



Atrial Fibrillation in Europe: **How AWARE are you?**



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Executive Summary

Introduction

Atrial fibrillation (AF) is a heart rhythm disturbance which can make those with the condition feel palpitations, chest pain or even loss of consciousness. AF increases the risk of mortality and those with AF are five times more likely to have a stroke than those without AF. AF is therefore a condition with a substantial impact upon those with the condition, and a challenge for the health care system.

This study was initiated in response to a perceived lack of awareness of AF and a lack of comparable information and data across Europe. This includes:

1. Incidence and prevalence of AF
2. Health care system response to AF (including management/treatment options, guidelines, and health care staff training and involvement in AF)
3. Patient information
4. Economic burden of AF (including hospitalisation data and potential costs of 'missed' diagnosis)

The objective was to assess what is currently known about each of these across Europe and Russia. At the outset it was recognised that there are a number of approaches which could be used to explore these issues, but reflecting on limited time and resources and applying pragmatism, the approach was to:

- Conduct a rapid evidence review: bringing together English language literature published between 2005 and 2010
- Survey member organisations of SAFE and the World Heart Federation by email

This study should be seen as a starting point for exploring these issues and not a definitive view.

Incidence and prevalence

AF affects between one and two per cent of the population as a whole, and across Europe six million people have AF. However, this study found relatively few countries within Europe have country level estimates of incidence and prevalence (see Figure 1).

Figure 1: Availability of incidence/prevalence estimates for AF across Europe



Note: countries in red where one or more estimates of incidence or prevalence of AF are available. Figure produced drawing upon data in Table 3, pg 12

In terms of absolute number of patients with diagnosed AF in countries where information is available, there are approximately:

- 50,000 people with AF in Finland
- 20,000 in Slovenia
- 7,500 new cases per year in Lithuania
- 800,000 in Germany
- 639,000 in England

Such estimates are unknown or unavailable (Belgium, Russia) or are not available due to patient confidentiality concerns which is hindering the ability to identify numbers of patients with AF (Norway).

The number of people with AF is expected to rise over time, and may more than double in the next 50 years. Respondents to the survey in Finland, Norway, Slovenia, Lithuania and Germany all believe that the number of people with AF will increase in the future.

The estimates that are available of the number of people with AF may not include all cases, as AF can be 'silent' and may be undiagnosed.

Disease registers can help in understanding incidence and prevalence (and a host of other issues such as management and health outcomes). These are few and far between with only a national registry in place in Germany, and potentially a national registry in Norway (subject to political debate and implementation). International registries are in place but will not necessarily look at the national picture.

Health care system response to AF

There are a number of ways that AF can be diagnosed and managed ranging from opportunistic screening, ECGs, cardioversion to return the heart to normal rhythm and anticoagulation to reduce the risk of blood clots which can cause stroke. Management differs according to the type of AF and according to specific patients' characteristics such as the presence of comorbidities. AF is therefore a complex disease to diagnose and manage.

The types of health care professionals involved in diagnosing and managing AF vary by country and can include GPs, neurologists, internists, cardiologists and nurses, AF can be treated across settings from primary care to outpatient and inpatient. A range of treatment options are available according to survey respondents. Newer treatments, such as the medicine dronedarone, may be not be available in some countries (Lithuania, Slovenia) or their availability may be unclear (Belgium, UK).

A range of guidelines exist, both national (eg National Institute for Health and Clinical Excellence guidelines for the national health service (NHS) in England and Wales) and European (eg European Society for Cardiology guidelines). However, adherence to guidelines is variable. This includes both over use and under use of oral anticoagulants and a lack of tailoring of management to specific patients' characteristics. The reasons are not well understood but potential solutions are likely to include education to overcome mis-perceptions of risk by clinicians.

No single country appears better or worse in their adherence to guidelines (or at least there is little comparable information to directly compare) and there is likely to be scope for improvement across many countries. Moving practice closer to guidelines could improve patient outcomes by reducing the risk of mortality and avoiding stroke. It would also bring benefits to the health care system by reducing the demand for relatively expensive hospitalisations. This presents a missed opportunity to benefit both patients and the health care system.

Patient information

There is a variety of information available to patients ranging from leaflets, websites and a telephone helpline (the latter in the UK). However, survey respondents are not convinced that what is available is sufficient to meet the needs of patients, and many had concerns about whether patients had the information that they needed to be a partner in treatment decisions with their clinician (Belgium, Norway, Lithuania and Germany). This finding accords with previous research that has asked doctors about their views of patient information; half of doctors thought patients needed more information, and a third that the available information is simply not good enough. There is also a gap in understanding patient preferences, which links back to adherence to guidelines for management; perhaps providing accessible information to patients will help to bridge the gaps.

Economic burden

Understanding the cost of illness is helpful to place a disease in context and to contribute to priority setting. The full economic burden of a disease is the cumulative burden across patients, carers, the health care system, employers and the welfare system (although welfare costs are treated differently as they are a transfer of wealth across parties in the economy).

A common starting point for understanding the cost of illness is to look at the number of people with the disease and then look at their use of resources (eg number of medical appointments, hospitalisations) and multiply those by unit costs. In AF, there is significant use of the health care system across both primary and secondary care, and this translates to significant costs (see table). Studies vary in their approach and how their estimates are expressed, but costs are in the order of one per cent of annual health care expenditure (estimated for the UK) with the majority of costs driven by hospitalisation/inpatient care. However, looking across Europe as a whole, relatively few studies quantify costs in financial terms (see Figure 2).

Figure 2: Availability of estimates of economic burden of AF across Europe

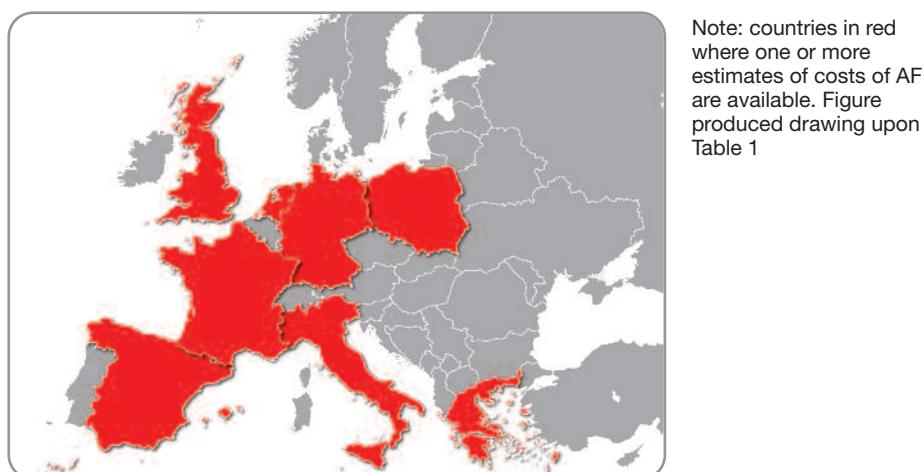


Table 1: Direct health care costs of AF, selected countries

Country	Direct health care cost	Source
France	€3,027 average per patient per year	Le Heuzey et al (2004)
Germany	AF related strokes cost more than non-AF related strokes; on average €11,799 vs €8,817 per patient	Brüggenjürgen, Rossnagel, Roll et al (2007)
Germany	€680m in total in 2006	Survey respondent ¹
Greece	€1,373 average per patient per year	Ringborg et al (2008)
Italy	€3,019 average per patient per year	Ringborg et al (2008)
Netherlands	€1,936 average per patient per year	Ringborg et al (2008)
Poland	€971 average per patient per year	Ringborg et al (2008)
Spain	€2,073 average per patient per year	Ringborg et al (2008)
Sweden	AF patients had on average €818 higher inpatient costs over 3 years than non-AF patients (€10,192 vs. €9,374)	Ghatnekar and Glader (2008)
UK	AF has been estimated to cost the UK to be £459 million (~€655 million) in 2000	Stewart et al (2004)

The ‘right’ level of expenditure in the health care system is difficult to determine but evidence suggests that achieving International Normalised Ratio (INR) for patients on warfarin in Sweden could lead to later cost offsets in the health care system by avoiding strokes. A similar value for money argument has also been put forward in the UK, where opportunistic screening of primary care patients can cost in the order of £200 per newly treated patient, but leads to fewer strokes, and hence reduced demand for relatively more expensive stroke care.

¹ From www.charite.de/epidemiologie/german/projekte/costflim.html

AF also results in lost work; both in terms of sickness absence and early retirement. Available estimates highlight a significant variation in this indirect cost of AF (see Table 2). These costs may well underestimate the burden, because they don't explicitly discuss the potential and scale of presenteeism (being at work, but not fully productive).

Table 2: Indirect (work) costs of AF, selected countries

Country	Indirect cost	Source
Germany	€3,125 average per patient per year	Brüggenjürgen, Rossnagel, Roll et al (2007)
Greece	€135 average per patient per year	Ringborg et al (2008)
Italy	€3,225 average per patient per year	Ringborg et al (2008)
Netherlands	€391 average per patient per year	Ringborg et al (2008)
Poland	€39 average per patient per year	Ringborg et al (2008)
Spain	€242 average per patient per year	Ringborg et al (2008)

Discussion and recommendations for the future

Looking across the survey and evidence reviewed, some key themes emerge. We know that:

- AF is increasingly common, affecting up to two per cent of the general population
- The number of people with AF is set to grow over time, perhaps even doubling in the next 50 years
- AF prevalence is likely to be underestimated because it can be silent
- AF is a complex disease to diagnose and manage with a need to tailor the management according to patients' characteristics
- There are missed opportunities to more successfully manage AF by adhering to guidelines which can contribute to better outcomes for patients, and reduce demand on health care systems
- Patient information is available but isn't sufficient, a concern shared by patient organisations and clinicians
- AF results in a substantial cost of illness because it uses significant resources across primary and secondary care. In particular hospitalisations are expensive, and this is a key driver of the costs of AF. Appropriate management, particularly the use of medicines can lead to reduced demand for expensive hospital care
- AF results in substantial loss of work

However, there is much more that we need to know to help make better decisions about the priority that should be placed on managing AF, how to make best use of resources in managing AF, and how best to implement this management across Europe. For example, this study suggests:

- **There is a lack of country estimates of incidence and prevalence of AF.** This implies that there may be scope for greater understanding of the extent of AF within countries. Perhaps the lack of country level estimates contributes to the concern expressed by SAFE and the World Heart Federation that there is a lack of awareness of AF. It is also likely to hinder effective planning within the health care system to provide treatment and management for those with AF.
- **Registries are not routinely available but more are being planned.** This should help meet some informational gaps.
- **There are guidelines for management but there is variation in adherence. The reasons are not fully known.** This implies a need for more in depth research to explore the key barriers and enablers to move closer to meeting these guidelines in practice. Promising solutions include more education for clinicians and providing information to patients.

This study is only a snapshot of the issues which need to be explored to ensure the best possible approach to manage AF within constraints of national settings (eg available budgets). It is not without its limitations; for example focusing upon English language literature may have missed relevant studies and focusing upon patient organisations provided insights from just one stakeholder group with relevant information and knowledge. There is significant potential to use other approaches to build a fuller understanding ranging from primary research and more country focused research which includes a wider group of relevant stakeholders. Some promising options to explore for the future include:

- **Updating the available costs of AF.** This would be useful to inform planning and resourcing in the future
- **Draw upon the estimates of the cost of stroke and apportion costs to AF.** This would be useful to highlight the burden where it is currently opaque
- **Explore the potential to extrapolate based upon available data to countries where no data exists**
- **Build on the momentum seen for disease registers and use them to collect as much information as is both useful and proportionate**
- **Explore reasons for lack of adherence to guidelines with clinicians and patients**
- **Work with patient organisations to identify the best approaches to fill the information gaps for patients**
- **Work with providers of clinical training to assess the appropriate content and frequency of training on AF**

1. Introduction

Atrial fibrillation (AF) is a heart rhythm disturbance. In clinical terms, it is an atrial tachyarrhythmia characterised by predominantly uncoordinated atrial activation with consequent deterioration of atrial mechanical function (Collaborating Centre for Chronic Conditions 2006). There are different types of AF (see Box 1).

