

**Supplementary Table 1.** Detailed classification of AF as defined by the ICD-10 code I48.

Code	Type of AF	Definition
I48.0	Paroxysmal atrial fibrillation	Atrial fibrillation with episodes that last from a few seconds to days and terminate spontaneously.
I48.1	Persistent atrial fibrillation	Atrial fibrillation that lasts for more than seven days and requires medical intervention for conversion to sinus rhythm.
I48.2	Chronic atrial fibrillation	Atrial fibrillation that has been ongoing for more than one year and is managed with long-term treatment strategies.
I48.3	Typical atrial flutter	A regular atrial rhythm at a rate of 250-350 beats per minute, usually with a 2:1 or 4:1 atrioventricular conduction ratio.
I48.4	Atypical atrial flutter	An irregular atrial rhythm with varying atrioventricular conduction ratios, not fitting the criteria for typical atrial flutter.
I48.9	Atrial fibrillation and atrial flutter, unspecified	The medical record lacks sufficient information to clearly distinguish between the specific types of atrial fibrillation and atrial flutter.

Abbreviations: AF= Atrial fibrillation; ICD-10= International Classification of Diseases, 10th Revision.

**Supplementary Table 2.** Definition of covariates in UK Biobank.

Covariates	Definition	Field ID
Age	Continuous variable (year).	34, 52, 53
Sex	Binary variable: male and female.	31
Race	Binary variable: white and non-white.	21000
Townsend Deprivation Index	Continuous variable, an integrated indicator of socioeconomic status calculated from participants' home postcodes.	189
Education degree	Multi-categorical variable. High level: College or University degree, NVQ or HND or HNC or equivalent. Middle level: A levels/AS levels or equivalent, Other professional qualifications e.g.: nursing, teaching. Low level: O levels/GCSEs or equivalent, CSEs or equivalent.	6138
Body mass index	Continuous variable (kg/m <sup>2</sup> ), calculated as body weight (kg) divided by square of height (m <sup>2</sup> ).	21001
Smoking status	Binary variable: current smoking, previous/never smoking.	20116
Alcohol consumption frequency	Binary variable: <3 times per week and ≥3 times per week.	1558
Diet	Binary variable measured by healthy diet score. It was measured using 3 food items: 1) total fruit and vegetable intake: >4.5 pieces or servings per day; 2) total fish intake: >2 times per week; 3) processed and red meat intake: ≤2 times of processed meat per week and ≤ 5times of red meat per week. If ≥2 healthy food items were fulfilled, healthy diet score was 1 (more advisable), otherwise healthy diet score was 0 (less advisable).	1289, 1299, 1309, 1319, 1329, 1339, 1349, 1369, 1379, 1389
Physical activity	Binary variable: Yes or no. Indicates whether a person met the 2017 UK Physical activity guidelines of 150 minutes of walking or moderate activity per week or 75 minutes of vigorous activity. For participants who reported the frequency of physical activity (10+ minutes) without information in the duration, we defined the duration as 10 minutes each time.	22036
Family history of CVDs	Binary variable: Yes or no. Illnesses of parents and siblings for coronary heart disease or stroke were aggregated. Included in sensitivity analyses.	20107, 20110, 20111
Chronic kidney disease at baseline	Binary variable: yes or no. Defined according to ICD-10 codes (N18). Participants with albumin to creatinine ratio more than 30 mg/g or estimated glomerular filtration rate less than 60 ml/min/1.73 m <sup>2</sup> were also diagnosed at baseline.	130814, 130815
Dyslipidemia at baseline	Binary variable: yes or no. Defined according to ICD-10 (E78).	130814, 130815
Depression at baseline	Binary variable: yes or no. Defined according to self-reported information (1286, 1531), ICD-10 codes (F32, F33, F34, F38, F39), and Patient Health Questionnaire-2.	2050, 2060, 20002, 41270, 41280
Cancer at baseline	Binary variable: yes or no. Defined according to self-reported information (20001).	134

