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Costs of atrial fibrillation in five European countries: results from the Euro Heart Survey on atrial fibrillation

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Aims To estimate costs of admission and costs incurred on an annual basis by patients with atrial fibrillation (AF) in Greece, Italy, Poland, Spain, and the Netherlands.
Methods and results The Euro Heart Survey on AF enrolled 5333 patients with AF in 35 European countries in 2003 and 2004. This was a bottom-up cost study conducted for the five largest contributors in terms of patients enrolled. Quantities of resource use during the enrolment admission and during 1-year follow-up were inferred from survey data and multiplied by national unit costs in order to estimate per patient costs associated with AF for each country. Mean costs of inpatient admission of an AF patient were estimated at €1363, €5252, €2322, €6360, and €6445 and mean costs incurred on an annual basis at €1507, €3225, €1010, €2315, and €2328 in Greece, Italy, Poland, Spain, and the Netherlands, respectively. Inpatient care and interventional procedures were identified as the main drivers of costs, accounting for more than 70% of total annual costs in all five countries.
Conclusion Estimates of the economic burden posed by AF are critical in light of the increasing importance of AF as a public health problem.

Introduction

There is a growing awareness of the economic burden posed by atrial fibrillation (AF) in Europe in light of an ageing population and constrained public finances. AF is well recognized as a disease of the elderly with the vast majority of cases occurring in patients above the age of 65.[1,2]

The prevalence of AF has been projected to increase as a consequence of population ageing,[3] a demographic trend that may be augmented by increased survival of patients with coronary heart disease.[4] This development will undoubtedly pose a challenge to health care systems during the coming decades in particular as AF patients are at increased risk of stroke, an event that entails high social and economic costs.[5,6]

There have been very few studies conducted on the cost of AF in Europe. Assessments of the resources devoted to care of patients with AF are important as a point of reference for economic evaluations of the cost-effectiveness of competing treatment strategies, as a means of highlighting the burden the condition imposes on society and as an aid to decision-makers and budget planners.

The objective of the present study was to estimate costs of admission and costs incurred on an annual basis by AF patients in Greece, Italy, Poland, Spain, and the Netherlands based on data collected through the Euro Heart Survey on AF.

Methods

The details of the Euro Heart Survey on AF have been described previously.[7] Consecutive patients per department were enrolled at outpatient cardiology clinics, cardiology wards, first (heart) aids, cardiac surgery wards, cardioversion departments and/or device implantation departments at university, non-university and specialized hospitals in European Society of Cardiology (ESC) member countries. Inclusion criteria were age 18 or older and AF on

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electrocardiogram (ECG) or Holter monitoring during the enrolment admission, or in the preceding 12 months. The period of study enrolment was September 2003 to August 2004. Data were collected through an electronic internet-based case report form covering patient characteristics, medical history, and management during the enrolment admission. A total of 5333 patients in 35 countries were enrolled in the Euro Heart Survey on AF. A follow-up of the cohort was conducted at 12 months at which data on AF status, treatment, medical events, consultations, and hospital admissions during the year of follow-up were collected through patient interview, review of patient medical records or both.

The present study included the five countries in which more than 200 patients were enrolled: Greece ($n = 323$), Italy ($n = 843$), Poland ($n = 267$), Spain ($n = 848$) and the Netherlands ($n = 714$). Total costs are a function of quantities of resource use and of the unit costs of these resources. Estimation of total costs associated with admission of an AF patient were based on resource data collected at enrolment while estimation of total annual costs incurred by AF patients were based on resource data collected at 1-year follow-up.

Resource use associated with admission

Data on resource use during the enrolment admission were classified into five modules: diagnostic procedures (including laboratory measurements), interventional procedures, drug therapy, inpatient care, and work loss. The admissions of patients enrolled in an outpatient cardiology clinic did not involve hospitalization, which has important implications for resource use. These admissions were therefore analysed separately from enrolment admissions taking place in the inpatient setting, i.e. at all enrolment sites except outpatient cardiology clinics.

The manner in which quantities of resource use were determined depended on the answer options given in the enrolment case report form. A quantity of one resource unit was assumed to be incurred by a patient during the enrolment admission for any given diagnostic procedure [ECG, transthoracic echocardiography (TTE), chest X-ray, exercise test, Holter monitoring, event recorder, transesophageal echocardiography (TEE) and electrophysiological procedure] or interventional procedure (electrical cardioversion, pharmacological conversion, catheter ablation, pacemaker implantation, ICD implantation, surgical therapy for AF) if it was recorded as being performed during the admission.

