The Cost of Illness of Atrial Fibrillation: A Systematic Review

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1. Background

- Atrial fibrillation (AF) is the most common cardiac arrhythmia, and the prevalence increases markedly with age. AF is strongly associated with increased risk of stroke and thromboembolism.
- In many countries, there is a growing awareness of the economic burden associated with AF due to aging populations and constrained public finances.

2. Objective

- The objective was to determine the cost of illness associated with AF and identify the main cost drivers of the disease.
- Separate searches were performed to identify studies investigating the cost of stroke and bleeding complications in patients with AF.

3. Methods

- **Method:** A systematic review was performed.
- **Databases and additional sources:** Sources included Medline, EMBASE, Cochrane Library, National Health Service Economic Evaluation, Health Technology Assessment, and Database of Abstracts of Reviews of Effectiveness databases from 1990 to April 21, 2009, and selected conference abstracts from 2005 to April 2009.
- **Screening:** A two-level screening process was performed. Level 1 screened titles and abstracts, and Level 2 screened full-text sources.
- **Language:** No language restrictions were applied in the search strategy.
- **Identification and selection of studies:**
  - The search strategy included combinations of free text and Medical Subject Headings. Separate sets of terms were used for the health condition of interest (AF or atrial flutter) and the study type (cost of illness and economic burden studies).
  - The inclusion criteria were patients with AF or atrial flutter, defined as persistent, permanent, and paroxysmal AF.
  - The exclusion criteria were studies of acute-onset AF and postoperative AF, and economic evaluations comparing costs and outcomes of alternative interventions.
- **Quality assessment:** Inclusion or exclusion of studies was performed in parallel by two researchers; disagreements were resolved by consensus.
- **Data extraction:** Data extracted included the study design, country, cost-year, population size and characteristics, and results (i.e., total costs, direct and indirect costs, and length of stay).
- **Data synthesis:** The range of direct annual cost and hospital cost estimates for the United States (US) and Western Europe was summarized. Disaggregated costs were reviewed to identify the main cost drivers.

4. Results

- **Identification of studies:** A total of 875 records were retrieved, and 37 studies were included in the review. (Figure 1).
- **Time horizon of retrieved studies:** cost-years ranged from 1991 to 2006.
- **Geographic zones considered:** The studies encompassed 16 countries (Australia, England, Finland, France, Germany, Greece, Hungary, Italy, The Netherlands, Poland, Portugal, Scotland, Spain, Sweden, the United Kingdom [UK], and the US).
- **Cost data:** The majority of studies estimated costs associated with AF in the US (18 studies) or Western Europe (14 studies). One study estimated the cost of AF in six countries worldwide (Australia, France, Portugal, Spain, Sweden, and the UK.[1] One study reported length of stay data for stroke patients with AF in seven European countries.[2] One study reported primary care contact rates in Scotland.[3] Two studies estimated the cost of stroke in AF patients in Western Europe.[4,5]
- **Study type:** A total of 15 studies were prospective, and 21 were retrospective. One study was a synthesis of published data.
- **Methodology used:** Ten studies were database analyses; two were registry analyses; two were based on survey data; and two were based on ancillary economic data collection within clinical trials. Twelve studies considered annual costs, and 16 considered hospitalization costs. The scope of the resource items included within individual studies varied widely from extremely specific (e.g., time and travel costs in attending anticoagulation clinics)[1] to more varied (e.g., diagnostic procedures, interventional procedures, drug therapy, inpatient care, consultations, work loss).[6]
- **National cost of AF:** The direct cost of managing AF represented 0.9% to 2.4% of the national health care budget for the UK (2000) and had approximately doubled over the previous 5 years.[7] Hospitalization rates for AF have been increasing steadily over the last 2 decades[8] and almost tripled in 2000 compared with the previous 2 decades.[9] Inpatient care and interventional procedures represented the largest cost component (where reported), accounting for 50% to 70% of total costs. In the US, AF hospitalizations alone cost an estimated $6.65 billion per annum (cost-year = 2006).[10]
- **Annual cost of AF:** Direct medical and nonmedical cost estimates ranged from approximately $10,100 to $14,200 per patient per year in the US (excluding one low outlier[11]), and from €450 to €3,000 in Western Europe (Table 1).
- **Cost of hospitalization for AF:** Direct cost estimates for inpatient stays ranged from approximately $1,700 to $19,300 in the US and from €1,300 to €6,400 in Western Europe (Figure 2).
- **Indirect costs:** If indirect costs were included, cost estimates increased by up to 20% in Europe and 79% in the US over direct costs alone (Table 1 and Figure 2).
- **Cost of hospitalization for major bleeding:** Hospitalization costs for major bleeding complications in patients with AF treated with warfarin have been estimated in the US as a mean US $15,988, with an average length of stay of 6 days (data-year = 2000-2003).[12] The average annual cost associated with bleeding per patient with AF receiving warfarin treatment has been estimated as US $19 in the US (data-year = 2000-2003),[12] £47.30 in the UK (cost-year = 1999/2000),[13] and €15 in Germany (cost-year = 2004).[14]
- **Cost of stroke in AF patients:** Direct costs associated with the management of stroke in patients with AF have been estimated as €11,799 in Germany (1-year period; cost-year not reported)[4] and €10,192 in Sweden (3-year period; data-year = 2001)[5] Mean hospitalization costs were significantly higher in AF-related strokes[4] (on average €818 higher over 3 years) than in non-AF patients (data-year = 2001).[5]

References: See poster handout.

