Lifetime risk of atrial fibrillation according to levels of risk factors

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Suppl. Methods. Statistical methods for lifetime risk prediction model and multiple imputation.

Statistical methods for the atrial fibrillation lifetime risk prediction model

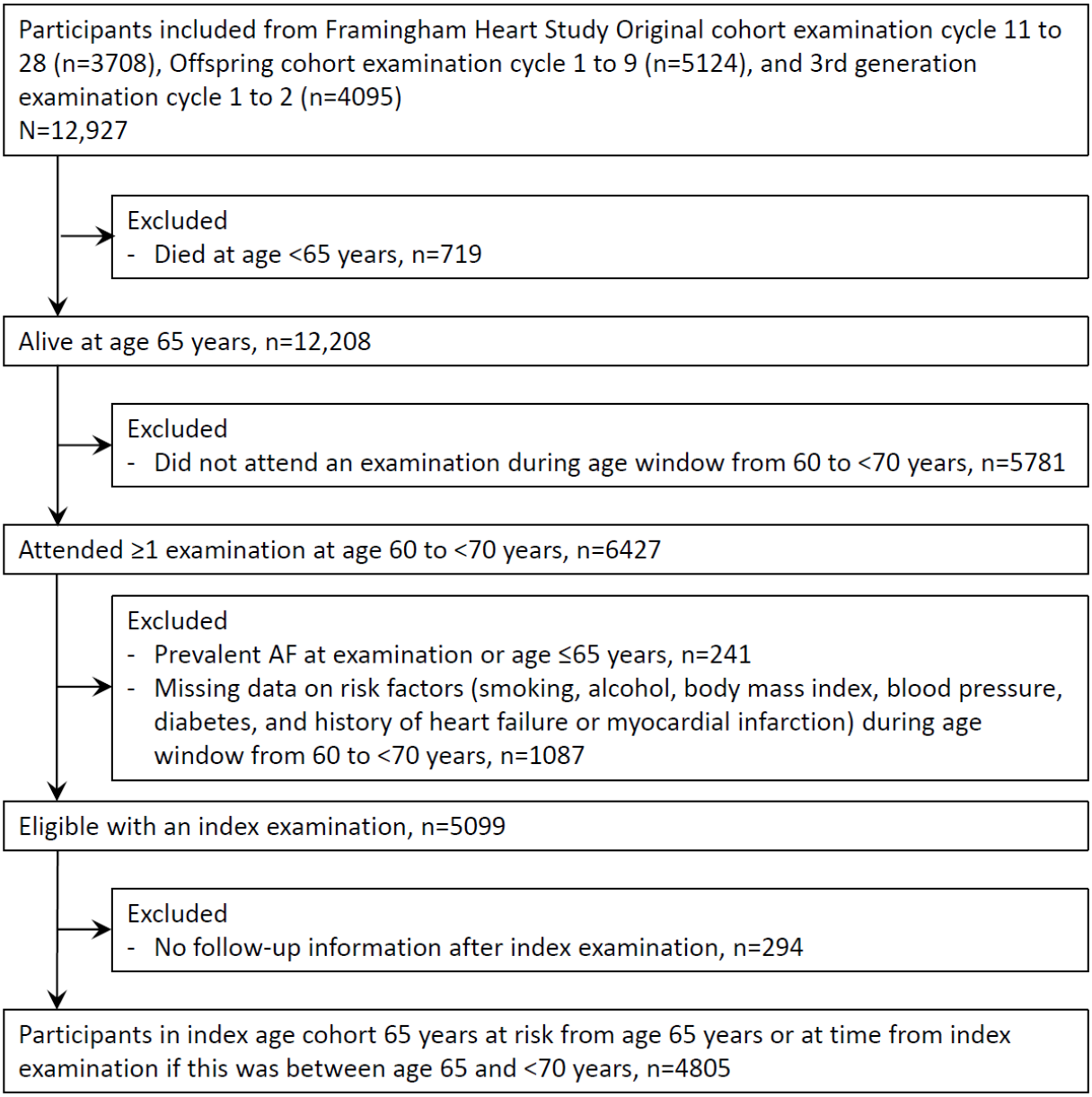
We developed a prediction model for the lifetime risk of atrial fibrillation (AF) at the index age 55 years. We used a multivariable Fine-Gray model accounting for the competing risk of death.[1] We included 9 covariates: Body mass index (BMI), systolic blood pressure, and diastolic blood pressure as continuous variables, and sex, smoking (never, past, or current), alcohol intake (optimal or elevated), diabetes (optimal, borderline, or elevated), treatment for hypertension, and history of myocardial infarction or heart failure as categorical variables. We did not perform any variable selection. We checked the assumptions of the Fine and Gray model.[2] We used goodness-of-fit test procedures based on the cumulative sums of residuals to assess the linear functional forms for BMI, systolic blood pressure, and diastolic blood pressure. All were satisfied. We also tested the proportionality of subdistribution hazards for the Fine and Gray model.[2,3] We found that the proportional hazards assumption was violated for BMI, sex, smoking, and history of myocardial infarction or heart failure. As a consequence, we added time-varying covariates $Z \times \log(t)$ to the model, i.e. an interaction term between each of these 4 covariates and the natural logarithmic transformation of time.

We used the cumulative subdistribution baseline hazard and the estimated regression coefficients of the Fine and Gray mode to derive the predicted cumulative incidence of AF at age 95 years for 16 risk profiles, in men and women separately.[4] We defined the profiles according to treatment for hypertension (yes or no), BMI (25 kg/m^2 or 35 kg/m^2), alcohol (elevated or optimal), and history of myocardial infarction or heart failure (yes or no). For each profile, we considered a participant with an average blood pressure level (mean systolic blood pressure 128 mm Hg and 124 mm Hg and mean diastolic blood pressure 80 mm Hg and 76 mm Hg for men and women respectively), who never smoked, and had no diabetes. Finally, we assessed the calibration and discrimination of the model. We plotted the AF lifetime risk estimate, computed within deciles of the predicted lifetime risk, against the average of the predicted AF lifetime risk within the same deciles.[5] We assessed discrimination by the c-index adapted for competing risk data.[6] These analyses were conducted in *R 3.3.2 cmprsk, crskdiag,* and *pec* packages.

