Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Creation of cohorts for present study based on data from previous study

In a previous study[1] we used the Danish Stroke Registry[2] (Stroke Registry) to identify 16,765 patients with first-ever intracerebral hemorrhage (ICH) admitted in 2005-2018 in Denmark. We matched each of these cases on age, sex, and index date (date of admission of case) to 660,477 general population controls.[1] The index date from the previous study is referred to here as inclusion date to avoid confusion with the nomenclature used in the nested case-control analysis planned as part of the present study (see main text). In the previous case-control study, we used risk-set sampling and controls were replaced after selection. This meant that individuals could be included as controls more than once and also that individuals sampled as controls could later become cases. In this study we defined the ICH-cohort and the comparison cohort to be mutually exclusive (i.e., individuals contributed only to one cohort). Therefore, we identified the chronologically first status of each individual and classified individuals accordingly as belonging to the ICH cohort or the comparison cohort (eFigure 1). In accordance with how we defined the source population (see main text), we excluded individuals aged <45 years on inclusion date (as ICH in this age-group is more likely to be non-spontaneous and ischemic events are less likely to occur in ICH survivors); and patients from the ICH-cohort who died within 30 days of their inclusion date (~30%) as well as patients from the comparison cohort who died within 30 days of their respective inclusion date (eFigure 1). For cohort members who survived the first 30 days, we ignored admissions with diagnosis codes corresponding to major vascular events recorded on day 0 to 30 post-inclusion date (i.e., we applied a 30-day blanking period). This was based on results of a previous validation study, where we found the positive predictive value (PPV) of a diagnosis of recurrent spontaneous symptomatic ICH (re-ICH) to be very low if the first 30-day period after an ICH is included. Conversely, if a 30-day blanking period is used, the PPV for re-ICH in DSR is high (90%) with an acceptable sensitivity (76%).[3] Consequently, the start date for the present study was 31 days after the inclusion date.

Assessment of exposure to medications

Information on prescriptions dispensed at community pharmacies in Denmark has been prospectively recorded in the Danish National Prescription Registry[4] (Prescription Registry) since 1995. For each prescription, the date of dispensing and a full account of the dispensed product, including the anatomical therapeutic chemical[5] (ATC) code, are recorded. The indication and prescribed dose are not available in the Prescription Registry.

To calculate date of end of supply of each prescription, we set each prescription to last the number of days that corresponded to the number of pills dispensed (for dipyridamole, ticagrelor, dabigatran, apixaban, and all nonsteroidal anti-inflammatory drugs divided by a factor of 2; and for warfarin divided by a factor of 1.5[6]); however, for proton pump inhibitors (PPI) we instead used the defined daily dose[5] (DDD; 1 DDD corresponds to 20 mg omeprazole, 40mg pantoprazole, 30mg lansoprazole, 20mg rabeprazole, 30mg esomeprazole).

After calculating the length of each supply as described above, we calculated episodes of treatment.

We did this based on prescriptions for drugs in the 10-year period up to inclusion date for the cohort analysis (eFigure 2). Between pairs of consecutive prescriptions, we allowed a grace period of 60 days between the end of supply of the first prescription of that pair and the date of the next prescription. Based on the most recent treatment episode before the inclusion date, we divided exposure by recency into current use (prescription supply covered the inclusion date or ended less than 30 days before the inclusion date), past use (prescription supply ended 31-365 days before inclusion date), and non-use (no recorded prescription, or prescription supply ended more than 365 days before inclusion date). A treatment episode for a drug or drug class comprised the length of consecutive prescriptions allowing for gaps between prescriptions of 60 days or less (grace period).

For the nested case-control analysis we used the same approach but with the index date as the reference point (as opposed to inclusion date in the cohort analysis) (eFigure 3). Using both the exposure history in the 10-year period before inclusion date and exposures to drugs during follow-up and based on the most recent treatment episode before the index date, we divided exposure by recency into current use (prescription supply covered the index date or ended less than 30 days before the index date), past use (prescription supply ended 31-365 days before index date), and non-use (no recorded prescription, or prescription supply ended more than 365 days before index date).

Statistical analysis

Nested case-control analysis

We performed subgroup analyses for sex, age (<75 years; ≥75 years), atrial fibrillation (AF), diabetes (DM), history of ischemic stroke (IS), history of major ischemic vascular event (including IS), and history of major ischemic vascular event other than IS. In these analyses, AF and DM were classified based on all available prior information, while history of major ischemic vascular events, IS, and ICH were classified based on information at baseline (cohort entry). For the subgroup analyses, we re-sampled cases and controls to achieve comparisons of e.g., cases with AF and controls with AF on index date. For the subgroup analyses, we used unconditional logistic regression and included the same covariates as in the main case-control analyses, in addition to covariates for sex, age (5-year bands), index date year (3-year bands), and duration of follow-up (4-year bands).

eTable 1. Diagnosis and Procedure Codes for Study Covariates Identified in Danish National Patient Registry or Danish National Prescription Registry as Specified

	Diagnosis code (ICD-10) or procedure code (sksube) from Danish National Patient Registry (unless otherwise specified)	**Drug (ATC) code**
Primary outcomes *For diagnosis codes inpatient hospital contacts with primary position codes only (unless otherwise specified)*		
1. Ischemic stroke	I63 [in Danish Stroke Registry]	
2. Intracerebral hemorrhage	I61 [in Danish Stroke Registry]	
3. Myocardial infarction	I21, I22, I23	
4. Major vascular event		
4a. Stroke		
4a1. Ischemic stroke	I63 [in Danish Stroke Registry]	
4a2. Intracerebral hemorrhage	I61 [in Danish Stroke Registry]	
4a3. Stroke of unspecified type	I64 [in Danish Stroke Registry]	
4b. Myocardial infarction	I21, I22, I23	
4c. Systemic embolism	I74	
4d. Vascular death – Death within 30 days if a hospital admission for one or more of the following events:		
4d1. Stroke		
4d1a. Intracerebral hemorrhage	I61 [in Danish Stroke Registry]	
4d1b. Ischemic stroke	I63 [in Danish Stroke Registry]	
4d1c. Stroke of unspecified type	I64 [in Danish Stroke Registry]	
Any of the following non-stroke events:		
4d2. Intracranial extraaxial hemorrhage		
4d2a. Subdural hematoma	S065, I620	
4d2b. Subarachnoid hemorrhage	I60	
4d2c. Epidural hematoma	I621	
4d2d. Intracranial unspecified	I629	
4d3. Myocardial infarction	I21, I22, I23	
4d4. Systemic embolism	I74	
4d5. Revascularization procedures		

4d5a. Thrombolysis (any organ)[1]	BOHA1 (sksube)	
4d5b. Percutaneous coronary intervention[1] [includes stenting]	KFNG, KFNF (sksube)	
4d5c. Coronary artery bypass grafting	KFNA, KFNB, KFNC, KFND, KFNE, KFNH20 (sksube)	
4d5d. Carotid artery procedures (includes all arteries derived from aortic arch and its branches)[2]	KPAF (endarterectomy), KPAE (thrombectomy) (sksube)	
4d4e. Visceral artery, thrombectomy/embolectomy (mesenteric, renal, visceral)[2]	KPCE, KPCF (sksube)	
4d4f. Lower limb revascularization[3] (thrombectomy/embolectomy, stents, bypass surgery etc)	KPDE, KPDF, KPDH, KPDN, KPDP, KPDQ, KPEE, KPEF, KPEH, KPEN, KPEP, KPEQ, KPFE, KPFH, KPFN, KPFP, KPFQ, KPDU74, KPDU84 (sksube)	
4d6. Mesenteric ischemia	K550E K550H	
4d7. Sudden cardiac death	I461	
4d8. Venous thromboembolism (DVT/PE)	I26, I801, I802, I803, I808, I809	
4d9. Extracranial hemorrhage		
4d9a. Gastrointestinal bleed (upper, lower, or unspecified)	K228F, K250, K252, K254, K256, K260, K262, K638B, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K298A, K625, K638B, K638C, K290-K292, K920, K921, K922	
4d9b. Esophageal varicose vein hemorrhage or esophageal hemorrhage	I850, I864A, K228F	
4d9c. Hematuria	N02, R31	
4d9d. Hemopericardium	I312	
4d9e. Peritoneal hemorrhage	K661	
4d9f. Hemothorax	J942	
4d9g. Hemorrhage in bile duct or pancreas	K838F, K868G	
4d9h. Hemorrhage in spinal cord	G951A	
4d9i. Acute bleeding anemia	D62	
Secondary outcomes		

For diagnosis codes inpatient hospital contacts with primary position codes only (unless otherwise specified)		
1. Stroke		
1a. Ischemic stroke	I63 [in Danish Stroke Registry]	
1b. Intracerebral hemorrhage	I61 [in Danish Stroke Registry]	
1c. Stroke of uncertain type	I64 [in Danish Stroke Registry]	
2. Intracranial extraaxial hemorrhage		
2a.Subdural	S065, I620	
2b.Subarachnoid	I60	
2c. Epidural	I621	
2d. Intracranial unspecified	I629	
3. Systemic embolism	I74	
4. Mesenteric ischemia	K550E K550H	
5. Venous thromboembolism (DVT or PE)	I26, I801, I802, I803, I808, I809	
6. Extracranial hemorrhage		
6a. Gastrointestinal bleed (upper, lower, or unspecified)	K228F, K250, K252, K254, K256, K260, K262, K638B, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K298A, K625, K638B, K638C, K290-K292, K920, K921, K922	
6b. Esophageal varicose vein hemorrhage or esophageal hemorrhage	I850, I864A, K228F	
6c. Hematuria	N02, R31	
6d. Hemopericardium	I312	
6e. Peritoneal hemorrhage	K661	
6f. Hemothorax	J942	
6g. Hemorrhage in bile duct or pancreas	K838F, K868G	
6h. Hemorrhage in spinal cord	G951A	
6i. Acute bleeding anemia	D62	
7. Sudden cardiac death	I461	
8. Major adverse cardiovascular event		
8a. Ischemic stroke	I63 [in Danish Stroke Registry]	
8b. Stroke of uncertain type	I64 [in Danish Stroke Registry]	

8c. Myocardial infarction	I21, I22, I23	
8d. Systemic embolism	I74	
8e. Revascularization procedures		
8e1. Thrombolysis (any organ)[1]	BOHA1 (sksube)	
8e2. Percutaneous coronary intervention[1] [includes stenting]	KFNG, KFNF (sksube)	
8e3. Coronary artery bypass grafting	KFNA, KFNB, KFNC, KFND, KFNE, KFNH20 (DNPR, sksube)	
8e4. Carotid artery procedures (includes all arteries derived from aortic arch and its branches)[2]	KPAF (endarterectomy), KPAE (thrombectomy) (sksube)	
8e5. Visceral artery, thrombectomy/embolectomy (mesenteric, renal, visceral)[2]	KPCE, KPCF (sksube)	
8e6. Lower limb revascularization[3] (thrombectomy/embolectomy, stents, bypass surgery etc)	KPDE, KPDF, KPDH, KPDN, KPDP, KPDQ, KPEE, KPEF, KPEH, KPEN, KPEP, KPEQ, KPFE, KPFH, KPFN, KPFP, KPFQ, KPDU74, KPDU84 (sksube)	
8f. Mesenteric ischemia	K550E K550H	
8g. Venous thrombosis (DVT or PE)	I26, I801, I802, I803, I808, I809 (	
8h. Sudden cardiac death	I461	
9. Major hemorrhagic vascular event		
9a. ICH	I61 [in Danish Stroke Registry]	
9b. Extracranial hemorrhage		
9b1. Gastrointestinal bleed (upper, lower, or unspecified)	K228F, K250, K252, K254, K256, K260, K262, K638B, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K298A, K625, K638B, K638C, K290-K292, K920, K921, K922	
9b2. Esophageal varicose vein hemorrhage or esophageal hemorrhage	I850, I864A, K228F	
9b3. Hematuria	N02, R31	
9b4. Hemopericardium	I312	
9b5. Peritoneal hemorrhage	K661	
9b6. Hemothorax	J942	

