Supplemental Material

Appendix

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Table S1 Incidence models.

Outcome	No. of events	py of follow-up	incidence per 100py
clinical AF progression	458	8866	5.2
clinical AF progression from paroxysmal AF	294	6031	4.9
clinical AF progression from persistent AF	164	2835	5.8
clinical AF progression among patients without a history of ECV or PVI at baseline	151	2772	5.4
RCI	617	5663	10.9
Newly prescribed amiodarone	199	7148	2.8
ECV	282	6759	4.2
PVI	358	6327	5.7
RCI among patients without a history of PVI or ECV	258	3207	8.0

AF=atrial fibrillation; py=patient years; ECV=electrical cardioversion; PVI=pulmonary vein isolation; RCI=rhythm control intervention

Table S2. Risk factors for clinical atrial fibrillation progression in paroxysmal vs. persistent atrial fibrillation.

Characteristic	Paroxysmal multivariable adj.	p-value	Persistent multivariable adj.	p-value	p-interaction
Age	1.14 [1.06; 1.22]	<0.001	1.31 [1.17; 1.45]	<0.001	0.029
Female Sex	0.84 [0.64; 1.10]	0.207	0.98 [0.68; 1.42]	0.908	0.537
BMI	1.03 [1.00; 1.05]	0.052	1.03 [0.99; 1.06]	0.181	0.966
Heart rate	1.07 [1.04; 1.11]	<0.001	1.02 [0.98; 1.07]	0.290	0.102
Systolic blood pressure	1.02 [0.99; 1.05]	0.233	1.04 [1.00; 1.09]	0.065	0.475
History of diabetes	0.84 [0.58; 1.21]	0.341	1.11 [0.71; 1.72]	0.650	0.329
History of coronary artery disease	0.99 [0.73; 1.32]	0.918	0.98 [0.66; 1.45]	0.913	0.968
History of hypertension	0.91 [0.69; 1.21]	0.255	1.09 [0.74; 1.62]	0.667	0.468
History of stroke and/or TIA	1.46 [1.09; 1.94]	0.010	1.54 [1.05; 2.27]	0.027	0.778
History of heart failure	2.07 [1.53; 2.80]	<0.001	1.24 [0.86; 1.78]	0.251	0.033
History of hyperthyroidism	1.92 [1.11; 3.31]	0.020	1.49 [0.85; 2.61]	0.162	0.556
History of renal failure	1.17 [0.83; 1.63]	0.375	1.03 [0.68; 1.58]	0.885	0.662
Regular physical activity	0.81 [0.63; 1.03]	0.084	0.80 [0.58; 1.12]	0.189	0.986
Current smoking	1.07 [0.69; 1.66]	0.775	0.97 [0.52; 1.84]	0.936	0.804
History of pulmonary vein isolation	0.87 [0.64; 1.20]	0.405	0.44 [0.26; 0.73]	0.002	0.026
AF related symptoms at baseline	0.95 [0.71; 1.25]	0.693	0.78 [0.55; 1.09]	0.148	0.390
Amiodarone use at baseline	0.99 [0.73; 1.36]	0.970	0.76 [0.51; 1.13]	0.169	0.289

Data are hazard ratios (HR) (95% confidence intervals [CI]) based on Cox regression models. Age per 5 years increase; Heart Rate per 5 beats/min increase, Systolic blood pressure per 5mmHg increase; Models included all variables from the table (age, sex, BMI, heart rate, systolic blood pressure, history of diabetes, history of coronary artery disease, history of hypertension, history of stroke/TIA, history of heart failure, history of hyperthyroidism, history of renal failure, regular physical activity, current smoking, history of pulmonary vein isolation, AF related symptoms, amiodarone).

A maximum of 85 (3.0%) observations were deleted due to missing variables.

Table S3. Risk factors for clinical atrial fibrillation progression in BEAT-AF vs. Swiss-AF.

