ORIGINAL ARTICLE

Atrial Fibrillation: Its Prevalence and Risk Factor Profile in the German General Population

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SUMMARY

Background: Atrial fibrillation (AF) is an increasingly common problem in primary care, but little is known about its prevalence and the distribution of AF risk factors in the general population.

Methods: We determined the prevalence of AF and the distribution of known AF risk factors among persons participating in the population-based Gutenberg Health Study. To this end, we used interview data about the medical diagnosis of AF and electrocardiograms (ECGs) that were performed for the study in 5000 persons aged 35 to 74. The response rate was 60.4%.

Results: There were 5000 persons in the study sample (age 52.2 ± 11 years; 50.6% were women). The prevalence of AF, weighted for the age and sex distribution of the general population, was 2.5%. AF was found to be more common in older persons, with a more pronounced increase in men: whereas its prevalence was 0.7% in 35- to 44-year-old men, the corresponding figure for the age group 65- to 74 was as high as 10.6%. Twenty five participants (15.5% of AF cases) received their initial diagnosis of AF on the basis of the study ECG. Compared to persons without AF, persons with AF were older and more commonly male, and they had a higher burden of cardiovascular risk factors. 14.3% of persons with AF had none of the well-established risk factors for AF (systolic blood pressure, antihypertensive medication, increased body-mass-index, heart failure). 42.7% of persons with AF were not taking either anticoagulants or platelet inhibitors.

Conclusion: These data indicate that the prevalence of AF in the middle-aged general population is 2.5% overall, and higher in the elderly. AF is thus a significant public health problem, and greater awareness of it is needed.

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Atrial fibrillation (AF) is an often underestimated disease, and its prevalence in the Western world is increasing (1, 2). The lifetime risk of developing AF is approximately 25%, and it mainly affects older persons (3). Major complications include thromboembolic events up to and including fatal stroke (4), heart failure (5), and increased morbidity and mortality not explained by cardiovascular comorbidity alone (6).

The reasons for the increase in prevalence are not fully clear. The main reasons are an aging population and longer survival times with cardiovascular diseases. The increasing awareness of AF, resulting in more frequent diagnosis, may also play a role (3, e1).

Data on AF are obtained mainly from registries or hospital databases. For example, the Euro Heart Survey on Atrial Fibrillation and the German Competence Network on Atrial Fibrillation (AFNET) contribute to the understanding of diagnostic measures, type of AF from paroxysmal to permanent, concomitant diseases, and treatment according to guidelines for patients diagnosed with AF (7). However, primary AF prevention mechanisms need to be implemented earlier. Few data are available on AF in the German general population. We have therefore investigated the prevalence of AF and the presence of known risk factors for AF and thromboembolic complications in the German population on the basis of the Gutenberg Health Study (GHS), an ongoing, population-based study.
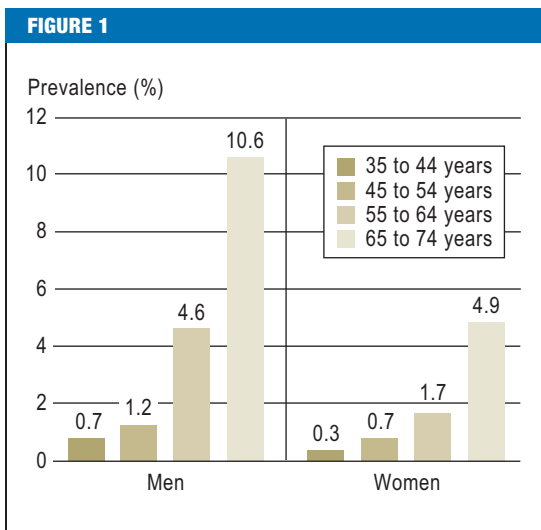
Methods

Study participants

Since 2007, persons from the city of Mainz and the region of Mainz-Bingen have been selected at random via the registration office and invited to take part in a five-hour examination at the University Medical Center of the Johannes Gutenberg University Mainz. This is the population-based GHS. Those invited to take part are aged between 35 and 74 and stratified in 10-year age groups. The main aim of the GHS is to investigate cardiovascular diseases and their risk factors. It has been designed to determine the incidence of cardiovascular morbidity and cardiovascular diseases such as myocardial infarction and atrial fibrillation. Its response rate is 60.4%.