9b7. Hemorrhage in bile duct or pancreas	K838F, K868G	
9b8. Hemorrhage in spinal cord	G951A	
9b9. Acute bleeding anemia	D62	
9c. Intracranial extraaxial hemorrhage		
9c1. Subdural	S065, I620	
9c2. Subarachnoid	I60	
9c3. Epidural	I621	
9c4. Intracranial unspecified	I629	
10. Major adverse cardiovascular event		
10a. Ischemic stroke	I63 [in Danish Stroke Registry]	
10b. Stroke of uncertain type	I64 [in Danish Stroke Registry]	
10c. Myocardial infarction	I21, I22, I23	
10d. Systemic embolism	I74	
10e. Revascularization procecdures		
10e1. Thrombolysis (any organ)[1]	BOHA1 (sksube)	
10e2. Percutaneous coronary intervention[1] [includes stenting]	KFNG, KFNF (sksube)	
10e3. Coronary artery bypass grafting	KFNA, KFNB, KFNC, KFND, KFNE, KFNH20 (sksube)	
10e4. Carotid artery procedures (includes all arteries derived from aortic arch and its branches)[2]	KPAF (endarterectomy), KPAE (thrombectomy) (sksube)	
10e5. Visceral artery, thrombectomy/embolectomy (mesenteric, renal, visceral)[2]	KPCE, KPCF (sksube)	
10e6. Lower limb revascularization[3] (thrombectomy/embolectomy, stents, bypass surgery etc)	KPDE, KPDF, KPDH, KPDN, KPDP, KPDQ, KPEE, KPEF, KPEH, KPEN, KPEP, KPEQ, KPFE, KPFH, KPFN, KPFP, KPFQ, KPDU74, KPDU84 (sksube)	
10f. Mesenteric ischemia	K550E K550H	
10g. Sudden cardiac death	I461	
11. All-cause death		
12. Vascular death – Death within 30 days of hospital admission for one or more of the following events:		

12a. Stroke		
12a1. Intracerebral hemorrhage	I61 [in Danish Stroke Registry]	
12a2. Ischemic stroke	I63 [in Danish Stroke Registry]	
12a3. Stroke of uncertain type	I64 [in Danish Stroke Registry]	
Any of the following non-stroke events:		
12b. Intracranial extraaxial hemorrhage		
12b1. Subdural	S065, I620	
12b2. Subarachnoid	I60	
12b3. Epidural	I621	
12b4. Intracranial unspecified	I629	
12c. Myocardial infarction	I21, I22, I23	
12d. Systemic embolism	I74	
12e. Revascularization procedures		
12e1. Thrombolysis (any organ)[1]	BOHA1 (sksube)	
12e2. Percutaneous coronary intervention[1] [includes stenting]	KFNG, KFNF (sksube)	
12e3. Coronary artery bypass grafting	KFNA, KFNB, KFNC, KFND, KFNE, KFNH20 (sksube)	
12e4. Carotid artery procedures (includes all arteries derived from aortic arch and its branches)[2]	KPAF (endarterectomy), KPAE (thrombectomy) (sksube)	
12e5. Visceral artery, thrombectomy/embolectomy (mesenteric, renal, visceral)[2]	KPCE, KPCF (sksube)	
12e6. Lower limb revascularization[3] (thrombectomy/embolectomy, stents, bypass surgery etc)	KPDE, KPDF, KPDH, KPDN, KPDP, KPDQ, KPEE, KPEF, KPEH, KPEN, KPEP, KPEQ, KPFE, KPFH, KPFN, KPFP, KPFQ, KPDU74, KPDU84 (sksube)	
12f. Mesenteric ischemia	K550E K550H	
12g. Sudden cardiac death	I461	
12h. Venous thromboembolism (DVT or PE)	I26, I801, I802, I803, I808, I809	
12i. Extracranial hemorrhage		
12i1.Gastrointestinal bleed (upper, lower, or unspecified)	K228F, K250, K252, K254, K256, K260, K262, K638B, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K298A,	

	K625, K638B, K638C, K290-K292, K920, K921, K922	
12i2. Esophageal varicose vein hemorrhage or esophageal hemorrhage	I850, I864A, K228F	
12i3. Hematuria	N02, R31	
12i4. Hemopericardium	I312	
12i5. Peritoneal hemorrhage	K661	
12i6. Hemothorax	J942	
12i7. Hemorrhage in bile duct or pancreas	K838F, K868G	
12i8. Hemorrhage in spinal cord	G951A	
12i9. Acute bleeding anemia	D62	
13. Non-vascular death (death not classified as vascular death)		
Covariates – Disorders *For diagnosis codes: Inpatient or outpatient, primary or secondary position (unless otherwise specified)*		
Hypertension	I10-I15	C03A, C08CA, C08DB01, C09A, C09B, C09C, C09D
Ischemic stroke	I63 [in Danish Stroke Registry]	
Myocardial infarction	I21, I22, I23	
Systemic embolism	I74	
Peripheral arterial disease	I702, I739	
Venous thromboembolism (DVT/PE)	I26, I801, I802, I803, I808, I809	
Diabetes	E10-E14	A10
Chronic kidney failure	N18 (excluding N181), N19, Z992, Z940	
Chronic hepatic diseases	K71-K77	
Atrial fibrillation	I48	
Congestive heart failure	I110, I130, I132, I420, I426, I427, I428, I429, I50	
Cancer	C00-C97 (C44 not included)	
Disorders/events or drug use indicative of alcohol misuse	E244, F10, G312, G621, G721, I426, K292, K70, K860, T510, T519, Z502, Z714, Z721,	N07BB

Chronic obstructive pulmonary disorder (COPD)	J42, J42, J44	R03 [in subjects aged 45+ years]
Covariates – use of medications		
Antiplatelet drugs		
Aspirin – low dose		B01AC06 – acetylsalicylic acid (75 mg, 100 mg, or 150 mg per tablet) B01AC30 - acetylsalicylic acid (50 mg per tablet) in combination with dipyridamole
Clopidogrel		B01AC04 (75 mg per tablet)
Dipyridamole		B01AC07 (100 mg per tablet, or 200 mg per tablet)
Other ADP-receptor blockers		B01AC22 – prasugrel (5 mg, or 10 mg per tablet) B01AC24 – ticagrelor (60 mg, or 90 mg per tablet)
Anticoagulant drugs		
Vitamin K antagonists		B01AA
Direct oral anticoagulants (DOAC)		
Dabigratran		B01AE07
Rivaroxaban		B01AF01
Apixaban		B01AF02
Edoxaban		B01AF03
Drugs with antihypertensive effects[a]		
Thiazides and other non-loop diuretics		C03A, C03D, C03E
Loop diuretics		C03C
Beta-blockers		C07
Calcium channel blockers		C08
ACE inhibitors and Angiotensin II receptor blockers (plain or in combinations)		C09A, C09B, C09C, C09D
Statins		C10AA

Selective serotonin reuptake inhibitors		N06AB
Nonsteroidal anti-inflammatory drugs		M01A (including Cox2 inhibitors), excluding M01AX
Proton pump inhibitors		A02BC

[a]Indication for drug use not available; some of the drugs may have been used for indications other than hypertension. Note that 'ever use' of some of these drugs was included in the definition of the hypertension covariate (i.e., C03A, C08CA, C08DB01, C09A, C09B, C09C, C09D).

eTable 2. Crude Incidence Rates of Primary Outcomes During Follow-up, Overall and Stratified by Baseline Comorbidities

	Ischemic stroke			**Myocardial infarct**			**Intracerebral hemorrhage**			**Major adverse cardiovascular events**[1]		
Baseline characteristic /comorbidity	Person-years	No. of events	Event rate per 100 pyrs (95% CI)	Person-years	No. of events	Event rate per 100 pyrs (95% CI)	Person-years	No. of events	Event rate per 100 pyrs (95% CI)	Person-years	No. of events	Event rate per 100 pyrs (95% CI)
All												
ICH-cohort	37,482	571	1.52 (1.40-1.65)	37,482	194	0.52 (0.45-0.60)	37,482	538	1.44 (1.32-1.56)	37,208	1,547	4.16 (3.96-4.37)
Comparison cohort	2,216,351	12,416	0.56 (0.55-0.57)	2,216,351	10,669	0.48 (0.47-0.49)	2,216,351	1,377	0.06 (0.06-0.07)	2,210,939	29,780	1.35 (1.33-1.36)
Male sex												
ICH-cohort	20,829	319	1.53 (1.37-1.71)	20,829	119	0.57 (0.48-0.68)	20,829	266	1.28 (1.13-1.44)	20,664	844	4.08 (3.82-4.37)
Comparison cohort	1,193,409	6,881	0.58 (0.56-0.59)	1,193,409	6,933	0.58 (0.57-0.59)	1,193,409	707	0.06 (0.06-0.06)	1,190,362	17,505	1.47 (1.45-1.49)
Female sex												
ICH-cohort	16,654	252	1.51 (1.34-1.71)	16,654	75	0.45 (0.36-0.56)	16,654	272	1.63 (1.45-1.84)	16,544	703	4.25 (3.95-4.58)
Comparison cohort	1,022,943	5,535	0.54 (0.53-0.56)	1,022,943	3,736	0.37 (0.35-0.38)	1,022,943	670	0.07 (0.06-0.07)	1,020,577	12,275	1.20 (1.18-1.22)
Age 45-59 years												

	Ischemic stroke			Myocardial infarct			Intracerebral hemorrhage			Major adverse cardiovascular events[1]		
ICH-cohort	10,047	100	1.00 (0.82-1.21)	10,047	43	0.43 (0.32-0.58)	10,047	75	0.75 (0.60-0.94)	9,999	247	2.47 (2.18-2.80)
Comparison cohort	499,588	1,029	0.21 (0.19-0.22)	499,588	1,298	0.26 (0.25-0.27)	499,588	97	0.02 (0.02-0.02)	499,025	2,680	0.54 (0.52-0.56)
Age 60-74 years												
ICH-cohort	17,160	248	1.45 (1.28-1.64)	17,160	77	0.45 (0.36-0.56)	17,160	247	1.44 (1.27-1.63)	17,010	655	3.85 (3.57-4.16)
Comparison cohort	966,747	4,791	0.50 (0.48-0.51)	966,747	4,317	0.45 (0.43-0.46)	966,747	481	0.05 (0.05-0.05)	964,582	11,145	1.16 (1.13-1.18)
Age 75-84 years												
ICH-cohort	8,118	178	2.19 (1.89-2.54)	8,118	54	0.67 (0.51-0.87)	8,118	176	2.17 (1.87-2.51)	8,048	512	6.36 (5.83-6.94)
Comparison cohort	564,451	4,885	0.87 (0.84-0.89)	564,451	3,818	0.68 (0.66-0.70)	564,451	625	0.11 (0.10-0.12)	562,369	11,720	2.08 (2.05-2.12)
Age 85+ years												
ICH-cohort	2,157	45	2.09 (1.56-2.79)	2,157	20	0.93 (0.60-1.44)	2,157	40	1.85 (1.36-2.53)	2,152	133	6.18 (5.21-7.33)
Comparison cohort	185,566	1,711	0.92 (0.88-0.97)	185,566	1,236	0.67 (0.63-0.70)	185,566	174	0.09 (0.08-0.11)	184,963	4,235	2.29 (2.22-2.36)

	Ischemic stroke			Myocardial infarct			Intracerebral hemorrhage			Major adverse cardiovascular events[1]		
Atrial Fibrillation[2]												
Yes												
ICH-cohort	4,015	114	2.84 (2.36-3.41)	4,015	30	0.75 (0.52-1.07)	4,015	59	1.47 (1.14-1.90)	3,947	251	6.36 (5.62-7.20)
Comparison cohort	133,293	1,254	0.94 (0.89-0.99)	133,293	845	0.63 (0.59-0.68)	133,293	167	0.13 (0.11-0.15)	132,759	3,028	2.28 (2.20-2.36)
No												
ICH-cohort	33,467	457	1.37 (1.25-1.50)	33,467	164	0.49 (0.42-0.57)	33,467	479	1.43 (1.31-1.57)	33,261	1,296	3.90 (3.69-4.11)
Comparison cohort	2,083,059	11,162	0.54 (0.53-0.55)	2,083,059	9,824	0.47 (0.46-0.48)	2,083,059	1,210	0.06 (0.05-0.06)	2,078,180	26,752	1.29 (1.27-1.30)
Hx of Ischemic stroke[2]												
Yes												
ICH-cohort	4,400	118	2.68 (2.24-3.21)	4,400	19	0.43 (0.28-0.68)	4,400	61	1.39 (1.08-1.78)	4,351	234	5.38 (4.73-6.11)
Comparison cohort	54,227	782	1.44 (1.34-1.55)	54,227	329	0.61 (0.54-0.68)	54,227	85	0.16 (0.13-0.19)	53,894	1,495	2.77 (2.64-2.92)
Hx of Ischemic stroke[2]												
No												

