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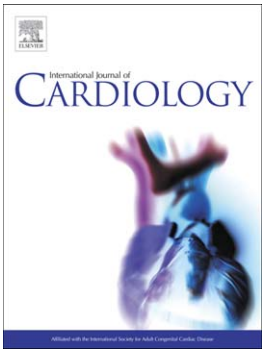

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Oral anticoagulant use in octogenarian European patients with atrial fibrillation: a subanalysis of PREFER in AF

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ABSTRACT

Background. Few studies describe oral anticoagulant (OAC) prescription practices in very elderly patients with atrial fibrillation (AF).

Methods. In this sub-analysis of the PREFER in AF study, performed in 2012, patients were stratified according to age (<80 [n = 5,575] and ≥80 years [n = 1,660]) and OAC treatment. Factors associated with OAC prescription were analyzed in a multivariate logistic regression model with backward elimination of variables least associated with OAC use.

Results. Patients ≥80 years presented with permanent AF more often (p<0.0001) and reported fatigue and dyspnea more frequently (p<0.0001) and palpitations less frequently (p<0.0001) than patients <80 years. Hypertension, stroke, heart failure, coronary heart disease, peripheral arterial disease, cancer, chronic kidney disease, and prior major bleeding were significantly more frequent in ≥80 years. Most patients were treated with OACs in both age groups. The overall use of vitamin K antagonists was similar in both groups (78.2% vs.78.2% p=0.98), while the use of non-vitamin K antagonist OACs was lower in the ≥80 years old group than in the <80 years group (4.5% vs. 6.6% p=0.001). Among patients ≥80 years, prior stroke and heart failure were significantly associated with OAC use, whereas higher age, prior bleeding, paroxysmal AF, chronic hepatic disease, and difficulties with self-care were associated with no OAC use.

Conclusions. The current use of OAC in European AF patients was satisfactorily high in octogenarians, suggesting reasonable implementation of current guidelines. Interestingly, patients with poor quality of life were less often anticoagulated. This may warrant further studies.

Introduction

Until a few years ago, only 50-60% of eligible patients with atrial fibrillation (AF) received anticoagulant treatments that were recommended to reduce the risk of stroke[1-6]. More recently, observational studies have shown that the percentage of AF patients treated with anticoagulant drugs has increased [7,8]. This trend suggests that physicians' practices have been likely influenced by the endorsement of the CHA_2DS_2-VASc score for the assessment of the risk of stroke[9] and by the AF guidelines by the European Society of Cardiology (ESC) [10,11].

Very elderly (≥ 80 years of age) patients constitute a specific population. Since the incidence of AF-related stroke rate increases with age[12-14], oral anticoagulant (OAC) treatment is particularly effective in the very elderly [15]. However, because very elderly patients are often frail and at higher risk of bleeding, the decision to treat them with an OAC is often more affected by the concern about bleeding than by the appraisal of the therapeutic benefits of anticoagulation [16-20]. Few data describe recent antithrombotic prescription practices in this specific population [7,21].

We performed a subanalysis of the large, cross-sectional, community-based Prevention of Thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF) study [8,22,23] to determine frequency and modalities of OAC prescription in AF patients older than 80 compared with younger patients.

Methods

This study is a subanalysis analysis of the PREFER in AF (Prevention of thromboembolic events – European Registry in Atrial Fibrillation) data set. Methodology of the study has previously been published [8]. In short, PREFER in AF registry was designed as a prospective observational study aiming at describing the characteristics and management of patients with AF with a particular focus on prevention of thromboembolic events. Inclusion criteria were age ≥ 18 years old and history of documented AF within the preceding 12 months. There were no explicit exclusion criteria. Furthermore, consecutive patients were included at each site in order to reduce selection bias. All data were entered into the European Registry for Atrial Fibrillation using electronic case report forms. Baseline data were collected from patients seen between January 2012 to January 2013 in seven representative European countries (Austria, France, Germany, Italy, Spain, Switzerland, and the UK). In addition to data on socio-demographics, medical history and therapies, quality of life was also measured using the EQ-5D, a validated standardized non-disease-specific instrument for describing and appraising health-related quality of life and generate a cardinal index of health. It evaluates 5-domains mobility (walking), self-care (washing and dressing), usual activities, pain/discomfort, and anxiety/depression [24].It is one of the most widely used questionnaires in research settings. The overall rate of response was 80% in the the study.

For the purpose of this subanalysis, patients were stratified according to their age at baseline (< 80 and ≥ 80 years). Data were then further stratified according to treatment with an OAC. OAC treatment was defined as treatment with vitamin K antagonist (VKA) or non-vitamin K antagonist oral anticoagulant (NOAC) and no OAC treatment was defined as neither NOAC nor VKA use. $CHADS_2$, CHA_2DS_2-VASC and HAS-BLED scores were calculated for each participant; however, because of missing values, they were only available for 91.1%, 91.2%, and 81.7% of participants over 80, respectively.

