

Supplementary Online Content

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eReferences

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

eTable 1. List of codes used to retrieve and classify data for the study

HOSPITAL CODES (DISCHARGE, OUTPATIENT, PROCEDURES)

Outcome of interest

Subdural hematoma (SDH)

ICD-8: 852.01, 852.11, 431.01, 431.91 [only used to exclude prevalent cases]

ICD-10: S065

Surgical procedures

Burr hole: AAD10

Craniotomy: AAD05

Covariates¹

Stroke (hemorrhagic, ischaemic, or “unspecified”)

ICD-8 : 43100, 43108, 43109, 43190, 43198, 43199, 433, 434, 43601, 43609, 43690

ICD-10: I61, I63, I64.9

Epilepsy

ICD-8: 345

ICD-10: G40, G41

Dementia

ICD-8: 29009, 29010, 29011, 29018, 29019, 29309

ICD-10: F00, F01, F02, F03, F05.1

Myocardial infarct

ICD-8: 410

ICD-10: I21

Unstable angina

ICD-8: No code available

ICD-10: I20.0

Angina, other

ICD-8: 413.09, 413.99

ICD-10: I20.1-I20.9

Peripheral artery disease

ICD-8: 443.89

ICD-10: I73.9

Diabetes

ICD-8: 249, 250

ICD-10: E10-E14

COPD

ICD-8: 49000, 49100, 49101, 49103

ICD-10: J42, J43, J44

Hypertension

ICD-8: 400-404

ICD-10: I10-I15

Chronic renal insufficiency

ICD-8: 593.2

ICD-10: N18-N19

Chronic hepatic diseases

ICD-8: 571.11, 571.19, 571.90, 571.91, 571.92, 571.93, 571.94, 571.99, 573

ICD-10: K71-K77

Coagulopathy

ICD-8: 286.09, 286.19, 286.29, 286.39, 286.99

ICD-10: D66, D67, D680, D681, D682, D689, D691, D693, D694

Codes of disorders indicative of alcohol misuse

ICD-8: 291, 303, 571.09, 571.10, 577.10, 979, 980

ICD-10: F10, G312, G621, G721, I426, K292, K70, K860, R780, T51, Z721

ATC CODES

*Antiplatelet drugs*²

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

Dipyridamole

B01AC07 (100 mg per tablet, or 200 mg per tablet)

Clopidogrel

B01AC04 (75 mg per tablet)

Other ADP drugs

B01AC22 – prasugrel (5 mg, or 10 mg per tablet)

B01AC24 - ticagrelor (60 mg, or 90 mg per tablet)

*Anticoagulant drugs*²

Vitamin K antagonists

B01AA

Direct oral anticoagulants (DOAC)

Dabigatran etexilate

B01AE07

Rivaroxaban

B01AF01

Apixaban

B01AF02

*Nonsteroidal anti-inflammatory drugs (NSAIDs)*³

M01A (including Cox2 inhibitors), excluding M01AX

*Selective serotonin reuptake inhibitors (SSRI)*³

N06AB

*Antidiabetics*³

A10

*Antihypertensives*³

Diuretics

C03 (except loop-diuretics, C03C)

Beta-blockers

C07

Calcium antagonists

C08 (except verapamil & diltiazem)

Agents that influence the renin-angiotensin system

C09

*Drugs used in treatment of Alzheimer's disease and other types of dementia*³

Cholinesterase inhibitors

N06DA

Memantin

N06DX01

*Statins*³

C10AA

*Postmenopausal hormone replacement therapy*³

G03C, G03DC, G03F

*Oral corticosteroids*³

H02AB

*Drugs used in treatment of alcohol dependency*²

N07BB

*Hypnotics and sedatives (including benzodiazepines)*³

N05BA, N05C

¹Based on hospital contacts in period 1977 to 1 month prior to index date.

²Based on prescriptions presented 1st January 1995 to 1 day prior to index date.

³Based on prescriptions presented in period 1 year to 1 month prior to index date.

eTable 2. Single use of antithrombotic drugs and risk of subdural hematoma in Denmark, 2000-2015

	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	OR ¹ (95% CI)	adjusted OR ² (95% CI)
Antiplatelet drugs				
Never use of any antithrombotic drug	5,013 (50.1)	252,593 (63.1)	1.00 (reference)	1.00 (reference)
Low-dose aspirin – current use	1,563 (15.6)	67,416 (16.8)	1.33 (1.25-1.42)	1.19 (1.10-1.29)
Duration of current use				
<1 month	122 (1.2)	2,364 (0.6)	3.04 (2.50-3.68)	2.70 (2.19-3.32)
≥1 month, ≤3 months	135 (1.3)	4,638 (1.2)	1.65 (1.38-1.97)	1.43 (1.18-1.74)
>3 months, ≤12 months	404 (4.0)	15,712 (3.9)	1.44 (1.29-1.60)	1.21 (1.07-1.37)
>1 year, ≤3 years	447 (4.5)	20,683 (5.2)	1.24 (1.11-1.37)	1.07 (0.95-1.21)
>3 years	455 (4.5)	24,019 (6.0)	1.11 (1.00-1.23)	0.92 (0.81-1.04)
Clopidogrel – current use	199 (2.0)	4,045 (1.0)	2.98 (2.55-3.50)	1.61 (1.30-1.98)
Duration of current use				
<1 month	9 (0.1)	134 (0.0)	4.24 (2.05-8.75)	2.13 (0.98-4.65)
≥1 month, ≤3 months	16 (0.2)	254 (0.1)	3.45 (2.02-5.92)	1.74 (0.97-3.14)
>3 months, ≤12 months	42 (0.4)	816 (0.2)	3.25 (2.33-4.53)	1.48 (1.02-2.16)
>1 year, ≤3 years	84 (0.8)	1,807 (0.5)	2.83 (2.23-3.58)	1.45 (1.08-1.93)
>3 years	48 (0.5)	1,034 (0.3)	2.82 (2.07-3.85)	1.44 (1.00-2.08)
Oral anticoagulant drugs				
DOAC ³ – current use	44 (0.4)	1,276 (0.3)	2.13 (1.53-2.96)	1.78 (1.26-2.53)
Duration of current use				
<1 month	3 (0.0)	86 (0.0)	2.07 (0.63-6.85)	NA ⁴
≥1 month, ≤3 months	7 (0.1)	153 (0.0)	2.77 (1.23-6.22)	2.72 (1.16-6.35)
>3 months, ≤12 months	9 (0.1)	355 (0.1)	1.60 (0.80-3.19)	1.27 (0.62-2.60)
>1 year, ≤3 years	23 (0.2)	571 (0.1)	2.56 (1.64-4.01)	2.05 (1.27-3.32)
>3 years	(n<3)	111 (0.03)	NA ⁴	NA ⁴

	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	OR¹ (95% CI)	adjusted OR² (95% CI)
Oral anticoagulant drugs				
VKA ⁵ – current use	853 (8.5)	12,940 (3.2)	3.99 (3.67-4.34)	3.51 (3.19-3.87)
Duration of current use				
<1 month	36 (0.4)	562 (0.1)	3.51 (2.45-5.02)	2.76 (1.88-4.06)
≥1 month, ≤3 months	94 (0.9)	1,087 (0.3)	5.12 (4.06-6.45)	4.32 (3.36-5.54)
>3 months, ≤12 months	193 (1.9)	2,732 (0.7)	4.14 (3.53-4.86)	3.42 (2.87-4.08)
>1 year, ≤3 years	225 (2.2)	3,356 (0.8)	3.91 (3.37-4.53)	3.33 (2.82-3.92)
>3 years	305 (3.0)	5,203 (1.3)	3.57 (3.14-4.07)	3.14 (2.72-3.63)

Single current users were defined as subjects with current use of a single antithrombotic drug and no concurrent use of other antithrombotic drugs or previous use (in the 12 months preceding their index date) of other antithrombotic drugs.

