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

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

- 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.

AF increasingly places a **critical financial burden** on the healthcare system, costing €660-€3,286 million annually across European countries.
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.\textsuperscript{25}

- Over 1 Million people suffer with AF in each of France, Germany, Italy, and the UK.\textsuperscript{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.\textsuperscript{25}

Prevalence and Incidence of AF & Atrial Flutter in Europe

<table>
<thead>
<tr>
<th>Total number of people with AF &amp; AFL (Prevalence)</th>
<th>Number of new people diagnosed with AF &amp; AFL per year (Incidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11,062,761 EUROPE**</td>
<td>886,500 EUROPE**</td>
</tr>
<tr>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
</tr>
<tr>
<td>1,001,409 FRANCE</td>
<td>77,837 FRANCE</td>
</tr>
<tr>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
</tr>
<tr>
<td>1,453,541 GERMANY</td>
<td>116,468 GERMANY</td>
</tr>
<tr>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
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<tr>
<td>1,014,483 ITALY</td>
<td>81,907 ITALY</td>
</tr>
<tr>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
</tr>
<tr>
<td>1,232,144 UNITED KINGDOM</td>
<td>97,555 UNITED KINGDOM</td>
</tr>
<tr>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
<td>Rate* for AF &amp; AFL per 100,000 of the population</td>
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</tbody>
</table>

*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.\textsuperscript{25}
AF is a common age-related arrhythmia: 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.\(^{27}\)

**DEMOGRAPHICS OF AF**

**Who is at risk for AF?**

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

### Distribution* of AF Types Among European Patients

<table>
<thead>
<tr>
<th>Type of AF</th>
<th>Patients WITH symptoms</th>
<th>Patients WITHOUT symptoms</th>
</tr>
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<tbody>
<tr>
<td>PAROXYSMAL</td>
<td>40%</td>
<td>34%</td>
</tr>
<tr>
<td>PERSISTENT</td>
<td>46%</td>
<td>24%</td>
</tr>
<tr>
<td>PERMANENT**</td>
<td>14%</td>
<td>42%</td>
</tr>
</tbody>
</table>

*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)
By 2050, Europe is expected to have the most patients with AF compared to other regions.\textsuperscript{29}

**THE NUMBER PEOPLE WITH AF IS EXPECTED TO INCREASE UP TO 70\%** \textsuperscript{31}

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

![Graph showing prevalence of AF in different regions](image)

Current estimated prevalence of AF 2050 estimates of AF prevalence of based on population protections by the USA Census Bureau

Source: Rahman et al. (2014)
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.\textsuperscript{31}

- \textbf{280K-340K} additional ischemic strokes
- \textbf{3.5-4 million} hospitalizations for AF
- \textbf{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

- An overactive thyroid gland or other metabolic imbalance
- Lung diseases
- Stress due to pneumonia, surgery or other illnesses
- High blood pressure
- Heart attacks
- Coronary artery disease
- Abnormal heart valves
- Heart defects you’re born with (i.e., congenital)
- Previous heart surgery
- Sick sinus syndrome (i.e., improper functioning of the heart’s natural pacemaker)

Other factors that cause AF:

- Exposure to stimulants, such as medications, caffeine, tobacco or alcohol
Lifestyle factors, other conditions, and non-modifiable factors increase the risk of developing AF.

**LIFESTYLE FACTORS**
- Obesity
- Alcohol consumption
- Risks for cardiovascular disease: smoking, stress, caffeine and other stimulants
- Activity level

**OTHER CONDITIONS**
- High blood pressure
- Heart failure
- History of heart attack
- Coronary artery and other heart disease
- Previous surgery
- Sleep-disordered breathing (e.g., obstructive sleep apnea)
- Diabetes

**NON-MODIFIABLE FACTORS**
- Older age
- Congenital heart defects
- Family history or other genetic factors
- Male sex
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.\textsuperscript{14, 49-50} The most common symptoms are:\textsuperscript{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 exercise.\textsuperscript{6}

