

Supplementary Table 1. Baseline table

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Agudo-Fernández et al., 2021 [19]	72.6 $\pm$ 14.6	639 (52.7)	Dabigatran Rivaroxaba Acenocoumaro	AF	1,213	January 1, 2012 to May 31, 2016	Retrospective cohort study	GIB 68	History of gastrointestinal bleeding (OR = 2.422, 95% CI: 1.101–5.327, $p$ = 0.028); Concomitant therapy with clopidogrel (OR = 2.373, 95% CI: 0.996–5.652, $p$ = 0.051); HasBled-Score (OR = 0.291, 95% CI: 0.170–0.496, $p$ = 0.000) Age (OR = 0.825, 95% CI: 0.455–1.497, $p$ = 0.527); Anticoagulant therapy (OR = 0.886, 95% CI: 0.591–1.330, $p$ = 0.561); Chronic kidney disease (OR = 1.505, 95% CI: 0.815–2.780, $p$ = 0.191); Other antiplatelet (OR = 4.497, 95% CI: 0.954–5.635, $p$ = 0.242); Corticosteroids (OR = 1.757, 95% CI: 0.719–4.295, $p$ = 0.216); Chads2-Score (OR = 0.765, 95% CI: 0.337–1.739, $p$ = 0.523)
Fanning et al., 2020 [20]	Median age CDARS: 78 THIN: 74	CDARS 14,492 (50) THIN 6,172 (53)	Aspirin Rivaroxaban	AF <sup>a)</sup>	CDARS: 29,213 THIN: 11,549	CDARS: 2010–2018 THIN: 2011–2017	Retrospective cohort study	GIB CDARS: 23,743 THIN: 10,111	Rivaroxaban 20 mg/day vs. aspirin (HR = 1.57, 95% CI: 1.08–2.29); PPIs/H2RAs (HR = 1.96, 95% CI: 1.14–3.37); Women (HR = 1.91, 95% CI = 1.08–3.40, $p$ = 0.53)
Graham et al., 2014 [21]	-	65,191 (48.5)	Dabigatran Warfarin	AF <sup>a)</sup>	134,414	October 19, 2010–December 31, 2012	Retrospective cohort study	2,715	Dabigatran 150 mg bid (HR = 1.51, 95% CI: 1.32–1.73)
Aisenberg et al., 2018 [22]	MGIB 75.0 (68.0–79.0) No MGIB 72.0 (64.0–78.0)	MGIB 382 (66.0) No MGIB 12 638 (61.8)	Edoxaban Warfarin	AF <sup>a)</sup>	21,105	-	RCT	MGIB 579	Concomitant aspirin intake (AHR = 1.31, 95% CI: 1.08–1.58, $p$ = 0.006)

