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[Intervention Protocol]

Prehabilitation exercise therapy before abdominal aortic aneurysm repair

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of exercise programmes on perioperative and postoperative morbidity and mortality associated with abdominal aortic aneurysm repair.

BACKGROUND

Description of the condition

An abdominal aortic aneurysm (AAA) is defined as an abnormal dilation in the diameter of the abdominal aorta of 3 cm or more (Hirsch 2006; Moll 2011). Most AAAs are asymptomatic and are frequently discovered incidentally during imaging or clinical examination for other conditions (Brown 2012). As well as having many risk factors in common with atherosclerosis (including tobacco smoking, advanced age, male sex, and hypertension), genetic factors and family history are likely to influence the development of abdominal aneurysms (Blanchard 2000; Larsson 2009; Lederle 1997).

The natural history of AAA is expansion (which in some cases causes the aneurysm to become symptomatic) and eventually, acute rupture. In the case of acute rupture, the classical presentation is the triad of sudden, severe abdominal or back pain (or both), a pulsatile abdominal mass and haemodynamic collapse. Mortality among people presenting with a ruptured aneurysm is high (particularly if the rupture occurs out of hospital), and even for those who do make it to hospital and undergo emergency surgery, mortality is approximately 35% (Gunnarsson 2016; Schermerhorn 2012; Sweeting 2015).

The average annual progression in diameter of small aneurysms (≤ 5.5 cm) is estimated to be between 2.0 and 3.0 mm/year, while progression is greater for aneurysms with a larger initial diameter (Bown 2013; Moll 2011). The risk of rupture increases with the diameter of the aneurysm, particularly above a diameter of approximately 5.5 cm (Powell 2008; Powell 2011).

Previously, the prevalence of AAA has been reported to range from 1.3% in women aged 65 to 80 years, to between 4% and 7.7% in men aged 65 to 80 years (Ashton 2002; Ashton 2007; Lindholt 2005; Nordon 2011; Norman 2004; Scott 2002). The annual incidence of AAA in Western populations has been estimated at between 0.4% and 0.67% (Forsdahl 2009; Lederle 2000; Nordon 2011; Vardulaki 1999), but may be lower for Asian populations (Spark 2001). More recent evidence suggests that AAA incidence is decreasing, most likely because of a reduction in tobacco smoking (Anjum 2012). The current prevalence rates are closer to 1.5% for men aged 65 and 0.7% for women over 60 years old (Jacomelli 2016; Svensjö 2014; Ulug 2016). There has also been discussion on the importance of the 'subaneurysmal' aorta (diameter 2.5 cm to 2.9 cm), since two-thirds of these will become aneurysmal over a period of five years (Wild 2013).

In asymptomatic people in whom AAA is suspected clinically, a definite diagnosis can be made using abdominal ultrasound to measure the diameter of the aneurysm (Moll 2011). More detailed information regarding the anatomy and relation to renal and visceral vessels can be obtained from computerised tomography (CT) scanning, if required. In the case of aneurysmal rupture, emergency CT scanning is widely used to confirm the diagnosis and enable the planning of aneurysm repair. Following trials of ultrasound screening, screening programmes to reduce male mortality from AAA have been recommended (Cosford 2007; LeFevre 2014). An example is the UK screening programme in which an ultrasound is offered to all men in their 65th year. Following an initial scan, individuals can be entered into regular surveillance if a small AAA is detected, while those with AAA larger than 5.4 cm can be referred for surgical evaluation (UK NSC 2017). A very similar programme is effective in Sweden, whereas screening is focused on older male smokers in the USA.