The quantities of antithrombotic, anti-arrhythmic/rate control and other drugs consumed during admission were determined for patients enrolled in an inpatient setting by multiplying the defined daily dose (DDD) according to the World Health Organization Collaborating Centre for Drugs Statistics Methodology[8] by the length of the patient's hospital stay in days. The drug therapy recorded at enrolment was assumed to prevail throughout the hospitalization unless the drug therapy recorded at discharge was different, in which case the patient was assumed to have switched treatment regimens halfway through the hospital stay.

Quantities of resource use related to inpatient care were determined in days through data on the length of hospital stay in cardiology wards, cardiac surgery and intensive and coronary care units (ICU/CCU), respectively.

Finally, for patients recorded as being employed the quantity of work loss in days was determined as the total length of stay of the enrolment admission. For employed patients enrolled in an outpatient setting, the quantity of work lost was assumed to equal half-a-day.

Annual resource use

Data on resources utilized by patients with AF during the year of follow-up were classified into six modules: diagnostic procedures, interventional procedures, drug therapy, inpatient care, consultations, and work loss. Patients enrolled in the study in an outpatient setting and in an inpatient setting were analysed jointly.

The number of diagnostic procedures (as above) performed since the enrolment admission was recorded at follow-up, and annual quantities could hence be inferred directly. In the case of the interventional procedures considered [catheter ablation, ICD implantation, coronary artery bypass grafting (CABG), valve replacement, pacemaker implantation, surgery for AF and percutaneous coronary intervention (PCI)], data solely indicated whether a procedure had been performed since the enrolment admission. A resource unit of one of the intervention in question was assumed for all non-missing, non-zero values.

In the module of drug therapy, patients recorded as receiving any given antithrombotic, anti-arrhythmic/rate control or other drug at 1-year follow-up as well as at discharge from the enrolment admission were assumed to have used DDDs of the drug for the full year. Patients recorded as receiving any given drug either at 1-year follow-up or at enrolment were assumed to have used DDDs of the drug for half-a-year.

In the module of inpatient care, the total number of nights spent in conjunction with hospital admissions for AF or other cardiovascular reasons since discharge from the enrolment admission were inferred from the follow-up data. Missing values of patients who had records of having undergone an interventional procedure during the year were imputed through best subset regression by country. The total number of consultations for AF with a doctor during the year and the total number of work days lost due to AF or other cardiovascular reason among the employed could be inferred directly.

Unit costs

Unit costs of the identified resource items are listed in *Table 1* and were obtained with the assistance of local professionals relying on the following country-specific sources: pharmacy price lists, price lists of two public hospitals in Greece, Health Ministry and hospital price lists in Italy, a bottom-up cost analysis conducted at the cardiology department of a representative hospital in Poland, the SOIKOS database of healthcare costs and Health Ministry price lists in Spain and published studies,[9,10] costing manuals and hospital price lists in the Netherlands. Unit costs of a work day lost were assumed to equal average daily earnings and were obtained from Eurostat for all countries.

Data analysis

Data analysis was performed with the Stata 9 software package at i3 Innovus, Stockholm, Sweden and University Hospital of Maastricht, Maastricht, the Netherlands. Costs of admission and total costs incurred on an annual basis by AF patients were determined per patient by multiplying the quantities of resources used with national unit costs of the corresponding resource items. Computations of mean costs were carried out by country and included patients with zero costs and missing values, the latter being set to zero. The analysis was carried out from the societal perspective implying that all available costs were considered regardless of payer. All costs are reported in 2006 Euros. The Polish zloty (PLN) was converted to Euros at the exchange rate of €1 = 4.64 PLN.

Results

This sub-study of the Euro Heart Survey of AF included all patients enrolled in Greece, Italy, Poland, Spain, and the Netherlands (*Table 2*).

The mean age lay between 66 and 70 with the majority of patients being male in all countries. Study patients were predominantly enrolled in an inpatient setting

Table 1 Unit costs of resources (Euros 2006)