The frequency and severity of symptoms varies a lot from patient to patient and, within a patient, symptoms can fluctuate widely over time.\textsuperscript{8}
Patients with AF often experience symptoms that impair functional status, disrupt daily life activities, and impact quality of life.\textsuperscript{49-51}

\begin{itemize}
  \item 19\% IMPAIRMENT IN FUNCTIONAL STATUS\textsuperscript{52*}
  \item 25\% DISRUPTION TO DAILY ACTIVITIES\textsuperscript{52**}
  \item UP TO 47\% REDUCTION IN QUALITY OF LIFE\textsuperscript{52, 53***}
\end{itemize}

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

\begin{itemize}
  \item 15\%-30\% have SILENT AF\textsuperscript{5, 28}
  \item AS MANY AS 1 in 4 PATIENTS are DIAGNOSED WITH AF AFTER SUFFERING A STROKE\textsuperscript{5, 8}
  \item PATIENTS WITH SILENT AF EXPERIENCE POORER general HEALTH and QUALITY OF LIFE than HEALTHY INDIVIDUALS\textsuperscript{54}
\end{itemize}

With disease progression, patients are more likely to experience:\textsuperscript{55}

\begin{itemize}
  \item More severe mobility problems
  \item Inability to continue regular activities
  \item Problems with self-care
  \item Increased pain and discomfort
  \item Anxiety and depression
\end{itemize}

*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:

- Older age⁹
- Heart failure⁹
- Valvular heart disease⁹, ¹², ³⁶
- Larger left atrium⁹
- Hyperthyroidism¹²
- Moderate to high alcohol consumption³⁶
- Asymptomatic and untreated AF¹¹, ⁵⁹

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

- New onset heart failure, or worsening heart failure
- Thromboembolism
AF increases a patient’s risk for life-threatening events and conditions, including stroke, heart failure, and death.

**WHAT ARE THE CONSEQUENCES OF AF?**

80% OF AF PATIENTS have another condition or cardiac disease.¹³

The seriousness of AF is critically misunderstood:
- 45% of patients believe it is not a life-threatening condition.⁶³

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

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**CLINICAL BURDEN**

<table>
<thead>
<tr>
<th>Number of concomitant conditions</th>
<th>Paroxysmal</th>
<th>Persistent</th>
<th>Permanent</th>
</tr>
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<tbody>
<tr>
<td>4 (n=283)</td>
<td>16</td>
<td>21</td>
<td>63</td>
</tr>
<tr>
<td>3 (n=923)</td>
<td>21</td>
<td>27</td>
<td>52</td>
</tr>
<tr>
<td>2 (n=1100)</td>
<td>28</td>
<td>29</td>
<td>42</td>
</tr>
<tr>
<td>1 (n=887)</td>
<td>35</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td>0 (n=258)</td>
<td>33</td>
<td>25</td>
<td>42</td>
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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), Odutayo 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
- Chronic kidney disease
- Prior stroke or transient ischemic attack
- Congestive heart failure
- Diabetes
- History of bleeding
Stroke is a serious complication of AF that is associated with long-term disability and mortality.\textsuperscript{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.\textsuperscript{64}

**What does stroke cause?\textsuperscript{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

\textbf{20\%-30\% of all strokes occur in AF patients}\textsuperscript{3, 31}

\textbf{142\% increased risk of any stroke}\textsuperscript{13}

\textbf{133\% increased risk of ischemic stroke}\textsuperscript{13}
In patients with AF, the risk of stroke is increased by:

- Older age\(^3\)\(^{,67}\)
- Chronic kidney disease\(^67\)
- Prior stroke, transient ischemic attack, or embolism\(^3\)\(^{,67}\)\(^{,68}\)
- Vascular disease and high blood pressure\(^3\)\(^{,68}\)
- Female sex\(^2\)\(^{,67}\)
- Congestive heart failure\(^3\)\(^{,67}\)
- Diabetes\(^3\)\(^{,67}\)\(^{,68}\)
- Obstructive sleep apnea\(^44\)

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.\(^69\)
Heart attack is a serious complication of AF that also significantly increases the risk of stroke and mortality.

