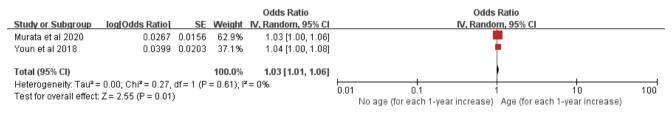


Supplementary Figure. Forest plots showing the association between risk factors and GIB (from S1-S49).

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Chan et al 2015		0.2031	11.2%	2.47 [1.66, 3.68]	
Chen et al 2014		0.3884	8.2%	2.57 [1.20, 5.50]	
Ferroni et al 2022 (1)	0.8278		10.2%	2.29 [1.36, 3.85]	
Ferroni et al 2022 (2)	0.3892	0.2523	10.5%	1.48 [0.90, 2.42]	+
Kato et al 2016	0.2761	0.1358	12.2%	1.32 [1.01, 1.72]	
Lauffenburger et al 2015 (1)	1.0003	0.2738	10.1%	2.72 [1.59, 4.65]	
Lauffenburger et al 2015 (2)	1.5096	0.2672	10.2%	4.52 [2.68, 7.64]	
Pourakari et al 2016	0.034	0.0237	13.0%	1.03 [0.99, 1.08]	t the second sec
Sandra et al 2021	-0.192	0.3038	9.6%	0.83 [0.46, 1.50]	
Sherid et al 2015	1.8948	0.6711	4.7%	6.65 [1.79, 24.78]	
Total (95% CI)			100.0%	1.95 [1.36, 2.79]	◆
Heterogeneity: Tau <sup>2</sup> = 0.26; Chi <sup>2</sup>		0.00001	); I <sup>z</sup> = 899	Хо	
Test for overall effect: Z = 3.66 (F	P = 0.0003)				No older age Older age

**S1.** Forest plot showing the association between older age and GIB.



**S2.** Forest plot showing the association between age: for each 1-year increase and GIB.

				Odds Ratio			Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl			IV, Random, 95% C	1	
Sherwood et al 2015	0.1076	0.0252	100.0%	1.11 [1.06, 1.17]			<b>—</b>		
Total (95% CI)			100.0%	1.11 [1.06, 1.17]	1	1	٠		
Heterogeneity: Not app Test for overall effect: Z		1)			0.01 No age	0.1 (for each 5-yea	i ar increase) Age (for	10 each 5-year increase	100 <sup>'</sup>

**S3.** Forest plot showing the association between age for each 5-year increase and GIB.

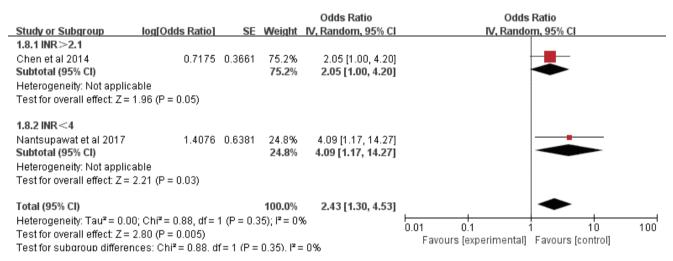
Study or Subgroup	log[Odds Ratio]	SE	Woight	Odds Ratio IV, Random, 95% Cl			Odds Ratio Random, 95%	CI	
Study of Subgroup	log ouus nauo	36	weight	IV, Kanuom, 95% CI		17,1	vanuom, 957		
Coates et al 2021	0.3639	0.1806	100.0%	1.44 [1.01, 2.05]					
Total (95% CI)			100.0%	1.44 [1.01, 2.05]			•		
Heterogeneity: Not ap Test for overall effect:	•				0.01	0.1 ≪1	1 20kg >120	10 Ikg	100

**S4.** Forest plot showing the association between obesity and GIB.



				Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl		IV, Random, 95% Cl
Delaney et al 2007	0.4094	0.0372	22.6%	1.51 [1.40, 1.62]		•
Fanning et al 2020	-0.6504	0.2926	11.7%	0.52 [0.29, 0.93]		
Ferroni et al 2022	-0.395	0.1923	16.2%	0.67 [0.46, 0.98]		
Lauffenburger et al 2015	0.2488	0.1008	20.6%	1.28 [1.05, 1.56]		-
Maruyama et al 2018	-1.2629	0.5305	5.5%	0.28 [0.10, 0.80]		
Sherid et al 2015	-1.0046	0.8521	2.5%	0.37 [0.07, 1.95]		
Sherwood et al 2015	0.1873	0.0905	21.0%	1.21 [1.01, 1.44]		-
Total (95% CI)			100.0%	0.95 [0.72, 1.26]		+
Heterogeneity: Tau <sup>2</sup> = 0.09;		6 (P ≤ 0.)	00001); P	'= 87%	L	0.1 1 10 100
Test for overall effect: Z = 0	.36 (P = 0.72)					Female Male