Supplementary Table 1. Continued

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Chan et al., 2015 [23]	72.0 $\pm$ 10.9	2,412 (47.8)	Dabigatran	AF, Prophylaxis of VTE	5,041	January 1, 2010 to December 31, 2013	Retrospective cohort study	GIB 124	Age $\geq$ 75 yr (IRR = 2.47, 95% CI: 1.66–3.68, $p < 0.05$ ); History of peptic ulcer/GIB (IRR = 2.31, 95% CI, 1.54–3.46, $p < 0.05$ ); Concomitant use of aspirin (IRR = 1.52, 95% CI, 1.03–2.24, $p < 0.05$ ); Gastroprotective agents (IRR = 0.52, 95% CI: 0.35–0.77, $p < 0.05$ ); Histamine type-2-receptor antagonists (IRR = 0.61, 95% CI: 0.40–0.94, $p < 0.05$ ); Proton pump inhibitors (IRR = 0.53, 95% CI: 0.31–0.91, $p < 0.05$ ); Histamine type-2-receptor antagonists Proton pump inhibitors both (IRR = 0.15, 95% CI: 0.06–0.39, $p < 0.05$ )
Chen et al., 2014 [24]	65.2 $\pm$ 16.6	234 (58)	Warfarin	DVT, AF, PE Valvular replacement other	401	July 1993 to May 2012	Retrospective cohort study	GIB 36	Age $>$ 65 yr (RR = 2.5, 95% CI: 1.2–5.5, $p = 0.02$ ); Mean INR $>$ 2.1 (RR = 2.1, 95% CI: 1.0–4.2, $p = 0.04$ ); History of GIB (RR = 5.1, 95% CI: 1.9–13.5, $p = 0.001$ ); Cirrhosis (RR = 6.9, 95% CI: 2.0–24.5, $p = 0.003$ )
Coates et al., 2021 [25]	63.9	70.2%	Dabigatran	AF <sup>a</sup> )	4,299	September 1, 2016–June 30, 2019	Retrospective cohort study	GIB 73	Weight $>$ 120 kg (AHR = 1.44, 95% CI: 1.01–2.05)
Delaney et al., 2007 [26]	Cases 69.3 $\pm$ 17.6 Control 69.1 $\pm$ 17.7	Cases 2,171 (53.9) Control 17,237 (42.9)	Warfarin	PE, DVT Stroke AF Congestive heart-failure	Cases 4,028 Control 40,171	January 1, 2000 to December 31, 2005	Case-control	GIB 4,028	Male (ARR = 1.50, 95% CI: 1.40–1.62); Heavy alcohol use (ARR = 4.00, 95% CI: 3.45–4.63); Smoking (ARR = 1.23, 95% CI: 1.15–1.34); Acetaminophen (paracetamol) use (ARR = 1.47, 95% CI: 1.35–1.60); Liver failure (ARR = 7.00, 95% CI: 4.78–10.27); Warfarin + ASA (ARR = 6.48, 95% CI: 4.25–9.87); Warfarin + NSAID (ARR = 4.79, 95% CI: 2.79–8.21); Warfarin + COX-2 inhibitor (ARR = 4.62, 95% CI: 1.48–14.43)

Supplementary Table 1. Continued

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Douros et al., 2019 [27]	DOAC 75.5 $\pm$ 9.1 VKA 78.0 $\pm$ 9.0	DOAC 2,819 (53.2) VKA 4,709 (51.7)	DOACs VKA	AF <sup>a)</sup>	14,407	January 2011 to March 2014	Retrospective cohort study	GIB 253	Current concomitant DOAC-antiplatelet use (AHR = 1.08, 95% CI: 0.81–1.45); Current concomitant rivaroxaban-antiplatelet use (AHR = 1.18, 95% CI: 0.75–1.87); Current concomitant DOAC-ASA use (AHR = 1.15, 95% CI: 0.82–1.62); Current concomitant use of a DOAC with multiple antiplatelets (AHR = 1.13, 95% CI: 0.63–2.04); Current concomitant dabigatran-antiplatelet use (AHR = 1.10, 95% CI: 0.79–1.54)
Ferroni et al., 2022 [28]	Male: DOAC 77.8 VKA 77.1 Female: DOAC 80.3 VKA 79.4	28,963 (48)	DOACs VKA	AF <sup>a)</sup>	59,880	July 1, 2013 to September 30, 2017	Retrospective cohort study	-	Female (AHR = 1.48, 95% CI: 1.02–2.16, $p = 0.04$ ); > 85 (AHR = 2.28, 95% CI: 1.36–3.85, $p = 0.01$ ); 74–84 (AHR = 1.47, 95% CI: 0.90–2.42, $p = 0.121$ ); History of GI disease (AHR = 1.89, 95% CI: 0.87–4.09, $p = 0.10$ ); Congestive heart failure (AHR = 1.46, 95% CI: 0.90–2.35, $p = 0.11$ ); History of bleeding (AHR = 3.27, 95% CI: 1.86–5.73, $p < 0.01$ ); Myocardial infarction (AHR = 2.23, 95% CI: 1.12–4.43, $p = 0.03$ ); Peripheral artery disease (AHR = 4.63, 95% CI: 2.24–9.56, $p < 0.01$ )
Gandhi et al., 2021 [29]	-	95,583 (60.3)	Apixaban Dabigatran Rivaroxaban	AF <sup>a)</sup>	158,476	January 2007–September 2017	Retrospective cohort study	GIB 4,290	Dabigatran + dronedarone (AHR = 1.40, 95% CI: 1.01–1.93, $p = 0.04$ ); Rivaroxaban + dronedarone (AHR = 1.39, 95% CI: 0.98–1.95, $p = 0.06$ ); Apixaban + dronedarone (AHR = 0.75, 95% CI: 0.39–1.44, $p = 0.38$ )
Garcia et al., 2019 [30]	Prior GI Bleed 73.5 (67.0–78.0) No Prior GI Bleed 70.0 (62.0–76.0)	Female Prior GI Bleed 205 (26.1) No Prior GI Bleed 6,211 (35.7)	Apixaban Warfarin	AF <sup>a)</sup>	18,197	-	RCT ARISTOTLE Trial	MGIB 218 Lower GI bleeding 97 Upper GI bleeding 118	Major GI bleeding: prior lower GI bleed (HR = 1.72, 95% CI: 0.86–3.42); prior upper GI bleed (HR = 3.13, 95% CI: 1.97–4.96) Upper GI bleeding: prior upper GI bleed (HR = 3.42, 95% CI: 2.02–5.81) Lower GI bleeding: prior lower GI bleed (HR = 5.47, 95% CI: 2.53–11.80)

