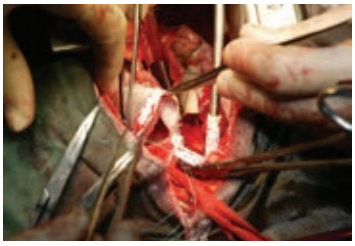
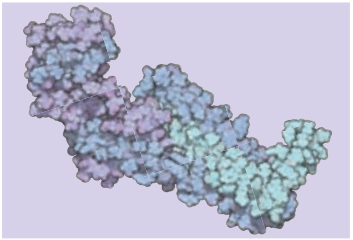
research

Weight loss diets may reduce premature mortality in adults with obesity p 269



Convincing support for the benefits of endovascular repair of aortic aneurysm p 270



Patient selection for cardiac troponin testing affects diagnosis of myocardial infarction p 272

ORIGINAL RESEARCH Systematic review and meta-analysis

Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer

Ma C, Avenell A, Bolland M, et al

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Study question Do weight loss interventions for adults with obesity affect all cause, cardiovascular, and cancer mortality, cardiovascular disease, cancer, and body weight?

Methods The authors performed a systematic review and meta-analysis of long term randomised controlled trials of dietary weight loss interventions, with or without exercise, for adults with obesity. They assessed the quality of evidence using the GRADE approach.

Study answer and limitations The review included 54 randomised controlled trials with 30 206 participants. All but one trial evaluated low fat, weight reducing diets. The authors found high quality evidence that premature all cause mortality was reduced after weight loss interventions (34 trials, 685 events; risk ratio 0.82, 95% confidence interval 0.71 to 0.95), with six fewer deaths per 1000 participants (95% confidence interval 2 to 10), moderate quality evidence for an effect on cardiovascular mortality (eight trials, 134 events; risk ratio 0.93, 95% confidence interval 0.67 to 1.31), and high quality evidence for participants having new cardiovascular events (24 trials, 1043 events; risk ratio 0.93, 95% confidence interval 0.83 to 1.04). Very low quality evidence was found for cancer mortality (eight trials, 34 events; risk ratio 0.58, 95% confidence interval 0.30 to 1.11) and for participants having new cancers (19 trials, 103 events; risk ratio 0.92, 95% confidence interval 0.63 to 1.36). These findings might be limited by failure to identify trials with relevant outcomes, by trials presenting outcome data as adverse events, and by the quality of the included trials.

What this study adds Weight reducing diets, usually low in total fat and saturated fat, with or without exercise advice or programmes, might reduce premature all cause mortality in adults who are obese.

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Study registration PROSPERO CRD42016033217

Surgical options for ruptured aortic aneurysm

ORIGINAL RESEARCH Three year results of the IMPROVE randomised trial

Comparative clinical effectiveness and cost effectiveness of endovascular strategy *v* open repair for ruptured abdominal aortic aneurysm

IMPROVE Trial Investigators

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Study question What is the three year effectiveness of a strategy of endovascular repair (in patients with suitable aortic morphology) versus open repair for patients with a clinical diagnosis of ruptured abdominal aortic aneurysm?

Methods Randomised controlled trial in 30 vascular centres (29 in the UK, one in Canada), 2009-16. In total, 316 patients were randomised to the endovascular strategy (275 confirmed ruptures) and 297 to open repair (261 confirmed ruptures), of whom 502 underwent emergency repair for rupture. Patients were followed up for survival and cost effectiveness.

Study answer and limitations After similar 90 day mortality, in the mid-term (three months to three years), there were fewer deaths in the endovascular strategy group than in the open repair group (hazard ratio 0.57, 95% confidence interval 0.36 to 0.90). Results for the 502 ruptures repaired were more pronounced: three year mortality was lower in the endovascular strategy group (42% *v* 54%; odds ratio 0.62, 95% confidence interval 0.43 to 0.88). At three years, compared with open repair, the endovascular strategy group also had an average gain of 0.17 (95% confidence interval 0.002 to 0.331) quality adjusted life years (QALYs), similar levels of reintervention, and lower average costs of −£2605 (−£5966 to £702). The probability that the endovascular strategy is cost effective was over 90% at all values of willingness to pay for a QALY gain. The pragmatic design, with about 10% non-compliance in each group, was addressed by a causal analysis of the 502 rupture repairs (the magnitude of survival and cost effectiveness gains for the endovascular strategy increased).