Box 1: Types of AF

Source: Camm et al (2010) p10

Type	Description
First diagnosed AF	First time AF is detected
Paroxysmal AF	Self-terminating, usually within 48 hrs
Persistent AF	AF is present when an AF episode either lasts longer than seven days or requires termination by cardioversion, either with drugs or by direct current cardioversion
Long-standing persistent AF	AF has lasted for ≥ 1 year when it is decided to adopt a rhythm control strategy
Permanent AF	AF when the presence of the arrhythmia is accepted by the patient (and physician)
Silent AF (asymptomatic)	May manifest as an AF-related complication (ischaemic stroke or tachycardiomypathy) or may be diagnosed by an opportunistic ECG. Silent AF may present as any of the temporal forms of AF

A person with AF may feel palpitations, chest pain, dizziness, or in extreme cases loss of consciousness. It may also occur asymptotically (National Collaborating Centre for Chronic Conditions 2006). AF also increases the risk of mortality (Lorgan 2006, DeWilde, Carey, Emmas et al 2006, Lip and Tello-Montoliu 2006, Lafuente-Lafuente, Mahé, Extramiana 2009, Jenkins and Dunn 2007, Finsterer and Stöllberger 2008, Singh 2008, Cea-Calvo, Redón, Lozano et al 2006, Kakar, Boos and Lip 2007, Maegdefessel, Azuma and Tsao 2010, Sherman, Kim, Boop, et al 2005). AF patients may not be diagnosed until after they have serious complications from AF including stroke, thromboembolism or heart failure (National Collaborating Centre for Chronic Conditions 2006). People with AF have an annual risk that is five to six times higher than patients in sinus rhythm for stroke (National Collaborating Centre for Chronic Conditions 2006). In the UK, five per cent of strokes occur in those with AF (BJHM 2009). Camm et al 2010 highlight the following clinical events from AF:

1. Death
2. Stroke
3. Hospitalisations
4. Quality of life and exercise capacity
5. Left ventricular function

AF risk factors include age, diabetes, hypertension, valve disease, and AF is associated with congestive heart failure and strokes (National Collaborating Centre for Chronic Conditions 2006). It is also common after surgery, such as thoracotomy and coronary artery bypass graft (National Collaborating Centre for Chronic Conditions 2006). It has also been linked to dietary and lifestyle factors (National Collaborating Centre for Chronic Conditions 2006).

It's therefore clear that AF is a condition that is not only significant for those suffering from the disease but also to the health care system.

This study was initiated in response to a perceived lack of awareness of AF across Europe and a lack of comparable information and data on AF across Europe. SAFE were interested in a variety of topics including:

1. Incidence and prevalence of AF
2. Health care system response to AF (including management / treatment options, guidelines, and health care staff training and involvement in AF)
3. Patient information
4. Economic burden of AF (including hospitalisation data and potential costs of ‘missed’ diagnosis)

The objective was to assess what is currently known about each of these across Europe.

The study set out to explore these topics using two approaches:

Rapid evidence review to bring together the evidence from published literature

This allows a baseline understanding of the evidence base as it stands drawing upon English language literature published between 2005 and 2010. A rapid evidence review completed by a single reviewer was a pragmatic approach² given limited time and resources.³

Survey of member organisations of SAFE and World Heart Federation

Surveys of patient organisations have been used to explore a variety of issues⁴ and although such approaches will have their limitations, patient organisations can act as advocates for patients and can bring together substantial expertise related to a disease area (NICE 2009). In some countries significant efforts are being made to involve patients and their representatives in health care related decision making (Barham forthcoming) and hence patient organisations are a legitimate source of views on a variety of issues related to a disease area.

From the outset, it was recognised that this is an exploratory study and that further work would most likely be required to enable a fuller and more robust understanding of the issues.⁵

The remainder of this report sets out:

- Incidence and prevalence estimates
- Health care system response to AF
- Patient information
- Economic burden of AF
- Discussion and recommendations for the future

Separate appendices provide details of survey questions, survey respondents, the approach to the rapid evidence review, and references.

² A systematic review with more than one researcher would be considered the ‘gold standard’ but would nevertheless require more time and resources

³ And there are precedents for taking such an approach as a starting point, see Øvretveit (2009) as an example

⁴ See for example Patient View (2009), Patient View (2010), and EURORDIS (2010)

⁵ A range of options were considered ranging from: surveys of academics, organisations representing health care staff, hospitals and clinics, review of Ministry of Health/Statistical Offices websites, focus groups with patients, clinicians etc. Such work would be feasible given sufficient resourcing and time

2. Incidence and prevalence

Key points:

- Up to two per cent of the general population will have AF
- Six million people across Europe have AF
- AF is expected to increase and perhaps even double in the next 50 years
- Diagnosing AF is complex, and many may have the condition and not yet be diagnosed

2.1 Up to two per cent of the general population will have AF

AF is the commonest sustained cardiac arrhythmia (National Collaborating Centre for Chronic Conditions 2006) occurring in one to two per cent of the general population (ESC 2010). It's likely that it is closer to two per cent than one per cent (Camm et al 2010). Across Europe the number of people with AF is estimated to be around six million (Camm et al 2010). AF was an underlying condition in 39 per cent of respondents to the European Heart Survey (Nieminen, Brutsaert, Dickstein et al 2006).

The available estimates of incidence and prevalence by country are presented below:

Table 3: Estimates of incidence and prevalence of AF by country

Country	Incidence and prevalence	Source
Denmark	Prevalence: 198 per 100,000 individuals aged 40–89 years (1980) 438 per 100,000 individuals aged 40–89 years (1999)	Frost, Vestergaard, Mosekilde et al (2005)
Italy	Prevalence: 7.4% those aged 65+	Bilato, Corti, Baggio et al (2009)
Italy	Prevalence: 9% of primary care patients those of which 63% had chronic AF, 37% newly diagnosed AF	Scalvini, Piepoli, Zanelli et al (2005)
Italy	Prevalence: 21.4% of heart failure patients in Heart Failure Clinics in hospitals	De Ferrari, Klersy, Ferrero et al (2007)
Italy	Prevalence: 3.9–3.0 cases, and 3.6–3.0 cases per 1,000 person-years in males and females respectively in primary care	Mazzaglia, Filippi, Alacqua et al (2010)
Lithuania	Prevalence: 3.8% at age 60 and 9.8% at age 80	Survey respondent
Netherlands	Prevalence: 5.5% of those aged 55+ Incidence: 9.9/1000 person-years	Heeringa, van der Kuip, Hofman et al (2006)
Norway	Prevalence: 10% of those aged over 75	Tveit, Abdelnoor, Enger et al (2008)
Portugal	Prevalence: 2.5% in those aged 40 and over	Bonhorst, Mendes, Adrago et al (2010)
Scotland (UK)	Prevalence: 9.4/1000 in men and 7.9/1000 in women Incidence: 1/1000 in men and .09/1000 in women (2001/2)	Murphy, Simpson, Jhund, et al (2007)
Spain	Incidence: 3.1 per 100 patient-years in those with hemodialysis	Vázquez-Ruiz de Castroviejoa, Sánchez-Perales, Lozano-Cabezas et al (2006)
Spain	Prevalence: 8.5% of those 60+	Cea-Calvo, Redón, Lozano et al (2006)
UK	Prevalence: 0.84% in men and 0.83% in women in primary care (1994) 1.49% in men and 1.29% in women in primary care (2003)	DeWilde, Carey, Emmas et al (2006)
UK	Prevalence: 1%	BJHM (2009)

In terms of available estimates of absolute numbers with AF only rough approximations are available from Finland (approximately 50,000), Slovenia (approximately 20,000), Lithuania (approximately 7,500 new cases per year), Germany (approximately 800,000), not known or unavailable (Belgium, Russia) or are not available due to patient confidentiality concerns, which is hindering the ability to identify numbers of patients with AF (Norway) (all survey responses). Approximately 639,000 people have AF in England (NICE 2006).

2.2 The prevalence of AF is increasing over time and could double in the next 50 years

The number of people with AF is increasing over time (Miyasaka, Barnes, Gersh et al 2006, Frost, Vestergaard, Mosekilde et al 2005, Santini and Ricci 2006, Rietbrock, Heeley, Plumb et al 2008).

The number of people with AF could double in the next 50 years (Camm et al 2010). However, there remain questions about the total number of people with AF as some may be undiagnosed, and some sources of data may under-report the true number of people with AF (Prineas, Soliman, Howard et al 2009, National Collaborating Centre for Chronic Conditions 2006, Murphy, Simpson, Jhund, et al 2007). AF incidence increases with age, estimated at 0.5 per cent prevalence at age 50–59 years to almost nine per cent prevalence at age 80–89 years (National Collaborating Centre for Chronic Conditions 2006).

Respondents to the survey believe that the number of people with AF will increase (Finland, Norway, Slovenia, Lithuania, Germany and UK).

2.3 AF prevalence is likely to be underestimated

Diagnosing AF is a challenge for the health care system because AF can be ‘silent’ with no symptoms and hence go undiagnosed (Camm et al 2010). AF can be diagnosed and managed across different settings (Kell 2009, Pisters, Nieuwlaat, de Vos et al 2009, Deasy undated, British Journal of Hospital Medicine 2009) and managed by different health care professionals including nurses (Gillis, Burland, Arnburg et al 2008), which poses a challenge to aggregate up estimates of cases (Murphy, Simpson, Jhund et al 2007). Technology for detecting AF is evolving with time and can pick up cases which would have been missed before (Camm et al 2010) which may be improving diagnosis. Thus, overall estimates of incidence and prevalence may well undercount the true numbers of people with this condition.

Disease registers can help to understand trends in incidence, prevalence (and many other issues⁶). Disease registers appear to be few and far between in Europe. Such registers are not available in Finland, Russia, Norway, Lithuania or respondents did not know (Belgium, Slovenia) but is available in Germany (the German Competence Network on Atrial Fibrillation (AFNET) survey respondent,⁷ Nabauer, Gerth, Limbourg et al 2009).

⁶ Including research and technology assessment, see Newton and Garner (2002). Registries can help explore patterns of practice and their presence may also contribute towards adherence to guidelines Ron Pisters, Robby Nieuwlaat, Cees B. de Vos et al Comprehensive upstream treatment for atrial fibrillation, when and how? *Europace* (2009) 11, 397–399.

⁷ Also see <http://www.kompetenznetz-vorhofflimmern.de/>

A national registry is planned in Norway and although it is still subject to debate and implementation, it may provide further insights on AF in the future (survey respondent).

A five-year follow up of patients (which could be thought of as quasi registry) has been undertaken in Italy allowing a better understanding of progression of AF (Pappone, Radinovic, Manguso et al 2008). The Euro Heart Survey on Atrial Fibrillation has been described as a registry (Wyse 2005), with results presented at the European level rather than country level. A separate registry, the International Registry for Atrial Fibrillation Surgery (RAFS), includes details on patients who have had surgery for their AF (Melo, Santiago, Aguiar et al 2008). Sanofi-aventis, have also set up registries including RECORD AF and REALISE AF to collect data on the disease and cardiovascular events across a number of countries (sanofi-aventis 2009). Progresses on such registries are likely to help fill the gaps that are seen in Europe.

