

Supplementary materials

Table 1: Embase search strategy

1. "incidence".ab,kw,ti.
2. "prevalence".ab,kw,ti.
3. incidence/
4. prevalence/
5. 1 or 2 or 3 or 4
6. "acute coronary syndrome".ab,kw,ti.
7. "myocardial infarction".ab,kw,ti.
8. "NSTEMI".ab,kw,ti.
9. "STEMI".ab,kw,ti.
10. "st segment elevation myocardial infarction".ab,kw,ti.
11. acute coronary syndrome/
12. heart infarction/
13. unstable angina pectoris/
14. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. "bleed* ".ab,kw,ti.
16. "h?emorrhage".ab,kw,ti.
17. exp bleeding/
18. 15 or 16 or 17
19. "post".ab,kw,ti.
20. "late onset".ab,kw,ti.
21. "discharge* ".ab,kw,ti.
22. "home".ab,kw,ti.
23. hospital discharge/
24. 19 or 20 or 21 or 22 or 23
25. "mortality".ab,kw,ti.
26. "death".ab,kw,ti.
27. "MACE".ab,kw,ti.
28. "major adverse cardi* event* ".ab,kw,ti.
29. "reinfarction".ab,kw,ti.
30. "readmi* ".ab,kw,ti.
31. hospital readmission/
32. heart reinfarction/
33. cardiovascular mortality/ or exp hospital mortality/ or mortality/ or mortality risk/
34. 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33
35. 5 and 14 and 18 and 24
36. 14 and 18 and 24 and 34
37. 35 or 36
38. limit 37 to human

Table 2: Bleeding definitions

Criteria	Severity	Definition
BARC	Type 0	No bleeding
	Type 1	Bleeding that is not actionable (Nuisance bleeds)
	Type 2	Actionable bleeding requiring hospitalisation, diagnostic studies and treatment by healthcare professional, but does not fit criteria for 3, 4 & 5.
	Type 3	
	A	Overt bleeding + hemoglobin drop of 3 to <5 g/dl
		Any transfusion with overt bleeding
	B	Overt bleeding + hemoglobin drop \geq 5 g/dl
		Cardiac tamponade
		Bleeding requiring surgical intervention
		Bleeding requiring intravenous vasoactive agents
	C	Intracranial bleed
		Intraocular bleed
	Type 4	CABG related bleeds
	Type 5	
		A
	B	Definite fatal bleeding: overt bleeding or autopsy or imaging confirmation
TIMI	Major	Intracranial or a \geq 5 g/dl decrease in hemoglobin or Bleeding resulting in death within 7 days
	Minor	Overt blood loss or \geq 3 to \leq 5 g/dl decrease in hemoglobin or requiring intervention (medical practitioner-guided medical or surgical treatment to stop or treat bleeding including temporarily or permanently stopping or changing the dose of a medication or study drug or leading to or prolonging hospitalisation or prompting evaluation (leading to unscheduled visit to a healthcare professional and diagnostic testing, either laboratory or imaging)
	Minimal	Any overt bleeding that does not meet Major or Minor bleeding criteria above.
GUSTO	Severe or life threatening	Intracerebral or resulting in substantial hemodynamic compromise requiring treatment
	Moderate	bleeding requiring blood transfusion or bleeding that does not cause hemodynamic compromise
	Mild	bleeding that does not meet criteria for severe or moderate bleeding