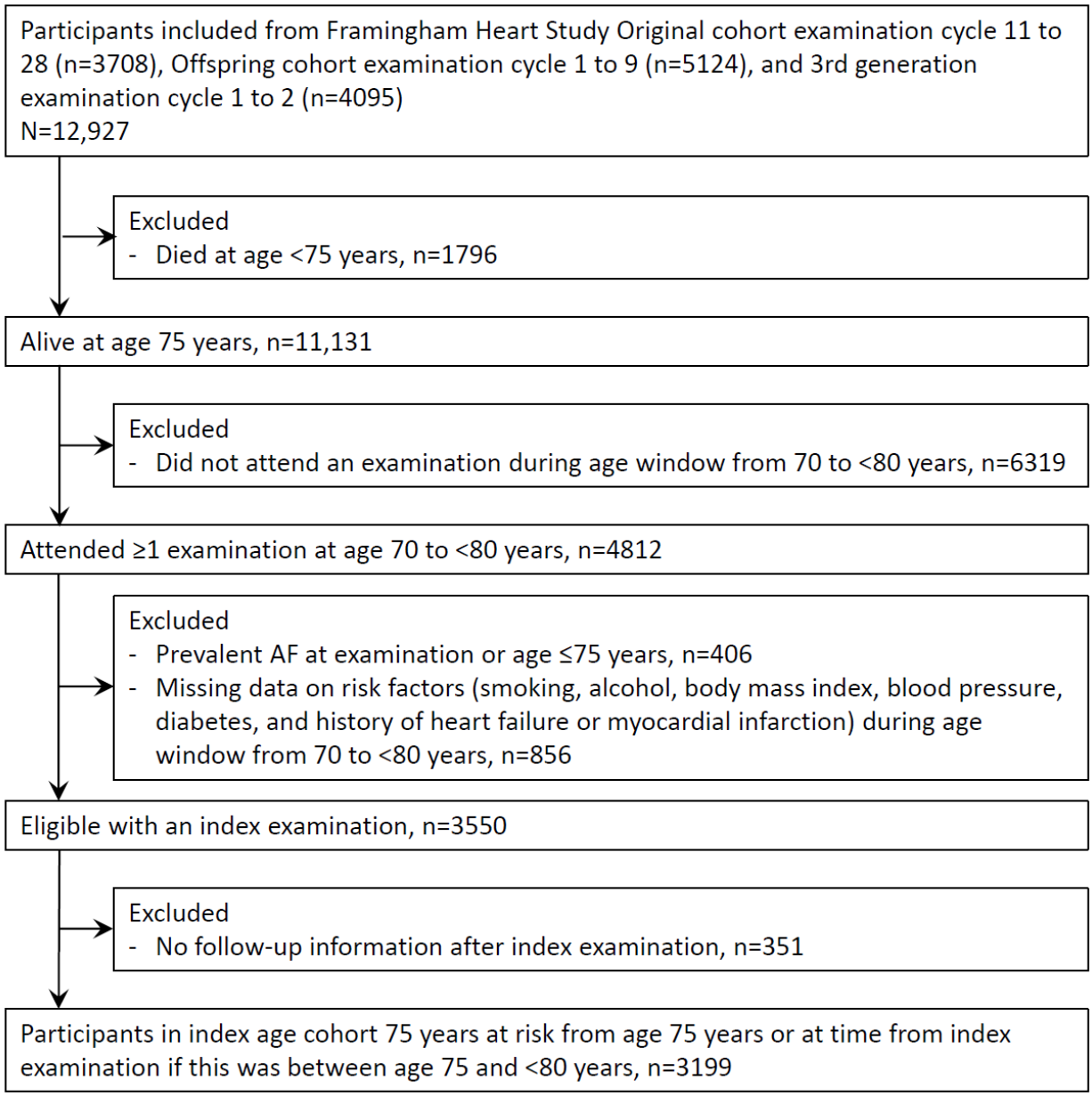
Multiple imputation analysis

We included 6778 participants (1201 AF cases), as compared to 5338 participants (489 AF cases) in the complete case analysis. Data were missing for the following 7 risk factors: diabetes (categorical; proportion of missing values 20.4%), BMI (continuous; 5.5%), smoking (categorical; 5.3%), treatment for hypertension (binary; 5.2%), systolic blood pressure (continuous; 0.1%), diastolic blood pressure (continuous; 0.1%), and alcohol (binary; 1.1%). We generated 25 imputed datasets by multiple imputation predictive mean matching method.[7] We included the following covariates in the predictive mean matching model: sex, age, BMI, diabetes, smoking, alcohol, systolic blood pressure, diastolic blood pressure, treatment for hypertension, history of myocardial infarction or heart failure. In addition, we used a generalization of the method proposed by White and Royston:[8] we included the outcome status variable (AF, death, censored), as well as the estimated subdistribution cumulative baseline hazards for AF and death, in the predictive mean matching model. In each imputed dataset, we categorized individuals into optimal, borderline, and elevated aggregated risk categories. The mean percentage, across the 25 imputed datasets, of individuals categorized into optimal, borderline, and elevated groups were 4.1%, 24.7%, and 71.2%, respectively. In each of the 25 imputed datasets, we estimated the lifetime risk at index age 55 years, and the associated standard error, for the optimal, borderline, and elevated risk categories, respectively. For each risk category, we combined the 25 estimates according to Rubin's rules.[9] Finally, we compared the multiple imputation analysis results with the complete case analysis results. The multiple imputation analysis was conducted by *R 3.3.2 cmprsk*, *survival*, *mice*, and *Amelia* packages.

