Screening for abdominal aortic aneurysm (Review)

Cosford PA, Leng GC

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

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Status: *Commented*

This record should be cited as:
Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD002945. DOI: 10.1002/14651858.CD002945.pub2.

This version first published online: 18 April 2007 in Issue 2, 2007.
Date of most recent substantive amendment: 26 January 2007

ABSTRACT

Background
Abdominal aortic aneurysm (AAA) is found in 5% to 10% of men aged 65 to 79 years. The major complication is rupture which presents as a surgical emergency. The mortality after rupture is high, 80% for patients reaching hospital and 50% for those undergoing surgery for emergency repair. Currently elective surgical repair is recommended for aneurysms discovered to be larger than 5.5 cm to prevent rupture. There is interest in population screening to detect, monitor and repair abdominal aortic aneurysms before rupture.

Objectives
To determine the effects of screening asymptomatic individuals for AAA on mortality, subsequent treatment, quality of life and cost effectiveness of screening.

Search strategy
The Cochrane Peripheral Vascular Diseases Group searched their Trials Register (last searched 26 January 2007) and CENTRAL (last searched Issue 1, 2007).

Selection criteria
Randomised controlled trials of population screening for AAA.

Data collection and analysis
Two authors independently assessed trials and extracted data.

Main results
Four studies involving 127,891 men and 9,342 women were included in this review. Only one study included women.

Results for men and women were analysed separately. Three to five years after screening there was no significant difference in all-cause mortality between screened and unscreened groups for men or women (men, odds ratio (OR) 0.95; 95% Confidence interval (CI) 0.85 to 1.07; for women OR 1.06; 95% CI 0.93 to 1.21).

There was a significant decrease in mortality from AAA in men (OR 0.60; 95% CI 0.47 to 0.78), but not for women (OR 1.99; 95% CI 0.36 to 10.88). In this analysis mortality includes death from rupture and from emergency or elective surgery for aneurysm repair. There was also a decreased incidence of ruptured aneurysm in men (OR 0.45; 95% CI 0.21 to 0.99) but not in women (OR 1.49; 95% CI 0.25 to 8.94).

There was a significant increase in surgery for AAA in men (OR 2.03; 95% CI 1.59 to 2.59). This was not reported in women. There were no data on life expectancy, complications of surgery or subjective quality of life.

Authors' conclusions
There is evidence of a significant reduction in mortality from AAA in men aged 65 to 79 years who undergo ultrasound screening. There is insufficient evidence to demonstrate benefit in women. The cost effectiveness may be acceptable, but needs further expert

analysis. These findings need careful consideration in judging whether a co-ordinated population-based screening programme should be introduced.

PLAIN LANGUAGE SUMMARY

Screening for abdominal aortic aneurysm

An aneurysm is a localised widening (dilation) of an artery. The blood vessel can burst (rupture) because the vessel wall is weakened. Some 5% to 10% of men aged between 65 and 79 years have an abdominal aneurysm in the area of the aorta, the main artery from the heart as it passes through the abdomen. Abdominal aortic aneurysms are often asymptomatic but a rupture is a surgical emergency and often leads to death. An aneurysm larger than 5 cm carries a high risk of rupture. Smaller aneurysms are monitored regularly using ultrasound to see if they are becoming larger. Elective surgical repair of aortic aneurysms aims to prevent death from rupture. The incidence of aortic aneurysm in women as they age is lower than for men.

This review identified four controlled trials involving 127,891 men and 9,342 women who were randomly assigned to aortic aneurysm screening using ultrasound or no screening. Only one trial included women. Two of the trials were conducted in the UK, one in Denmark and one in Australia. The results provide evidence of a benefit from screening in men with a strongly significant reduction in deaths from abdominal aortic aneurysm. The odds ratio (OR) for death was 0.60 (range 0.47 to 0.78, three trials) in men aged 65 to 83 years but was not reduced for women. From one trial there was also a decreased incidence of ruptured aneurysm in men but not women.

All-cause mortality was not significantly different between screened and unscreened groups some three to five years after screening, which is to be expected given the relative infrequency of abdominal aortic aneurysm as a cause of death.

Men who had been screened underwent more surgery for abdominal aortic aneurysm (OR 2.03; range 1.59 to 2.59, four trials) but resource analysis appears to demonstrate overall cost effectiveness of screening. There were no data on life expectancy, complications of surgery or quality of life.

BACKGROUND

Abdominal aortic aneurysm is a dilatation of the aorta (the main artery from the heart) as it passes through the abdomen. It is present in 5% to 10% of men aged between 65 and 79 years and is often asymptomatic (Vardulaki 1999). The major complication is rupture which presents as a surgical emergency. The mortality after rupture is high - approximately 80% of those who reach hospital and 50% of those undergoing emergency surgery for ruptured aortic aneurysm will die (Basnyat 1999; Johnston 1994). Elective surgical repair of aortic aneurysms aims to prevent death from rupture and the 30-day operative mortality for open surgery is approximately 5% to 6% (Anonymous 1998).

