Contents Supplementary Material

eMethods

Stratified analyses

First, we stratified by sex, age-groups (0-64, 65 – 74, 75 – 85, >85), and bleeding risk (HAS-BLED 0-2 and ≥3). Second, we stratified by concomitant antiplatelet and concomitant NSAID use. Third, we stratified by the individual NOACs apixaban, dabigatran, and rivaroxaban (edoxaban was not considered due to the very small sample size). We included an interaction term in our models and used the likelihood ratio test to test whether the interaction terms were significant. As it is not possible to pool results from different likelihood ratio tests through a meta-analysis, we considered a subgroup as an effect-modifier if the likelihood ratio test was significant in two or more databases. In each subgroup, we calculated the number needed to treat for one year (NNTY), by taking the multiplicative inverse of the absolute risk reduction. The absolute risk reduction was estimated with the incidence rate from the untreated group and the adjusted IRR.

Sensitivity analyses

We conducted several sensitivity analyses to test the robustness of our findings. First, we calculated E-values to identify the minimum strength of association that an unmeasured confounder would need to have with both PPI use and UGIB, conditional on the measured confounders, to explain away the observed associations [1]. Second, we tested the association between PPI use and non-GI major bleeds. As PPI use should not affect the risk for those bleeds, they could serve as falsification endpoints and we could assess potential residual confounding [2]. Third, we assessed how the results would be affected by including information on primary care diagnostic data by assessing the association between PPI use and UGIB in the Stockholm healthcare database with and without restricting the analyses to only secondary care data. Fourth, we conducted an analysis in which we had a maximum follow-up of one year. Fifth, we conducted an analysis in which we kept all covariates fixed at baseline. Finally, we conducted an analysis in which we excluded all patients suffering from the outcome of interest in the year prior to inclusion to remove high risk patients and an analysis where we excluded all patients suffering from any bleed or anemia in the year prior to inclusion.

To assess for each covariate how it influenced the exposure-outcome association, and thus what the effect of confounding adjustment is per covariate, we performed an additional analysis in which we created several adjusted Poisson regression models (i.e., without taking IPW into account). In these models we first: added each aforementioned covariate univariately, but still time-dependently; second: added groups of covariates (i.e., age-sex, CHADsVASc- and HAS-BLED comorbidities, GI comorbidities, comedication), and third: performed a full time-dependent covariate adjusted Poisson regression model.

eResults

The E-value for the point estimate for UGIB was 2.01. This indicates that a potential unobserved confounder would have required a relative risk of 2.01 with both the outcome and PPI use to move the point estimate to neutral.

We found a neutral association between PPI use and the first falsification endpoint of non-GI major bleed (IRR: 1.04; CI: 0.89 – 1.23). Censoring patients after one year of follow-up yielded similar results as in the main analysis (IRR: 0.72; CI: 0.54 – 0.96), as did excluding patients with a UGIB in the year prior to inclusion (IRR: 0.76; CI: 0.60 – 0.97) and exclusion of patients with any bleed or anemia in the year prior to the event (IRR: 0.78; CI 0.60 – 1.01). Keeping the covariates fixed at baseline yielded no different results (IRR: 0.81; CI 0.64 – 1.03).

Baseline characteristics were comparable to those observed in the main analysis when analyzing only secondary care data (Appendix Table 3). We found comparable results when we used only data from secondary care in Stockholm (IRR: 0.67; CI: 0.34 – 1.20), compared to data from both primary and secondary care (IRR: 0.79; CI: 0.49 – 1.26).

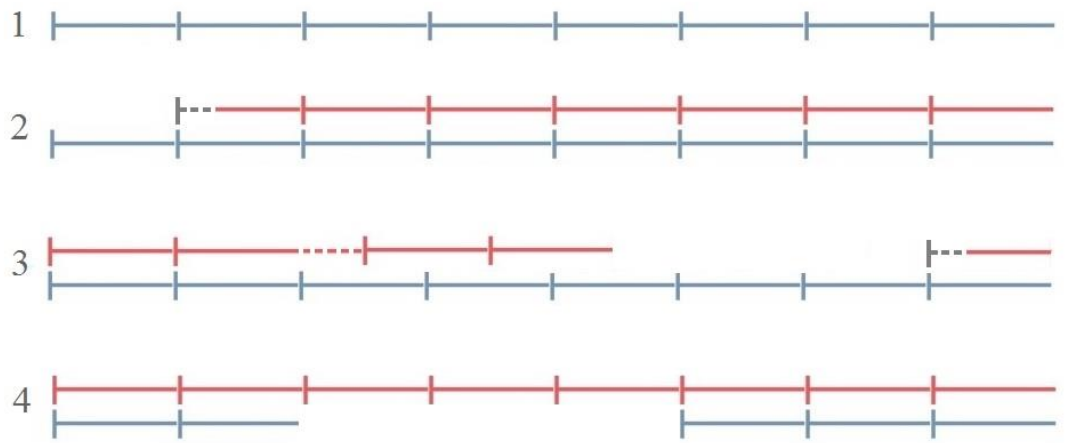
The stepwise adjusted models showed that anemia had the largest univariate effect when adjusting the models, followed by vascular disease and diuretics, and all three moved the point estimate towards a protective effect (Appendix Table 4). All groups of covariates were effective in removing confounding, but no group was as effective as the fully adjusted model and the full IPW model, indicating that adjustment for all covariates was needed. The fully adjusted models showed a larger protective effect compared to the IPW model.

