

Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes (Review)

Bosch X, Loma-Osorio P, Marrugat J



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ABSTRACT

Background

During percutaneous coronary intervention (PCI), and in non-ST segment elevation acute coronary syndromes (NSTEMACS), the risk of acute vessel occlusion by thrombosis is high. Glycoprotein (GP) IIb/IIIa blockers inhibit platelet aggregation and may prevent mortality and myocardial infarction (MI).

Objectives

To assess the efficacy and safety of GP IIb/IIIa blockers when administered during PCI, and as initial medical treatment in patients with NSTEMACS.

Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) on *The Cochrane Library* (Issue 2 2006), MEDLINE (1966 to June 2006), and EMBASE (1980 to April 2006). Reference list of articles, and relevant conference proceedings were checked. No language restrictions were applied.

Selection criteria

Randomised controlled trials (RCTs) comparing intravenous GP IIb/IIIa blockers with placebo were sought.

Data collection and analysis

2713 publications were screened separately by two reviewers who assessed trial quality and extracted data.

Main results

A total of 38 RCTs with 58,495 patients were included in the review. During PCI, GP IIb/IIIa blockers decreased mortality at 30 days (OR 0.74, 95% CI 0.58 to 0.94) but not at 6 months (OR 0.87, 95% CI 0.73 to 1.03). Death or MI was decreased both at 30 days (OR 0.67, 95% CI 0.61 to 0.74), and at 6 months (OR 0.71, 95% CI 0.62 to 0.82), although severe bleeding was slightly increased (OR 1.38, 95% CI 1.19 to 1.60; absolute risk increase 8.6 per 1000). The results were homogeneous for every endpoint according to the clinical condition of the patients that were studied, but were more marked when a stent was implanted and less marked for patients pre-treated with clopidogrel. As initial medical treatment of NSTEMACS, GP IIb/IIIa blockers did not decrease mortality at 30 days (OR 0.92, 95% CI 0.81 to 1.04) or at 6 months (OR 1.01, 95% CI 0.88 to 1.16). However, death or MI was decreased at 30 days (OR 0.92, 95% CI 0.86 to 0.99) and at 6 months (OR 0.88, 95% CI 0.81 to 0.96), although severe bleeding was slightly increased (OR 1.27, 95% CI 1.12 to 1.44, absolute risk increase 1.2 per 1000).

Authors' conclusions

In patients submitted to PCI, intravenous GP IIb/IIIa blockers reduce the risk of death at 30 days and markedly that of death or MI at 30 days and 6 months at a price of a moderate increase in the risk of severe bleeding. These effects were homogeneous for patients with or without an acute coronary syndrome but seem to decrease when patients are pre-treated with clopidogrel. In contrast, when

administered as initial medical treatment in patients with NSTEMI, these agents do not reduce mortality although they slightly reduce the risk of death or MI.

PLAIN LANGUAGE SUMMARY

During the last two decades, doctors have been looking for the best treatment to prevent clots in the coronary arteries of patients with heart disease. This review summarises the results of 38 studies which used a potent new class of antiplatelet drugs - glycoprotein IIb/IIIa blockers. This treatment was tested in two different conditions: in patients undergoing percutaneous coronary intervention (PCI) procedures (coronary angioplasty with or without stenting), and as the initial treatment of patients with acute coronary syndromes (unstable angina and non-ST segment elevation acute myocardial infarction).

Overall, the use of these drugs markedly reduced the risk of death or myocardial infarction at 30 days and 6 months in patients submitted to percutaneous coronary angioplasty or stent implantation. The results were similar for stable and for unstable patients with coronary artery disease, but there was comparatively less benefit for patients previously treated with clopidogrel, a new oral antiplatelet drug. Glycoprotein IIb/IIIa blockers only slightly reduced the risk of death or myocardial infarction when administered as initial medical treatment in patients with unstable angina or non-ST-elevation myocardial infarction. The benefits of glycoprotein IIb/IIIa blockers need to be balanced against the slightly increased risk of severe bleeding.

BACKGROUND

The mechanism of percutaneous coronary intervention (PCI) using balloon angioplasty with or without stent implantation, includes profound vessel injury and plaque rupture (Falk 1995), all of which triggers an immediate activation of the coagulation cascade, and adhesion, activation, and aggregation of platelets (ESC 2007; ACC/AHA 2007). Pre-treatment with aspirin and heparin has been shown to reduce the risk of acute vessel occlusion and of myocardial infarction in these patients, and is currently the standard antithrombotic treatment (ATC 2002). When a stent is implanted, the addition of ticlopidine or clopidogrel before the procedure and during follow-up to these two drugs has also shown to be of benefit (PCI-CURE) and is the standard antithrombotic treatment for this procedure (ESC 2007; ACC/AHA 2007).

The pathophysiology of non-ST segment elevation acute coronary syndrome (NSTEMI), i.e. unstable angina and non-ST segment elevation myocardial infarction (ESC/ACC 2000), involves the rupture or erosion of an atherosclerotic coronary plaque (Falk 1995), activation of the coagulation cascade, and adhesion, activation, and platelet aggregation. Treatment with aspirin and heparin has been shown to reduce the risk of cardiac events by 50% in patients with this syndrome (ATC 2002; Mehta 2003), and is currently the standard antithrombotic treatment (ESC 2007; ACC/AHA 2007). The addition of clopidogrel to aspirin and heparin has also shown to decrease the risk of vascular events in these patients (CURE) and its administration as initial medical treatment is now recommended in current clinical guidelines (ESC 2007; ACC/AHA 2007).

The glycoprotein IIb/IIIa (GP IIb/IIIa) integrin present in platelets mediates the final common pathway in platelet aggregation,

spawning the development of GP IIb/IIIa receptor blockers (Phillips 1988). In patients with NSTEMI, and also in patients submitted to PCI, intravenous GP IIb/IIIa blockade induces strong platelet inhibition (Gurbel 2005) and may prevent mural and intraluminal thrombus formation that can result in the prevention of both acute coronary occlusion and of embolisation of plaque thrombi to the distal microvasculature (Boersma 1999). However, because GP IIb/IIIa receptor blockers induce profound platelet inhibition, the risk of bleeding complications is increased, particularly when administered concomitantly with high-dose heparin treatment (Quinn 2002). Thus, safety is an important issue in the management of patients with these drugs, especially during PCI.

OBJECTIVES

The aim of this systematic review was to assess the effectiveness of GP IIb/IIIa blockers given in addition to standard medical treatment in:

1. Patients undergoing PCI.
2. As the initial medical treatment of patients with NSTEMI.

The first indication relates to a procedure rather than a health problem. The second relates to a clinical condition that includes a wide range of patient groups.

The standard medical treatment considered was aspirin and heparin in percutaneous transluminal coronary balloon angioplasty; aspirin, heparin and ticlopidine or clopidogrel in stent implantation; and aspirin and heparin in patients with NSTEMI.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We sought to identify all randomised controlled clinical trials, with or without blinding, studying intravenous GP IIb/IIIa blockers in patients submitted to PCI either with percutaneous transluminal coronary balloon angioplasty alone, or with stent placement; and in patients with NSTEMI treated with GP IIb/IIIa antagonists as the initial medical management, in which at least one of the pre-defined primary outcomes was measured.

We did not consider for this review trials performed in patients with ST-segment elevation acute myocardial infarction treated with thrombolytics or with facilitated or rescue PCI after thrombolytic treatment. We also did not consider trials on oral GP IIb/IIIa blockers since their clinical research has been stopped because their administration has been associated with increased mortality. Finally, we did not consider for this review trials in which the timing of the GP IIb/IIIa blockers administration was analysed (i.e. comparing pre-hospital administration vs. hospital administration or administration in the emergency room vs. in the catheterisation laboratory).

Types of participants

The following type of participants were considered for each of the two type of studies that we considered in this review:

1. Studies that randomised adult (18 years and older) male and female patients with or without an acute coronary syndrome submitted to PCI.

These studies were performed in stable or unstable coronary patients undergoing elective or urgent PCI with or without stent implantation. In all the studies performed during elective PCI, randomisation was performed when the exact coronary anatomy was known and inclusion criteria required the presence of one or more > 70% stenosis in a coronary segment amenable to PCI. Most of the studies also excluded patients with renal dysfunction and those at risk of bleeding.

2. Studies that included adult patients with NSTEMI in which GP IIb/IIIa antagonists were administered at the time of hospital admission as part of the initial medical management.

These studies were performed in patients with a recent (< 24 h) chest pain and with ischaemic changes in the admission ECG (ST-segment depression > 0.5 mm or transient elevation > 1 mm, > 1mm T-wave inversion) or CK-MB elevation above the upper limits of normality in each participant institution.

All of the studies excluded patients with moderate to severe renal dysfunction and those at risk of bleeding.

Types of intervention

Intravenous GP IIb/IIIa blockers administered as a bolus followed by an infusion, at any dose, compared with a control group treated with usual care (aspirin, heparin and ticlopidine or clopidogrel)

and GP IIb/IIIa blocker placebo. Three parenterally administered GP IIb/IIIa blockers in PCI (abciximab, eptifibatid and tirofiban) and four in NSTEMI (abciximab, eptifibatid, lamifiban and tirofiban) have been tested.

The daily doses of aspirin ranged in the studies from 50 mg to 325 mg and those of heparin were typically aimed at maintaining an activated clotting time > 200 s or an activated partial thromboplastin time between 50 s and 85 s, or twice that of laboratory control. Only in one study (Schulman 1996) was aspirin not allowed in the treatment group but administered in the placebo group.

Some studies had arms of active treatment with lower heparin doses (EPILOG 1997) or no heparin at all (PARAGON A 1998; PRISM Plus 1998) and even a complete study in which no heparin was given in the active treatment group (PRISM 1998). All patients of these studies were included in the present update since a prior meta-analysis performed with individual patient data reported similar results by including or excluding those patients (Boersma 2002). Patients of the control groups of all studies received heparin.

Comparators

The direct comparator to the GP IIb/IIIa blockers was typically placebo in the two indications.

Types of outcome measures

Primary outcomes

- All-cause mortality at 30 days and 6 months.
- Death or non-fatal myocardial infarction at 30 days and 6 months.

The combined endpoint of death or myocardial infarction was chosen because most deaths (all-cause mortality) occurring early after a NSTEMI or a PCI procedure are due to myocardial infarction.

Secondary outcomes

- Need for an urgent revascularisation procedure at 30 days and 6 months for patients who underwent PCI.

Urgent revascularisation was chosen as a secondary endpoint since this is a consequence of refractory ischaemia and since its indication is often clinician-driven and, in consequence, not entirely objective. This endpoint was combined with death and myocardial infarction because all share the same pathophysiology (i.e. acute vessel occlusion) also as a secondary endpoint.

- Safety: severe bleeding at 30 days.

This was the most important safety outcome that was appropriately described in all studies. Wherever reported the Thrombolysis In Myocardial Infarction (TIMI) classification was used to define severe bleeding (Bovill 1991); the investigator's definition was used otherwise. In one study (PRISM Plus 1998) severe bleeding was not reported in the arm that was prematurely stopped; in this

case we only included this endpoint for the placebo and tirofiban plus heparin groups.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Heart Group methods used in reviews.

In the original review, the following databases were searched: MEDLINE (1966 to June 30th 2001), EMBASE (1980 to Nov 1999), and *The Cochrane Library* (Issue 1 2000). The search strategy used on MEDLINE can be found in additional Table 01. This was adapted for use on other databases.

In the present update and because records are not necessarily added to CENTRAL on *The Cochrane Library* in chronological order search results from the current search were deduplicated (in Reference Manager) against a repeated search using the original strategy in Issue 1, 2000. Search strategies were checked and revised for the update.

Searches were updated on the Cochrane Central Register of Controlled Trials (CENTRAL) on *The Cochrane Library* (Issue 2 2006), MEDLINE (2001-June 2006) and EMBASE (2000 - April 2006). All records were loaded into Reference Manager and duplicates removed.

The search strategy for CENTRAL is detailed below (Terms in capitals are exploded MeSH terms and those in lower case are textword searches). See additional Table 02 and Table 03 for strategies for MEDLINE and EMBASE.

- #1 PLATELET GLYCOPROTEIN GPIIB-IIIa COMPLEX
- #2 (glycoprotein near inhibit*)
- #3 (glycoprotein near block*)
- #4 (glycoprotein near antagonist*)
- #5 gpiib*
- #6 abciximab
- #7 sibrafiban
- #8 tirofiban
- #9 lamifiban
- #10 aggrastat
- #11 eptifibatide
- #12 xemilofiban
- #13 lotrafiban
- #14 orbofiban
- #15 fradafiban
- #16 (fibrinogen next receptor next antagonist*)
- #17 roxifiban
- #18 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10)
- #19 (#11 or #12 or #13 or #14 or #15 or #16 or #17)
- #20 (#18 or #19)
- #21 ANGIOPLASTY TRANSLUMINAL PERCUTANEOUS CORONARY

- #22 ptca
- #23 (coronary near angioplasty)
- #24 pci
- #25 (percutaneous next coronary next intervention*)
- #26 ANGINA UNSTABLE
- #27 angina
- #28 stent*
- #29 MYOCARDIAL INFARCTION
- #30 (myocardial next infarction)
- #31 (heart next infarction)
- #32 (coronary next syndrome*)
- #33 (non next st next segment)
- #34 (non next st next elevation)
- #35 (without next st next segment)
- #36 (#21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30)
- #37 (#31 or #32 or #33 or #34 or #35)
- #38 (#36 or #37)
- #39 (#20 and #38)

Handsearches were done (to October 2006) of abstracts from conferences published in *Circulation* (American Heart Association Annual Meeting), *Journal of the American College of Cardiology* (American College of Cardiology Annual Congress), *American Heart Journal*, *European Heart Journal* (European Society Annual Congress), *Revista Española de Cardiología*, and online at Theheart.org, TIML.org, and Clinicaltrials.org. The references sections of reviews addressing GP IIb/IIIa inhibitors were also examined.

No language restrictions were applied to the search. English, French and Spanish language papers were read by the authors. No articles in other languages were identified as being relevant. Only one published study could not be retrieved from the bibliographic search (Gasior 2003).

METHODS OF THE REVIEW

The search strategy was designed to be very sensitive and yielded 2713 documents. All references from relevant reviews and meta-analyses (see "other references") were screened for studies possibly missed by our search strategy, however no additional studies were identified.

Results were screened separately by two reviewers (XB and JM). A paper was rejected only when both reviewers agreed that the article did not meet the inclusion criteria. 117 articles were retrieved for further examination. Each manuscript was scored independently by the same two reviewers using a pre-designed in/out form. Each manuscript was scored 1 (definitely "in", i.e. the study met the inclusion criteria); 2 (maybe in, i.e. small sample size or difficult to determine the type of control or of diagnosis); or 3 (definitely out, i.e. definitely did not meet the inclusion criteria). All manuscripts

which scored at least one “1” or one “2” were analysed in common by both reviewers. The decision for definitive inclusion was taken after detailed reading of each paper and by discussion between reviewers. Thirty-eight studies were selected for inclusion, this included 30 studies on GP IIb/IIIa blockers in patients submitted to PCI and 8 studies in which these drugs were tested as initial medical treatment in patients with NSTEMI (see QUOROM statement, Figure 01).

A data extraction form based on the RevMan form (version 4.2.8) was designed for the review. Original reports of trial results were abstracted by the three reviewers (XB, PL-O and JM). Differences between reviewers’ abstraction results were resolved by discussion. Data on characteristics of participants, interventions, outcomes, trial quality characteristics (i.e. adequacy of randomization, degree of blinding and losses to follow up) were abstracted onto this form. In addition, data were collected on potential confounding factors including participants’ baseline risk and characteristics, trial duration, intensity of intervention (dosing and duration of treatment), type and dose of concomitant medication used and revascularization procedures including stent implantation.

Data synthesis

Heterogeneity of studies was assessed by clinical judgement according to differences in type of patients enrolled, study quality, interventions and outcome. Pooled odds ratio (OR) of the individual and combined endpoints were calculated using RevMan 4.2.8 program. Fixed-effect meta-analyses are presented unless a chi-squared test for heterogeneity was statistically significant at a 5% level, in which case random-effects meta-analyses are presented. Risk differences were calculated after pooling together the studies for each meta-analysis.

The effects of GP IIb/IIIa blockers was examined in each of the two different clinical indications (i.e. during PCI, and as initial medical treatment of NSTEMI). In the former indication, six separate subgroup analysis were performed according to the clinical condition of the patients (NSTEMI, primary PCI, stable patients), the technique used (balloon PCI alone, PCI with stent implantation), and the concomitant treatment received (pretreatment with a high dose of clopidogrel at least 2 hours before the procedure).

Only the effect of the intravenous route of administration (i.e. bolus plus infusion) was examined and compared with placebo/control with usual care (i.e. aspirin and heparin or aspirin, heparin and ticlopidine/clopidogrel). To prevent attrition bias, all patients allocated to a treatment were analysed in this group regardless of whether they received it or not (i.e. intention-to-treat analysis). Intention-to-treat data were used in the pooled analyses of this review as it was possible to obtain them from the publications of all the studies.

DESCRIPTION OF STUDIES

A total of 38 randomised controlled trials with 58,495 patients were included in the review.

1. Percutaneous coronary intervention

PCI was the condition studied in 30 studies with 28,144 patients. Twenty-nine of the 30 studies reported outcomes at 30 days while 19 studies reported outcomes at 6 months.

Among the 30 studies and according to the clinical condition of the patients, there were six studies in patients with NSTEMI, four in primary PCI in patients with ST-segment elevation myocardial infarction (STEMI), and eight in stable coronary patients; the other 12 studies were performed in a mixed population. According to the technique used, there were 10 studies performed during balloon PCI, and 17 during PCI with stent. Finally, and according to the concomitant treatment that was administered there were nine studies performed in patients pre-treated with clopidogrel more than 2 hours before the procedure.

All patients included in trials with stent implantation received heparin, aspirin and ticlopidine or clopidogrel during and after the procedure except for the ERASER 1999 study in which ticlopidine was left to the investigator’s discretion. No study was performed specifically in patients in which a drug-eluting stent was implanted, and in only one study (ISAR-REACT 2) a drug-eluting stent was used in 50% of the cases. Abciximab was used in 19 trials, tirofiban in six, and eptifibatid in four. The doses varied among studies.

2. Initial medical treatment of patients with non-ST segment elevation acute coronary syndromes

Eight studies with 30,351 patients concerned GP IIb/IIIa use as initial medical treatment in patients with NSTEMI. All these eight studies presented 30-day follow-up results and four that of 6 months. Abciximab was used in one study, eptifibatid and tirofiban in two, and lamifiban in three.

PRISM 1998 differed from the other trials in that the GP IIb/IIIa blocker was given without heparin. PRISM Plus 1998 also initially contained an arm with GP IIb/IIIa blocker without heparin. The PARAGON A 1998 study also included an arm without heparin.

Variability

The potential sources of heterogeneity among the studies may include the variability in patient characteristics. For all the studies the mean age ranged from 59 years to 70 years. The proportion of males ranged from 61% to 95%. Prior myocardial infarction, which was described in most studies, ranged from 10% to 67% (see characteristics of included studies table).

In the PCI analysis, five trials were performed in patients with STEMI. The frequency of this diagnosis was of 0% in 22 other studies and ranged from 3% to 41% in the other three trials. A specific analysis of those five trials has been performed. In patients with NSTEMI treated medically, the prevalence of unstable angina ranged from 43% to 86%, and that of non-ST-segment

elevation myocardial infarction ranged from 14% to 57%. Thirty-two to 80% of patients had ST-segment depression at enrollment. The proportion of patients that underwent PCI procedures during the in-hospital period ranged from 14% to 31%, and in 1.6% to 25% of cases PCI was performed during drug-infusion which was administered within 24 to 72 hours after enrollment.

Dosing

Where trials had intervention arms with varying doses of GP IIb/IIIa inhibitor drugs, data from such intervention arms were pooled. In the EPIC 1994 study, one intervention arm had GP IIb/IIIa blocker administered in a bolus alone, i.e. with no subsequent perfusion; the results of that arm were not included.

Endpoints

All studies describing endpoints occurring within follow-up periods shorter than 30 days (i.e. in-hospital, 7-day, etc.) were pooled with 30-day follow-up studies (ERASER 1999; Kereiakes 1996; Simoons 1994) due to the fact that most of adverse events occur within the first week after the event or the procedure. Also, one study (ADVANCE 2004) that only reported events at 6 months was also included in the 30-day follow-up analysis, and three studies (ISAR-REACT 2004; ISAR-REACT 2; ISAR-SMART-2 2004) that reported the 1-year follow-up alone were pooled with the 6-month follow-up analysis.

In some instances, urgent PCI procedures (secondary endpoint in the PCI analyses) occurred more than once in the same patient. When the number of patients with at least one urgent revascularisation procedure was considered to be the difference between the overall number of patients with death, myocardial infarction and urgent revascularisation from the number of patients with death or myocardial infarction alone were considered to be. In some instances, the nature of PCI during follow up was not specified to be urgent or not. In such cases, overall revascularisations were considered.

METHODOLOGICAL QUALITY

In general the methodological quality of the 38 selected randomised clinical trials was good. Patients and clinicians were adequately blinded to treatment in most of them. In Claeys 2005 and ISAR-2 2000 the treatment strategy precluded blinding of the used drugs. However, allocation was adequately concealed. Given the importance of its approach these studies were retained in our analyses. All studies followed more than 95% of patients at 30 days and more than 90% at 6 months.

The definition of primary and secondary outcomes varied among studies. However, it was possible to obtain or calculate the number of cases with the primary and secondary endpoints of this review in most studies. We chose to combine death or non-fatal myocardial infarction because most deaths (all cause mortality) occurring early after NSTEMI or PCI are due to myocardial infarction and both

events share the same pathophysiology, i.e. acute coronary vessel occlusion or distal embolization.

Myocardial infarction was part of the composite efficacy endpoint of all trials, but the applied myocardial infarction definition was different especially regarding the required level of increased levels of the MB fraction of creatine kinase. In all cases we applied the trial-specific definition of myocardial infarction.

The secondary endpoint 'major bleeding', was assessed by the Thrombolysis In Myocardial Infarction (TIMI) classification when described (bleeding was classified as major if it involved intracranial haemorrhage or cardiac tamponade or if it was associated with a decrease in haemoglobin concentration of more than 50 g/L regardless of whether or not a bleeding site had been identified (Bovill 1991). Otherwise, the 'major' bleeding described in each study was used. When no description of major bleeding existed at all, brain haemorrhages and need for transfusion were selected as 'major' bleeding.

RESULTS

1. GP IIb/IIIa blockers during percutaneous coronary intervention

Primary endpoints

Data from 29 trials with 27,642 patients (98% of patients included in this meta-analysis) were available on 30-day mortality and myocardial infarction, while data from 19 trials with 21,542 patients (77% of patients included in the overall review) were available on 6-month mortality or myocardial infarction.

Treatment with intravenous GP IIb/IIIa blockers was associated with a significant reduction in the odds of mortality at 30 days (OR 0.74, 95% CI 0.58 to 0.94, $P = 0.01$) with a corresponding absolute risk reduction (ARR) per 1000 treated patients over 30 days of 4.1 (95% CI 1.7 to 6.6). The results were similar for all the different subgroups that were considered according to the clinical condition of the patients, the technique used and the concomitant treatment that was administered (Table 04). However, at 6 months the initial benefit was no longer observed in the overall group (OR 0.87, 95% CI 0.73 to 1.03, $P = 0.11$) and only the subgroup of patients treated with stent implantation showed the same degree of benefit observed at 30 days.

These agents were also associated with a significant decrease in the odds of death or MI both at 30 days (OR 0.67, 95% CI 0.61 to 0.74, $P < 0.00001$), and at 6 months (OR 0.71, 95% CI 0.62 to 0.82, $P < 0.00001$). The results were homogeneous for most of the subgroup of patients considered in the review but was less marked for patients pre-treated with clopidogrel.

Secondary endpoints

Data on urgent revascularisation and the combined endpoint of death, myocardial infarction or urgent revascularisation at 30 days were available from 28 trials with 27,317 patients (97% of patients

included in the overall review), and from 18 trials with 18,750 patients (68% of patients included in the overall review) at 6 months. Treatment with intravenous GP IIb/IIIa blockers was associated with a reduction in the risk of urgent revascularisation at 30 days (OR 0.60, 95% CI 0.52 to 0.69, $P < 0.00001$) and at 6 months (OR 0.86, 95% CI 0.79 to 0.93, $P = 0.0003$). The results were homogeneous for every subgroup of patients at 30 days and slightly more heterogeneous at 6 months (Table 05). Similar results were obtained for the combined endpoint of death, MI or urgent revascularisation.

Safety

Data were available from 26 trials with 26,931 patients (96% of patients included in the overall review). Major bleeding occurred in 3.33% patients in the treatment group and in 2.48% in controls. Treatment with intravenous GP IIb/IIIa blockers was associated with an increased risk of severe bleeding (OR 1.38, 95% CI 1.19 to 1.60; $P < 0.0001$) and the results were homogeneous in all subgroups (Table 06). The absolute risk increase per thousand treated patients over 30 days was of 8.6 (95% CI 4.6 to 12.6).

2. GP IIb/IIIa blockers as initial medical treatment in patients with non-ST segment elevation acute coronary syndromes

Primary endpoints

Data from eight trials with 30,351 patients (100% of patients included in this meta-analysis) were available on 1-month mortality and myocardial infarction, while data from only three trials but with 13,658 patients (45% of patients included in the overall review) were available on 6-month mortality or myocardial infarction.

Treatment with intravenous GP IIb/IIIa blockers was associated with a non-significant trend to a reduction in the risk of mortality at 30 days (OR 0.92, 95% CI 0.81 to 1.04; $P = 0.16$) and no difference was observed at 6 months (OR 1.01, 95% CI 0.88 to 1.16). However, these agents reduced the risk of mortality or myocardial infarction both at 30 days (OR 0.92, 95% CI 0.86 to 0.99, $P = 0.03$) and at 6 months (OR 0.88, 95% CI 0.81 to 0.96). The ARR per thousand treated patients over 30 days was of 12.8 (95% CI 5.7 to 20.0).

Safety

Data were available from eight trials with 29,920 patients (98.6% of patients included in the overall review). Treatment with intravenous GP IIb/IIIa blockers increased the incidence of severe bleeding at 30 days (OR 1.27, 95% CI 1.12 to 1.44, $P = 0.0002$). Major bleeding occurred in 3.72% and in 3.61% of patients in the treatment and control groups, respectively. The absolute risk increase per thousand treated patients over 30 days was of 1.2 (95% CI 0.3 to 5.4).

Summary of analyses

The main results for the primary outcomes can be found in Table 04, the main results for the secondary outcomes in Table 05 and the main results for safety outcomes in Table 06.

DISCUSSION

GP IIb/IIIa blockers during PCI

This systematic review has identified that GP IIb/IIIa blockers are safe and effective when administered during PCI with or without stent implantation. The conclusion is based on data from 30 trials including 28,144 patients. Overall, the administration of GP IIb/IIIa blockers as a bolus immediately before the intervention followed by a 12- to 24-hour infusion is beneficial. Although associated with a significant risk of severe bleeding (8.6 per 1000), this hazard is more than offset by the reduction in the 30-day mortality (4.1 patients per 1000 treated), mortality or non-fatal myocardial infarction (24.5 patients per 1000), need for urgent revascularisation (16 patients per 1000 treated) and the combined endpoint of mortality, myocardial infarction or urgent revascularisation (32.4 patients per 1000).

The results also show that the early benefit of GP IIb/IIIa blockers is maintained during follow-up. In spite of the fact that only 19 of the 30 trials have reported a 6-month follow-up, the studies include 77% of the total patients enrolled. Although the benefit on 30-day mortality is lost at 6 months, that observed on the combined endpoint of mortality or myocardial infarction is maintained with a similar odds ratio at 30-days and at 6 months. Furthermore, the benefit is also maintained for urgent revascularisation and for the combined secondary endpoint of death, myocardial infarction or need for urgent revascularisation.

The beneficial effect of these drugs is homogeneous in the different subgroups of patients according to their clinical condition (i.e. NSTEMI, STEMI or stable CAD), and the technique used (i.e. balloon PCI or PCI with stent), although 30-day and 6-month mortality was only reduced when administered in procedures with stent implantation. The use of drug-eluting stents have been reported to be associated with a higher risk of thrombosis. Accordingly, the results of this meta-analysis applies to patients in which a bare metal stent was implanted since no study was performed specifically in patients with drug-eluting stents, and since in only one of the 15 studies (ISAR-REACT 2) a drug-eluting stent was used in 50% of the cases.

The administration of clopidogrel during PCI in addition to aspirin and heparin has shown to reduce the risk of acute coronary occlusion. Since its administration during the year following PCI (PCI-CURE) has also shown to reduce the risk of mortality, myocardial infarction or recurrent ischaemia, the administration of clopidogrel during PCI and during the year following PCI is the standard medical treatment of patients subjected to this procedure (ACC/AHA 2007; ESC 2007). In recent years, the administration of clopidogrel in addition to aspirin and heparin has also been shown to be of benefit as initial medical treatment of patients with NSTEMI (CURE; PCI-CURE; ACC/AHA 2007; ESC 2007). Currently one of the main controversies in clinical cardiology is the effectiveness of GP IIb/IIIa blockers in patients submitted to

PCI who have been pre-treated with clopidogrel from the time of hospital admission or at least 2 hours before PCI.

Nine trials including 6,600 patients analysed the efficacy of these drugs in this setting. Five of these trials with 3,658 patients were performed in stable coronary patients (Claeys 2005; ISAR-REACT 2004; ISAR-SWEET 2004; ISAR-SMART-2 2004; TOPSTAR 2002), while three with 2,740 patients were performed in patients with acute coronary syndromes (ELISA-2 2006; ISAR-REACT 2; PRACTICE 2006), and another was performed in a mixed population (ADVANCE 2004). The results of this systematic review show that there appears to be less clear evidence of benefit in patients pre-treated with clopidogrel, with higher odds ratios for every endpoint. These results suggest that the effects of GP IIb/IIIa blockers may be decreased in patients pre-treated with clopidogrel. On the other hand, the risk for severe bleeding is not enhanced by these drugs when administered with aspirin, clopidogrel and heparin.

GP IIb/IIIa blockers as initial medical treatment in patients with non-ST segment elevation acute coronary syndromes

This systematic review has also identified that GP IIb/IIIa antagonists are safe but much less effective when administered as an initial medical treatment to patients with NSTEMACS than in patients who underwent PCI. This conclusion is based on data from over 30,000 patients. Overall, the administration of intravenous GP IIb/IIIa blockers as an initial bolus followed by a continuous infusion for 24 to 72 hours resulted in a modest benefit at 30 days (12.8 deaths or myocardial infarctions prevented per 1,000 patients treated) and at 6 months. This benefit was obtained in spite of a very acceptable excess of severe bleeding (1.2 per 1,000). However, the treatment provided no significant benefit on all-cause mortality at 30 days or 6 months.

These results contrast with those mentioned above in the overall population submitted to PCI, and also in the subgroup of patients with NSTEMACS that underwent PCI. It is worth noting that the beneficial effect obtained was higher in trials with a high use rate of PCI procedures (PRISM Plus 1998) than in trials with a low frequency of these procedures (PRISM 1998, GUSTO-IV 2001). In addition, in three trials (CAPTURE 1997; PRISM Plus 1998; PURSUIT 1998), patients that underwent percutaneous coronary revascularisation 24 to 72 hours after admission obtained greater benefit from GP IIb/IIIa antagonists after PCI than before the procedure (Boersma 1999), and in one trial (PARAGON B 2001), a benefit was observed only among patients that underwent PCI during drug infusion. These results strongly suggest the existence of a positive interaction between PCI and the effect of GP IIb/IIIa blockers. Finally, because the overall treatment effect of GP IIb/IIIa inhibitors when administered as initial medical management of patients with NSTEMACS is small and these drugs are expensive, the best cost-effectiveness ratio may be obtained when they are administered in high-risk patients scheduled for early PCI.

It is important to note that in spite of the proven effectiveness of these drugs, they are administered in less than half of the patients submitted to PCI and in only one third of patients with a NSTEMACS (CRUSADE; GRACE 2007). The reasons for this under-administration in clinical practice of drugs that have shown to be effective in RCTs are unclear, and some data even show that these drugs are less often offered to high-risk patients (GRACE 2007). Further applied clinical research would be desirable to enlarge the administration of these drugs as recommended in current guidelines (ESC 2007; ACC/AHA 2007; NICE 2002).

Characteristics and limitations of the review

Heterogeneity of studies was statistically important only in 7 of the 68 analyses performed, all of them related to PCI and regarding secondary endpoints. Such heterogeneity is likely to be due to the subjective nature of urgent revascularisation. Differences in patient's characteristics as age, gender, history of myocardial infarction, proportion of patients with acute coronary syndromes, although important, did not result in significant statistical heterogeneity. It is unlikely that other factors such as drug dosages or important concomitant treatments may have affected homogeneity, particularly heparin and aspirin.

It should be noted that the studied population might not be representative of all patients undergoing PCI or with NSTEMACS in clinical practice. Most of the studied PCI patients had an acute coronary syndrome or highly complicated coronary lesions. However, the subgroup analysis performed on these patients showed similar results than those obtained in the global analysis and those obtained in patients with stable CAD. In the group of patients with NSTEMACS treated medically, the inclusion was limited to patients with ST-segment changes during the admission ECG or with positive biological markers of myocardial necrosis. These features are present in half of patients and are known to select high-risk patients. In fact, in most university centres, patients with these characteristics are submitted to coronary angiography within 48 hours. In addition, some studies have shown a significant interaction between GP IIb/IIIa blockers and the presence of positive troponin levels at admission (Boersma 2002). On the other hand, all of these randomised controlled trials excluded patients with significant renal impairment, cerebrovascular disease and also any patient with a moderate to high risk for bleeding complications. Furthermore, the mean age of the studied patients is lower than what is generally seen in clinical practice. For these reasons, the generalisability of the findings of this review is limited to a moderate to high-risk population with a low risk of bleeding complications.

AUTHORS' CONCLUSIONS

Implications for practice

Intravenous GP IIb/IIIa blockers reduce the risk of death at 30 days and markedly that of death or myocardial infarction at 30

days and 6 months in patients submitted to PCI at a price of a moderate increase in the risk of severe bleeding. Mortality is reduced when a stent is implanted but not when coronary balloon angioplasty alone is performed. These effects are homogeneous for patients with or without an acute coronary syndrome. However, there appears to be less clear evidence of benefit in patients pre-treated with clopidogrel.

When administered as initial medical treatment in patients with NSTEMACS, these agents do not reduce mortality, but slightly reduce the risk of death or myocardial infarction at 30 days and at 6 months, with a minimal increase in the risk of severe bleeding.

Implications for research

Since the analysis of patients that underwent PCI after pre-treatment with clopidogrel showed less clear effects than in the main analysis, and since clopidogrel is currently administered in most patients with acute coronary syndromes (ESC 2007; ACC/AHA 2007), further trials are warranted in this subgroup of patients. Also, further research is needed to analyse if the favourable effects observed in patients in which a bare metal stent is implanted and how this can be extrapolated to patients with drug-eluting stents.

This review did not consider trials performed in patients with STEMI during facilitated thrombolysis or facilitated or rescue PCI. The number of trials performed in these settings is limited and their results variable, making further research desirable on this high-risk population.

POTENTIAL CONFLICT OF INTEREST

None known.

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TABLES

Characteristics of included studies

Study	ACE 2003
Methods	Follow-up: 30 days and 6 months Mean age: 66 y Male: 78% Diabetes: 18% Prior myocardial infarction: 11% Acute coronary syndrome: 100% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation myocardial infarction: 100% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 0% CK-MB elevation: 100% Troponin elevation: ?% Atherectomy: ?% Balloon PCI: 0% Stent: 99%
Participants	400 patients with ST-segment elevation acute myocardial infarction of less than 6 h or between 6 and 24 h if there was evidence of continuing ischaemia, including patients with cardiogenic shock
Interventions	Unblinded abciximab versus placebo
Outcomes	Primary: A composite of death, reinfarction, target vessel revascularization and stroke at 30 days. Secondary: ST-segment reduction, postprocedural corrected TIMI frame count, infarct size at 1 month, 6-month death, reinfarction, death or reinfarction, target vessel revascularization, and angiographic restenosis of the IRA.
Notes	All patients treated with 325 mg of aspirin and heparin. Immediately after the procedure patients received 500 mg of ticlopidine or 300 mg of clopidogrel. Aspirin and clopidogrel 75 mg or ticlopidine 500 mg were maintained for 1 month
Allocation concealment	A – Adequate

Study	ADMIRAL 2001
Methods	Follow-up: 30 days and 6 months Mean age: 61 y Male: 82% Prior myocardial infarction: 11% Acute coronary syndrome: 100 % Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation myocardial infarction: 100% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 0% CK-MB elevation: 100%

Characteristics of included studies (Continued)

	Troponin elevation: ?% Atherectomy: ?% Balloon PCI: 13% Stent: 87%
Participants	300 patients with ST-segment elevation acute myocardial infarction of less than 12 h with coronary anatomy suitable for stent implantation
Interventions	Abciximab versus placebo
Outcomes	Primary: A composite of death, myocardial infarction or urgent revascularization at 30 days. Secondary: A composite of death, myocardial infarction or any revascularization at 30 days and at 6 months; death or myocardial infarction, death, myocardial infarction or urgent revascularization at 6 months; TIMI flow grade; ejection fraction.
Notes	All patients treated with aspirin, heparin and ticlopidine
Allocation concealment	A – Adequate

Study ADVANCE 2004

Methods	Follow-up: 6 months Mean age: 69 y Male: 68% Diabetes: 49% Prior myocardial infarction: 48% Acute coronary syndrome: 56 % Unstable angina: ? Non-ST elevation myocardial infarction: ? ST-elevation myocardial infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: ? Balloon PCI: 2% Stent: 98%
Participants	202 stable coronary patients undergoing elective or urgent PCI + stent with clinical or angiographic high-risk features. Inclusion criteria were the presence of >1 stenosis >70% amenable to coronary stenting and the presence of diabetes mellitus, or a planned multivessel intervention, or the presence of non-ST-segment elevation ACS
Interventions	High-dose bolus tirofiban (25ng/kg/3 min) and infusion (0.15 ng/kg/min for 24-48 h) vs. placebo
Outcomes	Primary: A composite of death, nonfatal MI, urgent TVR, and thrombotic bailout GP IIb/IIIa inhibitor therapy. Secondary: Each component of the primary endpoint, the effects on troponin I release after the procedure and the effects on pre-specified subgroups: diabetes and ACS
Notes	All patients were pretreated with aspirin and a thienopyridine (clopidogrel 300 mg orally 6 h before the procedure -63%- or ticlopidine 500 mg 48 h before -37%-)
Allocation concealment	B – Unclear

Study CADILLAC 2003

Methods	Follow-up: 30 days and 1 year Mean age: 60 y
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Characteristics of included studies (Continued)

	<p>Male: 73%</p> <p>Diabetes: 16%</p> <p>Prior myocardial infarction: 14%</p> <p>Acute coronary syndrome: 100 %</p> <p>Unstable angina: 0%</p> <p>Non-ST elevation myocardial infarction: 12%</p> <p>ST-elevation myocardial infarction: 88%</p> <p>PCI:</p> <p>a) In-hospital: 100%</p> <p>b) Drug-infusion: 100%</p> <p>ST-segment depression: 0%</p> <p>CK-MB elevation: 100%</p> <p>Troponin elevation: ?%</p> <p>Atherectomy: ?%</p> <p>Balloon PCI: 50%</p> <p>Stent: 50%</p>
Participants	2082 patients with ST-segment elevation acute myocardial infarction of less than 12 h with a coronary stenosis no longer than 64 mm and with a reference diameter of 2.5 to 4 mm. Patients were randomized using a 2 by 2 factorial design to undergo PTCA alone, PTCA plus abciximab, stenting alone or stenting plus abciximab
Interventions	Abciximab vs control
Outcomes	Primary: A composite of death, reinfarction, repeated intervention or revascularization of the target vessel as a result of ischemia, or disabling stroke during the first 6 months after the index procedure
Notes	All patients received 324 mg of aspirin before the procedure, 500 mg ticlopidine or 300 mg clopidogrel orally, a 5000 U bolus of heparin and a beta-blocker i.v.
Allocation concealment	A – Adequate

Study	CANADIAN 1996
Methods	<p>Follow-up: 30 days</p> <p>Mean age: 60 y</p> <p>Male: 72%</p> <p>Prior myocardial infarction: 55%</p> <p>Acute coronary syndrome: 100%</p> <p>Unstable angina: 86%</p> <p>Non-ST elevation myocardial infarction: 14%</p> <p>ST-elevation myocardial infarction: 0%</p> <p>PCI:</p> <p>a) In-hospital: ?</p> <p>b) Drug-infusion: ?</p> <p>ST-segment depression: 65%</p> <p>CK-MB elevation: 14%</p> <p>Troponin elevation: ?</p> <p>Atherectomy: ?</p> <p>Balloon PCI: ?</p> <p>Stent: ?</p>
Participants	365 patients with unstable angina or myocardial infarction without ST-segment elevation
Interventions	Lamifiban vs. placebo
Outcomes	Primary: death, myocardial infarction, refractory ischemia, recurrent ischaemia (2 or more episodes of angina). Secondary: bleeding complications.
Notes	Dose-ranging trial: all four lamifiban arms were grouped for the analysis.

