Authors' objectives
To assess the efficacy of peri-operative beta-blockade in reducing myocardial ischaemia, myocardial infarction, and cardiac or all-cause mortality.

Searching
MEDLINE was searched from 1980 for articles published in the English language using the following MeSH terms: 'perioperative care', 'postoperative complications', 'adrenergic antagonists', 'adrenergic beta-blockade', 'myocardial ischaemia', 'myocardial infarction', 'mortality' and 'heart disease mortality'. These terms were combined with key title words related to peri-operative cardiac complications and adrenergic blockade. The reference lists from all relevant articles and publications for peri-operative cardiac risk management were examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible.

Specific interventions included in the review
Administrations of peri-operative beta-blockers were eligible. The beta-blockers included were:

- atenolol, 5 to 10 mg intravenously before and after surgery and 50 to 100 mg/day orally throughout the hospital stay;
- bisoprolol, 5 to 10 mg/day orally begun on average 37 days pre-operatively and continued for 30 days post-operatively;
- esmolol, either intravenously for 48 hours post-operatively or intravenously within 1 hour after surgery, and changed to metoprolol on the first post-operative morning; and
- labetalol (100 mg), oxprenolol (20 mg) or atenolol (50 mg), all given orally before and after induction of anaesthesia.

In all studies, the dose was titrated to a target heart rate; the target heart rate, where stated, ranged from 50 to less than 80 beats per minute.

Participants included in the review
Patients in the peri-operative period were eligible. The participants in the review included patients who met extensive study-specific clinical criteria, had positive tests on dobutamine echocardiography, had ischaemia on the Holter monitor, and had untreated hypertension. The participants were undergoing elective noncardiac surgery; elective abdominal aortic, infra-inguinal or carotid arterial surgery; and elective knee arthroplasty. Some studies included patients who were already being treated with beta-blockers, while others excluded this group of patients.

Outcomes assessed in the review
Studies that reported on peri-operative myocardial ischaemia, myocardial infarction, and mortality were eligible. Peri-operative myocardial ischaemia was assessed in one study using Holter monitoring.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Validity was assessed using the following criteria: the degree of blinding; baseline comparability of the treatment groups; completeness of follow-up; and important confounders or biases. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The information tabulated in the review included: author and year of publication; the inclusion and exclusion criteria for the participants; beta-blocker regimen; target heart rate (if set); and findings.

Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Differences were discussed in the text of the review, with particular reference to the differences in baseline cardiac risk between the studies.

Results of the review
Five RCTs (586 patients) were included.

Peri-operative ischaemia (4 RCTs). Three of the four RCTs found a statistically-significant reduction in peri-operative ischaemia among the patients treated with beta-blockers. The number-needed-to-treat ranged from 2.5 to 6.7. The fourth study found a non significant reduction in ischaemia in the treated group. It also reported a lower rate of ischaemia in the control group of 15%, compared with rates ranging from 28 to 73% in the control groups of studies finding a statistical difference.

Cardiac events and mortality (4 RCTs).

The number-needed-to-treat, where reported, ranged from 3.2 to 8.3.

One RCT involved 200 male veterans at risk of cardiac disease who were undergoing major noncardiac surgery. This study found no statistically-significant difference in the in-hospital cardiac or mortality, but found a relative reduction in all-cause mortality at 2 years in the treated group (2-year mortality was 9% versus 21%; p=0.02). These differences did not influence the results when adjusting for baseline differences between the treatment groups. Another RCT involved 112 high-risk patients undergoing vascular surgery. This study found that beta-blockade was associated with a significant reduction in peri-operative cardiac death (3.4% versus 17%; p=0.02) and nonfatal myocardial infarction (0% versus 17%; p<0.001). A further RCT involved 128 untreated hypertensive patients undergoing elective surgery; 30% of the patients in both treatment groups were already on beta-blockers. This study found that beta-blockade was associated with a reduction in post-operative myocardial infarction (2% versus 28%; p<0.001). The duration of follow-up was stated as being shorter than that for the other studies but no values were specified.

The fourth RCT involved 120 patients undergoing elective knee arthroplasty. This found no statistically-significant difference between the treatment groups in terms of the rates of post-operative myocardial infarction (2% versus 6%).

Authors' conclusions
Despite the heterogeneity of the trials, the growing amount of literature suggests a benefit for beta-blockade in preventing cardiac morbidity. Evidence from these trials can also be used to formulate an effective clinical approach while definitive trials are awaited.
CRD commentary
The aims were clearly stated and the inclusion criteria were defined in terms of the study design, intervention and outcomes. The methods used to determine ischaemia in the primary studies were not routinely described. By restricting the literature search to English language studies identified in one database, other relevant studies may have been omitted. In addition, the lack of an attempt to locate unpublished material raises the possibility of publication bias.

The methods used to select the studies were not described. The included studies were restricted to RCTs that were presumably placebo-controlled, although the control group was not explicitly specified a priori. Several aspects of validity were assessed and discussed in the text, and relevant data were extracted and tabulated clearly. However, the methods used to assess validity and extract the data were not described. It was not reported whether the analysis was conducted on an intention to treat basis.

A narrative synthesis was appropriate given the small number of studies in populations at varying risk of cardiac events. Potential causes of differences in the results between the studies were discussed.

The evidence presented appears to support the authors’ conclusions, although only one study appears to have reported follow-up beyond the in-hospital period.

Implications of the review for practice and research
Practice: The authors state that the review suggests the use of peri-operative beta-blockers is associated with significant reductions in cardiac morbidity and mortality. They went on to state that the studies included a relatively small number of patients (less than 700) who were selected and not consecutively enrolled, making generalisability to other populations uncertain.

Research: The authors state that large randomised trials in unselected populations are required. They also state that future research should address: the optimal duration of therapy; the identification of those populations in which beta-blockade is cost-effective; and the development of new peri-operative risk-management algorithms.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.