ICH-cohort	33,083	453	1.37 (1.25-1.50)	33,083	175	0.53 (0.46-0.61)	33,083	477	1.44 (1.32-1.58)	32,857	1,313	4.00 (3.79-4.22)
	Ischemic stroke			**Myocardial infarct**			**Intracerebral hemorrhage**			**Major adverse cardiovascular events**[1]		
ICH-cohort	33,083	453	1.37 (1.25-1.50)	33,083	175	0.53 (0.46-0.61)	33,083	477	1.44 (1.32-1.58)	32,857	1,313	4.00 (3.79-4.22)
Comparison cohort	2,162,124	11,634	0.54 (0.53-0.55)	2,162,124	10,340	0.48 (0.47-0.49)	2,162,124	1,292	0.06 (0.06-0.06)	2,157,045	28,285	1.31 (1.30-1.33)
Diabetes[2]												
Yes												
ICH-cohort	3,916	69	1.76 (1.39-2.23)	3,916	29	0.74 (0.51-1.07)	3,916	54	1.38 (1.06-1.80)	3,864	188	4.87 (4.22-5.61)
Comparison cohort	192,541	1,488	0.77 (0.73-0.81)	192,541	1,533	0.80 (0.76-0.84)	192,541	134	0.07 (0.06-0.08)	191,947	3,927	2.05 (1.98-2.11)
Diabetes[2]												
No												
ICH-cohort	33,567	502	1.50 (1.37-1.63)	33,567	165	0.49 (0.42-0.57)	33,567	484	1.44 (1.32-1.58)	33,344	1,359	4.08 (3.86-4.30)
Comparison cohort	2,023,810	10,928	0.54 (0.53-0.55)	2,023,810	9,136	0.45 (0.44-0.46)	2,023,810	1,243	0.06 (0.06-0.06)	2,018,992	25,853	1.28 (1.26-1.30)
Chronic kidney failure[2]												
Yes												
ICH-cohort	453	14	3.09	453	7	1.54	453	12	2.65	452	41	9.08

			(1.83-5.21)			(0.74-3.24)			(1.50-4.66)			(6.69-12.33)
	Ischemic stroke			**Myocardial infarct**			**Intracerebral hemorrhage**			**Major adverse cardiovascular events**[1]		
Comparison cohort	20,424	133	0.65 (0.55-0.77)	20,424	198	0.97 (0.84-1.11)	20,424	13	0.06 (0.04-0.11)	20,360	497	2.44 (2.24-2.67)
No												
ICH-cohort	37,029	557	1.50 (1.38-1.63)	37,029	187	0.51 (0.44-0.58)	37,029	526	1.42 (1.30-1.55)	36,756	1,506	4.10 (3.90-4.31)
Comparison cohort	2,195,927	12,283	0.56 (0.55-0.57)	2,195,927	10,471	0.48 (0.47-0.49)	2,195,927	1,364	0.06 (0.06-0.07)	2,190,579	29,283	1.34 (1.32-1.35)
Chronic hepatic disease[2]												
Yes												
ICH-cohort	464	10	2.15 (1.16-4.00)	464	<5	0.86 (0.32-2.30)	464	10	2.15 (1.16-4.00)	464	30	6.46 (4.52-9.24)
Comparison cohort	12,215	68	0.56 (0.44-0.71)	12,215	63	0.52 (0.40-0.66)	12,215	7	0.06 (0.03-0.12)	12,188	196	1.61 (1.40-1.85)
No												
ICH-cohort	37,018	561	1.52 (1.40-1.65)	37,018	190	0.51 (0.45-0.59)	37,018	528	1.43 (1.31-1.55)	36,744	1,517	4.13 (3.93-4.34)
Comparison cohort	2,204,136	12,348	0.56 (0.55-0.57)	2,204,136	10,606	0.48 (0.47-0.49)	2,204,136	1,370	0.06 (0.06-0.07)	2,198,752	29,584	1.35 (1.33-1.36)
COPD[2,3]												

	Ischemic stroke			Myocardial infarct			Intracerebral hemorrhage			Major adverse cardiovascular events[1]		
Yes												
ICH-cohort	7,499	133	1.77 (1.50-2.10)	7,499	48	0.64 (0.48-0.85)	7,499	110	1.47 (1.22-1.77)	7,447	353	4.74 (4.27-5.26)
Comparison cohort	426,751	2,563	0.60 (0.58-0.62)	426,751	2,495	0.58 (0.56-0.61)	426,751	299	0.07 (0.06-0.08)	425,459	6,751	1.59 (1.55-1.63)
No												
ICH-cohort	29,984	438	1.46 (1.33-1.60)	29,984	146	0.49 (0.41-0.57)	29,984	428	1.43 (1.30-1.57)	29,761	1194	4.01 (3.79-4.25)
Comparison cohort	1,789,600	9,853	0.55 (0.54-0.56)	1,789,600	8,174	0.46 (0.45-0.47)	1,789,600	1,078	0.06 (0.06-0.06)	1,785,480	23,029	1.29 (1.27-1.31)
High alcohol intake[2,4]												
Yes												
ICH-cohort	3,120	63	2.02 (1.58-2.58)	3,120	11	0.35 (0.20-0.64)	3,120	44	1.41 (1.05-1.90)	3,109	148	4.76 (4.05-5.59)
Comparison cohort	66,884	434	0.65 (0.59-0.71)	66,884	313	0.47 (0.42-0.52)	66,884	57	0.09 (0.07-0.11)	66,690	1,049	1.57 (1.48-1.67)
No												
ICH-cohort	34,362	508	1.48 (1.36-1.61)	34,362	183	0.53 (0.46-0.62)	34,362	494	1.44 (1.32-1.57)	34,098	1,399	4.10 (3.89-4.32)
Comparison cohort	2,149,468	11,982	0.56 (0.55-0.57)	2,149,468	10,356	0.48 (0.47-0.49)	2,149,468	1,320	0.06 (0.06-0.06)	2,144,249	28,731	1.34 (1.32-1.36)

[1]Defined as stroke [ischemic stroke, intracerebral hemorrhage, or ‘unspecified stroke’], myocardial infarction, systemic embolism, or vascular death
[2] Assessed at baseline based on data from previous 10 years.
[3]Chronic obstructive pulmonary disease.
[4]Disorder or drug use indicative of high alcohol intake.

eTable 3. Hazard Ratio of Primary Outcomes and Select Secondary Outcomes in ICH Cohort, Overall and Stratified by Age, Sex, and Baseline Comorbidities (Comparison Cohort Used as Reference)

	Event during follow-up						
	Ischemic stroke		Myocardial infarction		Intracerebral hemorrhage		
Baseline characteristic /comorbidity	HR[1] (95% CI)	aHR[2] (95% CI)	HR[1] (95% CI)	aHR[2] (95% CI)	HR[1] (95% CI)	aHR[2] (95% CI)	
All	2.79 (2.57-3.04)	2.64 (2.43-2.88)	1.08 (0.93-1.24)	1.12 (0.97-1.29)	23.7 (21.4-26.2)	23.5 (21.1-26.1)	
Male sex	2.71 (2.43-3.04)	2.48 (2.21-2.78)	0.98 (0.82-1.18)	1.03 (0.86-1.24)	22.1 (19.2-25.4)	22.1 (19.0-25.7)	
Female sex	2.89 (2.55-3.28)	2.88 (2.53-3.27)	1.24 (0.98-1.56)	1.29 (1.03-1.63)	25.6 (22.2-29.5)	25.6 (22.0-29.7)	
Age 45-59 years	4.98 (4.05-6.11)	3.21 (2.56-4.01)	1.66 (1.23-2.25)	1.42 (1.04-1.95)	38.6 (28.5-52.2)	31.2 (22.1-44.0)	
Age 60-74 years	3.03 (2.67-3.44)	2.44 (2.14-2.78)	1.02 (0.81-1.28)	0.98 (0.78-1.22)	30.5 (26.1-35.6)	28.1 (23.8-33.1)	
Age 75-84 years	2.71 (2.33-3.14)	2.46 (2.11-2.86)	1.00 (0.76-1.30)	1.04 (0.79-1.36)	20.8 (17.6-24.7)	18.2 (15.2-21.8)	
Age 85+ years	2.31 (1.71-3.10)	1.94 (1.44-2.61)	1.32 (0.85-2.06)	1.28 (0.82-2.00)	20.8 (14.7-29.5)	18.2 (12.7-26.3)	
Atrial Fibrillation[3]							
Yes	3.04 (2.51-3.68)	2.99 (2.46-3.64)	1.16 (0.81-1.67)	1.19 (0.82-1.72)	11.9 (8.8-16.9)	10.8 (7.9-14.8)	
No	2.63 (2.39-2.88)	2.56 (2.32-2.81)	1.04 (0.89-1.22)	1.10 (0.94-1.28)	25.3 (22.8-28.1)	26.2 (23.4-29.3)	
Hx of Ischemic stroke[3]							
Yes	1.83 (1.51-2.23)	2.01 (1.64-2.47)	0.71 (0.44-1.12)	0.85 (0.53-1.37)	8.5 (6.1-11.8)	9.7 (6.8-13.9)	
No	2.63 (2.39-2.89)	2.68 (2.44-2.95)	1.11 (0.96-1.29)	1.15 (0.99-1.33)	24.9 (22.4-27.7)	25.4 (22.7-28.4)	
Diabetes[3]							
Yes	2.31 (1.82-2.94)	2.16 (1.68-2.76)	0.93 (0.64-1.34)	1.03 (0.71-1.49)	19.9 (14.5-27.4)	21.6 (15.4-30.4)	
No	2.85 (2.61-3.12)	2.71 (2.47-2.97)	1.10 (0.94-1.28)	1.13 (0.97-1.32)	24.1 (21.7-26.8)	23.8 (21.3-26.6)	
Chronic kidney failure[3]							

	Ischemic stroke			Myocardial infarction			Intracerebral hemorrhage	
Yes	4.68 (2.70-8.14)	3.62 (2.01-6.54)		1.56 (0.73-3.31)	1.34 (0.61-2.93)		38.6 (17.5-85.0)	77.84 (25.74-235.42)
No	2.76 (2.54-3.01)	2.61 (2.40-2.85)		1.06 (0.92-1.23)	1.11 (0.96-1.28)		23.5 (21.2-26.0)	23.2 (20.8-25.9)
Chronic hepatic disease[3]								
Yes	3.97 (2.03-7.74)	4.17 (1.97-8.83)		1.57 (0.57-4.32)	1.96 (0.67-5.72)		40.5 (15.3-107.7)	582 (49.5-6841)
No	2.78 (2.55-3.02)	2.63 (2.41-2.86)		1.07 (0.93-1.23)	1.12 (0.97-1.29)		23.5 (21.3-26.0)	23.4 (21.0-26.0)
COPD[3, 4]								
Yes	3.00 (2.52-3.57)	2.81 (2.35-3.36)		1.08 (0.81-1.44)	1.14 (0.86-1.53)		21.6 (17.3-26.9)	20.5 (16.2-26.0)
No	2.73 (2.48-3.01)	2.58 (2.34-2.85)		1.07 (0.91-1.26)	1.11 (0.94-1.31)		24.2 (21.7-27.1)	24.7 (21.9-27.8)
High alcohol intake[3, 4]								
Yes	3.22 (2.47-4.20)	2.95 (2.23-3.90)		0.76 (0.42-1.38)	0.78 (0.42-1.43)		16.0 (10.8-23.8)	15.6 (10.2-24.0)
No	2.72 (2.49-2.97)	2.60 (2.37-2.84)		1.11 (0.96-1.28)	1.15 (0.99-1.33)		24.0 (21.7-26.7)	23.9 (21.5-26.7)

