National Institute for Health and Care Excellence

Final

Abdominal aortic aneurysm: diagnosis and management

Evidence review M: Goal-directed therapy during repair of unruptured and ruptured abdominal aortic aneurysms

NICE guideline NG156

Methods, evidence and recommendations

March 2020

Final

This evidence review was developed by the NICE Guideline Updates Team

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ISBN: 978-1-4731-3452-2

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Introduction

Goal directed therapy (GDT) 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. The intention of the technique is to reduce the risk of perioperative (30-day) morbidity and mortality after major surgery. Review questions 14 and 26 aim to assess the use of goal-directed therapy in people undergoing surgery for unruptured and ruptured abdominal aortic aneurysms (AAAs), respectively.

PICO table

Table 1: PICO table for GDT for unruptured or ruptured AAA

Parameter	Inclusion criteria
Population	People undergoing surgery for a confirmed unruptured or ruptured AAA
Intervention	Goal-directed fluid and/or ionotrope administration 'Goal-directed' refers to the use of cardiac output monitoring to tailor fluid administration to a maximal cardiac output
Comparators	Standard practice: fluid and/or ionotrope administration based on static preload parameters and traditional hemodynamics
Outcomes	• Mortality • Complications of surgery, including pain, blood loss, wound complications, respiratory complications, cardiovascular complications, gastrointestinal complications, and renal failure • Need for additional intervention, including the use of blood transfusions and other operative fluids • Adverse events • Quality of life • Resource use, including length of hospital or intensive care stay, and costs

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 2 review questions and identify studies that assessed the efficacy of goal-directed therapy for improving outcomes of surgical repair of unruptured and ruptured 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 that assessed whether goal-directed therapy improved outcomes of people undergoing surgical repair of unruptured or ruptured AAAs. Since limited evidence was identified from the RCT and systematic review literature search, the observational study database was sifted to identify non-randomised controlled trials which were potentially relevant to the review questions.

Studies were excluded if they:

- were not in English
- were not full reports of the study (for example, published only as an abstract)
- were not peer-reviewed
- were cohort studies, case series or case-control studies

Clinical evidence

Included studies

From an initial RCT database of 1,518 abstracts, 11 studies were identified as being potentially relevant to review question 14 and no questions were identified for review question 26. Following full-text review of the 14 ordered articles, 3 studies were included. No studies were identified as being potentially relevant to review questions 14 or 26 in an initial observational study database of 831 abstracts.

Update searches were conducted in December 2017, to identify any relevant studies published during guideline development. The update RCT and the observational study databases contained 42 and 45 abstracts, respectively. None of these were considered relevant. As a result no additional studies were identified.

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.

Table 2: Summary of included studies on GDT during repair of unruptured AAA

Study	Details
Bisgaard J, Gilsaa T, Ronholm E, and Toft P (2013) Optimising stroke volume and oxygen delivery in abdominal aortic surgery: a randomised controlled trial. Acta anaesthesiologica Scandinavica 57, 178-88	Study design: randomised controlled trial Location(s): Denmark Population: people with AAA undergoing elective open repair Sample size: 64; 70.3% (45/64) male Follow-up: 30 days Intervention: GDT – to maintain each patient's stroke volume index above 10% Comparators: control group – fluid therapy based on standard haemodynamic parameters Outcomes: mortality, postoperative complications, volume of blood products used (red blood cell concentrate, frozen plasma, and platelet transfusions), reoperation, need for mechanical ventilation, need for acute dialysis

Study	Details
Bonazzi M, Gentile F, Biasi G M, Migliavacca S, Esposti D, Cipolla M, Marsicano M, Prampolini F, Ornaghi M, Sternjakob S, and Tshomba Y (2002) Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients. A randomised pilot trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 23, 445-51	Study design: randomised controlled trial Location(s): Italy Population: people with AAA undergoing elective open repair Sample size: 100; sex-specific proportions were not reported Follow-up: not reported Intervention: GDT – cardiac output optimisation was performed to achieve a cardiac Index >3.0 l/min/sqm, pulmonary wedge pressure >10 and <18 mmHg, systemic vascular resistance <1450 dyne/sec/cm-5, oxygen delivery >600 ml/min/sqm. Comparators: control group – other than monitoring central venous pressure and invasive arterial pressure during surgery no haemodynamic monitoring was performed Outcomes: in-hospital mortality, cardiovascular morbidity, postoperative renal failure, length of stay
Funk Duane J, HayGlass Kent T, Koulack Joshua, Harding Greg, Boyd April, and Brinkman Ryan (2015) A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. Critical care (London, and England) 19, 247	Study design: randomised controlled trial Location(s): Canada Population: people with AAA undergoing elective open repair Sample size: 40; 67.5% (27/40) male Follow-up: not reported Intervention: GDT – cardiac optimisation was used to maintain the stroke volume variation below 13 %, the cardiac index at 2.2 l/minute per m2 and the mean arterial pressure less than 60 mmHg Comparators: control group – anaesthetists did not stroke volume variation or cardiac index information available as this information was covered by an opaque card Outcomes: mortality, postoperative complications, need for blood transfusion, length of stay

See Appendix D for full evidence tables.

GDT during repair of ruptured AAA

No studies were identified as being potentially relevant.

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 related to GDT during repair of unruptured AAA.

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 this review.

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

GDT during repair of unruptured AAA

Low-quality evidence from 2 RCTs, including 104 people undergoing elective open repair of AAA, indicated that people who received GDT during surgery needed more postoperative colloids than those who received traditional fluid administration during surgery.

Very low- to moderate-quality evidence from 3 RCTs, including 204 people who received goal-directed therapy or traditional fluid administration during elective open repair of AAA, could not differentiate the following outcome measures between groups:

- Mortality
- Cardiac complications (acute coronary syndrome, congestive heart failure arrhythmia and dysrhythmia)
- Pulmonary complications (pulmonary oedema and respiratory failure)
- Renal complications (acute kidney injury and
- Gastrointestinal complications (ischaemic gut and gastrointestinal paralysis)
- Cerebral thrombosis
- Lower limb paresis
- Infection (sepsis, pneumonia, wound infections and urinary tract infection)
- Blood loss
- Resource use (postoperative use of fluids, length of ICU or hospital stay, reoperations, the need for acute dialysis and the need for mechanical intervention)

GDT during repair of ruptured AAA

No studies assessing the efficacy of GDT during repair of ruptured AAA were identified.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee considered that the outcomes which matter most are perioperative morbidity and mortality. The committee considered that perioperative outcomes were more important than long-term outcomes because their clinical experience highlighted that people undergoing AAA surgery are more likely to experience negative outcomes immediately after surgery.

