Supplementary Table 1: Age, gender and treatment received in included studies

Study ID	Mean age	% male	Therapies received
Amlani 2010 [32]	62	80	Aspirin 99%, clopidogrel 99%, enoxaparin 17%, unfractionated heparin 84%, bivalirudin 21%, abciximab 27%, intra-aortic balloon pump 4%.
Ariza-Sole 2013 [33]	63	68	Aspirin 97%, clopidogrel 92%, glycoprotein IIb/IIIa 49%, unfractionated heparin 87%, low molecular weight heparin 15%, coumadin 9%, fondaparinux 8%, thrombolysis 47%, primary PCI 46%, coronary artery bypass graft 6%, intra-aortic balloon 10%.
Barthelemey 2012 [20]	63	77	In-hospital aspirin 95%, clopidogrel 95%, 900 mg loading dose 31%, unfractionated heparin 38%, low molecular weight heparin 67%, beta-blockers 82%, angiotensin converting enzyme inhibitor/angiotensin receptor blocker 83%, statins 95%, thrombolysis 7%, abciximab 78%.
Bertrand 2009 [34]	60	78	Clopidogrel ≥12 hours 90%, low molecular weight heparin prior 24%, glycoprotein IIb/IIIa inhibitor 5% and all patient received a bolus of abciximab.
Boden 2012 [35]	61	76	All received abciximab, periprocedural heparin and loading doses of aspirin and clopidogrel.
Budaj 2009 [36]	67	62	Patients randomized to fondaparinux 2.5 g once daily or subcutaneous enoxaparin 1 mg/kg twice daily. Aspirin 97%, clopidogrel 67%, intravenous unfractionated heparin 14%, angiogram or PCI 71%, coronary artery bypass graft 14%.
Cayla 2011 [18]	65	72	Patients randomized to immediate or next working day PCI. Aspirin 99%, mean clopidogrel 661 mg, abciximab 61%, unfractionated heparin on 4%, both unfractionated and low molecular weight heparin 68%.
Cayla 2012 [37]	Not reported.	Not reported.	Patients randomized to IV bolus of enoxaparin 0.5 mg/kg or unfractionated heparin before PCI. High dose clopidogrel 63%, glycoprotein IIb/IIIa inhibitors 80%.
Chhatriwalla 2013 [14]	35% age ≥75 years.	48	Patients matched for therapies received (ie heparin, glycoprotein IIb/IIIa, bivalirudin, PCI, etc).
Correia 2012 [38]	68	46	Aspirin 98%, clopidogrel 93%, low molecular weight heparin 89%, unfractionated heparin 3%, glycoprotein IIb/IIIa inhibitor 6%, coronary angiography 77%, coronary angioplasty 37%.
Eikelboom 2006 [28]	64	62	OASIS-2 was randomized trial of intravenous unfractionated heparin or hirudin. CURE was randomized trial of clopidogrel or placebo.
Fuchs 2009 [21]	61	72	Aspirin 94%, clopidogrel 38%.

Gitt 2010 [39]	64	84	Fibrinolysis 24%, primary /rescue PCI 66%, GP IIa/IIIb 32%, aspirin 96%, clopidogrel 86%, low molecular weight heparin 42%, unfractionated heparin 76%.
Giugliano 2010 [8]	Median age 59 to 68 depending on bleeding group.	77	Patients randomized to enoxaparin or unfractionated heparin after starting fibrinolysis.
Hermanides 2010 [22]	61	77	All patients received 300-500 mg aspirin IV and 5000-10,000 IU IV heparin. Clopidogrel was given since 1999. Glycoprotein IIb/IIIa inhibitor 59%.
Kaul 2013 [40]	50	68	In-hospital aspirin 97%, in-hospital unfractionated heparin 46%.
Kikkert 2013 [41]	62	70	Intra-aortic balloon pump 12%, load with clopidogrel 96%, glycoprotein IIb/IIIa inhibitor 28%.
Kinnaird 2003 [11]	64	70	Glycoprotein IIb/IIIa 5%.
Le May 2011 [42]	Not reported.	Not reported.	Standard therapy before catheterization included aspirin 160 mg, clopidogrel 600 mg and unfractionated heparin 60 U/kg (max 4000). Bivalirudin 29%, glycoprotein IIb/IIIa inhibitors 36%.
Lee 2009 [43]	Not reported.	Not reported.	Not reported.
Lemesle 2009 [27]	84	49	All patients received aspirin loading dose of 325 mg and clopidogrel loading dose of ≥300 mg and a 75 mg maintenance dose.
Lindsey 2009 [44]	65	68	Heparin alone 19%, heparin and glycoprotein IIb/IIIa inhibitor 34%, direct thrombin inhibitor 35%, therapeutic clopidogrel load 40%.
Lopes 2012 [45]	78	51	Aspirin 95%, anticoagulant 80%, heparin 87%, IV heparin 49%, low molecular weight heparin 44%, beta-blockers 90%, clopidogrel 56%, glycoprotein IIb/IIIa inhibitors 40%.
Matic 2010 [46]	59	75	Not reported.
Matic 2011 [47]	Not reported.	Not reported.	Not reported.
Matic 2012 [48]	Not reported.	Not reported.	Not reported.
Mehran 2011 [2]	62	74	Randomized trials of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors.
Montalescot 2009 [25]	64	75	Randomized trial of 0.50 mg/kg or 0.75 mg/kg enoxaparin or unfractionated heparin. All patients treated with aspirin 75 to 500 mg/day and thienopyridines. Approximately 40% had glycoprotein IIb/IIIa inhibitors in each arm.
Mrdovic 2013 [49]	59	73	Aspirin 99%, clopidogrel 99%, heparin 8%, tirofiban 42%, beta-blockers 86%, statin 93%, angiotensin converting enzyme inhibitors 71%, nitrates 37%, digitalis 3%, diuretics 15%, inotropes