	Event during follow-up						
	Major Vascular Event		Vascular death			Unspecified stroke	
Baseline characteristic /comorbidity	HR[1] (95% CI)	adjHR[2] (95% CI)	HR[1] (95% CI)	aHR[2] (95% CI)		HR[1] (95% CI)	aHR[2] (95% CI)
All	3.15 (2.99-3.31)	3.13 (2.97-3.30)	2.96 (2.58-3.41)	3.20 (2.78-3.69)		3.64 (2.74-4.84)	3.39 (2.53-4.53)
Male sex	2.82 (2.63-3.02)	2.77 (2.58-2.97)	2.85 (2.37-3.43)	3.04 (2.52-3.67)		3.96 (2.73-5.74)	3.50 (2.39-5.12)
Female sex	3.62 (3.36-3.91)	3.69 (3.42-3.99)	3.11 (2.51-3.84)	3.43 (2.76-4.26)		3.27 (2.11-5.09)	3.31 (2.12-5.19)
Age 45-59 years	4.69 (4.12-5.34)	3.38 (2.94-3.89)	8.80 (5.85-13.22)	4.97 (3.18-7.79)		7.77 (3.49-17.28)	4.09 (1.61-10.40)
Age 60-74 years	3.45 (3.19-3.73)	2.98 (2.75-3.23)	3.39 (2.65-4.35)	2.84 (2.20-3.65)		5.23 (3.40-8.03)	3.65 (2.33-5.71)
Age 75-84 years	3.23 (2.96-3.53)	3.10 (2.83-3.39)	3.46 (2.79-4.29)	3.31 (2.66-4.11)		3.18 (1.95-5.19)	2.95 (1.80-4.85)
Age 85+ years	2.72 (2.29-3.24)	2.43 (2.04-2.89)	2.61 (1.78-3.84)	2.36 (1.60-3.47)		1.83 (0.68-4.94)	1.77 (0.65-4.83)
Atrial Fibrillation[3]							
Yes	2.79 (2.46-3.18)	2.85 (2.49-3.25)	1.73 (1.22-2.46)	1.93 (1.35-2.75)		3.26 (1.70-6.27)	3.32 (1.70-6.51)
No	3.10 (2.93-3.27)	3.16 (2.98-3.34)	3.10 (2.66-3.61)	3.57 (3.06-4.17)		3.54 (2.58-4.85)	3.35 (2.43-4.63)
Hx of Ischemic stroke[3]							
Yes	1.91 (1.67-2.20)	2.24 (1.93; 2.59)	1.83 (1.28; 2.60)	2.90 (1.99; 4.24)		1.84 (0.94-3.59)	1.52 (0.75-3.11)
No	3.12 (2.95; 3.30)	3.21 (3.04- 3.40)	2.88 (2.47; 3.36)	3.19 (2.73-3.72)		3.56 (2.60-4.88)	3.62 (2.63-4.99)
Diabetes[3]							
Yes	2.41 (2.08-2.78)	2.49 (2.14-2.89)	2.23 (1.54-3.23)	2.65 (1.81-3.88)		3.85 (1.78-8.33)	2.96 (1.32-6.62)
No	3.26 (3.08-3.44)	3.22 (3.05-3.41)	3.08 (2.65-3.58)	3.29 (2.82-3.83)		3.60 (2.65-4.88)	3.42 (2.51-4.68)
Chronic kidney failure[3]							
Yes	3.68 (2.68-5.07)	3.27 (2.33-4.58)	2.05 (0.91-4.66)	2.09 (0.90-4.89)		9.70 (2.12-44.45)	12.29 (1.71-88.10)
No	3.13 (2.97-3.30)	3.10 (2.94-3.27)	2.99 (2.59-3.44)	3.23 (2.80-3.73)		3.55 (2.66-4.74)	3.30 (2.46-4.44)

	Major Vascular Event			Vascular death			Unspecified stroke	
Chronic hepatic disease[3]								
Yes	4.01 (2.72-5.90)	3.83 (2.50-5.88)		3.38 (1.53-7.45)	2.67 (1.09-6.52)		NA*	NA*
No	3.13 (2.97-3.30)	3.12 (2.96-3.29)		2.92 (2.53-3.37)	3.19 (2.76-3.68)		3.68 (2.77-4.89)	3.42 (2.56-4.57)
COPD[3,4]								
Yes	3.01 (2.71-3.36)	3.03 (2.71-3.38)		2.74 (2.08-3.60)	3.05 (2.30-4.03)		1.75 (0.78-3.95)	1.59 (0.70-3.62)
No	3.18 (3.00-3.38)	3.15 (2.97-3.34)		3.04 (2.59-3.57)	3.27 (2.77-3.85)		4.24 (3.13-5.75)	3.91 (2.87-5.34)
High alcohol intake[3, 5]								
Yes	3.07 (2.59-3.65)	2.90 (2.42-3.48)		2.78 (1.86-4.15)	2.73 (1.79-4.16)		3.09 (0.91-10.51)	2.54 (0.67-9.66)
No	3.12 (2.96-3.29)	3.13 (2.96-3.30)		2.87 (2.47-3.33)	3.18 (2.74-3.70)		3.73 (2.78-5.00)	3.45 (2.56-4.65)

Abbreviation: NA: Not Applicable (too few events).
[1]Hazard ratio, unadjusted.
[2]Hazard ratio adjusted for sex, age (5-year bands), study period (4-5 year bands), baseline comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, IS, MI, systemic embolism, PAD, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and baseline current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors].
[3]Assessed at baseline based on data from previous 10 years.
[4]Chronic obstructive pulmonary disease.
[5]Disorder indicative of high alcohol intake.

eTable 4. Hazard Ratios for Primary Outcomes and Select Secondary Outcomes in ICH Cohort With Comparison Cohort as Reference and Including Estimates That Adjust for Death as Competing Event

	ICH-cohort vs comparison cohort (reference)		
Primary outcomes and select secondary outcomes (in italics)	HR[1] (95% CI)	aHR[2] (95% CI)	sdHR[3] (95% CI)
Ischemic stroke	2.79 (2.57-3.04)	2.64 (2.43-2.88)	1.72 (1.58-1.88)
Intracerebral hemorrhage	23.7 (21.4-26.2)	23.5 (21.1-26.13)	15.5 (13.9-17.2)
'Unspecified stroke'	3.64 (2.74-4.84)	3.39 (2.53-4.53)	2.40 (1.79-3.20)
Myocardial infarction (MI)	1.08 (0.93-1.24)	1.12 (0.97-1.29)	0.77 (0.67-0.89)
MACE[4]	3.16 (3.01-3.33)	3.14 (2.98-3.31)	2.15 (2.04-2.27)
Vascular death[5]	3.06 (2.64-3.55)	3.30 (2.83-3.84)	1.77 (1.54-2.04)

[1]Hazard ratio, unadjusted.
[2]Hazard ratio adjusted for sex, age (5-year bands), study period (4-5 year bands), baseline comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and baseline current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors].
[3]Subdistibution hazard ratio adjusted for same covariates as above with all-cause-death as competing event.
[4]Major adverse cardiovascular event defined as stroke (ischemic stroke, intracerebral hemorrhage, or 'unspecified stroke'), myocardial infarction, systemic embolism, or vascular death.
[5]Death recorded as sudden cardiac death, or death within 30 days of any of following events: stroke (ischemic stroke, intracerebral hemorrhage, or unspecified stroke), myocardial infarction, systemic embolism, intracranial extra-axial hemorrhage, revascularization procedure, mesenteric ischemia, venous thromboembolism (i.e., deep vein thrombosis or pulmonary embolism), or extracranial hemorrhage.

eTable 5. Incidence Rates of Primary and Secondary Study Outcomes Based on Individual Follow-up for Each Outcome With Censoring Only Contingent on Migration, Death, or End of Study Period (as Opposed to Main Analysis, Where First Occurrence of a Primary Outcome Was Also a Censoring Criterion)

	ICH cohort			Comparison cohort	
Outcome during follow-up	No. of events / person-years	Event rate per 100 person-years (95% CI)		No. of events / person-years	Event rate per 100 person-years (95% CI)
Primary outcomes and select secondary outcomes (in italics)					
Ischemic stroke (IS)	595/39,279	1.51 (1.40-1.64)		12,855/2,256,688	0.57 (0.56-0.58)
Intracerebral hemorrhage (ICH)	577/39,813	1.45 (1.34-1.57)		1,504/2,295,631	0.07 (0.06-0.07)
'Unspecified stroke'	58/40,841	0.14 (0.11-0.18)		825/2,293,980	0.04 (0.03-0.04)
Myocardial infarct (MI)	212/40,469	0.52 (0.46-0.60)		10,949/2,258,156	0.48 (0.48-0.49)
MACE[1]	1,584/37,208	4.26 (4.05-4.47)		30,706/2,210,939	1.39 (1.37-1.40)
Vascular death[2]	521/41,114	1.27 (1.16-1.38)		7,961/2,297,952	0.35 (0.34-0.35)
Secondary outcomes					
Mesenteric ischemia	<5/41,109	0.00 (0.00-0.02)		29/2,297,907	0.00 (0.00-0.00)
Systemic embolism	32/41,046	0.08 (0.06-0.11)		859/2,295,486	0.04 (0.04-0.04)
Venous thromboembolism	250/40,457	0.62 (0.55-0.70)		8,787/2,269,424	0.39 (0.38-0.40)
Intracranial extra-axial hemorrhage[3]	213/40,411	0.53 (0.46-0.60)		2,473/2,291,304	0.11 (0.10-0.11)
Extracranial hemorrhage[4]	681/39,181	1.74 (1.61-1.87)		22,723/2,219,206	1.02 (1.01-1.04)
Sudden cardiac death	23/41,113	0.06 (0.04-0.08)		506/2,297,951	0.02 (0.02-0.02)
All-cause-death	4,340/41,114	10.56 (10.25-1 0.87)		78,200/2,297,952	3.40 (3.38-3.43)
Major ischemic vascular event[5]	1,346/36,940	3.64 (3.45-3.84)		45,570/2,131,314	2.14 (2.12-2.16)

	ICH cohort			Comparison cohort	
	No. of events / person-years	Event rate per 100 person-years (95% CI)		No. of events / person-years	Event rate per 100 person-years (95% CI)
Major hemorrhagic vascular event[6]	1,385/37,369	3.71 (3.52-3.91)		26,199/2,211,136	1.18 (1.17-1.20)
Major arterial vascular event[7]	1,137/37,518	3.03 (2.86-3.21)		38,450/2,155,634	1.78 (1.77-1.80)
Non-vascular death[9]	3,819/41,114	9.29 (9.00-9.59)		70,239/2,297,952	3.06 (3.03-3.08)

[1]Major adverse cardiovascular event defined as stroke (ischemic stroke, intracerebral hemorrhage, or 'unspecified stroke'), myocardial infarction, systemic embolism, or vascular death.
[2]Death recorded as sudden cardiac death, or death within 30 days of any of following events: stroke (ischemic stroke, intracerebral hemorrhage, or 'unspecified stroke'), myocardial infarction, systemic embolism, intracranial extraaxial hemorrhage, revascularization procedure, mesenteric ischemia, venous thromboembolism, or extracranial hemorrhage.
[3]Subdural hematoma, subarachnoid hemorrhage, or epidural hematoma.
[4]Gastrointestinal hemorrhage or other major extracranial hemorrhage (for full definition see text).
[5]Defined as ischemic stroke, 'unspecified stroke', myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, venous thromboembolism, or sudden cardiac death.
[6]Defined as gastrointestinal hemorrhage or other major extracranial hemorrhage (for full definition see text) and also including intracranial extraaxial hemorrhages.
[7]Defined as ischemic stroke, 'unspecified stroke', myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, or sudden cardiac death.
[8]Deaths that do not fulfill criteria for vascular death (see above).

eTable 6. Nested Case-Control Analysis of the Risk of Ischemic Stroke During Follow-up Associated With Having Had an Intracerebral Hemorrhage at Baseline

