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Low prevalence of atrial fibrillation in asymptomatic adults in Geneva, Switzerland

THESE

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Low prevalence of atrial fibrillation in asymptomatic adults in Geneva, Switzerland

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Rapport de synthèse

« Faible prévalence de la fibrillation auriculaire chez des adultes asymptomatiques à Genève, Suisse »

But : l'augmentation de la prévalence de la fibrillation auriculaire (FA) est dans les pays développés un problème de santé publique. L'ampleur de cette augmentation demeure cependant peu claire. L'objectif de ce travail est de déterminer la prévalence de la FA au sein d'un échantillon représentatif d'adultes asymptomatiques de plus de 50 ans.

Méthode : entre janvier 2005 et décembre 2007, des individus résidants du canton de Genève et ayant déjà participé précédemment à une étude randomisée ont été invités pour un examen de contrôle. Le diagnostic de FA a été posé à l'aide d'un tracé électrocardiographique 6 pistes. Tous les tracés ont étés revus par un cardiologue. Les prévalences de FA ont ensuite été standardisées pour la distribution d'âge dans la population genevoise. Une prise de sang veineuse a été réalisée chez tous les participants après 8 heures de jeûne et la glycémie, la triglyceridémie, le cholestérol sérique total ainsi que le cholestérol HDL sérique ont été déterminés.

Résultats : la participation a été de 72.8%. 29 cas de FA (22 hommes) ont été diagnostiqués parmi 3285 sujets (1696 hommes). La prévalence de la FA (95% CI) était de 0.88% (0.86, 0.90). La prévalence standardisée pour l'âge était légèrement plus élevée [0.94% (0.91, 0.97), hommes: 1.23% (1.19, 1.27), femmes: 0.54% (0.47, 0.61)]. Les sujets avec une FA étaient plus âgés (72.1 *vs.* 63.1 ans, $p < 0.0001$), plus souvent de sexe masculin (75.9% *vs.* 50.4%, $p = 0.0087$), avaient un indice de masse corporelle plus élevé (27.9 *vs.* 25,9 kg/m^2, $p = 0.011$), un périmètre abdominal plus important (98.8 *vs.* 90.2 cm, $p = 0.0034$), une tension artérielle diastolique plus élevée (80.9 *vs.* 75.7mmhg, $p = 0.0093$), un cholestérol sérique total plus bas (5.16 *vs.* 5.75mmol/L, $p = 0.0019$) et un HDL cholestérol sérique plus bas (1.31 *vs.* 1.48 mmol/L, $p = 0.02$). A l'anamnèse un antécédent « d'embolie artérielle » (cérébrale ou membres inferieurs) était significativement plus fréquent chez les sujets avec une FA (10.3 *vs.* 3.3%, $p = 0.03$).

Conclusion : cette étude basée sur une population suisse asymptomatique montre une prévalence de la FA inférieure à 1%. Ces résultats sont moins alarmants que ceux obtenus lors de précédentes études.

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CLINICAL RESEARCH

Low prevalence of atrial fibrillation in asymptomatic adults in Geneva, Switzerland

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Aims To determine the prevalence of atrial fibrillation (AF) in a population-based sample of adults.

Methods and results Between January 2005 and December 2007 individuals aged ≥50 years, residents of the city of Geneva, who had participated in a previous random survey were invited for follow-up examination. AF was assessed on a single resting 6-lead ECG. Reported prevalences were standardized for the age distribution of Canton Geneva. Overall participation was 72.8%. Twenty-nine cases of AF (22 men) were diagnosed among 3285 subjects (1696 men). The crude prevalence of AF (95% CI) was 0.88% (0.86, 0.90) overall, but higher in men [1.30% (1.26, 1.34)] than in women [0.44% (0.41, 0.47)]. The age-standardized AF prevalence was slightly higher [overall: 0.94% (0.91, 0.97), men: 1.23% (1.19, 1.27), women: 0.54% (0.47, 0.61)]. AF prevalence increased with age in both sexes. A 'history of suspected arterial embolism' (brain or legs) was higher in the AF cases (10.3 vs. 3.3%; $P = 0.03$).

Conclusion This population-based survey of a general Swiss population indicates that the prevalence of AF remains below 1%. These results are less alarming than those from previous studies based on patients seeking medical care.