Because the risk of rupture is low in small AAA (≤ 5.5 cm), management is usually non-surgical, using regular ultrasound monitoring to screen for expansion of the aneurysm as well as modifying general cardiovascular risk factors, in particular smoking cessation (Bown 2013; Brewster 2003; Filardo 2015; Hirsch 2006; Moll 2011). Medical therapies to reduce aneurysm growth rates are currently not widely used in clinical practice (Rughani 2012). National guidelines from the European Society of Vascular Surgery (ESVS) and from the American College of Cadiology (ACC) and American Heart Association (AHA) recommend that: when an AAA reaches a diameter of ≥ 5.5 cm (men) or ≥ 5.2 cm (women), demonstrates rapid expansion, or becomes symptomatic (regardless of size), the risk of rupture exceeds the risk of surgical repair and the individual should be referred to a vascular surgeon for consideration of surgical intervention (Hirsch 2006; Moll 2011). There are two main options for surgical intervention: open surgical repair (OSR) and endovascular aneurysm repair (EVAR). OSR involves replacement of the affected section of the aorta with a graft that is sutured in place. EVAR involves insertion of an intraluminal stent, via a catheter introduced in a distal artery (e.g. femoral artery). More recently, an alternative endovascular procedure called endovascular sealing is being evaluated: two grafts are introduced, one through each iliac artery, each attached to a bag of polymer that is used to completely seal the aneurysm sac. The main risks of OSR are perioperative cardiac events, infection and death. OSR has a higher 30-day mortality than endovascular stenting (3.0% versus 0.6%, respectively) (Waton 2018), but is prone to endoleak (blood flow in the remaining aneurysm) in the long term, which requires regular follow-up to detect and possible further surgery to treat (Greenhalgh 2010; Paravastu 2014; Patel 2016; Prinssen 2004). The choice of which surgical intervention to undertake is usually made on an individual basis, taking into account perioperative comorbidities (in particular, cardiac and respiratory conditions) and the individual risk of rupture. The anatomy of the aneurysm is also important because EVAR grafts are only suitable for particular anatomical configurations. Complications include cardiac problems, respiratory problems, haemorrhage, limb ischaemia and renal failure. People undergoing open repair are more susceptible to these complications than those undergoing EVAR (Waton 2018).

Description of the intervention

The majority of people with indications for elective AAA repair are older adults (Forsdahl 2009; Howard 2015; Kent 2010; Li 2013), who often present with multiple comorbidities (Mousa 2016). In addition to a common history of smoking (Jahangir 2015; Salzler 2015), and sedentary lifestyle, these people tend to have lower fitness levels compared to their age-matched controls (Myers 2014). Significant perioperative metabolic, cardiopulmonary and neuroendocrine challenges are associated with AAA repair (OSR or EVAR), which require the individual undergoing the procedure to have a good level of fitness to withstand the stress. There is evidence that level of fitness is associated with important perioperative and postoperative morbidity and mortality rates in people undergoing AAA repair (Moran 2016).

Exercise therapy is a prescribed and planned physical activity which aims to improve, maintain, or decrease the rate of

decline of physical capacity and function, as well as overall health and well being. Exercise therapy is routinely used in the management of many long-term conditions, such as cardiovascular diseases. In people with cardiovascular disease who are not undergoing surgery, exercise therapy has been shown to be beneficial in improving fitness and reducing morbidity and mortality risks (Boden 2014). Evidence also supports the use of exercise therapy to improve recovery, as well as to reduce perioperative and postoperative complications and length of hospital stay following cardiovascular surgeries (Hoogeboom 2014). This includes interventions for vascular conditions (Aherne 2015). Exercise therapy for cardiovascular conditions is safe, with the rate of adverse events ranging from 1 per 49,565 patient-hours of exercise training in cardiac patients (Pavy 2006), to 1 per 10,340 patient-hours in peripheral arterial disease (Gommans 2015).

How the intervention might work

Undergoing surgery promotes an inflammatory response, which increases the demand for oxygen consumption (Barakat 2015). Exercise improves cardiorespiratory fitness, which improves oxygen delivery to local tissue (Smith 2009), and is also associated with anti-inflammatory mechanisms (Petersen 2005). Older 2013 hypothesised that increased lactate production due to lower levels of cardiorespiratory fitness may contribute to postoperative complications, as the body has a reduced ability to metabolise lactate postoperatively.

Optimal fitness potentially provides people with the ability to withstand the metabolic, neuroendocrine and cardiopulmonary stress associated with surgery. Improved cardiovascular and respiratory fitness, and the potential benefit of improved response to surgery-related stress, may be the causal mechanism for the benefit of exercise in people undergoing AAA repair (Grant 2015; Prentis 2012; Thompson 2011).