**S5.** Forest plot showing the association between sex and GIB.



56. Forest plot showing the association between INR and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Nantsupawat et al2017	1.7669	0.7637	47.2%	5.85 [1.31, 26.15]	] — — — — — — — — — — — — — — — — — — —
Sandra et al 2021	-1.2366	0.2731	52.8%	0.29 [0.17, 0.50]	
Total (95% CI)			100.0%	1.20 [0.06, 22.63]	
Heterogeneity: Tau <sup>2</sup> = 4.1 Test for overall effect: Z =		= 1 (P = 0	).0002); I <sup>2</sup>	= 93%	0.01 0.1 1 10 100 HasBled-Score≤3 HasBled-Score≥3

**S7.** Forest plot showing the association between HasBled-Score > 3 and GIB.



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Pourakari et al 2016	-0.6143	0.6789	4.9%	0.54 [0.14, 2.05]	
Shimomura et al 2017	1.9042	0.5466	7.1%	6.71 [2.30, 19.60]	
Sandra et al 2021	0.4089	0.313	16.3%	1.51 [0.81, 2.78]	
Lauffenburger et al 2015	0.513	0.152	31.5%	1.67 [1.24, 2.25]	-
Schauer et al 2005	0.4776	0.0757	40.1%	1.61 [1.39, 1.87]	-
Total (95% CI)			100.0%	1.69 [1.24, 2.31]	◆
Heterogeneity: Tau² = 0.08	; Chi <sup>2</sup> = 9.46, df = 4	(P = 0.0)	5); I <sup>2</sup> = 58	%	
Test for overall effect: Z = 3	3.30 (P = 0.0010)				0.005 0.1 1 10 200 No kidney disease Kidney disease

**S8.** Forest plot showing the association between kidney disease and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl		Odds Ratio IV, Random, 95% Cl	
Chen et al 2014	1.9459	0.6392	47.7%	7.00 [2.00, 24.50]			<b></b>
Shimomura et al 2017	1.7269	0.6104	52.3%	5.62 [1.70, 18.60]			
Total (95% Cl)			100.0%	6.24 [2.63, 14.83]			
Heterogeneity: Tau <sup>2</sup> = 0. Test for overall effect: Z		L 0.01	0.1 1 No cirrhosis Cirrhosis	10 100			

**S9.** Forest plot showing the association between cirrhosis and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl		-	dds Ratio ndom, 95%	CI	
Delaney et al 2007	1.9468	0.1951	100.0%	7.01 [4.78, 10.27]				-	
Total (95% CI)			100.0%	7.01 [4.78, 10.27]		1		•	
Heterogeneity: Not ap Test for overall effect:		001)			0.01	0.1 No liver fail	1 ure Liverf	10 ailure	100

**S10.** Forest plot showing the association between liver failure and GIB.



01 . I 0. I.			100-1-0-0	Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.14.1 Chronic Heart Failu	ire				
Schauer et al 2005	0.2718	0.0947	53.2%	1.31 [1.09, 1.58]	
Subtotal (95% CI)			53.2%	1.31 [1.09, 1.58]	◆
Heterogeneity: Not applica	ible				
Test for overall effect: Z = 2	2.87 (P = 0.004)				
1.14.2 Congestive Heart F	ailure				
Ferroni et al 2022	0.2273	0.1109	38.8%	1.26 [1.01, 1.56]	<b>-</b>
Lauffenburger et al 2015	0.3745	0.2448	8.0%	1.45 [0.90, 2.35]	+
Subtotal (95% CI)			46.8%	1.29 [1.06, 1.57]	◆
Heterogeneity: Tau <sup>2</sup> = 0.00	); Chi <sup>2</sup> = 0.30, df = 1	(P = 0.5)	8); I <sup>z</sup> = 0%	5	
Test for overall effect: Z = 2	2.50 (P = 0.01)				
Total (95% CI)			100.0%	1.30 [1.14, 1.49]	•
Heterogeneity: Tau <sup>2</sup> = 0.00	); Chi <sup>2</sup> = 0.32, df = 2	(P = 0.8)	5); I <sup>2</sup> = 0%	, ,	
Test for overall effect: Z = 3		,			0.01 0.1 1 10 100
Test for subaroup differen	· · ·	= 1 (P = 1	0.89) P=	0%	No heart failure Heart failure

