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Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery (Review)

Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, Whitlock RP

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Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery.
Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD003611.
DOI: 10.1002/14651858.CD003611.pub3.

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[Intervention Review]

Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery

Kyle A Arsenault[1], Arif M Yusuf[2], Eugene Crystal[3], Jeff S Healey[4], Carlos A Morillo[5], Girish M Nair[6], Richard P Whitlock[1]

[1]Department of Surgery, McMaster University, Hamilton, Canada. [2]Thrombosis, Population Health Research Institute (McMaster University/Hamilton Health Sciences), Hamilton, Canada. [3]Electrophysiology Programme, Schulich Heart Centre, Toronto, Canada. [4]Medicine, McMaster University, Hamilton, Canada. [5]Department of Cardiac Sciences, Cumming School of Medicine, Foothills Medical Centre, Calgary, Canada. [6]Dept of Medicine, Cardiology Section, University of Ottawa Heart Institute, Ottawa, Canada

Contact address: Richard P Whitlock, richard.whitlock@phri.ca.

Editorial group: Cochrane Heart Group.
Publication status and date: Stable (no update expected for reasons given in 'What's new'), published in Issue 4, 2021.

Citation: Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, Whitlock RP. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database of Systematic Reviews* 2013, Issue 1. Art. No.: CD003611. DOI: 10.1002/14651858.CD003611.pub3.

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ABSTRACT

Background

Atrial fibrillation is a common post-operative complication of cardiac surgery and is associated with an increased risk of post-operative stroke, increased length of intensive care unit and hospital stays, healthcare costs and mortality. Numerous trials have evaluated various pharmacological and non-pharmacological prophylactic interventions for their efficacy in preventing post-operative atrial fibrillation. We conducted an update to a 2004 Cochrane systematic review and meta-analysis of the literature to gain a better understanding of the effectiveness of these interventions.

Objectives

The primary objective was to assess the effects of pharmacological and non-pharmacological interventions for preventing post-operative atrial fibrillation or supraventricular tachycardia after cardiac surgery. Secondary objectives were to determine the effects on post-operative stroke or cerebrovascular accident, mortality, cardiovascular mortality, length of hospital stay and cost of treatment during the hospital stay.

Search methods

We searched the Cochrane Central Register of ControlLed Trials (CENTRAL) (Issue 8, 2011), MEDLINE (from 1946 to July 2011), EMBASE (from 1974 to July 2011) and CINAHL (from 1981 to July 2011).

Selection criteria

We selected randomized controlled trials (RCTs) that included adult patients undergoing cardiac surgery who were allocated to pharmacological or non-pharmacological interventions for the prevention of post-operative atrial fibrillation or supraventricular tachycardia, except digoxin, potassium (K^+), or steroids.

Data collection and analysis

Two review authors independently abstracted study data and assessed trial quality.

Main results

One hundred and eighteen studies with 138 treatment groups and 17,364 participants were included in this review. Fifty-seven of these studies were included in the original version of this review while 61 were added, including 27 on interventions that were not considered in

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the original version. Interventions included amiodarone, beta-blockers, sotalol, magnesium, atrial pacing and posterior pericardiotomy. Each of the studied interventions significantly reduced the rate of post-operative atrial fibrillation after cardiac surgery compared with a control. Beta-blockers (odds ratio (OR) 0.33; 95% confidence interval) CI 0.26 to 0.43; I^2 = 55%) and sotalol (OR 0.34; 95% CI 0.26 to 0.43; I^2 = 3%) appear to have similar efficacy while magnesium's efficacy (OR 0.55; 95% CI 0.41 to 0.73; I^2 = 51%) may be slightly less. Amiodarone (OR 0.43; 95% CI 0.34 to 0.54; I^2 = 63%), atrial pacing (OR 0.47; 95% CI 0.36 to 0.61; I^2 = 50%) and posterior pericardiotomy (OR 0.35; 95% CI 0.18 to 0.67; I^2 = 66%) were all found to be effective. Prophylactic intervention decreased the hospital length of stay by approximately two-thirds of a day and decreased the cost of hospital treatment by roughly $1250 US. Intervention was also found to reduce the odds of post-operative stroke, though this reduction did not reach statistical significance (OR 0.69; 95% CI 0.47 to 1.01; I^2 = 0%). No significant effect on all-cause or cardiovascular mortality was demonstrated.

Authors' conclusions

Prophylaxis to prevent atrial fibrillation after cardiac surgery with any of the studied pharmacological or non-pharmacological interventions may be favored because of its reduction in the rate of atrial fibrillation, decrease in the length of stay and cost of hospital treatment and a possible decrease in the rate of stroke. However, this review is limited by the quality of the available data and heterogeneity between the included studies. Selection of appropriate interventions may depend on the individual patient situation and should take into consideration adverse effects and the cost associated with each approach.

PLAIN LANGUAGE SUMMARY

Intervention is favored in the prevention of post-operative atrial fibrillation after heart surgery

Atrial fibrillation after heart surgery is a common complication that has been associated with poor outcomes. We reviewed the literature to better understand the role of preventative interventions for this condition. By combining the results of 118 studies with 17,364 participants, we are able to gain a better understanding of the evidence behind each of these interventions. All of the interventions studied were effective in reducing the occurrence of atrial fibrillation, length of hospital stay, cost of hospital treatment and may be effective in reducing the risk of stroke. The interventions did not have an effect on death after heart surgery. It was not possible to analyze the adverse events associated with the medications studied in this review, but these should be considered by clinicians when choosing an appropriate intervention for their patients. Furthermore, differences in the design between the studies combined in this review may complicate interpretation of these results.

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BACKGROUND

Description of the condition

Atrial fibrillation is a common post-operative complication of cardiac surgery, occurring in 17% to 47% of patients (Almassi 1997; Chung 2000b; Frost 1992; Leitch 1990; Mathew 1996) with the incidence being greater in older patients (Leitch 1990). Besides directly causing patient discomfort and leading to hemodynamic compromise, several studies have demonstrated that post-operative atrial fibrillation is associated with an increased risk of post-operative stroke (Almassi 1997; Creswell 1993; Reed 1998) and mortality (Almassi 1997), longer intensive care unit and hospital stays (Almassi 1997; Aranki 1996; Creswell 1993; Loubani 2000; Mathew 1996) and greater costs of treatment (Kowey 1992; Taylor 1990). Atrial fibrillation, both paroxysmal and chronic, has been shown to significantly increase the risk of stroke, especially in older patients (Wolf 1991).The main mechanism of stroke in atrial fibrillation is believed to be intracardiac embolism. Blood stasis within the atrial chamber likely plays a role, but continuing research has identified multiple other factors that lead to thrombus formation (Whitlock 2009), including: atherosclerosis (SPAF Investigators Committee 1998), a pro-inflammatory state, and endothelial dysfunction (Guazzi 2009), as well as platelet activation (Müller 2002) that leads to a hypercoagulable state (Watson 2009). With the low rate and multifactorial etiology of post-operative stroke after cardiac surgery, it is difficult for any single trial to definitively demonstrate a benefit from atrial fibrillation prevention. Prophylaxis for post-operative atrial fibrillation is a common practice in the cardiac surgery population and aims to prevent the complications and outcomes discussed above.

Description of the intervention

Numerous trials have studied various interventions for their efficacy in preventing post-operative atrial fibrillation after cardiac surgery (Chung 2000b). These interventions fall into one of two categories: pharmacological or non-pharmacological. The most commonly studied prophylactic interventions to prevent atrial fibrillation after cardiac surgery are beta-blockers, including atenolol, metoprolol, propranolol and timolol, among others. This class of drugs works by blocking the effects of catecholamines on β_1-adrenergic receptors, thus decreasing the effects of the sympathetic nervous system on the heart. Amiodarone, a class III antiarrhythmic, has also been studied extensively in this setting. This agent primarily prolongs the repolarization phase of the cardiac cycle by blocking potassium channels. However, it also has other effect similar to those of antiarrhythmic classes Ia, II, and IV. Sotalol demonstrates properties of both Class III antiarrhythmics and beta-blockers. Finally, magnesium has been proposed as a prophylactic measure for atrial fibrillation after cardiac surgery and is thought to work through its effects on transmembrane ion gradients and catecholamines. Studies investigating non-pharmacological interventions for preventing post-operative atrial fibrillation have largely concentrated on atrial pacing, which controls the heart rate via electrical stimulation. However, posterior pericardiotomy, an intraoperative procedure that involves a 4 cm longitudinal incision in the pericardium posterior and parallel to the phrenic nerve, has also been evaluated. This technique is thought to work by allowing post-operative drainage of fluid and blood out of the pericardium, thereby preventing pericardial effusion, a condition known to be associated with the development of atrial fibrillation (Angelini 1987; Bryan 1990). Each of these interventions are associated with adverse effects that range from abnormal laboratory tests to hemodynamic instability. Knowledge of these possible adverse effects and the methods to address them are important skills for the clinician offering post-operative atrial fibrillation prophylaxis, as they may have important clinical consequences for this vulnerable patient population. While an in-depth discussion of the safety and monitoring of each of these interventions is beyond the scope of this review, the most common and most serious potential adverse events for each of these interventions are outlined in Table 1.

Why it is important to do this review

Many studies have investigated various proposed prophylactic interventions for their efficacy in preventing post-operative atrial fibrillation after cardiac surgery. However, few of these trials have been sufficiently powered to definitively determine the usefulness of these treatments in preventing this arrhythmia. Furthermore, no studies have had sufficient power to reliably estimate the effects of these treatments on the rates of clinically relevant outcomes such as stroke, mortality and the length and cost of hospital stay. This is an update of a Cochrane review originally published in 2004 (Crystal 2004). Since that date, a number of studies have been published that further evaluate the major interventions considered and re-explore interventions that were not included in the original review. We updated this systematic review and meta-analysis to determine the efficacy of various interventions for preventing post-operative atrial fibrillation after cardiac surgery and for their effects on stroke, mortality, cardiovascular mortality, length of hospital stay and cost of treatment.

OBJECTIVES

The primary objective was to assess the effects of pharmacological and non-pharmacological interventions for preventing post-operative atrial fibrillation or supraventricular tachycardia after cardiac surgery. Secondary objectives were to determine the effects on post-operative stroke or cerebrovascular accident, mortality, cardiovascular mortality, length of hospital stay and cost of treatment during the hospital stay.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) in which patients undergoing cardiac surgery, including coronary artery bypass graft (CABG), valvular and combined procedures with or without cardiopulmonary bypass (CPB), were randomized to pharmacological or non-pharmacological interventions for the prevention of post-operative atrial fibrillation or supraventricular tachycardia.

Types of participants

Adult (≥ 18 years old) undergoing CABG, valvular surgery or combined CABG and valvular surgery with or without CPB with no history of chronic atrial fibrillation.

Types of interventions

Any pharmacological or non-pharmacological intervention aimed at preventing post-operative atrial fibrillation except digoxin,

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potassium (K^+), or steroids. Digoxin is mainly used for its rate-control properties and therefore was not deemed to be important in this analysis of rhythm-control prophylaxis. While hypokalemia is an important factor in the generation of atrial fibrillation, its use is guided mainly by plasma levels and clinical decision-making rather than specific use for post-operative prophylaxis. Interest in steroids in the cardiac surgery setting has increased in recent years. We decided not to include steroids in this review because there have been several extensive reviews of this topic (Cappabianca 2011; Marik 2009; Whitlock 2008) and our literature search did not reveal any studies that would significantly add to the established review literature. We pooled the results of studies evaluating amiodarone, beta-blockers, sotalol, magnesium, atrial pacing and posterior pericardiotomy.

Types of outcome measures

Primary outcomes

Incidence of atrial fibrillation or supraventricular tachycardia.

Secondary outcomes

1. Incidence of stroke or cerebrovascular accident
2. Mortality rate
3. Cardiovascular mortality rate
4. Length of hospital stay
5. Cost of treatment during hospital stay

Adverse events associated with the interventions studied were not reported in a standardized format and the included trials were not powered to analyze these events. Therefore, data on adverse events were not collected.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 8, 2011), MEDLINE (from 1946 to July 2011), EMBASE (from 1974 to July 2011) and CINAHL (from 1981 to July 2011). The initial search was based on the following terms: "atrial fibrillation", "atrial flutter", or “atrial arrhythmia” and “heart surgery”, “cardiac surgery”, "CABG" or "valve surgery".

The search strategies used can be found in Appendix 1; Appendix 2; Appendix 3; Appendix 4. A standard RCT filter was used for MEDLINE (Dickersin 1994) and EMBASE (Lefebvre 2008).

Data collection and analysis

Selection of studies

Study eligibility was assessed in two stages. First, two review authors independently screened the titles and abstracts of each citation identified in our search. All articles identified as having any possibility of fulfilling the above eligibility criteria in the screening process were retrieved to undergo full text evaluation.

Two review authors independently evaluated each full text article selected during the screening stage. In cases of disagreement, the review authors discussed the reasoning for their decisions and came to a consensus. If disagreements were not resolved during this process, an independent third adjudicator assessed the paper in question and made a final decision. Non-English studies were assessed by third-party translators.

Data extraction and management

Two review authors independently abstracted the following descriptive data from eligible studies: year of publication, country of origin, interventions, treatment schema and doses, number of participants in each group, patient characteristics, concurrent antiarrhythmic medications, type of surgery, type of monitoring for outcomes, length of follow-up, definition of primary outcome and end points of atrial fibrillation, stroke, mortality, cardiovascular mortality, length of stay and cost. Data from the two review authors were compared and any discrepancies were resolved. We converted non-US currencies into 2011 US dollars using the Bank of Canada rates for June 21, 2011. Studies that did not present data on individual secondary outcomes were not included in those analyses. We did not contact trial authors for this missing data.

Trials that evaluated more than one dosage of a medication, more than one atrial pacing site or more than one intervention were entered into the analysis as multiple single trials, leading to control groups for these trials being counted twice in pooled analyses. Numbers of participants presented in the Effects of interventions section include these duplicated control groups.

Assessment of risk of bias in included studies

Risk of bias in included studies was assessed by two review authors using the criteria and technique described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Each study was assigned a level of risk of bias (high risk, unclear risk, low risk) for each of seven categories.

- Random sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of participants and personnel (performance bias)
- Blinding of outcome assessment (detection bias)
- Incomplete outcome data (attrition bias)
- Selective reporting (reporting bias)
- Intention-to-treat analysis

The use of intention-to-treat analysis was evaluated in addition to the categories suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* because it was felt that this analysis technique is important for, and specific to, the quality of randomized trials.

Using the primary outcome of incidence of atrial fibrillation or supraventricular tachycardia, studies were grouped by the assigned risk of bias level for each of the seven bias categories. Pharmacological and non-pharmacological interventions were separated for the performance bias and detection bias categories due to the technical difficulties of blinding in a non-pharmacological study.

Measures of treatment effect

Statistical analyses were performed using the statistical package provided by The Cochrane Collaboration (RevMan 5.1). We analyzed dichotomous outcomes using odds ratios within a Mantel-Haenszel random-effects model. We analyzed continuous variables using mean difference within an inverse variance random-effects model.

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Unit of analysis issues

All of the trials included in this review were of a simple parallel-group design, with individuals randomized to one intervention group and a single measurement for each outcome was collected from each participant.

Assessment of heterogeneity

Subgroup differences were assessed using the χ^2 test. Sensitivity analyses were undertaken for 'Risk of bias' categories that demonstrated significant subgroup differences, defined as $P < 0.10$. Sensitivity analyses compared all studies to studies that were at low risk of bias.

Heterogeneity was assessed using the I^2 statistic (Higgins 2002) due to its consistency for meta-analyses that include a large number of studies (Higgins 2003). An I^2 value greater than or equal to 50% was considered to be substantial in this analysis. When heterogeneity was identified, we explored individual trial characteristics within each intervention to determine possible sources.

RESULTS

Description of studies

Results of the search

Figure 1 displays a PRISMA diagram of our study selection process. Of the 3864 studies identified in the literature search and an additional three studies included from 'Studies awaiting classification' in the original review (Gerstenfeld 2001; Matsuura 2001; White 2002), 432 were reviewed in full text format and 170 met the inclusion criteria. Interventions included in fewer than four studies were not appropriate for pooling in our meta-analysis and therefore were not analyzed in this review. A total of 118 studies with 138 treatment groups and 17364 participants were considered in this review. Fifty-seven of these studies were included in the original version of this review (Crystal 2004) while 61 were added, including 27 on interventions that were not considered in the original version. The Kurz 1999 study was excluded from the original version of this review because the trial was prematurely aborted. We decided to include the preliminary results of this trial. The Tokmakoglu 2002 study was also excluded due to a lack of a control group. This trial was designed with three randomized groups: one that received amiodarone, one that received metoprolol and digoxin and one that received no prophylaxis. It is possible that the triple-group setup of this trial led to an error in its eligibility assessment in the original version of this review. Upon further assessment of this reference, it was included in our review. Twenty-three additional studies from the period covered by the literature search of the original review were identified (Arbatli 2003; Asimakopoulos 1997; Casthely 1994; Crystal 2003; Dagdelen 2002; England 1992; Fanning 1991; Farsak 2002; Gerstenfeld 2001; Jensen 1997; Kaplan 2003; Karmy-Jones 1995; Kuralay 1999; Matsuura 2001; Mulay 1995; Nurözler 1996; Parikka 1993; Speziale 2000; Toraman 2001; White 2002; White 2003; Wilkes 2002; Yeatman 2002) of which 13 studied the effects of magnesium (Casthely 1994; Dagdelen 2002; England 1992; Fanning 1991; Jensen 1997; Kaplan 2003; Karmy-Jones 1995; Nurözler 1996; Parikka 1993; Speziale 2000; Toraman 2001; Wilkes 2002; Yeatman 2002) and five evaluated posterior pericardiotomy (Arbatli 2003; Asimakopoulos 1997; Farsak 2002; Kuralay 1999; Mulay 1995), interventions that were not analyzed in the original version of this review.

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Figure 1. PRISMA diagram of study selection process

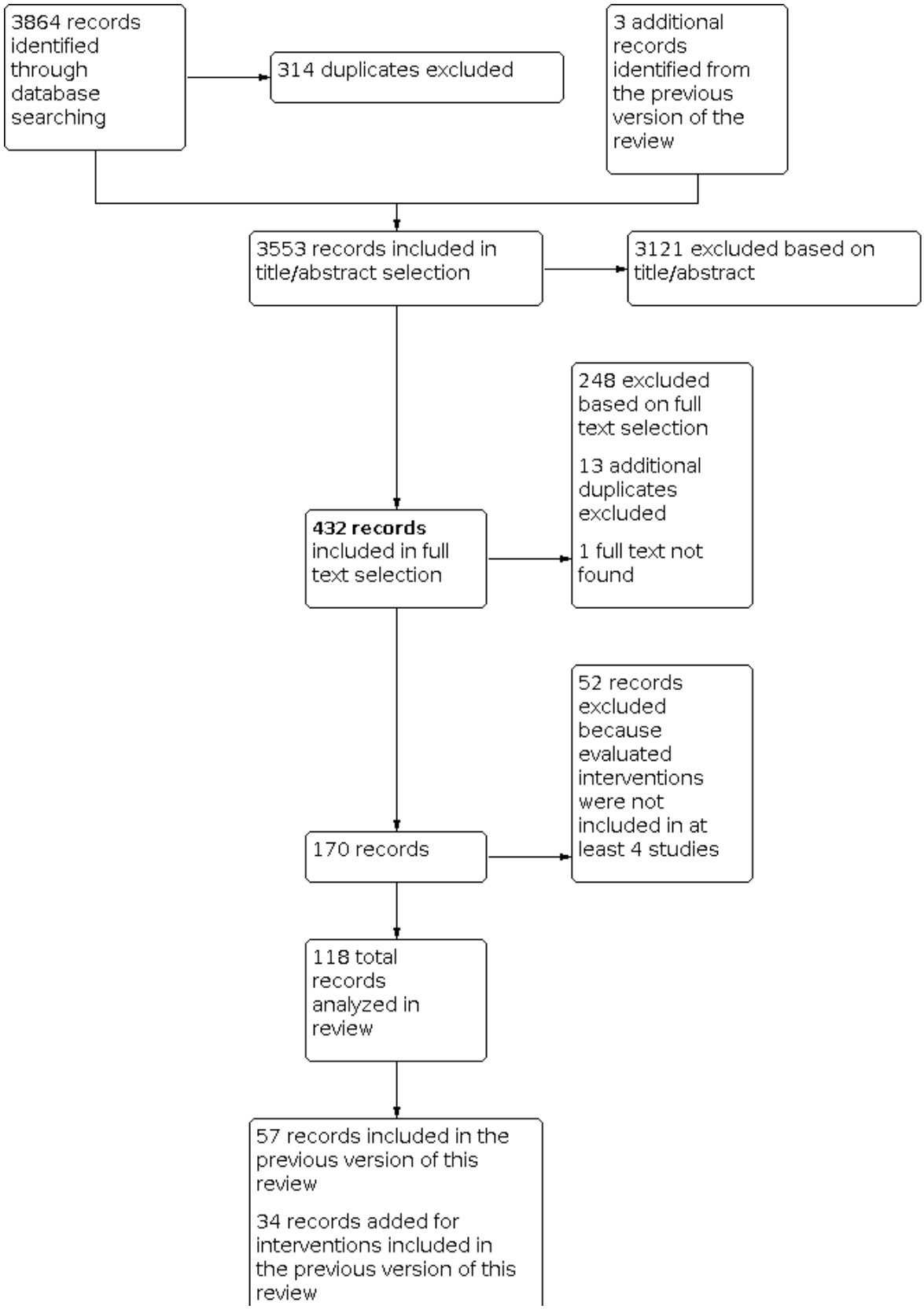

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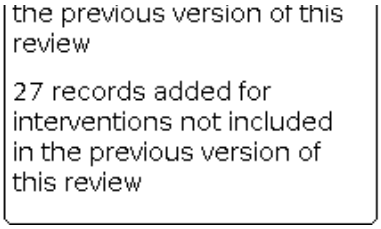
Figure 1. (Continued)



Included studies

See: Characteristics of included studies

We identified studies with the following pharmacological interventions.

- Amiodarone
- Beta-blockers
- Sotalol
- Magnesium

In the studies included in this review, beta-blockers included acebutolol, atenolol, landiolol, metoprolol, nadolol, propranolol and timolol.

We identified studies with the following non-pharmacological interventions.

- Atrial pacing
- Posterior pericardiotomy

In the studies included in this review, atrial pacing included Bachmann's bundle pacing, biatrial pacing, left atrial pacing, right atrial pacing and triple-site pacing.

Studies that included multiple intervention arms are marked in the analyses.

There were 17,364 participants in the 118 studies included in this review. The weighted mean age of trial participants was 60.2 years old. A weighted mean of 76.9% of participants were men. The trials were undertaken in various countries as outlined in Table 2.

Only three (2.5%) of the included studies described multicentre trials. The median length of follow-up was five days (interquartile range: three to seven). The length of treatment was not specifically reported in the majority of included studies, but was generally at least the duration of the follow-up period.

Excluded studies

Interventions included in fewer than four studies were not appropriate for pooling in our meta-analysis and therefore were not analyzed in this review.

Risk of bias in included studies

See: Characteristics of included studies

Combining the results from all seven of the categories considered in our study quality assessment, 41.5% of studies were at low risk for bias and 17.6% were at high risk. In 40.9% of studies, the risk of bias in the categories considered was unclear from the publication. There were 44 studies that were not at high risk for bias in any of the seven categories. Three of these (Auer 2004; Mitchell 2005; Zangrillo 2005) were deemed to be low risk in all of the categories. The results of the risk of bias assessments are displayed in Figure 2. Figure 3 displays a funnel plot of the results of all included studies for the primary outcome. While there were some outliers, the funnel plot was overall symmetrical and did not raise the concern of significant publication bias in this review.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

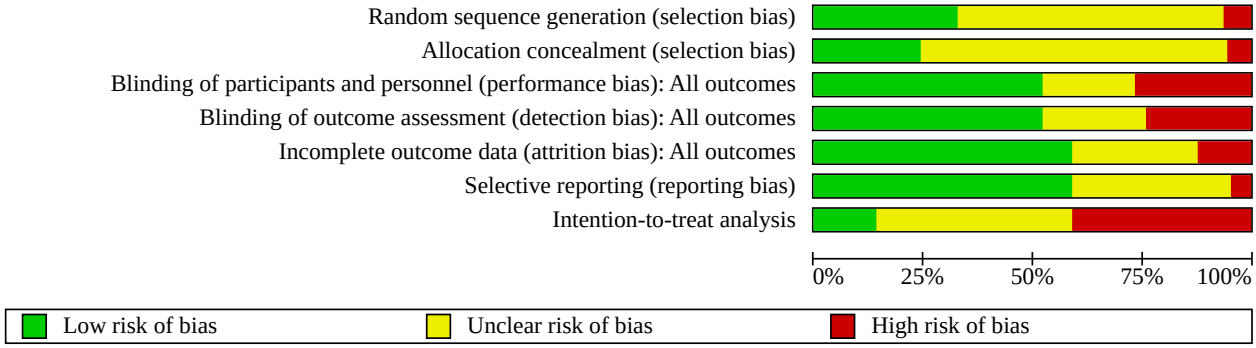


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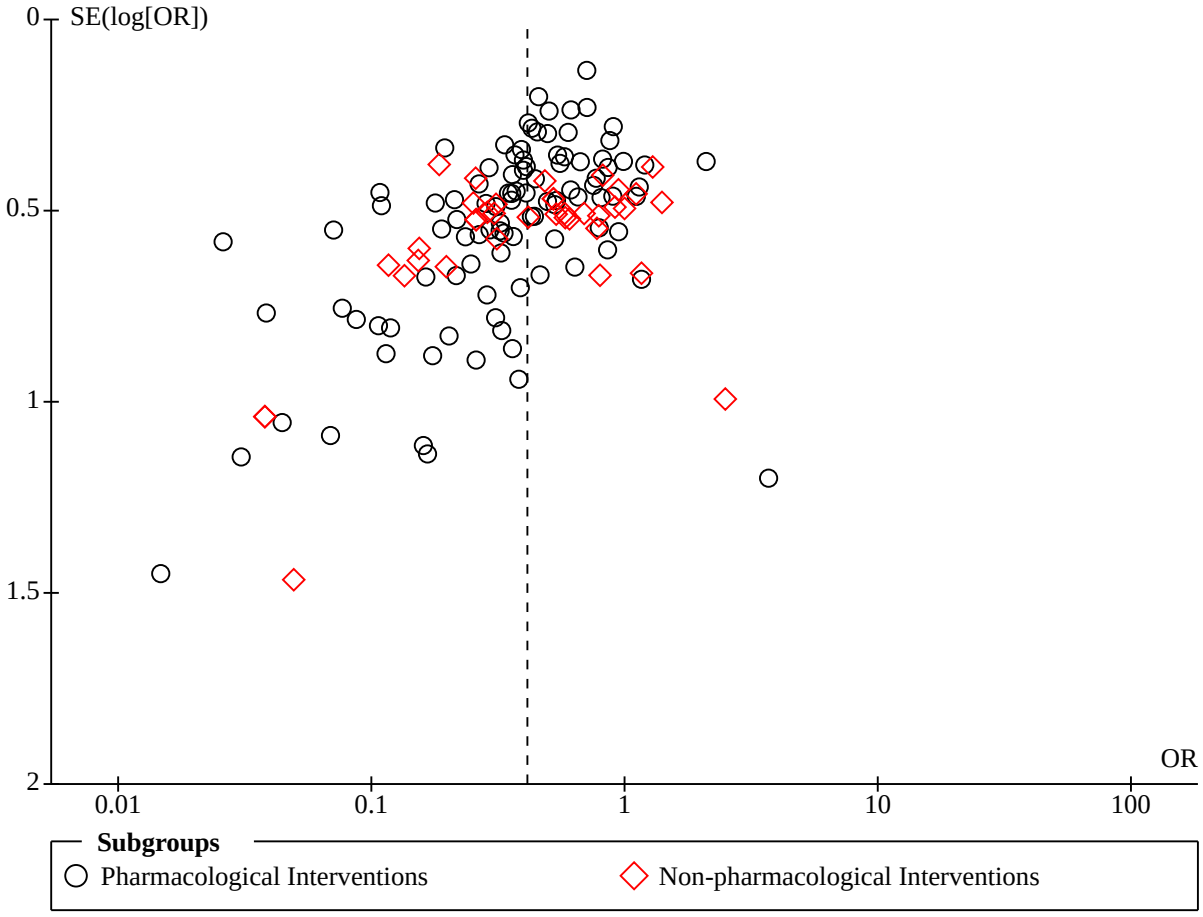
Figure 3. Funnel plot of comparison: 1 Atrial fibrillation or Supraventricular tachycardia, outcome: 1.1 All Treatments.



Allocation

See: Analysis 7.1; Analysis 7.2

As the inclusion criteria for this review required a study to be a randomized trial, the risk of selection bias was expected to be low. Unfortunately, the majority of studies did not provide sufficient information to judge the level of risk from inappropriate randomization sequence generation (61.0%) or allocation concealment (70.3%). Approximately one third (32.3%) of studies were deemed to be low risk in the randomization sequence generation category while approximately a quarter (24.6%) were at low risk for inappropriate allocation concealment (Figure 2).

When the studies were pooled according to the level of risk of bias, no significant difference between the subgroups was found for randomization sequence generation but significant differences were found in the allocation concealment analysis between high and low risk subgroups (P = 0.02). When only studies at low risk for this type of bias were considered, amiodarone (odds ratio (OR) 0.52; 95% confidence interval (CI) 0.38 to 0.70), beta-blockers (OR 0.44; 95% CI 0.30 to 0.66) and magnesium (OR 0.64; 95% CI 0.50 to 0.82) demonstrated summary odds ratios for post-operative atrial fibrillation closer to 1 while sotalol (OR 0.30; 95% CI 0.19 to 0.49), atrial pacing (OR 0.23; 95% CI 0.09 to 0.60) and posterior pericardiotomy (OR 0.19; 95% CI 0.09 to 0.39) had summary odds ratios further from 1. Each of these analyses, especially those of the non-pharmacological interventions, contained few studies.

Blinding

See: Analysis 7.3; Analysis 7.4; Analysis 7.5; Analysis 7.6

The majority of studies in this review were determined to be at low risk for performance (51.7%) or detection (51.7%) bias, as defined by appropriate blinding of the participants and healthcare providers or outcome assessors. Approximately one quarter of studies were at high risk for each bias (27.1% and 24.6%, respectively). Since a placebo cannot be used in non-pharmacological studies, blinding in these studies was rare. Only seven atrial pacing studies (Da Silva 2008; Eslami 2005; Fan 2000; Gerstenfeld 1999; Greenberg 2000; Levy 2000; Schweikert 1998) and one posterior pericardiotomy (Farsak 2002) utilized at least single-blinding; the majority blinded the outcome assessor to the treatment allocation (Figure 2).

Considering both performance and detection bias, pharmacological treatments demonstrated a trend towards differences between high and low risk subgroups (P = 0.12 and

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P = 0.11, respectively). This difference was not seen for non-pharmacological interventions (P = 0.84 and P = 0.81, respectively). Sensitivity analyses did not reveal any important change in the summary estimate for amiodarone, beta-blockers, sotalol or magnesium.

Incomplete outcome data

See: Analysis 7.7

The majority of studies in this review (57.6%) were categorized as having low risk for attrition bias. In over a quarter of studies (28.8%), insufficient information was given to determine the risk of attrition bias (Figure 2).

No significant difference was found between studies at high and low risk for attrition bias (P = 0.87).

Selective reporting

See: Analysis 7.8

Selective data reporting was not a major issue in the studies included in this review; 57.6% of studies were at low risk for reporting bias while only 5.9% were determined to be at high risk (Figure 2).

Despite the low percentage of high-risk studies, analysis demonstrated a significant difference between studies at high and low risk for reporting bias (P = 0.01). Sensitivity analyses considering only studies at low risk of bias resulted in a slight increase towards 1 in the summary estimates of beta-blockers (OR 0.39; 95% CI 0.28 to 0.54) and posterior pericardiotomy (OR 0.50; 95% CI 0.23 to 1.07).

Other potential sources of bias

Intention-to-treat analysis

See: Analysis 7.9

Only 18 studies (15.3%) specifically stated that they undertook an intention-to-treat analysis. Information to determine whether an intention-to-treat analysis was undertaken was insufficient in 44.9% of the studies. This category of bias had the greatest amount of studies in the high-risk category (39.8%) (Figure 2).

The results of analysis based on the use of an intention-to-treat analysis demonstrated a significant difference between all three subgroups (P = 0.01) but not between high and low risk groups (P = 0.17). Considering only studies that specifically stated that they undertook an intention-to-treat analysis, the summary odds ratios for post-operative atrial fibrillation for amiodarone treatment increased towards 1 (OR 0.56; 95% CI 0.45 to 0.69).

Effects of interventions

The effect of interventions on post-operative atrial fibrillation and supraventricular tachycardia

All included trials evaluated the effect of various pharmacological and non-pharmacological interventions on post-operative atrial fibrillation or supraventricular tachycardia. Definitions of an event varied between studies, from any occurrence of supraventricular tachycardia to atrial fibrillation lasting at least one hour or requiring therapy for hemodynamic compromise. Nearly all studies monitored patients for events using continuous electrocardiogram telemetry or Holter monitoring. The majority of studies followed patients until discharge from the intensive care unit or hospital while Forlani 2002 and Pfisterer 1997 followed up patients until 30 and 90 days post-operative, respectively. Jacquet 1994; Khuri 1987; White 2002; White 2003 and Yagdi 2003 re-evaluated patients at a follow-up clinic visit approximately 30 days after surgery. The median length of follow-up was five days (interquartile range: three to seven).

Considering all 118 studies, with 18,381 counted participants (including those control groups counted in multiple comparisons, as described in the Data extraction and management section), prophylactic intervention was associated with a significant reduction in atrial fibrillation in the treatment group (17.7%) compared to the control group (32.3%) (OR 0.41; 95% CI 0.37 to 0.47; I^2 = 56%; Figure 4). Pharmacological interventions were evaluated in a total of 93 studies with 14,685 participants. Analysis of these studies demonstrated a reduction in atrial fibrillation in the treatment group (17.7%) compared to the control group (32.2%) (OR 0.40; 95% CI 0.35 to 0.46; I^2 = 57%; Figure 4). Non-pharmacological interventions were associated with a reduction in atrial fibrillation in the treatment group (17.7%) compared to the control group (32.9%) (OR 0.44; 95% CI 0.34 to 0.57; I^2 = 54%; Figure 4) in 27 trials with 3696 participants.

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Figure 4. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.1 All Treatments.

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
1.1.1 Pharmacological Interventions						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Akbarzadeh 2009 (1)	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Auer 2004 (2)	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Auer 2004 (3)	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
Bert 2001 (4)	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Bert 2001 (5)	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	4	24	11	46	0.6%	0.64 [0.18 , 2.26]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Dörge 2000 (6)	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Dörge 2000 (7)	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Forlani 2002 (4)	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Forlani 2002 (3)	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Janssen 1986 (2)	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Janssen 1986 (3)	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]

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Figure 4. (Continued)

Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000 (4)	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Treggiari-Venzi 2000 (1)	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2002 (8)	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2002 (9)	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
White 2003 (1)	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Williams 1982	1	28	6	32	0.3%	0.16 [0.02 , 1.43]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**7251**		**7434**	**74.1%**	**0.40 [0.35 , 0.46]**
Total events:	1281		2391			
Heterogeneity: Tau² = 0.24; Chi² = 231.07, df = 99 (P < 0.00001); I² = 57%						
Test for overall effect: Z = 12.95 (P < 0.00001)						
1.1.2 Non-pharmacological Interventions						
Akbarzadeh 2009 (10)	7	70	12	70	0.7%	0.54 [0.20 , 1.46]

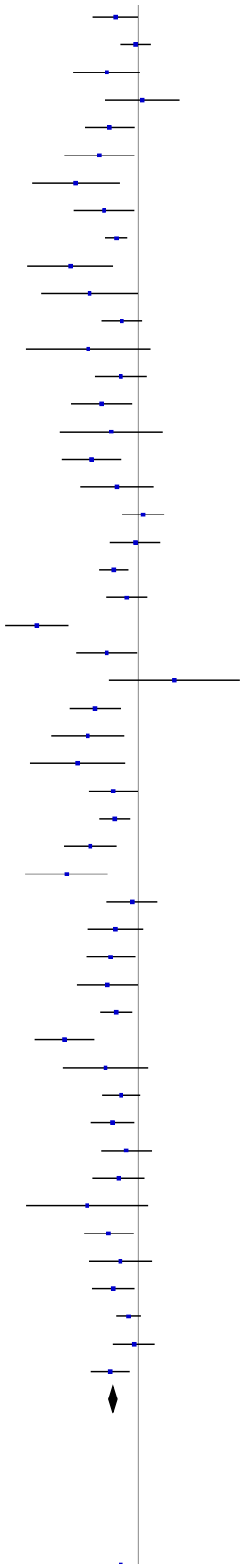

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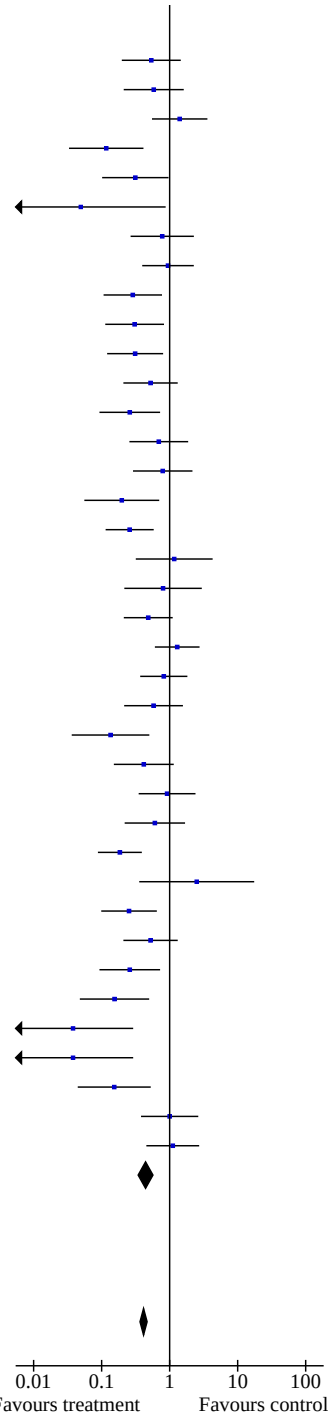
Figure 4. (Continued)

1.1.2 Non-pharmacological Interventions						
Akbarzadeh 2009 (10)	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Chavan 2010 (11)	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Chavan 2010 (12)	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
Eslami 2005 (13)	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Eslami 2005 (10)	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Fan 2000 (12)	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000 (13)	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000 (10)	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Gerstenfeld 1999 (10)	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 1999 (12)	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Goette 2002 (12)	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Goette 2002 (11)	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Greenberg 2000 (10)	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Greenberg 2000 (12)	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Greenberg 2000 (13)	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Hakala 2005 (14)	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hakala 2005 (15)	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Mirkhani 2005 (13)	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mirkhani 2005 (10)	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Neto 2007 (10)	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007 (12)	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
White 2003 (11)	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
Subtotal (95% CI)		**1825**		**1871**	**25.9%**	**0.44 [0.34 , 0.57]**
Total events:	323		614			
Heterogeneity: Tau² = 0.32; Chi² = 79.74, df = 37 (P < 0.0001); I² = 54%						
Test for overall effect: Z = 6.39 (P < 0.00001)						
Total (95% CI)		**9076**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1604		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.72, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%						



Footnotes

(1) Amiodarone
(2) Metoprolol
(3) Sotalol
(4) Magnesium
(5) Propanolol

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Figure 4. (Continued)

(4) Magnesium
(5) Propanolol
(6) Amiodarone (300mg)
(7) Amiodarone (150mg)
(8) Amiodarone (Fast-Load)
(9) Amiodarone (Slow-Load)
(10) Biatrial Pacing
(11) Bachmann's Bundle Pacing
(12) Right Atrial Pacing
(13) Left Atrial Pacing
(14) Right Atrial Pacing (Atrial Overdrive)
(15) Right Atrial Pacing (Bradycardia Prevention)

Amiodarone

Thirty-three of the studies included in this review, with a total of 5402 participants, evaluated the effect of amiodarone on post-operative atrial fibrillation and supraventricular tachycardia. Dosing regimens, including loading doses and infusion rates, varied between studies and were delivered both orally and intravenously. Approximately half of the studies began amiodarone administration pre-operatively and half post-operatively. Dörge 2000 and White 2002 each contained two separate treatment groups. The former utilized a high- and a low-dose group while the groups in the latter differed by the rate of the loading dose. Amiodarone was associated with a significant reduction in post-operative atrial fibrillation in the treatment group (19.4%) compared with the control group (33.3%) (OR 0.43; 95% CI 0.34 to 0.54; I^2 = 63%; Figure 5)

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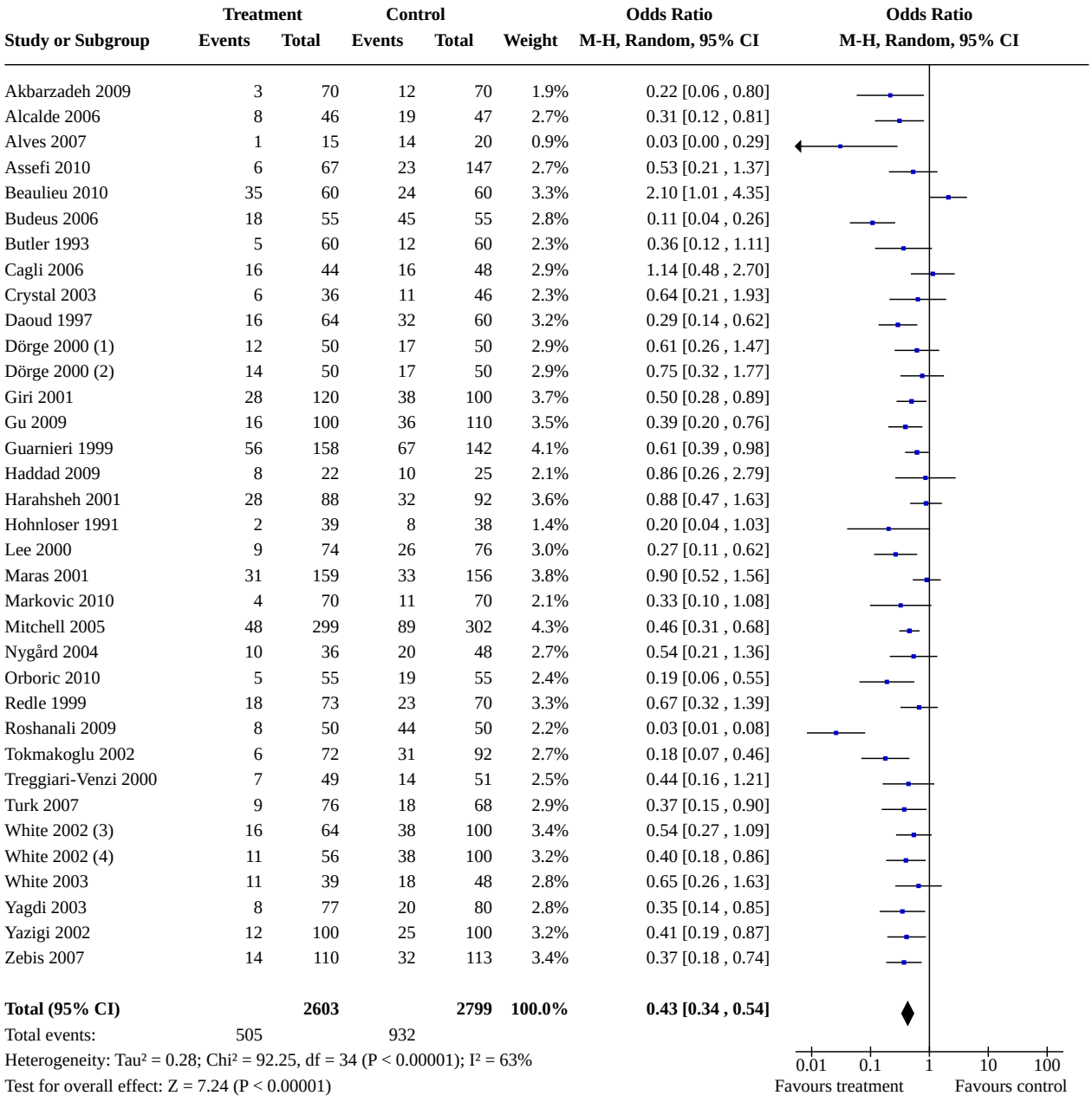
Figure 5. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.2 Amiodarone.



Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Akbarzadeh 2009	3	70	12	70	1.9%	0.22 [0.06 , 0.80]
Alcalde 2006	8	46	19	47	2.7%	0.31 [0.12 , 0.81]
Alves 2007	1	15	14	20	0.9%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	2.7%	0.53 [0.21 , 1.37]
Beaulieu 2010	35	60	24	60	3.3%	2.10 [1.01 , 4.35]
Budeus 2006	18	55	45	55	2.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	2.3%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	2.9%	1.14 [0.48 , 2.70]
Crystal 2003	6	36	11	46	2.3%	0.64 [0.21 , 1.93]
Daoud 1997	16	64	32	60	3.2%	0.29 [0.14 , 0.62]
Dörge 2000 (1)	12	50	17	50	2.9%	0.61 [0.26 , 1.47]
Dörge 2000 (2)	14	50	17	50	2.9%	0.75 [0.32 , 1.77]
Giri 2001	28	120	38	100	3.7%	0.50 [0.28 , 0.89]
Gu 2009	16	100	36	110	3.5%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	4.1%	0.61 [0.39 , 0.98]
Haddad 2009	8	22	10	25	2.1%	0.86 [0.26 , 2.79]
Harahsheh 2001	28	88	32	92	3.6%	0.88 [0.47 , 1.63]
Hohnloser 1991	2	39	8	38	1.4%	0.20 [0.04 , 1.03]
Lee 2000	9	74	26	76	3.0%	0.27 [0.11 , 0.62]
Maras 2001	31	159	33	156	3.8%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	2.1%	0.33 [0.10 , 1.08]
Mitchell 2005	48	299	89	302	4.3%	0.46 [0.31 , 0.68]
Nygård 2004	10	36	20	48	2.7%	0.54 [0.21 , 1.36]
Orboric 2010	5	55	19	55	2.4%	0.19 [0.06 , 0.55]
Redle 1999	18	73	23	70	3.3%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	2.2%	0.03 [0.01 , 0.08]
Tokmakoglu 2002	6	72	31	92	2.7%	0.18 [0.07 , 0.46]
Treggiari-Venzi 2000	7	49	14	51	2.5%	0.44 [0.16 , 1.21]
Turk 2007	9	76	18	68	2.9%	0.37 [0.15 , 0.90]
White 2002 (3)	16	64	38	100	3.4%	0.54 [0.27 , 1.09]
White 2002 (4)	11	56	38	100	3.2%	0.40 [0.18 , 0.86]
White 2003	11	39	18	48	2.8%	0.65 [0.26 , 1.63]
Yagdi 2003	8	77	20	80	2.8%	0.35 [0.14 , 0.85]
Yazigi 2002	12	100	25	100	3.2%	0.41 [0.19 , 0.87]
Zebis 2007	14	110	32	113	3.4%	0.37 [0.18 , 0.74]
Total (95% CI)		**2603**		**2799**	**100.0%**	**0.43 [0.34 , 0.54]**
Total events:	505		932			

Heterogeneity: Tau² = 0.28; Chi² = 92.25, df = 34 (P < 0.00001); I² = 63%
Test for overall effect: Z = 7.24 (P < 0.00001)
Test for subgroup differences: Not applicable

Footnotes
(1) Amiodarone (300mg)
(2) Amiodarone (150mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)

Beta-blockers

Thirty-three of the studies included in this review evaluated the effects of beta-blockers on post-operative atrial fibrillation and supraventricular tachycardia. These trials included 4698 participants. Half of these studies investigated propranolol. Dosing regimens varied between studies and were delivered both orally and intravenously. The majority of studies (81.8%) began beta-blocker administration post-operatively. Treatment with beta-blockers demonstrated a reduction in post-operative atrial fibrillation in the treatment group (16.3%) compared to the control group (31.7%) (OR 0.33; 95% CI 0.26 to 0.43; $I^2 = 55\%$; Figure 6).

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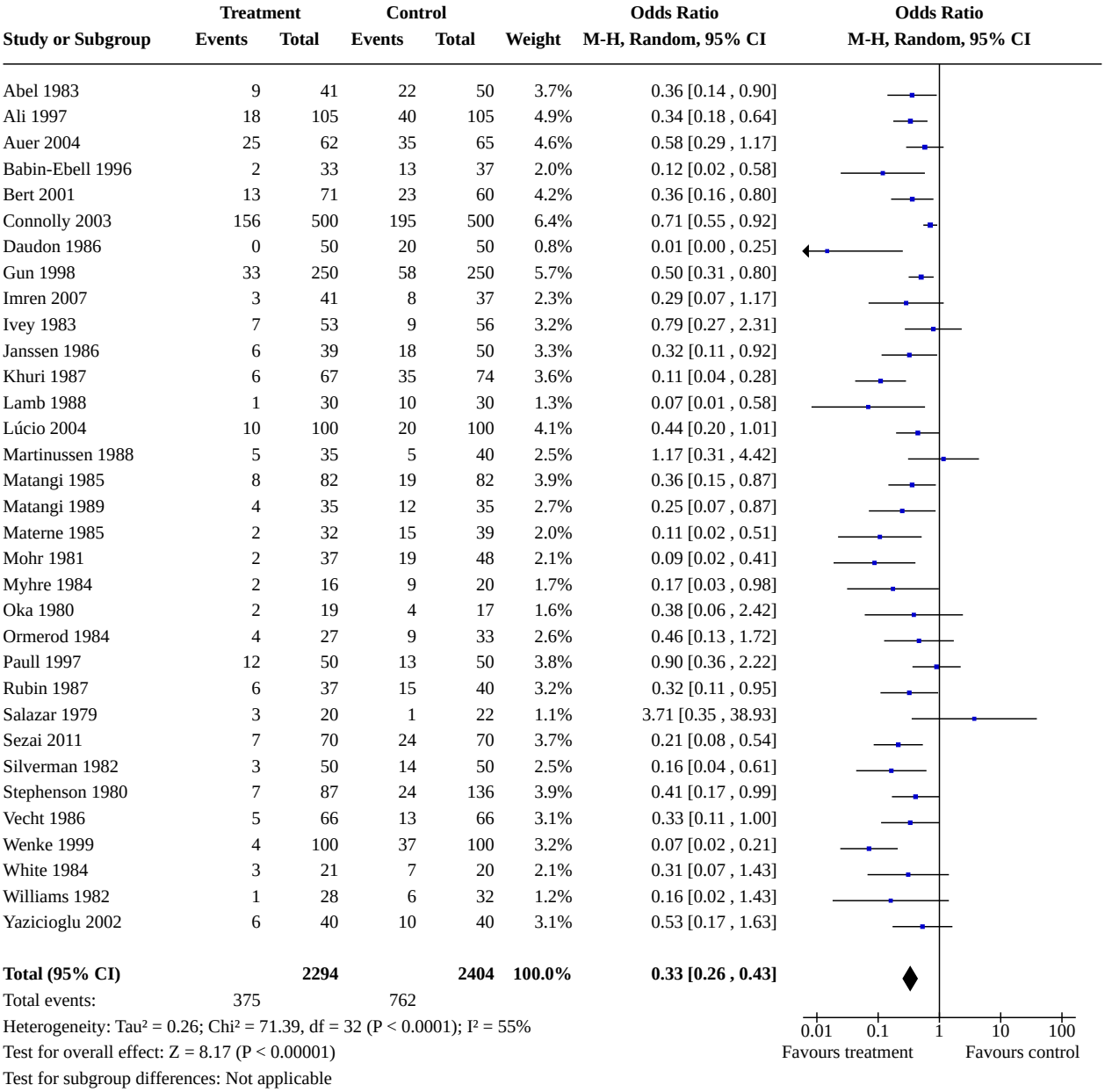
Figure 6. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.3 Beta-Blockers.



Sotalol

Eleven studies with 1609 participants evaluated the effects of sotalol on post-operative atrial fibrillation and supraventricular tachycardia. Dosing regimens varied between studies. All studies delivered sotalol orally but two studies (Jacquet 1994; Janssen 1986) began with intravenous infusions until the patients were able to receive pills. Six of the studies used a dose of 80 mg twice a day. The majority of studies (54.5%) began sotalol administration post-operatively. Sotalol was associated with a significant reduction in post-operative atrial fibrillation in the treatment group (18.1%) compared to the control group (40.0%) (OR 0.34; 95% CI 0.26 to 0.43; I^2 = 3%; Figure 7).

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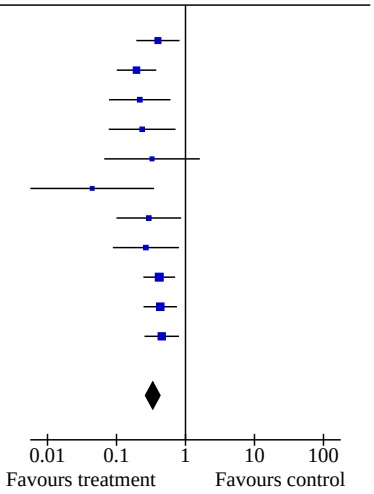
Figure 7. Forest plot:: 1 Atrial fibrillation or Supraventricular tachycardia; 1.4 Sotalol.

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Auer 2004	20	63	35	65	10.8%	0.40 [0.19 , 0.82]
Evrard 2000	16	103	50	103	12.8%	0.19 [0.10 , 0.38]
Forlani 2002	6	51	19	50	5.4%	0.22 [0.08 , 0.61]
Gomes 1999	5	40	17	45	4.6%	0.24 [0.08 , 0.72]
Jacquet 1994	3	25	5	17	2.3%	0.33 [0.07 , 1.61]
Janssen 1986	1	41	18	50	1.4%	0.04 [0.01 , 0.35]
Matsuura 2001	6	40	15	40	4.9%	0.29 [0.10 , 0.86]
Nyström 1993	5	50	15	51	4.7%	0.27 [0.09 , 0.80]
Pfisterer 1997	32	126	58	129	19.2%	0.42 [0.25 , 0.71]
Suttorp 1991	24	150	46	150	17.5%	0.43 [0.25 , 0.75]
Weber 1998	27	110	46	110	16.5%	0.45 [0.25 , 0.81]
Total (95% CI)		**799**		**810**	**100.0%**	**0.34 [0.26 , 0.43]**
Total events:	145		324			

Heterogeneity: Tau² = 0.01; Chi² = 10.34, df = 10 (P = 0.41); I² = 3%
Test for overall effect: Z = 8.88 (P < 0.00001)
Test for subgroup differences: Not applicable



Magnesium

Twenty-one of the studies included in this review investigated the effects of magnesium on post-operative atrial fibrillation and supraventricular tachycardia. These studies included 2988 participants. Dosing regimens varied between studies but all administration of magnesium was done intravenously. In 12 (57.1%) of these studies, magnesium was first administered intra-operatively. This analysis demonstrated a significant reduction in post-operative atrial fibrillation in the treatment group (16.5%) compared to the control group (26.2%) (OR 0.55; 95% CI 0.41 to 0.73; I^2 = 51%; Figure 8).

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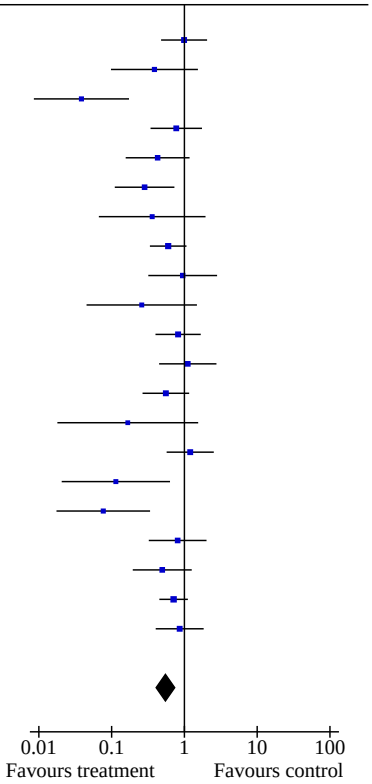
Figure 8. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.5 Magnesium.

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Bert 2001	24	63	23	60	6.4%	0.99 [0.48 , 2.05]
Casthely 1994	5	105	4	35	3.2%	0.39 [0.10 , 1.53]
Dagdelen 2002	2	93	20	55	2.8%	0.04 [0.01 , 0.17]
England 1992	17	50	20	50	5.8%	0.77 [0.34 , 1.74]
Fanning 1991	7	49	14	50	4.7%	0.43 [0.16 , 1.18]
Forlani 2002	8	54	19	50	5.0%	0.28 [0.11 , 0.73]
Hamid 2008	2	53	5	51	2.3%	0.36 [0.07 , 1.95]
Hazelrigg 2004	32	105	41	97	7.5%	0.60 [0.34 , 1.07]
Jensen 1997	10	29	10	28	4.3%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	2.2%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	6.5%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	5.2%	1.11 [0.45 , 2.76]
Najafi 2007	12	166	22	179	6.3%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	1.5%	0.17 [0.02 , 1.55]
Parikka 1993	20	69	18	71	6.3%	1.20 [0.57 , 2.53]
Speziale 2000	2	72	5	25	2.3%	0.11 [0.02 , 0.63]
Toraman 2001	2	100	21	100	2.9%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	11	47	14	51	5.2%	0.81 [0.32 , 2.01]
Wilkes 2002	11	41	17	40	5.1%	0.50 [0.20 , 1.26]
Yeatman 2002	45	200	58	200	8.4%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	6.2%	0.86 [0.40 , 1.84]
Total (95% CI)		**1567**		**1421**	**100.0%**	**0.55 [0.41 , 0.73]**
Total events:	258		373			

Heterogeneity: Tau² = 0.21; Chi² = 40.73, df = 20 (P = 0.004); I² = 51%
Test for overall effect: Z = 4.03 (P < 0.0001)
Test for subgroup differences: Not applicable



Atrial Pacing

Twenty-one of the papers included in this review studied the effects of atrial pacing on post-operative atrial fibrillation and supraventricular tachycardia. These trial included 2933 participants. Nine studies (Chavan 2010; Eslami 2005; Fan 2000; Gerstenfeld 1999; Goette 2002; Greenberg 2000; Hakala 2005; Mirkhani 2005; Neto 2007) contained more than one treatment group. Each of these groups were based on an alternate pacing location except for those in Hakala 2005, which were both right atrial pacing but differed in the target heart rate algorithms. There were 32 treatment groups in total, including three Bachmann's bundle pacing, 13 biatrial pacing, four left atrial pacing, 10 right atrial pacing, one triple-site atrial pacing and one not specified. The incidence of post-operative atrial fibrillation across all studies was 18.7% in the treatment group and 32.8% in the control group, a difference that was statistically significant (OR 0.47; 95% CI 0.36 to 0.61; I^2 = 50%; Figure 9).

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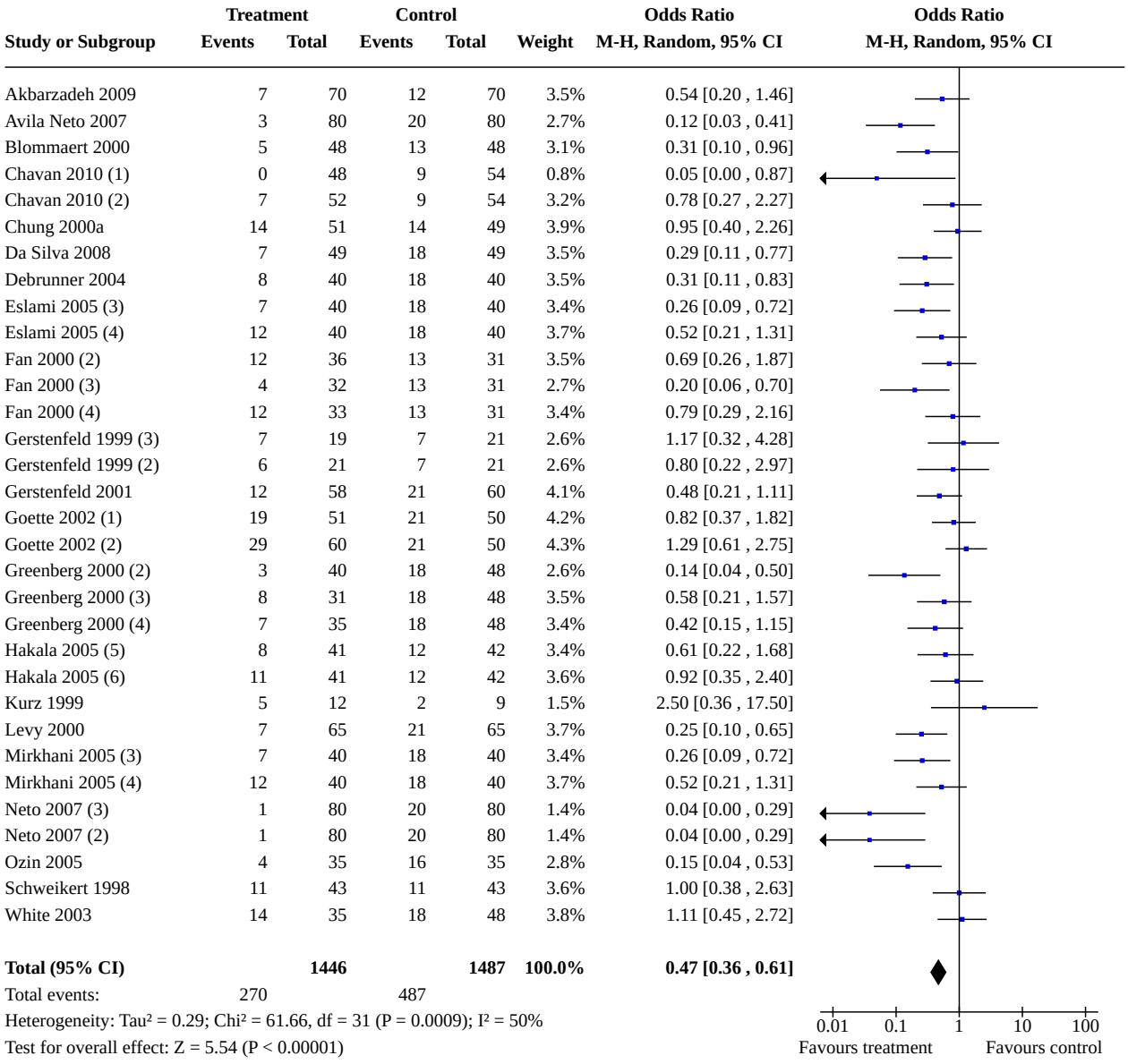
Figure 9. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.6 Atrial Pacing.



Footnotes

(1) Bachmann's Bundle Pacing
(2) Right Atrial Pacing
(3) Biatrial Pacing
(4) Left Atrial Pacing
(5) Right Atrial Pacing (Bradycardia Prevention)
(6) Right Atrial Pacing (Atrial Overdrive)

Posterior Pericardiotomy

There were six papers with 763 participants identified in this review that investigated posterior pericardiotomy for its effects on post-operative atrial fibrillation and supraventricular tachycardia. Surgical technique was similar in each of the studies and involved a 4 cm longitudinal incision in the pericardium posterior and parallel to the phrenic nerve. Posterior pericardiotomy was associated with a significant reduction in post-operative atrial fibrillation in the treatment group (14.0%) compared to the control group (33.1%) (OR 0.35; 95% CI 0.18 to 0.67; I^2 = 66%; Figure 10).

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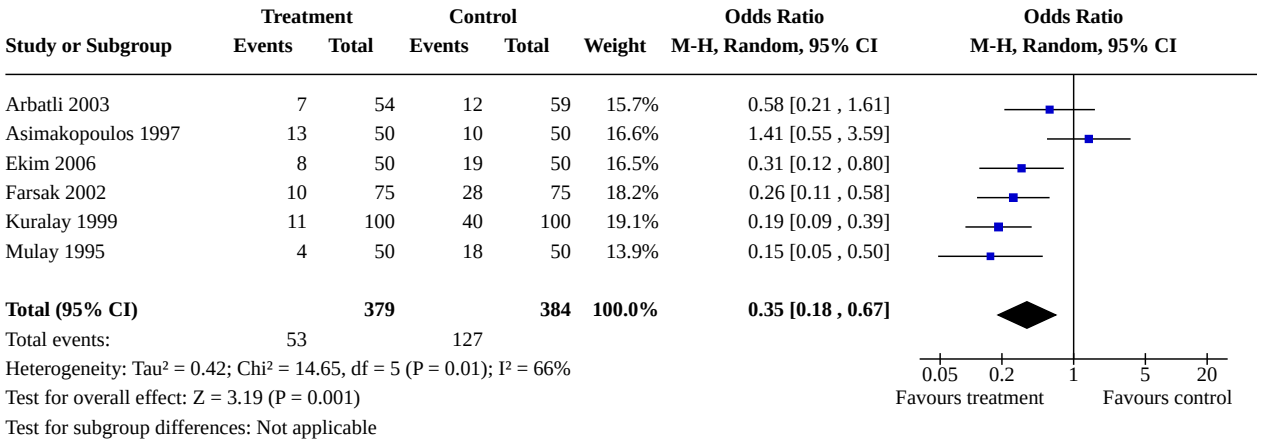
Figure 10. Forest plot: 1 Atrial fibrillation or Supraventricular tachycardia; 1.7 Posterior Pericardiotomy.



The effect of interventions on post-operative stroke and cerebrovascular accident

To determine if prophylactic treatment to prevent post-operative atrial fibrillation has a substantial effect on post-operative stroke, we collected all available data regarding this outcome from the studies included in this review. Twenty-eight studies with 34 treatment groups and 6361 participants provided data on the number of strokes. No patients in the Rubin 1987 study suffered a stroke and therefore this study did not contribute to the overall pooled summary estimate. Follow-up for stroke was identical to follow-up for atrial fibrillation in all studies. Only Auer 2004 specifically defined this outcome and required confirmation by brain computed tomography. Considering all interventions together, prophylactic treatment was associated with a borderline significant reduction in post-operative atrial fibrillation in the treatment group (1.5%) compared to the control group (2.3%) (OR 0.69; 95% CI 0.47 to 1.01; I^2 = 0%; Figure 11). There was insufficient data to judge the individual effects of beta-blockers, sotalol, magnesium or posterior pericardiotomy on post-operative stroke.

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Figure 11. Forest plot: 2 Stroke or Cerebrovascular Accident; 2.1 All Treatments.

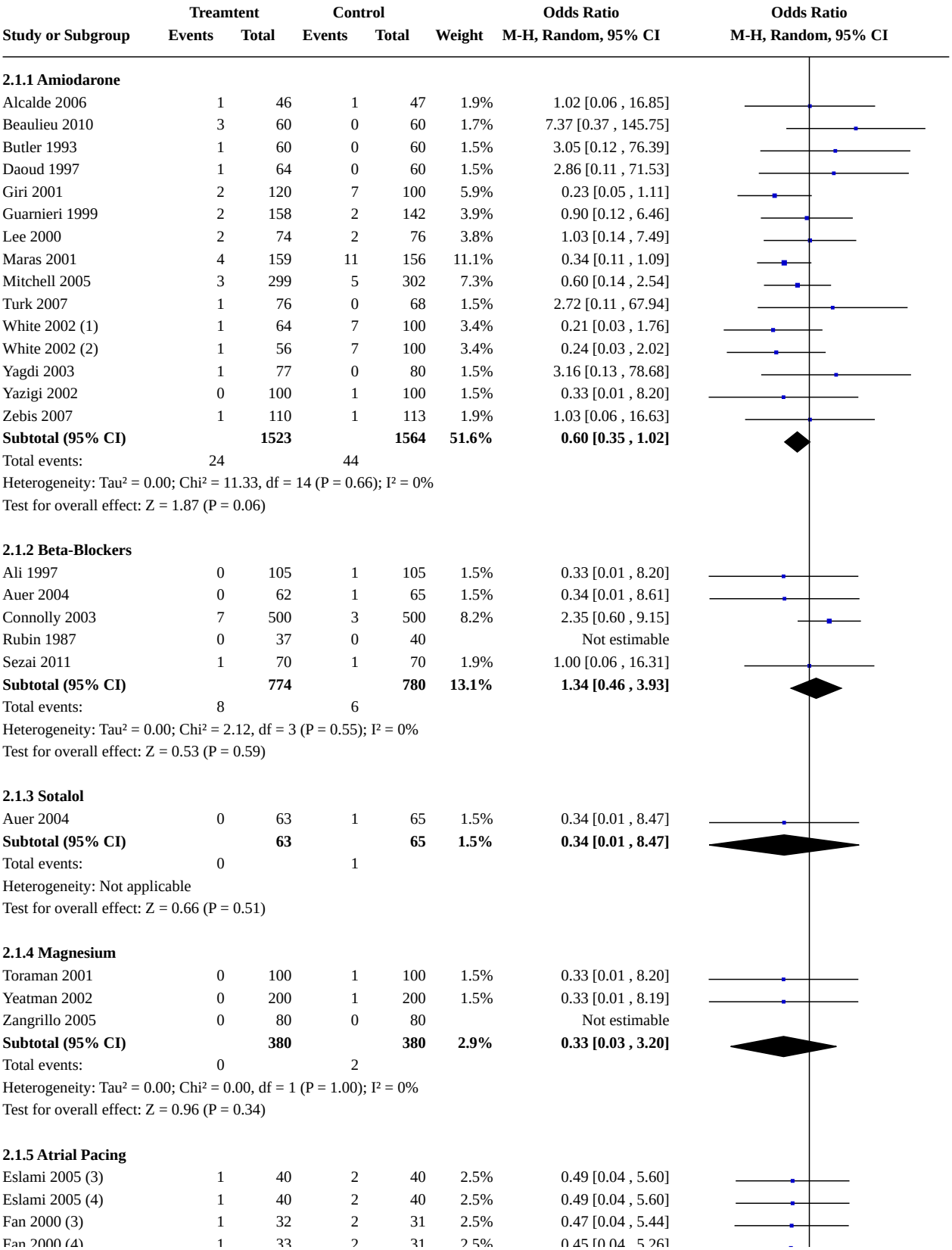

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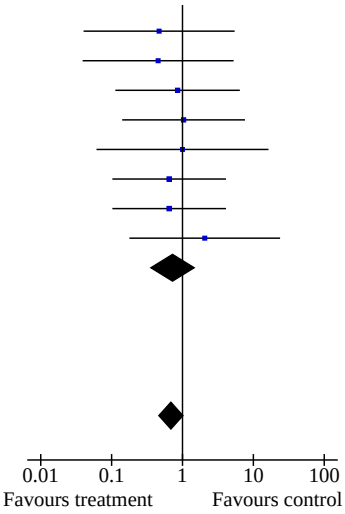
Figure 11. (Continued)

Fan 2000 (3)	1	32	2	31	2.5%	0.47 [0.04 , 5.44]
Fan 2000 (4)	1	33	2	31	2.5%	0.45 [0.04 , 5.26]
Fan 2000 (5)	2	36	2	31	3.7%	0.85 [0.11 , 6.44]
Gerstenfeld 1999	2	58	2	60	3.8%	1.04 [0.14 , 7.61]
Levy 2000	1	65	1	65	1.9%	1.00 [0.06 , 16.34]
Mirkhani 2005 (4)	2	40	3	40	4.4%	0.65 [0.10 , 4.11]
Mirkhani 2005 (3)	2	40	3	40	4.4%	0.65 [0.10 , 4.11]
Ozin 2005	2	35	1	35	2.5%	2.06 [0.18 , 23.83]
Subtotal (95% CI)		**419**		**413**	**30.9%**	**0.72 [0.36 , 1.46]**
Total events:	15		20			
Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 9 (P = 1.00); I² = 0%						
Test for overall effect: Z = 0.91 (P = 0.36)						
Total (95% CI)		**3159**		**3202**	**100.0%**	**0.69 [0.47 , 1.01]**
Total events:	47		73			
Heterogeneity: Tau² = 0.00; Chi² = 17.19, df = 31 (P = 0.98); I² = 0%						
Test for overall effect: Z = 1.90 (P = 0.06)						
Test for subgroup differences: Chi² = 2.35, df = 4 (P = 0.67), I² = 0%						



Footnotes
(1) Amiodarone (Fast-Load)
(2) Amiodarone (Slow-Load)
(3) Biatrial Pacing
(4) Left Atrial Pacing
(5) Right Atrial Pacing

Amiodarone

Fourteen studies, with 3087 participants, investigated amiodarone for its effect on post-operative atrial fibrillation provided data on post-operative stroke or cerebrovascular accident. The White 2002 study contained two separate treatment groups. Treatment with amiodarone demonstrated a borderline significant reduction in post-operative stroke in the treatment group (1.6%) compared to the control group (2.8%) (OR 0.60; 95% CI 0.35 to 1.02; $I^2 = 0\%$; Figure 11).

Atrial Pacing

Six studies with 10 treatment groups and 832 participants provided data on the effect of atrial pacing on post-operative stroke or cerebrovascular accident. Atrial pacing was associated with an insignificant reduction in post-operative stroke in the treatment group (3.6%) compared to the control group (4.8%) (OR 0.72; 95% CI 0.36 to 1.46; $I^2 = 0\%$; Figure 11).

The effect of interventions on post-operative mortality

Sixty-one studies with 72 treatment groups and 10,986 participants provided post-operative all-cause mortality rates for each group. The majority of studies recorded patient death for the duration of the follow-up for atrial fibrillation. Twenty studies (Auer 2004; Bert 2001; Butler 1993; Connolly 2003; Debrunner 2004; England 1992; Forlani 2002; Gerstenfeld 2001; Haddad 2009; Ivey 1983; Janssen 1986; Martinussen 1988; Matsuura 2001; Mulay 1995; Nyström 1993; Oka 1980; Paull 1997; Speziale 2000; Suttorp 1991; Zangrillo 2005) did not report an event in the control group and at least one of their treatment groups. Four studies (Beaulieu 2010; Crystal 2003; Giri 2001; Yeatman 2002) contacted study participants at 30 days post-operatively to assess mortality but not occurrence of atrial fibrillation. Considering all interventions together, prophylactic treatment for atrial fibrillation was not associated with a difference in all-cause post-operative mortality between the treatment group (1.9%) and the control group (1.8%) (OR 1.03; 95% CI 0.77 to 1.39; $I^2 = 0\%$; Figure 12). No individual intervention was associated with a significant effect on post-operative mortality.

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Figure 12. Forest plot: 3 Mortality; 3.1 All Treatments.

