SUPPLEMENTAL MATERIAL

Table S1. Parameters of the multivariate model including both gene scores for the prediction of prevalent AF

Variable	Estimate	SE	z-value	p-value
Intercept	-27.22	15.25	-1.79	0.074
AF-GS	**2.00**	**0.62**	**3.24**	**0.001**
BA-GS	**2.71**	**0.99**	**2.74**	**0.006**
Age	0.03	0.02	1.42	0.157
Sex	**1.08**	**0.42**	**2.55**	**0.011**
BMI	0.09	0.23	0.39	0.695
Height	0.09	0.08	1.14	0.255
Weight	-0.04	0.08	-0.49	0.625
SBP	**-0.03**	**0.01**	**-3.42**	**0.0006**
DBP	0.03	0.02	1.67	0.095
Hypertension	-0.03	0.38	-0.08	0.933
Coronary artery disease	-0.38	0.29	-1.29	0.197
Heart failure	**1.09**	**0.30**	**3.64**	**0.0003**
Valve	**0.90**	**0.45**	**1.97**	**0.048**
Smoking recent	-0.53	0.51	-1.04	0.300
Smoking ever	-0.06	0.31	-0.21	0.837
Diabetes	-0.09	0.34	-0.27	0.791
Dyslipidemia	-0.36	0.32	-1.13	0.259
Chronic renal failure	0.82	0.45	1.82	0.069
COPD	**0.85**	**0.38**	**2.25**	**0.025**
Lymphocytes	5.10	6.38	0.80	0.424
Neutrophils	-5.74	6.26	-0.92	0.359
Monocytes	9.18	8.29	1.11	0.268

BMI: Body-mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; COPD: Chronic obstructive pulmonary disease

Table S2. Detailed reclassification of participants when adding the gene scores to the clinical model

Outcome	Event up	Event down	Non-event up	Non-event down	Net absolute reclassification
All prevalent AF	**54**	37	106	**214**	125
Paroxysmal AF	**20**	11	116	**204**	97
Permanent AF	**26**	24	125	**195**	72

Reclassification when adding both gene scores to the clinical model (model 2)

Numbers in bold represent reclassification in the right direction

Net absolute reclassification represents the net number of participants correctly reclassified: (Event up - Event down) + (Non-event down - Non-event up)

Table S3. Predictive performance, reclassification and discrimination for Paroxysmal AF

	AUC (95% CI)	p-value	cNRI (95% CI)	p-value	IDI (95% CI)	p-value	Calibration χ^2 (p-value)
Compared to RF only							
RF only	0.691 (0.593 - 0.790)	---	---	---	---	---	1.24 (0.996)
RF + AF-GS	0.742 (0.656 - 0.828)	0.117	0.282 (-0.085 - 0.65)	0.132	0.039 (0.003 - 0.074)	0.032	8.27 (0.41)
RF + BA-GS	0.716 (0.626 - 0.806)	0.378	0.274 (-0.090 - 0.638)	0.141	0.010 (-0.006 - 0.026)	0.204	9.67 (0.29)
RF + Both GSs	0.752 (0.663 - 0.841)	0.167	0.565 (0.212 - 0.918)	0.002	0.052 (0.009 - 0.095)	0.018	10.28 (0.25)
Compared to RF + BA-GS							
RF + Both GSs	0.752 (0.663 - 0.841)	0.182	0.251 (-0.117 - 0.619)	0.181	0.042 (0.008 - 0.075)	0.015	10.28 (0.25)
Compared to RF + AF-GS							
RF + Both GSs	0.752 (0.663 - 0.841)	0.630	0.216 (-0.151 - 0.582)	0.250	0.013 (-0.002 - 0.029)	0.083	10.28 (0.25)

RF: risk factors for AF from model 2 (age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, congestive heart failure, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes)

AUC: Area under the ROC curve

cNRI: continuous net reclassification improvement index

IDI: integrated discrimination improvement index

Table S4. Predictive performance, reclassification and discrimination for Permanent AF