			7%, antiarrhythmics 9%.
Musumeci 2012 [50]	64	76	All patients treated with aspirin 100 mg and clopidogrel 75 mg daily. Glycoprotein IIb/IIIa inhibitor 32%.
Ndrepepa 2010 [17]	68	76	All patients received 325 to 500 mg aspirin and 600 mg loading dose of clopidogrel and were randomized to receive 0.75 mg/kg bolus of bivalirudin followed by an infusion at 1.75 mg/kg/hour for duration of procedure or 140 U/kg bolus of unfractionated heparin followed by placebo infusion.
Ndrepepa 2012 [23]	67	76	Pooled study of 6 randomized trials. Four were placebo control trials with abciximab and clopidogrel 600 mg. One was bivalirudin versus unfractionated heparin and the other was 100 U unfractionated heparin versus 140 U unfractionated heparin. All patients received 325-500 mg aspirin.
Pierre 2010 [51]	67	52	All patients had aspirin and clopidogrel. Unfractionated heparin 97%, low molecular weight heparin 24%, thrombolytics 12% and bivalirudin 2%.
Pilgrim 2010 [52]	63	76	Glycoprotein IIb/IIIa inhibitor 25%.
Polanska 2011 [53]	60	73	All patients had 300 mg aspirin and 300 mg clopidogrel. Abciximab in 47% of patients.
Poludasu 2011 [54]	Not reported.	Not reported.	Bivalirudin was the primary antithrombotic agent.
Rao 2005 [24]	Median age 64-70 depending on bleeding group.	66	GUSTO IIb patients randomized to heparin or hirudin. PURSUIT patients randomized to eptifibatide or placebo. PARAGON A and B randomized patients to intravenous lamifaiban or placebo.
Rossini 2010 [55]	Not reported.	Not reported.	Patient discharged on dual antiplatelet therapy.
Urban 2011 [56]	62	75	Aspirin 86%, ticlopidine 2%, clopidogrel 60%. Glycoprotein IIb/IIIa inhibitor 16%, bivalirudin 3%.
Valente 2011 [19]	Median age reported for bleeding and non-bleeding groups but not mean age.	74	Before PCI, a 70 U/kg IV bolus of unfractionated heparin was administered (maximum 5000 U) followed by additional weight adjusted doses. All patients given aspirin 500 mg and 300-600 mg clopidogrel.
Yoon 2013 [57]	Not reported.	Not reported.	Not reported.
Zheng 2009 [58]	65	62	Aspirin 300 mg.

Supplementary Table 2: Major bleeding definitions

Bleeding criteria	Definition
ACUITY/HORIZON-AMI	Major bleeding defined as intracranial or intraocular haemorrhage; bleeding at the access site, with a hematoma that was 5 cm or larger or that required intervention; a decrease in haemoglobin level of 4 g per decilitre or more without an overt bleeding source or 3 g per decilitre or more with an overt bleeding source; re-operation for bleeding or blood transfusion.
BARC	Type 0: no bleeding Type 1: bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalization, or treatment by a healthcare professional; may include episodes leading to self-discontinuation of medical therapy by the patient without consulting a healthcare professional. Type 2: any overt, actionable sign of haemorrhage (eg, more bleeding than would be expected for a clinical circumstance, including bleeding found by imaging alone) that does not fit the criteria for type 3, 4, or 5 but does meet at least on the following criteria: (1) requiring nonsurgical, medical intervention by a healthcare professional, (2) leading to hospitalization of increase level of care, or (3) prompting evaluation. Type 3 Type 3a: Overt bleeding plus haemoglobin drop of 3 to <5 g/dL. Any transfusion with overt bleeding. Type 3b: Overt bleeding plus haemoglobin drop ≥5 g/dL. Cardiac tamponade. Bleeding requiring surgical intervention for control (excluding dental/nasal/skin/haemorrhoid). Bleeding requiring intravenous vasoactive agents. Type 3c: Intracranial haemorrhage (does not include microbleeds or hemorrhagic transformation, dose include intraspinal). Subcategories confirmed by autopsy or imaging or lumbar puncture. Intraocular bleed compromising vision. Type 4: CABG-related bleeding, perioperative intracranial bleeding within 48 hours and reoperation after closure of sternotomy for the purposes of controlling bleeding.
CRUSADE	Major bleeding defined by intracranial haemorrhage, documented retroperitoneal bleed, haematocrit drop ≥12%, any red blood cell transfusion when baseline haematocrit was ≥28%, or any red blood cell transfusion when baseline haematocrit was <28% with witnessed bleed.
GUSTO	Severe or life-threatening bleeding defined as intracerebral or if they resulted in substantial hemodynamic compromise requiring treatment.