Statistical analysis was performed using SAS® 9.2 (SAS Institute Inc., Cary, North Carolina, USA). Continuous variables are presented as means and standard deviation (SD). Categorical variables are

presented as numbers and percentages. Percentages were calculated after the number of patients with missing data was subtracted from the denominator. Patient characteristics at baseline were compared according to age groups and then according to OAC use. Between-group comparisons were performed using Chi-Squared tests for categorical variables and Wilcoxon or Kruskall Wallis tests for continuous variables. Rates of OAC use was graphed by country (combing Austria, Switzerland and Germany into a single region) and compared according to the age groups at baseline. We studied factors associated with OAC use in 2 different sets of logistic regression models, one for participants < 80 and one for participants ≥ 80 years. Covariates associated with OAC use in univariate models ($p < 0.15$) were entered in the multivariate models; then, through a backward elimination process, only variables associated with OAC use in the multivariate models were finally presented using Forrest plots.

PREFER in AF study comprised 7,243 subjects, 7,225 patients were included for this analysis (18 subjects were missing), 5,565 < 80 years old (77%) and 1,660 (23%) ≥ 80 years old.

Results

Characteristics of the study population according to the age group

Comparison between the 2 age groups upon baseline patient characteristics is shown in **table 1**. Octogenarian patients were more often female. Rates of hypertension, previous stroke, heart failure, coronary heart disease, peripheral arterial disease, cancer, renal failure, bleeding history, valvular diseases were significantly higher in the ≥ 80-year than in the < 80-year group. Rate of dilated left atrial was higher in the ≥ 80-year group. Left ventricular ejection fraction was lower in the ≥ 80-year group. As a consequence of older age and these distributions, $CHADS_2$, CHA_2DS_2-VASC, and HAS-BLED were higher in the ≥ 80 year than in the < 80 year group (**table 2**).

In addition, octogenarians had more often permanent AF (51% vs. 35%, p<.0001) and reported more frequently AF-related symptoms such as fatigue and dyspnea and less frequently palpitations (**table 2**).

Responses to the EQ-5D health questionnaire (**figure 1**) showed that for all 5 domains patients in the ≥ 80 year group had more often problems with mobility, self-care, usual activities and pain/discomfort or anxiety/depression than patients in the < 80 year group (p < 0.0001 for all 5 domains).

Table 3 compares the 2 age-groups upon pharmacological and non-pharmacological strategies. The overall use of OACs was high in the whole population (82.6%), with no statistically significant difference between the two age groups. The frequency of use of VKAs was similar the two groups (78.2% vs.78.2% p=0.98), while NOACs were less frequently prescribed in the ≥ 80 year group (4.5% vs. 6.6% p=0.001)**.** Antiplatelet was overall used in 24.8% in < 80 year old and 25.4% in ≥ 80 year old patients (p=0.63). Antiplatelet was associated with OACs in 13.7% (13.9% in < 80 year old and 13.0% in ≥ 80 year old patient, p=0.30). Rhythm control therapy was less frequently used in older subjects (53.2% vs. 62.0%,

p < 0.0001). Amiodarone, dronedarone, flecainide and propafenone were less prescribed in ≥ 80 year old patients than in < 80 year old patients

When OAC prescriptions were stratified by country (**figure 2**), OAC prescription rates were high across all the countries with some variations from country to country. The lowest rate of OAC prescription was observed in the whole population and in octogenarian patients (71.7% and 68.1%, respectively) in Italy. Conversely the highest rate of OAC prescription was observed in the whole population (90.5%) in France. In the German region the highest rate was observed in octogenarian patients (89.0%). France was also the only country with a significant difference in OAC prescription between age-groups (< 80 yo, 91.6% vs. ≥ 80 yo, 88.2%, p < 0.05).

Factors associated with oral anticoagulant use according to age

Subjects ≥ 80 years old

In univariate analysis (**supplementary table**), among patients ≥ 80 years old, factors significantly associated with OAC use were prior ischemic stroke, heart failure and higher BMI, SBP and DBP. Factors significantly associated with OAC non-use were older age, paroxysmal and persistent AF, history of bleeding and chronic hepatic diseases. In the OAC use group compared to nonuse of-OAC, mean $CHADS_2$ and CHA_2DS_2-VASC score were higher (2.8 (1.2) vs. 2.5 (1.0), p=0.002 and 4.7 (1.4) vs. 4.4 (1.3), p=0.04 respectively) and HAS-BLED score was lower (2.4 (1.0) vs. 2.7 (0.9), p<0.0001). Results of the EQ-5D showed that factors significantly associated with no prescription of OACs were presence of problems for self-care and usual activities (**figure 1**).

In the multivariate analysis, (**figure 3a**), OAC use was significantly higher with prior ischemic stroke and heart failure. Factors associated with no prescription of OACs were older age, prior bleeding, paroxysmal AF, chronic hepatic disease and difficulties with self-care.

Subjects < 80 years old

In univariate analysis (**supplementary table**), among patients < 80 years old, factors significantly associated with OAC use were heart failure, prior stroke, coronary heart disease, hypertension, diabetes and COPD. Factors significantly associated with OAC non-use were paroxysmal AF and current smoking. In the OAC use group compared to nonuse of OAC, mean $CHADS_2$ and CHA_2DS_2-VASC score were higher (1.8 (1.2) vs. 1.3 (1.2), $p < 0.0001$and 3.2 (1.6) vs. 2.4 (1.8), $p < 0.0001$ respectively). HAS-BLED scores however were not significantly different between OAC subgroups (1.9 (1.1) vs. 1.9 (1.2), p=0.70). Results of the EQ-5D (see **figure 1**) showed use of OACs was significantly associated with mobility problem and pain/discomfort.