eReferences

1. Weele TJ Van Der, Ding P. Sensitivity analysis in observational research: Introducing the E-Value. *Ann Intern Med* American College of Physicians; 2017;**167**:268–274.

2. Prasad V, Jena AB. Prespecified Falsification End Points. *JAMA* American Medical Association; 2013;**309**:241.

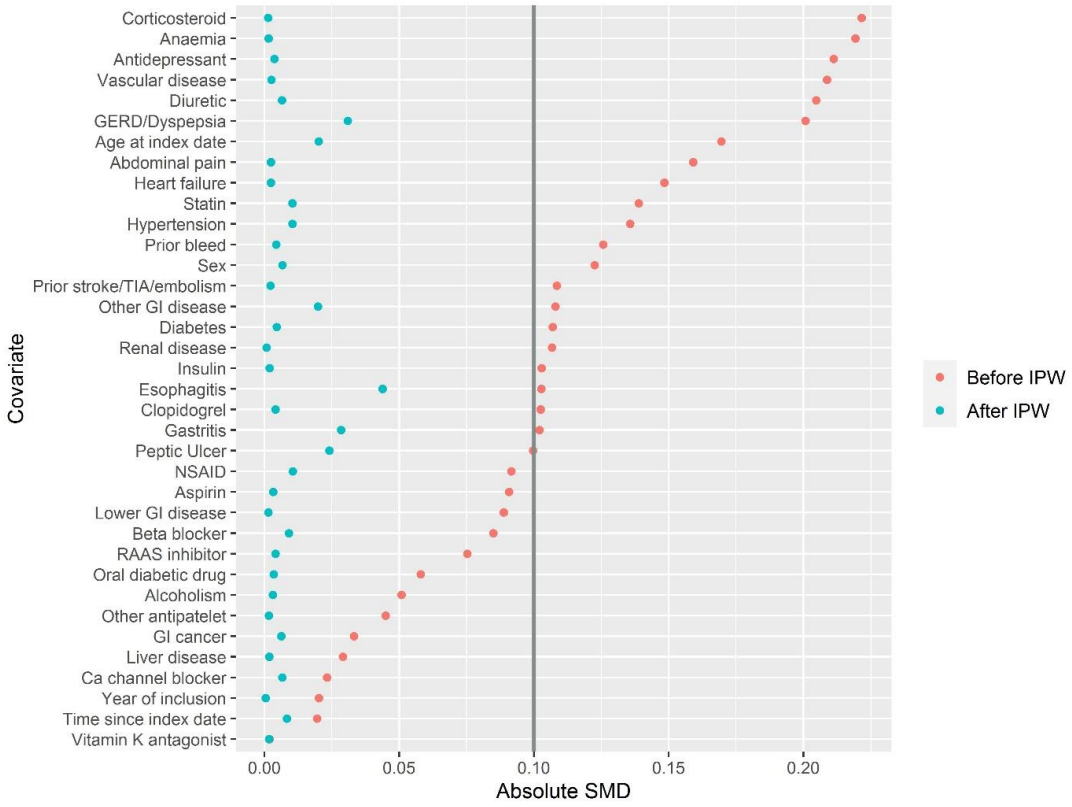
Appendix figure 1



Graphical presentation of four hypothetical patients with different exposure patterns. The vertical lines indicate that a patient claims a prescription and the horizontal lines indicate the duration of a prescription. A blue line is for a NOAC prescription and a red line is for a PPI prescription.

