SUPPLEMENTARY DATA

SUPPLEMENTARY METHODS

The study consecutively enrolled adult patients (age ≥ 18 years) presenting with ECG-documented AF as a primary or secondary diagnosis in 250 centers from 27 participating countries from October 2013 to September 2016. The institutional review board approved the study protocol for each institution. The study was performed according to the EU Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki. Participating countries were grouped into European regions as follows: *a)* Northern Europe—Denmark, Estonia, Latvia, Norway, UK; *b)* Western Europe—Belgium, France, Germany, Netherlands, Switzerland; *c)* Eastern Europe—Bulgaria, Czech Republic, Georgia, Kazakhstan, Kyrgyzstan, Poland, Romania, Russia; and *d)* Southern Europe— Albania, FYR Macedonia, Italy, Malta, Montenegro, Portugal, Serbia, Spain, Turkey.

Main inclusion criteria were the following: *a)* the qualifying AF event had to be recorded by a 12-lead ECG, 24-hour ECG Holter, or other electrocardiographic documentation within 12 months before enrollment; *b)* age should be 18 years and older; and *c)* a written informed consent form. The main exclusion criteria were the following: *a)* no objective proof of AF or *a)* being or planned to be enrolled in a pharmacological interventional clinical trial.

At the time of enrollment, investigators collected and recorded each patient's baseline characteristics, medical history, pharmacological treatment, and details of any prior clinical interventions or diagnostic procedures using a standardized electronic case report form.

Thromboembolic risk was defined according to the CHA2DS2-VASc score, and bleeding risk was assessed according to HAS-BLED. High-risk patients were defined as those with a CHA2DS2-VASc score greater than 2. Symptomatic status was defined according to the European Heart Rhythm Association (EHRA) score.

Statistical analysis (details on multivariable models and interaction analysis)

We built 2 different multivariable models: Model 1 was adjusted for CHA2DS2-VASc score, body mass index (BMI), chronic kidney disease (CKD, ie, creatinine clearance < 60 mL/min calculated with the

Cockcroft-Gault equation), type of AF, chronic obstructive pulmonary disease (COPD), and use of oral anticoagulants (OAC); Model 2 was adjusted for BMI, smoking, lipid disorder, the individual components of the CHA2DS2-VASc score (age, sex, heart failure, hypertension, diabetes, prior stroke, vascular disease), valvular heart disease, dementia, CKD, COPD, malignancy, obstructive sleep apnea, type of AF, EHRA score, use of OAC, region of enrollment, and site of inclusion (hospital/outpatient). Covariates included in the multivariable models were selected a priori based on their clinical relevance in the context of AF epidemiology and their potential role as confounders. The proportional hazard assumption for Cox models was assessed through Schoenfeld residuals, with no critical violation observed across physical activity groups. The results are expressed as hazard ratio (HR) and 95% confidence interval (CI).

Interaction analyses were conducted to explore the association between physical activity and the risk of the primary composite outcome among various subgroups. These subgroups were sex, age categories (< 65 years, 65-75 years, > 75 years), the presence of heart failure, obesity (defined as BMI ≥ 30 kg/m²), peripheral artery disease (PAD), COPD, CKD, coronary artery disease (CAD), European regions, CHA2DS2-VASc score < 2 vs ≥ 2 (low vs high), and AF type. All interaction analyses were adjusted for the same variables included in the Cox regression model (Model 1). The results are reported as adjusted hazard ratio (aHR), with 95% confidence interval (CI), and p-value for interaction (P_{int}). Moreover, we evaluated the interaction between age and left ventricular ejection fraction (LVEF), modeled as continuous variables, and physical activity on the risk of the primary outcome, using restricted cubic splines with 3 knots. For these analyses, we considered 65 years (for age) and 50% (for LVEF) as reference values (ie, HR = 1).