The quality of the evidence

The committee noted that the term GDT encompasses a broad range of practices, and the studies included in this review adopted different complex strategies for optimising cardiac output in people undergoing AAA surgery.

The committee considered that the identified evidence was very-low-to-moderate in quality. The main reason for downgrading evidence was imprecision of effect estimates: 95% confidence intervals of pooled estimates crossed 1 or 2 lines of predefined minimal important differences. Another reason for downgrading evidence was the statistical heterogeneity observed in some of the meta-analyses performed in this review.

The committee noted that pooled results from 2 RCTs indicated that people who receive GDT need more colloids after surgery; however, the committee considered that this was not a clinically important outcome. No differences in the remaining outcome measures were observed between people who received GDT and those treated by traditional haemodynamic management strategies.

The committee discussed whether it was appropriate to make a "do not offer GDT" recommendation. As GDT encompasses a broad range of different practices, it would be problematic to disentangle these differing elements and they agreed that it was not possible to point to 1 or 2 specific practices that should not be performed. It was also noted that haemodynamic monitoring and management are essential during major surgery. The committee agreed that a "do not offer" recommendation was too restrictive and could potentially limit the use of some basic techniques for managing people during surgery. As a result, the committee decided not to make any recommendations.

Benefits and harms

The committee noted that, although the identified evidence reported no differences in clinically important outcomes between people who received GDT and those managed using traditional approaches, the evidence comprised 3 small RCTs. As a result, the committee concluded that the evidence failed to show any benefit in performing GDT on people undergoing surgical repair of unruptured AAA.

Cost effectiveness and resource use

The committee noted that GDT is a complex and highly technical procedure that needs more staff and additional training compared with standard practice. These factors result in considerably higher costs associated with GDT. With this in mind, the committee believed that GDT was unlikely to be cost effective in AAA surgery; especially since the specialty generally has low operative mortality rates.

Other factors the committee took into account

The committee noted that studies had previously been published highlighting that GDT reduces morbidity but not mortality in people undergoing vascular surgery. The committee considered that these studies were not suitable for consideration because they included heterogeneous groups of people with different vascular conditions, making it impossible to extrapolate whether there were any benefits to people with AAA.

Appendices

Appendix A – Review protocols

Review protocol for review question 14: GDT during repair of unruptured abdominal aortic aneurysms

Review question 14	Is goal-directed therapy effective during the surgical repair of an unruptured abdominal aortic aneurysm?
Objectives	To assess the use of goal-directed therapy in people undergoing surgery for an unruptured abdominal aortic aneurysm
Type of review	Intervention
Language	English only
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 undergoing surgery for a confirmed unruptured abdominal aortic aneurysm
Intervention	Goal-directed fluid and/or ionotrope administration 'Goal-directed' refers to the use of cardiac output monitoring to tailor fluid administration to a maximal cardiac output
Comparator	Standard practice Fluid and/or ionotrope administration based on static preload parameters and traditional hemodynamics
Outcomes	• Mortality • Complications of surgery, including pain, blood loss, wound complications, respiratory complications, cardiovascular complications, gastrointestinal complications, and renal failure • Need for additional intervention, including the use of blood transfusions and other operative fluids • Adverse events • 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. 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.

Review question 14	Is goal-directed therapy effective during the surgical repair of an unruptured abdominal aortic aneurysm?
	All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.
Key papers	Funk DJ, HayGlass KT, Koulack J, Harding G, Boyd A, Brinkman R. A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. Crit Care. 2015 Jun 10;19:247

Review protocol for review question 26: GDT during repair of ruptured abdominal aortic aneurysms

Review question 26	Is goal-directed therapy effective during the surgical repair of a ruptured abdominal aortic aneurysm?
Objectives	To assess the use of goal-directed therapy in people undergoing surgery for a ruptured abdominal aortic aneurysm
Type of review	Intervention
Language	English only
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 undergoing surgery for a ruptured abdominal aortic aneurysm
Intervention	Goal-directed fluid and/or ionotrope administration 'Goal-directed' refers to the use of cardiac output monitoring to tailor fluid administration to a maximal cardiac output
Comparator	Standard practice Fluid and/or ionotrope administration based on static preload parameters and traditional hemodynamics
Outcomes	• Mortality • Complications of surgery, including pain, blood loss, wound complications, respiratory complications, cardiovascular complications, gastrointestinal complications, and renal failure • Need for additional intervention, including the use of blood transfusions and other operative fluids • Adverse events • 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 26	Is goal-directed therapy effective during the surgical repair of a ruptured 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	Funk DJ, HayGlass KT, Koulack J, Harding G, Boyd A, Brinkman R. A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. Crit Care. 2015 Jun 10;19:247

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 14 and 26

Medline Strategy, searched 27th June 2017
Database: Ovid MEDLINE(R) 1946 to June Week 3 2017
Search Strategy:

1 Aortic Aneurysm, Abdominal/
2 (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.
3 Aortic Rupture/
4 (AAA or RAAA).tw.
5 (endovascular* adj4 aneurysm* adj4 repair*).tw.
6 (endovascular* adj4 aort* adj4 repair*).tw.
7 (EVAR or EVRAR or FEVAR or F-EAVAR or BEVAR or B-EVAR).tw.
8 (Anaconda or Zenith Dynalink or Hemobahn or Luminex* or Memoth-erm or Wallstent).tw.
9 (Viabahn or Nitinol or Hemobahn or Intracoil or Tantalum).tw.
10 or/1-9
11 X-Rays/
12 (x-ray* or x ray* or xray* or x-radiation* or x radiation* or roentgen ray* or grenz ray* or radiograph*).tw.

