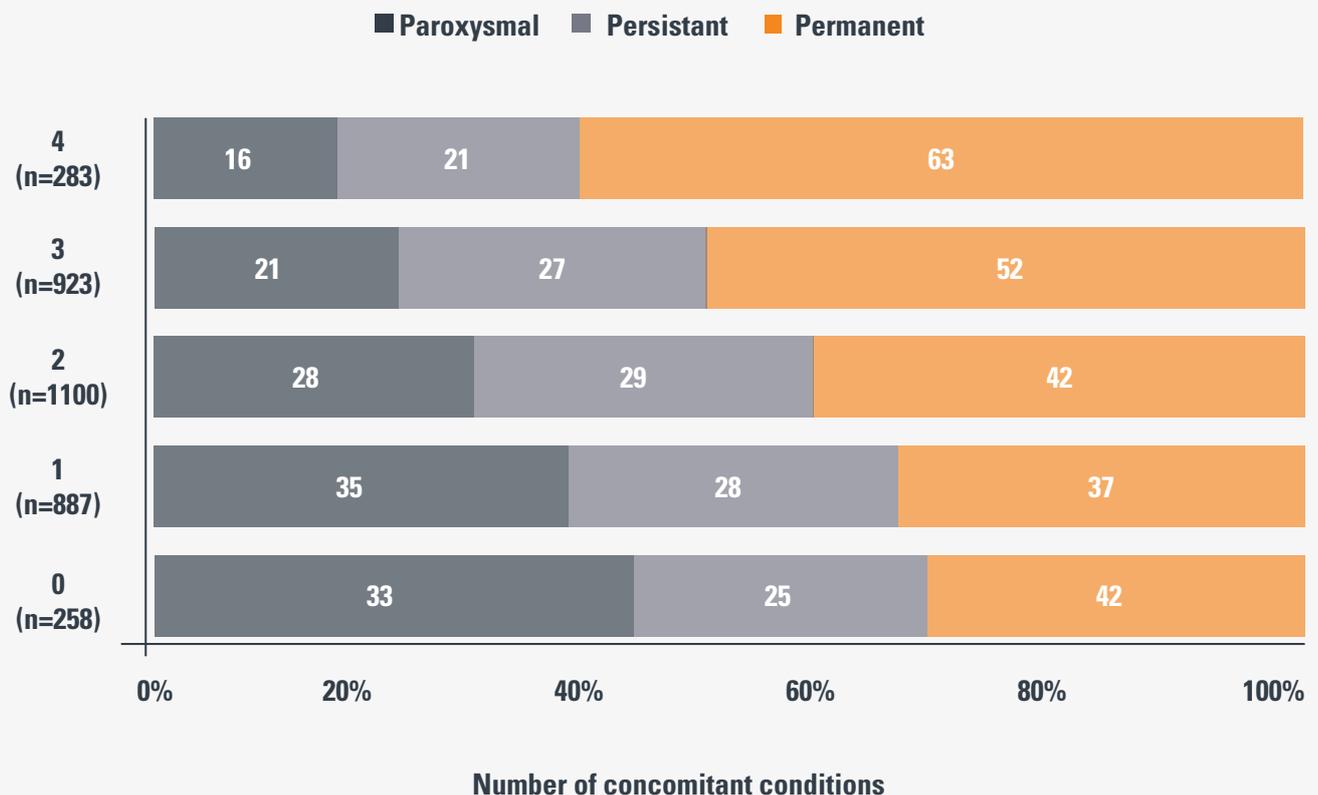
WHAT ARE THE CONSEQUENCES OF AF?

AF increases a patient's risk for life-threatening events and conditions, including stroke, heart failure, and death.



AS MANY AS
80%
OF AF PATIENTS
have **ANOTHER**
condition
or **CARDIAC**
DISEASE.³¹

- The seriousness of AF is critically misunderstood:
 - **45% of patients believe** it is not a life-threatening condition⁶⁰
- Most patients with AF have other serious conditions and complications:
 - **One-third have at least 3 other conditions.**^{31; 61}
 - **63% with 4 other conditions have permanent AF.**⁶¹



Source: Meinertz et al. (2011)

AF increases the risk of:^{31; 41; 44}

- Mortality:**
 AF is independently associated with a significantly greater risk of mortality.
- Stroke:**
 a serious complication of AF that is associated with long-term disability and mortality.
- Heart attack:**
 a serious complication of AF that also significantly increases the risk of stroke and mortality.
- Heart failure and left ventricular dysfunction:**
 a common complication of AF that increases the risk of mortality and lengthens hospital stay.
- Cognitive dysfunction or vascular dementia:**
 a complication of AF that causes a decline in memory and thinking skills, which can interrupt daily life and independent function.
- Obstructive sleep apnea:**
 is common in AF patients and may increase the risk of stroke, heart failure, and AF recurrence.

Increased risk* of morbidity and mortality in patients with AF.^{13; 35; 62}



142%
ANY STROKE

133%
ISCHEMIC STROKE

40%
DEMENTIA OR COGNITIVE IMPAIRMENT



399%
HEART FAILURE

103%
CARDIOVASCULAR MORTALITY

96%
MAJOR CARDIOVASCULAR EVENTS

61%
ISCHEMIC HEART DISEASE



64%
CHRONIC KIDNEY DISEASE



46%
ALL-CAUSE MORTALITY



31%
PERIPHERAL ARTERIAL DISEASE

*Relative increased risk based on the relative risk of morbidity and mortality when compared to patients without AF.
 Source: Boriani and Proietti (2017), Odotayo et al. (2016), Kalantarian et al. (2013)

WHAT IS THE RISK OF MORTALITY?

AF is independently associated with a significantly greater risk of mortality.



AF PATIENTS HAVE A **46%** GREATER RISK of death than patients WITHOUT AF.^{13; 35}

THE RATE OF MORTALITY IS **40%** in NEW AF PATIENTS after DIAGNOSIS³¹

- Even without the presence of other conditions, patients with AF have a 46% greater risk of mortality than patients without AF, based on pooled estimates from studies conducted in the last 5 years.^{13; 35}
- In a single year, **approximately 6%** of AF patients die.⁵¹
 - About 70% of these deaths were directly related to cardiovascular complications.⁵¹
- The rate of mortality is 40% in new AF patients after diagnosis and 60% within 5-10 years.³¹
- **Lack of symptoms increases the risk of mortality more**, with an added 2x risk compared to patients with symptoms.²⁸

Risk of death in patients with AF is increased by:^{28; 63}

■ Older age

■ Congestive heart failure

■ Chronic kidney disease

■ Diabetes

■ Prior stroke or transient ischemic attack

■ History of bleeding

WHAT IS THE RISK OF STROKE?