Characteristics of included studies (Continued)

All patients were treated with aspirin.

Allocation concealment A – Adequate

Study	CAPTURE 1997
Methods	Follow-up: 30 days and 6 months Mean age: 61 y Male: 72% Prior myocardial infarction: 50% Acute coronary syndrome: 100% Unstable angina: 100% Non-ST elevation myocardial infarction: 0% ST elevation myocardial infarction: 0% PCI: a) In-hospital: 98% b) Drug-infusion: 98% ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 98% Stent: 1%
Participants	1,265 patients with refractory unstable angina who underwent percutaneous transluminal coronary angioplasty
Interventions	Abciximab vs. placebo
Outcomes	Primary composite: death, myocardial infarction and urgent intervention for recurrent ischaemia at 30 days. Secondary: bleeding
Notes	CAPTURE Study. Intervention began 18 to 24 h before percutaneous transluminal coronary angioplasty and continued until 1h after it. Permits assessment of the effect of GP IIb/IIIa blockers as initial medical treatment of unstable angina and also during percutaneous transluminal coronary angioplasty
Allocation concealment	A – Adequate

Study	Chen 2000
Methods	Follow-up: 30 days Mean age: 70 y Male: 95% Diabetes: 35% Prior myocardial infarction: 46% Acute coronary syndrome: 29% Unstable angina: 29% Non-ST elevation myocardial infarction: ?% ST elevation myocardial infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0%

Characteristics of included studies (Continued)

	Balloon PCI: 100% Stent: 0%
Participants	42 coronary patients scheduled to undergo coronary angioplasty. They were eligible if they had early postinfarction angina or unstable angina with ≥ 2 episodes of angina at rest associated with ECG changes during the previous 24 h; or clinical or angiographic characteristics indicating high risk according to the AHA/ACC criteria
Interventions	Abciximab (bolus of 0.25 mg/kg, followed by an infusion of 10 mg/min for 12 h) vs. placebo
Outcomes	Primary: The composite of death, MI, unplanned revascularization or insertion of an intraaortic balloon pump for refractory ischaemia. Secondary: each individual endpoint and bleeding events
Notes	Small study with 42 patients
Allocation concealment	B – Unclear

Study **Claeys 2005**

Methods	Follow-up: 30 days and 6 months Mean age: 67 y Male: 70% Prior myocardial infarction: 19% Acute coronary syndrome: 33% Unstable angina: 31% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 0% Atherectomy: 0% Balloon PCI: 2% Stent: 98%
Participants	200 patients scheduled for elective PCI with stent implantation and pre-treated with aspirin and a loading dose of clopidogrel (450 mg) were randomized just before coronary intervention to treatment with or without abciximab. Exclusion criteria were ACS, recent AMI, intervention of lesions located in bypass grafts or near major side branches, and the presence of an angiographically visible intracoronary thrombus. Also, patients with creatinine value > 2 mg/dl, with hemostatic disorders or with a history of intolerance to thienopyridines or to abciximab were excluded.
Interventions	Abciximab (bolus of 0.25 mg/Kg, followed by an infusion of 0.125 μ g/Kg/min) vs Placebo. All patients treated with 160 mg ASA, unfractionated heparin, and 450 mg of Clopidogrel at randomization. patients received 300 mg Clopidogrel in the evening preceding PCI and 150 mg in the morning of the intervention
Outcomes	Primary: level of platelet aggregation inhibition, and of peri-procedural myonecrosis. Secondary: A composite endpoint of death, MI or urgent target-vessel revascularization within 30 days of randomization.
Notes	Low-risk patients scheduled for elective PCI with stent placement. All patients pretreated with high-dose clopidogrel
Allocation concealment	D – Not used

Study **ELISA-2 2006**

Methods Follow-up: 30 days

Characteristics of included studies (Continued)

	<p>Mean age: 63 y Male: 71% Diabetes: 18% Prior myocardial infarction: 21% Acute coronary syndrome: 100% Unstable angina: 22% Non-ST elevation myocardial infarction: 78% ST elevation myocardial infarction: 0% PCI: a) In-hospital: 59% b) Drug-infusion: 59% ST-Segment depression: 61% CK-MB elevation: ? Troponin elevation: 78% Atherectomy: 0% Balloon PCI: 10% Stent: 49%</p>
Participants	328 pts with NSTEMACS that underwent coronary angiography a median of 23 h after admission Inclusion criteria: Ischemic chest pain and new ST-depression or a positive biomarker of necrosis. Exclusion criteria: Age > 80 ys, persistent ST-elevation, previous PCI in the last 6 months, cardiogenic shock or contraindication to the use of triple antiplatelet therapy or invasive therapy
Interventions	Aspirin, clopidogrel 300 mg and tirofiban (10 microg/kg bolus + 0.15 microg/kg/min infusion) vs. aspirin and clopidogrel 600 mg. Study medication was given in an open-label manner. All patients were scheduled for coronary angiography within 48 h after admission
Outcomes	Primary: Enzymatic infarct size. Secondary: Initial TIMI flow of the culprit vessel
Notes	ELISA-2 Study to compare dual vs. triple antiplatelet pre-treatment in patients with NSTEMACS who were planned for early catheterization
Allocation concealment	A – Adequate

Study	EPIC 1994
Methods	<p>Follow-up: 30 days Mean age: 61 y Male: 72% Prior myocardial infarction: 56% Acute coronary syndrome: 100% Unstable angina: 43% Non-ST elevation myocardial infarction: ? ST elevation myocardial infarction: 41% PCI: a) In-hospital: 100% b) Drug-infusion: 100% (see notes) ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 10% . Balloon PCI: 90% Stent: 0%</p>
Participants	2,099 patients with unstable angina, angina post myocardial infarction or clinically or angiographically high-risk patients undergoing percutaneous transluminal coronary angioplasty or atherectomy

Characteristics of included studies (Continued)

Interventions	Abciximab bolus vs. abciximab bolus+infusion vs. placebo
Outcomes	Primary composite: death, myocardial infarction, revascularization for acute ischaemia and insertion of a stent because of procedural failure or placement of an intraaortic contrapulsation balloon pump.
Notes	EPIC Study 30-day Excluded bolus-alone arm from analysis. This was the only study using the bolus-alone arm.
Allocation concealment	A – Adequate

Study EPILOG 1997

Methods	Follow-up: 30 days Mean age: 60 y Male: 72% Prior myocardial infarction: % Acute coronary syndrome: 69% Unstable angina: 48% Non-ST elevation MI: ? ST elevation MI: ? PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 5% Balloon PCI: 95% Stent: 11%
Participants	2,792 patients with ST-segment elevation acute myocardial infarction, unstable or stable angina undergoing percutaneous transluminal coronary angioplasty. Exclusions: myocardial infarction in prior 24 h or angina with ECG changes or revascularization in prior 3 months
Interventions	Abciximab + low-dose heparin vs. abciximab + high-dose heparin vs. placebo + heparin
Outcomes	Primary composite: death, myocardial infarction and urgent reintervention Secondary: death, myocardial infarction, all revascularization
Notes	EPILOG 30-day follow-up The two abciximab groups have been grouped together for the analysis
Allocation concealment	A – Adequate

Study EPISTENT 1998

Methods	Follow-up: 30 days Mean age: 59 y Male: 75% Prior myocardial infarction: 35% Acute coronary syndrome: 52% Unstable angina: 36% Non-ST elevation myocardial infarction: ? ST elevation myocardial infarction: ? PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: ?
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Characteristics of included studies (Continued)

	CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 29% Stent: 71%
Participants	2,399 pts scheduled to elective or urgent coronary angioplasty or stent
Interventions	Abciximab+stent vs. abciximab+ balloon coronary angioplasty vs. placebo+stent
Outcomes	Primary composite: death, myocardial infarction and severe ischaemia requiring urgent revascularization Secondary: death, myocardial infarction, and death or large myocardial infarction
Notes	All patients treated with aspirin and heparin. The stent group received also ticlopidine 250 mg twice daily starting at the discretion of the investigator before the start of the study agent
Allocation concealment	A – Adequate

Study ERASER 1999

Methods	Follow-up: hospitalization and 6 months Mean age: 60 y Male: 79% Prior myocardial infarction: ? Acute coronary syndrome: 0% (see exclusions) Unstable angina: 56% Non-ST elevation myocardial infarction: - ST elevation myocardial infarction: - PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 0% Stent: 100%
Participants	215 angina patients with one stentable lesion (>/=50% reduction in intraluminal diameter) in an artery with an intraluminal diameter from 2.75 to 3 mm. Excluded were patients with acute coronary syndrome < 72 hours.
Interventions	Abciximab 12/24-h infusion vs. placebo.
Outcomes	Primary: proportion in stent obstruction volume of the target lesion Safety: major bleeding, death Secondary: target lesion mean and minimum lumen diameter, late loss and loss index by quantitative coronary angiography analysis and a composite of death, myocardial infarction and revascularization
Notes	ERASER trial. The 12-h and 24-h infusion groups were grouped together for the analysis. In-hospital was considered 30-day in this review. All patients treated with aspirin and heparin. Ticlopidine use was left to the investigator's discretion.
Allocation concealment	A – Adequate

Study ESPRIT 2000

Methods	Follow-up: 30 days Mean age: 62 y
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Characteristics of included studies (Continued)

	<p>Male: 73%</p> <p>Prior myocardial infarction: 32%</p> <p>Acute coronary syndrome: 18%</p> <p>Unstable angina: 14%</p> <p>Non-ST elevation myocardial infarction: %</p> <p>ST-elevation myocardial infarction: 5%</p> <p>PCI:</p> <p>a) In-hospital: 99%</p> <p>b) Drug-infusion: 99%</p> <p>ST-segment depression: ?</p> <p>CK-MB elevation: ?</p> <p>Troponin elevation: ?</p> <p>Atherectomy: 0%</p> <p>Balloon PCI: 99%</p> <p>Stent: 96%</p>
Participants	2,064 patients with coronary artery disease undergoing stent implantation on a native coronary artery
Interventions	Eptifibatide high-dose double-bolus + infusion vs. placebo
Outcomes	<p>Primary composite: death, myocardial infarction, urgent revascularization, and thrombotic bailout GP IIb/IIIa inhibitor within 48h after randomization</p> <p>Secondary: Death, myocardial infarction or urgent revascularization at 30 days and at 6 months.</p>
Notes	<p>ESPRIT trial.</p> <p>All patients treated with aspirin, heparin and clopidogrel or ticlopidine.</p>
Allocation concealment	A – Adequate

Study	GUSTO-IV 2001
Methods	<p>Follow-up: 30 days</p> <p>Mean age: 65 y</p> <p>Male: 62%</p> <p>Prior myocardial infarction: 31%</p> <p>Acute coronary syndrome: 100%</p> <p>Unstable angina: 72%</p> <p>Non-ST elevation infarction: 28%</p> <p>ST-elevation infarction: 0%</p> <p>PCI:</p> <p>a) In-hospital: 19%</p> <p>b) Drug-infusion: 1.6%</p> <p>ST-segment depression: 80%</p> <p>CK-MB elevation: 28%</p> <p>Troponin elevation: 59%</p> <p>Atherectomy: ?%</p> <p>Balloon PCI: ?%</p> <p>Stent: %?</p>
Participants	<p>7,800 average-risk patients with unstable angina or non-ST segment elevation myocardial infarction.</p> <p>Enrolment period: 1998-2000</p> <p>Last episode of chest pain: <24 h</p> <p>Indicator of myocardial ischaemia: >0.5 mm ST depression or >0.5 mm transient ST elevation or troponin T or I elevation above ULN</p>
Interventions	<p>Abciximab bolus+48-h infusion vs. abciximab bolus + 24-h infusion vs. placebo</p> <p>Dose:</p> <p>a) 250 ng/kg bolus + 0.125 ng/kg/min infusion (maximum 0.10 ng/min) for 24 h+ heparin</p>

Characteristics of included studies (Continued)

	b) 250 ng/kg bolus + 0.125 ng/kg/min infusion (maximum 0.10 ng/min) for 48 h+ heparin c) placebo + heparin Duration: 24 or 48 h
Outcomes	Primary: Death or myocardial infarction at 30 days. Secondary: Death or myocardial infarction in patients with positive troponin levels; death, myocardial infarction, revascularization or coronary angiography; death or myocardial infarction. Required level of CK or CK-MB elevation in MI definition: 3xULN. Safety: Intracranial haemorrhage; bleeding leading to decrease in haemoglobin concentration >50g/L.
Notes	GUSTO-IV Study Both abciximab groups were analyzed together in this review. All patients treated with 150-325 mg aspirin. Heparin was part of study regimen; initial dose weight-adjusted (maximum 5000 U bolus + 800 U/h infusion aiming for aPTT of 50-70 s; a subgroup treated with dalteparin (maximum dose 10000 U) Angiography was discouraged during infusion period. PCI was not scheduled ((just 1.6% had PCI within 48h).
Allocation concealment	A – Adequate

Study	Galassi 1999
Methods	Follow-up: 30 days Mean age: 62 y Male: 88% Diabetes: 27% Prior myocardial infarction: 67% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation myocardial infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: ?% Balloon PCI: 0% Stent: 100%
Participants	106 patients with CAD, demonstrable ischemia and a target de novo complex lesion stenosis >70% in a native vessel scheduled for elective implantation of a >20 mm stent or multiple stents.
Interventions	Patients were randomly assigned, in an open label fashion, to receive either a combination of abciximab (bolus and a 12 h infusion) and weight-adjusted low-dose heparin or weight-adjusted heparin alone. All patients received 325 mg of aspirin the day before the procedure and daily thereafter. Ticlopidine 250 mg twice daily was started the day before the intervention and was given to all patients for the first 4 weeks.
Outcomes	No Primary outcome was specified. Outcomes: mortality, MI, urgent revascularization, target lesion revascularization, acute or subacute stent thrombosis.
Notes	Patients were 'randomly allocated'. There is not description of the allocation concealment or the primary outcome of the study.
Allocation concealment	B – Unclear

Study	IMPACT 1995
Methods	Follow-up: 30 days

Characteristics of included studies (Continued)

	<p>Mean age: 62 y Male: 75% Prior myocardial infarction: 45% Acute coronary syndrome: 75% Unstable angina: 58% Non-ST elevation infarction: ?% ST-elevation myocardial infarction: 17% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ?% CK-MB elevation: ?% Troponin elevation: ?% Atherectomy: 13% Balloon PCI: 100% Stent: 0%</p>
Participants	150 patients with coronary artery disease scheduled for elective percutaneous coronary revascularization
Interventions	Eptifibatide bolus + 12-h infusion vs. eptifibatide bolus +4-h infusion vs. placebo
Outcomes	Primary composite: death, myocardial infarction and urgent revascularization, stent implantation or surgery. Safety endpoints: bleeding complications
Notes	IMPACT trial. The two eptifibatide groups were grouped together for the meta-analysis. All patients treated with aspirin and heparin
Allocation concealment	A – Adequate

Study	IMPACT-II 1997
Methods	<p>Follow-up: 30 days Mean age: 61 y Male: 75% Prior myocardial infarction: 41% Acute coronary syndrome: 42% Unstable angina: 38% Non-ST elevation myocardial infarction: ? % ST-elevation infarction: 4% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ?% CK-MB elevation: ?% Troponin elevation: ?% Atherectomy: 23% Balloon PCI: 92% Stent: 4%</p>
Participants	4,010 patients with coronary artery disease undergoing percutaneous revascularization
Interventions	2 Eptifibatide dose-ranging groups vs. placebo
Outcomes	Primary composite: death, myocardial infarction, urgent repeated revascularization or placement of a stent for acute closure Secondary: primary endpoint at 24 h and 6-month
Notes	IMPACT II Study Two arms with different doses of eptifibatide and a placebo arm.

Characteristics of included studies (Continued)

The two active treatment arms were grouped in our analysis.
All patients received aspirin and heparin

Allocation concealment A – Adequate

Study	ISAR-2 2000
Methods	Follow-up: 30 days Mean age: 61 y Male: 76% Prior myocardial infarction: ?% Acute coronary syndrome: 100% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 100% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 0% CK-MB elevation: 100% Troponin elevation: ?% Atherectomy: 0% Balloon PCI: 0% Stent: 100%
Participants	401 patients with ST-segment elevation acute myocardial infarction undergoing angioplasty with stent implantation within 48 hours after onset of chest pain.
Interventions	Abciximab plus reduced-dose heparin versus standard-dose heparin
Outcomes	Primary: angiographic restenosis at 6 months Secondary: a composite of death, myocardial infarction and target lesion revascularization at 30 days
Notes	ISAR-2 study Non-placebo controlled All patients treated with aspirin, heparin and ticlopidine
Allocation concealment	A – Adequate

Study	ISAR-REACT 2
Methods	Follow-up: 30 days Mean age: 66 y Male: 74% Prior myocardial infarction: 24% Acute coronary syndrome: 100% Unstable angina: 48% Non-ST elevation myocardial infarction: 52% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 52% Atherectomy: 0% Balloon PCI: 3% Stent: 97%

Characteristics of included studies (Continued)

Participants	2022 patients with NSTEMACS that underwent PCI in native coronary vessels within 6 h from diagnosis of ACS and after pretreatment with 600 mg of Clopidogrel >2 h before PCI. Coronary stenting was the target PCI.
Interventions	Abciximab (bolus of 0.25 mg/Kg, followed by an infusion of 0.125 µg/Kg/min) vs placebo. All patients treated with ASA, heparin and 600 mg of clopidogrel >2h before the procedure
Outcomes	Primary: All-cause death, MI or urgent target-vessel revascularization within 30 days of randomization. Safety: Major and minor bleeding, and thrombocytopenia.
Notes	High-risk patients with NSTEMACS treated with early (<6 h) PCI after diagnosis
Allocation concealment	A – Adequate

Study **ISAR-REACT 2004**

Methods	Follow-up: 30 days and 1 y Mean age: 66 y Male: 76% Prior myocardial infarction: 33% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 0% Percutaneous coronary revascularization: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 0% Atherectomy: ? Percutaneous transluminal balloon angioplasty: 10% Stent: 90%
Participants	2159 patients with CAD that underwent elective PCI in native coronary vessels and had been pretreated with 600 mg of clopidogrel >2 h before the intervention. Coronary stenting was the target PCI
Interventions	Abciximab (bolus of 0.25 mg/Kg, followed by an infusion of 0.125 µg/Kg/min) vs placebo. All patients treated with ASA and heparin
Outcomes	Primary: All-cause death, MI or urgent target-vessel revascularization within 30 days of randomization. Safety: Major and minor bleeding, and thrombocytopenia.
Notes	Low-risk patients scheduled for elective PCI with stent placement. All patients pretreated with high-dose clopidogrel
Allocation concealment	A – Adequate

Study **ISAR-SMART-2 2004**

Methods	Follow-up: one year Mean age: 66 y Male: 73% Prior myocardial infarction: 37% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 0%
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Characteristics of included studies (Continued)

	Atherectomy: 0% Balloon PCI: 50% Stent: 50%
Participants	502 patients with stable angina pectoris or a positive exercise test that underwent elective PCI in native coronary vessels <2.5 mm in size and after pretreatment with 600 mg of clopidogrel >2 h before PCI.
Interventions	Patients were randomized to either stenting or PCI and to either abciximab (bolus of 0.25 mg/kg, followed by an infusion of 0.125 µg/Kg/min) or placebo with the use of a 2x2 factorial design. All patients treated with ASA, heparin and 600 mg of clopidogrel >2h before the procedure
Outcomes	Primary: Angiographic restenosis at follow-up angiography. Secondary: Combined incidence of all-cause death and MI as well as target vessel revascularization during 1-year follow-up.
Notes	Low-risk patients scheduled for elective PCI with stent placement. All patients pretreated with high-dose clopidogrel
Allocation concealment	A – Adequate

Study ISAR-SWEET 2004

Methods	Follow-up: 30 days and 1 y Mean age: 67 y Male: 74% Prior myocardial infarction: 34% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 0% Atherectomy: ? Balloon PCI: 10% Stent: 90%
Participants	701 diabetic patients with CAD that underwent elective PCI in native coronary vessels and had been pretreated with 600 mg of Clopidogrel >2 h before the intervention. Coronary stenting was the target PCI.
Interventions	Abciximab (bolus of 0.25 mg/Kg, followed by an infusion for 12 h of 0.125 µg/Kg/min) vs placebo. All patients treated with ASA and heparin.
Outcomes	Primary: All-cause death and MI during the first 12 months after randomization. Safety: Major and minor bleeding, and thrombocytopenia.
Notes	Patients with diabetes mellitus (29% treated with insulin) scheduled for elective PCI with stent
Allocation concealment	A – Adequate

Study Juergens 2002

Methods	Follow-up: 30 days Mean age: 59 y Male: 83% Prior myocardial infarction: 46% Acute coronary syndrome: 46% Unstable angina: 46% Non-ST elevation myocardial infarction: ? ST-elevation infarction: 0%
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Characteristics of included studies (Continued)

	PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: 0% Troponin elevation: 0% Atherectomy: ? Balloon PCI: 2% Stent: 98%
Participants	894 patients scheduled to undergo PCI with stent placement
Interventions	Patients were randomized in a 3:2 ratio to receive an i.v. bolus (10 µg/Kg) and maintenance infusion for 36 h of tirofiban (0.10 µg/Kg/ min) or a bolus and infusion of placebo
Outcomes	Primary: any bleeding
Notes	This was primarily a tolerability study
Allocation concealment	A – Adequate

Study Keriakes 1996

Methods	Follow-up: hospitalization Mean age: 59 y Male: 82% Prior myocardial infarction: 47% Acute coronary syndrome: 52% Unstable angina: 39% Non-ST elevation myocardial infarction: 0% ST-elevation myocardial infarction: 13% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ?% CK-MB elevation: ?% Troponin elevation: ?% Atherectomy: 0% Balloon PCI: 100% Stent: 0%
Participants	93 high risk patients with coronary artery disease undergoing scheduled coronary angioplasty
Interventions	3 tirofiban dose-ranging groups versus placebo
Outcomes	Primary composite: death, myocardial infarction and need for urgent revascularization
Notes	Dose-ranging study All tirofiban groups were grouped together for the analysis
Allocation concealment	A – Adequate

Study PARAGON A 1998

Methods	Follow-up: 30 days and 6 months Mean age: 66 y Male: 65% Prior myocardial infarction: 35% Acute coronary syndrome: 100% Unstable angina: 100% Non-ST elevation myocardial infarction: ?%
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Characteristics of included studies (Continued)

	<p>ST-elevation myocardial infarction: 0%</p> <p>PCI: a) In-hospital: 14%</p> <p>b) Drug-infusion: ?</p> <p>ST-segment depression: ?%</p> <p>CK-MB elevation: ?%</p> <p>Troponin elevation: ?%</p> <p>Atherectomy: ?%</p> <p>Balloon PCI: 14%</p> <p>Stent: ?%</p>
Participants	<p>2,282 patients with unstable angina or non-ST segment elevation myocardial infarction</p> <p>Enrolment period: 1995-96</p> <p>Last episode of chest pain: <12 h</p> <p>Indicator of myocardial ischaemia: >0.5 mm ST depression or >0.5 mm transient ST elevation or T-wave inversion</p>
Interventions	<p>Low dose lamifiban vs. low dose lamifiban + heparin vs. high dose lamifiban vs. high dose lamifiban + heparin vs. placebo + heparin</p> <p>Dose:</p> <p>a) 300 ng bolus + 1 ng/min infusion + random assignment to heparin or heparin-placebo</p> <p>b) 750 ng bolus + 5 ng/min infusion + random assignment to heparin or heparin-placebo</p> <p>c) placebo + heparin</p> <p>Duration: 72-120 h; median:72 h</p>
Outcomes	<p>Primary: death or myocardial infarction at 30 days.</p> <p>Secondary: death, myocardial infarction, disabling stroke, major bleeding and intermediate bleeding; death and myocardial infarction at 6 months and death at 1 year.</p> <p>Required level of CK or CK-MB elevation in MI definition: 2xULN</p> <p>Safety: Intracranial haemorrhage; or bleeding leading to haemodynamic compromise requiring intervention.</p>
Notes	<p>PARAGON trial</p> <p>All patients treated with 75-325 mg aspirin.</p> <p>Heparin was part of study regimen; initial dose weight-adjusted (maximum 5000 U bolus + 1000 U/h infusion)</p> <p>Angiography was discouraged during the first 24 h.</p> <p>PCI at the discretion of treating physician</p> <p>All lamifiban + heparin groups grouped together in the analysis.</p>
Allocation concealment	A – Adequate

Study **PARAGON B 2001**

Methods	<p>Follow-up: 30 days and 6 months</p> <p>Mean age: 64 y</p> <p>Male: 66%</p> <p>Prior myocardial infarction: 30%</p> <p>Acute coronary syndrome: 100%</p> <p>Unstable angina: 43%</p> <p>Non-ST elevation myocardial infarction: 57%</p> <p>ST-segment elevation myocardial infarction: 0%</p> <p>PCI: a) In-hospital: 28%</p> <p>b) Drug-infusion: 12%</p> <p>ST-segment depression: 44%</p> <p>CK-MB elevation: 57%</p> <p>Troponin elevation: ?%</p> <p>Atherectomy: 4%</p> <p>Balloon PCI: 28%</p>
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Characteristics of included studies (Continued)

	Stent: 21%
Participants	5,225 patients with acute coronary syndrome without ST-segment elevation. Enrolment period: 1998-99 Last episode of chest pain: <12 h Indicator of myocardial ischaemia: >0.5 mm ST depression or >0.5 mm transient ST elevation or T-wave inversion or troponin T or I elevation above ULN
Interventions	Lamifiban (72 h infusion) vs. placebo Dose: a) 500 ng bolus + 1-2 ng/min infusion depending on creatinine clearance+ heparin b) placebo + heparin Duration: 72-120 h
Outcomes	Primary: A composite of death, myocardial infarction or severe recurrent ischaemia at 30 days. Secondary: death or myocardial infarction. Required level of CK or CK-MB elevation in MI definition: 2xULN in spontaneous MI; 3xULN in relation to PCI; 5xULN in relation to CABG. Safety: Intracranial haemorrhage; or bleeding leading to haemodynamic compromise requiring intervention.
Notes	PARAGON B Study The dose of lamifiban used was the one that had the best results in the previous PARAGON A study. All patients treated with 150-325 mg aspirin. Heparin was part of study regimen; initial dose weight-adjusted (maximum 5000 U bolus + 1000 U/h infusion aiming for aPTT of 50-70 s. Angiography at the discretion of treating physician. PCI at the discretion of treating physician
Allocation concealment	A – Adequate

Study	PRACTICE 2006
Methods	Follow-up: 30 d Acute coronary syndrome: 100% Unstable angina: 0% Non-ST elevation myocardial infarction: 100% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 0% CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 55% Stent: 45%
Participants	393 patients with NSTEMI treated with aspirin, clopidogrel with a loading dose of 300 mg followed by a daily dose of 75 mg, and heparin in both groups. An invasive strategy was planned within 6 to 48 h.
Interventions	Patients randomized to pretreatment with eptifibatide (n=196) or placebo (n=197)
Outcomes	Primary: A composite of death, MI or urgent revascularization at 30 days.
Notes	First study to evaluate the efficacy of a IIb/IIIa antagonist in patients with NSTEMACS pretreated with aspirin and clopidogrel
Allocation concealment	B – Unclear

Study	PRIDE 2001
Methods	Follow-up: 30 d

Characteristics of included studies (Continued)

	<p>Mean age: 59 y Male: ? Prior myocardial infarction: 51% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 0% CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 55% Stent: 45%</p>
Participants	127 coronary patients scheduled to undergo elective PCI were enrolled at 14 centers
Interventions	Pts randomized to 4 treatment regiments: 1) placebo bolus and infusion; 2) bolus of 135 µg/Kg Eptifibatide with a 0.75 µg/Kg/min infusion; 3) bolus of 180 µg/Kg Eptifibatide with a 2 µg/Kg/min infusion; 4) bolus of 250 µg/Kg Eptifibatide with a 3 µg/Kg/min infusion
Outcomes	Primary: To explore the pharmacodynamics of high doses of eptifibatide. Secondary: Safety
Notes	Dose-ranging study. 45% of pts underwent stent implantation
Allocation concealment	B – Unclear

Study	PRISM 1998
Methods	<p>Follow-up: 30 days Mean age: 62 y Male: 68% Prior myocardial infarction: 47% Acute coronary syndrome: 100% Unstable angina: 75% Non-ST elevation MI: 25% ST-elevation myocardial infarction: 0% PCI: a) In-hospital: 21% b) Drug-infusion: 2% ST-segment depression: 32% CK-MB elevation: 24% Troponin elevation: ?% Atherectomy: 0% Balloon PCI: 13% Stent: 8%</p>
Participants	<p>3,232 patients with unstable angina or non-ST segment elevation myocardial infarction Enrolment period: 1994-96 Last episode of chest pain: <24 h Indicator of myocardial ischaemia: >1 mm ST depression or >1 mm transient ST elevation or T-wave inversion or CK-MB elevation or prior evidence of CAD by history, stress test or coronary angiography</p>
Interventions	<p>Tirofiban vs. placebo Dose: a) 0.6 ng/Kg bolus + 0.15 ng/Kg/min infusion + placebo heparin b) placebo + heparin</p>

Characteristics of included studies (Continued)

	Duration: 48 h
Outcomes	Primary: A composite of death, myocardial infarction or refractory ischaemia at 48h. Secondary: A composite of death, myocardial infarction and refractory ischaemia at 7 days. Required level of CK or CK-MB elevation in MI definition: 2xULN Safety: Intracranial haemorrhage; bleeding leading to decrease in haemoglobin concentration >50g/L; or cardiac tamponade.
Notes	PRISM Study All patients treated with 300-325 mg aspirin. Heparin was part of study regimen; initial dose 5000 U bolus + 1000 U/h infusion Angiography was discouraged during the infusion period. PCI was not scheduled
Allocation concealment	A – Adequate

Study	PRISM Plus 1998
Methods	Follow-up: 30 days Mean age: 63 y Male: 67% Prior myocardial infarction: 43% Acute coronary syndrome: 100% Unstable angina: 55% Non-ST segment elevation myocardial infarction: 45% ST-elevation myocardial infarction: 0% PCI: a) In-hospital: 31% b) Drug-infusion: 25% ST-segment depression: 58% CK-MB elevation: 45% Troponin elevation: ?% Atherectomy: ?% Balloon PCI: ?% Stent: ?%
Participants	1,915 High risk patients with unstable angina or non-ST elevation MI. Enrolment period: 1994-96 Last episode of chest pain: <12 h Indicator of myocardial ischaemia: >1 mm ST depression or >1 mm transient ST elevation or >=3 mm T-wave inversion or CK-MB elevation
Interventions	Tirofiban-alone vs. tirofiban + heparin vs. placebo+heparin Dose: a) 0.4 ng/Kg bolus + 0.1 ng/Kg/min infusion + heparin b) 0.6 ng/kg bolus + 0.15 ng/kg/min infusion + placebo heparin c) placebo + heparin Duration: 48-96 h
Outcomes	Primary: A composite of death, myocardial infarction and refractory ischaemia at 7 days. Secondary: the same composite endpoint at 48 h and 30 days; The components of the primary endpoint as separate measures, and a composite of death or myocardial infarction. Required level of CK or CK-MB elevation in MI definition: 2xULN in spontaneous MI; 3xULN in relation to PCI. Safety: Intracranial haemorrhage; bleeding leading to decrease in haemoglobin concentration >40g/L or transfusion of >=2 U blood; or requiring corrective surgery.
Notes	PRISM plus All patients treated with 325 mg aspirin.

Characteristics of included studies (Continued)

Heparin was part of study regimen in the low-dose tirofiban arm but not in the high-dose arm; initial dose 5000 U bolus + 1000 U/h infusion
Angiography was recommended after the first 48 h of infusion (48-96 h) and during the infusion period.
PCI performed if indicated by angiography
The tirofiban-alone arm was prematurely stopped because of an early trend to increased mortality which disappeared after 6-month follow-up. Both tirofiban groups were grouped together for the analysis.