	Greece	Italy	Poland	Spain	The Netherlands
Diagnostics					
ECG	4	12	2	10	19
TTE	8	52	10	76	175
Chest X-ray	4	15	4	19	47
Holter monitoring	12	62	4	123	106
Exercise test	28	84	4	45	123
TEE	88	77	10	76	214
Electrophysiology	71	775	1242	71	1811
Event recorder	20	280	–	110	854
Thyroid function test	43	9	3	9	3
Interventions					
Pharmacological cardioversion	4	4	5	2	2
Electrical cardioversion	90	109	87	143	165
Catheter ablation	2935	5450	1549	4231	4149
Pacemaker implantation	7055	6084	834	6721	8817
ICD implantation	37 556	4211	4256	11 861	31 173
Surgical therapy	6175	5450	–	6665	6018
PCI	12 697	3925	1052	7734	3086
CABG	–	8030	1710	14 063	10 545
Valve replacement	16 000	10 562	1710	2922	14 000
Drug therapy (selected)[a]					
Acenocoumarol	0.1	0.2	0.1	0.1	0.1
Sotalol	0.2	0.2	0.1	0.3	0.1
Digoxin	0.1	0.1	0.1	0.1	0.1
Clopidogrel	2.3	2.3	2.3	2.0	1.8
Low molecular weight heparin	7.5	7.2	7.9	7.8	7.8
Inpatient care					
Inpatient day, cardiology ward	93	420	157	376	407
Inpatient day, cardiac surgery	93	588	201	527	407
Inpatient day, ICU/CCU	187	1402	247	1255	1324
Consultations					
Visit with doctor (GP)	22	21	12	21	25
Indirect costs					
Average daily cost of labour	101	154	40	106	196

[a]Cost of daily dose.

Sources – Greece: hospital and pharmacy price lists; Italy: hospital and pharmacy price lists, Health Ministry data; Poland: cost study conducted at cardiology department of Polish hospital, published cost data;[20] Spain: pharmacy price lists, SOIKOS database of health care costs, Health Ministry data; The Netherlands: hospital and pharmacy price lists, costing manuals and published studies.[24] Labour costs for all countries obtained from Eurostat.

Note: Unit costs for event recorder and surgical therapy in Poland and CABG in Greece were not collected since the resource was not utilized by any survey patient.

except in the Netherlands, where 61% of patients were enrolled in outpatient clinics. The enrolment site is important in the context of costs as it affects quantities of resource use. Larger quantities can be expected to be consumed in inpatient settings. Spain had the highest percentage of patients with permanent AF (43%; $P < 0.001$ for difference compared with the other countries). Poland had the highest percentage of patients with coronary artery disease (42%; $P < 0.001$ for difference compared with Greece, Italy, and Spain; non-significant difference compared with the Netherlands) while prevalence rates of valvular heart disease were similar in all five countries ranging from 25 to 28%.

Table 3 reports the number of patients undergoing the investigated diagnostic procedures and interventions during the enrolment admission by enrolment site and country and, for patients admitted in an inpatient setting, the mean length of the admission in days.

From a health economic perspective, the key resource items during admission are the interventional procedures and inpatient days as these entail the highest cost. In the inpatient setting, the percentages undergoing major interventions were fairly similar, though catheter ablation was performed to a somewhat higher extent on patients of the Spanish sample (7% compared with 4% in Poland, 3% in Greece and the Netherlands and 1% in Italy) and pacemaker implantation to a somewhat higher extent on patients of the Polish sample (9% compared with 6% in Italy, 5% in Spain and the Netherlands and 4% in Greece). Mean lengths of hospital stay were lower in Greece and Italy compared with the other countries (4 days compared with 7 days in the Netherlands and 8 days in Poland and Spain).

A few interventional procedures were recorded as being performed on patients enrolled in outpatient clinics, in particular in Italy. These patients are likely to undergo subsequent transfer to inpatient clinics but further data on

Table 2 Participating centre types and patient characteristics at enrolment, by country

	Greece	Italy	Poland	Spain	The Netherlands
Centres	($n = 10$)	($n = 32$)	($n = 11$)	($n = 29$)	($n = 13$)
University centres	1	6	6	20	2
Non-university centres	7	23	1	6	11
Specialized centres	2	3	4	3	0
Patients	($n = 323$)	($n = 843$)	($n = 267$)	($n = 848$)	($n = 714$)
Demographics					
Mean (SD) age, years	66 (12)	70 (11)	66 (11)	67 (13)	70 (12)
Female gender	41%	40%	46%	45%	41%
Enrolment site					
Outpatient clinic	16%	40%	15%	45%	61%
University hospital	14%	24%	60%	73%	23%
Clinical type of AF					
First detected	25%	18%	15%	20%	14%
Paroxysmal	34%	22%	40%	18%	38%
Persistent	18%	35%	21%	20%	17%
Permanent	23%	25%	24%	43%	31%
Concomitant disease					
Hypertension	64%	69%	70%	58%	53%
Coronary artery disease	29%	24%	42%	24%	38%
Heart failure	15%	23%	33%	33%	22%
Valvular heart disease	25%	28%	26%	27%	26%
Diabetes mellitus	22%	16%	13%	22%	16%

SD, standard deviation.

this were lacking. Cardioversion for patients presenting in outpatient clinics without subsequent admission is possible, but indeed not likely for catheter ablation and pacemaker and ICD implantation.