Table 1 of the supplementary data. Comparison of key clinical characteristics between excluded and included patients (cross-sectional phase)

	Excluded patients (n = 1571)	Included patients (N = 9525)	P
Age, y	71.00 [63.00-78.00]	71.00 [62.00-77.00]	.08
Female sex	608/1571 (38.7)	3904/9525 (41.0)	.08
Permanent AF	532/1528 (34.8)	3186/9378 (34.0)	.51
Hypertension	976/1549 (63.0)	5856/9450 (62.0)	.43
Diabetes mellitus	330/1543 (21.4)	2207/9485 (23.3)	.10
Smoking (current)	103/1048 (9.8)	879/9221 (9.5)	.75
Lipid disorder	599/1476 (40.6)	3794/9145 (41.5)	.51
Heart failure	447/1543 (29.0)	3899/9458 (41.2)	< .001
Dilated CMP	120/1544 (7.8)	867/9415 (9.2)	.06
Coronary artery disease	447/1506 (29.7)	2611/8925 (29.3)	.73
Prior TE events	178/1527 (11.7)	1096/9465 (11.6)	.93
Peripheral artery disease	108/1507 (7.2)	775/9346 (8.3)	.13
COPD	125/1552 (8.1)	855/9459 (9.0)	20
Malignancy (current + prior)	131/1558 (8.4)	687/9463 (7.3)	.10
CKD	174/1551 (11.2)	1207/9464 (12.8)	.09
Multimorbidity	981/1243 (78.9)	6169/7830 (78.8)	.91

AF, atrial fibrillation; CKD, chronic kidney disease; CMP, cardiomyopathy; COPD, chronic obstructive pulmonary disease; TE, thromboembolic.

The data are presented as No. (%) or median [interquartile range].

Table 2 of the supplementary data. Baseline characteristics of patients stratified by physical activity levels

	Occasional physical activity (n = 3089, 56.9%)	Regular physical activity (n = 1981, 36.5%)	Intense physical activity (n = 361, 6.6%)	All (n = 5431)	P
Age, y	69.00 [61.00-76.00]	68.00 [60.00-74.00]	64.00 [54.00-72.00]	69.00 [61.00-76.00]	< .001
Female	1211/3089 (39.2)	595/1981 (30.0)	78/361 (21.6)	1884/5431 (34.7)	< .001
BMI, kg/m²	27.20 [24.70-30.50]	26.80 [24.60-29.70]	26.70 [24.10-31.10]	27.20 [24.70–30.40]	.003
BSA, m²	1.91 [1-78-2.06]	1.94 [1.80-2.07]	1.97 [1.83-2.12]	1.94 [1.80–2.09]	< .001
LBM, kg	57.15 [48.55-63.83]	58.63 [50.61-64.10]	60.91 [53.98-66.82]	58.31 [49.75–64.59]	< .001
Site of inclusion					< .001
Hospital	1626/3089 (52.6)	905/1981 (45.7)	150/361 (41.6)	2681/5431 (49.4)	
Outpatient or office based	1463/3089 (47.4)	1076/1981 (54.3)	211/361 (58.4)	2750/5431 (50.6)	
*Region of enrolment**					< .001
Western Europe	706/3089 (22.9)	568/1981 (28.7)	95/361 (26.3)	1369/5431 (25.2)	
Southern Europe	1355/3089 (43.9)	724/1981 (36.5)	77/361 (21.3)	2156/5431 (39.7)	
Northern Europe	371/3089 (12.0)	397/1981 (20.0)	135/361 (37.4)	903/5431 (16.6)	
Eastern Europe	657/3089 (21.3)	292/1981 (14.7)	54/361 (15.0)	1003/5431 (18.5)	
AF type					< .001
First diagnosed	469/3050 (15.4)	377/1953 (19.3)	81/349 (23.2)	927/5352 (17.3)	
Paroxysmal	846/3050 (27.7)	588/1953 (30.1)	96/349 (27.5)	1530/5352 (28.6)	
Persistent	565/3050 (18.5)	415/1953 (21.2)	98/349 (28.1)	1078/5352 (20.1)	
Long-standing persistent	152/3050 (5.0)	83/1953 (4.2)	22/349 (6.3)	257/5352 (4.8)	
Permanent	1018/3050 (33.4)	490/1953 (25.1)	52/349 (14.9)	1560/5352 (29.1)	
Hypertension	1914/3064 (62.5)	1142/1972 (57.9)	148/358 (41.3)	3204/5394 (59.4)	< .001
Diabetes mellitus	709/3078 (23.0)	315/1972 (16.0)	39/361 (10.8)	1063/5411 (19.6)	< .001
Smoking (current)	311/2999 (10.4)	195/1938 (10.1)	45/358 (12.6)	551/5295 (10.4)	.36
Lipid disorder	1295/2969 (43.6)	725/1883 (38.5)	109/342 (31.9)	2129/5194 (41.0)	< .001
Obstructive sleep apnea	122/2985 (4.1)	59/1931 (3.1)	10/354 (2.8)	191/5270	.12
Heart failure	1242/3066 (40.5)	577/1972 (29.3)	75/357 (21.0)	1894/5395 (35.1)	< .001
Dilated CMP	269/3053 (8.8)	114/1966 (5.8)	22/355 (6.2)	405/5374 (7.5)	< .001
Hypertrophic CMP	102/3055 (3.3)	31/1968 (1.6)	7/355 (2.0)	140/5378 (2.6)	< .001
Restrictive CMP	3/3055 (0.1)	8/1967 (0.4)	1/355 (0.3)	12/5377 (0.2)	.07
Congenital heart disease	29/3063 (0.9)	21/1972 (1.1)	5/356 (1.4)	55/5391 (1.0)	.69
Pulmonary arterial hypertension	219/3040 (7.2)	81/1961 (4.1)	10/354 (2.8)	310/5355 (5.8)	< .001
Coronary artery disease	812/2879 (28.2)	462/1898 (24.3)	66/349 (18.9)	1340/5126 (26.1)	< .001
Prior MI	355/812 (43.7)	206/462 (44.6)	38/66 (57.6)	599/1340 (44.7)	.09
Prior PCI	303/812 (37.3)	206/462 (44.6)	34/66 (51.5)	543/1340 (40.5)	.007
Prior CABG	128/812 (15.8)	84/462 (18.2)	11/66 (16.7)	223/1340 (16.6)	.54
Prior angina	269/812 (33.1)	147/462 (31.8)	15/66 (22.7)	431/1340 (32.2)	.22
Valvular alterations	1441/3029 (47.6)	852/1948 (43.7)	136/355 (38.3)	2429/5332 (45.6)	< .001
Prior TE events	340/3072 (11.1)	192/1975 (9.7)	25/360 (6.9)	557/5407 (10.3)	.02