	No. (%) cases	No. (%) controls	OR[1] (95% CI)	Adj.OR[2] (95% CI)
All	12,987	216,885		
No previous ICH[3]	12,416 (95.6)	213,060 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	571 (4.4)	3,825 (1.8)	2.63 (2.40-2.87)	2.00 (1.82-2.20)
Sex				
Male	7,200	120,247		
No previous ICH[3]	6,881 (95.6)	118,086 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	319 (4.4)	2,161 (1.8)	2.55 (2.26-2.88)	1.89 (1.66-2.14)
Female	5,787	96,638		
No previous ICH[3]	5,535 (95.6)	94,974 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	252 (4.4)	1,664 (1.7)	2.73 (2.38-3.13)	2.17 (1.88-2.51)
Age on index date				
<75 years	6,168	119,085		
No previous ICH[3]	5,820 (94.4)	116,899 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	348 (5.6)	2,186 (1.8)	3.36 (2.98-3.78)	2.25 (1.98-2.56)
≥75 years	6,819	97,800		
No previous ICH[3]	6,596 (96.7)	96,161 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	223 (3.3)	1,639 (1.7)	2.00 (1.73-2.31)	1.62 (1.39-1.89)
	No. (%) cases	**No. (%) controls**	**OR[5] (95% CI)**	**Adj.OR[6] (95% CI)**
Atrial fibrillation[7]				
Yes	3,106	24,878		
No previous ICH[3]	2,952 (95.0)	24,225 (97.4)	1 (reference)	1 (reference)
Previous ICH[4]	154 (5.0)	653 (2.6)	2.11 (1.76-2.54)	1.61 (1.33-1.95)
No	9,881	192,007		
No previous ICH[3]	9,464 (95.8)	188,835 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	417 (4.2)	3,172 (1.7)	2.73 (2.46-3.03)	2.30 (2.07-2.57)
Diabetes[7]				
Yes	2,198	28,224		
No previous ICH[3]	2,101 (95.6)	27,660 (98.0)	1 (reference)	1 (reference)

	No. (%) cases	No. (%) controls	OR[5] (95% CI)	Adj.OR[6] (95% CI)
Previous ICH[4]	97 (4.4)	564 (2.0)	2.31 (1.85-2.88)	1.81 (1.44-2.28)
No	10,789	188,661		
No previous ICH[3]	10,315 (95.6)	185,400 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	474 (4.4)	3,261 (1.7)	2.74 (2.48-3.03)	2.16 (1.94-2.39)
History of major ischemic vascular event[8]				
Yes	2,091	24,811		
No previous ICH[3]	1,861 (89.0)	23,561 (95.0)	1 (reference)	1 (reference)
Previous ICH[4]	230 (11.0)	1,250 (5.0)	2.08 (1.79-2.42)	1.83 (1.55-2.15)
No	10,896	192,074		
No previous ICH[3]	10,555 (96.9)	189,499 (98.7)	1 (reference)	1 (reference)
Previous ICH[4]	341 (3.1)	2,575 (1.3)	2.56 (2.28-2.88)	2.12 (1.88-2.39)
History of ischemic stroke before baseline[9]				
Yes	722	5,588		
No previous ICH[3]	616 (85.3)	5,141 (92.0)	1 (reference)	1 (reference)
Previous ICH[4]	106 (14.7)	447 (8.0)	1.54 (1.22-1.96)	1.57 (1.22-2.02)
No	12,265	211,297		
No previous ICH[3]	11,800 (96.2)	207,919 (98.4)	1 (reference)	1 (reference)
Previous ICH[4]	465 (3.8)	3,378 (1.6)	2.55 (2.30-2.81)	2.11 (1.90-2.34)
History of major ischemic vascular event other than ischemic stroke[10]				
Yes	1,245	17,561		
No previous ICH[3]	1,166 (93.7)	17,153 (97.7)	1 (reference)	1 (reference)
Previous ICH[4]	79 (6.3)	408 (2.3)	2.87 (2.23-3.69)	2.31 (1.76-3.01)
No	11,742	199,324		
No previous ICH[3]	11,250 (95.8)	195,907 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	492 (4.2)	3,417 (1.7)	2.63 (2.39-2.90)	2.06 (1.86-2.28)

[1]Adjusted for age, sex, and index date (by design).

[2]Adjusted for sex, age, and index date (by design), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[3]No history of intracerebral hemorrhage at baseline (i.e., stems from comparison-cohort).
[4]First-ever intracerebral hemorrhage at baseline (i.e., stems from ICH-cohort).
[5]Adjusted for age (5-year bands), sex, and index date year (3-year bands).
[6]Adjusted for age (5-year bands), sex, index date year (3-year bands), duration of follow-up (4-year bands), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[7]At baseline or during follow-up.
[8]Defined as ischemic stroke or 'unspecified stroke' (only if recorded before inclusion into baseline), myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, venous thromboembolism, or sudden cardiac death.
[9]Only ischemic strokes recorded before baseline (i.e., before inclusion into cohorts) included.
[10]Defined as in footnote 8 but excluding ischemic stroke or 'unspecified stroke'.

eTable 7. Nested Case-Control Analysis of the Risk of Intracerebral Hemorrhage During Follow-up Associated With Having Had an Intracerebral Hemorrhage at Baseline

	No. (%) cases	No. (%) controls	OR[1] (95% CI)	Adj.OR[2] (95% CI)
All	1,915	64,955		
No previous ICH[3]	1,377 (71.9)	63,958 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	538 (28.1)	997 (1.5)	26.65 (23.56-30.16)	25.59 (22.30-29.36)
Sex				
Male	973	33,185		
No previous ICH[3]	707 (72.7)	32,689 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	266 (27.3)	496 (1.5)	26.27 (22.07-31.29)	26.87 (22.08-32.71)
Female	942	31,770		
No previous ICH[3]	670 (71.1)	31,269 (98.4)	1 (reference)	1 (reference)
Previous ICH[4]	272 (28.9)	501 (1.6)	27.04 (22.70-32.21)	24.89 (20.49-30.23)
Age on index date				
<75 years	900	32,087		
No previous ICH[3]	578 (64.2)	31,570 (98.4)	1 (reference)	1 (reference)
Previous ICH[4]	322 (35.8)	517 (1.6)	37.98 (31.78-45.38)	35.74 (29.09-43.91)
≥75 years	1,015	32,868		
No previous ICH[3]	799 (78.7)	32,388 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	216 (21.3)	480 (1.5)	18.82 (15.55-22.77)	19.27 (15.62-23.78)
	No. (%) cases	**No. (%) controls**	**OR[5] (95% CI)**	**Adj.OR[6] (95% CI)**
Atrial fibrillation[7]				
Yes	416	7,683		
No previous ICH[3]	334 (80.3)	7,510 (97.7)	1 (reference)	1 (reference)
Previous ICH[4]	82 (19.7)	173 (2.3)	10.97 (8.21-14.65)	13.38 (9.60-18.65)
No	1,499	57,272		
No previous ICH[3]	1,043 (69.6)	56,448 (98.6)	1 (reference)	1 (reference)
Previous ICH[4]	456 (30.4)	824 (1.4)	30.67 (26.91-34.96)	30.76 (26.54-35.66)
Diabetes[7]				
Yes	246	8,351		
No previous ICH[3]	178 (72.4)	8,212 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	68 (27.6)	139 (1.7)	23.22 (16.68-32.34)	23.27 (15.91-34.03)

	No. (%) cases	No. (%) controls	OR[5] (95% CI)	Adj.OR[6] (95% CI)
No	1,669	56,604		
No previous ICH[3]	1,199 (71.8)	55,746 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	470 (28.2)	858 (1.5)	26.16 (23.03-29.71)	27.47 (23.78-31.74)
History of major ischemic vascular event[8]				
Yes	361	6,998		
No previous ICH[3]	181 (50.1)	6,671 (95.3)	1 (reference)	1 (reference)
Previous ICH[4]	180 (49.9)	327 (4.7)	18.21 (14.26-23.26)	17.81 (13.42-23.62)
No	1,554	57,957		
No previous ICH[3]	1,196 (77.0)	57,287 (98.8)	1 (reference)	1 (reference)
Previous ICH[4]	358 (23.0)	670 (1.2)	27.03 (23.44-31.18)	29.52 (25.19-34.60)
History of ischemic stroke before baseline[9]				
Yes	128	1,581		
No previous ICH[3]	71 (55.5)	1,462 (92.5)	1 (reference)	1 (reference)
Previous ICH[4]	57 (44.5)	119 (7.5)	8.33 (5.49-12.64)	9.93 (6.03-16.35)
No	1,787	63,374		
No previous ICH[3]	1,306 (73.1)	62,496 (98.6)	1 (reference)	1 (reference)
Previous ICH[4]	481 (26.9)	878 (1.4)	27.12 (23.93-30.74)	28.55 (24.82-32.84)
History of major ischemic vascular event other than ischemic stroke[10]				
Yes	142	4,891		
No previous ICH[3]	89 (62.7)	4,802 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	53 (37.3)	89 (1.8)	31.11 (20.67-46.82)	37.24 (22.89-60.60)
No	1,773	60,064		
No previous ICH[3]	1,288 (72.6)	59,156 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	485 (27.4)	908 (1.5)	25.35 (22.38-28.71)	25.71 (22.34-29.60)

[1]Adjusted for age, sex, and index date (by design).
[2]Adjusted for sex, age, and index date (by design), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics,

loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[3]No history of intracerebral hemorrhage at baseline (i.e., stems from comparison-cohort).
[4]First-ever intracerebral hemorrhage at baseline (i.e., stems from ICH-cohort).
[5]Adjusted for age (5-year bands), sex, and index date year (3-year bands).
[6]Adjusted for age (5-year bands), sex, index date year (3-year bands), duration of follow-up (4-year bands), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[7]At baseline or during follow-up.
[8]Defined as ischemic stroke or 'unspecified stroke' (only if recorded before inclusion into baseline), myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, venous thromboembolism, or sudden cardiac death.
[9]Only ischemic strokes recorded before baseline (i.e., before inclusion into cohorts) included.
[10]Defined as in footnote 8 but excluding ischemic stroke or 'unspecified stroke'.

eTable 8. Nested Case-Control Analysis of the Risk of Myocardial Infarction During Follow-up Associated With Having Had an Intracerebral Hemorrhage at Baseline

	No. (%) cases	No. (%) controls	OR[1] (95% CI)	Adj.OR[2] (95% CI)
All	10,863	203,928		
No previous ICH[3]	10,669 (98.2)	200,237 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	194 (1.8)	3,691 (1.8)	0.98 (0.85-1.14)	0.89 (0.76-1.03)
Sex				
Male	7,052	121,590		
No previous ICH[3]	6,933 (98.3)	119,296 (98.1)	1 (reference)	1 (reference)
Previous ICH[4]	119 (1.7)	2,294 (1.9)	0.89 (0.74-1.08)	0.83 (0.68-1.00)
Female	3,811	82,338		
No previous ICH[3]	3,736 (98.0)	80,941 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	75 (2.0)	1,397 (1.7)	1.16 (0.92-1.47)	1.01 (0.79-1.29)
Age on index date				
<75 years	5,735	115,947		
No previous ICH[3]	5,615 (97.9)	113,724 (98.1)	1 (reference)	1 (reference)
Previous ICH[4]	120 (2.1)	2,223 (1.9)	1.09 (0.91-1.32)	0.92 (0.76-1.12)
≥75 years	5,128	87,981		
No previous ICH[3]	5,054 (98.6)	86,513 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	74 (1.4)	1,468 (1.7)	0.84 (0.66-1.07)	0.86 (0.67-1.10)
	No. (%) cases	**No. (%) controls**	**OR[5] (95% CI)**	**Adj.OR[6] (95% CI)**
Atrial fibrillation[7]				
Yes	1,898	22,510		
No previous ICH[3]	1,847 (97.3)	21,859 (97.1)	1 (reference)	1 (reference)
Previous ICH[4]	51 (2.7)	651 (2.9)	0.99 (0.74-1.32)	0.88 (0.65-1.18)
No	8,965	181,418		
No previous ICH[3]	8,822 (98.4)	178,378 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	143 (1.6)	3,040 (1.7)	0.97 (0.82-1.14)	0.92 (0.77-1.09)
Diabetes[7]				
Yes	2,081	25,971		
No previous ICH[3]	2,039 (98.0)	25,400 (97.8)	1 (reference)	1 (reference)