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
3.1.1 Amiodarone						
Akbarzadeh 2009	13	70	3	70	5.1%	5.09 [1.38 , 18.77]
Beaulieu 2010	1	60	1	60	1.1%	1.00 [0.06 , 16.37]
Budeus 2006	2	55	4	55	2.9%	0.48 [0.08 , 2.74]
Butler 1993	0	60	0	60		Not estimable
Crystal 2003	2	36	1	46	1.5%	2.65 [0.23 , 30.41]
Daoud 1997	3	64	2	60	2.6%	1.43 [0.23 , 8.85]
Dörge 2000 (1)	1	50	2	50	1.5%	0.49 [0.04 , 5.58]
Dörge 2000 (2)	2	50	2	50	2.2%	1.00 [0.14 , 7.39]
Giri 2001	4	120	4	100	4.4%	0.83 [0.20 , 3.40]
Gu 2009	1	100	1	110	1.1%	1.10 [0.07 , 17.84]
Guarnieri 1999	0	158	2	142	0.9%	0.18 [0.01 , 3.72]
Haddad 2009	0	22	0	25		Not estimable
Harahsheh 2001	3	88	3	92	3.3%	1.05 [0.21 , 5.33]
Lee 2000	4	74	5	76	4.7%	0.81 [0.21 , 3.15]
Maras 2001	9	159	7	156	8.5%	1.28 [0.46 , 3.52]
Mitchell 2005	7	299	10	302	9.1%	0.70 [0.26 , 1.86]
Nygård 2004	2	36	0	48	0.9%	7.03 [0.33 , 151.05]
Redle 1999	3	73	1	70	1.7%	2.96 [0.30 , 29.13]
Treggiari-Venzi 2000	1	49	1	51	1.1%	1.04 [0.06 , 17.13]
Turk 2007	2	76	1	68	1.5%	1.81 [0.16 , 20.43]
White 2002 (3)	1	64	4	100	1.8%	0.38 [0.04 , 3.49]
White 2002 (4)	3	56	4	100	3.7%	1.36 [0.29 , 6.30]
White 2003	1	39	2	48	1.5%	0.61 [0.05 , 6.93]
Yagdi 2003	1	77	3	80	1.7%	0.34 [0.03 , 3.32]
Zebis 2007	1	110	1	113	1.1%	1.03 [0.06 , 16.63]
Subtotal (95% CI)		**2045**		**2132**	**63.6%**	**1.08 [0.74 , 1.56]**
Total events:	67		64			
Heterogeneity: Tau² = 0.00; Chi² = 14.32, df = 22 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.38 (P = 0.70)						
3.1.2 Beta-Blockers						
Abel 1983	1	41	3	50	1.6%	0.39 [0.04 , 3.91]
Ali 1997	0	105	1	105	0.8%	0.33 [0.01 , 8.20]
Auer 2004	1	62	0	65	0.8%	3.20 [0.13 , 79.93]
Bert 2001	0	71	0	60		Not estimable
Connolly 2003	0	500	0	500		Not estimable
Imren 2007	1	41	2	37	1.5%	0.44 [0.04 , 5.03]
Ivey 1983	0	53	0	56		Not estimable
Janssen 1986	0	39	0	50		Not estimable
Lúcio 2004	2	100	1	100	1.5%	2.02 [0.18 , 22.65]
Martinussen 1988	0	35	0	40		Not estimable
Matangi 1985	1	82	1	82	1.1%	1.00 [0.06 , 16.26]
Oka 1980	0	19	0	17		Not estimable
Paull 1997	0	50	0	50		Not estimable
Sezai 2011	0	70	2	70	0.9%	0.19 [0.01 , 4.12]
White 1984	1	21	0	20	0.8%	3.00 [0.12 , 78.04]
Yazicioglu 2002	1	40	0	40	0.8%	3.08 [0.12 , 77.80]
Subtotal (95% CI)		**1329**		**1342**	**10.0%**	**0.87 [0.34 , 2.22]**
Total events:	8		10			
Heterogeneity: Tau² = 0.00; Chi² = 4.29, df = 8 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.28 (P = 0.78)						

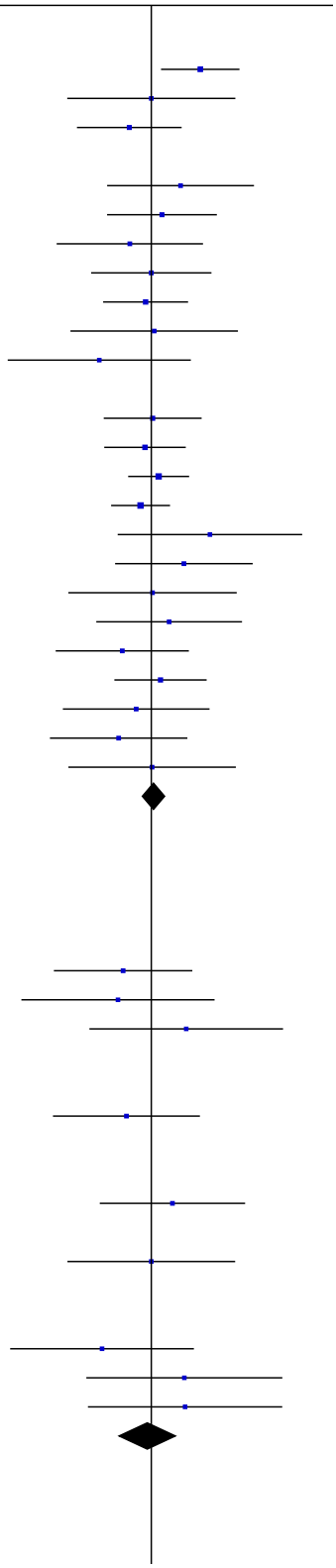

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Figure 12. (Continued)

Test for overall effect: Z = 0.28 (P = 0.78)						
3.1.3 Sotalol						
Auer 2004	0	63	0	65		Not estimable
Evrard 2000	1	103	1	103	1.1%	1.00 [0.06 , 16.21]
Forlani 2002	0	51	0	50		Not estimable
Gomes 1999	0	40	1	45	0.8%	0.37 [0.01 , 9.25]
Janssen 1986	0	41	0	50		Not estimable
Matsuura 2001	0	40	0	40		Not estimable
Nyström 1993	0	50	0	51		Not estimable
Suttorp 1991	0	150	0	150		Not estimable
Subtotal (95% CI)		**538**		**554**	**2.0%**	**0.65 [0.08 , 5.37]**
Total events:	1		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.64); I² = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						
3.1.4 Magnesium						
Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable
Fanning 1991	0	49	1	50	0.8%	0.33 [0.01 , 8.38]
Forlani 2002	1	54	0	50	0.8%	2.83 [0.11 , 71.13]
Hazelrigg 2004	1	105	2	97	1.5%	0.46 [0.04 , 5.12]
Kaplan 2003	1	100	1	100	1.1%	1.00 [0.06 , 16.21]
Karmy-Jones 1995	0	46	2	54	0.9%	0.23 [0.01 , 4.83]
Speziale 2000	0	72	0	25		Not estimable
Treggiari-Venzi 2000	0	47	1	51	0.8%	0.35 [0.01 , 8.91]
Wilkes 2002	1	41	1	40	1.1%	0.97 [0.06 , 16.14]
Yeatman 2002	3	200	1	200	1.7%	3.03 [0.31 , 29.38]
Zangrillo 2005	0	80	0	80		Not estimable
Subtotal (95% CI)		**907**		**857**	**8.8%**	**0.83 [0.31 , 2.24]**
Total events:	7		9			
Heterogeneity: Tau² = 0.00; Chi² = 3.34, df = 7 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.36 (P = 0.72)						
3.1.5 Atrial Pacing						
Akbarzadeh 2009	14	70	3	70	5.2%	5.58 [1.53 , 20.41]
Debrunner 2004	0	40	0	40		Not estimable
Gerstenfeld 2001	0	58	0	60		Not estimable
Goette 2002 (5)	0	51	1	50	0.8%	0.32 [0.01 , 8.05]
Goette 2002 (6)	0	60	1	50	0.8%	0.27 [0.01 , 6.84]
Levy 2000	1	65	2	65	1.5%	0.49 [0.04 , 5.57]
Neto 2007 (7)	2	80	3	80	2.6%	0.66 [0.11 , 4.05]
Neto 2007 (6)	2	80	3	80	2.6%	0.66 [0.11 , 4.05]
White 2003	0	35	2	48	0.9%	0.26 [0.01 , 5.63]
Subtotal (95% CI)		**539**		**543**	**14.5%**	**0.88 [0.32 , 2.47]**
Total events:	19		15			
Heterogeneity: Tau² = 0.64; Chi² = 9.20, df = 6 (P = 0.16); I² = 35%						
Test for overall effect: Z = 0.23 (P = 0.81)						
3.1.6 Posterior Pericardiotomy						
Asimakopoulos 1997	1	50	1	50	1.1%	1.00 [0.06 , 16.44]
Mulay 1995	0	50	0	50		Not estimable
Subtotal (95% CI)		**100**		**100**	**1.1%**	**1.00 [0.06 , 16.44]**
Total events:	1		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						

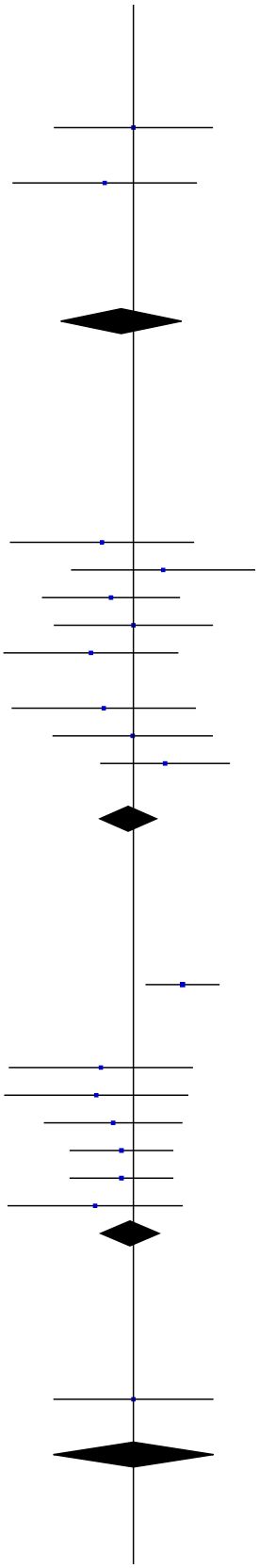

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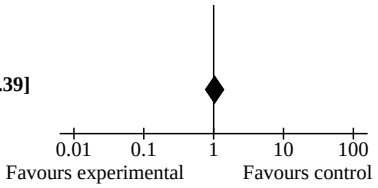
Figure 12. (Continued)

Test for overall effect: Z = 0.00 (P = 1.00)

Total (95% CI)		**5458**	**5528**	**100.0%**	**1.03 [0.77 , 1.39]**
Total events:	103		101		

Heterogeneity: Tau² = 0.00; Chi² = 31.98, df = 49 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.83)
Test for subgroup differences: Chi² = 0.57, df = 5 (P = 0.99), I² = 0%



Footnotes
(1) Amiodarone (150mg)
(2) Amiodarone (300mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)
(5) Bachmann's Bundle Pacing
(6) Right Atrial Pacing
(7) Biatrial Pacing

The effect of interventions on post-operative cardiovascular mortality

Of the studies that reported on post-operative mortality, 40 with 44 treatment groups and 6750 participants described the cause of death and allowed for categorization of certain events as cardiovascular mortality. The majority of these studies did not have any cardiovascular mortality events. Considering all interventions together, treatment was not associated with a difference in post-operative cardiovascular mortality between the treatment group (0.6%) and the control group (0.7%) (OR 0.87; 95% CI 0.47 to 1.62; I^2 = 0%; Figure 13). No individual intervention was associated with a significant effect on post-operative cardiovascular mortality.

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Figure 13. Forest plot: 4 Cardiovascular Mortality; 4.1 All Treatments.

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
4.1.1 Amiodarone						
Beaulieu 2010	0	60	1	60	3.7%	0.33 [0.01 , 8.21]
Budeus 2006	2	55	4	55	12.8%	0.48 [0.08 , 2.74]
Butler 1993	0	60	0	60		Not estimable
Daoud 1997	3	64	1	60	7.4%	2.90 [0.29 , 28.69]
Guarnieri 1999	0	158	1	142	3.8%	0.30 [0.01 , 7.36]
Haddad 2009	0	22	0	25		Not estimable
Lee 2000	2	74	2	76	9.8%	1.03 [0.14 , 7.49]
Maras 2001	5	159	4	156	21.8%	1.23 [0.33 , 4.68]
Mitchell 2005	0	299	5	302	4.6%	0.09 [0.00 , 1.64]
Nygård 2004	2	36	0	48	4.1%	7.03 [0.33 , 151.05]
Redle 1999	2	73	0	70	4.2%	4.93 [0.23 , 104.53]
Treggiari-Venzi 2000	1	49	0	51	3.7%	3.19 [0.13 , 80.09]
Turk 2007	0	76	0	68		Not estimable
Yagdi 2003	0	77	3	80	4.4%	0.14 [0.01 , 2.81]
Subtotal (95% CI)		**1262**		**1253**	**80.2%**	**0.93 [0.46 , 1.86]**
Total events:	17		21			
Heterogeneity: Tau² = 0.00; Chi² = 10.02, df = 10 (P = 0.44); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.83)						
4.1.2 Beta-Blockers						
Ali 1997	0	105	0	105		Not estimable
Bert 2001	0	71	0	60		Not estimable
Connolly 2003	0	500	0	500		Not estimable
Ivey 1983	0	53	0	56		Not estimable
Janssen 1986	0	39	0	50		Not estimable
Martinussen 1988	0	35	0	40		Not estimable
Oka 1980	0	19	0	17		Not estimable
Paull 1997	0	50	0	50		Not estimable
Sezai 2011	0	70	1	70	3.7%	0.33 [0.01 , 8.21]
White 1984	1	21	0	20	3.6%	3.00 [0.12 , 78.04]
Yazicioglu 2002	0	40	0	40		Not estimable
Subtotal (95% CI)		**1003**		**1008**	**7.4%**	**0.98 [0.10 , 9.66]**
Total events:	1		1			
Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 0.02 (P = 0.99)						
4.1.3 Sotalol						
Evrard 2000	0	103	0	103		Not estimable
Forlani 2002	0	51	0	50		Not estimable
Gomes 1999	0	40	0	45		Not estimable
Janssen 1986	0	41	0	50		Not estimable
Matsuura 2001	0	40	0	40		Not estimable
Nyström 1993	0	50	0	51		Not estimable
Suttorp 1991	0	150	0	150		Not estimable
Subtotal (95% CI)		**475**		**489**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
4.1.4 Magnesium						
Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable

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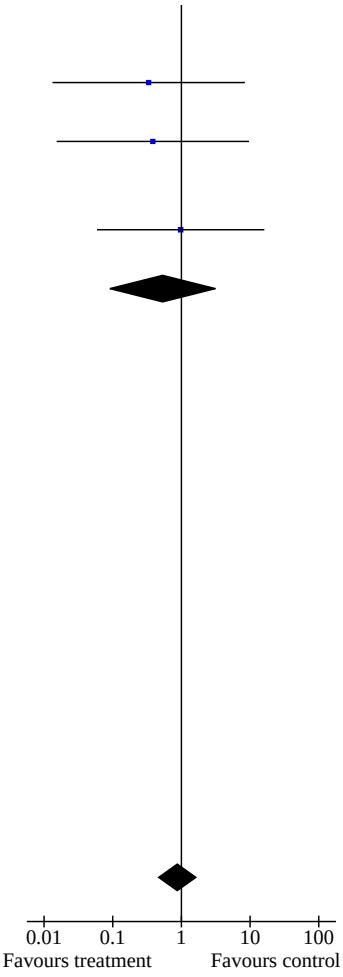
Figure 13. (Continued)

Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable
Fanning 1991	0	49	1	50	3.7%	0.33 [0.01 , 8.38]
Forlani 2002	0	54	0	50		Not estimable
Karmy-Jones 1995	0	46	1	54	3.7%	0.38 [0.02 , 9.64]
Speziale 2000	0	72	0	25		Not estimable
Treggiari-Venzi 2000	0	47	0	51		Not estimable
Wilkes 2002	1	41	1	40	4.9%	0.97 [0.06 , 16.14]
Zangrillo 2005	0	80	0	80		Not estimable
Subtotal (95% CI)		**502**		**460**	**12.4%**	**0.53 [0.09 , 3.13]**
Total events:	1		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 2 (P = 0.86); I² = 0%						
Test for overall effect: Z = 0.70 (P = 0.49)						
4.1.5 Atrial Pacing						
Debrunner 2004	0	40	0	40		Not estimable
Gerstenfeld 2001	0	58	0	60		Not estimable
Subtotal (95% CI)		**98**		**100**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
4.1.6 Posterior Pericardiotomy						
Mulay 1995	0	50	0	50		Not estimable
Subtotal (95% CI)		**50**		**50**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**3390**		**3360**	**100.0%**	**0.87 [0.47 , 1.62]**
Total events:	19		25			
Heterogeneity: Tau² = 0.00; Chi² = 11.53, df = 15 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.44 (P = 0.66)						
Test for subgroup differences: Chi² = 0.34, df = 2 (P = 0.84), I² = 0%						



The effect of interventions on hospital length of stay

There were 51 studies with 63 treatment groups and 9661 participants that reported on hospital length of stay. Three trials (Farsak 2002; Kuralay 1999; Redle 1999) did not contribute to the final pooled analysis due to lack of standard deviation data. Interventions were associated with a significant reduction in length of stay in the treatment group, demonstrated by a mean difference of -0.69 days (95% CI -0.95 to -0.43). All individual interventions were associated with similar significant or borderline significant reductions except for magnesium. Nine studies evaluating the effects of magnesium demonstrated a mean difference of 0.05 days (95% CI -0.47 to 0.57; I^2 = 69%; Figure 14).

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Figure 14. Forest plot: 5 Length of Stay; 5.1 All Treatments.

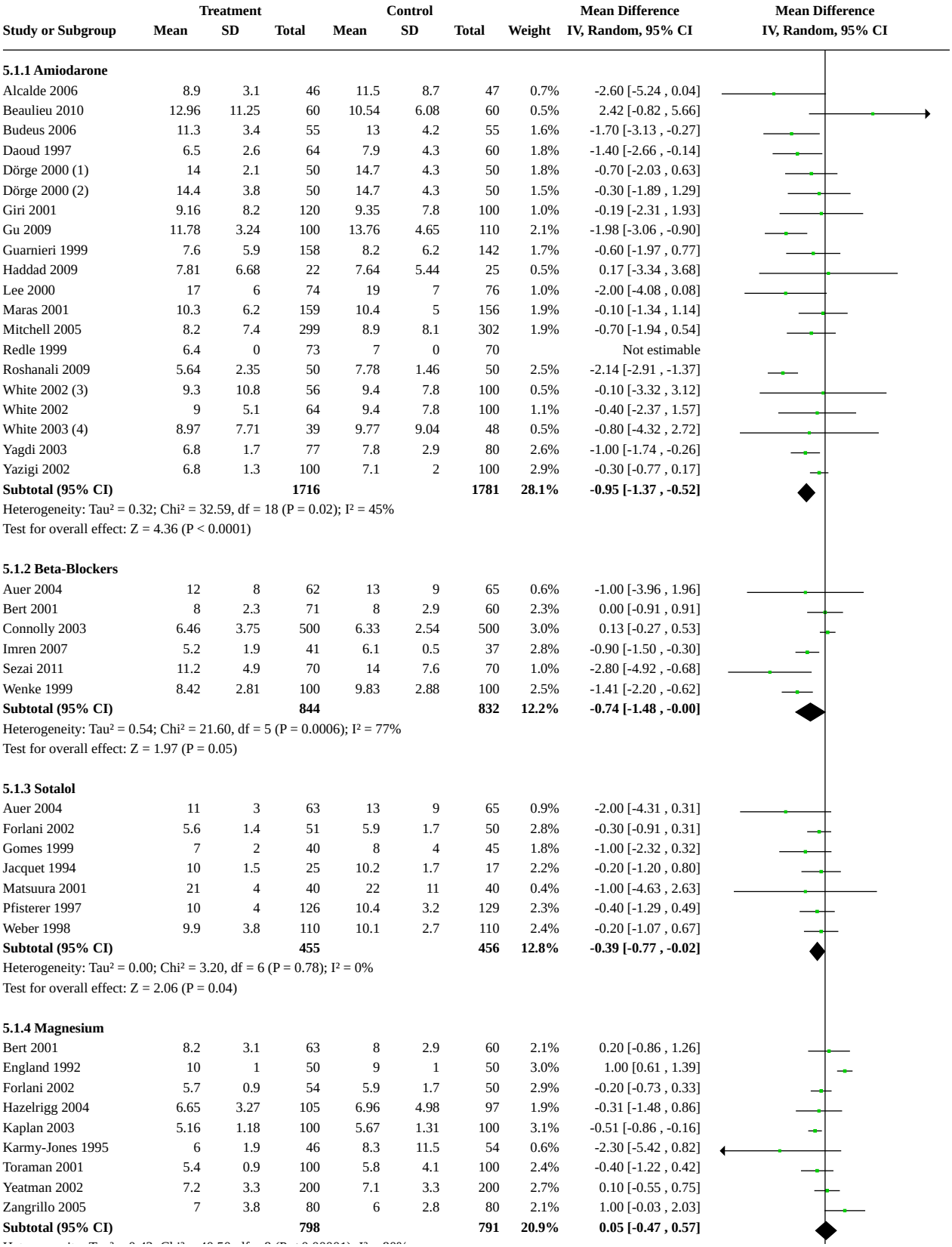

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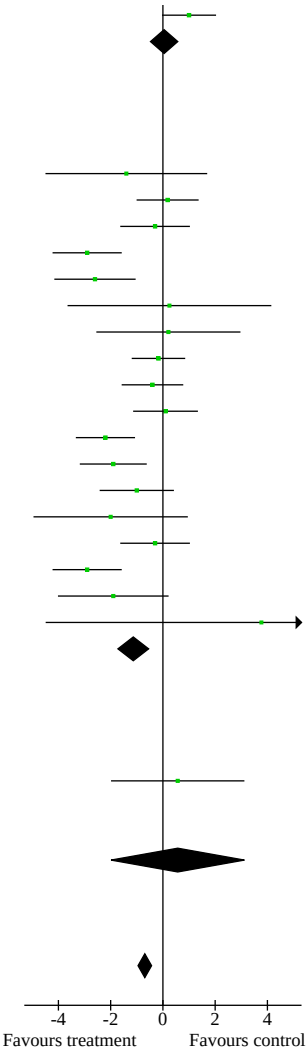
Figure 14. (Continued)

Zangrillo 2005	7	3.8	80	6	2.8	80	2.1%	1.00 [-0.03 , 2.03]
Subtotal (95% CI)			**798**			**791**	**20.9%**	**0.05 [-0.47 , 0.57]**
Heterogeneity: Tau² = 0.43; Chi² = 40.50, df = 8 (P < 0.00001); I² = 80%								
Test for overall effect: Z = 0.18 (P = 0.86)								
5.1.5 Atrial Pacing								
Chung 2000a	7.5	3.2	51	8.9	10.6	49	0.6%	-1.40 [-4.50 , 1.70]
Da Silva 2008	7.65	3.41	49	7.47	2.52	49	1.9%	0.18 [-1.01 , 1.37]
Eslami 2005 (5)	8.7	1.3	40	9	4.1	40	1.7%	-0.30 [-1.63 , 1.03]
Eslami 2005 (6)	6.1	1.2	40	9	4.1	40	1.8%	-2.90 [-4.22 , -1.58]
Fan 2000	7	1.4	32	9.6	4.2	31	1.5%	-2.60 [-4.16 , -1.04]
Gerstenfeld 1999 (7)	6.83	8.13	21	6.58	4.13	21	0.4%	0.25 [-3.65 , 4.15]
Gerstenfeld 1999 (6)	6.79	4.71	19	6.58	4.13	21	0.7%	0.21 [-2.55 , 2.97]
Gerstenfeld 2001	5.79	2.88	58	5.96	2.79	60	2.2%	-0.17 [-1.19 , 0.85]
Goette 2002 (7)	11.8	3.6	60	12.2	2.7	50	1.9%	-0.40 [-1.58 , 0.78]
Goette 2002 (8)	12.3	3.6	51	12.2	2.7	50	1.9%	0.10 [-1.14 , 1.34]
Greenberg 2000 (7)	5.6	1.4	40	7.8	3.7	48	2.0%	-2.20 [-3.33 , -1.07]
Greenberg 2000 (6)	5.9	2.1	31	7.8	3.7	48	1.8%	-1.90 [-3.18 , -0.62]
Greenberg 2000 (5)	6.8	2.9	35	7.8	3.7	48	1.6%	-1.00 [-2.42 , 0.42]
Levy 2000	7.7	6.9	65	9.7	10	65	0.6%	-2.00 [-4.95 , 0.95]
Mirkhani 2005 (5)	8.7	1.3	40	9	4.1	40	1.7%	-0.30 [-1.63 , 1.03]
Mirkhani 2005 (6)	6.1	1.2	40	9	4.1	40	1.8%	-2.90 [-4.22 , -1.58]
Ozin 2005	7.9	2.2	35	9.8	6	35	1.0%	-1.90 [-4.02 , 0.22]
White 2003	13.54	23.7	35	9.77	9.04	48	0.1%	3.77 [-4.49 , 12.03]
Subtotal (95% CI)			**742**			**783**	**25.2%**	**-1.13 [-1.72 , -0.55]**
Heterogeneity: Tau² = 0.85; Chi² = 41.87, df = 17 (P = 0.0007); I² = 59%								
Test for overall effect: Z = 3.79 (P = 0.0002)								
5.1.6 Posterior Pericardiotomy								
Arbatli 2003	13.889	8.46	54	13.322	4.674	59	0.8%	0.57 [-1.99 , 3.12]
Farsak 2002	8	0	75	7	0	75		Not estimable
Kuralay 1999	7	0	100	8	0	100		Not estimable
Subtotal (95% CI)			**229**			**234**	**0.8%**	**0.57 [-1.99 , 3.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.44 (P = 0.66)								
Total (95% CI)			**4784**			**4877**	**100.0%**	**-0.69 [-0.95 , -0.43]**
Heterogeneity: Tau² = 0.54; Chi² = 189.71, df = 59 (P < 0.00001); I² = 69%								
Test for overall effect: Z = 5.25 (P < 0.00001)								
Test for subgroup differences: Chi² = 13.76, df = 5 (P = 0.02), I² = 63.7%								



Footnotes

(1) Amiodarone (300mg)
(2) Amiodarone (150mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)
(5) Left Atrial Pacing
(6) Biatrial Pacing
(7) Right Atrial Pacing
(8) Bachmann's Bundle Pacing

The effect of interventions on cost of treatment during hospital stay

Twelve studies with 14 treatment groups and 2790 participants reported data on the cost of treatment during the hospital stay. Four trials (Connolly 2003; Eslami 2005; Fan 2000; Guarnieri 1999) did not contribute to the final pooled analysis due to lack of standard deviation data. Interventions were associated with a small but significant reduction in cost in the treatment group, demonstrated by a mean difference of -1.25 [1000s of US dollars] (95% CI -1.97 to -0.52; I^2 = 13%; Figure 15).

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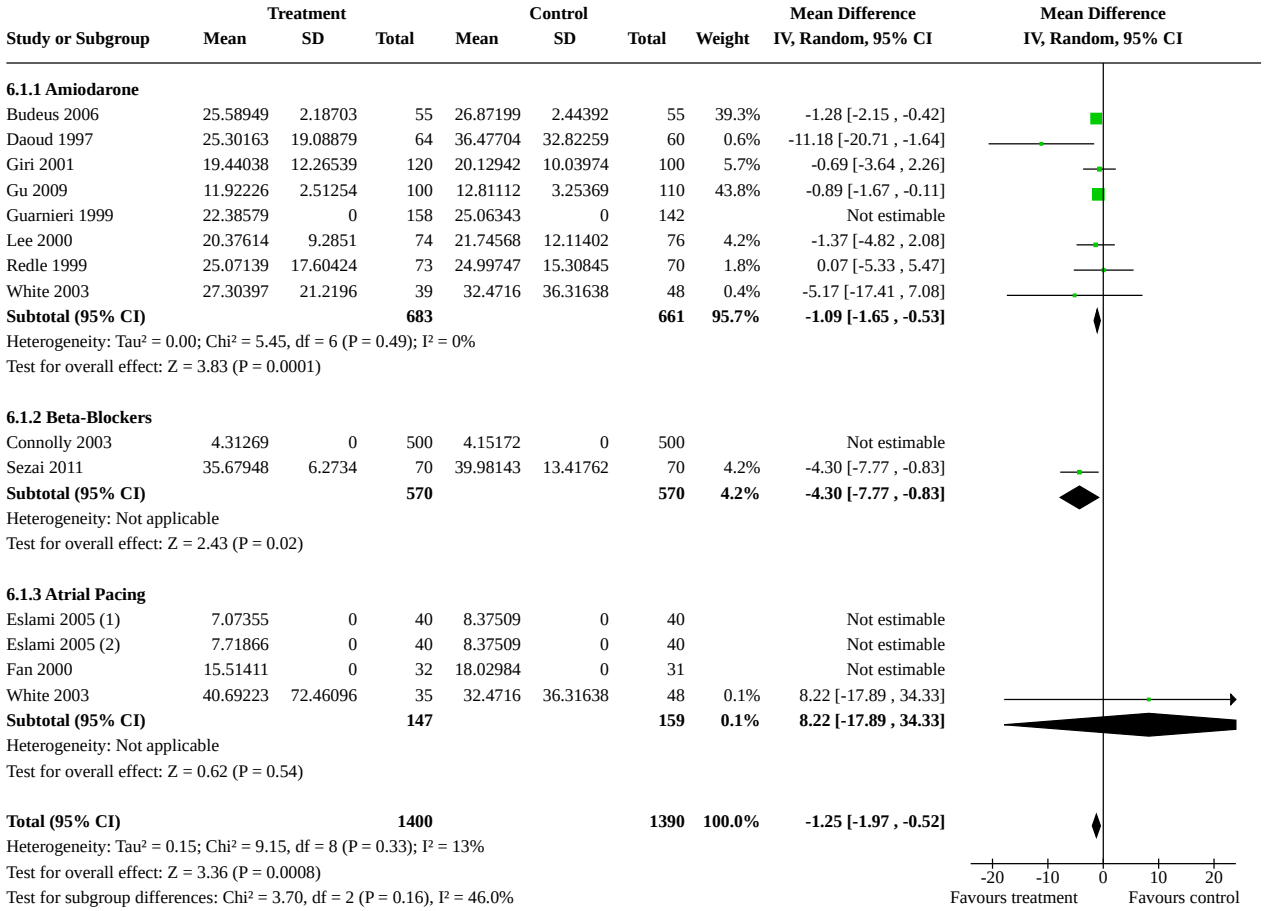
Figure 15. Forest plot: 6 Cost; 6.1 All Treatments.



Heterogeneity

Considerable heterogeneity was found in the primary outcome analyses for each of the reviewed interventions, except for sotalol (I^2 = 3%). However, much of this heterogeneity may be explained by primary trial characteristics.

In the amiodarone analysis, difference in treatment regimens between the studies, including dosages and timing of initial administration, likely contributed substantially to the heterogeneity. When considering only studies that began administration of amiodarone post-operatively, heterogeneity was numerically decreased (I^2 = 37%).

A source of heterogeneity in the beta-blocker analysis may have been the type of beta-blocker used. When considering only studies evaluating the effects of propranolol, only 18% of the variation between studies was found to be due to heterogeneity.

The pooled analysis of trials studying the efficacy of magnesium demonstrate borderline significant heterogeneity (I^2 = 51%). Treatment regimens varied from small doses added to the cardioplegia solution to continuous infusions over several days and possibly accounted for a large part of this variance.

Heterogeneity in the atrial pacing analysis may have been due to the pooling of studies utilizing different pacing methods, including Bachmann's bundle pacing, left atrial pacing, right atrial pacing and biatrial pacing.

Due to the small number of trials contained in the analysis of posterior pericardiotomy for prevention of post-operative atrial fibrillation, much of the heterogeneity found in this analysis (I^2 = 66%) was due to one study (Asimakopoulos 1997). This study differed from the others investigating this intervention in its definition of the primary outcome. Asimakopoulos 1997 considered all instances of supraventricular tachycardia while the other studies in this analysis specified the primary outcome as incidence of atrial fibrillation or set a minimum duration required for the event to be considered.

DISCUSSION

Summary of main results

This meta-analysis demonstrated that each of the studied interventions significantly reduced the rate of post-operative atrial fibrillation after cardiac surgery compared with a placebo control. Beta-blockers and sotalol appeared to have similar efficacy.

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Amiodarone, atrial pacing and posterior pericardiotomy were found to be effective. However, the summary estimate for the latter was based on only six trials. The ability of magnesium to prevent atrial fibrillation may be slightly less than that of the other pharmacological agents.

Prophylactic intervention of any kind in this setting appeared to reduce the odds of post-operative stroke, though this reduction did not reach statistical significance. Intervention also decreased the hospital length of stay by approximately two-thirds of a day and decreased the cost of hospital treatment by roughly $1250 US. There was insufficient evidence to appropriately compare the efficacy of the individual interventions for these secondary outcomes. However, it is important to note that magnesium and posterior pericardiotomy were not associated with a decreased length of hospital stay. With regards to the latter, this can possibly be explained by other positive effects of alternate interventions, including influencing hemodynamic stability, that are not benefits of posterior pericardiotomy. Atrial pacing was not associated with a decrease in the cost of hospital treatment, possibly due to the equipment costs associated with this intervention.

None of the interventions demonstrated a significant protective effect against post-operative all-cause or cardiovascular mortality.

Limitations

This meta-analysis was primarily limited by the lack of availability of relevant secondary outcome data. The incidence of stroke, all-cause mortality and cardiovascular mortality, as well as length of hospital stay and cost of hospital treatment were not collected in many of the included studies. Further, this review is limited by the quality of the available studies. Improper allocation concealment, lack of blinding within pharmacological trials, selective reporting and failure to utilize an intention-to-treat analysis were all associated with variation in the pooled summary estimates for prevention of post-operative atrial fibrillation. Although the results of sensitivity analyses based on the level of risk demonstrated some numerical differences, these adjusted results would not influence the overall implications of this review. Though many of the analyses in this review demonstrated significant heterogeneity, much of this variance may be explained by individual study characteristics that can be taken into account when applying the results of this review in the clinical setting. This review was not designed or powered to evaluate drug dosage or timing of interventions, which varied considerably between studies. Consensus on these factors through further research or more detailed analysis of data specific to these questions is warranted.

Agreements and disagreements with other studies or reviews

This review sought to update the previous version (Crystal 2004) with the available evidence from the seven years since its publication. In addition, the interventions of magnesium and posterior pericardiotomy were included due to their significant presence within the literature. Overall, the results of this meta-analysis are largely similar to those of the previous version. Increased evidence has lead to an improved estimated efficacy for both amiodarone and atrial pacing in preventing atrial fibrillation. Though the summary estimate for all interventions in relation to stroke still did not reach statistical significance, it is clearer from this updated review that there is a trend towards the protective effects of prophylaxis. The estimated reduction in hospital length of stay due to preventative intervention was nearly identical in the two versions of this review. Finally, additional evidence allowed this review to confirm the hypothesis of the previous version's authors that intervention in this setting leads to a decreased cost of hospital stay.

Since the publication of the previous version of this meta-analysis, a number of studies have reviewed the state of the literature surrounding this topic. However, few have done so in a systematic fashion. The most recent complete systematic review of this literature evaluated each of the pharmacological interventions we considered in this paper, as well as atrial pacing, digoxin and calcium-channel blockers (Burgess 2006). Our updated results are in agreement with those presented in this previous review.

A more recent analysis (Shepherd 2008) summarized the efficacy of magnesium for preventing post-operative atrial fibrillation after CABG. The authors reported a pooled odds ratio in a random-effects model of 14 studies of 0.61 (95% CI 0.41 to 0.90). Our summary estimate was similar.

A meta-analysis of posterior pericardiotomy in this setting retrieved the same six studies identified in our search and presented a nearly identical pooled summary estimate (Biancari 2010).

Clinical research has also focused on the use of steroids to decrease post-operative mortality and morbidity following cardiac surgery, including for prevention of atrial fibrillation. This class of drugs was not studied within this meta-analysis because several recent extensive reviews are readily available. Cappabianca 2011 reported in a review of 31 randomized trials that steroids were associated with a pooled odds ratio of 0.56 (95% CI 0.44 to 0.72) for atrial fibrillation, a result comparable to those of the interventions studied in this review.

AUTHORS' CONCLUSIONS

Implications for practice

Recent guidelines from both Canadian (Mitchell 2011) and American (Bradley 2005) expert groups have suggested that beta-blockers be adopted for routine prophylactic use following cardiac surgery to prevent post-operative atrial fibrillation in both patients regularly taking this type of medication at home and those not. In patients where the use of beta-blockers is contraindicated, amiodarone is considered to be the second choice. Due largely to possible adverse effects, sotalol is only recommended by these guidelines in patients at high risk of atrial fibrillation (e.g. the elderly, valvular surgery patients or those with congestive heart disease) (Shirzad 2010). The more recent Canadian guidelines (Mitchell 2011) state that magnesium and atrial pacing may be beneficial, but are only recommended if the patient has contraindications for both beta-blockers and amiodarone. This review largely supports these guidelines. Each of these interventions demonstrated strong efficacy in preventing post-operative atrial fibrillation. The selection of prophylaxis should reflect the individual patient's condition and take into account the risks and adverse events associated with each intervention. While the studies analyzed in this review were generally not powered to evaluate the adverse effects of each of the interventions and there was no standardized method of reporting these events, the known risks associated with each of the interventions are outlined

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in Table 1. These interventions should be administered by health professionals familiar with their use and with the assessment for and treatment of potential complications. The evidence presented in this review on posterior pericardiotomy is based on only a few randomized trials. Therefore, although it demonstrated promising results, we cannot recommend use of this surgical prophylactic intervention at this time.

Implications for research

This review presents evidence that post-operative atrial fibrillation can be reduced by several interventions with different mechanism of actions, for example, beta-blockers via catecholamine pathways and posterior pericardiotomy through diminution of cardiac irritation by blood. Further research should consider examining synergism between interventions for greater efficacy.

This review also demonstrates that intervention for preventing post-operative atrial fibrillation leads to a decreased hospital length of stay, lower costs of hospital treatment and a trend towards decreased risk of post-operative stroke. However, these data were unavailable from a number of the trials included in this review. Future studies should make note to properly collect and present these data as conclusive evidence of the beneficial effects of prophylactic intervention beyond the direct prevention of atrial fibrillation would be beneficial.

Finally, continued investigation into the physiological mechanisms of atrial fibrillation and especially the circumstances that lead to thrombus formation during this arrhythmia would benefit future research and lead to greater understanding of how to prevent this outcome.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abel 1983

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG using a saphenous vein graft only	
Interventions	Propranolol vs. Control	
Outcomes	AF or atrial flutter; Mortality	
Follow-Up	6 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Randomization based on last digit of hospital clinical record
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	No information of attempts to blind control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Withdrawn patients from treatment arm with high rate of clinical events
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

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Akbarzadeh 2009

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective on-pump CABG only	
Interventions	Amiodarone vs. Biatrial Pacing vs. Control	
Outcomes	AF lasting at least 1 hour or associated with hemodynamic compromise; Mortality	
Follow-Up	ICU discharge	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Externally validated sequence generator
Allocation concealment (selection bias)	Low risk	Allocation based on computer-generated randomizer
Blinding of participants and personnel (performance bias) All outcomes	High risk	Insufficient information; Pacing, therefore unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Single-blinded, therefore physicians know treatment regimen
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

Alcalde 2006

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. placebo

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Alcalde 2006 *(Continued)*

Outcomes	AF lasting at least 10 minutes or associated with hemodynamic instability; Stroke; LOS
Follow-Up	8.9-11.5 days
Concurrent Antiarrhythmic Medications	Beta-blockers (75% of patients)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded, identical looking pills
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

Ali 1997

Study characteristics

Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Beta-blocker (metoprolol, atenolol, sotalol or inderal) vs. Control
Outcomes	AF; Stroke; Mortality; CV Mortality
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

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Ali 1997 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

Alves 2007

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump cardiac surgery (79.7% CABG only, 2% mitral commissurotomy, 2% mitral valveplasty; 2% CABG + mitral valveplasty, 2% CABG + mitral valve replacement, 4.1% aortic valve replacement, 8.2% mitral valve replacement)
Interventions	Amiodarone vs. Control
Outcomes	AF
Follow-Up	7 days or hospital discharge
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

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Alves 2007 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

Arbatli 2003

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective, on-pump CABG only	
Interventions	Posterior pericardiotomy vs. Control	
Outcomes	AF lasting at least 15 minutes; LOS	
Follow-Up	2 days	
Concurrent Antiarrhythmic Medications	Diltiazem; Magnesium	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described

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Arbatli 2003 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Asimakopoulos 1997

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Posterior pericardiotomy vs. Control	
Outcomes	SVT; Mortality	
Follow-Up	Not reported	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgical Procedure
Blinding of outcome assessment (detection bias) All outcomes	High risk	Surgical Procedure
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

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Asimakopoulos 1997 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

Assefi 2010

Study characteristics		
Methods	Randomized, controlled	
Participants	CABG only	
Interventions	Amiodarone vs. Control	
Outcomes	AF	
Follow-Up	Not reported	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"Alternate Randomization" used
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Unclear risk	Not reported

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Auer 2004

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	Cardiac surgery (Valve surgery in 44.7% [Aortic 36%, Mitral 8.7%, Mitral and aortic 0.4%, Tricuspid 0.4%]; Combined CABG + valve in 9.9%)
Interventions	Metoprolol vs. sotalol vs. placebo
Outcomes	AF lasting at least 5 minutes or requiring intervention for angina or hemodynamic compromise; Stroke; Mortality; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Generation of a randomization table
Allocation concealment (selection bias)	Low risk	Assignment and treatment was blinded and isolated from patients and treaters
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded, identical looking pills
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Low risk	Yes

Avila Neto 2007

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only

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Avila Neto 2007 *(Continued)*

Interventions	Right atrial pacing vs. Control
Outcomes	AF
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Amiodarone and cardioversion in cases of clinical AF
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random assignment distribution
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgical Procedure
Blinding of outcome assessment (detection bias) All outcomes	High risk	Surgical Procedure
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Babin-Ebell 1996

Study characteristics

Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. Control
Outcomes	SVT
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None

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Babin-Ebell 1996 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random assignment
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	Due to discontinuations in treatment group
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Beaulieu 2010

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	Nonurgent on-pump valve surgery (isolated or CABG + valve)
Interventions	Amiodarone vs. placebo
Outcomes	AF lasting more than 30 minutes or requiring treatment for hemodynamic compromise or discomfort; Stroke; Mortality; CV Mortality; LOS
Follow-Up	Hospital Discharge; Telephone follow-up at 1 month
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

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Beaulieu 2010 *(Continued)*

Random sequence generation (selection bias)	Low risk	Computer-generated randomization program
Allocation concealment (selection bias)	Low risk	Pharmacy-controlled
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind, double dummy
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind, double dummy
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Bert 2001

Study characteristics	
Methods	Single-blind, randomized, controlled
Participants	On-pump CABG, CABG + mitral valve
Interventions	Magnesium vs. propranolol vs. control
Outcomes	AF, atrial flutter or SVT lasting more than 5 minutes and requiring treatment; Mortality; CV Mortality; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Beta-blockers, digoxin
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Unclear risk	Insufficient information

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Bert 2001 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No mention of placebo use
Blinding of outcome assessment (detection bias) All outcomes	Low risk	AF assessed by blinded physician
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Blommaert 2000

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Right atrial pacing vs. Control
Outcomes	AF lasting at least 15 minutes
Follow-Up	1 day
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgical Procedure
Blinding of outcome assessment (detection bias) All outcomes	High risk	Surgical Procedure

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Blommaert 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Budeus 2006

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Amiodarone vs. placebo
Outcomes	Af lasting at least 10 minutes; Mortality; CV Mortality; LOS; Cost
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomization program
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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Butler 1993

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Amiodarone vs. placebo
Outcomes	SVT lasting more than 5 minutes and requiring treatment; Stroke; Mortality; CV Mortality
Follow-Up	6 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Cagli 2006

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only

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Cagli 2006 *(Continued)*

Interventions	Amiodarone vs. placebo
Outcomes	AF lasting more than 30 minutes or requiring treatment for hemodynamic compromise or symptoms
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Casthely 1994

Study characteristics

Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Magnesium vs. Control
Outcomes	SVA
Follow-Up	2 days
Concurrent Antiarrhythmic Medications	None

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Casthely 1994 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No mention of placebo use
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Chavan 2010

Study characteristics

Methods	Randomized, controlled
Participants	CABG only
Interventions	Bachmann's bundle pacing vs. Right atrial pacing vs. Control
Outcomes	AF
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described

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Chavan 2010 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Chung 2000a

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective on-pump CABG only	
Interventions	Atrial pacing vs. Control	
Outcomes	AF or atrial flutter requiring treatment; LOS	
Follow-Up	7 days	
Concurrent Antiarrhythmic Medications	Beta-blockers, digoxin	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomization program
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgical Procedure

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Chung 2000a *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Surgical Procedure
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Connolly 2003

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	Elective on-pump cardiac surgery	
Interventions	Metoprolol vs. placebo	
Outcomes	AF or atrial flutter; Stroke; Mortality; CV Mortality; LOS; Cost	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Beta-blockers, digoxin, diltiazem/verapamil	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

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Connolly 2003 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Crystal 2003