Prevalence of
atrial fibrillation
in Gutenberg Health
Study (GHS)
patients by age
group and sex

FIGURE 1

Prevalence (%)

Legend:
- 35 to 44 years
- 45 to 54 years
- 55 to 64 years
- 65 to 74 years

Men: 0.7, 1.2, 4.6, 10.6
Women: 0.3, 0.7, 1.7, 4.9

While they are at the study site, patients undergo a detailed computer-assisted interview covering cardiovascular risk factors, lifestyle, socioeconomic status, and other areas. The prevalence of cardiovascular diseases such as myocardial infarction, cardiac failure, and stroke is determined by history taking. The definition of heart failure used is left ventricular ejection fraction (LVEF) below 55%, treated heart failure (determined by history taking), and/or shortness of breath (New York Heart Association [NYHA] Classification ≥1).

AF is diagnosed on the basis of a history of AF diagnosed by a physician and/or evidence of AF on the 12-lead resting ECG performed during the study, which lasts for 10 seconds. For this evaluation, all ECGs were interpreted by cardiologists, and the results generated automatically by the machine (GE Healthcare, CardioSoft v6) were verified. ECG-based diagnosis of AF was confirmed by at least two independent cardiologists. AF diagnosed on the basis of surface ECG is defined as absolutely irregular R peak intervals and an absence of P waves with a clear beginning and end (8). Thirty-eight individuals did not undergo ECG at the study site and/or had no history of AF. Extensive details of initial examination and the determination of cardiovascular risk factors have been published (9). Blood biomarkers were measured using standard techniques.

The GHS was approved by the Ethics Committee of the Rhineland-Palatinate State Medical Association. Every participant provides his/her written consent before beginning the study. Responsibility for data accuracy lies with the authors.

Statistics
As the population sample used in the GHS is stratified according to sex, age group, and urban versus suburban/rural origin, statistics describing the prevalence of AF and risk factors were calculated by age group (35 to 44, 45 to 54, 55 to 64, and 65 to 74 years) and weighted for the actual sex and age distribution of the city of Mainz and the region of Mainz-Bingen (n = 210 867, data of the German Federal Statistical Office, Wiesbaden 2011, as of December 31, 2007). They were also standardized for age according to the 1976 European standard population (WHO), in order to allow comparability with other studies.

The risk factors of the Framingham risk prediction algorithm for the occurrence of AF were used to determine the prevalence of classic AF risk factors (10). Risk of AF was assessed using the beta coefficient of the Framingham algorithm for 5-year AF prediction (11). CHADS$_2$ score (cardiac failure, hypertension, age, diabetes, stroke [doubled]) was calculated to assess the risk of stroke in individuals with AF, and CHA$_2$DS$_2$-VASc score (cardiac failure or dysfunction, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74, sex category) was calculated to estimate the risk of stroke in the next 12 months without anticoagulation therapy (12, 13). The data used to calculate these scores are shown in the *eBox*.

In addition, the relative and absolute risk reduction achieved using appropriate warfarin treatment for anticoagulation was calculated for persons with a potential indication for anticoagulation therapy (participants with AF not receiving antithrombotic therapy, i.e. not taking heparin, oral anticoagulants, and/or platelet aggregation inhibitors) (14, 15).

The publicly available program R Software, version 2.14.0 (R Development Core Team, 2011) was used for data analysis (e2).

Results
For the first 5000 GHS participants, the frequency of AF was 3.2% (n = 161). Men were more frequently affected than women, with a frequency of 4.6% (n = 115) versus 1.9% (n = 46). The weighted prevalence for the population of Mainz/Mainz-Bingen was 2.5%. There was a nonlinear increase with age in both men and women. In men aged 35 to 44 the prevalence was 0.7%, rising to 10.6% in those aged 65 to 74. In women there was an increase from 0.3% to 4.9% *(Figure 1)*.

The distribution in the subgroup containing participants with AF shown on the current ECG is similar (data not shown). The weighted characteristics of the first 5000 GHS participants are reproduced in *Table 1*, while the nonweighted data are shown in *eTable 1* and data standardized for age according to the European standard population are shown in *eTable 2*. Study participants with AF were older, and fewer than one-third of them were women. The cardiovascular risk profile was less favorable, and the prevalence of cardiovascular diseases such as heart attack and heart failure was higher. In particular, almost 10% of participants with AF reported a previous stroke, versus 1.5% in the other cohort.