ACUITY/HORIZON	Major	Intracranial or intraocular or access site bleeding requiring intervention or ≥ 5 -cm diameter hematoma or hemoglobin drop of ≥ 4 g/dl without an overt source or hemoglobin drop of ≥ 3 g/dl with an overt source or reoperation for bleeding or requiring blood product transfusion
CURE	Major	Significantly disabling, intraocular bleeding leading to loss of vision or requiring transfusion of ≥ 2 units of packed cells or bleeding that is life threatening (fatal or intracranial or results in decrease hemoglobin of at least 5 g/dl or leading to substantial hypotension requiring the use of inotropic agents or requiring surgical intervention or result in transfusion of ≥ 4 units of blood
	Minor	bleed leading to discontinuation of study medication
ISTH	Major	Fatal bleeding, and/or Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or Bleeding causing a fall in hemoglobin level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red cells
	Clinically non relevant non-major bleeding	Any sign or symptom of haemorrhage (e.g., more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for major bleeding but does meet at least one of the following criteria: 1) requiring medical intervention by a healthcare professional or 2) leading to hospitalization or increased level of care or 3) prompting a face to face (i.e., not just a telephone or electronic communication) evaluation.
OASIS 5	Major	Clinically overt bleeding that is fatal, symptomatic intracranial, retroperitoneal, or intraocular, an HGB decrease of at least 3.0 g/dL (with each blood transfusion unit counting for 1.0 g/dL of HGB), or requiring transfusion of at least 2 units of red blood cells
	Minor	Minor bleeding is considered to be any other clinically significant bleeding not meeting the definition for major bleeding and leading to interruption of study drug for at least 24 hours, surgical intervention or transfusion of one unit of blood (whole blood or PRBC)
Fosbol et al 2012		Re-hospitalisation for bleeding defined as gastrointestinal, intracranial, haemarthrosis, hemopericardium, haematuria, hemoptysis, epistaxis, haemorrhage not specified, acute post-hemorrhagic anaemia
Tsai et al 2010		Defined as hospitalisation with a primary diagnosis of gastrointestinal haemorrhage, or ulcer or GI bleed or perforation identified by surgery.
Carrero et al 2016		Defined as intracranial haemorrhage, gastrointestinal haemorrhage or anaemia.

Graipe et al 2015		Intracranial haemorrhage defined as subarachnoid haemorrhage, intracerebral haemorrhage and other intracranial haemorrhage using WHO ICD-10 classification.
Sorensen et al 2009		Defined as an admission to a Danish hospital with a diagnosis of non-fatal bleeding or fatal bleeding including cerebral bleed, respiratory tract bleeds, gastrointestinal bleed, urinary tract bleed, and anaemia from acute or chronic bleeding.
Cuschieri et al 2014		Gastrointestinal bleed defined as haematochezia, melena, hematemesis or coffee ground vomitus as documented by healthcare provider using ICD-9 codes
Buresly et al 2005		Bleeding was defined as any hospital admission that occurred after the index AMI hospitalization with a principal or new secondary diagnosis of intracranial haemorrhage, gastrointestinal tract haemorrhage, aortic aneurysm dissection or rupture, intraocular haemorrhage, haematuria, hemoptysis, epistaxis, or haemorrhage not otherwise specified.
Voss et al 2016		Defined as procedure related, gastrointestinal, respiratory, intracranial, intraocular, urogenital, and other, based on a list of ICD-10 codes.
Chamberlain et al 2016		Defined as intracranial haemorrhage, gastrointestinal tract haemorrhage, haemarthrosis, hemopericardium, haematuria, hemoptysis, epistaxis, or haemorrhage not otherwise specified or acute post-hemorrhagic anaemia
Atar et al 2006		Gastrointestinal bleeding was defined as blood loss from the GI tract of new onset, hematemesis, or melena with no other apparent source of acute blood loss. Severe or life-threatening GI bleeding was defined as bleeding associated with severe hemodynamic compromise. Major bleeding was defined as $\geq 15\%$ absolute reduction in haematocrit or need for a transfusion
Bergen et al 1994		Major bleeding defined as intracranial or fatal bleed or bleeding that led to admission for hospital treatment.
Blin et al 2017		Defined as hospitalization with a primary diagnosis of bleeding using relevant ICD-10 codes.
Brinkert et al 2017		Defined by ICD-10 codes as hospitalization with major bleeding.

