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Incidence, prevalence, and antithrombotic management of
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1 Incidence, prevalence and antithrombotic management of atrial fibrillation 2 in elderly Germans

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1Abstract

2

3Aims

4Data on the epidemiology of atrial fibrillation (AF) and its antithrombotic management in
5elderly populations are scarce. The aims of this study were to estimate the incidence and
6prevalence of AF in the elderly in Germany and to describe antithrombotic management of
7AF cases.

8

9Methods

10Estimation of prevalence and incidence was based on data of three German statutory health
11insurances, which insured more than 800,000 people aged 65 years and older in the study
12period. The one year period prevalence of AF was estimated for each of the years 2004-2007.
13The incidence rate of AF in 2007 was assessed in patients with a preceding continuous three-
14year insurance period without diagnoses of AF. Antithrombotic management of AF was
15described among incident AF cases in 2008 and predictors for lack of prescriptions of oral
16anticoagulants were identified.

17

18Results

19Age-standardised period prevalence of AF among those 65 years or older was 7.7% in 2004,
209.4% in 2005, 9.8% in 2006 and 10.3% in 2007. The age-standardised incidence of AF was
2127.4/1,000 person-years in 2007. Prevalence and incidence increased with age and were
22higher in men than in women. In 2008, 58.2% of new AF cases received antithrombotic
23drugs. Treatment was less common among women and older people.

24

25Conclusion

26Incidence and prevalence of AF are relatively high in the elderly in Germany. A considerable
27fraction of new AF cases did not receive antithrombotic drugs in routine care.

28

29Keywords

30Atrial fibrillation, health insurance data, epidemiology, antithrombotic medication, Germany

1 Condensed abstract

2 Using a large health care database, we estimated incidence and prevalence of atrial fibrillation
3 (27.4/100,000 person-years and 10.3%, respectively) in Germany among the ≥ 65 years old.

4 Around 60% of patients with new atrial fibrillation diagnoses received antithrombotic drugs;

5 this treatment was less common among women and at older age.

1 What's new?

- 2 • Information on the prevalence of atrial fibrillation in the elderly in Europe is scarce.
3 Our study showed that the condition is common in the ≥ 65 years old in routine care in
4 Germany (~10%).
- 5 • Based on consideration of also secondary hospital discharge diagnoses of atrial
6 fibrillation, our study revealed higher incidence and prevalence estimates as
7 previously reported, especially in the older age groups.
- 8 • Previous studies showed high proportions of patients with incident atrial fibrillation
9 receiving antithrombotic treatment, but were restricted mostly to patients from
10 specialised centres
- 11 • In contrast, our study showed that a considerably higher fraction of patients with new
12 atrial fibrillation diagnoses did not receive antithrombotic treatment in routine care,
13 which applied to both patients with rhythm and rate control.

1 Introduction

2 Atrial fibrillation (AF) is the most common cardiac rhythm disorder and affects mainly older
3 people (1, 2). The most serious complication of AF is stroke. AF is associated with an up to 5-
4 fold elevated risk for developing stroke, which is increasing with age (1). In people aged 80-
5 89 years, approximately 25% of all strokes are due to AF (1). Strokes associated with AF are
6 more likely to be severe and have a higher initial mortality than non-AF strokes (3, 4). In the
7 context of demographic changes, the number of people suffering from AF will increase in the
8 future. Modelling studies suggest a 2 to 3-fold increase in the number of AF cases by the year
9 2050 (1, 5, 6).

10 Antithrombotic management of AF was reported in several studies, but the results differed
11 substantially. Some of these studies did not reflect routine care (7, 8), failed to include elderly
12 AF patients (9) or were limited by low numbers of AF cases (9, 10). Moreover, the proportion
13 of AF patients receiving antithrombotic drugs was possibly overestimated, since field studies
14 based on voluntary participation of the treating physicians may have overrepresented those
15 who already provide adequate antithrombotic treatment to their AF patients (7, 8, 10, 11).

16 For adequate planning of health care resources, knowledge about the epidemiology of AF and
17 possible deficiencies in the care of AF patients is essential. However, reliable data on the
18 epidemiology of AF in Europe and antithrombotic management of elderly AF patients in
19 routine health care are scarce. Therefore, the aim of this study was to estimate incidence and
20 prevalence of AF in the elderly in Germany and to assess antithrombotic management in these
21 patients.

