National Institute for Health and Care Excellence

Draft for consultation

Abdominal aortic aneurysm: diagnosis and management

Evidence review J: Pre- and postoperative interventions to optimise outcomes after abdominal aortic aneurysm repair

NICE guideline <number>

Evidence reviews

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Pre- and postoperative interventions to optimise outcomes after abdominal aortic aneurysm repair

Review questions

What preoperative interventions are effective in optimising surgical outcome in people undergoing surgical repair of an unruptured abdominal aortic aneurysm?

What post-operative interventions are effective in reducing the risk of complications after surgical repair of an abdominal aortic aneurysm, as well as optimising postoperative outcomes and survival?

Introduction

These review questions aim to determine which interventions can be used preoperatively to 'optimise' surgical outcome; and to identify which post-operative interventions are effective in reducing the risk of further aneurysm growth or rupture, cardiovascular events, wound-related complications and graft-related complications (including endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion).

PICO tables:

Table 1: Inclusion criteria for preoperative interventions to optimise outcomes after AAA repair

Parameter	Inclusion criteria
Population	People with a confirmed unruptured abdominal aortic aneurysm (AAA) in whom surgery is planned
Interventions	Statins Beta-blockers Tranexamic acid Antiplatelet therapy Iron supplementation Coronary artery revascularisation Supervised exercise program Ischaemic preconditioning Respiratory training, including incentive spirometry and smoking cessation therapy
Comparators	Placebo, no intervention or each other
Outcomes	Mortality Peri- and post-operative complications Adverse effects of intervention Quality of life Resource use, including length of hospital or intensive care stay, and costs

Table 2: Inclusion criteria for postoperative interventions to optimise outcomes after AAA repair

Parameter	Inclusion criteria
Population	People who have undergone surgical repair of an AAA
Interventions	Surgical intervention Antifibrinolytic therapy with tranexamic acid Antiplatelet therapy (aspirin, clopidogrel, ticlopidine, cilostazol, prasugrel, ticagrelor, or any other antiplatelet drugs) Antihypertensive drugs (calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers (β-blockers; e.g. metoprolol, propranolol), angiotensin-II receptor antagonists, thiazide/ thiazide-like diuretics, or any other antihypertensive drugs) Lipid-lowering therapy (statins (simvastatin, pravastatin, atorvastatin)) Antibiotics (doxycycline, roxithromycin, azithromycin) Diabetic control, including metformin COPD control Smoking cessation Physical therapy/exercise Diet Weight control Control of alcohol consumption
Comparators	Placebo, no intervention or each other
Outcomes	Incidence of complications (AAA rupture, AAA growth/expansion, cardiovascular events, wound-related complications, endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion) Need for further surgical intervention Mortality (all-cause; AAA-related; cardiovascular; survival) Cardiovascular events Quality of life Adverse effects Resource use and cost

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

A 'bulk' search strategy was used to cover review questions relating to pre- and postoperative interventions. Two searches were performed to identify studies that assessed the efficacy of interventions that could potentially be used to improve outcomes of surgical repair of AAAs. The first literature search used a randomised controlled trial (RCT) and systematic review (SR) filter while the second search used an observational study filter to identify potentially relevant studies.

The reviewer sifted the RCT database first to identify systematic reviews, RCTs or quasi-randomised controlled trials exploring the efficacy of preoperative interventions for improving outcomes in people who were due to undergo elective surgical repair of unruptured AAAs, or postoperative interventions for improving outcomes in people who underwent elective AAA surgery. Studies were included if they met the set of criteria outlined in Tables 1 and 2 (the full protocol is available in Appendix A). If limited evidence was available from systematic reviews, RCTs or quasi-randomised controlled trials, the observational study database was sifted to identify potentially relevant non-randomised controlled trials.

Studies were excluded if they were not:

- were not in English
- were not full reports of the study (for example, published only as an abstract)
- were not peer-reviewed

Clinical evidence

Included studies

Preoperative interventions

From an initial RCT database of 916 abstracts, 24 were identified as being potentially relevant. Following full-text review of these articles, 8 studies were included. Additionally 1 study was identified via examination of the bibliography of an excluded systematic review. From an initial observational study database of 1,216 abstracts, 3 were identified as being potentially relevant. Following full-text review of these articles, no studies were included.

Update searches were conducted in December 2017, to identify any relevant studies published during guideline development. The update RCT and observational study databases contained 70 and 80 abstracts, respectively. Two abstracts from the RCT database and no abstracts from the observational study were considered potentially relevant. Following full text review of the 2 potentially relevant articles, 1 study was included

Overall, 10 studies were included in the evidence review for this review question.

Postoperative interventions

From the RCT database of 916 abstracts, 15 were identified as being potentially relevant. Following full-text review of these articles, 2 studies were included. From the observational study database of 1,216 abstracts, 2 were identified as being potentially relevant. Following full-text review of these articles, no studies were included.

Update searches were conducted in December 2017, to identify any relevant studies published during guideline development. The update RCT and observational study databases contained 70 and 80 abstracts, respectively. No abstracts from either database were considered potentially relevant, and no additional studies were included.

Overall, 2 studies were included in the evidence review for this review question.

Excluded studies

The list of papers excluded at full-text review, with reasons, is given in Appendix H.

Summary of clinical studies included in the evidence review

A summary of the included studies is provided in the tables below.

Preoperative interventions

Table 2: Beta-blockers

Study	Details
Yang H, Raymer K, Butler R, Parlow J, Roberts R. (2006) The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 152(5):983-90	Study design: randomised, placebo-controlled, double-blind trial Location(s): Canada Population: people undergoing elective abdominal aortic surgery (no additional details were provided) Sample size: 496; 76% (377/496) male Follow-up: 30 months Intervention: 25 to 100 mg of oral or intravenous metoprolol, administered 2 hours before and after surgery, then continued for 5 days or until hospital discharge. Comparators: matched placebo Outcomes: the primary outcome was the composite rate of cardiac death, myocardial infarction, congestive heart failure, unstable angina, dysrhythmia requiring treatment, and non-cardiac death at 6 month follow-up. Individual rates were also reported at 30-day follow-up. Secondary outcomes included the need for reoperation, cerebrovascular accidents, new or worsened renal insufficiency, rehospitalisation, and intraoperative adverse events.

Table 3: Exercise

Study	Details
Barakat H M, Shahin Y, Khan J A et al. (2016) Preoperative supervised exercise improves outcomes after elective abdominal aortic aneurysm repair. Annals of Surgery 264, 47-53	Study design: randomised, non-blinded trial Location(s): UK Population: people with AAAs undergoing elective EVAR or open surgical repair Sample size: 124; 89.5% (111/124) male Follow-up: 3 months Intervention: hospital-based exercise classes Comparators: no exercise Outcomes: the primary outcome was the composite rate of cardiac, pulmonary, and renal complications. Secondary outcomes included length of stay, APACHE II scores, occurrence of systematic inflammatory response syndrome, mortality, and bleeding requiring reoperation or transfusion.
Dronkers J, Veldman A, Hoberg E et al. (2008) Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. Clinical rehabilitation 22, 134-42	Study design: randomised, single-blind trial Location(s): Netherlands Population: people with AAAs undergoing elective surgical repair (not specified) who were considered to have a high risk of pulmonary complications Sample size: 20; 20% (5/15) male Follow-up: 7 days

Study	Details
	Intervention: inspiratory muscle training Comparators: no exercise Outcomes: incidence of atelectasis, patient satisfaction, and respiratory function
Tew GA, Batterham AM, Colling K, et al. (2017) Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. The British journal of surgery 104(13), 1791-1801	Study design: randomised, single-blind trial Location(s): UK Population: people with unruptured AAAs between 5.5 and 7.0 cm in diameter who were due to undergo elective EVAR or open surgical repair Sample size: 53; 94.3% (50/53) male Follow-up: 12 weeks Intervention: High intensity interval training Comparators: no exercise Outcomes: adverse events, length of stay, and quality of life

83 **Table 4: Remote ischaemic preconditioning (RIPC)**

Study	Details
Ali ZA, Callaghan CJ, Lim E et al. (2007) Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation 116, I98-105	Study design: randomised, double-blind trial Location(s): UK Population: people with AAAs undergoing elective open surgical repair Sample size: 82; 93% (76/82) male Follow-up: 7 days Intervention: lower limb RIPC Comparators: conventional open surgical repair without RIPC Outcomes: length of stay, mortality, myocardial injury, myocardial infarction, renal impairment, and adverse events
Li C, Li YS, Xu M et al. (2013) Limb remote ischemic preconditioning for intestinal and pulmonary protection during elective open infrarenal abdominal aortic aneurysm repair: a randomized controlled trial. Anesthesiology 118, 842-52	Study design: randomised, double-blind trial Location(s): China Population: people with AAAs undergoing elective open surgical repair Sample size: 62; 90.1% (55/61) male Follow-up: 24 hours Intervention: upper limb RIPC Comparators: sham RIPC Outcomes: the primary outcomes were haemodynamic data and variables reflecting lung function. Secondary outcomes included mortality, ventilator support time, ICU- and hospital-free days; new arrhythmia, perioperative myocardial infarction, diagnosis of congestive heart failure, symptoms and signs of pulmonary congestion, neurologic events, upper limb ischemia requiring intervention, intestinal injury markers, markers of oxidative stress and systemic inflammatory response, and scores of the severity of intestinal and pulmonary injury.
Mouton R, Pollock J, Soar J et al. (2015) Remote ischaemic preconditioning versus sham	Study design: randomised, double-blind trial Location(s): UK

Study	Details
procedure for abdominal aortic aneurysm repair: an external feasibility randomized controlled trial. Trials 16, 377	Population: people with AAAs undergoing elective EVAR or open surgical repair. Sample size: 69; sex-specific proportions were not reported. Follow-up: 48 hours Intervention: upper limb RIPC Comparators: sham RIPC Outcomes: acute kidney injury scores as classified by the acute injury network (AKIN), mortality, myocardial infarction, new postoperative ECG changes, new arrhythmia, troponin T levels above 14 ng/L, and adverse events
Murphy N, Vijayan A, Frohlich S et al. (2014) Remote ischemic preconditioning does not affect the incidence of acute kidney injury after elective abdominal aortic aneurysm repair. Journal of cardiothoracic and vascular anaesthesia 28, 1285-92	Study design: randomised, double-blind trial Location(s): UK Population: people with AAAs undergoing elective open surgical repair Sample size: 62; 85.5% (53/62) male Follow-up: 3 days Intervention: upper limb RIPC Comparators: sham RIPC Outcomes: mortality, kidney injury (measured by creatinine levels and AKIN scores), myocardial infarction, and length of hospital stay
Walsh SR, Boyle JR, Tang TY et al. (2009) Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 16, 680-9	Study design: randomised, non-blinded trial Location(s): UK Population: people with AAAs undergoing elective open surgical repair Sample size: 40 men Follow-up: 48 hours Intervention: lower limb RIPC Comparators: conventional open surgical repair without RIPC Outcomes: the primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and creatinine levels). Secondary outcomes included 30-day mortality, myocardial infarction, arrhythmia, congestive heart failure, pneumonia, renal failure, lower limb ischaemia requiring intervention, and postoperative length of stay.
Walsh SR, Sadat U, Boyle JR et al. (2010) Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vascular and endovascular surgery 44, 334-40	Study design: randomised, non-blinded trial Location(s): UK Population: people with AAAs undergoing elective EVAR Sample size: 40; 85% (34/40) male Follow-up: 48 hours Intervention: lower limb RIPC Comparators: conventional open surgical repair without RIPC. Outcomes: the primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and serum creatinine levels). Secondary outcomes included serum troponin levels

Study	Details
	and the incidence of major adverse cardiac events (cardiac arrest, cardiac death, cardiac failure, unstable angina, or myocardial infarction).

Postoperative interventions

Table 5: Doxycycline

Study	Details
Hackmann AE, Rubin BG, Sanchez LA et al. (2008) A randomized, placebo-controlled trial of doxycycline after endoluminal aneurysm repair. Journal of vascular surgery 48, 519-526	Study design: randomised, placebo-controlled, double-blind trial Location(s): USA Population: people with AAAs undergoing elective EVAR Sample size: 59; sex-specific proportions not reported Follow-up: 6 months Intervention: doxycycline 100 mg b.i.d Comparators: matched placebo Outcomes: aneurysm diameter, graft migration, incidence of endoleak, adverse events

Table 6: Physiotherapy plus walking exercises

Study	Details
Wnuk BR, Durmala J, Ziaja K et al. (2016) A Controlled Trial of the Efficacy of a Training Walking Program in Patients Recovering from Abdominal Aortic Aneurysm Surgery. Advances in clinical and experimental medicine : official organ Wroclaw Medical University 25, 1241-1371	Study design: randomised, single-blind trial Location(s): Poland Population: people with AAAs undergoing surgical repair (type not specified) Sample size: 65 males Follow-up: 2 years Intervention: basic physiotherapy plus backward or forward walking exercises Comparators: basic physiotherapy-alone Outcomes: 6-minute walking test distance, walking speed, spirometry measurements (FVC, FEV1, FEV1/FVC and PEF), length of hospital stay

See Appendix D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

See Appendix F for full GRADE tables, highlighting the quality of evidence from the included studies.

Economic evidence

Included studies

A literature search was conducted jointly for all review questions by applying standard health economic filters to a clinical search for AAA. This search returned a total of 5,173 citations. Following review of all titles and abstracts, no studies were identified as being potentially relevant to these review questions.

An update search was conducted in December 2017, to identify any relevant health economic analyses published during guideline development. The search found 814 abstracts; all of which were not considered relevant to this review. As a result no additional studies were included.

Excluded studies

No studies were retrieved for full-text review.

Evidence statements

Preoperative interventions

Beta-blockers

- Moderate- to high-quality evidence from 1 RCT, including 496 people who underwent elective AAA repair (type not specified), found higher rates of intraoperative hypotension and bradycardia requiring treatment in people who received preoperative beta-blockers compared with those who received placebo.
- Low-quality evidence from 1 RCT, including 496 people who underwent elective AAA repair (type not specified), could not differentiate between rates of cardiac-related mortality, non-cardiac-related mortality, unstable angina, myocardial infarction, congestive heart failure, postoperative cardiovascular accident, dysrhythmia, new or worsened renal insufficiency, and the need for reoperation in people who received preoperative beta-blockers compared with those who received placebo.

Exercise

- Low-quality evidence from 1 RCT, including 20 people who underwent elective AAA repair (type not specified), could not differentiate between atelectasis rates of people who had been performing inspiratory muscle training during the 2 weeks preceding surgery and those who had not been doing any training.
- Moderate-quality evidence from 1 RCT, including 124 people who underwent elective EVAR, indicated that cardiac complications and renal complications were less likely to occur in people who participated in preoperative hospital-based exercise classes compared with those who had not. Low-quality evidence from the same trial could not differentiate between rates of all-cause mortality, pulmonary complications, postoperative bleeding or the need for a blood transfusions of more than 4 units, and the need for reoperation between people who participated in preoperative hospital-based exercise classes and those who did not.
- Low- to moderate-quality evidence from 1 RCT, including 53 people who underwent elective EVAR or open surgical repair, could not differentiate preoperative dizziness, preoperative angina, and postoperative quality of life between people who participated in preoperative hospital-based exercise classes and those who did not.

Remote ischaemic preconditioning

- Low-quality evidence from 5 RCTs, including 273 people who underwent elective EVAR or open AAA repair, found higher rates of arrhythmia in people who received remote ischaemic preconditioning before surgery compared with those who received no preconditioning.
- Very low- to low-quality evidence from up to 6 RCTs, including 355 people who underwent elective EVAR or open AAA repair, could not differentiate rates of 30-day mortality, myocardial infarction, congestive heart failure, renal impairment or

failure, acute kidney injury, and rates of any type of complication between people who did and did not receive remote ischaemic preconditioning.

