

eTable 1. Definition of covariates.

eTable 2. Baseline characteristics before and after the Inverse Propensity of Treatment Weighting.

eTable 3. Characteristics of the Inverse Probability of Treatment Weighting cohort.

eTable 4. Incidence rate and risks of heart failure among the three groups without considering the Inverse Probability of Treatment Weighting.

eTable 5 Risks of heart failure at 2 years following atrial fibrillation index date according to pre-diabetes status changes without the Inverse Probability of Treatment Weighting.

eTable 6. BMI and blood pressure distribution in a subgroup of 3712 subjects with available data.

eTable 7. Risk of heart failure in sensitivity analysis that included a subgroup of 3712 subjects with available BMI and blood pressure.

eTable 8. Risks of heart failure in sensitivity analysis by censoring at last clinic visit date.

eFigure 1. Flow chart of the study cohort.

eFigure 2. Changes of glycaemic status among the pre-diabetes group.

Supplementary Appendix

eTable 1. Definition of covariates.

Entity	Definition
Atrial Fibrillation	ICD-9: 427.31
Heart Failure	ICD-9: 402, 404, 425, 428
Diabetes	ICD-9: 250
Hypertension	ICD-9: 401-405
Ischaemic stroke	ICD-9: 433, 434
Transient Ischaemic Attack	ICD-9: 435
Coronary Artery Disease	ICD-9: 410-414
Peripheral Vascular Disease	ICD-9: 440-444, 447
Venous Thromboembolism	ICD-9: 415.1, 451, 453
Rheumatoid Arthritis	ICD-9: 714
Ankylosing Spondylitis	ICD-9: 720-724
Systemic Sclerosis	ICD-9: 710.1
Systemic Lupus Erythematosus	ICD-9: 710.0
Liver Cirrhosis	ICD-9: 571.2, 571.5, 571.6, 572.2, 572.3, 572.4
Anaemia	ICD-9: 280,281-285
Cancer	ICD-9: 140-239
Gastrointestinal Bleeding	ICD-9: 456.0, 531-533, 578
Dyslipidaemia	ICD-9: 272, 272.1, 272.2, 272.3, 272.4
Obesity	ICD-9: 278
Smoking	ICD-9: 491, 492, 496

Abbreviation: ICD, International Classification of Diseases.

eTable 2. Baseline characteristics before and after the Inverse Propensity of Treatment Weighting.

	Overall	Normoglycaemia	Prediabetes	Diabetes	Unscreened	Standardized mean difference before IPTW	Standardized mean difference after IPTW
	N=25,142	N=3,711 (14.8%)	N=4,105 (16.3%)	N=10,127 (40.3%)	N= 7,199 (28.6%)		
Age, mean (SD)	75.2 (12.2)	75.0 (12.5)	75.1 (11.0)	75.8 (10.9)	74.5 (14.1)	0.065	0.018
Female, No. (%)	11,848 (47.1)	1,784 (48.1)	1,843 (44.9)	4,806 (47.5)	3415 (47.4)	0.037	0.009
Smoking, No. (%)	1,935 (7.7)	280 (7.5)	296 (7.2)	764 (7.5)	595 (8.3)	0.020	0.008
CHA <sub>2</sub> DS <sub>2</sub> -VASc score, median (IQR)	4.0 (2.0-5.0)	3.0 (2.0-4.0)	3.0 (2.0-4.0)	5.0 (4.0-6.0)	3.0 (2.0-4.0)	0.670	0.071
High-risk (≥2), No. (%)	19,809 (78.7)	2,677 (72.1)	3,010 (73.3)	9,310 (91.9)	4,812 (66.8)		
Intermediate-risk (=1), No. (%)	3,584 (14.3)	660 (17.8)	725 (17.7)	817 (8.1)	1,382 (19.2)		
Low-risk (=0), No. (%)	1,749 (7.0)	374 (10.1)	370 (9.0)	0 (0)	1,005 (14.0)		
Fasting blood glucose, mg/dl, median (IQR)	115.3 (95.5, 147.6)	91.0 (86.5, 95.5)	106.3 (102.7, 111.7)	149.6 (135.2, 175.5)	-	0.326	0.013
HbA1c, %, median (IQR)	6.9 (6.1, 7.7)	5.4 (5.2, 5.5)	6.0 (5.8, 6.1)	7.3 (6.9, 8.1)	-	0.279	0.006
eGFR, ml/min/1.73 m <sup>2</sup> , median (IQR)	65.4 (48.7, 80.8)	71.7 (58.5, 85.7)	69.6 (57.0, 82.9)	64.6 (47.5, 81.1)	65.7 (48.2, 81.2)	0.129	0.008