22

23 Methods

24 Data source

25 Source of data was the German Pharmacoepidemiological Research Database (GePaRD). This
26 study was based on data from three statutory health insurances (SHI) including more than 8
27 million insurants during the study period. The database was described elsewhere (12, 13). In
28 brief, GePaRD contains demographic variables, information on hospital admissions,
29 outpatient physician visits and data on outpatient prescriptions. The hospital data comprises
30 information on admission diagnoses, main and secondary hospital discharge diagnoses,
31 therapeutic and diagnostic procedures with their respective dates, admission and discharge
32 dates and the reason for hospital discharge. Outpatient claims include information on
33 outpatient treatments, procedures and diagnoses. Outpatient diagnoses, which are only related

1 to a quarter, can be distinguished into confirmed diagnoses, suspected diagnoses, diagnoses
2 ruled out and status post diagnoses. Both, outpatient and inpatient diagnoses, are coded
3 according to the German Modification of the International Classification of Diseases 10th
4 Revision (ICD-10 GM) (14). Data on outpatient prescriptions of reimbursed drugs contains
5 the date of prescription and dispensation, information on the prescribing physician, the
6 pharmaceutical reference number and the amount of substance prescribed. Using the
7 pharmaceutical reference number, prescriptions can be linked to the pharmaceutical reference
8 database containing information on the anatomical-therapeutical-chemical (ATC) code, the
9 defined daily dose (DDD), packaging size, strength, formulation, generic and trade name.

10 At the time of the study, data from two smaller SHIs were available for the years 2004-2007;
11 one large SHI provided data for 2004-2008. Use of the data for research purposes needs to be
12 approved by the SHIs contributing the data and by local or federal government authorities
13 responsible according to data protection legislation. In accordance with § 75 of Volume 10 of
14 the Social Insurance Code, informed consent of involved insurants was not required. Since the
15 study was based on pseudonymised routine data delivered by the SHIs, a vote of the ethics
16 committee was not required.

17

18 **Study design**

19 Estimation of the period prevalence of AF for each of the years 2004-2007 was based on
20 cross-sectional analysis. To assess the incidence of AF in 2007, a retrospective cohort study
21 was conducted. For 2008 data from only one company was available and this data was used to
22 assess antithrombotic management of AF.

23

24 **Study population**

25 Included in the study population were people insured in one of the participating SHIs, if they
26 had valid information on sex, year of birth and place of residence and were aged ≥ 65 years.
27 For each of the different study populations, further inclusion criteria were applied.

28

29 **Period prevalence of AF**

30 For each of the study years, separate study populations were defined. Insurants had to be
31 continuously insured during the study year or continuously insured until death in the
32 respective year to be eligible for the study population.

33

1 Incidence of AF

2 For inclusion in the study population, insurants had to have an active insurance period in
3 2007, preceded by a continuous three-year insurance period without outpatient or hospital
4 diagnoses indicating the presence of AF. Patients remained in the cohort until the end of the
5 study period (31.12.2007), end of insurance period, death or first AF diagnosis, whichever
6 came first.

7

8 Management of incident AF

9 The study population which was used to assess the management of incident AF included
10 insurants who had been insured in the first three quarters of 2008, preceded by a continuous
11 four-year insurance period without outpatient or hospital diagnoses indicating the presence of
12 AF. Finally, insurants were included in the study population, if they had been diagnosed with
13 AF in one of the first three quarters in 2008, so that data on prescriptions and procedures in
14 the quarter of the AF diagnosis and the subsequent quarter could be used to describe the
15 management of AF. Patients remained in the cohort until the end of the subsequent quarter,
16 end of insurance period or death, whichever came first.

17

18 Definitions

19 *Ascertainment of cases*

20 Cases of AF were ascertained by using one of the following ICD-10 GM codes: I48.10
21 (paroxysmal atrial fibrillation), I48.11 (chronic atrial fibrillation), I48.19 (atrial fibrillation not
22 further specified). To be identified as cases, insurants had to have at least one confirmed
23 outpatient diagnosis, one main hospital discharge diagnosis or one secondary hospital
24 discharge diagnosis with the above codes. Since an outpatient diagnosis can only be related to
25 a calendar quarter, the date of the outpatient diagnosis of AF was defined as the middle of the
26 quarter. In two sensitivity analyses we studied different combinations of the criteria for AF
27 cases: (i) two confirmed outpatient diagnoses in different quarters or one hospital discharge
28 diagnosis (main or secondary); or (ii) one confirmed outpatient diagnosis or one main hospital
29 discharge diagnosis without consideration of secondary hospital discharge diagnoses.