**Supplementary Table 1. Continued**

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Holm et al., 2020 [31]	72.1 $\pm$ 12.9	129,857 (53)	DOACs	AF <sup>a)</sup>	244,597	2008–2017	Retrospective cohort study	GIB 156,280	Rivaroxaban: co-treatment pharmacodynamic effect (HR = 1.68, 95% CI: 1.37–2.05); CYP3A4 and/or P-gp-inhibitors (HR = 1.54, 95% CI: 1.02–2.32); Apixaban:co-treatment pharmacodynamic effect (HR = 1.51, 95% CI: 1.28–1.78); CYP3A4 and/or P-gp-inhibitors (HR = 1.44, 95% CI: 1.06–1.95)
Holt et al., 2021 [32]	Median (IQR) 75 (68–82)	55,169 (56.1)	DOACs	AF <sup>a)</sup>	98,376	2012–2018	Retrospective case-control	GIB 4,946	Oral glucocorticoid < 20 mg daily dose (HR = 1.54, 95% CI: 1.29–1.84); Oral glucocorticoid $\geq$ 20 mg (HR = 2.19, 95% CI: 1.81–2.65)
Kato et al., 2016 [33]	< 65 yr: 59 (55.0–62.0) 65–74 yr: 70 (67.0–72.0) $\geq$ 75 yr: 79 (76.0–82.0)	< 65 yr: 3,987 (73) 65–74 yr: 4,381 (61) $\geq$ 75 yr: 4,697 (55)	Edoxaban Warfarin	AF <sup>a)</sup>	21,105	-	RCT ENGAGE AF-TIMI 48 Trial	MGIB 579	$\geq$ 75 yr (HR = 1.32, 95% CI: 1.01–1.72)
Kalil et al., 2016 [34]	Dabigatran 73.74 $\pm$ 6.86 Warfarin 73.85 $\pm$ 6.75	-	Dabigatran Warfarin	AF <sup>a)</sup>	69,467/25,74	June 1, 2010 to December 31	Retrospective cohort study	GIB 35	GFR 50–80 mL/min/1.73 m <sup>2</sup> (HR = 2.94, 95% CI: 1.24–7.02, $p$ = 0.015)
Kolb et al., 2018 [35]	-	-	Dabigatran Warfarin	AF <sup>a)</sup>	18,113	2005–2009	RCT (RE-LY) Trial	GIB 1,158	MGIB: D150 vs. W (RR = 1.57, 95% CI: 1.28–1.92, $p$ < 0.01); Life-threatening or fatal GI bleeding: D150 vs. W (RR = 1.62, 95% CI: 1.20–2.18, $p$ < 0.01); Upper GI: D150 vs. W (RR = 1.13, 95% CI: 0.81–1.58, $p$ = 0.49); Lower GI: D150 vs. W (RR = 2.23, 95% CI: 1.47–3.38, $p$ < 0.01)