**S11.** Forest plot showing the association between heart failure (HF) and GIB.

				Odds Ratio	Odds	Ratio	
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Rando	m, 95% Cl	
1.49.1 Bleeding							
Lauffenburger et al 2015	0.2761	0.1358	53.9%	1.32 [1.01, 1.72]		-	
Subtotal (95% CI)			<b>53.9</b> %	1.32 [1.01, 1.72]		◆	
Heterogeneity: Not applica	ble						
Test for overall effect: Z = 2	.03 (P = 0.04)						
1.49.2 History of bleeding							
Ferroni et al 2022	1.1831	0.287	46.1%	3.26 [1.86, 5.73]			
Subtotal (95% CI)			46.1%	3.26 [1.86, 5.73]		-	
Heterogeneity: Not applica	ble						
Test for overall effect: Z = 4	.12 (P < 0.0001)						
Total (95% CI)			100.0%	2.00 [0.83, 4.86]			
Heterogeneity: Tau <sup>2</sup> = 0.36	; Chi <sup>2</sup> = 8.16, df = 1	(P = 0.0)	04); I <sup>z</sup> = 8	8%	0.01 0.1	<del>   </del> 1 10	100
Test for overall effect: Z = 1	.54 (P = 0.12)						100
Test for subaroup difference	es: Chi <sup>2</sup> = 8.16. df:	= 1 (P = 0	0.004). I <sup>z</sup> :	= 87.7%	Favours [experimental]	Favours (control)	

**S12.** Forest plot showing the association between bleeding and GIB.

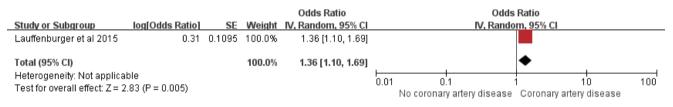
Cturks on Subarrown	la ri Odda Datial	er	Maint	Odds Ratio			Odds			
Study or Subgroup	log[Odds Ratio]	36	weight	IV, Random, 95% Cl			IV, Rando	n, 95% CI		
Ferroni et al 2022	0.8009	0.3508	100.0%	2.23 [1.12, 4.43]						
Total (95% CI)			100.0%	2.23 [1.12, 4.43]				-		
Heterogeneity: Not ap Test for overall effect:	•	)			0.01	0.1 No myocard	dial infarction	Myocardial	10 infarction	100

**\$13.** Forest plot showing the association between myocardial infarction and GIB.

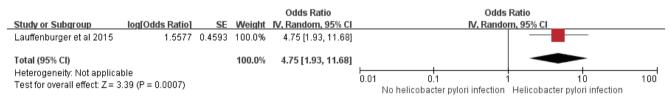


			Odds Ratio	Odds Ratio	
Study or Subgroup	log[Odds Ratio]	SE Weight	IV, Random, 95% Cl	IV, Random, 95% Cl	
1.50.1 GFR 50-80					
Kalil et al 2016	1.0819 0.4	423 82.7%	2.95 [1.24, 7.02]		
Subtotal (95% CI)		82.7%	2.95 [1.24, 7.02]		
Heterogeneity: Not ap	oplicable				
Test for overall effect	Z = 2.45 (P = 0.01)				
1.50.2 GFR ≤30					
Sherid et al 2015	1.5115 0.9	9665 17.3%	4.53 [0.68, 30.14]		
Subtotal (95% CI)		17.3%	4.53 [0.68, 30.14]		
Heterogeneity: Not a	oplicable				
Test for overall effect	: Z = 1.56 (P = 0.12)				
Total (95% CI)		100.0%	3.18 [1.44, 6.99]	•	
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi <sup>2</sup> = 0.16, df =	1 (P = 0.69); I <sup>a</sup>	²= 0%		00
Test for overall effect	: Z = 2.88 (P = 0.004)			Favours [experimental] Favours [control]	00
Test for subaroup dif	ferences: Chi <sup>2</sup> = 0.16. d	#f = 1 (P = 0.69	I), I² = 0%	ravou's (experimental) Favou's (control)	

**S14.** Forest plot showing the association between renal failure and GIB.



**\$15.** Forest plot showing the association between coronary artery disease and GIB.



**\$16.** Forest plot showing the association between helicobacter pylori infections and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
nawarawong et al 2018	1.5846	0.707	100.0%	4.88 [1.22, 19.50]	
Total (95% CI)			100.0%	4.88 [1.22, 19.50]	
Heterogeneity: Not applic: Test for overall effect: Z =					0.01 0.1 1 10 100 No hematochezia Hematochezia