REPLACE-2	Major bleeding defined as intracranial, intraocular, or retroperitoneal haemorrhage; clinically overt blood loss resulting in a decrease in haemoglobin of more than 3 g per decilitre; any decrease in haemoglobin of more than 4 g per decilitre; or transfusion of 2 or more units of packed red cells or whole blood.
STEEPLE	Major bleeding defined by fatal bleeding, retroperitoneal, intracranial or intraocular bleeding, bleeding that causes hemodynamic compromised requiring specific treatment, bleeding that requires intervention (surgical or endoscopic) or decompression of a closed space to stop or control the event, clinically overt bleeding, requiring any transfusion of ≥1 unit of packed red cells or whole blood, clinically overt bleeding, causing a decrease in haemoglobin of ≥3 g/dl or if haemoglobin level not available, a decrease of haematocrit of ≥10%.
TIMI	Major defined as intracranial or clinically significant overt signs of haemorrhage associated with a greater than 50 g/L decrease in haemoglobin level or an absolute decrease in haematocrit of greater than 15% (when haemoglobin levels not available). The diagnosis of intracranial bleeding required confirmation by computed tomography or magnetic resonance imaging of the head.

Supplementary Table 3: Quality assessment of included studies

Study ID	Ascertainment of bleeding	Ascertainment of outcome	Lost to follow up	Use of adjustments
Amlani 2010 [32]	Data collected by trained coordinator.	Data collected by trained coordinator. Patients and families were contacted by telephone at 30 days to determine mortality data.	Not reported.	TIMI STEMI risk score.
Ariza-Sole 2013 [33]	Data collected by trained physician using standardized case report form. Quality of data collection was assessed by checking source documentation in random samples.	Data collected by trained physician using standardized case report form. Quality of data collection was assessed by checking source documentation in random samples.	24 patients on chronic anticoagulation and 93 with missing data were excluded.	None.
Barthelemey 2012 [20]	Medical records and all available source documents.	Telephone call, medical consultation or re-hospitalization medical reports.	None.	None.
Bertrand 2009 [34]	End points adjudicated by clinical events committee blinded to study group.	End points adjudicated by clinical events committee blinded to study group.	None.	None (RCT data).
Boden 2012 [35]	Not reported.	Not reported.	Not reported.	None.
Budaj 2009 [36]	Safety outcomes adjudicated in a blinded fashion by a committee.	Safety outcomes adjudicated in a blinded fashion by a committee.	Not reported.	Adjusted for baseline characteristics (age, gender, diabetes, hypertension, myocardial infarction, stroke, systolic/diastolic blood pressure, Killip Class 3/4, haemoglobin, creatinine, creatinine clearance, aspirin, thienopyridines, intravenous unfractionated heparin, angiogram or PCI,

				coronary artery bypass graft and bleeding propensity.
Cayla 2011 [18]	End points adjudicated by clinical events committee unaware of treatment assignment of patients.	End points adjudicated by clinical events committee unaware of treatment assignment of patients.	None.	None (RCT data).
Cayla 2012 [37]	All clinical events were adjudicated by an independent clinical events committee unaware of treatment assignment of patients.	All clinical events were adjudicated by an independent clinical events committee unaware of treatment assignment of patients.	29 participants withdrew consent, 6 lost to follow up.	None (RCT data).
Chhatriwalla 2013 [14]	Data from CathPCI Registry which has an automated system validation, random auditing of participating centres and education and training of site managers are performed to promote quality assurance.	Data from CathPCI Registry which has an automated system validation, random auditing of participating centres and education and training of site managers are performed to promote quality assurance.	Propensity matching used.	Multivariate and propensity matching was used considering hospital characteristics, bleeding risk, mortality risk and patient demographics.
Correia 2012 [38]	Unclear.	In-hospital deaths were prospectively recorded.	Not reported.	Adjusted for propensity score with clinical characteristics (age, heart rate, troponin, severe coronary artery disease and treatment).
Eikelboom 2006 [28]	Not reported likely prospective collection in trial.	Not reported likely prospective collection in trial.	Not reported.	Adjusted for baseline characteristics (age, gender, diabetes, myocardial infarction, stroke, PCI, coronary artery bypass graft, heart failure, heart rate, systolic/diastolic blood pressure, creatinine, ST-segment changes, aspirin/clopidogrel,