Why it is important to do this review

Perioperative and postoperative morbidity and mortality are common following elective repair in people with AAA. There is a growing interest in the role of preoperative exercise therapy for people with AAA undergoing elective repair. Three previous reviews have been conducted on the impact of exercise in people with AAA (Kato 2019; Pouwels 2015; Wee 2019). However, these reviews focused on heterogeneous populations with or without indications for surgery. The outcomes of preoperative exercise therapy for people undergoing AAA repair is unclear from these reviews. If preoperative exercise decreases complications and the length of hospital stay, there is a potential for cost savings. We will perform a systematic review to synthesise evidence about the impact of exercise therapy prior to repair on mortality and morbidity in individuals with AAA. We will also evaluate the impact of different forms of exercise therapy, and investigate if the effect of exercise therapy is influenced by the subsequent type of repair. The findings of this review will provide evidence to help aid decision making and inform practice, with the aim of reducing the high risk of perioperative and preoperative events associated with AAA repair.

OBJECTIVES

To assess the effects of exercise programmes on perioperative and postoperative morbidity and mortality associated with abdominal aortic aneurysm repair.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised control trials (RCTs) that compare exercise therapy with usual care (no exercise) before elective abdominal aortic aneurysm (AAA) repair.

Types of participants

We will include participants aged 18 years and older, of either sex, with clinically diagnosed AAA deemed suitable for elective intervention (open surgical repair (OSR) or endovascular aneurysm repair (EVAR)). We will not apply restrictions on the size of the aneurysm. We will exclude studies that only involve participants undergoing emergency repair. If a study includes both elective and emergency participants, we will extract data for the elective participants only, if the trial reports these separately.

Types of interventions

We will include any exercise therapy before elective AAA repair, provided that the trial compared it against no exercise therapy. The exercise therapy may be in hospital, community or home-based settings. We will include, but not limit to, variations of exercise therapy, such as circuit training, moderate-intensity continuous exercise, high-intensity interval training, and inspiratory muscle training. We will include upper limb and lower limb exercises, as well as both aerobic and strength training programmes. We will include studies that combine exercise with other interventions (e.g. psychological counselling, structured education or behaviour change interventions) if both exercise and no exercise study arms received the same additional interventions, and multi-arm studies that compare exercise with no exercise and other interventions if data are available for the exercise versus no exercise comparison.

We will include both supervised and unsupervised exercise, and will not limit exercise to any frequency, duration, or intensity, but will take these variations into account in the meta-analysis. This review will also consider analysing supervised versus unsupervised exercise in the meta-analysis.

We define a supervised exercise therapy group as one in which participants undergo a programme of exercise delivered and formally supervised by a trained health professional. We define a unsupervised exercise therapy group as one in which participants receive advice to exercise without supervision (with or without a predetermined exercise regimen or logbook), or receive advice to exercise on their own, with regular contact and exercise support from trained personnel (structural home-based exercise programme). We define a no exercise group as one in which the participants maintain normal physical activity. We will aim to analyse supervised and unsupervised therapy where possible.

Types of outcome measures

Primary outcomes

- 30-day (or longer if reported) mortality post-AAA repair
- Incidence of perioperative and postoperative complications (cardiac, pulmonary, renal, infection, organ support, and reintervention)

Secondary outcomes

- Length of intensive care unit (ICU) recovery
- Length of hospital stay
- Number of ventilator days
- Change in aneurysm size pre- and post-exercise
- Quality of life (QoL, assessed using validated physical summary score scales such as Short Form 12 (SF-12) Health Survey (Ware 1996), Medical Outcomes Study (MOS) 36-Item Short-Form Health Survey (SF-36) (Ware 1992), and Assessment of Quality of Life (AQoL) instruments (AQoL-8D, 7D, 6D or 4D) (Hawthorne 1999).

We will report these outcomes at the last follow-up presented by the included studies. We will also report on adherence to exercise, if the included studies present this.

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist aims to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

The Information Specialist will search the following databases for relevant trials:

- the Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web);
- the Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO);
- MEDLINE (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) (1946 onwards);
- Embase Ovid (from 1974 onwards);
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; from 1982 onwards);
- PEDro (Physiotherapy Evidence Database), University of Sydney.