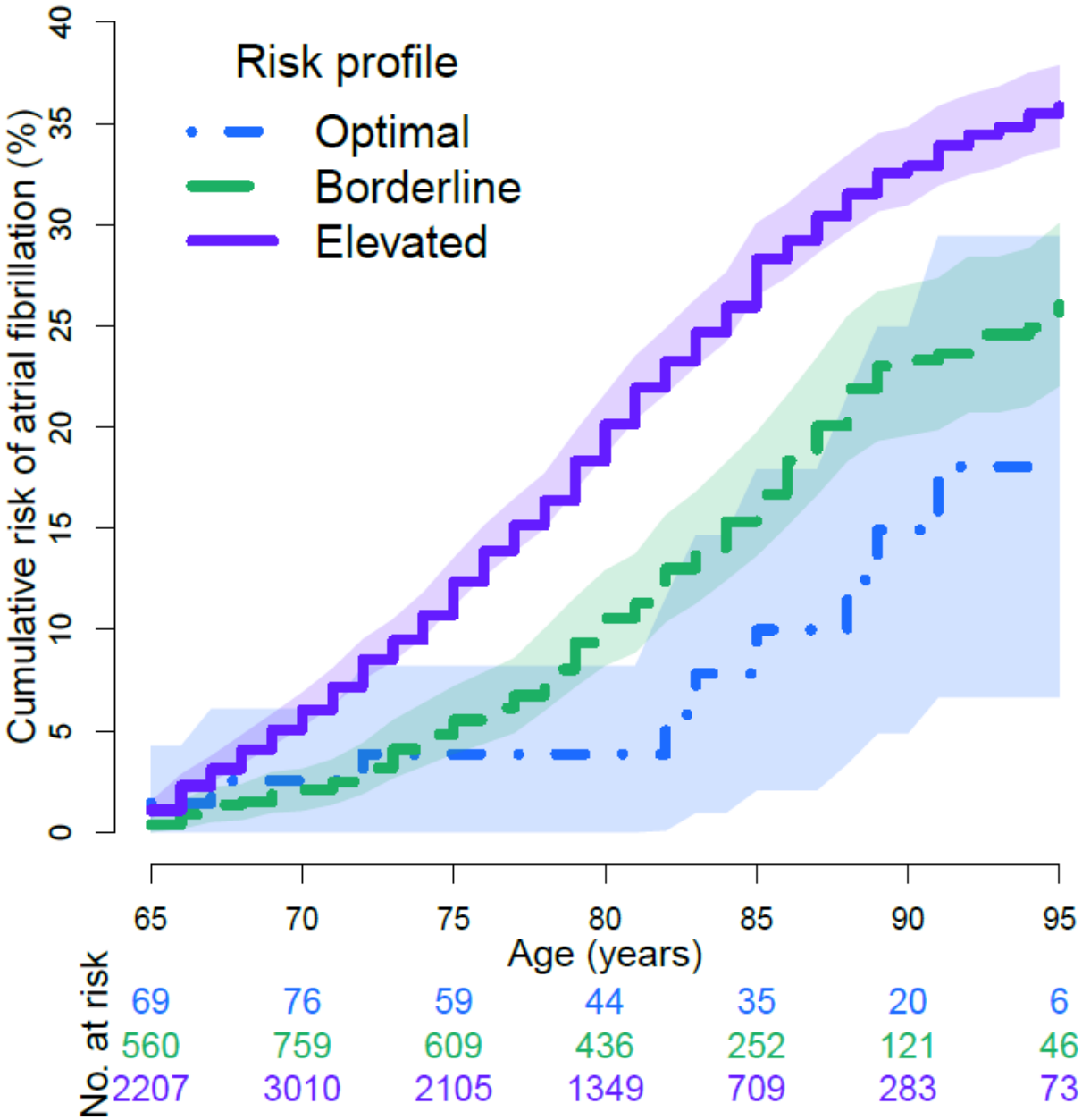
Suppl. Figure 1. Selection of the study sample with index age 65 years.



Suppl. Figure 2. Selection of the study sample with index age 75 years.