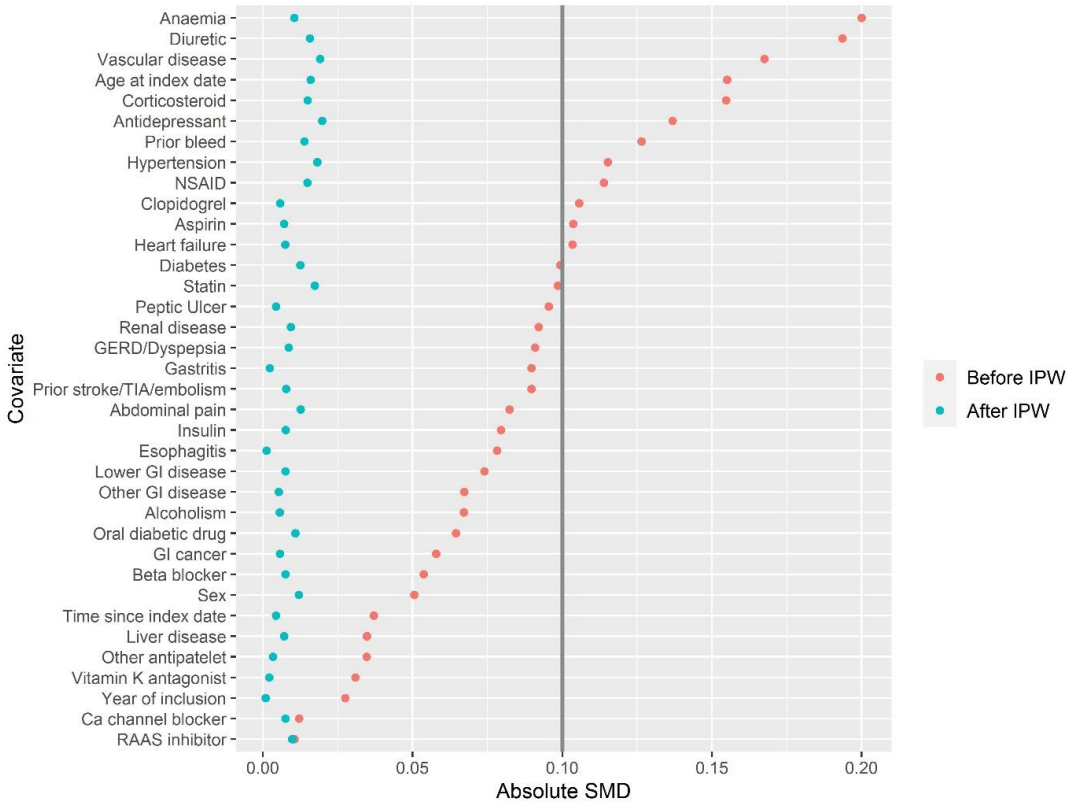
- Patient 1 is exposed to a NOAC the whole period and is therefore in the cohort the whole time, without any PPI exposure.
- Patient 2 claims a PPI prescription in the second period, and after a wash-in of 7 days (the grey area), the patient is considered exposed to a PPI the rest of the study period.
- Patient 3 is taking a PPI from the beginning of the study and is considered exposed to a PPI from the start. After the second PPI prescription, the patient claims a new PPI prescription after the calculated end of the second prescription, but within the 30-day grace period for non-compliance and, therefore, the patient is considered exposed to PPI treatment during that whole period. After the fourth PPI prescription, the patient fails to claim a new prescription within the 30-day grace period and is therefore considered unexposed from the end of the calculated end of the fourth prescription. At the end the patient claims a new PPI prescription and after a wash-in of 7 days the patient is considered exposed to PPI treatment.
- Patient 4 is taking a PPI from the beginning of the study and is considered exposed to a PPI from the start. After the second NOAC prescription, the patient fails to claim a new NOAC prescription within the 30-day grace period and, therefore, the patient is removed from the cohort during that period. After the patient claims a new NOAC prescription, the patient is once again included in the cohort.