Mean costs of admission of an AF patient in inpatient and outpatient settings are reported by country in *Table 4*. Mean costs of admission in an inpatient setting were estimated at €1363, €5252, €2322, €6360 and €6445 in Greece, Italy, Poland, Spain, and the Netherlands, respectively, with inpatient care accounting for the bulk of total costs. In Greece and Poland, relatively low costs of an inpatient day, explained by lower costs of labour and property, lead to markedly lower total costs of admission and to interventions accounting for an increased share of total costs. The lower cost of admission in Greece was also influenced by the relatively low mean length of stay. Likewise, the higher cost of admission in Spain and the Netherlands was heavily influenced by the higher mean length of stay.

In the outpatient setting, mean costs of admission were €68, €540, €229, €217, and €114 in the respective five countries. The higher cost of admission in Italy was driven by the execution of interventional procedures, which come at a high cost. If these were excluded, total costs of outpatient admission in Italy amounted to €59. Conversely, in the Greek patient sample, the lower cost of outpatient admission was explained by the absence of any major interventional procedure (catheter ablation, pacemaker or ICD implantation, surgical therapy) being carried out.

Table 5 reports resource use of study patients during the year of follow-up by country. An average 18% were lost to follow-up in these countries, which explains the lower number of patients compared with enrolment figures.

AF patients in all five countries made an average of two consultations with a doctor during the year. The percentage of patients requiring use of interventional procedures was generally low (2–3% for catheter ablation, 0–1% for ICD implantation, 1–2% for valve replacement) only slightly higher in Italy where 5% of patients had a pacemaker implantation. The average number of inpatient days spent during the year was 2 in the Netherlands, 3 in Spain and 4 in Greece, Italy, and Poland. Quantities of work loss exhibited more variation with employed patients in Greece losing an average of 9 days of work due to AF symptoms compared with an average of 26 days in the Netherlands. This did not appear to be due to differences in patients' age. As for drug therapy, the majority of patients were treated with a Vitamin K antagonist (VKA) at the time of follow-up in all countries except Greece where only 48% patients were receiving VKA. The percentage of patients treated with anti-arrhythmic/rate control drugs was equally lowest in Greece (62%) and highest in the Netherlands (78%).

Using the resource data collected at 1-year follow-up, mean annual costs of AF patients were estimated at €1507, €3225, €1010, €2315, and €2328 in Greece, Italy, Poland, Spain, and the Netherlands, respectively (*Table 6*). *Figure 1* illustrates the composition of annual costs and shows that costs were driven by inpatient care and interventions. These two resource items accounted for more than 70% of AF patients' costs in the five countries. The share of total costs accounted for by drug therapy was 11% in Greece, 6% in Italy, 9% in Poland, 10% in Spain, and 4% in the Netherlands.

As in the case of costs of inpatient admission, the lower annual costs observed in Greece and Poland were largely

Table 3 Key resource items used by atrial fibrillation patients during enrolment admission, by country and setting