Allocation concealment A – Adequate

Study	PURSUIT 1998
Methods	Follow-up: 30 days Mean age: 64 y Male: 65% Prior myocardial infarction: 32% Acute coronary syndrome: 100% Unstable angina: 54% Non-ST elevation myocardial infarction: 46% ST-elevation myocardial infarction: 0% PCI: a) In-hospital: 24% b) Drug-infusion: 11% ST-segment depression: 50% CK-MB elevation: 46% Troponin elevation: ?% Atherectomy: ?% Balloon PCI: 12% Stent: 12%
Participants	10,948 patients with unstable angina or non-ST segment elevation myocardial infarction Enrolment period: 1995-97 Last episode of chest pain: <24 h Indicator of myocardial ischaemia: >0.5 mm ST depression or >0.5 mm transient ST elevation or >1 mm T-wave inversion or CK-MB elevation above ULN
Interventions	Eptifibatide vs. placebo Dose: a) 180 ng/Kg bolus + 1.3 ng/Kg/min infusion + heparin b) 180 ng/kg bolus + 2.0 ng/kg/min infusion + heparin c) placebo + heparin Duration: 72-96 h
Outcomes	Primary: A composite of death or non-fatal myocardial infarction at 30 days. Secondary: Mortality at 30 days; myocardial infarction at 30 days; death or myocardial infarction at 96 h and 7 d; bleeding complications. Required level of CK or CK-MB elevation in MI definition: 1xULN in spontaneous MI; 3xULN in relation to PCI; 5xULN in relation to CABG. Safety: Intracranial haemorrhage; or bleeding leading to haemodynamic compromise requiring intervention.
Notes	PURSUIT Study All patients treated with aspirin. All patients treated with 80-325 mg aspirin. Heparin was part of study regimen; initial dose 5000 U bolus + 1000 U/h infusion Angiography at the discretion of treating physician. PCI at the discretion of treating physician

Allocation concealment A – Adequate

Characteristics of included studies (Continued)

Study	RAPPORT 1998
Methods	Follow-up: 30 days and 6 months Mean age: 61 y Male: 72% Prior myocardial infarction: 21% Acute coronary syndrome: 100% Unstable angina: 0% Non-ST elevation myocardial infarction: 0% ST elevation myocardial infarction: 100% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: 0% CK-MB elevation: 100% Troponin elevation: ? Atherectomy: 0% Balloon PCI: 85% Stent: 7% (unplanned)
Participants	483 patients with myocardial infarction (<12 hours) candidates for primary percutaneous transluminal coronary angioplasty
Interventions	Abciximab vs. placebo
Outcomes	Primary composite: death, myocardial infarction and any repeat revascularization, major bleeding
Notes	RAPPORT trial
Allocation concealment	A – Adequate

Study	RESTORE 1997
Methods	Follow-up: 30 days Mean age: 59 y Male: 72% Prior myocardial infarction: 35% Acute coronary syndrome: 100% Unstable angina: 67% Non-ST elevation myocardial infarction: ? ST elevation myocardial infarction: 32% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-Segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 8% Balloon PCI: 92% Stent: 0%
Participants	2,141 patients with unstable angina or myocardial infarction within 72 h from admission, undergoing atherectomy or percutaneous transluminal coronary angioplasty
Interventions	Tirofiban vs. placebo
Outcomes	Primary (individual and composite): death, myocardial infarction, revascularization due to recurrent ischaemia, insertion of a stent owing to actual or threatened acute closure of the target artery.
Notes	RESTORE trial

Characteristics of included studies (Continued)

Allocation concealment A – Adequate

Study	Schulman 1996
Methods	Follow-up: 30 days Mean age: 62 y Male: 63% Prior myocardial infarction: 55% Acute coronary syndrome: 100% Unstable angina: 100% Non-ST elevation myocardial infarction: ?% ST-elevation myocardial infarction: 0% PCI: a) In-hospital: ? b) Drug-infusion: ? ST-segment depression: 33% CK-MB elevation: ?% Troponin elevation: ?% Atherectomy: ?% Balloon PCI: ?% Stent: ?%
Participants	227 patients with unstable angina and ST-T changes on admission ECG, or known coronary artery disease.
Interventions	Two eptifibatid doses vs. placebo
Outcomes	Primary: number and duration of ischaemic episodes on continuous monitoring over the first 24 hours as well as for the entire duration of drug infusion Secondary: number and duration of symptomatic ischaemic episodes, number and duration of ECG episodes of ischaemia after study drug withdrawal, and clinical events of death, myocardial infarction and refractory ischaemia.
Notes	The placebo group received aspirin and heparin while the eptifibatid group received only heparin. Both active treatment groups have been grouped in our analysis
Allocation concealment	A – Adequate

Study	Simoons 1994
Methods	Follow-up: hospitalization Mean age: 61 y Male: 73% Prior myocardial infarction: 18% Acute coronary syndrome: 100% Unstable angina: 100% Non-ST segment elevation myocardial infarction: ?% ST-segment elevation myocardial infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: 67% CK-MB elevation: ?% Troponin elevation: ?% Atherectomy: 0% Balloon PCI: 100% Stent: 0%

Characteristics of included studies (Continued)

Participants	60 refractory unstable angina patients undergoing percutaneous coronary angioplasty.
Interventions	Abciximab vs. placebo
Outcomes	Primary: A composite of death, myocardial infarction and recurrent ischaemia requiring urgent revascularization Secondary: recurrent ischaemia and angiographic end points.
Notes	European Cooperative Study in which an in-hospital follow-up considered along with 30-day follow-up studies. All patients treated with i.v. nitroglycerin infusion, aspirin and heparin.
Allocation concealment	A – Adequate

Study TOPSTAR 2002

Methods	Follow-up: 30 days and 9 months Mean age: 65 y Male: 75% Prior myocardial infarction: 38% Acute coronary syndrome: 0% Unstable angina: 0% Non-ST segment elevation myocardial infarction: 0 % ST-segment elevation myocardial infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ? CK-MB elevation: ? Troponin elevation: ? Atherectomy: 0% Balloon PCI: 8% Stent: 92%
Participants	96 of 109 enrolled stable patients with a >70% stenosis that underwent elective PCI. All patients were pre-treated with ASA 500 mg and clopidogrel 375 mg at least one day before PCI
Interventions	Tirofiban bolus of 10 µg/Kg + infusion of 0.15 µg/Kg/min
Outcomes	Primary: presence of postinterventional release of troponin T after 24 h. Secondary: incidence of death, MI or target vessel revascularisation
Notes	All patients pre-treated with clopidogrel 375 mg and ASA 500 mg at least 1 day before PCI
Allocation concealment	B – Unclear

Study Tamburino 2002

Methods	Follow-up: 30 days and 6 m Mean age: 62 y Male: 88% Diabetes: 27% Prior myocardial infarction: 67% Acute Coronary Syndrome: 48% Unstable angina: 48% Non-ST elevation myocardial infarction: ?% ST-elevation infarction: 0% PCI: a) In-hospital: 100% b) Drug-infusion: 100% ST-segment depression: ?%
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CK-MB elevation: ?%
Troponin elevation: ?%
Atherectomy: 0%
Balloon PCI: 0%
Stent: 100%

Participants	107 patients with demonstrable reversible ischaemia and >70% de novo native coronary stenoses requiring implantation of either a stent longer than 20 mm or of multiple overlapping stents
Interventions	Abciximab (bolus of 0.25 mg/Kg, followed by an infusion of 0.125 µg/Kg/min for 12 h) vs placebo. All patients treated with ASA and heparin. Ticlopidine 250 mg twice daily was started the day before the intervention and was prescribed to all patients for 4 weeks following the procedure
Outcomes	Primary: safety (bleeding and vascular complications) and efficacy in reducing major in-hospital adverse cardiac events related to the procedure (death, MI and urgent revascularization) Secondary: reduction in death, MI, target lesion revascularization and angiographic binary restenosis at 6 months
Notes	
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
ACUITY 2006	Comparison of unfractionated heparin or enoxaparin plus any GP IIb/IIIa inhibitor vs. bivalirudin plus any GP IIb/IIIa inhibitor vs. bivalirudin alone.
ADVANCE MI 2005	Facilitated thrombolysis (eptifibatide + tenecteplase) vs. facilitated PCI (eptifibatide) in patients with STEMI
Alexander 1999	Substudy of the PURSUIT trial on the effect of prior use of aspirin in GP IIb/IIIa inhibitors use in unstable angina
BOCHUM 2004	Open-label pilot study to assess the practical application and safety of pre-hospital eptifibatide vs control in patients with suspected ACS. Patients were assigned eptifibatide or control in even/uneven days. Of the 356 patients included, only 42% had a NSTEMI, while 32% had a STEMI and 42% had a non specific chest pain.
Bellandi 2006	Comparison of Abciximab administered in the emergency room vs. in the catheterization laboratory
Blankenship 1998	EPIC substudy on local bleeding after GP IIb/IIIa inhibitors use
Boehrer 1994	EPIC substudy on the effect of abciximab in coronary artery bypass surgery
Brener 1999	RAPPORT substudy on the pattern of reperfusion in myocardial infarction patients treated with abciximab
CLOTILDA 2005	Comparison of tirofiban vs. provisional abciximab.
Cannon 1998	Trial with an oral GP IIb/IIIa antagonist (TIMI 12)
Casserly 1998	This is not a clinical trial but a case report
Clays 2002	Open-label, non-randomized study. Comparison of the degree of inhibition of platelet aggregation after the administration of a loading dose of clopidogrel vs. abciximab. Thirty-nine patients that underwent PCI with stent implantation
Costantini 2004	Substudy of the CADILLAC Trial
Cutlip 2003	Tirofiban vs control in the emergency room followed by any IIb/IIIa inhibitor during PCI a median of 90 min later
De Luca 2005	This is not a RCT but a descriptive study on the effects of abciximab in diabetic patients with or without metabolic control identified retrospectively

ELISA 2003	The ELISA pilot study. This study compared two different strategies in patients with UA/NSTEMI rather than two different treatments: immediate (median 6 h) ICP after randomization without pre-treatment with tirofiban versus delayed (median 50 h) ICP after prolonged pre-treatment with tirofiban. Thus, although tirofiban administration was randomized the basal conditions were different because of differences in timing of administration
EVEREST 2006	Comparison of tirofiban administered in the CCU vs. in the catheterization laboratory
Ercan 2004	Small study looking at differences in CRP at 48-72 h. No clinical events reported.
GRAPE 1999	Pilot study performed in 60 patients with STEMI treated with primary PCI without a control group. Not a randomized study
GUSTO V 2001	Trial comparing the addition of a GP IIb/IIIa antagonist to the fibrinolytic treatment in patients with ST-segment elevation acute myocardial infarction
Ghaffari 1998	EPILOG and EPIC joined subanalysis
Gunasekara 2006	A non-randomized comparison of abciximab vs. high-dose tirofiban
Hamm 1999	Substudy of the CAPTURE trial. Differential effects of abciximab in patients with refractory angina according to basal troponin levels
Hanefeld 2002	Pilot study of the BOCHUM trial
Heeschen 1999	Substudy of the PRISM trial. Effects of tirofiban in patients with UA/NSTEMI according to baseline troponin levels
IMPACT-AMI 1997	RCT on the effect of GP IIb/IIIa inhibitors in patients with ST-segment elevation acute myocardial infarction treated with thrombolytics
INTAMI 2005	Comparison of eptifibatid administered in the emergency room vs. in the cath lab in patients with STEMI submitted to primary PCI
Kereiakes 1997	Oral GP IIb/IIIa inhibitor xemilofiban. It is not a randomized clinical trial.
Kereiakes 1998a	Oral GP IIb/IIIa inhibitor xemilofiban
Kereiakes 1998b	Substudy of the EPILOG trial. Subanalysis in unplanned stent patients
Kleiman 1998	EPILOG subanalysis in patients with diabetes
Klootwijk 1998	CAPTURE substudy on silent ischaemia in GP IIb/IIIa inhibitors in unstable angina.
Krause 1996	Abstract from a Congress. A phase II RCT with 3 escalating doses of i.v. Fradafiban in 65 patients with stable angina submitted to elective PTCA. Aim: Safety and antiplatelet effects. No clinical events reported
Lefkovits 1996	EPIC substudy on the effects of abciximab on outcomes after percutaneous transluminal coronary angioplasty for acute myocardial infarction
Lenderink 2003	Substudy of the CAPTURE trial
Lincoff 1997	EPIC substudy of prevention of ischaemic complications in patients with unstable angina undergoing percutaneous transluminal coronary angioplasty
Mahaffey 1999	PURSUIT Substudy on stroke after GP IIb/IIIa inhibitors in unstable angina.
Mak 1997	EPIC non-randomized substudy on distal embolization during coronary artery bypass surgery
McClure 1999	PURSUIT substudy on the significance of thrombocytopenia after non-ST-elevation in acute coronary syndromes
McElwee 1997	Cost effectiveness analysis review
Miller 1999	Non-randomized GUSTO-III trial subanalysis on effectiveness of GP IIb/IIIa inhibitors in patients in whom thrombolysis failed.
Mockel 2005	Comparison of prehospital tirofiban versus fibrinolysis before direct PCI in patients with STEMI
Morrow 2001	Substudy of the TACTICS trial

Muller 1997	Analysis of the degree of platelet inhibition by an oral GP IIb/IIIa inhibitor fradafiban (ledrafiban is the active prodrug). Not a randomized clinical trial
Murdock 1997	Non-randomized study of patients with ST segment elevation acute myocardial infarction treated with GP IIb/IIIa inhibitors
Narins 1999	EPIC subanalysis on periprocedural myocardial infarction during percutaneous transluminal coronary angioplasty
Neumann 1998	Substudy on coronary flow and left ventricular ejection fraction after GP IIb/IIIa inhibitors in patients with ST-segment elevation acute myocardial infarction who underwent stent implantation.
Newby 1999	Design description of the SYMPHONY trial with oral GP IIb/IIIa inhibitor sibrafiban
Newby 2001	A substudy of the PARAGON-B study
On-TIME 2004	Pre-hospital tirofiban vs hospital (median delay 59 m) tirofiban during primary PCI in patients with ST-segment elevation acute myocardial infarction
PARADIGM 1998	Trial on GP IIb/IIIa blockers in patients with ST-segment elevation acute myocardial infarction treated with thrombolytics
PARAGON-B 2001	PARAGON-B substudy on the effects of lamifiban according to baseline troponin levels.
PROLOG 1997	Study on the effect of different doses of heparin in patients treated with abciximab during percutaneous revascularization
Petronio 2002	Rescue PCI in STEMI after thrombolysis
Prati 2005	Small study on the effects of abciximab on coronary microcirculation
REPLACE-2 2003	A comparison of bivalirudin plus any GP IIb/IIIa inhibitor on a provisional basis for complications during PCI, with heparin plus planned treatment with any GP IIb/IIIa inhibitor
ReoPro-BRIDGING 2004	Abciximab at admission versus abciximab immediately before primary PCI (mean difference 62 min) in patients with ST segment elevation myocardial infarction
Roe 2003	Treatment with eptifibatide vs placebo in the emergency department followed by open-label eptifibatide 12-24 h later.
SPEED P-St 2000	Primary PCI with or without GP IIb/IIIa antagonist in patients with ST-segment elevation acute myocardial infarction treated with a thrombolytic (facilitated PCI).
STOPAMI 2000	Primary PCI with stent and abciximab vs. thrombolysis in patients with STEMI
STOPAMI-2 2002	Controlled clinical trial with GP IIb/IIIa blockade in patients with ST-segment elevation acute myocardial infarction, comparing primary PCI with stenting and abciximab versus fibrinolysis and abciximab. No comparison was performed between abciximab and placebo or control.
SYMPHONY 2 2001	Controlled clinical trial with oral GP IIb/IIIa blockade with sibrafiban in patients with acute coronary syndromes 7 days or more after admission.
Simpfendorfer 1997	Controlled clinical trial with oral GP IIb/IIIa blockade with xemilofiban in patients with unstable angina undergoing percutaneous transluminal coronary angioplasty.
Steen 2005	Comparison of myocardial tissue perfusion with and without Tirofiban in patients with STEMI. No clinical events reported.
Svensson 2006	Thrombolysis vs facilitated PCI with abciximab in patients with STEMI
TAMI-8 1993	Pilot study on the effects of abciximab in patients with STEMI treated with thrombolytics
TARGET 2001	RCT comparing abciximab with tirofiban in patients submitted to PCI
TIGER-PA 2003	Open-label randomization of patients (n=100) with ST segment elevation MI to “early” administration of Tirofiban in the emergency room versus “late” administration in the catheterization laboratory immediately before primary PCI.
TIMI 14 1999	Thrombolysis with or without abciximab in patients with STEMI

Characteristics of excluded studies (Continued)

TIMI 15A 2000	A randomized open-label study of a new drug administered i.v. for 24 to 96 h in 91 patients. Patients were assigned to 1 of 9 regimens of RPR 109891. No Placebo group was included
Thiele 2005	Patients with STEMI were randomized to either pre-hospital facilitated fibrinolysis (half-dose reteplase+abciximab) or pre-hospital facilitated fibrinolysis (half-dose reteplase+abciximab) plus PCI
Valgimigli 2005	Comparison of tirofiban and an eluting stent vs. Abciximab + bare metal stent during primary PCI in patients with STEMI
Wong 2003	Small study (n=32) on the coronary flow reserve before and after stenting in patients receiving tirofiban vs. control. No data on clinical events
Zajdel 2002	Abstract from a congress, written in polish, with preliminary data. No clinical events.
Zhao 1999	PRISM plus substudy on angiographic results with tirofiban
van den Brand 1999	CAPTURE substudy on angiographic assessment of GPIIb/IIIa inhibitor use.
van den Merkhof 1999	Study on the TIMI perfusion grade of 60 patients with STEMI treated with abciximab in the emergency department. Not a RCT

Characteristics of ongoing studies

Study	EARLY-ACS
Trial name or title	The Early Glycoprotein IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndrome (EARLY ACS) trial
Participants	10,500 patients with high-risk unstable angina or non-ST elevation myocardial infarction. Patients have to have 2 of the following features: >0.1mm ST-segment depression or transient elevation in at least 2 contiguous leads, elevated troponin or CK-MB, or age>60 y. Patients must also be randomized within 12 h of presentation with a plan to undergo an invasive strategy no sooner than the next calendar day.
Interventions	Double bolus (10 min apart) of eptifibatide (180 µg/Kg i.v. + i.v. infusion of 2 µg/Kg/min for a maximum of 96 h, or matching placebo. Before initiation of PCI investigators may request an active kit to assure that the patients receives eptifibatide during PCI, in accordance with their standar practice. All patients will receive aspirin and heparin. At their discretion, investigators may select to administer 300 mg of clopidogrel at the time of randomization followed by 75 mg/day. Randomization will be stratified according to the investigator's plan to initiate clopidogrel early or not.
Outcomes	Primary: All-cause mortality, MI, urgent revascularization or thrombotic bailout within 96 h of randomization. Secondary: Death or MI within 30 days, death, MI or urgent revascularization within 30 d, death or MI within 96 h, and death within 30 d, 6 months and 1 year.
Starting date	March 2005
Contact information	The TIMI study group
Notes	

ADDITIONAL TABLES

Table 01. MEDLINE search strategy used for the original review

1 Clinical trial/ or Phase 1 clinical trial/ or Phase 2
clinical trial/ or Phase 3 clinical trial/ or Phase 4
clinical trial/ or Randomized controlled trial/

Table 01. MEDLINE search strategy used for the original review (Continued)

2 Randomization/
3 Double blind procedure/ or Meta analysis/ or Single blind
procedure/
4 exp controlled study/
5 Placebo/
6 ["150".tg.]
7 ["197".tg.]
8 (clinic\$ adj10 trial).ti,ab.
9 (clinic\$ adj10 trial\$).ti,ab.
10 (controlled adj trial\$).ti,ab.
11 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj10 (blind\$ or
mask\$)).ti,ab.
12 (placebo\$ or random\$).ti,ab.
13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 9 or 10 or 11 or 12
14limit 13 to human
15("glycoprotein IIb/IIIa" or "glycoprotein IIb-IIIa" or "glycoprotein-IIb/IIIa" or "Platelet IIb/IIIa" or "GP IIb-IIIa" or "GP IIb/IIIa"
or "IIb" or "IIIa").mp. [mp=Title, Abstract, registry number word, mesh subject heading]
16(Abciximab or 7E3 or Sibrafiban or Tirofiban or MK-383 or lamifiban or Aggrastat or Eptifibatide or Xemilofiban or Sibrafiban or
Orbofiban or Lefradafiban or Integrilin or Integrelin or Fradafiban or Lefradafiban).mp. [mp=Title, Abstract, registry number word,
mesh subject heading]
17(Inhibitor\$ or block\$ or antagonist\$).mp. [mp=Title, Abstract, registry number word, mesh subject heading]
1814 and (15 or 16) and 17

Table 02. MEDLINE search strategy for update

Database: Ovid MEDLINE(R) <1966 to June 2006>

Search Strategy:

1 Platelet Glycoprotein GPIIb-IIIa Complex/ (3571)
2 (glycoprotein adj5 (inhibit\$ or block\$ or antagonist\$)).tw. (5432)
3 gpIIb\$.tw. (2142)
4 abciximab.tw. (1005)
5 sibrafiban.tw. (31)
6 tirofiban.tw. (409)
7 lamifiban.tw. (47)
8 aggrastat.tw. (48)
9 eptifibatide.tw. (364)
10 xemilofiban.tw. (24)
11 lotrafiban.tw. (16)
12 orbofiban.tw. (33)
13 roxifiban.tw. (37)
14 or/1-13 (9629)
15 exp Angioplasty, Transluminal, Percutaneous Coronary/ (15946)
16 ptca.tw. (5386)
17 (coronary adj5 angioplasty).tw. (12103)
18 exp Angina, Unstable/ (7228)
19 angina.tw. (30002)
20 exp Stents/ (19760)
21 stent\$.tw. (22776)

Table 02. MEDLINE search strategy for update (Continued)

22 exp Myocardial Infarction/ (97227)
23 myocardial infarction.tw. (73572)
24 coronary syndrome\$.tw. (4479)
25 pci.tw. (2279)
26 percutaneous coronary intervention\$.tw. (2385)
27 or/15-26 (170987)
28 14 and 27 (2425)
29 randomized controlled trial.pt. (197725)
30 controlled clinical trial.pt. (67695)
31 Randomized controlled trials/ (36070)
32 random allocation.sh. (52478)
33 double blind method.sh. (80436)
34 single-blind method.sh. (8703)
35 or/29-34 (336066)
36 exp animal/ not human/ (2859420)
37 35 not 36 (317558)
38 clinical trial.pt. (399236)
39 exp Clinical trials/ (162490)
40 (clin\$ adj25 trial\$).ti,ab. (106928)
41 ((singl\$ or doubl\$ or trebl\$ or tripl\$) adj (blind\$ or mask\$)).ti,ab. (77018)
42 placebos.sh. (23449)
43 placebo\$.ti,ab. (87216)
44 random\$.ti,ab. (302049)
45 research design.sh. (39920)
46 or/38-45 (709458)
47 46 not 36 (659080)
48 37 or 47 (669641)
49 28 and 48 (1261)
50 limit 49 to yr=2001 - 2005 (759)

Table 03. EMBASE search strategy for update

Database: EMBASE <1980 to 2006 Week 15>

Search Strategy:

1 exp Fibrinogen Receptor/ (2876)
2 (glycoprotein adj5 (inhibit\$ or block\$ or antagonist\$)).tw. (5372)
3 gpIIb\$.tw. (2134)
4 abciximab.tw. (1093)
5 sibrafiban.tw. (34)
6 tirofiban.tw. (475)
7 lamifiban.tw. (62)
8 aggrastat.tw. (514)
9 eptifibatide.tw. (429)
10 xemilofiban.tw. (34)
11 lotrafiban.tw. (16)
12 orbofiban.tw. (43)
13 roxifiban.tw. (38)
14 or/1-13 (9853)

Table 03. EMBASE search strategy for update (Continued)

15 exp Transluminal Coronary Angioplasty/ (12578)
 16 ptca.tw. (5143)
 17 (coronary adj5 angioplasty).tw. (11403)
 18 exp Unstable Angina Pectoris/ (6443)
 19 angina.tw. (25018)
 20 exp coronary stent/ (5644)
 21 stent\$.tw. (22056)
 22 exp Heart Infarction/ (82147)
 23 myocardial infarction.tw. (62146)
 24 coronary syndrome\$.tw. (4572)
 25 pci.tw. (2533)
 26 percutaneous coronary intervention\$.tw. (2560)
 27 or/15-26 (139054)
 28 14 and 27 (2748)
 29 random\$.ti,ab. (271599)
 30 factorial\$.ti,ab. (5496)
 31 (crossover\$ or cross over\$ or cross-over\$).ti,ab. (31427)
 32 placebo\$.ti,ab. (84622)
 33 (double\$ adj blind\$).ti,ab. (68018)
 34 (singl\$ adj blind\$).ti,ab. (5722)
 35 assign\$.ti,ab. (78287)
 36 allocat\$.ti,ab. (24638)
 37 volunteer\$.ti,ab. (78791)
 38 Crossover Procedure/ (16005)
 39 Double Blind Procedure/ (55153)
 40 Randomized Controlled Trial/ (93598)
 41 Single Blind Procedure/ (5221)
 42 or/29-41 (478079)
 43 exp animal/ (88648)
 44 nonhuman/ (2535992)
 45 exp animal experiment/ (1072204)
 46 or/43-45 (2774573)
 47 exp human/ (4915811)
 48 46 not 47 (2422869)
 49 42 not 48 (418963)
 50 49 and 28 (763)
 51 limit 50 to yr=2000 - 2005 (569)
 52 from 51 keep 1-569 (569)

Table 04. Main results for the primary outcomes

Intervention	30-day mortality	30-day death or MI	6-month mortality	6-month death or MI
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
1. PCI (all patients)	0.74 (0.58 to 0.94)	0.67 (0.61 to 0.74)	0.86 (0.72 to 1.04)	0.71 (0.61 to 0.82)
Subgroup analysis by patient's condition				
PCI in NSTEMACS	0.73 (0.45 to 1.17)	0.73 (0.61 to 0.87)	1.04 (0.76 to 1.43)	0.81 (0.69 to 0.97)
PCI in STEMI	0.81 (0.53 to 1.26)	0.70 (0.49 to 1.01)	0.79 (0.57 to 1.10)	0.77 (0.59 to 1.00)

Table 04. Main results for the primary outcomes (Continued)

Intervention	30-day mortality	30-day death or MI	6-month mortality	6-month death or MI
PCI in stable CAD	0.77 (0.34 to 1.73)	0.75 (0.59 to 0.94)	0.84 (0.59 to 1.19)	0.79 (0.65 to 0.96)
Subgroup analysis by technique				
Balloon PCI	0.77 (0.54 to 1.12)	0.62 (0.49 to 0.79)	1.06 (0.75 to 1.50)	0.78 (0.65 to 0.94)
PCI + stent	0.67 (0.46 to 0.96)	0.67 (0.59 to 0.78)	0.75 (0.59 to 0.95)	0.68 (0.60 to 0.78)
Subgroup analysis by concomitant treatment				
PCI + clopidogrel	0.73 (0.42 to 1.27)	0.83 (0.69 to 1.01)	0.92 (0.70 to 1.22)	0.84 (0.71 to 1.00)
2. As initial medical treatment of NSTEMACS	0.92 (0.81 to 1.04)	0.92 (0.86 to 0.99)	1.01 (0.88 to 1.16)	0.88 (0.81 to 0.96)

MI, myocardial infarction; PCI, percutaneous coronary intervention; NSTEMACS, non-ST segment elevation acute coronary syndrome; STEMI, ST segment elevation myocardial infarction; CAD, coronary artery disease

Table 05. Main results for the secondary outcomes

Intervention	30-day urgent revasc	30-d death, MI, rev	6-m revasc	6-m death, MI, rev
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
1. PCI (all patients)	0.60 (0.52 to 0.69)	0.65 (0.57 to 0.74)	0.86 (0.79 to 0.93)	0.78 (0.71 to 0.87)
Subgroup analysis by patient's condition				
PCI in NSTEMACS	0.72 (0.55 to 0.93)	0.72 (0.61 to 0.85)	0.92 (0.79 to 1.06)	0.86 (0.76 to 0.97)
PCI in STEMI	0.43 (0.28 to 0.65)	0.54 (0.41 to 0.72)	0.76 (0.62 to 0.95)	0.77 (0.64 to 0.92)
PCI in stable CAD	0.86 (0.55 to 1.35)	0.78 (0.63 to 0.97)	0.93 (0.81 to 1.08)	0.88 (0.78 to 1.00)
Subgroup analysis by technique				
Balloon PCI	0.57 (0.48 to 0.69)	0.62 (0.50 to 0.76)	0.81 (0.60 to 1.10)	0.82 (0.73 to 0.93)
PCI + stent	0.70 (0.53 to 0.93)	0.68 (0.60 to 0.78)	0.87 (0.78 to 0.99)	0.73 (0.62 to 0.85)
Subgroup analysis by concomitant treatment				
PCI + clopidogrel	0.85 (0.58 to 1.24)	0.90 (0.74 to 1.09)	0.89 (0.78 to 1.02)	0.87 (0.77 to 0.98)

d, day; m, month; revasc (rev), revascularization; MI, myocardial infarction; PCI, percutaneous coronary intervention; NSTEMACS, non-ST elevation acute coronary syndrome;

Table 05. Main results for the secondary outcomes (Continued)

Intervention	30-day urgent revasc	30-d death, MI, rev	6-m revasc	6-m death, MI, rev
STEMI, ST segment elevation myocardial infarction; CAD, coronary artery disease				

Table 06. Main results for safety outcomes

Intervention	30-d major bleeding OR (95% CI)
1. PCI (all patients)	1.38 (1.19 to 1.60)
Subgroup analysis by patient's condition	
PCI in NSTEMACS	1.39 (1.04 to 1.85)
PCI in STEMI	1.71 (1.09 to 2.69)
PCI in stable CAD	1.74 (1.03 to 2.95)
Subgroup analysis by technique	
Balloon PCI	1.37 (1.01 to 1.88)
PCI + stent	1.30 (0.91 to 1.87)
Subgroup analysis by concomitant treatment	
PCI + clopidogrel	1.33 (0.89 to 1.98)
2. As initial medical treatment of NSTEMACS	1.27 (1.12 to 1.44)
d, day; PCI, percutaneous coronary intervention; NSTEMACS, non-ST elevation acute coronary syndrome; STEMI, ST elevation myocardial infarction; CAD, coronary artery disease	

ANALYSES**Comparison 01. PCI (all patients)**

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	29	27642	Odds Ratio (Fixed) 95% CI	0.74 [0.58, 0.94]
02 30-day mortality or myocardial infarction	29	27642	Odds Ratio (Fixed) 95% CI	0.67 [0.61, 0.74]
03 6-month mortality	19	21542	Odds Ratio (Fixed) 95% CI	0.87 [0.73, 1.03]
04 6-month mortality or myocardial infarction	19	21542	Odds Ratio (Random) 95% CI	0.71 [0.62, 0.82]
05 30-day urgent revascularisation	28	27317	Odds Ratio (Fixed) 95% CI	0.60 [0.52, 0.69]
06 30-day mortality, myocardial infarction or urgent revascularisation	28	27317	Odds Ratio (Random) 95% CI	0.65 [0.57, 0.74]
07 30-day major bleeding	26	26931	Odds Ratio (Fixed) 95% CI	1.38 [1.19, 1.60]
08 6-month urgent revascularisation	17	18654	Odds Ratio (Fixed) 95% CI	0.86 [0.79, 0.93]

09 6-month mortality, myocardial infarction or urgent revascularisation	18	18750	Odds Ratio (Random) 95% CI	0.78 [0.71, 0.87]
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Comparison 02. As initial medical treatment in patients with NSTEMACS

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	8	30351	Odds Ratio (Fixed) 95% CI	0.92 [0.81, 1.04]
02 30-day mortality or myocardial infarction	8	30351	Odds Ratio (Fixed) 95% CI	0.92 [0.86, 0.99]
03 6-month mortality	3	13658	Odds Ratio (Fixed) 95% CI	1.01 [0.88, 1.16]
04 6-month mortality or myocardial infarction	4	18883	Odds Ratio (Fixed) 95% CI	0.88 [0.81, 0.96]
05 30-day major bleeding	8	29920	Odds Ratio (Fixed) 95% CI	1.27 [1.12, 1.44]

Comparison 03. PCI in patients with NSTEMACS

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	6	6206	Odds Ratio (Fixed) 95% CI	0.73 [0.45, 1.17]
02 30-day mortality or myocardial infarction	6	6206	Odds Ratio (Fixed) 95% CI	0.73 [0.61, 0.87]
03 6-month mortality	3	5426	Odds Ratio (Fixed) 95% CI	1.04 [0.76, 1.43]
04 6-month mortality or myocardial infarction	3	5426	Odds Ratio (Fixed) 95% CI	0.81 [0.69, 0.97]
05 30-day urgent revascularisation	5	5881	Odds Ratio (Fixed) 95% CI	0.72 [0.55, 0.93]
06 30-day mortality, myocardial infarction or urgent revascularisation	5	5881	Odds Ratio (Fixed) 95% CI	0.72 [0.61, 0.85]
07 30-day major bleeding	5	5813	Odds Ratio (Fixed) 95% CI	1.39 [1.04, 1.85]
08 6-month urgent revascularisation	3	5426	Odds Ratio (Fixed) 95% CI	0.92 [0.79, 1.06]
09 6-month mortality, myocardial infarction or urgent revascularisation	3	5426	Odds Ratio (Fixed) 95% CI	0.86 [0.76, 0.97]

Comparison 04. Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	4	3265	Odds Ratio (Fixed) 95% CI	0.81 [0.53, 1.26]
02 30-day mortality or myocardial infarction	4	3265	Odds Ratio (Fixed) 95% CI	0.70 [0.49, 1.01]
03 6-month mortality	4	3265	Odds Ratio (Fixed) 95% CI	0.79 [0.57, 1.10]
04 6-month mortality or myocardial infarction	4	3265	Odds Ratio (Fixed) 95% CI	0.77 [0.59, 1.00]
05 30-day urgent revascularisation	4	3265	Odds Ratio (Fixed) 95% CI	0.43 [0.28, 0.65]
06 30-day mortality, myocardial infarction or urgent revascularisation	4	3265	Odds Ratio (Fixed) 95% CI	0.54 [0.41, 0.72]
07 30-day major bleeding	4	3265	Odds Ratio (Fixed) 95% CI	1.71 [1.09, 2.69]

08 6-month urgent revascularisation	4	3265	Odds Ratio (Fixed) 95% CI	0.76 [0.62, 0.95]
09 6-month mortality, myocardial infarction or urgent revascularisation	4	3265	Odds Ratio (Fixed) 95% CI	0.77 [0.64, 0.92]

Comparison 05. PCI in stable coronary patients

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	8	5494	Odds Ratio (Fixed) 95% CI	0.77 [0.34, 1.73]
02 30-day mortality or myocardial infarction	8	5494	Odds Ratio (Fixed) 95% CI	0.75 [0.59, 0.94]
03 6-month mortality	6	5722	Odds Ratio (Fixed) 95% CI	0.84 [0.59, 1.19]
04 6-month mortality or myocardial infarction	6	5722	Odds Ratio (Fixed) 95% CI	0.79 [0.65, 0.96]
05 30-day urgent revascularisation	8	5494	Odds Ratio (Fixed) 95% CI	0.86 [0.55, 1.35]
06 30-day mortality, myocardial infarction or urgent revascularisation	8	5494	Odds Ratio (Fixed) 95% CI	0.78 [0.63, 0.97]
07 30-day major bleeding	8	5494	Odds Ratio (Fixed) 95% CI	1.74 [1.03, 2.95]
08 6-month urgent revascularisation	6	5722	Odds Ratio (Fixed) 95% CI	0.93 [0.81, 1.08]
09 6-month mortality, myocardial infarction or urgent revascularisation	6	5722	Odds Ratio (Fixed) 95% CI	0.88 [0.78, 1.00]

Comparison 06. Balloon PCI

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	10	12440	Odds Ratio (Fixed) 95% CI	0.77 [0.54, 1.12]
02 30-day mortality or myocardial infarction	10	12440	Odds Ratio (Random) 95% CI	0.62 [0.49, 0.79]
03 6-month mortality	4	5291	Odds Ratio (Fixed) 95% CI	1.06 [0.75, 1.50]
04 6-month mortality or myocardial infarction	4	5291	Odds Ratio (Fixed) 95% CI	0.78 [0.65, 0.94]
05 30-day urgent revascularisation	10	12440	Odds Ratio (Fixed) 95% CI	0.57 [0.48, 0.69]
06 30-day mortality, myocardial infarction or urgent revascularisation	10	12440	Odds Ratio (Random) 95% CI	0.62 [0.50, 0.76]
07 30-day major bleeding	9	12347	Odds Ratio (Random) 95% CI	1.37 [1.01, 1.88]
08 6-month urgent revascularisation	4	5291	Odds Ratio (Random) 95% CI	0.81 [0.60, 1.10]
09 6-month mortality, myocardial infarction or urgent revascularisation	4	5291	Odds Ratio (Fixed) 95% CI	0.82 [0.73, 0.93]

Comparison 07. PCI with stent implantation

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	16	12669	Odds Ratio (Fixed) 95% CI	0.67 [0.46, 0.96]
02 30-day mortality or myocardial infarction	16	12669	Odds Ratio (Fixed) 95% CI	0.67 [0.59, 0.78]
03 6-month mortality	12	10875	Odds Ratio (Fixed) 95% CI	0.75 [0.59, 0.95]
04 6-month mortality or myocardial infarction	12	10875	Odds Ratio (Fixed) 95% CI	0.68 [0.60, 0.78]
05 30-day urgent revascularisation	16	12669	Odds Ratio (Fixed) 95% CI	0.70 [0.53, 0.93]
06 30-day mortality, myocardial infarction or urgent revascularisation	16	12669	Odds Ratio (Fixed) 95% CI	0.68 [0.60, 0.78]
07 30-day major bleeding	14	12051	Odds Ratio (Fixed) 95% CI	1.30 [0.91, 1.87]
08 6-month urgent revascularisation	11	10779	Odds Ratio (Fixed) 95% CI	0.87 [0.78, 0.99]
09 6-month mortality, myocardial infarction or urgent revascularisation	12	10874	Odds Ratio (Random) 95% CI	0.73 [0.62, 0.85]

Comparison 08. PCI in patients pre-treated with clopidogrel

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 30-day mortality	8	6098	Odds Ratio (Fixed) 95% CI	0.73 [0.42, 1.27]
02 30-day mortality or myocardial infarction	8	6098	Odds Ratio (Fixed) 95% CI	0.83 [0.69, 1.01]
03 6-month mortality	7	5882	Odds Ratio (Fixed) 95% CI	0.92 [0.70, 1.22]
04 6-month mortality or myocardial infarction	7	5882	Odds Ratio (Fixed) 95% CI	0.84 [0.71, 1.00]
05 30-day urgent revascularisation	7	5773	Odds Ratio (Fixed) 95% CI	0.85 [0.58, 1.24]
06 30-day mortality, myocardial infarction or urgent revascularisation	7	5682	Odds Ratio (Fixed) 95% CI	0.90 [0.74, 1.09]
07 30-day major bleeding	7	5705	Odds Ratio (Fixed) 95% CI	1.33 [0.89, 1.98]
08 6-month urgent revascularisation	6	5786	Odds Ratio (Fixed) 95% CI	0.89 [0.78, 1.02]
09 6-month mortality, myocardial infarction or urgent revascularisation	7	5882	Odds Ratio (Fixed) 95% CI	0.87 [0.77, 0.98]

INDEX TERMS

Medical Subject Headings (MeSH)

Angina, Unstable [complications]; Angioplasty, Transluminal, Percutaneous Coronary [*methods]; Aspirin [therapeutic use]; Fibrinolytic Agents [therapeutic use]; Heparin [therapeutic use]; Myocardial Infarction [drug therapy; mortality; *prevention & control]; Platelet Glycoprotein GPIIb-IIIa Complex [*antagonists & inhibitors]; Ticlopidine [therapeutic use]

MeSH check words

Humans

COVER SHEET

Title	Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes
Authors	Bosch X, Loma-Osorio P, Marrugat J
Contribution of author(s)	<p>Xavier Bosch originated and was primarily responsible for planning and carrying out the review, was the principal author and prepared the results and clinical discussion of the findings.</p> <p>Pablo Loma-Osorio participated in reviewing the studies and preparing the tables</p> <p>Jaume Marrugat, was active in the design of the review and in providing critical revisions of the manuscript. He had primary responsibility for the methods section and performed the statistical analyses.</p> <p>All three reviewers participated in the design of the review, study selection, review of pre-selected studies, data extraction and in the preparation of the manuscript.</p>
Issue protocol first published	2000/2
Review first published	2001/4
Date of most recent amendment	14 November 2007
Date of most recent SUBSTANTIVE amendment	22 December 2006
What's New	<p>Update September 2007</p> <p>In the current version we have used the terms percutaneous coronary intervention (PCI) and non-ST segment elevation acute coronary syndromes (NSTEMACS) for clarity, and addressed the efficacy of IIb/IIIa blockers in two main indications:</p> <ol style="list-style-type: none">1. During PCI (i.e. percutaneous transluminal coronary balloon angioplasty with or without stent implantation) in patients with or without an acute coronary syndrome.2. As the initial medical management of NSTEMACS (i.e. unstable angina and non-ST segment elevation acute myocardial infarction). <p>We have added 16 new studies in the PCI group and performed six new subanalyses in this group according to the patient's condition (NSTEMACS, STEMI, stable patients), the technique used (ballon PCI, stent) and concomitant treatment (clopidogrel).</p> <p>Conclusions about IIb/IIIa blockers during PCI are unchanged. Conclusions about IIb/IIIa blockers as initial treatment of NSTEMACS are unchanged.</p>
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	10 September 2007
Date authors' conclusions section amended	10 September 2007
Contact address	<p>Dr Xavier Bosch Director, Coronary Care Unit Department of Cardiology Hospital Clinic, University of Barcelona Villarroel 170 Barcelona 08036</p>

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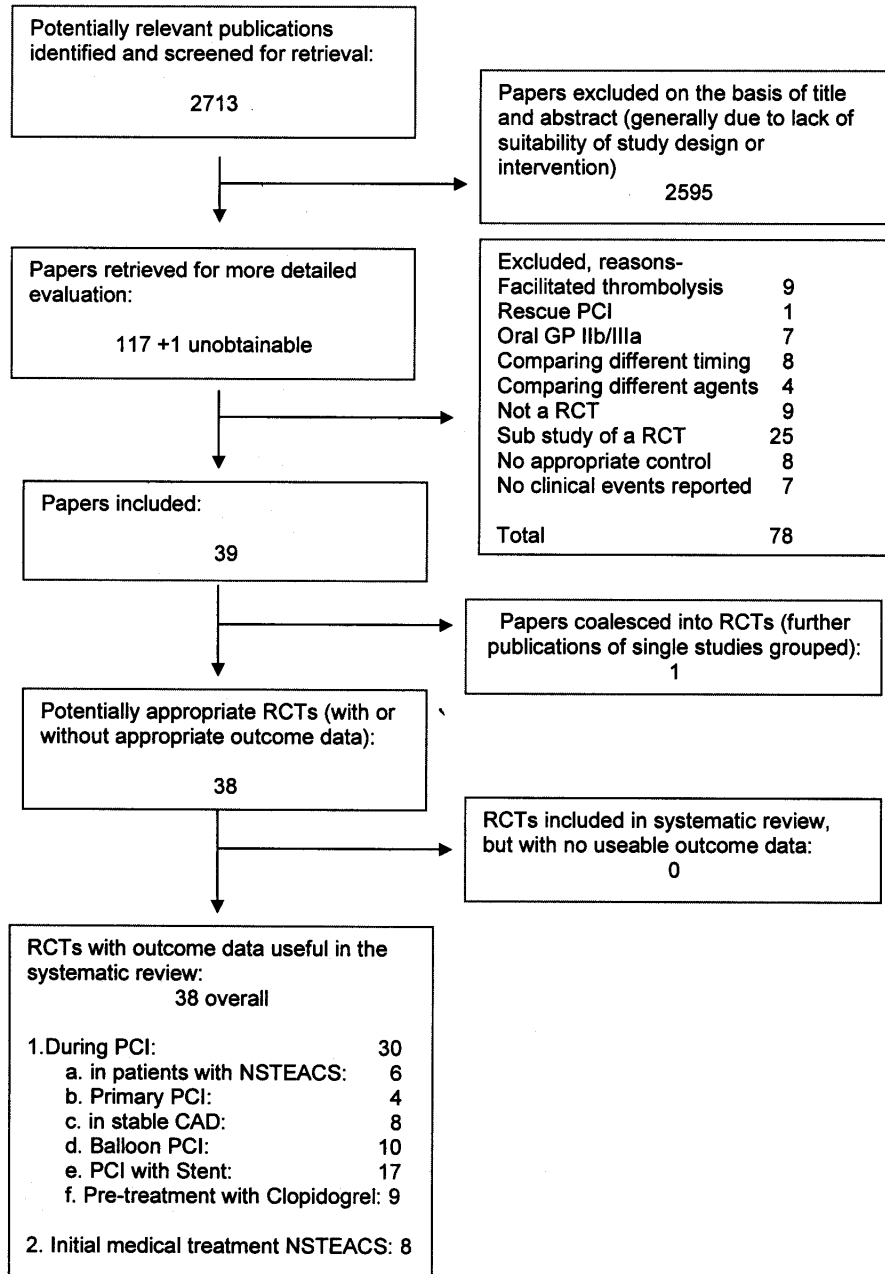
DOI 10.1002/14651858.CD002130
Cochrane Library number CD002130
Editorial group Cochrane Heart Group
Editorial group code HM-VASC

GRAPHS AND OTHER TABLES

Figure 01.