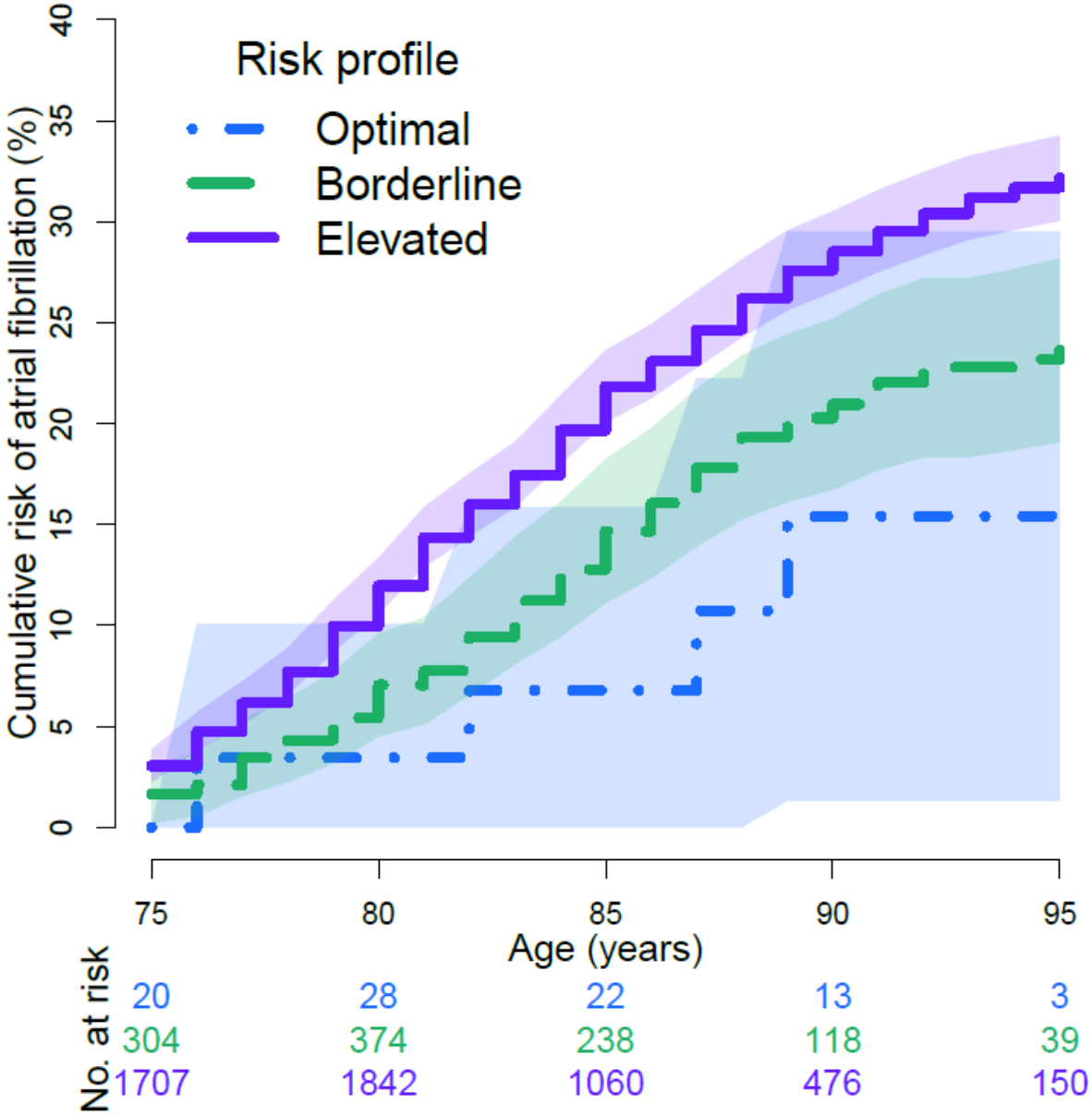


Suppl. Figure 3. Cumulative risk for atrial fibrillation according to risk factor burden (optimal, borderline, or elevated) at index age 65 years.



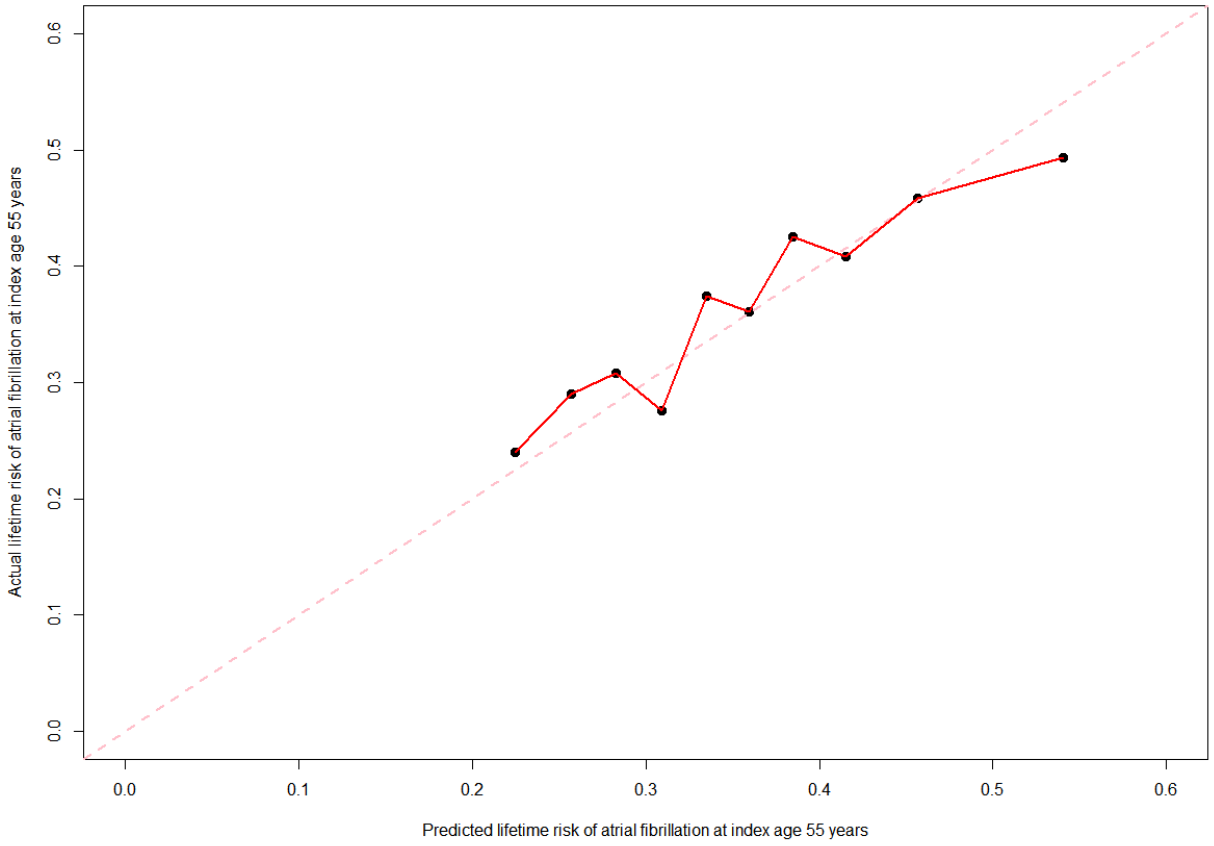
Shadings are 95% confidence boundaries. Participants entered the study sample between age 65 and 70 years; therefore, the number at risk increased from age 65 years to age 70 years.

Suppl. Figure 4. Cumulative risk for atrial fibrillation according to risk factor burden (optimal, borderline, or elevated) at index age 75 years.



Shadings are 95% confidence boundaries. Participants entered the study sample between age 75 and 80 years; therefore, the number at risk increased from age 75 years to age 80 years.

Suppl. Figure 5. Calibration plot of the prediction model for predicting lifetime risk at index age 55 years.



X-axis is the mean lifetime risk by Fine and Gray model adjusting competing risk of death, y-axis is the actual lifetime risk calculated by *cuminc* function in R *cmprsk* package in each decile of predicted lifetime risk.

Calibration was good, although the lifetime risk is slightly underestimated for moderate lifetime risk groups and overestimated for participants in the highest lifetime risk group. In addition, the C index for lifetime risk at index age 55 years adjusting competing risk of death is 59.4%, indicating relatively poor discrimination; but discrimination was hampered by the fact that the risk factors are also associated with the competing risk of death.

Suppl. Table 1. Characteristics of participants according to smoking divided into optimal, borderline, and elevated.