In the multivariate analysis (**figure 3b**), OAC use was significantly higher with age, prior stroke, heart failure, systolic blood pressure, dyslipidemia and significantly lower with paroxysmal AF, current smoking and difficulties with self-care.

Discussion

Analyzing data from an European multinational registry including 1660 participant 80 years and older, we found that the use of anticoagulant therapy was high in octogenarians and has increased compared to previous studies [3] suggesting that older age is a lesser issue for AC prescription and that current guideline are better implemented in this population. Compared with younger patients, octogenarian patients with AF had more comorbidities with higher CHA_2DS_2-VASC and HAS-BLED scores, and overall lower quality of life according to the EQ-5D health questionnaire. Patients in the ≥ 80 year group reported more frequently symptoms such as fatigue and dyspnea and less frequently palpitations and more frequently presented with a permanent AF. The percentage of use of VKAs was similar to that in younger patients while NOACs were less frequently prescribed to ≥ 80 patients.

Our results confirm prior reports on characteristics of very old patients with AF. It is known that in older subjects AF is often either non-symptomatic or presenting with non-specific symptoms, hence being often an incidental finding [25]. In our study, only 13% of octogenarians described palpitations, which is in line with previous studies reporting that less than 10% of AF patients over the age of 80 years had palpitations [26]. This is why an annual pulse assessment is recommended to improve AF detection in the elderly [10] as shown by SAFE study [27]. Furthermore, according to guidelines elderly patients had more often permanent AF and rate control strategy was preferred in octogenarian patients [10].

Oral anticoagulant prescription rates were high in the seven European countries participating in the study with a mean of 82.6% of OAC prescription rate in octogenarian subjects, although some variation from country to country was noted. Italy had the lowest rate of OAC prescription and France the highest. This rate of OAC use is higher than previously reported [3]. Recent studies have shown an increased prevalence of anticoagulant use [2,8,21,28]. However few studies were specifically focused on very old population. PREFER-AF is one of the most recent cohorts that included one of the largest proportions of octogenarian populations. A recent report on a French cohort, the SAGES study, including 447 subjects

over 80 years old, showed a similar rate of OAC prescription, i.e. 75.6% [7]. These findings show a progression in prescription practices towards a greater adherence to current European guidelines [10,11]. Factors for long considered barriers to anticoagulant use in the elderly, such as frequent comorbidities, fear of bleeding and unawareness of guidelines [3] might have been overcome because of the increase of evidence for the benefit of anticoagulant therapy especially in the AF elderly population [29]. On the other hand, the specific setting, i.e., patients, mostly outpatients, referred to cardiologists, might also explain the very high frequency of OAC use compared with what shown in other settings, e.g., inpatients admitted to internal medicine or geriatric wards [30].

In particular, we found that, among anticoagulants, vitamin K antagonists were prescribed more often than NOAC, with no significant differences between age groups. The overall rate of NOAC use was low (6.2%), consistently with the previous studies [21], and NOAC particularly low in the very elderly (4.6%). These results are not entirely surprising as in 2012 when the study was conducted, NOACs were just starting to become available and physicians would have been expected to exercise caution when prescribing a newly approved drug to a high risk population.

Analysis of determinant of OAC prescription showed some different factors between the 2 groups of age. Heart failure and stroke were associated with OAC use and paroxysmal AF and difficulty with self-care were associated with nonuse of OAC in both groups. In contrast history of bleeding and chronic hepatic disease were associated with nonuse of OAC only in the octogenarian group. Cardiovascular risk factors (dyslipidemia, SBP) were associated with OAC use only in < 80-year group. Interestingly, age had a different type of relationship with OAC use in the 2 age groups. It was associated with OAC use in < 80 year group and associated with nonuse in ≥ 80-year group. $CHADS_2$ and CHA_2DS_2-VASC scores were associated with OAC use in both age groups whereas HAS-BELD was only associated with nonuse of OAC in ≥ 80 year old group. These findings suggest that, despite the change in prescription frequency,

factors known to affect the patient risk of bleeding are still the main determinant of caution in OAC prescription.

The lower prescription of OAC in paroxysmal AF has already been observed [7,31] and may be related to the uncertainty of the diagnosis or to the belief that paroxysmal AF is less severe and at lower cardio-embolic risk than persistent/permanent AF.

In our population 13.7% (13.9% in < 80 year old and 13.0% in ≥ 80 year old patient) took simultaneously antiplatelet and anticoagulant. In recent randomized controlled trials with oral anticoagulants (NOAC vs Warfarin), aspirin was used at baseline in 34% of participants [32]. In RE-LY study aspirin was used continuously during the treatment period in 21.1%, 19.6%, and 20.8% of patients receiving 110 mg of dabigatran, 150 mg of dabigatran and warfarin, respectively [33]. In our octogenarian population the frequency of the association oral anticoagulant with antiplatelet drugs was lower because of the increased risk of bleeding of this dual therapy after 80 years.