What this study adds This is the first randomised trial comparing the use of minimally invasive endovascular aneurysm repair versus open surgery to report comprehensive mid-term outcomes. The results suggest that an endovascular strategy (endovascular repair when morphologically feasible) is both clinically effective and cost effective and should be adopted more widely.

Summary of health outcomes from the IMPROVE trial

Parameter	Differences between randomised groups	Quantitative differences (endovascular strategy *v* open repair)
30 and 90 day mortality	No difference	35% *v* 37% at 30 days; 38% *v* 40% at 90 days
3 year mortality	Endovascular strategy better for those with repaired ruptures	48% *v* 56% all patients; 42% *v* 54% repaired ruptures
Length of primary hospital stay	Shorter for endovascular strategy	15.7 *v* 19.6 days
Discharges directly to home	Higher for endovascular strategy	94% *v* 77% of discharges
Reintervention rate to 3 years	No difference	26 *v* 28 per 100 person years
Quality of life	Better at 3 months and 1 year for endovascular strategy, similar at 3 years	EQ-5D: 0.76 *v* 0.66 at 3 months; 0.78 *v* 0.71 at 1 year; EQ-5D: 0.74 *v* 0.73 at 3 years
QALYs to 3 years	Higher for endovascular strategy	1.14 *v* 0.97
Costs to 3 years	Endovascular strategy less	£16 900 *v* £19 500
Cost effectiveness to 3 years	Endovascular strategy cost effective	Incremental net monetary benefit: £7600

COMMENTARY The endovascular approach is better for patients and more cost effective for payers

The three year results of the IMPROVE trial[1] will change clinical practice in favour of endovascular repair for patients with suspected ruptured abdominal aortic aneurysms (AAA). Note, however, that long term trials of endovascular compared with open surgery have reported diverging results for patients with ruptured or intact aneurysms.

In previously reported analyses of outcomes at 30 days[2] and one year[3] IMPROVE Investigators found no difference in survival between the groups, the primary outcome. But there were other advantages to endovascular repair, including a greater likelihood of discharge to home at 30 days,[2] lower costs,[2 3] and a shorter average length of hospital stay at one year.[3]

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The potential benefits of endovascular treatment of ruptured AAA could be even greater than shown here

The new three year results are convincing.[1] The above advantages of endovascular repair have now transformed into a true survival benefit. The higher quality of life among survivors in the endovascular group is a further benefit that translates to better overall cost effectiveness. Reintervention rates were similar between the two groups.

Design strengths

The vascular surgeons in the UK and Canada have performed yet another large trial of excellent quality. About half of eligible patients were randomised, despite the obvious difficulties of performing a randomised trial in critically ill patients, often in severe pain and with traumatised relatives. More flexible legislation on consent in the UK and Canada made this possible and is laudable. The demands of securing fully informed consent before randomisation, as required in Sweden, can make this kind of research impossible. Supported by ethical oversight in both Canada and the UK, these authors were able to use a two stage consent process that secured brief initial consent followed by full consent after surgery. The study design was ideal, and only two patients in each group were lost to follow-up.

The potential benefits of endovascular treatment of ruptured AAA could be even greater than shown in an earlier report from the same investigators, only 36% of participants were managed under local