**WHAT IS THE RISK OF A HEART ATTACK?**

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.\(^{71}\)

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.\(^{1, 41, 64}\)

**THE RATE OF HEART ATTACKS IS**

0.4% - 2.5%\(^{3, 41}\) PER YEAR IN AF PATIENTS.
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.**

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 DYSFUNCTION**

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

**25% OF HEART FAILURE PATIENTS WILL DEVELOP AF WITHIN 5 YEARS.**

**15% OF AF PATIENTS WILL DEVELOP HEART FAILURE WITHIN 5 YEARS.**

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

**11X GREATER RISK IN WOMEN**

**3X GREATER RISK IN MEN**

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
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. \(^2\); \(^7\)

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. \(^3\); \(^1\); \(^2\); \(^4\)

Cognitive dysfunction and vascular dementia can even develop in AF patients receiving oral anticoagulation therapy. \(^3\); \(^7\)

WHAT IS THE RISK OF COGNITIVE DYSFUNCTION?

OF AF PATIENTS MAY HAVE COGNITIVE DYSFUNCTION OR DEMENTIA. \(^3\); \(^5\); \(^6\)

UP TO 18% OF AF PATIENTS MAY HAVE COGNITIVE DYSFUNCTION OR DEMENTIA. \(^3\); \(^5\); \(^6\)

INCREASED RISK OF COGNITIVE DECLINE, WHICH MAY OCCUR AT A FASTER RATE THAN IN NON-AF PATIENTS \(^1\); \(^2\); \(^4\); \(^7\)

UP TO 40% INCREASED RISK OF COGNITIVE DECLINE, WHICH MAY OCCUR AT A FASTER RATE THAN IN NON-AF PATIENTS \(^1\); \(^2\); \(^4\); \(^7\)
Obstructive sleep apnea is common in AF patients and may increase the risk of stroke, heart failure, and AF recurrence.

HOW DOES OBSTRUCTIVE SLEEP APNEA IMPACT AF?

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:

- **20%** of AF patients during 1 year\(^{31}\)
- **75%** of patients during 5 years\(^{31}\)
AF symptoms and repeated recurrence increase unplanned medical visits and hospitalizations.

WHY DO PEOPLE WITH AF SEEK MEDICAL TREATMENT?

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

2/3 of emergency room visits for symptoms leading to AF diagnosis result in hospital admissions.

PATIENT BURDEN
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

### Abbreviations:
- AF = atrial fibrillation
- SF-36 = Short Form 36 Quality of Life Questionnaire

Source: Dorian et al. (2000)

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)

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\(^{55; 85}\)
Caring for family members with AF can be burdensome. Some form of caregiver assistance is required in: 19, 86

**OF ELDERLY AF PATIENTS** 86

**OF PATIENTS RECOVERING FROM STROKE** 19

- **Opening medication packaging**
- **Assisting or confirming correct dosage of medication**
- **Driving to the primary care physician or anticoagulation clinic for regular monitoring**
- **Assisting with activities of daily living due to tiredness experienced due to AF**
- **Monitoring for signs of bleeding**
- **Ensuring adherence to any dietary restrictions**
Caregivers of AF patients experience considerable changes to their daily lives, including:

- 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:

- Patients are frail, sick, or disabled
- Patients have low quality of life
- Patients have had or are at high risk of stroke
- Patients have low level of independence
- Provide care for long hours (e.g., >4 hrs/week)

>40% of stroke patients receiving care need another caregiver by the third month of recovery.

Burden to caregivers may lead to less adequate patient support, physical and emotional stress, caregiver burnout, and suboptimal patient outcomes.
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.  
- Limitations after a stroke include:
  - Problems with communication
  - Anxiety
  - Memory loss
  - Cognitive impairment
  - Personality changes

STROKE in patients with AF is more severe and devastating than in patients who do not have AF.

30% of stroke patients will have a second stroke.