Finally, OAC use in both younger patients and in the very elderly was significantly associated with difficulties with self-care. Similarly, in the S.AGES study, lower autonomy was significantly associated with nonuse of VKA in patients < 80 [7]. As quality of life variables are not currently included in formalized risk/benefit assessments, these data support the idea that, regardless of age, some level of subjectivity is still influencing physician decisions. In particular, the association of problems with self-care and nonuse of OAC may reflect physician fears that patients would not be able to take medication consistently or adequately. Additional studies may be warranted in order to determine whether concerns about self-care impacting OAC use are justified.

Limitations

Selection bias could have been occurred during site selection within each country. Patient-selection could also have been subject to bias despite the instruction that physicians should enroll consecutive patients. However, overall patient characteristics in the PREFER AF registry were similar to those described in other registries [8]. Finally, as previously stated, our study was conducted in a specific setting of care, excluding very frail patients, such as residents in nursing homes with multiple comorbidities and major functional disability.

Strengths

The PREFER in AF study is a large cohort designed to provide a picture of the management of AF in seven European countries. All design aspects have been established by the scientific committee and accomplished by an independent CRO except the selection of the countries. Within each country representative sites have been selected in order to enroll a representative patient population that provided real-life data. The study includes a large proportion of subjects ≥ 80 years old with AF and contained quality of life data that are usually not assessed in such observational studies. Lastly, few studies assessed quality of life and its relationship with OAC therapies.

Conclusion

These data confirm the change in treatment patterns in Europe in recent years and show that the use of OACs for AF treatment has been integrated in daily, community-based practices both in younger patients and in the very elderly. Particularly use of anticoagulant therapy was higher even after 80 years than in previous studies suggesting that recent international guidelines are better implemented in this specific population. Factors associated with use of OAC vary according to age (> or < 80 years). Quality of life appears to influence the OAC prescription although no data support this fact. Additional studies are thus needed to assess the impact of quality of life on stroke and bleeding risk.

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RDC, JULH and PK have made substantial contributions to the analysis and the interpretation of data, revised the article critically and approved of the version to be submitted.

Table 1, Patient characteristics according to age

General characteristics. % (N)	Total	< 80 yo	≥ 80 yo	p
	N=7225	N=5565	N=1660	
Age, M (SD)	71.5 (7.9)	67.8 (9.34)	83.7 (3.17)	<.0001
Male gender	60.0 (4336)	63.7 (3543)	47.8 (793)	<.0001
Education level				
Primary school	47.9 (3461)	50.3 (2549)	60.4 (912)	
Secondary school	29.4 (2122)	33.3 (1691)	28.6 (431)	<.0001
High school diploma or above	13.8 (997)	16.4 (831)	11 (166)	
Body mass index (kg/m2), M (SD)	27.9 (4.9)	28.4 (5.08)	26.4 (4.27)	<.0001
Smoking status				
Never	56.6 (4088)	57.7 (3017)	68.4 (1071)	
Former	30.5 (2206)	33.3 (1744)	29.5 (462)	<.0001
Current	6.93 (501)	9 (469)	2 (32)	
Previous stroke	8.48 (613)	7.8 (430)	11.1 (183)	<.0001
COPD	11.3 (815)	10.8 (593)	13.6 (222)	0.0020
Arterial hypertension	72.5 (5239)	71.4 (3954)	78.3 (1285)	<.0001
Diabetes	22.4 (1616)	22.4 (1235)	23.1 (381)	0.51
Dyslipidemia	43.4 (3133)	45.5 (2469)	40.7 (664)	0.0007
Chronic heart failure	21.3 (1539)	19 (1045)	30.3 (494)	<.0001
Coronary heart disease	23.4 (1688)	22.2 (1214)	29.3 (474)	<.0001
Peripheral arterial disease	4.42 (319)	3.9 (215)	6.4 (104)	<.0001
Active cancer	3.22 (233)	2.9 (161)	4.4 (72)	0.003
Chronic hepatic diseases	2.05 (148)	2.1 (115)	2 (33)	0.85
History of thromboembolic events	2.49 (180)	2.4 (130)	3.1 (50)	0.11
Bleeding history	7.22 (522)	6.6 (367)	9.5 (155)	0.0001
SBP (mmHg), M (SD)	132 (17)	131.2 (16.4)	132.8 (17.3)	0.0007
DBP (mmHg), M (SD)	77.6 (10.2)	78.1 (10.2)	75.9 (10.3)	<.0001
Renal function				
eGFR ≥90	87.4 (6152)	90.2 (4896)	78.0 (1258)	
eGFR 60-89	2.34 (169)	2.6 (142)	1.7 (27)	
eGFR 30-59	8.30 (600)	6.2 (334)	16.5 (266)	<.0001
eGFR 15-29	1.51 (109)	0.9 (50)	3.7 (59)	
eGFR <15	0.12 (9)	0.1 (6)	0.2 (3)	
Ejection fraction %, M (SD)	56.5 (11.6)	56.7 (11.6)	55.9 (11.8)	0.008
Dilated left atrial (>40mm)	58.6 (4233)	68.2 (3190)	76.9 (1043)	<.0001
Severe aortic stenosis	0.78 (56)	0.6 (31)	1.5 (25)	0.0001
Severe mitral insufficiency	1.23 (89)	1.1 (61)	1.7 (28)	0.06
Heart valve replacement	5.37 (388)	5.4 (296)	5.7 (92)	<.0001

% (N), percentage (number); yo, years old; M (SD), Mean (standard deviation), Comparisons between groups were performed using Chi-Squared tests for categorical variables and Wilcoxon or Kruskall Wallis tests for continuous variables. COPD, chronic obstructive pulmonary disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate in mL/min/1.73 m^2 according to MDRD formula.