3. Health care system response to AF

Key points:

- AF is a complex disease to diagnose and manage
- Guidelines exist but there is evidence of variation in adherence to these guidelines across Europe
- Reasons for variation are not well understood and research is needed to explore barriers and enablers to best practice, including patients' preferences
- There could be missed opportunities to more effectively manage AF which could have knock on impacts on both patients in terms of preventable ill health and even mortality, but also a higher cost to the health care system

3.1 AF is a complex disease to diagnose and manage

AF can be managed using a variety of approaches. Box 2 provides an overview of options based upon UK guidance.⁸ It is also important to note that treatment options are evolving over time which can change the ways in which AF can be diagnosed and managed (Pietro Ricci, Morichelli, and Santini 2009, Kirchhof, Bax, Blomstrom-Lundquist et al 2009, Crandall et al 2009, Kalas 2009, Charokopos, Rouska, and Styliadis et al 2006, Neuberger, Mewis, van Veldhuisen et al 2007, Kistler and Habersberger 2007, Lafuente-Lafuente, Mahé, Extramiana 2009, Finsterer and Stöllberger 2008, Singh 2008, Wazni, Tsao, Chen et al 2006, Fuster, Ryden, Cannom, et al 2006, Saleem, Bharani, Madhusudhana Chetty et al, Kakar, Boos and Lip 2007, Gillinov 2007, Laughlin and Kowey 2008). Key priorities for implementing guidance have been identified in the UK (see Box 2 overleaf).

⁸ New guidance from the ESC is also available which provides much more clinical information on options, see Camm et al (2010)

Box 2: Main diagnostic and treatment options for AF from NICE Information for Patients (2006)

Diagnosis

ECG, and if appropriate ambulatory ECG, or echocardiography

Management

Cardioversion – either electrical cardioversion (which may also include medicines) or pharmacological cardioversion using antiarrhythmic medicines to help the heart return to a normal rhythm

Anticoagulation – to help reduce the risk of blood clots which can cause stroke. Example medicines include: aspirin, warfarin and heparin

Management of different types of AF

Management of persistent atrial fibrillation – medicines and possibly cardioversion. Example medicines include:

Medicine to control heart rate

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Calcium-channel blocker (verapamil or diltiazem)
Digoxin
Amiodarone

Medicine to control heart rhythm

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Amiodarone
Class 1c agent (flecainide, propafenone)
Sotalol

Medicine to prevent blood clots

Warfarin
Heparin

Management of permanent atrial fibrillation – regular medicines. Example medicines include:

Medicine to control heart rate

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Calcium-channel blocker (diltiazem, verapamil)
Digoxin

Medicine to prevent blood clots

Warfarin or
Aspirin

Management of paroxysmal atrial fibrillation – medicines but not necessarily taken regularly (also known as pill in the pocket). Example medicines include:

Medicine to control heart rhythm

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Amiodarone
Class 1c agent (flecainide, propafenone)
Sotalol

Medicine to prevent blood clots

Heparin (by injection)
Warfarin or
Aspirin

Management of acute-onset atrial fibrillation – electrical or pharmacological cardioversion. Example medicines include:

Medicine used for pharmacological cardioversion

Amiodarone
Class 1c agent (flecainide) (if there is also a Wolff-Parkinson–White syndrome)

Medicine to control heart rate

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Calcium-channel blocker (diltiazem, verapamil)
Amiodarone

Medicine to prevent blood clots

Heparin

Preventing and treating atrial fibrillation after surgery – medicines before and after surgery. Example medicines include:

Medicine to prevent atrial fibrillation after surgery

Amiodarone
Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Calcium-channel blocker (diltiazem, verapamil)
Sotalol

Medicine to treat atrial fibrillation after surgery

Beta-blocker (for example, atenolol, bisoprolol, metoprolol)
Calcium-channel blocker (diltiazem, verapamil)
Amiodarone

Box 3: Priorities for guidance implementation from the National Collaborating Centre for Chronic Conditions (2006)

1. An electrocardiogram (ECG) should be performed in all patients, whether symptomatic or not, in whom AF is suspected because an irregular pulse has been detected.
2. As some patients with persistent AF will satisfy criteria for either an initial rate-control or rhythm-control strategy (for example, aged over 65 but also symptomatic):
 - the indications for each option should not be regarded as mutually exclusive and the potential advantages and disadvantages of each strategy should be explained to patients before agreeing which to adopt
 - any comorbidities that might indicate one approach rather than the other should be taken into account
 - irrespective of whether a rate-control or a rhythm-control strategy is adopted in patients with persistent AF, appropriate antithrombotic therapy should be used.
3. In patients with permanent AF, who need treatment for rate control:
 - beta-blockers or rate-limiting calcium antagonists should be the preferred initial monotherapy in all patients
 - digoxin should only be considered as monotherapy in predominately sedentary patients.
4. In patients with newly diagnosed AF for whom antithrombotic therapy is indicated, such treatment should be initiated with minimal delay after the appropriate management of comorbidities.
5. The stroke risk stratification algorithm should be used in patients with AF to assess their risk of stroke and thromboembolism, and appropriate thromboprophylaxis given.

Source: National Collaborating Centre for Chronic Conditions (2006) p 17

Respondents to the survey suggest that AF can be diagnosed and managed by a variety of health care professionals, and commonly in the primary care and outpatient setting (see Tables 4, 5 & 6).

Table 4: Health care professionals commonly involved in diagnosis and management of AF, Belgium, Finland, Germany, Lithuania, Norway, Russia, Slovenia and UK

Country	Belgium	Finland	Germany	Lithuania	Norway	Russia	Slovenia	UK
Diagnosis								
GP	?	✓	✓	✓	✓	✓	✓	✓
Neurologist	?	✓			✓		✓	
Internist	?	✓		✓	✓	✓	✓	
Cardiologist	?	✓	✓	✓	✓	✓	✓	
Management								
GP	?		✓	✓	✓	✓	✓	✓
Neurologist	?							
Internist	?	✓		✓	✓		✓	
Cardiologist	?	✓	✓	✓	✓	✓	✓	✓
Nurse	?	✓						

Table 5: Setting where AF is commonly managed, Belgium, Finland, Germany, Lithuania, Norway, Russia, Slovenia and UK

Country	Belgium	Finland	Germany	Lithuania	Norway	Russia	Slovenia	UK
Primary care	?	✓	✓		✓	✓		✓
Outpatient	?	✓	✓	✓	✓	✓	✓	✓
Inpatient	?	✓	✓		✓			

A variety of treatment options may be appropriate and the survey respondents highlighted that many options are available (see Table 6). Newer treatments, such as dronedarone, are more likely not to be available (Slovenia, Lithuania) or their availability unknown (Belgium, UK⁹). Some options are limited by capacity, for example a decision has been taken to increase capacity for radiofrequency ablation (which currently has a one to three year waiting list) in Norway, which will be effective from 2011 (survey respondent). It must be noted however that this is based only upon responses from the survey, does not provide a definitive picture and hides complexities, such as whether treatments are available for use to different clinicians, different settings, any recommendations on their use, reimbursement status etc. This highlights the complexities in terms of ensuring appropriate access.

Table 6: Availability of treatment options for AF, Belgium, Finland, Germany, Lithuania, Norway, Russia, Slovenia and UK (Continued overleaf)

Country	Belgium	Finland	Germany	Lithuania	Norway	Russia	Slovenia	UK
Diagnostics								
ECG	✓	✓	✓	✓	✓	✓	✓	✓
TTE	?	✓	✓	✓	✓	✓	✓	✓
Chest x ray	✓	✓	✓	✓	✓	✓	✓	✓
Holter monitoring	?	✓	✓	✓	✓	✓	✓	?
Exercise test	✓	✓	✓	✓	✓	✓	✓	✓
TTE	?	✓	✓	✓	✓	✓	✓	✓
Electrophysiology	?	✓	?	✓	✓	✓	✓	✓
Event recorder	?	✓	✓	✓	✓	?	✓	✓
Interventions								
Pharmacological conversion	?	✓	✓	✓	✓	✓	✓	✓
Electrical cardioversion	?	✓	✓	✓	✓	✓	✓	✓
Catheter ablation	?	✓	✓	✓	✓	✓	✓	✓
Pacemaker implantation	✓	✓	✓	✓	✓	✓	✓	✓
ICD implantation	?	✓	✓	✓	✓	✓	✓	✓
Surgical therapy	?	✓	✓	✓	✓	✓	✓	✓

Key: ✓ = available, ✗ = not available, ? = unknown

⁹ While the research was ongoing Dronedarone was going through National Institute for Health and Clinical Excellence processes to provide recommendations on its use in the English and Welsh NHS. Final guidance is now available from: <http://guidance.nice.org.uk/TA197>

Table 6: Availability of treatment options for AF, Belgium, Finland, Germany, Lithuania, Norway, Russia, Slovenia and UK (Continued)

Country	Belgium	Finland	Germany	Lithuania	Norway	Russia	Slovenia	UK
Pharmaceuticals								
<i>Control heart rate</i>								
Beta-blocker (for example, atenolol, bisoprolol, metoprolol)	✓	✓		✓	✓	✓	✓	✓
Calcium-channel blocker (verapamil or diltiazem)	?	✓	?	✓	✓	✓	✓	✓
Digoxin	?	✓	?	✓	✓	✓	✓	✓
Amiodarone	?	✓	?	✓	✓	✓	✓	✓
<i>Medicine to control heart rhythm</i>								
Beta-blocker (for example, atenolol, bisoprolol, metoprolol)	✓	✓	?	✓	✓	✓	✓	✓
Amiodarone	?	✓	?	✓	✓	✓	✓	✓
Class 1c agent (flecainide, propafenone)	?	✓	?	✓	✓	✓	✓	✓
Sotalol	?	✓	?	✗	✓	✓	✓	✓
<i>Medicine to prevent blood clots</i>								
Warfarin/phenprocoumon or Vitamin K-antagonists in general	?	✓	?	✓	✓	✓	✓	✓
Heparin	?	✓	?	✓	✓	✓	✓	✓
Aspirin	✓	✓	?	✓	✓	✓	✓	✓
<i>Other</i>								
Dronedarone	?	✓	✓	✗	✓	✓	✗	?

Key: ✓ = available, ✗ = not available, ? = unknown

It should be noted that treatment for AF is complex; not all treatment options are appropriate for all patients reflecting specific clinical factors (Stürmer, Talajic, Thibault, et al 2005, Hoppe, Casares, and Eiskjær et al 2006, Kruchov Thygesen, Frost, Eagle et al 2009, Eduardo Vázquez-Ruiz de Castroviejoa, Carmen Sánchez-Perales, et al 2006, De Ferrari, Klersy, Ferrero et al 2007, Miyasaka, Barnes, Gersh et al 2006, Johansen, Brustad, Enger et al 2008, Neuberger, Mewis, van Veldhuisen et al 2007, Nucifora, Schuijf, Tops et al 2009, Lentine, Schnitzler, Abbott et al 2006, Schmitt, Duray, Gersh et al 2009, Del Arco, Martín, and Laguna, et al 2005). In addition, over time some patients may also experience side effects from treatment and/or become drug resistant (Leaver and Ho 2006, Jolobe 2006, Pisters, Nieuwlaat, de Vos et al 2009, Takahashi, Kuwahara and Takahashi 2009).