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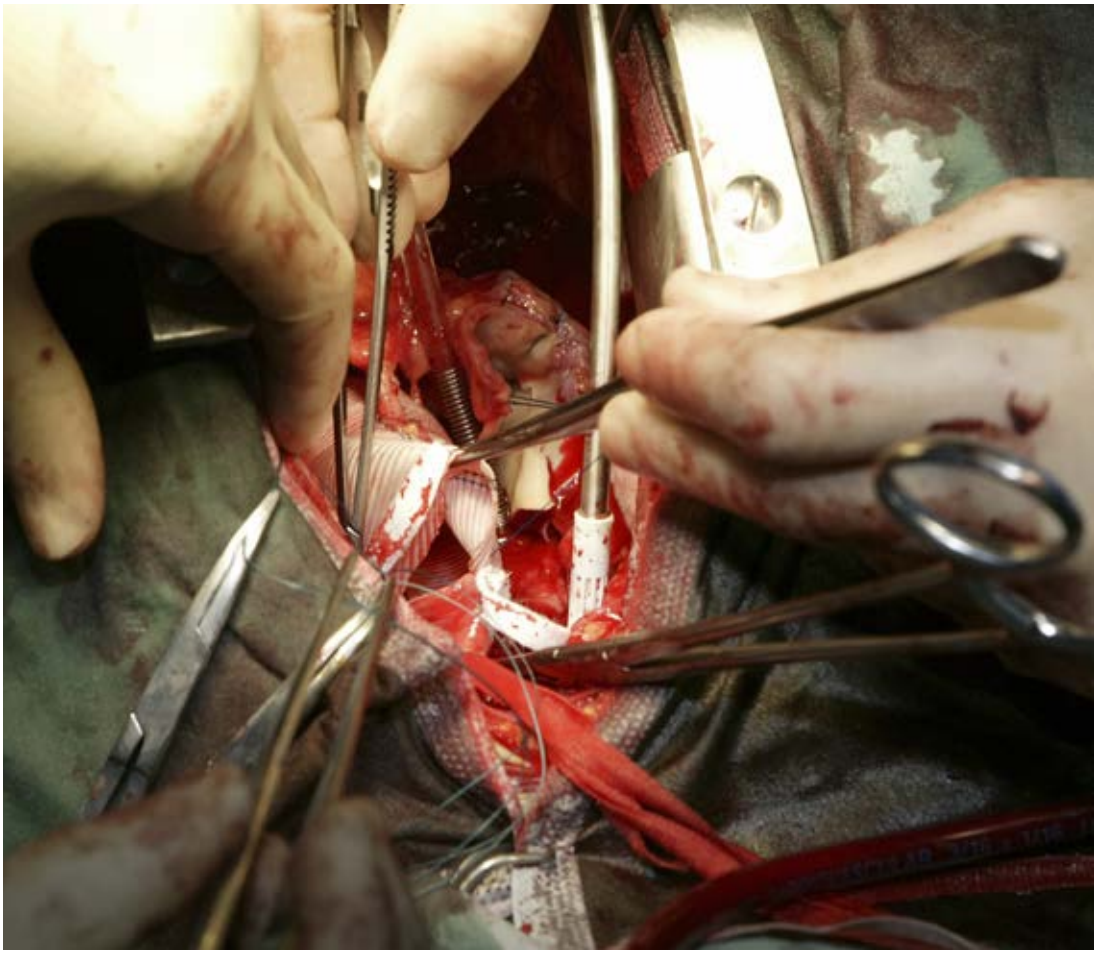
Trial registration
Current Controlled Trials ISRCTN48334791; ClinicalTrials.gov NCT00746122.



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anaesthesia,[2] about half the proportion reported by experienced centres.[4] In another analysis, patients managed with local anaesthesia had lower mortality than those managed with general anaesthesia (adjusted odds ratio 0.27, 95% confidence interval 0.10 to 0.70),[5] though there are confounders in this non-randomised comparison.

The EVAR1 trial of open compared with endovascular repair in 1252 patients with intact AAA recently reported 15 year follow-up data.[6] The early advantage of endovascular repair had disappeared by six months, and from eight years onward the open repair group had better survival. The 15 year results of the EVAR1 trial and the three year results of the IMPROVE trial can both be regarded as long term results as mean survival after rupture is much shorter.[7]

Reconciling differences

How should we reconcile these conflicting results for emergency and elective surgery? In the emergency setting of a ruptured AAA, we need to operate a "damage control" strategy to save a life in immediate danger. The "perfect" becomes the enemy of the "good." In the elective setting, patients and their surgeons have a longer term perspective. An operation associated with harm after eight years of follow-up is not good enough. The evidence gives a clear message to tailor treatment depending on the patient and the presentation.

Prevention is always better than cure, and the most effective way to prevent ruptured AAA is to avoid smoking.[8] Second best is early recognition and repair of aneurysms before rupture. In the large UK MASS trial, screening older men with ultrasonography reduced mortality from ruptured AAA by about 50%.[9] Long term results from that trial,[10] along with later meta-analyses,[11] showed that even all cause mortality rates can be reduced by ultrasound screening. Similar results were reported from the Swedish national screening programme.[12]

Does a haemodynamically stable patient with a ruptured AAA benefit from transport to a centre that can offer both open and endovascular repair? Probably, but this issue was not covered by the IMPROVE trial. How should we treat those with hostile anatomy today, when alternatives to open surgery exist, such as fenestrated endovascular grafts, available off the shelf? These and other remaining questions should be dealt with in future studies.