Table 2, AF characteristics and risk scores according to age groups

AF characteristics. % (N)	Total	< 80 yo	≥ 80 yo	p value
	7225	5565	1660	
Current AF type				
Paroxysmal	29.9 (2160)	32.6 (1806)	21.5 (354)	<.0001
Persistent	24.0 (1733)	25.5 (1412)	19.5 (321)	
Long standing persistent	7.14 (516)	6.9 (384)	8 (132)	
Permanent	38.6 (2786)	34.9 (1943)	51.1 (843)	
Current Heart rhythm				
Sinus rhythm	31.2 (2251)	34.7 (1916)	20.3 (335)	<.0001
Atrial fibrillation	64.4 (4652)	61.7 (3407)	75.6 (1245)	
Atrial flutter	1.94 (140)	2 (111)	1.8 (29)	
Other	1.73 (125)	1.6 (87)	2.3 (38)	
Palpitations				
Never or occasional	79.5 (5741)	79 (4336)	86.5 (1405)	<.0001
Intermediate or frequent	19.0 (1372)	21 (1153)	13.5 (219)	
Fatigue				
Never or occasional	64.7 (4672)	68 (3708)	59.4 (964)	<.0001
Intermediate or frequent	33.3 (2407)	32 (1747)	40.6 (660)	
Dyspnea				
Never or occasional	67.5 (4875)	70.2 (3852)	62.6 (1023)	<.0001
Intermediate or frequent	31.1 (2247)	29.8 (1636)	37.4 (611)	
Risk Scores, M (SD)				
$CHADS_2$	1.93 (1.22)	1.7 (1.23)	2.7 (1.18)	<.0001
CHA_2DS_2VASc	3.37 (1.62)	3 (1.68)	4.6 (1.41)	<.0001
HAS-BLED	2.04 (1.13)	1.9 (1.16)	2.5 (1.02)	<.0001

% (N), percentage (number); yo, years old; M (SD), Mean (standard deviation).

Table 3, Atrial fibrillation treatment according to age

AF treatment, % (N)	Total	< 80 yo	≥ 80 yo	P*
	7225	5565	1660	
Anticoagulants	82.6 (5967)	82.9 (4612)	81.6 (1355)	0.24
VKA (all)	78.2 (5651)	78.2 (4353)	78.2 (1298)	0.98
Warfarin	33.6 (2429)	34.3 (1908)	31.4 (521)	0.03
Phenprocoumon	18.3 (1320)	19.3 (1074)	14.6 (246)	<.0001
Acenocoumarol	13.0 (939)	12.7 (706)	14 (233)	0.15
Fluindione	13.2 (957)	11.8 (654)	18.3 (303)	<.0001
NOACs (all)	6.10 (441)	6.6 (367)	4.5 (74)	0.001
Dabigatran	4.04 (292)	4.4 (245)	2.8 (47)	0.004
Rivaroxaban	1.99 (144)	2.1 (117)	1.6 (27)	0.22
Apixaban	0.11 (8)	0.1 (8)	0 (0)	0.12
Antiplatelets agents (all)	24.9 (1800)	24.8 (1379)	25.4 (421)	0.63
Aspirin	19.9 (1438)	20.1 (1121)	19.1 (317)	0.35
Clopidogrel	4.10 (296)	3.9 (219)	4.6 (77)	0.20
Others	0.91 (66)	0.7 (39)	1.6 (27)	0.0005
APL as monotherapy	11.2 (809)	10.8 (603)	12.4 (206)	0.07
VKA as monotherapy	66.5 (4805)	66.1 (3681)	67.6 (1122)	0.27
No antithrombotic treatment	6.2 (450)	6.3 (350)	6.0 (99)	0.60
Rhythm control therapy	60.0 (4336)	62.0 (3453)	53.2 (883)	<.0001
Class I Flecainide	10.5 (762)	12.4 (691)	4.3 (71)	<.0001
Class I Propafenone	2.91 (210)	3.3 (183)	1.6 (27)	0.0004
Class I Quinidine	0.18 (13)	0.2 (12)	0.1 (1)	0.19
Class III Amiodarone	24.2 (1751)	25.6 (1423)	19.8 (328)	<.0001
Class III Dronedarone	4.03 (291)	4.6 (256)	2.1 (35)	<.0001
Class III d,l-Sotalol	5.51 (398)	5.6 (310)	5.3 (88)	0.67
Other antiarrhythmic drugs	28.3 (2047)	28.2 (1572)	28.6 (475)	0.77
Cardioversion				
Electrical cardioversion†	18.1 (1302)	20.8 (1153)	9 (149)	<.0001
Pharmacologic cardioversion*	19.5 (1401)	21.1 (1170)	14 (231)	<.0001
Catheter ablation*	5.18 (356)	6.3 (351)	0.3 (5)	<.0001
Pace maker or Defibrillator	9.03 (649)	8.1 (448)	12.3 (201)	<.0001

% (N), percentage (number); yo, years old; M (SD), * Comparisons between groups were performed using Chi-Squared tests for categorical variables and Wilcoxon/Kruskall Wallis tests for continuous variables; † in the past 12 months. AF, atrial fibrillation; APL, antiplatelet agent; VKA, vitamin K antagonist; NOAC, direct oral anticoagulant.