Figure 1. QUOROM Diagram for Study Inclusion and Exclusion

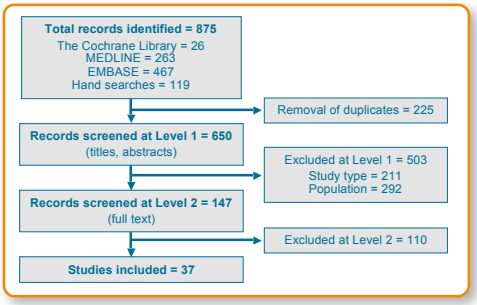
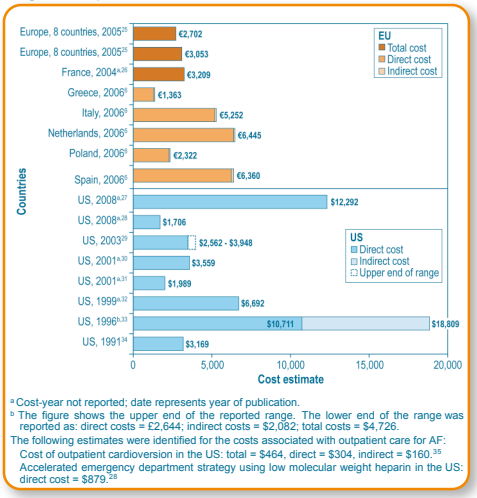


Table 1. Estimates of Annual Costs for AF (Arranged by Country and Publication Year)

Country	Cost Year	Total Cost	Direct Cost	Indirect Cost
France[15]	2001	-	€445-€1,590	-
France[16]	2000	-	€659-€1,092	-
Germany[17]	2005	€5,586	-	-
Germany[14]	2004	-	€827	-
Greece[6]	2006	€1,507	€1,372	€135
Italy[6]	2006	€3,225	€3,019	€206
The Netherlands[6]	2006	€2,328	€1,937	€391
Poland[6]	2006	-	-	-
Spain[6]	2006	€2,315	€2,073	€242
Sweden[17]	2005	€7,241	-	-
US[18]	2004	-	$14,199	-
US[11]	2002	-	$2,372-$10,312	-
US[19]	2001	-	$10,131-$10,560	-
US[20]	Not reported	-	$11,675	-

Four further studies reporting annual costs for patients with AF were identified but were not included in this table because costs represented only time and travel costs in attending anticoagulation clinics[1] or warfarin treatment only[22,23] or were reported in currency other than Euros or Dollars.

Figure 2. Inpatient Cost Estimates for AF



[a] Cost-year not reported; date represents year of publication.
[b] The figure shows the upper end of the reported range. The lower end of the range was reported as: direct costs = £2,644; indirect costs = $2,082; total costs = $4,726.

The following estimates were identified for the costs associated with outpatient care for AF:
Cost of outpatient cardioversion in the US: total = $464, direct = $304, indirect = $160.[35]
Accelerated emergency department strategy using low molecular weight heparin in the US: direct cost = $879.[28]

5. Discussion

- **Main findings:**
  - The cost of managing individual AF patients is high. The majority of direct cost estimates ranged from approximately $10,100 to $14,200 per patient per year in the US, and from €450 to €3,000 in Western Europe. Inpatient costs ranged from $1,700 to $18,800 in the US and from €1,300 to €6,400 in Western Europe. The lower end of the range in the US ($1,700) represented admissions for new onset AF in patients without comorbidity,[28] and the upper end ($18,800) was for ablation of the atrioventricular junction in drug refractory patients with an uncontrolled ventricular rate.[33]
  - The cost per patient-year is comparable to other chronic conditions such as diabetes[36] and chronic angina.[37] However, the economic burden of AF is expected to be lower on a national basis than that for other more prevalent diseases such as diabetes.
- **Justification of the approach used:** Publications were selected in compliance with prespecified eligibility criteria. Explicit, systematic methods were used in order to provide a comprehensive summary of the findings of cost of illness studies relating to AF management.
- **Limitations:**
  - The synthesis of cost estimates was confounded by substantial methodological heterogeneity between studies and diversity in the scope of resource items included.
  - The studies reported costs for years ranging from 1991 to 2006.
- **Perspectives:**
  - More accurate and standard estimations of AF costs seem to be necessary.
  - The economic burden of AF is increasing over time as a result of the increasing prevalence in aging populations. However, AF remains a much less common condition than many other cardiovascular diseases (e.g., hypertension, coronary heart disease, heart failure).

6. Conclusions

- The economic burden of AF is high, but is expected to be lower on a national basis than that for other more prevalent diseases such as diabetes. Hospitalizations represent the major cost driver, accounting for 50% to 70% of total costs. If indirect costs are included, costs increase by up to 20% over direct costs alone. Costs and hospitalizations attributable to AF have increased markedly over recent decades due to aging populations.
- The economic burden of AF is expected to decrease more on a national basis than other more prevalent diseases such as diabetes.

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