Stroke is a serious complication of AF that is associated with long-term disability and mortality.^{64; 65}

■ **What is stroke caused by?**

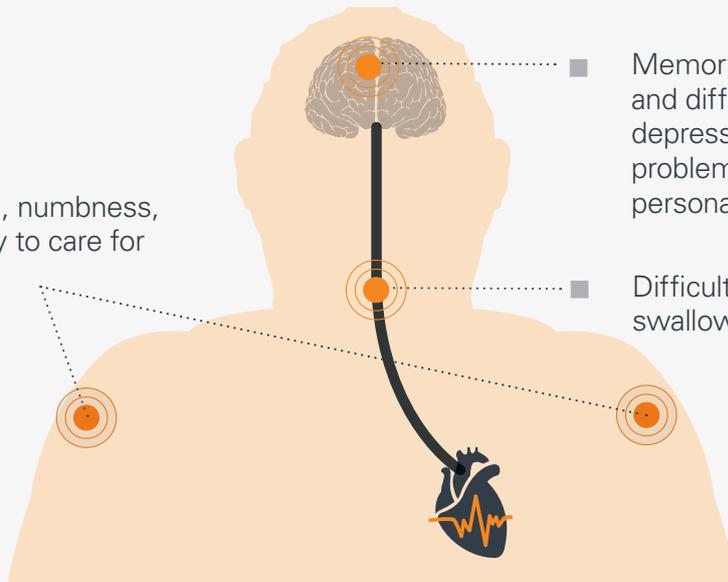
Uncoordinated contractions during AF can lead to clot formation within the heart that, when pumped out of the heart, can block an artery of the brain, resulting in stroke.⁶⁴

■ **What does stroke cause?**^{64; 65}

■ Paralysis, pain, numbness, reduced ability to care for oneself

■ Memory loss; cognitive impairment and difficulty understanding language; depression and other emotional problems; changes in behavior, personality, and independence

■ Difficulty speaking or swallowing



20%-30%
OF ALL STROKES
OCCUR IN
AF PATIENTS^{3; 31}

142%
INCREASED
RISK OF ANY
STROKE¹³

133%
INCREASED
RISK OF ISCHEMIC
STROKE¹³

- Patients with AF have a significantly greater risk of any stroke and ischemic stroke than those without AF, based on pooled estimates from studies conducted in the last 5 years.¹³
- The annual rate of stroke in AF patients is high:

2% for **ISCHEMIC STROKE**³¹

0.2% for **HEMORRHAGIC STROKE**³¹

- Undiagnosed silent AF is a likely cause of some strokes with an undetermined source.^{3; 11}
- Highest level of evidence suggests that patients with persistent AF have a higher risk of stroke than those with paroxysmal AF, whether treated with OACs or not.⁶⁶

In patients with AF, the risk of stroke is increased by:



■ Older age^{3; 67}



■ Chronic kidney disease⁶⁷



■ Prior stroke, transient ischemic attack, or embolism^{3; 67; 68}



■ Vascular disease and high blood pressure^{3; 68}



■ Female sex^{3; 67}



■ Congestive heart failure^{3; 67}



■ Diabetes^{3; 67; 68}

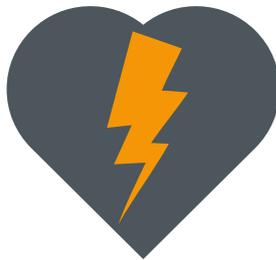


■ Obstructive sleep apnea⁴⁴

- Stroke in patients with AF is more severe and debilitating than in patients who do not have AF.^{69; 70}
 - Immediately after a stroke, patients with AF have **greater neurologic impairment and functional disability** than patients without AF.⁶⁹
 - Up to 3 months after a stroke, patients with AF were **significantly more disabled** than patients without AF.⁶⁹

WHAT IS THE RISK OF A HEART ATTACK?

Heart attack is a serious complication of AF that also significantly increases the risk of stroke and mortality.



THE RATE OF
HEART ATTACKS IS

0.4%-2.5%

PER YEAR IN
AF PATIENTS.^{3; 41}

- Uncoordinated contractions during AF can **lead to clot formation within the heart** that, when pumped out of the heart, can block an artery of the heart, resulting in heart attack.^{1; 41; 64}
- Heart attack is even more common in patients with AF **who also have other cardiovascular diseases** such as coronary artery disease, peripheral vascular disease, and heart failure.⁴¹
- Compared with patients without AF, those with AF who suffer a heart attack have worse medical outcomes.⁷¹
 - AF patients are more likely to have **a subsequent heart attack, ischemic stroke, or die.**⁷¹

WHAT IS THE RISK OF HEART FAILURE?

Heart failure is a common complication of AF that increases the risk of mortality and lengthens hospital stay.



2X
HIGHER RISK
of mortality
IN NEW AF
PATIENTS
WITH HEART
FAILURE.³¹

- AF and heart failure are both associated with a greater likelihood of death. New AF patients with heart failure have a 2x higher risk of mortality than with patients without AF.³¹
- Left ventricular (LV) dysfunction is an important risk factor for heart failure that is commonly caused or worsened by AF.^{3;38}

20%-30% OF PATIENTS WITH AF
HAVE LV DYSFUNCTION³

- Heart failure coexists with AF in **22%-42%** of AF patients.³¹



25%
OF HEART FAILURE
PATIENTS WILL
DEVELOP AF
WITHIN 5 YEARS.^{39; 40}



15%
OF AF PATIENTS
WILL DEVELOP
HEART FAILURE
WITHIN 5 YEARS.^{39; 40}

- The risk of developing heart failure for patients with AF varies by patient demographics.

11X  **GREATER RISK IN
WOMEN³¹**

(Background shows a row of 10 female icons, with the first one highlighted in dark blue.)

3X  **GREATER RISK IN
MEN³¹**

(Background shows a row of 3 male icons, with the first one highlighted in dark blue.)

- Patients with AF who also have heart failure tend to have **longer hospital stays** than patients who have only AF or only heart failure.^{37; 38}

WHAT IS THE RISK OF COGNITIVE DYSFUNCTION?

Cognitive dysfunction is a complication of AF that causes a decline in memory and thinking skills, which can interrupt daily life and independent function.

■ Decline in cognitive function and vascular dementia **severely impacts patients' quality of life**, including the ability to learn, function independently, and perform important daily and self-care tasks.^{72; 73}

■ In patients with AF, **cognitive decline and vascular dementia may arise** from poor blood supply to the brain and the equivalent of "mini-strokes" that lack symptoms.^{31; 72; 74}



18% OF AF PATIENTS MAY HAVE COGNITIVE DYSFUNCTION OR DEMENTIA.^{31; 75; 76}



UPTO 40% INCREASED RISK OF COGNITIVE DECLINE, WHICH MAY OCCUR AT A FASTER RATE THAN IN NON-AF PATIENTS^{13; 62; 74; 77}

■ Cognitive dysfunction and vascular dementia **can even develop in AF patients receiving oral anticoagulation therapy.**^{3; 78}

HOW DOES OBSTRUCTIVE SLEEP APNEA IMPACT AF?

Obstructive sleep apnea is common in AF patients and may increase the risk of stroke, heart failure, and AF recurrence.



32%-39%

**OF PATIENTS WITH AF
HAVE OBSTRUCTIVE
SLEEP APNEA²**

- Obstructive sleep apnea **may lead to AF** by causing changes to the size and shape of the heart.⁴⁴
- AF and obstructive sleep apnea **share several risk factors**, including obesity, heart failure, and hypertension.⁴⁴
- The severity of obstructive sleep apnea may be linked to AF prevalence and progression.²
- Obstructive sleep apnea may increase the risk of stroke, heart failure, and AF recurrence, particularly after treatment.^{2; 3; 79-80}

AF worsens the quality of life for patients, placing additional pressure on caregivers.