3.2 Missed opportunities to more successfully manage AF

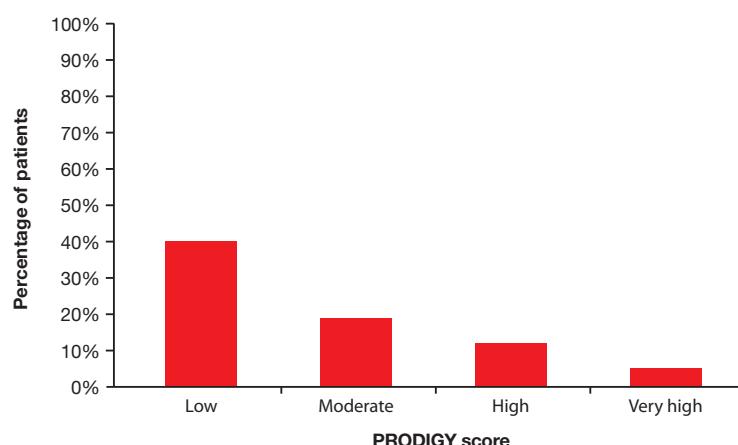
Although guidance exists, there is evidence of variation in practice in some countries in Europe (Nieuwlaat, Capucci, Lip et al 2006, Pisters, Nieuwlaat, de Vos et al 2009, Nabauer, Gerth, Limbourg et al 2009, DeWilde, Carey, Emmas et al 2006, Nieuwlaat, Prins, Le Heuzey et al, Nieuwlaat, Capucci, Camm et al 2005, Nieuwlaat, Eurlings, Capucci et al 2007, Zehnder, Schaer, Jeker et al 2006, Murphy, Simpson, Jhund, et al 2007, Monte, Macchia, Pellegrini et al 2006, Nieuwlaat, Eurlings, Cleland et al 2009, British Journal of Hospital Medicine 2009, Nieuwlaat, Olsson, Lip et al 2007, Mazzaglia, Filippi, Alacqua et al 2010). Such variation could mean missed opportunities to manage AF and avoid clinical outcomes such as stroke.

Some specific issues include:

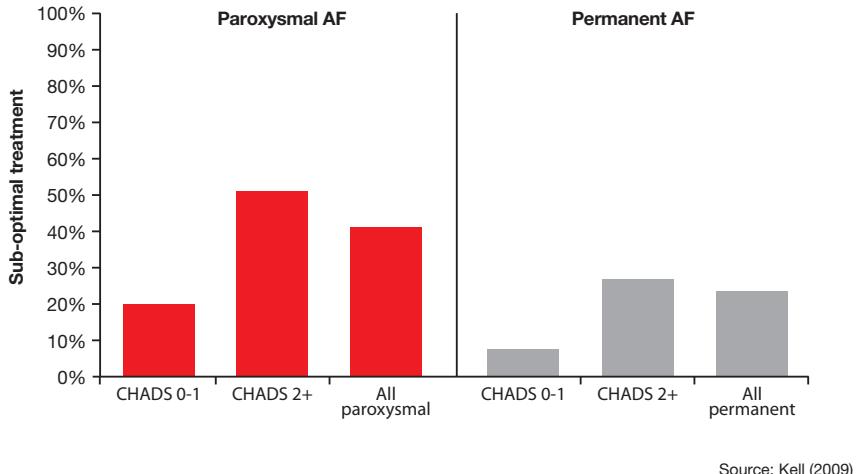
Prescribing

Although use of oral anticoagulants (OAs) increases when patients are at greater risk of stroke (indicated by PRODIGY score) there remain proportions who have no use of OAs in the primary care setting in the UK who could benefit (see Figure 3). The reasons are unknown and further research is recommended to explore both prescribers' decisions and patients' willingness to take certain medicines (DeWilde, Carey, Emmas et al 2006). Similar findings in local audits of AF patients, showed that sub-optimal treatment occurs in just over 50 per cent of existing AF patients (Kell 2009).

Figure 3: No use of oral anticoagulants (OA) by PRODIGY risk score in UK primary care



Source: DeWilde et al (2006)

Figure 4: Sub-optimal treatment by type of AF, North Somerset, UK

Underuse of OAs has also been seen as part of the Euro Heart Survey on Atrial Fibrillation. Patterns of prescribing suggested that OA was not tailored to the patient's risk profile as suggested by guidelines (Nieuwlaat, Capucci, Lip et al 2006). This includes potentially overuse of OA in patients least likely to benefit and with a risk of bleeding. Concerns of a lack of appropriate antithrombotic treatment have also been raised in Italy, both in post hospitalisation (Monte, Macchia, Pellegrini et al 2006), and in primary care (Mazzaglia, Filippi, Alacqua et al 2010).

The Euro Heart Survey on Atrial Fibrillation also allows exploration of issues to specific groups of patients. Those with both AF and heart failure may also not be treated according to guidelines and there are concerns of undertreatment in relation to drug therapy for stroke prevention, HF therapy, and rate control (Nieuwlaat, Eurlings, Cleland et al 2009).

The concern of a lack of tailoring of treatment to patients is echoed in results from the German Competence NETwork on Atrial Fibrillation (AFNET) registry including both over and under use of OA (Nabauer, Gerth, Limbourg et al 2009). 71 per cent of eligible patients for OA received it, and 49 per cent of ineligible patients for OA received it. Under and over treatment has also been seen in the Netherlands, although appropriate antithrombotic prescribing is relatively high occurring in 67 to 72 per cent of patients (Dinh, Nieuwlaat, Tielemans et al 2007).

Although causality cannot be confirmed, a higher level of mortality could be an outcome of underuse in those with first detected AF (Nieuwlaat et al 2008). In the Italian setting, patients receiving antithrombotic treatment following hospitalisation had more favourable survival rates (Monte, Macchia, Pellegrini et al 2006).

Thyroid hormone level measurement

30 per cent of patients included in the Euro Heart Survey did not undergo thyroid hormone levels measurement at any point in time, despite guidelines suggesting that this is undertaken (Nieuwlaat et al 2008)

The reasons for variation in practice are not well understood and may be a combination of (Nieuwlaat, Capucci, Lip et al 2006):

- Patient factors (eg awareness and understanding of AF and treatment options)
- Deficiencies in clinician knowledge of guidelines or deficiencies in the guidelines themselves
- Complexity of risk stratification schemes which guide prescribing decisions
- Unresolved debate about relative pros and cons of management options
- Need for refinement in tools and treatment options

Physician reluctance (including overestimation of risks of prescribing warfarin) may also be an issue (Lane and Lip 2005, Kell 2009). A potential approach is to improve dissemination of findings of clinical studies to increase awareness of risks amongst clinicians and generally improve education (Levi, Hobbs, Jacobson et al 2009).

Survey respondents indicated that training was available in the following countries: Germany and UK (but unknown if continuously updated), Finland, Norway, Slovenia, Lithuania (including being continuously updated), Russia (updated every five years), and one respondent did not know (Belgium).

In the Netherlands, the role of guidelines has been seen as instrumental for contributing to appropriate prescribing in AF (Dinh, Nieuwlaat, Tielemans et al 2007). In Norway, compliance is relatively high with guidance, when tested in two municipalities (Tveit, Abdelnoor, Enger et al 2008). This suggests that greater adherence may well be possible in other countries.

It should also be recognised that there is also ongoing debate about best practice (Lindsay 2009, Raja 2005, Nieuwlaat, Prins, Le Heuzey et al 2008, Healey, Baranchuk, Crystal, et al 2005, Lafuente-Lafuente, Mahé, Extramiana 2009, Jenkins and Dunn 2007, Singh 2008, Ogawa, Yamashita, Yamazaki, et al 2009, Israel 2009, Cosio, Aliot, Botto et al 2008, Calkins, Reynolds, Spector et al 2009, Lip, Huber, Andreotti et al 2010) and more research is needed (Cavalli, Kaya, Aslan et al 2008, Murtuza, Pepper, Stanbridge, et al 2008, Sleeswijk, Van Noord, Tulleken et al 2007, Pürerfellner, Urban, de Weerd et al 2009, Niv 2008, Levi, Hobbs, Jacobson et al 2009).

It is also relevant to note that following guidance can be cost increasing (and still value for money); in England the estimated cost of implementing NICE guidance for treatment and management of AF is £67.64million, a cost offset (due to reduction in strokes and bleeding) of £45.78million, leaving a net cost increase to the NHS of £21.86million (NICE 2006).

Finally, appropriate treatment and management in the health care system also requires the appropriate number and appropriately skilled health care professionals. Constraints can exist within systems; in particular a lack of arrhythmia specialists in the UK has been highlighted (BJHM 2009).

4. Patient information

Key points:

- There is a variety of information available to patients ranging from leaflets, websites and a telephone helpline
- What is available is insufficient to meet the needs of patients
- There is also a gap in understanding patient preferences

Patient information is variable across Europe. Survey responses suggest that there is a very mixed picture; particularly in terms of what is available, ranging from nothing through to multiple mechanisms to provide information including the internet, leaflets and telephone advice.

Table 7: Availability of patient information on AF, Belgium, Finland, Germany, Lithuania, Norway, Russia, Slovenia and UK

Country	Belgium	Finland	Germany	Lithuania	Norway	Russia	Slovenia	UK
Available?	X	?	✓	✓	✓	?	?	✓
Format								
Website(s)		✓	✓	✓				✓
Leaflet(s)		✓	✓	✓				✓
Telephone advice line(s)			✓					✓
Perceive a gap in patient information?	✓	?	✓	✓	✓	?	?	✓

Key: ✓ = available, X = not available, ? = unknown

It is clear that a range of resources are available, and the following have been highlighted in the literature and are set out in the in Box 4 below.

Box 4: Patient information on AF

Arrhythmia Alliance: www.heartrhythmcharity.org.uk

Atrial Fibrillation Association: <http://www.atrialfibrillation.org.uk/>

Shea JB, Sears SF. A patient's guide to living with atrial fibrillation. *Circulation*. 2008;117:e340-43. <http://circ.ahajournals.org/cgi/content/full/117/20/e340>

NHS Clinical Knowledge Summaries (patient information leaflet, atrial fibrillation). www.cks.nhs.uk/patient_information_leaflet/Atrial_fibrillation

Medline Plus. www.nlm.nih.gov/medlineplus/atrialfibrillation.html

Wikipedia. http://en.wikipedia.org/wiki/Atrial_fibrillation

World Heart Federation, SAFE, AFA, EHRA, Are you AF AWARE? http://www.world-heart-federation.org/fileadmin/user_upload/images/AF-Aware/AF%20AWARE%20booklet%20v11.pdf

Patient information in Germany provided by sanofi-aventis <http://www.vhf-portal.de/>

Source: BJHM (2009) and Lafuente, Lafuente et al (2009), World Heart Federation and survey respondent

Following on from the availability of patient information, survey respondents felt that patients did not have the information that they needed to be a partner in their treatment decisions with appropriate support from their clinician (Belgium, Norway, Lithuania, Germany) or didn't know (UK). The opposite was perceived by the respondent in Russia where they believed that patients did have the information that they needed. Specific issues were raised about the ways in which information was presented and/or co-ordinated where it is available.

These concerns about patient information are broadly consistent with previous survey research which has highlighted that (World Heart Federation, SAFE, AFA, European Heart Rhythm Association undated):

- 50 per cent of doctors thought that patients needed more information
- 33 per cent of physicians thought that the available patient education material was insufficient, of poor quality, or difficult to source

In addition, patient preferences are not well understood (Lane and Lip 2005) but patient preferences have been put forward as a potential driver for lack of adherence to guidelines. These issues may well be linked as information is likely to be a key part of patients' developing their preferences.

5. Economic burden of AF

Key points:

- Cost of illness studies are helpful to policy makers to understand the burden of a disease and to inform a host of decisions for the health care system
- AF results in significant primary care activity, particularly use of medicines
- AF results in significant secondary care activity, including hospitalisations with length of stay ranging from four to eight days
- This activity will translate into significant expenditure by the health care system on AF although this is not fully quantified across or within Europe
- Defining the appropriate level of health care system expenditure is challenging but wise use of resources in primary care (i.e. appropriate prescribing) may be able to reduce downstream burden in secondary care (i.e. through reduced incidence of stroke)
- AF can also limit ability to work which is a cost not only to the individual, but also to society more generally

5.1 Cost of illness is important for policy makers

The World Health Organisation (WHO) notes that understanding the burden of disease is “*an important input to health decision-making and planning processes*” (WHO 2010). Policy makers can use estimates of the cost of illness to: (1) define the magnitude of the disease or injury in financial terms; (2) justify intervention programs; (3) assist in the allocation of research funding on specific diseases; (4) provide a basis for policy and planning relative to prevention and control initiatives; and (5) provide an economic framework for program evaluation (Rice 2000, Finklestein and Corso 2003). Such estimates of the cost of an illness have been instrumental in public policy debates (Segel 2006).