Subjects with eGFR below 60 ml/min/1.73 m <sup>2</sup> , No. (%)	8,329 (33.1)	959 (25.8)	1,184 (28.8)	4,184 (41.3)	2,002 (27.8)	0.211	0.014
Medical conditions, No. (%)							
Hypertension	7,685 (30.6)	978 (26.4)	1,252 (30.5)	3,971 (39.2)	1,484 (20.6)	0.243	0.012
Ischaemic stroke	2,898 (11.5)	399 (10.8)	521 (12.7)	1,418 (14.0)	560 (7.8)	0.110	0.006
TIA	604 (2.4)	93 (2.5)	140 (3.4)	275 (2.7)	96 (1.3)	0.071	0.002
CAD	3,281 (13.0)	377 (10.2)	735 (17.9)	1,667 (16.5)	502 (7.0)	0.198	0.007
PVD	933 (3.7)	136 (3.7)	158 (3.8)	479 (4.7)	160 (2.2)	0.071	0.003
VTE	241 (1.0)	34 (0.9)	20 (0.5)	121 (1.2)	66 (0.9)	0.052	0.004
Autoimmune diseases*	3,793 (15.1)	600 (16.2)	595 (14.5)	1,533 (15.1)	1065 (14.8)	0.015	0.013
Liver cirrhosis	145 (0.6)	21 (0.6)	16 (0.4)	75 (0.7)	33 (0.5)	0.031	0.002
Anaemia	2,390 (9.5)	309 (8.3)	280 (6.8)	1,246 (12.3)	555 (7.7)	0.125	0.023
Cancer	4,039 (16.1)	596 (16.1)	635 (15.5)	1,754 (17.3)	1,054 (14.6)	0.040	0.004
GIB	2,737 (10.9)	380 (10.2)	422 (10.3)	1,217 (12.0)	718 (10.0)	0.042	0.005
Dyslipidaemia	2,427 (9.7)	246 (6.6)	448 (10.9)	1,431 (14.1)	302 (4.2)	0.210	0.007
Obesity	258 (1.0)	12 (0.3)	25 (0.6)	204 (2.0)	17 (0.2)	0.114	0.009
Medication use, No. (%)							
NOAC	13,196 (52.5)	2,006 (54.1)	2,562 (62.4)	5,401 (53.3)	3,227 (44.8)	0.195	0.006
Warfarin	4,333 (17.2)	586 (15.8)	753 (18.3)	2,014 (19.9)	980 (13.6)	0.098	0.002
Statins	10,024 (39.9)	1,245 (33.5)	1,851 (45.1)	5,562 (54.9)	1,366 (19.0)	0.441	0.078
Aspirin	9,830 (39.1)	1,378 (37.1)	1,935 (47.1)	4,657 (46.0)	1,860 (25.8)	0.243	0.042
Beta Blockers	8,032 (31.9)	1,202 (32.4)	1,447 (35.2)	3,603 (35.6)	1,780 (24.7)	0.119	0.010
ACEI/ARB	12,004 (47.7)	1,457 (39.3)	1,836 (44.7)	6,748 (66.6)	1,963 (27.3)	0.495	0.034

Procedure, No. (%)							
Ablation	144 (0.6)	22 (0.6)	25 (0.6)	27 (0.3)	70 (1.0)	0.052	0.002
Cardioversion	78 (0.3)	8 (0.2)	10 (0.2)	32 (0.3)	28 (0.4)	0.011	0.001

Abbreviation: N, number; IPTW, inverse probability of treatment weighting; SD, standard deviation; IQR, interquartile range; HF, heart failure; HbA1c, haemoglobin A1c; eGFR, estimated glomerular filtration rate; TIA, transient ischaemic attack; CAD, coronary artery disease; PVD, peripheral vascular disease; VTE, venous thromboembolism; GIB, gastrointestinal bleeding; NOAC, non-vitamin K antagonist oral anticoagulant; ACEI/ARB, angiotensin-converting enzyme/ angiotensin II receptor blocker.

