S1 Computerized requests made on electronic health records in every participating center (ICD-10 codes).

D62: acute post-haemorrhagic anaemia
D64.6: anaemia, unspecified

I98.2: oesophageal varices with bleeding

K22.6: gastro-oesophageal laceration-haemorrhage syndrome
K25.0: gastric ulcer
K26.0: duodenal ulcer
K62.5: haemorrhage of anus and rectum
K92.0: haematemesis
K92.1: meloena
K92.2 gastrointestinal haemorrhage, unspecified

R57.1: hypovolaemic shock
R58: haemorrhage, not elsewhere classified

Y44.2: agents primarily affecting blood constituents: anticoagulants
Y44.4: agents primarily affecting blood constituents: antithrombotic drugs

S2 Distribution and coagulation parameters of antithrombotic regimen

Oral anticoagulant	Antiplatelet	Parenteral anticoagulant	Frequency	Percent
.	Acetylsalicylic acid	.	319	29.54
.	Clopidogrel	.	70	6.48
.	Dual antiplatelet regimen	.	72	6.67
VKA	.	.	321	29.72
VKA	Acetylsalicylic acid	.	92	8.52
VKA	Clopidogrel	.	8	0.74
VKA	Dual antiplatelet regimen	.	13	1.20
DOAC	.	.	66	6.11
DOAC	Acetylsalicylic acid	.	9	0.83
DOAC	Clopidogrel	.	2	0.19
DOAC	Dual antiplatelet regimen	.	2	0.19
.	.	LMWH	42	3.89
.	.	Heparin	7	0.65
.	.	Fondaparinux	4	0.37
.	Acetylsalicylic acid	Heparin	7	0.65
.	Acetylsalicylic acid	LMWH	17	1.57
.	Acetylsalicylic acid	Fondaparinux	2	0.19
.	Clopidogrel	Fondaparinux	1	0.09
.	Dual antiplatelet regimen	Heparin	2	0.19
.	Dual antiplatelet regimen	LMWH	6	0.56
VKA	.	Heparin	2	0.19
VKA	.	LMWH	8	0.74
DOAC	.	LMWH	1	0.09
VKA	Acetylsalicylic acid	Heparin	2	0.19
VKA	Acetylsalicylic acid	LMWH	2	0.19
VKA	Clopidogrel	Heparin	1	0.09
.	.	.	2	0.19

DOAC denotes direct oral anticoagulant, LMWH denotes low molecular weight heparin, and VKA denotes vitamin K antagonist

Among 321 patients who were prescribed VKA alone, 192 (59.8%) were prescribed fluindione and 97 (30.2%) were prescribed warfarin, and 32 (9.97%) were prescribed acenocoumarol.

Among 66 patients who were prescribed DOAC alone, 40 (60.6%) were prescribed rivaroxaban, 23 (34.8%) were prescribed dabigatran, and 3 (4.55%) were prescribed apixaban.

For two patients, type of antithrombotic remained unknown.

Parenteral anticoagulant alone (n = 53)

	Frequency	Percent
Intravenous heparin	1	1.89
Subcutaneous heparin	6	11.32
Nadroparin	2	3.77
Tinzaparin	17	32.08
Enoxaparin	21	39.62
Dalteparin	2	3.77
Fondaparinux	4	7.55

Dual antiplatelet regiment alone (n = 72)

		Frequency	Percent
Acetylsalicylic acid	Clopidogrel	44	61.11
Acetylsalicylic acid + Clopidogrel		13	18.06
Acetylsalicylic acid	Prasugrel	7	9.72
Acetylsalicylic acid	Ticagrelor	8	11.11

Coagulation parameters according to antithrombotic regimen

Parameters	AP alone N = 461	VKA alone N = 321	Heparin alone * N = 53
Platelet count (Giga/L)	231 [179-294]	227 [186-296]	218 [168-284]
Missing values (%)	*36 (7.81)*	*14 (4.36)*	*5 (9.43)*
Prothrombin time (%)	66 [25-92]	67 [24-91]	75 [30-98]
Missing values (%)	*68 (14.7)*	*43 (13.4)*	*6 (11.3)*
aPTT ratio	1.11 [0.96-1.32]	1.10 [0.97-1.44]	1.14 [1.00-1.34]
Missing values (%)	*149 (32.3)*	*89 (27.7)*	*11 (20.7)*

values are median [Q1-Q3]; aPTT stands for activated partial thromboplastin time

* low molecular heparin (n = 46) and unfractionated heparin (n = 7)

S3 Gastrointestinal investigations / reasons for no investigation

Esophago-gastroduodenoscopy (EGD) (435/473 patients, 92%), abdominal CT scan (94/473, 19.9%), colonoscopy (72/473, 15.2%), video capsule endoscopy (26/473, 5.5%) in patients presenting upper GI bleeding symptoms (hematemesis or melena), and colonoscopy (258/368, 70.1%), EGD (157/368, 42.7%), abdominal CT scan (140/368, 38%), video capsule endoscopy (7/368, 1.9%) in patients presenting lower GI bleeding symptoms (hematochezia).