Effron et al 2018		Defined as rehospitalisation with bleeding or receipt of blood transfusion.
Kazi et al 2015		Defined as major spontaneous bleeding
Ko et al 2010		Defined as hospitalisation with bleeding post discharge
Erta et al 2018		Defined as physician-confirmed bleeding events.
Garay et al 2016		Defined as bleeding that required hospitalization, transfusion of more than 1 blood pack, or suspension of antithrombotic treatment
Garay et al 2018		Defined as intracranial bleeding or any other bleeding leading to hospitalization and/or red blood cell transfusion.

Table 3: Incidence of bleeding stratified by ACS presentation in observational studies and RCTs

Study design	Primary Author	Length of Follow-up	Bleeding Criteria	No with bleed	Crude Incidence of Bleeding per 100 persons and 95% CI
STEMI					
Observational Studies	Amin et al 2016	6 Months	BARC 1-5	1023	24.8 (23.5, 26.1) *
	Amin et al 2013	12 months	BARC 1	628	39.8 (37.4, 42.2) *
	Lattuca et al 2016	12 Months	BARC 1-3	132	35.8 (31.1, 40.8) *
	Bacquelin et al 2015	12 months	BARC 2-5	79	7.85 (6.35, 9.68) *
	Kassaian et al 2015	12 months	GUSTO mild, moderate, severe.	6	1.43 (0.65, 3.07) *
	Graipe et al 2015	12 months	Intracranial bleed	169	0.27 (0.23, 0.31) *
	Caneiro et al 2018	455 days (Median)	BARC 2 - 3	195	12.0 (10.5, 13.7) *
	Wong et al 2006	21 months	CURE major/life threatening	8	6.9 (3.54, 13.0) *
	Erta et al 2018	24 months	Physician-confirmed bleeding event	12	2.38 (1.37, 4.12) *
RCTs	Han et al 2015	12 months	BARC 1-5	42	2.37 (1.76, 3.19) *
	Mrdovic et al 2013	12 months	TIMI major/minor	25	1.29 (0.87, 1.89) *
	Nikolsky et al 2015	3 years	HORIZON major	63	2.15 (1.68, 2.74) *
NSTEMI/UA					
Observational Studies	Cuisset et al 2009	1 month	TIMI major/minor	16	2.68 (1.66, 4.31) *
	Amin et al 2016	6 Months	BARC 1-5	1044	24.2 (23.0, 25.5) *
	Amin et al 2013	12 months	BARC 1	707	35.7 (33.6, 37.8) *
	Palmerini et al 2014	12 months	BARC (any)	41	3.91 (2.89, 5.26) *
	Kassaian et al 2015	12 months	GUSTO mild, moderate, severe.	17	1.39 (0.87, 2.22) *
	Graipe et al 2015	12 months	Intracranial bleed	410	0.34 (0.31, 0.37) *
	Caneiro et al 2018	455 days (Median)	BARC 2 - 3	305	11.7 (10.5, 13.0) *
	Wong et al 2006	21 months	CURE major/life threatening	7	6.48 (3.17, 12.8) *

	Erta et al 2018	24 months	Physician-confirmed bleeding event	9	1.78 (0.94, 3.35) *
RCTs	Jolly et al 2009	8 months	CURE major	28	1.07 (0.74, 1.54) *
	Savonitto et al 2012	12 months	BARC 2, 3a & 3b	3	0.96 (0.33, 2.78) *
	Mahaffey et al 2013	502 days (Median)	TIMI major/minor	236	2.12 (1.87, 2.41) *

* Incidence and associated 95% CI calculated from data within study, **CI**: Confidence Interval, **TIMI**: Thrombolysis In Myocardial Infarction, **BARC**: Bleeding Academic Research Consortium, **GUSTO**: Global Use of Strategies To open Occluded arteries, **CURE**: Clopidogrel in Unstable angina to prevent Recurrent Events, **HORIZON**: Harmonising Outcomes with Revascularisation and stents.