				glycoprotein IIb/IIIa inhibitors, unfractionated heparin, low molecular weight heparin, hirudin, oral anticoagulation, fibrinolysis, coronary angiogram, PCI/stent/atherectomy, coronary artery bypass graft, intra-aortic balloon pump) and bleeding propensity.
Fuchs 2009 [21]	Hospital charts with standardized questionnaire completed by telephone or outpatient clinic. Data from hospitals and affiliated hospitals' databases were accessed.	Hospital charts with standardized questionnaire completed by telephone or outpatient clinic. Data from hospitals and affiliated hospitals' databases were accessed.	None.	None.
Gitt 2010 [39]	Unclear (Abstract only).	Unclear (Abstract only).	Not reported.	Baseline characteristics and treatment (age, gender, prior myocardial infarction, PCI, bypass, stroke, diabetes, renal failure, fibrinolysis, primary/rescue PCI, glycoprotein IIb/IIIa, aspirin, clopidogrel, low molecular weight heparin, unfractionated heparin)
Giugliano 2010 [8]	The bleeding severity and location were adjudicated by a blinded, independent clinical endpoint committee.	The cause of death was adjudicated by a blinded, independent clinical endpoint committee.	Not reported.	Baseline characteristics (Age, gender, race, weight, TIMI risk score >3, hypertension, hyperlipidaemia, current smoker, diabetes mellitus, prior MI,

				angina pectoris, anterior MI, left bundle branch block, heart rate, systolic blood pressure, Killip class ≥II, time from symptom to fibrinolytic), medications (aspirin or NSAID, unfractionated heparin, low molecular weight heparin, fibrinolysis type), in-hospital procedures, in-hospital events.
Hermanides 2010 [22]	Information was obtained from the patient's general physician or by direct telephone interview with the patient.	Information was obtained from the patient's general physician or by direct telephone interview with the patient.	204 patients were missing.	Age, gender and significantly different variables (anterior location, Killip ≥2 on admission, multivessel disease, initial treatment).
Kaul 2013 [40]	Bleeding events were determined by programmed algorithm or blinded adjudication.	All events, except death were adjudicated by independent clinical events committee.	Not reported.	Adjusted for radial versus femoral access, presence of obstructive coronary artery disease, treatment (medical management or PCI or CABG), and adverse events (MI, congestive heart failure or shock, and recurrent ischemia).
Kikkert 2013 [41]	Follow-up clinical outcomes were obtained by reviewing inpatient and outpatient charts.	Follow-up clinical outcomes were obtained by reviewing inpatient and outpatient charts.	Missing data for 19 out of 40 variables which were imputed.	Previously identified baseline predictors of 4-year mortality.
Kinnaird 2003 [11]	All data were confirmed by independent hospital chart	All data were confirmed by independent hospital chart	431 patients who underwent coronary artery	Age category, weight, gender, history of diabetes or myocardial

	review.	review.	bypass grafting and PCI during the same admission were excluded.	infarction, chronic renal insufficiency, hypertension, or coronary artery bypass surgery, admission diagnosis of unstable angina or myocardial infarction, use of glycoprotein IIb/IIIa, clotting time, use of any intra-aortic balloon pump, procedural hypotension, procedural time and saphenous vein graft intervention.
Le May 2011 [42]	Unclear. (Abstract only)	Unclear. (Abstract only)	Unclear. (Abstract only)	None.
Lee 2009 [43]	Occurrence of bleeding was prospectively evaluated.	Occurrence of cardiac death and myocardial infarction were prospectively evaluated.	Unclear. (Abstract only)	Patients' clinical, procedural and angiographic characteristics.
Lemesle 2009 [27]	Data managed by dedicated data coordinating centre. Data centre staff blinded to treatment objectives, abstracted demographic, clinical, and procedural information by hospital chart review. They also recorded hospital outcomes. Data centre staff obtained postdischarge follow-up information through telephone contact with the patient or referring physician. Source documentation of all reported clinical events was obtained and their nature adjudicated by independent	Data managed by dedicated data coordinating centre. Data centre staff blinded to treatment objectives, abstracted demographic, clinical, and procedural information by hospital chart review. They also recorded hospital outcomes. Data centre staff obtained postdischarge follow-up information through telephone contact with the patient or referring physician. Source documentation of all reported clinical events was obtained and their nature adjudicated by independent	Not reported.	Multivariate and propensity score analysis (unclear which variables included).