	No. (%) cases	No. (%) controls	OR[5] (95% CI)	Adj.OR[6] (95% CI)
Previous ICH[4]	42 (2.0)	571 (2.2)	0.93 (0.68-1.28)	0.92 (0.66-1.27)
No	8,782	177,957		
No previous ICH[3]	8,630 (98.3)	174,837 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	152 (1.7)	3,120 (1.8)	1.01 (0.85-1.19)	0.92 (0.78-1.09)
History of major ischemic vascular event[8]				
Yes	2,031	23,296		
No previous ICH[3]	1,940 (95.5)	22,075 (94.8)	1 (reference)	1 (reference)
Previous ICH[4]	91 (4.5)	1,221 (5.2)	0.74 (0.59-0.92)	1.06 (0.84-1.33)
No	8,832	180,632		
No previous ICH[3]	8,729 (98.8)	178,162 (98.6)	1 (reference)	1 (reference)
Previous ICH[4]	103 (1.2)	2,470 (1.4)	0.89 (0.73-1.09)	0.78 (0.63-0.96)
History of ischemic stroke before baseline[9]				
Yes	251	5,377		
No previous ICH[3]	234 (93.2)	4,937 (91.8)	1 (reference)	1 (reference)
Previous ICH[4]	17 (6.8)	440 (8.2)	0.78 (0.46-1.29)	0.80 (0.47-1.36)
No	10,612	198,551		
No previous ICH[3]	10,435 (98.3)	195,300 (98.4)	1 (reference)	1 (reference)
Previous ICH[4]	177 (1.7)	3,251 (1.6)	1.04 (0.89-1.21)	0.93 (0.80-1.09)
History of major ischemic vascular event other than ischemic stroke[10]				
Yes	1,725	16,249		
No previous ICH[3]	1,677 (97.2)	15,865 (97.6)	1 (reference)	1 (reference)
Previous ICH[4]	48 (2.8)	384 (2.4)	1.11 (0.81-1.51)	1.17 (0.85-1.62)
No	9,138	187,679		
No previous ICH[3]	8,992 (98.4)	184,372 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	146 (1.6)	3,307 (1.8)	0.93 (0.78-1.10)	0.84 (0.71-1.00)

[1]Adjusted for age, sex, and index date (by design).
[2]Adjusted for sex, age, and index date (by design), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake,

congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[3]No history of intracerebral hemorrhage at baseline (i.e., stems from comparison-cohort).
[4]First-ever intracerebral hemorrhage at baseline (i.e., stems from ICH-cohort).
[5]Adjusted for age (5-year bands), sex, and index date year (3-year bands).
[6]Adjusted for age (5-year bands), sex, index date year (3-year bands), duration of follow-up (4-year bands), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[7]At baseline or during follow-up.
[8]Defined as ischemic stroke or ‘unspecified stroke’ (only if recorded before inclusion into baseline), myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, venous thromboembolism, or sudden cardiac death.
[9]Only ischemic strokes recorded before baseline (i.e., before inclusion into cohorts) included.
[10]Defined as in footnote 8 but excluding ischemic stroke or ‘unspecified stroke’.

eTable 9. Nested Case-Control Analysis of the Risk of Major Adverse Cardiovascular Event (Stroke, Myocardial Infarction, Systemic Embolism, or Vascular Death) During Follow-up Associated With Having Had an Intracerebral Hemorrhage at Baseline

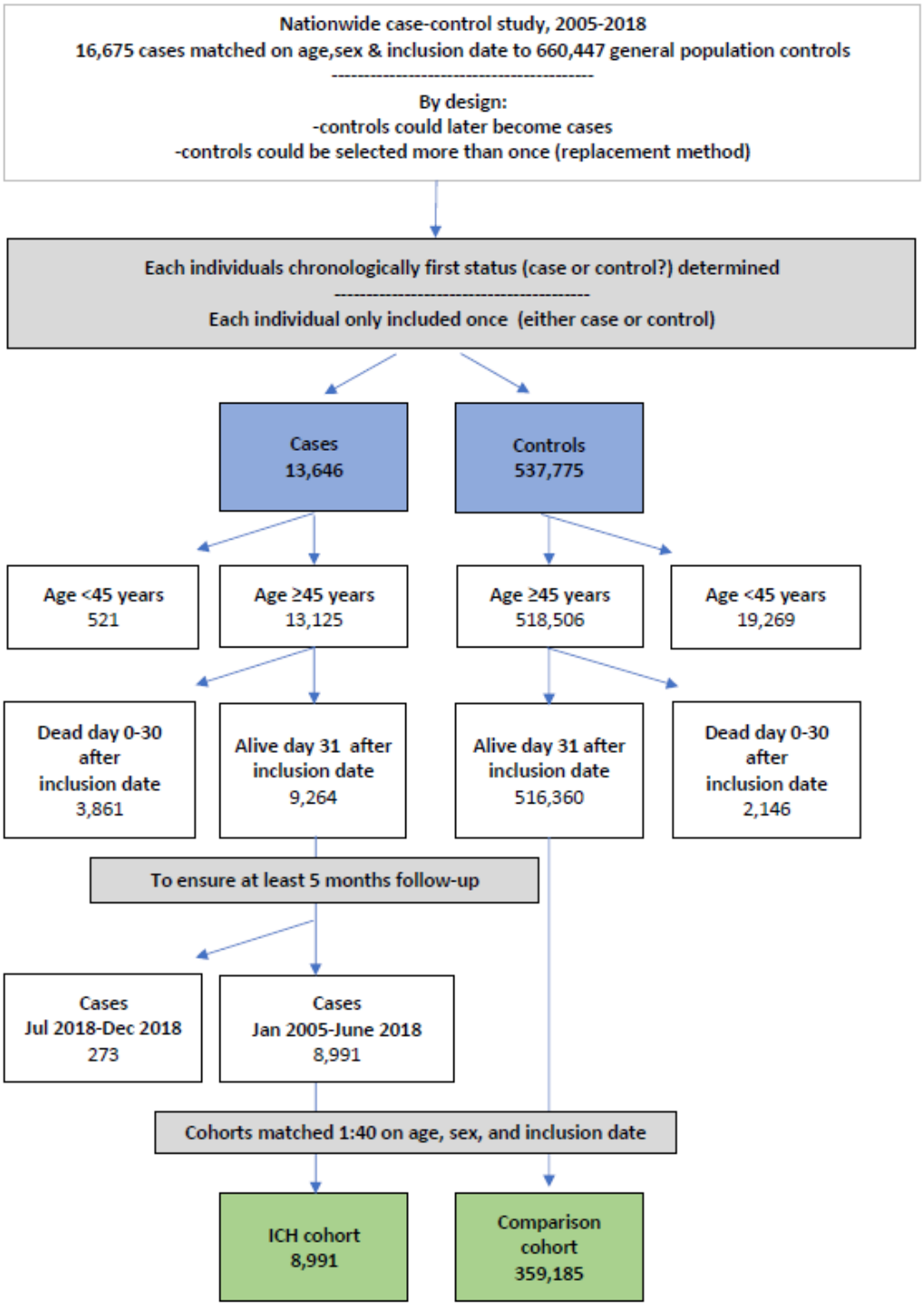
	No. (%) cases	No. (%) controls	OR[1] (95% CI)	Adj.OR[2] (95% CI)
All	31,327	269,891		
No previous ICH[3]	29,780 (95.1)	264,945 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	1,547 (4.9)	4,946 (1.8)	2.89 (2.72-3.07)	2.66 (2.49-2.84)
Sex				
Male	18,349	149,022		
No previous ICH[3]	17,505 (95.4)	146,191 (98.1)	1 (reference)	1 (reference)
Previous ICH[4]	844 (4.6)	2,831 (1.9)	2.57 (2.37-2.79)	2.29 (2.10-2.50)
Female	12,978	120,869		
No previous ICH[3]	12,275 (94.6)	118,754 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	703 (5.4)	2,115 (1.7)	3.38 (3.09-3.70)	3.29 (2.98-3.64)
Age on index date				
<75 years	14,727	159,131		
No previous ICH[3]	13,825 (93.9)	156,180 (98.1)	1 (reference)	1 (reference)
Previous ICH[4]	902 (6.1)	2,951 (1.9)	3.78 (3.49-4.10)	3.12 (2.85-3.41)
≥75 years	16,600	110,760		
No previous ICH[3]	15,955 (96.1)	108,765 (98.2)	1 (reference)	1 (reference)
Previous ICH[4]	645 (3.9)	1,995 (1.8)	2.19 (1.99-2.42)	2.24 (2.02-2.49)
	No. (%) cases	**No. (%) controls**	**OR[5] (95% CI)**	**Adj.OR[6] (95% CI)**
Atrial fibrillation[7]				
Yes	6,971	26,154		
No previous ICH[3]	6,618 (94.9)	25,448 (97.3)	1 (reference)	1 (reference)
Previous ICH[4]	353 (5.1)	706 (2.7)	2.15 (1.88-2.46)	1.98 (1.72-2.28)
No	24,265	210,517		
No previous ICH[3]	23,079 (95.1)	207,202 (98.4)	1 (reference)	1 (reference)
Previous ICH[4]	1,186 (4.9)	3,315 (1.6)	3.39 (3.16-3.63)	3.09 (2.88-3.32)
Diabetes[7]				
Yes	5,627	30,435		

	No. (%) cases	No. (%) controls	OR[5] (95% CI)	Adj.OR[6] (95% CI)
No previous ICH[3]	5,373 (95.5)	29,820 (98.0)	1 (reference)	1 (reference)
Previous ICH[4]	254 (4.5)	615 (2.0)	2.44 (2.10-2.84)	2.31 (1.97-2.71)
No	25,609	206,236		
No previous ICH[3]	24,324 (95.0)	202,830 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	1,285 (5.0)	3,406 (1.7)	3.34 (3.12-3.57)	2.93 (2.73-3.14)
History of major ischemic vascular event[8]				
Yes	5,622	26,243		
No previous ICH[3]	5,024 (89.4)	24,940 (95.0)	1 (reference)	1 (reference)
Previous ICH[4]	598 (10.6)	1,303 (5.0)	2.03 (1.83-2.25)	2.22 (1.98-2.49)
No	25,614	210,428		
No previous ICH[3]	24,673 (96.3)	207,710 (98.7)	1 (reference)	1 (reference)
Previous ICH[4]	941 (3.7)	2,718 (1.3)	3.21 (2.97-3.47)	2.99 (2.76-3.24)
History of ischemic stroke before baseline[9]				
Yes	1,348	6,039		
No previous ICH[3]	1,137 (84.3)	5,591 (92.6)	1 (reference)	1 (reference)
Previous ICH[4]	211 (15.7)	448 (7.4)	1.98 (1.65-2.38)	1.95 (1.60-2.37)
History of ischemic stroke before baseline[9]				
No	29,888	230,632		
No previous ICH[3]	28,560 (95.6)	227,059 (98.5)	1 (reference)	1 (reference)
Previous ICH[4]	1,328 (4.4)	3,573 (1.5)	3.15 (2.95-3.36)	2.86 (2.67-3.06)
History of major ischemic vascular event other than ischemic stroke[10]				
Yes	3,916	18,389		
No previous ICH[3]	3,696 (94.4)	17,978 (97.8)	1 (reference)	1 (reference)
Previous ICH[4]	220 (5.6)	411 (2.2)	2.58 (2.17-3.06)	2.30 (1.91-2.76)
No	27,320	218,282		