**S17.** Forest plot showing the association between hematochezia and GIB.



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl			Odds Ratio andom, 95%	CI	
Lauffenburger et al 2015	0.226	0.13	45.6%	1.25 [0.97, 1.62]			-		
Sherwood et al 2015	0.5283	0.0942	54.4%	1.70 [1.41, 2.04]					
Total (95% CI)			100.0%	1.48 [1.10, 1.98]			•		
Heterogeneity: Tau <sup>2</sup> = 0.03 Test for overall effect: Z = 2		(P = 0.0	6); I² = 72	%	0.01	0.1 No ane	1 mia Anemi	10 a	100

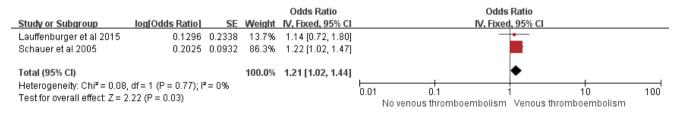
**S18.** Forest plot showing the association between anemia and GIB.

				Odds Ratio			Odds	Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl			IV, Rando	m, 95% Cl		
Sherwood et al 2015	0.4704	0.1385	100.0%	1.60 [1.22, 2.10]						
Total (95% CI)			100.0%	1.60 [1.22, 2.10]				•		
Heterogeneity: Not app Test for overall effect: 2		7)			0.01	0. Jo history	1 of sleep apnea		lO papnea	100

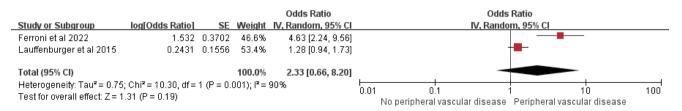
**\$19.** Forest plot showing the association between history of sleep apnea and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl		IV.	Odds Ratio Random, 95		
Schauer et al 2005	0.1794	0.0765	100.0%	1.20 [1.03, 1.39]					
Total (95% CI)			100.0%	1.20 [1.03, 1.39]			•		
Heterogeneity: Not ap Test for overall effect:	•	1			0.01 No	0.1 Psychiatric i	1 Ilness Psyc	10 hiatric illness	100

**\$20.** Forest plot showing the association between psychiatric illness and GIB.



**S21.** Forest plot showing the association between venous thromboembolism and GIB.



**s22.** Forest plot showing the association between peripheral vascular disease and GIB.



Study or Subgroup	la al Odda Datia)	65	Maight	Odds Ratio				Ratio		
Study or Subgroup	log[Odds Ratio]	3E	vveignt	IV, Random, 95% Cl			IV, Kando	m, 95% Cl		
Pourakari et al 2016	0.6782	0.779	100.0%	1.97 [0.43, 9.07]					-	
Total (95% CI)			100.0%	1.97 [0.43, 9.07]						
Heterogeneity: Not ap Test for overall effect: J					0.01 N	0. No mechani	1 cal valve implant		10 ve implant	100

**S23.** Forest plot showing the association between mechanical valve implant and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl		Odds Ra IV, Random,		
Schauer et al 2005	0.2729	0.1429	100.0%	1.31 [0.99, 1.74]				
<b>Total (95% CI)</b> Heterogeneity: Not ap Test for overall effect:	•		100.0%	1.31 [0.99, 1.74]	L	0.1 1 No liver disease Li	10 ver disease	100

**S24.** Forest plot showing the association between liver disease and GIB.

				Odds Ratio		Odd	s Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI		IV, Fixe	ed, 95% Cl		
Lauffenburger et al 2015	0.1859 0	0.1052	30.1%	1.20 [0.98, 1.48]			_ <b> </b> =-		
Schauer et al 2005	0.0301 0	0.0691	69.9%	1.03 [0.90, 1.18]			<b>#</b>		
Total (95% CI)			100.0%	1.08 [0.96, 1.21]			•		
Heterogeneity: Chi² = 1.53, Test for overall effect: Z = 1			L	0.1 No diabetes	1 5 Diabetes	10	100		