Prior ischemic stroke	174/3071 (5.7)	104/1975 (5.3)	9/360 (2.5)	287/5406 (5.3)	.04
Prior TIA	100/3071 (3.3)	58/1975 (2.9)	10/360 (2.8)	168/5406 (3.1)	.76
Prior EP/DVT	61/3071 (2.0)	31/1975 (1.6)	7/360 (1.9)	99/5406 (1.8)	.55
Prior hemorrhagic events	154/3070 (5.0)	89/1973 (4.5)	15/358 (4.2)	258/5401 (4.8)	.62
Peripheral vascular disease	251/3031 (8.3)	119/1942 (6.1)	12/358 (3.4)	382/5331 (7.2)	< .001
Liver disease	91/3078 (3.0)	52/1966 (2.6)	5/358 (1.4)	148/5402 (2.7)	.22
COPD	234/3068 (7.6)	130/1966 (6.6)	17/360 (4.7)	381/5394 (7.1)	.07
Dementia	27/3083 (0.9)	13/1978 (0.7)	0/361 (0.0)	40/5422 (0.7)	.16
Anemia	734/2696 (27.2)	464/1690 (27.5)	58/296 (19.6)	1256/4682 (26.8)	.01
Malignancy (current + prior)	199/3074 (6.5)	123/1968 (6.3)	25/361 (6.9)	347/5403 (6.4)	.88
Hyperthyroidism	128/3008 (4.3)	86/1950 (4.4)	13/352 (3.7)	227/5310 (4.3)	.83
Hypothyroidism	283/3012 (9.4)	164/1951 (8.4)	22/352 (6.3)	469/5315 (8.8)	.10
CKD	369/3079 (12.0)	136/1972 (6.9)	15/359 (4.2)	520/5410 (9.6)	< .001
Creatinine, mg/dL	0.98 (0.81-1.19)	0.97 (0.82-1.12)	0.94 (0.80-1.12)	0.98 (0.82–1.16)	.12
CrCl (C-G), mL/min	76.91 [57.28-99.18]	80.66 [62.43-101.33]	87.66 [69.14-114.86]	79.26 [60.01–101.03]	< .001
CHA_2DS_2-VASc	3.00 [2.00-4.00]	2.00 [1.00-3.00]	1.00 [1.00-3.00]	3.00 [2.00–4.00]	< .001
HAS-BLED	2.00 [1.00-2.00]	1.00 [1.00–2.00]	1.00 [1.00–2.00]	1.00 [1.00–2.00]	< .001
EHRA score	2.00 [1.00–2.00]	2.00 [1.00–2.00]	2.00 [1.00–2.00]	2.00 [1.00–2.00]	.03
Multimorbidity	2018/2541 (79.4)	1182/1686 (70.1)	178/309 (57.6)	3378/4536 (74.5)	< .001
No. of comorbidities	3 [2-5]	2 [1-4]	2 [1-3]	3 [1-4]	< .001
Echocardiographic parameters					
LVEF, %	55.00 [45.00-62.00]	57.00 [47.00-63.00]	58.00 [50.00-64.00]	55.00 [46.00–62.00]	.02
Left atrial enlargement	1669/2054 (81.3)	929/1196 (77.7)	133/185 (71.9)	2731/3435 (79.5)	.002
LA diameter indexed, cm/m²	2.28 (2.01-2.58)	2.22 (1.97-2.52)	2.19 (1.92-2.38)	2.25 (1.99–2.56)	< .001
ECG parameters					
Bundle branch block					
No	2501/2921 (85.6)	1644/1857 (88.5)	290/321 (90.3)	4435/5099 (87.0)	
LBBB	231/2921 (7.9)	105/1857 (5.7)	15/321 (4.7)	351/5099 (6.9)	
RBBB	189/2921 (6.5)	108/1857 (5.8)	16/321 (5.0)	313/5099 (6.1)	

