

# ATRIAL FIBRILLATION AND STROKE

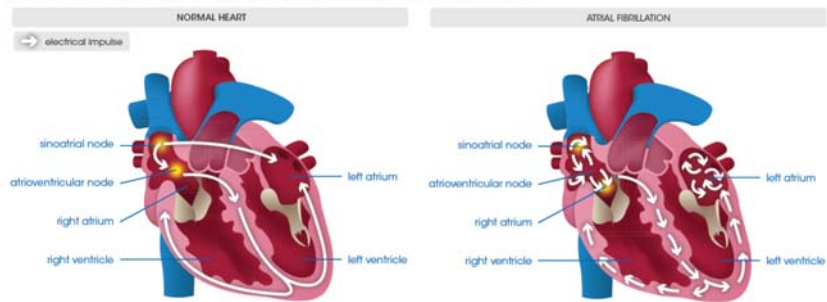
## EXECUTIVE SUMMARY

- Atrial fibrillation (AF) is the most common sustained heart rhythm condition, affecting approximately 2% of the total population, with one in four adults over 40 developing the arrhythmia in their lifetime<sup>1,2</sup>
- AF leads to a five-fold increase in the risk of stroke, resulting in up to three million patients worldwide suffering AF-related strokes each year<sup>2-4</sup>
- AF-related strokes tend to be severe, leading to an increased likelihood of death and disability<sup>5</sup>
- Vitamin K antagonists (VKA), like warfarin are effective in reducing the risk of stroke in patients with AF by approximately two-thirds (64%).<sup>6</sup> However, due to limitations associated with the treatment such as the need for regular monitoring and various food-drug and drug-drug interactions,<sup>4</sup> patients receiving warfarin spend half of their time outside the recommended narrow therapeutic range<sup>7</sup>
- Novel oral anticoagulants such as dabigatran etexilate, apixaban and rivaroxaban have been proven to provide benefits compared to warfarin<sup>2,8-11</sup>

## What is AF?

AF is the most common sustained heart rhythm condition, affecting approximately 2% of the total population, with one in four adults over the age of 40 developing the condition in their lifetime.<sup>1, 2</sup>

### How atrial fibrillation affects the heart



In patients with AF, the normal control of heart rhythm by the sinoatrial node is disrupted, leading to rapid and irregular electrical signals (tachyarrhythmia). This causes the upper chambers of the heart (atria) to quiver rather than contract in a co-ordinated fashion, reducing the efficiency with which blood is pumped from the atria to the ventricles and potentially leading to blood stasis (pooling) and blood clot development.<sup>12, 13</sup>

## What are the common symptoms?

Some people with AF have no symptoms and therefore the condition may only be discovered when the patient suffers complications such as a stroke.<sup>12</sup> AF can be diagnosed during routine tests such as a pulse check or ECG.<sup>2</sup>

Some patients experience symptoms due to AF causing a disrupted heart rhythm. Symptoms may include:<sup>13</sup>

- Dizziness or fainting
- Fatigue
- Palpitations
- Shortness of breath
- Weakness or difficulty exercising

## What are the risk factors?

AF risk factors include:<sup>14</sup>

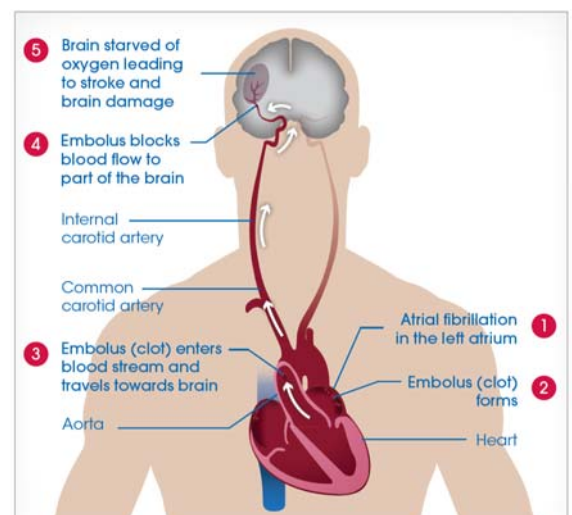
- Advancing age
- History of heart failure
- Hypertension
- Diabetes
- Echocardiographic abnormalities
- Thyroid disorders
- Excessive alcohol intake
- Sleep apnoea
- Family history of AF
- Cardiovascular disease

## Complications of AF

AF is associated with several serious complications. The rapid and irregular atrial activity in AF reduces the efficiency with which blood is pumped from the atria to the ventricles. Due to the pooling of blood (stasis), blood clots (thrombi) can form in the atria, which can dislodge and travel in the bloodstream, potentially blocking blood vessels in the brain and leading to an ischaemic stroke.<sup>12,13,15</sup>