Assessing the full economic costs of a disease requires analysis of (Segel 2006):

1. The direct costs (eg resources used in the health care system)
2. The indirect costs (eg sickness absence, presenteeism)
3. The intangible costs (eg worry and concern)

Assessing the full economic costs (taking the societal perspective¹⁰) of AF requires an assessment of the costs to:

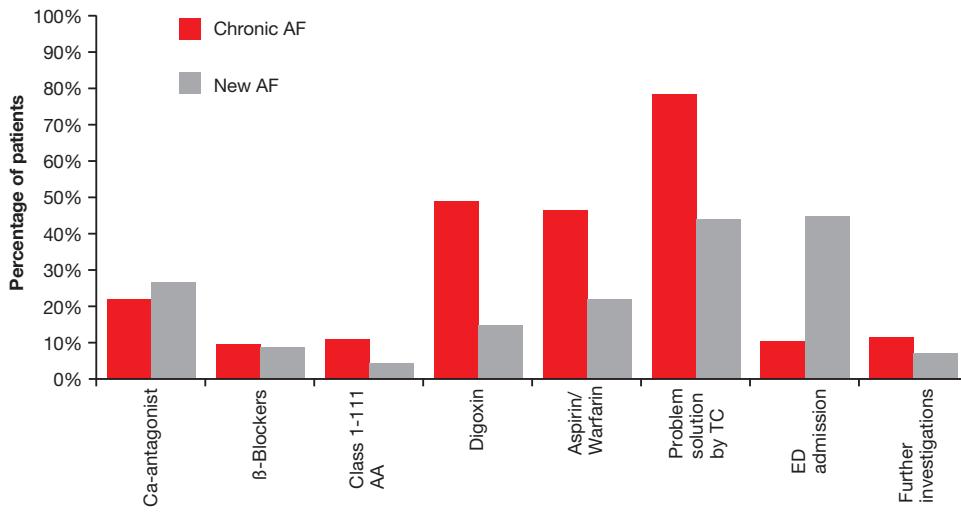
- Individuals with AF
- Carers of those with AF
- Potentially employer costs for those who may be absent from work due to AF (although this is less likely to occur as frequently than other diseases reflecting the increasing prevalence in those of retirement age)
- The health care system in providing treatment
- Potentially the welfare system in providing payments to those who are ill/cannot work (although this is a transfer payment and is not 'added up' because it represents a transfer of wealth from taxpayers to benefit recipients rather than consuming resources except for transaction costs of doing so)

In many cases the cost of an illness is worked bottom up by looking at activities and resources used and multiplying up by unit costs. Thus the amount of the activity is an indicator of the likely financial cost, even if the costing hasn't been completed.

5.2 Significant primary care activity

AF can be diagnosed and managed in both primary and secondary care settings. Primary care activity is varied ranging from the prescribing of a number of medicines through to referral to emergency care (see Figures 5 and 6).

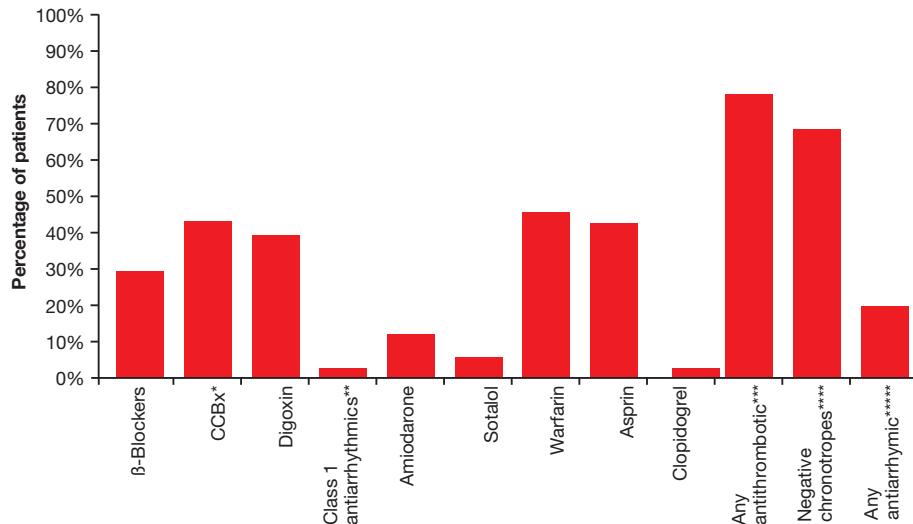
Figure 5: Therapy following identification of AF, Italian primary care patients



Source: Scalvining et al (2005)

¹⁰ See Byford and Rafferty (1998) and Jönsson (2009) for a discussion on the value of taking the societal perspective

Figure 6: Therapy, Scottish primary care patients



CCB = calcium channel blocker * =excluding dihydropyridines **=includes quinidine, disopyramide, propafenone and flecanide ***=warfarin or aspirin or clopidogrel ****=β-blocker or rate limiting CCB or digoxin *****=class 1 antiarrhythmic or amiodarone or sotalol

Source: Murphy et al (2007)

This level of activity implies not insignificant expense of AF to primary health care in both Italy and Scotland.

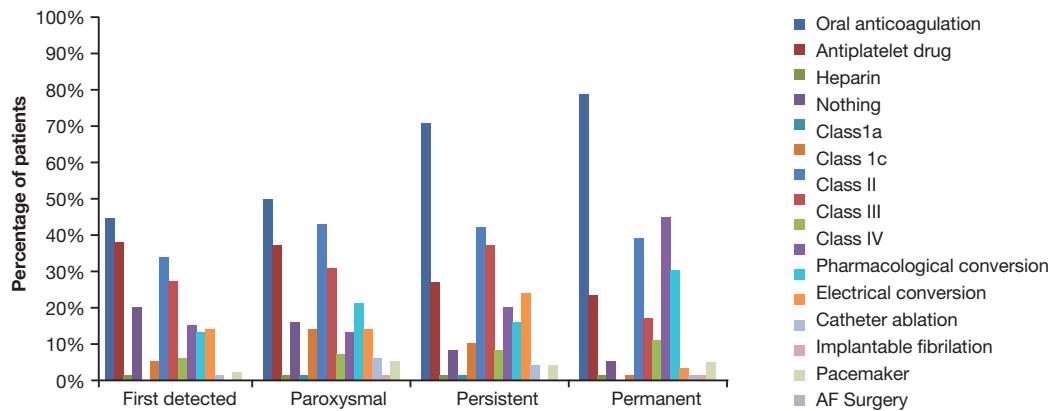
The appropriateness of expenditure is related to a number of factors. In Sweden, maintaining AF patients on warfarin in the International Normalised Ratio (INR) with the most commonly recommended range of INR 2–3, costs SEK16,244 for the first year, and SEK 8,904 for subsequent years in primary care. Björholt, Andersson, Nilsson et al (2007) highlight that this is not an insignificant cost but that “*warfarin prevents stroke in CAF, and the cost of monitoring may be off-set by the reduced incidence of this disorder*”. In Finland the costs of warfarin differ according to the degree of control; the mean costs were between €95.27 to €166.92 higher for patients who were not in the defined INR-balance (Hallinen, Martikainen and Soini et al 2008).

In the UK, opportunistic screening has been undertaken to more proactively identify AF patients and manage their risk of stroke (Kell 2009). In North Somerset, nine GP practices opportunistically screened patients over the age of 65. This led to one diagnosis of AF in every 107 patients screened (pulse taken) and amounted to 66 new patients treated. This, alongside an audit of treatment of existing AF patients, led to an estimate of 1.6 strokes avoided in the North Somerset area. This approach was underpinned by financial incentives; GP practices received payments ranging from £1 to £40 per patient, and £100 for producing baseline data, and £500 for attendance at three meetings. On balance, this pilot scheme is considered value for money in light of the relatively expensive cost of stroke treatment in the NHS versus an estimated cost of £191.38 for each new patient identified and treated.

5.3 Significant secondary care activity

In secondary care (focused upon cardiology clinics) there are a whole host of activities being undertaken across the different types of AF. The figure below highlights the frequent use of a range of medicines, with less frequent use of surgical interventions across patients in European countries.

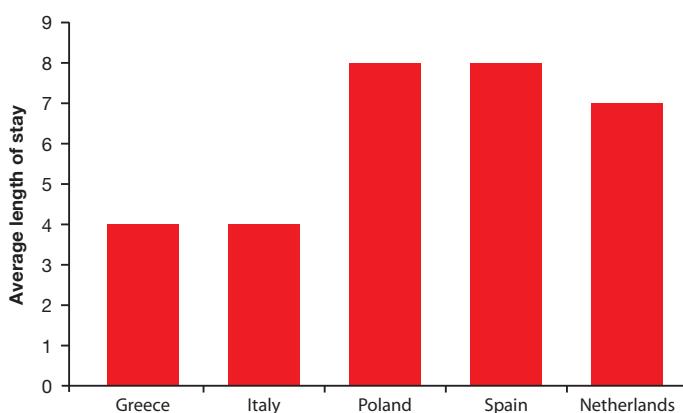
Figure 7: Management, European patients in cardiology clinics



Source: Nieuwlaat et al (2008)

Length of stay for hospitalised first-time ischemic stroke patients with AF is considerably longer than those without AF; in Denmark the median length of stay was 15 days vs 9 days (Kruchov Thygesen, Frost, Eagle et al 2009). Length of stay of those hospitalised in Greece, Italy, Poland, Spain and the Netherlands varies (see Figure 8).

Figure 8: Average length of stay for hospitalised AF patients, Greece, Italy, Poland, Spain, Netherlands

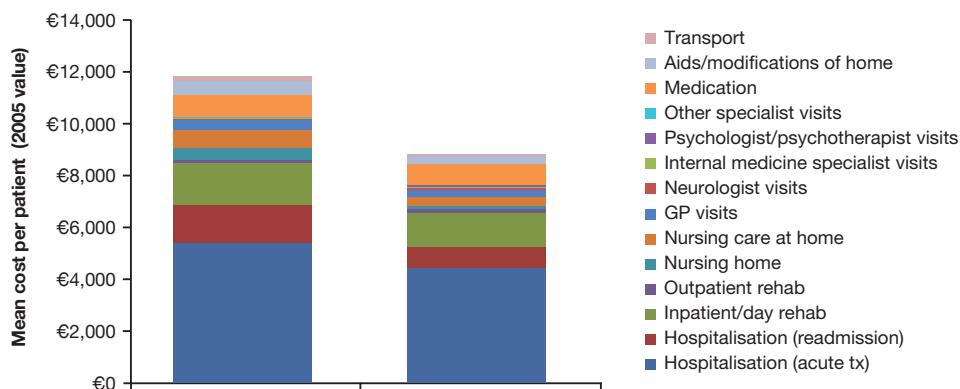


Source: Ringborg et al (2008)

In England, the latest available hospital statistics show 88,931 admissions for atrial fibrillation and flutter (~1% of all admissions in 2008/9). Of those, 62 per cent were classed as emergencies, with an average length of stay of 4.2 days (HES 2009). To give an indication of costs that may result from AF in hospital care in England, an elective (i.e. planned) Percutaneous Complex Ablation (includes Atrial Fibrillation or Ventricular Tachycardia) is estimated to cost, on average, £3,511 (in 2008/9) (DH 2010) with a length of stay around two days. The same procedure as an emergency costs £7,662 with a length of stay closer to eight days.