Figure legends

Figure 1, Patient EQ-5D according to age and oral anticoagulant use

Comparisons between groups with Chi-Squared tests; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

OAC +, use of oral anticoagulant; OAC –, nonuse of oral anticoagulant.

Figure 2, Treatment with oral anticoagulants according to age and country

The term 'Germany' was used to describe data from Germany, Austria, and Switzerland.

Figure 3a, Determinants of OACs use in < 80 year old subjects with atrial fibrillation.

Figure 3b, Determinants of OACs use in ≥ 80 year old subjects with atrial fibrillation

Logistic regression model with oral anticoagulant use as dependent variables and backward elimination of independent variables; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

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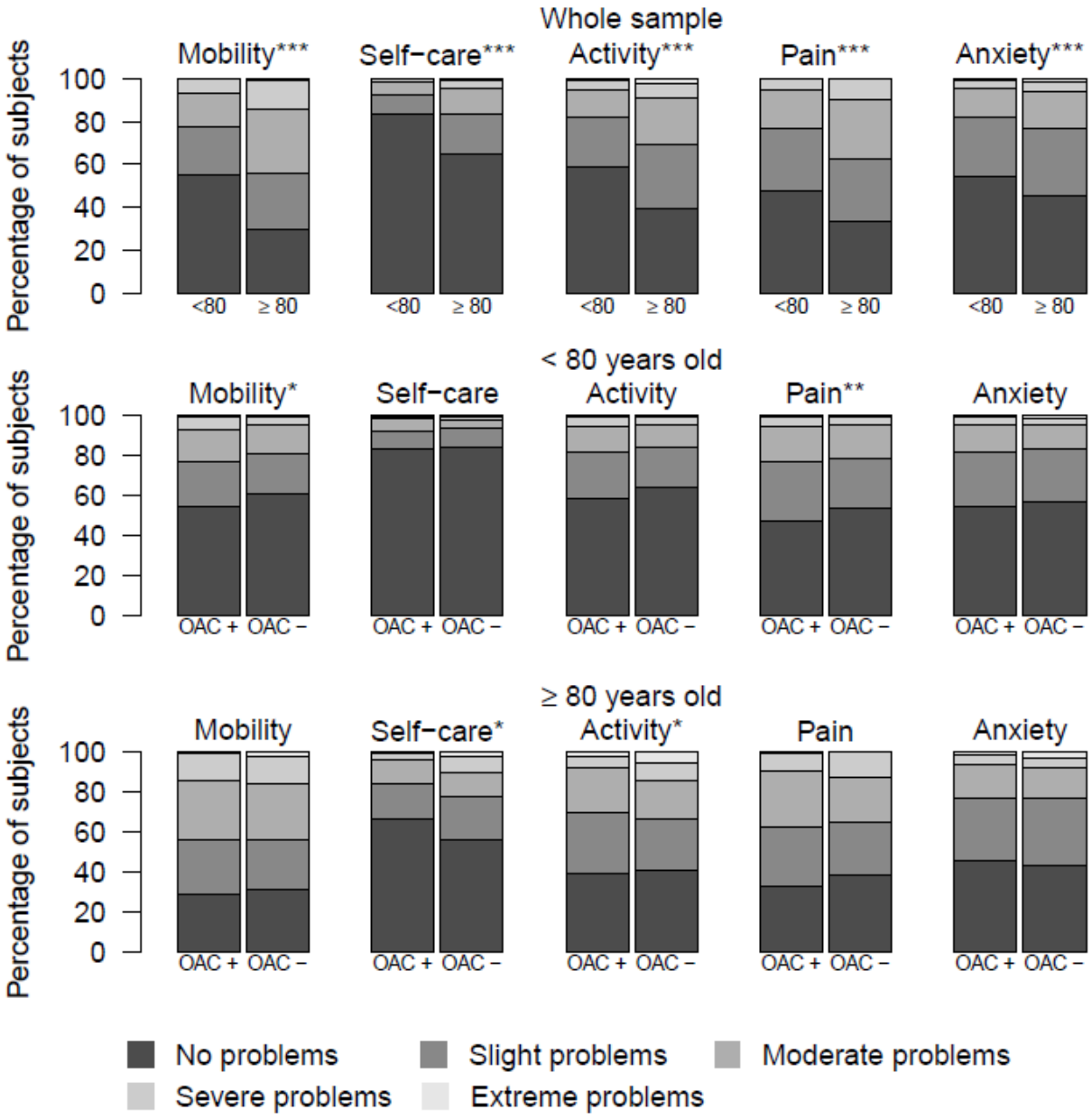