\*Autoimmune diseases include rheumatoid arthritis, systemic sclerosis, systemic lupus erythematosus, and ankylosing spondylitis.

The standardized mean difference is calculated across normoglycaemia, pre-diabetes and diabetes groups.

A variable is considered balanced between users and nonusers where the standardized mean difference is  $\leq 0.1$ .

eTable 3. Characteristics of the Inverse Probability of Treatment Weighting cohort.

	Normoglycaemia N=2,057	Prediabetes N=2,851	Diabetes N=7,448
Age, mean (SD), y	74.5 (9.0)	75.1 (11.0)	75.0 (11.3)
Female, No. (%)	1,025 (49.8)	1,272 (44.6)	3,494 (46.9)
Smoking, No. (%)	184 (8.9)	195 (6.8)	559 (7.5)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score, median (IQR)	3.0 (2.0-4.0)	3.0 (2.0-4.0)	4.0 (2.0-5.0)
Medical conditions, No. (%)			
Hypertension	623 (30.3)	879 (30.8)	2,860 (38.4)
Ischaemic stroke	250 (12.2)	351 (12.3)	1,018 (13.7)
TIA	57 ( 2.8)	99 ( 3.5)	201 ( 2.7)
CAD	225 (10.9)	522 (18.3)	1,220 (16.4)
PVD	83 ( 4.0)	110 ( 3.9)	332 ( 4.5)
VTE	21 ( 1.0)	14 ( 0.5)	93 ( 1.2)
Autoimmune diseases*	340 (16.5)	372 (13.0)	1,080 (14.5)
Liver cirrhosis	11 ( 0.5)	10 ( 0.4)	57 ( 0.8)
Anaemia	210 (10.2)	192 ( 6.7)	898 (12.1)
Cancer	360 (17.5)	431 (15.1)	1,270 (17.1)
GIB	235 (11.4)	289 (10.1)	883 (11.9)
Dyslipidaemia	143 ( 7.0)	314 (11.0)	1,020 (13.7)
Obesity	7 ( 0.3)	18 ( 0.6)	154 ( 2.1)
Medication use, No. (%)			
NOAC	1,125 (54.7)	1,753 (61.5)	4,052 (54.4)
Warfarin	324 (15.8)	526 (18.4)	1,487 (20.0)
Statins	727 (35.3)	1,276 (44.8)	4,066 (54.6)
Aspirin	808 (39.3)	1,335 (46.8)	3,349 (45.0)
Beta Blockers	698 (33.9)	994 (34.9)	2,623 (35.2)
ACEI/ARB	861 (41.9)	1,278 (44.8)	4,883 (65.6)
Procedure, No. (%)			
Ablation	9 (0.4)	10 (0.4)	20 (0.3)
Cardioversion	4 (0.2)	6 (0.2)	15 (0.2)

Abbreviation: N, number; SD, standard deviation; IQR, interquartile range; HF, heart failure; TIA, transient ischemia attack; CAD, coronary artery disease; PVD, peripheral vascular disease; VTE, venous thromboembolism; GIB, gastrointestinal bleeding; NOAC, non-vitamin K antagonist oral anticoagulant; ACEI/ARB, angiotensin-converting enzyme/ angiotensin II receptor blocker.

\*Autoimmune diseases include rheumatoid arthritis, systemic sclerosis, systemic lupus

erythematous, and ankylosing spondylitis.

eTable 4. Incidence rate and risks of heart failure among the three groups without considering the Inverse Probability of Treatment Weighting.

N= 17,943	Event number/Total No.(%)	Incidence rate	Unadjusted SHR (95%CI) P-value	Model 1 SHR (95%CI) P-value	Model 2 SHR (95%CI) P-value
Normoglycaemia	518/3,711 (14.0)	3.02	Ref	Ref	Ref
Pre-diabetes	646/4,105 (15.7)	3.14	1.10 (0.98-1.24) 0.09	1.13 (1.01-1.27) <0.01	1.06 (1.02-1.12) 0.03
Diabetes	1,795/10,127 (17.7)	3.38	1.26 (1.15-1.39) <0.01	1.25 (1.13-1.37) <0.01	1.23 (1.12-1.37) <0.01

Abbreviation: N, number; SHR, subdistribution hazard ratio; CI, confidence interval; Ref, reference.