In Germany, analysis of costs for those with stroke with and without AF suggest higher costs when AF is present (see Figure 9).

Figure 9: Stroke related direct costs with AF and without AF, Germany



Source: Brüggenjürgen et al (2007)

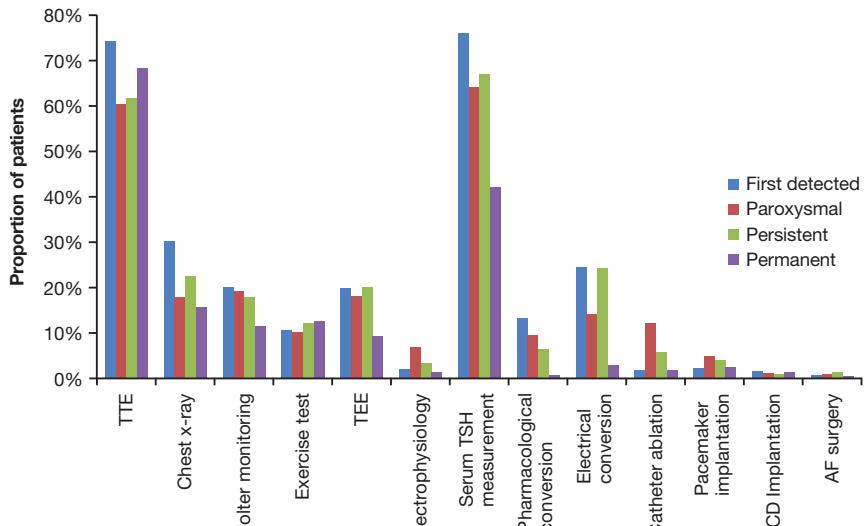
Adjusting for confounders suggests that AF related strokes cost more than non-AF related strokes; on average €11,799 vs €8,817 per patient (Brüggenjürgen, Rossnagel, Roll et al 2007). Similarly in Sweden, AF patients had on average €818 higher inpatient costs over three years than non-AF patients (€10,192 vs. €9374) (Ghatnekar and Glader 2008).

Although these statistics do not provide a complete understanding of the secondary burden of AF in Europe, they are suggestive of a need to use relatively more expensive health care resources.

5.4 Substantial health care system activity and costs

A range of activity is undertaken across the whole of the health care system. The AFNET registry provides an overview which reflects activity from GP practices through to hospitals. Intensity of different activities differs according to type of AF (see Figure 10).

Figure 10: Health care activity by type of AF, Germany

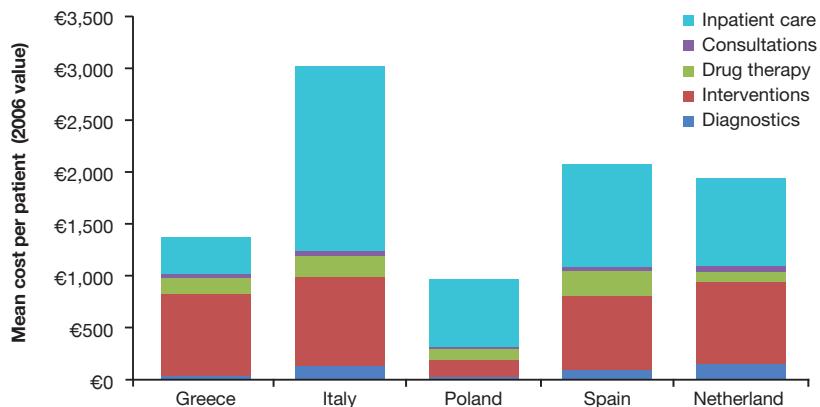


Source: Nabauer et al (2009)

Estimates of the cost of AF in Germany to the health care system are; €1,394 for paroxysmal AF, €2,130 for persistent AF, and €1,073 (2008 values) for permanent AF with hospitalisations driving the majority of these costs (Benkert et al 2009).

Although the full costs of AF to health care systems across Europe is not known estimates are available for some countries (Greece, Italy, Poland, Spain, Netherlands, UK, see Figures). These estimates are not all comparable but suggest that much of the costs of AF relate to hospitalisations. There is variation in costs which is likely to reflect a number of factors (eg local unit costs for labour, differences in clinical patterns of treatment etc).

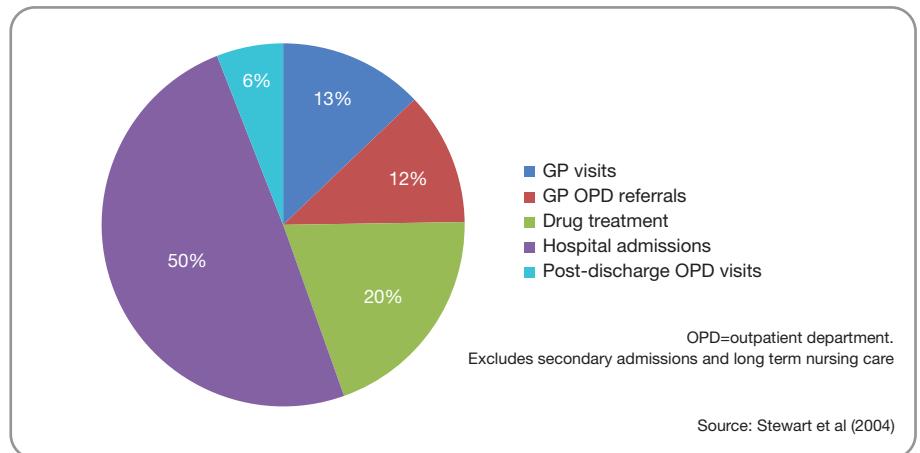
Figure 11: Health care system costs, Greece, Italy, Poland, Spain and the Netherlands



Source: Ringborg et al (2008)

In terms of relative importance, AF has been estimated to cost the UK £459 million (~€655 million) in 2000, equivalent to 0.97% of total NHS expenditure based on 1995 figures (Stewart et al 2004). A breakdown of the direct health care costs highlights the burden related to hospitalisations (see Figure 12 below).

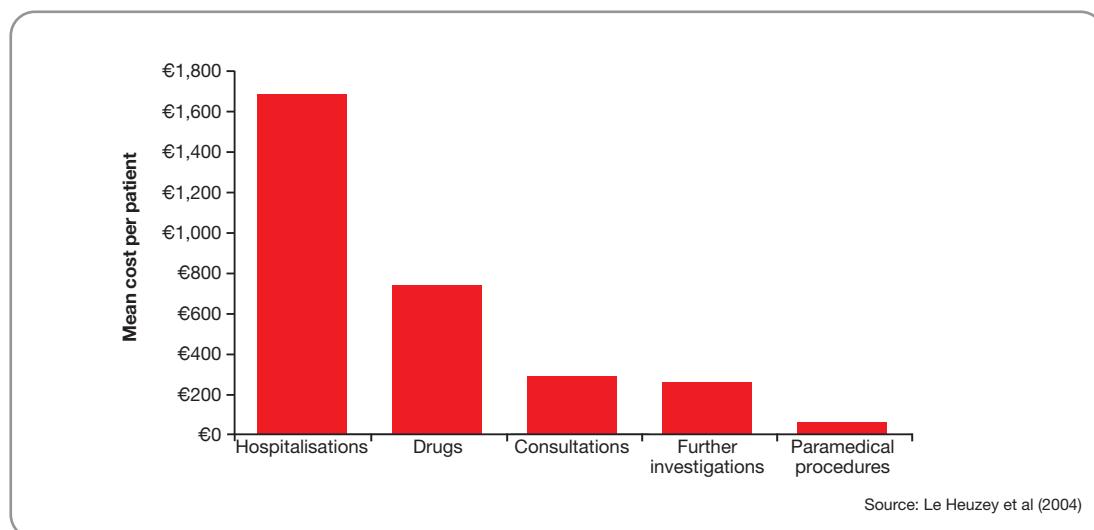
Figure 12: Breakdown of direct health care costs, UK



An estimate of €680million has been suggested for the cost of AF to the health care system in Germany (survey respondent^{11,12}).

In the French health care system, AF has been estimated to cost €3,027 on average per patient over a year. This is primarily because of hospitalisations (see Figure 13 below).

Figure 13: Health care system costs, France



Based upon the French estimate of total average cost per patient of €3,220, perhaps the total cost for AF is €10 billion for the European Union (Le Heuzey et al 2004).

Survey respondents found answering questions on economic burden particularly challenging; in some countries (Russia) estimates of economic burden are not undertaken at all. In others, one time studies have been conducted (UK, Germany¹³).

¹¹ It is based on the facts of a project made by a department of the Charité Berlin www.charite.de/epidemiologie/german/projekte/costflim.html

¹² Based upon estimates taken from a charity in Germany

¹³ And these papers are included in the preceding discussion, Stewart et al (2004) and Benkert et al (2009)

5.5 Substantial loss of work

Those with AF may also be limited in their ability to work and may retire early. Although estimating these indirect costs is challenging and subject to debate (Segel 2006) the available estimates for AF suggest that it could be substantial; ranging from €193 in France (Le Heuzey et al 2004) to in excess of €3,000 in Italy (Ringborg et al 2008, see Figure 14) and Germany (Bruggenjorgen et al 2007, see Figure 15). The costs vary across European countries and not all estimates separate out absenteeism and early retirement. None explicitly discuss any potential costs resulting from presenteeism (at work, but not fully productive).

Figure 14: Work loss costs, Greece, Italy, Poland, Spain and the Netherlands

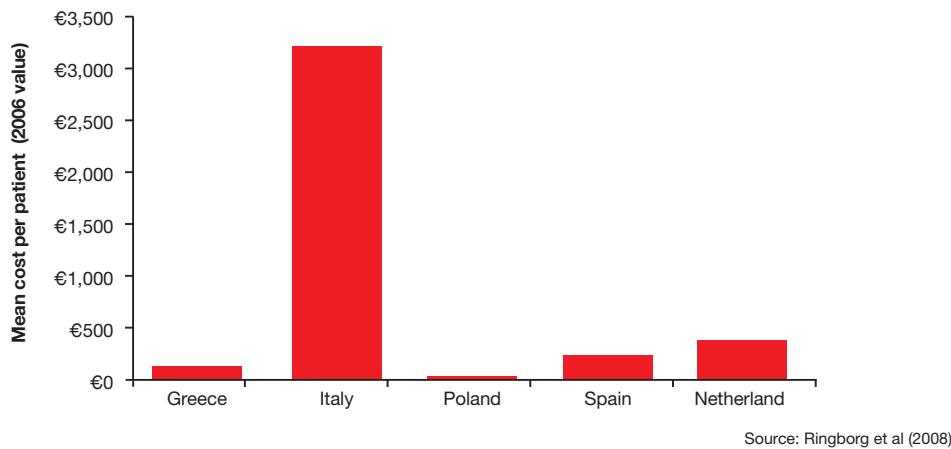
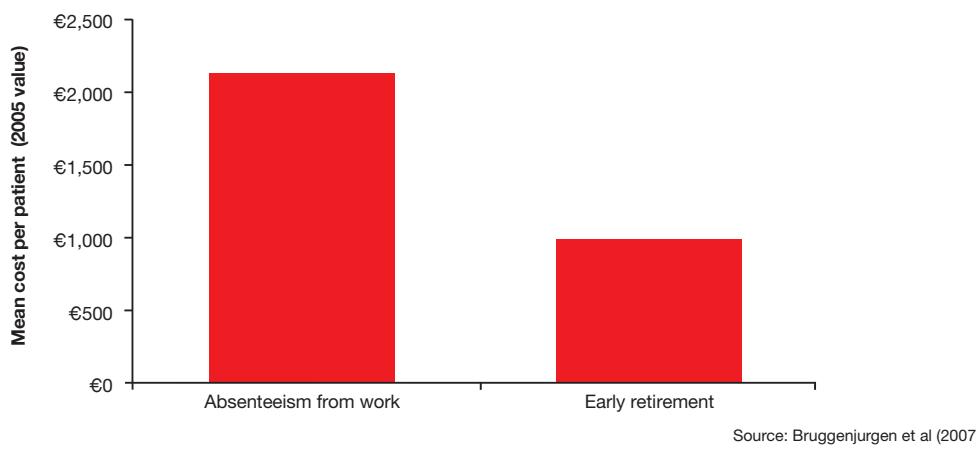