¹Adjusted for age, sex, and calendar period (year) by design

²Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, use of nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hypnotics and sedatives, hormone replacement therapy, oral corticosteroid drugs, and socioeconomic status (education level and income). Analyses for low-dose aspirin were adjusted for current use of clopidogrel and vice-versa. Analyses for antiplatelet drugs were adjusted for current use of oral anticoagulant drugs and vice-versa.

³Direct oral anticoagulant

⁴Not applicable

⁵Vitamin K antagonist

eTable 3. First-time use of antithrombotic drugs and risk of subdural hematoma in Denmark, 2000-2015

	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	OR¹ (95% CI)	adjusted OR² (95% CI)
Antiplatelet drugs				
Never use of any antithrombotic drug	5,013 (70.6)	252,593 (82.9)	1.00 (reference)	1.00 (reference)
Low-dose aspirin – current use	977 (13.8)	28,023 (9.2)	1.91 (1.78-2.06)	1.39 (1.26-1.52)
Duration of current use				
<1 month	125 (1.8)	1,410 (0.5)	4.87 (4.00-5.92)	4.17 (3.34-5.20)
≥1 month, ≤3 months	108 (1.5)	2,779 (0.9)	2.11 (1.73-2.58)	1.53 (1.21-1.95)
>3 months, ≤12 months	342 (4.8)	9,169 (3.0)	2.04 (1.81-2.29)	1.32 (1.14-1.53)
>1 year, ≤3 years	320 (4.5)	11,537 (3.8)	1.53 (1.36-1.73)	1.08 (0.93-1.25)
>3 years	82 (1.2)	3,128 (1.0)	1.41 (1.12-1.77)	0.87 (0.66-1.15)
Clopidogrel – current use	183 (2.6)	3,251 (1.1)	3.22 (2.74-3.78)	1.68 (1.31-2.16)
Duration of current use				
<1 month	13 (0.2)	215 (0.1)	3.52 (1.95-6.35)	2.30 (0.88-5.97)
≥1 month, ≤3 months	34 (0.5)	410 (0.1)	4.53 (3.10-6.61)	1.74 (0.90-3.36)
>3 months, ≤12 months	73 (1.0)	1,289 (0.4)	3.16 (2.46-4.07)	1.92 (1.32-2.80)
>1 year, ≤3 years	54 (0.8)	1,146 (0.4)	2.73 (2.04-3.65)	1.43 (0.98-2.09)
>3 years	9 (0.1)	191 (0.1)	3.06 (1.52-6.18)	1.14 (0.43-3.04)
Oral anticoagulant drugs				
DOAC ³ – current use	40 (0.6)	1,128 (0.4)	2.24 (1.59-3.14)	1.95 (1.35-2.82)
Duration of current use				
<1 month	7 (0.1)	108 (0.03)	4.03 (1.76-9.19)	4.18 (1.64-10.64)
≥1 month, ≤3 months	9 (0.1)	192 (0.1)	2.82 (1.39-5.71)	2.96 (1.40-6.26)
>3 months, ≤12 months	12 (0.2)	456 (0.1)	1.54 (0.85-2.79)	1.17 (0.62-2.23)
>1 year, ≤3 years	10 (0.1)	327 (0.1)	2.14 (1.10-4.16)	2.02 (1.01-4.02)
>3 years	(n<3)	45 (0.01)	NA ⁴	NA ⁴

	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	OR¹ (95% CI)	adjusted OR² (95% CI)
Oral anticoagulant drugs				
VKA ⁵ – current use	730 (10.3)	9,856 (3.2)	4.29 (3.93-4.69)	3.77 (3.40-4.19)
Duration of current use				
<1 month	37 (0.5)	497 (0.2)	3.80 (2.67-5.41)	3.10 (2.05-4.69)
≥1 month, ≤3 months	96 (1.4)	974 (0.3)	5.45 (4.34-6.86)	5.27 (4.04-6.87)
>3 months, ≤12 months	196 (2.8)	2,623 (0.9)	4.43 (3.78-5.19)	3.73 (3.09-4.51)
>1 year, ≤3 years	193 (2.7)	2,675 (0.9)	3.96 (3.38-4.64)	3.48 (2.89-4.19)
>3 years	208 (2.9)	3,087 (1.0)	3.97 (3.40-4.64)	3.43 (2.88-4.09)

First time users were defined as subjects who had initiated antiplatelet drug treatment (in antiplatelet drug analyses) or oral anticoagulant (in oral anticoagulant analyses) within the 4 years preceding their index date and with no use of any antithrombotic drug more than 4 years prior to index date.

¹Adjusted for age, sex, and calendar period (year) by design

²Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, use of nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hypnotics and sedatives, hormone replacement therapy, oral corticosteroid drugs, and socioeconomic status (education level and income). Analyses for low-dose aspirin were adjusted for current use of clopidogrel and vice-versa. Analyses for antiplatelet drugs were adjusted for current use of oral anticoagulant drugs and vice-versa.

³Direct oral anticoagulant

⁴Not applicable

⁵Vitamin K antagonis

eTable 4. Antithrombotic drug use and risk of subdural hematoma within sex and age strata, and by 30-day mortality of cases, Denmark 2000-2015

Type of antithrombotic	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	Adjusted odds ratio ¹ (95% CI)				
			Never use of any anti- thrombotics	Low-dose aspirin	P-value, Wald test	Clopidogrel	P-value, Wald test
Antiplatelet drugs							
Sex							
Male	6,548 (65.4)	261,920 (65.4)	1 (reference)	1.23 (1.13-1.34)		1.92 (1.57-2.35)	
Female	3,462 (34.6)	138,460 (34.6)	1 (reference)	1.51 (1.35-1.69)	.004	2.63 (2.01-3.44)	.06
Age, years							
20-64	3,166 (31.6)	126,620 (31.6)	1 (reference)	1.08 (0.90-1.30)		2.25 (1.54-3.28)	
65-74	2,403 (24.0)	96,120 (24.0)	1 (reference)	1.35 (1.18-1.55)	.05 ²	2.01 (1.49-2.72)	.69 ²
75-89	4,441 (44.4)	177,640 (44.4)	1 (reference)	1.46 (1.33-1.60)	.003 ³	2.45 (1.96-3.06)	.65 ³
30-day vital status of case ⁴							
Survived	8,402 (83.9)	NA ⁵	1 (reference)	1.29 (1.20-1.40)		2.01 (1.68-2.39)	
Died	1,608 (16.1)	NA ⁵	1 (reference)	1.66 (1.39-1.99)	.009	3.93 (2.51-6.16)	.005
Anticoagulant drugs							
Sex							
Male	6,548 (65.4)	261,920 (65.4)	1 (reference)	1.74 (1.24-2.45)		3.11 (2.79-3.47)	
Female	3,462 (34.6)	138,460 (34.6)	1 (reference)	1.71 (1.06-2.75)	.95	5.06 (4.35-5.88)	<.001
Age, years							
20-64	3,166 (31.6)	126,620 (31.6)	1 (reference)	1.20 (0.36-4.04)		4.04 (3.20-5.11)	
65-74	2,403 (24.0)	96,120 (24.0)	1 (reference)	1.69 (1.01-2.81)	.61 ²	3.90 (3.30-4.61)	.80 ²
75-89	4,441 (44.4)	177,640 (44.4)	1 (reference)	1.90 (1.34-2.68)	.47 ³	3.57 (3.18-4.01)	.34 ³