Index age 55 years			
	Optimal	**Borderline**	**Elevated**
Number of participants	1935	2275	1128
Male	822 (42.5)	1170 (51.4)	539 (47.8)
Age, mean (SD)	55 (2.1)	55 (1.9)	55 (1.9)
Calendar year for Framingham Heart Study exam, median (Q1, Q3)	1998 (1986, 2008)	1996 (1986, 2004)	1988 (1981, 1998)
Follow up, median (Q1, Q3)	13 (5, 23)	14 (8, 21)	16 (9, 24)
Alcohol in elevated	245 (12.7)	470 (20.7)	340 (30.1)
Body mass index (kg/m^2)	27.8 (5.4)	28.0 (5.3)	26.6 (4.8)
Systolic blood pressure (mm Hg)	125 (17)	126 (17)	128 (19)
Diastolic blood pressure (mm Hg)	78 (10)	78 (10)	78 (10)
Diabetes	123 (6.4)	156 (6.9)	67 (6.0)
History of heart failure or myocardial infarction	65 (3.4)	122 (5.4)	82 (7.3)
Index age 65 years			
	Optimal	**Borderline**	**Elevated**
Number of participants	1570	2414	821
Male	537 (34.2)	1252 (51.9)	337 (41.1)
Age, mean (SD)	65 (1.6)	65 (1.7)	65 (1.6)
Calendar year for Framingham Heart Study exam, median (Q1, Q3)	1994 (1982, 2006)	1996 (1983, 2006)	1984 (1979, 1995)
Follow up, median (Q1, Q3)	13 (6, 19)	11 (5, 17)	12 (6, 18)
Alcohol in elevated	177 (11.3)	528 (21.9)	243 (29.6)
Body mass index (kg/m^2)	27.9 (5.0)	28.0 (5.0)	26.1 (4.7)
Systolic blood pressure (mm Hg)	133 (18)	133 (18)	135 (20)
Diastolic blood pressure (mm Hg)	76 (10)	77 (10)	76 (10)

Diabetes	155 (9.9)	289 (12.0)	75 (9.1)
History of heart failure or myocardial infarction	141 (9.0)	319 (13.2)	109 (13.3)
Index age 75 years			
	Optimal	**Borderline**	**Elevated**
Number of participants	1233	1667	299
Male	329 (26.7)	856 (51.4)	106 (35.5)
Age, mean (SD)	75 (1.6)	75 (1.6)	74 (1.8)
Calendar year for Framingham Heart Study exam, median (Q1, Q3)	1991 (1982, 2000)	1993 (1986, 2005)	1987 (1981, 1994)
Alcohol in elevated	92 (7.5)	281 (16.9)	59 (19.7)
Follow up, median (Q1, Q3)	9 (5, 14)	7 (3, 12)	7 (3, 11)
Body mass index (kg/m^2)	27.2 (4.8)	27.3 (4.6)	25.0 (4.4)
Systolic blood pressure (mm Hg)	142 (20)	139 (20)	140 (22)
Diastolic blood pressure (mm Hg)	74 (10)	73 (10)	73 (11)
Diabetes	144 (11.7)	200 (12.0)	22 (7.4)
History of heart failure or myocardial infarction	206 (16.7)	325 (19.5)	45 (15.1)

Suppl. Table 2. Lifetime risk of atrial fibrillation by single risk factor and sex, adjusted for the competing risk of death at index age 55 years.

Risk factor	All			Men			Women		
	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*
Smoking									
Optimal	249/1935	38.1 (33.2-43.1)	0.23	116/822	43.0 (34.4-51.5)	0.28	133/1113	35.7 (29.6-41.8)	0.71
Borderline	343/2275	39.3 (34.9-43.6)		245/1170	43.3 (38.3-48.4)		98/1105	33.3 (25.3-41.4)	
Elevated	224/1128	32.1 (28.2-36.1)		128/539	36.4 (31.0-41.9)		96/589	28.3 (22.8-33.8)	
Alcohol									
Optimal	600/4283	35.1 (32.2-38.0)	0.0002	345/1957	40.1 (35.9-44.3)	0.006	255/2326	30.8 (26.8-34.8)	0.11
Elevated	216/1055	40.9 (36.1-45.7)		144/574	43.7 (37.8-49.5)		72/481	37.0 (29.2-44.9)	
Body mass index									
Optimal	236/1785	31.6 (27.5-35.7)	<0.0001	91/526	34.0 (27.4-40.5)	<0.0001	145/1259	30.4 (25.3-35.4)	0.002
Borderline	343/2136	38.2 (34.0-42.4)		247/1266	41.9 (37.0-46.9)		96/870	32.1 (24.8-39.5)	
Elevated	237/1417	44.2 (38.5-50.0)		151/739	48.1 (40.7-55.5)		86/678	39.4 (30.9-47.9)	
Blood pressure									
Optimal	152/1539	29.0 (24.2-33.9)	<0.0001	75/524	38.3 (30.3-46.3)	0.0008	77/1015	23.4 (17.6-29.2)	0.002
Borderline	272/1792	36.5 (32.0-41.0)		167/927	41.0 (35.1-46.9)		105/865	31.5 (25.0-38.0)	
Elevated	392/2007	41.1 (37.2-44.9)		247/1080	42.9 (37.9-47.8)		145/927	38.8 (32.9-44.8)	

Lifetime risk of atrial fibrillation according to levels of risk factors

Diabetes									
Optimal	624/3805	36.5 (33.7-39.4)	0.02	351/1599	41.2 (37.2-45.1)	0.51	273/2206	32.5 (28.5-36.4)	0.23
Borderline	128/1187	38.0 (24.6-51.5)		94/713	52.2 (36.2-68.1)		34/474	24.4 (13.8-35.1)	
Elevated	64/346	34.8 (27.3-42.4)		44/219	37.5 (27.7-47.3)		20/127	31.2 (19.2-43.3)	
History of heart failure or myocardial infarction									
Optimal	747/5069	37.0 (34.3-39.8)	<0.0001	438/2344	41.9 (38.1-45.6)	0.01	309/2725	32.6 (28.7-36.5)	0.05
Elevated	69/269	37.3 (29.1-45.4)		51/187	36.7 (27.6-45.8)		18/82	36.5 (21.1-51.8)	

The p values for interaction between sex and each risk factor were all <0.0001.