Model 1 adjusted for age and sex.

Model 2 adjusted for age, sex, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, hypertension, stroke, transient ischaemic attack, coronary artery disease, estimated glomerular filtration rate, peripheral vascular disease, rheumatoid arthritis, gastrointestinal bleeding, autoimmune diseases, anaemia, cancer, non-vitamin K antagonist oral anticoagulant, angiotensin-converting enzyme/ angiotensin II receptor blocker, Beta-blockers, statins, aspirin, warfarin, smoking, obesity, and dyslipidaemia.



eTable 5. Risks of heart failure at 2 years following atrial fibrillation index date according to pre-diabetes status changes without Inverse Probability of Treatment Weighting.

N=3,620	Incidence rate	Unadjusted	Model 1	Model 2
		SHR (95% CI) P-value	SHR (95% CI) P-value	SHR (95% CI) P-value
Reversion to normoglycaemia	0.94	0.79 (0.61-0.97) 0.01	0.72 (0.47-0.94) <0.01	0.63 (0.41-0.97) 0.03
Persistent pre-diabetes	1.29	Ref	Ref	Ref
Progression to diabetes	1.78	1.47 (1.18-1.74) <0.01	1.41 (1.15-1.70) <0.01	1.49 (1.11-1.99) 0.01

Abbreviation: N, number; SHR, subdistribution hazard ratio; CI, confidence interval; Ref, reference.

Model 1 adjusted for age and sex.

Model 2 adjusted for age, sex, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, hypertension, stroke, transient ischaemic attack, coronary artery disease, estimated glomerular filtration rate, peripheral vascular disease, rheumatoid arthritis, gastrointestinal bleeding, autoimmune diseases, anaemia, cancer, non-vitamin K antagonist oral anticoagulant, angiotensin-converting enzyme/ angiotensin II receptor blocker, Beta-blockers, statins, aspirin, warfarin, smoking, obesity, and dyslipidaemia.

eTable 6. BMI and blood pressure distribution in a subgroup of 3712 subjects with available data.

N= 3,712	Normoglycaemia	Pre-diabetes	Diabetes
Event number/Total No.(%)	113/740 (15.3)	163/822 (19.8)	374/2,150(17.4)
BMI, kg/m <sup>2</sup> , median (IQR)	22.3 (18.2, 26.2)	23.5 (18.7, 28.3)	23.8 (19.3, 28.3)
Systolic blood pressure, mmHg, mean (SD)	141.5 (23.2)	143.2 (23.5)	144.5 (23.8)
Diastolic blood pressure, mmHg, mean (SD)	78.5 (14.8)	79.6 (15.2)	77.3 (15.0)

Abbreviation: BMI, body mass index; N, number; IQR, interquartile range; SD, standard deviation; SHR, subdistribution hazard ratio; CI, confidence interval; Ref, reference.

eTable 7. Risk of heart failure in sensitivity analysis that included a subgroup of 3712 subjects with available BMI and blood pressure.

N= 3,712	Normoglycaemia	Pre-diabetes	Diabetes
Unadjusted		1.30	1.13
SHR (95% CI) P	Ref	(1.03-1.65)	(1.01-1.29)
		0.03	0.03
Model 1		1.34	1.14
SHR (95% CI) P	Ref	(1.16-1.59)	(1.02-1.30)
		0.02	0.02
Model 2		1.25	1.21
SHR (95% CI) P	Ref	(1.03-1.50)	(1.12-1.30)
		0.02	0.02
Model 2+ <b>BMI</b>		1.20	1.16
SHR (95% CI) P	Ref	(1.04-1.35)	(1.09-1.24)
		0.01	0.03
Model 2+ <b>BMI+blood pressure</b>		1.20	1.17
SHR (95% CI) P	Ref	(1.05-1.38)	(1.08-1.30)
		0.01	0.03

Abbreviation: BMI, body mass index; N, number; SHR, subdistribution hazard ratio; CI, confidence interval; Ref, reference.

Model 1 adjusted for age and sex.

Model 2 adjusted for age, sex, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, hypertension, stroke, transient ischaemic attack, coronary artery disease, estimated glomerular filtration rate, peripheral vascular disease, rheumatoid arthritis, gastrointestinal bleeding, autoimmune diseases, anaemia, cancer, non-vitamin K antagonist oral anticoagulant, angiotensin-converting enzyme/ angiotensin II receptor blocker, Beta-blockers, statins, aspirin, warfarin, smoking, obesity, and dyslipidaemia.

eTable 8. Risks of heart failure in sensitivity analysis by censoring at last clinic visit date.