Supplementary Table 1. Continued

Reference	Age (yr), Mean ± SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Lauffenburger et al., 2015 [36]	67.5 ± 12.4	No GIB Bleeding 13,104 (63.7) GI Bleeding 238 (53.4)	Dabigatran	AF <sup>a)</sup>	21,033	October 19, 2010 to De- cember 31, 2012	Retrospec- tive cohort study	GIB 446	65–74 (AHR = 2.72, 95% CI: 1.59–4.65, $p < 0.001$ ); $\geq 75$ (AHR = 4.52, 95% CI: 2.68–7.64, $p < 0.001$ ); Congestive heart failure (AHR = 1.25, 95% CI: 1.01–1.56, $p < 0.05$ ); Coronary artery disease (AHR = 1.37, 95% CI: 1.10–1.69, $p < 0.05$ ); Renal impairment (AHR = 1.67, 95% CI: 1.24–2.25, $p < 0.001$ ); Bleeding (AHR = 1.32, 95% CI: 1.01–1.72, $p < 0.05$ ); Alcohol abuse (AHR = 2.57, 95% CI: 1.52–4.35, $p < 0.001$ ); <i>Helicobacter pylori</i> infection (AHR = 4.75, 95% CI: 1.93–11.68, $p < 0.05$ ); Anti-platelet agent (AHR = 1.49, 95% CI: 1.19–1.88, $p < 0.001$ ); Male sex (AHR = 0.78, 95% CI: 0.64–0.95, $p < 0.05$ ); Digoxin use (AHR = 1.49, 95% CI: 1.19–1.88, $p < 0.05$ )
Lee et al., 2021 [37]	71.3 ± 10.0	25,868 (59.9)	DOACs	AF <sup>a)</sup>	43,173	January 2015 to Decem- ber 2017	Retrospec- tive cohort study	Hospital- ization of GIB 314	BMI $\geq 30$ kg/m <sup>2</sup> (AHR = 0.810, 95% CI: 0.494–1.328, $p = 0.018$ ); BMI per 5 kg/m <sup>2</sup> increase (AHR = 0.785, 95% CI: 0.658–0.937, $p = 0.007$ )
Leonard et al., 2016 [38]	Mean age 71	87,576 (37)	Warfarin	AF, VTE Valvular heart disease	236,691	1999–2011	Cohort	GIB 2,035	Warfarin + gemfibrozil (AHR = 2.29, 95% CI: 1.61–3.25)
Maruyama et al., 2018 [39]	72.2 ± 10.0	448 (68.1)	DOACs	AF <sup>a)</sup>	658	April 2011– November 2015	Cohort	GIB 27: Upper GI 9 Lower GI 18 MGIB 12	Upper gastrointestinal bleeding: PPI (AHR = 0, 95% CI: 0–2E + 134, $p < 0.001$ ); Past digestive ulcer (AHR = 29.114, 95% CI: 7.265–116.678, $p < 0.001$ ); Lower gastrointestinal bleeding: NSAIDs (AHR = 12.6, 95% CI: 3.2–49.1, $p < 0.001$ ); Dual antiplatelet (AHR = 8.6, 95% CI: 2.7–27.1, $p < 0.001$ ); Past GIB (AHR = 15.1, 95% CI: 3.2–72.0, $p = 0.001$ ); Female (AHR = 3.2, 95% CI: 0.1–0.8, $p = 0.019$ )