Appendix figure 2a



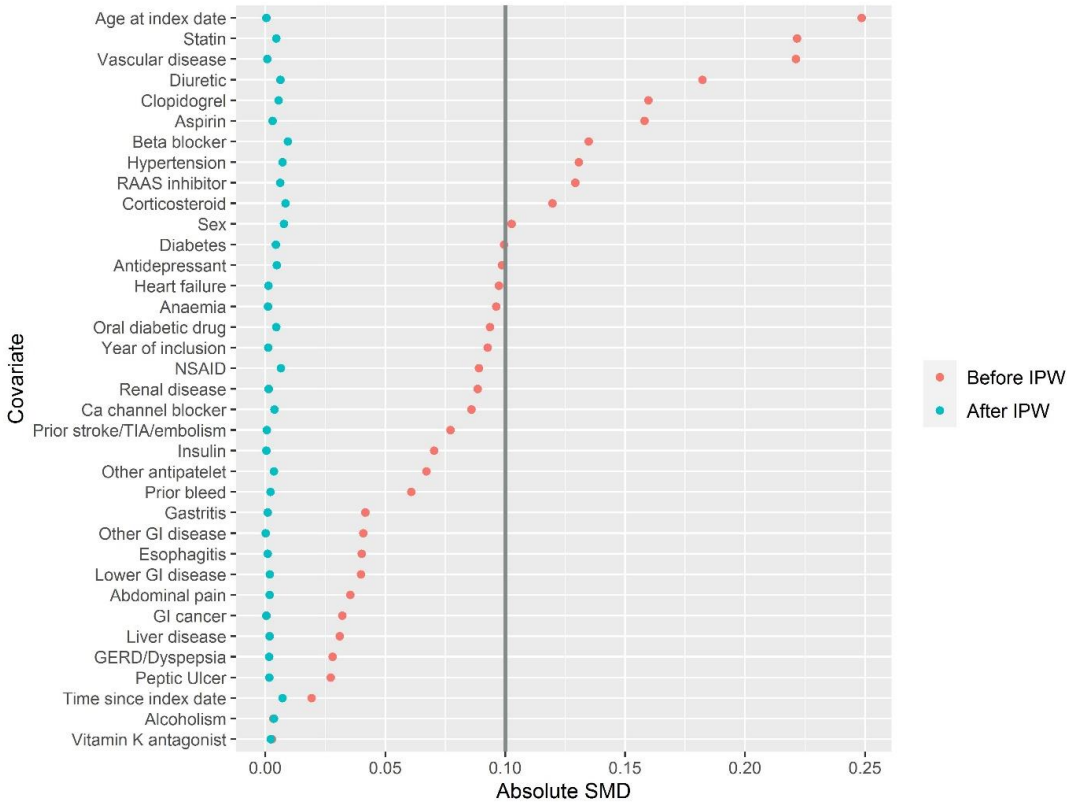
Standardized mean differences of covariates before and after applying inverse probability weighting in the Stockholm database.

Appendix table 2b



Standardized mean differences of covariates before and after applying inverse probability weighting in the Denmark database.

Appendix table 2c



Standardized mean differences of covariates before and after applying inverse probability weighting in the PHARMO database.

Appendix table 1

Outcome definition	**ICD-code beginning with**
Upper GI bleed	K25-K28 (sub codes 0, 2, 4, and 6 only) K290, K228, K298, I864
Baseline comorbidities	**ICD-code beginning with**
Hypertension	I10-I16
Renal disease	N183, N184, N185, N189, E102, E112, E122, E132, E142, I12, N03, N083, N085, N118C, N14, N150, N16, N19, N26, P960, Q601, Q602, Z992
Liver disease	K70-77
Stroke/TIA/embolism	I63, I64, I679, I693, I694, I698, I69, G453, G458, G459, I74, I26, I80, I81, I82
Prior bleed	I60, I61, I62, S064, S065, S066, I850, I983, K25-K28 (sub codes 0, 2, 4, and 6 only) K290, K228, K298, I864, K625, K922, D62, S063C, K920, G951A, I312, J942, K638B, K638C, K661, K868G, N02, R04, R31, R58
Anaemia	D50-59, D60-64
Alcohol abuse	E244, F10, G312, G621, G721, I426, K292, K70, K860, O354, P043, T51, Y90, Y91, Y91, Z502, Z714, E529A
Heart failure	I50, I099A, I971A, O754C, O291A, O742A, O754D, O891A, I30, Z035EA
Vascular disease	I20, I21, I22, I23, I24, I25, I70, I739
Diabetes	E10, E11, E12, E13, E14, G590, G632, H280, H360, N083, O240, O241, O242, O243
Peptic ulcer	K25-K28 (sub codes 1, 3, 5, 7, and 9 only)
GI cancer	C15-26
Gastritis	K29
Esophagitis	K20, K220, K2210, K222-229
GERD/dyspepsia	K21, K30
Abdominal pain	R10, R12
Lower GI problems	K57, K60-64
Other GI problems	K31, R11
Medication	**ATC code beginning with**
Apixaban	B01AF02
Dabigatran	B01AE07
Rivaroxaban	B01AF01
Edoxaban	B01AF03
PPI	A02BC
Aspirin	B01AC06
NSAID	M01A
Clopidogrel	B01AC04
Other antiplatelet	B01AC22, B01AC24, B01AC07
Corticosteroids	H02AA01, H02AA02, H02AA03, H02AB
Diuretic	C03A, C03B, C03C, C03D, C03E
Beta blocker	C07A, C07B, C07C, C07D, C07E, C07F
Ca channel blocker	C08C, C08D, C08E, C08G
RAAS inhibitor	C09A, C09B, C09C, C09D, C09X
Statin	C10AA
Oral antidiabetic drug	A10B
Insulin	A10A
Antidepressant	N06A
Falsification endpoint	**ICD code beginning with**
Non GI major bleed	I60, I61, I62, S064, S065, J942, I312, H431, H351