Table 4: Incidence of bleeding in observational studies stratified by discharge antithrombotic therapy and duration

Primary Author	Length of Follow-up	Bleeding definition	Discharge Antithrombotic combination	Duration	No with bleed	Crude Incidence of Bleeding per 100 persons and 95% CI
SAPT						
Fosbol et al 2012	12 months	Bleed leading to hospitalisation	Aspirin only	NR	223	10.1 (8.89, 11.4) *
Tsai et al 2010	12 months	Gastrointestinal bleed	Aspirin + PPI	NR	148	12.3 (10.6, 14.3) *
			Clopidogrel only		34	2.57 (1.84, 3.56) *
			Clopidogrel + PPI		91	8.65 (7.1, 10.5) *
Sorensen et al 2009	476.5 days (Mean)	Fatal and non-fatal bleed	Aspirin only	NR	709	3.78 (3.52, 4.06) *
			Clopidogrel only		158	2.18 (1.87, 2.54) *
Wong et al 2006	21 months	CURE major/life threatening	Aspirin	NR	7	6.48 (3.17, 12.8) *
Erta et al 2018	24 months	Physician-confirmed bleeding event	SAPT	NR	1	0.88 (0.16, 4.80) *
DAPT						
Cuisset et al 2009	1 month	TIMI major/minor	Aspirin (75 mg) + clopidogrel (75 mg)	1 month	16	2.68 (1.66, 4.31) *
Amin et al 2016	6 Months	BARC 1-5	Aspirin + thienopyridine	NR	2246	24.2 (23.3, 25.1) *
Lattuca et al 2016	12 Months	BARC 1-3	Aspirin + prasugrel	NR	68	33.3 (27.2, 40.1) *
			Aspirin + clopidogrel		64	38.8 (31.7, 46.4) *
Bacquelin et al 2015	12 Months	BARC 2-5	Aspirin + thienopyridine	NR	70	7.32 (5.84, 9.15) *
Palmerini et al 2014	12 months	BARC (any)	Aspirin (160 mg) + clopidogrel (75 mg)	12 months	41	3.91 (2.89, 5.26) *
Fosbol et al 2012	12 months	Bleed leading to hospitalisation	Aspirin + clopidogrel		336	11.8 (10.7, 13.1) *
Effron et al 2018	12 months	Bleed leading to hospitalisation or transfusion	Aspirin + prasugrel	NR	393	3.07 (2.79, 3.38) *
			Aspirin + ticagrelor		99	3.31 (2.73, 4.01) *

Carrero et al 2016	12 months	Major bleed	Aspirin + clopidogrel	12months	333	0.92 (0.83, 1.03) *
Sra et al 2016	15 months	BARC 1-5	Aspirin + thienopyridine	NR	353	20.1 (18.3, 22.0) *
Caneiro et al 2018	15 months	BARC 2 - 3	Aspirin + thienopyridine	NR	428	11.9 (10.9, 13.0) *
Sorensen et al 2009	476.5 days (Mean)	Fatal and non-fatal bleed	Aspirin + clopidogrel	NR	421	3.45 (3.14, 3.78) *
Cuschieri et al 2014	1.7 years (Mean)	Gastrointestinal bleed	Aspirin + clopidogrel	NR	107	3.33 (2.76, 4.00) *
Wong et al 2006	21 months	CURE major/life threatening	Aspirin + clopidogrel		8	6.9 (3.5, 13.0) *
Voss et al 2016	1.94 years (mean)	Other	Aspirin + clopidogrel	NR	206	5.88 (5.15, 6.71) *
Brener et al 2016	24 months	TIMI, GUSTO and AUCITY Major bleed	Aspirin + clopidogrel	NR	430	5.17 (4.71, 5.66) *
Erta et al 2018	24 months	Physician-confirmed bleeding event	DAPT	NR	20	2.20 (1.43, 3.37) *
Anticoagulant						
Braun et al 2014	3 months	BARC 2-5	Ticagrelor + warfarin	3 months	10	9.43 (5.21, 16.5) *
			Aspirin + clopidogrel + warfarin		16	10.2 (6.37, 15.9) *
Bacquelin et al 2015	12 Months	BARC 2-5	Aspirin + thienopyridine + vitamin k	NR	6	18.8 (8.89, 35.3) *
Fosbol et al 2012	12 months	Bleed leading to hospitalisation	Warfarin only	NR	78	13.9 (11.2, 16.9) *
			Warfarin + aspirin		182	14.3 (12.5, 16.4) *
			Warfarin + aspirin + clopidogrel		109	14.9 (12.5, 17.7) *
Sra et al 2016	15 months	BARC 1-5	Aspirin + thienopyridine + OAC	NR	87	31.4 (26.2, 37.1) *
Caneiro et al 2018	15 months	BARC 2 - 3	Anticoagulant	NR	101	21.1 (17.7, 25.0) *
Sorensen et al 2009	476.5 days (Mean)	Fatal and non-fatal bleed	Vitamin k only	NR	60	4.55 (3.55, 5.81) *
			Aspirin + vitamin k		133	17.8 (15.2, 20.7) *
			Clopidogrel + vitamin k		30	15.3 (10.9, 21.0) *