TABLE 1

Characterstics of the study sample for the total cohort and by prevalence of atrial fibrillation (weighted for the population of Mainz and the region of Mainz-Bingen)

Variable	Total population, n = 5000	Participants without atrial fibrillation, n = 4801	Participants with atrial fibrillation, n = 161
Age, years	52.2±11.1	51.9±11.0	63.2±9.5
Women, %	50.1*1	50.5 (50.3 to 50.7)	31.8 (24.3 to 39.3)
Smokers, %	20.9 (19.7 to 22.2)	21.2 (19.9 to 22.5)	11.6 (6.5 to 16.8)
Body mass index, kg/m^2	26.3 (23.6 to 29.6)	26.2 (23.6 to 29.5)	28.3 (25.7 to 32.1)
Systolic blood pressure, mm Hg	130.8±17.0	130.7±17.0	133.0±17.7
Diastolic blood pressure, mm Hg	82.9±9.4	83.0±9.3	82.5±11.0
Heart rate, bpm	69.0±10.7	69.0±10.6	69.4±12.7
Total cholesterol, mg/dL	222±41	222±41	212±44
Total/HDL cholesterol	4.00 (3.28 to 4.91)	4.00 (3.28 to 4.90)	4.53 (3.63 to 5.20)
Diabetes, %	6.0 (5.4 to 6.6)	5.8 (5.2 to 6.4)	12.2 (7.2 to 17.2)
Hypertension, %	45.4 (44.0 to 46.7)	44.7 (43.3 to 46.1)	71.6 (64.2 to 79.1)
Cardiac failure, %	17.7 (16.7 to 18.8)	17.1 (16.0 to 18.2)	46.3 (38.3 to 54.3)
Myocardial infarction, %	2.3 (1.9 to 2.6)	2.0 (1.7 to 2.4)	12.7 (7.6 to 17.8)
Stroke, %	1.5 (1.2 to 1.8)	1.3 (1.0 to 1.6)	9.8 (5.3 to 14.4)
PQ interval, ms	158±23	158±23	170±26*2
Biomarker			
Creatinine, mg/dL	0.87 (0.78 to 0.97)	0.87 (0.78 to 0.97)	0.93 (0.82 to 1.05)
C-reactive protein, mg/L	1.60 (0.50 to 3.20)	1.60 (0.50 to 3.10)	2.30 (1.30 to 4.71)
N-terminal pro-B-type natriuretic peptide, pg/mL	53.7 (23.5 to 108.0)	52.4 (23.0 to 104.4)	258.0 (65.0 to 931.7)

The data shown are mean±standard deviation for continuous variables, median and 25th to 75th percentile for skewed variables, and percentage and confidence interval for categorical variables. *1 For sex, confidence intervals have no informative value for the total population, because sex is a weight variable. *2 The PQ interval is shown for persons with sinus rhythm in the study ECG (n = 96 participants with a history of atrial fibrillation)

Creatinine, a renal function parameter; C-reactive protein, a marker for inflammation; and N-terminal pro-B-type natriuretic peptide, an indicator of cardiac stress, were all higher in the group with AF than in the total cohort *(Table 1)*.

In 40% (n = 65), AF was recorded in the study ECG. AF was detected in the study ECG in 29.4% (n = 40) of the 136 participants who reported that they had already been diagnosed with AF by a physician. Twenty-five participants, 0.5% of the total cohort and 15.5% of the participants with a GHS diagnosis of AF, were not aware that they had AF before the study and were first diagnosed during examination at the study site. According to the Framingham risk score for AF, these individuals had a mean risk of developing AF in the next five years of 2.0%.

The risk factor distribution of the Framingham risk score in participants with AF was similar for both sexes except for a trend towards a higher prevalence of cardiac failure in women (weighted distribution shown in *Table 2*, nonweighted distribution in *eTable 3*). *Figure 2* shows the cumulative number of risk factors in participants with AF. 14.3% of patients presented none of the risk factors measured other than age (13.0% of men, 17.1% of women). Only approximately 21.7% of participants presented three or more risk factors.

The risk stratification algorithms CHADS$_2$ and CHA$_2$DS$_2$-VASc scores were used to determine the risk of stroke in the next year for participants with AF if they did not receive suitable treatment. *Figure 3* shows the number of participants in each category. More than 80% of patients with AF had a risk of stroke of more than 2% if left untreated according to their CHADS$_2$ scores *(Figure 3a)*, and almost three-fourths of participants according to CHA$_2$DS$_2$-VASc scores *(Figure 3b)*. According to CHA$_2$DS$_2$-VASc scores, only 11.2% had

Prevalence of classic risk factors for atrial fibrillation* in men and women (weighted for the population of Mainz and the region of Mainz-Bingen)