Medline Strategy, searched 27th June 2017
Database: Ovid MEDLINE(R) 1946 to June Week 3 2017
Search Strategy:

13 Aortography/
14 aortograph*.tw.
15 Tomography, X-Ray Computed/
16 (cat scan* or ct scan* or cine ct or cine-ct or tomodensitomet*).tw.
17 ((computed or computer assisted or computeriz* or computeris* or electron beam* or axial*) adj4 tomograph*).tw.
18 Four-Dimensional Computed Tomography/
19 (4d ct or 4dct or 4-dimensional CT or four dimensional CT).tw.
20 exp Tomography, Spiral Computed/
21 ((helical or spiral) adj4 ct*).tw.
22 exp Magnetic Resonance Imaging/
23 (nmr tomograph* or mr tomograph* or nmr imag* or mri scan* or functional mri* or fmri* or zeugmatograph* or cine-mri* or cinemri*).tw.
24 (proton spin adj4 tomograph*).tw.
25 ((chemical shift or magnetic resonance or magneti* transfer) adj4 imag*).tw.
26 exp Angiography/
27 (angiograph* or arteriograph*).tw.
28 exp Ultrasonography/
29 (ultrasound* or ultrason* or sonograph* or echograph* or echotomograph*).tw.
30 exp Echocardiography/
31 echocardiograph*.tw.
32 Finite element analysis/
33 (finite adj4 element* adj4 analys*).tw.
34 (finite adj4 element* adj4 comput*).tw.
35 FEA.tw.
36 ((wall adj4 stress adj4 analys*) or (wall adj4 stress adj4 comput*)).tw.
37 exp Computer simulation/
38 Software/
39 Image interpretation, computer-assisted/ or Radiographic image interpretation, computer-assisted/
40 Imaging Three-Dimensional/
41 exp Image enhancement/
42 Stress, mechanical/
43 (stress* adj4 mechanical*).tw.
44 (scan* or imag*).tw.
45 Watchful waiting/
46 (watchful adj4 waiting*).tw.
47 Mass screening/
48 screen*.tw.
49 Population surveillance/
50 surveillan*.tw.
51 ((period* or test* or frequen* or regular* or routine* or rate or optimal* or optimis* or optimiz* or repeat* or interval*) adj4 (test* or monitor* or observ* or measur* or assess* or screen* or re-screen* or rescreen* or exam* or evaluat*)).tw.
52 ((aneursym* or sign* or diameter or risk*) adj4 (grow* or siz* or measur* or expan* or ruptur* or tear* or progress* or enlarg* or dilat* or bulg* or evaluat*)).tw.
53 Patient Selection/
54 ((patient or subject or criteria or treatment*) adj4 select*).tw.
55 ((follow-up or follow up) adj4 (visit* or repeat* or monitor* or assess* or care*)).tw.

Medline Strategy, searched 27th June 2017 Database: Ovid MEDLINE(R) 1946 to June Week 3 2017 Search Strategy:
56 Aftercare/
57 (aftercare or after-care).tw.
58 Disease progression/
59 ((disease or illness or condition) adj4 (progress* or worsen* or exacerbat* or deterior* or course or duration or trajector* or improv* or recur* or relaps* or remission)).tw.
60 endosure*.tw.
61 ((endosensor* or intrasac*) adj4 (monitor* or transduc*)).tw.
62 or/11-61
63 10 and 62
64 animals/ not humans/
65 63 not 64
66 limit 65 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.

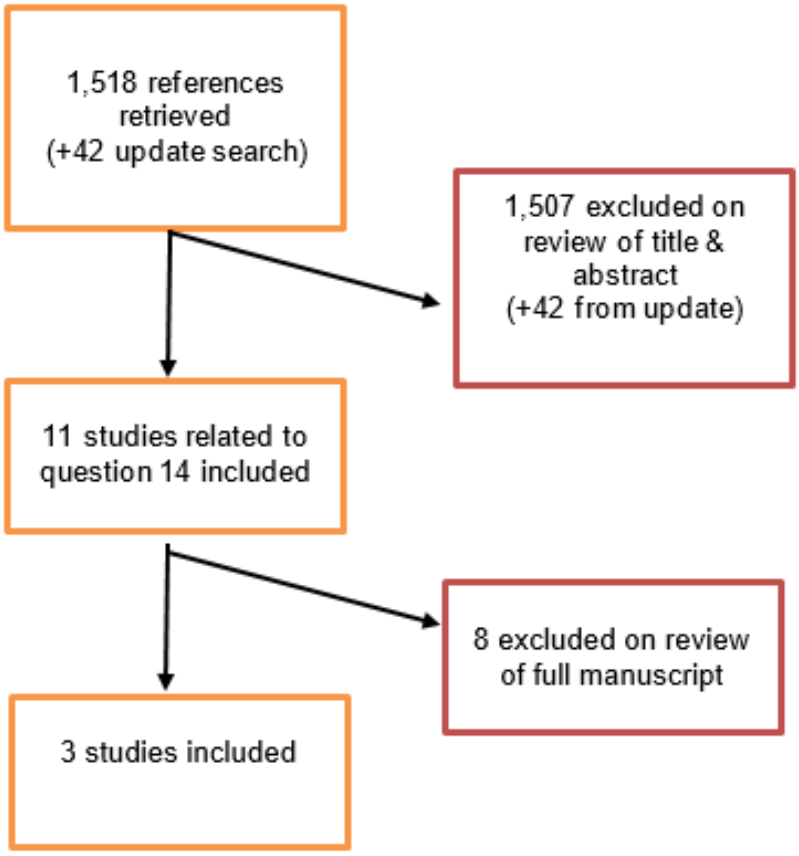
Medline Strategy

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.
24 (value adj3 (money or monetary)).tw.
25 (pharmacoeconomic* or (pharmaco adj economic*)).tw.
26 or/1-25

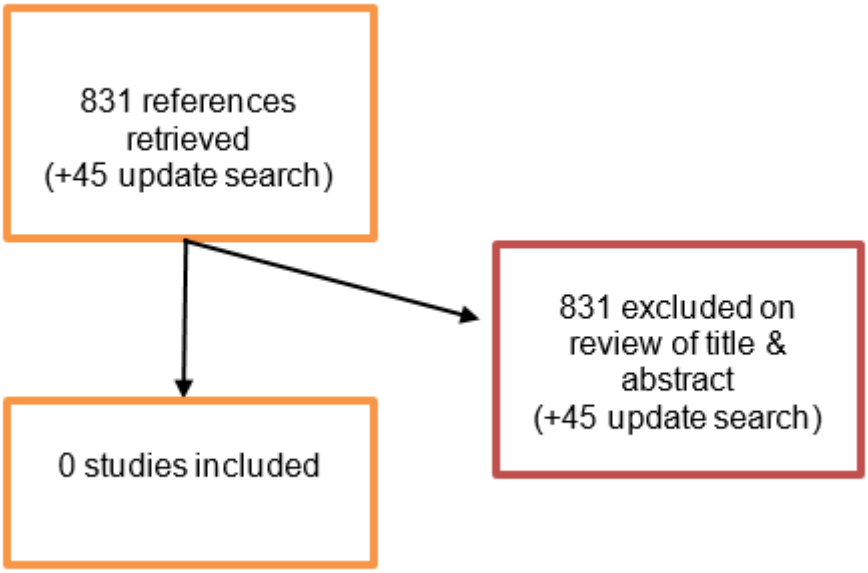
Quality of life
1 "Quality of Life"/
2 quality of life.tw.
3 "Value of Life"/
4 Quality-Adjusted Life Years/
5 quality adjusted life.tw.
6 (qaly* or qald* or qale* or qtime*).tw.
7 disability adjusted life.tw.
8 daly*.tw.
9 Health Status Indicators/
10 (sf36 or sf 36 or short form 36 or shortform 36 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