Keywords Atrial fibrillation • Crude overall prevalence • Age-standardized prevalence • Check-up

Introduction

The increasing prevalence of atrial fibrillation (AF), the most common sustained arrhythmia in western countries, is a public health concern[1–3] because it is associated with an increased risk of death,[4] congestive heart failure, and embolic events, including stroke.[3] The aim of this study was (i) to estimate the prevalence of AF in a population-based sample of adults aged 50 years or more and, (ii) to determine whether AF is associated with hypertension or a history of cardiovascular disease.

Methods

Between 1st January 2005 and 31st December 2007 men and women aged 50 years or more who were residents of the city and canton of Geneva, Switzerland and had participated in a previous random survey of the Geneva adult population aged 35–74 years were invited for follow-up examination. The ongoing, community-based surveillance project Bus Santé ('Health Bus') has been continuously monitoring chronic disease risk factors in the resident adult population of the canton of Geneva, Switzerland since 1993.[5] The canton of Geneva (246 km^2) has a population of ~438 500 primarily French-speaking inhabitants, of whom 61% are of Swiss and 39% of foreign origin. Of the latter approximately three-fourths are of European origin and just over one-half come from Mediterranean countries, namely Spain, France, Italy, and Portugal. Survey participants were selected independently and uniformly throughout each year since 1993 to represent the ~218 000 non-institutionalized men and women aged 35–74 years residing in the canton. Eligible subjects are identified using a standardized procedure from an annual residential database established, maintained and constantly updated by the cantonal government. All Swiss and foreign citizens living in the canton with an official residence permit are registered. The only specific information from the list used in the survey (gender, age, and Swiss or foreign origin) is highly accurate. Stratified random

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sampling by gender within 10-year age strata is proportional to the corresponding population distributions. Selected subjects are mailed an invitation to participate and, if they do not respond, up to seven telephone attempts at different times on various days of the week are made. If telephone contact is unsuccessful, two more letters are mailed. Each subject's recruitment lasts from 2 weeks to 2 months. Subjects who are not reached (15% of men, 19% of women) are replaced using the same selection protocol. Previous results have shown that such subjects usually no longer reside in the canton, so are not eligible for the study. Subjects who refuse to participate are not replaced. Participating subjects are not eligible in future surveys. Annual participation rates have ranged from 57 to 65%.

Recruitment for the follow-up visit was done by mail and telephone (up to five times). Subjects who could not be reached after this intensive recruitment process were not replaced. Overall participation was 72.8% (71.5% in men and 74.2% in women).

Participating subjects were invited to come to a mobile health unit (the *Bus Santé*) located alternatively during the week at three different fixed locations in Geneva. At the time of their appointment, subjects returned their completed self-administered questionnaires (previously sent by mail) on general health, diet, and physical activity. The health questionnaire requested, *inter alia*, information on the subject's medical history of myocardial infarction, angina pectoris, 'history of suspected arterial embolism', diabetes mellitus, hypertension, hypercholesterolemia, and their treatment. Trained technicians checked the questionnaires for correct completion and performed anthropometric (weight, height, and waist circumference) as well as clinical (ECG, venous blood sample, and blood pressure) measurements. All participants gave written informed consent for their inclusion in the study. The surveys were approved by the ethical committee for epidemiological research and public health, Institute for Social and Preventive medicine at the University of Geneva.

Electrocardiographic examination

A resting 6-lead body surface ECG (derivations: I, II, III, AVF, AVL, AVR) was recorded using a portable ECG machine (Schiller Reomed® AG, Dietikon, Switzerland). The recordings were performed in a sitting position at a paper speed of 25 mm/s. Data on basic rhythm, ventricular rate, P waves, PQ interval, QRS width, and QT interval were collected and a cardiologist reviewed all recordings. AF was defined by the absence of P waves, by the presence of an irregular atrial activity between 350 and 600 per minute, and by the presence of an irregular ventricular response. Atrial flutter was defined by the absence of P waves and the presence of regular f waves with an atrial activity between 250 and 350 per minutes.

Blood analysis

A venous blood sample was taken from each study participant after an 8 h fasting period. Analyses were performed in the Lipid Laboratory, Clinical Diabetes Unit, Geneva University Hospitals. Measurements included glycemia (colorimetric enzymatic assay, Labodia®, Switzerland), triglyceridemia (Randox Laboratories® Ltd., Crumlin, UK), total cholesterolemia (Randox Laboratories® Ltd., Crumlin, UK) and HDL cholesterolemia (Randox Laboratories® Ltd., Crumlin, UK).