Type of antithrombotic	Cases, no. (%) (n=10,010)	Controls, no. (%) (n=400,380)	Adjusted odds ratio ¹ (95% CI)				
			Never use of any anti- thrombotics	Direct oral anticoagulant	P-value, Wald test	Vitamin K antagonist	P-value, Wald test
30-day vital status of case ⁴							
Survived	8,402 (83.9)	NA ⁵	1 (reference)	1.44 (1.05-1.96)		3.33 (3.02-3.67)	
Died	1,608 (16.1)	NA ⁵	1 (reference)	3.87 (1.84-8.13)	.013	6.30 (5.04-7.88)	<.001

¹Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, use of nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hypnotics and sedatives, hormone replacement therapy, or oral corticosteroid drugs, and socioeconomic status (education level and income). Analyses for low-dose aspirin were adjusted for current use of clopidogrel and vice-versa. Analyses for antiplatelet drugs were adjusted for current use of oral anticoagulant drugs and vice-versa.

²Comparison of age strata 65-74 years vs. 20-64 years.

³Comparison of age strata 75-89 year vs. 20-64 years.

⁴Stratified by vital status of case on day 30 after subdural hematoma diagnosis, i.e., 30-day mortality of case.

⁵Not applicable: 30-day mortality was calculated for cases only.

eTable 5. Use of antithrombotic drugs and risk of subdural hematoma, Funen area, 2000-2012

	Cases, no. (%) (n=936)	Controls, no. (%) (n=18,689)	OR ¹ (95% CI)	Adjusted OR ² (95% CI)
Antiplatelet drug				
Never use of any antiplatelet drug	585 (62.5)	13,093 (70.1)	1.00 (reference)	1.00 (reference)
Low-dose aspirin, ever use ³	348 (37.2)	5,546 (29.7)	1.51 (1.30-1.77)	1.19 (0.99-1.43)
Recency of use				
Current use	242 (25.9)	3,600 (19.3)	1.62 (1.37-1.92)	1.30 (1.06-1.60)
Recent use	23 (2.5)	207 (1.1)	2.69 (1.72-4.20)	2.22 (1.40-3.53)
Past use	15 (1.6)	343 (1.8)	1.05 (0.62-1.78)	0.84 (0.49-1.44)
Distant use	68 (7.3)	1,396 (7.5)	1.17 (0.90-1.53)	0.93 (0.70-1.23)
Duration of current use				
<3 months	34 (3.6)	418 (2.2)	1.96 (1.36-2.84)	1.50 (1.00-2.23)
3-12 months	80 (8.5)	949 (5.1)	2.01 (1.56-2.59)	1.57 (1.18-2.09)
>1 year	128 (13.7)	2,233 (11.9)	1.37 (1.10-1.69)	1.02 (0.79-1.31)
Clopidogrel, ever use ³	46 (4.9)	741 (4.0)	1.50 (1.07-2.10)	1.36 (0.79-2.33)
Recency of use				
Current use	22 (2.4)	258 (1.4)	2.33 (1.45-3.72)	1.78 (0.96-3.29)
Recent use	2 (0.2)	21 (0.1)	3.18 (0.68-14.77)	NA
Past use	3 (0.3)	78 (0.4)	0.82 (0.26-2.65)	NA
Distant use	19 (2.0)	384 (2.1)	1.10 (0.67-1.80)	1.05 (0.52-2.10)
Duration of current use				
< 3 months	7 (0.7)	34 (0.2)	6.00 (2.40-15.04)	4.60 (1.54-13.73)
3-12 months	8 (0.9)	87 (0.5)	2.38 (1.11-5.08)	1.21 (0.46-3.22)
> 1 year	7 (0.7)	137 (0.7)	1.35 (0.61-2.99)	0.87 (0.33-2.28)
Anticoagulant drug⁴				
Never use of anticoagulant drug	780 (83.3)	17,219 (92.1)	1.00 (reference)	1.00 (reference)
Vitamin K antagonist, ever use ⁵	154 (16.5)	1450(7.8)	2.46 (2.04-2.98)	2.18 (1.79-2.66)
Recency of use				
Current use	107 (11.4)	707 (3.8)	3.54 (2.83-4.42)	3.27 (2.59-4.13)
Recent use	18 (1.9)	140 (0.7)	2.99 (1.81-4.93)	2.54 (1.52-4.25)
Past use	5 (0.5)	108 (0.6)	1.06 (0.43-2.61)	0.92 (0.37-2.31)
Distant use	23 (2.5)	495 (2.6)	1.08 (0.71-1.67)	0.88 (0.57-1.38)
Duration of current use				
<3 months	53 (5.7)	254 (1.4)	4.89 (3.56-6.70)	4.54 (3.27-6.29)
3-12 months	32 (3.4)	235 (1.3)	3.19 (2.17-4.68)	2.84 (1.92-4.23)
> 1 year	22 (2.4)	218 (1.2)	2.34 (1.49-3.67)	2.37 (1.50-3.77)

Only validated subdural hematoma cases and their corresponding controls included.

¹Adjusted for age, sex, and calendar period (year) by design

²Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, use of nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hormone replacement therapy, or oral corticosteroid drugs.

³Previous or concurrent use of other antiplatelet drugs or anticoagulant drugs included.

⁴23 users of non-vitamin K oral anticoagulants (3 cases and 20 controls) not included.