The likelihood of rupture depends on the size of the aneurysm. In the five years following diagnosis rupture occurs in approximately 2% of aneurysms found to be less than 4 cm in diameter and in over 25% of aneurysms larger than 5 cm (Ernst 1993). On this basis currently accepted practice for identified aneurysms is the following (Ballard 2000):

- Elective surgical repair for large aneurysms, usually taken to be 5.5 cm diameter or larger.
- Regular (e.g. six monthly) ultrasound surveillance for aneurysms below 5.5 cm diameter, with referral for surgery if the aneurysm grows at >1.0 cm per year or reaches 5.5 cm.

Ultrasound screening for asymptomatic abdominal aortic aneurysm has been identified as a possible means of reducing mortality (Wilmink 1998) in view of the greatly reduced mortality after elective repair compared to that following rupture (Anonymous 1998; Johnston 1994). However, screening is controversial for several reasons:

- People with large aneurysms do not necessarily die from them.
- The balance between risk of rupture and risk of elective surgical repair (which still has a significant mortality) is difficult to judge for people who are healthy, as opposed to people who already have symptoms of an aneurysm.
- Many healthy people will have a small aneurysm identified for which surgery is not advisable, but their awareness of their aneurysm could lead to significant anxiety.

Screening programmes should meet a standard set of criteria before their introduction. In the United Kingdom they are not introduced unless approved by the National Screening Committee. Approval requires programmes to meet criteria including evidence

from high quality randomised controlled trials that they are effective in reducing mortality or morbidity (Health Dept 1998). Whilst the National Screening Committee had considered that there was insufficient evidence on which to recommend introduction of a population screening programme (Health Dept 2000), they now consider that the evidence is sufficient to introduce screening, but its introduction should be through managed development of a co-ordinated service (Health Dept 2006). There are, however, no published systematic reviews of the evidence for screening from randomised controlled trials.

OBJECTIVES

1) To determine the effects of screening asymptomatic people for abdominal aortic aneurysm on their mortality, subsequent treatment for abdominal aortic aneurysm and quality of life. 2) To identify any available information from published data on the cost effectiveness of screening.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trials of screening versus no screening were eligible for this review. Any method of randomisation was eligible, including those in which individuals, locations or practices had been randomised. It was planned that differences in trial quality would be taken into account in the analysis. Trials were to be analysed on an intention-to-treat basis, but others would be included provided all randomised patients were accounted for.

Types of participants

Trials including people asymptomatic of aortic aneurysm were eligible for this review. Trials could be from any population, but major differences in the populations studied were to be considered in the analysis. For example, trials in the general population and in people with peripheral vascular disease were eligible, with differences in outcome to be identified in the analysis. The age-specific incidence of aortic aneurysm is lower in women than men, although the annual rate of rupture is higher (Brown 1999). This may alter the cost effectiveness of screening between men and women. Trials including both sexes were eligible and were analysed together, but sex differences in the outcome of screening were identified in the analysis.

Types of intervention

Studies of any screening technique for abdominal aortic aneurysm were eligible, although it was anticipated that trials would focus on ultrasound methods. It was planned that different screening techniques would be accounted for in the analysis to take account of different levels of sensitivity and specificity. Trials of screening followed by treatment and of screening alone were also to be included, provided long term outcome measures were identified.

Types of outcome measures

The following outcome measures were searched for and included where possible:

- mortality;
- life expectancy;
- progression to ruptured aortic aneurysm;
- complications of surgery including distal embolus, haemorrhage and graft failure, coronary and cerebrovascular events and renal complications;
- subjective measures including quality of life scores and impact on ability to work;
- use of resources including hospital stay and use of intensive care facilities.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The Cochrane Peripheral Vascular Diseases Group searched their Trials Register (last searched 26 January 2007) and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (last searched Issue 1, 2007) for publications describing randomised controlled trials of screening for abdominal aortic aneurysm. The PVD Group's Trials Register is constructed from electronic searches of MEDLINE (1966 to date), EMBASE (1980 to date), and CINAHL (1982 to date), and through handsearching relevant journals. The full list of journals that have been handsearched, as well as the search strategies used are described in the 'Search strategies for the identification of studies' section within the editorial information about the Cochrane PVD Group in *The Cochrane Library*.

For details of the search strategy used to search CENTRAL *see* (Table 01).

In addition, we searched the NHS economic evaluation database, the reference lists of articles found and handsearched relevant journals using the search strategy described by the Peripheral Vascular Diseases Group. We contacted the National Screening Committee and manufacturers of surgical and screening products to provide information on both published and unpublished trials. We sought information on current research programmes from the NHS Health Technology Assessment Programme and the Medical Research Council. We also contacted authors of major studies of the treatment of abdominal aortic aneurysm were approached (for example, the UK Small Aneurysm Trial).