The Information Specialist has devised a draft search strategy for RCTs for MEDLINE, which is displayed in Appendix 1. We will use this as the basis for search strategies for the other listed databases.

The Information Specialist will search the following trials registries:

- ClinicalTrials.gov (clinicaltrials.gov);
- World Health Organization International Clinical Trials Registry Platform (who.int/trialsearch).

Searching other resources

We will examine the included study reports' bibliographies to identify other relevant articles.

Data collection and analysis

Selection of studies

We will identify and exclude duplicates and will collate multiple reports of the same study. Two of three review authors (CF, UA, AT) will independently screen the titles and abstracts from the search results, identifying those to be retrieved for full-text review. Two of three review authors (CF, UA, AT) will independently screen the full texts and identify studies for inclusion. We will resolve any disagreement by discussion until we reach a consensus. Where necessary, we will consult a third review author (JM). We will illustrate the study selection process in a PRISMA diagram (Liberati 2009). We will list all articles excluded after full-text assessment in a 'Characteristics of excluded studies' table, and will provide the reasons for their exclusion.

Data extraction and management

Two of three review authors (CF, UA, AT) will independently extract relevant population and intervention characteristics, outcome data, and risk of bias components from the included studies using a standard data extraction form, which we will pilot on at least one study in the review. We will enter data into Review Manager 5 (RevMan 5, Review Manager 2014). We will resolve any disagreement about data extraction by discussion, and consult a third review author (JM) when necessary.

Assessment of risk of bias in included studies

Two review authors (CF, UA) will assess the risk of bias for all included studies, using the Cochrane 'Risk of Bias' tool, described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will judge the risk of bias in the following seven domains to be low, high or unclear.

- Random sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of participants and personnel (performance bias)
- Blinding of outcome assessment (detection bias)
- Incomeplete outcome data (attrition bias)
- Selective outcome reporting (reporting bias)
- Other sources of bias

Measures of treatment effect

Dichotomous outcomes

We will calculate risk ratios (RR) for dichotomous data, with 95% confidence intervals (CI).

Continuous outcomes

If studies measure continuous outcomes on the same scale, we will compare the mean difference (MD) in change scores. If studies use different scales to measure the same continuous outcomes, we will calculate the standardised mean difference (SMD). We will use 95% CIs for all continuous data.

We will narratively describe skewed data reported as medians and interquartile ranges.

Unit of analysis issues

We will consider each participant as the unit of analysis in the randomised trials. In RCTs with a parallel design, we will take multiple treatment arms into account, when relevant, to avoid double counting. For trials that considered multiple interventions in the same group, we will analyse only the partial data of interest.

Dealing with missing data

We will analyse the available data and contact trial authors to request missing data (such as the number of screened or randomised participants, lack of data regarding intention-to-treat

analyses, or data on as-treated or per-protocol analyses) in order to perform our analyses as thoroughly as possible. We will report dropout rates in the 'Characteristics of included studies' table of the review, and will use intention-to-treat analysis. Where possible, we will use the RevMan 5 calculator to calculate missing standard deviations (SD) using other data from the trial, such as CIs. Where this is not possible, and we consider the missing data to introduce serious bias, we will use a sensitivity analysis to explore the impact of including such studies in the overall assessment of results.

Assessment of heterogeneity

We will inspect forest plots visually to consider the direction and magnitude of effects, and the degree of overlap between CIs. We will quantify inconsistency among the pooled estimates using the I^2 statistic ($I^2 = ((Q - df)/Q) \times 100\%$, where Q is the Chi^2 statistic and 'df' represents the degree of freedom) (Higgins 2011). This will illustrate the percentage of the variability in effect estimates that results from heterogeneity rather than sampling error (Higgins 2011). If we identify substantial heterogeneity ($I^2 > 50\%$), we will report it and explore possible causes by prespecified subgroup analysis.

Assessment of reporting biases

We will assess the presence of publication bias and other reporting bias using funnel plots, if we identify sufficient studies (more than 10) for inclusion in the meta-analysis (Higgins 2011).