Postoperative interventions

Doxycycline versus placebo

- Very low-quality evidence from 1 RCT, including 27 people with AAAs who underwent elective EVAR, could not differentiate mean percentage changes in aneurysm diameters between people who received doxycycline after surgery and those who did not.
- Very low-quality evidence from 1 RCT, including 48 people who underwent elective EVAR of AAAs, could not differentiate endoleak and graft migration rates between people who received doxycycline after surgery and those who did not.

Physiotherapy plus walking exercises versus physiotherapy-alone

- Very low-quality evidence from 1 RCT, including 47 people who underwent elective AAA repair (type not specified) of AAAs, could not differentiate the average length of hospital stay between people who received postoperative physiotherapy plus forward or backward walking exercises and people who received physiotherapy-alone.

Recommendations

J1. Offer people with an AAA information, support and interventions for secondary prevention of cardiovascular disease. For more information refer to the NICE guidance on:

- stop smoking interventions and services
- diet, weight management and exercise
- medicines optimisation
- lipid modification and statin therapy
- diabetes management
- hypertension diagnosis and management
- antiplatelet therapy.

J2. Do not routinely start beta blockers immediately before surgery for people having AAA repair.

J3. Do not offer remote ischaemic preconditioning to people having AAA repair.

J4. For guidance on preventing and treating surgical site infections and on preventing venous thromboembolism, see the NICE guidelines on surgical site infections and reducing the risk of venous thromboembolism.

Research recommendations

Preoperative interventions

RR4. What is the clinical effectiveness and cost effectiveness of preoperative exercise programmes for improving outcomes of people who are having AAA repair?

Postoperative interventions

RR5. What are the benefits of postoperative use of Direct Oral Anticoagulants (DOACS) for improving outcomes after repair of AAA?

Rationale and impact

Why the committee made the recommendations

The committee made a recommendation on cardiovascular disease because it is common in people with AAA and it is best practice to reduce the risk of problems in people who have it.

The evidence showed that giving beta blockers just before surgery does not help, and that they cause problems such as low blood pressure and a slow heartbeat. The committee noted that some people with AAA may need to take beta blockers for other conditions (such as atrial fibrillation). As a result, they recommended against routine acute use before AAA repair, rather than recommending against beta blockers altogether.

Remote ischaemic preconditioning was not recommended because there was evidence that it does not improve outcomes and that it can cause problems such as an irregular heartbeat.

The committee recommended further research because there was not enough evidence to make recommendations on exercise programmes before surgery, or on any interventions after AAA repair.

Impact of the recommendations on practice

Providing support to reduce the risk of problems from cardiovascular disease is already current practice. In addition, beta blockers and routine ischaemic preconditioning are not currently in routine use before AAA repair, so these recommendations should have a minimal impact on practice.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

In relation to preoperative interventions, the outcomes that matter most are perioperative morbidity and mortality. With regards to postoperative interventions, the outcomes which matter most are postoperative morbidity and mortality, and the need for re-intervention.

The quality of the evidence

The committee considered that the identified evidence on preoperative exercise interventions was not robust enough to support a recommendation. Although the identified evidence for most outcomes were graded as being low-to-moderate in quality, the committee felt that the small sample sizes of included studies and relatively short follow-up periods precluded confidence in the reported outcomes. In relation to beta-blockers and RIPC, the committee considered that the evidence was of sufficient quality to draft recommendations.

This review excluded evidence on pre- and postoperative interventions for heterogeneous groups of people with vascular diseases who were treated by different types of surgical and non-surgical interventions, including AAA repair. It was noted that excluded studies did not report what proportions of people received AAA surgery or did not stratify analyses according to type of intervention received. As a result, the committee felt that this type of evidence could not be considered because of uncertain applicability to people with AAA.

The committee noted the existence of specialist society (Vascular Society of Great Britain and Ireland) guidelines related to AAA repair. It was noted that some of the recommendations in these guidelines relating to preoperative interventions were not based on evidence specific to people with AAA. The committee took these recommendations into account but refrained from cross-referring to specific recommendations.

With respect to postoperative interventions, the committee considered that the identified evidence was limited in both quantity and quality. The two identified studies were graded as very low to low in quality and indicated that postoperative use of doxycycline and physiotherapy plus walking exercises had no impact on the incidence of postoperative complications. As a result, the committee decided not to make any recommendations regarding these interventions.

Benefits and harms

The committee recognised that most people with AAA are likely to be older people with some form of cardiovascular disease. With this in mind the committee believed that optimisation of pre-existing medical conditions and minimisation of cardiovascular risks would increase the general health of people with AAA, leading to reduced postoperative morbidity and mortality. As a result, the committee felt that general principles of secondary prevention of cardiovascular disease, as outlined in other NICE guidelines, were applicable. The committee also agreed that it is important to reduce the risks of surgical site infections and venous thromboembolism in all people undergoing AAA repair. As result, recommendations were drafted cross-referring to other NICE guidance.

The committee agreed that the evidence on beta-blockers was clear that de novo beta-blockade in the immediate preoperative period was not effective and was potentially harmful. It was also considered that the evidence on beta-blockers in relation to AAA repair was consistent with broader evidence on the use of beta-blockade in other surgical cohorts, including people undergoing other types of vascular surgery. The committee felt that use of the word “routinely” allowed scope for clinician discretion given that there will be certain indications, for example atrial fibrillation, where beta blockade remains appropriate. It was clear that discontinuation of beta-blockers in such circumstances would be bad practice.

The committee felt that body of evidence on RIPC strongly indicated no benefit to postoperative outcomes, and the potential for harm (arrhythmia). Unlike beta-blockers, the committee felt that there was no particular circumstance where routine use of RIPC should be considered. Thus, a “do not use” recommendation was made.

The committee recognised the risk of thromboembolic events (such as deep venous thrombosis and pulmonary embolism) after AAA repair, and noted that no evidence was found relating to the use of postoperative anticoagulation in people who have undergone AAA repair. They noted that Direct-acting Oral Anticoagulants (DOACs) have become popular in clinical practice because they are easy to use, have good pharmacokinetic properties associated with fixed dosing, have few interactions with other medications, and require less frequent monitoring. With that in mind, the committee drafted a research recommendation to encourage research on how best to use DOACs in the postoperative period to balance the risk thromboembolic events with that of bleeding.

The committee noted that there is a widespread problem of people with AAA not having their medical therapy optimised, and that it would be good practice for clinicians to optimise medical therapy in all people identified as having an AAA, whether or not they were due to undergo AAA repair. The committee also agreed that it would be good practice for clinicians to perform preoperative medication assessments in order to optimise patient care.

Cost effectiveness and resource use

The committee considered that recommendations relating to secondary prevention of cardiovascular disease, prevention and treatment of surgical site infections, and reduction of the risk of venous thromboembolism were unlikely to have an impact on costs and resource use, because they simply cross-refer to existing guidance and reaffirm best clinical practice.

The committee considered the potential costs of treating intraoperative complications of preoperative beta-blockade (hypotension and bradycardia requiring treatment) and believed that a do not use recommendation would prevent such unnecessary expenses from occurring.

Other factors the committee took into account

The committee felt that NHS providers have already started devoting resources to exercise programmes based on a relatively small body of evidence. Thus, there is a role for further research to inform funding decisions. The committee agreed to make their research recommendation purposely broad, to maximise researcher uptake. It was agreed that the research recommendation should not explicitly state the need to monitor “cardiopulmonary” outcomes because there was some concern that researchers would focus on cardiac outcomes, at the expense of respiratory outcomes.

Appendices

Appendix A – Review protocols

Review protocol for review question 11: preoperative interventions to optimise outcomes after AAA repair

Review question 11	What presurgical interventions are effective in optimising surgical outcome in people undergoing surgical repair of an unruptured abdominal aortic aneurysm?
Objectives	To determine which interventions can be used preoperatively to 'optimise' surgical outcome.
Type of review	Intervention
Language	English
Study design	Systematic reviews of study designs listed below Randomised controlled trials Quasi-randomised controlled trials If insufficient evidence identified, non-randomised controlled trials
Status	Published papers only (full text) No date restrictions
Population	People with a confirmed unruptured abdominal aortic aneurysm in whom surgery is planned
Intervention	Statins Beta-blockers Tranexamic acid Antiplatelet therapy Iron supplementation Coronary artery revascularisation Supervised exercise program Ischaemic preconditioning Respiratory training, including incentive spirometry and smoking cessation therapy
Comparator	Placebo, no intervention or each other
Outcomes	Mortality Peri- and post-operative complications Adverse effects of intervention Quality of life Resource use, including length of hospital or intensive care stay, and costs
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published Pharmacological interventions not available in the UK
Baseline characteristics to be extracted in evidence tables	Age Sex Size of aneurysm Comorbidities
Search strategies	See Appendix B
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies.

Review question 11	**What presurgical interventions are effective in optimising surgical outcome in people undergoing surgical repair of an unruptured abdominal aortic aneurysm?**
	Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.
Key papers	Dronkers, A. Veldman, E. Hoberg, C. van der Waal, N. van Meeteren. Prevention of pulmonary complications after upper abdominal surgery by pre-operative intensive inspiratory muscle training: a randomized controlled pilot study. Clin Rehabil, 22 (2008), pp. 134–142 Kothmann, A.M. Batterham, S.J. Owen, A.J. Turley, M. Cheesman, A. Parry, et al. Effect of short-term exercise training on aerobic fitness in patients with abdominal aortic aneurysms: a pilot study. Br J Anaesth, 103 (2009), pp. 505–510 Myers, 2010. Effects of exercise training in patients with AAA: preliminary reslts from a randomised trial. J Cardiopulm Rehab Prev, 30 (2010), pp. 374–383 Tew, 2011. Endurance exercise training in patients with small abdominal aortic aneurysm: a randomised controlled pilot study. Arch Phys Med Rehabil, 93 (2012), pp. 2148–2153 Ali ZA, Callaghan CJ, Lim E, Ali AA, Nouraei SA, Akthar AM, Boyle JR, Varty K, Kharbanda RK, Dutka DP, Gaunt ME. Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation. 2007 Sep 11;116(11 Suppl):I98-105 Mouton R, Pollock J, Soar J, Mitchell DC, Rogers CA. Remote ischaemic preconditioning versus sham procedure for abdominal aortic aneurysm repair: an external feasibility randomized controlled trial. Trials. 2015 Aug 25;16:377 Walsh SR, Sadat U, Boyle JR, Tang TY, Lapsley M, Norden AG, Gaunt ME. Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vasc Endovascular Surg. 2010 Jul;44(5):334-40 Walsh SR, Boyle JR, Tang TY, Sadat U, Cooper DG, Lapsley M, Norden AG, Varty K, Hayes PD, Gaunt ME. Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. J Endovasc Ther. 2009 Dec;16(6):680-9

Review protocol for review question 30: postoperative interventions to optimise outcomes after AAA repair

Review question 30	**What postoperative interventions are effective in reducing the risk of complications after surgical repair of an abdominal aortic aneurysm, as well as optimising postoperative outcomes and survival?**
Objectives	To identify which postoperative interventions are effective in reducing the risk of further aneurysm growth or rupture, CV events, wound-related complications and graft-related complications (including endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion).
Type of review	Intervention
Language	English
Study design	Systematic reviews of study designs listed below Randomised controlled trials Quasi-randomised controlled trials If insufficient evidence identified, non-randomised controlled trials
Status	Published papers only (full text) No date restrictions

Review question 30	**What postoperative interventions are effective in reducing the risk of complications after surgical repair of an abdominal aortic aneurysm, as well as optimising postoperative outcomes and survival?**
Population	People who have undergone surgical repair of an abdominal aortic aneurysm
Intervention	Surgical intervention Antifibrinolytic therapy with tranexamic acid Antiplatelet therapy (aspirin, clopidogrel, ticlopidine, cilostazol, prasugrel, ticagrelor, or any other antiplatelet drugs) Antihypertensive drugs (calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers (β-blockers; e.g. metoprolol, propranolol), angiotensin-II receptor antagonists, thiazide/ thiazide-like diuretics, or any other antihypertensive drugs) Lipid-lowering therapy (statins (simvastatin, pravastatin, atorvastatin)) Antibiotics (doxycycline, roxithromycin, azithromycin) Diabetic control, including metformin COPD control Smoking cessation Physical therapy/exercise Diet Weight control Control of alcohol consumption
Comparator	Placebo, no intervention or each other
Outcomes	Incidence of complications (AAA rupture, AAA growth/expansion, cardiovascular events, wound-related complications, endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion) Need for further surgical intervention Mortality (all-cause; AAA-related; cardiovascular; survival) Cardiovascular events Quality of life Adverse effects Resource use and cost
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published Pharmacological interventions not available in the UK
Baseline characteristics to be extracted in evidence tables	Age Sex Size of aneurysm Comorbidities
Search strategies	See Appendix B
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.
Key papers	Yang H, Raymer K, Butler R, Parlow J, Roberts R. The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 2006 Nov;152(5):983-90

Appendix B – Literature search strategies

Clinical search literature search strategy

Main searches

Bibliographic databases searched for the guideline

- Cumulative Index to Nursing and Allied Health Literature - CINAHL (EBSCO)
- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (Wiley)
- Health Technology Assessment Database – HTA (Wiley)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE Epub Ahead of Print (Ovid)
- MEDLINE In-Process (Ovid)

Identification of evidence for review questions

The searches were conducted between November 2015 and October 2017 for 31 review questions (RQ). In collaboration with Cochrane, the evidence for several review questions was identified by an update of an existing Cochrane review. Review questions in this category are indicated below. Where review questions had a broader scope, supplement searches were undertaken by NICE.

Searches were re-run in December 2017.

Where appropriate, study design filters (either designed in-house or by McMaster) were used to limit the retrieval to, for example, randomised controlled trials. Details of the study design filters used can be found in section 4.

Search strategy review questions 11 and 30

Medline Strategy, searched 16th May 2017 **Database: Ovid MEDLINE(R) 1946 to May Week 1 2017** **Search Strategy:**
1 Aortic Aneurysm, Abdominal/
2 Aortic Rupture/
3 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort* or spontan* or juxtarenal* or juxta-renal* or juxta renal* or paraerenal* or para-renal* or para renal* or suprarenal* or supra renal* or supra-renal* or short neck* or short-neck* or shortneck* or visceral aortic segment*)).tw.
4 (AAA* or RAAA*).tw.
5 or/1-4
6 Preoperative Care/ or Perioperative Care/ or Perioperative Nursing/ or Postoperative Care/
7 home care services/ or home care services, hospital-based/
8 (presurg* or pre-surg* or pre surg* or preop* or pre-op* or pre op or periop* or peri-op* or peri op*).tw.
9 ((perianaesthe* or perianesthe* or surgical) adj4 nursing).tw.