Study characteristics		
Methods	Multicentre double-blind, randomized, placebo-controlled	
Participants	CABG (n = 69); Aortic valve (n = 1); Mitral valve (n = 2); Aneurysm resection (n = 6); Other (n = 2)	
Interventions	Amiodarone vs. placebo	
Outcomes	AF lasting at least 30 minutes	
Follow-Up	Not reported (30-day mortality)	
Concurrent Antiarrhythmic Medications	Verapamil, diltiazem, Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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Dagdelen 2002

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	On-pump valvular surgery with or without CABG
Interventions	Magnesium vs. placebo
Outcomes	AF lasting at least 2 minutes
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	Metoprolol, Nifedipine
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Daoud 1997

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. placebo

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Daoud 1997 *(Continued)*

Outcomes	AF lasting at least 5 minutes; Stroke; Mortality; CV Mortality; LOS; Cost
Follow-Up	Discharge
Concurrent Antiarrhythmic Medications	Beta-blockers, CCBs, Digitalis
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Da Silva 2008

Study characteristics

Methods	Single-blind, randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial pacing vs. Control
Outcomes	AF and atrial flutter
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Digoxin, beta-blockers, calcium channel blockers
Notes	

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Da Silva 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random numerical table
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Pacing, therefore unblinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Single-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Daudon 1986

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Acebutolol vs. Control
Outcomes	AF lasting at least 5 minutes
Follow-Up	9 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned

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Daudon 1986 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No mention of placebo use
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Debrunner 2004

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Biatrial pacing
Outcomes	SVA (AF lasting at least 20 minutes atrial flutter or SVT); Mortality; CV Mortality
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Pacing procedure

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Debrunner 2004 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Evaluated by 2 separate physicians
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Dörge 2000

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone (150mg) vs. Amiodarone (300mg) vs. placebo
Outcomes	AF; Mortality; LOS
Follow-Up	10 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

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Dörge 2000 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Ekim 2006

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective on-pump cardiac surgery (CABG n = 84; Valve n = 10; CABG + Valve n = 6)	
Interventions	Posterior pericardiotomy vs. Control	
Outcomes	SVT	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	During surgical procedure
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent ECG monitoring
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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England 1992

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Magnesium
Outcomes	AF; Mortality; CV Mortality; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Calcium channel blockers, Beta-blockers, Digoxin, Other antiarrythmic agents
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomized through pharmacy list system
Allocation concealment (selection bias)	Low risk	Pharmacy-controlled
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded, identical looking placebo therapy
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Eslami 2005

Study characteristics	
Methods	Double-blind, randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial pacing vs. Left atrial pacing vs. Control

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Eslami 2005 *(Continued)*

Outcomes	AF; Stroke; LOS; Cost
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	Beta-blockers, Digitalis
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Evrard 2000

Study characteristics

Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Sotalol vs. Control
Outcomes	AF lasting at least 10 minutes; Mortality; CV Mortality
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Not reported
Notes	

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Evrard 2000 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No mention of placebo use
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Fan 2000

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial pacing vs. Left atrial pacing vs. Right atrial pacing vs. Control
Outcomes	AF lasting at least 10 minutes
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned

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Fan 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent ECG monitoring
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some drop-out, but might not impact
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Low risk	Yes

Fanning 1991

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	SVT lasting at least 30 minutes; Mortality; CV Mortality	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	Beta-blockers until surgery; None postoperatively	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded

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Fanning 1991 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Farsak 2002

Study characteristics		
Methods	Double-blind, randomized, controlled	
Participants	On-pump CABG only	
Interventions	Posterior pericardiotomy vs. Control	
Outcomes	AF requiring treatment for symptoms or hemodynamic deterioration; LOS	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random digits, where first 75 are treatment, next 75 control
Allocation concealment (selection bias)	High risk	Randmization method visible
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded patients, and outcome assessors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

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Farsak 2002 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Forlani 2002

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Magnesium vs. sotalol vs. Control	
Outcomes	AF requiring treatment for symptoms or hemodynamic deterioration; Mortality; CV Mortality; LOS	
Follow-Up	30 days	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomization program
Allocation concealment (selection bias)	Low risk	Central allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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Gerstenfeld 1999

Study characteristics		
Methods	Single-blind, randomized, controlled	
Participants	Elective on-pump cardiac surgery (CABG n = 172; Valve n = 19; CABG + Valve n = 29)	
Interventions	Biatrial Pacing vs. Right atrial pacing vs. Control	
Outcomes	AF lasting at least 5 minutes or symptomatic or associated with hemodynamic compromise requiring treatment; LOS	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blinded, participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	AF determined through ECG
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Gerstenfeld 2001

Study characteristics	
Methods	Multicentre, randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial Pacing vs. Control

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Gerstenfeld 2001 *(Continued)*

Outcomes	AF; Stroke; Mortality; CV Mortality; LOS
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Low risk	AF determined through ECG
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Giri 2001

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG (86%) or CABG + valve (14%)
Interventions	Amiodarone vs. placebo
Outcomes	AF lasting at least 30 minutes or requiring treatment due to symptoms or hemodynamic compromise; Stroke; Mortality; LOS; Cost
Follow-Up	Hospital discharge, Follow-up at 30 days for mortality
Concurrent Antiarrhythmic Medications	Beta-blockers

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Giri 2001 *(Continued)*

Notes		

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization software
Allocation concealment (selection bias)	Low risk	Pharmacy controlled groupings
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Goette 2002

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG or AVR
Interventions	Bachmann's bundle pacing vs. Right atrial pacing vs. Control
Outcomes	AF lasting at least 1 hour or requiring therapy for hemodynamic compromise; Mortality; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned

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Goette 2002 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Insufficient information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Intention-to-treat analysis	High risk	No

Gomes 1999

Study characteristics		
Methods	Multicentre, double-blind, randomized, placebo-controlled	
Participants	On-pump CABG or AVR	
Interventions	Sotalol vs. placebo	
Outcomes	AF lasting at least 1 hour or requiring therapy for hemodynamic compromise; Mortality; CV Mortality; LOS	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	External randomization through pharmacy registry
Allocation concealment (selection bias)	Low risk	Pharmacy-controlled groupings
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind

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Gomes 1999 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Greenberg 2000

Study characteristics		
Methods	Double-blind, randomized, controlled	
Participants	Off-pump CABG only	
Interventions	Biatrial Pacing vs. Left atrial pacing vs. Right atrial pacing vs. Control	
Outcomes	AF lasting at least 10 minutes; LOS	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Beta-blockers (20mg qid)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded physician assessors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data

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Greenberg 2000 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Low risk	Yes

Gu 2009

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	Valve surgery (with or without CABG)	
Interventions	Amiodarone vs. placebo	
Outcomes	AF; Mortality; LOS; Cost	
Follow-Up	14 days	
Concurrent Antiarrhythmic Medications	Beta-blockers, Calcium channel blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomization software
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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Guarnieri 1999

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Amiodarone vs. Placebo
Outcomes	AF; Stroke; Mortality; CV Mortality; LOS; Cost
Follow-Up	30 days
Concurrent Antiarrhythmic Medications	Continuation if already using beta-blockers, calcium channel blockers or digitalis
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	Low risk	Yes

Gun 1998

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. placebo

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Gun 1998 *(Continued)*

Outcomes	AF
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Haddad 2009

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. placebo
Outcomes	AF; Mortality; CV Mortality; LOS
Follow-Up	42 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

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Haddad 2009 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind, placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind, placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Full details of outcomes not provided, although significance/non-sig stated
Selective reporting (reporting bias)	Unclear risk	Annotated version, not all outcome data reported
Intention-to-treat analysis	High risk	No

Hakala 2005

Study characteristics

Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Right atrial pacing (atrial overdrive) vs. Right atrial pacing (bradycardia prevention) vs. Control
Outcomes	AF
Follow-Up	From 24 to 72 hours postoperative
Concurrent Antiarrhythmic Medications	Metoprolol
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned

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Hakala 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation based on sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Pacing procedure, therefore unblinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	High risk	Patients excluded if ICU stay longer than 24hr; excluded if AF event within first 24 hrs postop
Intention-to-treat analysis	Low risk	Yes

Hamid 2008

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	Off-pump CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	AF lasting at least 15 minutes or requiring therapy for instability	
Follow-Up	1 day	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Pharmacy-controlled, computer-generated randomization software
Allocation concealment (selection bias)	Low risk	Allocation from pharmacy, administration of drug concealed through identical syringes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind, placebo-controlled

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Hamid 2008 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind, placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Harahsheh 2001

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	On-pump CABG only (with saphenous vein graft)
Interventions	Amiodarone vs. placebo
Outcomes	SVT; Mortality
Follow-Up	42 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Patients blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	High drop-out rate from treatment arm that could be related to therapy

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Harahsheh 2001 *(Continued)*

Selective reporting (reporting bias)	High risk	No defined protocol, limited outcomes reported, an outcome seems to be measured at an illogical time point
Intention-to-treat analysis	High risk	No

Hazelrigg 2004

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	AF, atrial flutter or SVT lasting more than one minute with hemodynamic deterioration; Mortality; LOS	
Follow-Up	5 days	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Pharmacy-controlled, statistician developed randomization sequence
Allocation concealment (selection bias)	Low risk	Pharmacy-controlled randomization
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blinded, placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blinded, placebo-controlled
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

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Hohnloser 1991

Study characteristics	
Methods	Single-blind, randomized, placebo-controlled
Participants	CABG only
Interventions	Amiodarone vs. placebo
Outcomes	SVT
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	Continuation if already on inotropic drugs, digitalis, nitrates, B-blockers, CCBs
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding of patients, no mention of physicians
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some missing data, but from both study arms that are likely to balance out
Selective reporting (reporting bias)	Unclear risk	Events only recorded within 2 day postop time frame
Intention-to-treat analysis	High risk	No

Imren 2007

Study characteristics	
Methods	Multicentre, double-blind, randomized, controlled
Participants	Off-pump CABG only
Interventions	Metoprolol vs. Control

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Imren 2007 *(Continued)*

Outcomes	AF lasting more than 15 minutes; Stroke; Mortality; LOS
Follow-Up	6 days
Concurrent Antiarrhythmic Medications	Esmolol during surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Isolated physician regulated randomization schemed based on random number list
Allocation concealment (selection bias)	Low risk	Allocation from a non-study related physician
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Ivey 1983

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. placebo
Outcomes	SVT; Mortality; CV Mortality
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

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Ivey 1983 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Pharmacy-controlled randomization and drug administration
Allocation concealment (selection bias)	Low risk	Double-blind, and pharmacy-controlled groupings
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Intention-to-treat analysis	High risk	No

Jacquet 1994

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Sotalol vs. Control
Outcomes	SVA lasting at least 1 minute with a heart rate of greater than 120 bpm; LOS
Follow-Up	Hospital discharge; 1-3 month postoperative follow-up
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No randomization method mentioned

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Jacquet 1994 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not placebo controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information
Incomplete outcome data (attrition bias) All outcomes	High risk	Event rates based on post-randomization drop-outs, but baseline characteristics not adjusted for
Selective reporting (reporting bias)	High risk	Adverse outcomes such as bradycardia not reported as risk factor, although high dropout rate due to complications
Intention-to-treat analysis	High risk	No

Janssen 1986

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Metoprolol vs. Sotalol vs. Control
Outcomes	SVT; Mortality; CV Mortality
Follow-Up	2 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization using sealed envelope
Allocation concealment (selection bias)	Low risk	Randomization using sealed envelope
Blinding of participants and personnel (performance bias) All outcomes	High risk	Treatment allocation was marked on patient chart. No blinding.

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Janssen 1986 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Treatment allocation was marked on patient chart. No blinding.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Jensen 1997

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	AF lasting more than 1 minute	
Follow-Up	3 days	
Concurrent Antiarrhythmic Medications	Beta-blockers; Calcium antagonists; Nitroglycerin	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	

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Jensen 1997 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Kanchi 2004

Study characteristics		
Methods	Randomized, placebo-controlled	
Participants	Off-pump CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	AF	
Follow-Up	1 day	
Concurrent Antiarrhythmic Medications	50 mg atenolol; 10 mg diazepam	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

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Kaplan 2003

Study characteristics		
Methods	Randomized, placebo-controlled	
Participants	Elective CABG only, both on and off-pump	
Interventions	Magnesium vs. placebo	
Outcomes	AF; LOS	
Follow-Up	Hospital stay (6 days)	
Concurrent Antiarrhythmic Medications	Calcium-channel blockers; ACE inhibitors; Digoxin	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Karmy-Jones 1995

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective CABG, valve or combination
Interventions	Magnesium vs. placebo

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Karmy-Jones 1995 *(Continued)*

Outcomes	SVT; Mortality; CV Mortality; LOS
Follow-Up	Hospital discharge (7 days)
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Physicians directing therapy were also blinded to all but the initial postoperative serum magnesium results"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Khuri 1987

Study characteristics

Methods	Multicentre, double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Nadolol vs. placebo
Outcomes	SVT
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

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Khuri 1987 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind, done centrally
Incomplete outcome data (attrition bias) All outcomes	High risk	"7 patients were excluded from the evaluation of efficacy because of insufficient postoperative data" - Allocation not reported
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Kuralay 1999

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Posterior pericardiotomy vs. Control
Outcomes	SVT lasting at least 30 minutes
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	

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Kuralay 1999 *(Continued)*

Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Kurz 1999

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective on-pump cardiac surgery	
Interventions	Biatrial pacing vs. Control	
Outcomes	Af lasting at least 2 minutes	
Follow-Up	3 days	
Concurrent Antiarrhythmic Medications	None	
Notes	Trial Prematurely Aborted	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization stratified by CABG vs valve
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described

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Kurz 1999 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	High risk	Trial prematurely aborted - Loss of atrial sensing in Tx group led to AF development
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Low risk	

Lamb 1988

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Atenolol vs. Control
Outcomes	AF
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed

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Lamb 1988 *(Continued)*

Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Lee 2000

Study characteristics		
Methods	Randomized, placebo-controlled	
Participants	Elective on-pump CABG only	
Interventions	Amiodarone vs. placebo	
Outcomes	AF lasting at least 10 minutes; Stroke; Mortality; CV Mortality; LOS, Cost	
Follow-Up	14 days	
Concurrent Antiarrhythmic Medications	Beta-blockers; Calcium channel blockers; Digitalis	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

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Levy 2000

Study characteristics	
Methods	Double-blind, randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial pacing vs. Control
Outcomes	AF lasting at least 1 hour; Stroke; Mortality; LOS
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	
Blinding of outcome assessment (detection bias) All outcomes	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	

Lúcio 2004

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Metoprolol vs. Control

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Lúcio 2004 *(Continued)*

Outcomes	Sustained AF and atrial flutter; Mortality
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	

Maras 2001

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. placebo
Outcomes	AF lasting at least 1 hour or associated with hemodynamic compromise; Stroke; Mortality; CV Mortality; LOS
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	Not reported (control group did remain on usual medications)

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Maras 2001 *(Continued)*

Notes		

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	

Markovic 2010

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	CABG only
Interventions	Amiodarone vs. placebo
Outcomes	AF
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described

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Markovic 2010 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Martinussen 1988

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Propranolol vs. placebo	
Outcomes	SVT; Mortality; CV Mortality	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind

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Martinussen 1988 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	High risk	14 patients removed from analysis because treatment/placebo not given
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Matangi 1985

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Propranolol vs. Control	
Outcomes	SVA (AF or atrial flutter or atrial tachycardia); Mortality	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat

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Matangi 1985 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Low risk	

Matangi 1989

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	Elective on-pump CABG only	
Interventions	Atenolol vs. placebo	
Outcomes	SVA	
Follow-Up	8 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

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Materne 1985

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Acebutolol vs. Control
Outcomes	SVT
Follow-Up	Hospital discharge (mean 10 days)
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Matsuura 2001

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Sotalol vs. Control

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Matsuura 2001 *(Continued)*

Outcomes	AF lasting at least 5 minutes; Mortality; CV Mortality; LOS
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	Digitalis; ACE inhibitors; Dihydropyridine calcium antagonists
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo was administered to controls
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of outcome assessors not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Mirkhani 2005

Study characteristics

Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Biatrial pacing vs. Left atrial pacing vs. Control
Outcomes	AF; Stroke; LOS
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	
Notes	

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Mirkhani 2005 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Mitchell 2005

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective CABG, valve or combo
Interventions	Amiodarone vs. placebo
Outcomes	SVT lasting at least 5 minutes and requiring treatment; Stroke; Mortality; CV Mortality; LOS
Follow-Up	6 days
Concurrent Antiarrhythmic Medications	Digoxin
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computer-generated"; Stratified by age, type of surgery and use of preoperative beta-blockers

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Mitchell 2005 *(Continued)*

Allocation concealment (selection bias)	Low risk	"Computer-generated" and "implemented by a hospital pharmacist who was not otherwise involved in the trial"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Study personnel were not aware of the allocation sequences or of patient allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Study personnel were not aware of the allocation sequences or of patient allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	

Mohr 1981

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Propranolol vs. Control	
Outcomes	SVT	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Randomization by odd or even last numbers on medical records
Allocation concealment (selection bias)	High risk	Randomization by odd or even last numbers on medical records
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding

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Mohr 1981 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Mulay 1995

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Posterior pericardiotomy vs. Control
Outcomes	SVT (AF or atrial flutter) that persisted despite correction of hypoxia or electrolyte imbalance; Mortality; CV Mortality
Follow-Up	Not reported
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed

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Mulay 1995 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

Myhre 1984

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Propranolol vs. Control	
Outcomes	"Clnically important SVA";	
Follow-Up	8 days	
Concurrent Antiarrhythmic Medications	Nitroglycerin	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"One patient in group B died peri-operatively and thus one more patient was included"
Allocation concealment (selection bias)	High risk	"One patient in group B died peri-operatively and thus one more patient was included"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	"Four patients were excluded from group B. Two patients did not receive propranolol at all, one because of arterial hypotension and one because propranolol was not administered as ordered"
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

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Najafi 2007

Study characteristics	
Methods	Double-blind, randomized, controlled
Participants	On-pump CABG only
Interventions	Magnesium vs. Control
Outcomes	AF
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The assignment of 345 patients to study group and control group was made possible with random number table at the time of admission to the operating room"
Allocation concealment (selection bias)	Low risk	"The assignment of 345 patients to study group and control group was made possible with random number table at the time of admission to the operating room"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Patients... were blind to the random allocation"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Clinical confirmation of occurrence of AF was made by a cardiologist who was blind to the random allocation"
Incomplete outcome data (attrition bias) All outcomes	High risk	"Eleven patients were dropped from the study due to... Mistake in Mg infusion dosage calculation (n = 2)"
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

Neto 2007

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only

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Neto 2007 *(Continued)*

Interventions	Biatrial pacing vs. Right atrial pacing vs. Control
Outcomes	AF; Mortality
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Beta-blockers (preoperative)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Nurözler 1996

Study characteristics

Methods	Double-blind, randomized, controlled
Participants	On-pump CABG only
Interventions	Magnesium vs. Control
Outcomes	AF that did not convert to sinus rhythm in 1 minute
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	None

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Nurözler 1996 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Nygård 2004

Study characteristics

Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. Control
Outcomes	AF lasting at least 5 minutes; Mortality; CV Mortality
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomization list was generated from a computerized table of random numbers"

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Nygård 2004 *(Continued)*

Allocation concealment (selection bias)	Low risk	"The randomization list was generated from a computerized table of random numbers"
Blinding of participants and personnel (performance bias) All outcomes	High risk	"The study was conducted in an open manner"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"The study was conducted in an open manner"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Nyström 1993

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective on-pump CABG only	
Interventions	Sotalol	
Outcomes	AF; Mortality; CV Mortality	
Follow-Up	6 days	
Concurrent Antiarrhythmic Medications	Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described

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Nyström 1993 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Oka 1980

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Propranolol vs. Control
Outcomes	Paroxysmal atrial tachyarrhythmia
Follow-Up	Not reported
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"Fifty-four consecutive patients... receiving long-term propranolol therapy, were entered in a randomized trial. They were compared with 17 patients... who were receiving no propranolol therapy prior to surgery"
Allocation concealment (selection bias)	High risk	"Fifty-four consecutive patients... receiving long-term propranolol therapy, were entered in a randomized trial. They were compared with 17 patients... who were receiving no propranolol therapy prior to surgery"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias)	Unclear risk	Not addressed

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Oka 1980 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Orboric 2010

Study characteristics		
Methods	Randomized, controlled	
Participants	Elective CABG only	
Interventions	Amiodarone vs. Control	
Outcomes	AF	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

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Ormerod 1984

Study characteristics	
Methods	Randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Propranolol vs. Control
Outcomes	AF
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Ozin 2005

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Triple-site Atrial Pacing

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Ozin 2005 *(Continued)*

Outcomes	AF; Stroke; LOS
Follow-Up	4 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Low risk	"randomized blindly"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Parikka 1993

Study characteristics

Methods	Single-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Magnesium vs. placebo
Outcomes	AF
Follow-Up	10 days
Concurrent Antiarrhythmic Medications	Metoprolol (25-50 mg tid), Digoxin
Notes	

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Parikka 1993 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Paull 1997

Study characteristics	
Methods	Single-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Metoprolol vs. placebo
Outcomes	AF; Mortality; CV Mortality
Follow-Up	Hospital discharge; First post-op visit (not specified)
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described

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Paull 1997 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blind
Blinding of outcome assessment (detection bias) All outcomes	High risk	Single-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Pfisterer 1997

Study characteristics		
Methods		
Participants	Elective on-pump CABG or aortic valve or both	
Interventions	Sotalol vs. placebo	
Outcomes	AF or atrial flutter; LOS	
Follow-Up	90 days	
Concurrent Antiarrhythmic Medications	Not reported	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind

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Pfisterer 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	Yes

Redle 1999

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Amiodarone vs. placebo	
Outcomes	AF; Mortality; CV Mortality; LOS; Cost	
Follow-Up	4 days	
Concurrent Antiarrhythmic Medications	Digoxin; Calcium channel blockers; Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Computer-generated randomized list"
Allocation concealment (selection bias)	Low risk	"Computer-generated randomized list that remained confidential until formal unblinding at the end of the study"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed

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Redle 1999 *(Continued)*

Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	Yes

Roshanali 2009

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Amiodarone vs. placebo	
Outcomes		
Follow-Up	Hospital discharge (approximately 7 days)	
Concurrent Antiarrhythmic Medications	Beta-blockers; Calcium channel blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

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Rubin 1987

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. Control
Outcomes	AF lasting at least 30 seconds ("chosen because all episodes in this series lasting longer than 30 seconds persisted until pharmacologic intervention"); Stroke
Follow-Up	Not reported
Concurrent Antiarrhythmic Medications	Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"randomized by lot"
Allocation concealment (selection bias)	Low risk	"randomized by lot"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	"Twenty-seven patients were excluded... 19 patients, protocol deviations"
Selective reporting (reporting bias)	High risk	Not all follow-up data collected were reported on
Intention-to-treat analysis	High risk	No

Salazar 1979

Study characteristics	
Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. Control

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Salazar 1979 *(Continued)*

Outcomes	Paroxysmal atrial tachycardia, Flutter-fibrillation, multiple atrial/nodal premature contractions
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	Not reported (No beta-blockers)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Schweikert 1998

Study characteristics

Methods	Randomized, controlled
Participants	On-pump CABG only
Interventions	Biatrial Pacing vs. Control
Outcomes	AF of at least 10 minutes requiring intervention
Follow-Up	Not reported
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

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Schweikert 1998 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"All patients were connected via temporary epicardial wires..."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	High risk	Abstract only
Intention-to-treat analysis	Unclear risk	Not reported

Sezai 2011

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only
Interventions	Landiolol vs. placebo
Outcomes	AF lasting at least 5 minutes or requiring intervention for hemodynamic compromise; Stroke; Mortality; CV Mortality; LOS; Cost
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization by lottery method

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Sezai 2011 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	High risk	No

Silverman 1982

Study characteristics	
Methods	Multicentre, randomized, controlled
Participants	On-pump CABG only
Interventions	Propranolol vs. Control
Outcomes	
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"Randomization was by birthdate"
Allocation concealment (selection bias)	High risk	"Randomization was by birthdate"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding

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Silverman 1982 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Speziale 2000

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	CABG only	
Interventions	Magnesium vs. placebo	
Outcomes	AF; Mortality; CV Mortality	
Follow-Up	2 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	

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Speziale 2000 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Stephenson 1980

Study characteristics		
Methods	Randomized, controlled	
Participants	CABG only	
Interventions	Propranolol vs. Control	
Outcomes	AF or atrial flutter	
Follow-Up	7 days	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"Randomization was by birthdate"
Allocation concealment (selection bias)	High risk	"Randomization was by birthdate"
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	"Two patients were excluded from this group because the resident responsible for writing the transfer orders had prescribed a higher dose of propranolol than 10mg every 6 hours"; "Other patients were excluded from the propranolol group, even though they had been randomly assigned to it by one of us, because the resident writing the transfer orders had neglected to prescribe the drug"
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

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Suttorp 1991

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	CABG, valve, combined, aortic or arrhythmia surgery
Interventions	Sotalol vs. placebo
Outcomes	SVA; Mortality; CV Mortality
Follow-Up	Not reported
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	"The data from 3 patients were excluded from analysis because of protocol violations (2 patients had taken the trial medication improperly)"
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

Tokmakoglu 2002

Study characteristics	
Methods	Randomized, controlled
Participants	Elective CABG only

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Tokmakoglu 2002 *(Continued)*

Interventions	Amiodarone vs. Control
Outcomes	AF
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Toraman 2001

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Magnesium vs. placebo
Outcomes	AF lasting 10 minutes or requiring therapy
Follow-Up	5 days
Concurrent Antiarrhythmic Medications	Metoprolol only (19 in Treatment group, 23 in Control group)

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Toraman 2001 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"All electrocardiograms were analyzed by a cardiologist who was blinded to the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Treggiari-Venzi 2000

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Amiodarone vs. Magnesium vs. placebo
Outcomes	AF; Mortality; CV Mortality
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Metoprolol only
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described

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Treggiari-Venzi 2000 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Turk 2007

Study characteristics	
Methods	Randomized, placebo-controlled
Participants	Elective off-pump CABG only
Interventions	Amiodarone vs. placebo
Outcomes	AF lasting 10 minutes or longer; Stroke; Mortality; CV Mortality
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described

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Turk 2007 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Vecht 1986

Study characteristics		
Methods	Randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Timolol vs. placebo	
Outcomes	SVT lasting at least 30 minutes	
Follow-Up	1 day	
Concurrent Antiarrhythmic Medications	Beta-blockers until day of surgery; Postop digoxin not allowed	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed

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Vecht 1986 *(Continued)*

Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Weber 1998

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	Elective on-pump CABG only	
Interventions	Sotalol vs. placebo	
Outcomes	AF, atrial flutter, SVT or AVNRT lasting at least 30 seconds; LOS	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Calcium channel blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	Yes

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Wenke 1999

Study characteristics	
Methods	Double-blind, randomized, controlled
Participants	CABG only
Interventions	Metoprolol vs. Control
Outcomes	SVA, AF or atrial flutter; LOS
Follow-Up	10 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random number series
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Not addressed
Selective reporting (reporting bias)	Low risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

White 1984

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only
Interventions	Timolol vs. placebo

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White 1984 *(Continued)*

Outcomes	AF or aflutter (divided into mild [< 30 sec, < 150 bpm], moderate [30 sec - 5 min, 150 - 200 bpm] or severe [> 5min, > 200 bpm]); Mortality; CV Mortality
Follow-Up	7 days
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

White 2002

Study characteristics

Methods	Double-blind, randomized, palcebo-controlled
Participants	Any open heart surgery (randomization was stratified by CABG vs valve)
Interventions	Fast-load amiodarone vs. Slow-load amiodarone vs. placebo
Outcomes	AF lasting more than 5 minutes or symptomatic; Mortality; Stroke; LOS
Follow-Up	Hospital discharge, 1 month postop
Concurrent Antiarrhythmic Medications	Beta-blockers

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White 2002 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The four randomization tables used in the study... were generated using commercially available statistical software"
Allocation concealment (selection bias)	Low risk	"The hospital pharmacy dispensed all study medication..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Low risk	Yes

White 2003

Study characteristics

Methods	Randomized, placebo-controlled
Participants	Any cardiothoracic surgery (randomization stratified by CABG vs valve)
Interventions	Amiodarone vs. Bachmann's Bundle Pacing vs. placebo
Outcomes	AF; LOS; Cost
Follow-Up	Hospital discharge, 1 week postop, 1 month postop
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	

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White 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	"This study was designed as a management trial in that the recommended treatment regimens were established by study investigators and available to clinicians but the patient's physician determined whether to adjust regimen intensity or to discontinue therapy without investigator consultation"
Blinding of outcome assessment (detection bias) All outcomes	High risk	"This study was designed as a management trial in that the recommended treatment regimens were established by study investigators and available to clinicians but the patient's physician determined whether to adjust regimen intensity or to discontinue therapy without investigator consultation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Wilkes 2002

Study characteristics	
Methods	Double-blind, randomized, controlled
Participants	Elective on-pump CABG only
Interventions	Magnesium vs. Control
Outcomes	AF; Mortality; CV Mortality
Follow-Up	3 days
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Patients were allocated to one of two groups by random numbers generated from random-number tables"
Allocation concealment (selection bias)	Low risk	"Patients were allocated to one of two groups by random numbers generated from random-number tables"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"To administer magnesium sulfate on the basis of ionized magnesium plasma levels and repeat this intervention as required, one nominated investigator remained unblinded to treatment group. All other clinicians involved in the care

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Wilkes 2002 *(Continued)*

		of patients and technicians concerned with the analysis of Holter tapes were rigorously blinded throughout the study period."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"To administer magnesium sulfate on the basis of ionized magnesium plasma levels and repeat this intervention as required, one nominated investigator remained unblinded to treatment group. All other clinicians involved in the care of patients and technicians concerned with the analysis of Holter tapes were rigorously blinded throughout the study period."
Incomplete outcome data (attrition bias) All outcomes	High risk	"Another two patients underwent mediastinal reexploration for bleeding complications (one in each group). All of these patients were excluded from further analysis of postoperative cardiac rhythm"
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Williams 1982

Study characteristics		
Methods	Randomized, controlled	
Participants	On-pump CABG only	
Interventions	Propranolol vs. Control	
Outcomes	AF	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	Digoxin (9 patients), Quinidine or procainamide (5 patients)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding

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Williams 1982 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

Yagdi 2003

Study characteristics		
Methods		
Participants	Elective on-pump CABG only	
Interventions	Amiodarone vs. placebo	
Outcomes	AF lasting more than 5 minutes or requiring therapy; Stroke; Mortality; LOS	
Follow-Up	Hospital discharge, 30 days postop	
Concurrent Antiarrhythmic Medications	Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	Unclear risk	Not reported

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Yazicioglu 2002

Study characteristics		
Methods	Randomized, placebo-controlled	
Participants	On-pump CABG only	
Interventions	Atenolol vs. placebo	
Outcomes	AF; Mortality; CV Mortality	
Follow-Up	Hospital discharge	
Concurrent Antiarrhythmic Medications	None	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Unclear risk	Concealment methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Yazigi 2002

Study characteristics	
Methods	Double-blind, randomized, placebo-controlled
Participants	Elective on-pump CABG only

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Yazigi 2002 *(Continued)*

Interventions	Amiodarone vs. placebo
Outcomes	AF lasting for > 5 minutes; Stroke; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomization methods not described
Allocation concealment (selection bias)	Low risk	"The hospital pharmacy dispensed all study medication..."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	Yes

Yeatman 2002

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	On-pump CABG only (elective and urgent but not emergency)
Interventions	Magnesium vs. placebo
Outcomes	AF; Stroke; Mortality; LOS
Follow-Up	Hospital discharge (mortality = 30 days)
Concurrent Antiarrhythmic Medications	Not reported

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Yeatman 2002 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomization sequence was performed by card allocation immediately before surgery"
Allocation concealment (selection bias)	Low risk	"The randomization sequence was performed by card allocation immediately before surgery"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not addressed
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Unclear risk	Not reported

Zangrillo 2005

Study characteristics

Methods	Double-blind, randomized, placebo-controlled
Participants	Elective off-pump CABG only
Interventions	Magnesium vs. placebo
Outcomes	AF lasting for > 10 minutes or requiring treatment; Stroke; Mortality; CV Mortality; LOS
Follow-Up	Hospital discharge
Concurrent Antiarrhythmic Medications	Beta-blockers
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Computer-generated list"

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Zangrillo 2005 *(Continued)*

Allocation concealment (selection bias)	Low risk	"Computer-generated list"; "Independent nurses dispensed either Mg or placebo in the operating room"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	
Intention-to-treat analysis	Low risk	Yes

Zebis 2007

Study characteristics		
Methods	Double-blind, randomized, placebo-controlled	
Participants	On-pump CABG only; Randomization stratified by age (65 yrs) and pre-op use of Beta-blockers	
Interventions	Amiodarone vs. placebo	
Outcomes	AF; Stroke; Mortality	
Follow-Up	5 days	
Concurrent Antiarrhythmic Medications	Beta-blockers	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Computerized prospective randomization schedule"
Allocation concealment (selection bias)	Low risk	"Each patient received a randomization number, which was recorded and sent by fax to the pharmacy... The pharmacy decoded the randomization number, prepared the appropriate infusion and pills, and forwarded them, together with a sealed opaque envelope containing the randomization assignment..."
Blinding of participants and personnel (performance bias)	Low risk	Double-blind

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Zebis 2007 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind
Incomplete outcome data (attrition bias) All outcomes	High risk	Intention-to-treat analysis stated, but not reported
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Intention-to-treat analysis	High risk	No

ACE: angiotensin-converting enzyme
AF: atrial fibrillation
AVNRT: atrioventricular nodal reentry tachycardia
AVR: aortic valve replacement
bpm: beats per minute
CABG: coronary artery bypass graft
CCBs: calcium channel blockers
CV: cardiovascular
ICU: intensive care unit
LOS: length of stay
SVT: supraventricular tachycardia
tid: three times per day

DATA AND ANALYSES

Comparison 1. Atrial fibrillation or Supraventricular tachycardia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 All Treatments	118	18381	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]
1.1.1 Pharmacological Interventions	93	14685	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.46]
1.1.2 Non-pharmacological Interventions	27	3696	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.34, 0.57]
1.2 Amiodarone	33	5402	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.34, 0.54]
1.3 Beta-Blockers	33	4698	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.26, 0.43]
1.4 Sotalol	11	1609	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.26, 0.43]
1.5 Magnesium	21	2988	Odds Ratio (M-H, Random, 95% CI)	0.55 [0.41, 0.73]
1.6 Atrial Pacing	21	2933	Odds Ratio (M-H, Random, 95% CI)	0.47 [0.36, 0.61]
1.7 Posterior Pericardiotomy	6	763	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.18, 0.67]

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Analysis 1.1. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 1: All Treatments

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
1.1.1 Pharmacological Interventions						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Akbarzadeh 2009 (1)	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Auer 2004 (2)	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Auer 2004 (3)	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
Bert 2001 (4)	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Bert 2001 (5)	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	4	24	11	46	0.6%	0.64 [0.18 , 2.26]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Dörge 2000 (6)	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Dörge 2000 (7)	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Forlani 2002 (4)	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Forlani 2002 (3)	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Janssen 1986 (2)	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Janssen 1986 (3)	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]

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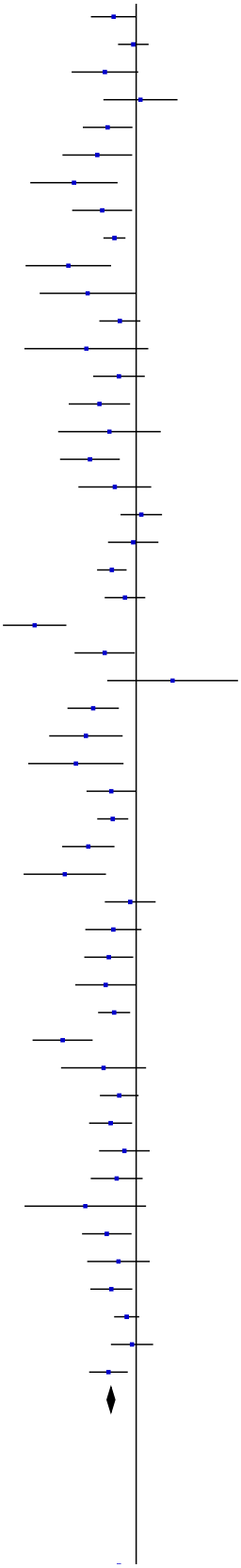
Analysis 1.1. (Continued)

Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000 (4)	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Treggiari-Venzi 2000 (1)	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2002 (8)	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2002 (9)	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
White 2003 (1)	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Williams 1982	1	28	6	32	0.3%	0.16 [0.02 , 1.43]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**7251**		**7434**	**74.1%**	**0.40 [0.35 , 0.46]**
Total events:	1281		2391			
Heterogeneity: Tau² = 0.24; Chi² = 231.07, df = 99 (P < 0.00001); I² = 57%						
Test for overall effect: Z = 12.95 (P < 0.00001)						
1.1.2 Non-pharmacological Interventions						
Akbarzadeh 2009 (10)	7	70	12	70	0.7%	0.54 [0.20 , 1.46]



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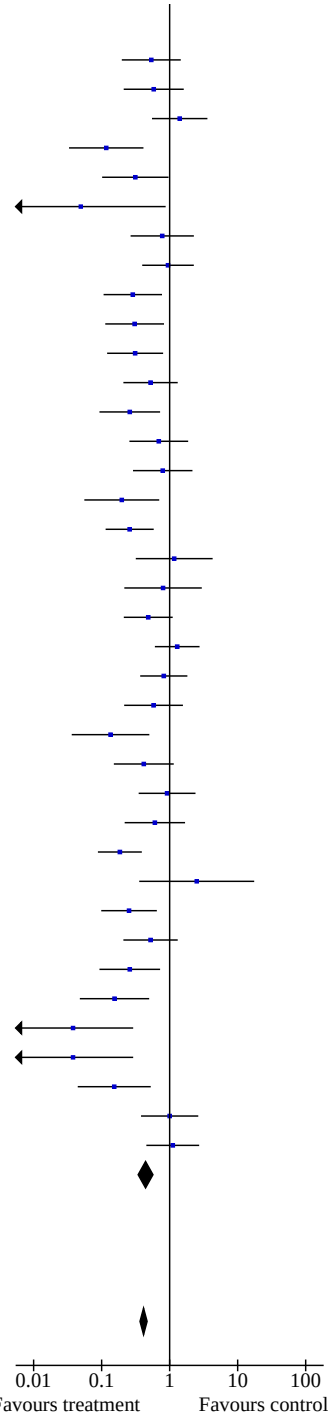
Analysis 1.1. (Continued)

1.1.2 Non-pharmacological Interventions						
Akbarzadeh 2009 (10)	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Chavan 2010 (11)	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Chavan 2010 (12)	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
Eslami 2005 (13)	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Eslami 2005 (10)	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Fan 2000 (12)	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000 (13)	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000 (10)	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Gerstenfeld 1999 (10)	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 1999 (12)	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Goette 2002 (12)	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Goette 2002 (11)	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Greenberg 2000 (10)	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Greenberg 2000 (12)	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Greenberg 2000 (13)	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Hakala 2005 (14)	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hakala 2005 (15)	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Mirkhani 2005 (13)	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mirkhani 2005 (10)	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Neto 2007 (10)	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007 (12)	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
White 2003 (11)	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
Subtotal (95% CI)		**1825**		**1871**	**25.9%**	**0.44 [0.34 , 0.57]**
Total events:	323		614			
Heterogeneity: Tau² = 0.32; Chi² = 79.74, df = 37 (P < 0.0001); I² = 54%						
Test for overall effect: Z = 6.39 (P < 0.00001)						
Total (95% CI)		**9076**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1604		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.72, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%						



Footnotes

(1) Amiodarone
(2) Metoprolol
(3) Sotalol
(4) Magnesium
(5) Propanolol

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Analysis 1.1. (Continued)

(4) Magnesium
(5) Propanolol
(6) Amiodarone (300mg)
(7) Amiodarone (150mg)
(8) Amiodarone (Fast-Load)
(9) Amiodarone (Slow-Load)
(10) Biatrial Pacing
(11) Bachmann's Bundle Pacing
(12) Right Atrial Pacing
(13) Left Atrial Pacing
(14) Right Atrial Pacing (Atrial Overdrive)
(15) Right Atrial Pacing (Bradycardia Prevention)