⁵Previous or concurrent use of antiplatelet drugs included.

eTable 6. Association between subdural hematoma type and preadmission antithrombotic drug use in Funen area, 2000-2012

	Subacute/chronic subdural hematoma			Acute subdural hematoma		
	Cases, no. (%) (n=517)	Controls, no. (%) (n=10,316)	Adjusted OR ¹ (95% CI)	Cases, no. (%) (n=419)	Controls, no. (%) (n=8,373)	Adjusted OR ¹ (95% CI)
Never use of any antiplatelet drug	307 (59.4)	6,819 (66.1)	1.00 (reference)	278 (66.3)	6,274 (74.9)	1.00 (reference)
Low-dose aspirin ²						
Current use	142 (27.5)	2,238 (21.7)	1.10 (0.83-1.45)	100 (23.9)	1,362 (16.3)	1.47 (1.04-2.08)
Duration of current use						
< 3 months	25 (4.8)	257 (2.5)	1.69 (1.05-2.72)	9 (2.1)	161 (1.9)	1.09 (0.52-2.29)
3-12 months	40 (7.7)	592 (5.7)	1.18 (0.80-1.73)	40 (9.5)	357 (4.3)	2.39 (1.55-3.70)
>1 year	77 (14.9)	1,389 (13.5)	0.95 (0.69-1.31)	51 (12.2)	844 (10.1)	1.17 (0.78-1.76)
Never use of any anticoagulant Vitamin K antagonist ³	430 (83.2)	9,379 (90.9)	1.00 (reference)	350 (83.5)	7,840 (93.6)	1.00 (reference)
Current use	55 (10.6)	448 (4.3)	2.59 (1.88-3.55)	52 (12.4)	262 (3.1)	4.72 (3.31-6.72)
Duration of current use						
< 3 months	27 (5.2)	156 (1.5)	3.42 (2.20-5.33)	26 (6.2)	99 (1.2)	6.64 (4.05-10.86)
3-12 months	15 (2.9)	150 (1.5)	2.13 (1.22-3.74)	17 (4.1)	86 (1.0)	4.12 (2.29-7.40)
>1 year	13 (2.5)	142 (1.4)	2.06 (1.14-3.73)	9 (2.1)	77 (0.9)	3.06 (1.48-6.33)

Only validated subdural hematoma cases and their corresponding controls included.

¹Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hormone replacement therapy, or oral corticosteroid drugs.

²Previous or concurrent use of other antiplatelet drugs or anticoagulant drugs included.

³Previous or concurrent use of antiplatelet drugs included. 23 users of non-vitamin K oral anticoagulants (3 cases and 20 controls) not included.

eTable 7. Association between subdural hematoma and preadmission antithrombotic drug use stratified by severity of head trauma in cases, Funen area, 2000-2012

	Mild/moderate head trauma ¹			Severe head trauma ¹		
	Cases, no. (%) (n=431)	Controls, no. (%) (n=8,604)	Adjusted OR ² (95% CI)	Cases, no. (%) (n=219)	Controls, no. (%) (n=4,375)	Adjusted OR ² (95% CI)
Never use of any antiplatelet drug	246 (57.1)	5,719 (66.5)	1 (reference)	169 (77.2)	3,477 (79.5)	1 (reference)
Low-dose aspirin ³						
Current use	130 (30.2)	1,887 (21.9)	1.41 (1.04-1.92)	30 (13.7)	562 (12.8)	0.93 (0.53-1.63)
Duration of current use						
< 3 months	17 (3.9)	208 (2.4)	1.68 (0.96-2.96)	6 (2.7)	74 (1.7)	1.42 (0.55-3.67)
3-12 months	49 (11.4)	489 (5.7)	2.01 (1.37-2.96)	6 (2.7)	155 (3.5)	0.62 (0.24-1.58)
>1 year	64 (14.8)	1,190 (13.8)	1.09 (0.76-1.56)	18 (8.2)	333 (7.6)	0.96 (0.50-1.84)
Never use of any anticoagulant Vitamin K antagonist ⁴	352 (81.7)	7,854 (91.3)	1 (reference)	199 (90.9)	4,123 (94.2)	1 (reference)
Current use	54 (12.5)	357 (4.1)	3.51 (2.51-4.89)	13 (5.9)	105 (2.4)	2.49 (1.31-4.73)
Duration of current use						
< 3 months	25 (5.8)	132 (1.5)	4.07 (2.54-6.54)	8 (3.7)	34 (0.8)	5.52 (2.34-13.05)
3-12 months	19 (4.4)	121 (1.4)	3.74 (2.22-6.31)	1 (0.5)	36 (0.8)	Not applicable
>1 year	10 (2.3)	104 (1.2)	2.41 (1.22-4.75)	4 (1.8)	35 (0.8)	2.47 (0.82-7.44)

Only 650 cases with confirmed history of trauma and information on trauma severity and their corresponding controls included.

¹Trauma severity was classified by neurosurgeons, blinded with regard to patients' use of antithrombotic drugs, based on their impression from the medical record information and guided by simple pre-defined examples provided to them (see online Supplement methods) into four mutually exclusive categories: "severe", "moderate", "mild", or "unclassifiable" (i.e., insufficient information). The latter group was not included in the present analysis.

²Adjusted for age, sex, and calendar period (by design) and the following, based on register data: hypertension, stroke, epilepsy, dementia, chronic obstructive pulmonary disease, high alcohol consumption, chronic hepatic disease, chronic renal insufficiency, diabetes, myocardial infarct, angina, unstable angina, peripheral artery disease, nonsteroidal anti-inflammatory drugs, selective serotonin reuptake inhibitors, hormone replacement therapy, or oral corticosteroid drugs.

³Previous or concurrent use of other antiplatelet drugs or anticoagulant drugs included.

⁴Previous or concurrent use of antiplatelet drugs included. 23 users of non-vitamin K oral anticoagulants (3 cases and 20 controls) not included.

eTable 8. Association between subdural hematoma imaging characteristics and preadmission antithrombotic drug use in cases, Funen area, 2000-2012

	Low-dose aspirin, current use (n=242)	Never use of antiplatelet drug (n=585)		
Subdural hematoma width, mm – mean (SD)			Difference (95% CI)	Adj. ¹ difference (95% CI)
Subacute/chronic subdural hematoma ²	18.0 (7.6)	17.7 (7.9)	0.3 (-1.4 to 2.0)	-0.7 (-2.6 to 1.2)
Acute subdural hematoma ³	12.0 (8.2)	10.4 (8.7)	1.5 (-0.7 to 3.8)	0.5 (-2.6 to 3.7)
Midline structure deviation presence – no (%)			OR (95% CI)	Adj. ⁴ OR (95% CI)
Subacute/chronic subdural hematoma ⁵	90 (63.8)	190 (63.8)	1.07 (0.65 to 1.77)	1.27 (0.69 to 2.31)
Acute subdural hematoma ⁶	49 (49.5)	127 (47.3)	0.99 (0.61 to 1.61)	1.01 (0.50 to 2.03)
	Vitamin K antagonist, current use (n=107)	Never use of anticoagulant (n=780)		
Subdural hematoma width, mm – mean (SD)			Difference (95% CI)	Adj. ¹ difference (95% CI)
Subacute/chronic subdural hematoma ⁷	18.1 (8.3)	17.6 (8.2)	0.5 (-2.0 to 2.9)	-0.7 (-3.1 to 1.7)
Acute subdural hematoma ⁸	13.1 (8.3)	10.5 (8.6)	2.6 (-0.3 to 5.4)	0.5 (-2.9 to 4.0)
Midline structure deviation presence – no (%)			OR (95% CI)	Adj. ⁴ OR (95% CI)
Subacute/chronic subdural hematoma ⁹	43 (78.2)	254 (59.1)	3.42 (1.32 to 8.89)	3.29 (1.14 to 9.51)
Acute subdural hematoma ¹⁰	35 (67.3)	153 (43.7)	2.15 (1.13 to 4.11)	2.80 (1.18 to 6.60)

Cases identified in Funen area, 2000-2012.