Variable	Men, n = 115	Women, n = 46
Age, years	66.0 (57.0 to 70.0)	66.0 (56.8 to 71.6)
Systolic blood pressure, mm Hg	133.8±17.4	131.3±18.6
Antihypertensive medication, %	70.9 (61.4 to 80.4)	67.0 (53.2 to 80.9)
Body mass index, kg/m^2	28.2 (26.2 to 32.1)	28.3 (23.9 to 33.1)
Cardiac failure, %	40.3 (31.1 to 49.5)	59.4 (44.5 to 74.3)
PQ interval, ms	170±25	171±27

* Based on the Framingham risk score (10)
The data shown are mean±standard deviation for continuous variables, median and 25th to 75th percentile for skewed variables, and percentage and 95% confidence interval for categorical variables. The PQ interval is shown for persons with sinus rhythm in the study ECG and a history of atrial fibrillation
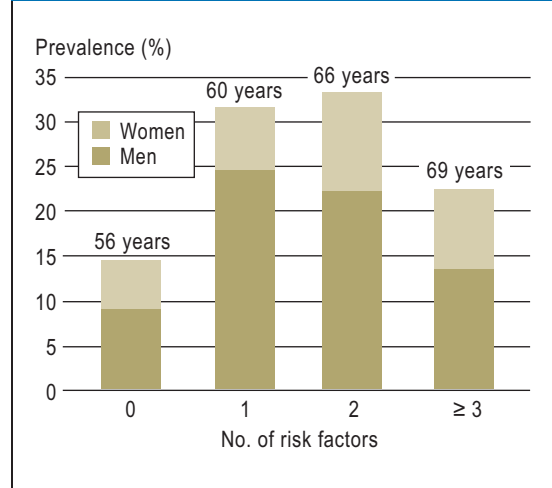
Distribution of risk factors according to the Framingham risk score (11) for atrial fibrillation in Gutenberg Health Study (GHS) participants with atrial fibrillation. The bars indicate percentages by sex. The median age of participants is stated above the bars. Prevalences are weighted for the population of Mainz and the region of Mainz-Bingen

a negligible risk. In the rest of the study population, the median CHADS$_2$ and CHA$_2$DS$_2$-VASc score was 1.0. The mean CHADS$_2$ and CHA$_2$DS$_2$-VASc scores of participants first diagnosed with AF on the basis of the study ECG were 2.0 and 3.0 respectively, with a mean 1-year risk of a thromboembolic event of 4.0% and 3.2% respectively.

Table 3 provides an overview of medication relevant to AF taken by all study participants and participants with AF (the nonweighted distribution is shown in *eTable 4*).

As expected, medication for cardiovascular diseases is taken more frequently by participants with AF. 42.7% of participants with AF reported that they took no anticoagulants or platelet inhibitors. The median CHADS$_2$ and CHA$_2$DS$_2$-VASc scores of these participants were 1.0 and 2.0 respectively. 58.7% had a CHADS score ≥1. According to study data (14, 15), appropriate warfarin treatment for anticoagulation would reduce these individuals' risk of a thromboembolic event in the next year from 2.1% to 0.75%. This represents a relative risk reduction of 65% and an absolute risk reduction of 1.4%.

Antiarrhythmic therapy other than beta-blockers was reported by approximately 20% of participants with AF, and 16% took digitalis medication. Also, thyroid hormone therapy was slightly more frequent in AF patients than in the study population as a whole.

Discussion

In a population-based German cohort, we observed an AF prevalence of 2.5% of participants aged between 35 and 74, with a significant rise in the number of cases with increasing age. The distribution of AF risk factors was similar for both sexes. The mean risk of stroke was 2.8% to 3.2% annually in participants with AF. The study ECG identified new-onset AF in 25 participants, with a mean 1-year risk of stroke (CHADS$_2$) of approximately 4.0%.

The weighted frequencies observed in this German cohort are in line with the data recently published in an Icelandic study (2). The prevalence reported, slightly less than 3%, may at first glance seem relatively low. However, this is due to the age distribution of the members of the cohort. AF occurs mainly in older persons, a fact also illustrated by the rise in AF with increasing age that was observed in this population. For the sake of comparison, the prevalence of myocardial infarction was 2.3%, and that of stroke 1.5%. This makes AF a relatively common disease. The cost of AF to the healthcare system is substantial (16). In addition, 83% of AF patients are symptomatic and it has a negative impact on quality of life (17).

It is also worth remembering that other cardiovascular diseases, such as coronary heart disease, are becoming less common as causes of death (18). The prevalence and therefore the total mortality of AF and its

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sequelae, however, are increasing, despite a slight improvement in survival times of individual patients with AF (1, 2).

