# The cost of atrial fibrillation in Italy: a five-year analysis of healthcare expenditure in the general population. From the Italian Survey of Atrial Fibrillation Management (ISAF) study

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**Abstract.** – OBJECTIVE: Atrial fibrillation (AF) is a relevant item of expenditure for the National Healthcare systems. The aim of the study was to estimate the annual costs of AF in Italy.

**PATIENTS AND METHODS:** The Italian Survey of Atrial Fibrillation Management Study enrolled 6.036 patients with AF among 295.906 subjects representative of the Italian population. Data were collected by 233 General Practitioners (GPs) distributed across Italy. Quantities of resources used during the 5 years preceding the ISAF screening were inferred from the survey data and multiplied by the current Italian unit costs of 2015 in order to estimate the mean per patient annual cumulative cost of AF. Patients were subdivided on the basis of the number of hospitalizations, invasive/non-invasive diagnostic tests and invasive therapeutic procedures in 3 different clinical subsets: "low cost", " medium cost" and "high cost clinical scenario".

RESULTS: The estimated mean costs per patient per year were 613 €, 891 € and 1213 € for the "Low cost", "Medium cost" and "High Cost Clinical Scenario" respectively. Hospitalizations and inpatient interventional procedures accounted for more than 80% of the cumulative annual costs. The mean annual costs among patients pursuing "Rhythm control" strategy was 956 €.

CONCLUSIONS: In Italy, the estimated costs of AF per patient per year are lower than those reported in other developed countries and vary widely related to the different characteristics of AF patients. Hospitalizations and interventional procedures are the main drivers of costs. The mean annual cost of AF is mainly influenced by the duration of the period of observation and the patients' characteristics. Measures to reduce hospitalizations are needed.

Key Words:

Arrhythmia, Atrial fibrillation, Cost, Economic, Resource use.

#### Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting approximately 2% of the general population. In Europe its prevalence is expected to rise to 2.7-3.3% in the next two decades due to the ageing of the population, the improved ability to suspect and diagnose AF and the greater ability to treat chronic cardiac and noncardiac diseases<sup>1,2</sup>. AF is generally associated with complex cardiac diseases, multiple comorbidities and hemodynamic or hemocoagulative consequences which cause frequent hospitalizations, permanent disabilities, cognitive disturbances, absences from work and death<sup>2-4</sup>. Therefore, AF is a relevant item of expenditure for the national health care systems.

A number of economic analyses have focused on AF-related costs. However, the majority of studies have assessed the cost of specific interventions or pharmacologic treatments during short periods (maximum 1 year) or the cumulative cost in patients hospitalized<sup>5,6</sup>. In particular, very few studies have been carried out to assess the cumulative cost of hospitalizations, diagnostic non-invasive tests and in-hospital/outside hospital interventional procedures during a long observational period in the general population or

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among large study populations<sup>6</sup>. Since AF is a long-lasting disease with an uneven use of resources during its different clinical phases (initial diagnose, stable/chronic course, complications, predeath period), for a correct analysis of AF costs the expenditure should be spread over a large time frame<sup>7</sup>. This can help assess the mean costs over long periods and to plan interventions to allocate human and economic resources more appropriately.

The aim of the present work is to assess the cumulative cost for hospitalizations, diagnostic and in-hospital/outside hospital interventional procedures related to AF management in a large sample of patients representative of the Italian population over a five-year period. To calculate the cumulative expenditure, the data of ISAF (Italian Survey of Atrial Fibrillation Management) study were used<sup>8</sup>.