Medline Strategy, searched 16th May 2017 **Database: Ovid MEDLINE(R) 1946 to May Week 1 2017** **Search Strategy:**
10 ((before or plan* or electiv* or ahead* or prepar* or prior) adj4 (surg* or operat* or procedure* or repair* or care* or outcome*)).tw. 11 (postsurg* or post-surg* or post surg* or postop* or post-op* or post op*).tw. 12 ((after or follow* or electiv* or post*) adj4 (surg* or operat* or procedure* or repair* or care* or outcome*)).tw. 13 (medical* adj4 (therap* or treat* or interven* or manag*)).tw. 14 Elective Surgical Procedures/ 15 Endovascular Procedures/ or Vascular Surgical Procedures/ 16 (endovascular* adj4 aneurysm* adj4 repair*).tw. 17 (endovascular* adj4 aort* adj4 repair*).tw. 18 (upper adj4 abdominal adj4 (repair* or surger* or surgic* or operat* or procedur*)).tw. 19 (EVAR or EVRAR or FEVAR or F-EAVAR or BEVAR or B-EVAR).tw. 20 (Anaconda or Zenith Dynalink or Hemobahn or Luminex* or Memoth-erm or Wallstent).tw. 21 (Viabahn or Nitinol or Hemobahn or Intracoil or Tantalum).tw. 22 or/6-21 23 exp Antifibrinolytic Agents/ 24 ((antifibrinolytic or anti-fibrinolytic) adj4 (hemostatic or haemostatic or agent*)).tw. 25 ((tranexam* or tranex-am* or tranex am* or tranexan or tranex-and or tranex an) adj4 acid*).tw. 26 TXA.tw. 27 (aminocaproic* adj4 acid*).tw. 28 vitamin k*.tw. 29 (anti plasmin* or anti-plasmin* or (plasmin* adj4 inhibitor*)).tw. 30 Iron/ 31 iron.tw. 32 exp Coronary Artery Bypass/ 33 ((coronary adj4 arter* adj4 bypass*) or (aortocoronary adj4 bypass*)).tw. 34 ((off-pump or off pump) adj4 bypass*).tw. 35 CABG.tw. 36 ((blood-flow or blood flow or perfus*) adj4 restor*).tw. 37 (coronary adj4 (revasculari* or recanali* or reperfus*)).tw. 38 Antibiotic Prophylaxis/ 39 (antibiotic* adj4 (premed* or prophyla*)).tw. 40 (Doxycyclin* or Atridox or Cyclodox or Demix or Doxylar or Efracea or Nordox or Periostat or Ramysis or Vibramycin or Vibramycin).tw. 41 Roxithromycin*.tw. 42 (Azithromycin* or Azyter or Clamelle or Zedbac or Zithromax).tw. 43 Smoking Cessation/ 44 "Tobacco Use Cessation"/ 45 ((cigarette* or smok* or tobacco or nicotine*) adj4 (cessation or withdrawal or ceas*)).tw. 46 ((quit* or stop* or giv* or abstin* or abstain*) adj4 (tobacco or cigarette or smoking or nicotine*)).tw. 47 (smoking adj4 (therap* or rehab*)).tw. 48 (cessation adj4 (treat* or therap* or assist* or advice or advis* or program* or interven* or service*)).tw. 49 Motor Activity/

Medline Strategy, searched 16th May 2017
Database: Ovid MEDLINE(R) 1946 to May Week 1 2017
Search Strategy:

50 ((motor or physical* or locomotor or supervis*) adj4 activit*).tw.
51 exp Exercise/ or Exercise Therapy/
52 (exercise* or exercisi* or kinesiotherap*).tw.
53 exp Physical Fitness/
54 Physical endurance/
55 fitness*.tw.
56 (walk* or swim* or jog* or cycl* or bicycl* or bike* or gym*).tw.
57 ((physical* or keep* or cardio* or aerobic or fitness or endurance) adj4 (fit* or activit* or active or train* or therap*)).tw.
58 (aerobic adj4 condition*).tw.
59 Muscle strength/
60 (muscle adj4 strength*).tw.
61 Ischemic Preconditioning/
62 ((ischemic* or ischaemic* or remote) adj4 (precondition* or pre-condition* or pre condition*)).tw.
63 (IPC or RIC or RIPC).tw.
64 Respiratory therapy/
65 exp Breathing Exercises/
66 ((breath* or respirat* or inhal*) adj4 (exercis* or therap* or train* or alter* or chang* or deepen* or physio* or rehab*)).tw.
67 exp Spirometry/
68 (spirometr* or bronchospirometr*).tw.
69 exp Diet/
70 (diet or diets or dieting).tw.
71 (health* adj4 eat*).tw.
72 exp Food/
73 food*.tw.
74 (weight adj4 (manag* or control* or maintain* or achiev* or goal* or health*)).tw.
75 exp Alcohol-Related Disorders/
76 (alcohol* adj4 (use* or abus* or drink* or reduc* or intake or consum* or control* or abstain* or abstinen* or depend* or addict* or chonic*)).tw.
77 ((problem* adj4 drink*) or (alcoholic* or alcoholism)).tw.
78 exp Pulmonary Disease, Chronic Obstructive/
79 Lung diseases, obstructive/
80 (COPD* or COAD* or COBD* or AECB*).tw.
81 (chronic adj4 obstruct* adj4 (disease* or airway*)).tw.
82 (chronic* adj4 (airflow* or airway* or bronch* or lung* or respirat* or pulmonary) adj4 obstruct*).tw.
83 exp Diabetes Mellitus/
84 diabet*.tw.
85 or/23-84
86 5 and 22 and 85
87 Aortic Aneurysm, Abdominal/su [Surgery]
88 85 and 87
89 86 or 88
90 animals/ not humans/

Medline Strategy, searched 16th May 2017 Database: Ovid MEDLINE(R) 1946 to May Week 1 2017 Search Strategy:
91 89 not 90
92 limit 91 to english language

Health Economics literature search strategy

Sources searched to identify economic evaluations

- NHS Economic Evaluation Database – NHS EED (Wiley) last updated Dec 2014
- Health Technology Assessment Database – HTA (Wiley) last updated Oct 2016
- Embase (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

Search filters to retrieve economic evaluations and quality of life papers were appended to the population and intervention terms to identify relevant evidence. Searches were not undertaken for qualitative RQs. For social care topic questions additional terms were added. Searches were re-run in September 2017 where the filters were added to the population terms.

Health economics search strategy

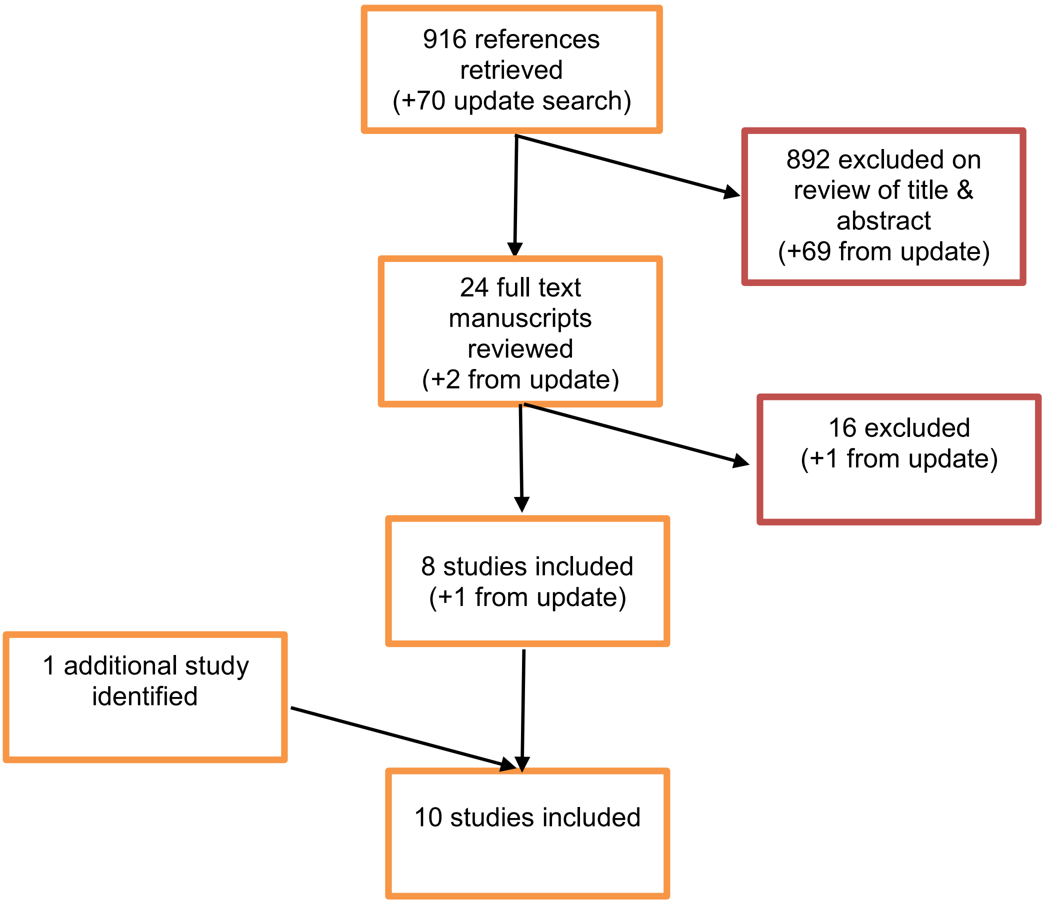
Medline Strategy
Economic evaluations
1 Economics/
2 exp "Costs and Cost Analysis"/
3 Economics, Dental/
4 exp Economics, Hospital/
5 exp Economics, Medical/
6 Economics, Nursing/
7 Economics, Pharmaceutical/
8 Budgets/
9 exp Models, Economic/
10 Markov Chains/
11 Monte Carlo Method/
12 Decision Trees/
13 econom*.tw.
14 cba.tw.
15 cea.tw.
16 cua.tw.
17 markov*.tw.
18 (monte adj carlo).tw.
19 (decision adj3 (tree* or analys*)).tw.
20 (cost or costs or costing* or costly or costed).tw.
21 (price* or pricing*).tw.
22 budget*.tw.
23 expenditure*.tw.

Medline Strategy
24 (value adj3 (money or monetary)).tw. 25 (pharmacoeconomic* or (pharmaco adj economic*)).tw. 26 or/1-25 Quality of life 1 "Quality of Life"/ 2 quality of life.tw. 3 "Value of Life"/ 4 Quality-Adjusted Life Years/ 5 quality adjusted life.tw. 6 (qaly* or qald* or qale* or qtime*).tw. 7 disability adjusted life.tw. 8 daly*.tw. 9 Health Status Indicators/ 10 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw. 11 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw. 12 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw. 13 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw. 14 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw. 15 (euroqol or euro qol or eq5d or eq 5d).tw. 16 (qol or hql or hqol or hrqol).tw. 17 (hye or hyes).tw. 18 health* year* equivalent*.tw. 19 utilit*.tw. 20 (hui or hui1 or hui2 or hui3).tw. 21 disutili*.tw. 22 rosser.tw. 23 quality of wellbeing.tw. 24 quality of well-being.tw. 25 qwb.tw. 26 willingness to pay.tw. 27 standard gamble*.tw. 28 time trade off.tw. 29 time tradeoff.tw. 30 tto.tw. 31 or/1-30

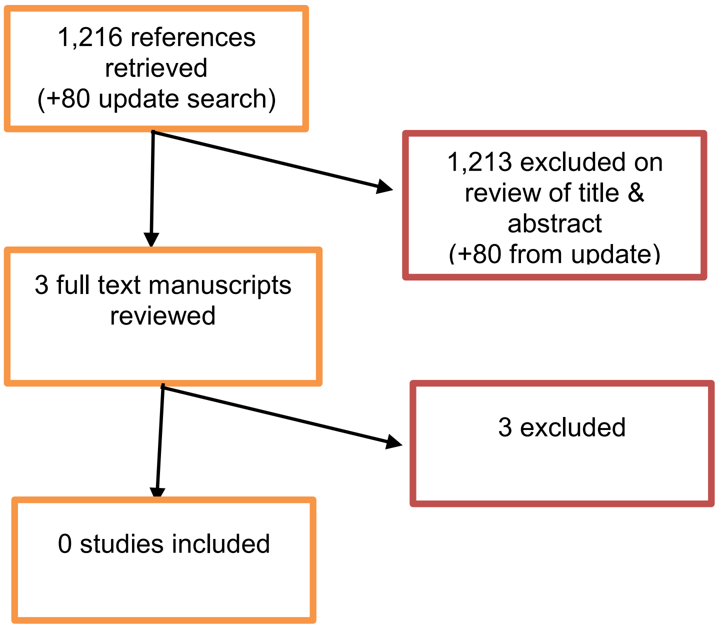
Appendix C – Clinical evidence study selection

Review question 11 (preoperative interventions) study selection

RCT filter

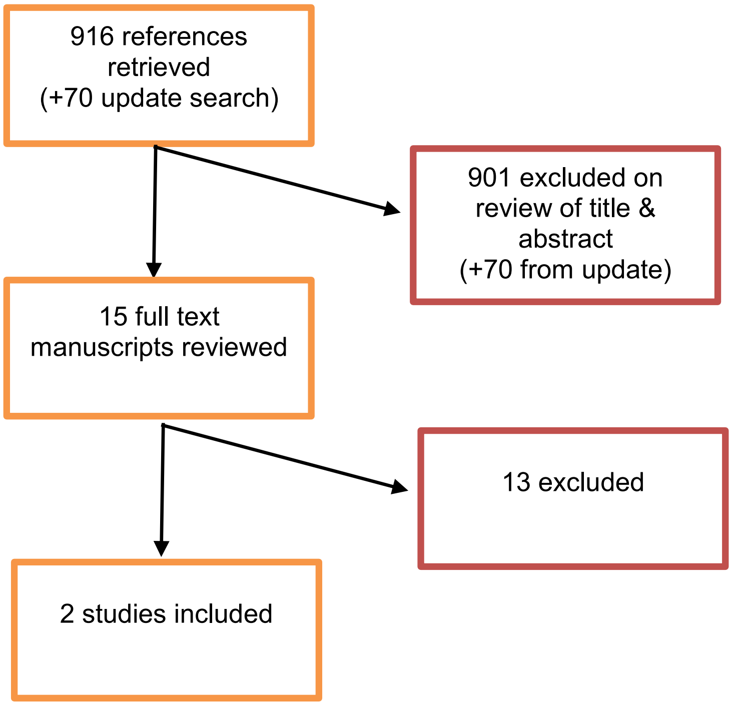


Observational study filter



Review question 30 (postoperative interventions) study selection

RCT filter



Observational study filter

Appendix D – Clinical evidence tables

Evidence tables for review question 11 (preoperative interventions)

Beta-blockers

Full citation	**Yang H, Raymer K, Butler R, Parlow J, Roberts R. (2006) The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 152(5):983-90.**
Study details	Study type: randomised, placebo-controlled, double-blind trial Location(s): Canada Aim(s): to assess the efficacy of perioperative metoprolol on postoperative outcomes of patients undergoing abdominal aortic surgery Study dates: 1999 to 2002 Follow-up: 30 months Sources of funding: Heart and Stroke Foundation of Canada
Participants	Population: patients undergoing elective abdominal aortic surgery (no additional details were provided). Sample size: 496; 76% (377/496) male Inclusion criteria: patients with American Society of Anaesthesiology class of 3 or less undergoing abdominal aortic surgery and infrainguinal or axillofemoral revascularization were included Exclusion criteria: current or recent use of beta-blockers or amiodarone, an airflow obstruction requiring treatment, history of congestive heart failure, a history of atrioventricular block, or previous adverse drug reactions to beta-blockers Baseline characteristics: • Mean age: Beta-blocker group, 66.4 years; control group, 65.9 years • Sex: Beta-blocker group, 78.5% male; control group, 73.6% male • Mean aneurysm size: not reported • Prior myocardial infarction: Beta-blocker group, 15.0%; control group, 12.0% • Angina: Beta-blocker group, 7.3%; control group, 10.0% • Diabetes: Beta-blocker group, 22.0%; control group, 14.8% • Permanent pace maker: Beta-blocker group, 0.4%; control group, 0% • Renal insufficiency: Beta-blocker group, 1.2%; control group, 2.8%
Intervention	25 to 100 mg of metoprolol was administered orally or intravenously, 2 hours before and after surgery. Treatment was continued intravenously every 6 hours or orally twice a day for 5 days or until hospital discharge (whichever occurred sooner).