9810 Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention, and as initial treatment in Non-ST segment elevation Acute Coronary Syndromes

Figure 1. Flow diagram of systematic review (Quorum statement flow diagram)

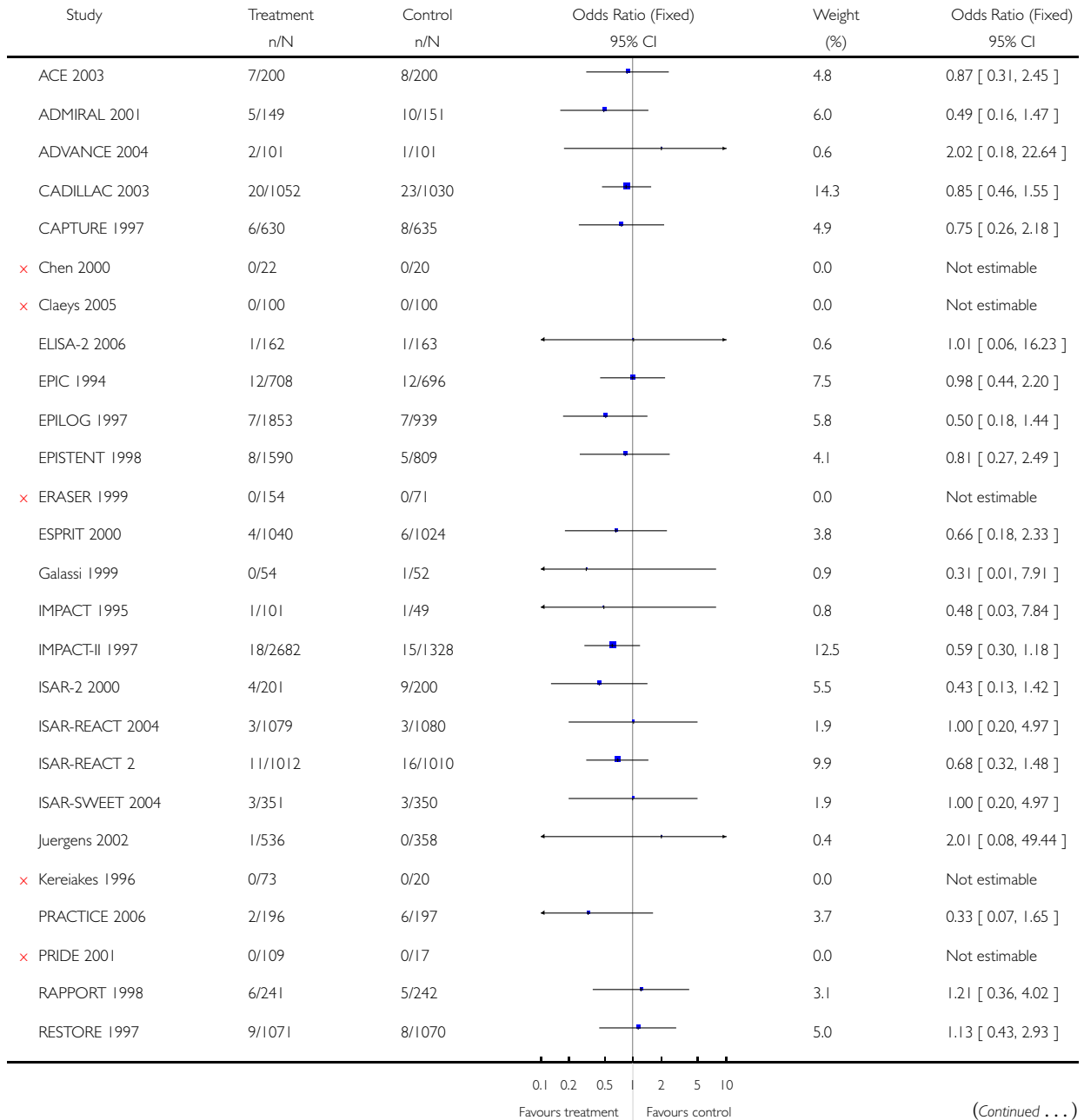


Analysis 01.01. Comparison 01 PCI (all patients), Outcome 01 30-day mortality

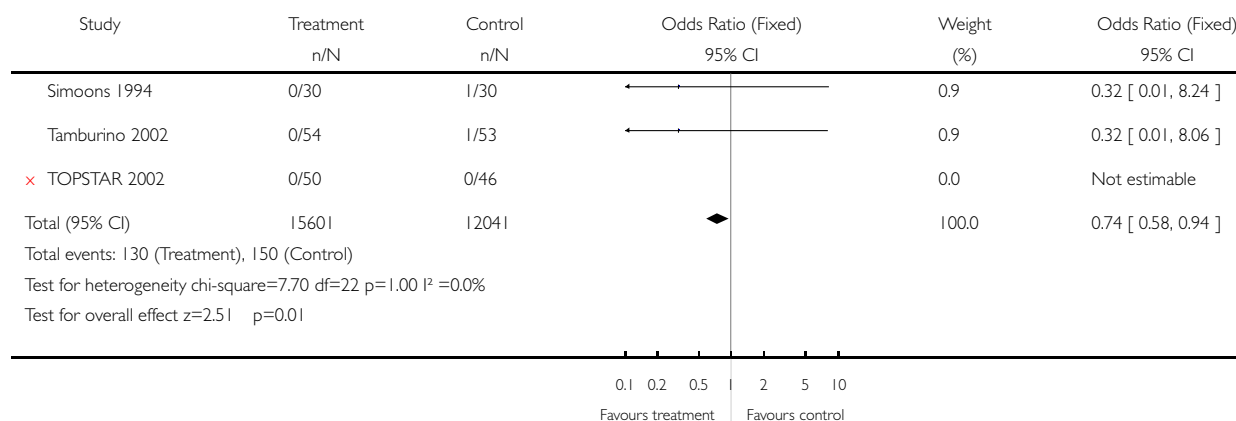
Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 01 30-day mortality



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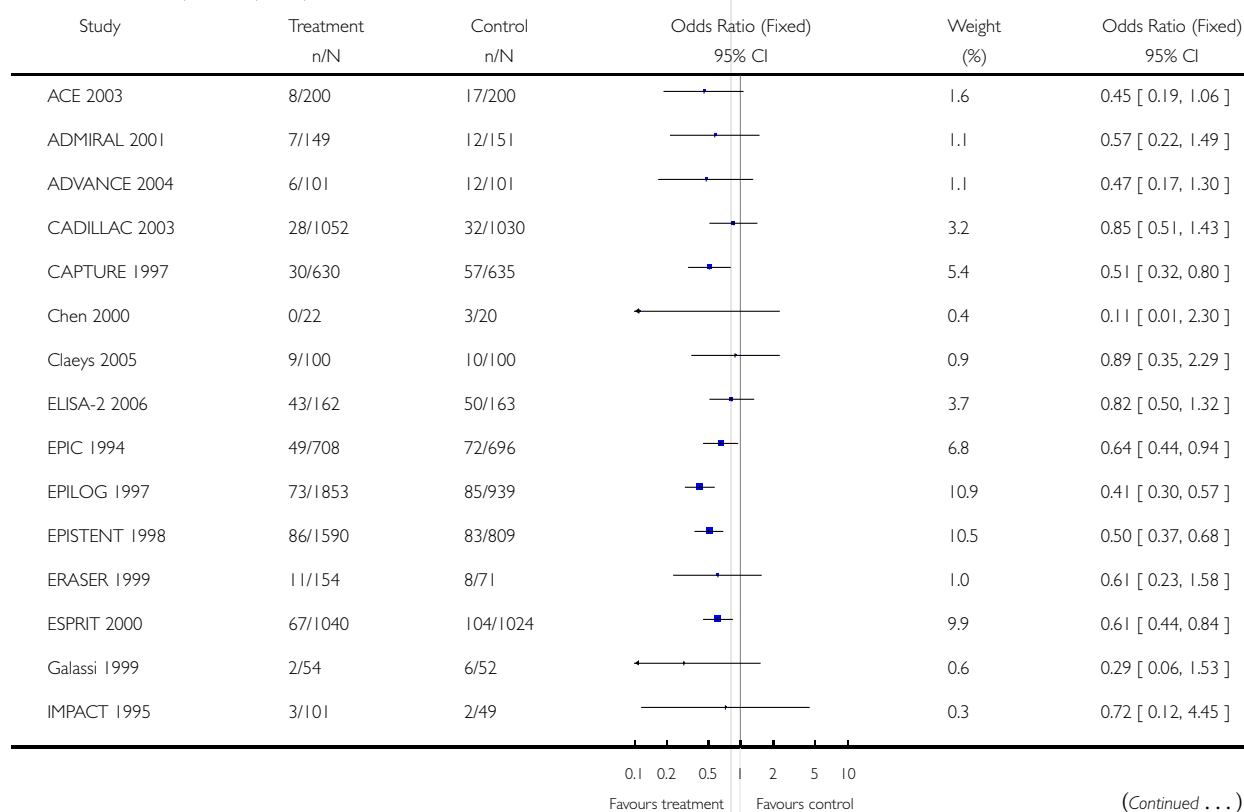


Analysis 01.02. Comparison 01 PCI (all patients), Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

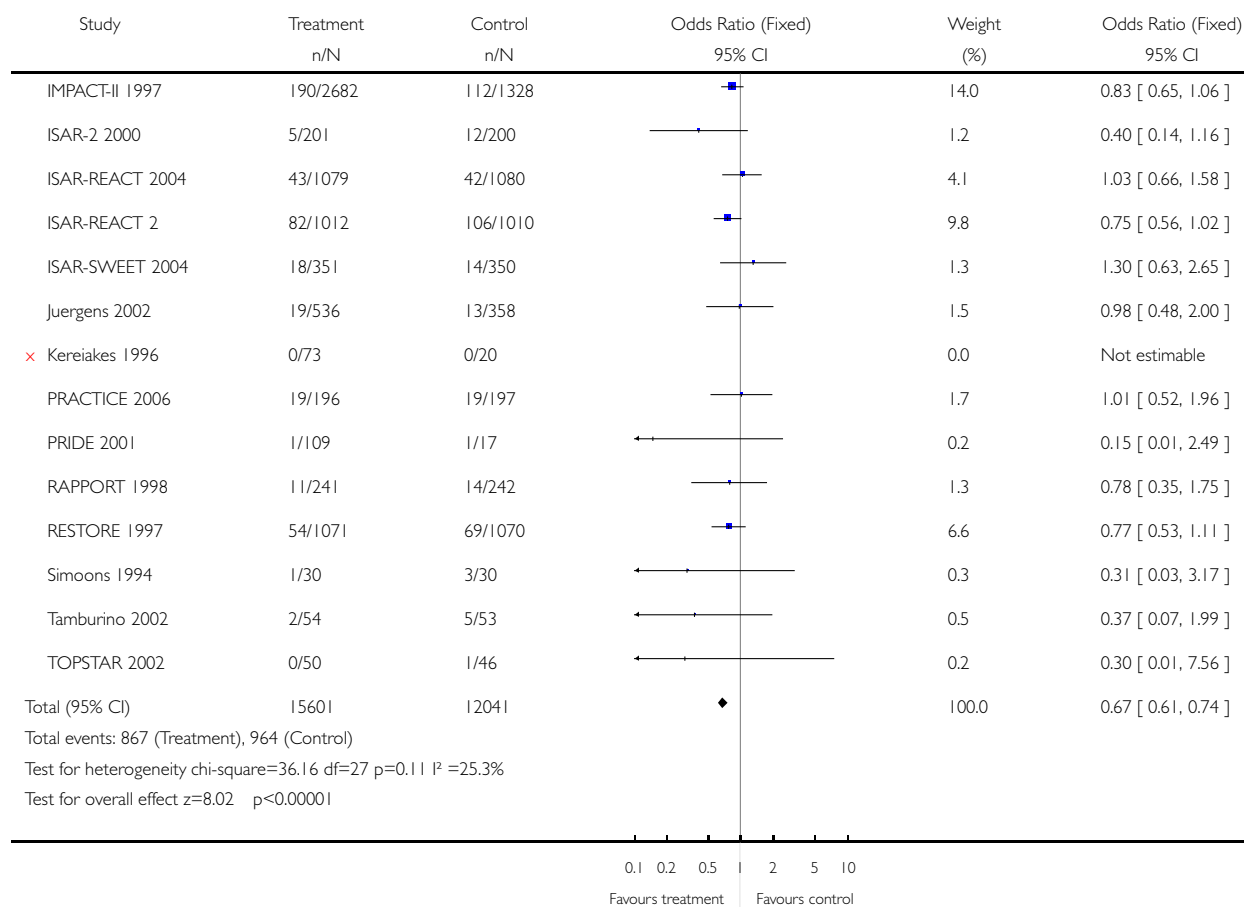
Comparison: 01 PCI (all patients)

Outcome: 02 30-day mortality or myocardial infarction



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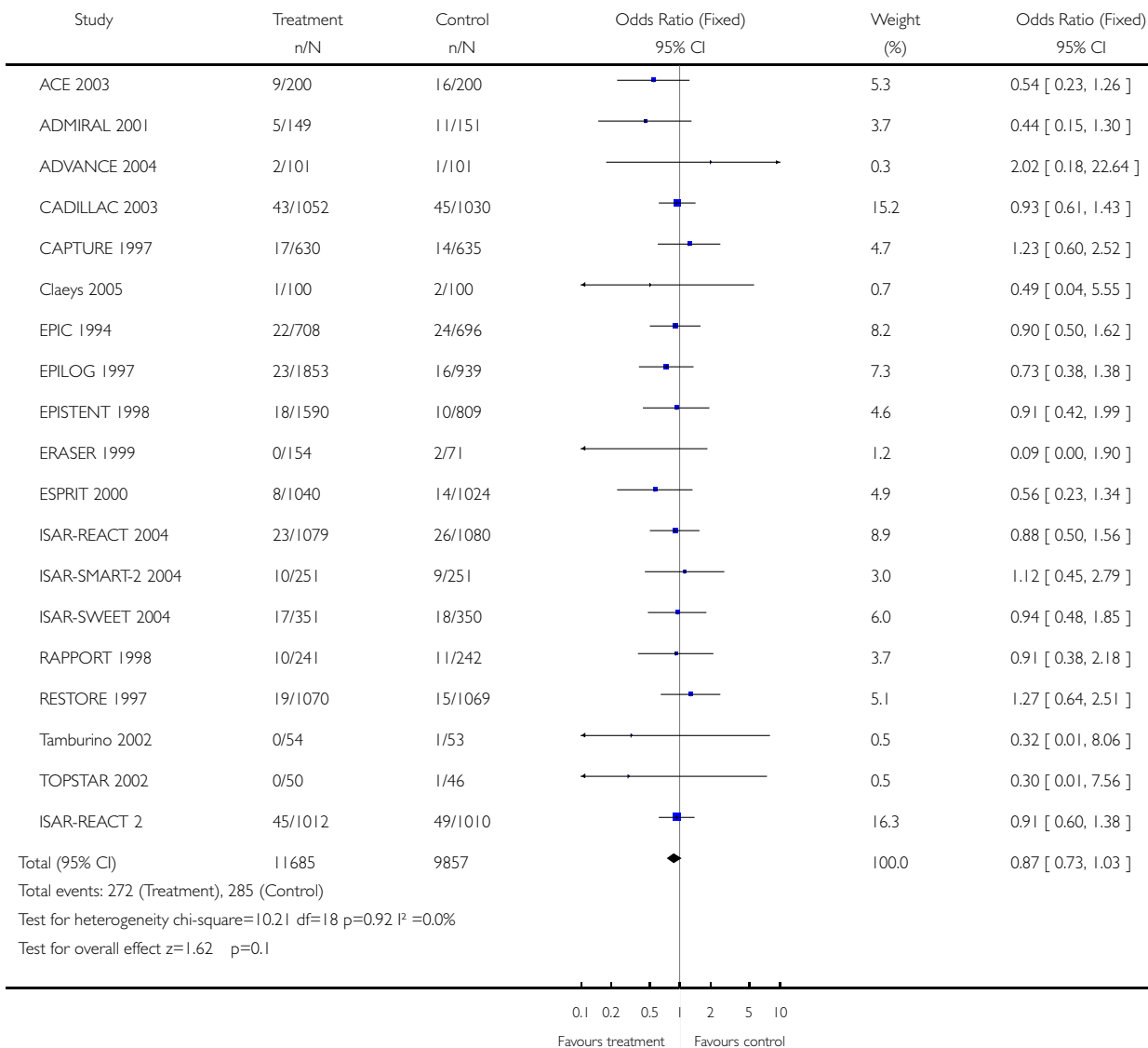


Analysis 01.03. Comparison 01 PCI (all patients), Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 03 6-month mortality

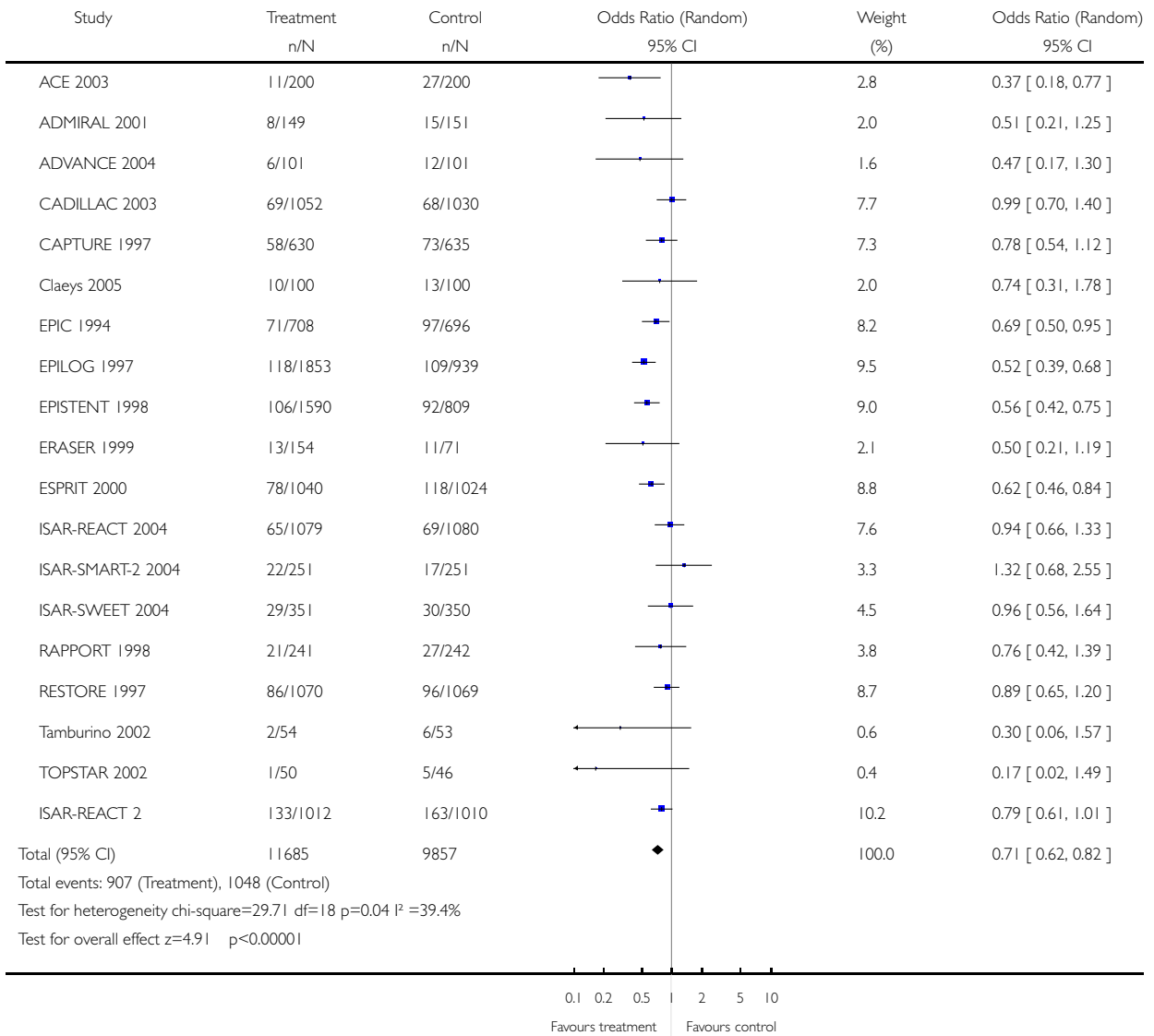


Analysis 01.04. Comparison 01 PCI (all patients), Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 04 6-month mortality or myocardial infarction

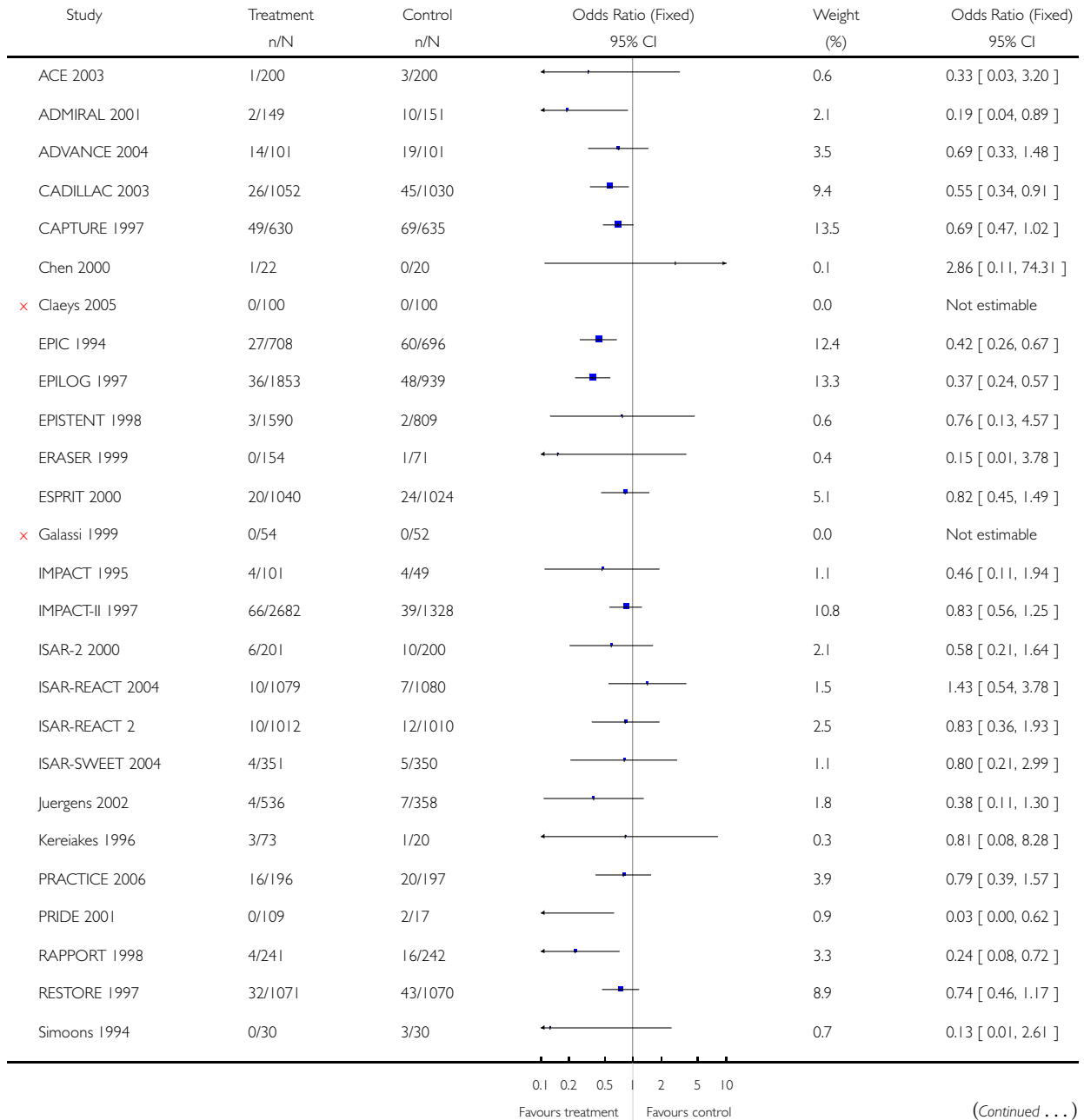


Analysis 01.05. Comparison 01 PCI (all patients), Outcome 05 30-day urgent revascularisation

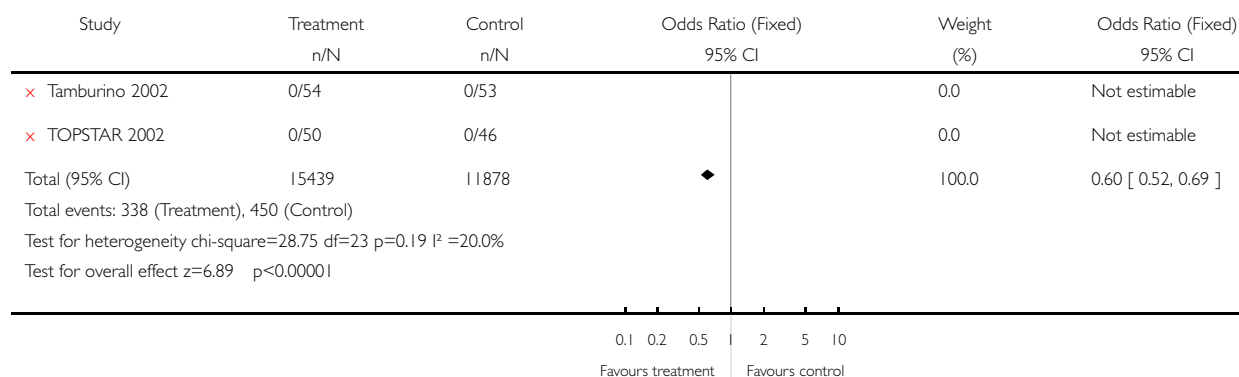
Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 05 30-day urgent revascularisation



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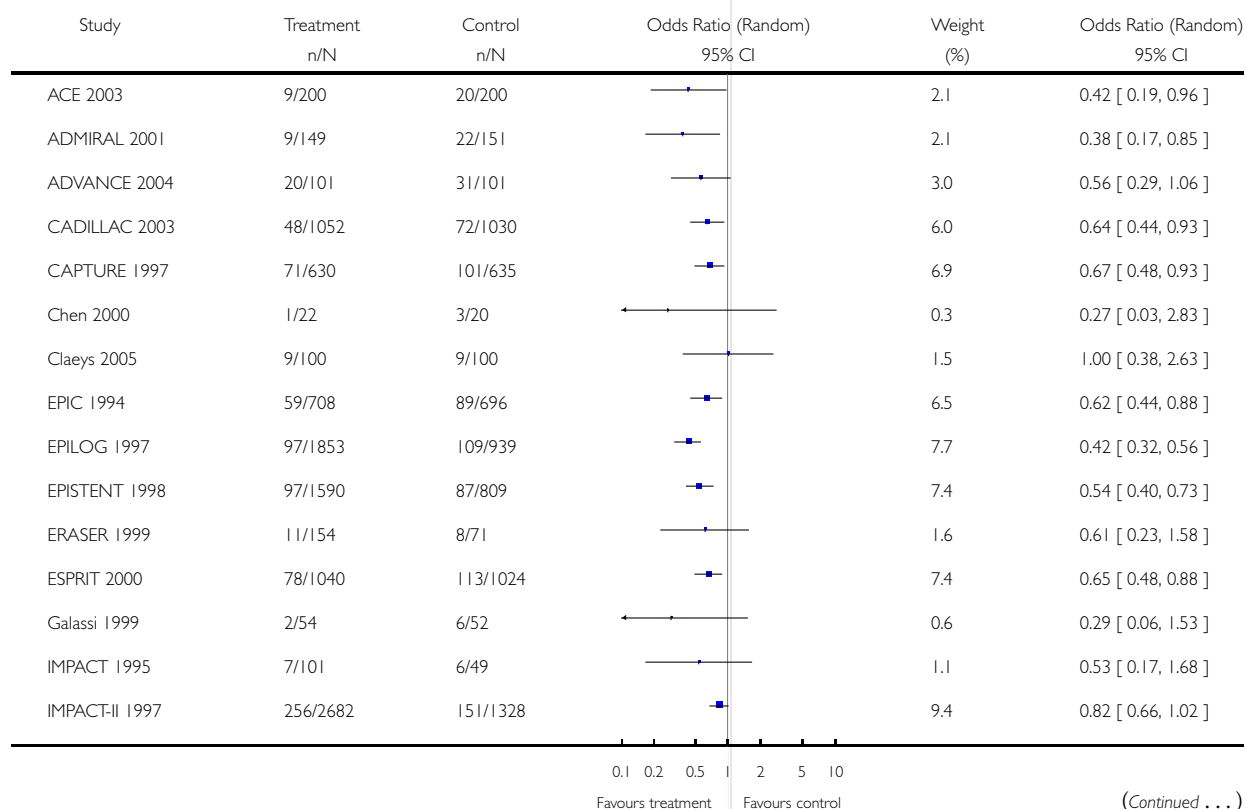


Analysis 01.06. Comparison 01 PCI (all patients), Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

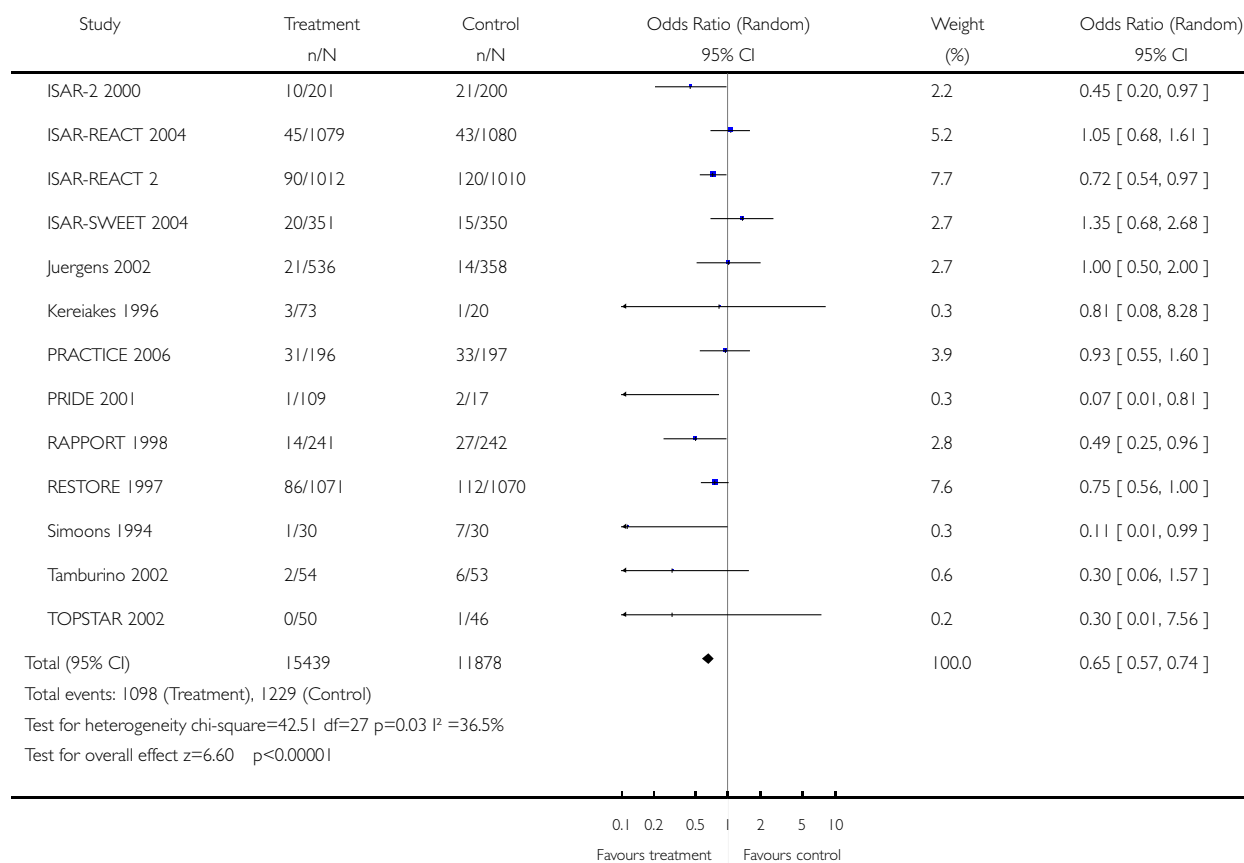
Comparison: 01 PCI (all patients)

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation



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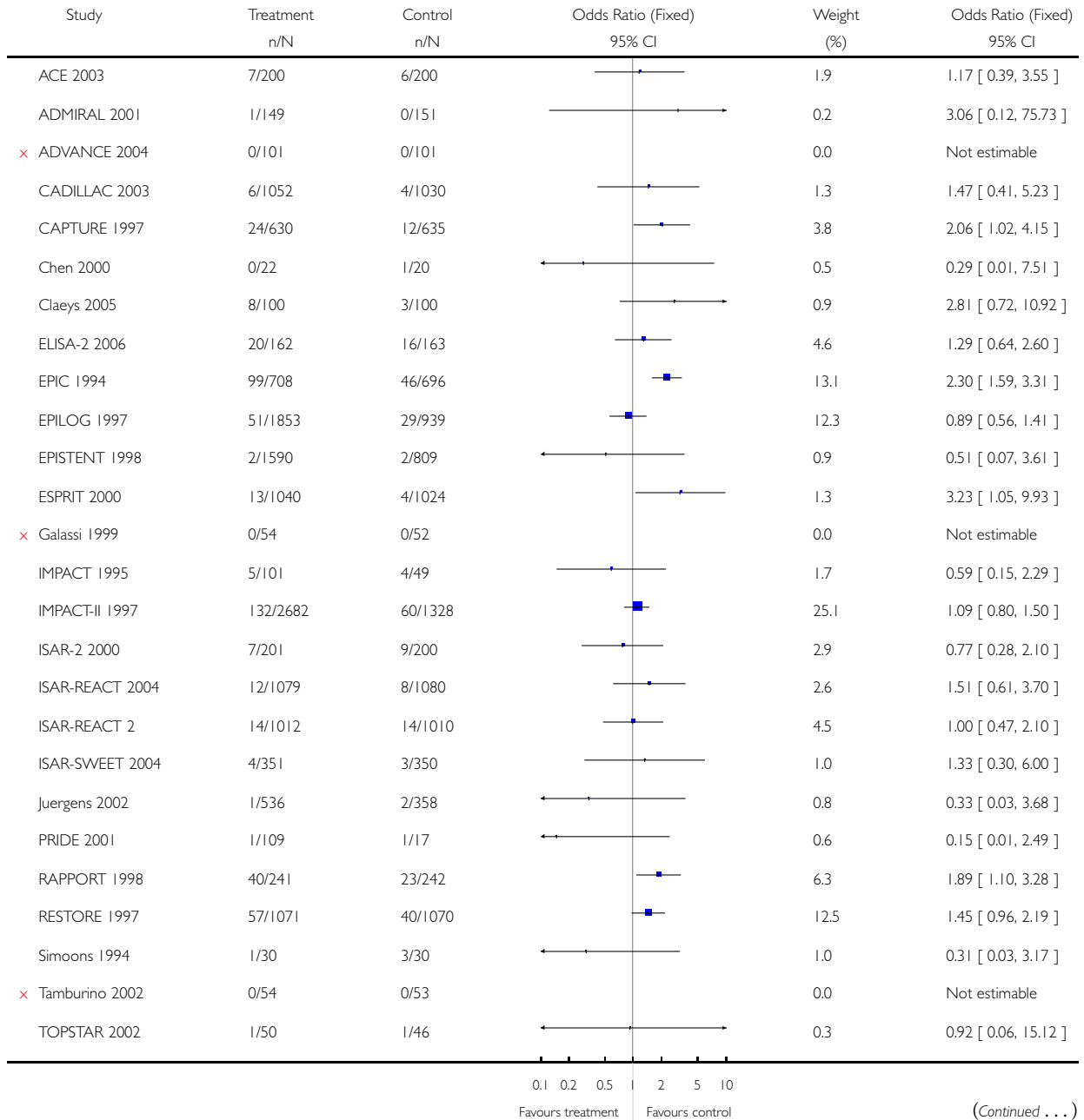