Resource	Greece	Italy	Poland	Spain	The Netherlands
Inpatient setting	($n = 272$)	($n = 509$)	($n = 226$)	($n = 464$)	($n = 280$)
Diagnostics					
ECG	241 (89)	449 (88)	216 (96)	393 (85)	258 (92)
TTE	179 (66)	291 (57)	122 (54)	252 (54)	62 (22)
Chest X-ray	184 (68)	194 (38)	128 (57)	353 (76)	137 (49)
Holter monitoring	18 (7)	30 (6)	27 (12)	38 (8)	5 (2)
Exercise test	19 (7)	13 (3)	19 (8)	20 (4)	13 (5)
TEE	26 (10)	88 (17)	13 (6)	39 (8)	11 (4)
Electrophysiology	8 (3)	8 (2)	11 (5)	7 (2)	9 (3)
Event recorder	13 (5)	12 (2)	0	0	5 (2)
Interventions					
Pharmacological conversion	154 (57)	89 (17)	81 (36)	67 (14)	46 (16)
Electrical cardioversion	35 (13)	208 (41)	74 (33)	72 (16)	80 (29)
Catheter ablation	7 (3)	4 (1)	8 (4)	31 (7)	8 (3)
Pacemaker implantation	10 (4)	28 (6)	20 (9)	25 (5)	14 (5)
ICD implantation	1 (0.5)	1 (0.5)	5 (2)	3 (1)	4 (1)
Surgical therapy	1 (0.5)	0	0	0	2 (1)
Inpatient care					
Mean (SD) length of stay, days	4 (4)	4 (6)	8 (9)	8 (8)	7 (10)
Outpatient setting	($n = 51$)	($n = 334$)	($n = 41$)	($n = 384$)	($n = 430$)
Diagnostics					
ECG	43 (84)	170 (51)	22 (54)	296 (77)	329 (77)
TTE	23 (45)	36 (11)	8 (20)	108 (28)	37 (9)
Chest X-ray	9 (18)	13 (4)	0	126 (33)	20 (5)
Holter monitoring	2 (4)	18 (5)	5 (12)	14 (4)	3 (1)
Exercise test	0	1 (0.5)	0	4 (1)	13 (3)
TEE	0	5 (2)	1 (2)	3 (1)	1 (0.5)
Electrophysiology	0	1 (0.5)	0	1 (0.5)	1 (0.5)
Event recorder	0	1 (0.5)	0	1 (0.5)	1 (0.5)
Interventions					
Pharmacological conversion	12 (24)	60 (18)	2 (5)	33 (9)	3 (1)
Electrical cardioversion	0	47 (14)	4 (10)	18 (5)	6 (1)
Catheter ablation	0	9 (3)	2 (5)	4 (1)	1 (0.5)
Pacemaker implantation	0	15 (5)	1 (2)	5 (1)	1 (0.5)
ICD implantation	0	1 (0.5)	1 (2)	0	0
Surgical therapy	0	2 (0.5)	0	0	0

Data are presented as observed number (%) within country unless otherwise indicated.
ECG, electrocardiogram; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; ICD, implantable cardioverter defibrillator; SD standard deviation.

explained by the relatively low cost of an inpatient day (*Table 1*). At €2315 and €2328, annual costs of AF patients in Spain and the Netherlands were very similar, though the cost of interventions was somewhat higher in the Netherlands, possibly influenced by the high unit cost of ICD implantation (€31 173 compared with €11 861 in Spain). The higher mean cost of drug therapy observed among Spanish patients was due to comparatively high utilization rates of low molecular weight heparin, which is more costly than other antithrombotic treatments. Overall, annual costs were the highest in Italy, where unit costs of an inpatient day were elevated (€420, cardiology ward) in addition to the proportion of patients undergoing electrical cardioversion, PCI, ICD and pacemaker implantations being greater than in Spain and the Netherlands. Costs of work loss in the five countries were not negligible but were not as elevated as those of diseases that affect younger individuals, e.g. multiple sclerosis.[11] Nevertheless they accounted for 9%, 6%, 4%, 10%, and 17% of total costs in Greece, Italy, Poland, Spain, and the Netherlands, respectively. The higher indirect costs observed for the Dutch sample were driven by the high number of working days lost (mean of 26 days).

To take into account differences in price levels between countries, costs were adjusted for purchasing power parities (PPP) from 2006 (Greece 89.2; Italy 104.4; Poland 62.9; Spain 93.2; Netherlands 104.2; EU 27 = 100).[12] These are conversion rates applied to equalize the purchasing power in different countries. From *Figure 2* it is clear that PPP-adjustment did not eliminate differences in costs between countries, implying that resource use in AF management does in fact vary. However, comparing the PPP factors with the relation between unit costs in the five

Table 4 Mean (SD) costs of admission, by country and setting

Resource	Greece	Italy	Poland	Spain	The Netherlands
Inpatient setting	($n = 272$)	($n = 509$)	($n = 226$)	($n = 464$)	($n = 280$)
Diagnostics	56 (34)	81 (108)	72 (270)	87 (67)	155 (352)
Interventions	508 (2678)	431 (1497)	252 (729)	744 (2209)	1081 (4149)
Drug therapy	10 (17)	10 (22)	10 (22)	29 (49)	29 (94)
Inpatient care	721 (427)	4632 (3651)	1946 (1654)	5362 (4583)	5099 (4948)
Work loss	68 (147)	98 (327)	42 (121)	138 (502)	81 (619)
Total cost	1363 (2739)	5252 (4317)	2322 (1995)	6360 (5748)	6445 (7531)
Outpatient setting	($n = 51$)	($n = 334$)	($n = 41$)	($n = 384$)	($n = 430$)
Diagnostics	35 (23)	21 (49)	4 (5)	45 (52)	44 (116)
Interventions	1 (1)	481 (1751)	208 (936)	138 (878)	32 (470)
Consultation	22 (–)	21 (–)	12 (–)	21 (–)	25 (–)
Work loss	11 (21)	17 (30)	5 (7)	13 (21)	13 (31)
Total cost	68 (29)	540 (1759)	229 (936)	217 (883)	114 (520)

All costs are expressed in year 2006 Euros.
SD, standard deviation.

countries (*Table 1*), it is clear that the PPP-index failed to completely equalize the price level.