Reasons for no GI investigations were the following: unfavorable benefit-to-risk ratio (n = 83), unknown (n = 50), palliative care including decision of care limitation (n = 33), patient refusal (n = 24), and miscellaneous reasons (n = 19).

S4 Clinical characteristics according to gastrointestinal lesion location

Variables		Total, N = 1080	Gastro-duodenal ulcer, N = 209	Other upper GI lesion, N = 199	Lower GI lesion, N = 289	Unknown lesion, N = 383	p
Female		454	39.2 (82)	31.2 (62)	43.9 (127)	47.8 (183)	0.0012
Age, years			76.7 ± 12.4	76.4 ± 11.9	79.9 ± 10.3	82.2 ± 10.7	<.0001
Arterial hypertension		735	70.8 (148)	63.3 (126)	69.6 (201)	67.9 (260)	0.3781
CAD		439	43.1 (90)	45.7 (91)	36 (104)	40.2 (154)	0.1532
Heart failure		166	13.4 (28)	12.6 (25)	16.3 (47)	17.2 (66)	0.3871
Diabetes mellitus		302	30.1 (63)	30.2 (60)	25.3 (73)	27.7 (106)	0.5661
Cancer		231	15.8 (33)	27.6 (55)	21.8 (63)	20.9 (80)	0.0350
PVD		190	17.7 (37)	20.6 (41)	12.5 (36)	19.8 (76)	0.0494
Chronic renal insufficiency		217	18.7 (39)	18.1 (36)	17.3 (50)	24 (92)	0.1193
Liver cirrhosis		58	2.9 (6)	15.1 (30)	2.8 (8)	3.7 (14)	<.0001
Alcohol consumption		117	12.4 (26)	16.6 (33)	8.3 (24)	8.9 (34)	0.0129
Tobacco use		93	13.4 (28)	14.1 (28)	4.5 (13)	6.3 (24)	<.0001
History of bleeding		357	27.3 (57)	31.7 (63)	35.3 (102)	35.2 (135)	0.1854
Gastro-duodenal ulcer		195	46.4 (97)	11.6 (23)	9.7 (28)	12.3 (47)	<.0001
Antithrombotic treatment	VKA alone	321	27.3 (57)	30.2 (60)	30.2 (87)	30.6 (117)	0.2358
	DOAC alone	66	2.4 (5)	5.5 (11)	9 (26)	6.3 (24)	
	AP mono. alone	389	36.8 (77)	40.2 (80)	34.7 (100)	34.6 (132)	
	Dual AP alone	72	10.5 (22)	5 (10)	5.9 (17)	6 (23)	
	Parenteral alone	53	5.7 (12)	3.5 (7)	4.5 (13)	5.5 (21)	
	Combo	177	17.2 (36)	15.6 (31)	15.6 (45)	17 (65)	
MAP (mm Hg)	on admission		75 ± 15	79 ± 17	82 ± 18	79 ± 18	0.0002
Creatinine (µmol/L)	on admission		135 ± 132	115 ± 94	110 ± 71	129 ± 111	0.0240
Hemoglobin (g/dL)	on admission		8.3 ± 2.2	8.8 ± 2.4	10.5 ± 2.7	9.1 ± 2.8	<.0001

S5 Antithrombotic drug across upper GI causative lesion

	Gastro-duodenal ulcer N = 209	Gastric erosive lesion N = 75	Angiodysplasia N = 51	Other N = 23	Cancer N = 23	Esophageal varices N = 23	Polyp N = 4	Total N = 408
VKA	27.3 (57)	32.0 (24)	25.5 (13)	30.4 (7)	30.4 (7)	26.1 (6)	75.0 (3)	117
Dabigatran	-	4.00 (3)	1.96 (1)	-	-	-	-	4
Rivaroxaban	2.39 (5)	2.67 (2)	5.88 (3)	8.70 (2)	-	-	-	12
Dual AP	10.5 (22)	6.67 (5)	3.92 (2)	-	8.70 (2)	4.35 (1)	-	32
Parenteral	5.74 (12)	-	3.92 (2)	8.70 (2)	8.70 (2)	4.35 (1)	-	19
AAS	30.1 (63)	34.7 (26)	23.5 (12)	34.8 (8)	43.5 (10)	52.2 (12)	-	131
P2Y12-I	6.70 (14)	4.00 (3)	7.84 (4)	4.35 (1)	8.70 (2)	8.70 (2)	-	26
Parenteral combo	6.22 (13)	2.67 (2)	1.96 (1)	4.35 (1)	-	-	-	17
Oral antithrombotic combo	11.0 (23)	13.3 (10)	25.5 (13)	8.70 (2)	-	4.35 (1)	25.0 (1)	50

Values are percentage (frequency); GI denotes gastrointestinal, VKA vitamin K antagonist, AP antiplatelet agent, AAS acetylsalicylic acid, P2Y12-I P2Y12 inhibitor.