Characteristic	BEAT-AF multivariable adj.	p-value	Swiss-AF multivariable adj.	p-value
Age	1.22 [1.12; 1.33]	<0.001	1.09 [1.00; 1.18]	0.063
Female Sex	0.83 [0.59; 1.16]	0.270	0.87 [0.66; 1.16]	0.355
BMI	1.02 [0.99; 1.06]	0.216	1.01 [0.98; 1.04]	0.458
Heart rate	1.01 [0.97; 1.05]	0.619	1.12 [1.08; 1.16]	<0.001
Systolic blood pressure	1.04 [1.00; 1.09]	0.069	1.01 [0.98; 1.05]	0.421
History of diabetes	0.80 [0.48; 1.33]	0.382	0.83 [0.59; 1.17]	0.282
History of coronary artery disease	1.06 [0.71; 1.58]	0.763	0.92 [0.69; 1.23]	0.558
History of hypertension	0.87 [0.61; 1.23]	0.414	1.10 [0.81; 1.49]	0.536
History of stroke and/or TIA	1.12 [0.72; 1.72]	0.620	1.42 [1.08; 1.88]	0.012
History of heart failure	2.28 [1.56; 3.34]	<0.001	1.37 [1.03; 1.82]	0.032
History of hyperthyroidism	2.72 [1.61; 4.60]	<0.001	1.08 [0.59; 2.00]	0.800
History of renal failure	0.66 [0.40; 1.10]	0.112	1.31 [0.97; 1.78]	0.081
Regular physical activity	0.74 [0.54; 1.00]	0.051	0.87 [0.67; 1.12]	0.263
Current smoking	1.00 [0.56; 1.80]	0.999	1.03 [0.65; 1.64]	0.902
Paroxysmal AF at baseline	0.86 [0.61; 1.20]	0.367	1.27 [0.97; 1.65]	0.077
History of pulmonary vein isolation	0.86 [0.59; 1.25]	0.432	0.45 [0.31; 0.68]	<0.001
AF related symptoms at baseline	1.12 [0.76; 1.65]	0.565	0.78 [0.60; 1.02]	0.068
Amiodarone use at baseline	0.92 [0.63; 1.35]	0.669	0.94 [0.69; 1.30]	0.713

Data are hazard ratios (HR) (95% confidence intervals [CI]) based on Cox regression models. Age per 5 years increase; Heart Rate per 5 beats/min increase, Systolic blood pressure per 5mmHg increase; Models included all variables from the table (age, sex, BMI, heart rate, systolic blood pressure, history of diabetes, history of coronary artery disease, history of hypertension, history of stroke/TIA, history of heart failure, history of hyperthyroidism, history of renal failure, regular physical activity, current smoking, AF type, history of pulmonary vein isolation, AF related symptoms, amiodarone). A maximum of 33 (2.8%) [BEAT-AF] and 52 (3.1%) [Swiss-AF] observations were deleted due to missing variables.

Table S4. Baseline characteristics stratified by rhythm control intervention.

Characteristic	No intervention n=1655	PVI n=221	ECV n=107	Amiodarone n=101	>1 intervention n=188	p-value
Age [years]	71 ± 10	62 ± 10	68 ± 10	73 ± 6	66 ± 9	<0.001
Female sex, No. (%)	491 (29.7)	71 (32.1)	32 (29.9)	35 (34.7)	56 (29.8)	0.812
Body mass index [kg/m^2]	26.9 ± 4.6	26.4 ± 3.9	27.6 ± 4.3	27.6 ± 4.6	27.8 ± 4.3	<0.001
Heart rate [beats/min]	65 [58; 75]	63 [54; 72]	68 [60; 82]	66 [57; 73]	68 [58; 79]	0.006
Systolic blood pressure [mmHg]	134 ± 18	134 ± 18	134 ± 20	136 ± 19	135 ± 20	0.025
History of coronary heart disease, No. (%)	409 (24.7)	20 (9.1)	23 (21.5)	28 (27.7)	21 (11.2)	<0.001
History of stroke/TIA, No. (%)	375 (17.9)	23 (8.4)	30 (17.8)	20 (19.8)	23 (10.1)	<0.001
History of hypertension, No. (%)	1096 (66.2)	105 (47.5)	72 (67.3)	80 (79.2)	121 (64.4)	<0.001
History of heart failure, No. (%)	279 (16.9)	12 (5.4)	24 (22.4)	21 (20.8)	29 (15.4)	<0.001
History of diabetes mellitus, No. (%)	224 (13.5)	15 (6.8)	20 (18.7)	13 (12.9)	17 (9.0)	0.008
History of renal failure, No. (%)	264 (16.0)	5 (2.3)	19 (17.8)	19 (18.8)	14 (7.5)	<0.001
History of hyperthyroidism, No. (%)	66 (4.0)	11 (5.0)	7 (6.5)	3 (3.0)	9 (4.8)	0.646
Current Smoker, No. (%)	129 (7.8)	27 (12.2)	10 (9.4)	11 (11.1)	12 (6.4)	0.133
Regular physical activity, No. (%)	834 (50.5)	144 (65.5)	64 (59.8)	56 (56.6)	108 (57.5)	<0.001
AF related symptoms, No. (%)	1105 (68.1)	207 (93.7)	79 (73.8)	73 (73.7)	153 (81.4)	<0.001