RCT filter



Observational study filter



Appendix D – Clinical evidence tables

GDT during repair of unruptured AAA

Full citation	**Bisgaard J, Gilsaa T, Ronholm E, and Toft P (2013) Optimising stroke volume and oxygen delivery in abdominal aortic surgery: a randomised controlled trial. Acta anaesthesiologica Scandinavica 57, 178-88**
Study details	Study type: randomised controlled trial Location(s): Denmark Aim(s): to evaluate the effect of perioperative goal-directed therapy (GDT) on the incidence of complications and length of stay after elective open repair of AAA Study dates: June 2008 to July 2010 Follow-up: 30 days Sources of funding: This study was funded by the local research fund, the Toyota fund and the Research Initiative of the Danish Society of Anaesthesiology and Intensive Care Medicine
Participants	Population: patients with AAA undergoing elective open repair Sample size: 64; 70.3% (45/64) male Inclusion criteria: adults with AAA who were scheduled for elective open repair were included Exclusion criteria: end-stage renal failure, receiving lithium therapy, or body weight less than 40 kg Baseline characteristics: • Mean age: GDT group, 68 years; control group, 68 years • Sex: GDT group, 81.2% male; control group, 59.3% male • Mean aneurysm size: not reported • History of myocardial infarction, coronary artery bypass grafting or percutaneous coronary intervention: GDT group, 43.8%; control group, 18.8%
Intervention	GDT: an epidural catheter was inserted at the low thoracic or high lumbar level. Patients received aliquots of hydroxyethyl starch as colloid when hypovolaemia was suspected. Fluid challenges, using hydroxyethyl starch aliquots, were performed until the patient's stroke volume index (SVI) rose by 10% or higher for more than 20 minutes. This was repeated whenever the SVI decreased. Intravenous vasopressors were administered intraoperatively in fractionated doses to maintain a desired blood pressure. Dobutamine was not used intraoperatively but was administered during the postoperative period to maximise to maximise cardiac output.
Comparison	Control group (fluid therapy based on standard haemodynamic parameters)

Full citation	**Bisgaard J, Gilsaa T, Ronholm E, and Toft P (2013) Optimising stroke volume and oxygen delivery in abdominal aortic surgery: a randomised controlled trial. Acta anaesthesiologica Scandinavica 57, 178-88**
Outcomes measures	Mortality, postoperative complications (myocardial ischaemia, septic shock, pneumonia, wound infections, acute coronary syndrome, cardiac arrhythmia, pulmonary oedema, acute kidney injury, gastrointestinal bleeding, volume of blood products used (red blood cell concentrate, frozen plasma, and platelet transfusions), reoperation, readmission to ICU, need for mechanical ventilation, need for acute dialysis
Risk of bias assessment (using the Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – patients were allocated to GDT or control group by computer generated random sequence on the day of surgery. 2. Allocation concealment (selection bias): Unclear risk – authors did not state whether efforts were made to conceal group allocations 3. Blinding of participants and personnel (performance bias): Low risk – both participants and personnel were blinded to treatment. allocations. “The surgical, anaesthetic and ICU clinical teams were blinded to all cardiac output values by coverage of the screen throughout the study period.” 4. Blinding of outcome assessment (detection bias): Low risk – complications and length of stay were registered by a study group member without knowledge of study group allocation. 5. Incomplete outcome data (attrition bias): Low risk – all participants were accounted for with losses to follow-up adequately reported. 6. Selective reporting (reporting bias): Low risk – most of the study protocol was outlined in the manuscript and all relevant outcomes were reported. 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: Directly applicable

Full citation	**Bonazzi M, Gentile F, Biasi G M, Migliavacca S, Esposti D, Cipolla M, Marsicano M, Prampolini F, Ornaghi M, Sternjakob S, and Tshomba Y (2002) Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients. A randomised pilot trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 23, 445-51**
Study details	Study type: randomised controlled trial Location(s): Italy Aim(s): to evaluate whether perioperative haemodynamic optimisation influences outcomes of infrarenal AAA repair Study dates: April 1996 to March 2000 Follow-up: not reported Sources of funding: not reported
Participants	Population: patients with AAA undergoing elective open repair Sample size: 100; sex-specific proportions were not reported Inclusion criteria: patients less than 75 years old, without angina and arrhythmias without alterations of ventricular repolarisation on a resting electrocardiogram, without evidence of left ventricular wall motion abnormalities on preoperative transthoracic echocardiography at rest and with an ejection fraction ≥50% were included Exclusion criteria: presence of advanced chronic renal failure, severe Chronic Obstructive Pulmonary Disease requiring postoperative ventilator support, or concomitant aortoiliac obstructive disease Baseline characteristics: • Mean age: GDT group, 67 years; control group, 68 years • Sex: proportions not reported • Mean aneurysm size: not reported • Diabetes: GDT group, 5%; control group, 7% • Hypertension: GDT group, 16%; control group, 15% • Renal failure: GDT group, 3%; control group, 4%
Intervention	GDT: the radial artery of the patient's non-dominant hand was cannulated and a pulmonary artery catheter was inserted through the basilic vein under fluoroscopic guidance. Cardiac output optimisation was performed to achieve the following parameters: cardiac index >3.0 l/min/sqm, pulmonary wedge pressure >10 and <18 mmHg, systemic vascular resistance <1450 dyne/sec/cm^{-5}, oxygen delivery >600 ml/min/sqm.
Comparison	Control group: other than monitoring central venous pressure and invasive arterial pressure during surgery no haemodynamic monitoring was performed
Outcomes measures	In-hospital mortality, cardiovascular morbidity (non-fatal myocardial infarction, arrhythmias, congestive heart failure), postoperative renal failure, length of stay