	AUC (95% CI)	p-value	cNRI (95% CI)	p-value	IDI (95% CI)	p-value	Calibration χ^2 (p-value)
Compared to RF only							
RF only	0.853 (0.795 - 0.911)	---	---	---	---	---	8.36 (0.40)
RF + AF GS	0.855 (0.799 - 0.911)	0.709	0.438 (0.146 - 0.729)	0.003	0.006 (-0.006 - 0.017)	0.353	11.57 (0.17)
RF + BA GS	0.854 (0.797 - 0.911)	0.905	0.276 (-0.019 - 0.572)	0.067	0.023 (0.003 - 0.044)	0.027	11.31 (0.18)
RF + Both GSs	0.860 (0.806 - 0.915)	0.419	0.259 (-0.038 - 0.556)	0.088	0.029 (0.004 - 0.054)	0.022	5.73 (0.68)
Compared to RF + BA-GS							
RF + Both GSs	0.860 (0.806 - 0.915)	0.162	0.335 (0.041 - 0.629)	0.026	0.006 (-0.005 - 0.017)	0.260	5.73 (0.68)
Compared to RF + AF-GS							
RF + Both GSs	0.860 (0.806 - 0.915)	0.540	0.239 (-0.057 - 0.535)	0.114	0.023 (0.004 - 0.043)	0.018	5.73 (0.68)

RF: risk factors for AF from model 2 (age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, congestive heart failure, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes)

AUC: Area under the ROC curve

cNRI: continuous net reclassification improvement index

IDI: integrated discrimination improvement index

Figure S1.

	OR [95% CI]	P-value
AF-GS		
Univariate	1.41 [1.07 - 1.87]	0.016
Model 1	1.45 [1.09 - 1.93]	0.012
Model 2	1.57 [1.09 - 2.27]	0.015
Model 2 + BA-GS	1.61 [1.12 - 2.31]	0.011
BA-GS		
Univariate	1.24 [0.91 - 1.70]	0.17
Model 1	1.17 [0.85 - 1.62]	0.33
Model 2	1.95 [1.03 - 3.68]	0.04
Model 2 + AF-GS	2.09 [1.08 - 4.03]	0.029
Both GSs		
Univariate	1.46 [1.09 - 1.97]	0.011
Model 1	1.42 [1.05 - 1.93]	0.021
Model 2	2.23 [1.36 - 3.65]	0.0014
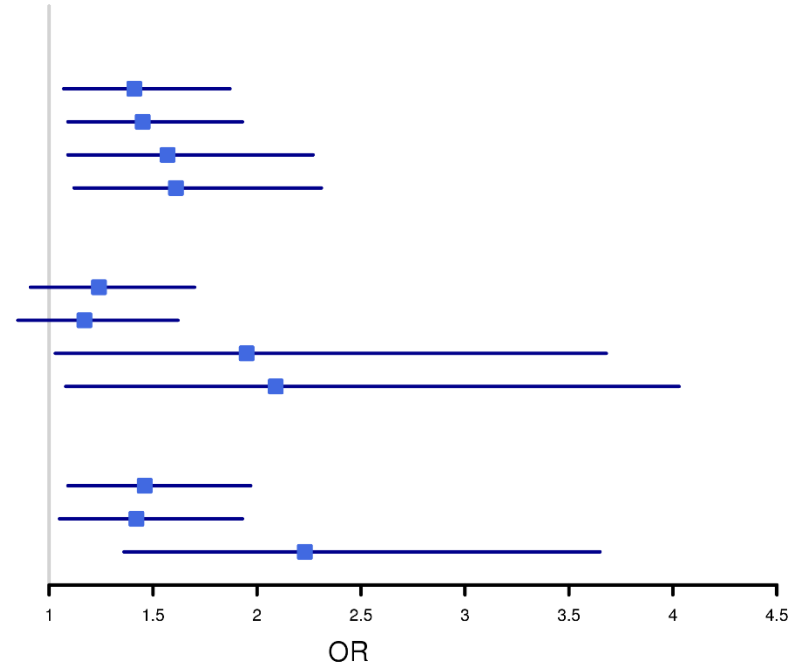
Figure S2.