30

31 *Drug therapy*

32 The proportion of incident AF patients receiving at least one antithrombotic drug and the
33 proportion of incident AF patients receiving more than one antithrombotic drug was described

1 overall and stratified by treatment strategies of rhythm versus rate control. Both treatment
2 strategies were defined by applying a modified definition originally proposed by *Nieuwlaat et*
3 *al.* (7). A patient was assigned to rhythm control, if a class IA, IC or III antiarrhythmic drug
4 (Vaughan Williams Classification (15)) had been prescribed or an electrical cardioversion had
5 been conducted. Patients not included in the rhythm control group were classified into the rate
6 control group, if they received prescriptions of digitalis, class II or class IV antiarrhythmic
7 drugs. Cordichin (a combination drug of verapamil and quinidine) was classified as rhythm
8 controlling agent.

9 Antithrombotic therapy was defined as at least one prescription of a vitamin K antagonist,
10 antiplatelet drug, low molecular weight heparin, unfractionated heparin, heparinoid, direct
11 thrombin inhibitor or other antithrombotic drug in the quarter of the AF diagnosis or the
12 subsequent quarter.

13

14 *Comorbidities*

15 A range of comorbidities including risk factors and secondary diseases of AF was selected to
16 describe the study population. These comorbidities were assessed using ICD-10 GM codes
17 related to confirmed outpatient diagnoses, main hospital discharge diagnoses or secondary
18 hospital discharge diagnoses during the respective study year (relevant codes are displayed in
19 table 1 of the supplementary material).

20

21 **Statistical analysis**

22 Period prevalence of AF was calculated by dividing the cumulative number of AF cases in a
23 given year by the mid-year population of the respective year. Corresponding confidence
24 intervals (CIs) were calculated using the Wilson-Score method (16). CIs for age-standardised
25 estimates were calculated according to the method based on the gamma distribution (17).
26 Incidence rates of AF were calculated by dividing the number of incident AF cases by the
27 accumulated person-time in the corresponding time period. CIs for incidence rates were
28 calculated using the substitution method (18). Prevalence and incidence estimates were
29 standardised using direct standardisation for the population distribution of ≥ 65 year-aged
30 Germans in the respective year obtained from the German Federal Statistical Office. In two
31 sensitivity analyses, the incidence and prevalence estimations were repeated applying both
32 case definitions described above.

1Using a logistic regression model, we determined predictors of lack of therapy with oral
2anticoagulants in incident AF patients. Independent variables contained in the full model
3included sex, age (5-year age categories), cardiac treatment strategy (rate control, rhythm
4control, neither), physician speciality of the AF diagnosing doctor (General Practitioner (GP),
5internist, other physician in private practice, physician in hospital), the CHA₂DS₂-VASc score
6(dichotomised into ≥ 2 and < 2) and selected comorbidities ascertained during a four-year
7period preceding the incident AF diagnosis (as shown in **Table 1**). Relevant factors were
8selected by backward elimination using the Wald test ($p < 0.05$) to determine the final model.
9All statistical analyses were conducted using SAS 9.2 (SAS Institute Inc., Cary, NC).

10

11Results

12Prevalence of AF

13AF cases were older and the proportion of men among AF cases was higher than in the total
14study population (**Table 1**). Assessed comorbidities were more frequent in AF cases than in
15the study population.

16In 2007, the standardised prevalence of AF was 10.3% and was higher in men (11.4%) than in
17women (8.7%) (**Table 2**). The prevalence was 5.1% in the age-group 65-69 years and
18increased to 19.7% in the age-group 85-89 years (**Figure 1**). In patients aged ≥ 90 years, the
19prevalence was slightly lower than in the preceding age group. Throughout the four study
20years, the prevalence of AF increased steadily. The increase in the prevalence of AF was seen
21in both sexes and all age-groups. The first sensitivity analysis in which two confirmed
22outpatient diagnoses were required for case ascertainment revealed slightly lower prevalence
23estimates. Here, the prevalence of AF in 2007 was 4.5% in patients aged 65-69 years and
24increased with advancing age to 18.1% in the age-group 85-89 years. Similar differences
25between the two estimation approaches were seen in both sexes (data not shown). The second
26sensitivity analysis which did not consider secondary hospital discharge diagnoses for case
27ascertainment resulted in lower prevalence estimates than the first sensitivity analysis,
28particularly in the oldest age groups. In this analysis, the AF prevalence was 4.6% in patients
29aged 65-69 years and 15.3% in those aged 85-89 years.