Fig. 1

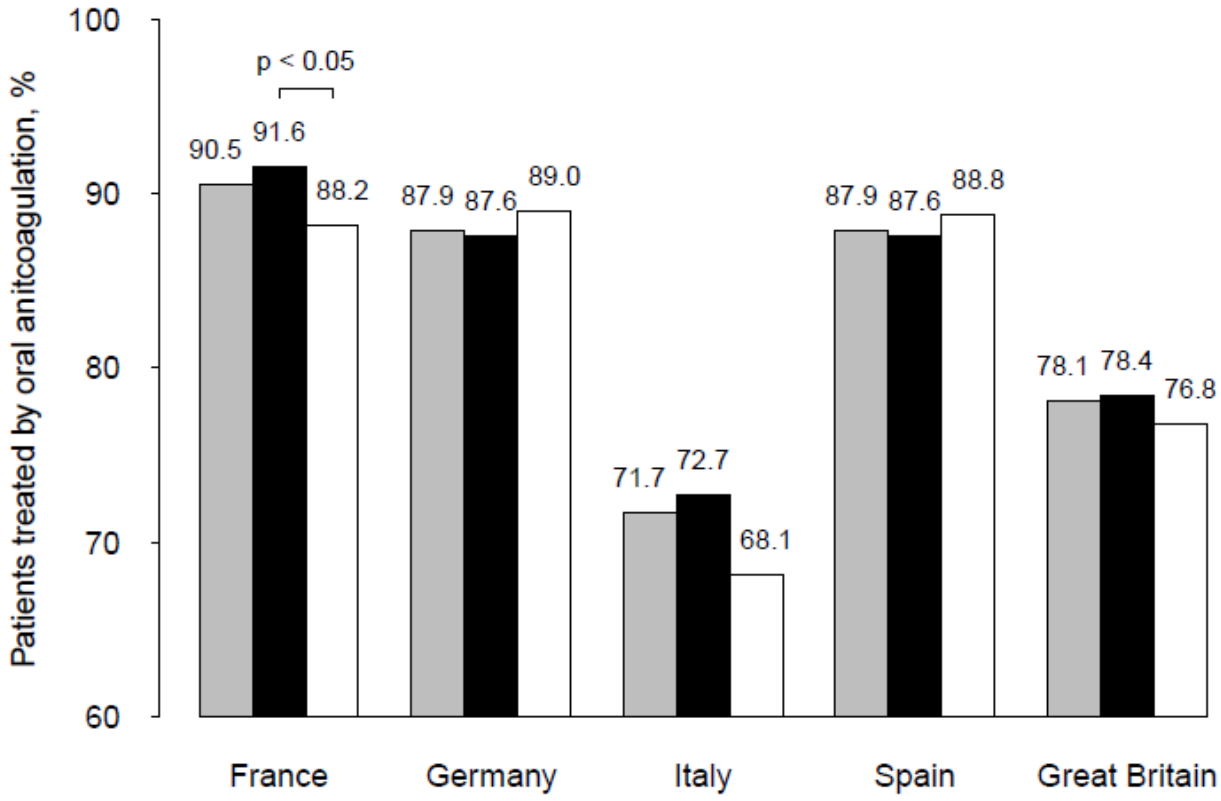

Fig. 2

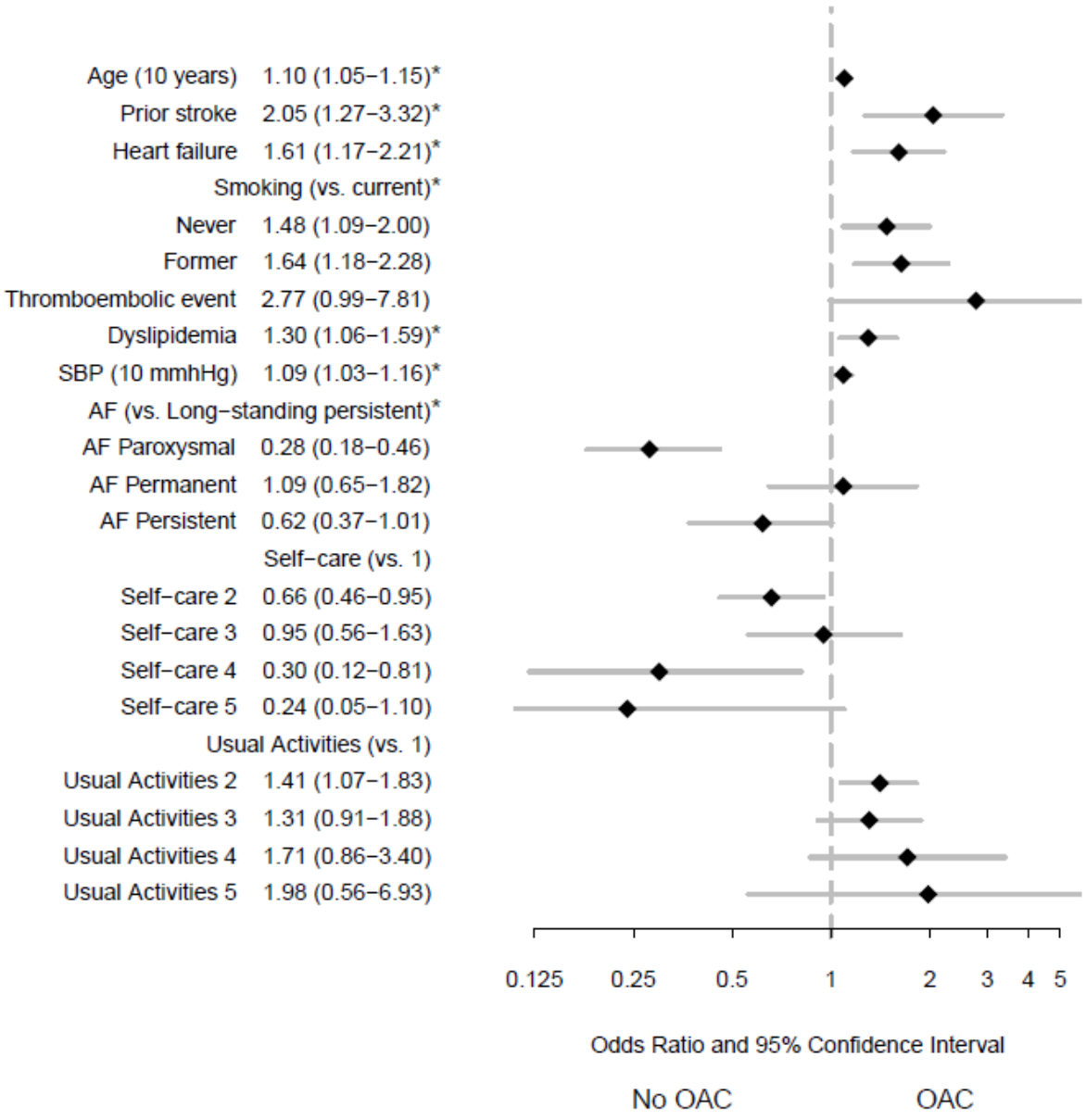