			Aspirin + clopidogrel + vitamin k		61	19.4 (15.4, 24.1) *
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* Incidence and associated 95% CI calculated from data within study, **CI**: Confidence Interval, **SD**: Standard deviation, **SAPT**: Single antiplatelet, **DAPT**: Dual antiplatelet, **PPI**: Proton Pump Inhibitor, **OAC**: Oral Anticoagulation, **NR**; not reported, **CURE**: Clopidogrel in Unstable angina to prevent Recurrent Events, **TIMI**: Thrombolysis In Myocardial Infarction, **BARC**: Bleeding Academic Research Consortium, **GUSTO**: Global Use of Strategies To open Occluded arteries, **ACUITY**; acute catheterisation and urgent intervention triage strategy.

Table 5: Incidence of bleeding in randomised controlled trials stratified by discharge antithrombotic therapy and duration

Primary Author	Length of Follow-up	Bleeding definition	Discharge Antithrombotic combination	Duration	No with bleed	Crude Incidence of Bleeding per 100 persons and 95% CI
SAPT						
Yeh et al 2015	18 months	BARC 2-5	Aspirin + placebo	18 months	35	1.98 (1.42, 2.74) *
Bonaca et al 2015	33 months	TIMI major	Aspirin (75 -150 mg) + placebo	33 months	72	1.03 (0.82, 1.29) *
DAPT						
Carrabba et al 2016	12 months	BARC 1-3	Aspirin (100 mg) + prasugrel (10 mg)	12 months	45	47.4 (37.6, 57.3) *
			Aspirin (100 mg) + prasugrel (5 mg)		31	31.6 (23.3, 41.4) *
Cuisset et al 2017	12 months	BARC \geq 2	Aspirin + clopidogrel	NR	30	9.49 (6.73, 13.2) *
			Aspirin + prasugrel/ticagrelor		76	23.9 (19.5, 28.9) *
Han et al 2015	12 months	BARC 1-5	Aspirin + clopidogrel	NR	47	2.33 (1.76, 3.08) *
Savonitto et al 2012	12 months	BARC 2, 3a & 3b	Aspirin + thienopyridine	NR	3	0.96 (0.33, 2.78) *
Kohli et al 2014	450 days	TIMI major/minor	Aspirin (\leq 150 mg) + clopidogrel (75 mg)	NR	103	2.75 (2.27, 3.32) *
			Aspirin (\geq 150 mg) + clopidogrel (75 mg)		70	2.80 (2.22, 3.52) *
			Aspirin (\leq 150 mg) + prasugrel (75 mg)		137	3.60 (3.05, 4.24) *
			Aspirin (\geq 150 mg) + prasugrel (75 mg)		97	3.82 (3.14, 4.64) *
Yeh et al 2015	18 months	BARC 2-5	Aspirin + thienopyridine	18 months	76	4.21 (3.38, 5.24) *