¹Age and sex adjusted using linear regression.

²Information missing for 21 patients with current low-dose aspirin use and 70 patients with never use of antiplatelet drugs.

³Information missing for 17 patients with current low-dose aspirin use and 80 patients with never use of antiplatelet drugs.

⁴Age and sex adjusted using logistic regression.

⁵Information missing for 23 patients with current low-dose aspirin use and 58 patients with never use of antiplatelet drugs.

⁶Information missing for 11 patients with current low-dose aspirin use and 56 patients with never use of antiplatelet drugs.

⁷Information missing for 7 patients with current vitamin K antagonist use and 101 patients with never use of anticoagulant drugs.

⁸Information missing for 11 patients with current vitamin K antagonist use and 93 patients with never use of anticoagulant drugs.

⁹Information missing for 7 patients with current vitamin K antagonist use and 87 patients with never use of anticoagulant drugs.

¹⁰Information missing for 3 patients with current vitamin K antagonist use and 65 patients with never use of anticoagulant drugs.

eTable 9. Association between subdural hematoma surgical treatment, 30-day mortality, and preadmission antithrombotic drug use in cases, Funen area, 2000-2012

	Low-dose aspirin, current use (n=307)	Never use of antiplatelet drug (n=585)	OR (95% CI)	Adj. ¹ OR (95% CI)
Subacute/chronic subdural hematoma – no. (%)				
Surgical procedure performed				
Yes, performed	98 (69.0)	237 (77.2)	0.66 (0.42-1.02)	0.80 (0.45-1.38)
No, not performed	44 (31.0)	70 (22.8)	1 (reference)	1 (reference)
Reason for operation not performed				
Prognosis too poor	3 (2.1)	2 (0.7)	NA ²	NA ²
Mild symptoms	38 (26.7)	62 (20.2)	NA ²	NA ²
Other reasons	3 (2.1)	4 (1.4)	NA ²	NA ²
Information missing	0 (0.0)	2 (0.7)	NA ²	NA ²
30-day mortality – no. (%)	9 (6.3)	14 (4.6)	1.41 (0.60-3.35)	1.07 (0.39-2.98)
Acute subdural hematoma – no. (%)				
Surgical procedure performed				
Yes, performed	27 (27.0)	93 (33.5)	0.74 (0.44-1.22)	0.73 (0.38-1.40)
No, not performed	73 (73.0)	185 (66.6)	1 (reference)	1 (reference)
Reason for operation not performed				
Prognosis too poor	15 (15.0)	25 (9.0)	NA ²	NA ²
Mild symptoms	47 (47.0)	129 (46.4)	NA ²	NA ²
Other reasons	16 (5.8)	6 (6.0)	NA ²	NA ²
Information missing	5 (5.0)	15 (5.4)	NA ²	NA ²
30-day mortality – no. (%)	29 (29)	52 (18.7)	1.78 (1.05-3.00)	1.15 (0.57-2.34)
	Vitamin K antagonist, current use (n=107)	Never use of anticoagulant (n=780)	OR (95% CI)	Adj. ⁴ OR (95% CI)
Subacute/chronic subdural hematoma – no. (%)				
Surgical procedure performed				
Yes, performed	44 (80.0)	317 (73.7)	1.43 (0.71-2.86)	1.19 (0.55-2.56)
No, not performed	11 (20.0)	113 (26.3)	1 (reference)	1 (reference)
Reason for operation not performed				
Prognosis too poor	2 (3.6)	3 (0.7)	NA ²	NA ²
Mild symptoms	8 (14.6)	99 (23.0)	NA ²	NA ²
Other reasons	1 (1.8)	7 (1.6)	NA ²	NA ²
Information missing	0 (0.0)	4 (0.9)	NA ²	NA ²

	Vitamin K antagonist, current use (n=107)	Never use of anticoagulant (n=780)	OR (95% CI)	Adj. ¹ OR (95% CI)
Subacute/chronic subdural hematoma – no. (%)				
30-day mortality – no. (%)	6 (10.9)	17 (4.0)	2.97 (1.12-7.90)	2.77 (0.94-8.18)
Acute subdural hematoma – no. (%)				
Surgical procedure performed				
Yes, performed	19 (36.5)	110 (31.4)	0.93 (0.76-1.15)	0.95 (0.73-1.23)
No, not performed	33 (63.5)	240 (68.6)	1 (reference)	1 (reference)
Reason for operation not performed				
Prognosis too poor	10 (19.2)	32 (9.1)	NA ²	NA ²
Mild symptoms	21 (40.4)	169 (48.3)	NA ²	NA ²
Other reasons	1 (1.9)	23 (6.6)	NA ²	NA ²
Information missing	1 (1.9)	16 (4.6)	NA ²	NA ²
30-day mortality – no. (%)	15 (28.9)	68 (19.4)	1.68 (0.87-3.23)	1.33 (0.62-2.89)

Cases identified in Funen area, 2000-2012.

¹Age and sex adjusted using logistic regression.

²NA: Not applicable.

Table 10. Incidence rate of subdural hematoma and percentage of subdural hematoma patients with current use of antithrombotic drugs in Denmark, 2000-2015

A. Men, 20-64 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	1,658,158	121	7.3 (6.1-8.7)	5.8	0.0	4.1	0.0	1.7
2001	1,660,585	122	7.3 (6.1-8.8)	6.6	0.0	0.8	0.0	5.7
2002	1,660,273	136	8.2 (6.9-9.7)	14.0	0.0	5.9	0.0	8.1
2003	1,658,858	131	7.9 (6.6-9.4)	9.9	0.0	3.1	0.8	6.1
2004	1,655,201	127	7.7 (6.4-9.1)	10.2	0.0	1.6	2.4	6.3
2005	1,651,851	141	8.5 (7.2-10.1)	13.5	0.0	2.8	2.1	8.5
2006	1,650,067	146	8.8 (7.5-10.4)	17.8	0.0	6.2	1.4	10.3
2007	1,649,976	149	9.0 (7.6-10.6)	17.4	0.0	6.0	0.7	10.7
2008	1,651,595	174	10.5 (9.0-12.2)	17.2	0.0	6.9	0.6	9.8
2009	1,655,150	149	9.0 (7.6-10.6)	16.1	0.0	6.0	2.0	8.1
2010	1,650,539	148	9.0 (7.6-10.5)	12.8	0.0	2.7	0.7	9.5
2011	1,647,264	150	9.1 (7.7-10.7)	19.3	0.0	8.0	2.7	8.7
2012	1,642,171	156	9.5 (8.1-11.1)	19.9	0.0	4.5	4.5	10.9
2013	1,642,363	139	8.5 (7.1-10.0)	18.7	0.7	7.9	4.3	5.8
2014	1,646,910	127	7.7 (6.4-9.2)	15.7	0.0	7.1	3.9	4.7
2015	1,657,805	135	8.1 (6.8-9.6)	17.0	0.0	3.0	5.9	8.1