30

31Incidence of AF

32The overall standardised incidence of AF in 2007 was 27.4/1,000 py and was higher in men
33than in women (**Table 3**). The incidence of AF increased with advancing age from 13.2/1,000

1py in patients aged 65-69 years to 67.7/1,000 py in the age-group ≥ 90 years and was higher in
2men than in women across all age-groups. The incidence estimates from the first sensitivity
3analysis which required two confirmed outpatient diagnoses for case ascertainment were
4somewhat lower in both sexes. Here, the incidence rate of AF in 2007 was 7.7/1,000 py in the
5age-group 65-69 and increased to 51.7/1,000 py in patients aged ≥ 90 years (data not shown).
6The second sensitivity analysis which did not include secondary hospital discharge diagnoses
7in the case ascertainment revealed considerably lower incidence rates of AF compared to the
8main analysis. In this estimation approach, the incidence of AF was 10.1/1,000 py in the age
9group 65-69 years and 31.3/1,000 py in patients aged ≥ 90 years.

10

11 *Antithrombotic drug management*

12Of the 10,177 incident AF cases identified in 2008, 59.3% were newly diagnosed in hospital.
13Of the 40.7% who were newly diagnosed in the outpatient sector, 52.5% received the first AF
14diagnosis by an internist and 39.1% were diagnosed by a GP. Of the newly diagnosed AF
15cases, 58.2% received antithrombotic drugs in the quarter of the AF diagnosis or in the
16subsequent quarter (**Figure 2**). Antithrombotic drugs were more often prescribed to men
17(61.8%) than to women (51.6%). The proportion of incident AF cases receiving
18antithrombotic drug therapy declined with advancing age. In the age-group 65-69 years,
1960.2% were supplied with antithrombotic medications, however, in the age-group ≥ 90 years
20only 32.2% received an antithrombotic drug.

21In 59.1% of the incident AF cases, treatment was classified as rate control, whereas in 19.3%
22of the cases - as rhythm control. The remaining 21.6% received no medications classified as
23rhythm or rate control in the quarter of the AF diagnosis or in the following quarter. AF
24patients treated with rhythm control received more often antithrombotic agents (75.2%) than
25patients treated with rate control (61.3%) (**Table 4**). In particular, vitamin K antagonists and
26low-molecular-weight heparin were more rarely prescribed in patients with rate control than
27in those with rhythm control. Patients, whose rhythm disorder remained untreated, were
28considerably less often treated with antithrombotics (34.7%). Heparinoids and direct thrombin
29inhibitors were not prescribed in our study population of AF patients. With regard to the
30dichotomised CHA₂DS₂-VASc score, only slight differences in the proportion of patients
31without oral anticoagulation treatment were observed between patients with a CHA₂DS₂-
32VASc score of 0-1 compared to those with a CHA₂DS₂-VASc score of ≥ 2 (69.2% versus
3361.7%). The multivariate analysis showed that increasing age, female sex, rate control or no

1therapy strategy (neither rhythm control nor rate control) compared to rhythm control
2myocardial infarction, valvular heart disease, diabetes mellitus, chronic renal failure and a
3CHA₂DS₂-VASc score of 0-1 were associated with a significantly increased risk of not
4receiving oral anticoagulants after incident AF diagnosis, whereby especially subjects aged 90
5years or older were less likely to receive oral anticoagulants (**Table 5**).

6

7**Discussion**

8Using data from a large German health insurance database we assessed prevalence, incidence
9and antithrombotic drug treatment of AF in Germany. The incidence and prevalence increased
10with advancing age and were higher among men than women. More than 40% of incident AF
11cases received no antithrombotic drug treatment in 2008.

12The prevalence of AF estimated in our study is somewhat higher than the estimates derived
13from the considerably older, population-based Rotterdam Study which was conducted
14between 1990 and 1999 (19). In this study, the prevalence of AF was 4.0% in the age-group
1565-69 years (5.1% in our study) and similarly showed a marked increase with age. In subjects
16aged 80-84 years, the prevalence of AF was 13.5% in the Rotterdam Study compared to
1716.5% in our study. In contrast, we found a lower AF prevalence in our study than the
18recently published population-based Gutenberg Health Study (GHS) in Rhineland Palatinate
19(9). This is not surprising since in the GHS active screening for AF with a 12-lead
20electrocardiogram was conducted in addition to obtaining the medical history of the patient in
21an anamnestic interview. In the GHS, the prevalence of AF was provided in 10-year age
22bands up to the age of 74 years and was 10.6% in men and 4.9% in women aged 65-74 years,
23whereas it was 7.7% and 4.2% in this age group in our study, respectively.