Costa et al 2015	6 months	BARC 2-5	Aspirin (80 - 160 mg) + clopidogrel (75 mg)	6 months	30	4.09 (2.88, 5.78) *
	24 months		Aspirin (80 - 160 mg) + clopidogrel (75 mg)	24 months	52	7.10 (5.46, 9.20) *
Bonaca et al 2015	33 months	TIMI major	Aspirin + ticagrelor (60 mg)	33 months	170	2.44 (2.11, 2.83) *
			Aspirin + ticagrelor (90 mg)		193	2.76 (2.40, 3.17) *
Nikolsky et al 2015	3 years	HORIZON major	Aspirin + thienopyridine	NR	63	2.15 (1.68, 2.74) *
Anticoagulant						
Bergen et al 1994	37 months	Major bleed	Nicoumalone or phenprocoumon	37 months	73	4.29 (3.43, 5.37) *

* Incidence and associated 95% CI calculated from data within study, **CI**: Confidence Interval, **SD**: Standard deviation, **SAPT**: Single antiplatelet, **DAPT**: Dual antiplatelet, **PPI**: Proton Pump Inhibitor, **NR**: not reported, **BARC**: Bleeding Academic Research Consortium, **TIMI**: Thrombolysis In Myocardial Infarction, **HORIZON**: Harmonising Outcomes with Revascularisation and stents.

Table 6: Incidence of major, minor and nuisance bleeding events in observational studies and RCTs that used any of the formal bleeding definitions stratified by length of follow-up.

Observational Studies				Randomised Controlled Trials			
Length of follow-up	Study ID	Bleeding definition used	Incidence of bleeds per 100 persons and 95% CI	Length of follow-up	Study ID	Bleeding definition used	Incidence of bleeds per 100 persons and 95% CI
Major bleeds				Major bleeds			
30 days	Cuisset et al 2009	TIMI major	0.84 (0.36, 1.95) *	6 months	Yusuf et al 2006	OASIS-5 major	1.84 (1.66, 2.03) *
3 months	Braun et al 2014	BARC 3 - 5	5.32 (3.20, 8.74) *	8 months	Jolly et al 2009	CURE major	1.07 (0.74, 1.54) *
12 months	Lattuca et al 2016	BARC 3	3.25 (1.87, 5.60) *	12 months	Carrabba et al 2016	BARC 3	2.07 (0.81, 5.21) *
	Raposeiras et al 2018	BARC 3 - 5	1.53 (1.21, 1.94) *		Han et al 2015	BARC 3 - 5	0.10 (0.03, 0.36) *
	Bacquelin et al 2015	BARC 3 - 5	1.29 (0.76, 2.20) *		Cuisset et al 2017	TIMI major	0.79 (0.34, 1.83) *
	Yetgin et al 2018	TIMI major	0.94 (0.63, 1.41) *		Mrdovic et al 2013	TIMI major	0.15 (0.05, 0.45) *
	Kassaian et al 2015	GUSTO severe	0.67 (0.37, 1.20) *		15 months	Mahaffey et al 2013	TIMI major
15 months	Caneiro et al 2018	BARC 3	3.33 (2.83, 3.92) *	Kohli et al 2014		TIMI major	1.20 (1.02, 1.40) *
	Sra et al 2016	BARC 3 - 5	1.03 (0.68, 1.57) *	> 15 months	Costa et al 2015	BARC 3 - 5	2.73 (2.01, 3.70) *
> 15 months	Brener et al 2016	TIMI/GUSTO/ACUITY	5.17 (4.71, 5.66) *		Yeh et al 2015	BARC 3 - 5	1.48 (1.13, 1.93) *
	Wong et al 2006	CURE major	3.13 (1.52, 6.31) *		Bonaca et al 2015	TIMI major	1.41 (1.26, 1.58) *
					Nikolsky et al 2015	Horizon major	2.15 (1.68, 2.74) *
Minor bleeds				Minor bleeds			
30 days	Cuisset et al 2009	TIMI minor	1.84 (1.03, 3.27) *	12 months	Carrabba et al 2016	BARC 2	6.22 (3.59, 10.6) *