Data synthesis

We will perform statistical analysis using RevMan 5 software (Review Manager 2014). We will undertake meta-analyses where it is meaningful to do so, i.e. if the included studies' treatments, participants, and underlying clinical questions are similar enough for pooling to make sense. We will summarise the data for each study in a forest plot, and present 95% CI for all summary estimates. We will report data narratively if it is not appropriate to combine data in a meta-analysis.

We will perform meta-analyses according to the recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will consider a fixed-effect model where we find no substantial heterogeneity ($I^2 < 50\%$). We will use a random-effects model if we find substantial heterogeneity ($I^2 > 50\%$).

Subgroup analysis and investigation of heterogeneity

We will perform subgroup analyses to investigate possible reasons for heterogeneity. We plan to carry out subgroup analyses based on:

- participants age (< 80 versus > 80 years) as the over 80s are known to have higher rates of complications (Sonesson 2018);
- type of repair (OSR versus EVAR);
- type of exercise therapy (e.g. aerobic versus isometric; supervised versus unsupervised).

Sensitivity analysis

We will conduct sensitivity analyses to establish whether findings are robust by limiting the analyses to studies with low risk of bias in the selection bias domain, the detection bias domain or both. Additionally, where missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results.

Summary of findings and assessment of the certainty of the evidence

We will create a 'Summary of findings' table to provide the key information presented in the review for the exercise versus no exercise comparison, using GRADEpro software (GRADEpro GDT). We will include the following outcomes, which are of most clinical relevance, in each table:

- 30-day (or longer if reported) mortality post-AAA repair;
- incidence of perioperative and postoperative complications (cardiac, pulmonary, renal, infection and organ support, and reintervention);
- length of ICU recovery;
- length of hospital stay;
- number of ventilator days;
- QoL.

We will assess the certainty of the evidence for each outcome as high, moderate, low or very low, based on the five GRADE considerations of risk of bias, inconsistency, indirectness, imprecision, and publication bias, using the GRADE approach (Atkins 2004). We will base the tables on methods described in Chapters 11 and 12 of the *Cochrane Handbook for Systematic Reviews of Interventions*, and will justify any departures from the standard methods (Atkins 2004; Higgins 2011). Two of three review authors (CF, UA, AT) will independently judge the certainty of the evidence and, if required, will resolve any disagreements by consensus or discussion with a third review author (JM). We will justify all decisions to downgrade the evidence using footnotes and we will make comments to aid the reader's understanding of the review where necessary. We have included a draft 'Summary of findings' table in this protocol (Table 1).

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ADDITIONAL TABLES

Table 1. Draft 'Summary of findings' table

Exercise programmes compared with no exercise programmes before AAA repair

Patient or population: people who have undergone repair for AAA

Settings: hospital, community or home-based settings

Intervention: exercise programme[a]

Comparison: no exercise programme[b]

Outcomes	Anticipated absolute effects * (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no exercise programme	Risk with exercise programme				
30 day (or longer if reported) mortality post-AAA repair	Study population		RR [value] ([val-	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low**	
	[value] per 1000	[value] per 1000 ([value] to [value])				

Table 1. Draft 'Summary of findings' table *(Continued)*

			ue] to [value])		⊕⊕⊖⊖ **low** ⊕⊕⊕⊖ **moderate** ⊕⊕⊕⊕ **high**
Incidence of perioperative and postoperative complications (cardiac, pulmonary, renal, infection, organ support, and reintervention) (follow-up)	**Study population** **[value] per 1000**	**[value] per 1000** ([value] to [value])	**RR [value]** ([value] to [value])	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low** ⊕⊕⊖⊖ **low** ⊕⊕⊕⊖ **moderate** ⊕⊕⊕⊕ **high**
Length of ICU recovery (follow-up)	The mean [outcome] ranged across control groups from [value][measure]	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]	—	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low** ⊕⊕⊖⊖ **low** ⊕⊕⊕⊖ **moderate** ⊕⊕⊕⊕ **high**
Length of hospital stay (follow-up)	The mean [outcome] ranged across control groups from [value][measure]	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]	—	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low** ⊕⊕⊖⊖ **low** ⊕⊕⊕⊖ **moderate** ⊕⊕⊕⊕ **high**
Number of ventilator days (follow-up)	The mean [outcome] ranged across control groups from [value][measure]	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]	—	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low** ⊕⊕⊖⊖ **low** ⊕⊕⊕⊖