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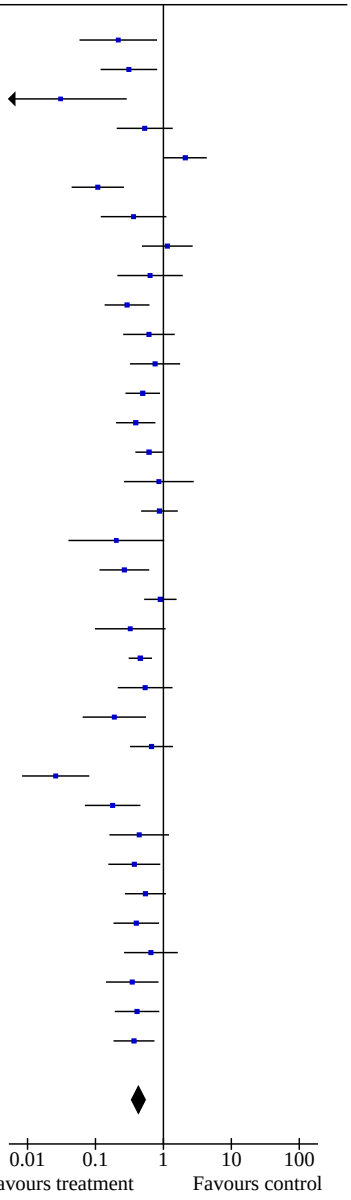
Analysis 1.2. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 2: Amiodarone

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Akbarzadeh 2009	3	70	12	70	1.9%	0.22 [0.06 , 0.80]
Alcalde 2006	8	46	19	47	2.7%	0.31 [0.12 , 0.81]
Alves 2007	1	15	14	20	0.9%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	2.7%	0.53 [0.21 , 1.37]
Beaulieu 2010	35	60	24	60	3.3%	2.10 [1.01 , 4.35]
Budeus 2006	18	55	45	55	2.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	2.3%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	2.9%	1.14 [0.48 , 2.70]
Crystal 2003	6	36	11	46	2.3%	0.64 [0.21 , 1.93]
Daoud 1997	16	64	32	60	3.2%	0.29 [0.14 , 0.62]
Dörge 2000 (1)	12	50	17	50	2.9%	0.61 [0.26 , 1.47]
Dörge 2000 (2)	14	50	17	50	2.9%	0.75 [0.32 , 1.77]
Giri 2001	28	120	38	100	3.7%	0.50 [0.28 , 0.89]
Gu 2009	16	100	36	110	3.5%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	4.1%	0.61 [0.39 , 0.98]
Haddad 2009	8	22	10	25	2.1%	0.86 [0.26 , 2.79]
Harahsheh 2001	28	88	32	92	3.6%	0.88 [0.47 , 1.63]
Hohnloser 1991	2	39	8	38	1.4%	0.20 [0.04 , 1.03]
Lee 2000	9	74	26	76	3.0%	0.27 [0.11 , 0.62]
Maras 2001	31	159	33	156	3.8%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	2.1%	0.33 [0.10 , 1.08]
Mitchell 2005	48	299	89	302	4.3%	0.46 [0.31 , 0.68]
Nygård 2004	10	36	20	48	2.7%	0.54 [0.21 , 1.36]
Orboric 2010	5	55	19	55	2.4%	0.19 [0.06 , 0.55]
Redle 1999	18	73	23	70	3.3%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	2.2%	0.03 [0.01 , 0.08]
Tokmakoglu 2002	6	72	31	92	2.7%	0.18 [0.07 , 0.46]
Treggiari-Venzi 2000	7	49	14	51	2.5%	0.44 [0.16 , 1.21]
Turk 2007	9	76	18	68	2.9%	0.37 [0.15 , 0.90]
White 2002 (3)	16	64	38	100	3.4%	0.54 [0.27 , 1.09]
White 2002 (4)	11	56	38	100	3.2%	0.40 [0.18 , 0.86]
White 2003	11	39	18	48	2.8%	0.65 [0.26 , 1.63]
Yagdi 2003	8	77	20	80	2.8%	0.35 [0.14 , 0.85]
Yazigi 2002	12	100	25	100	3.2%	0.41 [0.19 , 0.87]
Zebis 2007	14	110	32	113	3.4%	0.37 [0.18 , 0.74]
Total (95% CI)		**2603**		**2799**	**100.0%**	**0.43 [0.34 , 0.54]**
Total events:	505		932			



Heterogeneity: Tau² = 0.28; Chi² = 92.25, df = 34 (P < 0.00001); I² = 63%
Test for overall effect: Z = 7.24 (P < 0.00001)
Test for subgroup differences: Not applicable

Footnotes

(1) Amiodarone (300mg)
(2) Amiodarone (150mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)

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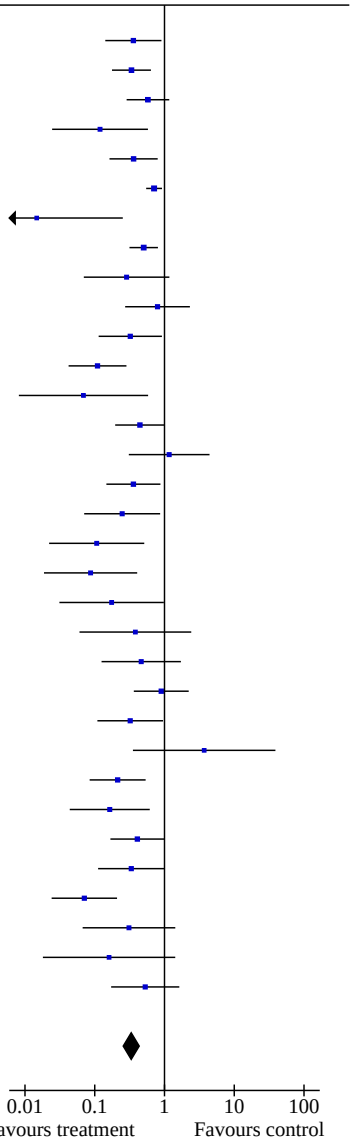
Analysis 1.3. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 3: Beta-Blockers

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Abel 1983	9	41	22	50	3.7%	0.36 [0.14 , 0.90]
Ali 1997	18	105	40	105	4.9%	0.34 [0.18 , 0.64]
Auer 2004	25	62	35	65	4.6%	0.58 [0.29 , 1.17]
Babin-Ebell 1996	2	33	13	37	2.0%	0.12 [0.02 , 0.58]
Bert 2001	13	71	23	60	4.2%	0.36 [0.16 , 0.80]
Connolly 2003	156	500	195	500	6.4%	0.71 [0.55 , 0.92]
Daudon 1986	0	50	20	50	0.8%	0.01 [0.00 , 0.25]
Gun 1998	33	250	58	250	5.7%	0.50 [0.31 , 0.80]
Imren 2007	3	41	8	37	2.3%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	3.2%	0.79 [0.27 , 2.31]
Janssen 1986	6	39	18	50	3.3%	0.32 [0.11 , 0.92]
Khuri 1987	6	67	35	74	3.6%	0.11 [0.04 , 0.28]
Lamb 1988	1	30	10	30	1.3%	0.07 [0.01 , 0.58]
Lúcio 2004	10	100	20	100	4.1%	0.44 [0.20 , 1.01]
Martinussen 1988	5	35	5	40	2.5%	1.17 [0.31 , 4.42]
Matangi 1985	8	82	19	82	3.9%	0.36 [0.15 , 0.87]
Matangi 1989	4	35	12	35	2.7%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	2.0%	0.11 [0.02 , 0.51]
Mohr 1981	2	37	19	48	2.1%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	1.7%	0.17 [0.03 , 0.98]
Oka 1980	2	19	4	17	1.6%	0.38 [0.06 , 2.42]
Ormerod 1984	4	27	9	33	2.6%	0.46 [0.13 , 1.72]
Paull 1997	12	50	13	50	3.8%	0.90 [0.36 , 2.22]
Rubin 1987	6	37	15	40	3.2%	0.32 [0.11 , 0.95]
Salazar 1979	3	20	1	22	1.1%	3.71 [0.35 , 38.93]
Sezai 2011	7	70	24	70	3.7%	0.21 [0.08 , 0.54]
Silverman 1982	3	50	14	50	2.5%	0.16 [0.04 , 0.61]
Stephenson 1980	7	87	24	136	3.9%	0.41 [0.17 , 0.99]
Vecht 1986	5	66	13	66	3.1%	0.33 [0.11 , 1.00]
Wenke 1999	4	100	37	100	3.2%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	2.1%	0.31 [0.07 , 1.43]
Williams 1982	1	28	6	32	1.2%	0.16 [0.02 , 1.43]
Yazicioglu 2002	6	40	10	40	3.1%	0.53 [0.17 , 1.63]
Total (95% CI)		**2294**		**2404**	**100.0%**	**0.33 [0.26 , 0.43]**
Total events:	375		762			

Heterogeneity: Tau² = 0.26; Chi² = 71.39, df = 32 (P < 0.0001); I² = 55%
Test for overall effect: Z = 8.17 (P < 0.00001)
Test for subgroup differences: Not applicable



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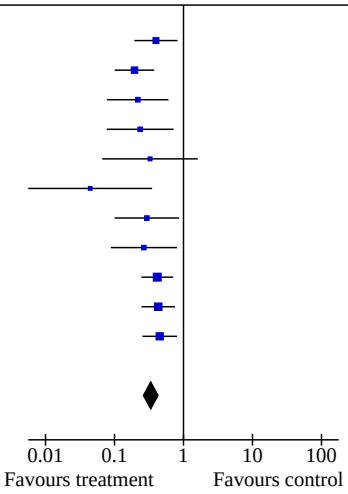
Analysis 1.4. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 4: Sotalol

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Auer 2004	20	63	35	65	10.8%	0.40 [0.19 , 0.82]
Evrard 2000	16	103	50	103	12.8%	0.19 [0.10 , 0.38]
Forlani 2002	6	51	19	50	5.4%	0.22 [0.08 , 0.61]
Gomes 1999	5	40	17	45	4.6%	0.24 [0.08 , 0.72]
Jacquet 1994	3	25	5	17	2.3%	0.33 [0.07 , 1.61]
Janssen 1986	1	41	18	50	1.4%	0.04 [0.01 , 0.35]
Matsuura 2001	6	40	15	40	4.9%	0.29 [0.10 , 0.86]
Nyström 1993	5	50	15	51	4.7%	0.27 [0.09 , 0.80]
Pfisterer 1997	32	126	58	129	19.2%	0.42 [0.25 , 0.71]
Suttorp 1991	24	150	46	150	17.5%	0.43 [0.25 , 0.75]
Weber 1998	27	110	46	110	16.5%	0.45 [0.25 , 0.81]
Total (95% CI)		**799**		**810**	**100.0%**	**0.34 [0.26 , 0.43]**
Total events:	145		324			

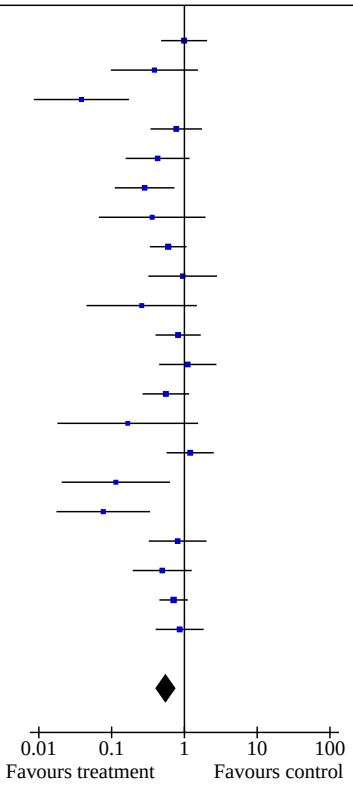
Heterogeneity: Tau² = 0.01; Chi² = 10.34, df = 10 (P = 0.41); I² = 3%
Test for overall effect: Z = 8.88 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 5: Magnesium

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Bert 2001	24	63	23	60	6.4%	0.99 [0.48 , 2.05]
Casthely 1994	5	105	4	35	3.2%	0.39 [0.10 , 1.53]
Dagdelen 2002	2	93	20	55	2.8%	0.04 [0.01 , 0.17]
England 1992	17	50	20	50	5.8%	0.77 [0.34 , 1.74]
Fanning 1991	7	49	14	50	4.7%	0.43 [0.16 , 1.18]
Forlani 2002	8	54	19	50	5.0%	0.28 [0.11 , 0.73]
Hamid 2008	2	53	5	51	2.3%	0.36 [0.07 , 1.95]
Hazelrigg 2004	32	105	41	97	7.5%	0.60 [0.34 , 1.07]
Jensen 1997	10	29	10	28	4.3%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	2.2%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	6.5%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	5.2%	1.11 [0.45 , 2.76]
Najafi 2007	12	166	22	179	6.3%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	1.5%	0.17 [0.02 , 1.55]
Parikka 1993	20	69	18	71	6.3%	1.20 [0.57 , 2.53]
Speziale 2000	2	72	5	25	2.3%	0.11 [0.02 , 0.63]
Toraman 2001	2	100	21	100	2.9%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	11	47	14	51	5.2%	0.81 [0.32 , 2.01]
Wilkes 2002	11	41	17	40	5.1%	0.50 [0.20 , 1.26]
Yeatman 2002	45	200	58	200	8.4%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	6.2%	0.86 [0.40 , 1.84]
Total (95% CI)		**1567**		**1421**	**100.0%**	**0.55 [0.41 , 0.73]**
Total events:	258		373			

Heterogeneity: Tau² = 0.21; Chi² = 40.73, df = 20 (P = 0.004); I² = 51%
Test for overall effect: Z = 4.03 (P < 0.0001)
Test for subgroup differences: Not applicable



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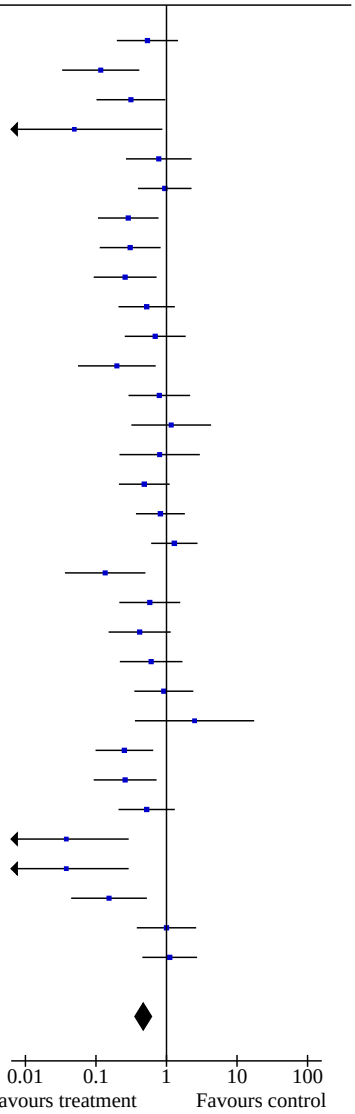
Analysis 1.6. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 6: Atrial Pacing

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Akbarzadeh 2009	7	70	12	70	3.5%	0.54 [0.20 , 1.46]
Avila Neto 2007	3	80	20	80	2.7%	0.12 [0.03 , 0.41]
Blommaert 2000	5	48	13	48	3.1%	0.31 [0.10 , 0.96]
Chavan 2010 (1)	0	48	9	54	0.8%	0.05 [0.00 , 0.87]
Chavan 2010 (2)	7	52	9	54	3.2%	0.78 [0.27 , 2.27]
Chung 2000a	14	51	14	49	3.9%	0.95 [0.40 , 2.26]
Da Silva 2008	7	49	18	49	3.5%	0.29 [0.11 , 0.77]
Debrunner 2004	8	40	18	40	3.5%	0.31 [0.11 , 0.83]
Eslami 2005 (3)	7	40	18	40	3.4%	0.26 [0.09 , 0.72]
Eslami 2005 (4)	12	40	18	40	3.7%	0.52 [0.21 , 1.31]
Fan 2000 (2)	12	36	13	31	3.5%	0.69 [0.26 , 1.87]
Fan 2000 (3)	4	32	13	31	2.7%	0.20 [0.06 , 0.70]
Fan 2000 (4)	12	33	13	31	3.4%	0.79 [0.29 , 2.16]
Gerstenfeld 1999 (3)	7	19	7	21	2.6%	1.17 [0.32 , 4.28]
Gerstenfeld 1999 (2)	6	21	7	21	2.6%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	4.1%	0.48 [0.21 , 1.11]
Goette 2002 (1)	19	51	21	50	4.2%	0.82 [0.37 , 1.82]
Goette 2002 (2)	29	60	21	50	4.3%	1.29 [0.61 , 2.75]
Greenberg 2000 (2)	3	40	18	48	2.6%	0.14 [0.04 , 0.50]
Greenberg 2000 (3)	8	31	18	48	3.5%	0.58 [0.21 , 1.57]
Greenberg 2000 (4)	7	35	18	48	3.4%	0.42 [0.15 , 1.15]
Hakala 2005 (5)	8	41	12	42	3.4%	0.61 [0.22 , 1.68]
Hakala 2005 (6)	11	41	12	42	3.6%	0.92 [0.35 , 2.40]
Kurz 1999	5	12	2	9	1.5%	2.50 [0.36 , 17.50]
Levy 2000	7	65	21	65	3.7%	0.25 [0.10 , 0.65]
Mirkhani 2005 (3)	7	40	18	40	3.4%	0.26 [0.09 , 0.72]
Mirkhani 2005 (4)	12	40	18	40	3.7%	0.52 [0.21 , 1.31]
Neto 2007 (3)	1	80	20	80	1.4%	0.04 [0.00 , 0.29]
Neto 2007 (2)	1	80	20	80	1.4%	0.04 [0.00 , 0.29]
Ozin 2005	4	35	16	35	2.8%	0.15 [0.04 , 0.53]
Schweikert 1998	11	43	11	43	3.6%	1.00 [0.38 , 2.63]
White 2003	14	35	18	48	3.8%	1.11 [0.45 , 2.72]
Total (95% CI)		**1446**		**1487**	**100.0%**	**0.47 [0.36 , 0.61]**
Total events:	270		487			

Heterogeneity: Tau² = 0.29; Chi² = 61.66, df = 31 (P = 0.0009); I² = 50%
Test for overall effect: Z = 5.54 (P < 0.00001)
Test for subgroup differences: Not applicable



Footnotes

(1) Bachmann's Bundle Pacing
(2) Right Atrial Pacing
(3) Biatrial Pacing
(4) Left Atrial Pacing
(5) Right Atrial Pacing (Bradycardia Prevention)
(6) Right Atrial Pacing (Atrial Overdrive)

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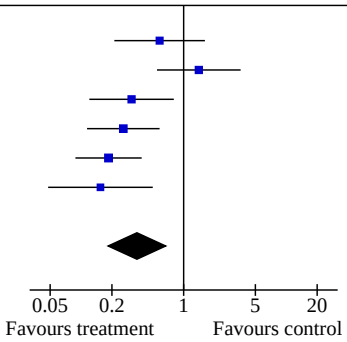
Analysis 1.7. Comparison 1: Atrial fibrillation or Supraventricular tachycardia, Outcome 7: Posterior Pericardiotomy

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Arbatli 2003	7	54	12	59	15.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	16.6%	1.41 [0.55 , 3.59]
Ekim 2006	8	50	19	50	16.5%	0.31 [0.12 , 0.80]
Farsak 2002	10	75	28	75	18.2%	0.26 [0.11 , 0.58]
Kuralay 1999	11	100	40	100	19.1%	0.19 [0.09 , 0.39]
Mulay 1995	4	50	18	50	13.9%	0.15 [0.05 , 0.50]
Total (95% CI)		**379**		**384**	**100.0%**	**0.35 [0.18 , 0.67]**
Total events:	53		127			

Heterogeneity: Tau² = 0.42; Chi² = 14.65, df = 5 (P = 0.01); I² = 66%
Test for overall effect: Z = 3.19 (P = 0.001)
Test for subgroup differences: Not applicable



Comparison 2. Stroke or Cerebrovascular Accident

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 All Treatments	28	6361	Odds Ratio (M-H, Random, 95% CI)	0.69 [0.47, 1.01]
2.1.1 Amiodarone	14	3087	Odds Ratio (M-H, Random, 95% CI)	0.60 [0.35, 1.02]
2.1.2 Beta-Blockers	5	1554	Odds Ratio (M-H, Random, 95% CI)	1.34 [0.46, 3.93]
2.1.3 Sotalol	1	128	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.01, 8.47]
2.1.4 Magnesium	3	760	Odds Ratio (M-H, Random, 95% CI)	0.33 [0.03, 3.20]
2.1.5 Atrial Pacing	6	832	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.36, 1.46]

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Analysis 2.1. Comparison 2: Stroke or Cerebrovascular Accident, Outcome 1: All Treatments

Study or Subgroup	Treamtent Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
2.1.1 Amiodarone						
Alcalde 2006	1	46	1	47	1.9%	1.02 [0.06 , 16.85]
Beaulieu 2010	3	60	0	60	1.7%	7.37 [0.37 , 145.75]
Butler 1993	1	60	0	60	1.5%	3.05 [0.12 , 76.39]
Daoud 1997	1	64	0	60	1.5%	2.86 [0.11 , 71.53]
Giri 2001	2	120	7	100	5.9%	0.23 [0.05 , 1.11]
Guarnieri 1999	2	158	2	142	3.9%	0.90 [0.12 , 6.46]
Lee 2000	2	74	2	76	3.8%	1.03 [0.14 , 7.49]
Maras 2001	4	159	11	156	11.1%	0.34 [0.11 , 1.09]
Mitchell 2005	3	299	5	302	7.3%	0.60 [0.14 , 2.54]
Turk 2007	1	76	0	68	1.5%	2.72 [0.11 , 67.94]
White 2002 (1)	1	64	7	100	3.4%	0.21 [0.03 , 1.76]
White 2002 (2)	1	56	7	100	3.4%	0.24 [0.03 , 2.02]
Yagdi 2003	1	77	0	80	1.5%	3.16 [0.13 , 78.68]
Yazigi 2002	0	100	1	100	1.5%	0.33 [0.01 , 8.20]
Zebis 2007	1	110	1	113	1.9%	1.03 [0.06 , 16.63]
Subtotal (95% CI)		**1523**		**1564**	**51.6%**	**0.60 [0.35 , 1.02]**
Total events:	24		44			
Heterogeneity: Tau² = 0.00; Chi² = 11.33, df = 14 (P = 0.66); I² = 0%						
Test for overall effect: Z = 1.87 (P = 0.06)						
2.1.2 Beta-Blockers						
Ali 1997	0	105	1	105	1.5%	0.33 [0.01 , 8.20]
Auer 2004	0	62	1	65	1.5%	0.34 [0.01 , 8.61]
Connolly 2003	7	500	3	500	8.2%	2.35 [0.60 , 9.15]
Rubin 1987	0	37	0	40		Not estimable
Sezai 2011	1	70	1	70	1.9%	1.00 [0.06 , 16.31]
Subtotal (95% CI)		**774**		**780**	**13.1%**	**1.34 [0.46 , 3.93]**
Total events:	8		6			
Heterogeneity: Tau² = 0.00; Chi² = 2.12, df = 3 (P = 0.55); I² = 0%						
Test for overall effect: Z = 0.53 (P = 0.59)						
2.1.3 Sotalol						
Auer 2004	0	63	1	65	1.5%	0.34 [0.01 , 8.47]
Subtotal (95% CI)		**63**		**65**	**1.5%**	**0.34 [0.01 , 8.47]**
Total events:	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.66 (P = 0.51)						
2.1.4 Magnesium						
Toraman 2001	0	100	1	100	1.5%	0.33 [0.01 , 8.20]
Yeatman 2002	0	200	1	200	1.5%	0.33 [0.01 , 8.19]
Zangrillo 2005	0	80	0	80		Not estimable
Subtotal (95% CI)		**380**		**380**	**2.9%**	**0.33 [0.03 , 3.20]**
Total events:	0		2			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%						
Test for overall effect: Z = 0.96 (P = 0.34)						
2.1.5 Atrial Pacing						
Eslami 2005 (3)	1	40	2	40	2.5%	0.49 [0.04 , 5.60]
Eslami 2005 (4)	1	40	2	40	2.5%	0.49 [0.04 , 5.60]
Fan 2000 (3)	1	32	2	31	2.5%	0.47 [0.04 , 5.44]
Fan 2000 (4)	1	33	2	31	2.5%	0.45 [0.04 , 5.26]

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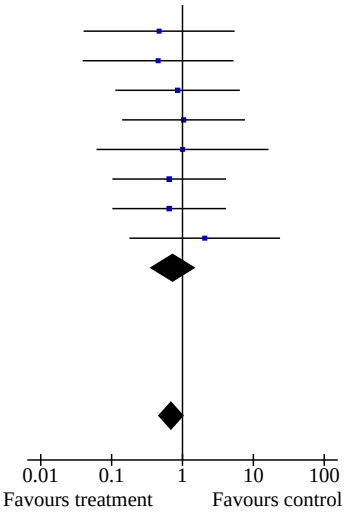
Analysis 2.1. (Continued)

Fan 2000 (3)	1	32	2	31	2.5%	0.47 [0.04 , 5.44]
Fan 2000 (4)	1	33	2	31	2.5%	0.45 [0.04 , 5.26]
Fan 2000 (5)	2	36	2	31	3.7%	0.85 [0.11 , 6.44]
Gerstenfeld 1999	2	58	2	60	3.8%	1.04 [0.14 , 7.61]
Levy 2000	1	65	1	65	1.9%	1.00 [0.06 , 16.34]
Mirkhani 2005 (4)	2	40	3	40	4.4%	0.65 [0.10 , 4.11]
Mirkhani 2005 (3)	2	40	3	40	4.4%	0.65 [0.10 , 4.11]
Ozin 2005	2	35	1	35	2.5%	2.06 [0.18 , 23.83]
Subtotal (95% CI)		**419**		**413**	**30.9%**	**0.72 [0.36 , 1.46]**
Total events:	15		20			
Heterogeneity: Tau² = 0.00; Chi² = 1.39, df = 9 (P = 1.00); I² = 0%						
Test for overall effect: Z = 0.91 (P = 0.36)						
Total (95% CI)		**3159**		**3202**	**100.0%**	**0.69 [0.47 , 1.01]**
Total events:	47		73			
Heterogeneity: Tau² = 0.00; Chi² = 17.19, df = 31 (P = 0.98); I² = 0%						
Test for overall effect: Z = 1.90 (P = 0.06)						
Test for subgroup differences: Chi² = 2.35, df = 4 (P = 0.67), I² = 0%						



Footnotes

(1) Amiodarone (Fast-Load)
(2) Amiodarone (Slow-Load)
(3) Biatrial Pacing
(4) Left Atrial Pacing
(5) Right Atrial Pacing

Comparison 3. Mortality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 All Treatments	61	10986	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.77, 1.39]
3.1.1 Amiodarone	23	4177	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.74, 1.56]
3.1.2 Beta-Blockers	16	2671	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.34, 2.22]
3.1.3 Sotalol	8	1092	Odds Ratio (M-H, Random, 95% CI)	0.65 [0.08, 5.37]
3.1.4 Magnesium	12	1764	Odds Ratio (M-H, Random, 95% CI)	0.83 [0.31, 2.24]
3.1.5 Atrial Pacing	7	1082	Odds Ratio (M-H, Random, 95% CI)	0.88 [0.32, 2.47]
3.1.6 Posterior Pericardiotomy	2	200	Odds Ratio (M-H, Random, 95% CI)	1.00 [0.06, 16.44]

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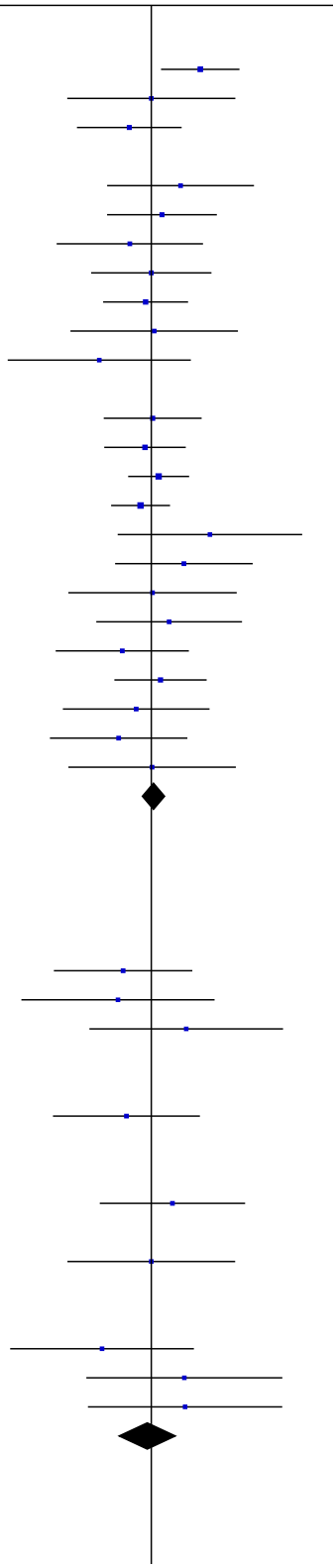
Analysis 3.1. Comparison 3: Mortality, Outcome 1: All Treatments

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
3.1.1 Amiodarone						
Akbarzadeh 2009	13	70	3	70	5.1%	5.09 [1.38 , 18.77]
Beaulieu 2010	1	60	1	60	1.1%	1.00 [0.06 , 16.37]
Budeus 2006	2	55	4	55	2.9%	0.48 [0.08 , 2.74]
Butler 1993	0	60	0	60		Not estimable
Crystal 2003	2	36	1	46	1.5%	2.65 [0.23 , 30.41]
Daoud 1997	3	64	2	60	2.6%	1.43 [0.23 , 8.85]
Dörge 2000 (1)	1	50	2	50	1.5%	0.49 [0.04 , 5.58]
Dörge 2000 (2)	2	50	2	50	2.2%	1.00 [0.14 , 7.39]
Giri 2001	4	120	4	100	4.4%	0.83 [0.20 , 3.40]
Gu 2009	1	100	1	110	1.1%	1.10 [0.07 , 17.84]
Guarnieri 1999	0	158	2	142	0.9%	0.18 [0.01 , 3.72]
Haddad 2009	0	22	0	25		Not estimable
Harahsheh 2001	3	88	3	92	3.3%	1.05 [0.21 , 5.33]
Lee 2000	4	74	5	76	4.7%	0.81 [0.21 , 3.15]
Maras 2001	9	159	7	156	8.5%	1.28 [0.46 , 3.52]
Mitchell 2005	7	299	10	302	9.1%	0.70 [0.26 , 1.86]
Nygård 2004	2	36	0	48	0.9%	7.03 [0.33 , 151.05]
Redle 1999	3	73	1	70	1.7%	2.96 [0.30 , 29.13]
Treggiari-Venzi 2000	1	49	1	51	1.1%	1.04 [0.06 , 17.13]
Turk 2007	2	76	1	68	1.5%	1.81 [0.16 , 20.43]
White 2002 (3)	1	64	4	100	1.8%	0.38 [0.04 , 3.49]
White 2002 (4)	3	56	4	100	3.7%	1.36 [0.29 , 6.30]
White 2003	1	39	2	48	1.5%	0.61 [0.05 , 6.93]
Yagdi 2003	1	77	3	80	1.7%	0.34 [0.03 , 3.32]
Zebis 2007	1	110	1	113	1.1%	1.03 [0.06 , 16.63]
Subtotal (95% CI)		**2045**		**2132**	**63.6%**	**1.08 [0.74 , 1.56]**
Total events:	67		64			
Heterogeneity: Tau² = 0.00; Chi² = 14.32, df = 22 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.38 (P = 0.70)						
3.1.2 Beta-Blockers						
Abel 1983	1	41	3	50	1.6%	0.39 [0.04 , 3.91]
Ali 1997	0	105	1	105	0.8%	0.33 [0.01 , 8.20]
Auer 2004	1	62	0	65	0.8%	3.20 [0.13 , 79.93]
Bert 2001	0	71	0	60		Not estimable
Connolly 2003	0	500	0	500		Not estimable
Imren 2007	1	41	2	37	1.5%	0.44 [0.04 , 5.03]
Ivey 1983	0	53	0	56		Not estimable
Janssen 1986	0	39	0	50		Not estimable
Lúcio 2004	2	100	1	100	1.5%	2.02 [0.18 , 22.65]
Martinussen 1988	0	35	0	40		Not estimable
Matangi 1985	1	82	1	82	1.1%	1.00 [0.06 , 16.26]
Oka 1980	0	19	0	17		Not estimable
Paull 1997	0	50	0	50		Not estimable
Sezai 2011	0	70	2	70	0.9%	0.19 [0.01 , 4.12]
White 1984	1	21	0	20	0.8%	3.00 [0.12 , 78.04]
Yazicioglu 2002	1	40	0	40	0.8%	3.08 [0.12 , 77.80]
Subtotal (95% CI)		**1329**		**1342**	**10.0%**	**0.87 [0.34 , 2.22]**
Total events:	8		10			
Heterogeneity: Tau² = 0.00; Chi² = 4.29, df = 8 (P = 0.83); I² = 0%						
Test for overall effect: Z = 0.28 (P = 0.78)						



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Analysis 3.1. (Continued)

Test for overall effect: Z = 0.28 (P = 0.78)

3.1.3 Sotalol

Auer 2004	0	63	0	65		Not estimable
Evrard 2000	1	103	1	103	1.1%	1.00 [0.06 , 16.21]
Forlani 2002	0	51	0	50		Not estimable
Gomes 1999	0	40	1	45	0.8%	0.37 [0.01 , 9.25]
Janssen 1986	0	41	0	50		Not estimable
Matsuura 2001	0	40	0	40		Not estimable
Nyström 1993	0	50	0	51		Not estimable
Suttorp 1991	0	150	0	150		Not estimable
Subtotal (95% CI)		**538**		**554**	**2.0%**	**0.65 [0.08 , 5.37]**
Total events:	1		2			

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.64); I² = 0%

Test for overall effect: Z = 0.40 (P = 0.69)

3.1.4 Magnesium

Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable
Fanning 1991	0	49	1	50	0.8%	0.33 [0.01 , 8.38]
Forlani 2002	1	54	0	50	0.8%	2.83 [0.11 , 71.13]
Hazelrigg 2004	1	105	2	97	1.5%	0.46 [0.04 , 5.12]
Kaplan 2003	1	100	1	100	1.1%	1.00 [0.06 , 16.21]
Karmy-Jones 1995	0	46	2	54	0.9%	0.23 [0.01 , 4.83]
Speziale 2000	0	72	0	25		Not estimable
Treggiari-Venzi 2000	0	47	1	51	0.8%	0.35 [0.01 , 8.91]
Wilkes 2002	1	41	1	40	1.1%	0.97 [0.06 , 16.14]
Yeatman 2002	3	200	1	200	1.7%	3.03 [0.31 , 29.38]
Zangrillo 2005	0	80	0	80		Not estimable
Subtotal (95% CI)		**907**		**857**	**8.8%**	**0.83 [0.31 , 2.24]**
Total events:	7		9			

Heterogeneity: Tau² = 0.00; Chi² = 3.34, df = 7 (P = 0.85); I² = 0%

Test for overall effect: Z = 0.36 (P = 0.72)

3.1.5 Atrial Pacing

Akbarzadeh 2009	14	70	3	70	5.2%	5.58 [1.53 , 20.41]
Debrunner 2004	0	40	0	40		Not estimable
Gerstenfeld 2001	0	58	0	60		Not estimable
Goette 2002 (5)	0	51	1	50	0.8%	0.32 [0.01 , 8.05]
Goette 2002 (6)	0	60	1	50	0.8%	0.27 [0.01 , 6.84]
Levy 2000	1	65	2	65	1.5%	0.49 [0.04 , 5.57]
Neto 2007 (7)	2	80	3	80	2.6%	0.66 [0.11 , 4.05]
Neto 2007 (6)	2	80	3	80	2.6%	0.66 [0.11 , 4.05]
White 2003	0	35	2	48	0.9%	0.26 [0.01 , 5.63]
Subtotal (95% CI)		**539**		**543**	**14.5%**	**0.88 [0.32 , 2.47]**
Total events:	19		15			

Heterogeneity: Tau² = 0.64; Chi² = 9.20, df = 6 (P = 0.16); I² = 35%

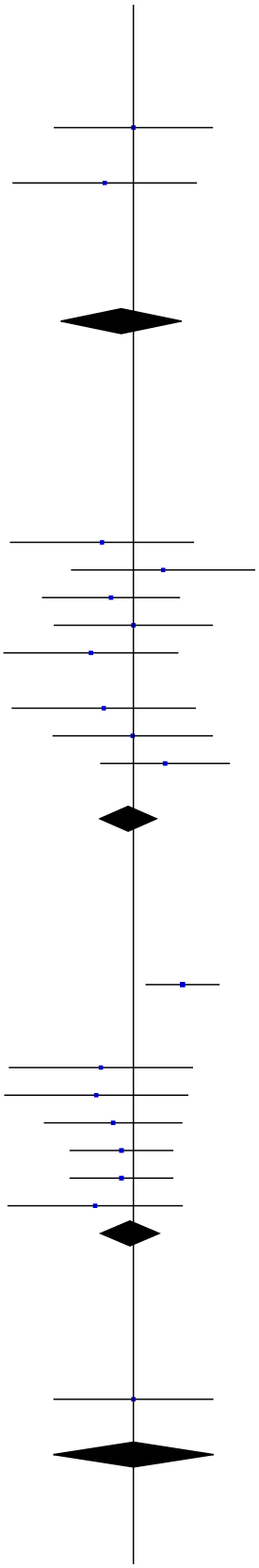
Test for overall effect: Z = 0.23 (P = 0.81)

3.1.6 Posterior Pericardiotomy

Asimakopoulos 1997	1	50	1	50	1.1%	1.00 [0.06 , 16.44]
Mulay 1995	0	50	0	50		Not estimable
Subtotal (95% CI)		**100**		**100**	**1.1%**	**1.00 [0.06 , 16.44]**
Total events:	1		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 0.00 (P = 1.00)



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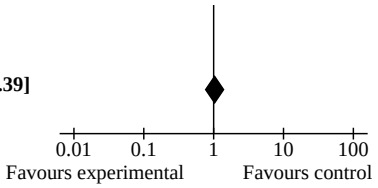
Analysis 3.1. (Continued)

Test for overall effect: Z = 0.00 (P = 1.00)

Total (95% CI)	**5458**	**5528**	**100.0%**	**1.03 [0.77 , 1.39]**	
Total events:	103	101			

Heterogeneity: Tau² = 0.00; Chi² = 31.98, df = 49 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.21 (P = 0.83)
Test for subgroup differences: Chi² = 0.57, df = 5 (P = 0.99), I² = 0%



Footnotes
(1) Amiodarone (150mg)
(2) Amiodarone (300mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)
(5) Bachmann's Bundle Pacing
(6) Right Atrial Pacing
(7) Biatrial Pacing

Comparison 4. Cardiovascular Mortality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 All Treatments	40	6750	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.47, 1.62]
4.1.1 Amiodarone	14	2515	Odds Ratio (M-H, Random, 95% CI)	0.93 [0.46, 1.86]
4.1.2 Beta-Blockers	11	2011	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.10, 9.66]
4.1.3 Sotalol	7	964	Odds Ratio (M-H, Random, 95% CI)	Not estimable
4.1.4 Magnesium	9	962	Odds Ratio (M-H, Random, 95% CI)	0.53 [0.09, 3.13]
4.1.5 Atrial Pacing	2	198	Odds Ratio (M-H, Random, 95% CI)	Not estimable
4.1.6 Posterior Pericardiotomy	1	100	Odds Ratio (M-H, Random, 95% CI)	Not estimable