Discussion

Though primarily designed to investigate management of AF in daily clinical practice, clinical outcomes and adherence to guidelines, the Euro Heart Survey on AF also had the specific objective of evaluating the influence of AF on health economical costs. The data collected through the survey are a valuable source of information on resource utilization associated with AF across Europe.

Mean total costs of inpatient admission of an AF patient were estimated at €1363, €5252, €2322, €6360, and €6445 and mean total costs incurred on an annual basis at €1507, €3225, €1010, €2315, and €2328 in Greece, Italy, Poland, Spain, and the Netherlands, respectively. These were the five countries in which more than 200 patients were enrolled in the Euro Heart Survey on AF and where cost estimates consequently could be expected to be sufficiently stable. A rough approximation of the economic burden of AF at the national level can be obtained by applying a recent European estimate of AF prevalence of 5.5% among persons aged 55 years and above[2] and country population statistics[13] to the annual per patient cost estimates provided in this study. The total annual cost of AF in the five studied countries thus amounts to €6.2 billion (€272 million in Greece, €3286 million in Italy, €526 million in Poland, €1545 million in Spain, and €554 million in the Netherlands).

Data on the costs of AF in Europe are lacking and to our knowledge there are no previous AF cost studies from Greece, Italy or Spain. The present study is unique in this respect and also in its European perspective with the standardized methodology of the Euro Heart Survey on AF allowing for direct comparison of costs between countries.

A few cost-of-illness studies of AF have been conducted in the US[14–16] but they are difficult to compare due to differences in health care systems. The most thorough European study to which our estimates can be compared is the COCAF survey,[17] which estimated the mean annual cost incurred by AF patients in France at €3209. This is similar to the annual cost of AF patients in Italy estimated by the present study. Stewart *et al.*[18] found the annual per patient cost of AF in the UK to total €680, which is substantially lower. However, this study used a top-down methodology, which is known to run the risk of underestimation due to not all types of costs being present in register data, which this approach relies on.

Costs of AF have been investigated previously in the Netherlands and in Poland in the context of cost-effectiveness studies of rate control vs. rhythm control in patients with persistent AF. The Dutch study found mean costs during the year after randomization to equal €3445 in the rate control group and €4100 in the rhythm control group.[19] The Polish study found mean annual costs to equal €1225 in the rate control group and €2526 in the rhythm control group.[20] These estimates are higher than the annual costs of €2328 and €1010 we found for AF patients in the Netherlands and Poland, respectively, but a substantial portion of total costs in treatment groups of the cited studies was protocol-driven and might not reflect AF management in clinical practice.

Nevertheless, there is chance that we have underestimated annual costs incurred by AF patients since the data available through the 1-year follow-up survey did not permit quantification of all relevant resource items. Questions regarding the number of consultations with specialists other than a doctor, home help and day care during the year were not included. Data on certain resource items, e.g. International Normalized Ratio (INR) monitoring visits were not collected. Furthermore, quantities of the examined resource items could not be ascertained in all cases. For example, a patient may have undergone an interventional procedure (e.g. PCI) several times during the year of follow-up but the data collected did not indicate the number of procedures, only whether or not one was performed. The cost of a single procedure was assigned in these cases.

Another factor that is likely to have lead costs to be underestimated was the presence of missing values. In cases where information on resource use of a given variable