3 months	Braun et al 2014	BARC 2	4.56 (2.63, 7.80) *			Han et al 2015	BARC 2	0.35 (0.17, 0.71) *
12 months	Lattuca et al 2016	BARC 2	10.6 (7.83, 14.1) *			Cuisset et al 2017	TIMI minor	5.52 (4.00, 7.58) *
	Bacquelin et al 2015	BARC 2	6.56 (5.19, 8.26) *			Mrdovic et al 2013	TIMI minor	0.36 (0.17, 0.74) *
	Kassaian et al 2015	GUSTO mild	0.73 (0.42, 12.7) *		15 months	Kohli et al 2014	TIMI minor	2.03 (1.80, 2.29) *
15 months	Caneiro et al 2018	BARC 2	8.49 (7.69, 9.37) *			Mahaffey et al 2013	TIMI minor	0.76 (0.61, 0.93) *
	Sra et al 2016	BARC 2	4.67 (3.78, 5.76) *			Costa et al 2015	BARC 2	2.87 (2.13, 3.85) *
> 15 months	Wong et al 2006	CURE minor	3.57 (1.82, 6.89) *		> 15 months	Yeh et al 2015	BARC 2	1.71 (1.33, 2.18) *
						Bonaca et al 2015	TIMI minor	0.66 (0.56, 0.78) *
Nuisance bleeds				Nuisance bleeds				
6 months	Amin et al 2016	BARC 1	9.14 (8.57, 9.74) *			Carrabba et al 2016	BARC 1	31.9 (24.9, 37.9) *
12 months	Amin et al 2013	BARC 1	37.5 (35.9, 39.1) *		12 months	Han et al 2015	BARC 1	1.88 (1.37, 2.57) *
	Lattuca et al 2016	BARC 1	21.9 (18.0, 26.5) *			Cuisset et al 2017	TIMI minimal	10.4 (8.27, 13.0) *
15 months	Sra et al 2016	BARC 1	19.2 (17.4, 21.1) *			Mrdovic et al 2013	TIMI minimal	0.77 (0.47, 1.27) *

*Incidence and associated 95% CI calculated from data within study, **CI**: Confidence Interval, **TIMI**: Thrombolysis In Myocardial Infarction, **BARC**: Bleeding Academic Research Consortium, **GUSTO**: Global Use of Strategies To open Occluded arteries, **ACUITY**; acute catheterisation and urgent intervention triage strategy. **CURE**: Clopidogrel in Unstable angina to prevent Recurrent Events, **HORIZON**: Harmonising Outcomes with Revascularisation and stents, **OASIS-5**: the fifth Organization to Assess Strategies In acute ischemic Syndromes

Table 7: Incidence of different types of bleeding events stratified by length of follow-up.