	physicians not involved in the study.	physicians not involved in the study.		
Lindsey 2009 [44]	Data regarding patient characteristics, presentation, treatment and outcomes collected prospectively on standardized care report forms and submitted to data coordinating centre.	Patients were contacted by telephone at 6 and 12 months after index PCI. Events ascertained at follow-up included death, stent thrombosis, revascularization and MI. All outcomes adjudicated by 2 cardiologist blinded to treatment factors and subsequent outcomes.	468 excluded because they had STEMI. 621 excluded because baseline CK-MB ≥1 x ULN, 537 excluded missing ≥1 candidate variables.	Sociodemographic factors, covariates, clinical factors, angiographic and procedural factors, periprocedural myocardial infarction.
Lopes 2012 [45]	Retrospective chart review for detailed process of care and in-hospital outcomes and standardized data collection form.	Retrospective chart review for detailed process of care and in-hospital outcomes and standardized data collection form. All-cause mortality was available through CMS linkage.	30,419 excluded STEMI patients due to missing variables. 566 excluded whose CMS data discrepancies. 10,950 excluded who died in hospital, were transferred out, underwent coronary artery bypass graft and with inconsistent bleeding data. 1,449 subsequent admission for patient with multiple admissions.	Age, systolic blood pressure on admission, serum creatinine, signs of heart failure, prior heart failure, weight, heart rate on admission, initial haematocrit, prior stroke, diabetes, initial troponin ratio, prior peripheral artery disease, sex, race, family history of coronary artery disease, hypertension, current/recent smoker, dyslipidaemia, prior myocardial infarction, prior PCI, prior CABG and ECG finding and plus 10 additional interactions, discharge anti-platelet medications, cardiac catheterization and revascularization with PCI.

Matic 2010 [46]	Unclear. (Abstract only).	Unclear. (Abstract only).	Unclear. (Abstract only).	Multivariate but unclear adjustments (Abstract only).
Matic 2011 [47]	Unclear. (Abstract only).	Unclear. (Abstract only).	Unclear. (Abstract only).	Multivariate but unclear adjustments (Abstract only).
Matic 2012 [48]	Unclear. (Abstract only).	Unclear. (Abstract only).	Not reported.	Multivariate with demographic and clinical characteristics of patients. (Abstract only).
Mehran 2011 [2]	Bleeding was adjudicated by a blinded clinical events committee.	Endpoints were adjudicated by a blinded clinical events committee.	7 excluded as they experienced a TIMI major bleed before their index PCI.	Adjusted for baseline predictors (unclear which).
Montalescot 2009 [25]	Not reported likely prospectively recorded within 48 hours of admission.	Data on all-cause mortality at 1 year were gathered by telephone or by visiting participating sites.	892 patients were lost to follow up beyond day 30.	Age, sex, obesity, diabetes, hypertension, smoking habits, hypercholesterolemia, renal insufficiency, peripheral arterial disease, family history of coronary heart disease, unstable angina or MI within the previous 7 days, low haemoglobin at entry, PCI characteristics, previous medication within 1 week before enrolment, concomitant medications, anticoagulant crossover during index hospitalization, country, nonfata MI or urgent target vessel revascularization, creatinine kinase and major

				bleeding up to 48 hours.
Mrdovic 2013 [49]	Follow up data were obtained by scheduled telephone interviews and outpatient visits.	Follow up data were obtained by scheduled telephone interviews and outpatient visits.	No lost to follow up at 30 days and at 1 year 51 were lost to follow up.	None.
Musumeci 2012 [50]	Follow up by telephone contact or outpatient clinical visits and whenever adverse cardiac events and/or major bleeding events occurred, patients charts were reviewed.	Follow up by telephone contact or outpatient clinical visits and whenever adverse cardiac events and/or major bleeding events occurred, patients charts were reviewed.	14 patients were lost to follow-up or excluded from analysis.	Age, body mass index, male gender, left ventricular ejection fraction, use of glycoprotein IIb/IIIa inhibitors, femoral access, atrial fibrillation, prior stroke, prior myocardial infarction, prior PCI, prior coronary artery bypass graft, hypertension, diabetes mellitus, aspirin at discharge, proton pump inhibitor at discharge, oral anticoagulants at discharge, clopidogrel at discharge, ticlopidine at discharge, baseline anaemia prior to PCI and platelets at admission.
Ndrepepa 2010 [17]	Follow up with telephone interview and visits up to 12 months.	Follow up with telephone interview and visits up to 12 months with information about death obtained from hospital records, death certificates or telephone contact with relatives of the patient or attending physician.	48 patients did not complete 1 year follow up.	None.
Ndrepepa 2012 [23]	For every case with bleeding, source documentation was available and it	All patients were seen by their physician or interviewed by telephone	Not reported.	Adjusted models used but not clear what was in the models.

	was reevaluated. All patients were seen by their physician or interviewed by telephone at 30 days, 6 months and 1 year after the procedure. Local research coordinators collected the data and forwarded them to the data coordinating centre. The quality of data collection was assessed by checking source documentation in random samples.	at 30 days, 6 months and 1 year after the procedure. Local research coordinators collected the data and forwarded them to the data coordinating centre. The quality of data collection was assessed by checking source documentation in random samples.		
Pierre 2010 [51]	Unclear.	Unclear.	Not reported.	None.
Pilgrim 2010 [52]	Unclear. (Abstract only).	Unclear. (Abstract only).	242 patients had missing laboratory parameters and 62 patients had non-PCI related bleeding during the index hospitalization and were excluded.	None.
Polanska 2011 [53]	Unclear. (Abstract only).	Unclear. (Abstract only).	Not reported.	Unclear. (Abstract only).
Poludasu 2011 [54]	Unclear. (Abstract only).	Unclear. (Abstract only).	Not reported.	Adjusted for significant univariate predictors of mortality (unclear which predictors).
Rao 2005 [24]	Bleeding events were not adjudicated by were determined by the investigator.	All death and MI events were adjudicated by an independent blinded events committee.	Not reported.	Patient characteristics, presenting signs and symptoms and treatments, including blood transfusion. In addition, coronary artery bypass grafting and use of procedures was considered in analysis.