Analysis 01.07. Comparison 01 PCI (all patients), Outcome 07 30-day major bleeding

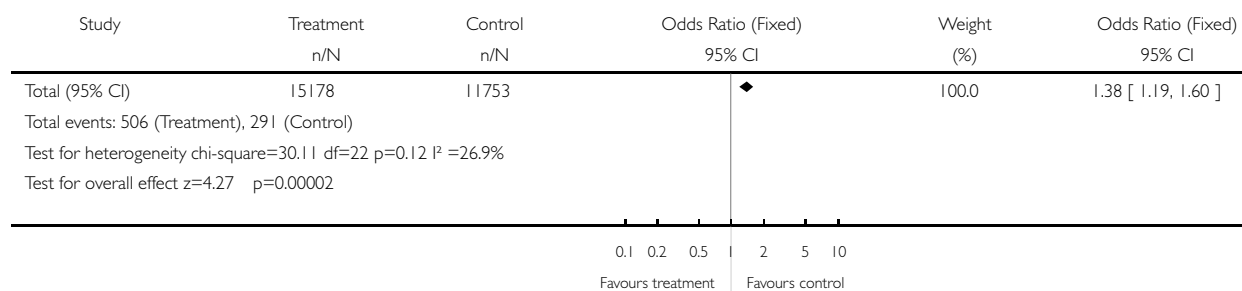
Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 07 30-day major bleeding



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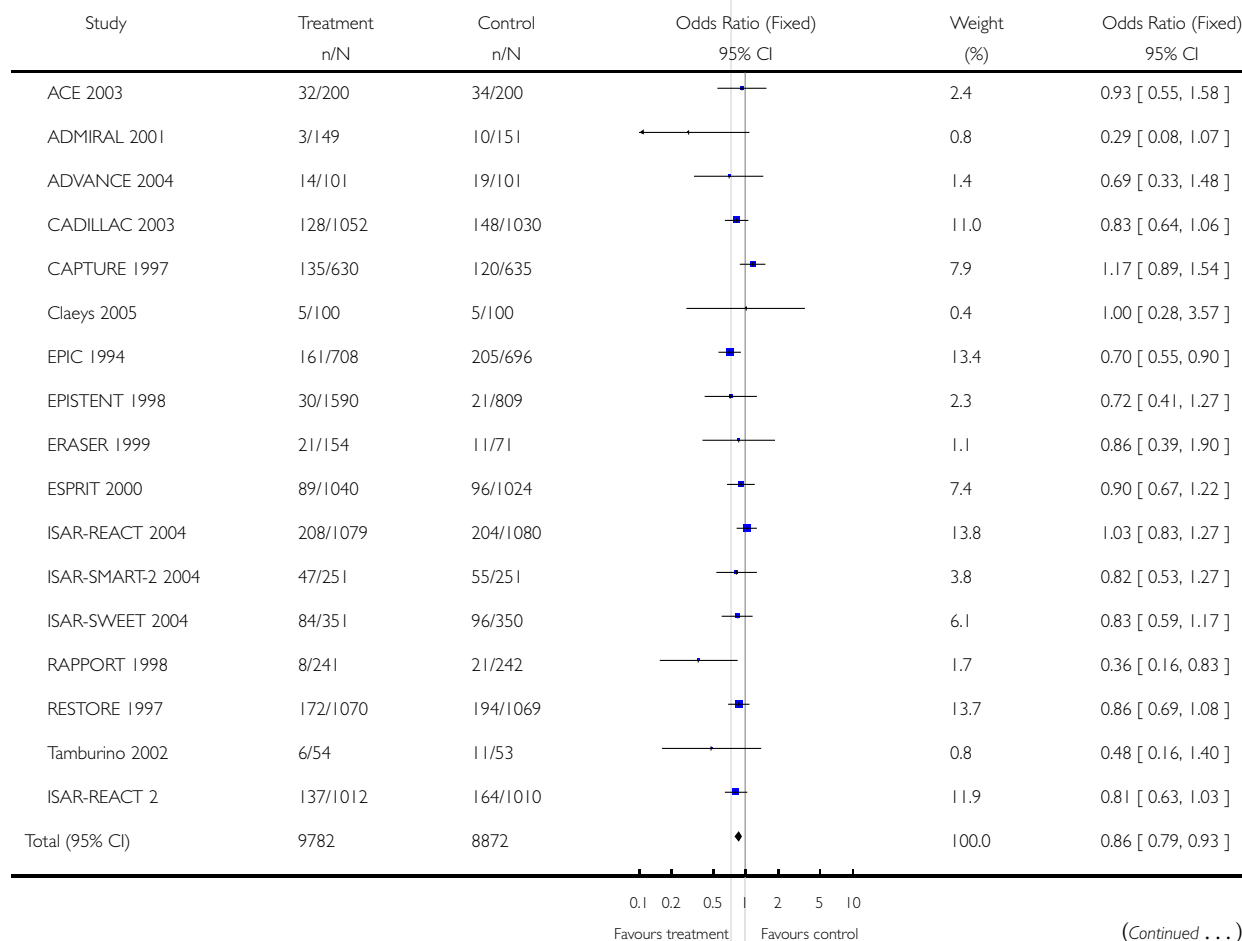


Analysis 01.08. Comparison 01 PCI (all patients), Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 01 PCI (all patients)

Outcome: 08 6-month urgent revascularisation



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Study	Treatment n/N	Control n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
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Total events: 1280 (Treatment), 1414 (Control)
 Test for heterogeneity chi-square=19.34 df=16 p=0.25 I² =17.3%
 Test for overall effect z=3.60 p=0.0003

Analysis 01.09. Comparison 01 PCI (all patients), Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

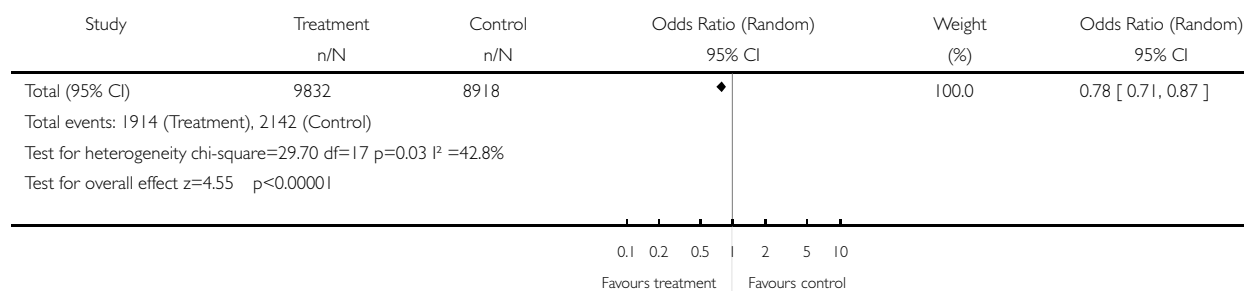
Comparison: 01 PCI (all patients)

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

Study	Treatment n/N	Control n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
ACE 2003	43/200	61/200	0.62 [0.40, 0.98]	4.0	0.62 [0.40, 0.98]
ADMIRAL 2001	11/149	24/151	0.42 [0.20, 0.90]	1.7	0.42 [0.20, 0.90]
ADVANCE 2004	20/101	31/101	0.56 [0.29, 1.06]	2.2	0.56 [0.29, 1.06]
CADILLAC 2003	178/1052	190/1030	0.90 [0.72, 1.13]	9.0	0.90 [0.72, 1.13]
CAPTURE 1997	193/630	193/635	1.01 [0.80, 1.28]	8.6	1.01 [0.80, 1.28]
Claeys 2005	13/100	16/100	0.78 [0.36, 1.73]	1.6	0.78 [0.36, 1.73]
EPIC 1994	191/708	244/696	0.68 [0.55, 0.86]	8.9	0.68 [0.55, 0.86]
EPISTENT 1998	124/1590	98/809	0.61 [0.46, 0.81]	7.4	0.61 [0.46, 0.81]
ERASER 1999	33/154	18/71	0.80 [0.42, 1.55]	2.2	0.80 [0.42, 1.55]
ESPRIT 2000	148/1040	187/1024	0.74 [0.59, 0.94]	8.7	0.74 [0.59, 0.94]
ISAR-REACT 2004	257/1079	257/1080	1.00 [0.82, 1.22]	10.0	1.00 [0.82, 1.22]
ISAR-SMART-2 2004	69/251	72/251	0.94 [0.64, 1.39]	4.9	0.94 [0.64, 1.39]
ISAR-SWEET 2004	105/351	112/350	0.91 [0.66, 1.25]	6.3	0.91 [0.66, 1.25]
RAPPORT 1998	28/241	43/242	0.61 [0.36, 1.02]	3.3	0.61 [0.36, 1.02]
RESTORE 1997	258/1070	290/1069	0.85 [0.70, 1.04]	10.1	0.85 [0.70, 1.04]
Tamburino 2002	8/54	19/53	0.31 [0.12, 0.79]	1.2	0.31 [0.12, 0.79]
TOPSTAR 2002	1/50	6/46	0.14 [0.02, 1.18]	0.2	0.14 [0.02, 1.18]
ISAR-REACT 2	234/1012	281/1010	0.78 [0.64, 0.95]	9.9	0.78 [0.64, 0.95]

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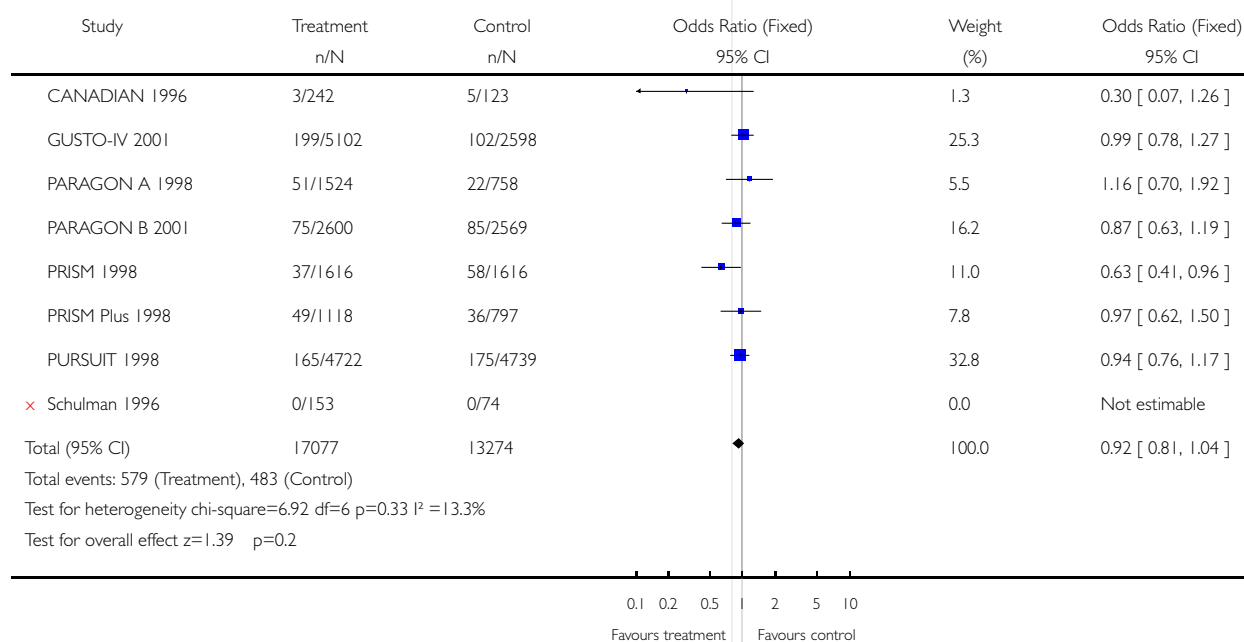


Analysis 02.01. Comparison 02 As initial medical treatment in patients with NSTEMACS, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 02 As initial medical treatment in patients with NSTEMACS

Outcome: 01 30-day mortality

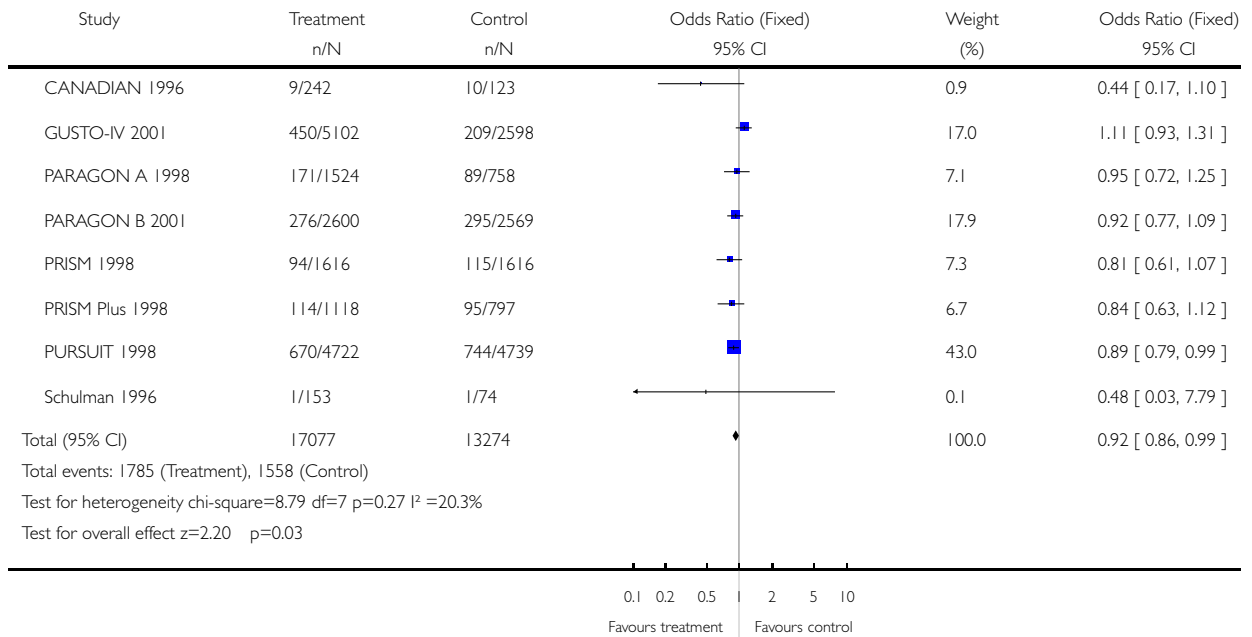


Analysis 02.02. Comparison 02 As initial medical treatment in patients with NSTEMACS, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 02 As initial medical treatment in patients with NSTEMACS

Outcome: 02 30-day mortality or myocardial infarction

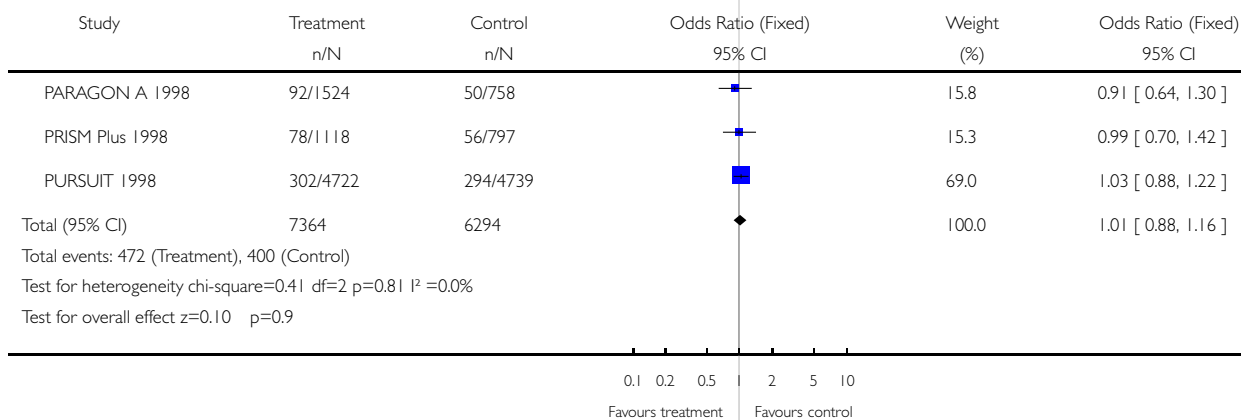


Analysis 02.03. Comparison 02 As initial medical treatment in patients with NSTEMACS, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 02 As initial medical treatment in patients with NSTEMACS

Outcome: 03 6-month mortality

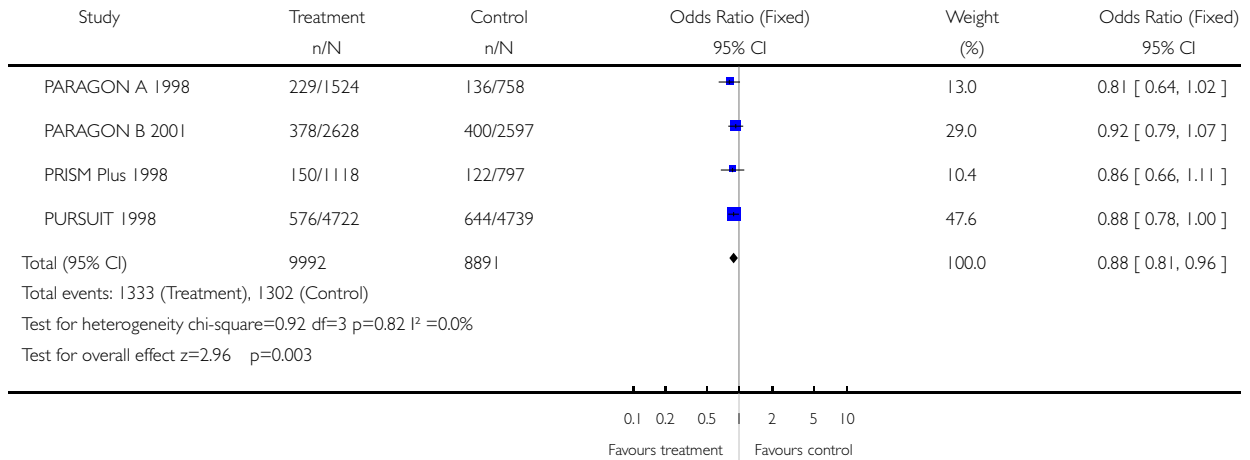


Analysis 02.04. Comparison 02 As initial medical treatment in patients with NSTEMACS, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 02 As initial medical treatment in patients with NSTEMACS

Outcome: 04 6-month mortality or myocardial infarction

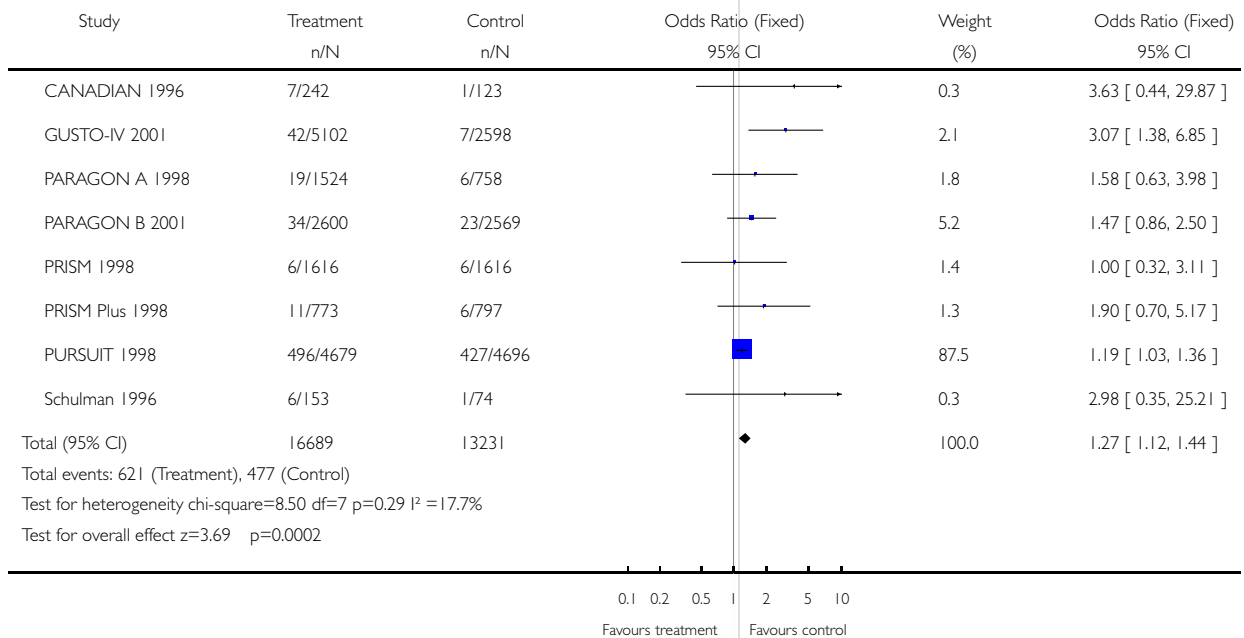


Analysis 02.05. Comparison 02 As initial medical treatment in patients with NSTEMACS, Outcome 05 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 02 As initial medical treatment in patients with NSTEMACS

Outcome: 05 30-day major bleeding

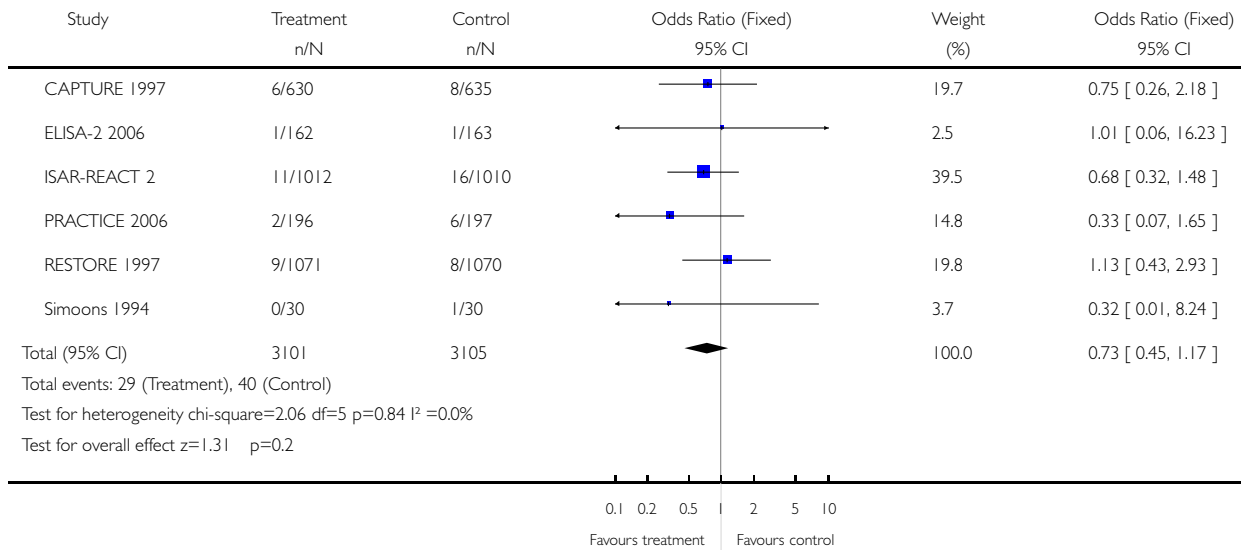


Analysis 03.01. Comparison 03 PCI in patients with NSTEMACS, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 01 30-day mortality

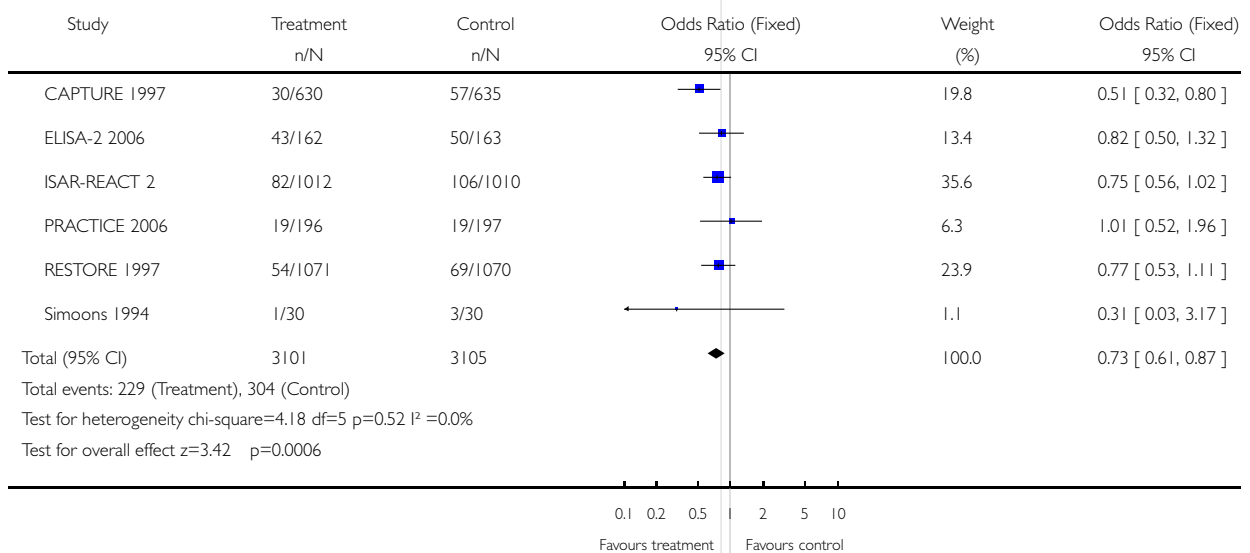


Analysis 03.02. Comparison 03 PCI in patients with NSTEMACS, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 02 30-day mortality or myocardial infarction

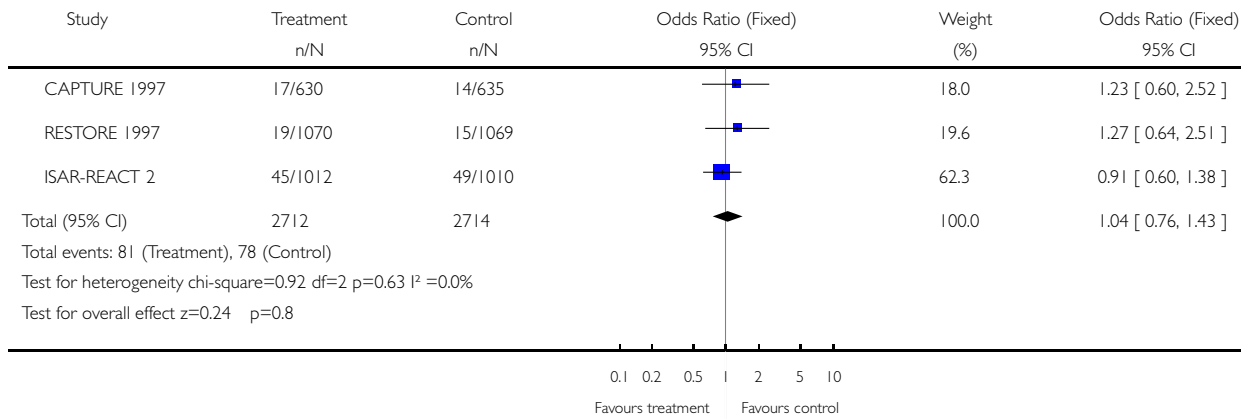


Analysis 03.03. Comparison 03 PCI in patients with NSTEMACS, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 03 6-month mortality

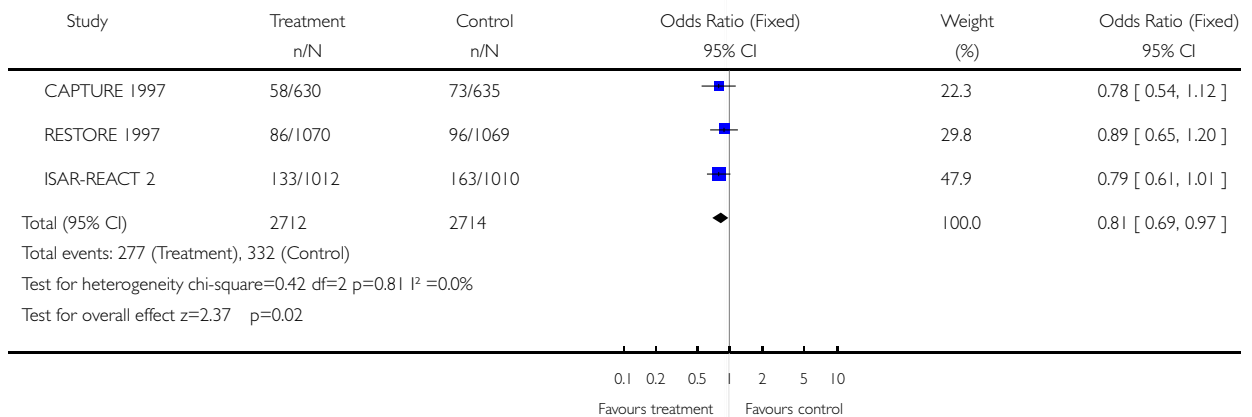


Analysis 03.04. Comparison 03 PCI in patients with NSTEMACS, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 04 6-month mortality or myocardial infarction

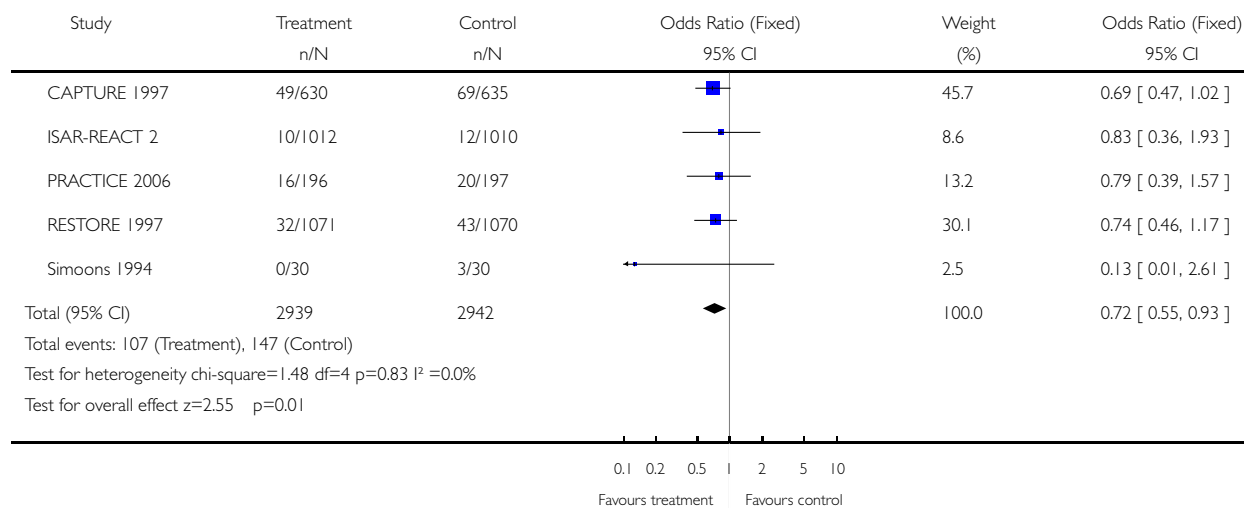


Analysis 03.05. Comparison 03 PCI in patients with NSTEMACS, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 05 30-day urgent revascularisation

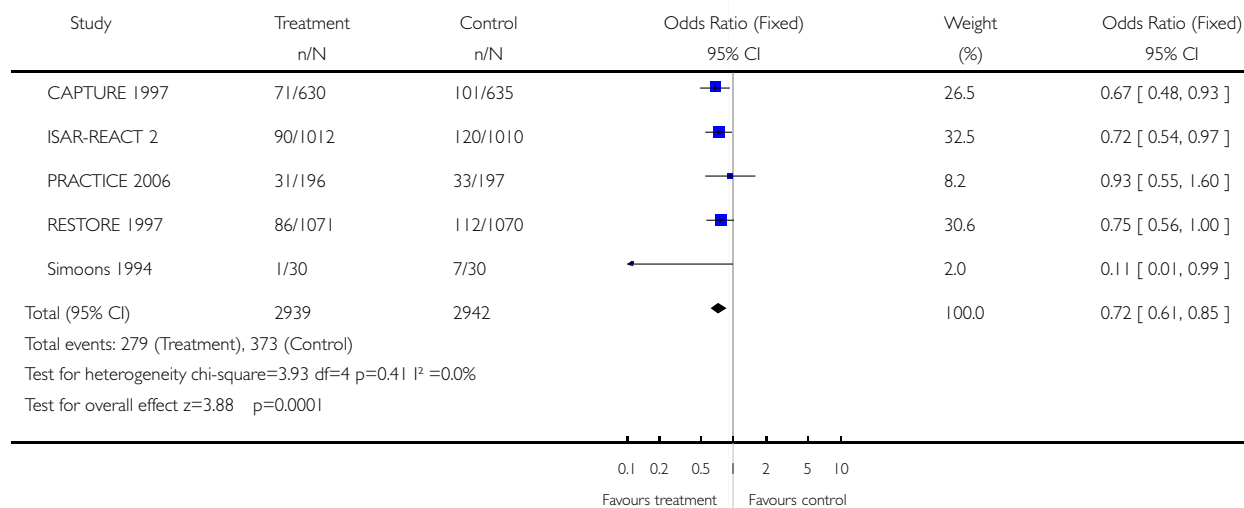


Analysis 03.06. Comparison 03 PCI in patients with NSTEMACS, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

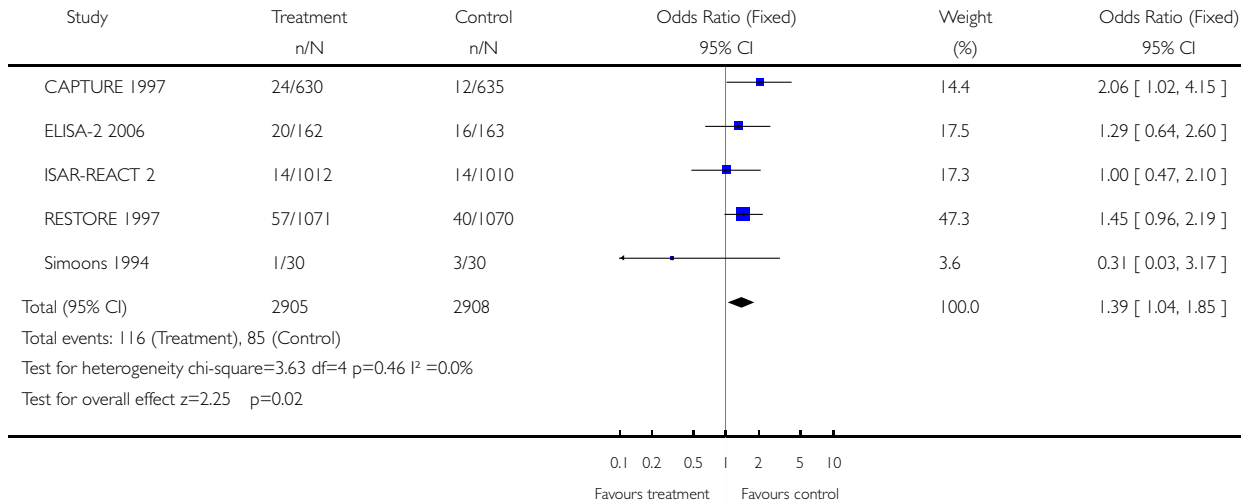


Analysis 03.07. Comparison 03 PCI in patients with NSTEMACS, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 07 30-day major bleeding

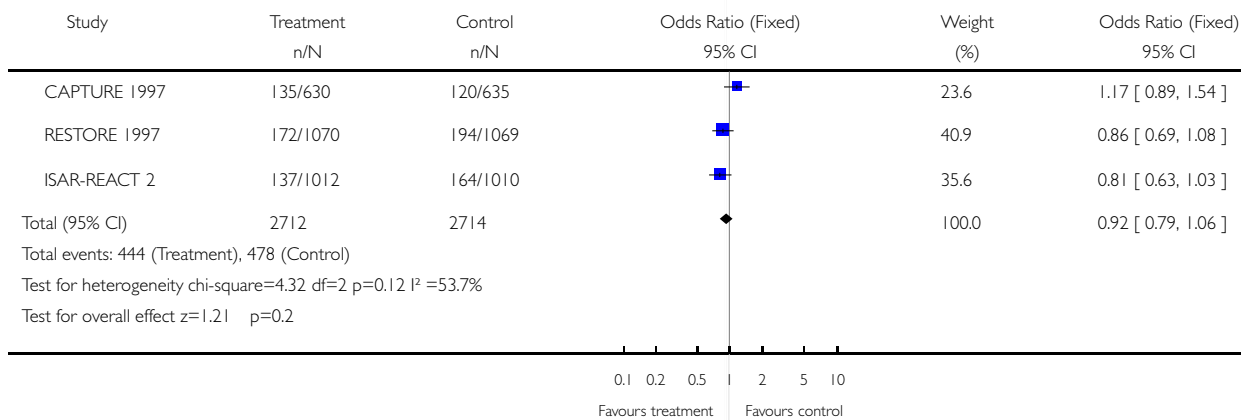


Analysis 03.08. Comparison 03 PCI in patients with NSTEMACS, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 08 6-month urgent revascularisation

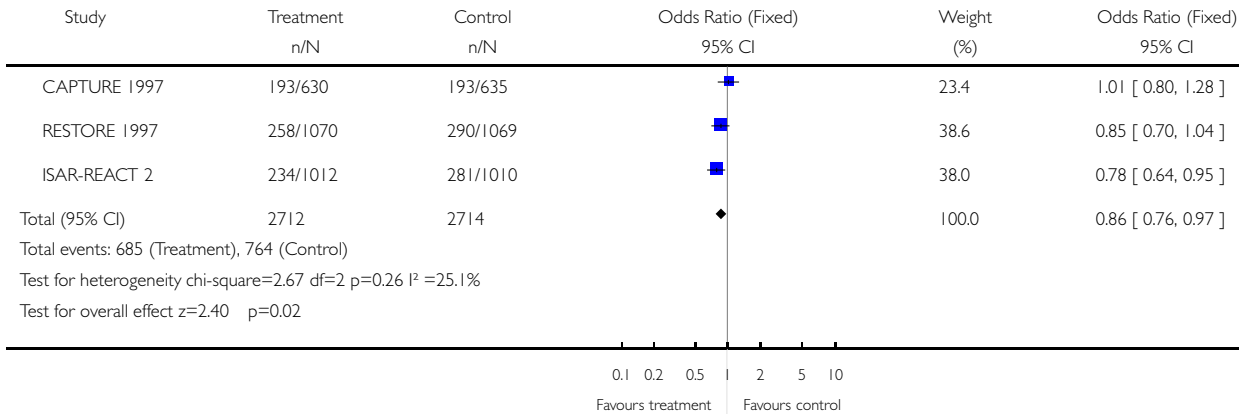


Analysis 03.09. Comparison 03 PCI in patients with NSTEMACS, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 03 PCI in patients with NSTEMACS