AF, atrial fibrillation; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; CMP, cardiomyopathy; COPD, chronic obstructive pulmonary disease; CrCl C-G, creatinine clearance according to Cockroft-Gault formula; DVT, deep vein thrombosis; EHRA, European Heart Rate Association; IQR, interquartile range; LA, left atrium; LBBB, left bundle branch block; LBM, lean body mass; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; PE, pulmonary embolism; RBBB, right bundle branch block; TE, thromboembolic; TIA, transient ischemic attack.

The data are presented as No. (%) or median [interquartile range].

*Regions of enrolment. Northern Europe: Denmark, Estonia, Latvia, Norway, UK; Western Europe: Belgium, France, Germany, Netherlands, Switzerland; Eastern Europe: Bulgaria, Czech Republic, Georgia, Kazakhstan, Kyrgyzstan, Poland, Romania, Russia; Southern Europe: Albania, FYR Macedonia, Italy, Malta, Montenegro, Portugal, Serbia, Spain, Turkey. Left atrial enlargement was defined based on American Society Echocardiography guidelines, with an indexed anteroposterior dimension > 2.3 cm/m² considered abnormal for both men and women.

Table 3 of the supplementary data. Multivariable logistic regression analysis for factors associated with physical inactivity

	Multivariable analysis		
	OR	95%CI	*P*
Age	1.02	1.01-1.02	< .001
Female sex	1.90	1.70-2.12	< .001
BMI	1.04	1.03-1.05	< .001
Permanent AF	1.26	1.12-1.42	< .001
Hypertension	0.90	0.80-1.00	.050
Diabetes mellitus	1.25	1.11-1.43	< .001
Smoking	1.16	0.96-1.39	.107
Obstructive sleep apnea	1.36	1.06-1.75	.015
Heart failure	1.40	1.24-1.58	< .001
Dilated cardiomyopathy	1.31	1.08-1.61	.008
Hypertrophic cardiomyopathy	1.48	1.08-2.03	.014
Pulmonary arterial hypertension	1.16	0.93-1.46	.192
Coronary artery disease	1.07	0.95-1.20	.296
Valvular alterations	1.10	0.98-1.23	.079
Prior thromboembolic events	1.15	0.98-1.35	.103
Prior hemorrhagic events	1.04	0.83-1.29	.754
Peripheral vascular disease	0.91	0.75-1.10	.331
COPD	1.29	1.08-1.58	.006
Dementia	1.55	0.94-2.57	.088
Anemia	1.24	1.11-1.39	< .001
Malignancy	1.13	0.93-1.37	.220
Hyperthyroidism	1.11	0.86-1.42	.429
Chronic kidney disease	1.38	1.18-1.63	< .001

AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; OR, odds ratio.