Full citation	**Yang H, Raymer K, Butler R, Parlow J, Roberts R. (2006) The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. Am Heart J. 152(5):983-90.**
Comparison	Matched placebo
Outcomes measures	The primary outcome was the composite rate of cardiac death, myocardial infarction, congestive heart failure, unstable angina, dysrhythmia requiring treatment, and non-cardiac death at 6 month follow-up. Individual rates were also reported at 30-day follow-up. Secondary outcomes included the need for reoperation, cerebrovascular accidents, new or worsened renal insufficiency, rehospitalisation, and intraoperative adverse events.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Authors state that randomisation was constructed in block of 4 by the study statistician; however it is not clear how allocation sequences were generated. 2. Allocation concealment (selection bias): Unclear risk – Insufficient information was provided in the manuscript to ascertain whether appropriate steps were taken to conceal group allocations 3. Blinding of participants and personnel (performance bias): Low risk – Authors state that patients, investigators, and all caretakers were blinded to the study randomisation 4. Blinding of outcome assessment (detection bias): Low risk – Authors state that patients, investigators, and all caretakers were blinded to the study randomisation 5. Incomplete outcome data (attrition bias): Low risk – "Completion of study protocol was 77.6% and 75.2% in the placebo and treatment groups, respectively." All losses to follow-up were accounted for and equally balanced across the 2 groups. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: – Unclear risk – Intraoperative use of esmolol was allowed if deemed absolutely necessary. However, it was not clear what proportions of patients in each group received esmolol. Overall risk of bias: Low Directness: directly applicable

Exercise

Full citation	**Barakat H M, Shahin Y, Khan J A et al. (2016) Preoperative supervised exercise improves outcomes after elective abdominal aortic aneurysm repair. Annals of Surgery 264, 47-53**
Study details	Study type: randomised, non-blinded trial Location(s): UK Aim(s): to assess the impact of a preoperative medically supervised exercise programme on postoperative outcomes of elective AAA repair Study dates: September 2009 to January 2014 Follow-up: 3 months Sources of funding: University of Hull (self-funded)
Participants	Population: patients with AAAs undergoing EVAR or open surgical repair. Sample size: 124; 89.5% (111/124) male Inclusion criteria: patients older than 18 years with AAAs greater than 5.5 cm in diameter were included Exclusion criteria: thoracic aortic aneurysms, presence of factors that would limit exercise participation, patients requiring expedited or urgent aneurysm repair Baseline characteristics: • Mean age: Exercise group, 73.8 years; control group, 72.9 years • Sex: Exercise group, 90.3% male; control group, 88.7% male • Mean aneurysm size: Exercise group 6.0 cm; control group, 6.3 cm • Hypertension: Exercise group, 72.6%; control group, 69.4% • Coronary artery disease: Exercise group, 38.7%; control group, 37.1% • Hyperlipidaemia: Exercise group, 43.5%; control group, 40.3% • Peripheral artery disease: Exercise group, 14.5%; control group, 12.9% • Diabetes: Exercise group, 6.5%; control group, 14.5% • Cerebrovascular disease: Exercise group, 16.1%; control group, 17% • COPD: Exercise group, 29.0%; control group, 37.1%
Intervention	Hospital based exercise classes: Patients attended 1 hour-long classes, 3 times a week. Exercises comprised a 5-minute warm up, using a cycle ergometer, heel-raise repetitions, knee extensions, dumbbells' biceps/arm curls, step-up lunges, knee bends (bodyweight), and 5 minutes for cool down and stretching.
Comparison	No exercise (controls)

Full citation	**Barakat H M, Shahin Y, Khan J A et al. (2016) Preoperative supervised exercise improves outcomes after elective abdominal aortic aneurysm repair. Annals of Surgery 264, 47-53**
Outcomes measures	The primary outcome was the composite rate of cardiac, pulmonary, and renal complications. Secondary outcomes included length of stay, APACHE II scores, occurrence of systematic inflammatory response syndrome, mortality, and bleeding requiring reoperation or transfusion.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Randomisation was performed using a computer-generated sequence prepared by an independent professional 2. Allocation concealment (selection bias): Low risk – Randomisation was performed using opaque, sealed, identical 3. envelopes containing the treatment allocation 4. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured 5. Blinding of outcome assessment (detection bias): Low risk – Clinicians including consultant surgeons, anaesthetists, medical staff and interventional radiologists were blinded to group allocations 6. Incomplete outcome data (attrition bias): Low risk – There were no losses to follow-up. 7. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported. 8. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**Dronkers J, Veldman A, Hoberg E et al. (2008) Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. Clinical rehabilitation 22, 134-42**
Study details	Study type: randomised, single-blind trial Location(s): Netherlands Aim(s): to investigate the effects of preoperative inspiratory muscle training on the incidence of atelectasis in patients at high risk of pulmonary complications scheduled for elective AAA surgery Study dates: not reported Follow-up: 7 days Sources of funding: not reported
Participants	Population: patients with AAAs undergoing elective surgical repair (not specified) who were considered to have a high risk of pulmonary complications. Sample size: 20; 20% (5/15) male Inclusion criteria: patients who were due to undergo AAA surgical repair, with a scheduled delay of at least 2 weeks, and at least 1 of the following risk factors were included: age over 65 years, smoking within 2 months before surgery, presence of COPD, and a BMI greater than 27 were included Exclusion criteria: cerebrovascular disorders, neuromuscular diseases, a history of lung surgery, cardiovascular instability, receiving immunosuppressive treatment within 30 days of surgery, or treatment by a physical therapist within 8 weeks of surgery Baseline characteristics: • Mean age: Exercise group, 70 years; control group, 59 years • Sex: Exercise group, 80% male; control group, 70% male • Mean aneurysm size: not reported • COPD: Exercise group, 10%; control group, 10%
Intervention	Inspiratory muscle training: Patients took part in a training programme involving one 15-minute exercise session, 6 days a week, for at least 2 weeks prior to surgery. One session per week was supervised by the same physical therapist and the other 5 sessions were unsupervised.
Comparison	No exercise
Outcomes measures	Outcomes included incidence of atelectasis, patient satisfaction, and respiratory function.
Risk of bias assessment (using	1. Random sequence generation (selection bias): Unclear risk – Authors state that an independent research assistant randomly assigned patients to treatment groups. No further information was provided. 2. Allocation concealment (selection bias): Low risk – Group allocations were concealed using sealed and numbered envelopes.

Full citation	**Dronkers J, Veldman A, Hoberg E et al. (2008) Prevention of pulmonary complications after upper abdominal surgery by preoperative intensive inspiratory muscle training: a randomized controlled pilot study. Clinical rehabilitation 22, 134-42**
Cochrane risk of bias tool)	3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Low risk – Assessment of the primary outcome (atelectasis) was performed by radiologists who were blinded to treatment outcomes. 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Tew GA, Batterham AM, Colling K, et al. (2017) Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. The British journal of surgery 104(13), 1791-1801**
Study details	Study type: randomised, single-blind trial Location(s): UK Aim(s): to assess the feasibility of a preoperative high-intensity interval training (HIT) programme in patients awaiting elective abdominal aortic aneurysm repair Study dates: not reported Follow-up: 12 weeks Sources of funding: This study was funded by the National Institute for Health Research under its Research for Patient Benefit Programme
Participants	Population: patients with unruptured AAAs undergoing elective EVAR or open surgical repair Sample size: 53; 94.3% (50/53) male Inclusion criteria: patients > 18 years, with infrarenal AAAs 5.5 to 7.0 cm in diameter who were due to undergo AAA surgical repair open repair or EVAR were included Exclusion criteria: AAA managed non-operatively, not an infrarenal aneurysm (juxtarenal, suprarenal or thoracic), infrarenal AAA diameter exceeding 7·0 cm, emergency AAA repair, contraindication to exercise testing or training Baseline characteristics: • Mean age: Exercise group, 74.6 years; control group, 74.9 years • Sex: Exercise group, 92.6% male; control group, 96.2% male • Mean aneurysm size: Exercise group 6.0 cm; control group, 5.8 cm • Coronary artery disease: Exercise group, 40.7%; control group, 53.8% • Cerebrovascular disease: Exercise group, 25.9%; control group, 26.9% • Peripheral arterial disease: Exercise group, 0%; control group, 7.7% • Diabetes: Exercise group, 14.8%; control group, 7.7% • COPD: Exercise group, 22.2%; control group, 26.9%
Intervention	HIT: Patients in the exercise group were invited to complete three hospital-based exercise sessions per week, for the 4 consecutive weeks immediately preceding their intended operation date
Comparison	No exercise
Outcomes measures	Adverse events, quality of life, and length of stay

Full citation	**Tew GA, Batterham AM, Colling K, et al. (2017) Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. The British journal of surgery 104(13), 1791-1801**
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Authors stated that participants were randomised to groups using minimastion. Minimisation was performed with a 1:1 allocation ratio and equal weighting for the three minimisation factors (sex, type of procedure and study centre). 2. Allocation concealment (selection bias): Low risk – Allocation was concealed from those assessing eligibility and recruiting patients, with eligible patients allocated remotely via e-mail by the trial statistician. 3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Low risk – Authors stated that tests were performed by 2 experienced investigators blinded to group allocations, 5. Incomplete outcome data (attrition bias): Low risk – All losses to follow-up were reported and accounted for in a consort diagram. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Remote ischaemic preconditioning

Full citation	**Ali ZA, Callaghan CJ, Lim E et al. (2007) Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation 116, I98-105**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to investigate the potential of RIPC on myocardial and renal protection after elective open AAA repair Study dates: February 2003 and December 2005 Follow-up: 7 days Sources of funding: Cambridge University Hospitals NHS Foundation Trust
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 82; 93% (76/82) male Inclusion criteria: patients referred for primary elective open AAA repair were included. No additional information was provided Exclusion criteria: over 90 years of age, needed concomitant procedures other than AAA repair, history of an acute coronary syndrome or myocardial infraction within 3 months, or taking sulfonylurea oral hypoglycaemic agents or nicorandil drug therapy Baseline characteristics: • Mean age: RIPC group, 74 years; control group, 75 years • Sex: RIPC group, 93% male; control group, 93% male • Mean aneurysm size: not reported • History of angina: RIPC group, 24%; control group, 27% • History of hypertension: RIPC group, 51%; control group, 63% • History of diabetes: RIPC group, 5%; control group, 5% • History of hypercholesterolaemia : RIPC group, 39%; control group, 46%
Intervention	Lower limb RIPC: This involved sequential cross-clamping of the common iliac arteries with 10 minutes ischaemia, followed by 10 minutes of reperfusion (RIPC stimulus). In order to reduce the risk of trash foot, sequential cross-clamping was performed to minimise repeat clamping of a single iliac artery. To prevent prolonged operating times, surgeons used a standardised approach whereby the iliac vessels were dissected before the neck of the aneurysm. The right iliac vessel was cross-clamped for 10 minutes followed by reperfusion during which time the left iliac was prepared. The cross-clamp was then placed to the left iliac vessel for 10 minutes and subsequently released, providing a total of 20 minutes of lower limb ischemia. During this time, the remainder of the operative dissection was carried out until the surgeon was prepared to cross-clamp the aorta before opening the aneurysm sac.
Comparison	Conventional open surgical repair without RIPC

Full citation	**Ali ZA, Callaghan CJ, Lim E et al. (2007) Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation 116, I98-105**
Outcomes measures	Outcomes included length of stay, mortality, myocardial injury, myocardial infarction, renal impairment, and adverse events.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Patients were randomized by a computer-generated list in randomly sequenced blocks of 5, 6, 8, or 12. 2. Allocation concealment (selection bias): Low risk – Treatment allocations were concealed using numbered, sealed, opaque envelopes. 3. Blinding of participants and personnel (performance bias): Low risk – Patients and data collectors not present in the operating room were blinded of treatment allocations. 4. Blinding of outcome assessment (detection bias): Low risk – Results were compared and analysed by 2 blinded groups of assessors, labelled A and B. 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported and all participants were included in the analyses. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	Li C, Li YS, Xu M et al. (2013) Limb remote ischemic preconditioning for intestinal and pulmonary protection during elective open infrarenal abdominal aortic aneurysm repair: a randomized controlled trial. Anesthesiology 118, 842-52
Study details	Study type: randomised, double-blind trial Location(s): China Aim(s): to assess whether limb RIPC would reduce intestinal and pulmonary injuries in patients undergoing open surgical repair of infrarenal AAAs Study dates: January 2008 to June 2011 Follow-up: 24 hours Sources of funding: Sun Yat-Sen University hospital (self-funded)
Participants	Population: patients with AAAs undergoing elective open surgical repair. Sample size: 62; 90.1% (55/61) male Inclusion criteria: patients less than 80 years who were due to receive open surgical repair. No additional information was provided Exclusion criteria: infarction within 3 months, angina pain within 48 hours of surgery, ejection fraction less than 40%, poor pulmonary function (PaO2 < 60 mmHg), COPD, history of inflammatory bowel disease, history of diarrhoea within 1 week of surgery, or intestinal chronic inflammatory disease Baseline characteristics: • Mean age: RIPC group, 62 years; control group, 67 years • Sex: RIPC group, 93% male; control group, 84% male • Mean aneurysm size: RIPC group, 72 mm; control group, 69 mm • Hypertension: RIPC group, 77%; control group, 58% • Diabetes: RIPC group, 45%; control group, 29% • Previous myocardial infarction: RIPC group, 16%; control group, 26%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the left upper arm and 3 inflating–deflating cycles were performed. Each cycle consisted of 5 minutes of inflation to 200 mmHg followed by 5 minutes of reperfusion by deflating the cuff. All procedures were consistently performed by the same surgeon.
Comparison	Sham RIPC: an uninflated cuff was placed on the left upper arm for 30 min.
Outcomes measures	The primary outcomes were haemodynamic data and variables reflecting lung function. Secondary outcomes included mortality, ventilator support time, ICU- and hospital-free days; new arrhythmia, perioperative myocardial infarction, diagnosis of congestive heart failure, symptoms and signs of pulmonary congestion, neurologic events, upper limb ischemia requiring intervention,

Full citation	**Li C, Li YS, Xu M et al. (2013) Limb remote ischemic preconditioning for intestinal and pulmonary protection during elective open infrarenal abdominal aortic aneurysm repair: a randomized controlled trial. Anesthesiology 118, 842-52**
	intestinal injury markers, markers of oxidative stress and systemic inflammatory response, and scores of the severity of intestinal and pulmonary injury.
Risk of bias assessment (using Cochrane risk of bias)	1. Random sequence generation (selection bias): Low risk – randomisation was performed by an independent person using a computer random number generator with a 1:1 allocation using blocks of varying sizes. 2. Allocation concealment (selection bias): Low risk – Allocation details were stored in numbered, sealed, and opaque envelopes. Treatment allocation was revealed by anaesthetists opening the envelope on the morning of surgery. 3. Blinding of participants and personnel (performance bias): Low risk – Patients, investigators, surgeons, critical care teams, and individuals participating in data analysis were all blinded to group allocations. 4. Blinding of outcome assessment (detection bias): Low risk – as stated above. 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported and all participants were included in the analyses. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Mouton R, Pollock J, Soar J et al. (2015) Remote ischaemic preconditioning versus sham procedure for abdominal aortic aneurysm repair: an external feasibility randomized controlled trial. Trials 16, 377**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to investigate whether RIPC could be successfully introduced in elective AAA repair Study dates: January 2010 to December 2012 Follow-up: 48 hours Sources of funding: the National Institute of Health Research and the North Bristol NHS Trust
Participants	Population: patients with AAAs undergoing elective EVAR or open surgical repair. Sample size: 69; sex-specific proportions were not reported. Inclusion criteria: patients referred for a primary elective AAA repair (EVAR or open surgery) were included. No additional information was provided Exclusion criteria: patients taking sulphonylurea oral hypoglycaemic drugs or nicorandil were excluded Baseline characteristics: • Mean age: RIPC group, 72 years; control group, 72 years • Sex: not reported • Mean aneurysm size: not reported • Hypertension: RIPC group, 77%; control group, 71% • Ischaemic heart disease: RIPC group, 38%; control group, 26% • Cerebrovascular disease: RIPC group, 18%; control group, 20% • Congestive heart failure: RIPC group, 15%; control group, 3%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the upper arm (side not specified) and three 10-minute cycles of conditioning were performed. Each cycle consisted of 5 minutes of ischaemia (inflation of a blood pressure cuff to 40 mmHg above the patient's systolic blood pressure) followed by 5 minutes of reperfusion.
Comparison	Sham RIPC: a pressure cuff was inflated for the same periods as the RIPC intervention but only to 40 mmHg.
Outcomes measures	Outcomes included acute kidney injury scores as classified by the acute injury network (AKIN), mortality, myocardial infarction, new postoperative ECG changes, new arrhythmia, troponin T levels above 14 ng/L, and adverse events.
Risk of bias assessment (using	1. Random sequence generation (selection bias): Low risk – Randomisation was performed with a 1:1 allocation, using computer-generated randomisation sequences of varying block sizes and stratified by type of surgery. 2. Allocation concealment (selection bias): Low risk – Allocations were concealed and accessed via a secure password protected.