*overall test comparing sub-distribution hazards across risk categories by Fine and Gray method.

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 3. Lifetime risk of atrial fibrillation by single risk factor and sex, adjusted for the competing risk of death at index age 65 years.

Risk factor	All			Men			Women		
	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*
Smoking									
Optimal	316/1570	33.7 (30.4-36.9)	0.009	115/537	38.6 (32.5-44.7)	0.06	201/1033	31.6 (27.8-35.4)	0.62
Borderline	525/2414	36.3 (33.6-39.1)		339/1252	41.1 (37.4-44.8)		186/1162	30.5 (26.5-34.5)	
Elevated	182/821	27.5 (24.0-31.0)		81/337	28.6 (23.1-34.0)		101/484	26.8 (22.2-31.4)	
Alcohol									
Optimal	799/3857	33.2 (31.2-35.3)	0.05	405/1669	37.7 (34.6-40.9)	0.15	394/2188	29.9 (27.3-32.6)	0.39
Elevated	224/948	35.6 (31.6-39.5)		130/457	39.7 (34.1-45.4)		94/491	31.5 (26.0-37.0)	
Body mass index									
Optimal	314/1537	29.9 (27.0-32.8)	<0.0001	117/476	33.4 (28.1-38.7)	0.01	197/1061	28.3 (24.8-31.8)	0.002
Borderline	422/2008	33.3 (30.5-36.1)		265/1056	37.9 (34.0-41.8)		157/952	28.1 (24.2-32.0)	
Elevated	287/1260	40.7 (36.7-44.8)		153/594	44.9 (38.9-50.8)		134/666	37.5 (32.0-43.0)	
Blood pressure									
Optimal	118/778	27.5 (22.9-32.1)	<0.0001	61/283	34.5 (26.7-42.2)	0.04	57/495	23.2 (17.5-28.9)	<0.0001
Borderline	254/1303	30.2 (26.9-33.5)		140/579	36.3 (31.2-41.5)		114/724	25.3 (21.1-29.5)	
Elevated	651/2724	37.1 (34.6-39.5)		334/1264	40.1 (36.4-43.7)		317/1460	34.7 (31.4-37.9)	

Lifetime risk of atrial fibrillation according to levels of risk factors

Diabetes									
Optimal	726/3137	32.8 (30.8-34.8)	0.0007	345/1221	37.2 (33.9-40.4)	0.08	381/1916	29.8 (27.2-32.4)	0.04
Borderline	171/1149	32.9 (27.0-38.7)		109/602	33.9 (27.8-40)		62/547	32.2 (21.8-42.6)	
Elevated	126/519	36.5 (30.7-42.2)		81/303	40.4 (32.5-48.4)		45/216	31.0 (23.1-39.0)	
History of heart failure or myocardial infarction									
Optimal	864/4236	33.4 (31.4-35.3)	0.0002	433/1777	38.3 (35.2-41.4)	0.07	431/2459	29.9 (27.4-32.4)	0.01
Elevated	159/569	35.9 (31.2-40.7)		102/349	38.3 (32.0-44.6)		57/220	33.3 (25.7-40.8)	

The p values for interaction between sex and each risk factor were all <0.0001.

*overall test comparing sub-distribution hazards across risk categories by Fine and Gray method.

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 4. Lifetime risk of atrial fibrillation by single risk factor and sex, adjusted for the competing risk of death at index age 75 years.

Risk factor	All			Men			Women		
	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*	AF cases/total	Lifetime risk (95%CI)	p value*
Smoking									
Optimal	294/1233	30.2 (27.1-33.2)	0.21	88/329	36.1 (29.6-42.6)	0.25	206/904	28.2 (24.8-31.6)	0.97
Borderline	410/1667	32.2 (29.4-35.0)		244/856	36.3 (32.3-40.3)		166/811	27.7 (24-31.5)	
Elevated	72/299	26.0 (20.6-31.3)		26/106	25.3 (16.7-33.9)		46/193	26.4 (19.5-33.2)	
Alcohol									
Optimal	671/2767	30.8 (28.7-32.8)	0.95	303/1100	35.2 (31.7-38.6)	0.81	368/1667	28.0 (25.4-30.5)	0.59
Elevated	105/432	30.7 (25.4-36.0)		55/191	35.9 (27.5-44.3)		50/241	26.7 (20.0-33.4)	
Body mass index									
Optimal	255/1126	27.2 (24.2-30.2)	<0.0001	106/364	33.9 (28.3-39.6)	0.02	149/762	23.8 (20.3-27.3)	0.002
Borderline	319/1364	30.1 (27.2-33.0)		164/652	32.1 (27.7-36.5)		155/712	28.2 (24.3-32.1)	
Elevated	202/709	38.7 (34.2-43.2)		88/275	45.5 (37.8-53.1)		114/434	34.9 (29.4-40.5)	
Blood pressure									
Optimal	45/272	22.4 (16.4-28.5)	<0.0001	26/117	30.5 (19.8-41.3)	0.03	19/155	16.6 (9.6-23.5)	0.0005
Borderline	140/675	25.9 (22.1-29.8)		66/271	29.7 (23.3-36.1)		74/404	23.4 (18.6-28.3)	
Elevated	591/2252	33.1 (30.8-35.4)		266/903	37.7 (33.8-41.6)		325/1349	30.3 (27.4-33.2)	

Lifetime risk of atrial fibrillation according to levels of risk factors

Diabetes									
Optimal	580/2249	30.1 (28.0-32.3)	0.59	251/810	35.3 (31.5-39.1)	0.76	329/1439	27.2 (24.6-29.8)	0.37
Borderline	110/584	31.7 (25.7-37.7)		63/294	34.1 (26.0-42.1)		47/290	28.6 (20.3-36.8)	
Elevated	86/366	32.3 (26.1-38.5)		44/187	33.8 (25.0-42.6)		42/179	31.6 (22.8-40.4)	
History of heart failure or myocardial infarction									
Optimal	607/2623	29.8 (27.7-31.9)	0.002	261/988	34.2 (30.6-37.8)	0.05	346/1635	27.2 (24.6-29.7)	0.08
Elevated	169/576	35.1 (30.4-39.8)		97/303	38.5 (31.8-45.1)		72/273	31.7 (25.1-38.3)	

p values for interaction between sex and risk profile <0.0001.