TIA=transient ischaemic attack; p-values were based on Chi-squared or Kruskal Wallis tests as appropriate

Table S5. Factors associated with rhythm control interventions among patients without a history of pulmonary vein isolation and/or electrical cardioversion.

Characteristic n=1221	HR (95% CI) age/sex adj.	p-value	HR (95% CI) multivariable adj.	p-value
Age	0.83 [0.79; 0.87]	<0.001	0.86 [0.81; 0.91]	<0.001
Female Sex	1.11 (0.86; 1.43)	0.440	0.99 [0.76; 1.30]	0.953
BMI	1.00 [0.98; 1.03]	0.975	1.01 [0.98; 1.04]	0.474
Heart Rate	1.04 [1.01; 1.08]	0.014	1.05 [1.02; 1.09]	0.005
Systolic blood pressure	1.03 [1.00; 1.07]	0.073	1.04 [1.00; 1.08]	0.038
History of diabetes	0.78 [0.53; 1.17]	0.235	0.84 [0.55; 1.28]	0.412
History of coronary artery disease	0.62 [0.44; 0.89]	0.008	0.69 [0.48; 0.99]	0.044
History of hypertension	1.05 [0.80; 1.39]	0.705	1.06 [0.80; 1.42]	0.682
History of heart failure	0.94 [0.64; 1.38]	0.752	1.21 [0.81; 1.81]	0.361
History of stroke/TIA	0.76 [0.54; 1.07]	0.1118	0.76 [0.53; 1.08]	0.125
History of hyperthyroidism	1.21 [0.57; 2.57]	0.618	1.27 [0.59; 2.70]	0.542
History of renal failure	0.82 [0.54; 1.24]	0.352	0.90 [0.58; 1.39]	0.629
Regular physical activity	1.58 [1.23; 2.03]	<0.001	1.68 [1.29; 2.18]	<0.001
Current smoking	0.93 [0.60; 1.44]	0.744	1.06 [0.68; 1.65]	0.815
Paroxysmal AF	0.81 [0.58; 1.13]	0.218	0.80 [0.57; 1.13]	0.208
AF related symptoms at baseline	1.81 [1.28; 2.57]	<0.001	1.78 [1.25; 2.54]	0.001

Data are hazard ratios (HR) (95% confidence intervals [CI]) based on Cox regression models.
Rhythm control intervention was defined as either pulmonary vein isolation, electrical cardioversion and/or new amiodarone.
Age per 5 years increase; Heart Rate per 5 beats/min increase, Systolic blood pressure per 5mmHg increase; Multivariable models included all variables from the table (age, sex, BMI, heart rate, systolic blood pressure, history of diabetes, history of coronary artery disease, history of hypertension, history of heart failure, history of stroke /TIA, history of hyperthyroidism, history of renal failure, regular physical activity, current smoking, paroxysmal AF, AF related symptoms).
A maximum of 32 (2.6%) observations were deleted due to missing predictor variables