Figure 15: Work loss costs, Germany



6. Discussion and recommendations for the future

6.1 Overarching conclusions

There are key themes which are clear across the survey responses and evidence reviewed in this report:

- AF is increasingly common affecting up to two per cent of the general population
- The number of people with AF is set to grow over time, perhaps even doubling in the next 50 years
- AF prevalence is likely to be underestimated because it can be silent
- AF is a complex disease to diagnose and manage with a need to tailor the management according to patients' characteristics
- There are missed opportunities to more successfully manage AF by adhering to guidelines which can contribute to better outcomes for patients, and less demand on health care systems
- Patient information is available but isn't sufficient, a concern shared by patient organisations and clinicians
- AF results in a substantial cost of illness because it uses significant resources across primary and secondary care. In particular hospitalisations are expensive, and this is a key driver of the costs of AF. Appropriate management, particularly the use of medicines can lead to reduced demand for expensive hospital care
- AF results in substantial loss of work

6.2 Limitations

This study recognised from the outset that there are a large number of key areas to explore on AF in Europe and that there will be value in using a variety of approaches to explore these. This study used two methods to begin to explore incidence and prevalence of AF, health care system response to AF, patient information and economic burden of AF. These were selected to maximise the geographic scope and to bring consistency (eg in asking the same question using the same approach in the survey) within limited time and resources.

The rapid evidence review includes the following limitations: (1) only English-language literature was reviewed - expanding the coverage to non-English literature could reveal more evidence across Europe, (2) the time period of the literature reviewed was 2005 to 2010 - including earlier research could reveal more evidence but it would be more dated, (3) it was based upon searches and review by a single author and (4) it did not include the grey literature which could reveal work in progress and/or unpublished but relevant work.

The survey includes the following limitations: (1) patient organisations (who have drawn on contacts in some instances, such as clinicians or academics to help fill in the questions) were the only stakeholder group surveyed who will have information and knowledge relevant to the issues. Many others (eg individual clinicians, Hospitals including outpatient clinics, primary care clinics, Departments/Ministries of Health, Universities, professional associations and Trade Unions, manufacturers of technologies) are also likely to have relevant information and knowledge, (2) limited topics, (3) English language.

6.3 Potential future research

A number of potential pieces of further research could be helpful including:

- **Updating the available costs of AF**, for example estimates for the UK are now more than five years out of date. This would allow an understanding of the evolution of costs over time, particularly exploring the rate of increase. This would be useful to inform planning and resourcing in the future
- **Draw upon the estimates of the cost of stroke¹⁴ and apportion costs to AF.** This would exploit the link between AF and stroke and potentially allow estimates to be made of the cost of AF in countries where no estimates currently exist. This would be useful to highlight the burden where it is currently opaque
- **Explore the potential to extrapolate based upon available data to countries where no data exists.** Such approaches have been undertaken in other disease areas¹⁵
- **Build on the momentum seen for disease registers and use them to collect as much information as is both useful and proportionate** to explore burden and insights into disease progression and explore the costs and benefits of different treatment options
- **Explore reasons for lack of adherence to guidelines with clinicians and patients** to help understand barriers and explore potential enablers. This may be best approached initially via focus group discussion
- **Work with patient organisations to identify the best approaches to fill the information gaps for patients.** This may be best approached initially via focus group discussion
- **Work with providers of clinical training to assess the appropriate content and frequency of training on AF.** This may be best approached in partnership with professional organisations

¹⁴ Luengo-Fernandez, Gray and Rothwell (2009) provides a review of studies looking at the cost of stroke including studies in Western Europe and Eastern Europe

¹⁵ Lundkvist et al (2008) takes this approach for rheumatoid arthritis

7. Appendix 1: Survey questions

About you and your organisation

Please fill in your answers in this column in English

Example: What is your name?

A patient organisation

1 What is your name?

2 What is the name or your organisation?

3 What is your telephone number?

Please provide the international dialling code

4 What is your email address?

5 What is your postal address?

Street number/building name

Street

Town

Country

Postcode

6 What is your role in the organisation?

Eg Policy Officer, Researcher, Chief Executive etc

Please tell us about your organisation

7 How long has your organisation been operating in years?

Please delete as appropriate

8 Do you work just on AF?

Yes/No

9 If you would like to provide more of a description about your organisation please feel free to do so

10 Can we identify your organisation in the public report of this research?

Please delete as appropriate

Yes/No

Incidence and prevalence of AF

Please fill in your answers in this column in English

Example: How many people are newly diagnosed with AF per year on average?

	1000			
	Estimate	Exact number	Year	Source if exact number provided

11 How many people are newly diagnosed with AF per year on average in your country?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

12 How many people have AF in total in your country?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

13 Do you expect the total number of people with AF in your country to increase, decrease or stay the same in the next 5 years?

14 Is there/are there disease register(s) in your country that separately identify patients with AF?

15 If yes, please tell us how many you know about?

If yes, how do these operate?

16 Primary care or secondary care or both?

Please delete as appropriate

Increase/Decrease/Stay the same

17 Updated monthly/quarterly/annually?

Yes/No/Don't know

18 Who is responsible for the register(s)?

Primary care/Secondary care/Both

Monthly/Quarterly/Annually/Don't Know

Can you recommend who and where we might look for information in your country*

This might include for example: Government Departments, Organisations that represent health care staff, Academics, Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

* This is relevant if there is future research so that we can efficiently conduct future research on this issue

Management and treatment of AF

Please fill in your answers in this column in English

Please delete as appropriate

19 Who commonly diagnoses AF?

GP*, Neurologist, Internist, Cardiologist, Nurse, Other

20 Who commonly manages AF?

GP*, Neurologist, Internist, Cardiologist, Nurse, Other

21 How many years will patients have had AF, on average, by the time they are diagnosed?

22 Where are patients commonly treated?

Primary Care/Out patient/In patient/Other

What treatment options are available in your country?**

Diagnostics

23 ECG

Please delete as appropriate

Yes/No/Don't Know

24 TTE

Yes/No/Don't Know

25 Chest x ray

Yes/No/Don't Know

26 Holter monitoring

Yes/No/Don't Know

27 Exercise test

Yes/No/Don't Know

28 TEE

Yes/No/Don't Know

29 Electrophysiology

Yes/No/Don't Know

30 Event recorder

Yes/No/Don't Know

31 Other please specify:

Yes/No/Don't Know

Interventions

32 Pharmacological conversion

Yes/No/Don't Know

33 Electrical cardioversion

Yes/No/Don't Know

34 Catheter ablation

Yes/No/Don't Know

35 Pacemaker implantation

Yes/No/Don't Know

36 ICD implantation

Yes/No/Don't Know

37 Surgical therapy

Yes/No/Don't Know

38 Other please specify:

Yes/No/Don't Know

Pharmaceuticals

Control heart rate

39 Beta-blocker (for example, atenolol, bisoprolol, metoprolol)

Yes/No/Don't Know

40 Calcium-channel blocker (verapamil or diltiazem)

Yes/No/Don't Know

41 Digoxin

Yes/No/Don't Know

42 Amiodarone

Yes/No/Don't Know

Medicine to control heart rhythm

43 Beta-blocker (for example, atenolol, bisoprolol, metoprolol)

Yes/No/Don't Know

44 Amiodarone

Yes/No/Don't Know

45 Class 1c agent (flecainide, propafenone)

Yes/No/Don't Know

46 Sotalol

Yes/No/Don't Know

* GP = General Practitioner and may also be known as Family Doctor, or Primary Care Physician

** Note these are the options listed by NICE

(see <http://www.nice.org.uk/nicemedia/live/10982/30056/30056.pdf>)

Continued next page

Management and treatment of AF (continued)

Please fill in your answers in this column in English

Please delete as appropriate

Medicine to prevent blood clots

47 Warfarin/phenprocoumon or Vitamin K-antagonists in general

48 Heparin

49 Aspirin

Other

50 Dronedarone

51 Other please specify:

52 If you would like to provide more of a description about treatment options that are available in your country then please feel free do so

53 If you would like to provide more of a description about treatment options that are not available in your country then please feel free do so

54 If treatments are not available in your country, why do you think that is?

(e.g. medical insurance issues, drug availability, lack of funds etc)

Can you recommend who and where we might look for information***

This might include for example: Government Departments, Organisations that represent health care staff, Academics, Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

*** This is relevant if there is future research so that we can efficiently conduct future research on this issue

Training of health care professionals

Please fill in your answers in this column in English

Please delete as appropriate

Yes/No/Don't Know

55 Is there training for health care professionals (including all types of health care professionals including for example, doctors, nurses, allied health professionals) on AF?

56 If yes, is this continuously updated?

Yes/No/Don't Know

57 If yes, who provides this training?

Can you recommend who and where we might look for information*

This might include for example: Government Departments, Organisations that represent health care staff, Academics, Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

* This is relevant if there is future research so that we can efficiently conduct future research on this issue

Patient information

Please fill in your answers in this column in English

Please delete as appropriate

58 Is information available for patients about AF in your country?

Yes/No/Don't Know

What format is this information in?

59 Website(s)

Yes/No

60 Leaflets

Yes/No

61 Telephone advice line(s)

Yes/No

62 Other (please specify):

Who provides this information?

63 Health care system/staff

Yes/No

64 Government

Yes/No

65 Patient organisation

Yes/No

66 Other (please specify):

67 Do you perceive any gaps in the information available to patients?

Yes/No/Don't Know

68 If yes, please describe:**69 Do you believe that patients have the information that they need to be able to understand their condition?**

Yes/No/Don't Know

70 Do you believe that patients have the information that they need to be able to be a partner in their treatment decisions with appropriate support from their clinician?

Yes/No/Don't Know

71 Do other patient organisations exist in your country who represent AF patients?

Yes/No/Don't Know

If yes, can you please tell us the names of the organisations***Name of organisation**

Contact person**Telephone number****Email address****Website****Name of organisation**

Contact person**Telephone number****Email address****Website**

* This is relevant if there is future research so that we can efficiently conduct future research on this issue

Costs of AF in primary care

Please fill in your answers in this column in English

Please delete as appropriate

72 Are data on primary care activity for AF collected in your country?

Yes/No/Don't Know

73 If yes, who by?

74 If collected, how reliable are the data on AF primary care activity?

Very reliable/Not very reliable/Don't know

75 How much does AF cost in primary care in total per year on average in your country (in Euro)?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

Estimate	Exact number	Year	Source if exact number provided
----------	--------------	------	---------------------------------

How much activity takes place in primary care per year on average in your country?*

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

--	--	--	--

76 Primary care consultations

--	--	--	--

77 Primary care referred outpatient consultations which occur before hospitalisation

--	--	--	--

78 Anticoagulation visits

--	--	--	--

79 Pharmaceutical costs

--	--	--	--

80 Other (please specify):

--	--	--	--

* Note these are the main categories used in previous costing work, primary care component (see <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1768125/pdf/hrt09000286.pdf>)

How much does each activity in primary care cost in total per year on average in your country (in Euro)?*

--	--	--	--

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

81 Primary care consultations

--	--	--	--

82 Primary care referred outpatient consultations which occur before hospitalisation

--	--	--	--

83 Anticoagulation visits

--	--	--	--

84 Pharmaceutical costs

--	--	--	--

85 Other (please specify):

--	--	--	--

* Note these are the main categories used in previous costing work

(see <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1768125/pdf/hrt09000286.pdf>). Note that tests were not separately identified.