Rossini 2010 [55]	Unclear. (Abstract only).	Unclear. (Abstract only).	Not reported.	Multivariate analysis to estimate odds ratios but unclear which variables in model.
Urban 2011 [56]	Patients were followed up to 360 days by telephone communication or office visit by contacts with primary physicians or referring cardiologists. Data were collected electronically and transferred to an independent data management organization. The accuracy of data collection was monitored by an independent organization. Accuracy of baseline data was 96% and adverse events were 93.2%.	Patients were followed up to 360 days by telephone communication or office visit by contacts with primary physicians or referring cardiologists. Data were collected electronically and transferred to an independent data management organization. The accuracy of data collection was monitored by an independent organization. Accuracy of baseline data was 96% and adverse events were 93.2%.	253 were de-registered after online data queries and on-site monitoring of source data.	Multivariate models with independent correlates of death (index procedure ST, insulin-dependent diabetes, age, Charlson comorbidity index, total number of lesions, glycoprotein IIb/IIIa inhibitor, hyperlipidaemia at baseline, bypass graft target lesions).
Valente 2011 [19]	Data prospectively collected onto dedicated database.	Data prospectively collected onto dedicated database.	Not reported.	Age, weight, gender, admission systolic blood pressure, admission heart rate, Killip class, myocardial infarction location, left ventricular ejection fraction, PCI failure, eGFR, admission haemoglobin, intra-aortic balloon pump, ultrafiltration and mechanical ventilation.
Yoon 2013 [57]	Unclear. (Abstract).	Unclear. (Abstract).	Not reported. (Abstract).	Adjusted hazards ratios reported but unclear covariates in model.
Zheng 2009 [58]	Follow up with phone calls or visits.	Follow up with phone calls or visits.	Not reported.	Adjusted hazards ratios reported but unclear covariates in model.

Supplementary Table 4: Risk of MACE and mortality with and without major bleeding

Study ID	Crude MACE (major bleeding vs no major bleeding)	Risk of MACE with bleeding.	Crude mortality (major bleeding vs no major bleeding)	Risk of mortality with bleeding.
Amlani 2010 [32]	NA.	NA.	30 day: 13/66 (20%) vs 42/568 (7%).	30 day: primary PCI OR 3.1 (1.5-6.1).
Ariza-Sole 2013 [33]	NA.	NA.	HR 6.91 (3.72-12.82) at mean of 344 days.	NA.
Barthelemey 2012 [20]	NA.	NA.	In-hospital bleed and 1 year: TIMI major: 8/17 (47%) vs 29/654 (4%). GUSTO severe: 5/10 (50%) vs 32/661 (5%). STEEPLE major: 18/73 (25%) vs 19/598 (3%).	NA.
Bertrand 2009 [34]	30 day: 7/19 vs 44/1329. 6 month: 8/19 vs 108/1329. 1 year: 10/19 vs 164/1329.	1 year: HR 2.41 (1.42-4.35).	30 day: 2/19 (11%) vs 0/1329 (0%). 6 month: 2/19 (11%) vs 2/1329 (0.1%). 1 year: 3/19 (16%) vs 8/1329 (0.6%).	NA.
Boden 2012 [35]	NA.	NA.	1 year: 19/203 (9.2%) vs 19/762 (2.5%).	NA.
Budaj 2009 [36]	30 day: 168/771 vs 1160/18851. 6 month: 276/937 vs 1940/18665.	30 day Death/MI/Stroke (MACE): HR 3.99 (3.30-4.82). 6 month Death/MI/Stroke (MACE): HR 2.97 (2.55-3.45).	30 day: 65/771 (8%) vs 517/18851 (3%). 6 month: 132/937 (14%) vs 985/18665 (5%).	30 day: HR 3.46 (2.6-4.60). 6 month: HR 3.11 (2.55-3.79).
Cayla 2011 [18]	30 day: 5/19 vs 37/333.	NA.	30 day: 5/19 (26%) vs 2/333 (0.6%).	30 day: OR: 50.3 (10.1-248.7).
Cayla 2012 [37]	NA.	NA.	NA.	30 day: OR 6.5 (2.8-14.6).
Chhatriwalla 2013 [14]	NA.	NA.	In-hospital: 3194/57246 (5.6%) vs 18978/3329442 (0.6%).	In-hospital propensity matched cohort: 5.26% (2950/56078) vs 1.87% (4195/224312).
Correia 2012 [38]	NA.	NA.	In-hospital: 6/29 (21%) vs 25/455 (5%)	In-hospital morality: adjusted OR 3.34 (1.2-9.5).