The reduction in cardiac output observed with AF can lead to heart failure and increased risk of mortality.<sup>2, 13</sup>

Stroke is the leading complication of



## AF

AF raises the risk of stroke five-fold, with approximately one in five strokes being attributed to AF.<sup>2,4</sup> Three million patients suffer AF-related strokes each year.<sup>3,4</sup>

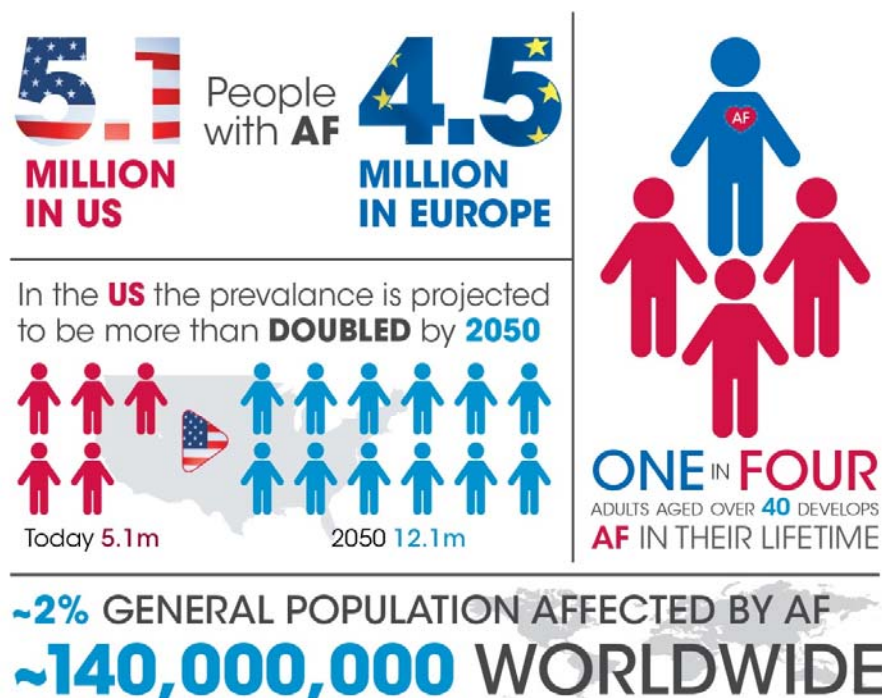
Strokes can be classified into two main types: ischaemic and haemorrhagic.<sup>15</sup> Ischaemic strokes account for 92% of strokes experienced by patients with AF.<sup>16</sup> Ischaemic strokes occur when a blood clot blocks a vessel in the brain and frequently lead to severe disability or death.<sup>5, 15</sup> Haemorrhagic strokes account for approximately 8% of strokes in patients with AF and occur when a blood vessel in the brain bursts or ruptures.<sup>15, 16</sup>

## Personal burden of AF & Stroke

AF negatively impacts patients' quality-of-life. Their emotional wellbeing, mental health and social functioning may be more negatively affected compared to people with other cardiac conditions.<sup>17</sup>

Results from 'SPEAK about AF' (Stroke Prevention Education, Awareness and Knowledge), the largest survey ever conducted in patients diagnosed with AF and their treating physicians, showed that over half of patients with AF (55%) felt that living with the condition was a burden.<sup>18</sup>

## AF – an increasing problem



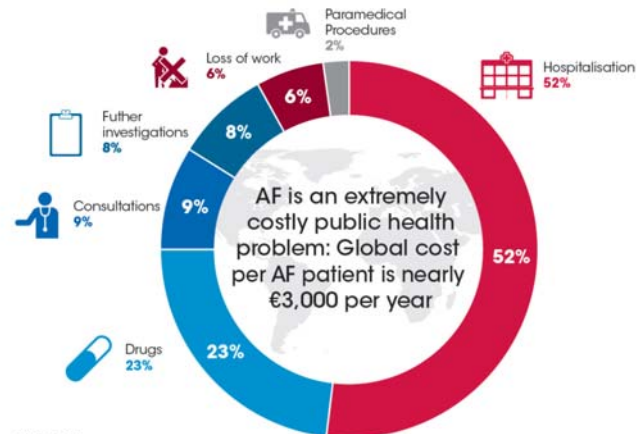
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## The costs associated with AF

AF is an extremely expensive public health problem.<sup>19</sup> Given the ageing population, atrial fibrillation is expected to become an increasing burden on healthcare systems worldwide.<sup>20</sup>