HOW LONG DO PEOPLE LIVE WITH AF?

AF is a life-long chronic disease and patients are burdened with frequent and repeated episodes over their lifetime.

IN AN ITALIAN REGISTRY OF PATIENTS WITH AF,

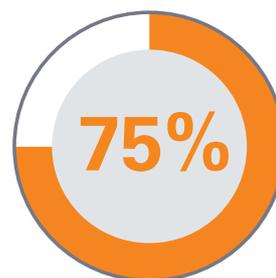


**13% had AF for <1 year;
30% for 5-10 years;
and 18% for >10 years.^{31; 75}**

■ Recurrence of AF is frequent, with ≥ 2 recurrences occurring in:



**OF AF PATIENTS
DURING 1 YEAR³¹**



**OF PATIENTS
DURING 5 YEARS³¹**

WHY DO PEOPLE WITH AF SEEK MEDICAL TREATMENT?

AF symptoms and repeated recurrence increase unplanned medical visits and hospitalizations.



SYMPTOMS OCCUR IN 69% PATIENTS WITH AF, EVEN IF THEY ARE BEING TREATED^{8; 81}

- Symptoms are a major reason why patients with AF seek medical attention.⁸
- Clinical decision-making can be challenging because symptoms related to AF can differ a lot between patients and within patients at different time points.⁸
- AF and its related symptoms are a major therapeutic challenge and burden to healthcare systems.⁸

2/3 of

**EMERGENCY ROOM VISITS
for SYMPTOMS LEADING
to AF DIAGNOSIS result in**

**HOSPITAL
ADMISSIONS⁸**

HOW DOES AF IMPACT PATIENT QUALITY OF LIFE?

Quality of life is significantly poorer in patients with AF than patients with other cardiovascular conditions.

■ The Short Form 36 (SF-36) Health Survey is the most common questionnaire used to measure patient quality of life.

■ The questionnaire measures the impact on physical and mental health using 8 subscales:⁸²

PHYSICAL COMPONENT SUBSCALES

PHYSICAL FUNCTION

ROLE PHYSICAL

BODILY PAIN

GENERAL HEALTH

MENTAL COMPONENT SUBSCALES

MENTAL HEALTH

ROLE EMOTIONAL

SOCIAL FUNCTION

VITALITY

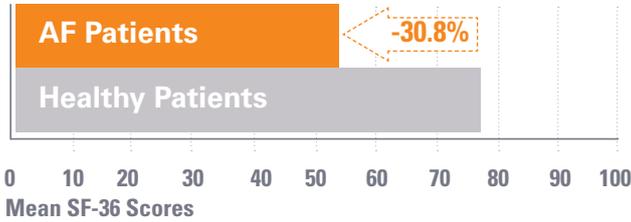
■ Lower total scores on each subscale indicate poorer quality of life.

■ Patients with AF have **significantly poorer quality of life** than the general population in several SF-36 subscales, with reductions of **up to 47%**.^{14-17; 52}

Comparison of Quality of Life between AF Patients and the General Population

SF-36 Quality of Life Subscales

General Health



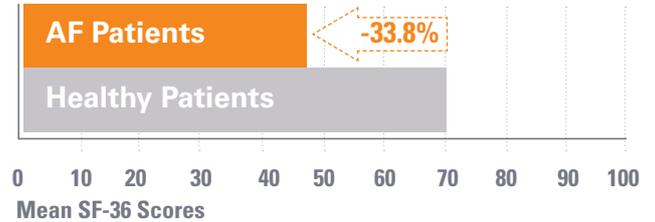
Physical Functioning



Role Physical



Vitality



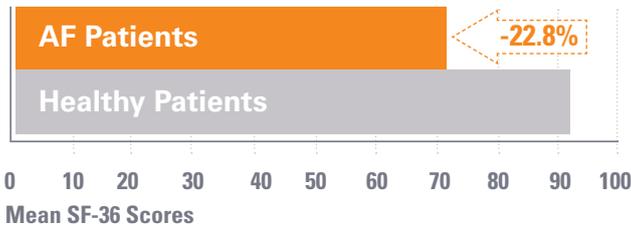
Mental Health



Role Emotional



Social Functioning



Bodily Pain



Abbreviations: AF = atrial fibrillation; SF-36 = Short Form 36 Quality of Life Questionnaire
Source: Dorian et al. (2000)⁵²

Healthy Patients (n=47) AF Patients (n=152)

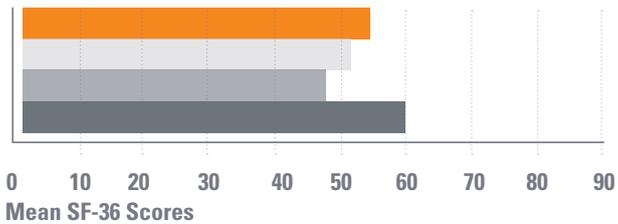
Patients with AF or other cardiovascular diseases such as coronary artery disease, congestive heart failure, and history of heart attack have **similar reductions in quality of life.**^{15; 52}

Comparison of Quality of Life between Patients with AF and other Cardiovascular Conditions

SF-36 Quality of Life Subscales

■ AF Patients (n=152)
 ■ PTCA Patients (n=69)
 ■ CHF Patients (n=216)
 ■ Post-Heart Attack Patients (n=69)

General Health



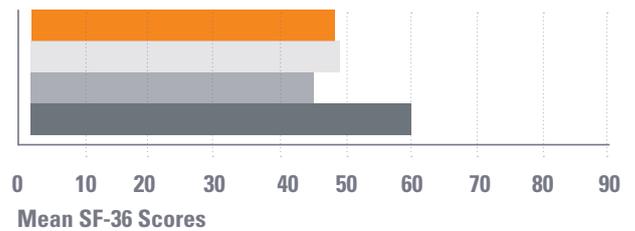
Physical Functioning



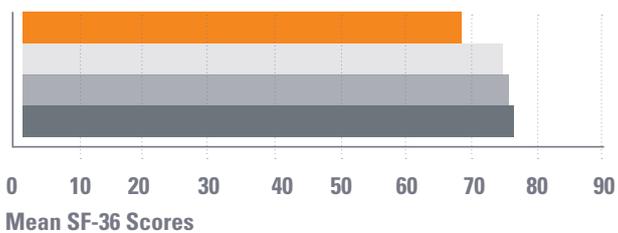
Role Physical



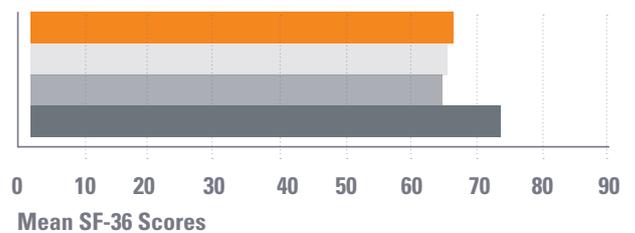
Vitality



Mental Health



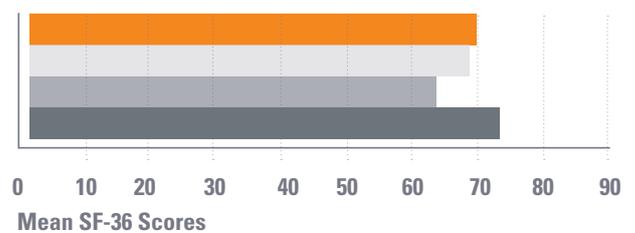
Role Emotional



Social Functioning



Bodily Pain



Abbreviations: AF = atrial fibrillation; CHF = congestive heart failure; PTCA = percutaneous transluminal coronary angioplasty in patients with coronary artery disease
 Source: Dorian et al. (2000)¹²