ATC and ICD-10 codes

Appendix table 2.

	Stockholm		**Denmark**		**PHARMO**	
	Total (N=34977)		**Total (N = 108322)**		**Total (N=19034)**	
	PPI user	**PPI non-user**	**PPI user**	**PPI non-user**	**PPI user**	**PPI non-user**
n	11 682	23 349	26 220	84 005	8 806	10 228
Person time (years)	9993	45586	21762	169226	8183	17820
Age, sex, risk scores						
Female	5771 (49.6%)	10028 (42.9%)	12323 (47.0%)	36962 (44.0%)	3954 (44.9%)	4146 (40.5%)
Age	75.31 (10.36)	74.30 (11.07)	75.83 (10.19)	74.50 (11.11)	73.26 (10.11)	70.97 (10.96)
CHADsVASc (mean (sd))	3.77 (1.84)	3.29 (1.78)	3.22 (1.68)	2.83 (1.66)	2.85 (1.66)	2.37 (1.63)
HAS-BLED (mean(sd))	2.55 (1.22)	2.16 (1.14)	2.19 (1.16)	1.86 (1.12)	1.89 (1.12)	1.52 (1.09)
≥1 GI comorbidity, n (%)	2330 (20.0%)	1951 (8.4%)	2944 (11.2%)	5159 (6.1%)	562 (6.4%)	450 (4.4%)
NOAC						
Apixaban	7154 (61.5%)	15876 (68.0%)	8299 (31.7%)	28439 (33.9%)	2072 (23.5%)	2548 (24.9%)
Dabigatran	2526 (21.7%)	3930 (16.8%)	9154 (34.9%)	23957 (28.5%)	3673 (41.7%)	3711 (36.3%)
Rivaroxaban	1929 (16.6%)	3486 (14.9%)	8506 (32.4%)	30295 (36.1%)	2649 (30.1%)	3362 (32.9%)
Edoxaban	19 (0.2%)	57 (0.2%)	261 (1.0%)	1314 (1.6%)	412 (4.7%)	607 (5.9%)
Main comorbidities						
Hypertension	7966 (68.5%)	14393 (61.6%)	9558 (36.5%)	25212 (30.0%)	2912 (33.1%)	2737 (26.8%)
Renal disease	906 (7.8%)	1135 (4.9%)	1142 (4.4%)	2460 (2.9%)	610 (6.9%)	522 (5.1%)
Liver disease	140 (1.2%)	189 (0.8%)	268 (1.0%)	580 (0.7%)	148 (1.7%)	124 (1.2%)
Prior stroke/TIA/embolism	2624 (22.6%)	4270 (18.3%)	5408 (20.6%)	14471 (17.2%)	1023 (11.6%)	994 (9.7%)
Alcoholism	368 (3.2%)	601 (2.6%)	677 (2.6%)	1423 (1.7%)	112 (1.3%)	127 (1.2%)
Prior bleed	1692 (14.6%)	2316 (9.9%)	3190 (12.2%)	6691 (8.0%)	410 (4.7%)	335 (3.3%)
Anaemia	1791 (15.4%)	1699 (7.3%)	2426 (9.3%)	3539 (4.2%)	720 (8.2%)	548 (5.4%)
Heart failure	3065 (26.4%)	4850 (20.8%)	4351 (16.6%)	11131 (13.3%)	1221 (13.9%)	1121 (11.0%)
Vascular disease	3031 (26.1%)	3755 (16.1%)	6228 (23.8%)	14048 (16.7%)	2188 (24.8%)	1459 (14.3%)