S6 Antithrombotic drug across lower GI causative lesion

	Colonic diverticulum N = 120	Colon cancer N = 51	Other N = 40	Colitis N = 25	Hemorrhoids N = 24	Colonic ulcer N = 20	Colonic polyp N = 8	Total N = 288
VKA	27.5 (33)	25.5 (13)	32.5 (13)	32.0 (8)	33.3 (8)	45.0 (9)	37.5 (3)	87
Dabigatran	2.50 (3)	3.92 (2)		4.00 (1)	8.33 (2)	15.0 (3)		11
Rivaroxaban	6.67 (8)	7.84 (4)	2.50 (1)		8.33 (2)			15
Dual AP	7.50 (9)	5.88 (3)	2.50 (1)		16.7 (4)			17
Parenteral	0.83 (1)	7.84 (4)	10.0 (4)		4.17 (1)	5.00 (1)	25.0 (2)	13
AAS	34.2 (41)	27.5 (14)	22.5 (9)	36.0 (9)	20.8 (5)	20.0 (4)	12.5 (1)	83
P2Y12-I	5.83 (7)	9.80 (5)	7.50 (3)	4.00 (1)		5.00 (1)		17
Parenteral combo	4.17 (5)	1.96 (1)	2.50 (1)	8.00 (2)	4.17 (1)	5.00 (1)		11
Oral antithrombotic combo	10.8 (13)	9.80 (5)	20.0 (8)	16.0 (4)	4.17 (1)	5.00 (1)	25.0 (2)	34

Values are percentage (frequency); GI denotes gastrointestinal, VKA vitamin K antagonist, AP antiplatelet agent,, AAS acetylsalicylic acid, P2Y12-I P2Y12 inhibitor. There was one missing value for antithrombotic drug type.

S7 Gastrointestinal lesion location and antithrombotic class cross-tabulation among 696 patients with a known lesion

Antithrombotic drug type	Upper GI lesion N = 408	Lower GI lesion N = 288
VKA alone	117 (28.7)	87 (30.2)
DOAC alone	16 (3.92)	26 (9.03)
AP alone	189 (46.3)	117 (40.6)
Parenteral or combo	86 (21.1)	58 (20.1)

Overall chi-square test p-value = 0.03

all pair-wise comparisons with Bonferroni correction > 0.10 except for DOAC compared to antiplatelet drugs (p-value = 0.02)

S8 Therapeutic management of major GI bleeding according to antithrombotic drug type (excluding combo and patients with limitation of care support)

Panel A. Upper GI bleeding symptoms (hematemesis or melena)

	VKA N = 168	DOAC N = 26	AP mono. N = 207	Dual AP N = 38	Parenteral N = 23	p value [a]
Surgery	8.33 (14)	7.69 (2)	4.83 (10)	7.89 (3)	4.35 (1)	0.63
Embolization	0.60 (1)	3.85 (1)	-	-	-	0.11
Endoscopy [b]	26.2 (44)	19.2 (5)	26.6 (55)	31.6 (12)	30.4 (7)	0.84
PPI	78.6 (132)	73.1 (19)	80.2 (166)	92.1 (35)	73.9 (17)	0.24
Transfusion						
Red cells	78.0 (131)	73.1 (19)	79.2 (164)	84.2 (32)	82.6 (19)	0.85
Platelets	0.60 (1)	-	4.35 (9)	-	4.35 (1)	0.11
Freeze plasma	2.98 (5)	3.85 (1)	2.90 (6)	2.63 (1)	-	0.96
Reversal therapy						
PCC	31.5 (53)	23.1 (6)	-	-	-	0.49
Vitamin K	50.6 (85)	3.85 (1)	0.97 (2)	2.63 (1)	-	<.001
Other	-	-				

Hemostatic procedures were: sclerotherapy with epinephrine injection, electrocautery therapy, argon plasma coagulation and banding clip.