It is interesting that 14.3% of participants with AF presented none of the known, repeatedly validated AF risk factors of the Framingham risk score other than age (10, 19, 20), that almost half the individuals with AF had no more than one risk factor, and that only around one-fifth presented three or more risk factors. This indicates that other risk factors also play a role in the development of AF. The Framingham risk factors can only explain up to 60% of the risk in the population (11, 19), which means that there is considerable room for improvement in risk prediction.

As expected, the values of easy-to-measure biomarkers for inflammation (C-reactive protein) and cardiac stress (N-terminal pro-B-type natriuretic peptide) are higher in the group of participants with AF. However, it was also shown that additional measurement of both biomarkers only slightly increases the predictive value of the known risk factors (21). The search for specific biomarkers and clinical risk factors for AF continues. While research and the development of guidelines have seen major efforts regarding risk and the prevention of AF sequelae, knowledge of predisposition towards AF and primary prevention is still at an early stage.

AF patients' main contacts are primary care and hospital physicians (17). The Outpatient Registry Upon Morbidity of Atrial Fibrillation (ATRIUM) shows that most AF patients are treated by primary care physicians (22). This makes it even more important to raise awareness of AF among these categories of physicians. The percentage of persons first diagnosed during the GHS was 0.5% of the total study population, or 15.5% of participants with AF. $CHADS_2$ and CHA_2DS_2-VASc scores showed a mean 1-year risk of a thromboembolic stroke event of 3.6%. This means that the risk in this subgroup is considerable. The presented data show how important a simple ECG can be for at-risk patients. Data reported in the literature suggest that fewer than half of initial diagnoses of AF are based on AF-specific symptoms. Most AF diagnoses are made during visits to doctors for other complaints or, in almost one-fourth of cases, during routine examinations (17).

Stroke prevention therapy for AF patients according to guidelines has reduced the incidence of this serious sequela (23). Oral anticoagulation therapy is also increasingly being recommended for patients with a moderate risk of stroke, i.e. scores of 1.0 or higher (8, 24). In our cohort, more than one-third of participants with AF were not receiving anticoagulation therapy, although their mean CHA_2DS_2-VASc score was 2.0. Of all participants with AF, 14.3% had a negligible risk of stroke, with a CHA_2DS_2-VASc score of 0, meaning that according to current recommendations they did not require anticoagulation therapy. It remains to be seen how new anticoagulants will alter anticoagulation strategies in the near future.

FIGURE 3
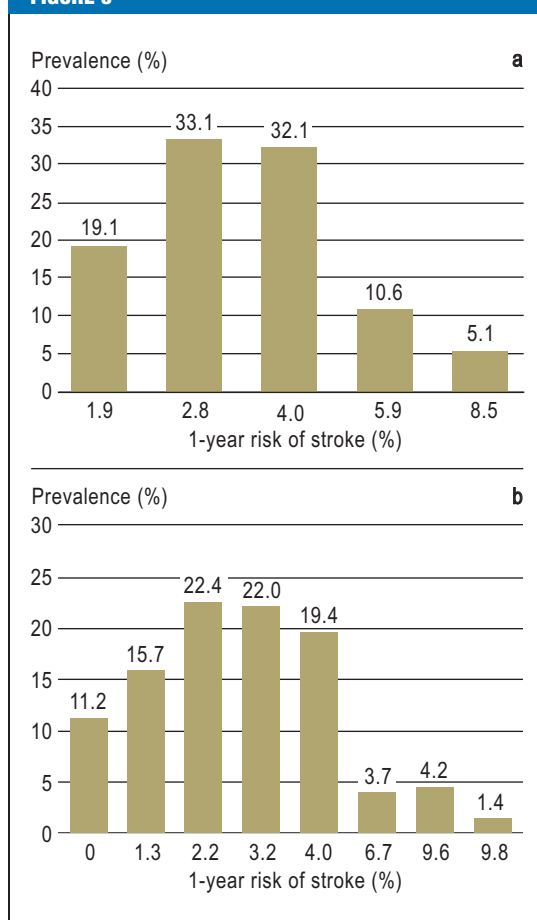
Risk of stroke according to a) $CHADS_2$ score (adjusted for aspirin intake); and b) CHA_2DS_2-VASc score (adjusted for warfarin intake) (12, 13) in Gutenberg Health Study (GHS) participants with atrial fibrillation. Prevalences are weighted for the population of Mainz and the region of Mainz-Bingen

Limitations

As expected, the number of cases of AF in a population-based cohort of middle-aged persons is small, so the conclusions presented here must be interpreted with caution. A study involving older persons would be needed to estimate the prevalence of AF in the general population more precisely, because AF is a disease of old age.