## **Patients and Methods**

# Data Sources and Study Population

The ISAF Study is a nationwide retrospective, observational study promoted by the Italian Association of Hospital Cardiologists (ANMCO) and the Italian College of General Practitioners (SIMG) to assess the epidemiology, the treatment strategies and the resources used to manage patients with AF in Italy. The methods used in this study have been previously described<sup>8</sup>. In summary, data were collected by 233 General Practitioners (GPs) included in the Research Network of the Italian College of General Practitioners that consists of 800 selected GPs interested in research in primary care and trained for high-quality data entry. All the 800 researchers were invited to participate the ISAF study and 233 accepted to participate it<sup>8</sup>. The 233 GPs were distributed across Italy (31% in the northern regions, 24% in the central regions, and 17% in the southern regions). The screened ISAF population consisted of 295,906 subjects aged 15 years or older and was representative of the Italian population. Data collection started on May 17 and ended on June 22, 2011. The diagnosis of AF had to be supported by an electrocardiogram or by the diagnosis recorded on a hospital discharge summary. The diagnosis of AF was recorded and confirmed in 6,036 patients. For each of the 6,036 AF patients data on some selected clinical events, diagnostic tests and therapeutic invasive procedures related to AF that occurred or were performed in the 5

years preceding the ISAF screening were collected. Data were collected as aggregate. No identifiers linking individuals to the data were provided to the researchers who analyzed data. Neither Ethical Committee approval nor informed consent was required for using encrypted retrospective information.

# Cost Analysis

For the cost analysis we assessed the number of hospital admissions due to AF (1), cerebrovascular accidents (2), Holter ECG recordings (3), exercise stress tests (4), echocardiograms (5), cardioversions (6), pacemaker implantations (7), electrophysiologic studies (8) and ablation procedures (9) related to AF management that occurred or were performed in the 5 years preceding the ISAF screening. The variables of interest identified as 2, 7, 8 (see above) occurred or were performed only one time during the 5 years of observation, those identified as 1, 3-6, 9 one or more times. Patients who underwent one to 3 of these last events/procedures were classified as Group A, those who underwent 4 or more as Group B. To estimate the cumulative cost of AF, patients were furtherly subdivided into 3 different clinical subsets on the basis of the following criteria: (1) "low cost clinical scenario": expenditure for the variables of interest 2, 7, 8 (occurred/performed one time during the observational period) plus expenditures for the variables 1, 3-6, 9 (arbitrarily considered as performed one time in the Group A and 4 times in the Group B); (2) "high cost clinical scenario": expenditure for the variables of interest 2, 7, 8 (occurred/performed one time during the observational period) plus expenditure for the variables 1, 3-6, 9 (arbitrarily considered as occurred/performed 3 times in the Group A and 7 times in the Group B); (3) "medium cost clinical scenario": expenditure for the variables of interest 2, 7, 8 (occurred/performed one time during the observational period) plus expenditure for the variables of interest 1, 3-6, 9 (arbitrarily considered as occurred/performed 2 times in the Group A and 5 times in the Group B). The cost of hospitalizations, diagnostic/therapeutic tests and therapeutic procedures was that established in 2015 by the Italian Healthcare System. The cumulative expenditures for each variable of interest was estimated by multiplying the reimbursement fees paid by the Italian Healthcare System for the total number of events/diagnostic-therapeutic procedures occurred/performed during the 5 years of analysis. The cumulative annual cost of AF per patient was estimated by dividing by 5 the total cost of each variable of interest and then by adding up the expenditure for each single variable. The cumulative hospitalization cost per patient per year related to pacemaker implants, cardioversions and transcatheter ablation related to AF has been estimated also for the subgroup of patients assigned to the "Rhythm control" treatment strategy.

## Results

The characteristics of the 6.036 AF patients are shown in Table I. From these data it appears that permanent AF prevails (55%) on both the persistent and paroxysmal forms. AF is generally a long-term condition with a duration of 5 years or more in half of the patients, and moderately/heavily symptomatic in two-thirds. AF is associated with cardiac diseases in two-thirds of cases and with comorbidities in almost the totality of patients (91.5%). In particular, one-third of the patients suffers from 3 or more comor-

bidities. Hospitalizations due to AF, invasive and non-invasive diagnostic procedures and interventional treatments for AF performed in the 5 years preceding ISAF screening are shown in Tables II-IV. Forty-one per cent of patients were referred with a primary diagnosis of AF at least once (6.7% more than 3 times), 23.2% received at least one electrical or pharmacological cardioversion (4.6% more than 3 attempts). In addition: 8.6% were referred for stroke and 9.3% for TIA. Approximately in 3% of AF patients one electrophysiologic study, 2.9% one or more transcatheter AF ablation and 2.7% one pacemaker implant (0.7%: ablate and pace) were carried out. Half of the patients performed at least one ECG Holter recording, three fourth one echocardiogram and one fourth one exercise stress test.