Table 5 Resource use of study patients during 1-year follow-up

Resource	Greece ($n = 251$)	Italy ($n = 645$)	Poland ($n = 203$)	Spain ($n = 720$)	The Netherlands ($n = 685$)
Diagnostics					
TEE	20 (8)	107 (17)	16 (8)	79 (11)	65 (9)
TTE	100 (40)	360 (56)	78 (38)	264 (37)	92 (13)
Chest X-ray	53 (21)	222 (34)	50 (25)	303 (42)	179 (26)
Holter monitoring	62 (25)	266 (41)	56 (28)	158 (22)	86 (13)
Exercise test	35 (14)	74 (11)	19 (9)	79 (11)	72 (11)
Electrophysiology	6 (2)	27 (4)	3 (1)	14 (2)	12 (2)
Event recorder	5 (2)	4 (1)	0	4 (1)	15 (2)
Thyroid function test	70 (28)	217 (34)	50 (25)	196 (27)	179 (26)
Conversion					
Pharmacological cardioversion	57 (23)	89 (14)	40 (20)	63 (9)	26 (4)
Electrical cardioversion	7 (3)	147 (23)	39 (19)	48 (7)	77 (11)
Interventions					
CABG	0	4 (1)	4 (2)	5 (1)	7 (1)
Valve replacement	4 (2)	10 (2)	2 (1)	14 (2)	4 (0.5)
Catheter ablation	6 (2)	22 (3)	6 (3)	19 (3)	15 (2)
Pacemaker implantation	7 (3)	35 (5)	6 (3)	26 (4)	25 (4)
ICD implantation	0	5 (1)	0	3 (0.5)	3 (0.5)
Surgical therapy	0	1 (0.2)	0	2 (0.5)	4 (0.5)
PCI	5 (2)	17 (3)	5 (2)	11 (2)	4 (0.5)
Drug therapy[a]					
Vitamin K antagonist	121 (48)	383 (59)	113 (56)	494 (69)	473 (69)
Other antithrombotic treatment	66 (26)	195 (30)	29 (14)	184 (26)	126 (18)
Anti-arrhythmic/rate control treatment	156 (62)	533 (70)	143 (70)	550 (76)	532 (78)
Inpatient care					
Mean (SD) no. of inpatient days[b]	4 (24)	4 (10)	4 (8)	3 (6)	2 (7)
Consultations					
Mean (SD) no. of consultations with doctor[b]	2 (2)	2 (4)	2 (2)	2 (3)	2 (2)
Work loss	($n = 49$)	($n = 112$)	($n = 24$)	($n = 135$)	($n = 71$)
Mean (SD) no. of days lost[b], employed patients	9 (22)	11 (22)	12 (12)	14 (48)	26 (56)
Mean (SD) no. of days lost[b], all patients	1 (9)	1 (9)	1 (5)	2 (20)	3 (19)

Data are presented as observed number of patients (%) within country unless otherwise indicated.
TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; CABG, coronary artery bypass grafting; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary intervention; CVD, cardiovascular disease; SD standard deviation.
[a]Treatment recorded at 1-year follow-up.
[b]Due to AF or other cardiovascular disease.

Table 6 Mean (SD) annual costs of AF patients, by resource category and country

Resource	Greece ($n = 251$)	Italy ($n = 645$)	Poland ($n = 203$)	Spain ($n = 720$)	The Netherlands ($n = 685$)
Diagnostics	45 (121)	147 (223)	28 (153)	104 (140)	160 (384)
Interventions	780 (3091)	851 (2441)	172 (456)	708 (2547)	798 (3488)
Drug therapy	159 (296)	199 (311)	96 (325)	237 (358)	87 (150)
Consultations	37 (46)	44 (88)	24 (26)	37 (67)	57 (56)
Inpatient care	352 (2248)	1778 (4075)	651 (1271)	987 (2234)	834 (3036)
Work loss	135 (999)	206 (1395)	39 (186)	242 (2253)	391 (3596)
Total annual cost	1507 (5238)	3225 (5975)	1010 (1667)	2315 (4931)	2328 (6834)

All costs are expressed in year 2006 Euros.
SD, standard deviation.

was missing, the cost was set to zero, except in the case of inpatient days during follow-up where imputation techniques for filling in missing values could be applied.[21] Some of the patients whose values were missing were likely to have used resources and setting their costs to zero will have pulled down mean values.

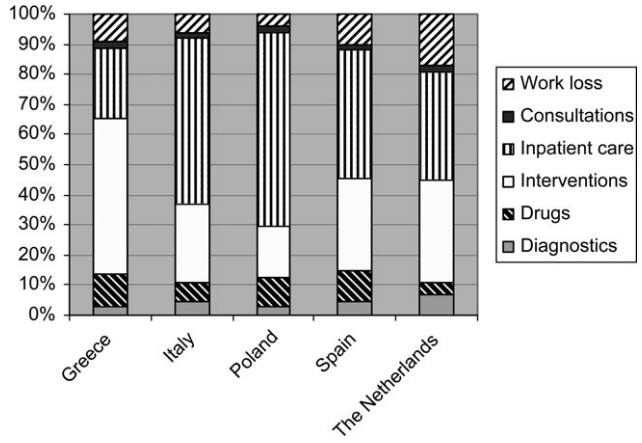

Figure 1 Distribution of annual costs of atrial fibrillation patients.