**S25.** Forest plot showing the association between diabetes and GIB.

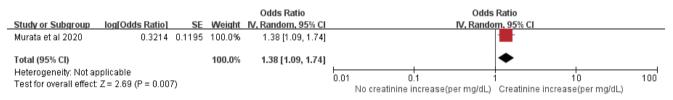
Churche on Culture out	las/Odda Datial	er	Mainht	Odds Ratio			Odds Ratio		
Study or Subgroup	log[Odds Ratio]	36	weight	IV, Random, 95% Cl		IV, F	<u>tandom, 959</u>	% CI	
Sherwood et al 2015	0.2625	0.109	60.9%	1.30 [1.05, 1.61]					
Shimomura et al 2017	1.3762 (	0.5305	39.1%	3.96 [1.40, 11.20]					
Total (95% CI)			100.0%	2.01 [0.69, 5.83]					
Heterogeneity: Tau <sup>2</sup> = 0 Test for overall effect: Z =		1 (P = 0.	.04); I² = ;	76%	0.01	0.1 No C	1 OPD COPI	10 D	100

**S26.** Forest plot showing the association between COPD and GIB.

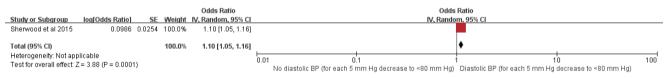


				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Chan et al 2015	0.8365	0.2065	6.6%	2.31 [1.54, 3.46]	
Chen et al 2014	1.6223	0.5002	5.9%	5.06 [1.90, 13.50]	
Ferroni et al 2022	0.6346	0.3949	6.2%	1.89 [0.87, 4.09]	
Garcia et al 2019 (1)	0.5394	0.3522	6.3%	1.71 [0.86, 3.42]	
Garcia et al 2019 (2)	1.1397	0.2356	6.6%	3.13 [1.97, 4.96]	
Garcia et al 2019 (3)	1.2313	0.2695	6.5%	3.43 [2.02, 5.81]	
Garcia et al 2019 (4)	1.6982	0.3928	6.2%	5.46 [2.53, 11.80]	
Maruyama et al 2018 (1)	3.3712	0.7083	5.2%	29.11 [7.26, 116.68]	
Maruyama et al 2018 (2)	2.7199	0.7943	4.9%	15.18 [3.20, 72.00]	
Nantsupawat et al 2017	3.2238	1.1105	3.9%	25.12 [2.85, 221.48]	· · · · · · · · · · · · · · · · · · ·
Pourakari et al 2016	4.7113	0.7306	5.1%	111.20 [26.56, 465.56]	
Sandra et al 2021	0.8845	0.4022	6.2%	2.42 [1.10, 5.33]	
Sherid et al 2014	1.431	0.9807	4.3%	4.18 [0.61, 28.59]	
Sherid et al 2015	2.7408	0.0005	6.8%	15.50 [15.48, 15.51]	· · · · · · · · · · · · · · · · · · ·
Sherwood et al 2015	0.7488	0.1359	6.7%	2.11 [1.62, 2.76]	
Shimomura et al 2017	0.6148	0.3399	6.4%	1.85 [0.95, 3.60]	
Youn et al 2018	1.7802	0.44	6.1%	5.93 [2.50, 14.05]	
Total (95% Cl)			100.0%	5.26 [2.76, 10.05]	
Heterogeneity: Tau <sup>2</sup> = 1.60; C	⊳hi² = 532.22, df = 1	I6 (P < 0.	00001); P	<b>²</b> = 97%	
Test for overall effect: Z = 5.0	3 (P < 0.00001)	-			0.01 0.1 1 10 100
					No history of peptic ulcer/GIB History of peptic ulcer/GIB

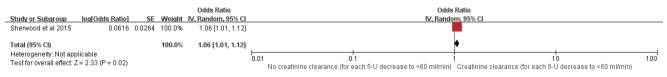
**S27.** Forest plot showing the association between history of peptic ulcer/GIB and GIB.



**S28.** Forest plot showing the association between creatinine level (per 1 mg/dL increase) and GIB.



**\$29.** Forest plot showing the association between diastolic BP and GIB.



S30. Forest plot showing the association between creatinine clearance < 60 ml/min and GIB.