24Our prevalence estimates of AF are somewhat higher than those of another recently published
25German study which was also based on claims data (20). This study by Wilke et al. (20)
26estimated the prevalence of AF at 4.8% in patients aged 65-69 years and at 15.1% in the age
27group 85-89 years (5.1% and 19.7% in our study, respectively) using a different algorithm for
28case ascertainment. This algorithm required one main hospital discharge diagnosis or two
29outpatient diagnoses in two different quarters and was used in analogy to the algorithms
30applied in the German morbidity-based risk structure equalisation scheme (21), where two
31outpatient diagnoses are required in order to improve security of the diagnosis. Since AF is an
32intermittent disease, which is characterised by short and rare episodes particularly at the
33beginning of the disease, a first AF diagnosis has not necessarily to be followed by a second

1AF diagnosis in the same year (22). Therefore we applied an algorithm based on a single
2diagnosis only. Requiring a second outpatient diagnosis of AF in another quarter in our first
3sensitivity analysis resulted in a similar prevalence for those aged 65-69 years as in the study
4by Wilke et al. (20), but still yielded a higher prevalence in the older age groups in our study.
5As our second sensitivity analysis which did not consider secondary hospital discharge
6diagnoses for case ascertainment revealed prevalences similar to those of Wilke et al., the
7difference between our and the Wilke study at higher age is likely due to the fact that the
8algorithm for case ascertainment by Wilke et al. did not consider secondary hospital discharge
9diagnoses of AF. From the hospital diagnoses, Wilke et al. only included patients with a main
10hospital discharge diagnosis, which in the German coding system states the disease giving rise
11to the hospitalisation. Since up to 30% of AF patients have asymptomatic AF (23), it might
12not be infrequent that AF is detected first during the routine examinations in the context of a
13hospital stay which was due to another disease.

14The incidence rates of AF from our study are most comparable with the results of the
15Cardiovascular Health Study (24). In this study, 18.0% of the incident AF cases were solely
16identified based on diagnoses reported by the patients which may have led to over- or
17underestimation of incidence, since patients could have forgotten about the arrhythmia or
18could have confused AF with another arrhythmia (24). The Rotterdam study (19), the US
19ARIC-Study (25) and another US study reported by Miyasaka *et al.* (5) reported lower
20incidence rates of AF in comparison to our study. In the ARIC study, only inpatient diagnoses
21were used to identify AF cases which presumably led to a considerable underestimation of the
22incidence rate, since AF does not necessarily require inpatient treatment. Only 67% of AF
23patients in our study were identified by inpatient diagnoses so that 33% of the patients would
24have been missed had the outpatient diagnoses not been considered. In comparison to the
25study by Wilke et al. (20), the incidence estimates in our study were also higher with the
26difference being most pronounced in the oldest age groups. These differences likely result
27from the different case finding algorithms used in both studies, as already discussed above. In
28particular, the non-consideration of secondary hospital discharge diagnoses may have led to
29the lower incidence estimates in the study by Wilke et al. since our second sensitivity
30analysis, in which only confirmed outpatient diagnoses and main hospital discharge diagnoses
31were considered revealed comparable estimates to the results provided by Wilke et al.

32Comparing our incidence and prevalence estimates with those from other studies, it has to be
33taken into account that most other studies were conducted in the late 1980's or 1990's (1, 19,

124, 25) and this has several implications. Improved survival of patients with cardiac diseases
2has led to an increase in elderly patients who are at high risk of AF. Furthermore, a growing
3awareness of AF among physicians may have resulted in a smaller proportion of undetected
4AF cases. Therefore the higher estimates in our study were to be expected compared to those
5from these earlier studies. Our similar prevalence estimates to those of the considerably older
6Rotterdam study (19) may be explained by the active screening approach for AF in the
7Rotterdam study which would be expected to outweigh the lower prevalence during the time
8period of its study conduct (26).

9Our estimates regarding the proportion of incident AF cases receiving antithrombotic therapy
10in general as well as defined antithrombotic agents compare well with the results of the
11recently published GHS study (9), but are considerably lower than the estimates reported by
12the Euro Heart Survey (7) or those of the Registry of the German Competence Network on
13Atrial Fibrillation (AFNET) (8). All AF patients participating in the Euro Heart Survey and
1467% of AF patients participating in the AFNET were treated in specialized university
15hospitals or cardiologist centres (7, 8) who have been shown to provide adequate
16antithrombotic treatment more frequently (27). In our study, a more balanced distribution
17regarding the sector of the diagnosis and the physician speciality of the AF diagnosing doctor
18was seen. Both in the Euro Heart Survey and the AFNET, the participating centres are
19presumably not representative for anticoagulant management of AF patients in routine care,
20but are likely to include a selected sample of physicians who due to their scientific interest in
21the study question are more likely to provide adequate antithrombotic therapy in accordance
22with current guidelines. It is an advantage of our study that it includes all physicians who care
23for AF patients thereby avoiding a selected sample of physicians. A further explanation for
24the lower proportion of AF patients with antithrombotic therapy in our study may be that
25acetylsalicylic acid (ASA) in the therapy of AF is not reimbursed by the SHIs in Germany, so
26that the data source of our study did not contain such claims. Wilke et al. (28) also evaluated
27the antithrombotic management of patients with AF and also showed an underuse of treatment
28with antithrombotic drugs, but since this study focussed on the antithrombotic therapy of
29prevalent AF cases and used other methods to evaluate the antithrombotic treatment, we did
30not compare our results to this study.