Eikelboom 2006 [28]	30 day MI: 46/436 vs 1375/33710. 6 months: 55/553 vs 1965/32125. 30 day stroke: 12/469 vs 187/33677. 6 months: 17/641 vs 388/33285.	30 day: MI HR 4.44 (3.16-6.24). Between 30 day and 6 month: MI HR 1.14 (0.59-2.21). 30-day: stroke HR 6.46 (3.54-11.79). Between 30 day and 6 month: stroke HR 1.30 (0.48-3.54).	30 day: 60/470 (13%) vs 833/33676 (25%). 6 months: 86/560 (15%) vs 1781/32634 (5%).	30 day: HR 5.37 (3.97 - 7.26). Between 30 day and 6 month: HR 1.54 (1.01-2.36).
Fuchs 2009 [21]	30 day: 8/27 (31%) vs 100/804 (12.4%). 6 month: 11/27 (41%) vs 177/804 (22%).	NA.	30 day: 7/27(26%) vs 61/804 (7.6%). 6 month: 10/27 (37%) vs 80/804 (10%).	NA.
Gitt 2010 [39]	NA.	NA.	In-hospital: 40/281 (14.2%) vs 600/8451 (7.1%).	In-hospital mortality: adjusted OR 2.18 95% CI 1.45-3.29.
Giugliano 2010 [8]	NA.	NA.	30 day: 37.6% (116/309) vs 6.6% (1295/19628). 1 year: 42.9% (133/309) vs 9.9% (1943/19628).	30 day mortality: adjusted HR 2.9 (2.4-3.6). Day 31 to 365 mortality: adjusted HR 2.1 (1.2-3.6).
Hermanides 2010 [22]	30 day MI: 3/80 (3.8%) vs 122/4371 (2.8%). 1 year MI:3/80 (3.8%) vs 214/4371 (4.9%). 30 day stroke: 5/80 (6.3%) vs 13/4371 (0.3%). 1 year stroke: 6/80 (7.5%) vs 35/4371 (0.8%).	NA.	30 day: 22/80 (27.5%) vs 140/4371 (3.2%). 1 year: 26/80 (32.5%) vs 254/4371 (5.8%).	1 year mortality: adjusted HR 3.5 (2.3-5.4).
Kaul 2013 [40]	NA.	NA.	NA.	Adjusted risk for men OR 5.8 (3.9-8.6), women OR 1.5 (0.8-2.9). Combined OR 4.01 (2.86-5.61).
Kikkert 2013 [41]	NA.	NA.	NA.	Adjusted risk up to 30 days: HR 2.74 (1.65-4.55).
Kinnaird 2003 [11]	In-hospital: 39/588 (6.6%) vs 198/8992 (2.2%).	NA.	In-hospital: 45/588 (7.5%) vs 162/8992 (1.8%).	NA.
Le May 2011	NA.	NA.	6 month: 22/91 (24%) vs 134/1941	6 month mortality OR 4.47 (2.21-9.03).

[42]			(7%).	
Lee 2009 [43]	MACE: unadjusted HR 5.18 (3.26-8.24).	MACE: adjusted HR 3.19 (1.89-5.37).	Cardiac death: unadjusted HR 6.16 (3.60-10.54)	Cardiac death: adjusted HR 3.36 (1.79-6.31).
Lemesle 2009 [27]	NA.	NA.	NA.	6-month mortality: adjusted HR 3.0 (2-4.6).
Lindsey 2009 [44]	NA.	NA.	1-year: 28/180 vs 139/5781.	1-year mortality: adjusted HR 6.85 (3.37-13.89).
Lopes 2012 [45]	NA.	NA.	30-day: 57/1625 (16%) vs 138/11465 (2%). 1 year: 253/1625 (4%) vs 825/11465 (1%). 3 years: 551/1625 (34%) vs 2155/11465 (19%).	30-day mortality: HR 2.00 (1.44-2.77), 1 year mortality: HR 1.48 (1.25-1.75), 3 year mortality: HR 1.23 (1.07-1.42), >3 years HR 1.25 (1.01-1.54).
Matic 2010 [46]	NA.	NA.	In-hospital: 3/32 (9%) vs 21/738 (3%).	NA.
Matic 2011 [47]	30-day: 18/88 vs 83/1154.	NA.	30-days: 10/88 (11%) vs 66/1154 (6%).	NA.
Matic 2012 [48]	NA.	NA.	1 year: BARC 3a 15/55 (27%) vs 189/1558 (12%). BARC 3b 10/23 (43%) vs 189/1558 (12%).	Adjusted OR BARC 3a 2.37 (1.16-4.84), BARC 3b 4.62 (1.75-12.16).
Mehran 2011 [2]	NA.	NA.	NA.	1-year mortality: HR 4.2 (3.1-5.7). Day 0-1 HR 6.8 (3.5-13.1), day 2-7 HR 6.0 (3.1-11.6), day 8-30 HR 8.7 (4.8-15.9), day 31+ HR 2.6 (1.6-4.1).
Montalescot 2009 [25]	NA.	NA.	NA.	1-year mortality: HR 3.0 (1.1-8.4).
Mrdovic 2013 [49]	NA.	NA.	30 days: OR 14.90 (6.21-35.76), 1 year: OR 9.47 (4.13-21.70).	NA.
Musumeci 2012 [50]	Bleeding 30 days: 20/52 (38.9%) vs 194/1385 (14.0%).	NA.	Bleeding 30 days: 9/52 (16.7%) vs 71/1385 (5.1%). Bleeding 12	NA.