Panel B. Lower GI bleeding symptoms (hematochezia)

	VKA N = 143	DOAC N = 38	AP mono. N = 175	Dual AP N = 34	Parenteral N = 29	p value [a]
Surgery	6.29 (9)	10.5 (4)	12.0 (21)	2.94 (1)	20.7 (6)	0.07
Embolization	2.10 (3)	-	4.00 (7)	5.88 (2)	6.90 (2)	0.30
Endoscopy [b]	13.3 (19)	10.5 (4)	9.71 (17)	11.8 (4)	20.7 (6)	0.49
PPI	23.1 (33)	31.6 (12)	26.9 (47)	35.3 (12)	31.0 (9)	0.53
Transfusions						
Red cells	55.2 (79)	63.2 (24)	55.4 (97)	67.6 (23)	62.1 (18)	0.61
Platelets	0.70 (1)	-	2.29 (4)	-	6.90 (2)	0.19
Freeze plasma	2.10 (3)	-	4.00 (7)	2.94 (1)	6.90 (2)	0.42
Reversal therapy						
PCC	27.3 (39)	7.89 (3)	0.57 (1)	-	3.45 (1)	<.001
Vitamin K	48.2 (69)	2.63 (1)	1.14 (2)	-	-	<.001
Other	-	-	-	-	3.45 (1)	-

Endoscopic hemostatic procedures were: diverticular cautery, mucosal resection, polyp ablation and vasoconstrictor infusion.

Values are percentage (frequency). PCC denotes prothrombin complex concentrate, PPI denotes proton pump inhibitor, VKA vitamin K antagonist, DOAC direct oral anticoagulant, and AP antiplatelet agent.

[a] Fisher exact test, [b] with hemostatic procedure

S9 Outcome from emergency department (ED) according to gastrointestinal bleeding symptoms and antithrombotic drug types (excluding combo and patients with limitation of care support)

Bleeding symptoms	VKA	DOAC	AP mono	Dual AP	Parenteral	Any combo	p values for hospitalization items	p value for outcome*
Hematemesis or melena	N = 168	N = 26	N = 207	N = 38	N = 23	N = 100		
Death in ED*	0.60 (1)	-	0.97 (2)	-	13.0 (3)	1.00 (1)		0.060[a]
Hospitalization*	86.9 (146)	92.4 (24)	86.5 (179)	89.5 (34)	78.3 (18)	91.0 (91)		
Length of stay (days)	6 [0-116]	5 [0-35]	5 [0-83]	6 [1-73]	4.5 [0-34]	6 [0-51]	0.749[b]	
Critical care unit (CCU)	39.0 (57)	25.0 (6)	33.0 (59)	67.6 (23)	44.4 (8)	39.6 (36)	0.005[a]	
Length of stay (days) in CCU	4 [1-45]	3 [0-19]	4 [1-83]	3 [1-7]	3.5 [1-11]	3.5 [1-20]	0.532[b]	
Death during hospitalization	8.22 (12)	-	5.59 (10)	8.82 (3)	5.56 (1)	6.59 (6)	0.594[a]	
Back home*	11.3 (19)	3.85 (1)	10.1 (24)	7.89 (3)	4.35 (1)	6.00 (6)		
Secondary care*	1.19 (2)	3.85 (1)	2.42 (5)	2.63 (1)	4.35 (1)	2.00 (2)		
Hematochezia	N = 143	N = 38	N = 175	N = 34	N = 29	N = 76		
Death in ED*	-	2.63 (1)	1.71 (3)	-	3.45 (1)	3.95 (3)		0.269[a]
Hospitalization*	83.9 (120)	84.2 (32)	81.1 (142)	76.5 (26)	72.4 (21)	82.9 (63)		
Length of stay (days)	6 [0-51]	7 [1-43]	5 [0-46]	4.5 [0-33]	6 [1-51]	6 [1-30]	0.032[b]	
Critical care unit (CCU)	31.1 (37)	34.4 (11)	35.9 (51)	34.6 (9)	28.6 (6)	39.7 (25)	0.926[a]	
Length of stay (days) in CCU	3 [1-14]	6 [1-9]	3.5 [0-15]	5 [1-7]	3.5 [1-5]	4 [2-13]	0.574[b]	
Death during hospitalization	4.20 (5)	-	4.23 (6)	7.69 (2)	9.52 (2)	-	0.358[a]	
Back home*	14.0 (20)	7.89 (3)	16.6 (29)	17.6 (6)	20.7 (6)	11.8 (9)		
Secondary care*	2.10 (3)	5.26 (2)	0.57 (1)	5.88 (2)	3.45 (1)	1.32 (1)		

Values are percentage (frequency) or median [min-max]; [a] Fisher exact test or [b] Kruskal-Wallis test. VKA denotes vitamin K antagonist, DOAC direct oral anticoagulant, and AP antiplatelet agent. *outcome is a mutually exclusive four-class variable (death in ED, hospitalization, back home or moving to secondary care facility)