AF type has been associated with perceived symptom severity and reductions in quality of life.¹⁴

- Patients with intermittent AF (paroxysmal and early persistent AF) **had worse impairment of quality of life** than those with chronic AF (persistent and permanent AF).¹⁴

In patients with AF, factors that may impair quality of life include:



■ **Greater disability**⁸³



■ **High number of prescribed drugs (7 or more)**⁸³



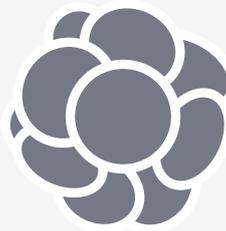
■ **Greater number of visits to emergency department**⁵⁶



■ **Greater number of symptomatic episodes**⁵⁶



■ **Increased anxiety and the perception of more severe palpitations**^{14; 56; 84}



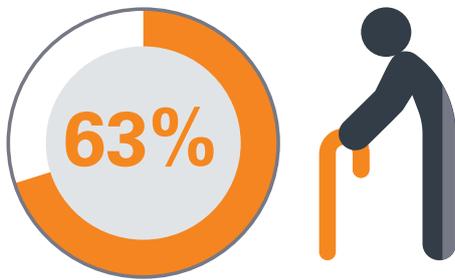
■ **Disease progression**⁵⁵



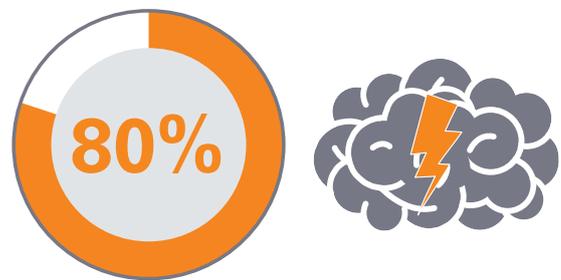
■ **Major complications and other conditions** such as stroke, heart failure, obstructive sleep apnea, chronic obstructive pulmonary disease, and coronary artery disease^{55; 85}

HOW DOES AF IMPACT FAMILY MEMBERS?

Caring for family members with AF can be burdensome. Some form of caregiver assistance is required in:^{19; 86}



OF ELDERLY AF PATIENTS⁸⁶



OF PATIENTS RECOVERING FROM STROKE¹⁹

■ AF patients require caregiver assistance for several activities of daily living, including:⁸⁷

- **Opening** medication packaging
- **Assisting** with activities of daily living due to tiredness experienced due to AF
- **Assisting or confirming** correct dosage of medication
- **Monitoring** for signs of bleeding
- **Driving** to the primary care physician or anticoagulation clinic for regular monitoring
- **Ensuring adherence** to any dietary restrictions

- Caregivers of AF patients experience considerable changes to their daily lives, including:¹⁸



**Disrupted
schedules**



**Financial
burden**



**Lack of
family support**



**Health
problems**

- Caregivers experience considerable disruption to their schedules and are at high risk of burnout when:^{18; 19}

- Patients are **frail, sick, or disabled**¹⁸

- Patients have low **quality of life**¹⁹

- Patients have had or are at **high risk of stroke**^{18; 19}

- Patients have low level of **independence**¹⁹

- Provide care for **long hours** (e.g., >4 hrs/week)^{18; 19}

**>40% OF STROKE PATIENTS
RECEIVING CARE**

**NEED ANOTHER caregiver by the
THIRD MONTH of
RECOVERY.**¹⁹

- Burden to caregivers may lead to less adequate patient support, physical and emotional stress, caregiver burnout, and suboptimal patient outcomes.⁸⁷

HOW DOES STROKE IMPACT QUALITY OF LIFE?

The occurrence of stroke can have a devastating impact on patient quality of life and the ability to perform daily activities.

- Stroke can cause significant impairment in physical, psychological, and social function, and can reduce a patient's ability to carry out routine activities.⁸⁸
- Limitations after a stroke include:⁸⁸

- Paralysis
- Depression
- Personality changes
- Problems with communication
- Anxiety
- Memory loss
- Cognitive impairment



STROKE in patients with AF IS MORE SEVERE AND DEVASTATING than in patients who do not have AF⁶⁹⁻⁷⁰

30% OF STROKE PATIENTS WILL HAVE A SECOND STROKE⁸⁹

- Patients who experience a stroke are at risk of suffering a second stroke.⁸⁹
 - In stroke patients, the risk of a second stroke is nearly 9x higher than the risk of stroke in the general population.⁸⁹

HOW DOES STROKE TREATMENT AFFECT QUALITY OF LIFE?

Oral anticoagulant therapy is a psychological, logistical, and therapeutic challenge for patients and their physicians.

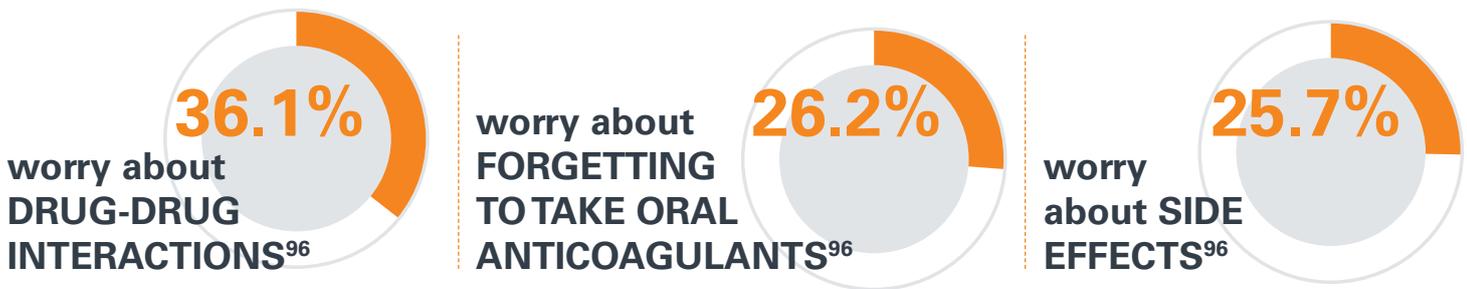
■ Oral anticoagulation therapy reduces the risk of stroke and prolongs life, **but increases the risk of bleeding** in patients with AF.⁹⁰⁻⁹³

■ Oral anticoagulation therapy can be **burdensome** to patients, as it requires:

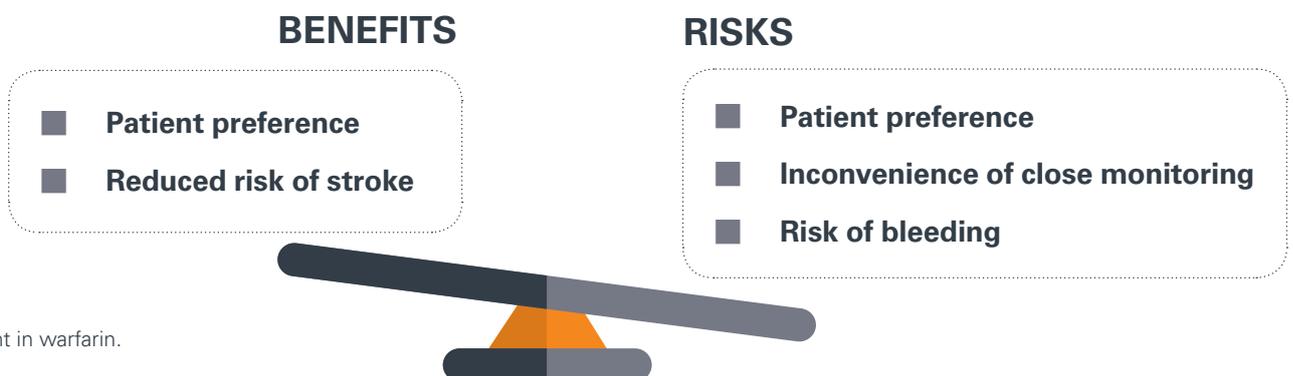
■ **FREQUENT AND REGULAR VISITS**
to monitor and optimize dosage^{*72; 94; 95}

■ **CHANGES TO PATIENT BEHAVIOR AND LIFESTYLE**
that disrupt daily activities and negatively impact quality of life.⁹⁴⁻⁹⁵

■ Common concerns for AF patients on oral anticoagulants such as warfarin:



■ Prescription of oral anticoagulants requires physicians to weigh the **benefit of stroke prevention** against the **risk of bleeding**, as well as consider the **inconvenience of close monitoring and patient preference**.⁹⁷⁻⁹⁸



*For patient in warfarin.

HOW DOES AF TREATMENT AFFECT QUALITY OF LIFE?

Pharmaceutical treatment for AF carries risks of serious side effects and may increase patient anxiety and worsen quality of life.

■ Antiarrhythmic drugs for managing AF have many side effects, including **drug-drug interactions and irregular heartbeats** that cannot be distinguished from AF.^{3; 99}

■ Concern over side effects may contribute to **patient anxiety**, which reduces quality of life.^{14; 56; 84; 96}

Safety Risks Associated with Pharmaceutical Treatment of AF – Rate Control Drugs

DRUGS

- Metoprolol
- Bisoprolol
- Atenolol
- Verapamil
- Diltiazem
- Digoxin
- Digitoxin

POTENTIAL SIDE EFFECTS

- Lethargy
- Headache
- Swelling in the lower limbs
- Upper respiratory tract symptoms
- Gastro-intestinal upset
- Malaise
- Dizziness
- Blurred vision
- Rash

POTENTIAL ADVERSE EVENTS

- Slowed heartbeat
- Blocked electrical signals in the heart
- Low blood pressure
- Sudden narrowing of airways in the lungs
- Death

Safety Risks Associated with Pharmaceutical Treatment of AF – Rhythm Control Drugs

- Flecainide
- Amiodarone
- Propafenone
- Ibutilide
- Vernakalant

- Low blood pressure
- Atrial flutter
- Increased risk of ventricular tachycardia
- Inflammation of the veins

- Slowed heartbeat
- Blocked electrical signals in the heart
- Pulmonary fibrosis
- Heart failure

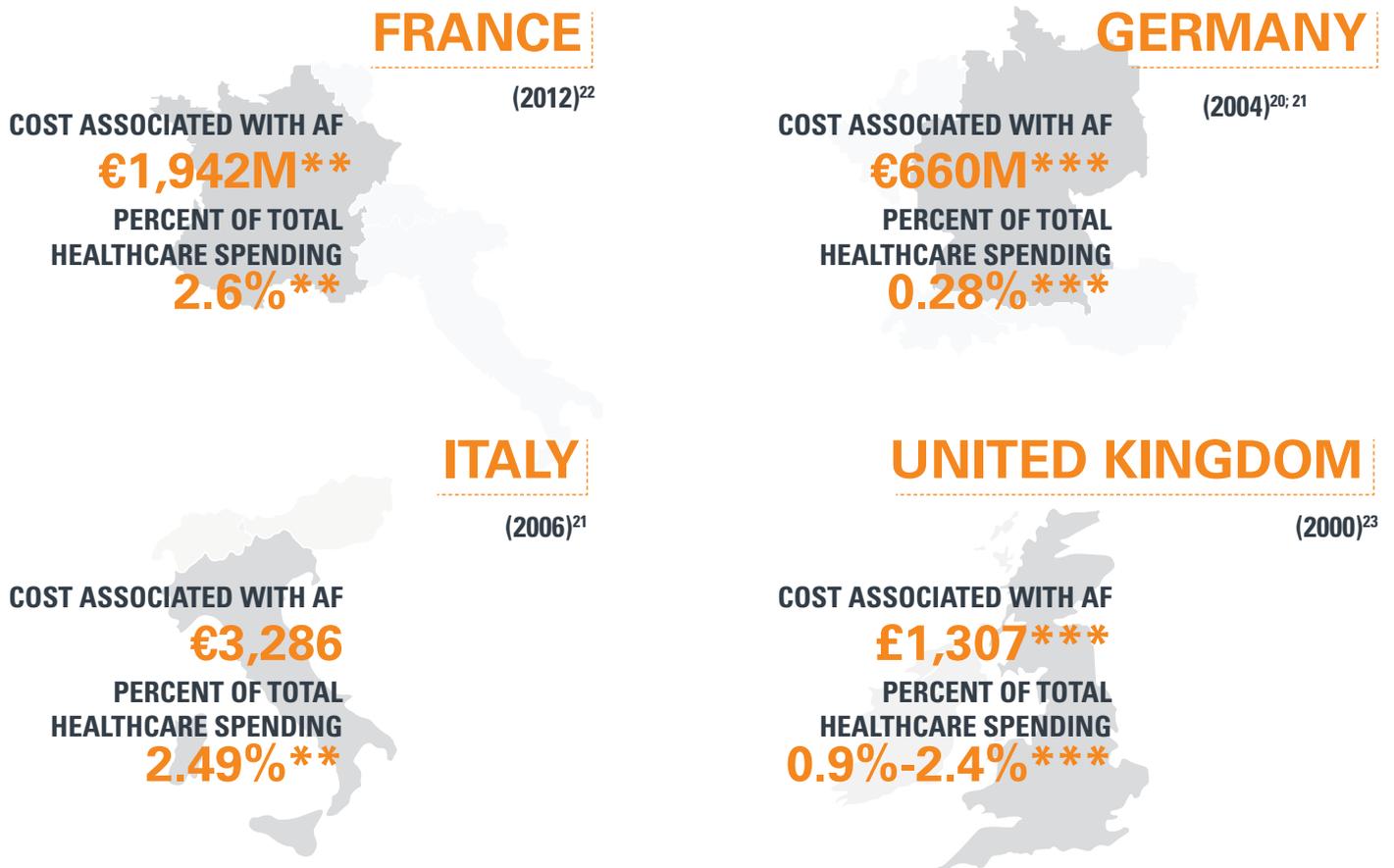
AF increasingly places a critical financial burden on healthcare systems.