	Bleeding 12 months: 24/52 (46.5%) vs 184/1385 (13.3%). Bleeding at follow up: 25/52 (48.1%) vs 181/1385 (13.1%).		months: 12/52 (23.3%) vs 65/1385 (4.7%). Bleeding at follow up: 13/52 (25%) vs 62/1385 (4.5%).	
Ndrepepa 2010 [17]	NA.	NA.	1-year: 13/174 vs 53/4015.	1 year mortality: OR 6.04 (3.22-11.29).
Ndrepepa 2012 [23]	NA.	NA.	BARC ≥2: 30 days 22/679 (3%) vs 32/11780 (0.3%). 30 day to 1 year 41/679 (6%) vs 245/11780 (2%). 1 year 63/679 (9%) vs 277/11780 (2%). BARC ≥3 30 days 20/500 (4%) vs 34/11959 (0.3%). 30 day to 1 year 31/500 (6%) vs 255/11959 (2%). 1 year 51/500 (10%) vs 289/11959 (2%). TIMI major: 30 day 7/111 (6%) vs 47/12348 (0.4%). 30 day to 1 year: 6/111 (5%) vs 280/12348 (2%). 1 year 13/111 (12%) vs 327/12348 (3%).	BARC ≥2: 30 days mortality: HR 12.1 95% CI 7.1-20.9. 1 year mortality: HR 4.2 95% CI 3.2-5.5. BARC ≥3 30 days mortality: HR 14.4 95% CI 8.3-25.1. 1 year mortality: HR 4.5 95% CI 3.3-6.1. TIMI major: 30 days mortality: HR 17.2 95% CI 7.8-38. 1 year mortality: HR 4.9 95% CI 2.8-8.5. REPLACE-2 major: 30 day mortality: HR 13.3 95% CI 7.7-23.7. 1 year mortaltiy: HR 4.5 95% CI 3.3-6.0. REPLACE-2 (major): HR 3.14 (2.30-4.29). BARC class ≥2: HR 2.72 (2.03-3.63). BARC class ≥3: HR3.19 (2.34-4.35).
Pierre 2010 [51]	NA.	NA.	30 day: 6/48 (13%) vs 59/3799 (2%). 9 month: 9/48 (19%) vs 108/3799 (3%).	NA.
Pilgrim 2010 [52]	NA.	NA.	In-hospital: 5/34 (15%) vs 0/347 (0%)	NA.
Polanska 2011 [53]	NA.	NA.	In-hospital: 9/40 (23%) vs 36/1024 (4%). 1 year: 10/40 (25%) vs 43/1024 (4%).	1 year: HR 5.98 (2.78-12.82).
Poludasu 2011	NA.	NA.	NA.	2.3 year: adjusted HR 1.4 (1.04-1.8).

[54]				
Rao 2005 [24]	NA.	Adjusted HR for death/MI: moderate 3.3 (2.9-3.7), severe 5.6 (4.6-6.8).	NA.	Adjusted HR for 30-day death: moderate 2.7 (2.3-3.4), severe 10.6 (8.3-13.6). 6-month death: moderate 2.1 (1.8-3.4), severe 7.5 (6.1-9.3).
Rossini 2010 [55]	1 year: 27/57 (47.3%) vs 163/1301 (12.5%).	NA.	1 year: 13/57 (23.6%) vs 49/1301 (3.8%).	NA.
Urban 2011 [56]	NA.	NA.	NA.	360 day mortality: HR 6.0 (3.3-10.8).
Valente 2011 [19]	NA.	NA.	TIMI major: 18/88 (20%) vs 27/903 (3%). ACUITY major 19/170 (11.2%) vs 26/821 (3.2%).	NA.
Yoon 2013 [57]	2 year: 44/234 vs 641/5932.	2 year MACE: 1.50 (1.10-2.05).	NA.	NA.
Zheng 2009 [58]	In-hospital: 5/27 (18.5%) vs 22/385 (5.7%). 1 year: 10/27 (37%) vs 55/385 (14.3%).	1 year MACE: 2.79 (2.21-5.90).	NA.	NA.

Supplementary Figure 1: Flow diagram of study selection