The estimated costs per patient per year for hospitalizations, non-invasive/invasive tests and therapeutic procedures are shown in Tables II-IV. The "Low", "Medium" and "High Cost Clinical Scenario" show an estimated mean expenditure per patient per year of  $613 \in 891 \in 1.213 \in 1.213$ 

**Table I.** Characteristics of patients with atrial fibrillation.

Characteristics	Total No. 6,036	Characteristics	Total No. 6.036
Females	3,080 (51%)	Diabetes mellitus	1,343 (22.2%)
Type of AF		Diabetes + VC	420 (7%)
Paroxysmal	1,218 (20.2%)	Cerebrovascular disease#	
Persistent	1,465 (24.3%)	Ischemic stroke	448 (7.5%)
Permanent	3,353 (55.5%)	Haemorragic stroke	70 (1.2%)
Lone AF	73 (1.2%)	TIA	560 (9.3%)
Duration of AF history*		Dementia	891 (14.9%)
< 1 yr	760 (12.7%)	Obesity (BMI $\geq 30$ )	1,198 (20%)
1-5 yrs	2,339 (39.1%)	Renal Failure#	
6-10 yrs	1,811 (30.3%)	GFR 30-60 ml/min	1,350 (22.6%)
> 10 yrs	1,074 (17.9%)	GFR < 30 ml/min	218 (3.6%)
Current AF symptoms		Dialysis	36 (0.6%)
Palpitations	2,457 (39.4%)	Hyperthyroidism	267 (4.5%)
Asthenia	1,471 (24.6%)	Hypothyroidism	456 (7.6%)
Dyspnoea	1,417 (23.7%)	COPD	1,114 (18.7%)
No heart disease	1,433 (23.7%)	OSAS	268 (4.5%)
Coronary artery disease	1,145 (19%)	Other pulmonary diseases	226 (3.8%)
Valvular disease	735 (12.2%)	≥ 3 Comorbidities	1,770 (29.3%)
Hypertension + LVH	2,203 (36.5%)	Heart failure#	1,486 (24.8%)
Non-ischemic DCMP	122 (2%)	No comorbidity	512 (8.5%)
Other heart disease	153 (2.5%)	Smoke	542 (9%)
Hypertension	4,023 (66.7%)	Alcool abuse	143 (2.4%)

Abbreviations – AF: atrial fibrillation; BMI: body mass index; COPD: chronic obstructive pulmonary disease; DCMP: dilated cardiomyopathy; AF: atrial fibrillation; GFR: glomerular filtration rate; LVH: left ventricular hypertrophy; n: number; OSAS: obstructive sleep-apnea syndrome; TIA: transient ischemic attack; VC: vascular complications; \*Data related to 5,984 patients; \*Data related to 5,996 patients.

**Table II.** "Low cost clinical scenario": cumulative annual cost per patient for hospitalizations due to AF, noninvasive tests and interventional diagnostic-therapeutic procedures in the 5 years preceding ISAF screening.