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

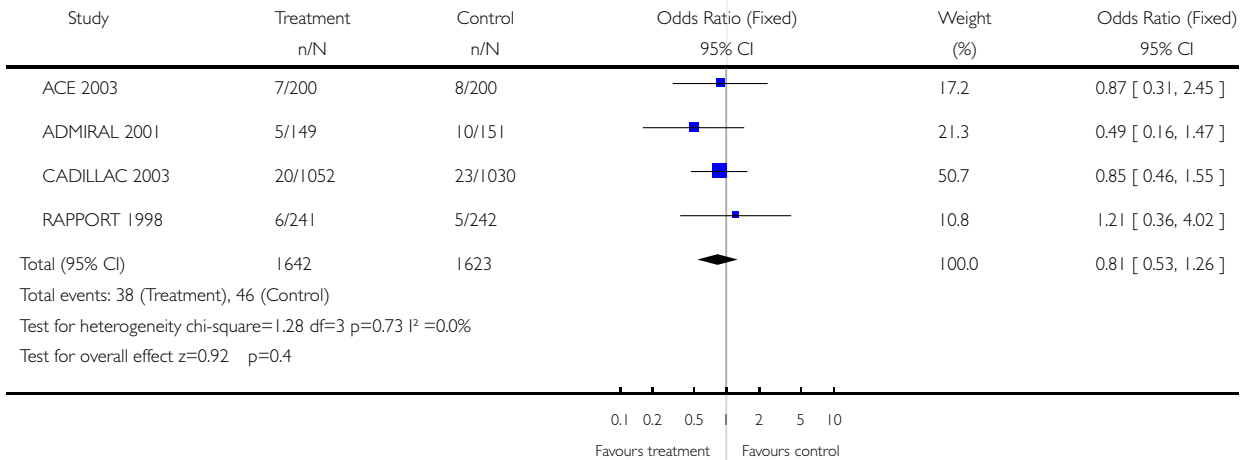


Analysis 04.01. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 01 30-day mortality

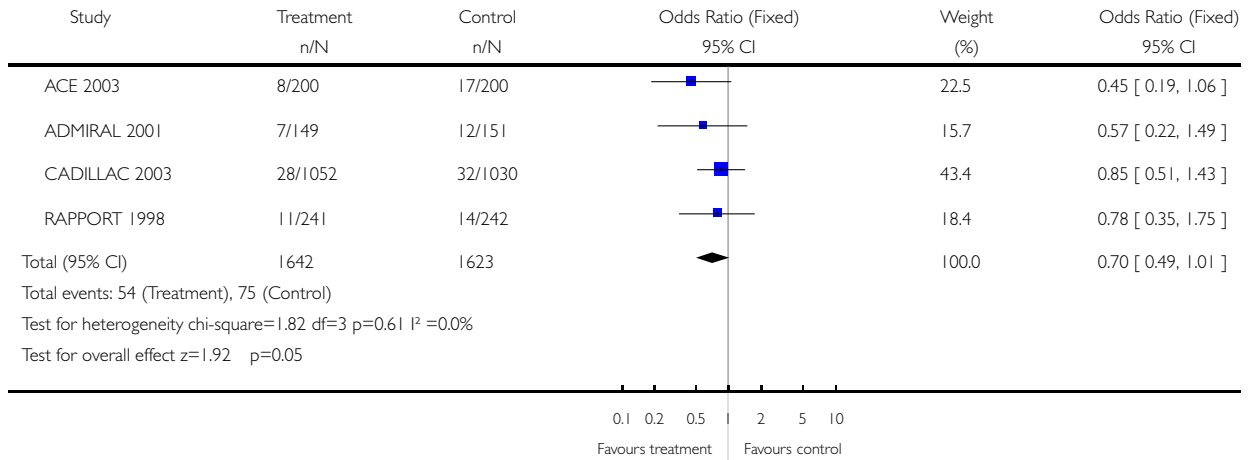


Analysis 04.02. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 02 30-day mortality or myocardial infarction

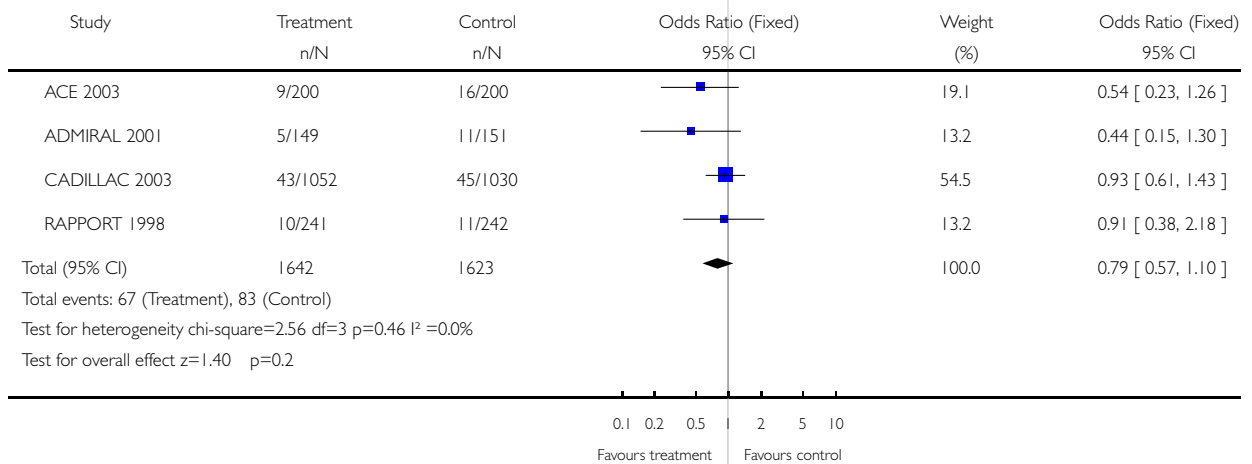


Analysis 04.03. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 03 6-month mortality

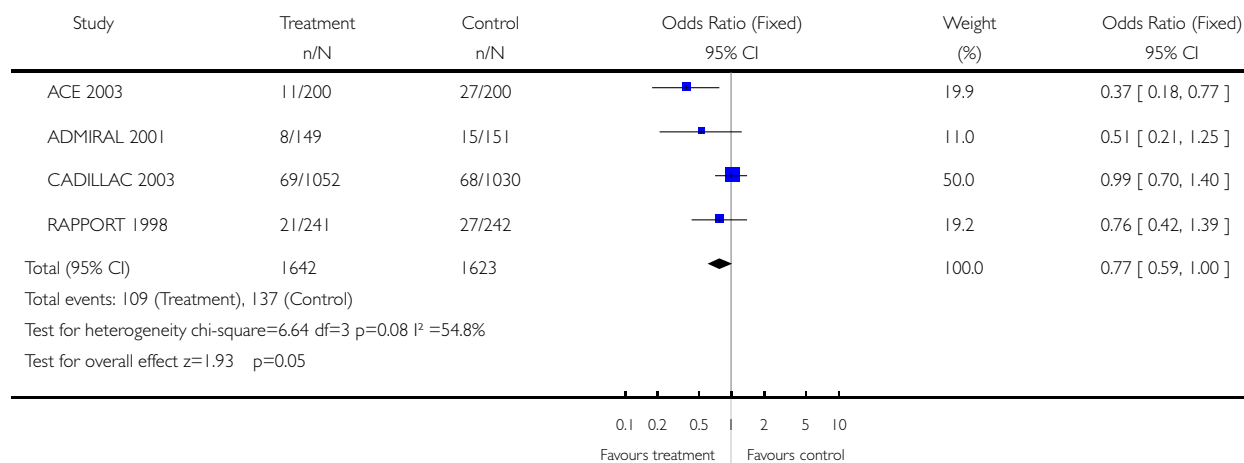


Analysis 04.04. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 04 6-month mortality or myocardial infarction

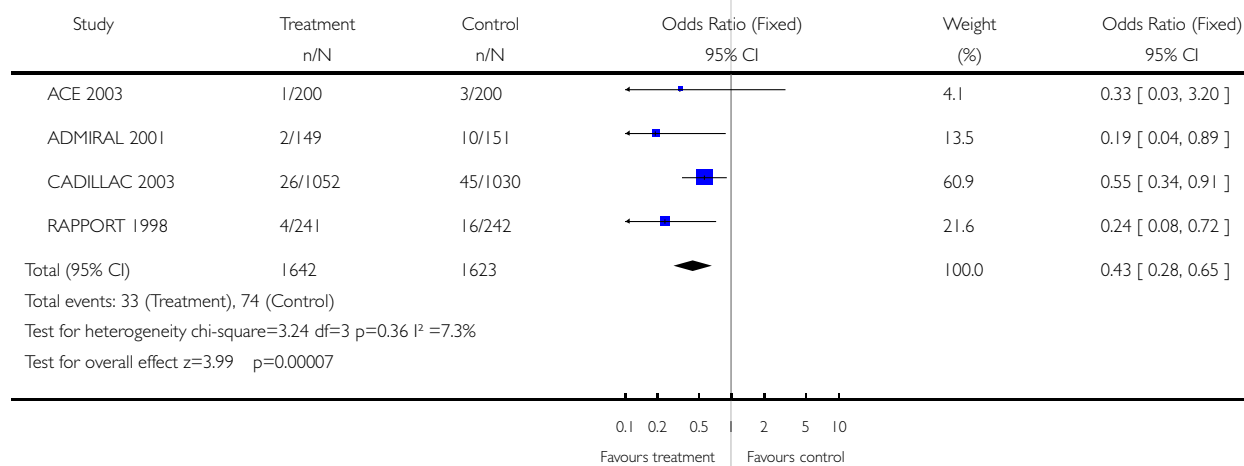


Analysis 04.05. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 05 30-day urgent revascularisation

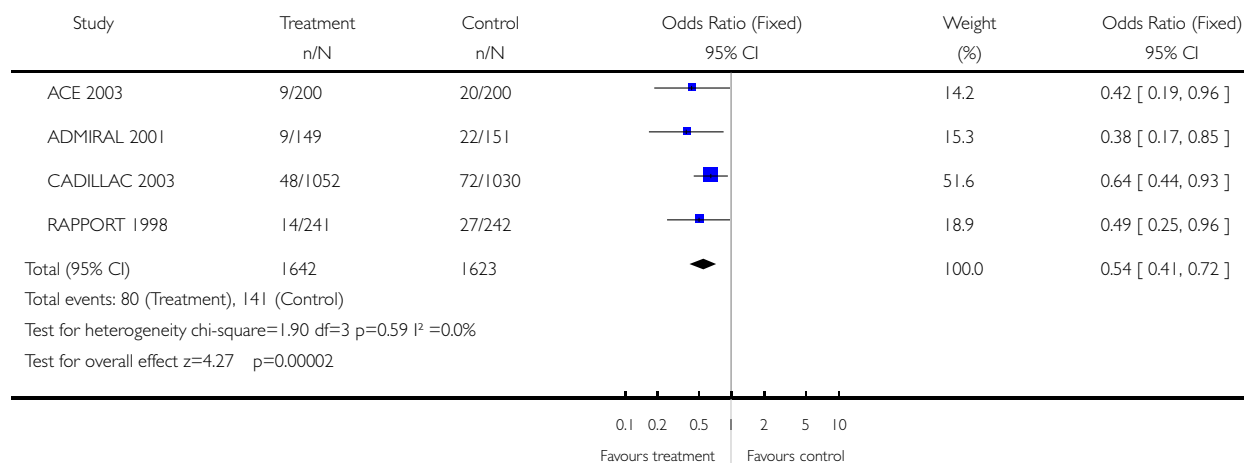


Analysis 04.06. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

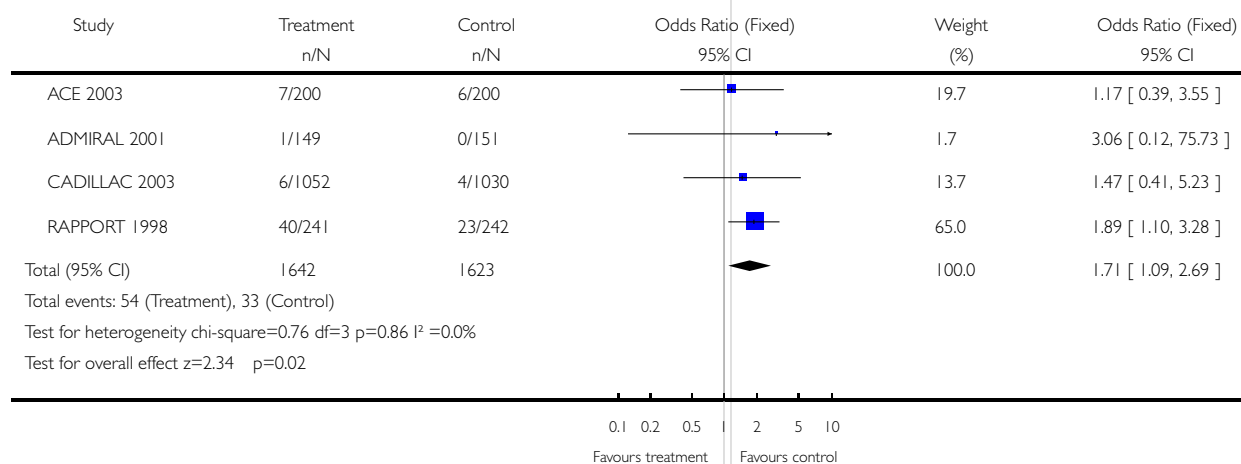


Analysis 04.07. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 07 30-day major bleeding

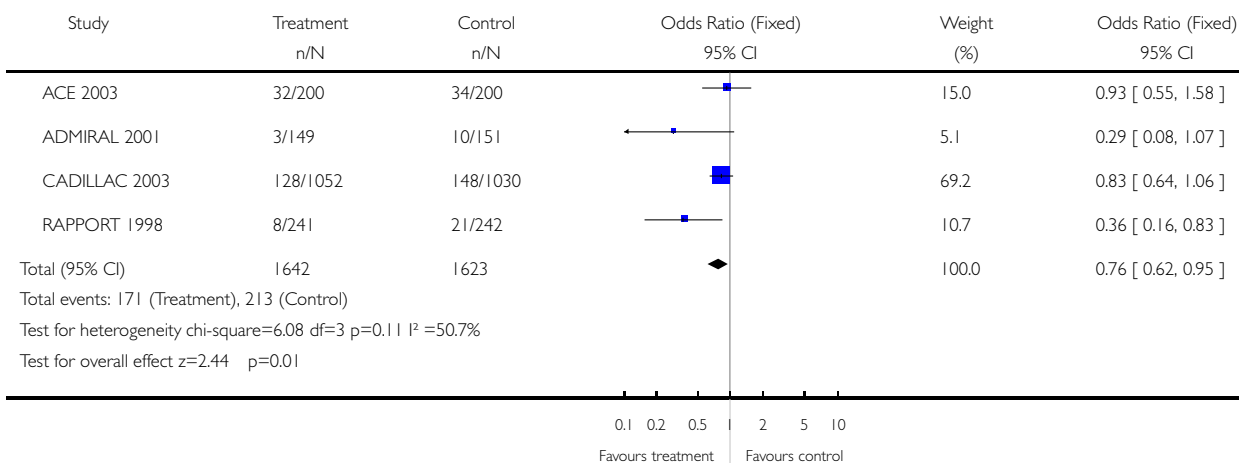


Analysis 04.08. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 08 6-month urgent revascularisation

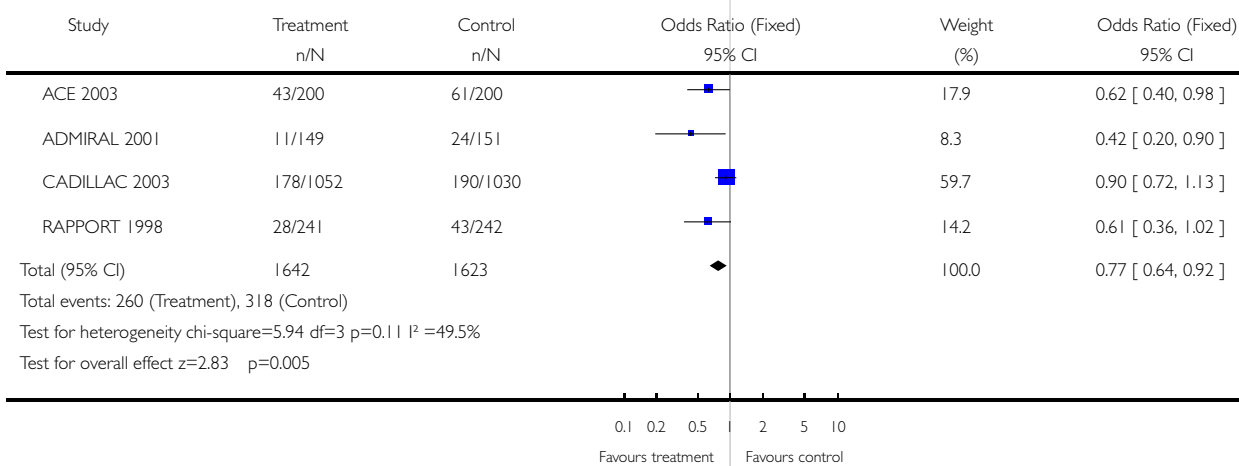


Analysis 04.09. Comparison 04 Primary PCI in patients with ST segment elevation acute myocardial infarction, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 04 Primary PCI in patients with ST segment elevation acute myocardial infarction

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

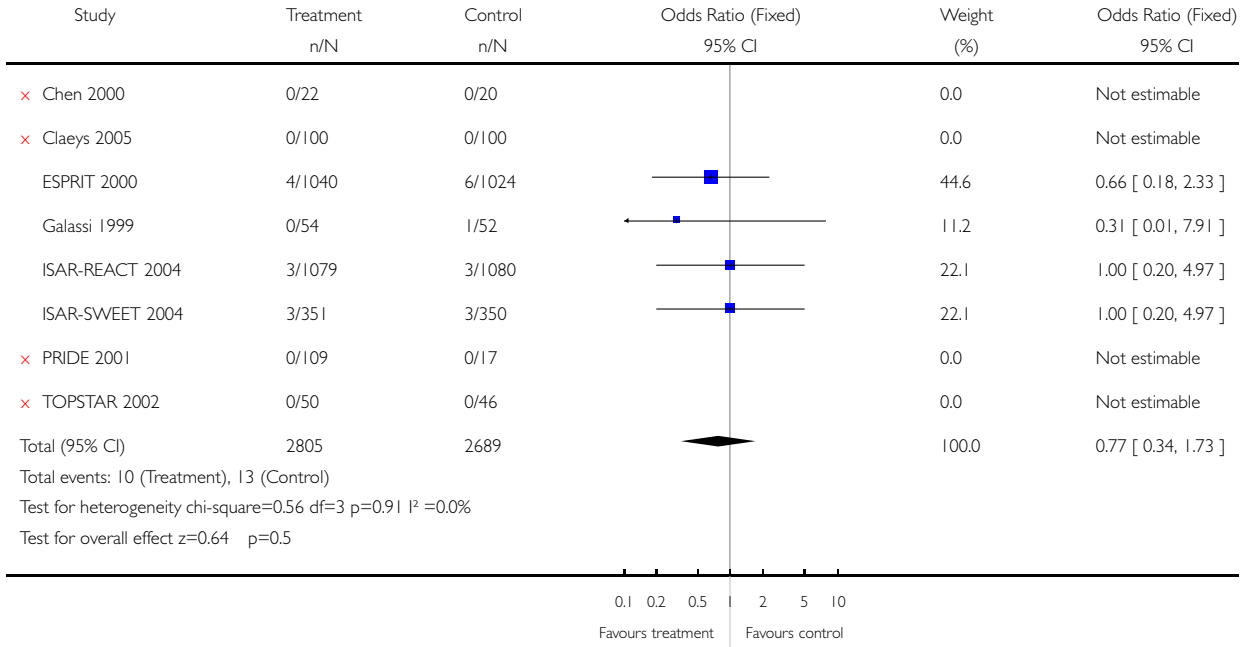


Analysis 05.01. Comparison 05 PCI in stable coronary patients, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 01 30-day mortality

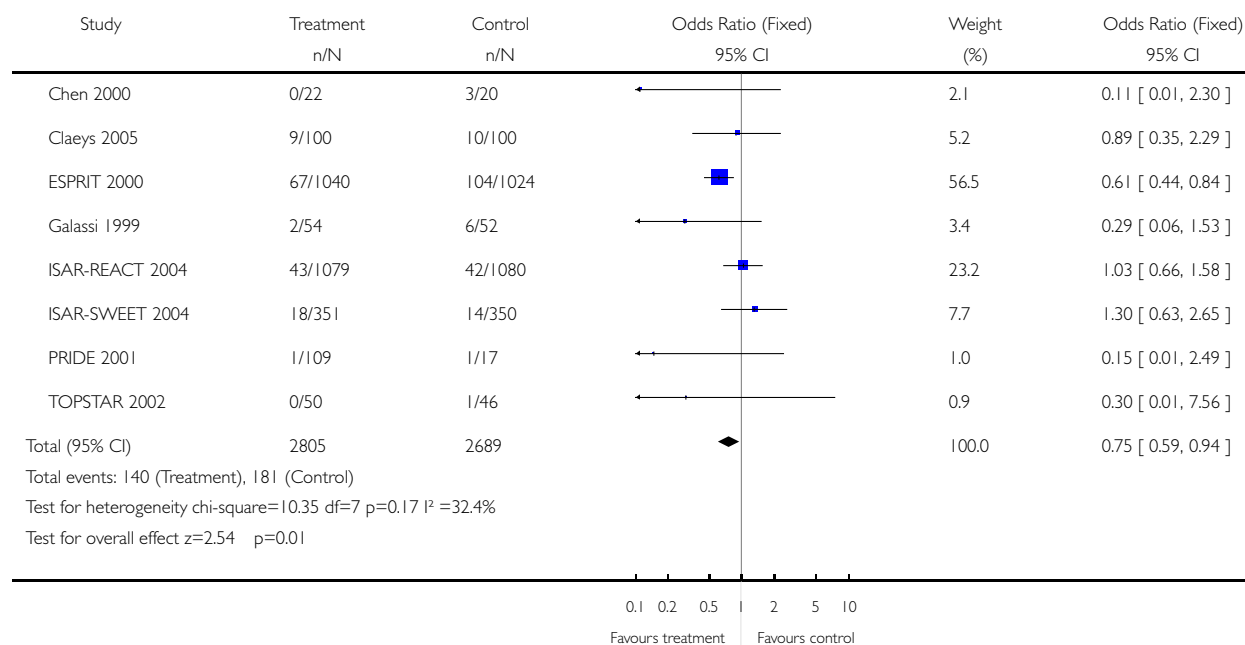


Analysis 05.02. Comparison 05 PCI in stable coronary patients, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 02 30-day mortality or myocardial infarction

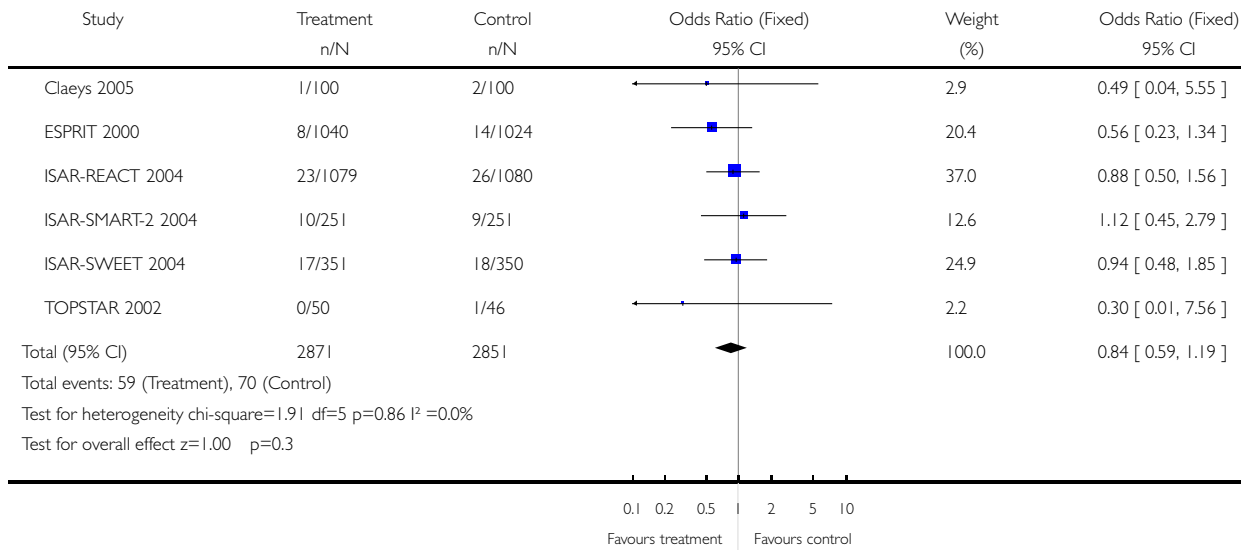


Analysis 05.03. Comparison 05 PCI in stable coronary patients, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 03 6-month mortality

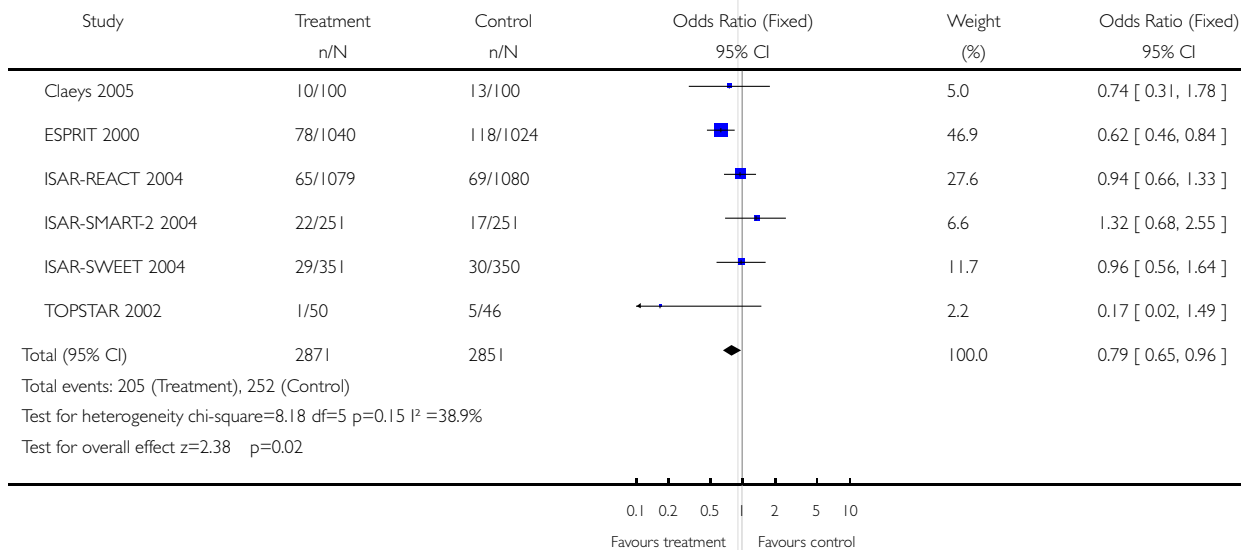


Analysis 05.04. Comparison 05 PCI in stable coronary patients, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 04 6-month mortality or myocardial infarction

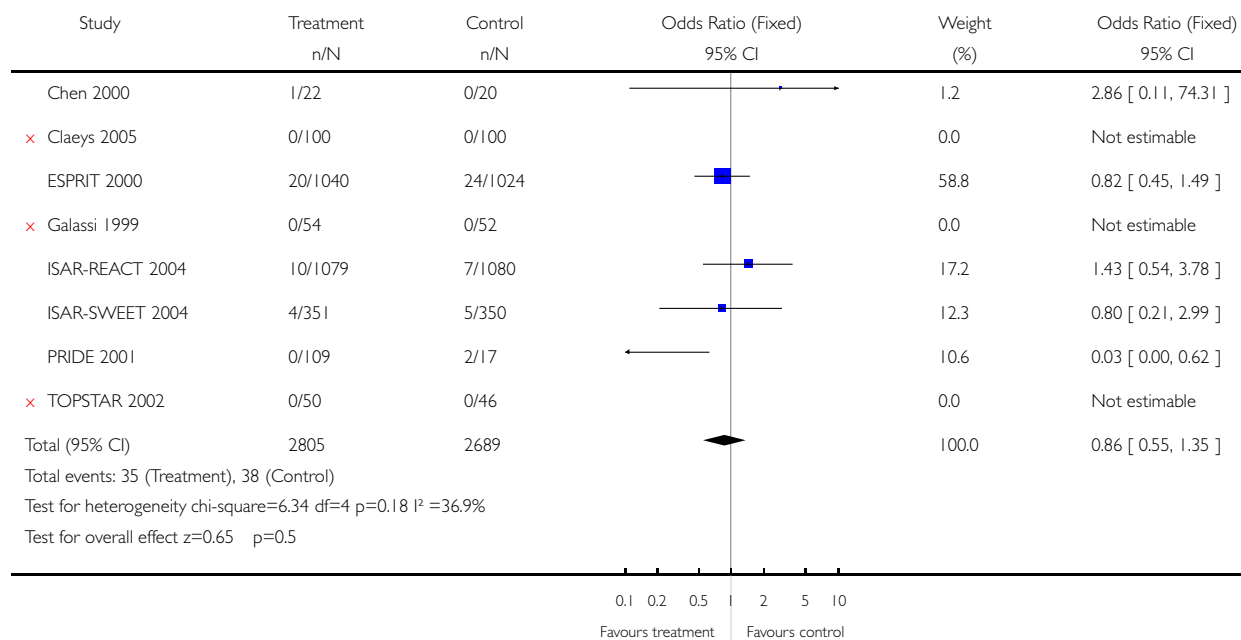


Analysis 05.05. Comparison 05 PCI in stable coronary patients, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 05 30-day urgent revascularisation

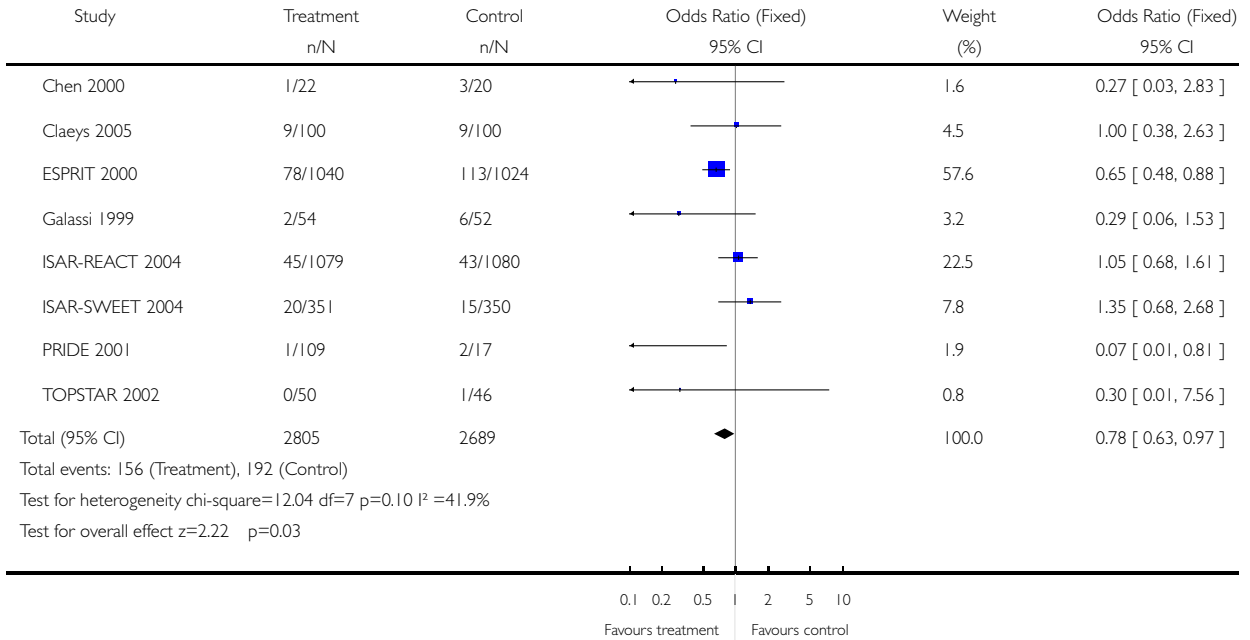


Analysis 05.06. Comparison 05 PCI in stable coronary patients, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

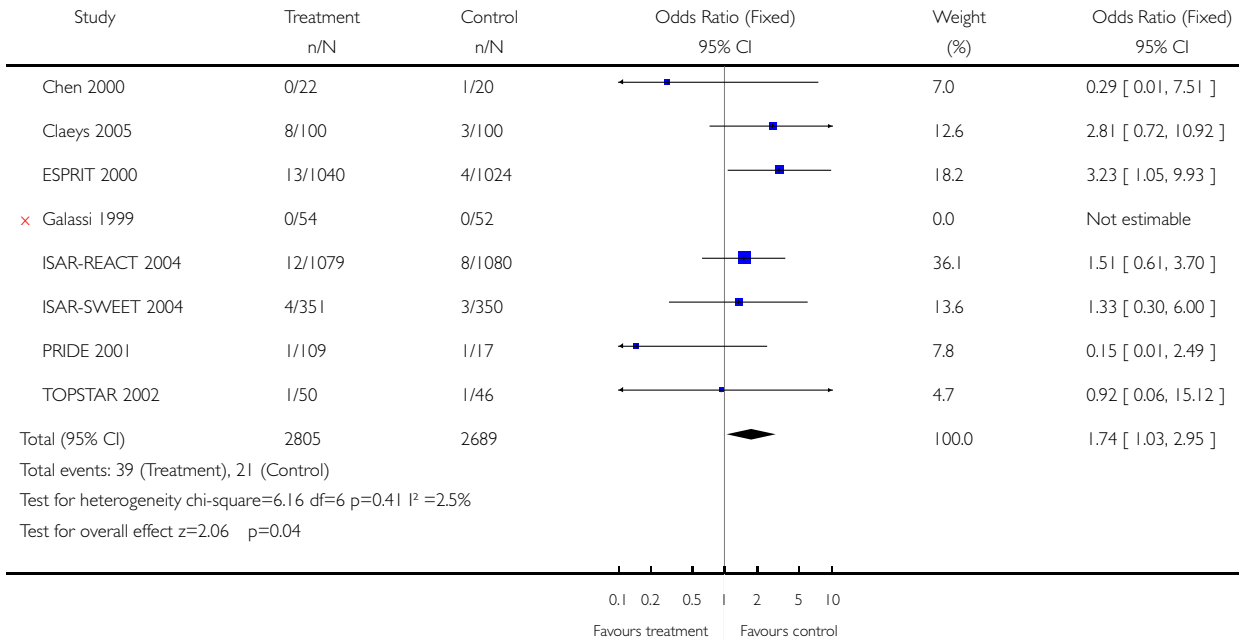


Analysis 05.07. Comparison 05 PCI in stable coronary patients, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 07 30-day major bleeding

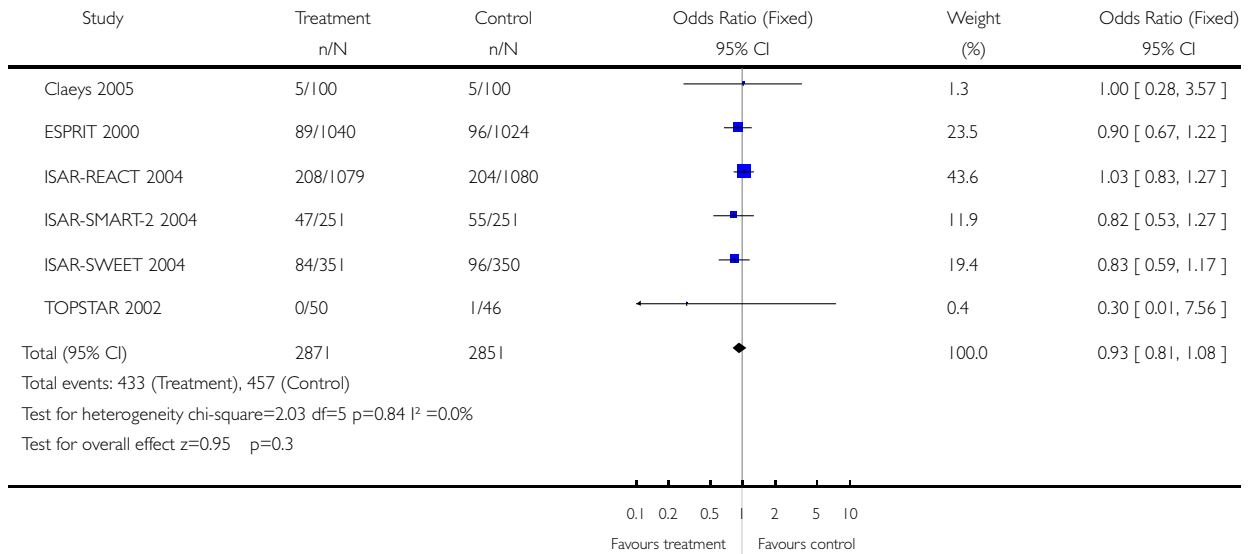


Analysis 05.08. Comparison 05 PCI in stable coronary patients, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 08 6-month urgent revascularisation

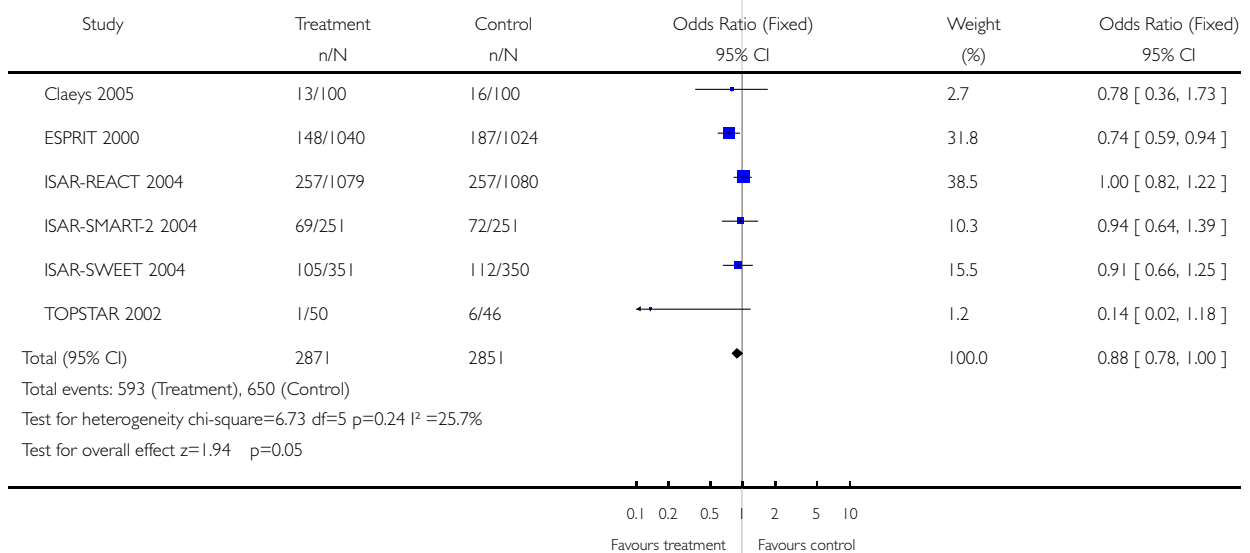


Analysis 05.09. Comparison 05 PCI in stable coronary patients, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 05 PCI in stable coronary patients