*N= 17,621	Event number/Total No.(%)	Unadjusted SHR (95% CI) P-value	Model 1 SHR (95% CI) P-value	Model 2 SHR (95% CI) P-value
Normoglycaemia	518/3638 (14.2)	Ref	Ref	Ref
Pre-diabetes	646/4019 (16.1)	1.10 (0.98-1.24) 0.09	1.14 (1.02-1.28) 0.03	1.11 (1.03-1.20) 0.01
Diabetes	1795/9964 (18.0)	1.20 (1.07-1.33) <0.01	1.20 (1.09-1.32) <0.01	1.21 (1.11-1.30) <0.01

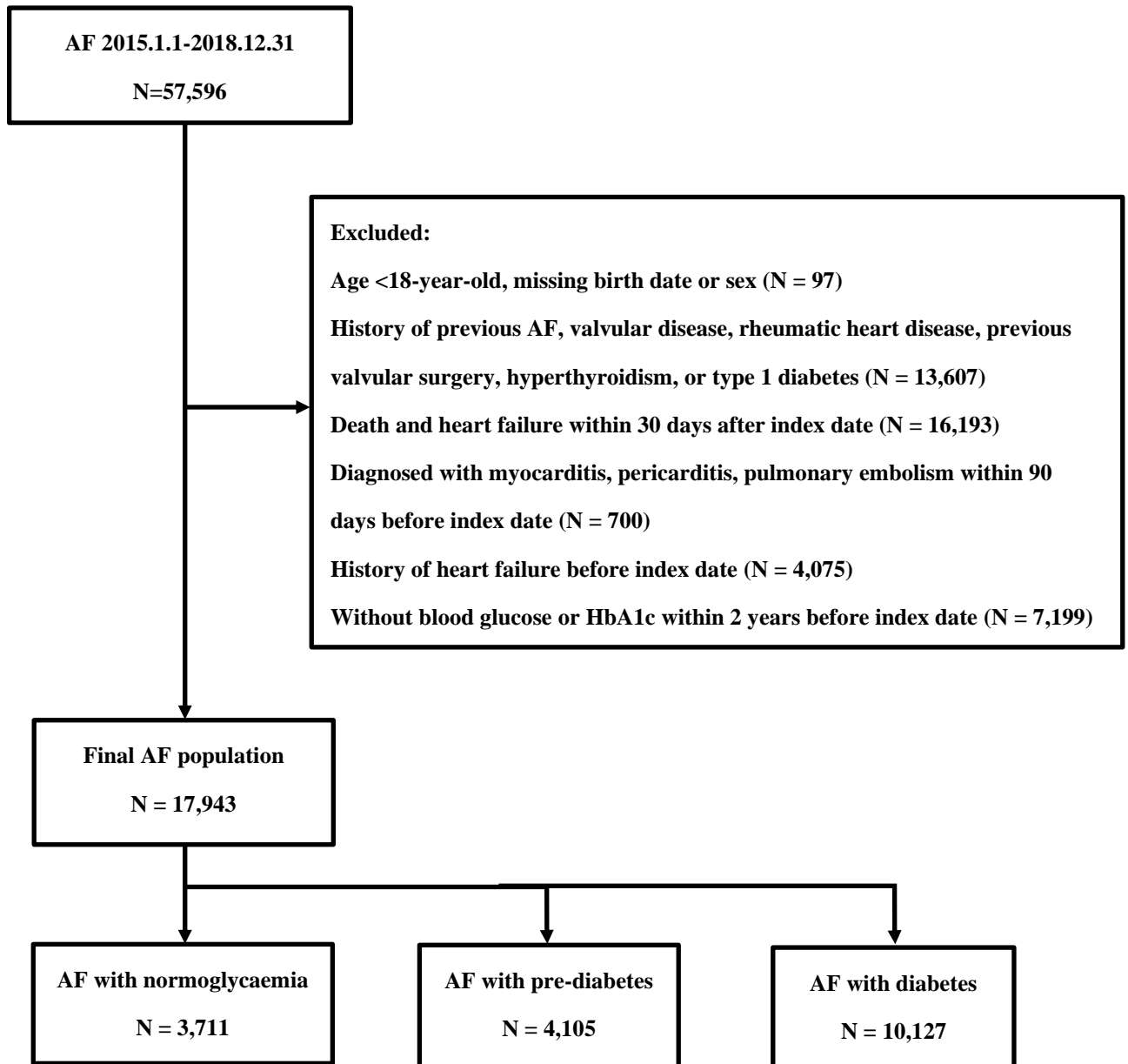
Abbreviation: N, number; SHR, subdistribution hazard ratio; CI, confidence interval; Ref, reference.