	OR [95% CI]	P-value
AF-GS		
Univariate	1.84 [1.35 - 2.51]	0.00012
Model 1	1.78 [1.30 - 2.43]	0.00035
Model 2	1.81 [1.22 - 2.70]	0.0034
Model 2 + BA-GS	1.78 [1.20 - 2.64]	0.0043
BA-GS		
Univariate	1.41 [0.97 - 2.07]	0.076
Model 1	1.51 [1.01 - 2.25]	0.043
Model 2	1.87 [0.93 - 3.73]	0.077
Model 2 + AF-GS	1.83 [0.89 - 3.79]	0.1
Both GSs		
Univariate	1.92 [1.37 - 2.71]	0.00017
Model 1	1.87 [1.33 - 2.64]	0.00032
Model 2	2.46 [1.47 - 4.10]	0.00057

Figure S3.

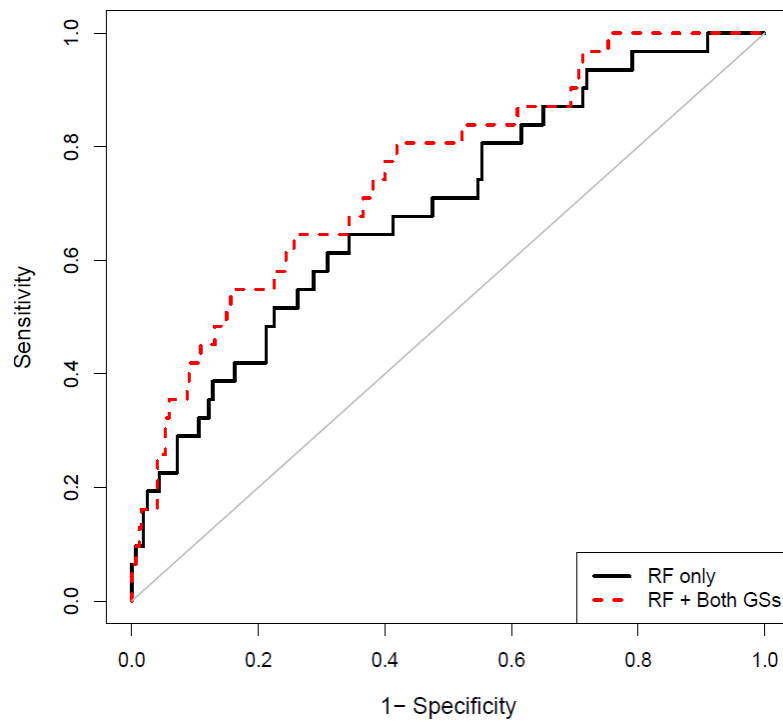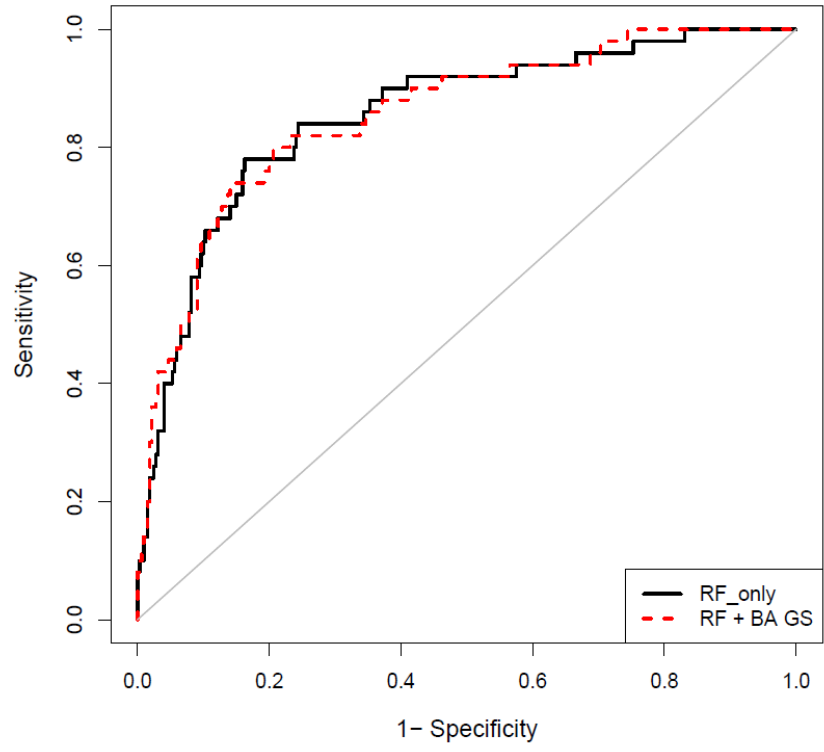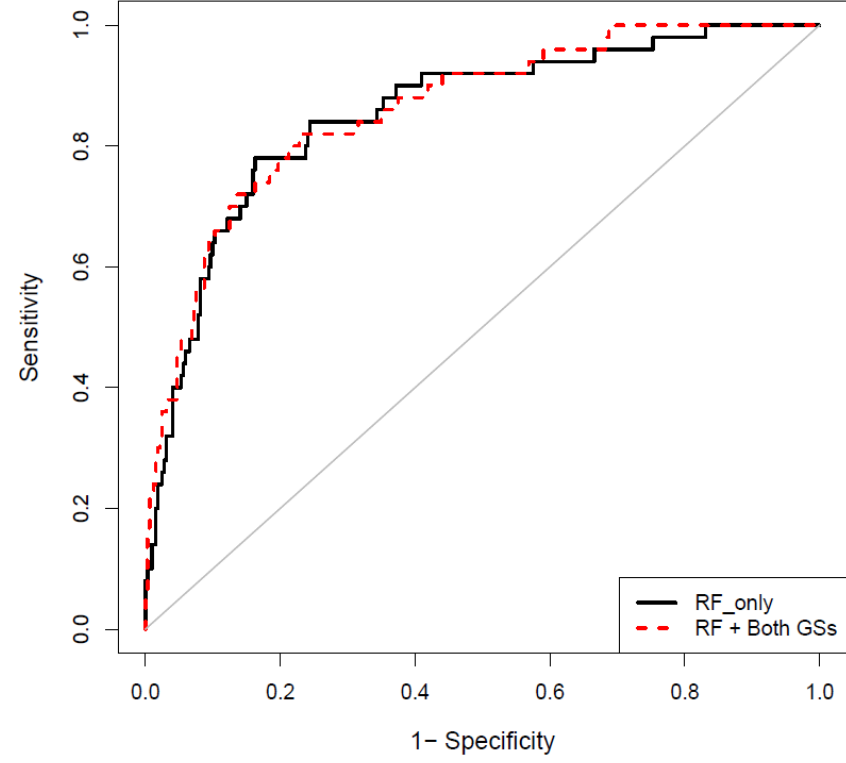|	OR [95% CI]	P-value
AF-GS		
Univariate	1.35 [1.01 - 1.80]	0.041
Model 1	1.42 [1.06 - 1.91]	0.12
Model 2	1.33 [0.93 - 1.91]	0.12
Model 2 + BA-GS	1.29 [0.90 - 1.85]	0.16
BA-GS		
Univariate	1.69 [1.23 - 2.33]	0.0014
Model 1	1.60 [1.15 - 2.23]	0.0051
Model 2	2.30 [1.16 - 4.56]	0.017
Model 2 + AF-GS	2.26 [1.13 - 4.52]	0.021
Both GSs		
Univariate	1.70 [1.26 - 2.29]	0.00052
Model 1	1.69 [1.24 - 2.30]	0.00082
Model 2	1.70 [1.07 - 2.71]	0.025

Figure S4.