			Estimated	Estimated total		
	Pati	ients	numbers of	numbers of events/proced	Total cost per yr	Mean cost per pt
	(No.)	(%)	events/proced per pt in 5 yrs	per yr	(million €)	per yr (€)
Hospitalizations for AF						
Group A (n 1-3)	2,079	(34.4)	1	416	1.040	
Group B $(n > 3)$	406	(6.7)	4	325	0.813	207.0
Hospitalizations for					1.853	307.0
Ischemic stroke	448	(7.4)	1	90	0.323	
Haemorragic stroke	70	(1.2)	1	14	0.100	
	560	(9.3)	1	112	0.251	
					0.674	111.6
Ecg Holter recordings						
Group A (n 1-3)	2,505	(41.5)	1	501	0.031	
Group B $(n > 3)$	636	(10.5)	4	509	0.032	10.4
Exercise stress tests					0.063	10.4
Group A (n 1-3)	1,317	(21.8)	1	263	0.015	
Group B $(n > 3)$	251	(4.2)	4	201	0.013	
		()		201	0.026	4.3
Echocardiograms						
Group A (n 1-3)	3,518	(58.3)	1	704	0.036	
Group B $(n > 3)$	1,083	(17.9)	4	866	0.045	
					0.081	13.4
Cardioversions Group A (n 1-3)	1 122	(10.6)	1	224	0.202	
Group B (n > 3)	1,122 283	(18.6) (4.6)	1 4	224	0.202	
Group B (ii > 3)	203	(4.0)		220	0.406	67.2
Electrophysiologic study	189	(3.1)	1	38	0.207	34.3
Pacemaker implants		(- ' )				
Rhythm control	110	(1.8)	1	22	0.105	
Rate control (A&P)	56	(0.7)	1	11	0.052	
T					0.157	26.0
Transcatheter ablation	117	(1.0)	1	23	0.127	
$\begin{bmatrix} 1\\2 \end{bmatrix}$	40	(1.9) (0.7)	1 2	23 16	0.127	
$\begin{bmatrix} 2\\3 \end{bmatrix}$	6	(0.7) $(0.1)$	3	4	0.020	
		(0.1)		•	0.214	38.8
Total costs (€)						890.8

Abbreviations - No.: number; proced: procedures; pt: patient; yr: year.

pacemaker implant and transcatheter ablation is 517 € in the "Low Cost", 735 € in the "Medium Cost" and 987 € in the "High Cost Clinical Scenario", respectively 84.3%, 82.4% and 81.3% of the cumulative costs.

"Rhythm control" treatment strategy was pursued in 2,643 patients (43.8%). The number of hospitalizations, cardioversions, pacemaker implants and transcatheter ablations for AF performed in the 5 years preceding ISAF screening and their cumulative costs are shown in Table V. The mean estimated cost per patient per year was  $956 \in$ .

# Discussion

Our research on a large series of patients with AF primarily provides information on the cumulative costs of AF in the general population and clinical practice. Additionally, for the first time to our best knowledge, it provides data on the estimated mean annual cost of AF assessed on the basis of a long period of observation (5-year time frame). Finally, since the population screened in the ISAF study is representative of the Italian population, it allows to estimate the cost of AF, non-inclusive of drug therapy, in Italy.

**Table III.** "Medium cost clinical scenario": cumulative annual cost per patient for hospitalizations due to AF, noninvasive tests and interventional diagnostic-therapeutic procedures in the 5 years preceding ISAF screening.

	Patients		Estimated numbers of events/proced	Estimated total numbers of events/proced	Total cost	Mean cost
	(No.)	(%)	per pt in 5 yrs	per yr	(million €)	per yr (€)
Hospitalizations for AF						
Group A (n 1-3)	2,079	(34.4)	2	832	2.079	
Group B $(n > 3)$	406	(6.7)	5	406	1.015	
Hospitalizations for					3.094	512.6
Ischemic stroke	448	(7.4)	1	90	0.323	
Haemorragic stroke	70	(7.4) $(1.2)$	1	14	0.100	
TIA	560	(9.3)	1	112	0.251	
		(>10)			0.674	111.6
Ecg Holter recordings						
Group A (n 1-3)	2,505	(41.5)	2	1.002	0.062	
Group B $(n > 3)$	636	(10.5)	5	635	0.039	
					0.091	16.8
Exercise stress tests	1 215	(21.0)		505	0.020	
Group A (n 1-3)	1,317	(21.8)	2 5	527	0.029	
Group B (n > 3)	251	(4.2)	3	251	0.014 <b>0.043</b>	7.2
Echocardiograms					0.043	1.2
Group A (n 1-3)	3,518	(58.3)	2	1.408	0.073	
Group B $(n > 3)$	1,083	(17.9)	5	1.083	0.056	
	-,	(-,,,)			0.129	21.3
Cardioversions						
Group A (n 1-3)	1,122	(18.6)	2	449	0.404	
Group B $(n > 3)$	283	(4.6)	5	283	0.255	
					0.659	109.1
Electrophysiologic study	189	(3.1)	1	38	0.207	34.3
Pacemaker implants	110	(1.0)	1	22	0.156	
Rhythm control	56	(1.8)	1 1	11	0.156	
Rate control (A&P)	30	(0.7)	1	11	0.078 <b>0.234</b>	38.8
Transcatheter ablation					U•#JT	20.0
1	117	(1.9)	1	23	0.127	
2	40	(0.7)	2	16	0.087	
3	6	(0.1)	3	4	0.022	
					0.236	39.1
Total costs (€)						1213.