Arterial blood pressure measurements

Blood pressure was measured using an oscillometer (Omron® HEM 907), which was calibrated every 12 months with a standard sphygmomanometer. The standardized measurements were performed with the study participant seated after a 10 min rest, and were repeated three successive times at 1-min intervals. For analyses the mean of the first and second measurements were calculated, however, if the difference was larger than 10 mmHg, the mean of the two closest values was calculated.

Statistical analysis

Comparisons between the characteristics of the subgroups of study participants (i) free of AF (Non-AF) vs. (ii) those diagnosed with AF (AF cases) were made with independent sample Student's *t*-tests for continuous variables and by χ^2 tests for categorical variables. Atrial flutters were not included in the AF cases.

Overall and sex-specific crude (unadjusted) and age-adjusted prevalence of AF were estimated using the large sample normal theory approximation to the Poisson distribution.[6] The age-adjustment involved estimating the age-subgroup-specific expected numbers of AF cases and weighting by the sample vs. population age subgroup sizes. These AF prevalences were also estimated with approximate 95% percent confidence intervals (95% CI).

Results

Atrial fibrillation prevalence

A total of 3285 participating study subjects (1696 men and 1589 women) who had at least reached their 50th birthday in 2005–07 were investigated. The overall mean (SD) age was 63.2 (8.6) years. There were in total 29 cases of AF comprising 22 men and 7 women identified during the 3-year study period. There was only 1 case of atrial flutter (typical atrial flutter).

Characteristics of the two subgroups (i) free of AF (Non-AF, $n = 3256$) and (ii) those diagnosed with AF (AF cases, $n = 29$) are presented in *Table 1*. On average, the AF cases were significantly older (72.1 vs. 63.1 years, $P < 0.0001$); showed a significant male predominance (75.9 vs. 50.4%, $P = 0.0087$); had a significantly higher body mass index (body mass index 27.9 vs. 25.9 kg/m^2, $P = 0.011$) and had a larger waist circumference (98.8 vs. 90.2 cm, $P = 0.0034$). AF subjects also had a significantly higher diastolic blood pressure (80.9 vs. 75.7 mmHg, $P = 0.0093$); a significantly lower total serum cholesterol (5.16 vs. 5.75 mmol/L, $P = 0.0019$) and a lower high-density lipoprotein (HDL) cholesterol (1.31 vs. 1.48 mmol/L, $P = 0.02$).

The crude overall prevalence of AF (95% CI) was 0.88% (0.86, 0.90) (*Figure 1*). The crude prevalence of AF was higher in men [1.30% (1.26, 1.34)] than in women [0.44% (0.41, 0.47)]. The corresponding age-adjusted AF overall prevalence was slightly higher [0.94% (0.91, 0.97)] than the overall AF crude prevalence. The corresponding age-adjusted prevalence of AF for men was slightly lower [1.23% (1.19, 1.27)] than their crude AF prevalence, but the age-adjusted AF prevalence for women was slightly higher [0.54% (0.47, 0.61)] than their AF crude prevalence. AF prevalence was higher in older age groups in both sexes (*Figure 1*). Indeed, the crude AF prevalence is nearly triple among study participants aged 70 years or more (*Figure 1*), among whom over two thirds of the AF cases were identified overall and in both sexes, compared with the corresponding AF prevalence among study participants aged 50 years or more.

In patients with AF, the overall mean (SD) rate of ventricular response was 79.2 (14.6) beats per minute (range 54–135). Among the 29 cases of AF, eight (28%; seven men and one woman) were previously known to their attending physician.

Table 1 Characteristics of the subgroups of study participants free of atrial fibrillation vs. those diagnosed with atrial fibrillation, Geneva, Switzerland, 2005–07