Full citation	**Bonazzi M, Gentile F, Biasi G M, Migliavacca S, Esposti D, Cipolla M, Marsicano M, Prampolini F, Ornaghi M, Sternjakob S, and Tshomba Y (2002) Impact of perioperative haemodynamic monitoring on cardiac morbidity after major vascular surgery in low risk patients. A randomised pilot trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 23, 445-51**
Risk of bias assessment (using the Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – a computer-generated random number was obtained by phone-call to the Statistical Centre of the hospital on the day before surgery. 2. Allocation concealment (selection bias): Unclear risk – authors did not state whether efforts were made to conceal group allocations. 3. Blinding of participants and personnel (performance bias): Low risk – it is unclear whether participants or personnel were blinded to treatment allocations; however, this is was unlikely to affect results as objective outcomes were assessed. 4. Blinding of outcome assessment (detection bias): Unclear risk – it is unclear whether outcome assessors were blinded to treatment allocations. 5. Incomplete outcome data (attrition bias): Low risk – all participants were accounted for and there were no losses to follow-up. 6. Selective reporting (reporting bias): Low risk – most of the study protocol was outlined in the manuscript and all relevant outcomes were reported. 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**Funk Duane J, HayGlass Kent T, Koulack Joshua, Harding Greg, Boyd April, and Brinkman Ryan (2015) A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. Critical care (London, and England) 19, 247**
Study details	Study type: randomised controlled trial Location(s): Canada Aim(s): to determine if GDT is associated with lower levels of inflammatory markers Study dates: not reported Follow-up: not reported Sources of funding:
Participants	Population: patients with AAA undergoing elective open repair Sample size: 40; 67.5% (27/40) male Inclusion criteria: patients over 18 years who were scheduled to undergo elective open AAA repair were included Exclusion criteria: over 80 years old, weight greater than 120 kg, known or suspected aortic insufficiency, renal dysfunction, active congestive heart failure, or atrial fibrillation Baseline characteristics: • Mean age: GDT group, 70 years; control group, 67 years • Sex: GDT group, 60% male; control group, 75% male • Mean aneurysm size: not reported • Diabetes: GDT group, 15%; control group, 10% • Hypertension: GDT group, 70%; control group, 65% • Hyperlipidaemia: GDT group, 60%; control group, 50% • COPD: GDT group, 55%; control group, 35% • Ischaemic heart disease: GDT group, 40%; control group, 40% • Myocardial infarction: GDT group, 40%; control group, 35%
Intervention	GDT: an epidural catheter was inserted at the thoracic level and patients received a background crystalloid infusion of 3 cm^3/kg ideal body weight of lactated Ringers solution. Hydroxyethyl starch solution was used to maintain the stroke volume variation (SVV) below 13 %. Inotropic therapy was started when the SVV was less than 13 % and cardiac index (CI) was less than 2.2 l/minute per m^2. Phenylephrine was used if SVV was less than 13 %, the CI was more than 2.2 l/minute per m^2 and mean arterial pressure was less than 60 mmHg.
Comparison	Control group: anaesthetists did not have CI or SVV information available as this information was covered by an opaque card
Outcomes measures	Mortality, complications (myocardial infarction, pneumonia, respiratory failure, sepsis, rhabdomyolysis, acute kidney injury, dysrhythmia, bleeding, ischaemic guy, and delirium) ICU admission, length of stay
Risk of bias assessment	• Did the trial address a clearly focused issue? Yes

Full citation	Funk Duane J, HayGlass Kent T, Koulack Joshua, Harding Greg, Boyd April, and Brinkman Ryan (2015) A randomized controlled trial on the effects of goal-directed therapy on the inflammatory response open abdominal aortic aneurysm repair. Critical care (London, and England) 19, 247
(using the Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – authors state that participants were randomised by way of a sealed envelope but no details are provided as to how randomisation was performed. 2. Allocation concealment (selection bias): Unclear risk – authors did not state whether efforts were made to conceal group allocations. 3. Blinding of participants and personnel (performance bias): Low risk – authors stated that patients and personnel were blinded to treatment allocations. 4. Blinding of outcome assessment (detection bias): Low risk – authors highlighted that a blinded assessor determined the occurrence of postoperative outcomes and statistical analysis was performed independently. 5. Incomplete outcome data (attrition bias): Low risk – all participants were accounted for and there were no losses to follow-up. 6. Selective reporting (reporting bias): Low risk – all appropriate outcomes were adequately reported. 7. Other bias: Low risk – none identified Overall risk of bias: moderate Unclear – authors state that participants were randomised by way of a sealed envelope but no details are provided as to how randomisation was performedYes – authors highlight that a blinded assessor determined the occurrence of postoperative complicationsDirectness: directly applicable

GDT during repair of ruptured AAA

No studies were identified as being relevant to review question 26.

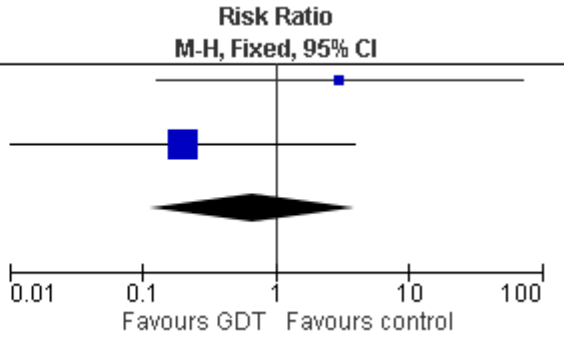
Appendix E – Forest plots

GDT during repair of unruptured AAA

Mortality

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bisgaard 2013	1	32	0	32	16.7%	3.00 [0.13, 71.00]
Bonazzi 2002	0	50	0	50		Not estimable
Funk 2015	0	20	2	20	83.3%	0.20 [0.01, 3.92]
Total (95% CI)		**102**		**102**	**100.0%**	**0.67 [0.11, 3.87]**
Total events	1		2			