WHAT IS THE TOTAL COST OF AF TO NATIONAL HEALTHCARE SYSTEMS?

It is estimated that up to 2.6% of total annual health care expenditure is associated with AF in European countries.

- The national economic burden of AF is high and varies across European countries.^{21; 100; 101}
- The total healthcare costs of AF account for **0.28% to 2.6% of total healthcare spending** in European countries.^{3; 21-23; 100*}

Annual National Healthcare Costs of AF



*Based on limited country data reporting.

**Based on in-patient and rehabilitation costs to hospitals for AF patients hospitalized for cardiovascular reasons. The study noted exclusion of minor cardiovascular complications, community consultation, and prescription; as such, these costs do not represent the total cost in France.

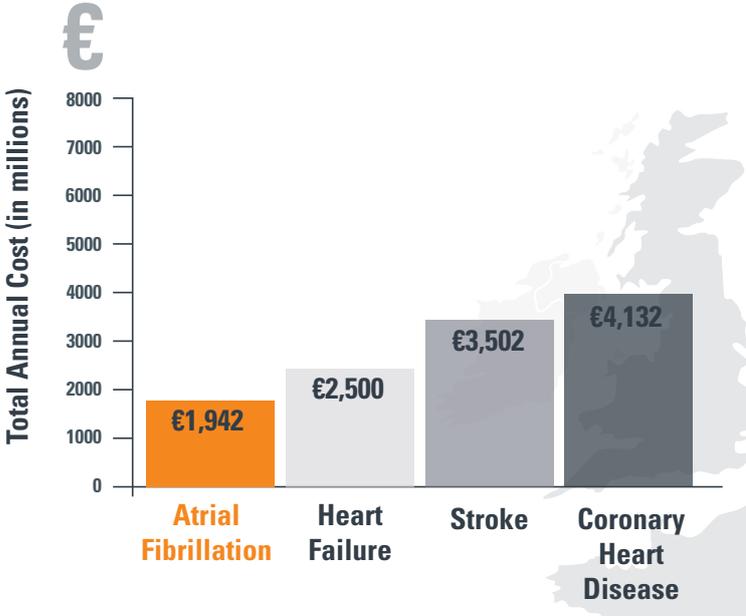
***Based on direct costs.

ECONOMIC BURDEN

- The high cost of AF is largely due to **hospitalizations and complications** such as stroke.^{21; 23}
- **National healthcare costs for AF are similar** to those for other cardiovascular diseases.^{20; 22; 23; 102-106}

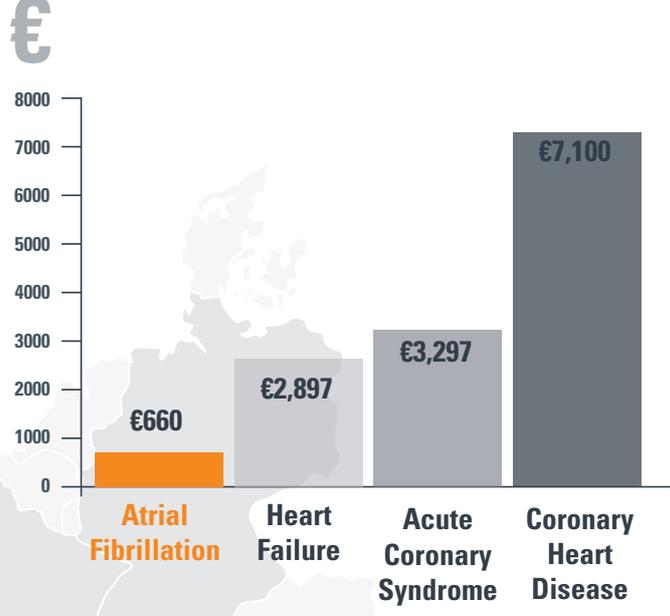
FRANCE

(Cost Year 2012/2013)



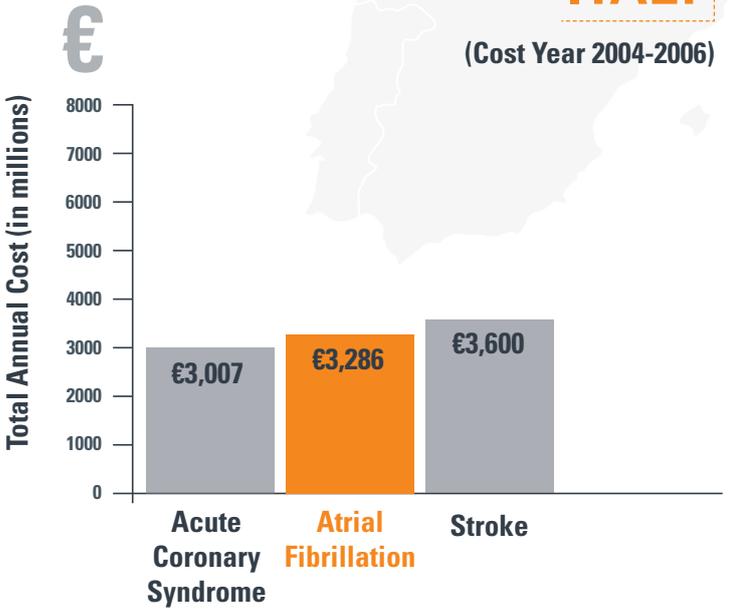
GERMANY

(Cost Year 2004-2006)



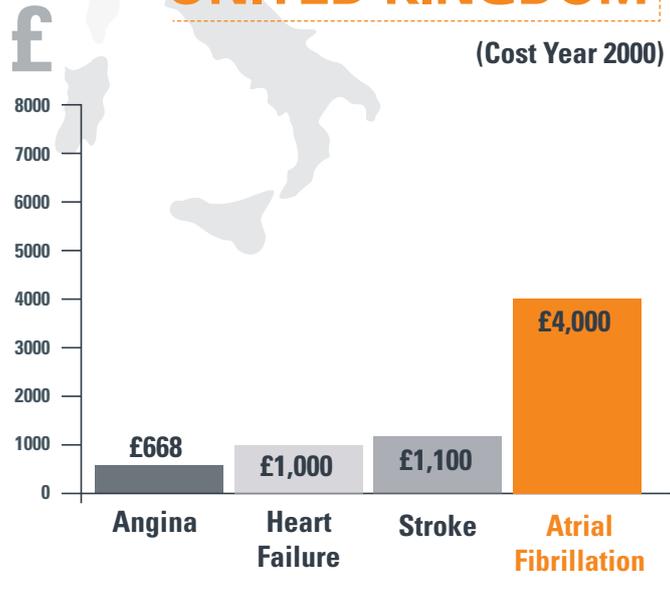
ITALY

(Cost Year 2004-2006)



UNITED KINGDOM

(Cost Year 2000)



WHAT ARE THE DIRECT AND INDIRECT COSTS OF AF?

Direct and indirect costs for the management of AF are highly variable across European countries.