- The total cost burden of AF reaches €13.5 billion per year in the European Union alone. This can include direct AF treatment costs as well as costs associated with lost work including sickness absence or early retirement<sup>19, 21, 22</sup>
- Direct AF treatment costs include in-patient hospital and outpatient care, as well as costs associated with medications. This totals \$6.65 billion in the US, and over €6.2 billion per year in Europe<sup>20, 23</sup>
- Due to AF-related strokes tending to be more severe, direct hospital costs following AF-stroke may be up to 30% higher than the costs associated with strokes unrelated to the arrhythmia<sup>24</sup>



References:  
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## Managing AF

The management of AF has two broad objectives: to prevent life-threatening complications, including stroke and heart failure, and to relieve symptoms from the arrhythmia itself.<sup>19</sup>

Symptom relief can be achieved by either controlling the heart rate or restoring sinus rhythm depending on the individual patient characteristics:<sup>19</sup>

- Rate-control aims to normalise the heart rate and relieve symptoms of AF
- Rhythm-control aims to restore normal sinus rhythm

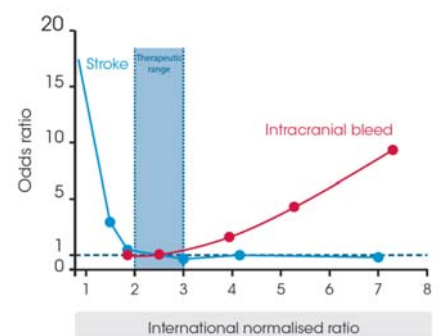
Anticoagulant treatments reduce blood clotting and are important for the prevention of stroke and systemic embolism in patients with AF.<sup>25</sup>

## A history of stroke prevention in AF

Vitamin K antagonists (VKAs), like warfarin, have been used for stroke prevention in AF for decades. However, due to the limitations associated with the treatment, such as the need for regular monitoring and various food-drug and drug-drug interactions, considerable fluctuations in the treatment's efficacy and safety can occur.<sup>4</sup>

Furthermore, real-life studies have shown that patients receiving warfarin spend less than half of their time inside the recommended narrow therapeutic range between an INR\* value of 2.0–3.0, leading to an increased risk of bleeding or suffering a stroke due to blood clots.<sup>4</sup>

- Under-anticoagulation (INR<2) increases stroke risk significantly, doubling at INR of 1.7, tripling at 1.5 and increasing six-fold at INR of 1.3<sup>26</sup>
- Over-anticoagulation (INR>4.0) increases risk of brain haemorrhage (intracranial bleeding) substantially<sup>27</sup>



\*INR – International Normalization Ratio is a measure of how fast the blood clots

## Stroke prevention in AF with novel oral anticoagulants

To address the shortcomings of VKAs, several novel oral anticoagulants (direct thrombin inhibitors and factor Xa inhibitors) have been developed.

Dabigatran etexilate (Pradaxa<sup>®</sup>) was the first novel oral anticoagulant (NOAC) to be approved for stroke prevention in AF, and has now been approved in over 100 countries worldwide.<sup>28</sup> Clinical experience of dabigatran etexilate is already well established and continues to grow, equating to over 3 million patient-years globally in all licensed indications.<sup>28</sup>

Dabigatran etexilate is the first and only NOAC with controlled long-term clinical trial data extending beyond 6 years of ongoing treatment. Results demonstrate the sustained efficacy and safety profile of the treatment in the clinical setting with protection provided against stroke and intracranial haemorrhage.<sup>29,30</sup>

Two Factor Xa inhibitors, rivaroxaban and apixaban, have also been approved for the prevention of stroke in AF.<sup>2</sup>

## AF Treatment Guidelines

The 2012 Focused Update of the European Society of Cardiology Guidelines for the Management of Atrial Fibrillation reinforce the importance of anticoagulation for stroke prevention in patients with AF. The guidelines state that all AF patients at risk of stroke as defined by a CHA<sub>2</sub>DS<sub>2</sub>-VASc\*\* score  $\geq 1$  should be considered for oral anticoagulant treatment, taking into account risk of bleeding complications and patient preferences. For AF patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ , anticoagulant treatment is recommended in all instances except when contraindicated.<sup>2</sup>

The guidelines also highlight the better efficacy, safety and convenience of the NOACs in comparison to oral anticoagulation with VKAs and state that when oral anticoagulant therapy is recommended NOACs should be considered in preference to VKAs.<sup>2</sup>

\*\*CHA<sub>2</sub>DS<sub>2</sub>-VASc is a scoring system to assess risk factors for stroke in patients with non-valvular AF. CHA<sub>2</sub>DS<sub>2</sub>-VASc considers the following patient characteristics to assist physicians with their decision on whether or not to anticoagulate a patient - congestive heart failure, hypertension, age  $\geq 75$  (doubled), diabetes, stroke (doubled), vascular disease, age 65–74, and sex category (female)

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