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

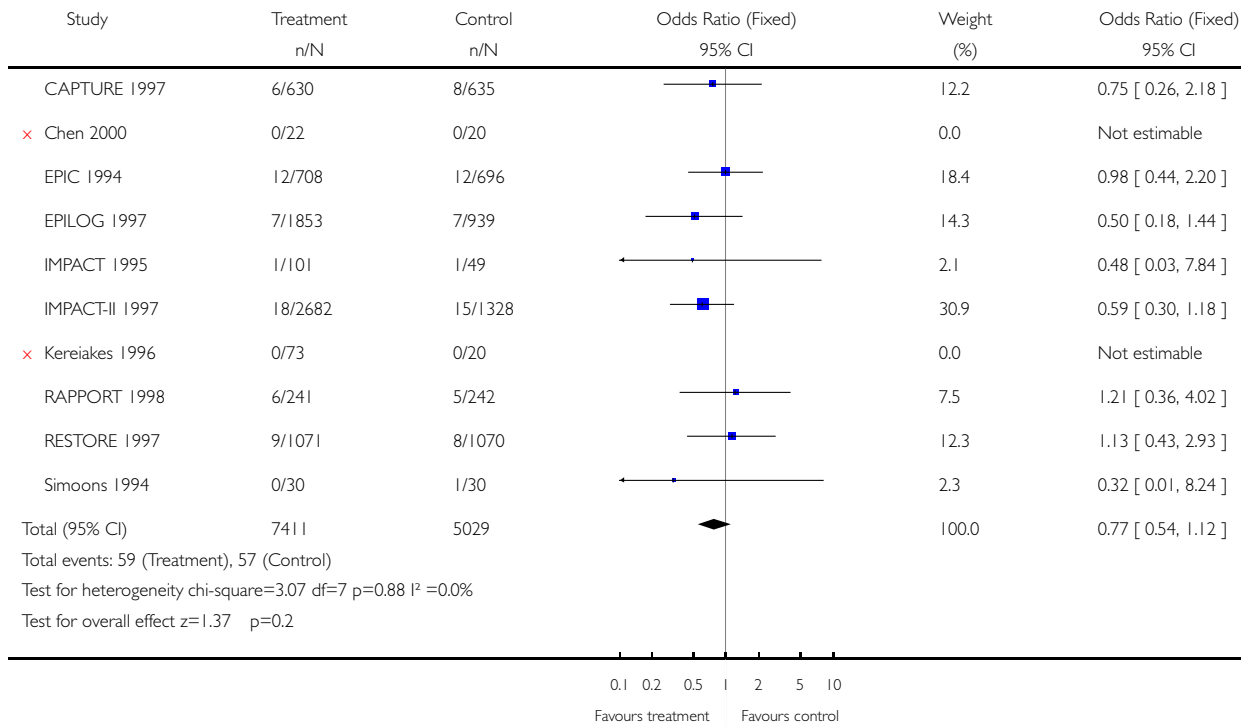


Analysis 06.01. Comparison 06 Balloon PCI, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 01 30-day mortality

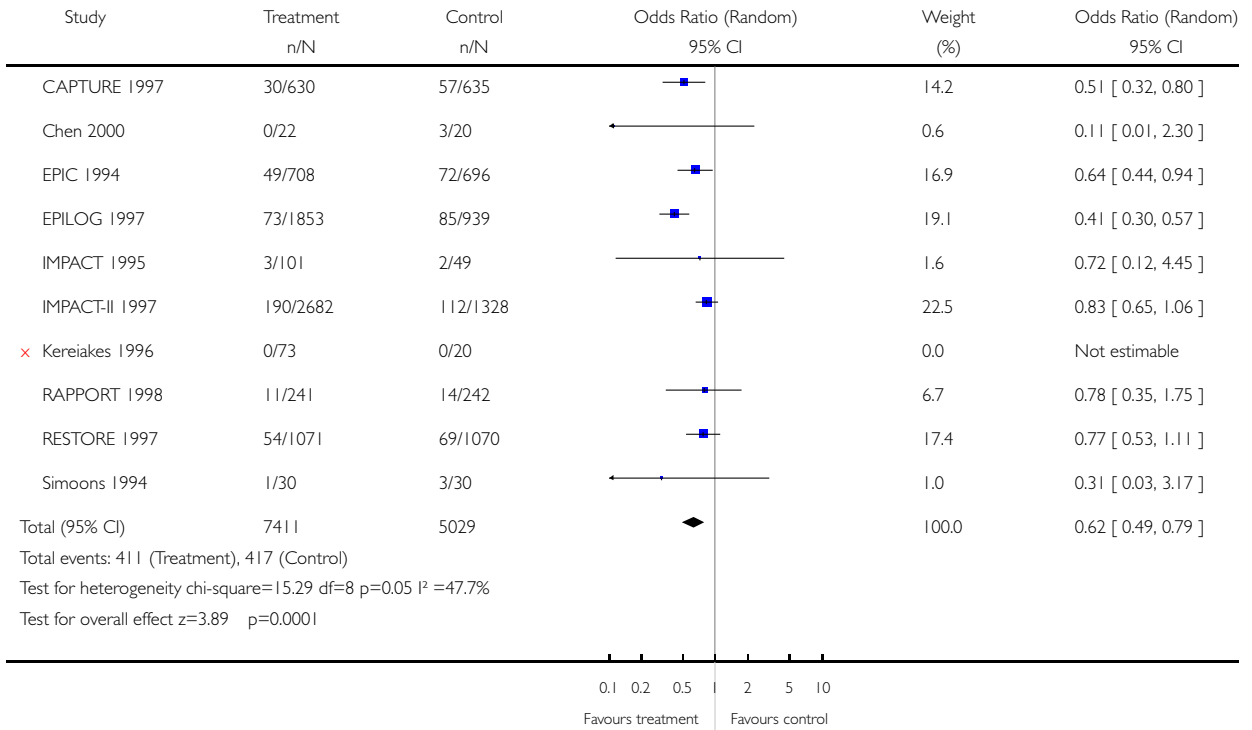


Analysis 06.02. Comparison 06 Balloon PCI, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 02 30-day mortality or myocardial infarction

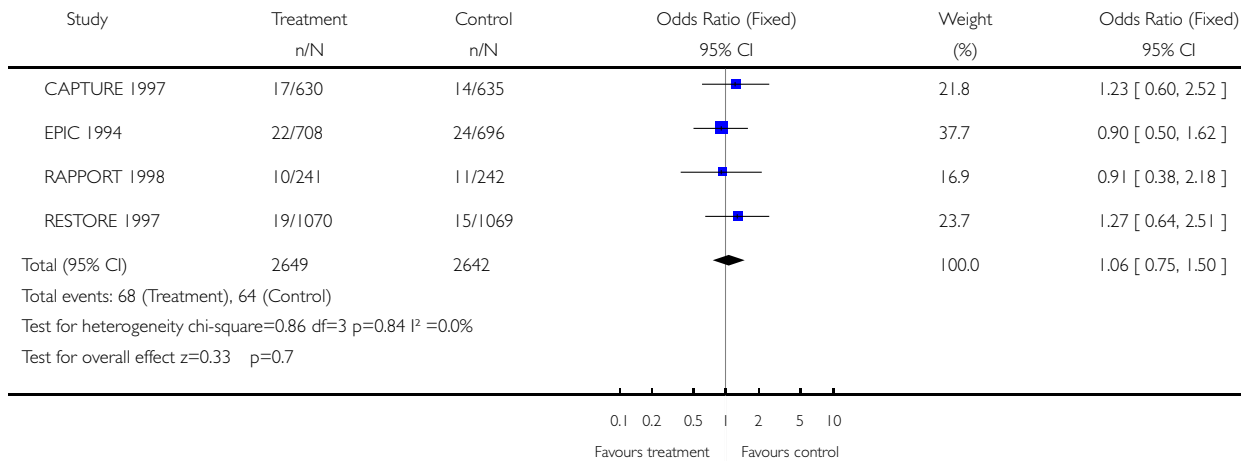


Analysis 06.03. Comparison 06 Balloon PCI, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 03 6-month mortality

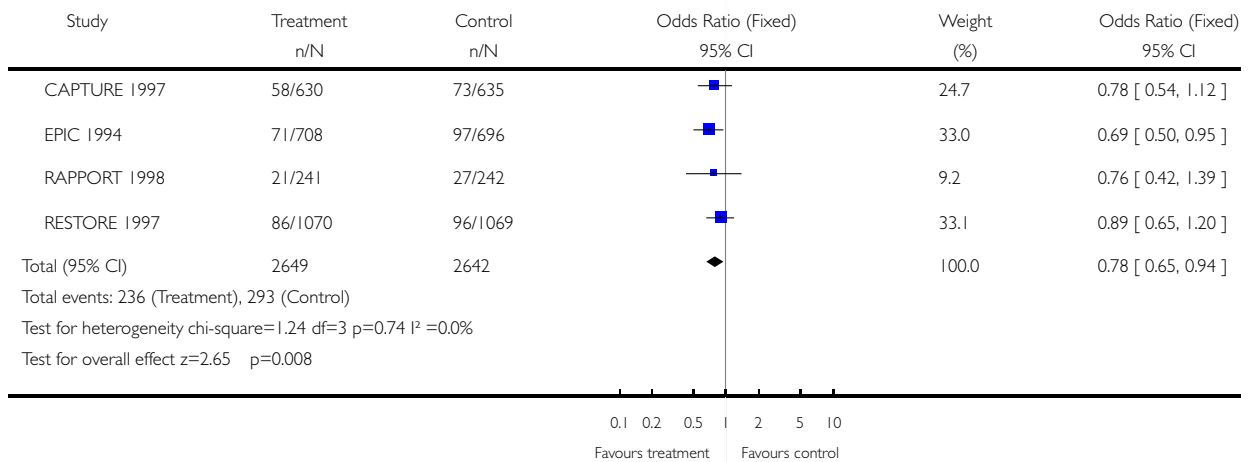


Analysis 06.04. Comparison 06 Balloon PCI, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 04 6-month mortality or myocardial infarction

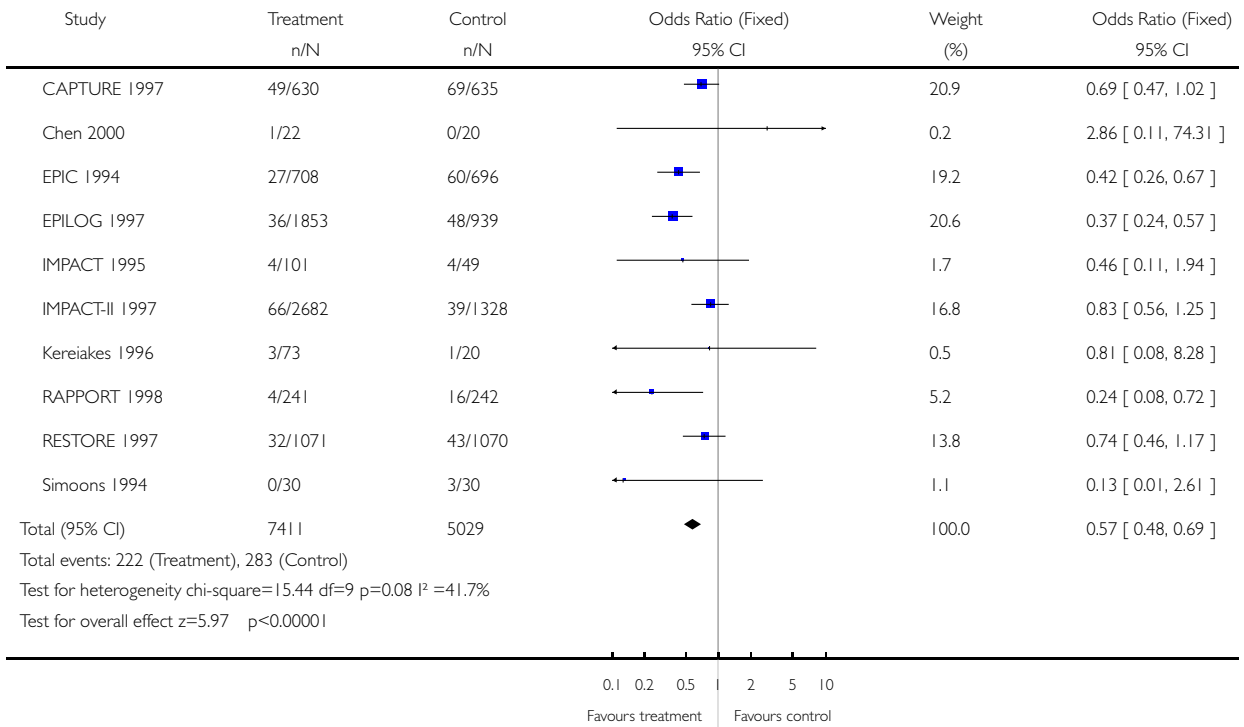


Analysis 06.05. Comparison 06 Balloon PCI, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 05 30-day urgent revascularisation

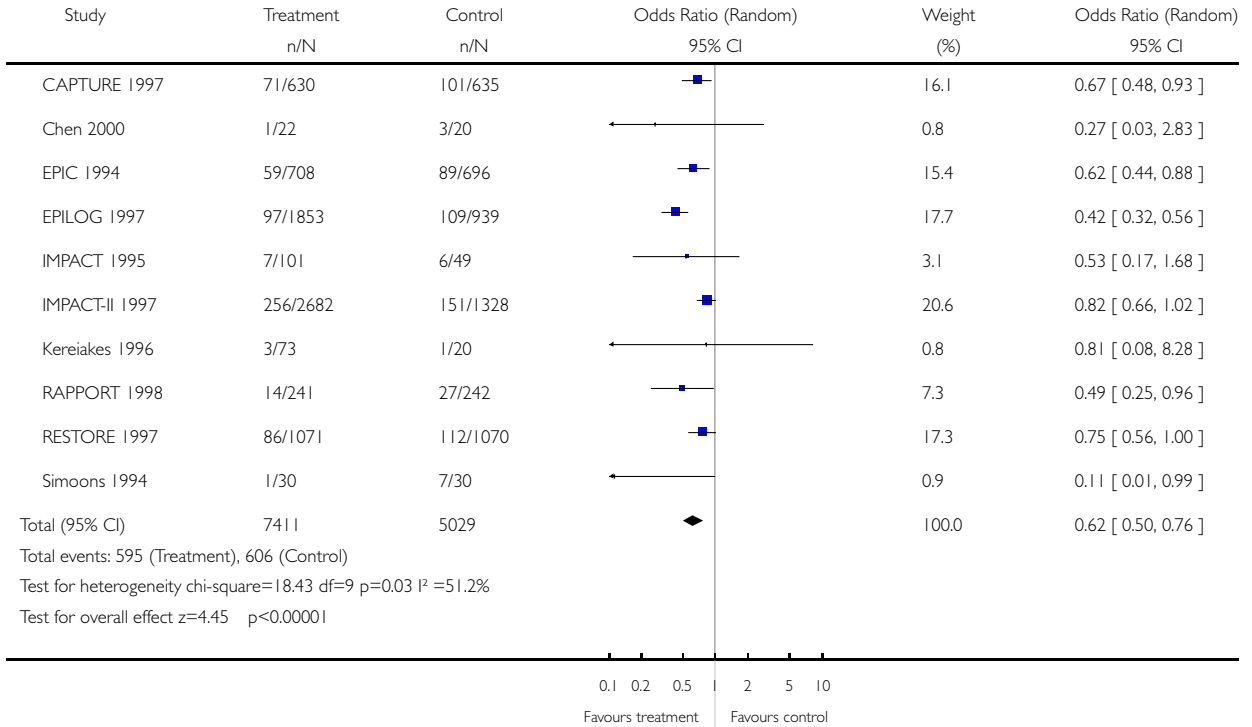


Analysis 06.06. Comparison 06 Balloon PCI, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

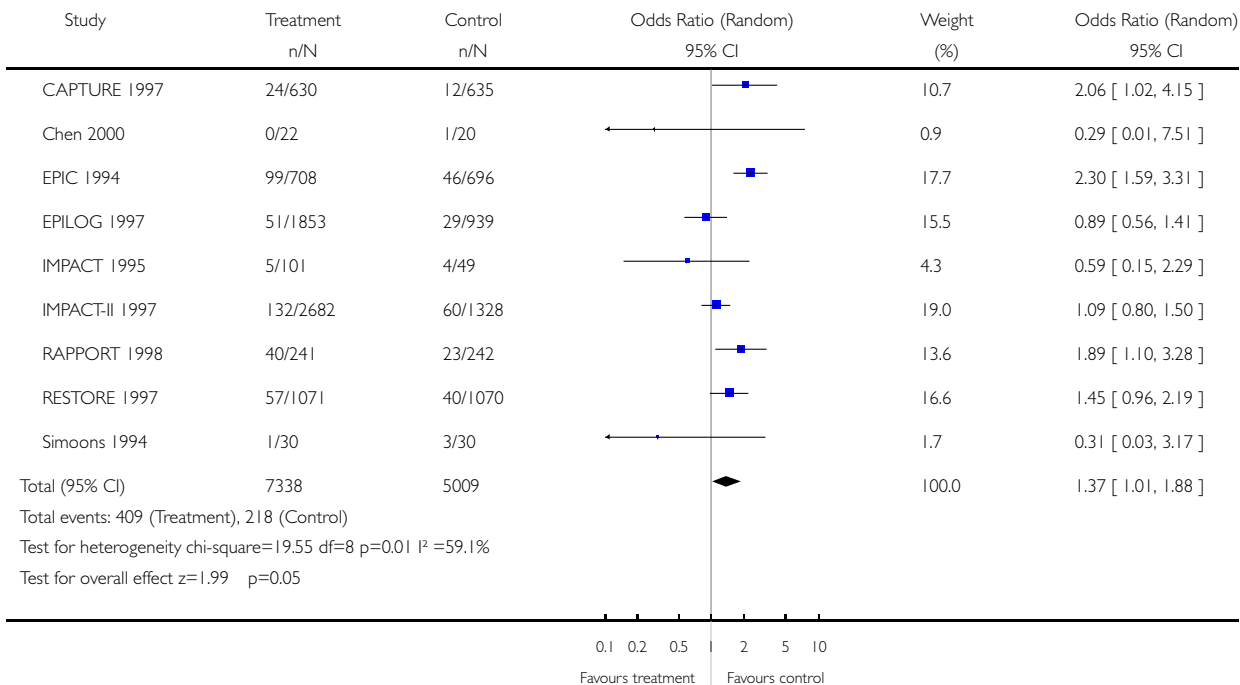


Analysis 06.07. Comparison 06 Balloon PCI, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 07 30-day major bleeding

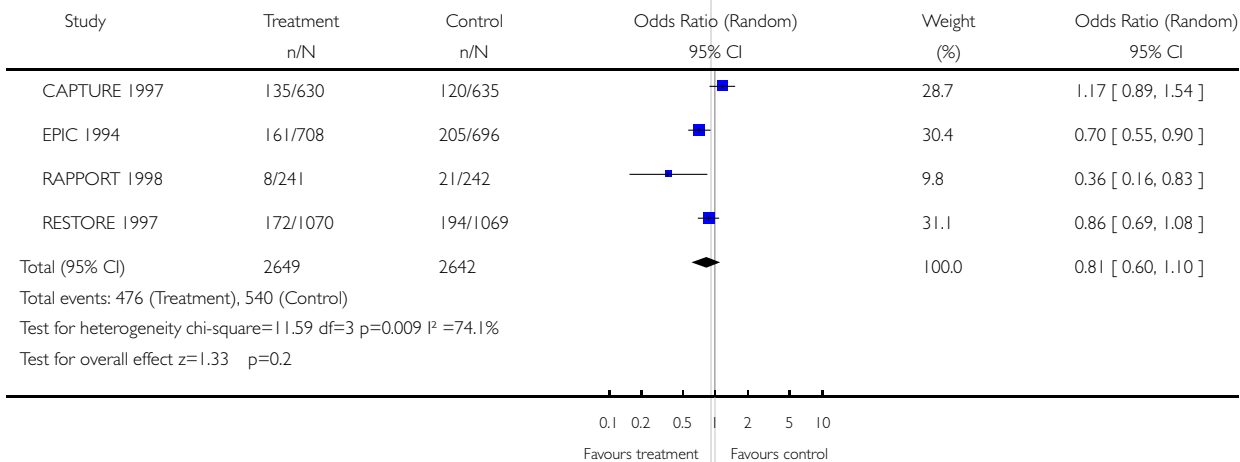


Analysis 06.08. Comparison 06 Balloon PCI, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 08 6-month urgent revascularisation

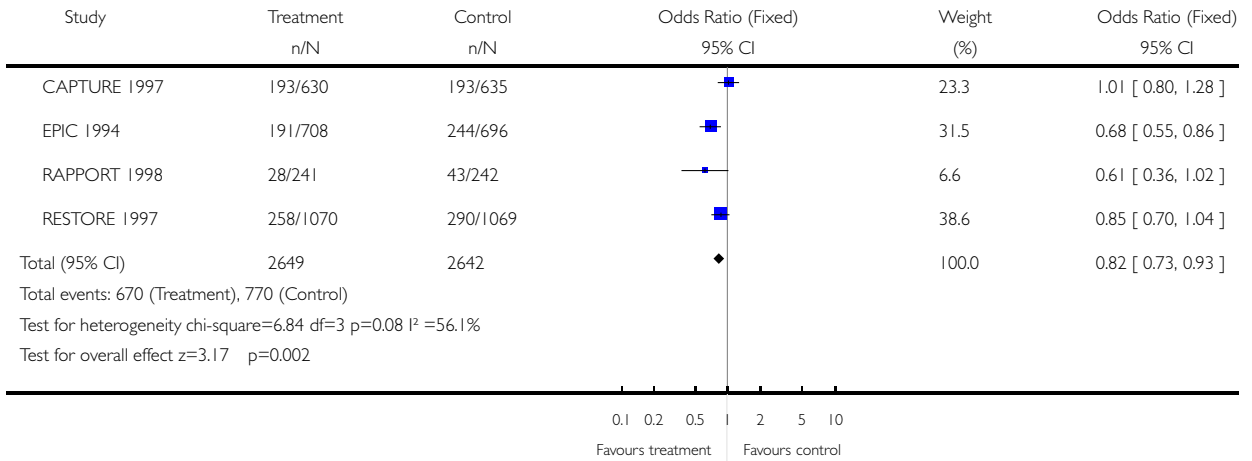


Analysis 06.09. Comparison 06 Balloon PCI, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 06 Balloon PCI

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

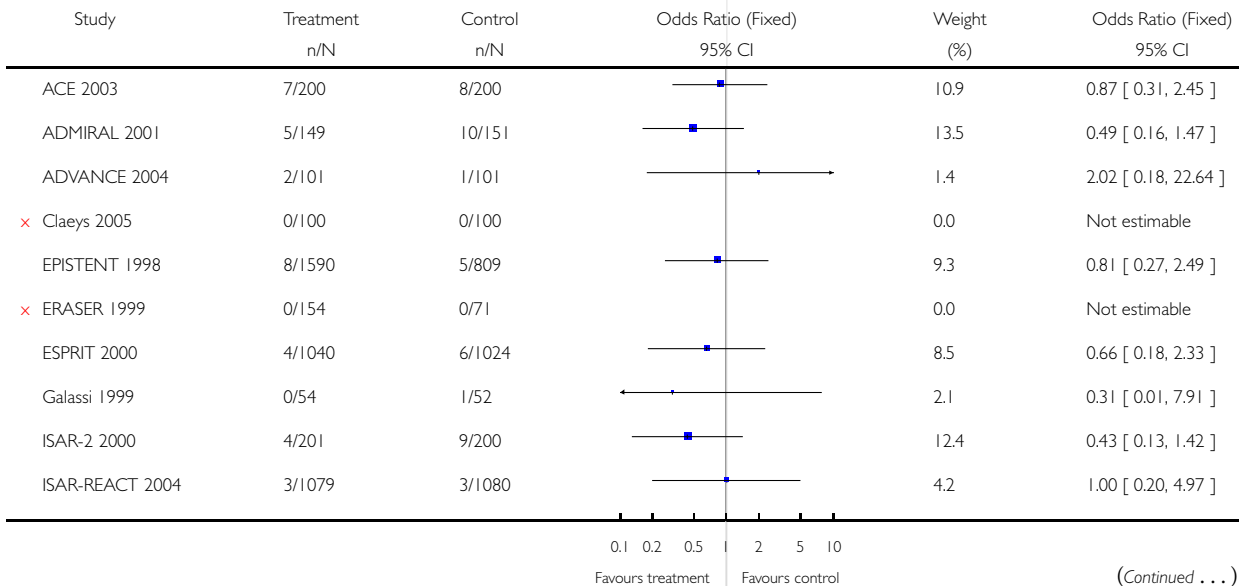


Analysis 07.01. Comparison 07 PCI with stent implantation, Outcome 01 30-day mortality

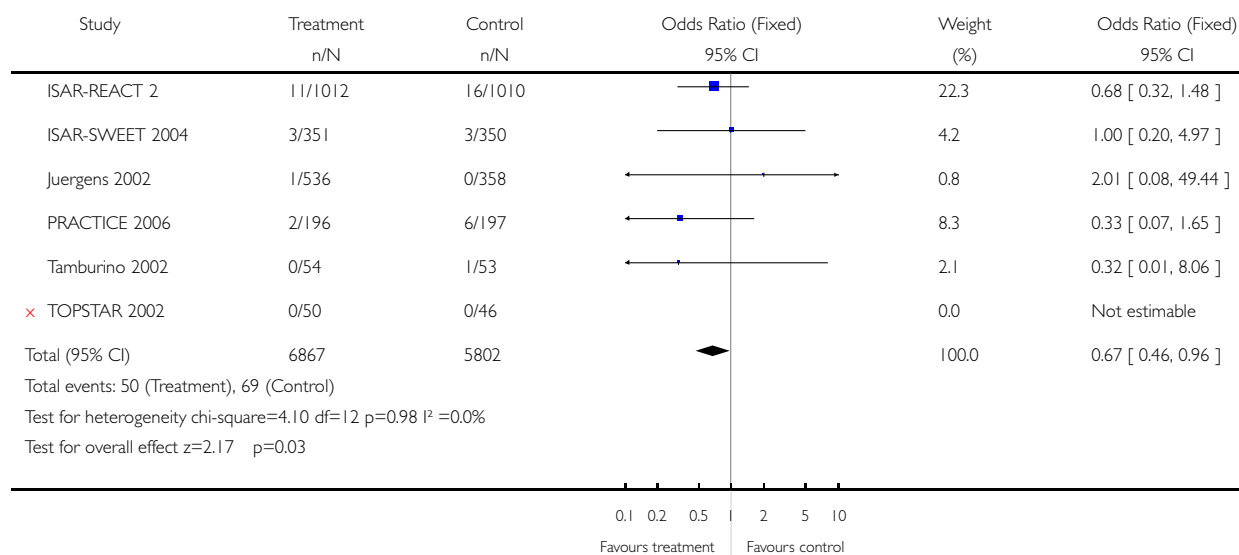
Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 01 30-day mortality



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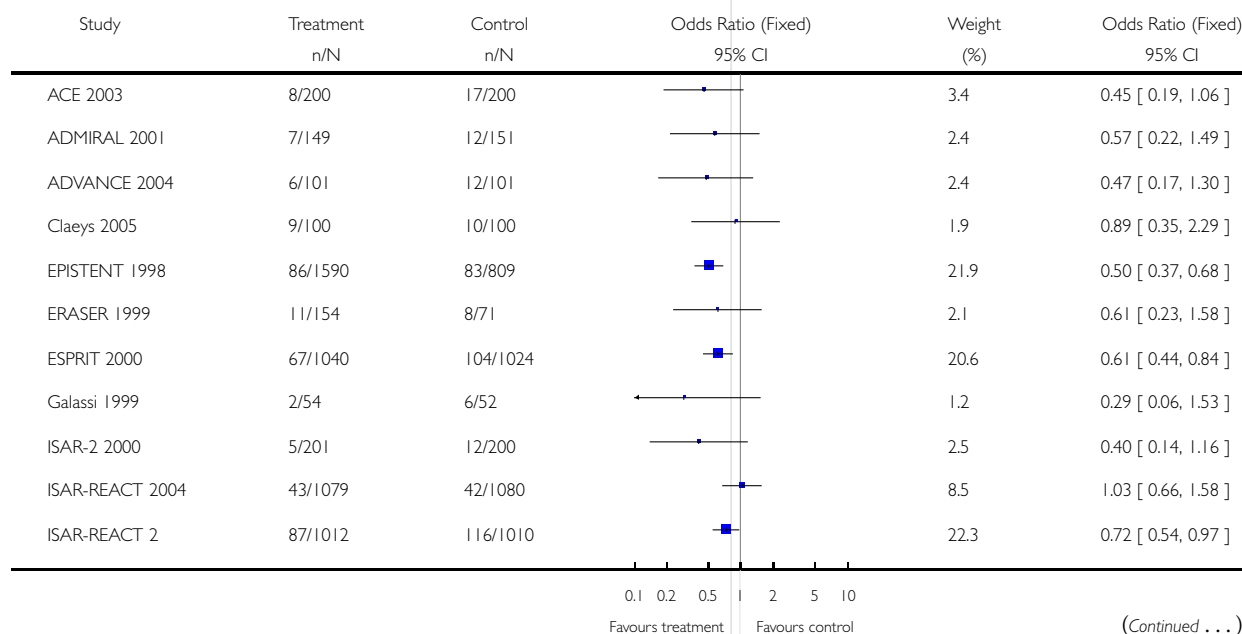


Analysis 07.02. Comparison 07 PCI with stent implantation, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

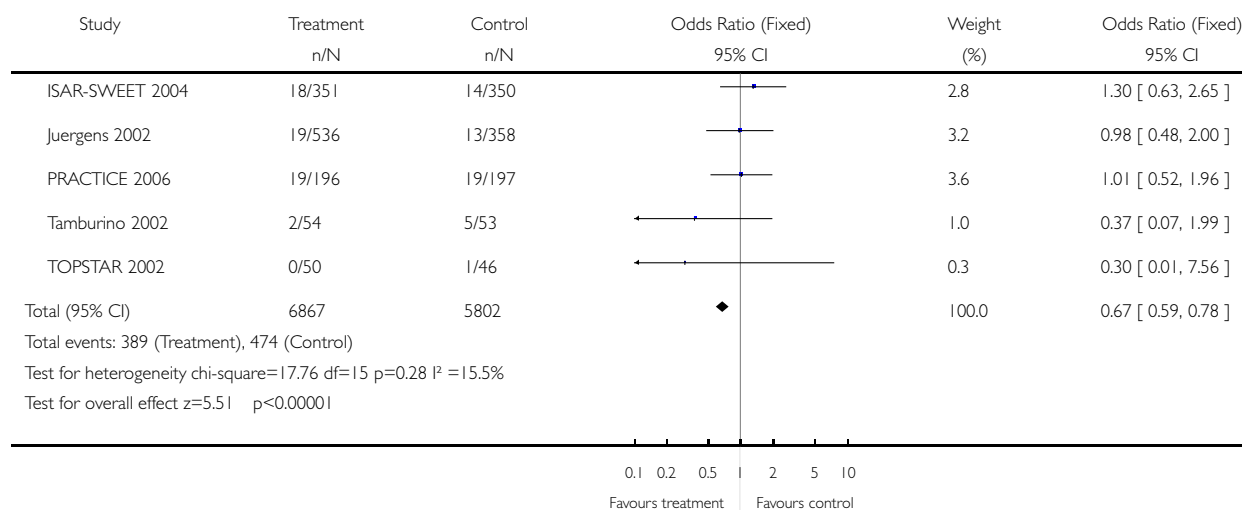
Comparison: 07 PCI with stent implantation

Outcome: 02 30-day mortality or myocardial infarction



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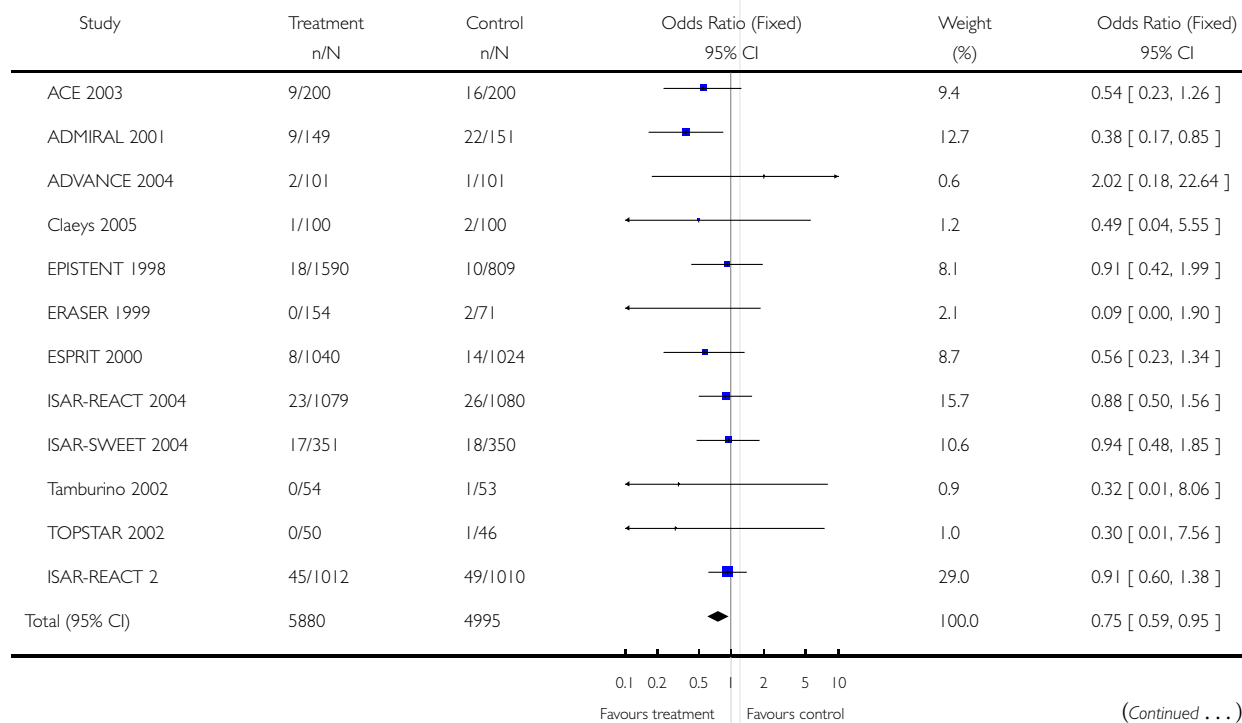


Analysis 07.03. Comparison 07 PCI with stent implantation, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 03 6-month mortality



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Study	Treatment n/N	Control n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
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Total events: 132 (Treatment), 162 (Control)
 Test for heterogeneity chi-square=8.81 df=11 p=0.64 I²=0.0%
 Test for overall effect z=2.40 p=0.02



Analysis 07.04. Comparison 07 PCI with stent implantation, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 04 6-month mortality or myocardial infarction

Study	Treatment n/N	Control n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
ACE 2003	11/200	27/200		4.7	0.37 [0.18, 0.77]
ADMIRAL 2001	8/149	15/151		2.6	0.51 [0.21, 1.25]
ADVANCE 2004	6/101	12/101		2.1	0.47 [0.17, 1.30]
Claeys 2005	10/100	13/100		2.1	0.74 [0.31, 1.78]
EPISTENT 1998	106/1590	92/809		20.9	0.56 [0.42, 0.75]
ERASER 1999	13/154	11/71		2.5	0.50 [0.21, 1.19]
ESPRIT 2000	78/1040	118/1024		20.2	0.62 [0.46, 0.84]
ISAR-REACT 2004	65/1079	69/1080		11.9	0.94 [0.66, 1.33]
ISAR-SWEET 2004	29/351	30/350		5.1	0.96 [0.56, 1.64]
Tamburino 2002	2/54	6/53		1.1	0.30 [0.06, 1.57]
TOPSTAR 2002	1/50	5/46		0.9	0.17 [0.02, 1.49]
ISAR-REACT 2	133/1012	163/1010		26.0	0.79 [0.61, 1.01]
Total (95% CI)	5880	4995		100.0	0.68 [0.60, 0.78]

Total events: 462 (Treatment), 561 (Control)
 Test for heterogeneity chi-square=14.85 df=11 p=0.19 I²=25.9%
 Test for overall effect z=5.77 p<0.00001