Supplementary Table 1. Continued

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Murata et al., 2020 [40]	Warfarin 72.2 $\pm$ 9.3 DOAC 71.8 $\pm$ 9.5	2,390 (74)	Warfarin, DOACs	AF <sup>a)</sup>	3,237	2013–2015	Prospective cohort	GIB 68	Creatinine (per mg/dL increase) (AHR = 1.379, 95% CI: 1.091–1.743, $p$ = 0.007); Age (per year increase) (AHR = 1.027, 95% CI: 0.996–1.059, $p$ = 0.86); Hemoglobin (per g/dL) (AHR = 0.814, 95% CI: 0.705–0.941, $p$ = 0.005)
Nantsupawat et al., 2017 [41]	Mean age 72.2	128 (51.8)	Dabigatran	AF <sup>a)</sup>	247	2010–2013	Retrospective cohort study	GIB 10	History of GIB (OR = 25.14, 95% CI: 2.85–221.47, $p$ < 0.01); HAS-BLED $\geq$ 3 (OR = 5.85, 95% CI: 1.31–26.15, $p$ = 0.021); Corticosteroid use (OR = 4.30, 95% CI: 0.81–22.79, $p$ = 0.087)
Nawarawong et al., 2018 [42]	71.6 $\pm$ 10.8	47 (50)	Warfarin, UFH, LMWH, NOAC	AF, vascular thrombosis, Stroke, Valvular heart diseases	94	October 2010 to February 2013	Retrospective cohort study	Acute GIB 94	Hematochezia (OR = 4.90, 95% CI: 1.22–19.50, $p$ = 0.024); INR < 4 (OR = 4.07, 95% CI: 1.17–14.27, $p$ = 0.028); Concomitant antiplatelets (OR = 0.32, 95% CI: 0.12–0.88, $p$ = 0.027)
Olsen et al., 2019 [43]	Moderate age 70 (IQR 64–78)	22,651 (55)	VKA DOACs	AF <sup>a)</sup>	41,183	January 1, 2012–December 31, 2015	Retrospective cohort study	GIB 1,642	NSAIDs + NOAC vs. NOAC (HR = 2.01, 95% CI: 1.40–2.61); NSAIDs + VKA vs. VKA (HR = 1.95, 95% CI: 1.21–2.69); NSAIDs + apixaban vs. apixaban (HR = 2.98, 95% CI: 1.82–4.87); NSAIDs + rivaroxaban vs. rivaroxaban (HR = 1.94, 95% CI: 1.06–3.55); NSAIDs + dabigatran vs. dabigatran (HR = 1.52, 95% CI: 0.92–2.50)
Pham et al., 2020 [44]	-	-	DOACs	AF <sup>a)</sup>	48,442	October 19, 2010 to June 30, 2015	Retrospective cohort study	GIB 687	Overall GI bleeding: dabigatran with verapamil or diltiazem vs amlodipine (AHR = 2.16, 95% CI: 1.30–3.60, $p$ < 0.05); dabigatran + verapamil or diltiazem vs. metoprolol (AHR = 2.32, 95% CI: 1.42–3.79, $p$ < 0.05); GI minor bleeding: dabigatran with verapamil or diltiazem vs. amlodipine (AHR = 2.16, 95% CI: 1.29–3.63, $p$ < 0.05); dabigatran + verapamil or diltiazem vs. metoprolol (AHR = 2.33, 95% CI: 1.42–3.82, $p$ < 0.05); Major/moderate GI bleeding: dabigatran + verapamil or diltiazem vs. metoprolol (AHR = 5.49, 95% CI: 1.67–18.03, $p$ < 0.05)