Table 4 of the supplementary data. Comparison of key clinical characteristics between excluded and included patients (longitudinal phase)

	Excluded patients (n = 1104)	Included patients (n = 8421)	P
Age, y	69.00 [62.00-76.00]	71.00 (62.00-77.00]	.002
Female sex	492/1104 (44.6)	3412/8421 (40.5)	.01
Permanent AF	387/1094 (35.4)	2799/8282 (33.8)	.29
Hypertension	727/1095 (66.4)	5129/8355 (61.4)	.001
Diabetes mellitus	236/1099 (21.5)	1971/8386 (23.5)	.13
Smoking (current)	136/1057 (12.9)	743/8164 (9.1)	< .001
Lipid disorder	439/1059 (41.5)	3355/8086 (41.5)	.98
Heart failure	478/1098 (43.5)	3421/8360 (40.9)	.09
Dilated CMP	123/1087 (11.3)	744/8328 (8.9)	.01
Coronary artery disease	330/983 (33.6)	2281/7942 (28.7)	.002
Prior TE events	109/1095 (10.0)	987/8370 (11.8)	.07
Peripheral artery disease	89/1065 (8.4)	686/8281 (8.3)	.93
COPD	86/1095 (7.9)	769/8364 (9.2)	.14
Malignancy (current + prior)	43/1092 (3.9)	644/8371 (7.7)	< .001
CKD	140/1100 (12.7)	1067/8364 (12.8)	.98
Multimorbidity	692/860 (80.5)	5477/6970 (78.6)	.20

AF, atrial fibrillation; CKD, chronic kidney disease; CMP, cardiomyopathy; COPD, chronic obstructive pulmonary disease; TE, thromboembolic.

Table 5 of the supplementary data. Risk of adverse outcomes across different levels of physical activity

|	Unadjusted analysis			Adjusted analysis Model 1			Adjusted analysis Model 2		
	HR	[95%CI]	*P*	HR	[95%CI]	*P*	HR	[95%CI]	*P*
Primary outcome									
Composite outcome[a]									
Physical inactivity (ref)	-	-	-	-	-	-	-	-	-
Occasional physical activity	**0.63**	**0.55-0.71**	**< .001**	**0.75**	**0.65-0.86**	**< .001**	**0.82**	**0.71-0.96**	**.01**
Regular physical activity	**0.42**	**0.35-0.50**	**< .001**	**0.57**	**0.47-0.68**	**< .001**	**0.65**	**0.53-0.80**	**< .001**
Intense physical activity	**0.31**	**0.20-0.47**	**< .001**	**0.52**	**0.33-0.82**	**.006**	**0.59**	**0.36-0.95**	**.03**
Secondary outcomes									
MACE[b]									
Physical inactivity (ref)	-	-	**-**	-	-	-	-	-	-
Occasional physical activity	0.62	0.52-0.74	< .001	0.76	0.64-0.91	.004	0.81	0.66-1.00	.05
Regular physical activity	0.50	0.41-0.63	< .001	0.71	0.56-0.89	.004	0.83	0.64-1.01	.16
Intense physical activity	0.26	0.14-0.48	< .001	0.44	0.22-0.85	.01	0.53	0.27-1.00	.06
All-cause mortality									
Physical inactivity (ref)	-	-	**-**	-	-	-	-	-	-
Occasional physical activity	0.58	0.49-0.67	< .001	0.69	0.59-0.81	< .001	0.80	0.67-0.96	.01
Regular physical activity	0.31	0.25-0.39	< .001	0.43	0.33-0.54	< .001	0.52	0.39-0.67	< .001
Intense physical activity	0.22	0.12-0.39	< .001	0.42	0.23-0.77	.005	0.48	0.25-0.91	.02

ACS, acute coronary syndrome; AF, atrial fibrillation; aHR, adjusted hazard ratio; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; MACE, major adverse cardiovascular events; OAC, oral anticoagulants; TE, thromboembolic events.

[a]Composite outcome: composite MACE and all-cause mortality.

[b]MACE = composite of any TE/ACS/CV death. Model 1 was adjusted for CHA_2DS_2-VASc score, BMI, use of OAC, chronic kidney disease, type of AF and COPD. Model 2 was adjusted for age, sex, BMI, smoking, lipid disorder, the individual components of the CHA2DS2-VASc score (heart failure,

hypertension, diabetes, prior stroke, vascular disease), valvular heart disease, dementia, chronic kidney disease, COPD, malignancy, obstructive sleep apnea, type of AF, EHRA score, use of OAC, region of enrolment and site of inclusion (hospital/outpatient).