■ Costs for AF management can be divided into 2 groups:

DIRECT COSTS

- Hospitalization
- Outpatient and Physicians Visits
- Prescriptions
- Laboratory Testing
- Long-term Care

INDIRECT COSTS

- Work Productivity Losses
- Support Provided By Caregivers

■ Direct costs of AF are high, accounting for*:



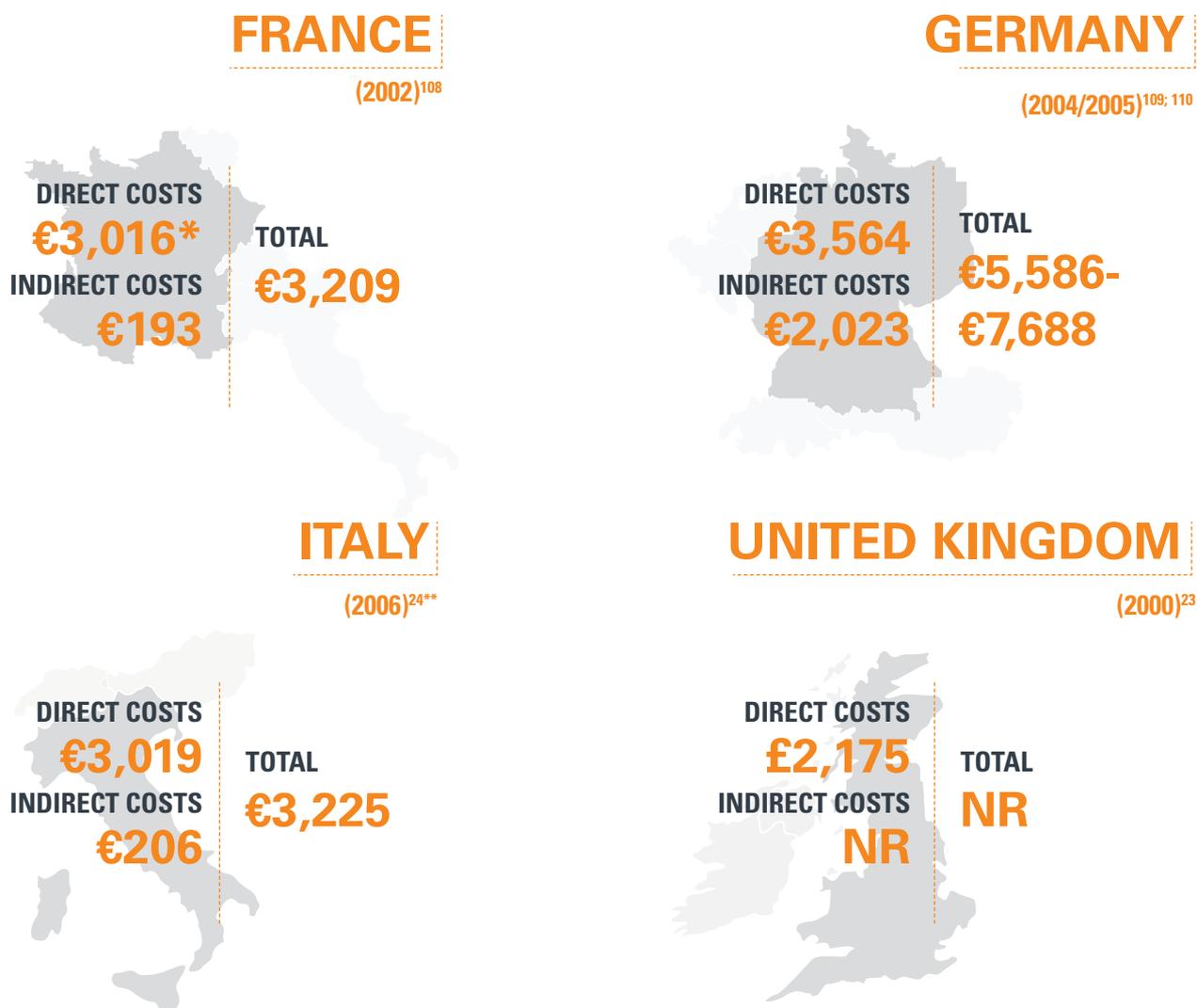
■ Annual direct per-patient costs of AF are **similar in France, Germany, Italy, and the UK.** ^{23; 24; 107-109}

■ Indirect costs reported are **highly variable by country, with highest costs in Germany.** ^{24; 108; 109}

- Indirect costs related to AF were higher for paroxysmal and persistent AF, whereas those not related to AF were higher for permanent AF.¹⁰⁸

*Based on limited country data reporting.

Annual Direct and Indirect Cost of AF per Patient



- Persistent AF can **cost significantly more to treat** than paroxysmal or permanent AF in some countries.¹⁰⁸
 - In Germany, **costs were lowest** for permanent AF and highest for persistent AF.¹⁰⁸
 - In Sweden, **costs were equally high** for paroxysmal and persistent AF.¹⁰⁸

*Direct cost was calculated by excluding costs for loss of work from the total per-patient cost reported for the societal perspective in Le Heuzey et al. (2004). Drug costs contained out-of-pocket costs, however, the authors noted that these costs were not statistically different from the those in the healthcare payer perspective; as such, drug costs were assumed to be direct costs.

**Based 1-year follow-up costs after index admission.

Abbreviations: NR = not reported.

WHAT FACTORS INFLUENCE DIRECT COSTS OF AF?



HOSPITALIZATIONS
AT 44%-78%
OF AF MANAGEMENT COSTS^{20; 21; 23; 24; 109*}



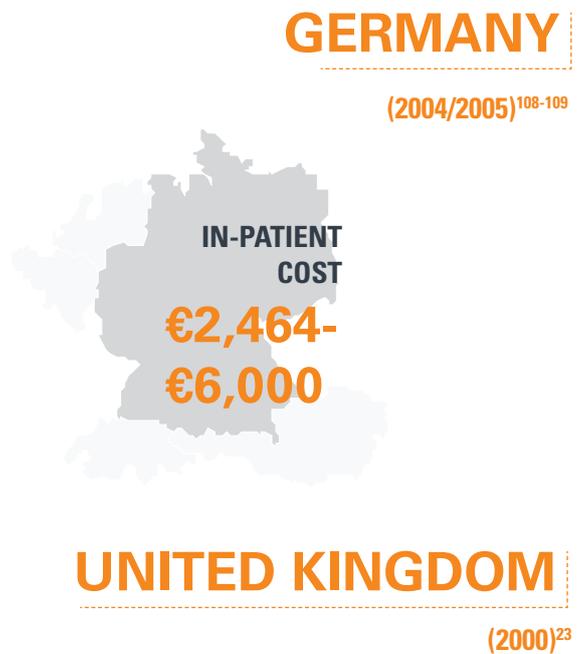
ANTIARRHYTHMIC DRUGS
AT 15%-20%
OF AF MANAGEMENT COSTS^{20; 21; 23; 109*}

Hospital costs represent the largest expense in AF management.

IN-PATIENT COSTS
ACCOUNT FOR **50%-70%** OF ANNUAL DIRECT
COSTS¹⁰⁰

- Healthcare resource use in AF patients is high, with **up to 40%** of AF patients hospitalized each year primarily due to heart failure and arrhythmia recurrence.^{3; 110}
- **Hospitalization costs can be 2x higher** for persistent AF than paroxysmal AF.¹⁰⁷
- Other factors associated with a high hospital cost include stroke and bleeding events, high stroke risk, high bleeding risk, and presence of other conditions.¹¹¹

Mean Annual Cost of In-patient Care per Patient*



*Data is based on limited countries reporting.