Covariates	Definition	Field ID
Autoimmune diseases at baseline	Binary variable: yes or no. Including the 19 most common autoimmune diseases across the U.K.: polymyalgia rheumatica, Sjogren's disease, systemic lupus erythematosus [SLE], systemic sclerosis, vasculitis, coeliac disease, inflammatory bowel disease including Crohn's disease and ulcerative colitis, primary biliary cirrhosis, Addison's disease, type 1 diabetes, Graves' disease, Hashimoto's disease, multiple sclerosis, myasthenia gravis, psoriasis, vitiligo, pernicious anemia, ankylosing spondylitis and rheumatoid arthritis.	41270, 41280, 131912, 130706, 130700, 131626, 131628, 131042, 131742,
	Defined according to ICD-10 (E271, E272, M081, M45, K900, O240, E10, E05, P721, E063, K50, K51, M074, M075, M091, M092, G35, G700, P940, D510, M315, M353, , K743, L40, M070, M072, M073, M090, M05, M06, M080, J990, , M350, M32, L93, M34, I677, I681, I682, I731, I776, K101, L95, M052, M30, M310, M313, M314, M315, M316, M317, M352, N002, N003, N004, N005, N007, N012, N013, N014, N015, N017, N022, N023, N024, N025, N027, N032, N033, N034, N035, N037, N042, N043, N044, N045, N047, N052, N053, N054, N055, N057, N062, N063, N064, N065, N067, N072, N073, N074, N075, N077, L80).	131848, 131850, 131894, 131828, 131898, 131832, 131890, 131802
Heart failure at baseline	Binary variable: yes or no. Defined according to ICD-10 I50).	131354
Valve diseases at baseline	Binary variable: yes or no. Defined according to ICD-10 (I05, I06, I07, I08, I34, I35, I36, I37, I39.0, I39.1, I39.3, I39.4).	41270, 41280, 131276, 131278, 131280,
		131282, 131322, 131324, 131326, 131328
Myocarditis at baseline	Binary variable: yes or no. Defined according to ICD-10 (I40, I41).	131334, 131336

Abbreviations: CVDs=Cardiovascular diseases; HNC=Higher national certificate; HND=Higher national diploma; NVQ=National vocational qualification.

Supplementary Table 3. Sensitivity analyses.

CMD numbers	Analysis 1		Analysis 2		Analysis 3		Analysis 4		Analysis 5		Analysis 6		Analysis 7	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
1	1.41	(1.35; 1.47)	1.54	(1.48; 1.60)	1.54	(1.49; 1.60)	1.96	(1.88; 2.04)	1.42	(1.38; 1.46)	1.53	(1.47, 1.59)	1.52	(1.47, 1.58)
2	2.05	(1.89; 2.21)	2.07	(1.96; 2.19)	2.06	(1.95; 2.17)	2.68	(2.51; 2.87)	1.80	(1.72; 1.88)	2.02	(1.90, 2.14)	1.98	(1.88, 2.09)
≥3	2.55	(2.06; 3.17)	3.16	(2.90; 3.45)	3.14	(2.89; 3.40)	3.82	(3.32; 4.39)	2.57	(2.40; 2.76)	3.01	(2.74, 3.31)	2.92	(2.67, 3.18)
Accumulative dose effect	1.41	(1.37; 1.46)	1.46	(1.43; 1.49)	1.46	(1.43; 1.49)	1.69	(1.65; 1.74)	1.36	(1.34; 1.39)	1.44	(1.41, 1.48)	1.43	(1.40, 1.46)

Analysis 1: CMDs were defined to include coronary artery disease, diabetes, stroke (n = 308,916).

Analysis 2: Exclusion of participants with less than 2 years of follow-up (n = 305,912).

Analysis 3: Exclusion of participants with only a self-reported history of atrial fibrillation (n = 308,761).

Analysis 4: Exclusion of participants with only self-reported CMDs (n = 273,149).

Analysis 5: Inclusion of participants with new-onset CMDs during the follow-up period (n = 396,356).

Analysis 6: Exclusion of participants with history of cancer or any autoimmune diseases at baseline (n = 266,694).

Analysis 7: Exclusion of participants with history of heart failure, any valve diseases, or myocarditis at baseline (n = 306,758).

Reference group: participants free of CMDs. HRs were calculated in Cox proportional hazards after adjusting for age, sex, ethnicity, current smoking status, Townsend deprivation index, body mass index, alcohol consumption, education degree, healthy diet, physical activity, dyslipidemia, family history of cardiovascular diseases, depression, and chronic kidney disease based. *P*<0.001.

Abbreviations: CI=Confidence interval; CMD=Cardiometabolic diseases; HR=Hazard ratio.

**Supplementary Figure 1.** Flowchart of the study design for main analysis.