Characteristics	Non-AF cases (n = 3,256)[a]	AF cases (n = 29)	P-value[b]
Age (years)	63.1 (8.6)[c]	72.1 (7.0)	**<0.0001**
Sex (% men)	50.4[d]	75.9	**0.0087**
Body mass index (kg/m^2)	25.9 (4.1)	27.9 (3.4)	**0.011**
Waist circumference (cm)	90.2 (15.7)	98.8 (10.2)	**0.0034**
Systolic blood pressure (SBP, mmHg)	132.8 (18.7)	135.0 (20.7)	0.53
Diastolic blood pressure (DBP, mmHg)	75.7 (10.6)	80.9 (12.9)	**0.0093**
Total serum cholesterol (mmol/L)	5.75 (1.01)	5.16 (1.04)	**0.0019**
High density lipoprotein cholesterol (mmol/L)	1.48 (0.39)	1.31 (0.32)	**0.020**
Triglycerides (mmol/L)	1.30 (0.79)	1.34 (.74)	0.80
Blood glucose (mmol/L)	5.32 (1.20)	5.62 (1.24)	0.19
History of myocardial infarction (%)	3.4	3.6	0.97
History of angina pectoris (%)	3.4	3.4	0.99
History of suspected arterial embolism (%)	3.3	10.7	**0.032**
Current smoker (%)	3.8	10.3	0.46
Ex-smoker (%)	43.6	34.5	(2 df)
Cholesterol treatment (%)	21.6	24.1	0.74
Hypertension treatment (%)	26.5	44.8	**0.026**
Diabetes treatment (%)	4.6	20.7	**<0.0001**

[a]Excludes AF cases, [b]Independent sample Student's t-test for continuous variables; χ^2 test (1 degree of freedom unless noted otherwise) for categorical variables, [c]Mean (SD) for continuous variables, [d]Percentage for categorical variables; Bold: $P < 0.05$. AF, atrial fibrillation; df, degree of freedom.

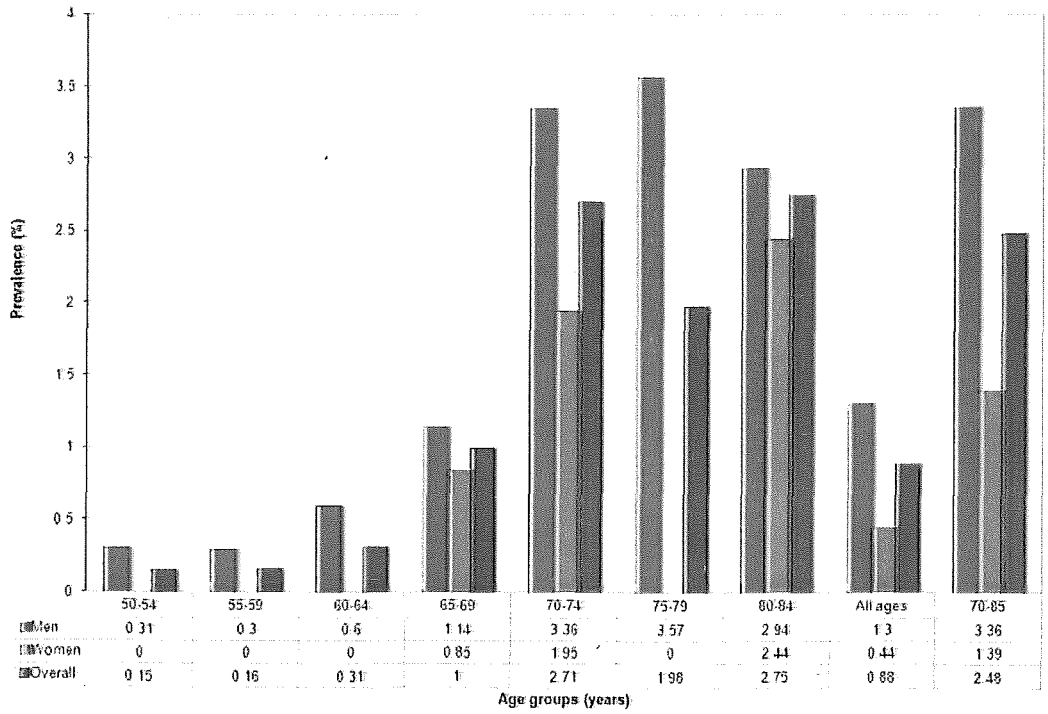

Figure 1 Crude prevalence of atrial fibrillation by sex and age. Geneva, Switzerland, 2005–07.