Model 1 adjusted for age and sex.

Model 2 adjusted for age, sex, CHA2DS2-VASc score, hypertension, stroke, transient ischaemic attack, coronary artery disease, estimated glomerular filtration rate, peripheral vascular disease, rheumatoid arthritis, gastrointestinal bleeding, autoimmune diseases, anaemia, cancer, non-vitamin K antagonist oral anticoagulant, angiotensin-converting enzyme/ angiotensin II receptor blocker, Beta-blockers, statins, aspirin, warfarin, smoking, obesity, and dyslipidaemia.

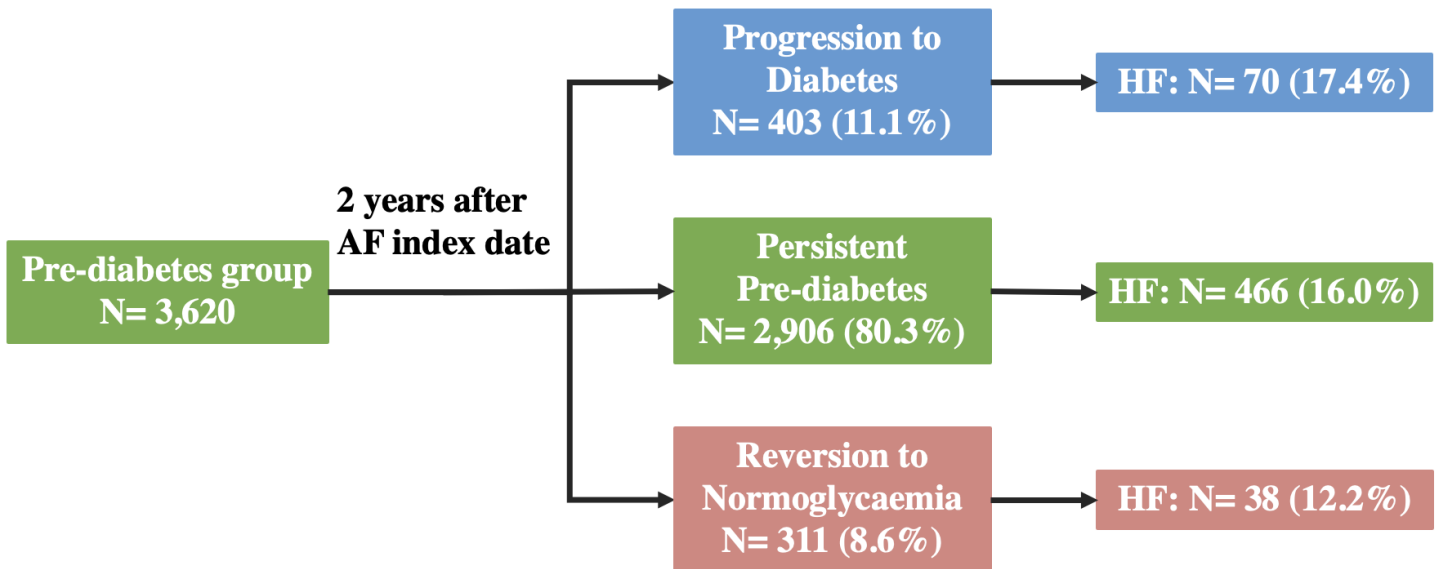
\*Among 17,943 patients in the entire study cohort, 322 (1.8%) patients without clinic visits after the index date.

**eFigure 1. Flow chart of the study cohort.**



Abbreviation: AF, atrial fibrillation; N, number; HbA1c, haemoglobin A1c.

eFigure 2. Changes of glycaemic status among the pre-diabetes group.



Abbreviation: N, number; AF, atrial fibrillation; HF, heart failure.