Diabetes	2414 (20.8%)	3895 (16.7%)	3459 (13.2%)	8566 (10.2%)	1362 (15.5%)	1237 (12.1%)
GI comorbidities						
Peptic ulcer	189 (1.6%)	42 (0.2%)	309 (1.2%)	191 (0.2%)	13 (0.1%)	3 (0.0%)
Gastrointestinal cancer	124 (1.1%)	149 (0.6%)	414 (1.6%)	765 (0.9%)	141 (1.6%)	109 (1.1%)
Gastritis	199 (1.7%)	72 (0.3%)	294 (1.1%)	265 (0.3%)	41 (0.5%)	16 (0.2%)
Esophagitis	136 (1.2%)	37 (0.2%)	227 (0.9%)	221 (0.3%)	36 (0.4%)	26 (0.3%)
GERD/dyspepsia	530 (4.6%)	188 (0.8%)	370 (1.4%)	495 (0.6%)	40 (0.5%)	16 (0.2%)
Abdominal pain	1028 (8.8%)	881 (3.8%)	857 (3.3%)	1868 (2.2%)	92 (1.0%)	77 (0.8%)
Lower GI problems	611 (5.3%)	681 (2.9%)	949 (3.6%)	2019 (2.4%)	193 (2.2%)	183 (1.8%)
Other GI problems	276 (2.4%)	184 (0.8%)	242 (0.9%)	402 (0.5%)	104 (1.2%)	81 (0.8%)
Comedication						
Aspirin	3837 (33.0%)	5892 (25.2%)	8748 (33.4%)	22930 (27.3%)	2448 (27.8%)	1680 (16.4%)
Vitamin K antagonist	1978 (17.0%)	2438 (10.4%)	6525 (24.9%)	19625 (23.4%)	2371 (26.9%)	2984 (29.2%)
Clopidogrel	560 (4.8%)	600 (2.6%)	2536 (9.7%)	6816 (8.1%)	734 (8.3%)	531 (5.2%)
Other antiplatelets	241 (2.1%)	253 (1.1%)	773 (2.9%)	1614 (1.9%)	348 (4.0%)	189 (1.8%)
NSAID	1380 (11.9%)	1737 (7.4%)	4467 (17.0%)	9975 (11.9%)	1164 (13.2%)	939 (9.2%)
Corticosteroid	1708 (14.7%)	1375 (5.9%)	3207 (12.2%)	6364 (7.6%)	1237 (14.0%)	983 (9.6%)
Diuretic	3663 (31.5%)	5492 (23.5%)	11557 (44.1%)	30465 (36.3%)	2904 (33.0%)	2624 (25.7%)
Beta blocker	7302 (62.8%)	13445 (57.6%)	12591 (48.0%)	36831 (43.8%)	5166 (58.7%)	5395 (52.7%)
Calcium channel blocker	3089 (26.6%)	5932 (25.4%)	7425 (28.3%)	21921 (26.1%)	2196 (24.9%)	2163 (21.1%)
RAAS inhibitor	5312 (45.7%)	9599 (41.1%)	12466 (47.5%)	37509 (44.7%)	4522 (51.4%)	4425 (43.3%)
Statin	4161 (35.8%)	6864 (29.4%)	10788 (41.1%)	30781 (36.6%)	4139 (47.0%)	3676 (35.9%)
Diabetic drug	1199 (10.3%)	2036 (8.7%)	3641 (13.9%)	9917 (11.8%)	1394 (15.8%)	1256 (12.3%)
Insulin	806 (6.9%)	1089 (4.7%)	1280 (4.9%)	3225 (3.8%)	481 (5.5%)	451 (4.4%)
Antidepressant	1978 (17.0%)	2438 (10.4%)	4147 (15.8%)	10768 (12.8%)	783 (8.9%)	657 (6.4%)