**Based on direct costs that were calculated by excluding costs for loss of work from the total per-patient cost reported for the societal perspective in Le Heuzey et al. (2004).

WHY ARE AF PATIENTS ADMITTED TO HOSPITAL?

AF represents a significant portion of admissions for cardiac arrhythmias.



■ Main reasons for AF admissions include:^{22; 107; 113}



■ Atrial fibrillation



■ Heart Failure



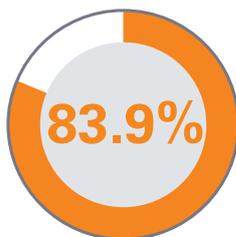
■ Vascular and ischemic diseases



■ Stroke, transient ischemic attack, or systemic emboli

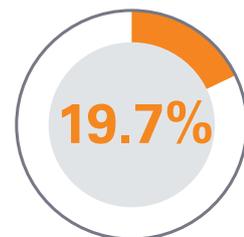
■ Reasons for admission or consultation differ by AF type:

AF WAS THE MOST COMMON REASON



IN PERSISTENT AF PATIENTS WHEN COMPARED TO OTHER AF TYPES¹¹³

HEART FAILURE WAS MOST COMMON REASON



IN PERMANENT AF PATIENTS WHEN COMPARED TO OTHER AF TYPES¹¹³

HOW DOES STROKE AFFECT THE COST OF AF?

The cost for the treatment and prevention of stroke in AF is high, contributing substantially to the total cost of AF management.

- In Europe, the cost of stroke in patients with AF is **7% to nearly 60% higher** than in patients without AF.^{70; 114-120}

In 2015, stroke was estimated to cost **€45 billion** a year in the European Union:¹²¹



Higher costs are due to:^{100; 120}



- Hospitalizations
- Longer hospital stays
- Greater use of nursing care
- In-patient rehabilitation
- Hospital readmissions

Cost of Stroke in AF (Annual Per-patient Cost)

FRANCE

(2002)²²

OVERALL

€10,094

HEMORRHAGIC STROKE

€12,748

ISCHEMIC STROKE

€11,243

SYSTEMIC EMBOLISM

€9,087

UNSPECIFIED STROKE

€8,108

TRANSIENT ISCHEMIC ATTACK

€3,734

GERMANY

(2001)¹²⁰

HOSPITAL ADMISSION FOR STROKE

€5,447

DIRECT COST OF STROKE WITH AF

€11,799

ITALY

(2015)¹²²

TOTAL HEALTHCARE COSTS FOR STROKE SURVIVORS WITH AF:

€13,054

UNITED KINGDOM

(2008-2009)¹¹⁵

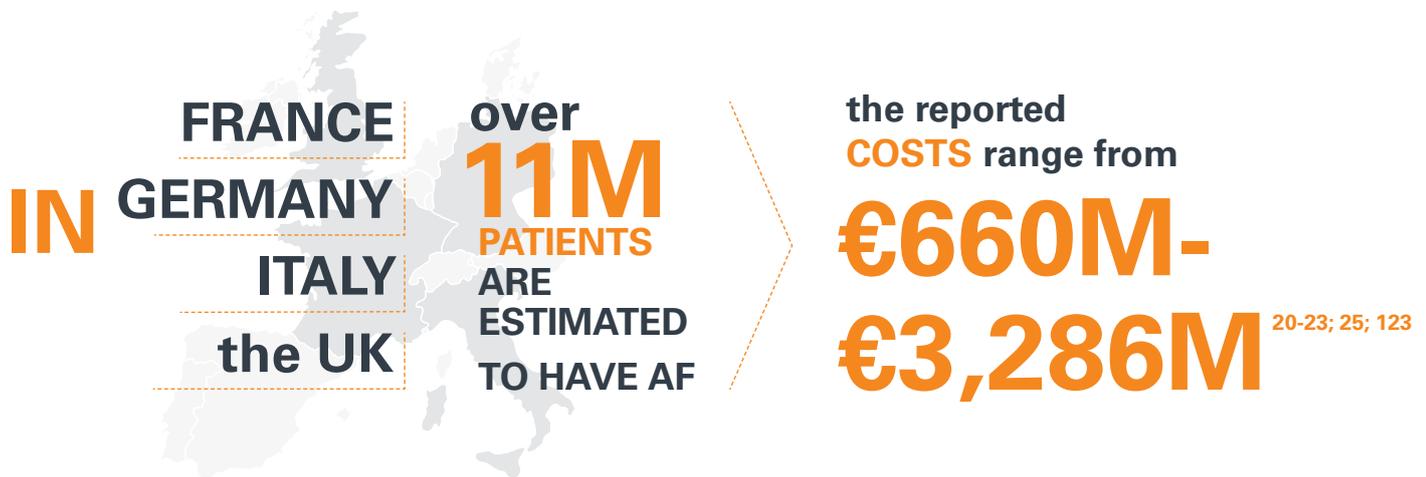
MEAN HOSPITAL AND 5-YEAR CARE COSTS - ISCHEMIC STROKE

£22,423 - £23,345

MEAN HOSPITAL AND 5-YEAR CARE COSTS - SYSTEMIC EMBOLISM

£13,634 - £13,720

The burden of AF is high and places a critical financial burden on healthcare systems in Europe.



BY 2050 Europe is projected to have **the greatest number of AF patients** compared to other regions globally.²⁹ This is expected to increase the number of stroke events, hospitalizations, and doctor visits, **ultimately raising the cost to national healthcare systems.**³¹

- The 2016 European Society of Cardiology’s Guidelines for the Management of AF and the 2017 HRS/EHRA/ECAS/APHS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation highlight several gaps in the evidence, where evidence is currently being developed or requires more recent and/or better studies.^{2;3} **Key areas for future research include the following:**

■ National and regional burden of AF

Most of the evidence on the national or regional burden of AF in Europe, particularly future projections on the total number of patients affected, number of new patients, and cost of AF, are based on data collected over 10 years ago, and are therefore outdated. **Recent data from methodologically robust studies are needed to understand the current epidemiologic and cost burden of AF for Europe and individual European countries.**

Risk of stroke in specific AF populations

Several specific AF groups should be studied to better characterize their risk for AF, stroke, and other AF-related comorbidities (e.g., patients with one stroke risk factor, non-Caucasian patients, women patients).³

Differences in overall patient management (e.g., different treatment for concomitant cardiovascular diseases) **may help explain** the variability in the reported rates of new (incident) AF cases, all (prevalent) AF cases, and AF complications.

Major health modifiers that cause AF

THE CAUSES
OF AF
DIFFER BY
PATIENT



The major causes of AF require **better characterization** by patient group, and should consider the key comorbidities associated with AF and pathophysiologically distinct types of AF.³ In the different patient subgroups, **how many patients have AF, what is the impact on disease progression, and what are the management costs?**

Treatment outcomes and quality of life and risk of stroke

The totality of evidence on AF underscores its role in reducing quality of life and in increasing the risk of stroke.



If treatments for AF aim to reduce or eliminate AF, **how do different treatment outcomes relate to quality of life and stroke risk?**

AF patient pathway

Will a **full pathway approach achieve better outcomes** for patients and Health Care Services (HCSs) **than a siloed approach?**

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