Abbreviations - No.: number; proced: procedures; pt: patient; yr: year.

In the past, the costs of AF have been estimated generally in selected study populations (inhospital patients, patients treated in outpatient cardiology clinics or in emergency departments or in anticoagulation clinics) over relatively short periods (maximum 12 months) or with the aim of evaluating the economic burden of specific interventions (transcatheter ablation, cardioversion, anticoagulation monitoring, drug therapy)<sup>6,9-12</sup>. In addition, in the few studies where the costs of drug therapy have been assessed over a longer than 1 year time-basis, only subgroups of patients generally aged 65 years or more have been

analyzed<sup>7</sup>. In the present study, the estimated cost per patient per year is the result of an average expenditure made over a 5 years period (2006-2011). In our opinion, this is a crucial information because previous researches have shown that health-related costs are not constant over patients' life span, but rather have distinct peaks of rapid cost accumulation, alternated by lower cost phases<sup>7,13</sup>. Our data showed that in Italy the estimated annual cost of AF per patient ranges from a minimum of  $613 \in$  in the "Low cost clinical scenario" to  $891 \in$  in the "Medium cost clinical scenario" (presumably the most common sub-

**Table IV.** "High cost clinical scenario": cumulative annual cost per patient for hospitalizations due to AF, noninvasive tests and interventional diagnostic-therapeutic procedures in the 5 years preceding ISAF screening.

	Patients		Estimated numbers of	Estimated total numbers of	Total cost	Mean cost
	(No.)	(%)	events/proced per pt in 5 yrs	events/proced per yr	per yr (million €)	per yr (€)
Hospitalizations for AF						
Group A (n 1-3)	2,079	(34.4)	3	1,247	3,117	
Group B $(n > 3)$	406	(6.7)	7	568	1,420	751 7
Hospitalizations for					4,537	751.7
Ischemic stroke	448	(7.4)	1	90	0,323	
Haemorragic stroke	70	(1.2)	1	14	0,100	
TIA	560	(9.3)	1	112	0,251	
					0,674	111.6
Ecg Holter						
Group A (n 1-3)	2,505	(41.5)	3	1,503	0,093	
Group B $(n > 3)$	636	(10.5)	7	890	0,055	24.6
Exercise stress tests					0,148	24.6
Group A (n 1-3)	1.317	(21.8)	3	790	0,044	
Group B $(n > 3)$	251	(4.2)	7	351	0.020	
Group B (ii x 3)	231	(1.2)	,	331	0,064	10.6
Echocardiograms					,	
Group A (n 1-3)	3,518	(58.3)	3	2,111	0,109	
Group B $(n > 3)$	1,083	(17.9)	7	1,516	0,079	
					0,188	31.0
Cardioversions	1 100	(10.6)	2	(72	0.606	
Group A (n 1-3)	1,122	(18.6)	3 7	673	0,606	
Group B (n > 3)	283	(4.6)	/	396	0,356 <b>0,962</b>	159.4
Electrophysiologic study	189	(3.1)	1	38	0,207	34.3
Pacemaker implants	10)	(3.1)	1	50	0,207	54.5
Rhythm control	110	(1.8)	1	22	0,206	
Rate control (A&P)	56	(0.7)	1	11	0,103	
					0,309	51.3
Transcatheter ablation						
1	117	(1.9)	1	23	0,127	
2	40	(0.7)	2	16	0,087	
3	6	(0.1)	3	4	0,020	20.0
T 4 1 (2)					0,214	38.8
Total costs (€)					1213.3	