B. Women, 20-64 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	1,618,979	55	3.4 (2.6-4.4)	5.5	0.0	3.6	0.0	1.8
2001	1,623,315	47	2.9 (2.1-3.9)	2.1	0.0	0.0	0.0	2.1
2002	1,625,742	60	3.7 (2.8-4.8)	3.3	0.0	0.0	0.0	3.3
2003	1,626,486	48	3.0 (2.2-3.9)	10.4	0.0	2.1	2.1	6.3
2004	1,625,189	47	2.9 (2.1-3.8)	21.3	0.0	6.4	6.4	8.5
2005	1,624,323	59	3.6 (2.8-4.7)	6.8	0.0	1.7	0.0	5.1
2006	1,624,273	63	3.9 (3.0-5.0)	22.2	0.0	9.5	1.6	11.1
2007	1,625,389	62	3.8 (2.9-4.9)	19.4	0.0	8.1	0.0	11.3
2008	1,626,975	62	3.8 (2.9-4.9)	14.5	0.0	4.8	3.2	6.5
2009	1,629,792	48	2.9 (2.2-3.9)	16.7	0.0	4.2	2.1	10.4
2010	1,629,094	62	3.8 (2.9-4.9)	11.3	0.0	6.5	1.6	3.2
2011	1,628,030	66	4.1 (3.1-5.2)	12.1	0.0	4.5	3.0	4.5
2012	1,624,678	50	3.1 (2.3-4.1)	18.0	0.0	6.0	6.0	6.0
2013	1,624,644	76	4.7 (3.7-5.9)	15.8	2.6	6.6	1.3	5.3
2014	1,628,175	60	3.7 (2.8-4.7)	30.0	0.0	11.7	10.0	8.3
2015	1,635,230	50	3.1 (2.3-4.0)	10.0	0.0	2.0	2.0	6.0

C. Men, 65-74 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	191,166	56	29.3 (22.1-38.0)	30.4	0.0	7.1	0.0	23.2
2001	192,059	68	35.4 (27.5-44.9)	26.5	0.0	13.2	0.0	13.2
2002	193,882	82	42.3 (33.6-52.5)	24.4	0.0	8.5	1.2	14.6
2003	196,733	80	40.7 (32.2-50.6)	30.0	0.0	10.0	2.5	17.5
2004	200,222	79	39.5 (31.2-49.2)	34.2	0.0	12.7	3.8	17.7
2005	204,647	81	39.6 (31.4-49.2)	49.4	0.0	24.7	1.2	23.5
2006	209,882	85	40.5 (32.3-50.1)	44.7	0.0	14.1	2.4	28.2
2007	215,868	110	51.0 (41.9-61.4)	42.7	0.0	17.3	0.9	24.5
2008	225,190	104	46.2 (37.7-56.0)	49.0	0.0	17.3	6.7	25.0
2009	235,605	92	39.0 (31.5-47.9)	55.4	0.0	22.8	2.2	30.4
2010	248,309	118	47.5 (39.3-56.9)	31.4	0.0	12.7	1.7	16.9
2011	262,250	122	46.5 (38.6-55.5)	54.1	0.8	19.7	9.8	23.8
2012	276,428	145	52.5 (44.3-61.7)	49.0	1.4	19.3	6.9	21.4
2013	288,496	129	44.7 (37.3-53.1)	53.5	3.9	16.3	7.8	25.6
2014	297,234	157	52.8 (44.9-61.8)	48.4	3.8	18.5	8.9	17.2
2015	303,739	174	57.3 (49.1-66.5)	43.1	5.7	12.6	10.3	14.4

D. Women, 65-74 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	222,133	18	8.1 (4.8-12.8)	33.3	0.0	11.1	0.0	22.2
2001	220,986	31	14.0 (9.5-19.9)	22.6	0.0	9.7	0.0	12.9
2002	221,369	19	8.6 (5.2-13.4)	26.3	0.0	10.5	0.0	15.8
2003	223,166	33	14.8 (10.2-20.8)	33.3	0.0	18.2	3.0	12.1
2004	225,430	41	18.2 (13.1-24.7)	29.3	0.0	9.8	2.4	17.1
2005	228,413	34	14.9 (10.3-20.8)	47.1	0.0	17.6	2.9	26.5
2006	232,512	32	13.8 (9.4-19.4)	34.4	0.0	3.1	6.2	25.0
2007	237,449	28	11.8 (7.8-17.0)	25.0	0.0	7.1	3.6	14.3
2008	245,315	54	22.0 (16.5-28.7)	44.4	0.0	11.1	9.3	24.1
2009	255,552	50	19.6 (14.5-25.8)	38.0	0.0	12.0	4.0	22.0
2010	267,400	59	22.1 (16.8-28.5)	45.8	0.0	11.9	3.4	30.5
2011	280,393	61	21.8 (16.6-27.9)	52.5	0.0	18.0	8.2	26.2
2012	294,027	50	17.0 (12.6-22.4)	36.0	0.0	18.0	4.0	14.0
2013	305,533	67	21.9 (17.0-27.8)	32.8	0.0	14.9	3.0	14.9
2014	314,445	66	21.0 (16.2-26.7)	33.3	3.0	7.6	9.1	13.6
2015	321,587	78	24.3 (19.2-30.3)	39.7	1.3	11.5	6.4	20.5

E. Men, 75-89 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	130,899	102	77.9 (63.5-94.6)	49.0	0.0	13.7	0.0	35.3
2001	131,644	106	80.5 (65.9-97.4)	32.1	0.0	9.4	0.0	22.6
2002	132,177	110	83.2 (68.4-100.3)	50.0	0.0	12.7	0.9	36.4
2003	132,419	135	101.9 (85.5-120.7)	51.9	0.0	14.8	0.7	36.3
2004	133,375	141	105.7 (89.0-124.7)	49.6	0.0	17.0	1.4	31.2
2005	134,167	149	111.1 (93.9-130.4)	57.7	0.0	18.8	2.0	36.9
2006	135,476	132	97.4 (81.5-115.5)	57.6	0.0	14.4	2.3	40.9
2007	136,702	156	114.1 (96.9-133.5)	55.8	0.0	17.3	1.9	36.5
2008	138,177	162	117.2 (99.9-136.7)	64.2	0.0	21.0	4.9	38.3
2009	139,975	174	124.3 (106.5-144.2)	62.6	0.0	28.7	1.1	32.8
2010	142,289	179	125.8 (108.0-145.6)	62.6	0.0	24.0	5.6	33.0
2011	144,843	211	145.7 (126.7-166.7)	65.4	0.0	24.2	6.6	34.6
2012	148,575	189	127.2 (109.7-146.7)	67.2	2.6	25.9	10.6	28.0
2013	152,955	225	147.1 (128.5-167.6)	70.2	2.2	25.8	14.7	27.6
2014	158,128	222	140.4 (122.5-160.1)	68.5	6.8	25.2	14.0	22.5
2015	163,778	222	135.5 (118.3-154.6)	68.9	7.2	27.9	14.4	19.4