Fig. 3a

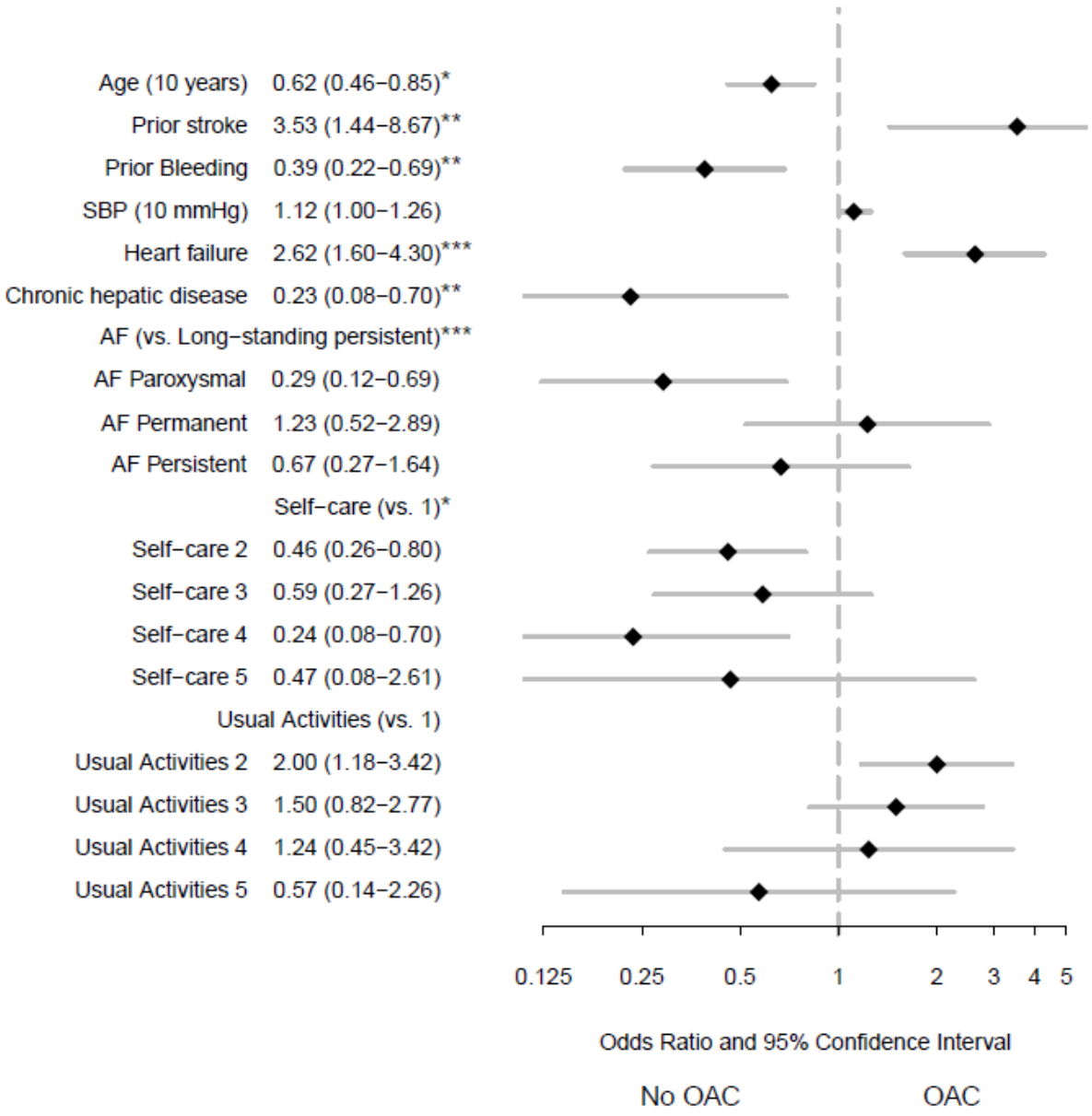

Fig. 3b