Abbreviations - No.: number; proced: procedures; pt: patient; yr: year.

group of patient with AF in the real world and in clinical practice) to a maximum of 1.213 € in the "High cost clinical scenario". This means that the cost of treatment for each single patient may vary consistently (even doubling) based on the characteristics and the needs of care. In our study, this is particularly evident when considering those patients pursuing the "Rhythm control" strategy where the cost for hospitalizations, cardioversions, pacemaker implants and catheter ablations is higher than that for all the variables of interest analyzed in both the "Low cost" and the

"Medium cost clinical scenario" (956 € vs. 613 € and 891 € respectively). This is in agreement with the results of the study of Bennell et al<sup>7</sup> who showed that significant predictors of increasing costs in the management of AF are not only the number of hospitalizations but also the selected diagnostic/treatment strategies, age-classes of patients and the presence of comorbidities.

In agreement with the findings of other health economics works<sup>5-7,9</sup>, our data show that in-hospital costs represent the most important determinant of the total costs of AF. In all three "clinical"

**Table V.** Cumulative annual cost per patient submitted to the "Rhythm control" treatment strategy: costs for hospitalizations, cardioversions, pacemaker implant, transcatheter ablation in the 5 years preceding ISAF screening.

	Patients		Estimated numbers of events/proced	Estimated total numbers of events/proced	Total cost	Mean cost per pt
	(No.)	(%)	per pt in 5 yrs	per yr	(million €)	per yr (€)
Hospitalizations for AF						
Group A (n 1-3)	1,017	(38.5)	2 5	407	1.017	
Group B $(n > 3)$	185	(7.0)	5	185	0.462	
					1.479	559.6
Cardioversions						
Group A (n 1-3)	1,122	(42.5)	2 5	44	0.404	
Group B $(n > 3)$	283	(10.7)	5	283	0.255	
_					0.659	249.2
Pacemaker implants						
Rhythm control	110	(4.2)	1	22	0.156	58.9
Transcatheter ablation						
1	117	(1.9)	1	23	0.127	
2	40	(0.7)	2 3	16	0.087	
3	6	(0.1)	3	4	0.022	
					0.236	88.6
Total costs (€)						956.3

Abbreviations - No.: number; proced: procedures; pt: patient; yr: year

scenarios" such expenditure represents more than 80% of the total costs. This suggests that the maximum effort must be done to improve our ability to treat AF out of the hospital.

The estimated annual cumulative costs in our 3 "clinical scenarios" are not easily comparable to those reported in the previous investigations performed in developed countries since we did not assess the cost of drug therapy. In Germany (2011), among 14,800 patients identified in the database of a health insurance company on the basis of the International Classification of Disease (ICD-10 diagnosis code), the cumulative cost per patient in the first year following an AF attack is 2,233 € (expenditure for hospitalization, drugs, remedies, adjuvants and outpatient doctor-patient contacts)<sup>14</sup>. In USA (2009), Kim et al<sup>5</sup> showed that among 32,000 patients included in the Integrated Health Care System National Database, aged 20 years or older and identified on the basis of an ICD-9 diagnosis of AF the cumulative cost during the 12 months following enrollment (expenditure for patient hospital stay, outpatient medical services and medical therapy) was 14,133 \$ (12,719 €). Again, in USA in 2005, Pelletier et al<sup>14</sup> showed that among 68,000 Medicare AF patients aged 65 years or older, the average cost of one access to the hospital for AF and the following one year management was