- Patients who experience a stroke are at risk of suffering a second stroke.
- In stroke patients, the risk of a second stroke is nearly 9x higher than the risk of stroke in the general population.
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.\textsuperscript{90-93}

- Oral anticoagulation therapy can be burdensome to patients, as it requires:
  - **FREQUENT AND REGULAR VISITS** to monitor and optimize dosage\textsuperscript{72, 94, 95}
  - **CHANGES TO PATIENT BEHAVIOR AND LIFESTYLE** that disrupt daily activities and negatively impact quality of life.\textsuperscript{94-96}

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

- **36.1%** worry about DRUG-DRUG INTERACTIONS\textsuperscript{96}
- **26.2%** worry about FORGETTING TO TAKE ORAL ANTICOAGULANTS\textsuperscript{96}
- **25.7%** worry about SIDE EFFECTS\textsuperscript{96}

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.\textsuperscript{97-98}

**BENEFITS**
- Patient preference
- Reduced risk of stroke

**RISKS**
- Patient preference
- Inconvenience of close monitoring
- Risk of bleeding

*For patient in warfarin.*
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.\textsuperscript{3,99}

- Concern over side effects may contribute to patient anxiety, which reduces quality of life.\textsuperscript{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**

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Cost Associated with AF</th>
<th>Percent of Total Healthcare Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>2012</td>
<td>€1,942M**</td>
<td>2.6%**</td>
</tr>
<tr>
<td>Germany</td>
<td>2004</td>
<td>€660M***</td>
<td>0.28%***</td>
</tr>
<tr>
<td>Italy</td>
<td>2006</td>
<td>€3,286</td>
<td>2.49%**</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2000</td>
<td>£1,307***</td>
<td>0.9%-2.4%***</td>
</tr>
</tbody>
</table>

*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.
The high cost of AF is largely due to hospitalizations and complications such as stroke.\textsuperscript{21, 23}

National healthcare costs for AF are similar to those for other cardiovascular diseases.\textsuperscript{20, 22, 23, 102-106}
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:

- **2.6%** of hospital expenditures in France\(^{22}\)
- **0.9% - 2.4%** of total annual healthcare expenditures in the UK\(^{23}\)

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.
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 COSTS20; 21; 23; 24; 109*

ANTIARRHYTHMIC DRUGS
AT 15%–20%
OF AF MANAGEMENT COSTS20; 21; 23; 109*

Hospital costs represent the largest expense in AF management.

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

*Data is based on only 5 country experience.
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.\textsuperscript{3, 110}

Hospitalization costs can be 2x higher for persistent AF than paroxysmal AF.\textsuperscript{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.\textsuperscript{111}

Mean Annual Cost of In-patient Care per Patient*

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Estimated Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>2002\textsuperscript{107}</td>
<td>€3,016**</td>
</tr>
<tr>
<td>Germany</td>
<td>2004/2005\textsuperscript{108-109}</td>
<td>€2,464 - €6,000</td>
</tr>
<tr>
<td>Italy</td>
<td>2006\textsuperscript{114}</td>
<td>€1,778</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2000\textsuperscript{123}</td>
<td>£1,679</td>
</tr>
</tbody>
</table>

*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.

~1/3 of all cardiac arrhythmia admissions are for AF.112

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 types.113
- Heart failure was most common reason in permanent AF patients when compared to other AF types.113
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.\textsuperscript{70, 114-120}

In 2015, stroke was estimated to cost €45 billion a year in the European Union:\textsuperscript{121}

- €16 billion due to informal care
- €20 billion due to direct healthcare costs
- €9 billion due to productivity losses
Higher costs are due to:

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

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

**FRANCE**

- Overall: €10,094
- Hemorrhagic Stroke: €12,748
- Ischemic Stroke: €11,243

**GERMANY**

- Hospital Admission for Stroke: €5,447
- Direct Cost of Stroke with AF: €11,799

**ITALY**

- Total Healthcare Costs for Stroke Survivors with AF: €13,054

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**UNITED KINGDOM**

- 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.

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

The 2016 European Society of Cardiology’s Guidelines for the Management of AF and the 2017 HRS/EHRA/ECAS/APHRS/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.

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.
Conclusions

- 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). 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 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. 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?