*overall test comparing sub-distribution hazards across risk categories by Fine and Gray method

Suppl. Table 5. Distribution of risk factor categories.

Risk factor profile	**Number of elevated risk factors**	**Number of borderline risk factors**	**Index age 55 years** n=5338	**Index age 65 years** n=4805	**Index age 75 years** n=3199
Optimal	0	0	247 (4.6)	100 (2.1)	33 (1.0)
Borderline	0	1	520 (9.7)	279 (5.8)	138 (4.3)
	0	2	549 (10.3)	377 (7.9)	214 (6.7)
	0	≥3	346 (6.7)	265 (5.5)	140 (4.4)
Elevated	1	Any	1863 (34.9)	1671 (34.8)	1253 (39.2)
	2	Any	1220 (22.9)	1355 (28.2)	972 (30.4)
	≥3	Any	593 (11.1)	758 (15.8)	449 (14.0)

Suppl. Table 6. Lifetime risk of atrial fibrillation by risk factor profile, adjusted for the competing risk of death in men.

			Index age 55 years		Index age 65 years		Index age 75 years	
Risk factor profile	**Number of elevated risk factors**	**Number of borderline risk factors**	**AF cases/total**	**Lifetime risk (95%CI)**	**AF cases/total**	**Lifetime risk (95%CI)**	**AF cases/total**	**Lifetime risk (95%CI)**
Optimal	0	0	7/55	29.8 (9.7-49.9)	4/21	28.8 (3.0-54.6)	1/5	25.0 (0.0-67.4)
Borderline	0	1	21/136	42.0 (24.3-59.7)	8/61	20.1 (7.3-32.9)	6/39	20.9 (5.9-35.9)
	0	2	46/255	46.0 (33.6-58.5)	40/154	44.1 (33.2-55.0)	19/77	29.4 (17.8-41.0)
	0	≥3	27/226	28.3 (17.8-38.9)	19/144	22.0 (12.8-31.3)	17/75	29.6 (16.5-42.8)
Elevated	1	Any	150/856	43.7 (37.2-50.3)	200/715	42.3 (37.5-47.1)	131/476	34.4 (29.2-39.5)
	2	Any	139/626	41.1 (34.9-47.4)	148/618	36.5 (31.3-41.7)	125/417	37.9 (32.2-43.6)
	≥3	Any	99/377	42.7 (35.4-49.9)	116/413	39.4 (33.5-45.4)	59/202	38.6 (30.3-47.0)

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 7. Lifetime risk of atrial fibrillation by risk factor profile, adjusted for the competing risk of death in women.

			Index age 55 years		Index age 65 years		Index age 75 years	
Risk factor profile	**Number of elevated risk factors**	**Number of borderline risk factors**	**AF cases/total**	**Lifetime risk (95%CI)**	**AF cases/total**	**Lifetime risk (95%CI)**	**AF cases/total**	**Lifetime risk (95%CI)**
Optimal	0	0	11/192	20.5 (7.3-33.7)	5/79	14.9 (2.2-27.6)	3/28	13.8 (0.0-28.3)
Borderline	0	1	37/384	28.8 (19.3-38.3)	36/218	26.1 (18.4-33.9)	12/99	16.9 (7.9-26.0)
	0	2	22/294	31.7 (14.4-48.9)	25/223	21.3 (13.4-29.1)	21/137	20.2 (12.3-28.1)
	0	≥3	10/120	25.3 (8.8-41.8)	8/121	15.0 (4.6-25.4)	12/65	27.9 (14.0-41.8)
Elevated	1	Any	116/1007	33.1 (26.6-39.6)	173/956	30.6 (26.6-34.6)	165/777	26.2 (22.6-29.7)
	2	Any	86/594	36.2 (29.0-43.4)	165/737	35.6 (31.0-40.2)	143/555	32.7 (28.0-37.3)
	≥3	Any	45/216	34.7 (26.0-43.3)	76/345	31.6 (25.5-37.7)	62/247	31.8 (24.7-39.0)

Suppl. Table 8. Multivariable prediction model of the lifetime risk of atrial fibrillation at age index 55 years.

	Coef.	SE(Coef.)	Covariance	p-value
Women vs. men	-1.30439	0.31235	-0.03434	0.0000
Women vs. men x log(t)	0.31037	0.11317		0.0061
Systolic blood pressure (mm Hg)	0.00963	0.00288		0.0008
Diastolic blood pressure (mm Hg)	-0.00739	0.00520		0.1600
Treatment of hypertension	0.21862	0.08298		0.0084
Body mass index (kg/m2)	0.07474	0.01878	-0.00012	0.0001
Body mass index x log(t)	-0.01629	0.00708		0.0210
Past smoker vs. never smoker	0.36787	0.29734	-0.03097	0.2200
Past smoker vs. never smoker x log(t)	-0.12982	0.10857		0.2300
Current smoker vs. never smoker	0.91243	0.31326	-0.03393	0.0036
Current smoker vs. never smoker x log(t)	-0.33899	0.11352		0.0028
Borderline diabetes vs. optimal diabetes	-0.12940	0.09926		0.1900
Elevated diabetes vs. optimal diabetes	-0.03556	0.13884		0.8000
History of MI or HF	1.77197	0.26611	-0.02520	0.0000
History of MI or HF x log(t)	-0.62349	0.11017		0.0000
Elevated alcohol vs. optimal alcohol	0.25184	0.08103		0.0019

We entered the 9 covariates in the model and we did not perform any variable selection.

Coef.: coefficient; SE(Coef): standard error of the coefficient. log(t): natural logarithm of time (years since index age 55 years).

The subdistribution hazard ratio is exp(Coef) and the associated 95% confidence interval is from exp[Coef-1.96*SE(Coef)] to exp[Coef+1.96*SE(Coef)].