Full citation	Mouton R, Pollock J, Soar J et al. (2015) Remote ischaemic preconditioning versus sham procedure for abdominal aortic aneurysm repair: an external feasibility randomized controlled trial. Trials 16, 377
Cochrane risk of bias tool)	website and were concealed until sufficient information to uniquely identify the individual had been entered. 3. Blinding of participants and personnel (performance bias): Low risk – With the exception of the in-theatre anaesthetic team who administered the intervention, everyone (participants, surgeons, nursing staff and research nurses) was blinded to the intervention received. 4. Blinding of outcome assessment (detection bias): Low risk – as stated above. 5. Incomplete outcome data (attrition bias): Low risk – All loses to follow-up were adequately explained. Furthermore analyses were performed using an intention to treat approach. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Murphy N, Vijayan A, Frohlich S et al. (2014) Remote ischemic preconditioning does not affect the incidence of acute kidney injury after elective abdominal aortic aneurysm repair. Journal of cardiothoracic and vascular anaesthesia 28, 1285-92**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to assess the effects of RIPC on renal outcome in patients with AAAs having elective open surgical repair. Study dates: September 2009 to December 2012 Follow-up: 3 days Sources of funding: not reported
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 62; 85.5% (53/62) male Inclusion criteria: adults with AAAs referred for primary elective open surgical repair were included. No additional information was provided Exclusion criteria: myocardial infarction within 2 weeks of surgery, history of upper limb vascular insufficiency, kidney disease requiring renal replacement, or AAAs requiring emergency AAA repair Baseline characteristics: • Median age: RIPC group, 75 years; control group, 69 years • Sex: RIPC group, 94% male; control group, 77% male • Mean aneurysm size: not reported • Previous myocardial infarction: RIPC group, 22%; control group, 13% • Angina: RIPC group, 13%; control group, 16% • Hypertension: RIPC group, 64%; control group, 52% • Hypercholesterolemia: RIPC group, 23%; control group, 16% • Chronic kidney disease: RIPC group, 61%; control group, 55%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the upper arm (side not specified) and three 10-minute cycles of conditioning were performed. Each cycle consisted of 5 minutes of ischaemia (inflation of a blood pressure cuff to 100 mmHg above the patient's systolic blood pressure) followed by 5 minutes of reperfusion.
Comparison	Sham RIPC: method not specified
Outcomes measures	Outcomes included mortality, kidney injury (measured by creatinine levels and AKIN scores), myocardial infarction, and length of hospital stay.

Full citation	**Murphy N, Vijayan A, Frohlich S et al. (2014) Remote ischemic preconditioning does not affect the incidence of acute kidney injury after elective abdominal aortic aneurysm repair. Journal of cardiothoracic and vascular anaesthesia 28, 1285-92**
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Patients were assigned randomly, using a random number computer generator in a 1:1 ratio for parallel arms 2. Allocation concealment (selection bias): Unclear risk – Allocations were concealed using sealed envelopes. No further details were provided. 3. Blinding of participants and personnel (performance bias): Low risk – Authors do not explicitly state that participants were blinded to group allocations. However, the trial is described as a double-blind trial and it is unlikely that patients would have been aware what was being done to them while under general anaesthesia. 4. Blinding of outcome assessment (detection bias): Low risk – Study investigators, attending anaesthetists and surgical staff were blinded to treatment assignments. 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Walsh SR, Boyle JR, Tang TY et al. (2009) Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 16, 680-9**
Study details	Study type: randomised, non-blinded trial Location(s): UK Aim(s): to determine whether RIPC reduces renal damage in patients with AAAs having elective open surgical repair Study dates: February 2006 to October 2007 Follow-up: 48 hours Sources of funding: The Mouton Charitable Foundation
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 40 men Inclusion criteria: patients with AAAs and no history of acute renal failure, no history of renal replacement therapy, no previous renal transplant, no history of renal disease, serum creatinine values less than 1.5 mg/dL and a serum urea values less than 20 mmol/L were included Exclusion criteria: a history of previous EVAR, a history of a lower limb amputation, or patients scheduled to receive suprarenal aneurysm repairs Baseline characteristics: • Mean age: RIPC group, 74 years; control group, 76 years • Sex: 100% in both arms • Mean aneurysm size: RIPC group, 60.7 mm; control group, 63.9 mm • Diabetes: RIPC group, 17%; control group, 9% • Previous myocardial infarction: RIPC group, 33%; control group, 18% • Angina: RIPC group, 28%; control group, 18% • COPD: RIPC group, 17%; control group, 18% • Hypertension: RIPC group, 44%; control group, 55%
Intervention	Lower limb RIPC: A cross-clamp was applied to the right common iliac artery for 10 minutes. Subsequently, the right iliac territory was reperfused and the clamp was applied to the left common iliac artery. Once each common iliac artery territory had undergone one 10-minute cycle of ischemia followed by 10 minutes of reperfusion, the aorta was cross-clamped and the aneurysm sac was opened.
Comparison	Conventional open surgical repair without RIPC

Full citation	**Walsh SR, Boyle JR, Tang TY et al. (2009) Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 16, 680-9**
Outcomes measures	The primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and creatinine levels). Secondary outcomes included 30-day mortality, myocardial infarction, arrhythmia, congestive heart failure, pneumonia, renal failure, lower limb ischaemia requiring intervention, and postoperative length of stay.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Participants were randomised in blocks of 4 using computer-generated sequences. 2. Allocation concealment (selection bias): Low risk – Group allocations were concealed with sealed, opaque, envelopes which were opened on the day of surgery 3. Blinding of participants and personnel (performance bias): Unclear risk – It was unclear whether participants were blinded to treatment allocations. This was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): High risk – Outcome assessors were not blinded of treatment allocations 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported in either treatment arm. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Moderate Directness: directly applicable

Full citation	**Walsh SR, Sadat U, Boyle JR et al. (2010) Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vascular and endovascular surgery 44, 334-40**
Study details	Study type: randomised, non-blinded trial Location(s): UK Aim(s): to determine whether RIPC reduces renal and cardiac damage in patients with AAAs having elective open surgical repair. Study dates: November 2006 to January 2008 Follow-up: 48 hours Sources of funding: The Mouton Charitable Foundation
Participants	Population: patients with AAAs undergoing elective EVAR Sample size: 40; 85% (34/40) male Inclusion criteria: patients with AAAs and no history of acute renal failure, no history of renal replacement therapy, no previous renal transplant, no history of renal disease, serum creatinine values less than 1.5 mg/dL and a serum urea values less than 20 mmol/L were included Exclusion criteria: a history of previous EVAR, a history of a lower limb amputation, or patients scheduled to receive fenestrated or branched aneurysm repairs Baseline characteristics: • Median age: RIPC group, 75 years; control group, 72 years • Sex: RIPC group, 72% male; control group, 100% male • Mean aneurysm size: RIPC group, 67.8 mm; control group, 77.4 mm • Diabetes: RIPC group, 4.5%; control group, 0% • Previous myocardial infarction: RIPC group, 18%; control group, 22% • Angina: RIPC group, 4.5%; control group, 16% • COPD: RIPC group, 4.5%; control group, 5.5% • Hypertension: RIPC group, 54%; control group, 88%
Intervention	Lower limb RIPC: Ischaemia was induced by placing an inflatable tourniquet around the thigh and inflating it until there was no audible doppler signal in either pedal artery. After 10 minutes the cuff was deflated and the procedure was repeated on the other leg.
Comparison	Conventional open surgical repair without RIPC
Outcomes measures	The primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and serum creatinine levels). Secondary outcomes included serum troponin levels and the incidence of major adverse cardiac events (cardiac arrest, cardiac death, cardiac failure, unstable angina, or myocardial infarction).

Full citation	**Walsh SR, Sadat U, Boyle JR et al. (2010) Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vascular and endovascular surgery 44, 334-40**
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Participants were randomised in blocks of 4 using computer-generated sequences. 2. Allocation concealment (selection bias): Low risk – Group allocations were concealed with sealed, opaque, envelopes which were opened on the day of surgery. 3. Blinding of participants and personnel (performance bias): Unclear risk – It was unclear whether participants were blinded to treatment allocations. This was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): High risk – Outcome assessors were not blinded of treatment allocations 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Moderate Directness: directly applicable

Evidence tables for review question 30 (postoperative interventions)

Doxycycline versus placebo

Full citation	**Hackmann AE, Rubin BG, Sanchez LA et al. (2008) A randomized, placebo-controlled trial of doxycycline after endoluminal aneurysm repair. Journal of vascular surgery 48, 519-526**
Study details	Study type: randomised, placebo-controlled, double-blind trial Location(s): USA Aim(s): to evaluate the effect of a MMP inhibitor, doxycycline, on EVAR Study dates: not reported Follow-up: 6 months Sources of funding: Barnes-Jewish Hospital Foundation, National Institutes for Health, Department of Veteran's Affairs, Flight Attendants Medical Research Institute, and the American Heart Association
Participants	Population: patients with AAAs undergoing elective EVAR Sample size: 59; sex-specific proportions not reported Inclusion criteria: patients with AAAs less than 5.0 cm in diameter were included Exclusion criteria: not reported Baseline characteristics: • Mean age: Doxycycline group, 68.9 years; control group, 74.0 years • Sex: Doxycycline group, 80% male; control group, 79.2% male • Mean aneurysm size: Doxycycline group; 57.2 mm; control group, 57.2 mm • Hypertension: Doxycycline group, 90%; control group, 79.2% • Coronary artery disease: Doxycycline group, 60%; control group, 45.8% • Diabetes: Doxycycline group, 10%; control group, 12.5% • Peripheral artery disease: Doxycycline group, 40%; control group, 29.2% • COPD: Doxycycline group, 30%; control group, 41.7% • Renal insufficiency: Doxycycline group, 10%; control group, 25%
Intervention	Doxycycline 100 mg b.i.d, starting from the day after surgery and continued for 6 months
Comparison	Matched placebo
Outcomes measures	Aneurysm diameter, graft migration, incidence of endoleak, adverse events
Risk of bias assessment	1. Random sequence generation (selection bias): Unclear risk – Authors stated that randomisation was performed in the pharmacy utilising a pre-assigned table of codes. No further details were provided.

Full citation	Hackmann AE, Rubin BG, Sanchez LA et al. (2008) A randomized, placebo-controlled trial of doxycycline after endoluminal aneurysm repair. Journal of vascular surgery 48, 519-526
(using Cochrane risk of bias tool)	2. Allocation concealment (selection bias): Unclear risk – It is unclear whether treatment allocations were concealed. 3. Blinding of participants and personnel (performance bias): Low risk – Participants were blinded to treatment allocations as both doxycycline and placebo tablets had similar packaging and coating. 4. Blinding of outcome assessment (detection bias): Low risk – Data were collected from the CT scans, by individuals blinded as to treatment group 5. Incomplete outcome data (attrition bias): High risk – At final follow-up, 7 participants in the doxycycline group and 4 participants in the placebo group were either lost to follow-up or withdrew from the study. 6. Selective reporting (reporting bias): High risk – Authors reported some outcome measures for the whole study population whereas other outcome measures were only reported for the intervention group; omitting results for the placebo group. 7. Other bias: High risk – Patients in the placebo group were significantly older than those in the doxycycline group. A higher proportion of patients in the doxycycline group were smokers. 8. Overall risk of bias: High Directness: directly applicable

Physiotherapy plus walking exercises versus physiotherapy-alone

Full citation	**Wnuk BR, Durmala J, Ziaja K et al. (2016) A Controlled Trial of the Efficacy of a Training Walking Program in Patients Recovering from Abdominal Aortic Aneurysm Surgery. Advances in clinical and experimental medicine : official organ Wroclaw Medical University 25, 1241-1371**
Study details	Study type: randomised, single-blind trial Location(s): Poland Aim(s): to evaluate the impact of a physical training (backward walking) programme on patients after AAA surgery Study dates: not specified Follow-up: 2 years Sources of funding: not specified
Participants	Population: patients with AAAs undergoing surgical repair (not specified) Sample size: 65 males Inclusion criteria: patients with unruptured, non-symptomatic AAAs, between 65 and 75 years, who had a stable cardiologic status, no neurological disorders, and no motor system impairment were included Exclusion criteria: patients with neurological disorders, unstable coronary heart disease, aortic dissection, psychiatric diseases, difficulty in locomotion, or medical contraindications were excluded Baseline characteristics: • Mean age: Forward walking exercise group, 68 years; Forward walking exercise group, 70 years; control group, 69 years • Sex: 100% male in all groups
Intervention	Participants were divided into 2 intervention groups: • Basic physiotherapy plus backward walking exercises • Basic physiotherapy plus forward walking exercises Basic physiotherapy involved general conditioning exercises of low intensity. In addition to basic physiotherapy, participants in the intervention groups performed backward or forward walking exercises, conducted on an interval training cycle. The intensity (workload) of exercises were tailored to each patient by calculating “training heart rates”.
Comparison	Basic physiotherapy-alone
Outcomes measures	6-minute walking test distance, walking speed, spirometry measurements (FVC, FEV_1, FEV_1/FVC and PEF), length of hospital stay
Risk of bias assessment (using	1. Random sequence generation (selection bias): Low risk – randomisation was performed by drawing identical sealed envelopes which contained the number of the allocated group. 2. Allocation concealment (selection bias): Low risk – It is unclear whether treatment allocations were concealed.

Full citation	**Wnuk BR, Durmala J, Ziaja K et al. (2016) A Controlled Trial of the Efficacy of a Training Walking Program in Patients Recovering from Abdominal Aortic Aneurysm Surgery. Advances in clinical and experimental medicine : official organ Wroclaw Medical University 25, 1241-1371**
Cochrane risk of bias tool)	3. Blinding of participants and personnel (performance bias): Low risk – It was not possible to blind participants but this was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): Low risk – Outcome assessors were blinded to treatment allocations. 5. Incomplete outcome data (attrition bias): High risk – During the postoperative period, 17 participants were excluded from the study due to cardiac complications or disorders preventing their participation in exercise training. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported. 7. Other bias: High risk – It is unclear whether groups were similar at the start of the trial as limited demographic data was reported. Overall risk of bias: Moderate Directness: directly applicable

Appendix E – Forest plots

Forest plots for review question 11 (preoperative interventions)

Beta-blockers

No meta-analysis was performed.

Exercise

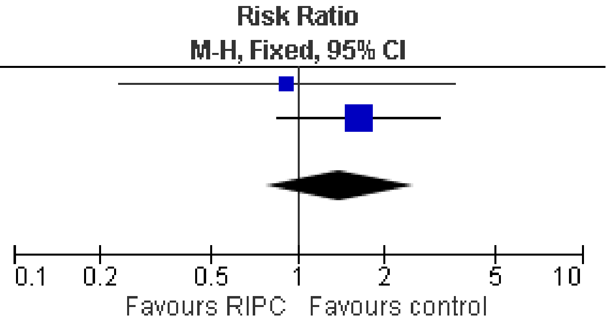
No meta-analysis was performed.