A

B
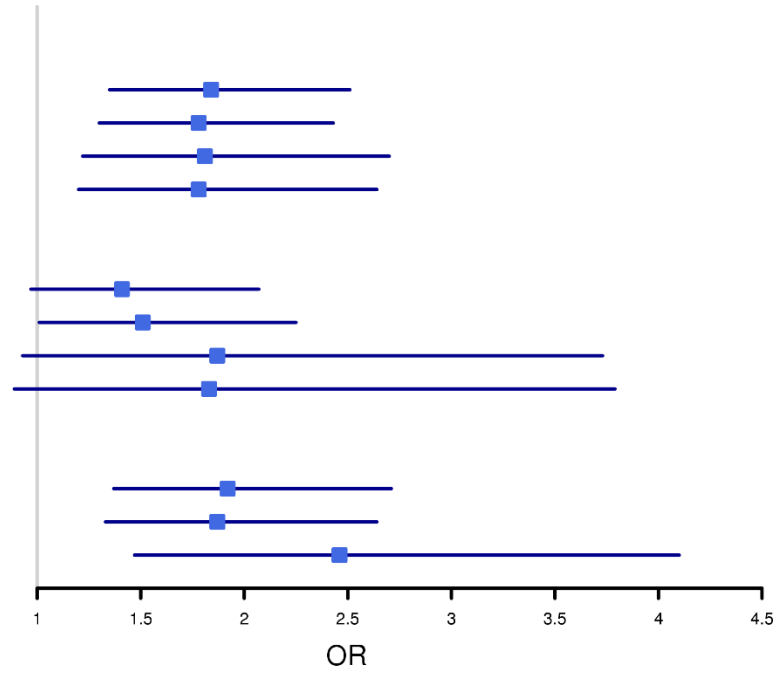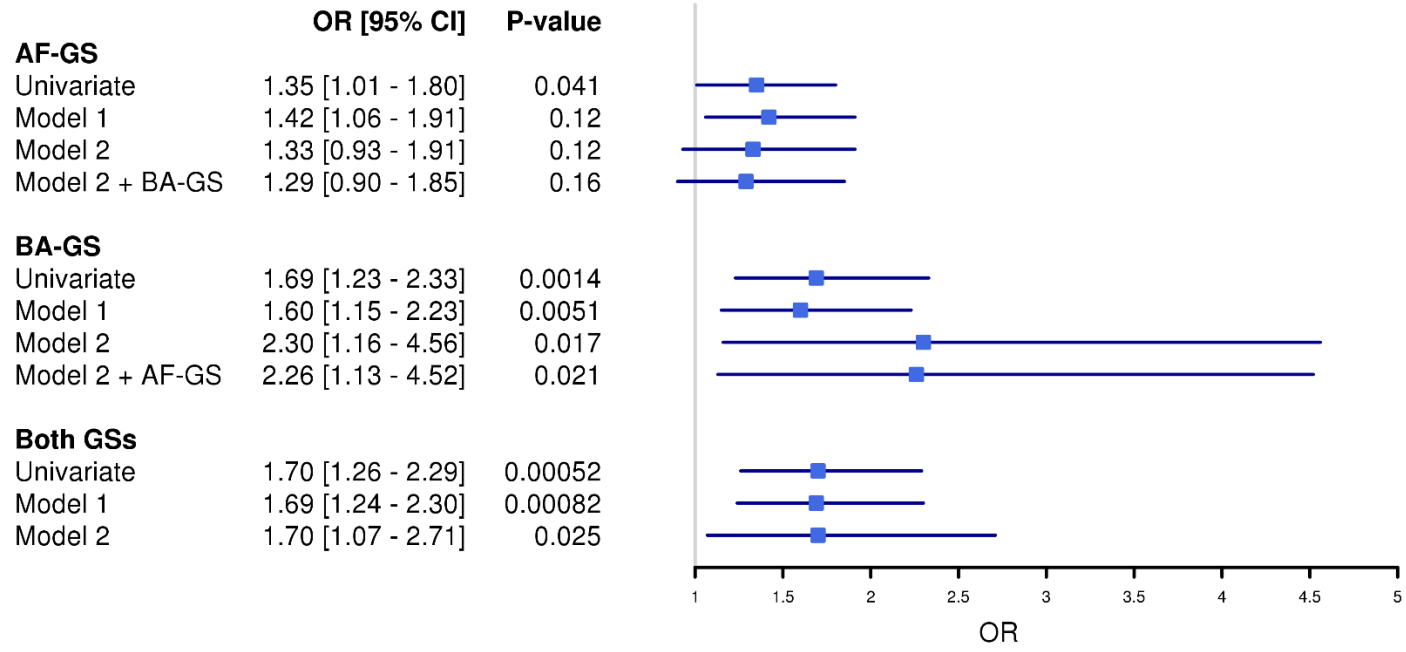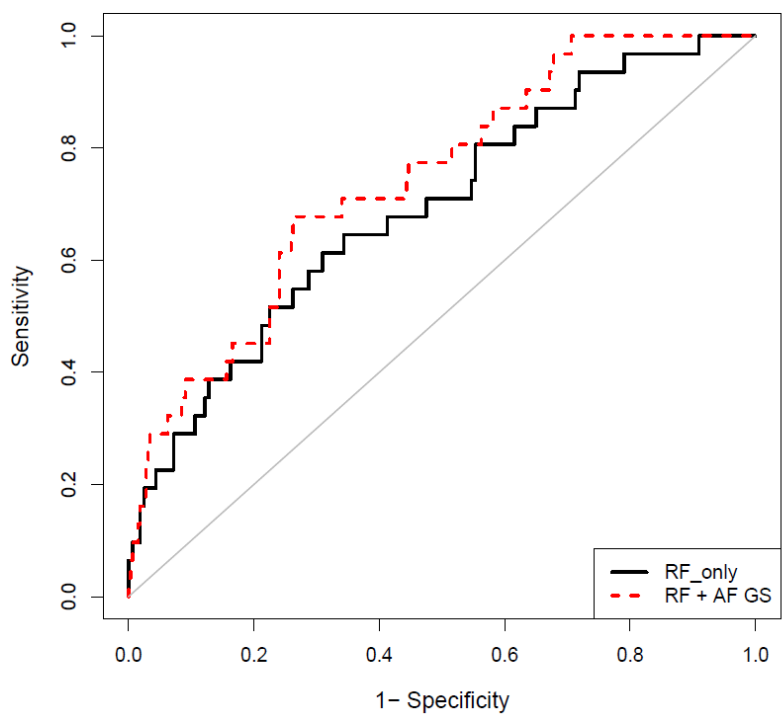
Supplemental Figure Legends:

Figure S1. Multivariate models for the prediction of AF excluding patients with heart failure.

OR: Odds ratios (95% confidence intervals) for AF for a 1-SD increase in the score; AF-GS: Atrial fibrillation gene score; BA-GS: Biological age gene score; GS: Gene score

Model 1 was adjusted for age and sex

Model 2 was adjusted for age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes

Figure S2. Multivariate models for the prediction of Paroxysmal AF

OR: Odds ratios (95% confidence intervals) for AF for a 1-SD increase in the score; AF-GS: Atrial fibrillation gene score; BA-GS: Biological age gene score; GS: Gene score

Model 1 was adjusted for age and sex

Model 2 was adjusted for age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes

Figure S3. Multivariate models for the prediction of Permanent AF

OR: Odds ratios (95% confidence intervals) for AF for a 1-SD increase in the score; AF-GS: Atrial fibrillation gene score; BA-GS: Biological age gene score; GS: Gene score

Model 1 was adjusted for age and sex

Model 2 was adjusted for age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes

Figure S4. ROC Curves for the identification of prevalent AF by subtypes

A: Model including AF-GS compared to model including clinical risk factors alone for the identification of Paroxysmal AF; B: Model including both GSs compared to model including clinical risk factors alone for the identification of Paroxysmal AF; C: Model including BA-GS compared to model including clinical risk factors alone for the identification of Permanent AF; D: Model including both GSs compared to model including clinical risk factors alone for the identification of Permanent AF.

RF: Risk factors (age, sex, BMI, height, weight, smoking status (in the last 12 months and ever), systolic blood pressure, diastolic blood pressure, hypertension, diabetes, coronary artery disease, dyslipidemia, congestive heart failure, valvular heart disease, chronic renal failure, chronic obstructive pulmonary disease, relative lymphocytes, neutrophils and monocytes); AF-GS: Atrial fibrillation gene score; BA-GS: Biological age gene score; GS: Gene score