Table 2 Review of published reports on prevalence of atrial fibrillation

Authors	Place	Sample (*n*)	Year	AF diagnosis	Age (years)	% of women	Prevalence (%)
Majeed *et al.*[1]	England & Wales, UK	211 practitioners ($n = 1.4$ millions)	1998	Medical records	All ages	Unknown	Overall; m 1.2; w 1.3 0–34; m 0.1; w 0.1 35–44; m 0.3; w 0.2 45–54; m 0.7; w 0.4 55–64; m 1.8; w 1.1 65–74; m 4.6; w 3.3 75–84; m 9.1; w 7.2 ≥85; m 10.6; w 10.9
Wolf *et al.*[3]	Framingham (MA), USA	All inhabitants invited ($n = 5070$)	1948–82	Medical files, ECG/2 years	50–89	Unknown	50–59; 0.5 60–69; 1.8 70–79; 4.8 80–89; 8.8
Önundarson *et al.*[11]	Reykjavik, Island	All inhabitants invited ($n = 9067$)	1968–71	ECG	32–64	52	Overall; m 0.41 ; w 0.15
Heeringa *et al.*[12]	Rotterdam, NL	All inhabitants invited ($n = 6808$)	1993–94	Single ECG	≥55	59	Overall; 5.5 55–59; m 0.8; w 0.6 60–64; m 2.6; w 1.0 65–69; m 5.2; w 2.9 70–74; m 6.9; w 5.4 75–79; m 13.0; w 6.5 80–84; m 15.2; w 12.7 ≥85; m 17.9; w 17.5
Lake *et al.*[13]	Busselton, Australia	All inhabitants invited ($n = 1770$)	1966–81	ECG/3 years	>60	48	Overall; 1.5 60–64; m 1.1; w 2.3 65–69; m 3.3; w 2.7 70–74; m 8.6; w 5.5 ≥75; m 15.0; w 8.4
Langenberg *et al.*[17]	Netherlands	10 practitioners ($n = 40\,185$)	1996	Medical file, ECG if irregular pulse	≥60	Unknown	Overall; 5.1 60–69; m 3.3; w 2.3 70–79; m 7.0; w 6.3 ≥80; m 12.1; w 8.7
Furberg *et al.*[18]	Four communities, USA	Medicare recipients ($n = 5201$)	1993	Single ECG Anamnesis	≥65	57	Overall; m 6.2; w 4.8 65–69; m 5.9; w 2.8 70–79; m 5.8; w 5.9 >80; m 8.0; w 6.7

Wheeldon *et al.*[19]	Sheffield, UK	Four practitioners ($n = 1207$)	1998	Single ECG	≥65	Unknown	Overall; 5.4 65–69; 2.3 70–74; 4.1 75–79; 5.8 80–84; 6.4 ≥85; 8.1
Nakayama *et al.*[26]	Shibata, Japan	All inhabitants invited ($n = 2651$)	1997	Single ECG	≥40	58	Overall; 1.3
Labrador Garcia *et al.*[27]	Toledo, Spain	All inhabitants invited ($n = 1206$)	1998	Single ECG Anamnesis	≥65	55	Overall; m 4.5; w 6.4 65–74; m 3.1; w 4.6 75–84; m 8.5; w 7.2 ≥85; m 4.5; w 27.3
Sudlow *et al.*[28]	Northumberland, UK	26 practitioners ($n = 4843$)	1998	Single ECG	≥65	Unknown	≥65; 4.7 ≥75; m 10; w 5.6
Gehring *et al.*[29]	Germany	Random sample ($n = 4003$)	1984–85	Single ECG	25–64	50	Overall; m 0.2; w 0.3 25–44; m 0.0; w 0.0 45–54; m 0.2; w 0.0 55–64; m 0.9; w 1.4
Hobbs *et al.*[30]	West Midlands, UK	50 health centers ($n = 14\,781$)	2005	Medical file	≥65	57	Overall; 7.2 65–69; m 3.0; w 1.7 70–74; m 5.0; w 3.4 75–79; m 7.3; w 5.0 80–84; m 10.3; w 7.2 ≥85; m 11.1; w 9.1

Co-morbidities

A 'history of suspected arterial embolism' involving brain or legs was significantly higher in the AF cases compared with the non-AF subjects (10.7 vs. 3.3%, $P = 0.032$) (*Table 1*). There were no significant differences for either history of myocardial infarction or angina pectoris between the latter two subgroups (range 3.4–3.6%, *Table 1*).

Discussion

This population-based survey of a European population found a lower prevalence of AF in subjects aged 50 years or more than in most other studies, with an overall prevalence of 0.9%. The overall AF prevalence for all age classes has been estimated in the literature to be between 0.2 and 1.2%.[1,7,8–11] For populations over 50 years of age this figure is much higher, between 1.5 and 5.5%.[2,3,12,13] *Table 2* shows comparative data on the estimated AF prevalence rates reported in other studies. The very high density of primary care physicians and cardiologists in the canton of Geneva leads possibly to a broader screening and treatment of AF risk factors, what might explain the low prevalence in the present study.