RIPC versus sham RIPC or no RIPC (control)

RIPC versus control: any complications

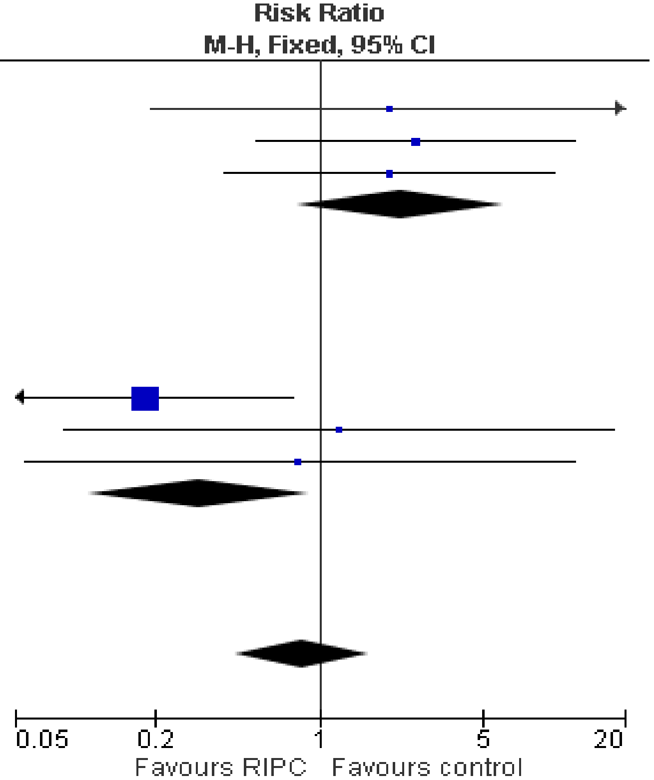
	RIPC		Control			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
Walsh 2009	3	18	4	22	31.9%	0.92 [0.23, 3.58]
Walsh 2010	14	22	7	18	68.1%	1.64 [0.85, 3.16]
Total (95% CI)		**40**		**40**	**100.0%**	**1.41 [0.77, 2.56]**
Total events	17		11			

Heterogeneity: Chi² = 0.58, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)



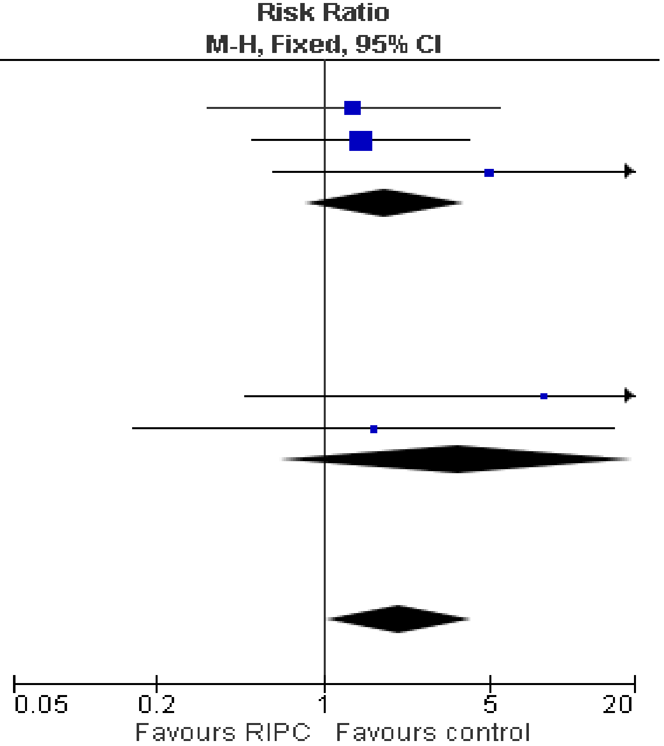
RIPC versus control: myocardial infarction

Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.2.1 Upper limb RIPC						
Li 2013	2	31	1	31	5.6%	2.00 [0.19, 20.93]
Mouton 2010	5	34	2	35	11.0%	2.57 [0.54, 12.38]
Murphy 2014	4	31	2	31	11.1%	2.00 [0.39, 10.13]
Subtotal (95% CI)		**96**		**97**	**27.7%**	**2.23 [0.81, 6.15]**
Total events	11		5			
Heterogeneity: Chi² = 0.06, df = 2 (P = 0.97); I² = 0%						
Test for overall effect: Z = 1.55 (P = 0.12)						
4.2.2 Lower limb RIPC						
Ali 2007	2	41	11	41	61.2%	0.18 [0.04, 0.77]
Walsh 2009	1	18	1	22	5.0%	1.22 [0.08, 18.20]
Walsh 2010	1	22	1	18	6.1%	0.82 [0.05, 12.19]
Subtotal (95% CI)		**81**		**81**	**72.3%**	**0.31 [0.10, 0.90]**
Total events	4		13			
Heterogeneity: Chi² = 2.02, df = 2 (P = 0.36); I² = 1%						
Test for overall effect: Z = 2.15 (P = 0.03)						
Total (95% CI)		**177**		**178**	**100.0%**	**0.84 [0.43, 1.62]**
Total events	15		18			
Heterogeneity: Chi² = 7.97, df = 5 (P = 0.16); I² = 37%						
Test for overall effect: Z = 0.52 (P = 0.60)						
Test for subgroup differences: Chi² = 6.87, df = 1 (P = 0.009), I² = 85.5%						



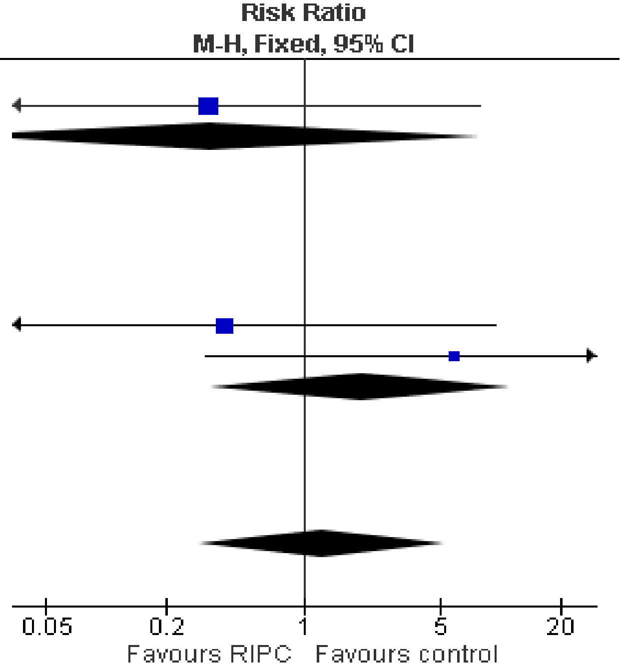
RIPC versus control: arrhythmia

Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.3.1 Upper limb RIPC						
Li 2013	4	31	3	31	28.6%	1.33 [0.32, 5.47]
Mouton 2010	7	34	5	35	47.0%	1.44 [0.51, 4.10]
Murphy 2014	5	31	1	31	9.5%	5.00 [0.62, 40.36]
Subtotal (95% CI)		**96**		**97**	**85.2%**	**1.80 [0.84, 3.87]**
Total events	16		9			
Heterogeneity: Chi² = 1.27, df = 2 (P = 0.53); I² = 0%						
Test for overall effect: Z = 1.51 (P = 0.13)						
4.3.2 Lower limb RIPC						
Walsh 2009	3	18	0	22	4.3%	8.47 [0.47, 154.04]
Walsh 2010	2	22	1	18	10.5%	1.64 [0.16, 16.62]
Subtotal (95% CI)		**40**		**40**	**14.8%**	**3.63 [0.66, 19.83]**
Total events	5		1			
Heterogeneity: Chi² = 0.78, df = 1 (P = 0.38); I² = 0%						
Test for overall effect: Z = 1.49 (P = 0.14)						
Total (95% CI)		**136**		**137**	**100.0%**	**2.07 [1.04, 4.15]**
Total events	21		10			
Heterogeneity: Chi² = 2.47, df = 4 (P = 0.65); I² = 0%						
Test for overall effect: Z = 2.06 (P = 0.04)						
Test for subgroup differences: Chi² = 0.54, df = 1 (P = 0.46), I² = 0%						



RIPC versus control: congestive heart failure

Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.4.1 Upper limb RIPC						
Li 2013	0	31	1	31	44.1%	0.33 [0.01, 7.88]
Subtotal (95% CI)		**31**		**31**	**44.1%**	**0.33 [0.01, 7.88]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						
4.4.2 Lower limb RIPC						
Walsh 2009	0	18	1	22	39.9%	0.40 [0.02, 9.35]
Walsh 2010	3	22	0	18	16.1%	5.78 [0.32, 105.12]
Subtotal (95% CI)		**40**		**40**	**55.9%**	**1.95 [0.34, 11.34]**
Total events	3		1			
Heterogeneity: Chi² = 1.51, df = 1 (P = 0.22); I² = 34%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**71**		**71**	**100.0%**	**1.24 [0.30, 5.18]**
Total events	3		2			
Heterogeneity: Chi² = 2.23, df = 2 (P = 0.33); I² = 11%						
Test for overall effect: Z = 0.29 (P = 0.77)						
Test for subgroup differences: Chi² = 0.91, df = 1 (P = 0.34), I² = 0%						



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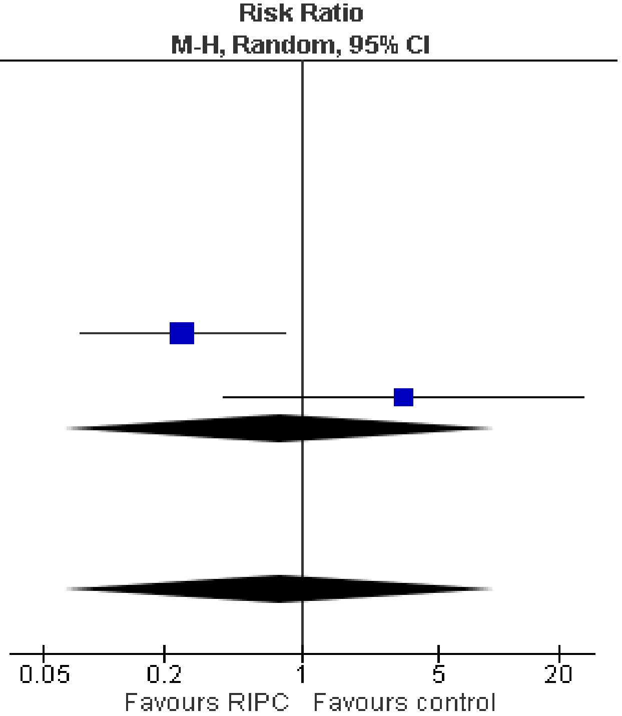
RIPC versus control: renal impairment or failure

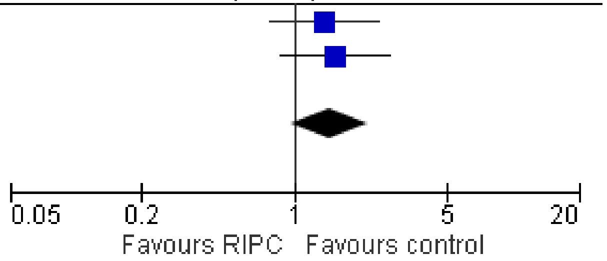
Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
4.5.1 Upper limb RIPC						
Li 2013	0	31	0	31		Not estimable
Subtotal (95% CI)		**31**		**31**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
4.5.2 Lower limb RIPC						
Ali 2007	3	41	12	41	55.9%	0.25 [0.08, 0.82]
Walsh 2009	0	18	0	22		Not estimable
Walsh 2010	4	22	1	18	44.1%	3.27 [0.40, 26.75]
Subtotal (95% CI)		**81**		**81**	**100.0%**	**0.78 [0.06, 9.56]**
Total events	7		13			
Heterogeneity: Tau² = 2.57; Chi² = 4.38, df = 1 (P = 0.04); I² = 77%						
Test for overall effect: Z = 0.20 (P = 0.84)						
Total (95% CI)		**112**		**112**	**100.0%**	**0.78 [0.06, 9.56]**
Total events	7		13			
Heterogeneity: Tau² = 2.57; Chi² = 4.38, df = 1 (P = 0.04); I² = 77%						
Test for overall effect: Z = 0.20 (P = 0.84)						
Test for subgroup differences: Not applicable						



RIPC versus control: acute kidney injury

Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Mouton 2010	16	34	12	35	51.8%	1.37 [0.77, 2.45]	
Murphy 2014	17	31	11	31	48.2%	1.55 [0.87, 2.74]	
Total (95% CI)		**65**		**66**	**100.0%**	**1.46 [0.97, 2.19]**	
Total events	33		23				

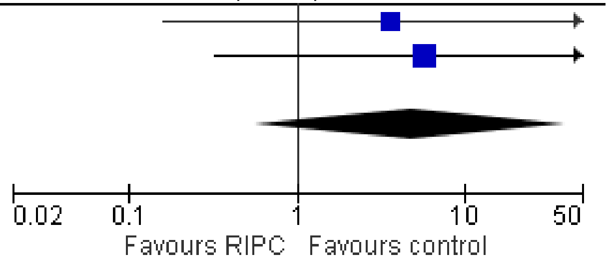
Heterogeneity: Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 1.81 (P = 0.07)



RIPC versus control: 30-day mortality

Study or Subgroup	RIPC Events	RIPC Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Walsh 2009	1	18	0	22	45.2%	3.63 [0.16, 84.11]	
Walsh 2010	3	22	0	18	54.8%	5.78 [0.32, 105.12]	
Total (95% CI)		**40**		**40**	**100.0%**	**4.81 [0.57, 40.68]**	
Total events	4		0				

Heterogeneity: Chi² = 0.05, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)



Forest plots for review question 30 (postoperative interventions)

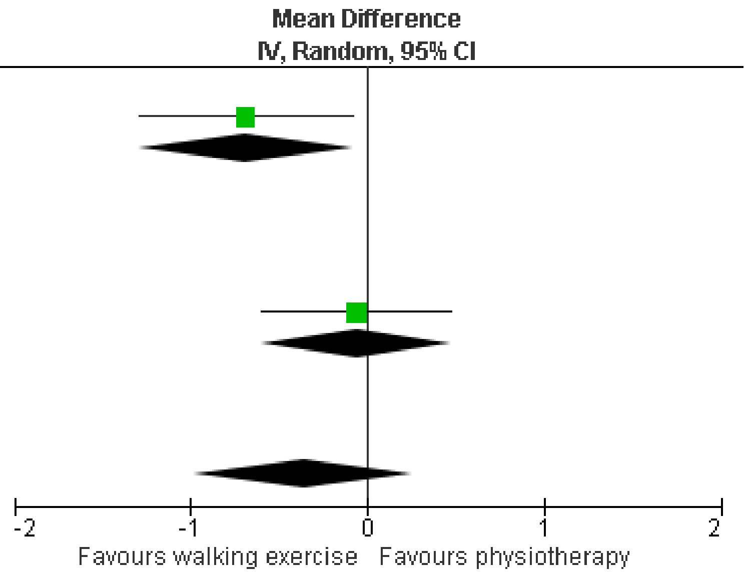
Doxycycline versus placebo

Meta-analysis was not possible.

Physiotherapy plus walking exercises versus physiotherapy-alone

Length of hospital stay

	Walking exercise			Physiotherapy-alone				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
1.1.1 Backward walking exercises								
Wnuk 2016	5.87	0.83	15	6.56	0.63	8	47.3%	-0.69 [-1.30, -0.08]
Subtotal (95% CI)			**15**			**8**	**47.3%**	**-0.69 [-1.30, -0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.23 (P = 0.03)								
1.1.2 Forward walking exercises								
Wnuk 2016	6.5	0.63	16	6.56	0.63	8	52.7%	-0.06 [-0.59, 0.47]
Subtotal (95% CI)			**16**			**8**	**52.7%**	**-0.06 [-0.59, 0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.22 (P = 0.83)								
Total (95% CI)			**31**			**16**	**100.0%**	**-0.36 [-0.97, 0.26]**
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 2.34$, df = 1 (P = 0.13); $I^2 = 57\%$								
Test for overall effect: Z = 1.14 (P = 0.25)								
Test for subgroup differences: $Chi^2 = 2.34$, df = 1 (P = 0.13), $I^2 = 57.2\%$								



Appendix F – GRADE tables

Grade tables for review question 11 (preoperative interventions)

Beta-blockers versus placebo

Intraoperative complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
Hypotension requiring treatment; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Serious[1]	250	246	RR 1.37 (1.10, 1.71)	Moderate
Bradycardia requiring treatment; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Not serious	250	246	RR 2.81 (1.72, 4.61)	High
1. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level.									

