

SUPPLEMENTAL DATA FILE

Table S1. Equations of the risk scores

GARFIELD-AF stroke/SE (original)	$100 * (1 - (0.991344397^{**} (\exp(0.0304823 * (\text{Age} - 60) + 0.952524717 * \text{stroke/TIA/SE} + 0.432357326 * \text{Bleeding} + 0.319129628 * \text{Heart failure} + 0.574919171 * \text{Chronic kidney disease} + 0.654249546 * \text{other region} + 0.671380382 * \text{race} - 0.582045773 * \text{OAC}))))))$
GARFIELD-AF stroke/SE (modified for this analysis)	$100 * (1 - (0.991344397^{**} (\exp(0.0304823 * (\text{Age} - 60) + 0.952524717 * \text{stroke/TIA/SE} + 0.432357326 * \text{Bleeding} + 0.319129628 * \text{Heart failure} + 0.574919171 * \text{Chronic kidney disease} - 0.582045773 * \text{OAC}))))))$
GARFIELD-AF major bleeding	$100 * (1 - (0.994488926^{**} (\exp(0.0389958 * (\text{AGE} - 60) + 0.515013074 * \text{vascular disease} + 0.577378429 * \text{Chronic kidney disease}))))))$
CHA ₂ DS ₂ -VASc	65 ≤ age < 75: 1 point Age ≥ 75: 2 point Female sex: 1 point Heart failure: 1 point Hypertension: 1 point Ischemic stroke / TCI / Systemic embolism and thrombosis: 2 points Ischemic Heart Disease or Peripheral atherosclerosis: 1 point Diabetes: 1 point
HAS-BLED	Age > 65: 1 point Hypertension: 1 point Chronic kidney disease: 1 point Liver disease: 1 point Ischemic stroke / TCI / Systemic embolism and thrombosis: 1

	points Bleeding: 1 point ASA or ADP inhibitors or Dipyridamole or NSAID: 1 point Alcohol: 1 point
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Table S2. Definitions of covariates.

	ICD-10 codes
Atrial Fibrillation	I48
Non-Valvular Atrial Fibrillation	Presence of: I48 With absence of: Rheumatic heart valve disease, prostatic heart valve
Rheumatic heart valve disease	ICD10: Z952, Z954, I05, I06, I080A, I081A, I082A, I083A
Prostatic heart valve	KFKD, KFKH, KFMD, KFMH, KFGE, KFJF
Stroke / TIA / Systemic embolism and thrombosis (without hemorrhagic stroke), baseline	Ischemic: I63, I64 TIA: G458, G459 Systemic embolism and thrombosis: I74
Stroke/SE, endpoint	Ischemic: I63, I64 Systemic embolism and thrombosis: I74
Hospitalization for any bleeding, baseline	Heart: I312 Urine: N02, R31 Airways: R04 Eye: H313, H356, H431, H450, H052A Gastrointestinal: K228F, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K298A, K625, K638B, K638C, K838F, K868G, K920, K921, K922, I850, I864A Intra-dural bleeds not hemorrhagic stroke: S064, S065, S066 Hemorrhagic stroke: I60, I61, I62, I690, I691, I692 Retro-peritoneal: K661 Thorax: J942 Anemia due to bleeding: D500, D62
Major bleeding (with hemorrhagic stroke)	Heart: I312 Urine; N02, R31 Eye: H313, H356, H431, H450 Airways: R04 Gastrointestinal: K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K280, K282, K284, K286, K920, K921, K922 Intra-dural bleeds not hemorrhagic stroke: S064, S065, S066, I692 Hemorrhagic stroke: I60, I61, I62, I690, I691 Thorax: J942 Retro-peritoneal: K661

	Anemia due to bleeding: D62
Heart Failure	Cardiomyopathy: I42 Heart failure: I50, I110 Lung edema: J81
IHD	Ischemic Heart Disease: I20-I25 <ul style="list-style-type: none"> • Angina pectoris: I20 • Acute myocardial infarction: I21, I22 • Complications to AMI: I23, • Other forms of ischemic heart disease: I24, I25
Peripheral artery disease	I70
Vascular disease	Presence of Ischemic heart disease or peripheral artery disease
Chronic Kidney Disease	N02, N03, N04, N05, N06, N07, N08, N11, N12, N14, N18, N19, N26, N158, N159, N160, N162, N163, N164, N168 Q61, E102, E112, E132, E142, I120, M321B
Pulmonary embolism	I26
Alcohol	F10, K70, E52, T51, K860, E244, G312, I426, O354, Z714, Z721, G621, G721, K292, L278A
Liver disease	B15, B16, B17, B18, B19, C22, K70, K71, K72, K73, K74, K75, K76, K77, Z944, I982, D684C
Diabetes Mellitus	Insulin: A10A Non-Insulin: A10B
OAC	VKA: Warfarin: B01AA03, Phenprocoumon: B01AA04 NOAC: Dabigatran: B01AE07, Rivaroxaban: B01AF01, Apixaban: B01AF02
Acetylsalicylic acid	B01AC06, N02BA01
ADP-inhibitors	B01AC04, B01AC24, B10AC22
NSAID	M01A without M01AX05
Hypertension as usage of combination of at least two of the seven different drugs classes at the same time.	<ol style="list-style-type: none"> 1. Non-Loop: Thiazides C02L, C02DA, C07B, C07D, C09XA52, C03A, C03EA; Low-ceiling diuretics (excl. thiazides): C03B, C03X, C07C, C08G, C09BA, C09DA; Potassium-sparing agents (spiron): C03D, C03E, C03EB 2. Loop: High-ceiling diuretics (Loop) C03C, C03EB 3. Antiadrenergic agents: C02A, C02B, C02C