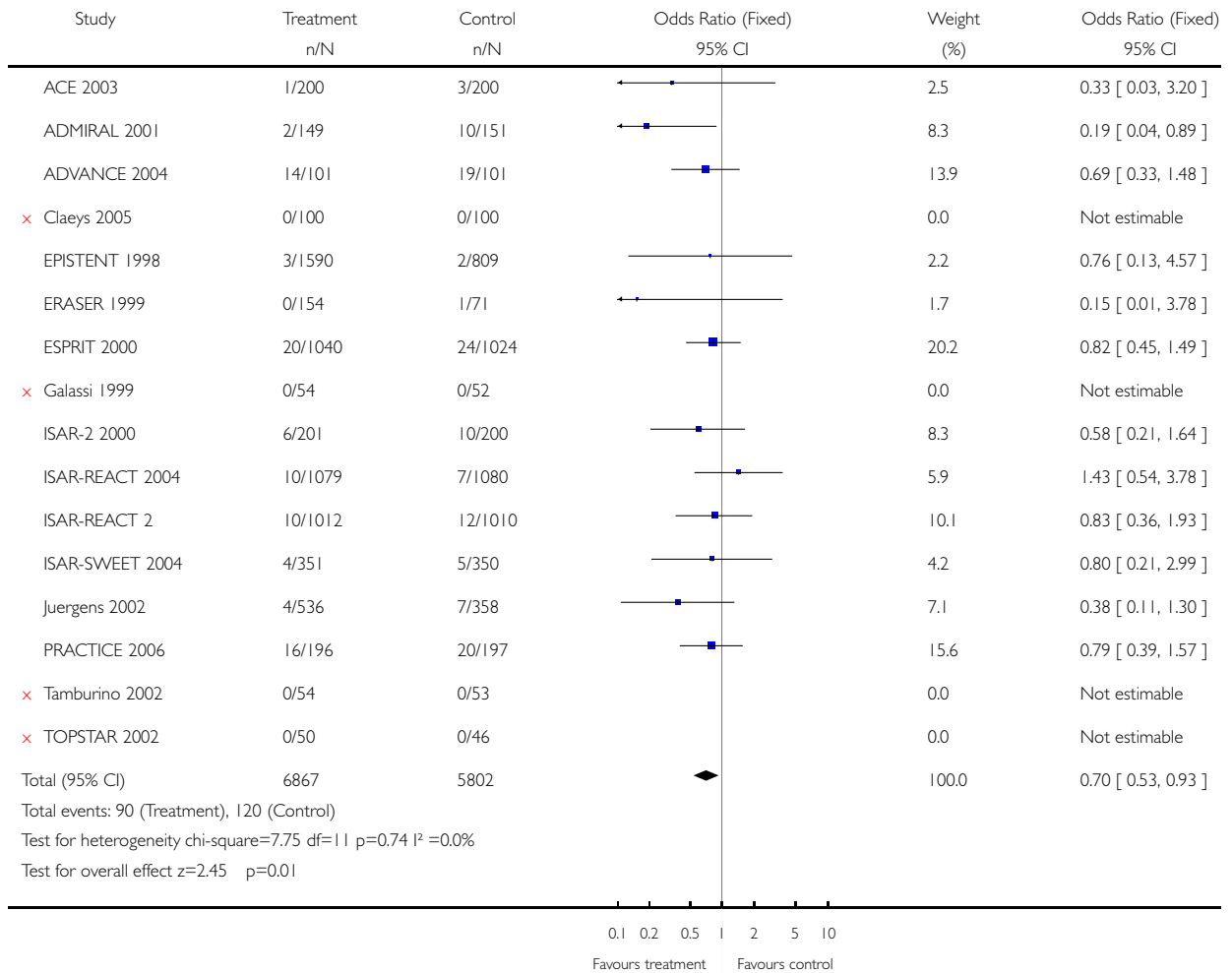


Analysis 07.05. Comparison 07 PCI with stent implantation, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 05 30-day urgent revascularisation

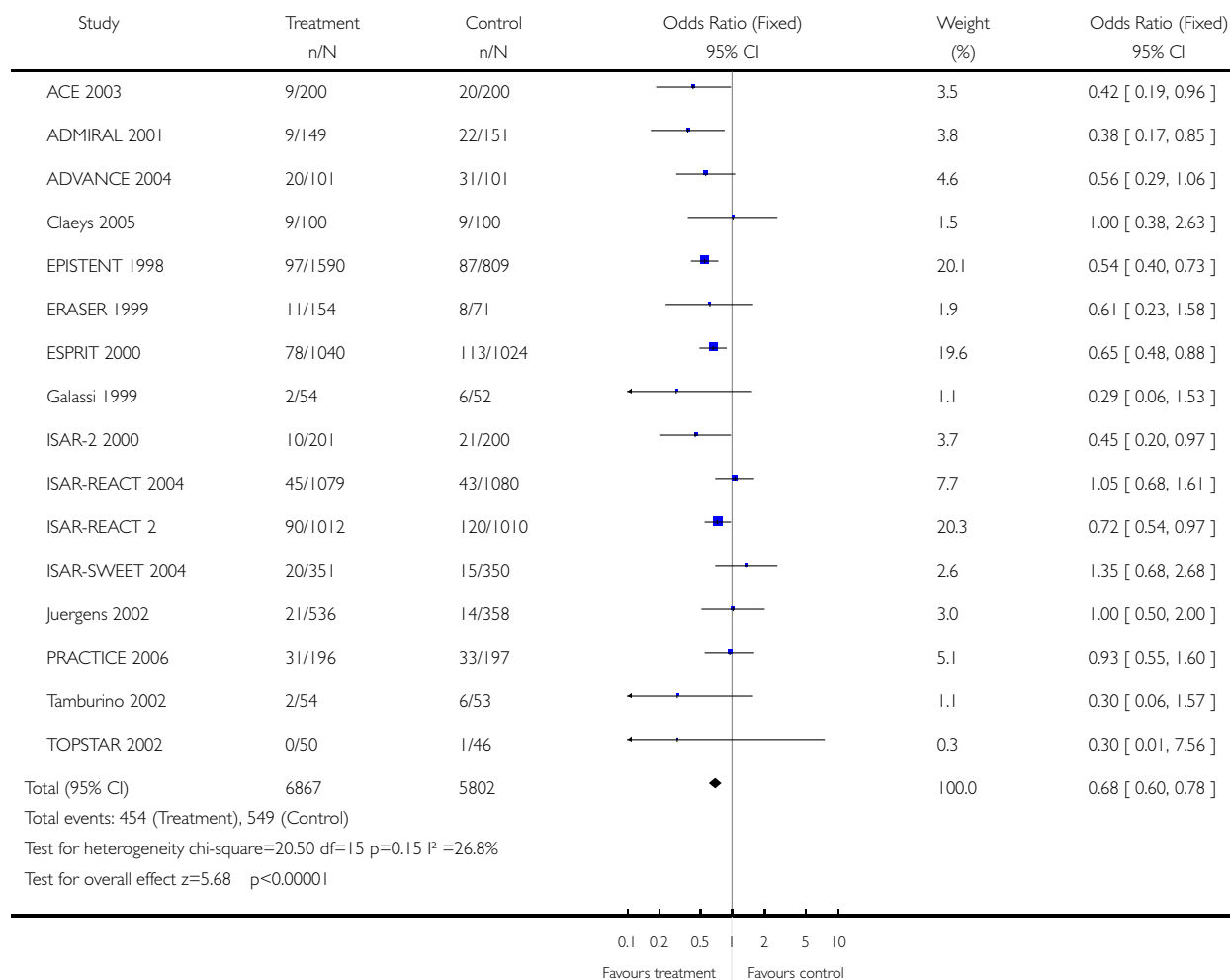


Analysis 07.06. Comparison 07 PCI with stent implantation, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

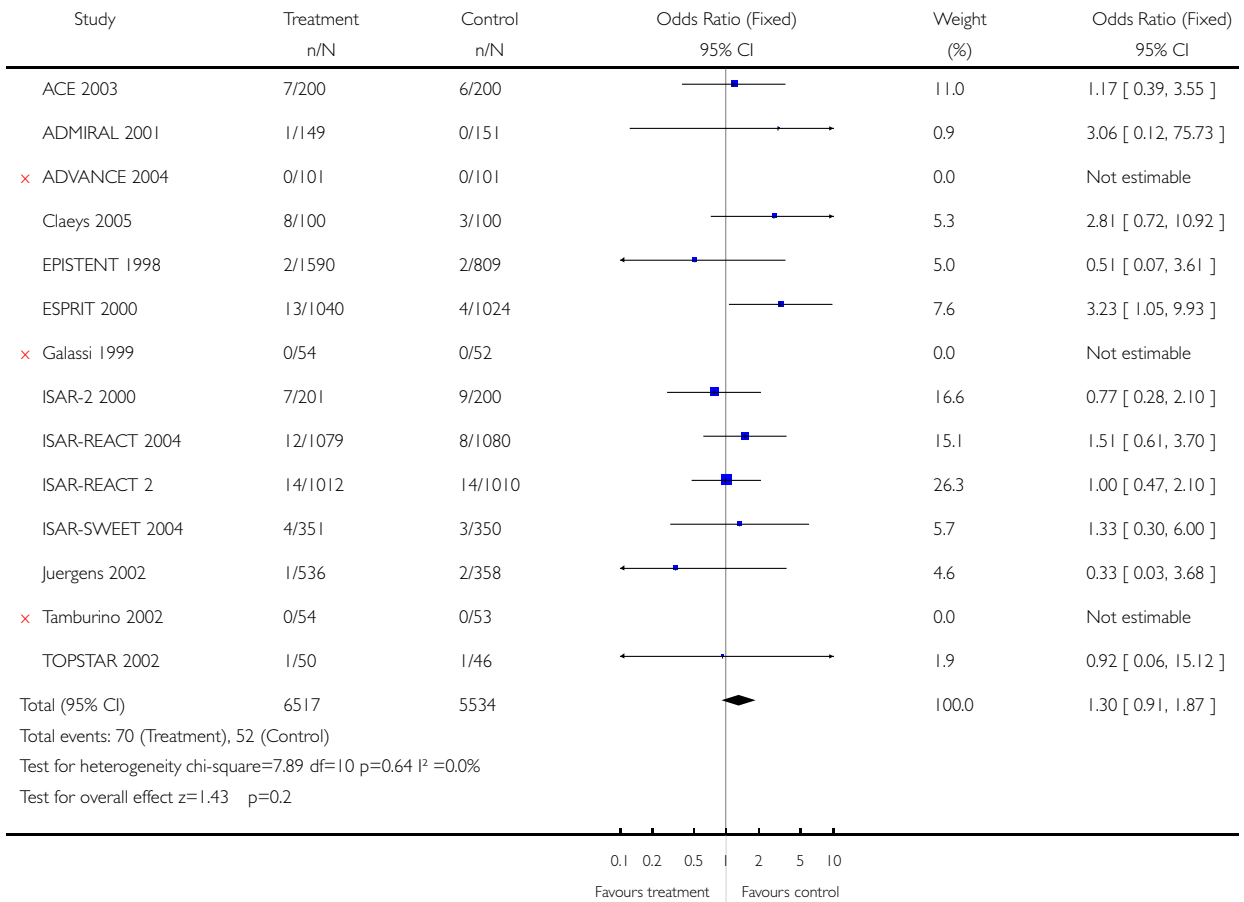


Analysis 07.07. Comparison 07 PCI with stent implantation, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 07 30-day major bleeding

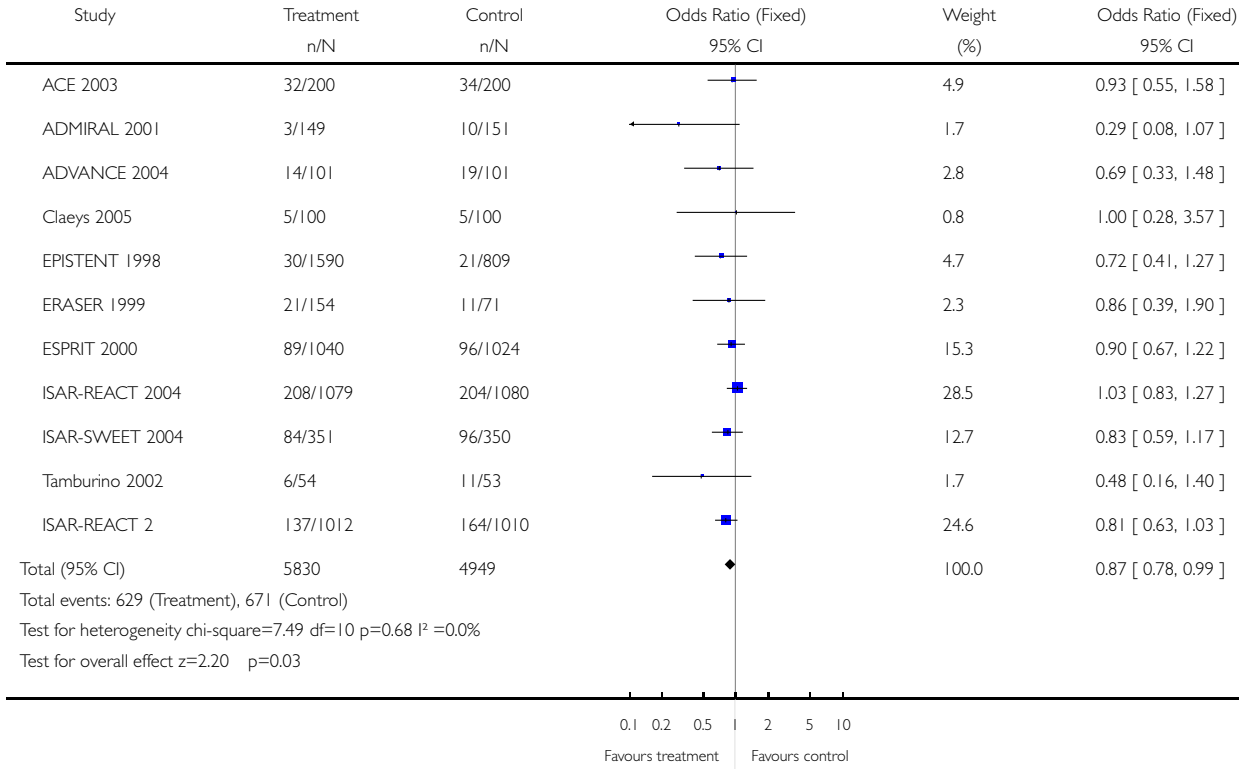


Analysis 07.08. Comparison 07 PCI with stent implantation, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 08 6-month urgent revascularisation

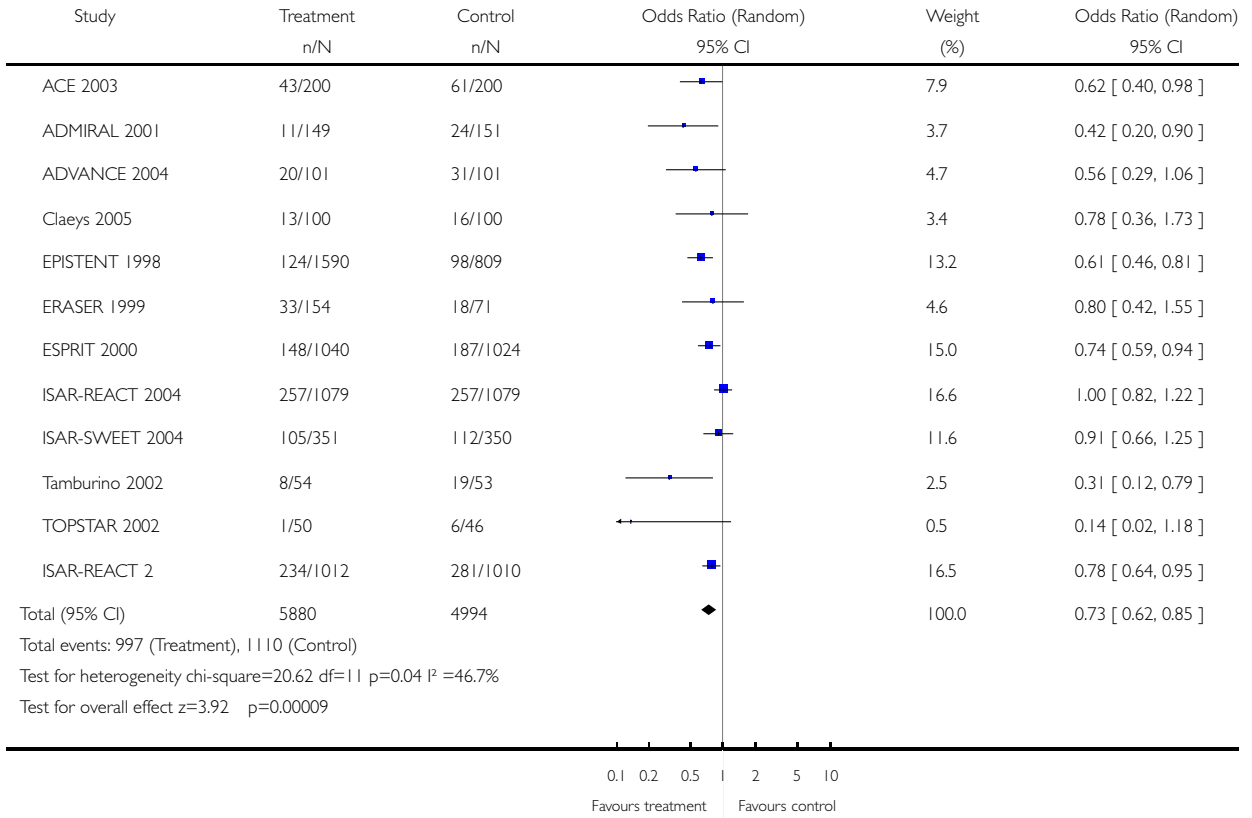


Analysis 07.09. Comparison 07 PCI with stent implantation, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 07 PCI with stent implantation

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation

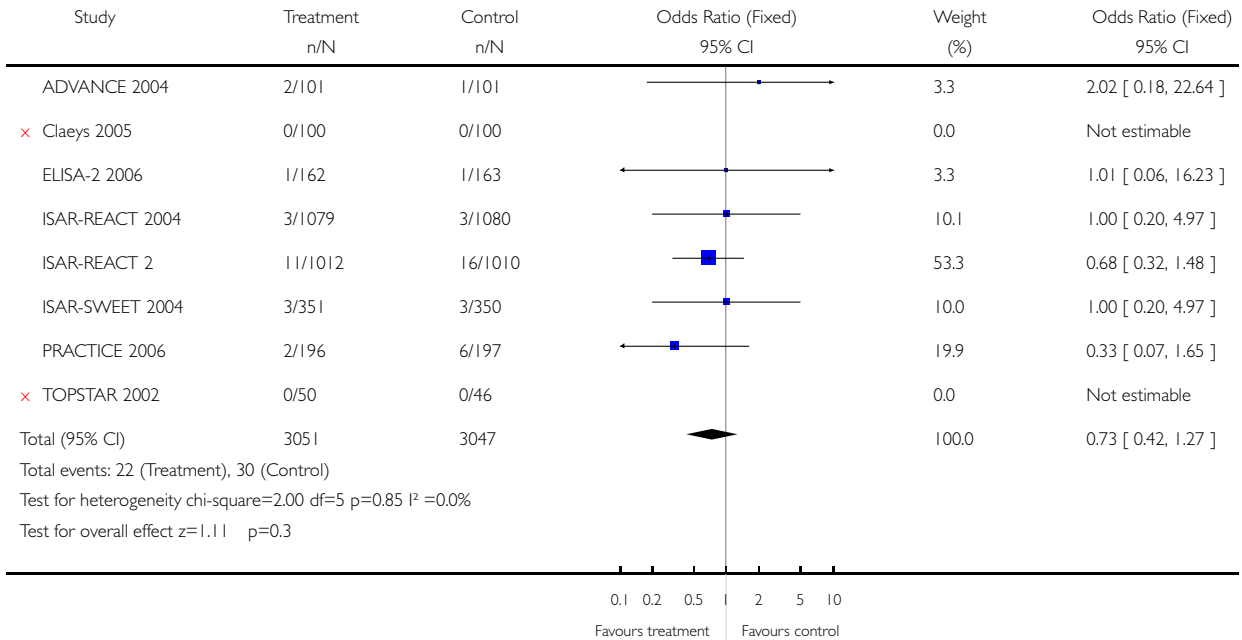


Analysis 08.01. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 01 30-day mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 01 30-day mortality

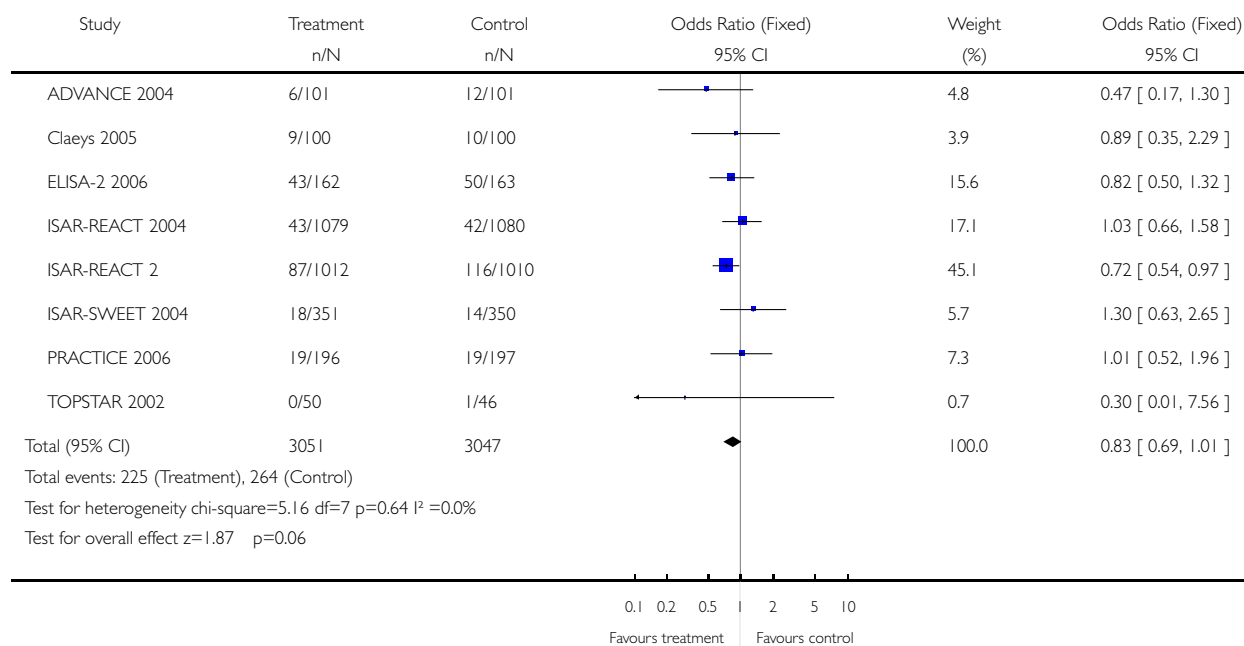


Analysis 08.02. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 02 30-day mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 02 30-day mortality or myocardial infarction

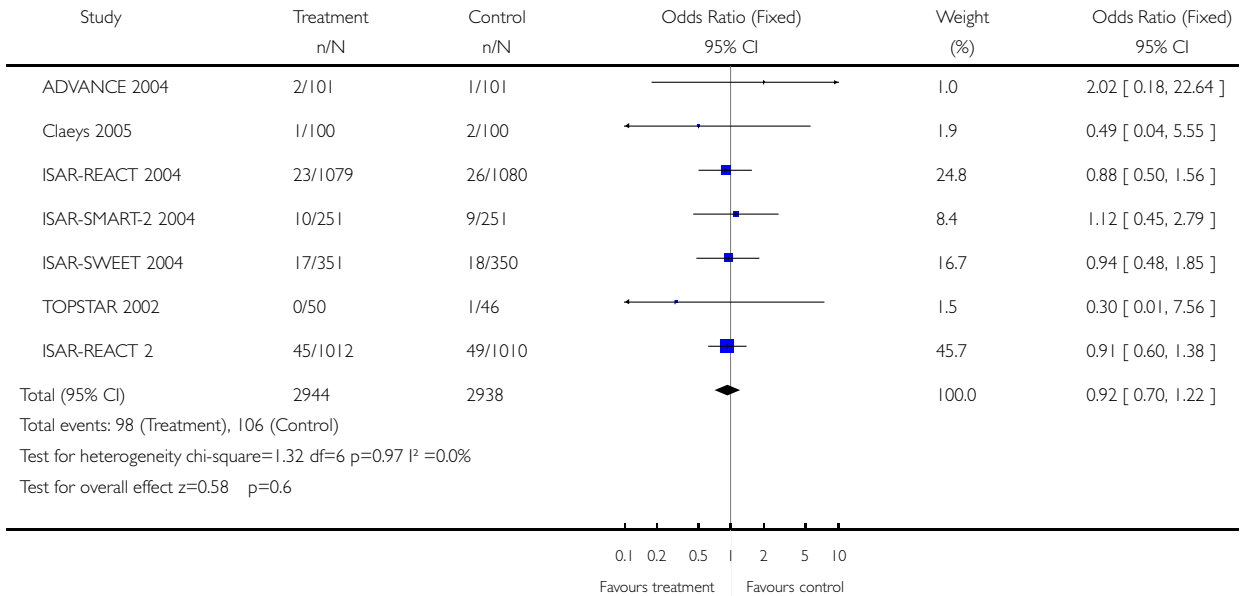


Analysis 08.03. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 03 6-month mortality

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 03 6-month mortality

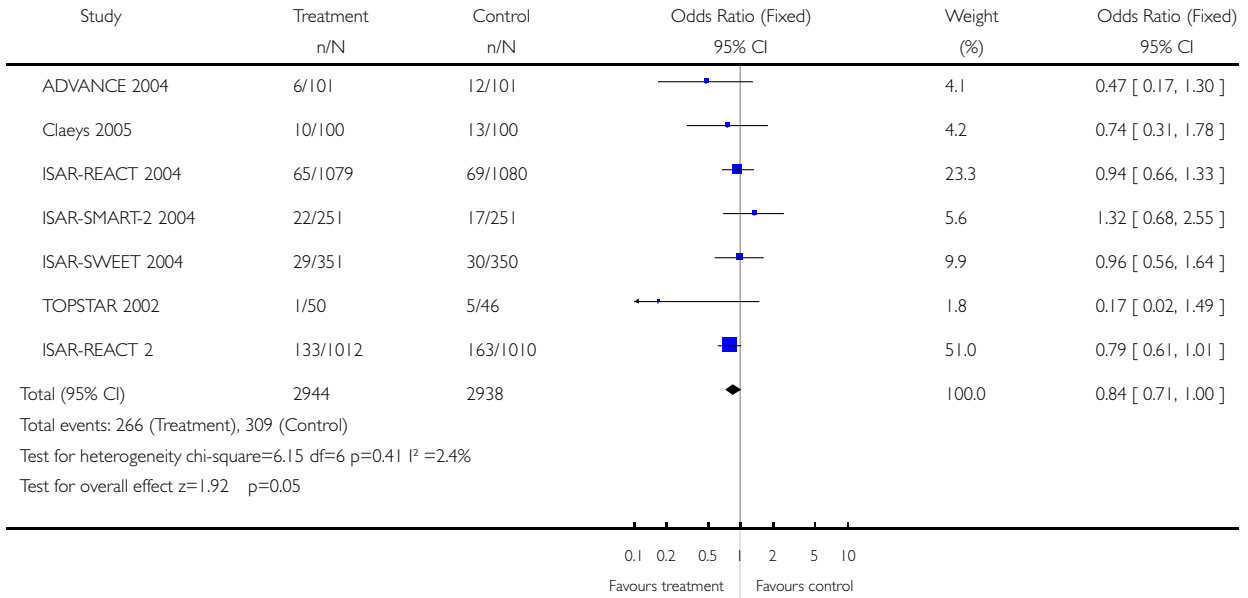


Analysis 08.04. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 04 6-month mortality or myocardial infarction

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 04 6-month mortality or myocardial infarction

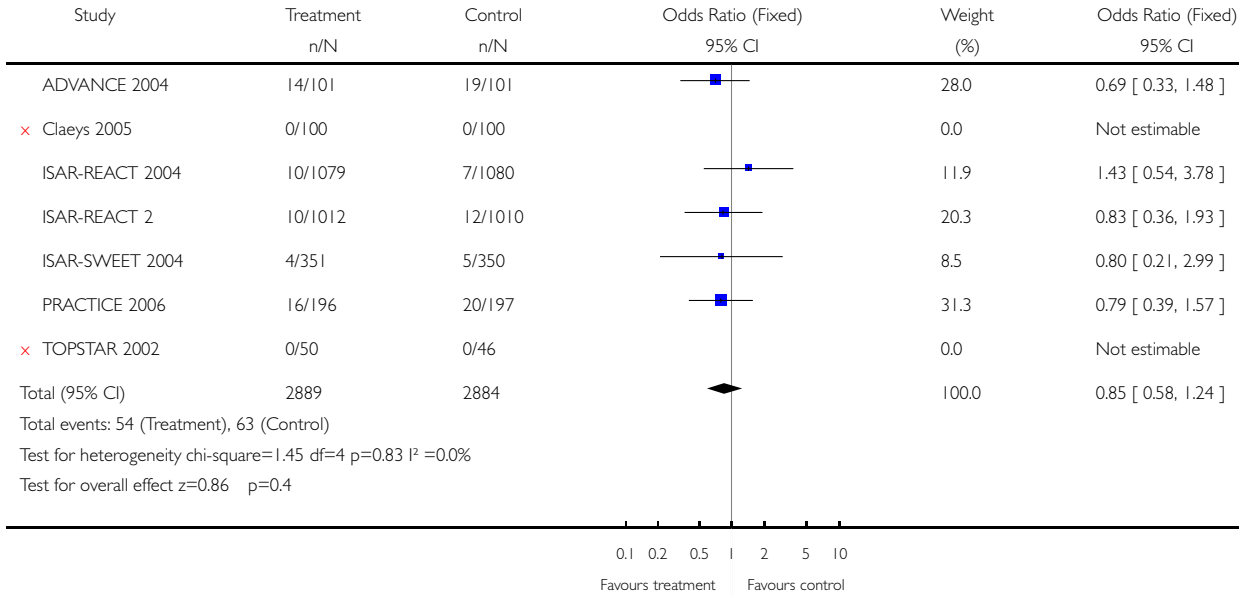


Analysis 08.05. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 05 30-day urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 05 30-day urgent revascularisation

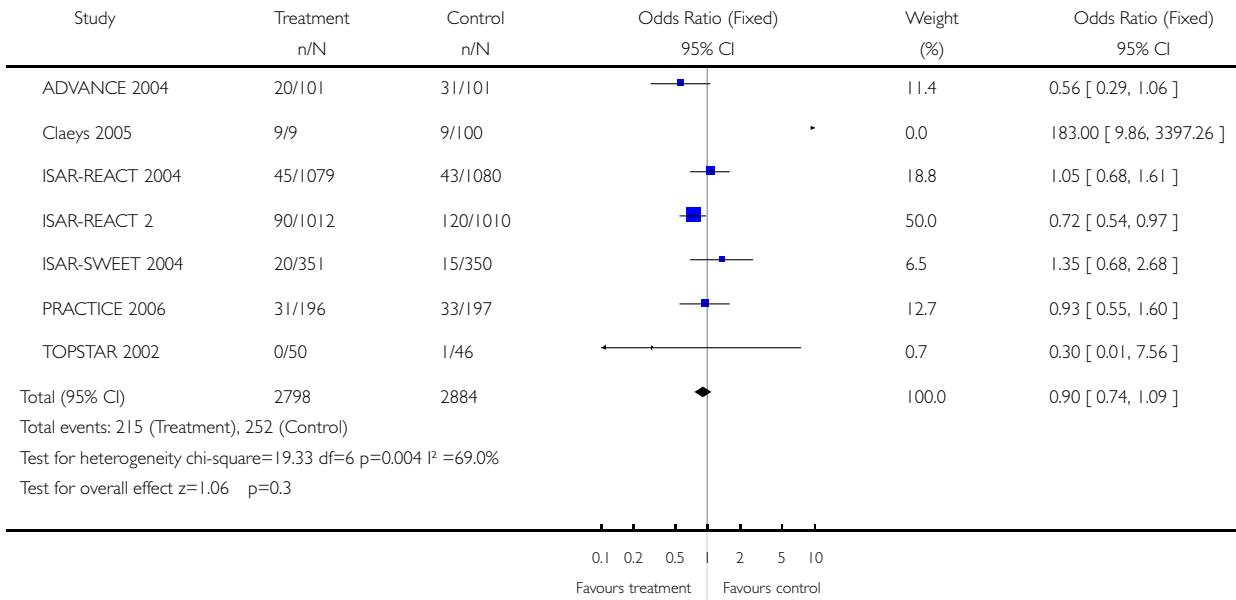


Analysis 08.06. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 06 30-day mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 06 30-day mortality, myocardial infarction or urgent revascularisation

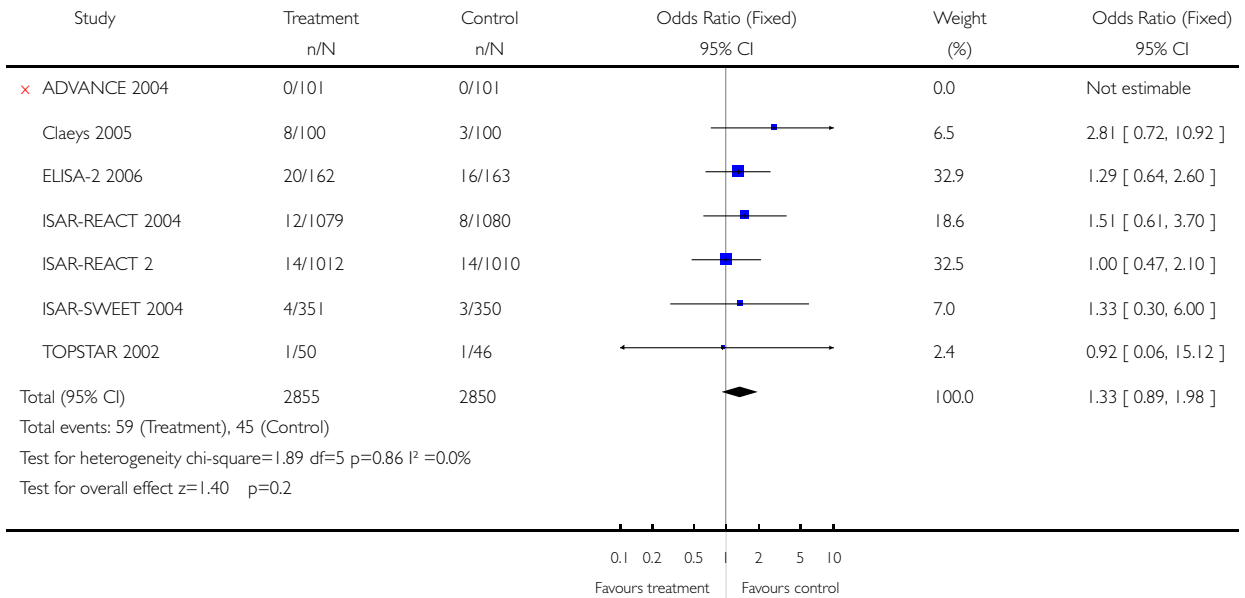


Analysis 08.07. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 07 30-day major bleeding

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 07 30-day major bleeding

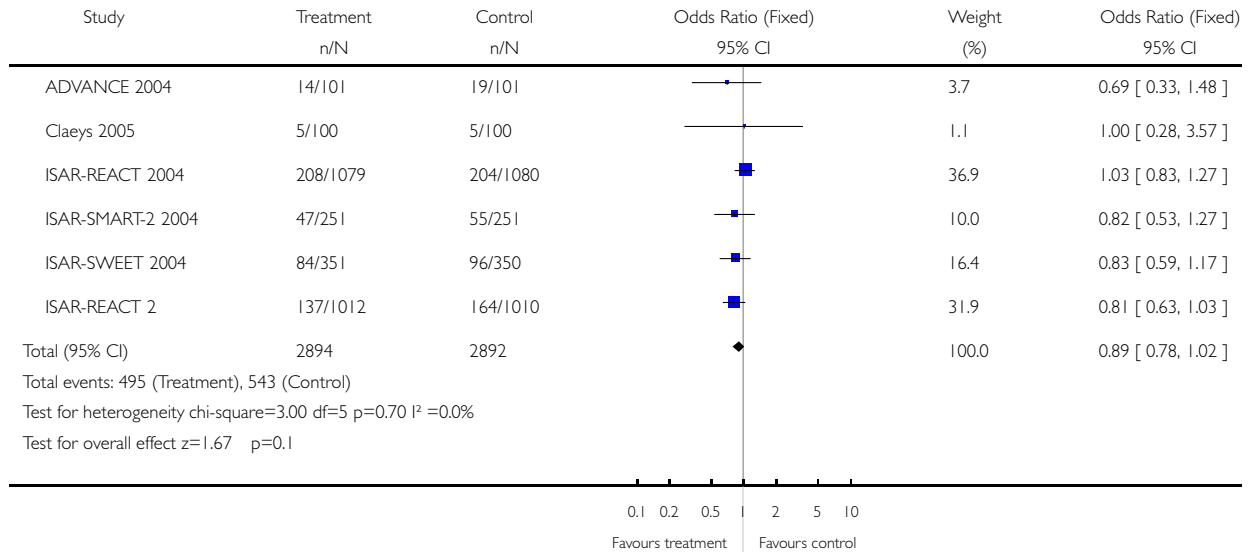


Analysis 08.08. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 08 6-month urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 08 6-month urgent revascularisation

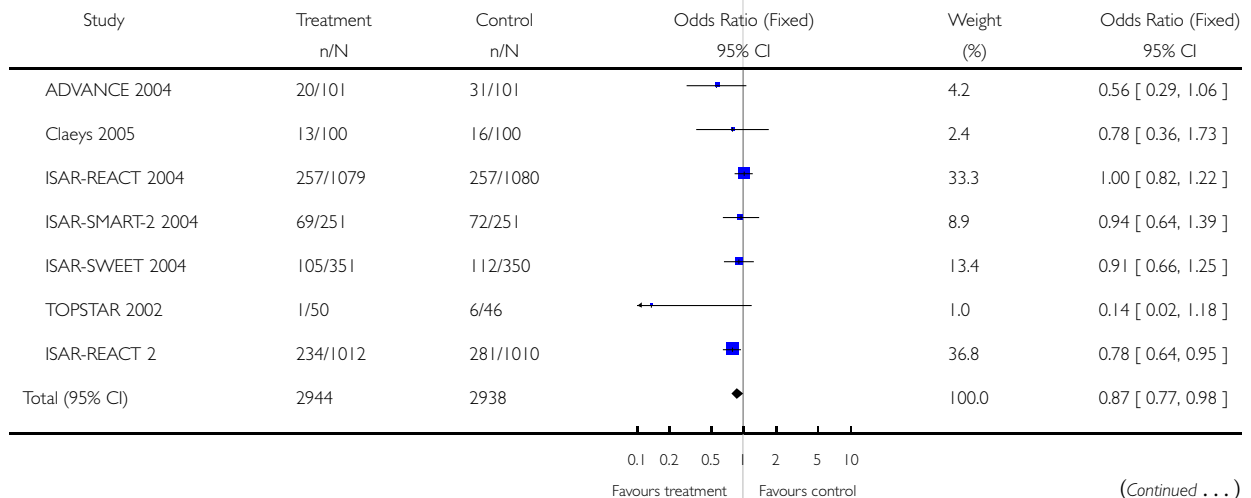


Analysis 08.09. Comparison 08 PCI in patients pre-treated with clopidogrel, Outcome 09 6-month mortality, myocardial infarction or urgent revascularisation

Review: Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary intervention and the initial treatment of non-ST segment elevation acute coronary syndromes

Comparison: 08 PCI in patients pre-treated with clopidogrel

Outcome: 09 6-month mortality, myocardial infarction or urgent revascularisation



(... Continued)

Study	Treatment n/N	Control n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI
Total events: 699 (Treatment), 775 (Control)					
Test for heterogeneity chi-square=8.01 df=6 p=0.24 I ² =25.1%					
Test for overall effect z=2.32 p=0.02					
			0.1 0.2 0.5		2 5 10
			Favours treatment		Favours control