31

32*Limitations*

1At the time of the analysis, health insurance data were only available to us until the end of
22008. It was therefore not possible to study which impact the newer oral anticoagulants might
3have on the antithrombotic management of AF patients. Further, health insurance data have
4only been available to us since 2004. Calculation of the **CHA₂DS₂-VASc** score was limited by
5this fact, since prior diagnoses of stroke or ischaemic attack were not available to us before
6this time. In some cases, patients could have had diagnoses of AF prior to 2004 and would
7thus be misclassified as incident cases in 2007, although they were prevalent cases. However,
8such misclassification is probably of low magnitude, since it is unlikely that an AF patient
9will not see his physician for three years and will not obtain the AF diagnosis in his records.

10A validation of the AF diagnosis in our data by chart review could not be carried out for
11reasons of protection of personal data. However, we assume a valid coding of AF diagnoses
12in SHI data, since our results regarding the prevalence of AF were similar to the German
13GHS-study or showed expected differences (9).

14Due to lack of specific codes it could not be clearly distinguished between rhythm and rate
15controlling catheter ablations. Therefore catheter ablations could not be taken into account
16when defining rhythm and rate control, which could have led to an underestimation of both
17treatment strategies. However, this potential underestimation is suspected to be rather small,
18since catheter ablations are rarely performed in incident AF cases.

19Since many contraindications for the use of antithrombotic agents in patients with AF cannot
20adequately be operationalized in claims data, we did not exclude patients with
21contraindications when evaluating the antithrombotic treatment in incident AF patients, which
22could have led to an overestimation of undertreatment. However, since these contraindications
23are rare disorders, not accounting for them will likely not change the results of undertreatment
24with antithrombotics to a relevant extent.

25The categorization of the physician speciality in claims data is rather unspecific, as for
26example cardiologists cannot be distinguished from gastroenterologists, since both are coded
27as internists in our data. This presumably led to the fact that the physician speciality had no
28influence on receiving oral anticoagulants in the multivariate logistic regression model,
29although this is a known association in other studies (27).

30*Strengths*

31The major strength of this study is the large study sample, which allowed a precise estimation
32of incidence, prevalence and antithrombotic treatment even in the highest age-categories.

1 Since this study is based on administrative data, recall bias or selection bias (e.g. due to
2 voluntary participation of patients or physicians) could be avoided. We further did not restrict
3 our analyses on the antithrombotic treatment of incident AF to selected physician specialities,
4 so that our results are more likely to reflect routine care. In addition, it could be shown that
5 the age- and sex-distribution as well as drug use of patients included in GePaRD is similar to
6 that of Germany, leading to a high external validity of the results (12, 29).

7

8 In conclusion, our study showed that the incidence and prevalence of AF in elderly people in
9 Germany is rather high. Compared with incidence and prevalence estimates of older studies,
10 an increase of the incidence and prevalence can be assumed. Our analysis revealed a
11 considerable fraction of AF patients who were not treated with antithrombotic drugs, whereby
12 especially old-aged people and women had a high risk of not receiving antithrombotic
13 treatment.

14 In the context of an aging society and therefore increasing numbers of multi-morbid AF cases
15 at a high risk of stroke, providing adequate antithrombotic therapy is an important task for the
16 physicians and interventions are necessary to improve the current situation.

17

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22

23 **Conflict of interest**

24 Christoph Ohlmeier: None declared

25 Rafael Mikolajczyk: Rafael Mikolajczyk received research funding from Sanofi Pasteur MSD
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27 Wilhelm Haverkamp: Wilhelm Haverkamp has received honoraria and research funding from
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29 relationship.

30 Edeltraut Garbe: Edeltraut Garbe is running a department that occasionally performs studies
31 for pharmaceutical industries with the full freedom to publish. The companies include
32 Mundipharma, Bayer, Stada, Sanofi-Aventis, Sanofi-Pasteur, Novartis, Celgene, and GSK.

1She has been consultant to Bayer-Schering, Nycomed, Teva, GSK, Schwabe and Novartis in
2the past. The present work is unrelated to the above grants and relationships.

3

1

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1 Figure legends

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3 Figure 1: Age- and sex-stratified prevalence of atrial fibrillation in 2007. Error bars represent
4 95% confidence intervals.