11,675 \\$. In Spain and in The Netherlands among patients enrolled in the Euro Heart Survey (enrolled in Hospital Cardiology Wards or Outpatient Cardiology Clinics)9 aged 18 years or older, the mean cumulative cost per patient was 6,360 € and 6,445 € respectively for in-hospital stay and 2,315 € and 2,328 € respectively for the one-year outpatient management. Apart from the differences in the cost of the diagnostic procedures, therapeutic treatments or hospitalizations present in each of the above mentioned countries (e.g., the cost of a pacemaker implant in Italy, Spain and The Netherlands in 2006:  $6,084 ext{ } €, 6,721 ext{ } € and 8,817 ext{ } € respectively)<sup>9</sup>, the$ most relevant differences between our study and the others are the followings: 1] the duration of the cost analysis (5 years vs. 1 year), and 2] the characteristics of the study population and site of management (general population vs. selected clinical settings, in-Hospital Cardiology Wards vs. no specific in-Hospital Wards). Our costs are possibly underestimated since additional expenses such as those related to drug therapy (which are a small component of total costs ranging from 4% to 11%)9 were not included in the present study. Anyhow, even if we include additional costs to the "Low", "Medium" and "High cost" clinical scenarios (e.g., those related to one-year antiarrhythmic therapy and anticoagulation as reported in the Euro Heart Survey for Italy:  $533 \in$  and  $383 \in$  respectively) <sup>9</sup>, it appears that the mean annual costs of AF are significantly lower  $(1,529 \in, 1,807 \in$  and  $2,129 \in$  respectively) than those reported in the majority of the studies in the literature<sup>5-7,9,15</sup>.

According to our data, the total costs of AF in Italy (population aged 15 years or older: 51.5 million people; AF prevalence: 1.9%)<sup>8,16</sup> should be 631 million €, 918 million € and 1.25 billion € respectively in a hypothetical "Low cost" "Medium cost" and "High cost clinical scenario".

The study has some limitations. Participation of the GPs in the ISAF study was voluntary and restricted to those with greater interest in the clinical research. It is very likely that this might have influenced AF management and treatment resulting in an overestimation of the use of procedures and investigations. Data have been provided as an "aggregate", thus the expenses for AF management have been calculated in some selected patient subgroups ("Low", "Medium" and "High cost clinical scenario") on the basis of a reasonably pre-established set of events/procedures that allowed to assess most of the possible clinical scenarios in the real world of AF. The costs of drug treatment was not included in our analysis since the clinical course of AF and consequently medical therapy varies significantly over time in particular during a long observational period as in our study and since the actual use (in terms of prevalence) of the new oral anticoagulants in the general population is not yet well known. A correct analysis of this particular problem needs an "ad hoc" assessment. We tried to overcome this lack of information using the results of the previously published study on the Italian reality. The evaluation of hospitalizations due to AF was done by the GPs, with the potential for some underestimate of the role of AF in the case of concomitant heart failure.

## Conclusions

Our report shows that the estimated costs of AF in Italy are relatively low; thus, the expenditure for the Healthcare National System should be less than expected on the basis of the findings present in the literature. The reason of this consideration lies not only in the fact that our data represent an average cost resulting from a long period of observation, but also in the fact that they refer to the general population which often

includes patients who do not need expensive diagnostic or therapeutic procedures or frequent hospitalizations. Our data confirms that most of the costs of AF are related to in-hospital stay. Thus, in the context of a cost containment, measures to reduce the risk of hospitalization are strongly needed. This can be achieved by a careful application of Guideline recommendations.

## Acknowledgements

The study was supported with an unrestricted grant by Boehringer Ingelheim, Italy and Sanofi-Aventis, Italy. Dr Massimo Zoni Berisso has received modest fees as a speaker from Bayer Italy, Daiichi-Sankyo Italy, Amgen Italy, Merck-Sharp-Dohme Italy; dr Maurizio Landolina has received modest fees as a speaker and an Advisory Board Member from Medtronic Italy and St Jude Medical Italy; dr Luca Degli Esposti is the Chief Executive of the Clicon S.r.l. Health, Economics & Outcomes Research (Ravenna, Italy) that carried out the analysis of the data and received an ad-hoc unrestricted grant from Boehringer-Ingelheim Italy; prof Giuseppe Boriani has received modest fees as a speaker from Medtronic Italy, Boston Italy and Boehringer-Ingelheim Italy.

#### **Conflict of Interest**

No conflict of interests to declare by the remaining authors.

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