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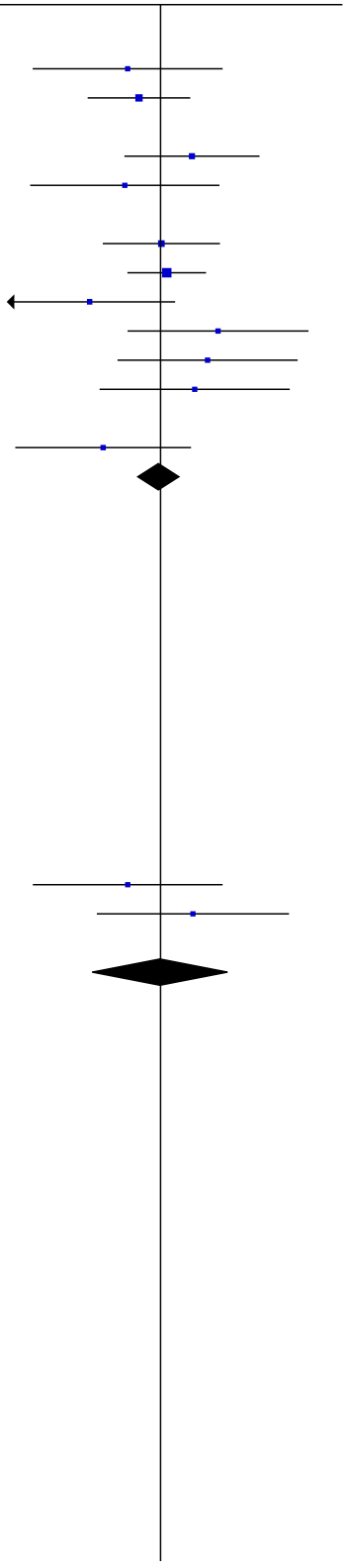
Analysis 4.1. Comparison 4: Cardiovascular Mortality, Outcome 1: All Treatments

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
4.1.1 Amiodarone						
Beaulieu 2010	0	60	1	60	3.7%	0.33 [0.01 , 8.21]
Budeus 2006	2	55	4	55	12.8%	0.48 [0.08 , 2.74]
Butler 1993	0	60	0	60		Not estimable
Daoud 1997	3	64	1	60	7.4%	2.90 [0.29 , 28.69]
Guarnieri 1999	0	158	1	142	3.8%	0.30 [0.01 , 7.36]
Haddad 2009	0	22	0	25		Not estimable
Lee 2000	2	74	2	76	9.8%	1.03 [0.14 , 7.49]
Maras 2001	5	159	4	156	21.8%	1.23 [0.33 , 4.68]
Mitchell 2005	0	299	5	302	4.6%	0.09 [0.00 , 1.64]
Nygård 2004	2	36	0	48	4.1%	7.03 [0.33 , 151.05]
Redle 1999	2	73	0	70	4.2%	4.93 [0.23 , 104.53]
Treggiari-Venzi 2000	1	49	0	51	3.7%	3.19 [0.13 , 80.09]
Turk 2007	0	76	0	68		Not estimable
Yagdi 2003	0	77	3	80	4.4%	0.14 [0.01 , 2.81]
Subtotal (95% CI)		**1262**		**1253**	**80.2%**	**0.93 [0.46 , 1.86]**
Total events:	17		21			
Heterogeneity: Tau² = 0.00; Chi² = 10.02, df = 10 (P = 0.44); I² = 0%						
Test for overall effect: Z = 0.21 (P = 0.83)						
4.1.2 Beta-Blockers						
Ali 1997	0	105	0	105		Not estimable
Bert 2001	0	71	0	60		Not estimable
Connolly 2003	0	500	0	500		Not estimable
Ivey 1983	0	53	0	56		Not estimable
Janssen 1986	0	39	0	50		Not estimable
Martinussen 1988	0	35	0	40		Not estimable
Oka 1980	0	19	0	17		Not estimable
Paull 1997	0	50	0	50		Not estimable
Sezai 2011	0	70	1	70	3.7%	0.33 [0.01 , 8.21]
White 1984	1	21	0	20	3.6%	3.00 [0.12 , 78.04]
Yazicioglu 2002	0	40	0	40		Not estimable
Subtotal (95% CI)		**1003**		**1008**	**7.4%**	**0.98 [0.10 , 9.66]**
Total events:	1		1			
Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 0.02 (P = 0.99)						
4.1.3 Sotalol						
Evrard 2000	0	103	0	103		Not estimable
Forlani 2002	0	51	0	50		Not estimable
Gomes 1999	0	40	0	45		Not estimable
Janssen 1986	0	41	0	50		Not estimable
Matsuura 2001	0	40	0	40		Not estimable
Nyström 1993	0	50	0	51		Not estimable
Suttorp 1991	0	150	0	150		Not estimable
Subtotal (95% CI)		**475**		**489**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
4.1.4 Magnesium						
Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable



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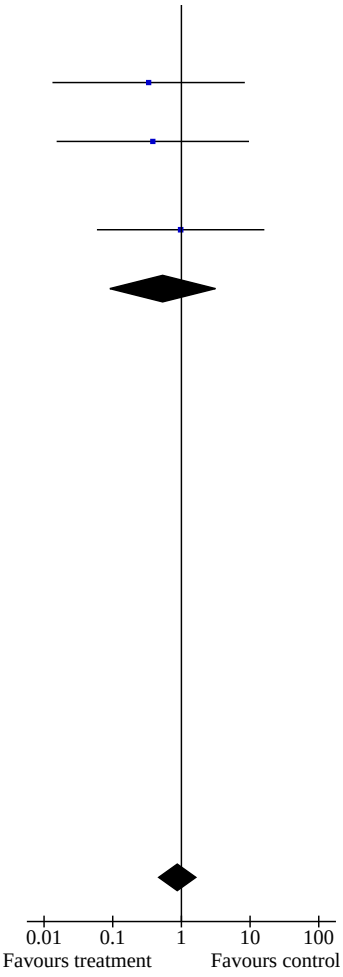
Analysis 4.1. (Continued)

Bert 2001	0	63	0	60		Not estimable
England 1992	0	50	0	50		Not estimable
Fanning 1991	0	49	1	50	3.7%	0.33 [0.01 , 8.38]
Forlani 2002	0	54	0	50		Not estimable
Karmy-Jones 1995	0	46	1	54	3.7%	0.38 [0.02 , 9.64]
Speziale 2000	0	72	0	25		Not estimable
Treggiari-Venzi 2000	0	47	0	51		Not estimable
Wilkes 2002	1	41	1	40	4.9%	0.97 [0.06 , 16.14]
Zangrillo 2005	0	80	0	80		Not estimable
Subtotal (95% CI)		**502**		**460**	**12.4%**	**0.53 [0.09 , 3.13]**
Total events:	1		3			
Heterogeneity: Tau² = 0.00; Chi² = 0.30, df = 2 (P = 0.86); I² = 0%						
Test for overall effect: Z = 0.70 (P = 0.49)						
4.1.5 Atrial Pacing						
Debrunner 2004	0	40	0	40		Not estimable
Gerstenfeld 2001	0	58	0	60		Not estimable
Subtotal (95% CI)		**98**		**100**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
4.1.6 Posterior Pericardiotomy						
Mulay 1995	0	50	0	50		Not estimable
Subtotal (95% CI)		**50**		**50**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**3390**		**3360**	**100.0%**	**0.87 [0.47 , 1.62]**
Total events:	19		25			
Heterogeneity: Tau² = 0.00; Chi² = 11.53, df = 15 (P = 0.71); I² = 0%						
Test for overall effect: Z = 0.44 (P = 0.66)						
Test for subgroup differences: Chi² = 0.34, df = 2 (P = 0.84), I² = 0%						



Comparison 5. Length of Stay

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 All Treatments	51	9661	Mean Difference (IV, Random, 95% CI)	-0.69 [-0.95, -0.43]
5.1.1 Amiodarone	18	3497	Mean Difference (IV, Random, 95% CI)	-0.95 [-1.37, -0.52]
5.1.2 Beta-Blockers	6	1676	Mean Difference (IV, Random, 95% CI)	-0.74 [-1.48, -0.00]
5.1.3 Sotalol	7	911	Mean Difference (IV, Random, 95% CI)	-0.39 [-0.77, -0.02]
5.1.4 Magnesium	9	1589	Mean Difference (IV, Random, 95% CI)	0.05 [-0.47, 0.57]
5.1.5 Atrial Pacing	12	1525	Mean Difference (IV, Random, 95% CI)	-1.13 [-1.72, -0.55]
5.1.6 Posterior Pericardiotomy	3	463	Mean Difference (IV, Random, 95% CI)	0.57 [-1.99, 3.12]

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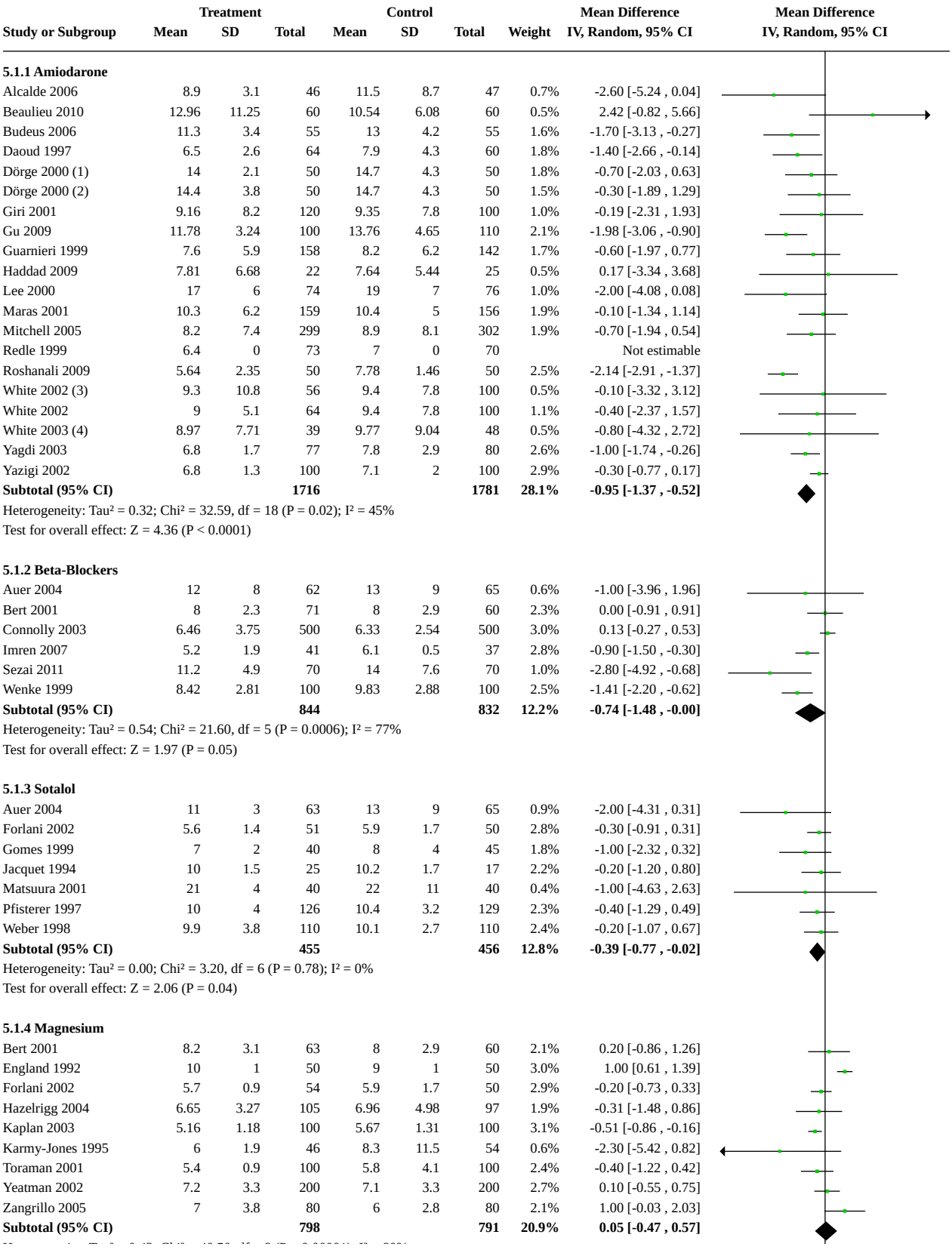
Analysis 5.1. Comparison 5: Length of Stay, Outcome 1: All Treatments



Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
5.1.1 Amiodarone								
Alcalde 2006	8.9	3.1	46	11.5	8.7	47	0.7%	-2.60 [-5.24 , 0.04]
Beaulieu 2010	12.96	11.25	60	10.54	6.08	60	0.5%	2.42 [-0.82 , 5.66]
Budeus 2006	11.3	3.4	55	13	4.2	55	1.6%	-1.70 [-3.13 , -0.27]
Daoud 1997	6.5	2.6	64	7.9	4.3	60	1.8%	-1.40 [-2.66 , -0.14]
Dörge 2000 (1)	14	2.1	50	14.7	4.3	50	1.8%	-0.70 [-2.03 , 0.63]
Dörge 2000 (2)	14.4	3.8	50	14.7	4.3	50	1.5%	-0.30 [-1.89 , 1.29]
Giri 2001	9.16	8.2	120	9.35	7.8	100	1.0%	-0.19 [-2.31 , 1.93]
Gu 2009	11.78	3.24	100	13.76	4.65	110	2.1%	-1.98 [-3.06 , -0.90]
Guarnieri 1999	7.6	5.9	158	8.2	6.2	142	1.7%	-0.60 [-1.97 , 0.77]
Haddad 2009	7.81	6.68	22	7.64	5.44	25	0.5%	0.17 [-3.34 , 3.68]
Lee 2000	17	6	74	19	7	76	1.0%	-2.00 [-4.08 , 0.08]
Maras 2001	10.3	6.2	159	10.4	5	156	1.9%	-0.10 [-1.34 , 1.14]
Mitchell 2005	8.2	7.4	299	8.9	8.1	302	1.9%	-0.70 [-1.94 , 0.54]
Redle 1999	6.4	0	73	7	0	70		Not estimable
Roshanali 2009	5.64	2.35	50	7.78	1.46	50	2.5%	-2.14 [-2.91 , -1.37]
White 2002 (3)	9.3	10.8	56	9.4	7.8	100	0.5%	-0.10 [-3.32 , 3.12]
White 2002	9	5.1	64	9.4	7.8	100	1.1%	-0.40 [-2.37 , 1.57]
White 2003 (4)	8.97	7.71	39	9.77	9.04	48	0.5%	-0.80 [-4.32 , 2.72]
Yagdi 2003	6.8	1.7	77	7.8	2.9	80	2.6%	-1.00 [-1.74 , -0.26]
Yazigi 2002	6.8	1.3	100	7.1	2	100	2.9%	-0.30 [-0.77 , 0.17]
Subtotal (95% CI)			**1716**			**1781**	**28.1%**	**-0.95 [-1.37 , -0.52]**
Heterogeneity: Tau² = 0.32; Chi² = 32.59, df = 18 (P = 0.02); I² = 45%								
Test for overall effect: Z = 4.36 (P < 0.0001)								
5.1.2 Beta-Blockers								
Auer 2004	12	8	62	13	9	65	0.6%	-1.00 [-3.96 , 1.96]
Bert 2001	8	2.3	71	8	2.9	60	2.3%	0.00 [-0.91 , 0.91]
Connolly 2003	6.46	3.75	500	6.33	2.54	500	3.0%	0.13 [-0.27 , 0.53]
Imren 2007	5.2	1.9	41	6.1	0.5	37	2.8%	-0.90 [-1.50 , -0.30]
Sezai 2011	11.2	4.9	70	14	7.6	70	1.0%	-2.80 [-4.92 , -0.68]
Wenke 1999	8.42	2.81	100	9.83	2.88	100	2.5%	-1.41 [-2.20 , -0.62]
Subtotal (95% CI)			**844**			**832**	**12.2%**	**-0.74 [-1.48 , -0.00]**
Heterogeneity: Tau² = 0.54; Chi² = 21.60, df = 5 (P = 0.0006); I² = 77%								
Test for overall effect: Z = 1.97 (P = 0.05)								
5.1.3 Sotalol								
Auer 2004	11	3	63	13	9	65	0.9%	-2.00 [-4.31 , 0.31]
Forlani 2002	5.6	1.4	51	5.9	1.7	50	2.8%	-0.30 [-0.91 , 0.31]
Gomes 1999	7	2	40	8	4	45	1.8%	-1.00 [-2.32 , 0.32]
Jacquet 1994	10	1.5	25	10.2	1.7	17	2.2%	-0.20 [-1.20 , 0.80]
Matsuura 2001	21	4	40	22	11	40	0.4%	-1.00 [-4.63 , 2.63]
Pfisterer 1997	10	4	126	10.4	3.2	129	2.3%	-0.40 [-1.29 , 0.49]
Weber 1998	9.9	3.8	110	10.1	2.7	110	2.4%	-0.20 [-1.07 , 0.67]
Subtotal (95% CI)			**455**			**456**	**12.8%**	**-0.39 [-0.77 , -0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 3.20, df = 6 (P = 0.78); I² = 0%								
Test for overall effect: Z = 2.06 (P = 0.04)								
5.1.4 Magnesium								
Bert 2001	8.2	3.1	63	8	2.9	60	2.1%	0.20 [-0.86 , 1.26]
England 1992	10	1	50	9	1	50	3.0%	1.00 [0.61 , 1.39]
Forlani 2002	5.7	0.9	54	5.9	1.7	50	2.9%	-0.20 [-0.73 , 0.33]
Hazelrigg 2004	6.65	3.27	105	6.96	4.98	97	1.9%	-0.31 [-1.48 , 0.86]
Kaplan 2003	5.16	1.18	100	5.67	1.31	100	3.1%	-0.51 [-0.86 , -0.16]
Karmy-Jones 1995	6	1.9	46	8.3	11.5	54	0.6%	-2.30 [-5.42 , 0.82]
Toraman 2001	5.4	0.9	100	5.8	4.1	100	2.4%	-0.40 [-1.22 , 0.42]
Yeatman 2002	7.2	3.3	200	7.1	3.3	200	2.7%	0.10 [-0.55 , 0.75]
Zangrillo 2005	7	3.8	80	6	2.8	80	2.1%	1.00 [-0.03 , 2.03]
Subtotal (95% CI)			**798**			**791**	**20.9%**	**0.05 [-0.47 , 0.57]**

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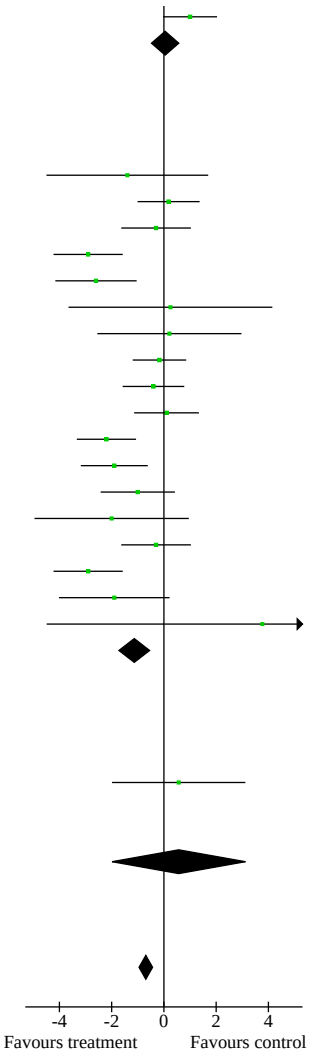
Analysis 5.1. (Continued)

Zangrillo 2005	7	3.8	80	6	2.8	80	2.1%	1.00 [-0.03 , 2.03]
Subtotal (95% CI)			**798**			**791**	**20.9%**	**0.05 [-0.47 , 0.57]**
Heterogeneity: Tau² = 0.43; Chi² = 40.50, df = 8 (P < 0.00001); I² = 80%								
Test for overall effect: Z = 0.18 (P = 0.86)								
5.1.5 Atrial Pacing								
Chung 2000a	7.5	3.2	51	8.9	10.6	49	0.6%	-1.40 [-4.50 , 1.70]
Da Silva 2008	7.65	3.41	49	7.47	2.52	49	1.9%	0.18 [-1.01 , 1.37]
Eslami 2005 (5)	8.7	1.3	40	9	4.1	40	1.7%	-0.30 [-1.63 , 1.03]
Eslami 2005 (6)	6.1	1.2	40	9	4.1	40	1.8%	-2.90 [-4.22 , -1.58]
Fan 2000	7	1.4	32	9.6	4.2	31	1.5%	-2.60 [-4.16 , -1.04]
Gerstenfeld 1999 (7)	6.83	8.13	21	6.58	4.13	21	0.4%	0.25 [-3.65 , 4.15]
Gerstenfeld 1999 (6)	6.79	4.71	19	6.58	4.13	21	0.7%	0.21 [-2.55 , 2.97]
Gerstenfeld 2001	5.79	2.88	58	5.96	2.79	60	2.2%	-0.17 [-1.19 , 0.85]
Goette 2002 (7)	11.8	3.6	60	12.2	2.7	50	1.9%	-0.40 [-1.58 , 0.78]
Goette 2002 (8)	12.3	3.6	51	12.2	2.7	50	1.9%	0.10 [-1.14 , 1.34]
Greenberg 2000 (7)	5.6	1.4	40	7.8	3.7	48	2.0%	-2.20 [-3.33 , -1.07]
Greenberg 2000 (6)	5.9	2.1	31	7.8	3.7	48	1.8%	-1.90 [-3.18 , -0.62]
Greenberg 2000 (5)	6.8	2.9	35	7.8	3.7	48	1.6%	-1.00 [-2.42 , 0.42]
Levy 2000	7.7	6.9	65	9.7	10	65	0.6%	-2.00 [-4.95 , 0.95]
Mirkhani 2005 (5)	8.7	1.3	40	9	4.1	40	1.7%	-0.30 [-1.63 , 1.03]
Mirkhani 2005 (6)	6.1	1.2	40	9	4.1	40	1.8%	-2.90 [-4.22 , -1.58]
Ozin 2005	7.9	2.2	35	9.8	6	35	1.0%	-1.90 [-4.02 , 0.22]
White 2003	13.54	23.7	35	9.77	9.04	48	0.1%	3.77 [-4.49 , 12.03]
Subtotal (95% CI)			**742**			**783**	**25.2%**	**-1.13 [-1.72 , -0.55]**
Heterogeneity: Tau² = 0.85; Chi² = 41.87, df = 17 (P = 0.0007); I² = 59%								
Test for overall effect: Z = 3.79 (P = 0.0002)								
5.1.6 Posterior Pericardiotomy								
Arbatli 2003	13.889	8.46	54	13.322	4.674	59	0.8%	0.57 [-1.99 , 3.12]
Farsak 2002	8	0	75	7	0	75		Not estimable
Kuralay 1999	7	0	100	8	0	100		Not estimable
Subtotal (95% CI)			**229**			**234**	**0.8%**	**0.57 [-1.99 , 3.12]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.44 (P = 0.66)								
Total (95% CI)			**4784**			**4877**	**100.0%**	**-0.69 [-0.95 , -0.43]**
Heterogeneity: Tau² = 0.54; Chi² = 189.71, df = 59 (P < 0.00001); I² = 69%								
Test for overall effect: Z = 5.25 (P < 0.00001)								
Test for subgroup differences: Chi² = 13.76, df = 5 (P = 0.02), I² = 63.7%								



Footnotes

(1) Amiodarone (300mg)
(2) Amiodarone (150mg)
(3) Amiodarone (Fast-Load)
(4) Amiodarone (Slow-Load)
(5) Left Atrial Pacing
(6) Biatrial Pacing
(7) Right Atrial Pacing
(8) Bachmann's Bundle Pacing

Comparison 6. Cost

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 All Treatments	12	2790	Mean Difference (IV, Random, 95% CI)	-1.25 [-1.97, -0.52]
6.1.1 Amiodarone	8	1344	Mean Difference (IV, Random, 95% CI)	-1.09 [-1.65, -0.53]

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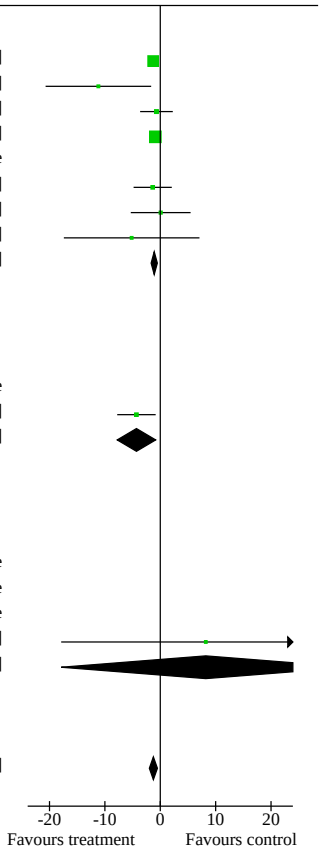
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1.2 Beta-Blockers	2	1140	Mean Difference (IV, Random, 95% CI)	-4.30 [-7.77, -0.83]
6.1.3 Atrial Pacing	3	306	Mean Difference (IV, Random, 95% CI)	8.22 [-17.89, 34.33]

Analysis 6.1. Comparison 6: Cost, Outcome 1: All Treatments

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
6.1.1 Amiodarone								
Budeus 2006	25.58949	2.18703	55	26.87199	2.44392	55	39.3%	-1.28 [-2.15 , -0.42]
Daoud 1997	25.30163	19.08879	64	36.47704	32.82259	60	0.6%	-11.18 [-20.71 , -1.64]
Giri 2001	19.44038	12.26539	120	20.12942	10.03974	100	5.7%	-0.69 [-3.64 , 2.26]
Gu 2009	11.92226	2.51254	100	12.81112	3.25369	110	43.8%	-0.89 [-1.67 , -0.11]
Guarnieri 1999	22.38579	0	158	25.06343	0	142		Not estimable
Lee 2000	20.37614	9.2851	74	21.74568	12.11402	76	4.2%	-1.37 [-4.82 , 2.08]
Redle 1999	25.07139	17.60424	73	24.99747	15.30845	70	1.8%	0.07 [-5.33 , 5.47]
White 2003	27.30397	21.2196	39	32.4716	36.31638	48	0.4%	-5.17 [-17.41 , 7.08]
Subtotal (95% CI)			**683**			**661**	**95.7%**	**-1.09 [-1.65 , -0.53]**
Heterogeneity: Tau² = 0.00; Chi² = 5.45, df = 6 (P = 0.49); I² = 0%								
Test for overall effect: Z = 3.83 (P = 0.0001)								
6.1.2 Beta-Blockers								
Connolly 2003	4.31269	0	500	4.15172	0	500		Not estimable
Sezai 2011	35.67948	6.2734	70	39.98143	13.41762	70	4.2%	-4.30 [-7.77 , -0.83]
Subtotal (95% CI)			**570**			**570**	**4.2%**	**-4.30 [-7.77 , -0.83]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.43 (P = 0.02)								
6.1.3 Atrial Pacing								
Eslami 2005 (1)	7.07355	0	40	8.37509	0	40		Not estimable
Eslami 2005 (2)	7.71866	0	40	8.37509	0	40		Not estimable
Fan 2000	15.51411	0	32	18.02984	0	31		Not estimable
White 2003	40.69223	72.46096	35	32.4716	36.31638	48	0.1%	8.22 [-17.89 , 34.33]
Subtotal (95% CI)			**147**			**159**	**0.1%**	**8.22 [-17.89 , 34.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.54)								
Total (95% CI)			**1400**			**1390**	**100.0%**	**-1.25 [-1.97 , -0.52]**
Heterogeneity: Tau² = 0.15; Chi² = 9.15, df = 8 (P = 0.33); I² = 13%								
Test for overall effect: Z = 3.36 (P = 0.0008)								
Test for subgroup differences: Chi² = 3.70, df = 2 (P = 0.16), I² = 46.0%								



Footnotes
(1) Biatrial Pacing
(2) Left Atrial Pacing

Comparison 7. Risk of Bias Assessment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 All Treatments - Randomization sequence generation	118	18393	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]
7.1.1 High Risk	7	785	Odds Ratio (M-H, Random, 95% CI)	0.31 [0.20, 0.49]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1.2 Unclear Risk	71	10437	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.34, 0.47]
7.1.3 Low Risk	40	7171	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.38, 0.55]
7.2 All Treatments - Allocation concealment	118	18393	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]
7.2.1 High Risk	6	630	Odds Ratio (M-H, Random, 95% CI)	0.25 [0.15, 0.40]
7.2.2 Unclear Risk	83	12185	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.35, 0.48]
7.2.3 Low Risk	29	5578	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.37, 0.54]
7.3 Pharmacological Treatments - Blinding of participants and personnel	93	14617	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.46]
7.3.1 High Risk	19	1873	Odds Ratio (M-H, Random, 95% CI)	0.35 [0.26, 0.48]
7.3.2 Unclear Risk	18	2388	Odds Ratio (M-H, Random, 95% CI)	0.29 [0.21, 0.39]
7.3.3 Low Risk	56	10356	Odds Ratio (M-H, Random, 95% CI)	0.46 [0.39, 0.55]
7.4 Non-Pharmacological Treatments - Blinding of participants and personnel	27	3696	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.34, 0.57]
7.4.1 High Risk	13	1691	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.30, 0.65]
7.4.2 Unclear Risk	7	1047	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.25, 0.81]
7.4.3 Low Risk	7	958	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.29, 0.59]
7.5 Pharmacological Treatments - Blinding of outcome assessment	93	14697	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.46]
7.5.1 High Risk	19	2066	Odds Ratio (M-H, Random, 95% CI)	0.32 [0.22, 0.47]
7.5.2 Unclear Risk	21	2518	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.26, 0.45]
7.5.3 Low Risk	53	10113	Odds Ratio (M-H, Random, 95% CI)	0.45 [0.38, 0.53]
7.6 Non-Pharmacological Treatments - Blinding of outcome assessment	27	3696	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.34, 0.57]
7.6.1 High Risk	10	1317	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.25, 0.70]
7.6.2 Unclear Risk	7	1017	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.27, 0.99]
7.6.3 Low Risk	10	1362	Odds Ratio (M-H, Random, 95% CI)	0.39 [0.31, 0.51]
7.7 All Treatments - Incomplete outcome data	118	18393	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]

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Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.7.1 High Risk	14	1905	Odds Ratio (M-H, Random, 95% CI)	0.42 [0.30, 0.59]
7.7.2 Unclear Risk	34	4249	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.34, 0.55]
7.7.3 Low Risk	70	12239	Odds Ratio (M-H, Random, 95% CI)	0.40 [0.35, 0.47]
7.8 All Treatments - Selective reporting	118	18233	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]
7.8.1 High Risk	5	551	Odds Ratio (M-H, Random, 95% CI)	0.72 [0.49, 1.05]
7.8.2 Unclear Risk	43	5712	Odds Ratio (M-H, Random, 95% CI)	0.36 [0.28, 0.47]
7.8.3 Low Risk	70	11970	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.37, 0.49]
7.9 All Treatments - Intention-to-treat analysis	118	18393	Odds Ratio (M-H, Random, 95% CI)	0.41 [0.37, 0.47]
7.9.1 High Risk	49	8017	Odds Ratio (M-H, Random, 95% CI)	0.44 [0.37, 0.52]
7.9.2 Unclear Risk	53	6676	Odds Ratio (M-H, Random, 95% CI)	0.34 [0.27, 0.43]
7.9.3 Low Risk	16	3700	Odds Ratio (M-H, Random, 95% CI)	0.52 [0.44, 0.60]

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Analysis 7.1. Comparison 7: Risk of Bias Assessment, Outcome 1: All Treatments - Randomization sequence generation

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.1.1 High Risk						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Subtotal (95% CI)		**317**		**468**	**4.0%**	**0.31 [0.20 , 0.49]**
Total events:	31		115			
Heterogeneity: Tau² = 0.00; Chi² = 5.70, df = 6 (P = 0.46); I² = 0%						
Test for overall effect: Z = 5.15 (P < 0.00001)						
7.1.2 Unclear Risk						
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Chavan 2010	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Chavan 2010	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.7%	0.64 [0.21 , 1.93]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Dörge 2000	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
Dörge 2000	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
Eslami 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Eslami 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fan 2000	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Gerstenfeld 1999	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 1999	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Greenberg 2000	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Greenberg 2000	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Greenberg 2000	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]

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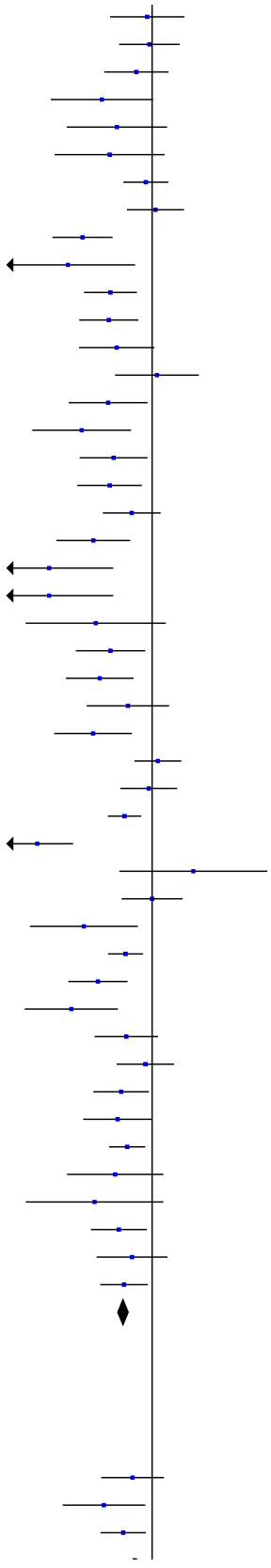
Analysis 7.1. (Continued)

Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hakala 2005	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mirkhani 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mirkhani 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Treggiari-Venzi 2000	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
Williams 1982	1	28	6	32	0.2%	0.16 [0.02 , 1.43]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Subtotal (95% CI)		**5246**		**5191**	**57.5%**	**0.40 [0.34 , 0.47]**
Total events:	917		1717			
Heterogeneity: Tau² = 0.29; Chi² = 193.96, df = 83 (P < 0.00001); I² = 57%						
Test for overall effect: Z = 11.10 (P < 0.00001)						
7.1.3 Low Risk						
Akbarzadeh 2009	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Akbarzadeh 2009	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]



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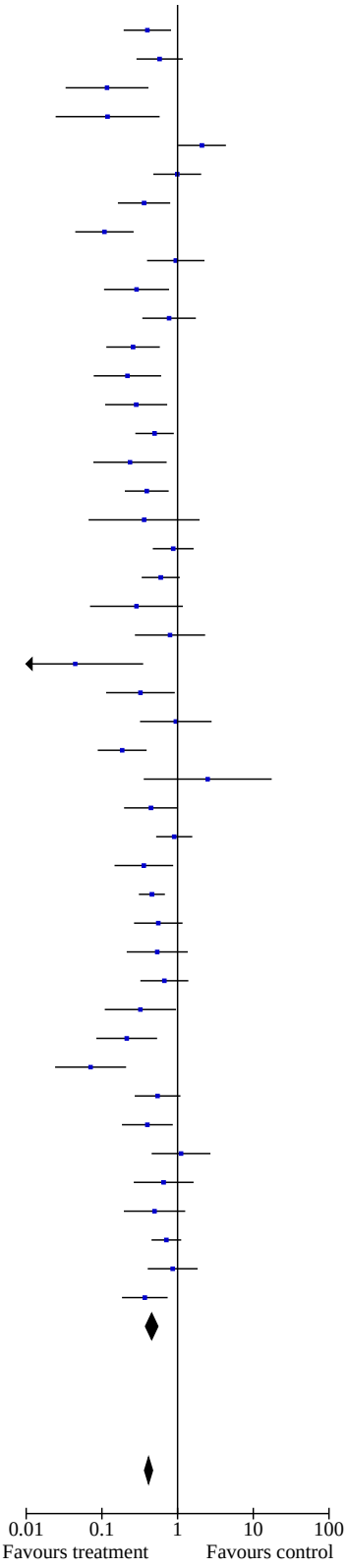
Analysis 7.1. (Continued)

Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
Bert 2001	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Bert 2001	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Forlani 2002	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Forlani 2002	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Janssen 1986	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Janssen 1986	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 2002	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2002	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
White 2003	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**3525**		**3646**	**38.4%**	**0.45 [0.38 , 0.55]**
Total events:	658		1173			
Heterogeneity: Tau² = 0.22; Chi² = 107.26, df = 46 (P < 0.00001); I² = 57%						
Test for overall effect: Z = 8.28 (P < 0.00001)						
Total (95% CI)		**9088**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1606		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.79, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 2.73, df = 2 (P = 0.25), I² = 26.9%						



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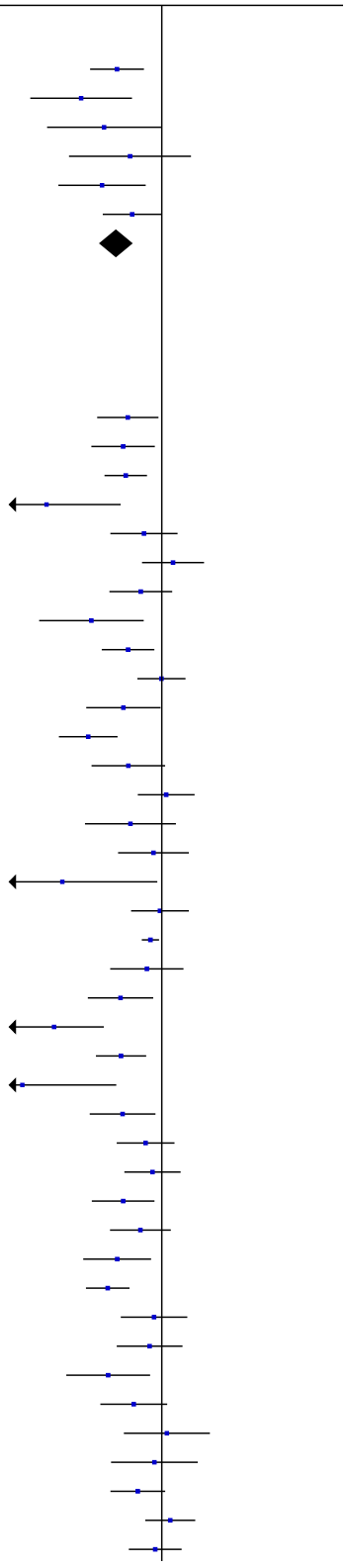
Analysis 7.2. Comparison 7: Risk of Bias Assessment, Outcome 2: All Treatments - Allocation concealment

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.2.1 High Risk						
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Subtotal (95% CI)		**284**		**346**	**3.4%**	**0.25 [0.15 , 0.40]**
Total events:	26		98			
Heterogeneity: Tau² = 0.00; Chi² = 3.76, df = 5 (P = 0.58); I² = 0%						
Test for overall effect: Z = 5.71 (P < 0.00001)						
7.2.2 Unclear Risk						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Bert 2001	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Bert 2001	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Chavan 2010	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Chavan 2010	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.7%	0.64 [0.21 , 1.93]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Dörge 2000	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Dörge 2000	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
Eslami 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Eslami 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Gerstenfeld 1999	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 1999	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]



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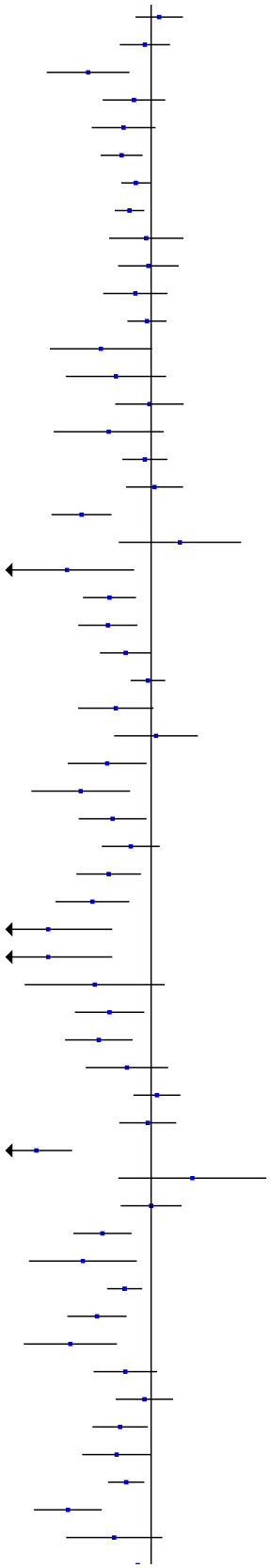
Analysis 7.2. (Continued)

Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Greenberg 2000	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Greenberg 2000	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Greenberg 2000	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hakala 2005	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mirkhani 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mirkhani 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Treggiari-Venzi 2000	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]



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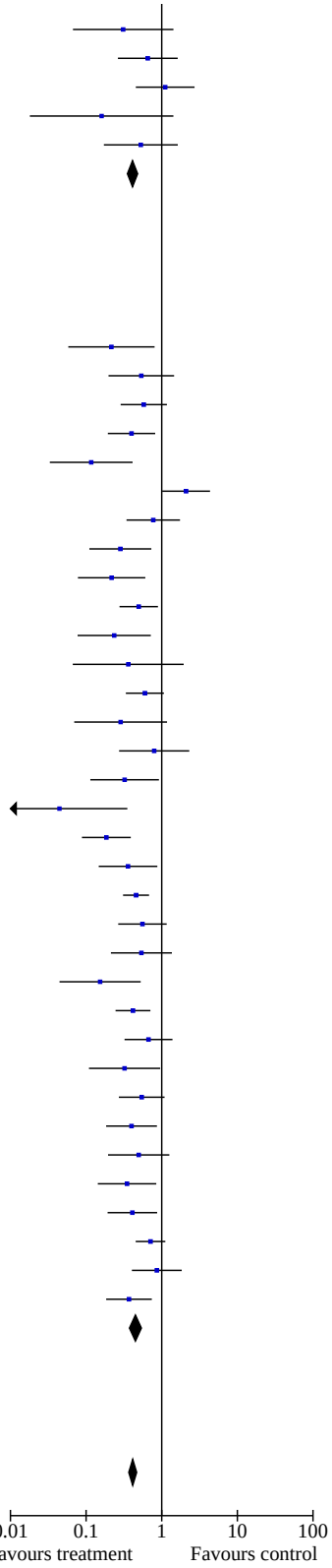
Analysis 7.2. (Continued)

White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
White 2003	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
Williams 1982	1	28	6	32	0.2%	0.16 [0.02 , 1.43]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Subtotal (95% CI)		**6070**		**6115**	**68.4%**	**0.41 [0.35 , 0.48]**
Total events:	1090		2009			
Heterogeneity: Tau² = 0.32; Chi² = 245.09, df = 97 (P < 0.00001); I² = 60%						
Test for overall effect: Z = 11.21 (P < 0.00001)						
7.2.3 Low Risk						
Akbarzadeh 2009	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Akbarzadeh 2009	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Forlani 2002	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Forlani 2002	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Janssen 1986	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Janssen 1986	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
White 2002	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2002	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**2734**		**2844**	**28.2%**	**0.45 [0.37 , 0.54]**
Total events:	490		898			
Heterogeneity: Tau² = 0.11; Chi² = 55.37, df = 33 (P = 0.009); I² = 40%						
Test for overall effect: Z = 8.67 (P < 0.00001)						
Total (95% CI)		**9088**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1606		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.79, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 5.13, df = 2 (P = 0.08), I² = 61.0%						



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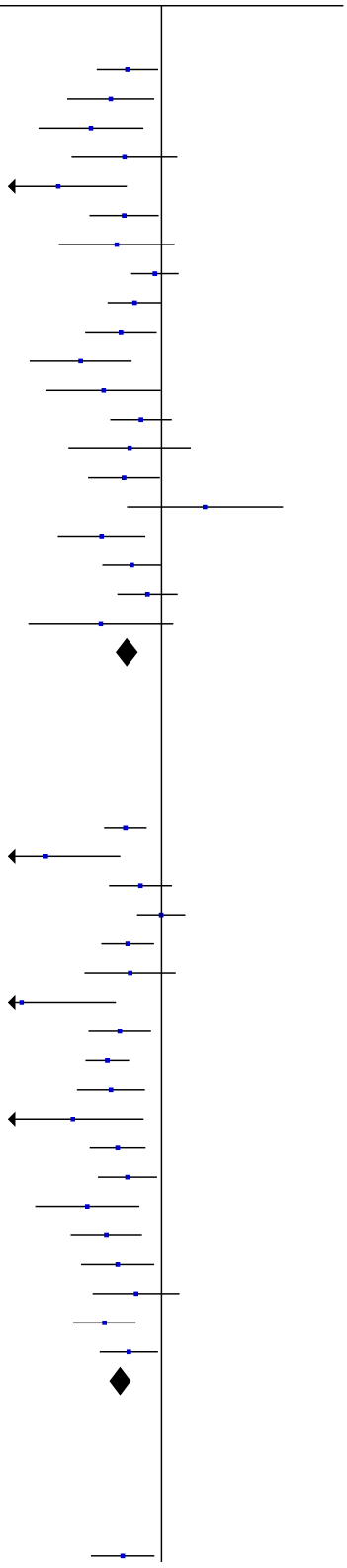
Analysis 7.3. Comparison 7: Risk of Bias Assessment, Outcome 3: Pharmacological Treatments - Blinding of participants and personnel

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.3.1 High Risk						
Abel 1983	9	41	22	50	1.1%	0.36 [0.14 , 0.90]
Akbarzadeh 2009	3	70	12	70	0.7%	0.22 [0.06 , 0.80]
Babin-Ebell 1996	2	33	13	37	0.6%	0.12 [0.02 , 0.58]
Jacquet 1994	3	25	5	17	0.6%	0.33 [0.07 , 1.61]
Janssen 1986	1	41	18	50	0.4%	0.04 [0.01 , 0.35]
Janssen 1986	6	39	18	50	0.9%	0.32 [0.11 , 0.92]
Kanchi 2004	2	20	6	20	0.5%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.3%	0.82 [0.40 , 1.68]
Lúcio 2004	10	100	20	100	1.2%	0.44 [0.20 , 1.01]
Matsuura 2001	6	40	15	40	0.9%	0.29 [0.10 , 0.86]
Mohr 1981	2	37	19	48	0.6%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.5%	0.17 [0.03 , 0.98]
Nygård 2004	10	36	20	48	1.1%	0.54 [0.21 , 1.36]
Oka 1980	2	19	4	17	0.4%	0.38 [0.06 , 2.42]
Rubin 1987	6	37	15	40	0.9%	0.32 [0.11 , 0.95]
Salazar 1979	3	20	1	22	0.3%	3.71 [0.35 , 38.93]
Silverman 1982	3	50	14	50	0.7%	0.16 [0.04 , 0.61]
Stephenson 1980	7	87	24	136	1.1%	0.41 [0.17 , 0.99]
White 2003	11	39	18	48	1.1%	0.65 [0.26 , 1.63]
Williams 1982	1	28	6	32	0.3%	0.16 [0.02 , 1.43]
Subtotal (95% CI)		**878**		**995**	**15.2%**	**0.35 [0.26 , 0.48]**
Total events:	106		279			
Heterogeneity: Tau² = 0.10; Chi² = 24.35, df = 19 (P = 0.18); I² = 22%						
Test for overall effect: Z = 6.73 (P < 0.00001)						
7.3.2 Unclear Risk						
Ali 1997	18	105	40	105	1.4%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.3%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	1.0%	0.53 [0.21 , 1.37]
Bert 2001	24	63	23	60	1.3%	0.99 [0.48 , 2.05]
Casthely 1994	13	71	23	60	1.2%	0.36 [0.16 , 0.80]
Daudon 1986	5	105	4	35	0.7%	0.39 [0.10 , 1.53]
Evrard 2000	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Forlani 2002	8	54	19	50	1.1%	0.28 [0.11 , 0.73]
Forlani 2002	16	103	50	103	1.4%	0.19 [0.10 , 0.38]
Lamb 1988	6	51	19	50	1.0%	0.22 [0.08 , 0.61]
Lee 2000	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Matangi 1985	9	74	26	76	1.2%	0.27 [0.11 , 0.62]
Materne 1985	8	82	19	82	1.1%	0.36 [0.15 , 0.87]
Nyström 1993	2	32	15	39	0.6%	0.11 [0.02 , 0.51]
Orboric 2010	5	55	19	55	0.9%	0.19 [0.06 , 0.55]
Ormerod 1984	5	50	15	51	0.9%	0.27 [0.09 , 0.80]
Tokmakoglu 2002	4	27	9	33	0.7%	0.46 [0.13 , 1.72]
Turk 2007	6	72	31	92	1.1%	0.18 [0.07 , 0.46]
Yazicioglu 2002	9	76	18	68	1.1%	0.37 [0.15 , 0.90]
Subtotal (95% CI)		**1182**		**1206**	**17.5%**	**0.29 [0.21 , 0.39]**
Total events:	146		397			
Heterogeneity: Tau² = 0.16; Chi² = 29.23, df = 18 (P = 0.05); I² = 38%						
Test for overall effect: Z = 8.22 (P < 0.00001)						
7.3.3 Low Risk						
Alcalde 2006	8	46	19	47	1.0%	0.31 [0.12 , 0.81]



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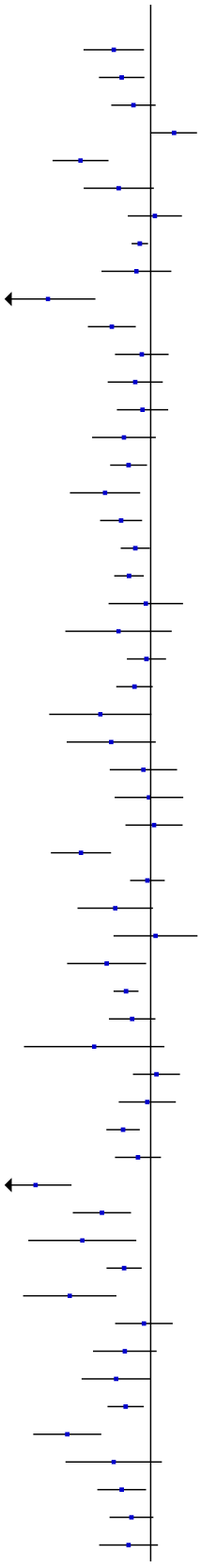
Analysis 7.3. (Continued)

7.3.3 Low Risk						
Alcalde 2006	8	46	19	47	1.0%	0.31 [0.12 , 0.81]
Auer 2004	20	63	35	65	1.3%	0.40 [0.19 , 0.82]
Auer 2004	25	62	35	65	1.3%	0.58 [0.29 , 1.17]
Beaulieu 2010	35	60	24	60	1.3%	2.10 [1.01 , 4.35]
Budeus 2006	18	55	45	55	1.1%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.9%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	1.1%	1.14 [0.48 , 2.70]
Connolly 2003	156	500	195	500	1.9%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.9%	0.64 [0.21 , 1.93]
Dagdelen 2002	2	93	20	55	0.6%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	1.3%	0.29 [0.14 , 0.62]
Dörge 2000	14	50	17	50	1.2%	0.75 [0.32 , 1.77]
Dörge 2000	12	50	17	50	1.1%	0.61 [0.26 , 1.47]
England 1992	17	50	20	50	1.2%	0.77 [0.34 , 1.74]
Fanning 1991	7	49	14	50	1.0%	0.43 [0.16 , 1.18]
Giri 2001	28	120	38	100	1.5%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.9%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.4%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.7%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.7%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.8%	0.86 [0.26 , 2.79]
Hamid 2008	2	53	5	51	0.5%	0.36 [0.07 , 1.95]
Harahsheh 2001	28	88	32	92	1.5%	0.88 [0.47 , 1.63]
Hazelrigg 2004	32	105	41	97	1.5%	0.60 [0.34 , 1.07]
Hohnloser 1991	2	39	8	38	0.5%	0.20 [0.04 , 1.03]
Imren 2007	3	41	8	37	0.7%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.9%	0.79 [0.27 , 2.31]
Jensen 1997	10	29	10	28	0.9%	0.95 [0.32 , 2.81]
Karmy-Jones 1995	12	46	13	54	1.1%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	1.0%	0.11 [0.04 , 0.28]
Maras 2001	31	159	33	156	1.6%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.8%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.7%	1.17 [0.31 , 4.42]
Matangi 1989	4	35	12	35	0.8%	0.25 [0.07 , 0.87]
Mitchell 2005	48	299	89	302	1.8%	0.46 [0.31 , 0.68]
Najafi 2007	12	166	22	179	1.3%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	0.3%	0.17 [0.02 , 1.55]
Parikka 1993	20	69	18	71	1.3%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	1.1%	0.90 [0.36 , 2.22]
Pfisterer 1997	32	126	58	129	1.6%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.3%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	0.9%	0.03 [0.01 , 0.08]
Sezai 2011	7	70	24	70	1.1%	0.21 [0.08 , 0.54]
Speziale 2000	2	72	5	25	0.5%	0.11 [0.02 , 0.63]
Suttorp 1991	24	150	46	150	1.5%	0.43 [0.25 , 0.75]
Toraman 2001	2	100	21	100	0.6%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	11	47	14	51	1.1%	0.81 [0.32 , 2.01]
Treggiari-Venzi 2000	7	49	14	51	1.0%	0.44 [0.16 , 1.21]
Vecht 1986	5	66	13	66	0.9%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.5%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.9%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.6%	0.31 [0.07 , 1.43]
White 2002	11	56	38	100	1.3%	0.40 [0.18 , 0.86]
White 2002	16	64	38	100	1.4%	0.54 [0.27 , 1.09]
Wilkes 2002	11	41	17	40	1.1%	0.50 [0.20 , 1.26]



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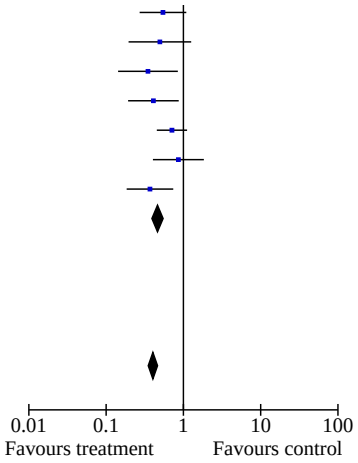
Analysis 7.3. (Continued)

White 2002	16	64	38	100	1.4%	0.54 [0.27 , 1.09]
Wilkes 2002	11	41	17	40	1.1%	0.50 [0.20 , 1.26]
Yagdi 2003	8	77	20	80	1.1%	0.35 [0.14 , 0.85]
Yazigi 2002	12	100	25	100	1.3%	0.41 [0.19 , 0.87]
Yeatman 2002	45	200	58	200	1.7%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	1.3%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.4%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**5163**		**5193**	**67.3%**	**0.46 [0.39 , 0.55]**
Total events:	1025		1705			
Heterogeneity: Tau² = 0.23; Chi² = 154.70, df = 59 (P < 0.00001); I² = 62%						
Test for overall effect: Z = 9.09 (P < 0.00001)						
Total (95% CI)		**7223**		**7394**	**100.0%**	**0.40 [0.35 , 0.46]**
Total events:	1277		2381			
Heterogeneity: Tau² = 0.24; Chi² = 231.10, df = 98 (P < 0.00001); I² = 58%						
Test for overall effect: Z = 12.90 (P < 0.00001)						
Test for subgroup differences: Chi² = 8.42, df = 2 (P = 0.01), I² = 76.3%						



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Analysis 7.4. Comparison 7: Risk of Bias Assessment, Outcome 4: Non-Pharmacological Treatments - Blinding of participants and personnel

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.4.1 High Risk						
Akbarzadeh 2009	7	70	12	70	2.8%	0.54 [0.20 , 1.46]
Asimakopoulos 1997	13	50	10	50	3.0%	1.41 [0.55 , 3.59]
Avila Neto 2007	3	80	20	80	2.2%	0.12 [0.03 , 0.41]
Blommaert 2000	5	48	13	48	2.5%	0.31 [0.10 , 0.96]
Chavan 2010	0	48	9	54	0.7%	0.05 [0.00 , 0.87]
Chavan 2010	7	52	9	54	2.6%	0.78 [0.27 , 2.27]
Chung 2000a	14	51	14	49	3.2%	0.95 [0.40 , 2.26]
Da Silva 2008	7	49	18	49	2.9%	0.29 [0.11 , 0.77]
Debrunner 2004	8	40	18	40	2.8%	0.31 [0.11 , 0.83]
Hakala 2005	11	41	12	42	2.9%	0.92 [0.35 , 2.40]
Hakala 2005	8	41	12	42	2.8%	0.61 [0.22 , 1.68]
Kuralay 1999	11	100	40	100	3.5%	0.19 [0.09 , 0.39]
Mirkhani 2005	7	40	18	40	2.8%	0.26 [0.09 , 0.72]
Mirkhani 2005	12	40	18	40	3.0%	0.52 [0.21 , 1.31]
Mulay 1995	4	50	18	50	2.4%	0.15 [0.05 , 0.50]
White 2003	14	35	18	48	3.1%	1.11 [0.45 , 2.72]
Subtotal (95% CI)		**835**		**856**	**43.3%**	**0.44 [0.30 , 0.65]**
Total events:	131		259			
Heterogeneity: Tau² = 0.34; Chi² = 34.48, df = 15 (P = 0.003); I² = 57%						
Test for overall effect: Z = 4.16 (P < 0.0001)						
7.4.2 Unclear Risk						
Arbatli 2003	7	54	12	59	2.8%	0.58 [0.21 , 1.61]
Fan 2000	12	36	13	31	2.8%	0.69 [0.26 , 1.87]
Fan 2000	4	32	13	31	2.2%	0.20 [0.06 , 0.70]
Fan 2000	12	33	13	31	2.8%	0.79 [0.29 , 2.16]
Gerstenfeld 2001	12	58	21	60	3.3%	0.48 [0.21 , 1.11]
Goette 2002	29	60	21	50	3.5%	1.29 [0.61 , 2.75]
Goette 2002	19	51	21	50	3.4%	0.82 [0.37 , 1.82]
Kurz 1999	5	12	2	9	1.3%	2.50 [0.36 , 17.50]
Neto 2007	1	80	20	80	1.2%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	1.2%	0.04 [0.00 , 0.29]
Ozin 2005	4	35	16	35	2.3%	0.15 [0.04 , 0.53]
Subtotal (95% CI)		**531**		**516**	**26.7%**	**0.45 [0.25 , 0.81]**
Total events:	106		172			
Heterogeneity: Tau² = 0.62; Chi² = 30.36, df = 10 (P = 0.0007); I² = 67%						
Test for overall effect: Z = 2.66 (P = 0.008)						
7.4.3 Low Risk						
Ekim 2006	8	50	19	50	3.0%	0.31 [0.12 , 0.80]
Eslami 2005	7	40	18	40	2.8%	0.26 [0.09 , 0.72]
Eslami 2005	12	40	18	40	3.0%	0.52 [0.21 , 1.31]
Farsak 2002	10	75	28	75	3.3%	0.26 [0.11 , 0.58]
Gerstenfeld 1999	7	19	7	21	2.2%	1.17 [0.32 , 4.28]
Gerstenfeld 1999	6	21	7	21	2.1%	0.80 [0.22 , 2.97]
Greenberg 2000	7	35	18	48	2.8%	0.42 [0.15 , 1.15]
Greenberg 2000	3	40	18	48	2.1%	0.14 [0.04 , 0.50]
Greenberg 2000	8	31	18	48	2.8%	0.58 [0.21 , 1.57]
Levy 2000	7	65	21	65	3.0%	0.25 [0.10 , 0.65]
Schweikert 1998	11	43	11	43	2.9%	1.00 [0.38 , 2.63]
Subtotal (95% CI)		**459**		**499**	**30.0%**	**0.41 [0.29 , 0.59]**
Total events:	86		183			

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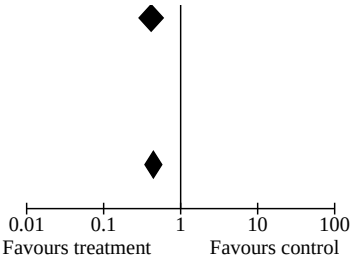
Analysis 7.4. (Continued)

Subtotal (95% CI)		**459**	**499**	**30.0%**	**0.41 [0.29 , 0.59]**
Total events:	86	183			
Heterogeneity: Tau² = 0.10; Chi² = 13.58, df = 10 (P = 0.19); I² = 26%					
Test for overall effect: Z = 4.81 (P < 0.00001)					
Total (95% CI)		**1825**	**1871**	**100.0%**	**0.44 [0.34 , 0.57]**
Total events:	323	614			
Heterogeneity: Tau² = 0.32; Chi² = 79.74, df = 37 (P < 0.0001); I² = 54%					
Test for overall effect: Z = 6.39 (P < 0.00001)					
Test for subgroup differences: Chi² = 0.07, df = 2 (P = 0.97), I² = 0%					



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Analysis 7.5. Comparison 7: Risk of Bias Assessment, Outcome 5: Pharmacological Treatments - Blinding of outcome assessment

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.5.1 High Risk						
Akbarzadeh 2009	3	70	12	70	0.7%	0.22 [0.06 , 0.80]
Babin-Ebell 1996	2	33	13	37	0.6%	0.12 [0.02 , 0.58]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Evrard 2000	16	103	50	103	1.4%	0.19 [0.10 , 0.38]
Janssen 1986	6	39	18	50	0.9%	0.32 [0.11 , 0.92]
Janssen 1986	1	41	18	50	0.4%	0.04 [0.01 , 0.35]
Kanchi 2004	2	20	6	20	0.5%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.3%	0.82 [0.40 , 1.68]
Lúcio 2004	10	100	20	100	1.2%	0.44 [0.20 , 1.01]
Mohr 1981	2	37	19	48	0.6%	0.09 [0.02 , 0.41]
Myhre 1984	2	16	9	20	0.5%	0.17 [0.03 , 0.98]
Nygård 2004	10	36	20	48	1.1%	0.54 [0.21 , 1.36]
Oka 1980	2	19	4	17	0.4%	0.38 [0.06 , 2.42]
Paull 1997	12	50	13	50	1.1%	0.90 [0.36 , 2.22]
Rubin 1987	6	37	15	40	0.9%	0.32 [0.11 , 0.95]
Salazar 1979	3	20	1	22	0.3%	3.71 [0.35 , 38.93]
Silverman 1982	3	50	14	50	0.7%	0.16 [0.04 , 0.61]
Stephenson 1980	7	87	24	136	1.1%	0.41 [0.17 , 0.99]
White 2003	11	39	18	48	1.1%	0.65 [0.26 , 1.63]
Williams 1982	1	28	6	32	0.3%	0.16 [0.02 , 1.43]
Subtotal (95% CI)		**975**		**1091**	**15.2%**	**0.32 [0.22 , 0.47]**
Total events:	116		320			
Heterogeneity: Tau² = 0.32; Chi² = 36.96, df = 19 (P = 0.008); I² = 49%						
Test for overall effect: Z = 5.88 (P < 0.00001)						
7.5.2 Unclear Risk						
Abel 1983	9	41	22	50	1.1%	0.36 [0.14 , 0.90]
Ali 1997	18	105	40	105	1.4%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.3%	0.03 [0.00 , 0.29]
Assefi 2010	6	67	23	147	1.0%	0.53 [0.21 , 1.37]
Casthely 1994	5	105	4	35	0.7%	0.39 [0.10 , 1.53]
Forlani 2002	8	54	19	50	1.0%	0.28 [0.11 , 0.73]
Forlani 2002	6	51	19	50	1.0%	0.22 [0.08 , 0.61]
Harahsheh 2001	28	88	32	92	1.4%	0.88 [0.47 , 1.63]
Hohnloser 1991	2	39	8	38	0.5%	0.20 [0.04 , 1.03]
Jacquet 1994	3	25	5	17	0.5%	0.33 [0.07 , 1.61]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	1.2%	0.27 [0.11 , 0.62]
Matangi 1985	8	82	19	82	1.1%	0.36 [0.15 , 0.87]
Materne 1985	2	32	15	39	0.6%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.9%	0.29 [0.10 , 0.86]
Nyström 1993	5	50	15	51	0.9%	0.27 [0.09 , 0.80]
Orboric 2010	5	55	19	55	0.9%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.7%	0.46 [0.13 , 1.72]
Parikka 1993	20	69	18	71	1.3%	1.20 [0.57 , 2.53]
Tokmakoglu 2002	6	72	31	92	1.0%	0.18 [0.07 , 0.46]
Turk 2007	9	76	18	68	1.1%	0.37 [0.15 , 0.90]
Yazicioglu 2002	6	40	10	40	0.9%	0.53 [0.17 , 1.63]
Subtotal (95% CI)		**1237**		**1281**	**19.9%**	**0.34 [0.26 , 0.45]**
Total events:	167		391			
Heterogeneity: Tau² = 0.17; Chi² = 34.57, df = 21 (P = 0.03); I² = 39%						
Test for overall effect: Z = 7.43 (P < 0.00001)						

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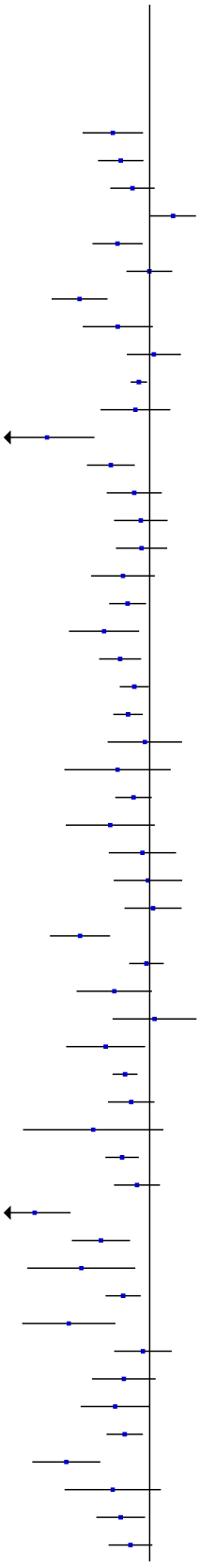
Analysis 7.5. (Continued)

Heterogeneity: Tau² = 0.17; Chi² = 34.57, df = 21 (P = 0.03); I² = 39%
Test for overall effect: Z = 7.43 (P < 0.00001)

7.5.3 Low Risk

Alcalde 2006	8	46	19	47	1.0%	0.31 [0.12 , 0.81]
Auer 2004	20	63	35	65	1.3%	0.40 [0.19 , 0.82]
Auer 2004	25	62	35	65	1.3%	0.58 [0.29 , 1.17]
Beaulieu 2010	35	60	24	60	1.3%	2.10 [1.01 , 4.35]
Bert 2001	13	71	23	60	1.2%	0.36 [0.16 , 0.80]
Bert 2001	24	63	23	60	1.3%	0.99 [0.48 , 2.05]
Budeus 2006	18	55	45	55	1.1%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.9%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	1.1%	1.14 [0.48 , 2.70]
Connolly 2003	156	500	195	500	1.9%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.9%	0.64 [0.21 , 1.93]
Dagdelen 2002	2	93	20	55	0.6%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	1.3%	0.29 [0.14 , 0.62]
Dörge 2000	12	50	17	50	1.1%	0.61 [0.26 , 1.47]
Dörge 2000	14	50	17	50	1.1%	0.75 [0.32 , 1.77]
England 1992	17	50	20	50	1.2%	0.77 [0.34 , 1.74]
Fanning 1991	7	49	14	50	1.0%	0.43 [0.16 , 1.18]
Giri 2001	28	120	38	100	1.5%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.9%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.4%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.7%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.7%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.8%	0.86 [0.26 , 2.79]
Hamid 2008	2	53	5	51	0.5%	0.36 [0.07 , 1.95]
Hazelrigg 2004	32	105	41	97	1.5%	0.60 [0.34 , 1.07]
Imren 2007	3	41	8	37	0.6%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.9%	0.79 [0.27 , 2.31]
Jensen 1997	10	29	10	28	0.9%	0.95 [0.32 , 2.81]
Karmy-Jones 1995	12	46	13	54	1.1%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	1.0%	0.11 [0.04 , 0.28]
Maras 2001	31	159	33	156	1.5%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.8%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.7%	1.17 [0.31 , 4.42]
Matangi 1989	4	35	12	35	0.8%	0.25 [0.07 , 0.87]
Mitchell 2005	48	299	89	302	1.8%	0.46 [0.31 , 0.68]
Najafi 2007	12	166	22	179	1.3%	0.56 [0.27 , 1.16]
Nurözler 1996	1	25	5	25	0.3%	0.17 [0.02 , 1.55]
Pfisterer 1997	32	126	58	129	1.6%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.3%	0.67 [0.32 , 1.39]
Roshanali 2009	8	50	44	50	0.8%	0.03 [0.01 , 0.08]
Sezai 2011	7	70	24	70	1.1%	0.21 [0.08 , 0.54]
Speziale 2000	2	72	5	25	0.5%	0.11 [0.02 , 0.63]
Suttorp 1991	24	150	46	150	1.5%	0.43 [0.25 , 0.75]
Toraman 2001	2	100	21	100	0.6%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	11	47	14	51	1.1%	0.81 [0.32 , 2.01]
Treggiari-Venzi 2000	7	49	14	51	1.0%	0.44 [0.16 , 1.21]
Vecht 1986	5	66	13	66	0.9%	0.33 [0.11 , 1.00]
Weber 1998	27	110	46	110	1.5%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.9%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.6%	0.31 [0.07 , 1.43]
White 2002	11	56	38	100	1.2%	0.40 [0.18 , 0.86]
White 2002	16	64	38	100	1.3%	0.54 [0.27 , 1.09]



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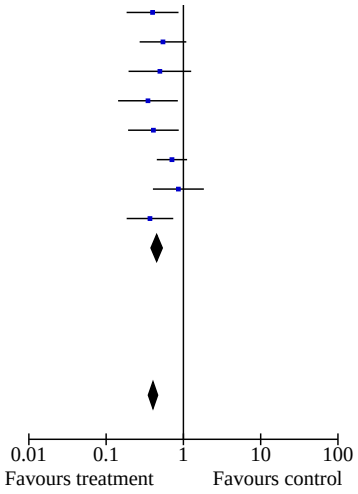
Analysis 7.5. (Continued)

White 2002	11	56	38	100	1.2%	0.40 [0.18 , 0.86]
White 2002	16	64	38	100	1.3%	0.54 [0.27 , 1.09]
Wilkes 2002	11	41	17	40	1.1%	0.50 [0.20 , 1.26]
Yagdi 2003	8	77	20	80	1.1%	0.35 [0.14 , 0.85]
Yazigi 2002	12	100	25	100	1.3%	0.41 [0.19 , 0.87]
Yeatman 2002	45	200	58	200	1.7%	0.71 [0.45 , 1.12]
Zangrillo 2005	16	80	18	80	1.3%	0.86 [0.40 , 1.84]
Zebis 2007	14	110	32	113	1.3%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**5051**		**5062**	**64.9%**	**0.45 [0.38 , 0.53]**
Total events:	1000		1680			
Heterogeneity: Tau² = 0.23; Chi² = 148.01, df = 57 (P < 0.00001); I² = 61%						
Test for overall effect: Z = 9.34 (P < 0.00001)						
Total (95% CI)		**7263**		**7434**	**100.0%**	**0.40 [0.35 , 0.46]**
Total events:	1283		2391			
Heterogeneity: Tau² = 0.24; Chi² = 231.14, df = 99 (P < 0.00001); I² = 57%						
Test for overall effect: Z = 12.95 (P < 0.00001)						
Test for subgroup differences: Chi² = 4.38, df = 2 (P = 0.11), I² = 54.4%						



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Analysis 7.6. Comparison 7: Risk of Bias Assessment, Outcome 6: Non-Pharmacological Treatments - Blinding of outcome assessment

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.6.1 High Risk						
Akbarzadeh 2009	7	70	12	70	2.8%	0.54 [0.20 , 1.46]
Asimakopoulos 1997	13	50	10	50	3.0%	1.41 [0.55 , 3.59]
Avila Neto 2007	3	80	20	80	2.2%	0.12 [0.03 , 0.41]
Blommaert 2000	5	48	13	48	2.5%	0.31 [0.10 , 0.96]
Chavan 2010	0	48	9	54	0.7%	0.05 [0.00 , 0.87]
Chavan 2010	7	52	9	54	2.6%	0.78 [0.27 , 2.27]
Chung 2000a	14	51	14	49	3.2%	0.95 [0.40 , 2.26]
Kuralay 1999	11	100	40	100	3.5%	0.19 [0.09 , 0.39]
Mirkhani 2005	12	40	18	40	3.0%	0.52 [0.21 , 1.31]
Mirkhani 2005	7	40	18	40	2.8%	0.26 [0.09 , 0.72]
Ozin 2005	4	35	16	35	2.3%	0.15 [0.04 , 0.53]
White 2003	14	35	18	48	3.1%	1.11 [0.45 , 2.72]
Subtotal (95% CI)		**649**		**668**	**31.8%**	**0.42 [0.25 , 0.70]**
Total events:	97		197			
Heterogeneity: Tau² = 0.48; Chi² = 30.44, df = 11 (P = 0.001); I² = 64%						
Test for overall effect: Z = 3.37 (P = 0.0007)						
7.6.2 Unclear Risk						
Arbatli 2003	7	54	12	59	2.8%	0.58 [0.21 , 1.61]
Goette 2002	19	51	21	50	3.4%	0.82 [0.37 , 1.82]
Goette 2002	29	60	21	50	3.5%	1.29 [0.61 , 2.75]
Hakala 2005	11	41	12	42	2.9%	0.92 [0.35 , 2.40]
Hakala 2005	8	41	12	42	2.8%	0.61 [0.22 , 1.68]
Kurz 1999	5	12	2	9	1.3%	2.50 [0.36 , 17.50]
Mulay 1995	4	50	18	50	2.4%	0.15 [0.05 , 0.50]
Neto 2007	1	80	20	80	1.2%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	1.2%	0.04 [0.00 , 0.29]
Schweikert 1998	11	43	11	43	2.9%	1.00 [0.38 , 2.63]
Subtotal (95% CI)		**512**		**505**	**24.3%**	**0.52 [0.27 , 0.99]**
Total events:	96		149			
Heterogeneity: Tau² = 0.69; Chi² = 29.46, df = 9 (P = 0.0005); I² = 69%						
Test for overall effect: Z = 1.98 (P = 0.05)						
7.6.3 Low Risk						
Da Silva 2008	7	49	18	49	2.9%	0.29 [0.11 , 0.77]
Debrunner 2004	8	40	18	40	2.8%	0.31 [0.11 , 0.83]
Ekim 2006	8	50	19	50	3.0%	0.31 [0.12 , 0.80]
Eslami 2005	7	40	18	40	2.8%	0.26 [0.09 , 0.72]
Eslami 2005	12	40	18	40	3.0%	0.52 [0.21 , 1.31]
Fan 2000	12	36	13	31	2.8%	0.69 [0.26 , 1.87]
Fan 2000	12	33	13	31	2.8%	0.79 [0.29 , 2.16]
Fan 2000	4	32	13	31	2.2%	0.20 [0.06 , 0.70]
Farsak 2002	10	75	28	75	3.3%	0.26 [0.11 , 0.58]
Gerstenfeld 1999	7	19	7	21	2.2%	1.17 [0.32 , 4.28]
Gerstenfeld 1999	6	21	7	21	2.1%	0.80 [0.22 , 2.97]
Gerstenfeld 2001	12	58	21	60	3.3%	0.48 [0.21 , 1.11]
Greenberg 2000	8	31	18	48	2.8%	0.58 [0.21 , 1.57]
Greenberg 2000	7	35	18	48	2.8%	0.42 [0.15 , 1.15]
Greenberg 2000	3	40	18	48	2.1%	0.14 [0.04 , 0.50]
Levy 2000	7	65	21	65	3.0%	0.25 [0.10 , 0.65]
Subtotal (95% CI)		**664**		**698**	**44.0%**	**0.39 [0.31 , 0.51]**
Total events:	130		268			

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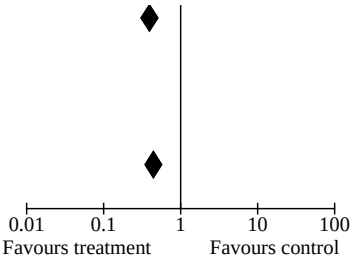
Analysis 7.6. (Continued)

Subtotal (95% CI)	**664**	**698**	**44.0%**	**0.39 [0.31 , 0.51]**	
Total events:	130	268			
Heterogeneity: Tau² = 0.00; Chi² = 15.19, df = 15 (P = 0.44); I² = 1%					
Test for overall effect: Z = 7.21 (P < 0.00001)					
Total (95% CI)	**1825**	**1871**	**100.0%**	**0.44 [0.34 , 0.57]**	
Total events:	323	614			
Heterogeneity: Tau² = 0.32; Chi² = 79.74, df = 37 (P < 0.0001); I² = 54%					
Test for overall effect: Z = 6.39 (P < 0.00001)					
Test for subgroup differences: Chi² = 0.65, df = 2 (P = 0.72), I² = 0%					



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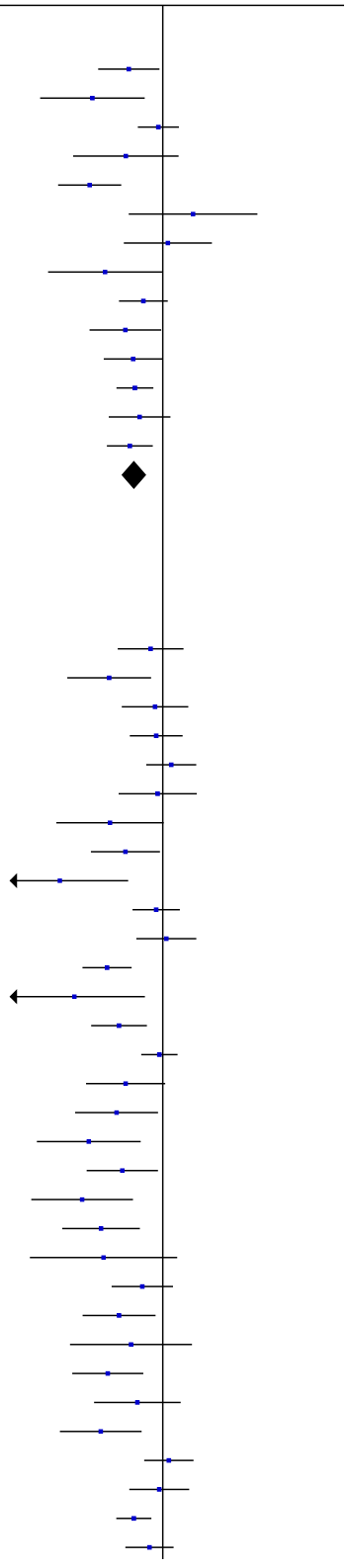
Analysis 7.7. Comparison 7: Risk of Bias Assessment, Outcome 7: All Treatments - Incomplete outcome data

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.7.1 High Risk						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**908**		**997**	**10.0%**	**0.42 [0.30 , 0.59]**
Total events:	134		279			
Heterogeneity: Tau² = 0.17; Chi² = 23.13, df = 13 (P = 0.04); I² = 44%						
Test for overall effect: Z = 4.98 (P < 0.00001)						
7.7.2 Unclear Risk						
Fan 2000	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Janssen 1986	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Janssen 1986	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]



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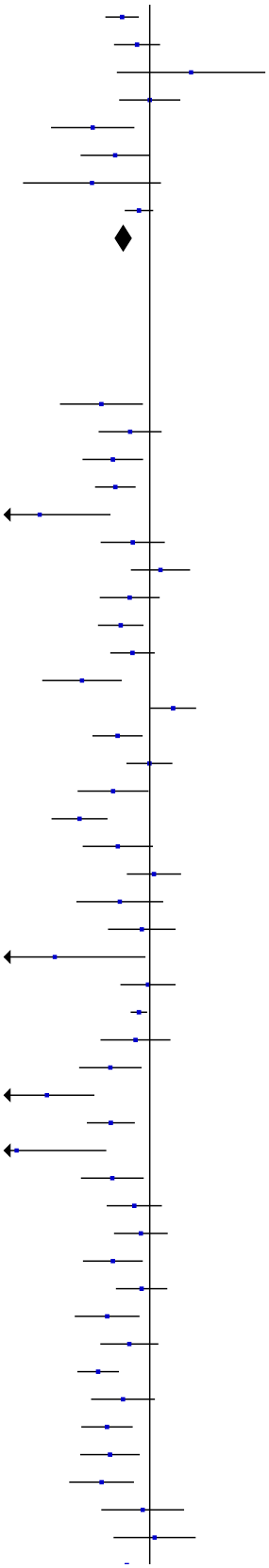
Analysis 7.7. (Continued)

Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Williams 1982	1	28	6	32	0.2%	0.16 [0.02 , 1.43]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Subtotal (95% CI)		**2098**		**2151**	**25.4%**	**0.43 [0.34 , 0.55]**
Total events:	377		670			
Heterogeneity: Tau² = 0.30; Chi² = 84.43, df = 37 (P < 0.0001); I² = 56%						
Test for overall effect: Z = 6.59 (P < 0.00001)						
7.7.3 Low Risk						
Akbarzadeh 2009	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Akbarzadeh 2009	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
Bert 2001	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Bert 2001	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Chavan 2010	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Chavan 2010	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.7%	0.64 [0.21 , 1.93]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Dörge 2000	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Dörge 2000	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Eslami 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Eslami 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Forlani 2002	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Forlani 2002	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Gerstenfeld 1999	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 1999	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]



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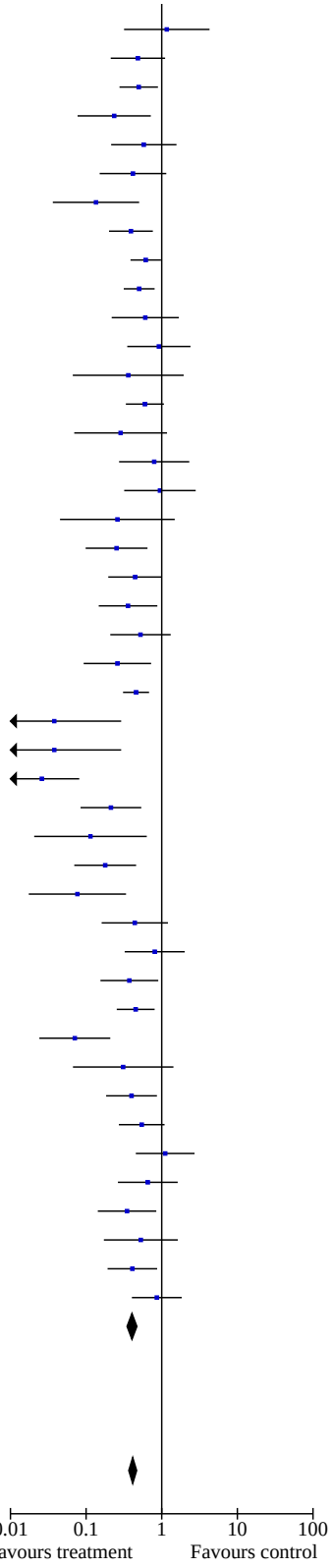
Analysis 7.7. (Continued)

Gerstenfeld 1999	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Greenberg 2000	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Greenberg 2000	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Greenberg 2000	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Hakala 2005	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Mirkhani 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mirkhani 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Treggiari-Venzi 2000	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2002	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
White 2002	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2003	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Subtotal (95% CI)		**6082**		**6157**	**64.6%**	**0.40 [0.35 , 0.47]**
Total events:	1095		2056			
Heterogeneity: Tau² = 0.25; Chi² = 201.83, df = 85 (P < 0.00001); I² = 58%						
Test for overall effect: Z = 11.89 (P < 0.00001)						
Total (95% CI)		**9088**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1606		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.79, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 0.19, df = 2 (P = 0.91), I² = 0%						



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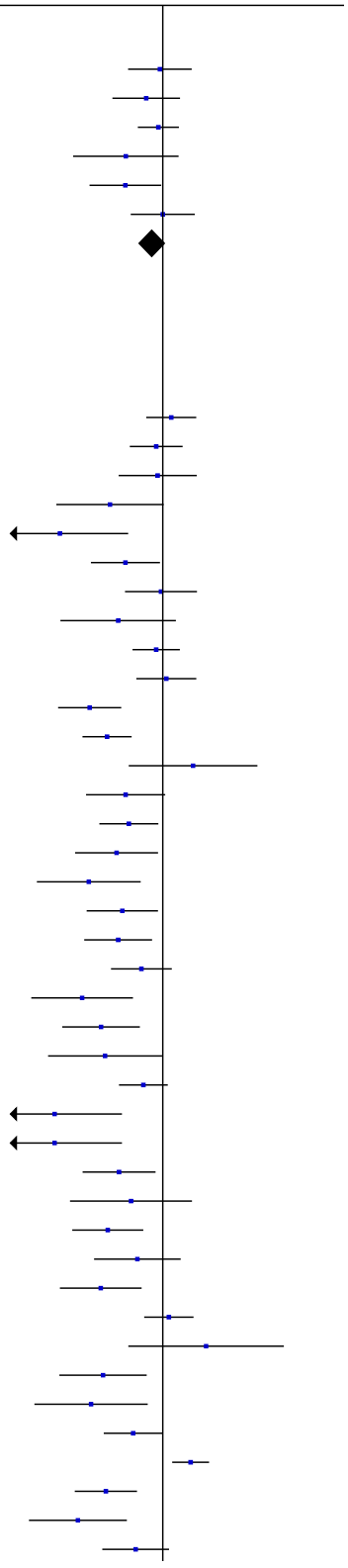
Analysis 7.8. Comparison 7: Risk of Bias Assessment, Outcome 8: All Treatments - Selective reporting

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.8.1 High Risk						
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Hakala 2005	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Harahsheh 2001	28	88	32	92	1.0%	0.88 [0.47 , 1.63]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Subtotal (95% CI)		**275**		**276**	**4.4%**	**0.72 [0.49 , 1.05]**
Total events:	67		87			
Heterogeneity: Tau² = 0.00; Chi² = 4.22, df = 5 (P = 0.52); I² = 0%						
Test for overall effect: Z = 1.73 (P = 0.08)						
7.8.2 Unclear Risk						
Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Janssen 1986	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Janssen 1986	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mirkhani 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mirkhani 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mohr 1981	2	37	19	48	0.5%	0.09 [0.02 , 0.41]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	0.9%	0.56 [0.27 , 1.16]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.6%	0.46 [0.13 , 1.72]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Silverman 1982	3	50	14	50	0.6%	0.16 [0.04 , 0.61]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Suttorp 1991	46	150	24	150	1.1%	2.32 [1.33 , 4.06]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]



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Analysis 7.8. (Continued)

Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]	
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]	
Treggiari-Venzi 2000	11	47	14	51	0.8%	0.81 [0.32 , 2.01]	
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]	
White 1984	3	21	7	20	0.5%	0.31 [0.07 , 1.43]	
White 2002	16	64	38	100	1.0%	0.54 [0.27 , 1.09]	
White 2002	11	56	38	100	0.9%	0.40 [0.18 , 0.86]	
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]	
Williams 1982	1	28	6	32	0.3%	0.16 [0.02 , 1.43]	
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]	
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]	
Subtotal (95% CI)		**2769**		**2943**	**32.2%**	**0.36 [0.28 , 0.47]**	
Total events:	393		843				
Heterogeneity: Tau² = 0.51; Chi² = 137.62, df = 48 (P < 0.00001); I² = 65%							
Test for overall effect: Z = 7.64 (P < 0.00001)							
7.8.3 Low Risk							
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]	
Akbarzadeh 2009	7	70	12	70	0.7%	0.54 [0.20 , 1.46]	
Akbarzadeh 2009	3	70	12	70	0.6%	0.22 [0.06 , 0.80]	
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]	
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]	
Alves 2007	1	15	14	20	0.3%	0.03 [0.00 , 0.29]	
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]	
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]	
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]	
Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]	
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]	
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]	
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]	
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]	
Bert 2001	13	71	23	60	0.9%	0.36 [0.16 , 0.80]	
Bert 2001	24	63	23	60	1.0%	0.99 [0.48 , 2.05]	
Blommaert 2000	5	48	13	48	0.7%	0.31 [0.10 , 0.96]	
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]	
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]	
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]	
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]	
Chavan 2010	7	52	9	54	0.7%	0.78 [0.27 , 2.27]	
Chavan 2010	0	48	9	54	0.2%	0.05 [0.00 , 0.87]	
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]	
Connolly 2003	156	500	195	500	1.3%	0.71 [0.55 , 0.92]	
Crystal 2003	6	36	11	46	0.7%	0.64 [0.21 , 1.93]	
Da Silva 2008	7	49	18	49	0.8%	0.29 [0.11 , 0.77]	
Dagdelen 2002	2	93	20	55	0.5%	0.04 [0.01 , 0.17]	
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]	
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]	
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]	
Dörge 2000	14	50	17	50	0.9%	0.75 [0.32 , 1.77]	
Ekim 2006	12	50	17	50	0.8%	0.61 [0.26 , 1.47]	
England 1992	8	50	19	50	0.8%	0.31 [0.12 , 0.80]	
Eslami 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]	
Eslami 2005	17	50	20	50	0.9%	0.77 [0.34 , 1.74]	
Evrard 2000	12	40	18	40	0.8%	0.52 [0.21 , 1.31]	
Fan 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]	
Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]	
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]	

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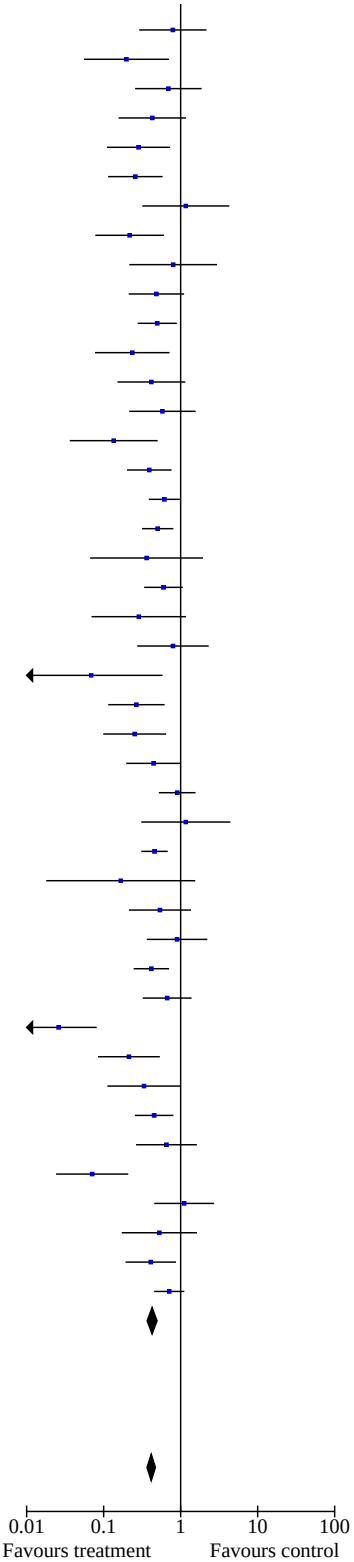
Analysis 7.8. (Continued)

Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Fanning 1991	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Farsak 2002	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Forlani 2002	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Forlani 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Gerstenfeld 1999	7	19	7	21	0.6%	1.17 [0.32 , 4.28]
Gerstenfeld 1999	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Gerstenfeld 2001	6	21	7	21	0.6%	0.80 [0.22 , 2.97]
Giri 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Gomes 1999	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Greenberg 2000	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Greenberg 2000	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Greenberg 2000	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Gu 2009	3	40	18	48	0.6%	0.14 [0.04 , 0.50]
Guarnieri 1999	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Gun 1998	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Hamid 2008	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Hazelrigg 2004	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Imren 2007	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Ivey 1983	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Lamb 1988	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Lee 2000	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Levy 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Lúcio 2004	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Maras 2001	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Martinussen 1988	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Mitchell 2005	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Nurözler 1996	48	299	89	302	1.2%	0.46 [0.31 , 0.68]
Nygård 2004	1	25	5	25	0.3%	0.17 [0.02 , 1.55]
Paull 1997	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Pfisterer 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Redle 1999	32	126	58	129	1.1%	0.42 [0.25 , 0.71]
Roshanali 2009	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Sezai 2011	8	50	44	50	0.7%	0.03 [0.01 , 0.08]
Vecht 1986	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Weber 1998	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Wenke 1999	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
White 2003	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
Yazicioglu 2002	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
Yazigi 2002	6	40	10	40	0.7%	0.53 [0.17 , 1.63]
Yeatman 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Zangrillo 2005	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Subtotal (95% CI)		**5964**		**6006**	**63.3%**	**0.43 [0.37 , 0.49]**
Total events:	1152		2035			
Heterogeneity: Tau² = 0.23; Chi² = 192.29, df = 81 (P < 0.00001); I² = 58%						
Test for overall effect: Z = 11.32 (P < 0.00001)						
Total (95% CI)		**9008**		**9225**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1612		2965			
Heterogeneity: Tau² = 0.30; Chi² = 339.51, df = 136 (P < 0.00001); I² = 60%						
Test for overall effect: Z = 13.69 (P < 0.00001)						
Test for subgroup differences: Chi² = 8.52, df = 2 (P = 0.01), I² = 76.5%						



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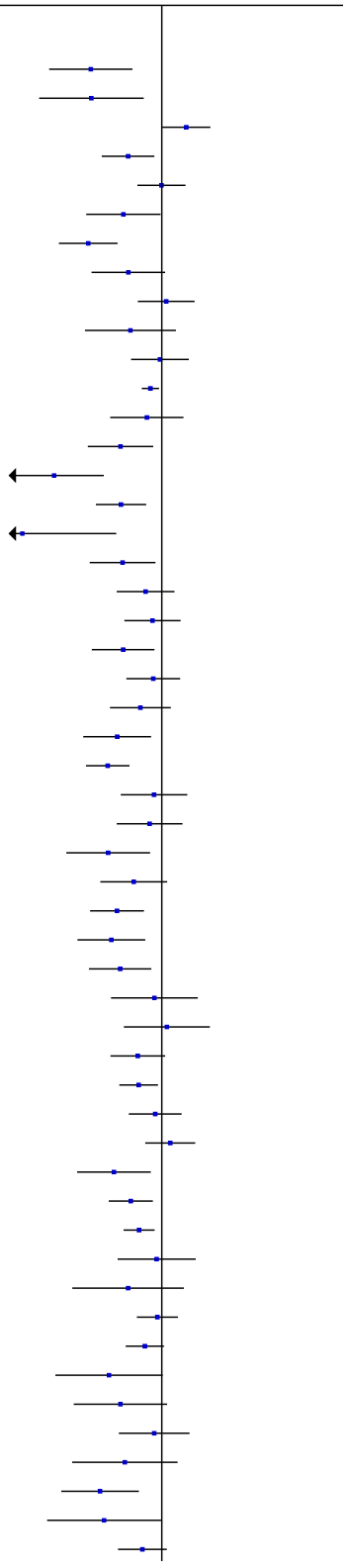
Analysis 7.9. Comparison 7: Risk of Bias Assessment, Outcome 9: All Treatments - Intention-to-treat analysis

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
7.9.1 High Risk						
Avila Neto 2007	3	80	20	80	0.6%	0.12 [0.03 , 0.41]
Babin-Ebell 1996	2	33	13	37	0.4%	0.12 [0.02 , 0.58]
Beaulieu 2010	35	60	24	60	1.0%	2.10 [1.01 , 4.35]
Bert 2001	13	71	23	60	0.9%	0.36 [0.16 , 0.80]
Bert 2001	24	63	23	60	1.0%	0.99 [0.48 , 2.05]
Blommaert 2000	5	48	13	48	0.6%	0.31 [0.10 , 0.96]
Budeus 2006	18	55	45	55	0.8%	0.11 [0.04 , 0.26]
Butler 1993	5	60	12	60	0.7%	0.36 [0.12 , 1.11]
Cagli 2006	16	44	16	48	0.8%	1.14 [0.48 , 2.70]
Casthely 1994	5	105	4	35	0.5%	0.39 [0.10 , 1.53]
Chung 2000a	14	51	14	49	0.8%	0.95 [0.40 , 2.26]
Connolly 2003	156	500	195	500	1.4%	0.71 [0.55 , 0.92]
Crystal 2003	6	36	11	46	0.7%	0.64 [0.21 , 1.93]
Da Silva 2008	7	49	18	49	0.7%	0.29 [0.11 , 0.77]
Dagdelen 2002	2	93	20	55	0.4%	0.04 [0.01 , 0.17]
Daoud 1997	16	64	32	60	0.9%	0.29 [0.14 , 0.62]
Daudon 1986	0	50	20	50	0.2%	0.01 [0.00 , 0.25]
Debrunner 2004	8	40	18	40	0.7%	0.31 [0.11 , 0.83]
Dörge 2000	12	50	17	50	0.8%	0.61 [0.26 , 1.47]
Dörge 2000	14	50	17	50	0.9%	0.75 [0.32 , 1.77]
Ekim 2006	8	50	19	50	0.8%	0.31 [0.12 , 0.80]
England 1992	17	50	20	50	0.9%	0.77 [0.34 , 1.74]
Eslami 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Eslami 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Evrard 2000	16	103	50	103	1.0%	0.19 [0.10 , 0.38]
Fan 2000	12	33	13	31	0.7%	0.79 [0.29 , 2.16]
Fan 2000	12	36	13	31	0.7%	0.69 [0.26 , 1.87]
Fan 2000	4	32	13	31	0.6%	0.20 [0.06 , 0.70]
Fanning 1991	7	49	14	50	0.7%	0.43 [0.16 , 1.18]
Farsak 2002	10	75	28	75	0.9%	0.26 [0.11 , 0.58]
Forlani 2002	6	51	19	50	0.7%	0.22 [0.08 , 0.61]
Forlani 2002	8	54	19	50	0.8%	0.28 [0.11 , 0.73]
Gerstenfeld 1999	6	21	7	21	0.5%	0.80 [0.22 , 2.97]
Gerstenfeld 1999	7	19	7	21	0.5%	1.17 [0.32 , 4.28]
Gerstenfeld 2001	12	58	21	60	0.9%	0.48 [0.21 , 1.11]
Giri 2001	28	120	38	100	1.1%	0.50 [0.28 , 0.89]
Goette 2002	19	51	21	50	0.9%	0.82 [0.37 , 1.82]
Goette 2002	29	60	21	50	0.9%	1.29 [0.61 , 2.75]
Gomes 1999	5	40	17	45	0.7%	0.24 [0.08 , 0.72]
Gu 2009	16	100	36	110	1.0%	0.39 [0.20 , 0.76]
Gun 1998	33	250	58	250	1.2%	0.50 [0.31 , 0.80]
Haddad 2009	8	22	10	25	0.6%	0.86 [0.26 , 2.79]
Hamid 2008	2	53	5	51	0.4%	0.36 [0.07 , 1.95]
Harahsheh 2001	28	88	32	92	1.1%	0.88 [0.47 , 1.63]
Hazelrigg 2004	32	105	41	97	1.1%	0.60 [0.34 , 1.07]
Hohnloser 1991	2	39	8	38	0.4%	0.20 [0.04 , 1.03]
Imren 2007	3	41	8	37	0.5%	0.29 [0.07 , 1.17]
Ivey 1983	7	53	9	56	0.7%	0.79 [0.27 , 2.31]
Jacquet 1994	3	25	5	17	0.4%	0.33 [0.07 , 1.61]
Mulay 1995	4	50	18	50	0.6%	0.15 [0.05 , 0.50]
Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]



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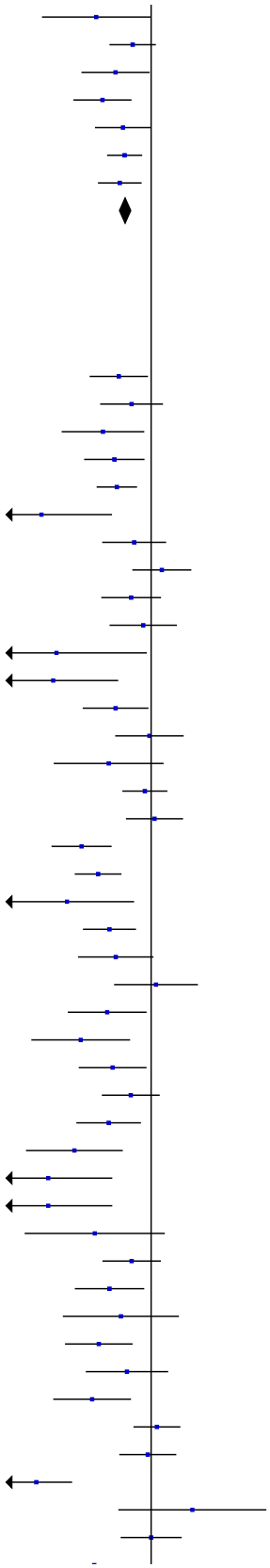
Analysis 7.9. (Continued)

Myhre 1984	2	16	9	20	0.4%	0.17 [0.03 , 0.98]
Najafi 2007	12	166	22	179	1.0%	0.56 [0.27 , 1.16]
Rubin 1987	6	37	15	40	0.7%	0.32 [0.11 , 0.95]
Sezai 2011	7	70	24	70	0.8%	0.21 [0.08 , 0.54]
Stephenson 1980	7	87	24	136	0.8%	0.41 [0.17 , 0.99]
Suttorp 1991	24	150	46	150	1.1%	0.43 [0.25 , 0.75]
Zebis 2007	14	110	32	113	1.0%	0.37 [0.18 , 0.74]
Subtotal (95% CI)		**4046**		**3971**	**43.3%**	**0.44 [0.37 , 0.52]**
Total events:	796		1333			
Heterogeneity: Tau² = 0.22; Chi² = 126.26, df = 56 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 9.20 (P < 0.00001)						
7.9.2 Unclear Risk						
Abel 1983	9	41	22	50	0.8%	0.36 [0.14 , 0.90]
Akbarzadeh 2009	7	70	12	70	0.7%	0.54 [0.20 , 1.46]
Akbarzadeh 2009	3	70	12	70	0.5%	0.22 [0.06 , 0.80]
Alcalde 2006	8	46	19	47	0.8%	0.31 [0.12 , 0.81]
Ali 1997	18	105	40	105	1.0%	0.34 [0.18 , 0.64]
Alves 2007	1	15	14	20	0.2%	0.03 [0.00 , 0.29]
Arbatli 2003	7	54	12	59	0.7%	0.58 [0.21 , 1.61]
Asimakopoulos 1997	13	50	10	50	0.8%	1.41 [0.55 , 3.59]
Assefi 2010	6	67	23	147	0.8%	0.53 [0.21 , 1.37]
Chavan 2010	7	52	9	54	0.7%	0.78 [0.27 , 2.27]
Chavan 2010	0	48	9	54	0.2%	0.05 [0.00 , 0.87]
Janssen 1986	1	41	18	50	0.3%	0.04 [0.01 , 0.35]
Janssen 1986	6	39	18	50	0.7%	0.32 [0.11 , 0.92]
Jensen 1997	10	29	10	28	0.7%	0.95 [0.32 , 2.81]
Kanchi 2004	2	20	6	20	0.4%	0.26 [0.05 , 1.49]
Kaplan 2003	17	100	20	100	1.0%	0.82 [0.40 , 1.68]
Karmy-Jones 1995	12	46	13	54	0.8%	1.11 [0.45 , 2.76]
Khuri 1987	6	67	35	74	0.8%	0.11 [0.04 , 0.28]
Kuralay 1999	11	100	40	100	0.9%	0.19 [0.09 , 0.39]
Lamb 1988	1	30	10	30	0.3%	0.07 [0.01 , 0.58]
Lee 2000	9	74	26	76	0.9%	0.27 [0.11 , 0.62]
Markovic 2010	4	70	11	70	0.6%	0.33 [0.10 , 1.08]
Martinussen 1988	5	35	5	40	0.5%	1.17 [0.31 , 4.42]
Matangi 1989	4	35	12	35	0.6%	0.25 [0.07 , 0.87]
Materne 1985	2	32	15	39	0.4%	0.11 [0.02 , 0.51]
Matsuura 2001	6	40	15	40	0.7%	0.29 [0.10 , 0.86]
Mirkhani 2005	12	40	18	40	0.8%	0.52 [0.21 , 1.31]
Mirkhani 2005	7	40	18	40	0.7%	0.26 [0.09 , 0.72]
Mohr 1981	2	37	19	48	0.4%	0.09 [0.02 , 0.41]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Neto 2007	1	80	20	80	0.3%	0.04 [0.00 , 0.29]
Nurözler 1996	1	25	5	25	0.2%	0.17 [0.02 , 1.55]
Nygård 2004	10	36	20	48	0.8%	0.54 [0.21 , 1.36]
Nyström 1993	5	50	15	51	0.7%	0.27 [0.09 , 0.80]
Oka 1980	2	19	4	17	0.3%	0.38 [0.06 , 2.42]
Orboric 2010	5	55	19	55	0.7%	0.19 [0.06 , 0.55]
Ormerod 1984	4	27	9	33	0.5%	0.46 [0.13 , 1.72]
Ozin 2005	4	35	16	35	0.6%	0.15 [0.04 , 0.53]
Parikka 1993	20	69	18	71	0.9%	1.20 [0.57 , 2.53]
Paull 1997	12	50	13	50	0.8%	0.90 [0.36 , 2.22]
Roshanali 2009	8	50	44	50	0.6%	0.03 [0.01 , 0.08]
Salazar 1979	3	20	1	22	0.2%	3.71 [0.35 , 38.93]
Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]



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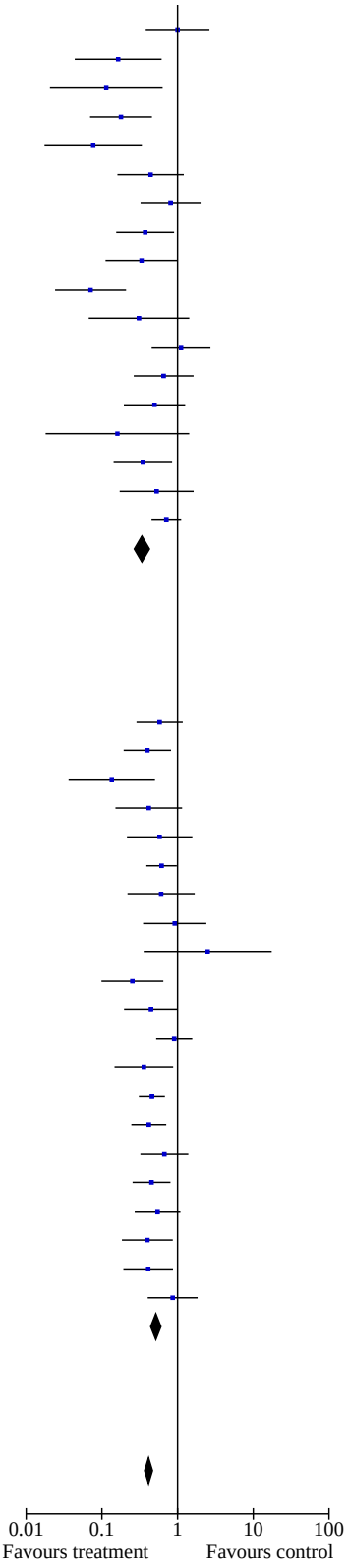
Analysis 7.9. (Continued)

Schweikert 1998	11	43	11	43	0.8%	1.00 [0.38 , 2.63]
Silverman 1982	3	50	14	50	0.5%	0.16 [0.04 , 0.61]
Speziale 2000	2	72	5	25	0.4%	0.11 [0.02 , 0.63]
Tokmakoglu 2002	6	72	31	92	0.8%	0.18 [0.07 , 0.46]
Toraman 2001	2	100	21	100	0.5%	0.08 [0.02 , 0.34]
Treggiari-Venzi 2000	7	49	14	51	0.7%	0.44 [0.16 , 1.21]
Treggiari-Venzi 2000	11	47	14	51	0.8%	0.81 [0.32 , 2.01]
Turk 2007	9	76	18	68	0.8%	0.37 [0.15 , 0.90]
Vecht 1986	5	66	13	66	0.7%	0.33 [0.11 , 1.00]
Wenke 1999	4	100	37	100	0.7%	0.07 [0.02 , 0.21]
White 1984	3	21	7	20	0.4%	0.31 [0.07 , 1.43]
White 2003	14	35	18	48	0.8%	1.11 [0.45 , 2.72]
White 2003	11	39	18	48	0.8%	0.65 [0.26 , 1.63]
Wilkes 2002	11	41	17	40	0.8%	0.50 [0.20 , 1.26]
Williams 1982	1	28	6	32	0.2%	0.16 [0.02 , 1.43]
Yagdi 2003	8	77	20	80	0.8%	0.35 [0.14 , 0.85]
Yazicioglu 2002	6	40	10	40	0.6%	0.53 [0.17 , 1.63]
Yeatman 2002	45	200	58	200	1.2%	0.71 [0.45 , 1.12]
Subtotal (95% CI)		**3245**		**3431**	**37.8%**	**0.34 [0.27 , 0.43]**
Total events:	431		1027			
Heterogeneity: Tau² = 0.47; Chi² = 155.83, df = 59 (P < 0.00001); I² = 62%						
Test for overall effect: Z = 9.22 (P < 0.00001)						
7.9.3 Low Risk						
Auer 2004	25	62	35	65	1.0%	0.58 [0.29 , 1.17]
Auer 2004	20	63	35	65	1.0%	0.40 [0.19 , 0.82]
Greenberg 2000	3	40	18	48	0.5%	0.14 [0.04 , 0.50]
Greenberg 2000	7	35	18	48	0.7%	0.42 [0.15 , 1.15]
Greenberg 2000	8	31	18	48	0.7%	0.58 [0.21 , 1.57]
Guarnieri 1999	56	158	67	142	1.2%	0.61 [0.39 , 0.98]
Hakala 2005	8	41	12	42	0.7%	0.61 [0.22 , 1.68]
Hakala 2005	11	41	12	42	0.8%	0.92 [0.35 , 2.40]
Kurz 1999	5	12	2	9	0.3%	2.50 [0.36 , 17.50]
Levy 2000	7	65	21	65	0.8%	0.25 [0.10 , 0.65]
Lúcio 2004	10	100	20	100	0.9%	0.44 [0.20 , 1.01]
Maras 2001	31	159	33	156	1.1%	0.90 [0.52 , 1.56]
Matangi 1985	8	82	19	82	0.8%	0.36 [0.15 , 0.87]
Mitchell 2005	48	299	89	302	1.3%	0.46 [0.31 , 0.68]
Pfisterer 1997	32	126	58	129	1.2%	0.42 [0.25 , 0.71]
Redle 1999	18	73	23	70	1.0%	0.67 [0.32 , 1.39]
Weber 1998	27	110	46	110	1.1%	0.45 [0.25 , 0.81]
White 2002	16	64	38	100	1.0%	0.54 [0.27 , 1.09]
White 2002	11	56	38	100	0.9%	0.40 [0.18 , 0.86]
Yazigi 2002	12	100	25	100	0.9%	0.41 [0.19 , 0.87]
Zangrillo 2005	16	80	18	80	0.9%	0.86 [0.40 , 1.84]
Subtotal (95% CI)		**1797**		**1903**	**18.8%**	**0.52 [0.44 , 0.60]**
Total events:	379		645			
Heterogeneity: Tau² = 0.00; Chi² = 20.55, df = 20 (P = 0.42); I² = 3%						
Test for overall effect: Z = 8.32 (P < 0.00001)						
Total (95% CI)		**9088**		**9305**	**100.0%**	**0.41 [0.37 , 0.47]**
Total events:	1606		3005			
Heterogeneity: Tau² = 0.25; Chi² = 310.79, df = 137 (P < 0.00001); I² = 56%						
Test for overall effect: Z = 14.46 (P < 0.00001)						
Test for subgroup differences: Chi² = 8.95, df = 2 (P = 0.01), I² = 77.7%						



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ADDITIONAL TABLES

Table 1. Potential adverse events associated with interventions for prevention of post-operative atrial fibrillation

Intervention	Potential Adverse Events (% incidence)
Pharmacological Interventions	
Amiodarone	- Serum creatinine increase (93%) - Hypotension (16%) - Phlebitis of administration site (not defined) - Ventricular arrhythmias (2%-5%) - Hepatotoxicity (3%-20%)
Beta-blockers	- Bradycardia (3%) - Hypotension (1%) - Exacerbation of decompensated congestive heart failure (< 1%) - Bronchospasm (rare)
Sotalol	- Dyspnea (21%) - Bradycardia (16%) - Hypotension (6%) - Torsades de pointes or new ventricular arrhythmia (4% in patients with supraventricular arrhythmia)
Magnesium	- Hypotension (rare)
Non-Pharmacological Interventions	
Atrial Pacing	- Atrial irritability (not defined)
Posterior Pericardiotomy	- Not defined

Table 2. Country of origin of included trials

Country	Number of Trials
Austria	1
Belgium	4
Brazil	7
Canada	7
China	2

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Table 2. Country of origin of included trials *(Continued)*

Denmark	4
Finland	2
France	1
Germany	6
India	2
Iran	6
Israel	1
Italy	3
Japan	2
Jordan	1
Lebanon	1
Netherlands	2
New Zealand	1
Norway	1
Pakistan	1
Serbia	2
Sweden	1
Switzerland	5
Taiwan	1
Turkey	15
UK	9
USA	29
Yugoslavia	1

APPENDICES

Appendix 1. CENTRAL Search Strategy

1. MeSH descriptor Atrial Fibrillation explode all trees
2. MeSH descriptor Atrial Flutter explode all trees

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3. MeSH descriptor Tachycardia, Supraventricular explode all trees
4. atrial NEAR/ fibrillat*
5. atrial NEAR/ flutter*
6. auricular* NEAR/ fibrillat*
7. auricular* NEAR/ flutter*
8. atrium NEAR/ fibrillat*
9. atrium NEAR/ flutter*
10. tachycardia NEAR/ supraventricular
11. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)
12. MeSH descriptor Cardiac Surgical Procedures explode all trees
13. heart NEAR/ surg*
14. cardiac NEAR/ surg*
15. coronary NEAR/ surg*
16. coronary NEAR/ bypass
17. CABG
18. valv* NEAR/ surg*
19. valv* NEAR/ replace*
20. (#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19)
21. (#11 AND #20)

Appendix 2. CINAHL Search Strategy

1. (MH "Atrial Fibrillation")
2. (MH "Atrial Flutter")
3. atrial N5 fibrillat*
4. atrial N5 flutter*
5. auricular* N5 fibrillat*
6. auricular* N5 flutter*
7. atrium N5 fibrillat*
8. atrium N5 flutter*
9. (MH "Tachycardia, Supraventricular")
10. tachycardia N5 supraventricular
11. S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10
12. (MH "Surgery, Cardiovascular")
13. heart N5 surg*
14. cardiac N5 surg*
15. coronary N5 surg*

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16. coronary N5 bypass

17. CABG

18. valv* N5 surg*

19. valv* N5 replace*

20. S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19

21. S11 and S20

Appendix 3. EMBASE Search Strategy

RCT Search Filter:

1. random*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

2. factorial*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

3. (crossover* or cross-over*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

4. placebo*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

5. (doubl* adj blind*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

6. (singl* adj blind*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

7. assign*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

8. allocat*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

9. volunteer*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

10. crossover procedure.sh.

11. double-blind procedure.sh.

12. randomized controlled trial.sh.

13. single-blind procedure.sh.

14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

Search:

15. heart atrium fibrillation/

16. heart atrium flutter/

17. (atrial adj6 fibrillat*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

18. (atrial adj6 flutter*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

19. (auricular* adj6 fibrillat*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

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20. (auricular* adj6 flutter*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

21. (atrium adj6 fibrillat*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

22. (atrium adj6 flutter*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

23. supraventricular tachycardia/

24. (tachycardia adj6 supraventricular).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

25. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24

26. exp heart surgery/

27. (heart adj6 surg*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

28. (cardiac adj6 surg*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

29. (coronary adj6 surg*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

30. (coronary adj6 bypass).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

31. CABG.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

32. (valv* adj6 surg*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

33. (valv* adj6 replace*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer]

34. 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33

35. 14 and 25 and 34

Appendix 4. MEDLINE Search Strategy

RCT Search Filter:

1. randomized-controlled-trial.pt.

2. Randomized Controlled Trial/

3. Random Allocation/

4. Double-Blind Method/

5. Single-Blind Method/

6. 1 or 2 or 3 or 4 or 5

7. limit 6 to humans

8. clinical trial.pt.

9. exp Clinical Trial/

10. (clin* adj5 trial*).ti,ab.

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11. ((singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

12. ((singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)).ti,ab.

13. Placebos/

14. placebo*.ti,ab.

15. random*.ti,ab.

16. Research Design/

17. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16

18. limit 17 to humans

19. exp Evaluation Studies/

20. Follow-Up Studies/

21. Prospective Studies/

22. (control* or prospectiv* or volunteer*).mp,ti,ab.

23. 18 or 19 or 20 or 21 or 22

24. limit 23 to humans

25. 7 or 18 or 24

Search:

26. Atrial Fibrillation/

27. Atrial Flutter/

28. (atrial adj5 fibrillat*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

29. (atrial adj5 flutter*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

30. (auricular* adj5 fibrillat*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

31. (auricular* adj5 flutter*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

32. Tachycardia, Supraventricular/

33. (tachycardia adj5 supraventricular).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

34. 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33

35. Cardiac Surgical Procedures/

36. (heart adj5 surg*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

37. (cardiac adj5 surg*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

38. (coronary adj5 surg*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

39. (coronary adj5 bypass).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

40. CABG.mp.

41. (valv* adj5 surg*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

42. (valv* adj5 replace*).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

43. 35 or 36 or 37 or 38 or 39 or 41 or 42

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44. 34 and 43

45. 25 and 44

WHAT'S NEW

Date	Event	Description
31 March 2021	Review declared as stable	This review question is considered low priority for the current scope of Cochrane Heart.

HISTORY

Protocol first published: Issue 2, 2002
Review first published: Issue 4, 2004

Date	Event	Description
30 October 2012	New citation required but conclusions have not changed	Increased evidence has lead to an improved estimated efficacy for both amiodarone and atrial pacing in preventing atrial fibrillation. Though the summary estimate for all interventions in relation to stroke still did not reach statistical significance, it is clearer from this updated review that there is a trend towards the protective effects of prophylaxis. Finally, additional evidence allowed this review to confirm the hypothesis of the previous version's authors that intervention in this setting leads to a decreased cost of hospital stay. No major changes to the conclusions were made.
30 July 2011	New search has been performed	We reran the search strategy up to July 2011. Two additional interventions, magnesium and posterior pericardiotomy, were included due to their significant presence within the literature. Three studies that were awaiting assessment (Gerstenfeld 2001; Matsuura 2001; White 2002) and two that were excluded (Kurz 1999; Tokmakoglu 2002) in the original review were included. Twenty-one additional studies from the time period covered in the original literature search were identified, The background section was updated. The methodology section was updated to include the 'Risk of bias' assessment suggested in the Cochrane Handbook and sensitivity analyses on this assessment.

CONTRIBUTIONS OF AUTHORS

Kyle Arsenault

- Protocol preparation

- Search strategy development and initiation

- Study selection

- Obtaining copies of studies

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- Data extraction

- Data analysis and interpretation

- Manuscript preparation

- Final editing

Arif Yusuf

- Study selection

- Obtaining copies of studies

- Data extraction

- Final editing

Eugene Crystal

- Original review

- Final editing

Carlos Morillo

- Protocol preparation

- Data interpretation

- Final editing

Jeff Healey

- Data interpretation

- Final editing

Girish Nair

- Data interpretation

- Final editing

Richard Whitlock

- Lead research effort

- Protocol preparation

- Data interpretation

- Manuscript preparation

- Final editing

DECLARATIONS OF INTEREST

The authors have no declarations of interest.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

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External sources

- Beamish Family Foundation Chair in Vascular Surgery, Canada

  Kyle Arsenault was supported by the Beamish Family Foundation Chair in Vascular Surgery, held by Dr. Jacques G. Tittley

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Two additional interventions, magnesium and posterior pericardiotomy, were included due to their significant presence within the literature.

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenergic beta-Antagonists [therapeutic use]; Amiodarone [therapeutic use]; Anti-Arrhythmia Agents [therapeutic use]; Atrial Fibrillation [*prevention & control]; Cardiac Pacing, Artificial; Cardiac Surgical Procedures [*adverse effects]; Magnesium Compounds [therapeutic use]; Pericardiectomy [methods]; Randomized Controlled Trials as Topic; Sotalol [therapeutic use]; Tachycardia, Supraventricular [*prevention & control]

MeSH check words

Adult; Humans

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