Figure 1 of the supplementary data. Kaplan–Meier curves for MACE (Any TE/ACS/CV death). A. Cumulative curves according to physical activity vs physical inactivity. B. Cumulative curves according to increasing levels of physical activity
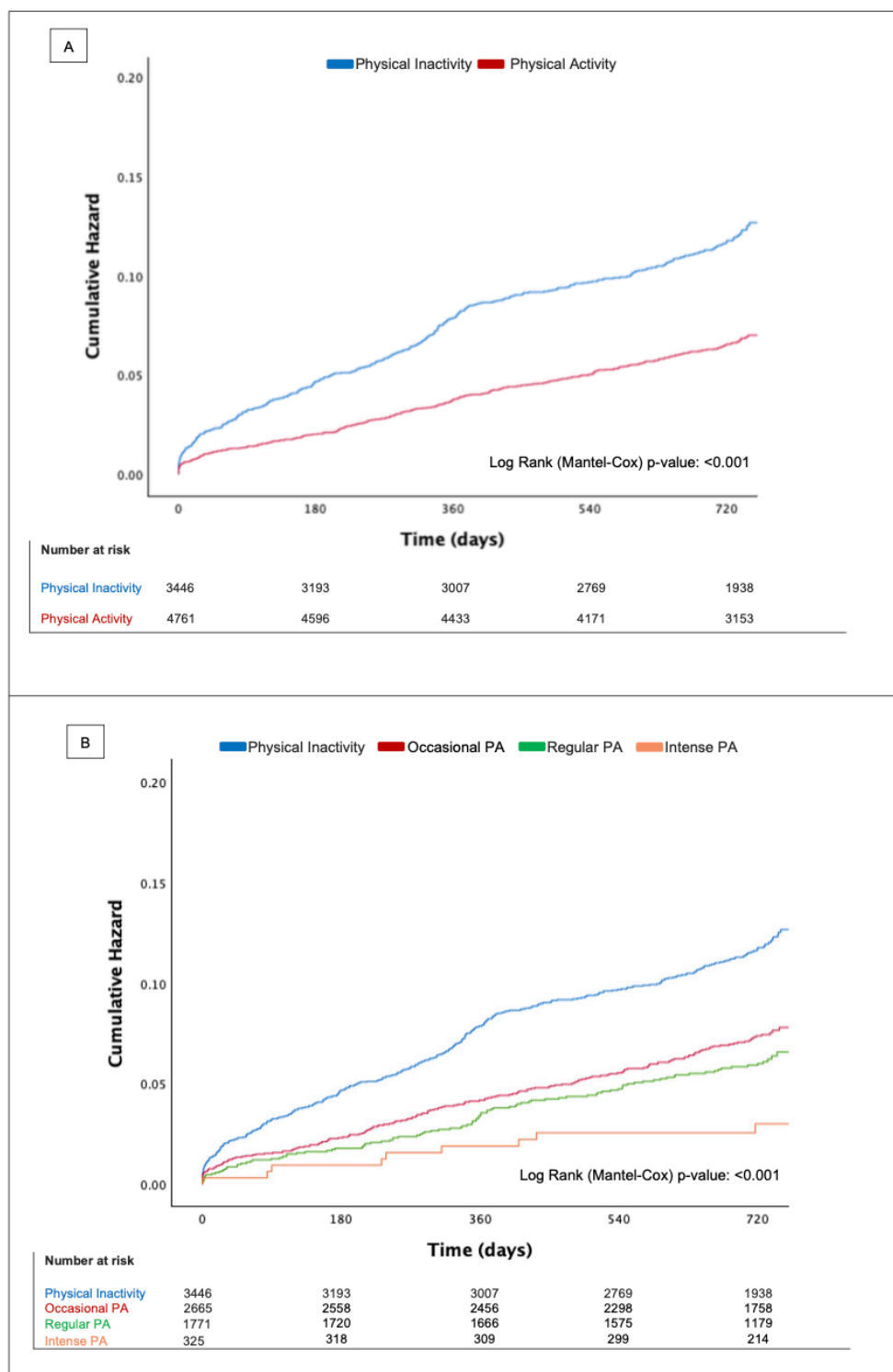
Figure 2 of the supplementary data. Kaplan–Meier curves for All-Cause Mortality. A. Cumulative