Supplementary Table 1. Continued

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Pourakari et al., 2016 [45]	No GI bleeding 63.8 $\pm$ 16.8 GI bleeding 68.6 $\pm$ 13.1	121 (43.5)	Warfarin	AF, DVT, Mechanical heart, Valve implantation	278	2003–2015	Retrospective cohort study	UGIB 41	History of peptic ulcer (HR = 111.19, 95% CI: 26.56–465.56, $p < 0.001$ ); Older age (HR = 1.032, 95% CI: 0.985–1.081, $p = 0.183$ ); Mechanical valve implant (HR = 1.971, 95% CI: 0.428–9.070, $p = 0.384$ ); Chronic kidney disease (HR = 0.542, 95% CI: 0.143–2.047, $p = 0.366$ )
Schauer et al., 2005 [46]	73 $\pm$ 13.8	2,974 (31.8)	Warfarin	AF <sup>a</sup>	9,345	January 1, 1997 to May 31, 2002	Retrospective cohort study	GIB 864	Substance abuse (AHR = 1.41, 95% CI: 1.07–1.87); Psychiatric illness (AHR = 1.19, 95% CI: 1.03–1.39); Social risk factors (AHR = 1.28, 95% CI: 1.12–1.48); Chronic heart failure (AHR = 1.31, 95% CI: 1.09–1.58); Liver disease (AHR = 1.31, 95% CI: 0.99–1.74); Renal disease (AHR = 1.61, 95% CI: 1.39–1.87); Deep vein thrombosis (AHR = 1.22, 95% CI: 1.02–1.47); Diabetes mellitus (AHR = 1.03, 95% CI: 0.90–1.18); Refill time 432 d (AHR = 0.79, 95% CI: 0.69–0.91)
Sherid et al., 2015 [47]	Dabigatran 72.72 Warfarin 71.83	Dabigatran 104 (50.0) Warfarin 96 (45.9)	Dabigatran Warfarin	AF, DVT, PE Portal venous thrombosis	417	2010–2012	Retrospective cohort study	GIB 31	Dabigatran group: duration < 100 days (AOR = 8.176, 95% CI: 1.993–38.547, $p = 0.0007$ ); Age > 65 yr (AOR = 2.989, 95% CI: 1.785–24.782, $p = 0.0453$ ); Previous GI bleeding (AOR = 6.284, 95% CI: 0.612–28.591, $p = 0.036$ ); Sex (female) (AOR = 2.732, 95% CI: 0.514–14.509, $p = 0.238$ ); Race (Caucasian) (AOR = 0.612, 95% CI: 1.33–2.816, $p = 0.528$ ); GFR $\leq 30$ mL/min/1.73 m <sup>2</sup> (AOR = 4.534, 95% CI: 0.682–30.138, $p = 0.118$ ); Concomitant with aspirin (AOR = 1.739, 95% CI: 1.64–4.781, $p = 0.657$ ); Concomitant with thienopyridines (AOR = 1.051, 95% CI: 0.752–7.438, $p = 0.279$ ); Concomitant with dual antiplatelet (AOR = 0.856, 95% CI: 0.675–9.409, $p = 0.492$ ); Concomitant with NSAIDs (AOR = 1.297, 95% CI: 1.824–5.721, $p = 0.573$ )