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6 Figure 2: Age- and sex-stratified proportions of incident cases with atrial fibrillation receiving
7 antithrombotic therapy. Error bars represent 95% confidence intervals.

1Text tables

2Table 1: Characteristics of the study population and patients with atrial fibrillation in 2007

Characteristics	Study population			AF-cases		
	<i>n</i>	%	95% CI	<i>n</i>	%	95% CI
Age groups						
65-69	383,966	47.3		19,369	28.5	
70-74	211,713	26.1		17,644	26.0	
75-79	120,154	14.8		14,718	21.7	
80-84	62,325	7.8		9,947	14.7	
85+	34,313	4.2		6,224	9.2	
All	812,471	100.0		67,902	100.0	
Age (Mean, SD)	72.6	6.1		75.5	6.8	
Sex						
Women	361,280	44.8		24,293	35.6	
Comorbidity						
Heart failure	84,325	10.4	(10.3-10.4)	24,310	35.8	(35.4-36.2)
Myocardial infarction	15,316	1.9	(1.8- 1.9)	3,285	4.8	(4.7-5.0)
Ischaemic stroke	16,304	1.9	(1.9- 1.9)	4,146	6.1	(5.9-6.3)
Hypertension	519,694	64.0	(63.9-64.1)	56,604	83.4	(83.1-83.8)
Ischaemic heart disease	184,421	20.6	(20.5-20.7)	32,508	47.9	(47.5-48.3)
Cardiomyopathy	11,474	1.4	(1.4- 1.4)	4,270	6.3	(6.1- 6.5)
Valvular heart disease	74,949	9.2	(9.2- 9.3)	20,151	29.7	(29.3-30.0)
Diabetes mellitus	167,444	20.6	(20.5-20.7)	21,725	32.0	(31.6-32.4)
COPD*	65,566	8.1	(8.0- 8.1)	9,880	14.6	(14.3-14.8)
Sleep apnea	18,847	2.3	(2.3- 2.4)	2,987	4.4	(4.3- 4.6)
Hyperthyroidism	30,284	3.7	(3.7- 3.8)	5,009	7.4	(7.2- 7.6)
Chronic renal failure	45,280	5.6	(5.5- 5.6)	11,269	16.6	(16.3-16.9)
Hospitalisation						
≥ 1 Hospitalisation	204,983	25.2	(25.1-25.3)	36,684	54.0	(53.7-54.4)

*COPD: Chronic obstructive pulmonary disease

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1 Table 2: Sex-stratified crude and standardised prevalence of atrial fibrillation in 2004 to 2007

Year	Men				Women				All			
	Crude (%)	95% CI	Stand.	95% CI	Crude (%)	95% CI	Stand.	95% CI	Crude (%)	95% CI	Stand.	95% CI
2004	8.1	(8.0-8.2)	9.3	(9.2-9.4)	5.9	(5.8-6.0)	7.2	(7.1-7.3)	7.1	(7.1-7.2)	7.7	(7.6-7.8)
2005	8.9	(8.8-9.0)	10.3	(10.2-10.4)	6.4	(6.3-6.5)	8.0	(7.8-8.1)	7.8	(7.7-7.9)	9.4	(9.3-9.4)
2006	9.3	(9.2-9.4)	10.8	(10.7-10.9)	6.5	(6.4-6.6)	8.2	(8.1-8.4)	8.1	(8.0-8.1)	9.8	(9.7-9.8)
2007	9.8	(9.7-9.9)	11.4	(11.3-11.5)	6.8	(6.7-6.9)	8.7	(8.6-8.8)	8.5	(8.4-8.5)	10.3	(10.2-10.4)

*Stand.= Standardised (Standardisation was based on the population distribution of Germany of the respective year)

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1 Table 3: Sex-stratified crude and standardised incidence rate of atrial fibrillation per 1,000 person-years in 2007

	Men				Women				All			
	<i>py*</i>	<i>Cases*</i>	<i>Rate**</i>	<i>95% CI</i>	<i>py</i>	<i>Cases</i>	<i>e</i>	<i>95% CI</i>	<i>py</i>	<i>Cases</i>	<i>e</i>	<i>95% CI</i>
Age groups												
65-69	197,042	3,128	15.9	(15.3-16.4)	147,851	1,413	9.6	(9.1-10.1)	344,893	4,541	13.2	(12.8-13.6)
70-74	105,412	2,765	26.2	(25.3-27.2)	77,589	1,221	15.7	(14.9-16.6)	183,001	3,986	21.8	(21.1-22.5)
75-79	52,526	1,975	37.6	(36.0-39.3)	45,173	1,185	26.2	(24.8-27.8)	97,699	3,160	32.3	(31.2-33.5)
80-84	20,468	1,084	53.0	(49.9-56.2)	27,001	1,095	40.6	(38.2-43.0)	47,469	2,179	45.9	(44.0-47.9)
85-89	6,041	426	70.5	(64.0-77.5)	11,015	604	54.8	(50.6-59.4)	17,056	1,030	60.4	(56.8-64.2)
90+	1,716	137	79.9	(67.1-94.4)	5,208	332	63.8	(57.1-71.0)	6,924	469	67.7	(61.8-74.2)
All	383,205	9,515	24.8	(24.3-25.3)	313,836	5,850	18.6	(18.2-19.1)	697,041	15,365	22.0	(21.7-22.4)
Stand.****			30.3	(29.6-31.0)			25.3	(24.6-26.1)			28.4	(27.9-29.0)