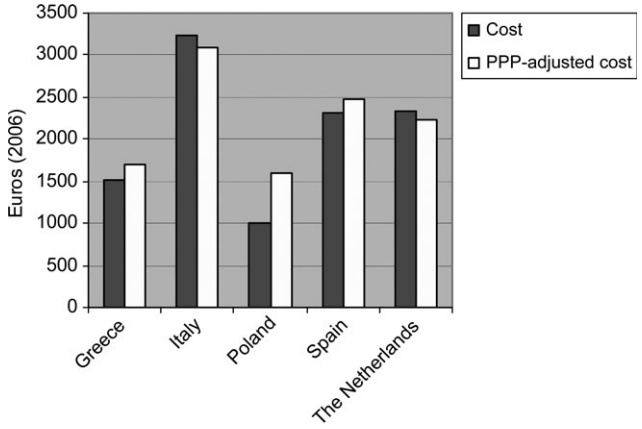

Figure 2 Annual costs of atrial fibrillation patients in absolute terms and adjusted for purchasing power parity (PPP).

The cardiology-based population and overrepresentation of highly specialized centres with an interest in AF participating in the Euro Heart Survey on AF has been discussed previously[7] and is a factor that influences the generalizability of the estimated costs. These centres may attract more severely ill patients and provide advanced care, which may lead costs of admission to be higher than what they are in typical clinical practice. On the other hand, costs incurred during follow-up may be lower if patients are better managed. The issue of the representativity of participating centres is common to all Euro Heart Surveys; results are representative of the participating centres but not necessarily of the countries as a whole. This is true also for the cost results of the present study.

Estimated costs were directly related to treatment of AF or to prevention and treatment of the cardiovascular complications of AF. It is strength of the study that the economic burden thus inferred is not confounded by comorbidities unrelated to AF that study patients may suffer from (e.g. depression, dementia).

As expected, there were some notable differences in costs of admission and costs incurred on an annual basis by AF patients between countries. Total costs are a function of quantities of resource use and of unit costs, both of which vary with health care systems and prices of inputs. Differences in price levels were evident in the case of Poland and Greece. In particular, unit costs of a bed-day were significantly lower in Poland and Greece than in Spain, Italy, and the Netherlands leading to lower costs of inpatient care at admission and on an annual basis, despite similar quantities of inpatient days. PPP-adjustment failed to completely equalize price levels. The unit cost data used for calculations of total costs in each country were obtained locally. This type of data is not always readily accessible and was notably difficult to obtain in Greece. National averages were requested but the uniformity of the unit cost data across countries was difficult to verify and this may have had an unduly effect on results.

Total costs related to AF are also influenced by the severity of disease of patients recruited to the survey in each country and the type of centres participating. Higher proportions of severely ill patients and specialized centres presumably entail greater use of resources. The patients enrolled in Spain had the highest prevalence of permanent AF (43%) and Poland had the highest proportion of specialized centres (36%) but the extent to which this has impacted on costs of admission and annual costs is difficult to judge. In fact, a higher prevalence of permanent AF and comorbidities and high proportions of patients enrolled in specialized centres only affects total management costs inasmuch as it entails greater use of resources. Hence the resource data, summarized in *Tables 3* and *5*, are central.

A key finding of the present study is the role of interventional procedures and inpatient care as major drivers of total costs of AF management. Despite relatively small quantities used, the high costs of these resource items led them to account for more than 70% of total annual costs in the five countries studied. This is in line with the results of the COCAF study[17] and highlights the potential cost-effectiveness of disease management targeted at reducing risks of serious cardiovascular events among AF patients, e.g. stroke prevention. Costs of drug therapy and consultations accounted for a relatively small share of total costs. AF hospitalization rates have been seen to increase in recent years in Europe as well as the US,[22,23] which could have important economic consequences given the resource burden this entails.

In conclusion, the Euro Heart Survey on AF provided a unique opportunity of assessing resource use and costs associated with management of AF in Europe, which is critical in light of the increasing importance of AF as a public health problem. Costs of AF were seen to be substantial in the five countries studied with inpatient care and interventional procedures identified as the principal cost components.

Conflict of interest: A.R. and P.L. are employed by a contract research organization, performing consultancy for pharmaceutical companies. D.F. is employed by Sanofi-Aventis.

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