Continued next page

Costs of AF in primary care (continued)

Can you recommend who and where we might look for information **

This might include for example: Government Departments,
Organisations that represent health care staff, Academics,
Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

** This is relevant if there is future research so that we can efficiently conduct future research on this issue

Costs of AF in secondary care

Please fill in your answers in this column in English

Please delete as appropriate

86 Are data on secondary care activity for AF collected in your country? Yes/No/Don't Know

87 If yes, who by?

88 If collected, how reliable are the data on AF secondary care activity? Very reliable/Not very reliable/Don't know

89 How much does AF cost in secondary care in total per year on average in your country (in Euro)? Source if exact number provided

Estimate Exact number Year

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

How much activity takes place in secondary care per year on average in your country?*

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

Inpatient setting/hospital setting

90 Diagnostics (eg ECG, TTE, chest x ray, holter monitoring, exercise test, TEE, electrophysiology, event recorder)

91 Interventions (eg pharmacological conversion, electrical cardioversion, catheter ablation, pacemaker implantation, ICD implantation, Surgical therapy)

92 Pharmaceutical costs

93 Inpatient care admission/hospitalisation

94 Other (please specify):

Outpatient setting

95 Diagnostics (eg ECG, TTE, chest x ray, holter monitoring, exercise test, TEE, electrophysiology, event recorder)

96 Interventions (eg pharmacological conversion, electrical cardioversion, catheter ablation, pacemaker implantation, ICD implantation, Surgical therapy)

97 Pharmaceutical costs

98 Consultations which occur after hospitalisation

99 Other (please specify):

* Note these are the main categories used in previous secondary care setting costing work
(see <http://europace.oxfordjournals.org/content/10/4/403.full>)

100 What is the average length of stay for an emergency admission for AF?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

Continued next page

Costs of AF in secondary care (continued)

Please fill in your answers in this column in English

	Estimate	Exact number	Year	Source if exact number provided
101 What is the average length of stay for a non-emergency admission for AF?				

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

How much does each activity in secondary care cost in total per year on average in your country (in Euro)?*

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

Inpatient setting

102 Diagnostics (eg ECG, transthoracic echocardiogram (TTE), chest x ray, holter monitoring, exercise test, TEE, electrophysiology, event recorder)

--	--	--	--

103 Interventions (eg pharmacological conversion, electrical cardioversion, catheter ablation, pacemaker implantation, ICD implantation, Surgical therapy)

--	--	--	--

104 Pharmaceutical costs

--	--	--	--

105 Inpatient care admission/hospitalisation

--	--	--	--

106 Other (please specify):

--	--	--	--

Outpatient setting

107 Diagnostics (eg ECG, TTE, chest x ray, holter monitoring, exercise test, TEE, electrophysiology, event recorder)

--	--	--	--

108 Interventions (eg pharmacological conversion, electrical cardioversion, catheter ablation, pacemaker implantation, ICD implantation, Surgical therapy)

--	--	--	--

109 Pharmaceutical costs

--	--	--	--

110 Consultations which occur after hospitalisation

--	--	--	--

111 Other (please specify):

--	--	--	--

Can you recommend who and where we might look for information in your country**

This might include for example: Government Departments, Organisations that represent health care staff, Academics, Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

** This is relevant if there is future research so that we can efficiently conduct future research on this issue

Total economic costs of AF

Please fill in your answers in this column in English

112 How much does AF cost the health care system in total per year on average in your country (in Euro)?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

Estimate	Exact number	Year	Source if exact number provided

113 How much does AF cost the economy (eg in terms of sickness absence, lower productivity of those with AF at work, cost to carers for caring for those with AF) in total per year on average in your country (in Euro)?

If you know the exact number and the year that this relates to, please also fill this in, otherwise please use your best available information and judgement

--	--	--	--

Further information

Please fill in your answers in this column in English

Can you recommend who and where we might look for information in your country*

This might include for example: Government Departments, Organisations that represent health care staff, Academics, Websites, Published articles etc.

Please feel free to expand and add

Government Departments

Trade Unions

Organisations that represent health care staff

Academics

Websites

Published articles

* This is relevant if there is future research so that we can efficiently conduct future research on this issue

Can you provide guidance as to how we might access further data? If yes, please do so

--

8. Appendix 2: Respondents

All members of SAFE and the World Heart Federation were invited to take part in the survey from July to September 2010. As such the sample can be characterised as a ‘convenience sample’.

The survey was developed in a stepped approach:

1. The rapid evidence review was used to inform some of the content of the survey eg to inform the list of treatment options, terminology and economic costs to the health care system
2. Discussion with clinicians was undertaken to explore issues in AF and to inform questions to be explored (eg patient information and their involvement as a partner in treatment was a key issue highlighted by one clinician)
3. A subset of topics were prioritised via discussion with SAFE for inclusion in the survey due to a concern about the length of the survey which would limit motivation to participate (including all the topics initially set out by SAFE would have led to a survey approximately twice the length of the one used)¹⁶
4. The survey questions and Excel tool were developed and then piloted with three organisations to test that practicalities worked (eg that the Excel spreadsheet could be opened) and that the questions were meaningful and relevant. Feedback suggested that the practicalities worked but that the questions were detailed but did fit with the clinical context of AF. Given that the scope of the survey had already been reduced, the survey was not further reduced as it would limit further the areas of interest to SAFE

The approach to inviting participation was to:

- Send a letter from SAFE or the World Heart Federation to member organisations to alert them to the research and encourage participation via email
- Send an email invitation to participate from Leela Barham with a further reminder email
- Send an email to encourage participation from SAFE to SAFE members
- Phone calls to encourage participation from Leela Barham to World Heart Federation members and from SAFE staff to SAFE members

The final respondents included:

1. Belgium – Anonymous
2. Finland – Finnish Heart Association
3. Germany – German Stroke Foundation
4. Lithuania – Kaunas University of Medicine hospital, Cardiology dept
5. Norway – Norwegian Society of Cardiology
6. Russia – Anonymous
7. Slovenia – Slovenian Stroke Association
8. UK – Stroke Association

¹⁶ The following topics were not included in the survey but are of interest to SAFE: Guidelines, social care costs, patient costs, carer costs, transfer payments, and future research

This is a relatively small number of respondents in comparison to the membership of SAFE and the World Heart Federation (who have 72 member organisations). The low response rate is likely to reflect a number of challenges for organisations:

- The timing as many organisations close over the summer and/or relevant staff may take holidays during the months of June to September
- A lack of detailed knowledge on AF
- A lack of availability of specialists in the field, whom the organisation may have wished to work with to fill in the survey (eg local cardiologists)
- A lack of confidence in being able to provide answers to the relatively detailed questions that were asked in the survey; for example perhaps there is a lack of confidence in being able to answer health economic questions
- A lack of resources to devote to filling in the survey in the light of competing priorities (because for example, the organisation covers other disease areas and/or is minimally staffed and participating in the survey was a lower priority than their other work demands)
- The request that responses be filled in, in English
- Perhaps a concern about the approach taken to gather the information

In terms of lessons for the future, some suggestions include:

- Avoiding the holiday period for eliciting responses
- Providing a face to face briefing meeting to prepare organisations for taking part in the survey and reassuring them that ‘blanks’ are acceptable and to reassure them of the value of feeding back constraints to taking part. This should include a discussion of the rationale for the approach and why other approaches are not being used (eg because of practical constraints of time and funding and language barriers)
- Double checking of contact details prior to formal invitations to participate to minimise ‘bounce backs’ from email invitations

9. Appendix 3: Approach to rapid evidence review

This project adopted a rapid evidence review approach to identify relevant published research. A rapid evidence review follows the principles of a systematic review, but concessions are made in order to complete reviews in a shorter time scale (Thornley, Robert Quigley, Carolyn Watts et al 2007).

The following tables provide the search terms, limits and number of hits produced by searching Google Scholar and Pubmed. All searches were conducted in April 2010.

Table 8: Searches completed in Google Scholar

Search terms in Google Scholar	Date searched	# of hits
Limits: Exact phrase in title, 2005 to date, only in subject areas: biology, life sciences, and environment science, business, administration, finance and economics, medicine, pharmacology, and veterinary science, social sciences, arts and humanities		
Incidence of atrial fibrillation	18th April 2010	122
Prevalence of atrial fibrillation	18th April 2010	61
Clinical guidelines for atrial fibrillation	18th April 2010	0
Clinical guidelines for the treatment of atrial fibrillation	18th April 2010	0
Clinical guidelines for the management of atrial fibrillation	18th April 2010	0
Patient information for atrial fibrillation	18th April 2010	0
Patient information on atrial fibrillation	18th April 2010	0
Treatment options for atrial fibrillation	18th April 2010	0
Treatment for atrial fibrillation	18th April 2010	44
Management options for atrial fibrillation	18th April 2010	0
Management of atrial fibrillation	18th April 2010	220
Economics of atrial fibrillation	18th April 2010	0
Cost of atrial fibrillation	18th April 2010	3
Costs of atrial fibrillation	18th April 2010	1
Burden of atrial fibrillation	18th April 2010	0
Registries of atrial fibrillation	18th April 2010	0
Health care costs of atrial fibrillation	18th April 2010	0
Societal costs of atrial fibrillation	18th April 2010	0
Patient costs of atrial fibrillation	18th April 2010	0
		451

Table 9: Searches completed in Pubmed

Search terms in Pubmed	Date searched	# of hits
(Incidence[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	109
(prevalence[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	49
(Clinical[Title] AND guidelines[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	5
(Clinical[Title] AND guidelines[Title] AND treatment[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	0
Clinical[Title] AND guidelines[Title] AND management[Title] AND atrial[Title] AND fibrillation[Title] AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	1
(Patient[Title] AND information[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	0
(Patient[Title] AND information[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	0
(Treatment[Title] AND options[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/20"[PDat])	20th April 2010	5
(Treatment[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/28"[PDat])	20th April 2010	261
(Management[Title] AND options[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	1
(Management[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	166
economics[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	1
(cost[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	28
(costs[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	10
(burden[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	27
(Registries[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/28"[PDat])	28th April 2010	0
(health[Title] AND care[Title] AND costs[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/30"[PDat] : "2010/04/28"[PDat])	28th April 2010	2
(Societal[Title] AND costs[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/28"[PDat])	28th April 2010	0
(Patient[Title] AND costs[Title] AND atrial[Title] AND fibrillation[Title]) AND ("humans"[MeSH Terms] AND English[lang] AND "2005/04/22"[PDat] : "2010/04/28"[PDat])	28th April 2010	0
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Titles were screened for relevance, followed by abstracts. This identified 33 articles which provided evidence relating to Europe, and a further five which were international (ie discussed AF in the international setting).¹⁷ Many of the other articles discussed provided relevant background and context but often focused upon the US. Reference lists were not checked which could have identified further studies.

¹⁷ Note that two studies of economic costs of AF (Stewart et al 2004 and Le Heuzey et al 2004) were out of scope based upon the date range and are not included in these numbers, however they were located via general searches and are included in the report on the pragmatic basis that they provide insight, albeit more dated. Note that one study was sent by a survey respondent which is in German (Benkert et al 2009). Again this is included in the report on the pragmatic basis that it provides insight, although the full article could not be reviewed.

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36 studies which related to European countries or were international in scope are marked with a *.

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