As AF is often asymptomatic and can be intermittent, the prevalence of AF found in this research should be treated as an underestimate, as a result of underdiagnosis. Even in patients with symptomatic episodes of AF, asymptomatic episodes of AF can be detected in up to 62% of cases (25). The extent to which more intensive screening for AF in primary prevention, for example by ECG, leads to a higher AF detection rate

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TABLE 3

Medication of the study sample for the total cohort and participants with atrial fibrillation (weighted for the population of Mainz and the region of Mainz-Bingen)

Variable	Total population, n = 5000	Participants with atrial fibrillation, n = 161
Antithrombotic therapy		
Heparin, %	0.1 (0.0 to 0.2)	0.5 (0.0 to 1.5)
Oral anticoagulants, %	1.6 (1.3 to 1.9)	37.1 (29.5 to 44.7)
Platelet inhibitors, %	8.1 (7.4 to 8.8)	23.1 (16.7 to 29.6)
None of the above, %	90.3 (89.6 to 91.0)	42.7 (34.6 to 50.8)
Antiarrhythmic medication		
Class I, %	0.1 (0.0 to 0.2)	2.8 (0.3 to 5.2)
Class III, %	0.3 (0.2 to 0.5)	8.8 (4.4 to 13.1)
Class IV, %	0.9 (0.7 to 1.2)	8.1 (3.2 to 12.9)
Digitalis, %	0.5 (0.4 to 0.7)	16.4 (10.8 to 22.1)
Other medication		
ACE inhibitors, %	12.0 (11.2 to 12.9)	36.4 (28.9 to 43.9)
AT-II antagonists, %	7.2 (6.5 to 7.8)	18.4 (12.2 to 24.5)
Beta-blockers, %	13.5 (12.6 to 14.4)	56.1 (48.0 to 64.2)
Dihydropyridine, %	5.5 (4.9 to 6.1)	17.8 (11.7 to 23.9)
Diuretics, %	13.4 (12.5 to 14.2)	43.0 (35.1 to 50.9)
Nitrates, %	0.7 (0.5 to 0.9)	6.5 (2.7 to 10.3)
Renin inhibitors, %	0.1 (0.0 to 0.2)	0.7 (0.0 to 2.2)
Statins, %	9.8 (9.0 to 10.5)	34.9 (27.3 to 42.5)
Insulin, %	2.1 (1.7 to 2.5)	5.0 (1.6 to 8.3)
Oral antidiabetic medication, %	3.6 (3.2 to 4.1)	6.5 (2.7 to 10.3)
Thyroid hormone therapy, %	11.4 (10.5 to 12.3)	16.5 (10.5 to 22.5)

The data shown are percentage and 95% confidence interval for medication intake; ACE: angiotensin-converting enzyme

and the consequences of this in allowing early intervention and individual treatment strategies remain to be seen (e1).

This systematic, detailed research (including research into cardiovascular risk factors and patients' medication history) into a random, population-based sample and analysis of cases of AF in the study have allowed us to describe up-to-date, population-based data on AF and on the distribution of stroke risk factors in the studied cohort. Follow-up lasting several years will provide valuable information on AF risk factors and incidence.

At present, we can demonstrate that AF is a disease significant for the general population, and that its prevalence rises substantially with increasing age.

Screening using 12-lead ECG can reveal cases not yet diagnosed. Knowledge of how AF develops and of the distribution of risk factors in the general population is essential if long-term preventive measures are to be developed and gaps in care are to be closed.

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Further explanation of methods

In the Gutenberg Health Study, standard anthropometric data are measured to determine classic cardiovascular risk factors. Participants' medication history is obtained from information they provide and from drug packaging. Drugs are classified according to the Anatomical Therapeutic Chemical (ATC) Classification System.

Classic cardiovascular risk factors are defined as follows:

- Smoking divides participants into nonsmokers (people who have never smoked or no longer smoke) and current smokers.

- Diagnosis of diabetes mellitus is based on a medical history taken by a physician, or fasting blood glucose ≥126 mg/dL, or blood glucose ≥200 mg/dL in nonfasting participants.

- Dyslipidemia is defined as diagnosis by a physician or LDL/HDL ratio >3.5.

- Antihypertensive medication or mean systolic blood pressure ≥140 mm Hg or mean diastolic blood pressure ≥90 mm Hg results in a diagnosis of hypertension.