Type of bleed	Study design	Length of follow-up	Study ID	Incidence of bleeds per 100 persons and 95% CI
Bruising	<i>Observational studies</i>	<i>12 months</i>	Bacquelin et al 2015	1.49 (0.91, 2.45) *
			Amin et al 2013	20.1 (18.8, 21.4) *
			Lattuca et al 2016	22.5 (18.5, 27.0) *
Gastrointestinal	<i>Observational studies</i>	<i>30 days</i>	Cuisset et al 2009	0.50 (0.17, 1.47) *
		<i>3 months</i>	Braun et al 2014	4.56 (2.63, 7.80) *
		<i>12 months</i>	Yetgin et al 2018	0.25 (0.11, 0.53) *
			Garay et al 2016	1.16 (0.72, 1.88) *
			Bacquelin et al 2015	1.79 (1.13, 2.81) *
		Lattuca et al 2016	4.88 (3.11, 7.58) *	
		Tsai et al 2010	7.63 (6.80, 8.54) *	
		<i>15 months</i>	Sorensen et al 2009	1.88 (1.75, 2.02) *
		<i>> 15 months</i>	Cuschieri et al 2014	3.33 (2.76, 4.00) *
	Voss et al 2016		3.65 (3.08, 4.33) *	
	<i>RCTs</i>	<i>12 months</i>	Atar et al 2006	1.02 (0.84, 1.24) *
			Mrdovic et al 2013	0.67 (0.39, 1.14) *
Kohli et al 2014			0.66 (0.53, 0.82) *	
Respiratory	<i>Observational studies</i>	<i>12 months</i>	Bacquelin et al 2015	0.50 (0.21, 1.16) *
			Garay et al 2016	1.09 (0.66, 1.79) *
		<i>15 months</i>	Sorensen et al 2009	0.54 (0.47, 0.62) *
		<i>> 15 months</i>	Voss et al 2016	0.91 (0.65, 1.29) *
	<i>RCTs</i>	<i>12 months</i>	Mrdovic et al 2013	0.51 (0.28, 0.95) *
Genito-Urinary	<i>Observational studies</i>	<i>12 months</i>	Bacquelin et al 2015	0.50 (0.21, 1.16) *
			Garay et al 2016	1.75 (1.18, 2.58) *
			Lattuca et al 2016	2.17 (1.10, 4.22) *
		<i>15 months</i>	Sorensen et al 2009	0.70 (0.62, 0.78) *

		> 15 months	Voss et al 2016	0.80 (0.55, 1.15) *
	<i>RCTs</i>	12 months	Mrdovic et al 2013	0.15 (0.05, 0.45) *
Intracranial	<i>Observational studies</i>	30 days	Cuisset et al 2009	0.34 (0.09, 1.21) *
		3 months	Braun et al 2014	0.76 (0.21, 2.73) *
		12 months	Yetgin et al 2018	0.25 (0.11, 0.53) *
			Garay et al 2016	0.36 (0.16, 0.85) *
			Bacquelin et al 2015	0.40 (0.15, 10.2) *
			Graipe et al 2015	0.31 (0.29, 0.34) *
			Wang et al 2015	0.20 (0.18, 0.22) *
		15 months	Sorensen et al 2009	0.46 (0.40, 0.53) *
		> 15 months	Voss et al 2016	0.43 (0.26, 0.70) *
<i>RCTs</i>	> 15 months	Bonaca et al 2015	0.45 (0.37, 0.55) *	
Intraocular	<i>Observational studies</i>	12 months	Lattuca et al 2016	0.27 (0.05, 1.52) *
		> 15 months	Voss et al 2016	0.20 (0.10, 0.41) *
Unspecified†	<i>Observational studies</i>	3 months	Braun et al 2014	1.90 (0.81, 4.37) *
		12 months	Yetgin et al 2018	0.25 (0.11, 0.53) *
			Bacquelin et al 2015	0.60 (0.27, 1.30) *
			Lattuca et al 2016	0.81 (0.28, 2.36) *
> 15 months	Voss et al 2016	0.20 (0.10, 0.41) *		

* Incidence and associated 95% CI calculated from data within study, †Bleeds from unspecified location, CI: Confidence, RCT: Randomised controlled trial

Table 8: Summary of the assessment of the strength of evidence for each secondary outcome

Outcome and length of follow-up post hospital discharge	Strength of Evidence
All-cause mortality (within 1 to 3.5 years)	SOE = Low (5 observational studies and 1 RCT; 142,945 participants) Low level of evidence due to moderate risk of bias, and residual confounding.
MACE (within 476 days)	SOE = Insufficient (1 observational study; 40812 participants) Insufficient, because evidence was derived from only one study which is at high risk of bias, as such conclusion cannot be drawn.
Re-hospitalisation (within 12 months)	SOE = Insufficient (1 observational study; 3560 participants) Insufficient, because evidence was derived from only one study which is at high risk of bias, as such conclusion cannot be drawn.

SOE: strength of evidence, MACE: major adverse cardiovascular event, RCT: randomised controlled trial.