				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Aisenberg et al 2018	0.2672	0.0971	21.5%	1.31 [1.08, 1.58]	
Chan et al 2015	0.418	0.1982	20.0%	1.52 [1.03, 2.24]	
Delaney et al 2007	1.8682	0.2149	19.7%	6.48 [4.25, 9.87]	
Douros et al 2019	0.142	0.1737	20.4%	1.15 [0.82, 1.62]	
Sherid et al 2015	1.0297	0.273	18.4%	2.80 [1.64, 4.78]	
Total (95% CI)			100.0%	2.07 [1.17, 3.66]	◆
Heterogeneity: Tau <sup>2</sup> = (	0.38; Chi <sup>2</sup> = 54.45,	df = 4 (P	< 0.00001	1); I² = 93%	
Test for overall effect: Z	Z = 2.50 (P = 0.01)				0.01 0.1 1 10 100
	(,,				No concomitant use of aspirin Concomitant use of aspirin

**S31.** Forest plot showing the association between concomitant use of aspirin and GIB.

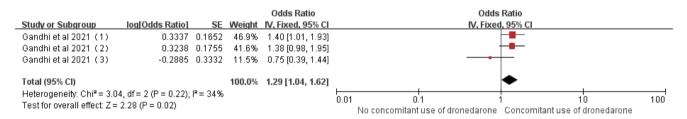
~		~5		Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.52.1 NSAID use					
Delaney et al 2007(1)		0.2753	9.5%	4.79 [2.79, 8.21]	
Delaney et al 2007(2)	1.5307	0.5809	3.0%	4.62 [1.48, 14.43]	
Delaney et al 2007(3)	0.3851	0.0433	24.3%	1.47 [1.35, 1.60]	•
Maruyama et al 2018	2.5285	0.6966	2.2%	12.53 [3.20, 49.10]	
Olsen et al 2019 (1)	0.6479	0.1589	16.2%	1.91 [1.40, 2.61]	
Olsen et al 2019 (2)	0.5901	0.2038	13.2%	1.80 [1.21, 2.69]	
Sherid et al 2015	0.2601	0.4615	4.4%	1.30 [0.52, 3.20]	
Subtotal (95% CI)			72.7%	2.37 [1.61, 3.50]	•
Heterogeneity: Tau <sup>2</sup> = 0.17; 0	Chi² = 33.22, df = 6	6 (P ≤ 0.0	0001); I <sup>z</sup> :	= 82%	
Test for overall effect: Z = 4.3	6 (P < 0.0001)				
<b>1.52.2 Paracetamol use</b> Delaney et al 2007 <b>Subtotal (95% CI)</b> Heterogeneity: Not applicabl Test for overall effect: Z = 8.8	e	0.0433	24.3% <b>24.3</b> %	1.47 [1.35, 1.60] 1.47 [1.35, 1.60]	•
1.52.3 COX-2 inhibitor use					
Delaney et al 2007	1.5307	0.5809	3.0%	4.62 [1.48, 14.43]	
Subtotal (95% CI)			3.0%	4.62 [1.48, 14.43]	
Heterogeneity: Not applicabl	e				
Test for overall effect: Z = 2.6	4 (P = 0.008)				
Total (95% CI)			100.0%	1.97 [1.59, 2.42]	•
Heterogeneity: Tau <sup>2</sup> = 0.05; (	:hi≓= 37 96 df- 9	(P < ∩ ∩			
Test for overall effect: Z = 6.3		, (i ~ 0.0	0007/,1 -	-1370	0.01 0.1 i 10 10
Test for subgroup difference	· /	2/0-0	010\ 12-	70 50	Favours [experimental] Favours [control]

**S32.** Forest plot showing the association between concomitant with NSAID and GIB.



				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Douros et al 2019 (1)	0.0804	0.1485	13.8%	1.08 [0.81, 1.45]	-
Douros et al 2019 (2)	0.1691	0.2331	11.1%	1.18 [0.75, 1.87]	
Douros et al 2019 (3)	0.1255	0.2997	9.2%	1.13 [0.63, 2.04]	
Douros et al 2019 (4)	0.098	0.1703	13.1%	1.10 [0.79, 1.54]	
Lauffenburger et al 2015	0.4026	0.1167	14.8%	1.50 [1.19, 1.88]	-
Maruyama et al 2018	2.1464	0.5883	4.0%	8.55 [2.70, 27.10]	
nawarawong et al 2018	-1.124	0.5083	5.0%	0.32 [0.12, 0.88]	
Sandra et al 2021	0.841	0.4531	5.8%	2.32 [0.95, 5.64]	
Sherid et al 2014	2.0015	0.9636	1.8%	7.40 [1.12, 48.92]	
Sherid et al 2015	0.9243	0.6721	3.3%	2.52 [0.68, 9.41]	
Sherwood et al 2015	0.4064	0.1972	12.3%	1.50 [1.02, 2.21]	
Youn et al 2018	1.1383	0.4608	5.7%	3.12 [1.27, 7.70]	
Total (95% Cl)			100.0%	1.45 [1.11, 1.90]	◆
Heterogeneity: Tau <sup>2</sup> = 0.11	; Chi <sup>2</sup> = 31.72, df =	11 (P = 0	.0008); I <sup>z</sup>	= 65%	
Test for overall effect: Z = 2					0.01 0.1 1 10 100
	· ·····,				No antiplatelet agent use Antiplatelet agent use