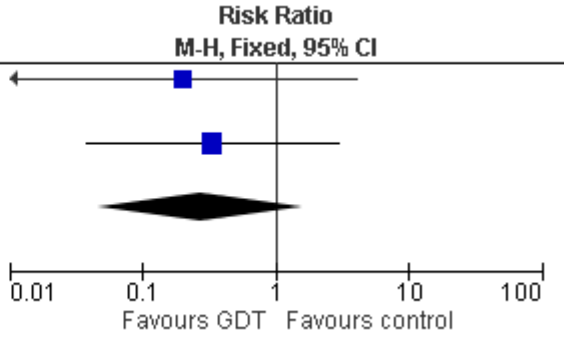
Heterogeneity: Chi² = 1.50, df = 1 (P = 0.22); I² = 33%
Test for overall effect: Z = 0.45 (P = 0.65)



Acute coronary syndrome

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bisgaard 2013	0	32	2	32	45.5%	0.20 [0.01, 4.01]
Bonazzi 2002	0	50	0	50		Not estimable
Funk 2015	1	20	3	20	54.5%	0.33 [0.04, 2.94]
Total (95% CI)		**102**		**102**	**100.0%**	**0.27 [0.05, 1.58]**
Total events	1		5			

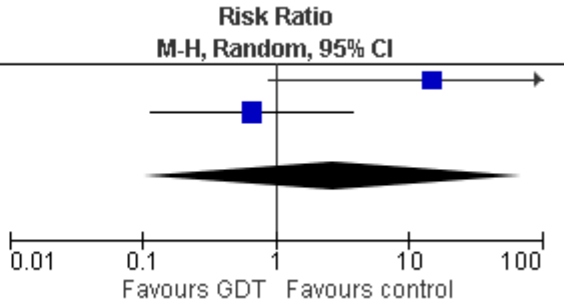
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.45 (P = 0.15)



Arrhythmia

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Bisgaard 2013	7	32	0	32	44.3%	15.00 [0.89, 252.09]
Bonazzi 2002	2	50	3	50	55.7%	0.67 [0.12, 3.82]
Total (95% CI)		**82**		**82**	**100.0%**	**2.65 [0.10, 68.40]**
Total events	9		3			

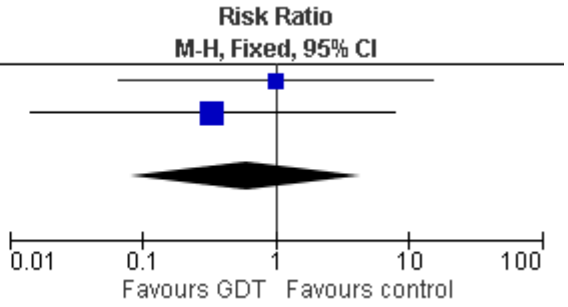
Heterogeneity: Tau² = 4.15; Chi² = 3.89, df = 1 (P = 0.05); I² = 74%
Test for overall effect: Z = 0.59 (P = 0.56)



Sepsis or septic shock

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bisgaard 2013	1	32	1	32	40.0%	1.00 [0.07, 15.30]
Funk 2015	0	20	1	20	60.0%	0.33 [0.01, 7.72]
Total (95% CI)		**52**		**52**	**100.0%**	**0.60 [0.08, 4.39]**
Total events	1		2			

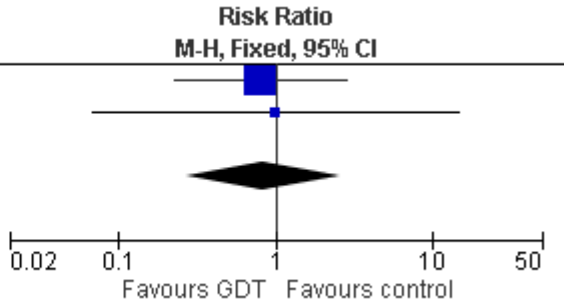
Heterogeneity: Chi² = 0.27, df = 1 (P = 0.60); I² = 0%
Test for overall effect: Z = 0.50 (P = 0.61)



Pneumonia

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bonazzi 2002	4	50	5	50	83.3%	0.80 [0.23, 2.81]
Funk 2015	1	20	1	20	16.7%	1.00 [0.07, 14.90]
Total (95% CI)		**70**		**70**	**100.0%**	**0.83 [0.27, 2.60]**
Total events	5		6			

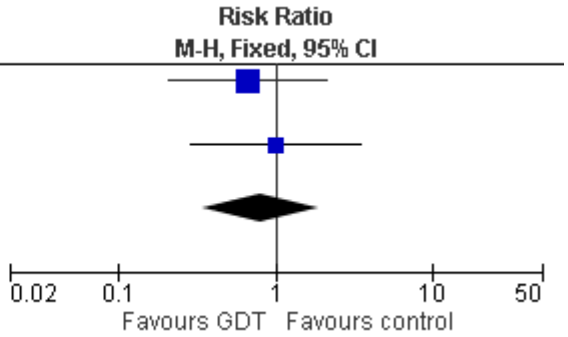
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.75)



Acute kidney injury or renal failure

Study or Subgroup	GDT Events	GDT Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bisgaard 2013	4	32	6	32	60.0%	0.67 [0.21, 2.14]
Bonazzi 2002	0	50	0	50		Not estimable
Funk 2015	4	20	4	20	40.0%	1.00 [0.29, 3.45]
Total (95% CI)		**102**		**102**	**100.0%**	**0.80 [0.34, 1.86]**
Total events	8		10			

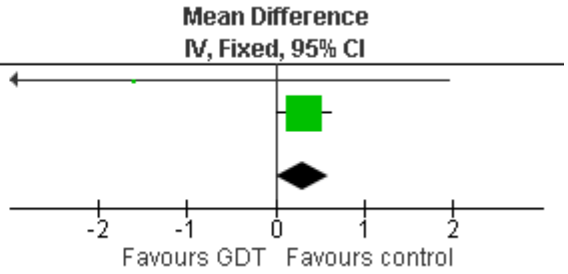
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.52 (P = 0.61)



Postoperative use of crystalloids (litres)

Study or Subgroup	GDT Mean	GDT SD	GDT Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Funk 2015	11.8	4.4	20	13.4	6.8	20	0.7%	-1.60 [-5.15, 1.95]
Bisgaard 2013	1.173	0.743	32	0.859	0.435	32	99.3%	0.31 [0.02, 0.61]
Total (95% CI)			52			52	**100.0%**	**0.30 [0.00, 0.60]**