Full baseline characteristics per database

Appendix table 3.

	Primary + Secondary	**Secondary only**
Characteristic		
Female	15799 (45.2%)	12472 (46.6%)
Age	74.64 (10.85)	75.50 (11.05)
CHADsVASc (mean (sd))	3.45 (1.81)	3.25 (1.82)
HAS-BLED (mean(sd))	2.29 (1.18)	2.02 (1.15)
≥1 GI comorbidity	4281 (12.2%)	2302 (8.6%)
NOAC		
Apixaban	23030 (65.8%)	17335 (64.8%)
Dabigatran	6456 (18.5%)	5197 (19.4%)
Rivaroxaban	5415 (15.5%)	4156 (15.5%)
Edoxaban	76 (0.2%)	58 (0.2%)
Comorbidities		
Hypertension	22359 (63.9%)	12864 (48.1%)
Renal disease	2041 (5.8%)	1312 (4.9%)
Liver disease	329 (0.9%)	166 (0.6%)
Prior stroke/TIA/embolism	6894 (19.7%)	4776 (17.9%)
Alcoholism	969 (2.8%)	552 (2.1%)
Prior bleed	4008 (11.5%)	1921 (7.2%)
Anaemia	3490 (10.0%)	2035 (7.6%)
Heart failure	7915 (22.6%)	6100 (22.8%)
Vascular disease	6786 (19.4%)	4503 (16.8%)
Diabetes	6309 (18.0%)	3808 (14.2%)
GI comorbidities		
Peptic ulcer	231 (0.7%)	159 (0.6%)
Gastrointestinal cancer	273 (0.8%)	190 (0.7%)
Gastritis	271 (0.8%)	91 (0.3%)
Esophagitis	173 (0.5%)	84 (0.3%)
GERD/dyspepsia	718 (2.1%)	125 (0.5%)
Abdominal pain	1909 (5.5%)	212 (0.8%)
Lower GI problems	1292 (3.7%)	395 (1.5%)
Other GI problems	460 (1.3%)	130 (0.5%)
Comedication		
Aspirin	9729 (27.8%)	6783 (25.4%)
Vitamin K antagonist	4416 (12.6%)	3302 (12.3%)
Clopidogrel	1160 (3.3%)	822 (3.1%)
Other antiplatelets	494 (1.4%)	330 (1.2%)
NSAID	3117 (8.9%)	2150 (8.0%)
Corticosteroid	3083 (8.8%)	2647 (9.9%)
Diuretic	9155 (26.2%)	8157 (30.5%)
Beta blocker	20747 (59.3%)	17015 (63.6%)
Calcium channel blocker	9021 (25.8%)	6643 (24.8%)
RAAS inhibitor	14911 (42.6%)	11966 (44.7%)
Statin	11025 (31.5%)	8638 (32.3%)
Diabetic drug	3235 (9.2%)	2522 (9.4%)
Insulin	1895 (5.4%)	1655 (6.2%)
Antidepressant	4416 (12.6%)	3823 (14.3%)

Baseline characteristics of the Stockholm cohort with and without access to primary care data

Appendix table 4.