Postoperative complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
Unstable angina; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 3.02 (0.12, 73.88)	Low
Myocardial infarction; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 0.91 (0.50, 1.65)	Low
Congestive heart failure at 30 days; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 1.68 (0.41, 6.95)	Low
Postoperative cerebrovascular accident ; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 1.26 (0.34, 4.64)	Low
Dysrhythmia; effect sizes below 1 favour beta blockers									

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 0.71 (0.27, 1.38)	Low
New or worsened renal insufficiency; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 1.41 (0.45, 4.39)	Low
Need for reoperation; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 1.15 (0.42, 3.13)	Low
1. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

30-day mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
All-cause mortality; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 0.20 (0.02, 1.69)	Low
Cardiac death; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 0.33 (0.01, 8.08)	Low
Non-cardiac death; effect sizes below 1 favour beta blockers									
Yang (2006)	RCT	Not serious	Not serious	N/A	Very serious[1]	250	246	RR 0.14 (0.01, 2.73)	Low
1. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Exercises

Inspiratory muscle training versus no training: postoperative complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Atelectasis; effect sizes below 1 favour exercise group									
Dronkers (2008)	RCT	Serious[1]	Not serious	N/A	Serious[2]	10	10	RR 0.38 (0.14, 1.02)	Low
1. Very small sample size, downgrade 1 level. 2. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level									

Physical exercise versus no exercise: preoperative intervention-related adverse events

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
Dizziness; effect sizes below 1 favour exercise group									
Tew (2016)	RCT	Not serious	Not serious	N/A	Very serious[1]	27	26	RR 2.89 (0.12, 67.69)	Low
Angina; effect sizes below 1 favour exercise group									
Tew (2016)	RCT	Not serious	Not serious	N/A	Very serious[1]	27	26	RR 2.89 (0.12, 67.69)	Low
1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 level									

Physical exercise versus no exercise: postoperative complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
Cardiac complications (including myocardial infarction, prolonged inotropic support, new onset arrhythmia, and unstable angina); effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Serious[1]	62	62	RR 0.36 (0.14, 0.93)	Moderate
Pulmonary complications (including pneumonia, pneumonia requiring reintubation, exacerbation of COPD, and reintubation); effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Very serious[2]	62	62	RR 0.54 (0.23, 1.26)	Low
Renal complications (including acute renal failure and renal insufficiency); effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Serious[1]	62	62	RR 0.31 (0.11, 0.89)	Moderate
Postoperative bleeding or need for a blood transfusion of more than 4 units; effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Very serious[2]	62	62	RR 0.57 (0.18, 1.85)	Low
Need for reoperation; effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Very serious[2]	62	62	RR 0.67 (0.12, 3.84)	Low
1. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 level. 2. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Physical exercise versus no exercise: 30-day mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
All-cause mortality; effect sizes below 1 favour exercise group									
Barakat (2016)	RCT	Not serious	Not serious	N/A	Very serious[2]	62	62	RR 1.10 (0.15, 6.88)	Low
1. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Physical exercise versus no exercise: length of stay

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
Median length of stay									
Tew (2016)	RCT	Not serious	Not serious	N/A	Very serious[1]	27	26	Difference in medians: 1 day (Statistical significance not reported)	Low
1. Level of statistical significance not reported, downgrade 2 levels									

Physical exercise versus no exercise: quality of life

Quality assessment						No of patients		Effect estimate	Quality
No of studies	**Design**	**Risk of bias**	**Indirectness**	**Inconsistency**	**Imprecision**	**Intervention**	**Control**	**Summary of results**	
SF-36 Physical function subscale scores at 12 weeks; effect sizes below 0 favour exercise group									
Tew (2016)	RCT	Not serious	Not serious	N/A	Serious[1]	27	26	MD -0.3 (-2.7, 2.1)	Moderate
SF-36 mental health subscale scores at 12 weeks; effect sizes below 0 favour exercise group									
Tew (2016)	RCT	Not serious	Not serious	N/A	Serious[1]	27	26	MD -0.5 (-3.3, 2.3)	Moderate
1. Non-significant result, downgrade 1 level.									

RIPC

Postoperative complications

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Any complications; effect sizes below 1 favour RIPC									
2 studies	RCT	Serious[1]	Not serious	Serious[2]	Very serious[3]	40	38	RR 1.41 (0.77, 2.56)	Very low
Myocardial infarction; effect sizes below 1 favour RIPC									
6 studies	RCT	Not serious	Not serious	Very serious[2,3]	Very serious[4]	177	178	RR 0.84 (0.43, 1.62)	Very low
Arrhythmia; effect sizes below 1 favour RIPC									
5 studies	RCT	Not serious	Not serious	Serious[2]	Serious[5]	136	137	RR 2.07 (1.04, 4.15)	Low
Congestive heart failure; effect sizes below 1 favour RIPC									
3 studies	RCT	Serious[1]	Not serious	Serious[2]	Very serious[4]	71	71	RR 1.24 (0.30, 5.18)	Very low
Renal impairment or failure; effect sizes below 1 favour RIPC									
4 studies	RCT	Serious[1]	Not serious	Very serious[2,6]	Very serious[4]	71	71	RR 0.78 (0.06, 9.56)	Very low
Acute kidney injury; effect sizes below 1 favour RIPC									
2 studies	RCT	Not serious	Not serious	Serious[2]	Serious[5]	146	147	RR 1.46 (0.97, 2.19)	Low

1. Outcome assessors were not blinded of treatment allocations, downgrade 1 level.
2. Different surgical techniques (EVAR or open surgical repair) were used across included studies, downgrade 1 level.
3. I^2 between 33% and 66.7%, downgrade 1 level.
4. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
5. Confidence interval crosses one line of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 1 levels.
6. I^2 between >66.7%, downgrade 2 levels.

Mortality

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
30-day mortality; effect sizes below 1 favour RIPC									
2 studies	RCT	Serious[1]	Not serious	Serious[2]	Very serious[3]	40	40	RR 4.81 (0.57, 40.68)	Very low

1. Outcome assessors were not blinded of treatment allocations, downgrade 1 level.
2. Different surgical techniques (EVAR or open surgical repair) were used across included studies, downgrade 1 level.

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
3. Confidence interval crosses two lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Grade tables for review question 30 (postoperative interventions)

Doxycycline versus placebo

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Mean percentage change in aneurysm diameter									
Hackmann (2008)	RCT	Very serious[1]	Not serious	N/A	Very serious[2]	12	15	Non-significant (MD not reported)	Very low
Presence of endoleak									
Hackmann (2008)	RCT	Very serious[1]	Not serious	N/A	Very serious[2]	20	24	Non-significant (RR not reported)	Very low
Occurrence of graft migration									
Hackmann (2008)	RCT	Very serious[1]	Not serious	N/A	Very serious[2]	20	24	Non-significant (RR not reported)	Very low
1. Patients in the placebo group were significantly older than those in the doxycycline group. A higher proportion of patients in the doxycycline group were smokers. Finally, authors reported some outcome measures for the whole study population whereas other outcome measures were only reported for the intervention group; omitting results for the placebo group. Downgrade 2 levels. 2. Risk ratio and measures of dispersion not reported. Downgrade 2 levels.									

Physiotherapy plus walking exercises versus physiotherapy-alone

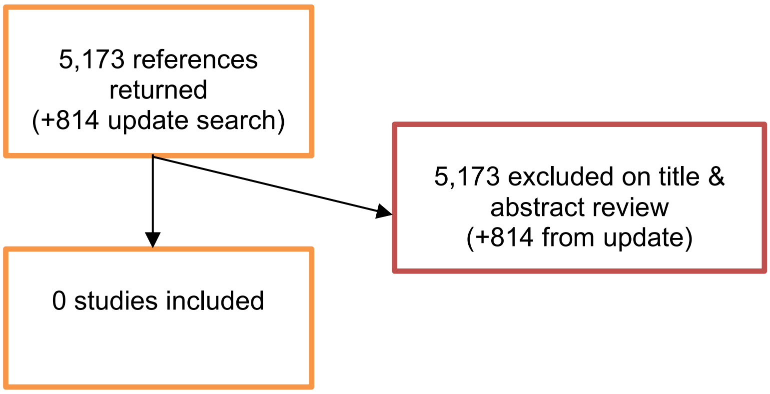
Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Hospital length of stay (days); effect sizes below 0 favour exercise group									
Wnuk (2016)	RCT	Serious[1]	Not serious	Serious[2]	Serious[3]	31	16	MD -0.36 (-0.97, 0.26)	Very low

Quality assessment						No of patients		Effect estimate	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	

1. Unclear whether intervention arms were similar at the start of the trial. Furthermore, there were moderate levels of losses to follow-up: 17 participants were excluded from the study during the postoperative period due to cardiac complications. Downgrade 1 level.
2. I^2 value between 33.3% and 66.7%, downgrade 1 level.
3. Non-significant result. Downgrade 1 level.

Appendix G – Economic evidence study selection

Review questions 11 and 30 study selection



Appendix H – Excluded studies

Clinical studies

Review question 11 (preoperative interventions)

No.	Study	Reason for exclusion
1	Alreja G, Bugano D, and Lotfi A (2012) Effect of remote ischemic preconditioning on myocardial and renal injury: meta-analysis of randomized controlled trials. The Journal of invasive cardiology 24, 42-8	Meta-analysis assessed the efficacy of remote ischaemic preconditioning by pooling data from 3 studies of patients undergoing AAA repair and 2 studies of patients undergoing coronary artery bypass grafting. No subgroup or sensitivity analysis was performed.
2	Bani-Hani M, Titi M A, Jaradat I, and al-Khaffaf H (2008) Interventions for preventing venous thromboembolism following abdominal aortic surgery (Cochrane review) [with consumer summary]. Cochrane Database of Systematic Reviews 2008, andIssue 1 ,	The systematic review included studies of patients who underwent aortic surgery not related to AAAs: aortic bifurcation graft surgery and aortic reconstruction surgery.
3	Chello M, Mastroroberto P, Romano R et al. (1996) Protection by coenzyme Q10 of tissue reperfusion injury during abdominal aortic cross-clamping. The Journal of cardiovascular surgery 37, 229-35	Intervention (antioxidant supplement) is not outlined in the review protocol.
4	Desai M, Gurusamy K, Ghanbari H et al. (2011) Remote ischaemic preconditioning does not improve morbidity or mortality following open or endovascular aneurysm repair: A meta-analysis. Interactive cardiovascular and thoracic surgery 12, S139	Conference abstract.
5	Kertai M D, Boersma E, Westerhout C et al. (2004) A combination of statins and beta-blockers is independently associated with a reduction in the incidence of perioperative mortality and nonfatal myocardial infarction in patients undergoing abdominal aortic aneurysm surgery. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 28, 343-52	Not a controlled trial. The study is a retrospective study which assessed the perioperative outcomes of patients with AAAs that had been taking statins and compared with those who had not been taking statins.
6	Kothmann E, Batterham A M, Owen S J et al. (2009) Effect of short-term exercise training on aerobic fitness in patients with abdominal aortic aneurysms: a pilot study. British Journal of Anaesthesia 2009 Oct, and103(4):505-510 ,	Participants in this study did not go on to receive surgery. As a result, this study does not assess whether exercise training is effective in optimising surgical outcomes in people undergoing surgical repair.
7	Hayashi K, Hirashiki A, Kodama A et al. (2016) Impact of preoperative regular	Not a controlled trial. This is a prospective cohort study which assessed whether

No.	Study	Reason for exclusion
	physical activity on postoperative course after open abdominal aortic aneurysm surgery. Heart and vessels 31, 578-83	patients preoperative physical activity levels affected postoperative outcomes of people undergoing AAA surgery.
8	Holzheimer R G (2003) Oral antibiotic prophylaxis can influence the inflammatory response in aortic aneurysm repair: results of a randomized clinical study. Journal of chemotherapy (Florence, and Italy) 15, 157-64	Outcome measure not of interest. Study assesses how oral antibiotic administration affects circulating inflammatory markers. No definitive outcomes were assessed.
9	Lo Sapio, P , Chechi T, Gensini GF et al. (2014) Impact of two different cardiac work-up strategies in patients undergoing abdominal aortic aneurysm repair. International journal of cardiology 175, e1-e3	Study is not directly relevant to this review question. This is a non-randomised comparative study comparing 2 algorithms for preoperative work-up: no comparisons were made with a control group (standard care).
10	McElrath M, Myers J, Chan K, et al. (2017) Exercise adherence in the elderly: Experience with abdominal aortic aneurysm simple treatment and prevention. Journal of vascular nursing : official publication of the Society for Peripheral Vascular Nursing 35(1), 12-20	Participants in this study did not go on to receive surgery. As a result, this study does not assess whether exercise training is effective in optimising surgical outcomes in people undergoing surgical repair.
11	Mouton R, Pollock J, Soar J et al. (2014) Remote ischaemic preconditioning for elective abdominal aortic aneurysm (AAA) repair: a randomized controlled trial to assess feasibility. Applied cardiopulmonary pathophysiology 18, 35	Conference abstract.
12	Myers JN, White JJ, Narasimhan B et al. (2010) Effects of exercise training in patients with abdominal aortic aneurysm: preliminary results from a randomized trial. Journal of cardiopulmonary rehabilitation and prevention 30, 374-83	Participants in this study did not go on to receive surgery. As a result, this study does not assess whether exercise training is effective in optimising surgical outcomes in people undergoing surgical repair.
13	Myers J, McElrath M, Jaffe A et al. (2014) A randomized trial of exercise training in abdominal aortic aneurysm disease. Medicine and science in sports and exercise 46, 2-9	Participants in this study did not go on to receive surgery. As a result, this study does not assess whether exercise training is effective in optimising surgical outcomes in people undergoing surgical repair.
14	Pouwels S, Willigendael EM, van Sambeek M R H et al. (2015) Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 49, 66-76	No quantitative synthesis was performed. Instead authors discussed the results of individual studies. Identified studies were assessed to ascertain their relevance to this NICE review question.

No.	Study	Reason for exclusion
15	Railton CJ, Wolpin J, Lam-McCulloch J et al. (2010) Renin-angiotensin blockade is associated with increased mortality after vascular surgery. Canadian journal of anaesthesia = Journal canadien d'anesthesie 57, 736-44	Not a controlled trial. The study is a cohort study which assessed outcomes of patients with preoperative renin-angiotensin system blockade, achieved either by angiotensin converting enzyme inhibitors or angiotensin receptor blocking agents.
16	Richardson K, Sanders G, Hayden P et al. (2014) The effect of preoperative exercise on postoperative outcome in abdominal aortic aneurysm (AAA) patients: Pilot study. Intensive care medicine 40, S136	Conference abstract.
17	Robertson L, Atallah E, and Stansby G (2017) Pharmacological treatment of vascular risk factors for reducing mortality and cardiovascular events in patients with abdominal aortic aneurysm. Cochrane Database of Systematic Reviews	Systematic review included one RCT which is already considered in this NICE review.
18	Tew G A, Moss J, Crank H et al. (2012) Endurance exercise training in patients with small abdominal aortic aneurysm: a randomised controlled pilot study. Archives of Physical Medicine and Rehabilitation 2012 Dec, and93(12):2148-2153 ,	Participants in this study did not go on to receive surgery. As a result, this study does not assess whether exercise training is effective in optimising surgical outcomes in people undergoing surgical repair.
19	Wijnen M, Vader HL, Van Den Wall Bake, A et al. (2002) Can renal dysfunction after infra-renal aortic aneurysm repair be modified by multi-antioxidant supplementation?. The Journal of cardiovascular surgery 43, 483-8	Intervention (antioxidant supplements) is not outlined in the review protocol.
20	Wijnen M, Roumen R, Vader HL, et al. (2002) A multiantioxidant supplementation reduces damage from ischaemia reperfusion in patients after lower torso ischaemia. A randomised trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 23, 486-90	Intervention (antioxidant supplements) is not outlined in the review protocol.