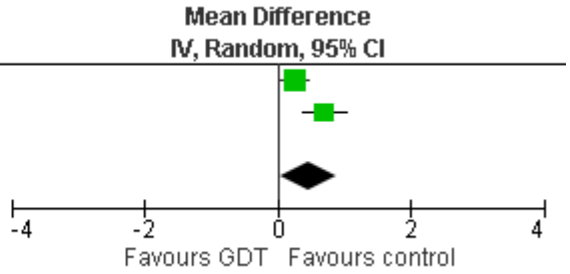
Heterogeneity: Chi² = 1.11, df = 1 (P = 0.29); I² = 10%
Test for overall effect: Z = 1.98 (P = 0.05)



Postoperative use of colloids (litres)

Study or Subgroup	GDT Mean	GDT SD	GDT Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Bisgaard 2013	0.675	0.556	32	0.413	0.294	32	54.3%	0.26 [0.04, 0.48]
Funk 2015	1.298	0.667	20	0.595	0.366	20	45.7%	0.70 [0.37, 1.04]
Total (95% CI)			52			52	**100.0%**	**0.46 [0.03, 0.89]**

Heterogeneity: Tau² = 0.08; Chi² = 4.71, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 2.11 (P = 0.03)



GDT during repair of ruptured AAA

No studies were identified as being relevant to review question 26.

Appendix F – GRADE tables

GDT during repair of unruptured AAA

Mortality

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Need for reoperation (lower numbers favour intervention); effect sizes below 1 favour GDT									
3, (Bisgaard 2013, Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	102	102	RR 0.67 (0.11, 3.87)	Low
1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Intraoperative blood loss

Quality assessment						No of patients		Difference in medians (intervention minus control group)	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Estimated blood loss (ml; lower numbers favour intervention)									
3 (Bisgaard 2013, Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	102	102	Bisgaard diff in medians: -10 Bonazzi diff in medians: -100 Funk diff in medians: 200 (All non-significant according to the Mann-Whitney or Wilcoxon rank test)	Low
1. Only median values were reported, downgrade 2 levels.									

Postoperative complications: any complications

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Any complications (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard 2013	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 1.13 (0.69, 1.85)	Low

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

Postoperative complications: cardiovascular complications

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Acute coronary syndrome (including myocardial infarction; lower numbers favour intervention); effect sizes below 1 favour GDT									
3 (Bisgaard 2013, Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	102	102	RR 0.27 (0.05, 1.58)	Low
Arrhythmia (lower numbers favour intervention); effect sizes below 1 favour GDT									
2 (Bisgaard 2013, Bonazzi 2002)	RCT	Not serious	Not serious	Very serious[2]	Very serious[1]	82	82	RR 2.65 (0.10, 68.40)	Very low
Dysrhythmia (lower numbers favour intervention); effect sizes below 1 favour GDT									
Funk (2015)	RCT	Serious[3]	Not serious	N/A	Very serious[1]	20	20	RR 0.67 (0.12, 3.57)	Very low
Congestive heart failure (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bonazzi (2002)	RCT	Not serious	Not serious	N/A	Very serious[1]	50	50	RR 0.33 (0.01, 7.99)	Low
1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels. 2. I^2 value >66.7%, downgrade 2 levels. 3. Unclear whether an appropriate approach was used to perform randomisation, downgrade 1 level.									

Postoperative complications: infection

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Sepsis or septic shock (lower numbers favour intervention); effect sizes below 1 favour GDT									
2 (Bisgaard 2013, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	52	52	RR 0.60 (0.08, 4.39)	Low
Pneumonia (lower numbers favour intervention); effect sizes below 1 favour GDT									
2 (Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	70	70	RR 0.83 (0.27, 2.60)	Low
Abdominal infection (lower numbers favour intervention); effect sizes below 1 favour GDT									

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 2.00 (0.08, 20.97)	Low
Deep wound infection (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 3.00 (0.13, 71.00)	Low
Superficial wound infection (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.50 (0.05, 5.24)	Low
Urinary tract infection (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 3.00 (0.13, 71.00)	Low
1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.									

Postoperative complications: other complications

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Pulmonary oedema (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.20 (0.01, 4.01)	Low
Respiratory failure (lower numbers favour intervention); effect sizes below 1 favour GDT									
Funk (2015)	RCT	Serious[2]	Not serious	N/A	Very serious[1]	20	20	RR 0.33 (0.01, 7.72)	Very low
Acute kidney injury or renal failure (lower numbers favour intervention); effect sizes below 1 favour GDT									
3 (Bisgaard 2013, Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[1]	102	102	RR 0.80 (0.34, 1.86)	Low
Creatinine kinase levels above 5000 U/l (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[2]	32	32	RR 1.00 (0.15, 6.67)	Low
Ischaemic gut									
Funk (2015)	RCT	Serious[2]	Not serious	N/A	Very serious[1]	20	20	RR 0.33 (0.01, 7.72)	Very low
Gastrointestinal paralysis (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 1.75 (0.57, 5.40)	Low
Severe upper gastrointestinal bleeding (lower numbers favour intervention); effect sizes below 1 favour GDT									

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.33 (0.01, 7.89)	Low
Cerebral thrombosis (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 3.00 (0.13, 71.00)	Low
Lower limb paresis (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.33 (0.01, 7.89)	Low

1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
2. Unclear whether an appropriate approach was used to perform randomisation, downgrade 1 level.

Need for additional intervention

Quality assessment						No of patients			Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Need for reoperation (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.82 (0.39, 1.70)	Low
Need for mechanical intervention (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 0.43 (0.12, 1.51)	Low
Need for acute dialysis (lower numbers favour intervention); effect sizes below 1 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[1]	32	32	RR 1.00 (0.15, 6.67)	Low
Postoperative blood transfusions (ml; lower numbers favour intervention); effect sizes below 0 favour GDT									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Serious[2]	32	32	MD 77.00 (-38.76, 192.76)	Moderate
Postoperative use of crystalloids (Litres; lower numbers favour intervention); effect sizes below 0 favour GDT									
2 (Bisgaard 2013, Funk 2015)	RCT	Not serious	Not serious	Not serious	Serious[2]	52	52	MD 0.30 (0.00, 0.60	Moderate
Postoperative use of colloids (Litres; lower numbers favour intervention); effect sizes below 0 favour GDT									
2 (Bisgaard 2013, Funk 2015)	RCT	Not serious	Not serious	Very serious[3]	Not serious	52	52	MD 0.39 (0.21, 0.58)	Low

1. Confidence interval crosses 2 lines of a defined minimum clinically important difference (RR MIDs of 0.8 and 1.25), downgrade 2 levels.
2. Non-significant result, downgrade 1 level.
3. I^2 value >66.7%, downgrade 2 levels.