	Stockholm	Denmark	PHARMO	Pooled
Model	IRR	IRR	IRR	IRR
Main analysis (IPW)	**0,79 (0,48-1,23)**	**0,72 (0,53-0,96)**	**0,85 (0,37-1,78)**	**0,75 (0,59-0,95)**
Full covariate adjustment	**0,72 (0,45-1,13)**	**0,67 (0,52-0,86)**	**0,74 (0,30-1,66)**	**0,69 (0,56-0,85)**
Unadjusted	**1,21 (0,77-1,82)**	**1,02 (0,79-1,28)**	**1,03 (0,44-2,22)**	**1,06 (0,86-1,30)**
Age sex adjusted	**1,12 (0,72-1,82)**	**0,96 (0,74-1,27)**	**0,99 (0,42-2,23)**	**0,99 (0,81-1,29)**
Age	1,11 (0,71-1,67)	0,95 (0,74-1,20)	0,97 (0,41-2,10)	0,99 (0,81-1,21)
Sex	1,21 (0,77-1,82)	1,02 (0,79-1,29)	1,06 (0,46-2,29)	1,06 (0,87-1,30)
HASBLED CHADSVASC adjustment	**0,98 (0,62-1,49)**	**0,83 (0,64-1,05)**	**0,89 (0,38-1,94)**	**0,86 (0,70-1,06)**
Hypertension	1,17 (0,75-1,77)	0,99 (0,78-1,26)	0,99 (0,43-2,14)	1,03 (0,84-1,27)
Renal disease	1,15 (0,74-1,73)	1,02 (0,79-1,28)	1,04 (0,45-2,24)	1,05 (0,85-1,28)
Liver disease	1,21 (0,78-1,82)	1,00 (0,78-1,27)	1,04 (0,45-2,23)	1,05 (0,86-1,29)
Stroke/TIA/Embolism	1,15 (0,74-1,73)	1,00 (0,78-1,27)	1,03 (0,44-2,21)	1,03 (0,84-1,27)
Alcoholism	1,18 (0,76-1,78)	0,99 (0,77-1,25)	1,03 (0,44-2,22)	1,03 (0,84-1,26)
Prior bleed	1,14 (0,73-1,71)	1,00 (0,78-1,26)	0,99 (0,43-2,14)	1,03 (0,84-1,26)
Anaemia	1,02 (0,65-1,55)	0,91 (0,71-1,16)	0,89 (0,38-1,94)	0,94 (0,76-1,15)
Heart failure	1,11 (0,71-1,68)	0,98 (0,77-1,24)	1,00 (0,43-2,15)	1,01 (0,83-1,24)
Vascular disease	1,11 (0,71-1,67)	0,97 (0,75-1,22)	0,91 (0,39-1,98)	0,99 (0,81-1,22)
Diabetes	1,19 (0,76-1,79)	0,99 (0,77-1,25)	0,98 (0,42-2,11)	1,03 (0,84-1,27)
GI covariate adjustment	**1,08 (0,68-1,65)**	**0,94 (0,73-1,19)**	**0,94 (0,40-2,05)**	**0,97 (0,78-1,19)**
Peptic ulcer	1,14 (0,73-1,73)	0,98 (0,76-1,24)	1,03 (0,44-2,22)	1,02 (0,83-1,25)
GI cancer	1,21 (0,77-1,82)	1,00 (0,78-1,27)	1,04 (0,45-2,23)	1,05 (0,86-1,29)
Gastritis	1,19 (0,76-1,79)	1,01 (0,79-1,28)	0,99 (0,42-2,14)	1,05 (0,86-1,29)
Esophagitis	1,11 (0,71-1,69)	0,99 (0,77-1,25)	0,99 (0,42-2,14)	1,02 (0,83-1,25)
GERD/Dyspepsia	1,18 (0,76-1,79)	1,02 (0,79-1,28)	1,00 (0,43-2,15)	1,05 (0,86-1,29)
Abdominal pain	1,24 (0,79-1,86)	1,00 (0,78-1,26)	1,04 (0,45-2,23)	1,05 (0,86-1,29)
Lower GI disease	1,18 (0,76-1,78)	1,01 (0,79-1,27)	1,03 (0,44-2,21)	1,05 (0,85-1,28)
Other GI disease	1,22 (0,78-1,83)	1,00 (0,78-1,27)	1,04 (0,45-2,23)	1,05 (0,86-1,29)
Full drug adjustment	**0,98 (0,62-1,49)**	**0,83 (0,64-1,05)**	**0,89 (0,38-1,94)**	**0,86 (0,70-1,06)**
Aspirin	1,15 (0,74-1,74)	0,96 (0,75-1,21)	1,00 (0,43-2,17)	1,00 (0,82-1,23)
NSAID	1,20 (0,77-1,81)	0,99 (0,77-1,25)	1,01 (0,43-2,16)	1,03 (0,84-1,27)
Clopidogrel	1,18 (0,75-1,78)	0,98 (0,77-1,24)	1,08 (0,47-2,33)	1,03 (0,84-1,26)
Other antiplatelets	1,21 (0,78-1,83)	1,00 (0,78-1,27)	1,04 (0,45-2,24)	1,05 (0,86-1,29)
Corticosteroids	1,23 (0,79-1,86)	0,97 (0,76-1,23)	1,03 (0,44-2,22)	1,03 (0,84-1,26)
Diuretics	1,10 (0,70-1,65)	0,94 (0,73-1,18)	0,93 (0,40-2,01)	0,97 (0,79-1,19)
Beta blocker	1,21 (0,78-1,83)	1,02 (0,80-1,29)	1,05 (0,45-2,26)	1,06 (0,87-1,30)
Ca channel blocker	1,20 (0,77-1,81)	1,02 (0,79-1,28)	1,00 (0,43-2,16)	1,05 (0,86-1,29)
RAAS inhibitor	1,19 (0,76-1,79)	0,98 (0,76-1,24)	0,99 (0,42-2,13)	1,03 (0,84-1,26)
Statin	1,19 (0,76-1,79)	1,02 (0,80-1,29)	1,03 (0,44-2,23)	1,06 (0,86-1,30)
Oral diabetic drug	1,21 (0,77-1,82)	1,01 (0,79-1,27)	0,96 (0,41-2,07)	1,05 (0,85-1,28)
Insulin	1,13 (0,73-1,71)	1,01 (0,78-1,27)	1,02 (0,44-2,20)	1,04 (0,84-1,27)
Antidepressant	1,13 (0,72-1,70)	1,00 (0,78-1,26)	0,99 (0,43-2,15)	1,02 (0,84-1,26)
Vitamin K antagonist	1,21 (0,77-1,82)	1,01 (0,79-1,27)	1,03 (0,44-2,22)	1,05 (0,86-1,29)

Effect of adjustment on association per covariate or set of covariates. First three columns are for the databases separately, and the final column is for the pooled analysis.