For sex, BMI, smoking, and history of myocardial infarction or heart failure, one needs to account for the interaction between the covariate Z and log(t). Let us note Coef1 is the coefficient for Z and Coef2 is the coefficient for the interaction between Z and log(t). The subdistribution hazard ratio is $\exp(\text{Coef1})t^{\text{Coef2}}$. The 95% confidence interval is from exp[Coef1+Coef2 x log(t)-1.96*SE{Coef1+Coef2 x log(t)}] to exp[Coef1+Coef2 x log(t)+1.96*SE(Coef1+Coef2 x log(t))]. The standard error is $SE\{Coef1+Coef2 \times \log(t)\}=\text{sqrt}[\ SE(Coef1)^2 + \log(t)^2\ SE(Coef2)^2 + 2\log(t)\ \text{Covariance}(Coef1,Coef2)\ ]$

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 9. Lifetime risk AF by single risk factor, unadjusted for the competing risk of death.

Risk factor	Risk factor	Index age 55 years		Index age 65 years		Index age 75 years	
		AF cases/total	Lifetime risk (95%CI)	AF cases/total	Lifetime risk (95%CI)	AF cases/total	Lifetime risk (95%CI)
Smoking	Optimal	249/1935	56.4 (45.3-67.6)	316/1570	47.4 (42.1-52.6)	294/1233	42.3 (37.8-46.7)
	Borderline	343/2275	54.3 (46.6-61.9)	525/2414	53.2 (48.4-57.9)	410/1667	49.5 (45.0-54.0)
	Elevated	224/1128	59.5 (48.6-70.3)	182/821	61.4 (52.0-70.7)	72/299	54.4 (42.1-66.7)
Alcohol	Optimal	600/4283	50.9 (45.3-56.4)	799/3857	50.2 (46.6-53.7)	671/2767	46.2 (43.0-49.4)
	Elevated	216/1055	74.3 (60.5-88.0)	224/948	61.1 (52.6-69.6)	105/432	49.2 (40.3-58.2)
Body mass	Optimal	236/1785	49.6 (40.7-58.7)	314/1537	45.7 (40.8-50.6)	255/1126	41.9 (37.0-46.9)
index	Borderline	343/2136	60.6 (49.4-71.9)	422/2008	53.5 (48.1-58.9)	319/1364	47.2 (42.4-52.0)
	Elevated	237/1417	66.7 (54.4-79.1)	287/1260	61.5 (54.0-69.1)	202/709	53.3 (46.9-59.8)
Blood	Optimal	152/1539	38.4 (30.0-46.8)	118/778	38.1 (30.7-45.5)	45/272	34.0 (24.0-43.9)
pressure	Borderline	272/1792	58.5 (47.6-69.5)	254/1303	45.0 (39.5-50.4)	140/675	37.8 (31.9-43.7)
	Elevated	392/2007	66.5 (56.7-76.2)	651/2724	60.7 (55.9-65.4)	591/2252	50.8 (47.1-54.6)
Diabetes	Optimal	624/3805	56.6 (50.0-63.2)	726/3137	51.1 (47.5-54.6)	580/2249	45.7 (42.4-49.1)
	Borderline	128/1187	53.4 (26.2-80.6)	171/1149	48.1 (34.3-61.8)	110/584	48.2 (32.8-63.7)
	Elevated	64/346	53.4 (40.6-66.1)	126/519	60.9 (44.9-76.9)	86/366	53.2 (40.8-65.7)
History of	Optimal	747/5069	56.9 (50.4-63.5)	864/4236	50.9 (47.5-54.4)	607/2623	44.1 (40.8-47.4)
heart failure	Elevated	69/269	57.4 (41.5-73.3)	159/569	61.6 (51.2-72.0)	169/576	60.7 (52.1-69.4)
or							
myocardial							
infarction							

These results do not account for competing risk of death and overestimates the lifetime risk of atrial fibrillation.

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 10. Lifetime risk of atrial fibrillation at index age 55 years according to burden of risk factors with multiple imputation.

Analysis	Risk category	Men	Women
		Lifetime risk (95%CI)	Lifetime risk (95%CI)
Multiple imputation	Optimal	31.6 (10.3-52.8)	23.9 (12.0-35.9)
	Borderline	36.0 (29.8-42.2)	30.0 (24.4-35.7)
	Elevated	39.2 (36.4-42.0)	31.1 (28.3-33.8)
Complete case	Optimal	29.8 (9.7-49.9)	20.5 (7.3-33.7)
	Borderline	39.7 (31.7-47.7)	28.0 (20.6-35.4)
	Elevated	43.3 (38.4-46.2)	34.6 (30.3-39.0)

In the multiple imputation analysis, we included 6778 participants among which 1201 developed atrial fibrillation during follow-up. The mean percentage of individuals belonging to optimal, borderline, and elevated groups were 4.1%, 24.7%, and 71.2% respectively across 25 imputed datasets. Among those 6778 participants, 5338 participants (489 AF cases) didn't have any missing data for the risk factors and were included in the complete case analysis.

Lifetime risk of atrial fibrillation according to levels of risk factors

Suppl. Table 11. Lifetime risk of atrial fibrillation by BMI adjusted for the competing risk of death excluding underweighted individuals.

Risk Factor		Index age 55 years		Index age 65 years		Index age 75 years	
		AF cases/total	Lifetime risk (95%CI)	AF cases/total	Lifetime risk (95%CI)	AF cases/total	Lifetime risk (95%CI)
Body mass index	Optimal	233/1751	31.8 (27.7-36.0)	309/1493	30.3 (27.3-33.3)	247/1082	27.4 (24.4-30.5)
	Borderline	343/2136	38.2 (34.0-42.4)	422/2008	33.3 (30.5-36.1)	319/1364	30.1 (27.2-33.0)
	Elevated	237/1417	44.2 (38.5-50.0)	287/1260	40.7 (36.7-44.8)	202/709	38.7 (34.2-43.2)

The number of underweighted (BMI<18.5 kg/m^2) individuals excluded from the optimal category were 34, 44, and 44 for index age 55 years, index age 65 years, and index age 75 years respectively.

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