F. Women, 75-89 years

Year	Person-time, years	Incident cases, no.	Incidence rate (95% CI)	Incident cases with current antithrombotic drug use, %				
				Any AT	DOAC	VKA	Clopidogrel	Low-dose aspirin
2000	215,630	89	41.3 (33.1-50.8)	41.6	0.0	9.0	0.0	32.6
2001	215,363	91	42.3 (34.0-51.9)	36.3	0.0	3.3	0.0	33.0
2002	214,565	74	34.5 (27.1-43.3)	47.3	0.0	12.2	1.4	33.8
2003	212,692	78	36.7 (29.0-45.8)	42.3	0.0	7.7	2.6	32.1
2004	211,596	87	41.1 (32.9-50.7)	63.2	0.0	20.7	2.3	40.2
2005	210,524	93	44.2 (35.7-54.1)	53.8	0.0	17.2	1.1	35.5
2006	210,186	114	54.2 (44.7-65.2)	51.8	0.0	20.2	3.5	28.1
2007	209,245	111	53.0 (43.6-63.9)	55.0	0.0	20.7	1.8	32.4
2008	208,479	94	45.1 (36.4-55.2)	60.6	0.0	22.3	4.3	34.0
2009	208,009	116	55.8 (46.1-66.9)	62.9	0.0	21.6	6.0	35.3
2010	208,242	135	64.8 (54.4-76.7)	57.0	0.0	18.5	3.7	34.8
2011	207,929	131	63.0 (52.7-74.8)	55.7	0.0	19.1	4.6	32.1
2012	209,219	145	69.3 (58.5-81.5)	68.3	0.7	26.9	13.1	27.6
2013	212,185	149	70.2 (59.4-82.4)	59.1	2.7	22.1	10.1	24.2
2014	215,402	159	73.8 (62.8-86.2)	64.8	4.4	20.8	10.7	28.9
2015	219,252	160	73.0 (62.1-85.2)	62.5	10.6	21.3	13.7	16.9

AT: antithrombotic drug; DOAC: direct oral anticoagulant; VKA: vitamin K antagonist.

eMethods

Cases

International Classification of Diseases 10th Edition (ICD-10) code S065 (“traumatic SDH” in Danish ICD-10 version) was used to identify cases of subdural hematoma (SDH). Only incident cases with S065 code as principal discharge diagnosis were included.¹ This algorithm was developed based on the results of a previous large validation study, where medical records of more than 1,000 patients with SDH codes (inpatient, outpatient, and emergency room data) were assessed. Likewise, code I620 (“non-traumatic SDH”) was not included, as the positive predictive value of this code was low, according to the previously mentioned validation study.¹

Cases were classified with regard to (i) admission or transferal to neurosurgery departments during the first week of hospitalization, and (ii) recorded surgical intervention codes, i.e., burr hole, craniotomy, or none. Cases that underwent both procedures during the same episode of care were classified as craniotomy.

Assessment of antithrombotic drug exposure

For low-dose aspirin (ASA), an estimated daily dose was calculated defined as the most frequently prescribed tablet strength during the last five years in the exposure period.

To calculate length of supply of each prescription, each prescription was set to last the number of days that corresponded to the number of pills dispensed (divided by 2 for dipyridamole, dabigatran, and apixaban, and 1.5 for warfarin,² and divided by 1 for all other antithrombotic drugs) plus a grace period of 60 days (to allow some degree of non-compliance or irregular dispensing). A treatment episode lasted for as long as consecutive prescriptions were presented with no gap, i.e., presented within the time-window defined by the coverage of the preceding prescription including the grace period. Based on the most recent treatment episode prior to the index date, exposure was divided into current use (use at index-date), recent use (treatment episode ending 1-90 days before index date), past use (91-365 days), and distant use (>365 days before index-date). Similar to a previous study,³ current use was further subdivided by the duration of the current treatment episode into <1 month; ≥1 month, ≤3 months; >3 months to ≤12 months; >1 year to ≤3 years; and >3 years.

Some subjects switch between antithrombotic drugs. To analyze the effect of use of individual antithrombotic drugs, analyses on duration of current use were therefore repeated in subjects that had only used a single antithrombotic drug within 12 months of their index date (i.e, subjects switching antithrombotic drugs in the last 12 months were excluded). The effect of dipyridamole only (with no concurrent use of ASA) was not analyzed, since, in accordance with Danish guidelines on stroke prevention, this drug is only recommended in combination with ASA.⁴ Accordingly, only the combination ASA/dipyridamole was studied. Further, analyses were performed restricted to first time users of the drug. First-time users were defined as subjects who had initiated antiplatelet drug treatment within the 4 years preceding their index date and with no use prior to this time window.

Finally, the risk of SDH was calculated in subjects with concurrent multiple use of antithrombotics (dual therapy and triple therapy). In these analyses, use of dipyridamole was disregarded (except in the analysis concerning dual therapy with ASA and dipyridamole).

Regional analyses

Using a regional Patient Registry and methods similar to the above, all residents of the area admitted under SDH diagnostic codes in the catchment area (Funen area) in 2000-2012 were identified and the diagnoses codes were validated as previously described.¹ In this regional material, information was retrieved from medical records on history of head trauma, including timing in relation to admission, and severity. Two neurosurgeons classified trauma severity based on their impression from the medical record information and guided by simple pre-defined examples provided to them (see parentheses) into four mutually exclusive categories: “severe” (e.g., high-impact motor vehicle head trauma, fall from flight of stairs), “moderate” (e.g., fall on level ground), “mild” (e.g., hit head against cupboard lid), or “unclassifiable”. Information on

alcohol overuse was also retrieved from the medical records, and brain scans of all potential cases were visually assessed. The two neurosurgeons evaluating the medical records and brain scans were blinded with regard to patients' use of antithrombotic drugs.

Using a local register,⁵ eligible subjects were selected from the general population in the catchment area and matched to cases on age, sex, and calendar period (year) with a 1:20 case to control ratio. For cases and controls, information was retrieved from local registries on all hospital contacts, and prescription fills. Prehospital use of antithrombotic drugs was classified in all patients using the same methods as described above.

Statistical analyses

Supplementary analyses were performed to address: (i) the presence of potential effect measure modification of age and sex by stratifying analyses according to these variables; and (ii) subgroup analyses by fatal vs. non-fatal cases.