Table 1. Draft 'Summary of findings' table *(Continued)*

					moderate ⊕⊕⊕⊕ **high**
QoL (using validated summary score, follow-up)	The mean [outcome] ranged across control groups from [value][measure]	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]	—	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **very low** ⊕⊕⊖⊖ **low** ⊕⊕⊕⊖ **moderate** ⊕⊕⊕⊕ **high**

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
AAA: abdominal aortic aneurysm; **CI:** confidence interval; **ICU**: intensive care unit; **QoL**: quality of life; **RR:** risk ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Exercise includes both supervised and unsupervised exercise therapies. Supervised exercise therapy consists of a programme of exercise delivered and formally supervised by a trained health professional. Programme inclusion is not limited by frequency or intensity of the exercise programme. Unsupervised exercise therapy consists of advice to exercise without supervision (with or without a predetermined exercise regimen or logbook), or to exercise on their own with regular contact and exercise support from trained personnel (structural home-based exercise programme).
[b]No exercise consists of maintained normal physical activity (i.e. participants did not undergo/receive supervised exercise, or unsupervised exercise).

APPENDICES

Appendix 1. MEDLINE search strategy

1 exp Aortic Aneurysm/

2 exp Aneurysm, Ruptured/

3 exp Aorta, Abdominal/

4 AAA*.ti,ab.

5 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort*)).ti,ab.

6 (aort* adj3 (balloon* or dilat* or bulg*)).ti,ab.

7 (abdom* adj3 (balloon* or dilat* or bulg*)).ti,ab.

8 (aneurism* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort*)).ti,ab.

9 or/1-8

10 exp Exercise/

11 exp Exercise Therapy/

12 exp Preoperative Care/

13 "home based train*".ti,ab.

14 "Interval Train*".ti,ab.

15 "Physical activit*".ti,ab.

16 "Physical train*".ti,ab.

17 "Physical Therap*".ti,ab.

18 Exercis*.ti,ab.

19 physiotherapy.ti,ab.

20 prehabilitat*.ti,ab.

21 pre-habilitation.ti,ab.

22 "physical fitness".ti,ab.

23 pre-habilitation.ti,ab.

24 or/10-23

25 9 and 24

26 randomized controlled trial.pt.

27 controlled clinical trial.pt.

28 randomized.ab.

29 placebo.ab.

30 drug therapy.fs.

31 randomly.ab.

32 trial.ab.

33 groups.ab.

34 or/26-33

35 exp animals/ not humans.sh.

36 34 not 35

37 25 and 36

HISTORY

Protocol first published: Issue 7, 2020

CONTRIBUTIONS OF AUTHORS

CF: designing and drafting the protocol, designing literature searches, acquiring trial reports, trial selection, data extraction, data analysis, data interpretation, review drafting and future review updates
UA: designing and drafting the protocol, acquiring trial reports, trial selection, data extraction, data analysis, data interpretation, review drafting and future review updates

AT: designing and drafting the protocol, acquiring trial reports, trial selection, data extraction, data analysis, data interpretation, review drafting and future review updates
JM: designing and drafting the protocol, data interpretation, review drafting and future review updates

DECLARATIONS OF INTEREST

CF: none known
UA: none known
AT: is employed as a Network Support Fellow for Cochrane (based in University College London). She receives payment from the Royal College of Obstetricians and Gynaecologists for freelance systematic reviewing to develop NICE guidelines.
JM: has declared that he has received travel, course fees, accommodation and meals from Medtronic, Gore, Abbott and Vascutek to attend various educational courses/meetings. He has not received any other financial remuneration. He received speakers fees along with travel and accommodation from Gore to attend/speak at the 2015 VSGBI meeting and other educational events. He is a cofounder of UKETS, a trainee initiative which receives funding through sponsorship from endovascular technology and simulation companies. The majority of this is non-financial (the companies supply trainers on the courses or allow use of their simulators), although Vascutek, Abbott, Cook, Medtronic and Mentice give some direct financial input that is used to run events. JM derives no personal profit from this initiative.

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