- The data used to calculate $CHADS_2$ score are shown in *eBox Table 1*. Those used to calculate CHA_2DS_2-VASc score are shown in *eBox Table 2*.

eBOX TABLE 1

$CHADS_2$ score and risk of stroke adapted according to Gage et al. (e3)

$CHADS_2$ score	Patients (n = 1733)	Adjusted stroke rate (% per year) (95% confidence interval)
0	120	1.9 (1.2 to 3.0)
1	463	2.8 (2.0 to 3.8)
2	523	4.0 (3.1 to 5.1)
3	337	5.9 (4.6 to 7.3)
4	220	8.5 (6.3 to 11.1)
5	65	12.5 (8.2 to 1..5)
6	5	18.2 (10.5 to 27.4)

$CHADS_2$: cardiac failure, hypertension, age, diabetes, stroke (doubled)

eBOX TABLE 2

Adjusted stroke rate, corresponding to CHA_2DS_2-VASc score according to Lip et al. (e4)

CHA_2DS_2-VASc score	Patients (n = 7329)	Adjusted stroke rate (% per year)
0	1	0
1	422	1.3
2	1230	2.2
3	1730	3.2
4	1718	4
5	1159	6.7
6	679	9.8
7	294	9.6
8	82	6.7
9	14	15.2

CHA_2DS_2-VASc: cardiac failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74, sex category (female)

eTABLE 1

Characterstics of the study sample for the total cohort and by prevalence of atrial fibrillation
(nonweighted distribution in the Gutenberg Health Study)

Variable	Total population, n = 5000	Participants without atrial fibrillation, n = 4801	Participants with atrial fibrillation, n = 161
Age, years	55.5±10.9	55.2±10.9	64.9±8.3
Women, n (%)	2460 (49.2; 47.8 to 50.6)	2390 (49.8; 48.4 to 51.2)	46 (28.6; 21.5 to 35.6)
Smokers, n (%)	959 (19.2; 18.1 to 20.3)	935 (19.5; 18.4 to 20.6)	18 (11.2; 6.3 to 16.1)
Body mass index, kg/m^2	26.5 (23.9 to 29.8)	26.5 (23.8 to 29.7)	28.2 (25.8 to 32.1)
Systolic blood pressure, mm Hg	132.8±17.7	132.8±17.7	133.8±17.8
Diastolic blood pressure, mm Hg	83.2±9.5	83.2±9.4	82.4±11.1
Heart rate, bpm	68.9±10.9	68.8±10.8	69.5±13.0
Total cholesterol, mg/dL	223±41	224±41	211±44
Total/HDL cholesterol	4.02 (3.30 to 4.92)	4.02 (3.30 to 4.90)	4.50 (3.63 to 5.20)
Diabetes, n (%)	374 (7.5; 6.8 to 8.2)	349 (7.3; 6.5 to 8.0)	21(13.0; 7.8 to 18.3)
Hypertension, n (%)	2 564 (51.3; 49.9 to 52.7)	2 427 (50.6; 49.1 to 52.0)	118 (73.3; 66.4 to 80.2)
Cardiac failure, n (%)	965 (19.4; 18.3 to 20.5)	883 (18.4; 17.3 to 19.5)	78 (48.8; 40.9 to 56.6)
Myocardial infarction, n (%)	156 (3.1; 2.6 to 3.6)	134 (2.8; 2.3 to 3.3)	22 (13.8; 8.4 to 19.3)
Stroke, n (%)	95 (1.9; 1.5 to 2.3)	78 (1.6; 1.3 to 2.0)	17 (10.6; 5.8 to 15.4)
PQ interval, ms	160±24	160±24	171±26*
Biomarker			
Creatinine, mg/dL	0.88 (0.79 to 0.98)	0.88 (0.79 to 0.97)	0.95 (0.83 to 1.06)
C-reactive protein, mg/L	1.70 (0.50 to 3.30)	1.60 (0.50 to 3.20)	2.50 (1.37 to 4.93)
N-terminal pro-B-type natriuretic peptide, pg/mL	61.9 (28.5 to 124.4)	60.1 (27.7 to 118.2)	290.6 (90.4 to 977.7)

The data shown are mean±standard deviation for continuous variables and number, percentage, and 95% confidence interval for categorical variables.
* The PQ interval is shown for persons with sinus rhythm in the study ECG (n = 96 participants with a history of atrial fibrillation)

eTABLE 2

**Characterstics of the study sample for the total cohort and by prevalence of atrial fibrillation
(standardized for age according to the 1976 European standard population [*1])**