Descriptive analyses

Trends in incidence rate of SDH

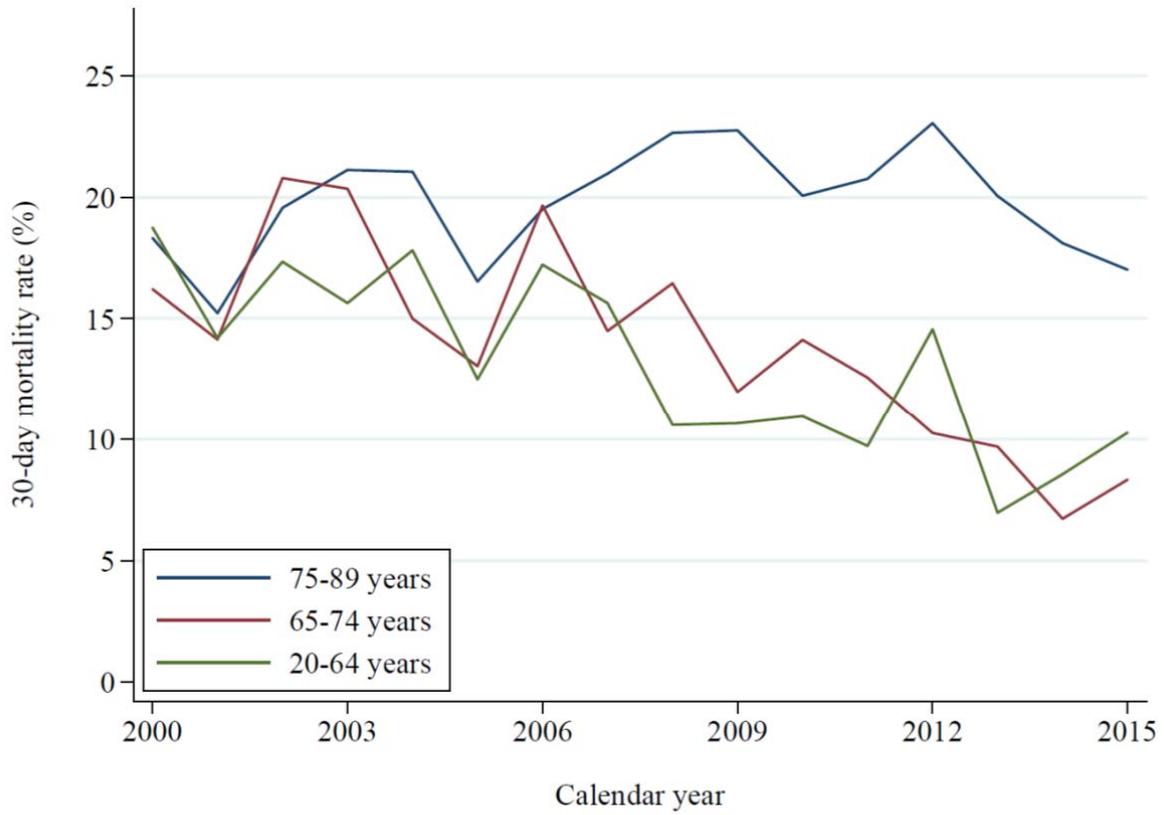
Using linear regression, the trend was calculated in the incidence rate of SDH.

Trends in the 30-day case fatality rate of SDH patients were also tested (by direct age- and sex-standardization).

Patterns of antithrombotic drug use

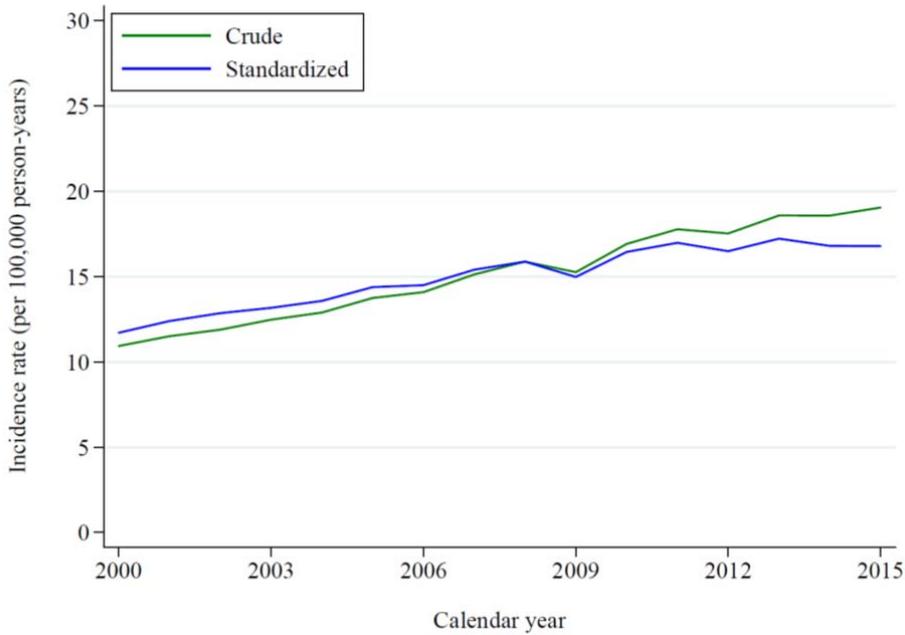
To describe patterns of antithrombotic drug use, data from a regional prescription register,⁵ were used. From this register all 2,887,336 prescriptions for antithrombotic drugs redeemed by all residents of the previously described Funen area (population 484,346) for the period 2000 to 2015 were retrieved. Data were limited to residents of the area ages 20-89 years and the same exposure criteria were used as when exposure status was assigned to cases and controls. All users were charted with respect to periods of single and concomitant current use within each calendar year.

eFigure 1. Short-term (30-day) mortality after subdural hematoma diagnosis stratified by age, Denmark, 2000-2015

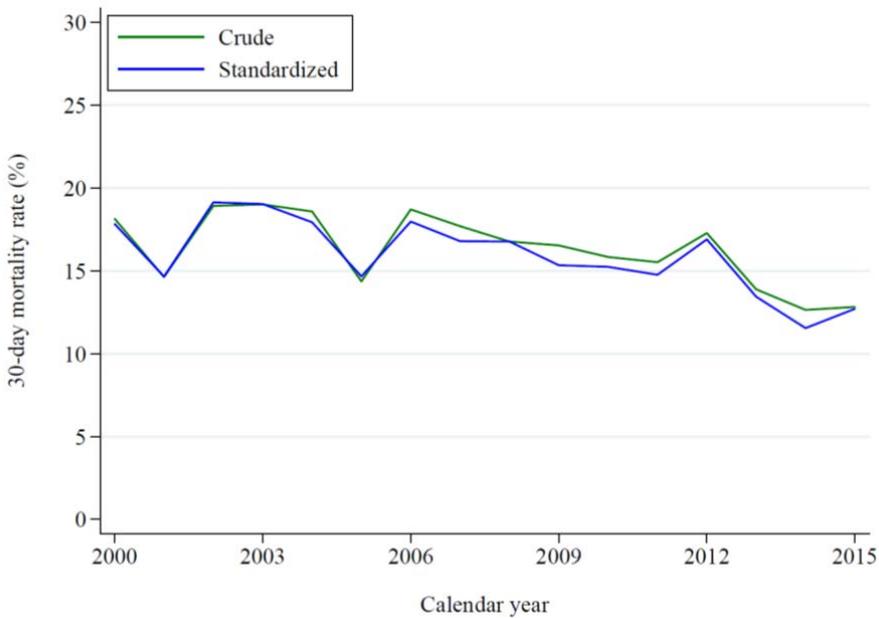


eFigure 2. Crude and age- and sex standardized incidence rate of subdural hematoma (panel A) and 30-day mortality (panel B) after subdural hematoma diagnosis, Denmark, 2000-2015

A.



B.



eReferences

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