Review question 30 (postoperative interventions)

No.	Study	Reason for exclusion
1	Abdul-Hussien H, Hanemaaijer R, Verheijen JH et al. (2009) Doxycycline therapy for abdominal aneurysm: Improved proteolytic balance through	Outcome measure not of interest. Study assesses how doxycycline affects aortic wall expression of the enzyme, matrix metalloproteinase.

No.	Study	Reason for exclusion
	reduced neutrophil content. Journal of vascular surgery 49, 741-9	
2	Aoki A, Suezawa T, Yamamoto S et al. (2014) Effect of antifibrinolytic therapy with tranexamic acid on abdominal aortic aneurysm shrinkage after endovascular repair. Journal of vascular surgery 59, 1203-8	Not a controlled trial. The study involved a retrospective review of medical records of patients treated before and after 5 institutions started administering tranexamic acid as part of their EVAR treatment protocols.
3	Boker A, Haberman CJ, Girling L et al. (2004) Variable ventilation improves perioperative lung function in patients undergoing abdominal aortic aneurysmectomy. Anesthesiology 100, 608-16	Perioperative intervention: study assessed the efficacy of variable ventilation delivered during surgery.
4	Brinkmann S J. H, Buijs N, Vermeulen M A et al. (2016) Perioperative glutamine supplementation restores disturbed renal arginine synthesis after open aortic surgery: A randomized controlled clinical trial. American Journal of Physiology - Renal Physiology 311, F567-f575	Outcome measure not of interest. Study assesses how perioperative glutamine administration affects arginine biosynthesis.
5	de Bruin JL, Baas AF, Heymans MW et al. (2014) Statin therapy is associated with improved survival after endovascular and open aneurysm repair. Journal of vascular surgery 59, 39-44.e1	Post-hoc analysis of an RCT comparing EVAR and open aneurysm repair. One of the secondary outcomes assessed was whether statin therapy reduced the risk of cardiovascular deaths. Unfortunately, it was not clear whether patients received statins before or after surgery.
6	Duffy MJ, O'Kane CM, Stevenson M et al. (2015) A randomized clinical trial of ascorbic acid in open abdominal aortic aneurysm repair. Intensive Care Medicine Experimental 3,	Perioperative intervention: study assessed the efficacy of parenteral ascorbic acid, administered during surgery.
7	Jones CI, Payne DA, Hayes PD et al.(2008) The antithrombotic effect of dextran-40 in man is due to enhanced fibrinolysis in vivo. Journal of vascular surgery 48, 715-22	Perioperative intervention: study assessed the efficacy of dextran-40, administered over 1 hour during surgery.
8	Kalimeris K, Nikolakopoulos N, Riga M et al. (2014) Mannitol and renal dysfunction after endovascular aortic aneurysm repair procedures: a randomized trial. Journal of cardiothoracic and vascular anesthesia 28, 954-9	Perioperative intervention: study assessed the efficacy of mannitol, administered within 15 minutes of surgery commencement.
9	Kertai MD, Boersma E, Westerhout CM et al. (2004) Association between long-term statin use and mortality after successful abdominal aortic aneurysm surgery. The American journal of medicine 116, 96-103	Not a controlled trial. The study is a retrospective study which assessed the outcomes of patients with AAAs that had been taking statins and compared with those who had not been taking statins.

No.	Study	Reason for exclusion
10	Leijdekkers VJ, Vahl AC, Mackaay A J et al. (2006) Aprotinin does not diminish blood loss in elective operations for infrarenal abdominal aneurysms: A randomized double-blind controlled trial. Annals of Vascular Surgery 20, 322-329	Perioperative intervention: study assessed the efficacy of aprotinin, administered during surgery.
11	Nicholson ML, Baker DM, Hopkinson BR et al. (1996) Randomized controlled trial of the effect of mannitol on renal reperfusion injury during aortic aneurysm surgery. The British journal of surgery 83, 1230-3	Perioperative intervention: study assessed the efficacy of mannitol, administered during surgery.
12	Rittoo D, Gosling P, Burnley S et al. (2004) Randomized study comparing the effects of hydroxyethyl starch solution with Gelofusine on pulmonary function in patients undergoing abdominal aortic aneurysm surgery. British journal of anaesthesia 92, 61-6	Perioperative intervention: study compared the efficacy hydroxyethyl starch solution with gelofusine, administered during surgery.
13	Smaka TJ, Cobas M, Velazquez OC et al. (2011) Perioperative management of endovascular abdominal aortic aneurysm repair: update 2010. Journal of cardiothoracic and vascular anesthesia 25, 166-76	Literature review.
14	Tisi PV, and Shearman CP (1997) Randomized controlled trial of the effect of mannitol on renal reperfusion injury during aortic aneurysm surgery. The British journal of surgery 84, 587	Letter to editor.
15	West MA, Parry M, Asher R et al. (2015) The Effect of beta-blockade on objectively measured physical fitness in patients with abdominal aortic aneurysms--A blinded interventional study. British journal of anaesthesia 114, 878-85	Study did not assess postoperative outcomes.

Economic studies

No full text papers were retrieved. All studies were excluded at review of titles and abstracts.

Appendix I – Research recommendations

Preoperative exercise programmes

Research recommendation	**What is the clinical and cost-effectiveness of preoperative exercise programmes for improving outcomes of people who are having repair of an AAA?**
Population	People with a confirmed unruptured abdominal aortic aneurysm in whom surgery is planned.
Intervention(s)	Exercise programmes incorporating physical exercise, preoperative physiotherapy or respiratory muscle training.
Comparator(s)	Each other, or no exercise
Outcomes	• Perioperative morbidity and mortality • Incidence of postoperative complications (AAA rupture, AAA growth/expansion, cardiovascular events, wound-related complications, endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion) • Need for further surgical intervention • Mortality (all-cause; AAA-related; cardiovascular; survival) • Cardiovascular events • Quality of life • Adverse effects • Resource use and cost
Study design	Randomised controlled trial

Potential criterion	**Explanation**
Importance to patients, service users or the population	NHS providers have started devoting resources to exercise programmes, based on a relatively small body of evidence. Further research on the effectiveness of these programmes is needed to inform funding decisions.
Relevance to NICE guidance	Medium priority: no recommendations were made in this guideline due to limited evidence, and further research would allow for recommendations to be possible in future guideline updates.
Current evidence base	There is a growing body of evidence on preoperative exercise interventions for people undergoing various types of surgical procedures; however, the evidence relating to people with AAA was limited in quantity. Identified studies evaluating preoperative exercise interventions, in people with AAAs, were not considered robust enough to draft recommendations. The study evaluating the efficacy of inspiratory muscle training, by Dronkers et al. (2008), was considered low in quality as it had a small sample size (20 participants) and a short follow-up period. The study assessing the efficacy on supervised exercise, by Barakat et al (2016) was considered moderate in quality; however, reporting of composite outcomes, made it difficult to establish specific benefits (or harms) associated with the intervention.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	Postoperative growth and rupture is very rare, such that the committee suggested that it would require a very large RCT to detect an effect.

Postoperative use of Direct Oral Anticoagulants (DOACs)

Research recommendation	What are the benefits of postoperative use of Direct Oral Anticoagulants (DOACS) for improving outcomes after repair of AAA?
Population	People who have undergone surgical repair of an abdominal aortic aneurysm.
Intervention(s)	• Apixaban • Dabigatran • Edoxaban • Rivaroxaban • Betrixaban
Comparator(s)	• Each other • Matched placebo
Outcomes	• Incidence of postoperative complications (AAA rupture, AAA growth/expansion, cardiovascular events, wound-related complications, endoleak, graft migration, graft kinking, incisional hernia, graft occlusion, aortic neck expansion) • Need for further surgical intervention • Mortality (all-cause; AAA-related; cardiovascular; survival) • Cardiovascular events • Quality of life • Adverse effects • Resource use and cost
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	The committee recognised the risk of thromboembolic events (such as deep venous thrombosis and pulmonary embolism) following AAA surgery, and noted that postoperative anticoagulation, with or without the use of mechanical devices, can safely reduce the risk of such complications. DOACs are becoming increasingly popular because they are easy to use, have good pharmacokinetic properties associated with fixed dosing, have few interactions with other medications, and require less frequent monitoring. With that in mind, it is important to establish how best to use DOACs in the postoperative period to balance the risk thromboembolic events with that of bleeding.
Relevance to NICE guidance	Medium priority: no recommendations were made in this guideline due to the lack of evidence, and studies would allow for recommendations to be possible in future guideline updates.
Current evidence base	No studies were identified that specifically assessed the efficacy of postoperative use of DOACs for improving outcomes after repair of AAA.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	Postoperative growth and rupture is very rare, such that the committee suggested that it would require a very large RCT to detect an effect.

Appendix J – Glossary

Abdominal Aortic Aneurysm (AAA)

A localised bulge in the abdominal aorta (the major blood vessel that supplies blood to the lower half of the body including the abdomen, pelvis and lower limbs) caused by weakening of the aortic wall. It is defined as an aortic diameter greater than 3 cm or a diameter more than 50% larger than the normal width of a healthy aorta. The clinical relevance of AAA is that the condition may lead to a life threatening rupture of the affected artery. Abdominal aortic aneurysms are generally characterised by their shape, size and cause:

- Infrarenal AAA: an aneurysm located in the lower segment of the abdominal aorta below the kidneys.
- Juxtarenal AAA: a type of infrarenal aneurysm that extends to, and sometimes, includes the lower margin of renal artery origins.
- Suprarenal AAA: an aneurysm involving the aorta below the diaphragm and above the renal arteries involving some or all of the visceral aortic segment and hence the origins of the renal, superior mesenteric, and celiac arteries, it may extend down to the aortic bifurcation.

Abdominal compartment syndrome

Abdominal compartment syndrome occurs when the pressure within the abdominal cavity increases above 20 mm Hg (intra-abdominal hypertension). In the context of a ruptured AAA this is due to the mass effect of a volume of blood within or behind the abdominal cavity. The increased abdominal pressure reduces blood flow to abdominal organs and impairs pulmonary, cardiovascular, renal, and gastro-intestinal function. This can cause multiple organ dysfunction and eventually lead to death.

Cardiopulmonary exercise testing

Cardiopulmonary Exercise Testing (CPET, sometimes also called CPX testing) is a non-invasive approach used to assess how the body performs before and during exercise. During CPET, the patient performs exercise on a stationary bicycle while breathing through a mouthpiece. Each breath is measured to assess the performance of the lungs and cardiovascular system. A heart tracing device (Electrocardiogram) will also record the hearts electrical activity before, during and after exercise.

Device migration

Migration can occur after device implantation when there is any movement or displacement of a stent-graft from its original position relative to the aorta or renal arteries. The risk of migration increases with time and can result in the loss of device fixation. Device migration may not need further treatment but should be monitored as it can lead to complications such as aneurysm rupture or endoleak.

Endoleak

An endoleak is the persistence of blood flow outside an endovascular stent - graft but within the aneurysm sac in which the graft is placed.

- Type I – Perigraft (at the proximal or distal seal zones): This form of endoleak is caused by blood flowing into the aneurysm because of an incomplete or ineffective seal at either end of an endograft. The blood flow creates pressure within the sac and significantly increases the risk of sac enlargement and rupture. As a result, Type I endoleaks typically require urgent attention.
- Type II – Retrograde or collateral (mesenteric, lumbar, renal accessory): These endoleaks are the most common type of endoleak. They occur when blood bleeds into the sac from small side branches of the aorta. They are generally considered benign because they are usually at low pressure and tend to resolve spontaneously over time without any need for intervention. Treatment of the endoleak is indicated if the aneurysm sac continues to expand.
- Type III – Midgraft (fabric tear, graft dislocation, graft disintegration): These endoleaks occur when blood flows into the aneurysm sac through defects in the endograft (such as graft fractures, misaligned graft joints and holes in the graft fabric). Similarly to Type I endoleak, a Type III endoleak results in systemic blood pressure within the aneurysm sac that increases the risk of rupture. Therefore, Type III endoleaks typically require urgent attention.
- Type IV– Graft porosity: These endoleaks often occur soon after AAA repair and are associated with the porosity of certain graft materials. They are caused by blood flowing through the graft fabric into the aneurysm sac. They do not usually require treatment and tend to resolve within a few days of graft placement.
- Type V – Endotension: A Type V endoleak is a phenomenon in which there is continued sac expansion without radiographic evidence of a leak site. It is a poorly understood abnormality. One theory that it is caused by pulsation of the graft wall, with transmission of the pulse wave through the aneurysm sac to the native aneurysm wall. Alternatively it may be due to intermittent leaks which are not apparent at imaging. It can be difficult to identify and treat any cause.

Endovascular aneurysm repair

Endovascular aneurysm repair (EVAR) is a technique that involves placing a stent –graft prosthesis within an aneurysm. The stent-graft is inserted through a small incision in the femoral artery in the groin, then delivered to the site of the aneurysm using catheters and guidewires and placed in position under X-ray guidance.

- Conventional EVAR refers to placement of an endovascular stent graft in an AAA where the anatomy of the aneurysm is such that the ‘instructions for use’ of that particular device are adhered to. Instructions for use define tolerances for AAA anatomy that the device manufacturer considers appropriate for that device. Common limitations on AAA anatomy are infrarenal neck length (usually >10mm), diameter (usually ≤30mm) and neck angle relative to the main body of the AAA
- Complex EVAR refers to a number of endovascular strategies that have been developed to address the challenges of aortic proximal neck fixation associated with complicated aneurysm anatomies like those seen in juxtarenal and suprarenal AAAs.

These strategies include using conventional infrarenal aortic stent grafts outside their 'instructions for use', using physician-modified endografts, utilisation of customised fenestrated endografts, and employing snorkel or chimney approaches with parallel covered stents.

Goal directed therapy

Goal directed therapy refers to a method of fluid administration that relies on minimally invasive cardiac output monitoring to tailor fluid administration to a maximal cardiac output or other reliable markers of cardiac function such as stroke volume variation or pulse pressure variation.

Post processing technique

For the purpose of this review, a post-processing technique refers to a software package that is used to augment imaging obtained from CT scans, (which are conventionally presented as axial images), to provide additional 2- or 3-dimensional imaging and data relating to an aneurysm's, size, position and anatomy.

Permissive hypotension

Permissive hypotension (also known as hypotensive resuscitation and restrictive volume resuscitation) is a method of fluid administration commonly used in people with haemorrhage after trauma. The basic principle of the technique is to maintain haemostasis (the stopping of blood flow) by keeping a person's blood pressure within a lower than normal range. In theory, a lower blood pressure means that blood loss will be slower, and more easily controlled by the pressure of internal self-tamponade and clot formation.

Remote ischemic preconditioning

Remote ischemic preconditioning is a procedure that aims to reduce damage (ischaemic injury) that may occur from a restriction in the blood supply to tissues during surgery. The technique aims to trigger the body's natural protective functions. It is sometimes performed before surgery and involves repeated, temporary cessation of blood flow to a limb to create ischemia (lack of oxygen and glucose) in the tissue. In theory, this "conditioning" activates physiological pathways that render the heart muscle resistant to subsequent prolonged periods of ischaemia.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent (medication that promotes blood clotting) that can be used to prevent, stop or reduce unwanted bleeding. It is often used to reduce the need for blood transfusion in adults having surgery, in trauma and in massive obstetric haemorrhage.