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Patient selection for high sensitivity cardiac troponin testing and diagnosis of myocardial infarction

Shah ASV, Sandoval Y, Noaman A

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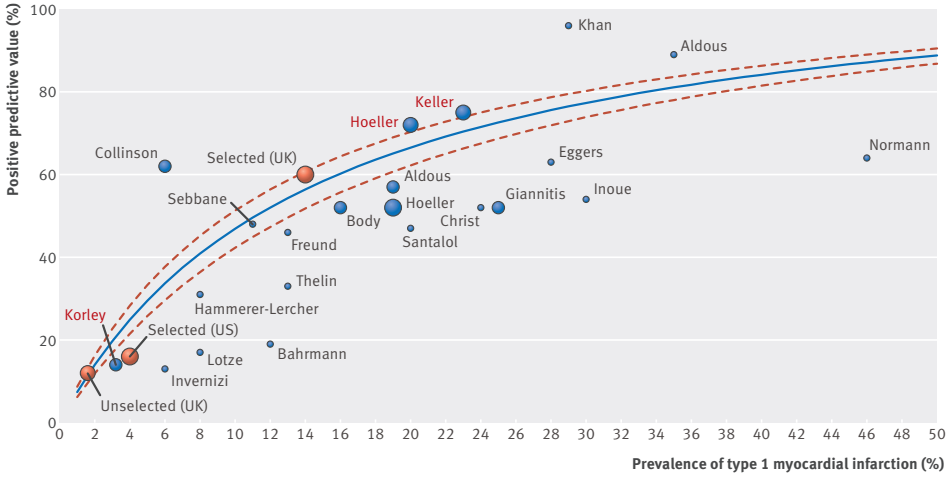
Study question How does selection of patients for high sensitivity cardiac troponin testing affect the diagnosis of myocardial infarction?

Methods This was a prospective study of 8500 consecutive patients presenting to the emergency department in three cohorts: one unselected patient population in the United Kingdom (n=1054) and two selected patient populations in whom troponin testing was requested by the attending clinician in the UK (n=5815) and the United States (n=1631). The final diagnosis of type 1 myocardial infarction, type 2 myocardial infarction, or myocardial injury was independently adjudicated. The primary outcome was the positive predictive value of an elevated cardiac troponin concentration for a diagnosis of type 1 myocardial infarction.

Study answer and limitations When testing is done indiscriminately or without previous clinical assessment, elevated high sensitivity cardiac troponin concentrations are common (one in eight patients), predominantly reflecting myocardial injury rather than infarction, and the positive predictive value for type 1 myocardial infarction is markedly reduced. When troponin testing was guided by the attending clinician, the positive predictive value improved and was highest in patients with chest pain, myocardial ischaemia on the electrocardiogram, or known ischaemic heart disease. The frequency of elevated troponin concentrations in the unselected patient population may have been underestimated, as serial samples were not available for all patients.

What this study adds Selection of patients with a higher pretest probability based on simple clinical features markedly enhances the positive predictive value of high sensitivity cardiac troponin, highlighting the importance of undertaking clinical assessment before testing.



Influence of prevalence on positive predictive value (PPV) of elevated high sensitivity cardiac troponin concentration for diagnosis of type 1 myocardial infarction. Red dots=populations of unselected patients in emergency department (n=1054) and selected patients in UK (n=5815) and US (n=1631). Blue dots=reported PPV for high sensitivity cardiac troponin by prevalence of type 1 myocardial infarction in previously published cohorts using high sensitivity cardiac troponin T (black text) and high sensitivity cardiac troponin I (red text) assays. Dot size reflects number of patients in cohort. Blue line shows central estimate of PPV with 95% CI derived from unselected emergency department population in UK

Funding, competing interests, data sharing
This study was funded by the British Heart Foundation. See full version on bmj.com for competing interests. Patient level data and statistical code will be available from the corresponding author following publication of the primary study.