curves according to physical activity vs physical inactivity. B. Cumulative curves according to increasing levels of physical activity.
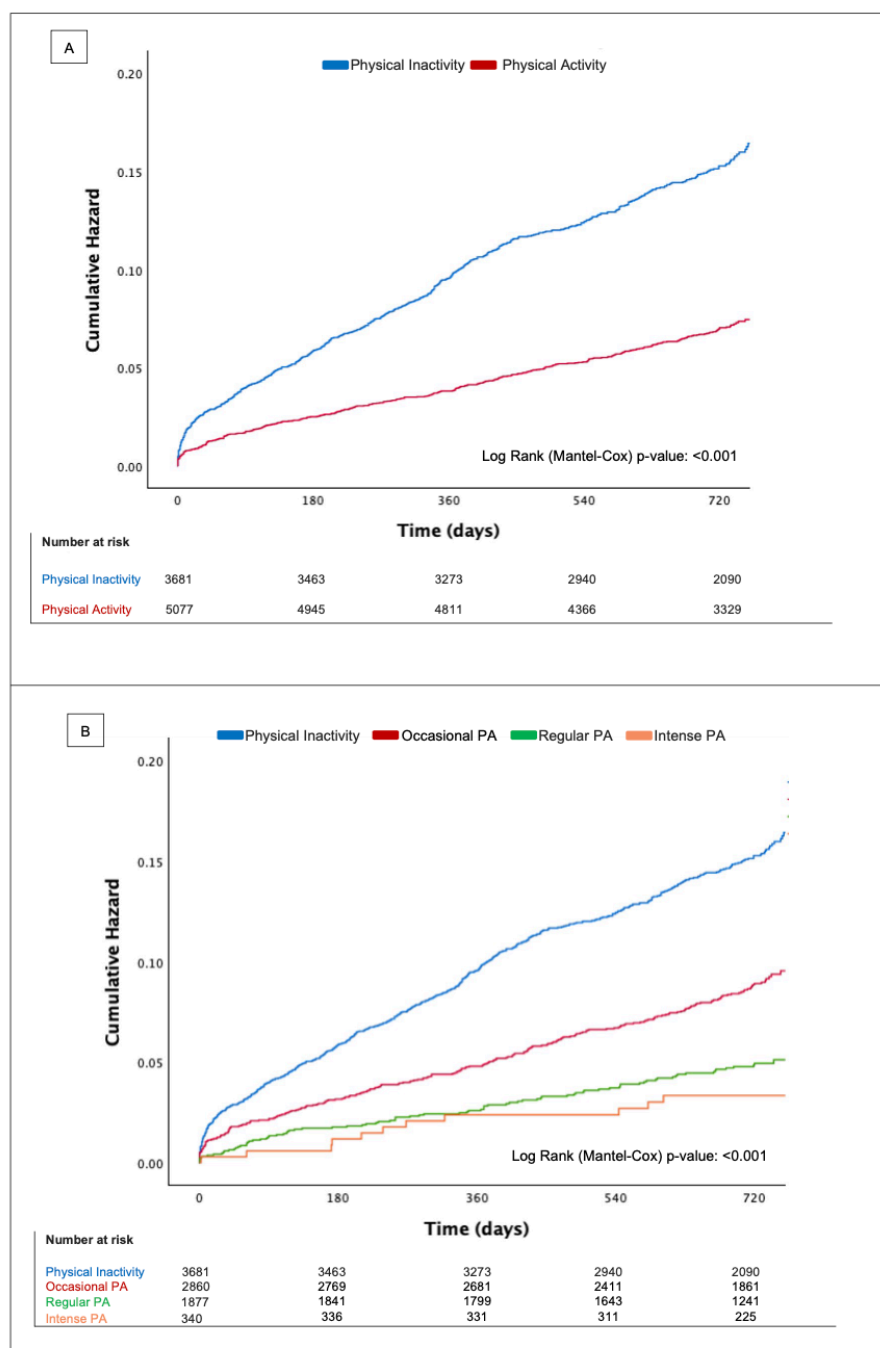
Figure 3 of the supplementary data. Sensitivity analysis. Kaplan–Meier curves and Cox regression analysis for study outcomes according to physical activity levels (excluding inactive AF patients)