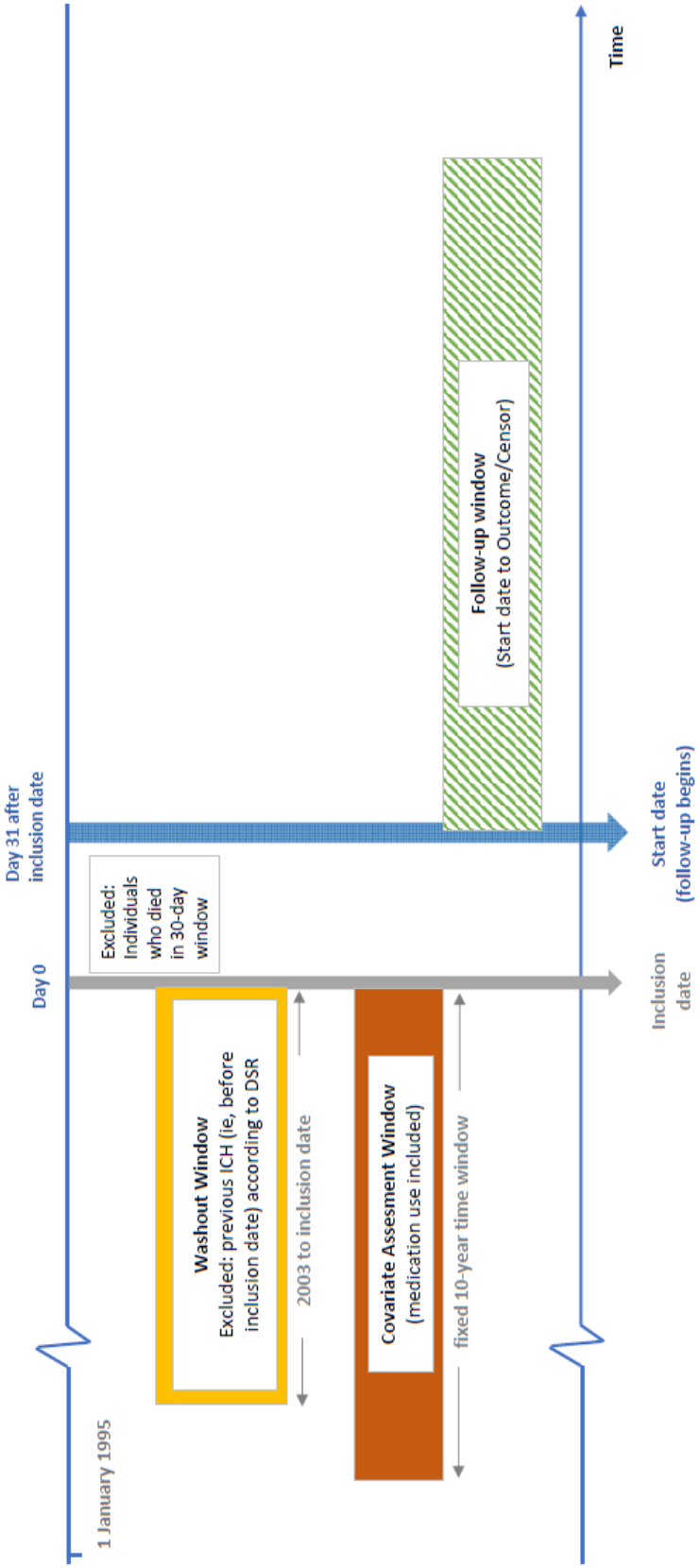
	No. (%) cases	No. (%) controls	OR[5] (95% CI)	Adj.OR[6] (95% CI)
No previous ICH[3]	26,001 (95.2)	214,672 (98.3)	1 (reference)	1 (reference)
Previous ICH[4]	1,319 (4.8)	3,610 (1.7)	3.23 (3.02-3.45)	2.90 (2.70-3.11)

[1]Adjusted for age, sex, and index date (by design).
[2]Adjusted for sex, age, and index date (by design), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[3]No history of intracerebral hemorrhage at baseline (i.e., stems from comparison-cohort).
[4]First-ever intracerebral hemorrhage at baseline (i.e., stems from ICH-cohort).
[5]Adjusted for age (5-year bands), sex, and index date year (3-year bands).
[6]Adjusted for age (5-year bands), sex, index date year (3-year bands), duration of follow-up (4-year bands), comorbidity [separate covariates for each of the following: hypertension, atrial fibrillation, ischemic stroke, myocardial infarction, systemic embolism, peripheral arterial disease, venous thromboembolism, diabetes, chronic kidney failure, chronic hepatic diseases, chronic obstructive pulmonary disorder, disorders indicative of high alcohol intake, congestive heart failure, and cancer] and current use of drugs [separate covariates for each of the following drugs/drug classes: low-dose aspirin, clopidogrel, dipyridamole, vitamin K antagonist, direct oral anticoagulant, statins, thiazides and other non-loop diuretics, loop diuretics, beta blockers, calcium channel blockers, ACE-inhibitors and angiotensin II receptor blockers, nonsteroidal anti-inflammatory drugs, selective serotonin re-uptake inhibitors, and proton pump inhibitors]. All covariates were determined on index-date and based on all available data, i.e., from 10 years before baseline and up to index-date.
[7]At baseline or during follow-up.
[8]Defined as ischemic stroke or 'unspecified stroke' (only if recorded before inclusion into baseline), myocardial infarction, systemic embolism, revascularization procedures, mesenteric ischemia, venous thromboembolism, or sudden cardiac death.
[9]Only ischemic strokes recorded before baseline (i.e., before inclusion into cohorts) included.
[10]Defined as in footnote 8 but excluding ischemic stroke or 'unspecified stroke'.

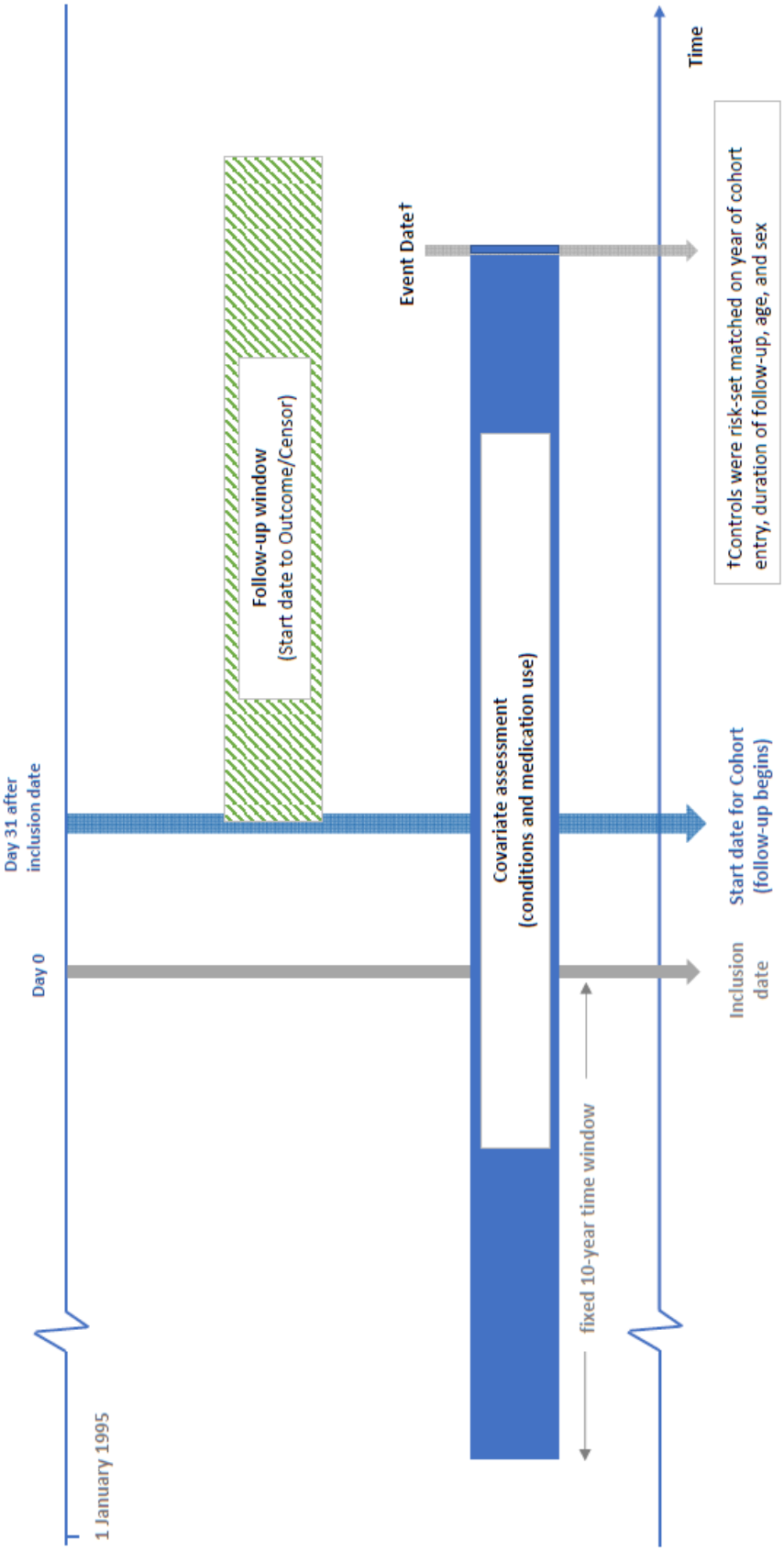
eFigure 1. Flow Chart of Creation of Intracerebral Hemorrhage (ICH) Cohort and Comparison Cohort Based on Data From a Previous Study



eFigure 2. Cohort Design

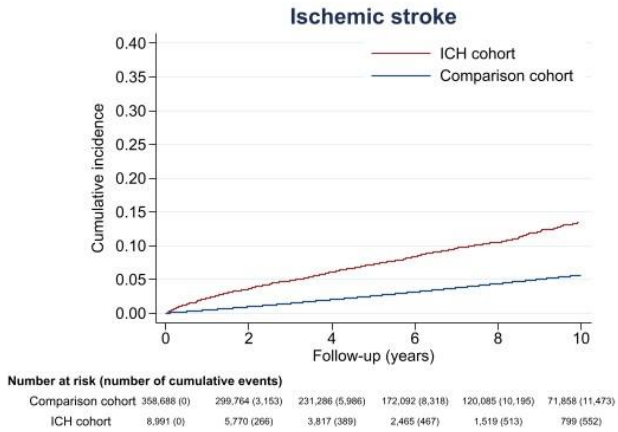


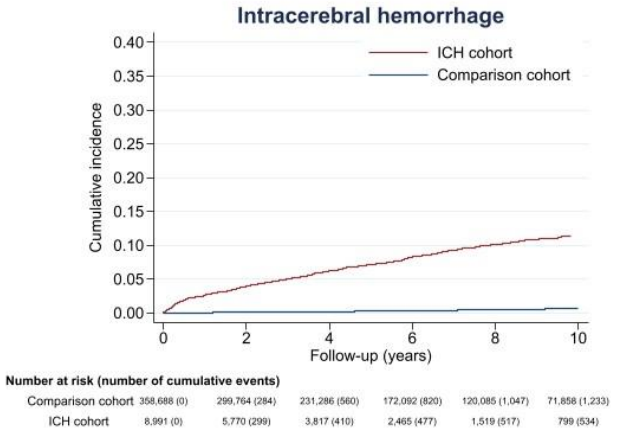
eFigure 3. Nested Case-Control Design

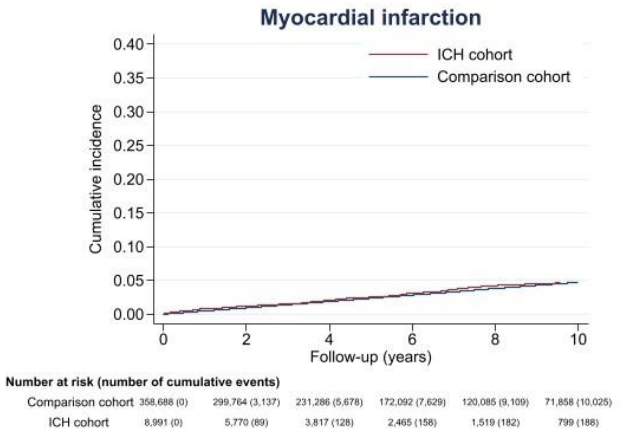


eFigure 4. Cumulative Incidence of Ischemic Stroke, Intracerebral Hemorrhage, and Myocardial Infarction