Resource use

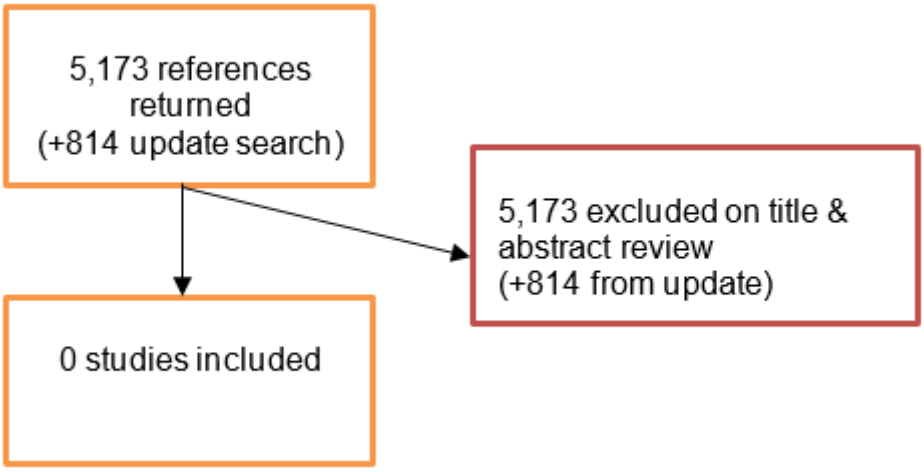
Quality assessment						No of patients		Difference in medians (intervention minus control group)	Quality
No of studies	Design	Risk of bias	Indirectness	Inconsistency	Imprecision	Intervention	Control	Summary of results	
Hospital length of stay (days; lower numbers favour intervention)									
3 (Bisgaard 2013, Bonazzi 2002, Funk 2015)	RCT	Not serious	Not serious	Not serious	Very serious[2]	102	102	Bisgaard diff in medians: 0 Bonazzi diff in medians: 1 Funk diff in medians: 0 (All non-significant according to the Mann-Whitney or Wilcoxon rank test)	Low
Intensive Care Unit length of stay (hours; lower numbers favour intervention)									
Bisgaard (2013)	RCT	Not serious	Not serious	N/A	Very serious[2]	32	32	Difference in medians: -1 (non-significant)	Low

1. Only median values were reported, downgrade 2 levels.

GDT during repair of ruptured AAA

No studies were identified as being relevant to GDT during repair of ruptured AAA.

Appendix G – Economic evidence study selection



Appendix H – Excluded studies

Clinical studies

GDT during repair of unruptured AAA

No.	Study	Reason for exclusion
1	Dentz M E, Lubarsky D A, Smith L R, McCann R L, Moskop R J, Inge W, and Grichnik K P (1995) A comparison of amrinone with sodium nitroprusside for control of hemodynamics during infrarenal abdominal aortic surgery. Journal of cardiothoracic and vascular anesthesia 9, 486-90	It is unclear whether cardiac output monitoring was used to follow a goal-oriented protocol that tailored fluid administration in order to maintain maximal cardiac output.
2	Leijdekkers V J, Vahl A C, Mackaay A J. C, Huijgens P C, and Rauwerda J A (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	This study assessed the use of a fibrinolysis inhibitor (aprotinin) during elective AAA repair. It is unclear whether cardiac output monitoring was used to follow a goal-oriented protocol that tailored fluid administration in order to maintain maximal cardiac output.
3	Kassim D Y, and Esmat I M (2016) Goal directed fluid therapy reduces major complications in elective surgery for abdominal aortic aneurysm: Liberal versus restrictive strategies. Egyptian Journal of Anaesthesia 32, 167-173	This study does not compare the efficacy of GDT with that of standard practice. Instead the study compares 2 different GDT strategies in which patients were assigned to receive 6 ml/kg/h of crystalloid (restrictive strategy) or 12 ml/kg/h of crystalloid (liberal strategy).
4	McGinley J, Lynch L, Hubbard K, McCoy D, and Cunningham A J (2001) Dopexamine hydrochloride does not modify hemodynamic response or tissue oxygenation or gut permeability during abdominal aortic surgery. Canadian journal of anaesthesia = Journal canadien d'anesthesie 48, 238-44	Investigators assessed haemodynamic, biochemical and cardiovascular effects of using dopexamine during AAA repair. These types of outcome are not listed for inclusion in the review protocol.
5	Piper S N, Boldt J, Schmidt C C, Brosch C, Maleck W H, and Berchtold C (2000) Influence of dopexamine on hemodynamics, intramucosal pH, and regulators of the macrocirculation and microcirculation in patients undergoing abdominal aortic surgery. Journal of Cardiothoracic and Vascular Anesthesia 14, 281-287	Investigators assessed haemodynamic, biochemical and cardiovascular effects of using dopexamine during AAA repair. These types of outcome are not listed for inclusion in the review protocol.
6	Ragaller M, Muller M, Bleyl J U, Strecker A, Segiet T W, Ellinger K, and Albrecht D M (2000) Hemodynamic effects of hypertonic hydroxyethyl starch 6% solution and isotonic hydroxyethyl starch 6% solution after declamping during abdominal aortic aneurysm repair. Shock (Augusta, and Ga.) 13, 367-73	Study assessed the haemodynamic, and biochemical effects of using 2 different starch solutions during AAA surgery. These types of outcome are not listed for inclusion in the review protocol.
7	Waters J H, Gottlieb A, Schoenwald P, Popovich M J, Sprung J, and Nelson D R (2001) Normal saline versus lactated	This study does not explicitly compare the efficacy of GDT with that of standard practice. All patients undergoing were

No.	Study	Reason for exclusion
	Ringer's solution for intraoperative fluid management in patients undergoing abdominal aortic aneurysm repair: an outcome study. Anesthesia and analgesia 93, 817-822	monitored via arterial or venous catheters but some were randomised to receive normal saline or lactated ringer's solution for fluid management during surgery.
8	Valentine R J, Duke M L, Inman M H, Grayburn P A, Hagino R T, Kakish H B, and Clagett G P (1998) Effectiveness of pulmonary artery catheters in aortic surgery: a randomized trial. Journal of vascular surgery 27, 203-11; discussion 211-2	Study is not specific to AAA: only 51% of the study sample were people with AAAs and results were not reported separately for this subgroup

GDT during repair of ruptured AAA

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

Economic studies

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

Appendix I – 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.