	<ol style="list-style-type: none">4. Beta-blockers: C07A, C07B, C07C, C07D, C07F5. Vasodilators: C02DB, C02DD, C02DG6. Calcium channel blockers: C08, C09BB, C09DB7. RASi: C09AA, C09BA, C09BB, C09CA, C09DA, C09DB, C09XA02, C09XA52
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Table S3. Baseline characteristics for the Danish population, stratified by CHA₂DS₂VASC score. Low (0-1 men, 1-2 women) risk and high-risk.

	Low risk	High risk
n	20,673	70,020
age (median [IQR])	61 [54, 68]	78 [71, 85]
Sex, male (%)	13083 (63.3)	35403 (50.6)
Diabetes (%)	286 (1.4)	10614 (15.2)
Stroke/TIA (%)	0 (0.0)	12827 (18.3)
Systemic embolism (%)	0 (0.0)	448 (0.6)
History of bleeding (%)	1154 (5.6)	9176 (13.1)
Chronic kidney disease (%)	296 (1.4)	3928 (5.6)
Heart failure (%)	225 (1.1)	14736 (21.0)
Ischemic heart disease (%)	492 (2.4)	12953 (18.5)
OAC (%)	8801 (42.6)	42379 (60.5)
NOAC (%)	4307 (20.8)	18905 (27.0)
VKA (%)	4494 (21.7)	23474 (33.5)
venous thromboembolism (%)	380 (1.8)	2301 (3.3)
Pulmonary embolism (%)	0 (0.0)	2460 (3.5)
Dipyridamole (%)	78 (0.4)	2629 (3.8)
Hypertension (%)	3601 (17.4)	52064 (74.4)
NSAID (%)	3113 (15.1)	9965 (14.2)
Acetylsalicylic acid (%)	3685 (17.8)	29205 (41.7)
ADP-inhibitor (%)	335 (1.6)	8793 (12.6)
PCI (%)	252 (1.2)	6104 (8.7)
CABG (%)	109 (0.5)	3182 (4.5)
CHA ₂ DS ₂ VASC (median [IQR])	1.0 [0.0, 1.0]	4.0 [3.0, 5.0]
CHA ₂ DS ₂ VASC (%)		
0	5678 (27.5)	-

1	10231 (49.5)	-
2	4764 (23.0)	11373 (16.2)
3	-	20143 (28.8)
4	-	19378 (27.7)
5	-	11020 (15.7)
>5	-	8106 (11.6)
HAS-BLED (median [IQR])	1.0 [0.0, 1.0]	2.0 [2.0, 3.0]
HAS-BLED category (%)		
0	7844 (37.9)	453 (0.6)
1	9297 (45.0)	10659 (15.2)
2	3083 (14.9)	28087 (40.1)
3	400 (1.9)	24598 (35.1)
>3	49 (0.2)	6223 (8.9)
GARFIELD-AF stroke (median [IQR])	0.68 [0.52, 0.94]	1.33 [0.89, 2.09]
GARFIELD-AF, bleed (median [IQR])	0.59 [0.44, 0.76]	1.27 [0.95, 1.69]

Table S3 footnotes. Abbreviations. TIA; transient ischemic attack, SE; systemic embolism, OAC; oral anticoagulants, NOAC; non-vitamin-K antagonist, VKA; vitamin-K antagonist; NSAID; non-steroidal anti-inflammatory drug, ADP; adenosine diphosphate, PCI; Percutaneous coronary intervention, CABG; Coronary Artery Bypass Grafting.

Table S4. Logistic regression coefficients of GARFIELD-AF model for stroke/SE and major bleeding in the GARFIELD-AF Global cohort and the Danish AF cohort.

Variable	GARFIELD-AF Global registry	Danish AF cohort	P value*
Stroke/SE			
Age	0.030	0.026	<0.001
Prior Stroke/SE	0.952	1.572	<0.001
Bleeding	0.432	0.191	0.001
Heart failure	0.319	0.065	0.269
Chronic kidney disease	0.574	0.091	0.332
OAC	-0.582	-0.396	<0.001
Major bleeding			
Age	0.039	0.041	<0.001
Vascular disease	0.515	0.363	<0.001
Chronic kidney disease	0.577	0.865	<0.001

Table S4 footnotes. Abbreviations. SE; systemic embolism, OAC; oral anticoagulant.