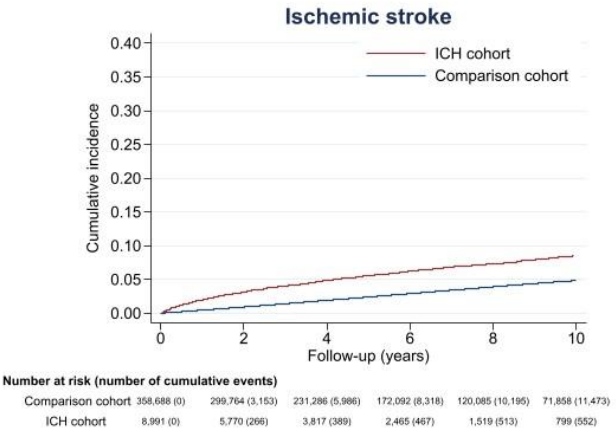
A. Cumulative Incidence

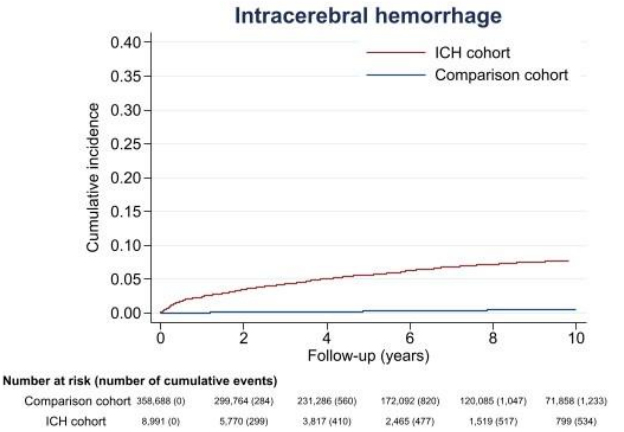


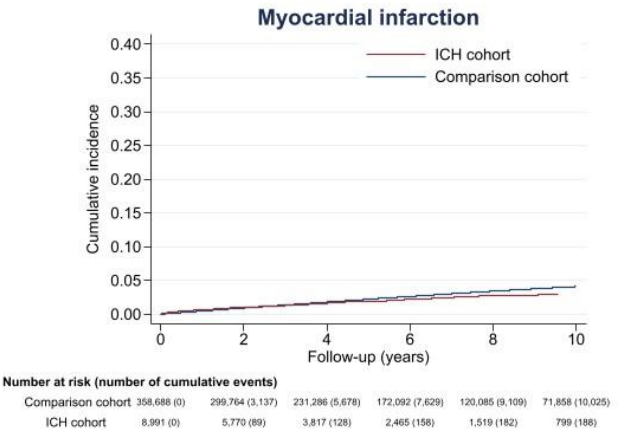




B. Cumulative incidence with death as competing risk

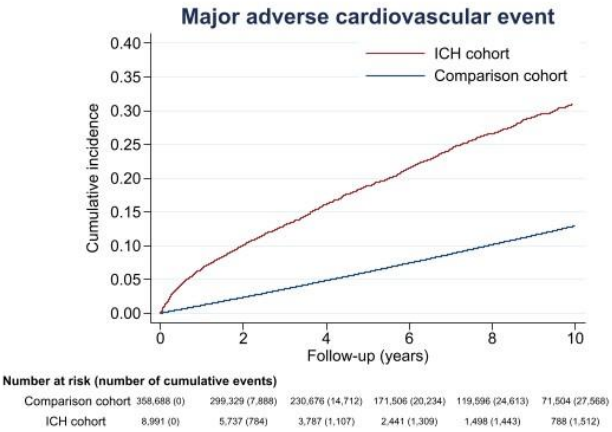




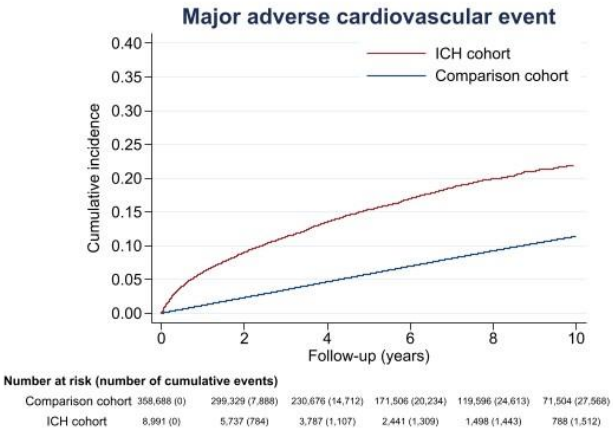


eFigure 5. Cumulative Incidence of Major Adverse Cardiovascular Event (Stroke, Myocardial Infarction, Systemic Embolism, or Vascular Death) and All-Cause Death

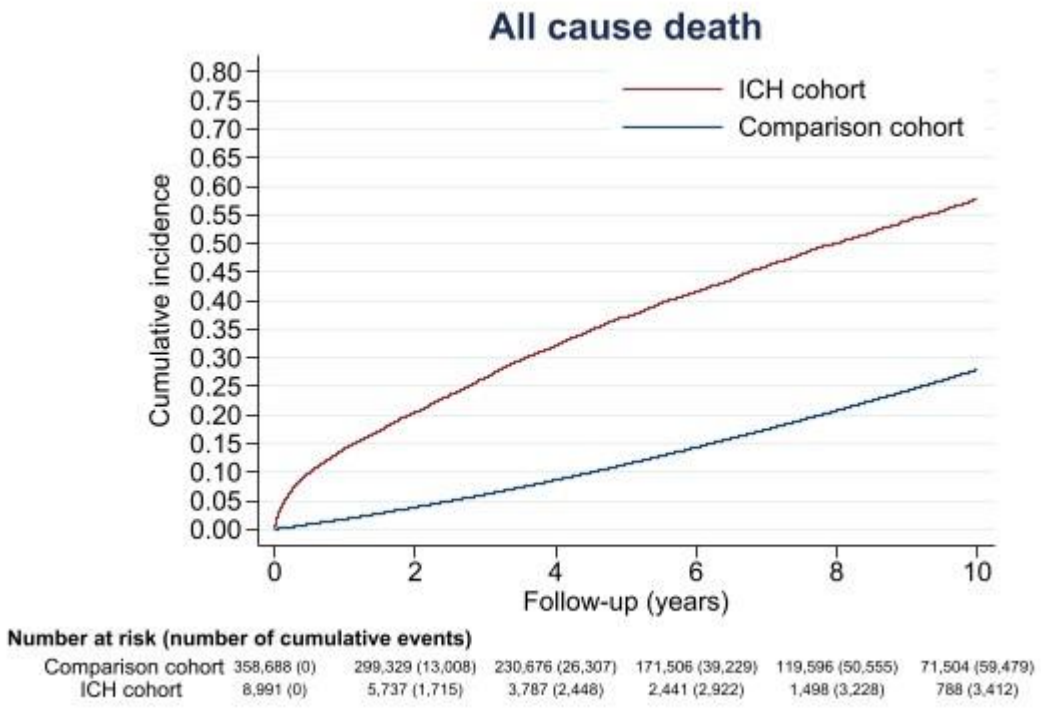
A. Cumulative Incidence



B. Cumulative incidence with death as competing risk

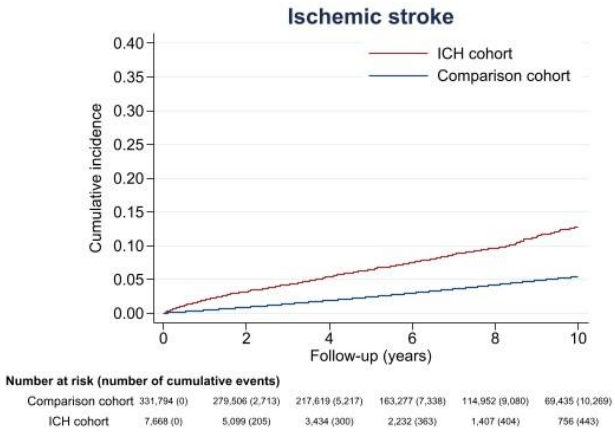


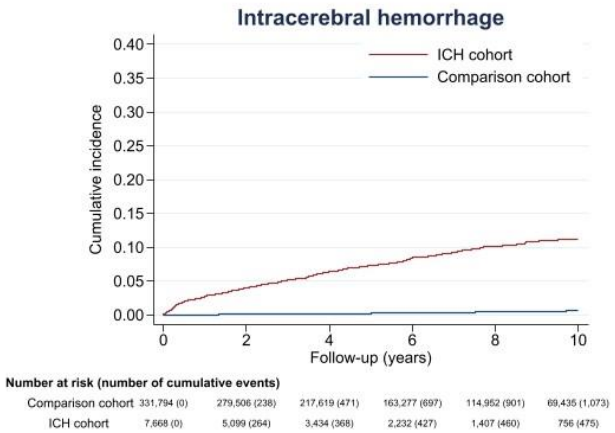
C. All cause death

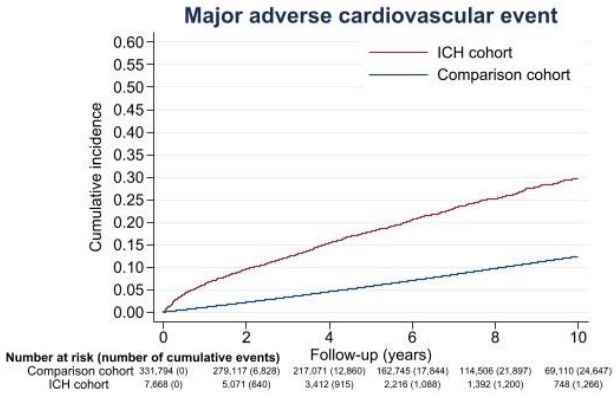


eFigure 6. Cumulative Incidence of Ischemic Stroke, Intracerebral Hemorrhage, and Major Adverse Cardiovascular Event Stratified by Comorbid Atrial Fibrillation

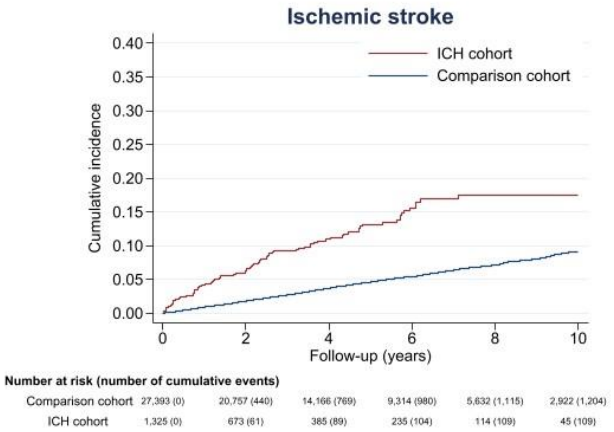
A. No atrial fibrillation at baseline

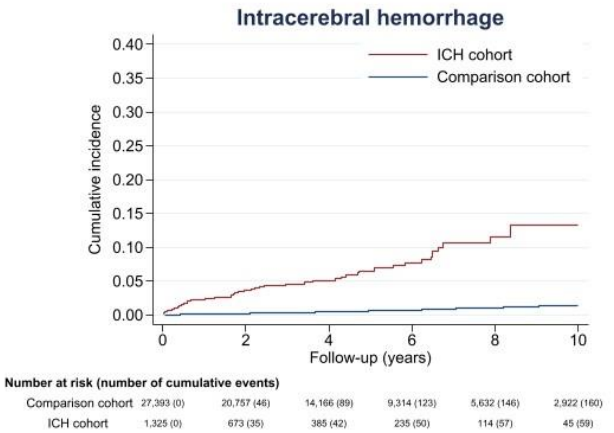


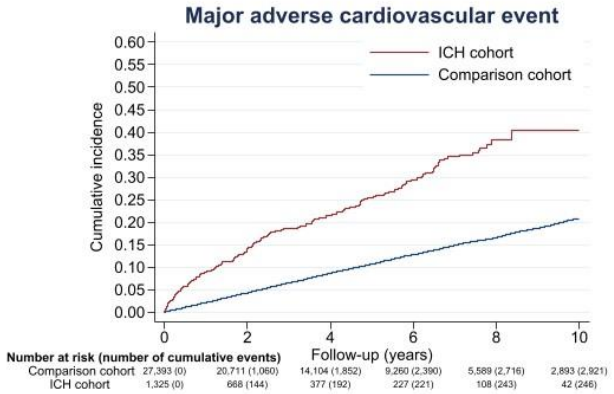




B. Atrial fibrillation at baseline







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