**S33.** Forest plot showing the association between antiplatelet theapy and GIB.



**S34.** Forest plot showing the association between concomitant use of dronedarone and GIB.

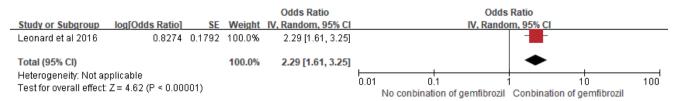
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% Cl		Odds Ratio IV. Fixed, 95% Cl	
Holm et al 2020 (1)				1.54 [1.02, 2.32]			
Holm et al 2020 (2)	0.363	0.1555	64.5%	1.44 [1.06, 1.95]			
Total (95% CI)			100.0%	1.47 [1.15, 1.88]			
Heterogeneity: Chi² = 0. Test for overall effect: Z			)		0.01	0.1 10 10 No CYP3A4 and/or P-gp-inhibitors use CYP3A4 and/or P-gp-inhibitors use	100

S35. Forest plot showing the association between conbination of CYP3A4 and/or P-gp-inhibitors and GIB.

				Odds Ratio		(	Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl		IV, R	andom, 95%	6 CI	
Lauffenburger et al 2015	0.4026	0.1167	100.0%	1.50 [1.19, 1.88]					
Total (95% CI)			100.0%	1.50 [1.19, 1.88]			•		
Heterogeneity: Not applica Test for overall effect: Z = 3					0.01	0.1 No digoxin	1 use Digox	10 in use	100

**S36.** Forest plot showing the association between conbination of digoxin and GIB.





**S37.** Forest plot showing the association between conbination of gemfibrozil and GIB.

			Odds Ratio	Odds Ratio	
Study or Subgroup log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl	
Pham et al 2020 (1) 0.7716	0.2598	23.3%	2.16 [1.30, 3.60]		
Pham et al 2020 (2) 0.8415	0.2504	25.1%	2.32 [1.42, 3.79]		
Pham et al 2020 (3) 0.7719	0.2639	22.6%	2.16 [1.29, 3.63]		
Pham et al 2020 (4) 0.8455	0.2525	24.7%	2.33 [1.42, 3.82]		
Pham et al 2020 (5) 1.7024	0.607	4.3%	5.49 [1.67, 18.03]		
Total (95% CI)		100.0%	2.33 [1.82, 2.98]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.15, df = Test for overall effect: Z = 6.75 (P < 0.00001	•	71); I² = (	)%	0.01 0.1 1 10 No verapamil or diltiazem use Verapamil or diltiazem use	100

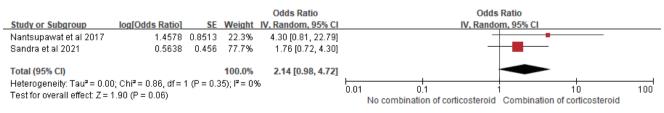
**S38.** Forest plot showing the association between conbination of verapamil or diltiazem and GIB.

				Odds Ratio			Odds	Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl			IV, Rando	m, 95% Cl		
Sherwood et al 2015	0.3867	0.0794	100.0%	1.47 [1.26, 1.72]						
Total (95% CI)			100.0%	1.47 [1.26, 1.72]				•		
Heterogeneity: Not app Test for overall effect: 2		01)			0.01	0. No long-term A	1 SA use at screening	1 Long-term ASA us	10 e at screening	100

**S39.** Forest plot showing the association between long-term ASA use at screening and GIB.

				Odds Ratio			Odds	Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl			IV, Rando	m, 95% Cl		
Sandra et al 2021	0.864	0.4429	100.0%	2.37 [1.00, 5.65]						
Total (95% CI)			100.0%	2.37 [1.00, 5.65]						
Heterogeneity: Not ap Test for overall effect:		)			0.005 No	0. concomitant therap	1 y with clopidogrel	1 1 concomitant ther	i 10 apy with clopidogrel	200

**\$40.** Forest plot showing the association between concomitant therapy with clopidogrel and GIB.



**S41.** Forest plot showing the association between combination of corticosteroid and GIB.



				Odds Ratio			Ode	ls Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl			IV, Ran	dom, 95% C		
Sherid et al 2015	0.8608	0.5846	100.0%	2.37 [0.75, 7.44]						
Total (95% CI)			100.0%	2.37 [0.75, 7.44]						
Heterogeneity: Not ap Test for overall effect:		)			0.01	0. No thieno	1 pyridines us	1 e Thienop	10 vridines use	100