The studies in *Table 2* are not strictly comparable because of their design heterogeneity. Prevalence varies according to the sex, age or ethnicity distributions of patients. Methods of diagnosing AF (e.g. single ECG, multiple ECG distributed in time, history with the patient, medical records review or a combination of these parameters) also influence the results of the survey. A study based on biennial electrocardiographic recordings and on a systematic medical record review[3] may miss less intermittent AF. AF seems to have a lower prevalence in Afro-Americans than in Caucasians.[14,15] Two other studies based on a single electrocardiogram within the framework of a free and voluntary screening among asymptomatic people also showed a low AF prevalence. Jeong[9] in a study conducted in patients more than 40 years of age reported a AF prevalence of 1.2% for men and of 0.4% for women. Guize *et al.*[8] reported in patients older than 30 years of age values of 0.24 and 0.11% for men and women, respectively. Finally, an additional cause of heterogeneity across studies is related to the context: AF prevalence is considerably higher in hospitalized patients as shown by Patel[16] reporting an AF prevalence of 22% in an elderly hospitalized population.

The general characteristics of AF prevalence in this random population-based survey are similar to those found in other studies. First, the AF prevalence is higher in men,[1,2,7,9,10,12,17,18] even after adjustment for the co-morbidities.[4] The reason for this difference remains unclear. Despite a higher prevalence in men, the absolute number of women with AF is more important because of their longer life expectancy.[10] Second, the incidence of AF increases with age both in men and in women.[2,3,9,10,12,13,17,19]

AF prevalence is increasing all over the world.[1–3] This increase is probably due to aging of the populations and possibly related to an increase in risk factor exposures. For example, an increase in the prevalence of ischemic heart disease[20–23] could contribute to an increase in AF prevalence. In our survey a 'history of suspected arterial embolism' (involving brain or legs) was significantly higher in the AF cases compared with the non-AF subjects but a history of myocardial infarction or angina did not differ between the two groups, suggesting that 'arterial embolism' may be a consequence of AF rather than a predisposing factor for AF.

There are some limitations in this study. (i) A selection bias can explain the relatively low AF prevalence in our study. It is difficult to compare characteristics of our regional populations with those of the general Swiss population. However, the MONICA study of the cantons of Fribourg and Vaud[24] (population of 784 000 inhabitants) between 1992 and 1993 in subjects aged 55–75 yielded a mean body mass index in men of 27.3 kg/m^2 and in women of 26.7 kg/m^2; a mean systolic blood pressure in men of 143.9 mmHg and in women of 138.9 mmHg; a mean diastolic blood pressure in men of 85.5 mmHg and in women of 80.8 mmHg; a mean total serum cholesterol level in men 6.38 mmol/L and in women of 6.8 mmol/L; a proportion of active smokers in men of 20.2% and in women of 13.7%. When compared with values in *Table 1*, even if the age distribution is not exactly the same, it seems that mean body mass index, blood pressure (systolic and diastolic) and mean total serum cholesterol level are less elevated and that there are clearly less active smokers in our population. For diabetes mellitus a similar study conducted in the city of Lausanne (canton of Vaud)[25] in 2006 among subjects aged 35–75 showed an impaired fasting glucose prevalence of 25% and a diabetes mellitus prevalence of 7%. Thus it seems that our population is less exposed to traditional cardiovascular risk factors and resulting AF risk factors (hypertensive heart disease, coronary heart disease, cardiac failure). We cannot rule out that patients already followed medically for AF or patients too sick because of the invalidating effects of AF chose not to participate in this survey. (ii) The sample was based on a follow-up of a population-based, representative sample of the Geneva adult population. Losses to follow-up may have compromised its representativeness. There is, however, no reason to consider that AF *per se* would have constituted an obstacle to participate in the follow-up, especially among people familiar with the survey. Moreover, standardizing prevalence of AF on the age distribution of the target population compensated for random imbalances on the sample age distribution resulting from the 27% non-participation. (iii) The probability of underestimation of the AF prevalence using a single electrocardiogram should be taken into account when comparing AF prevalence rates reported by other studies. For example, Furberg *et al.*[18] found that 50% of the diagnosed AF cases were missed on a single ECG and were only diagnosed after accounting for the patient history.

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