*py = person years

**Newly diagnosed AF patients

***per 1,000 py

****Stand.=Standardised (Standardisation was based on the population distribution of Germany of the respective year)

Table 4: Antithrombotic therapy in patients with newly diagnosed atrial fibrillation by therapy approach

Antithrombotic therapy*	Rhythm control			Rate control			Neither			All		
	<i>n</i>	%	95% CI	<i>n</i>	%	95% CI	<i>n</i>	%	95% CI	<i>n</i>	%	95% CI
All	1,475	75.2	(73.2-77.0)	3,690	61.3	(60.1-62.5)	761	34.7	(32.7-36.7)	5,926	58.2	(57.3-59.2)
Vitamin K antagonists	1,143	58.3	(56.1-60.4)	2,286	38.0	(36.8-39.2)	445	20.3	(18.6-22.0)	3,874	38.1	(37.1-39.0)
≥ 2 prescriptions	456	23.2	(21.4-25.2)	854	14.2	(13.3-15.1)	181	8.2	(7.2-9.5)	1,491	14.7	(14.0-15.4)
Antiplatelet drugs	444	22.6	(20.8-24.5)	1,453	24.1	(23.1-25.2)	256	11.7	(10.4-13.1)	2,153	21.2	(20.4-22.0)
≥ 2 prescriptions	192	9.8	(8.6-11.2)	678	11.3	10.5-12.1)	99	4.5	(3.7-5.5)	969	9.5	(9.0-10.1)
Low molecular weight heparin	565	28.8	(26.8-30.8)	1,148	19.1	(18.1-20.1)	253	11.5	(10.3-12.9)	1,966	19.3	(18.6-20.1)
≥ 2 prescriptions	226	11.5	(10.2-13.0)	481	8.0	(7.3-8.7)	127	5.8	(4.9-6.8)	834	8.2	(7.3-8.7)
Unfractionated heparin	13	0.7	(0.4- 1.1)	32	0.5	(0.4- 0.8)	6	0.3	(0.1- 0.6)	51	0.5	(0.4- 0.7)
≥ 2 prescriptions	5	0.3	(0.1-0.6)	9	0.2	(0.1-0.3)	3	0.1	(0.1-0.4)	17	0.2	(0.1-0.3)
Other antithrombotic agents	14	0.7	(0.4- 1.2)	28	0.5	(0.3- 0.7)	5	0.2	(0.1- 0.5)	47	0.5	(0.4- 0.6)
≥ 2 prescriptions	5	0.3	(0.1-0.6)	10	0.2	(0.1-0.3)	0	0.0	(0.0-0.2)	15	0.2	(0.1-0.2)

*Patients could have received more than one drug

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Table 5: Adjusted risk for lack of therapy with oral anticoagulants after incident AF diagnosis

Characteristics	Risk for lack of therapy	
	OR	95% CI
Age		
65-69	1.0	
70-74	1.0	(0.9 - 1.1)
75-79	1.0	(0.9 - 1.1)
80-84	1.6	(1.4 - 1.8)
85-89	2.2	(1.8 - 2.7)
≥90	12.4	(6.3 - 24.4)
Sex		
Men	1.0	
Women	1.3	(1.2 - 1.4)
Therapy approach		
Rhythm control	1.0	
Rate control	2.1	(1.9 - 2.3)
Neither	5.0	(4.4 - 5.8)
Comorbidities		
Ischaemic stroke*	0.8	(0.7 - 0.9)
Myocardial infarction*	1.2	(1.1 - 1.4)
Valvular heart disease*	0.8	(0.7 - 0.8)
Diabetes mellitus*	0.9	(0.8 - 1.0)
Chronic renal failure*	1.3	(1.1 - 1.4)
CHA₂DS₂-VASc score		
≥2	1.0	
0-1	1.5	(1.2 - 1.9)

*Reference category = No

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