**\$42.** Forest plot showing the association between conbination of thienopyridines and GIB.

Study or Subgroup	log[Odds Ratio]	SE.	Woight	Odds Ratio IV, Random, 95% Cl			Ratio m, 95% Cl	
Study of Subgroup	logi ouus ratio	3E	weight	IV, Random, 95% CI		iv, Kanuu	m, 95% Ci	
Holt et al 2021 (1)	0.4322	0.0906	50.5%	1.54 [1.29, 1.84]			-	
Holt et al 2021 (2)	0.7839	0.0973	49.5%	2.19 [1.81, 2.65]			-	
Total (95% CI)			100.0%	1.83 [1.30, 2.59]			•	
Heterogeneity: Tau² = Test for overall effect:			= 0.008);	I² = 86%	0.01	0.1 No oral glucocorticoid use	1 10 Oral glucocorticoid use	100

**S43.** Forest plot showing the association between conbination of oral glucocorticoid and GIB.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV. Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Schauer et al 2005			100.0%	1.29 [1.12, 1.48]	
Total (95% CI)			100.0%	1.29 [1.12, 1.48]	◆
Heterogeneity: Not ap Test for overall effect:		D4)			0.01 0.1 1 10 100 No social risk factors Social risk factors

**S44.** Forest plot showing the association between social risk factors and GIB.

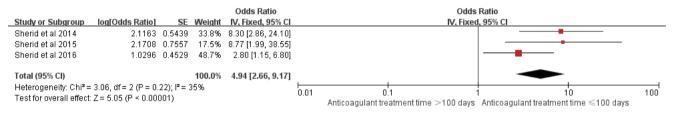
				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	I IV, Random, 95% Cl
Delaney et al 2007	1.3855	0.075	67.0%	4.00 [3.45, 4.63]	ı] 🔰 📕
Lauffenburger et al 2015	0.9444	0.2682	33.0%	2.57 [1.52, 4.35]	i] ————————————————————————————————————
Total (95% CI)			100.0%	3.46 [2.30, 5.19]	1 •
Heterogeneity: Tau² = 0.06 Test for overall effect: Z = 5		(P = 0.1	1); I <sup>z</sup> = 60'	%	0.01 0.1 1 10 100 No alcohol use Alcohol use

**S45.** Forest plot showing the association between alcohol use and GIB.



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% Cl		Odds Rat IV, Fixed, 95		
Delaney et al 2007	0.2162	0.039	82.7%	1.24 [1.15, 1.34]				
Sherwood et al 2015	0.3154	0.0852	17.3%	1.37 [1.16, 1.62]		+		
Total (95% CI)				1.26 [1.18, 1.35]		•		
Heterogeneity: Chi <sup>2</sup> = 1 Test for overall effect: 2		<i></i>	%		0.01	0.1 1 No smoking Sm	10 loking	100

**\$46.** Forest plot showing the association between smoking and GIB.





				Odds Ratio			Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl		IV, F	andom, 95%	6 CI	
Schauer et al 2005	0.3468	0.1424	100.0%	1.41 [1.07, 1.87]					
Total (95% CI)			100.0%	1.41 [1.07, 1.87]			•		
Heterogeneity: Not ap Test for overall effect:	•	)			0.01 No	0.1 substance al	1 ouse Subs	10 tance abuse	100

**S48.** Forest plot showing the association between substance abuse and GIB.

				Odds Ratio		Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI		
Graham et al 2014	0.4129	0.069	52.1%	1.51 [1.32, 1.73]				
Kolb et al 2018 (1)	0.4496	0.1034	23.2%	1.57 [1.28, 1.92]		-		
Kolb et al 2018 (2)	0.4808	0.1523	10.7%	1.62 [1.20, 2.18]				
Kolb et al 2018 (3)	0.1234	0.1704	8.5%	1.13 [0.81, 1.58]				
Kolb et al 2018 (4)	0.8016	0.2124	5.5%	2.23 [1.47, 3.38]				
Total (95% CI)			100.0%	1.53 [1.39, 1.69]		•		
Heterogeneity: Chi <sup>2</sup> =			38%		0.01 0	1 1	10	100
Test for overall effect:	001)			0.01 0	Warfarin Dabigatr			

**S49.** Forest plot showing the association between dabigatran 150mg and GIB.