Supplementary Table 1. Continued

Reference	Age (yr), Mean ± SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Sherid et al., 2014 [48]	Rivaroxaban 68.25 ± 14.97 Dabigatran 72.71 ± 12.37	Rivarox- aban 70 (47.62) Dabiga- tran 114 (50.22)	Rivaroxaban Dabigatran	AF VTE treat- ment VTE pro- phylaxi	374	2010–2013	Retrospec- tive cohort study	GIB 19	Rivaroxaban group: ≤ 40 days vs. > 40 days (OR = 2.8, <i>p</i> = 0.023); DAPT with rivaroxaban (OR = 7.4, <i>p</i> = 0.0378); Prior GI bleeding (OR = 15.5, <i>p</i> = 0.0002); Dabigatran group:dabiga- tran for ≤ 40 days when compared to ≥ 40 days (OR = 8.3, <i>p</i> < 0.0001)
Sherid et al., 2016 [49]	Rivaroxaban 68.25 ± 14.97 Warfarin 71.35 ± 13.09	Rivarox- aban 70 (47.62) Warfarin 70 (45.75)	Rivaroxaban Warfarin	AF VTE treat- ment VTE pro- phylaxi	300	2011–2013	Retrospec- tive cohort study	GIB 22	Rivaroxaban group: ≤ 40 days vs. > 40 days (OR = 2.8, <i>p</i> = 0.023); DAPT with rivaroxaban (OR = 7.4, <i>p</i> = 0.0378); Prior GI bleeding (OR = 15.5, <i>p</i> = 0.0002)
Sherwood et al., 2015 [50]	73 (65–78)	8,591 (60)	Rivaroxaban Warfarin	AF <sup>a)</sup>	14,236	2010-2011	RCT (Rocket AF Trial)	GIB 684	Anemia at baseline (HR = 1.70, 95% CI: 1.41– 2.04, <i>p</i> < 0.0001); Previous GI bleeding (HR = 2.11, 95% CI: 1.62–2.76, <i>p</i> < 0.0001); Long- term ASA use at screening HR = 1.47, 95% CI: 1.26–1.72, <i>p</i> < 0.0001); Age (for each 5-yr increase) (HR = 1.11, 95% CI: 1.06–1.17, <i>p</i> < 0.0001); Diastolic BP (for each 5 mmHg decrease to < 80 mmHg) (HR = 1.10, 95% CI: 1.05–1.16, <i>p</i> = 0.0002); Smoking history (cur- rent or former) (HR = 1.37, 95% CI: 1.16–1.62), <i>p</i> = 0.0002); History of sleep apnea (HR = 1.60, 95% CI: 1.22–2.10, <i>p</i> = 0.0007); PPI at baseline (HR = 1.36, 95% CI: 1.12–1.65, <i>p</i> = 0.0018); Creatinine clearance (for each 5-U decrease to < 60 mL/min) (HR = 1.06, 95% CI: 1.01–1.12, <i>p</i> = 0.015); COPD (HR = 1.30, 95% CI: 1.05–1.61, <i>p</i> = 0.016); Male (HR = 1.21, 95% CI: 1.01–1.44, <i>p</i> = 0.037); Baseline antiplatelet (other than ASA) (HR = 1.50, 95% CI: 1.02–2.21, <i>p</i> = 0.039)



Supplementary Table 1. Continued

Reference	Age (yr), Mean $\pm$ SD (range)	Sex, male, n (%)	Drug	Population	Sample size	Time	Study design	Number of GIB	Risk factor
Shimomura et al., 2018 [52]	69.4 $\pm$ 9.9	329 (64.8)	Warfarin DOACs	AF, Valve replace- ment or valvu- loplasty history	508	2001–2015	Retrospec- tive cohort study	GIB 42	PPI therapy (AHR = 0.52, 95% CI: 0.27–1.0, $p$ = 0.053); Chronic kidney disease (AHR = 6.7, 95% CI: 2.3–19.6, $p$ < 0.001); COPD (AHR = 4.0, 95% CI: 1.4–11.2, $p$ = 0.011); History of peptic ulcer disease (AHR = 1.8, 95% CI: 0.95–3.6, $p$ = 0.071); Liver cirrhosis (AHR = 5.6, 95% CI: 1.7–18.6, $p$ = 0.005)
Youn et al., 2018 [51]	Mean Non-GPA 70.4 (18–99) GPA 73.3 (22–96)	Male Non-GPA 837 (48.8) GPA 164 (45.6)	DOACs	AF, VTE, DVT, PE, ACS Pro- phylaxis of DVT/ PTE	2,076	2008–2016	Retrospec- tive cohort study	UGIB 30	Age, 1-year increase (HR = 1.041, 95% CI: 1.000–1.083, $p$ = 0.048); Antiplatelet agent use (HR = 3.121, 95% CI: 1.265–7.702, $p$ = 0.014); History of peptic ulcer/UGIB (HR = 5.931, 95% CI: 2.504–14.049, $p$ < 0.001)

ACS, acute coronary syndrome; ARR, adjust risk ratio; DVT, deep vein thrombosis; IRR, incidence risk ratio; PE, pulmonary embolism; RR, risk ratio.

<sup>a)</sup>The populations of 23 studies were only stroke patients.