Variable	Total population, n = 5000	Participants without atrial fibrillation, n = 4801	Participants with atrial fibrillation, n = 161
Age, years	51.9±10.6	51.6±10.5	62.2±9.5
Women, %	50	50.4	30.1
Smokers, %	21.4	21.6	12.7
Body mass index, kg/m^2	26.3 (23.6 to 29.6)	26.2 (23.6 to 29.5)	28.2 (25.5 to 32.2)
Systolic blood pressure, mm Hg	130.6±16.9	130.5±16.9	133.0±17.6
Diastolic blood pressure, mm Hg	83.1±9.4	83.1±9.3	82.8±10.9
Heart rate, bpm	69.0±10.7	69.0±10.6	69.3±12.4
Total cholesterol, mg/dL	222±41	222±41	212±43
Total/HDL cholesterol	4.01 (3.28 to 4.92)	4.00 (3.28 to 4.91)	4.54 (3.64 to 5.21)
Diabetes, %	5.9	5.7	11.7
Hypertension, %	45	44.4	70
Cardiac failure, %	17.4	16.8	43.1
Myocardial infarction, %	2.1	1.9	12.2
Stroke, %	1.4	1.2	9.2
PQ interval, ms	158±23	158±23	169±25[*2]
Biomarker			
Creatinine, mg/dL	0.87 (0.78 to 0.97)	0.87 (0.78 to 0.97)	0.94 (0.82 to 1.05)
C-reactive protein, mg/L	1.60 (0.50 to 3.10)	1.60 (0.50 to 3.10)	2.30 (1.30 to 4.68)
N-terminal pro-B-type natriuretic peptide, pg/mL	52.6 (23.1 to 104.9)	51.5 (22.9 to 102.0)	234.5 (60.9 to 884.4)

The data shown are mean±standard deviation for continuous variables and percentage for categorical variables.
[*1] The data in this table were standardized for age according to the 1976 European standard population (WHO), in order to allow comparability with other studies.
[*2] The PQ interval is shown for persons with sinus rhythm in the study ECG (n = 96 participants with a history of atrial fibrillation)

eTABLE 3

Prevalence of classic risk factors for atrial fibrillation (e5) in men and women (nonweighted distribution in the Gutenberg Health Study)

Variable	Men, n = 115	Women, n = 46
Age, years	67.0 (60.3 to 71.8)	67.0 (60.0 to 72.0)
Systolic blood pressure, mm Hg	134.5±17.5	132.0±18.5
Antihypertensive medication, n (%)	88 (76.5)	31 (67.4)
Body mass index, kg/m^2	29.2±4.7	29.6±6.7
Cardiac failure, n (%)	50 (43.5)	28 (62.2)
PQ interval, ms	170.8±25.1	170.8±27.2

The data shown are mean±standard deviation for continuous variables and number and percentage for categorical variables. The PQ interval is shown for persons with sinus rhythm in the study ECG and a history of atrial fibrillation

eTABLE 4

Medication of the study sample for the total cohort and participants with atrial fibrillation (nonweighted distribution in the Gutenberg Health Study)

Variable	Total population, n = 5000	Participants with atrial fibrillation, n = 161
Antithrombotic therapy		
Heparin, n (%)	6 (0.1)	1 (0.6)
Oral anticoagulants, n (%)	104 (2.1)	63 (39.1)
Platelet inhibitors, n (%)	516 (10.3)	41 (25.5)
None of the above, n (%)	4 370 (87.6)	62 (38.5)
Antiarrhythmic medication		
Class I, n (%)	7 (0.1)	5 (3.1)
Class III, n (%)	24 (0.5)	15 (9.3)
Class IV, n (%)	56 (1.1)	12 (7.5)
Digitalis, n (%)	37 (0.7)	29 (18.0)
Other medication		
ACE inhibitors, n (%)	746 (15.0)	65 (40.4)
AT-II antagonists, n (%)	441 (8.8)	30 (18.6)
Beta-blockers, n (%)	821 (16.5)	94 (58.4)
Dihydropyridine, n (%)	344 (6.9)	29 (18.0)
Diuretics, n (%)	832 (16.7)	75 (46.6)
Nitrates, n (%)	49 (1.0)	11 (6.8)
Renin inhibitors, n (%)	6 (0.1)	1 (0.6)
Statins, n (%)	610 (12.2)	58 (36.0)
Insulin, n (%)	130 (2.6)	8 (5.0)
Oral antidiabetic medication, n (%)	230 (4.6)	11 (6.8)
Thyroid hormone therapy, n (%)	600 (12.0)	25 (15.5)

The data shown are number and percentage for medication intake; ACE: angiotensin-converting enzyme.