* P value for coefficients in the Danish AF cohort

Figure S1. Flowchart of study population

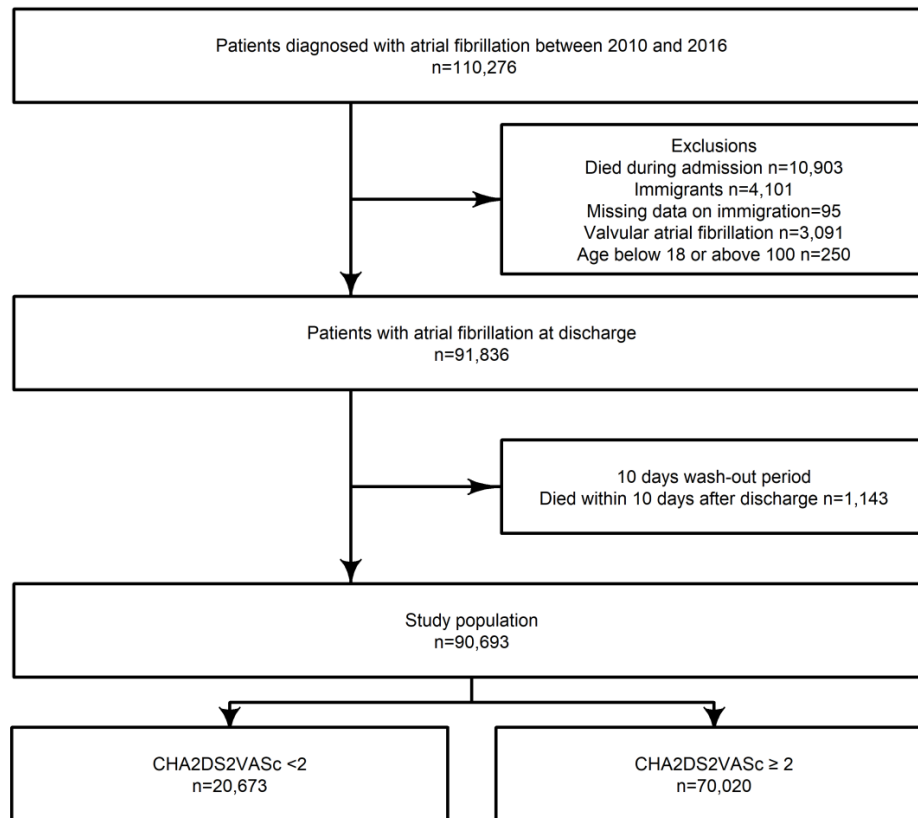


Figure S2. Cumulative incidence of ischemic stroke in the Danish population stratified by low and high stroke risk

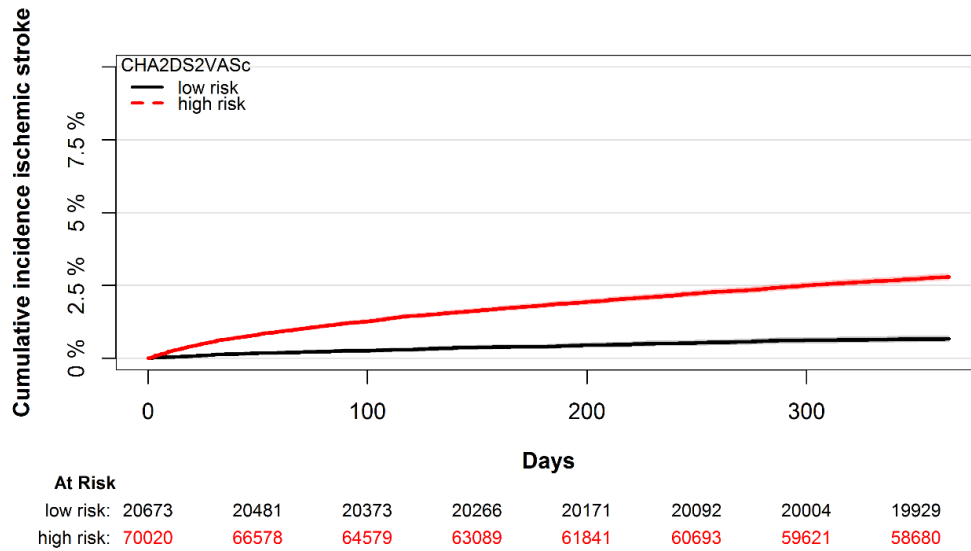


Figure S2 legend. Low risk patients were defined as CHA₂DS₂-VASc score (≤ 2 for women, 0-1 for men and > 2 for women and > 1 for men).