METHODS OF THE REVIEW

Selection of trials
One author (PAC) identified possible trials, and the second author (GL) assessed unblinded trial reports independently to confirm eligibility for inclusion in the review. PAC contacted trial authors for additional information where necessary for all trials which appeared to meet the inclusion criteria.

Quality of trials
Both authors independently assessed the methodological quality of included trials and resolved discrepancies by discussion. Assessment was based on the methods described by Jadad (Jadad 1996) and Schulz (Schulz 1995), including method and concealment of allocation, blinding and withdrawals and drop outs from the study. This assessment was not used to exclude trials from the study but to explore heterogeneity.

Data extraction
Both authors extracted data independently using a standard pro forma. Disagreements were resolved by discussion and, where necessary, seeking additional information from the authors.

Statistical analysis
We performed statistical analysis according to statistical guidelines for review authors in the Cochrane Peripheral Vascular Diseases Group. We used the odds ratio as the measure of effect for each dichotomous outcome. We planned that heterogeneity in the data would be explored using identified characteristics of the studies, in particular assessments of quality. We intended to analyse continuous outcome measures using the weighted mean difference; if different scales were used we planned to standardise and combined them to calculate the standardised mean difference.

We considered some categories of trial subjects separately in subgroup analyses, where sufficient information was available. For example, we analysed studies of men separately from women, and we also planned to analyse separately people with other manifestations of atherosclerosis such as intermittent claudication, or other major illnesses such as diabetes.

DESCRIPTION OF STUDIES

Four completed randomised controlled studies met the criteria for inclusion in the review. These were conducted in Chichester, UK (Chichester), Viborg, Denmark (Viborg), Perth, Western Australia (Western Australia), and an MRC trial in the UK (Multicentre Aneurysm Screening Study) (MASS).

The Chichester trial (Chichester) identified 15,775 men and women aged 65 to 80 years from family practices in Chichester, UK and randomly allocated them to ultrasound screening or no intervention. Those in whom an abdominal aortic aneurysm of 3 cm to 4.4 cm was identified were rescanned annually, and those with an aneurysm of 4.5 cm to 5.9 cm were rescanned every three months. In both these groups surgery was offered if the rate of growth was greater than 1 cm per year or if symptoms developed. Those with an abdominal aortic aneurysm of 6 cm or larger were offered surgery directly. The mean follow up was 30.5 months.

The Mass study (MASS) included 67,800 men aged 65 to 74 years from family practices in Oxford, Portsmouth, Winchester and Southampton, UK, and randomly allocated them to ultrasound screening or no intervention. Those in whom an abdominal aortic aneurysm of 3 cm to 4.4 cm was identified were rescanned annually, and those with an aneurysm of 4.4 cm to 5.4 cm were rescanned every three months. Growth of an aneurysm of greater than 1 cm per year, or development of symptoms led to referral for surgery. Surgery was also offered directly for people with aneurysms of 5.5 cm or larger. Mean follow up was 4.1 years. The MASS study also collected data on costs associated with screening and subsequent interventions to derive estimates of cost effectiveness.

The Western Australian Study (Western Australia) included 41,000 men aged 65 to 79 years identified from the electoral roll in Perth, Australia. They were randomly allocated to receive ultrasound screening or no intervention. Screening took place over the subsequent 32 months, and the age of men on screening therefore ranged from 65 to 83 years. Men were provided with a letter detailing the outcome of screening with a copy for their general practitioner, who arranged follow-up investigations or surgical referral as they considered appropriate. Median follow up was 43 months.

The Viborg trial included 12,658 men aged 65 to 73 years, identified from the health department as residents of the County of Viborg, Denmark. They were randomly allocated to ultrasound screening or no intervention. Patients identified with aneurysms above 3.0 cm were offered annual rescreening, and surgery was offered when an aneurysm was 5.0 cm or larger. Mean follow up was 5.1 years. The Viborg study also collected data on hospital costs associated with screening and subsequent interventions to derive estimates of cost effectiveness.

Further details on the studies completed and currently in progress are shown in the section on characteristics of included studies.

METHODOLOGICAL QUALITY

All four trials met the inclusion criteria for this review. In the Chichester trial (Chichester) all eligible individuals were identified from practice registers and family health service lists, and randomisation was generated by computer. The same method was used by the Mass study (MASS). The Western Australia trial (Western Australia) identified individuals from the electoral role, excluding those living in nursing homes, and those who lived in a community too far distant for the researchers to establish a screening clinic

within their resources. The remainder were randomised by computer generated random numbering (Jamrozik 2000), into intervention and control groups of equal size defined by five year age group and postcode. The Viborg trial (Viborg) identified all eligible men in the County of Viborg from health department lists. Randomisation was computer generated in blocks of of approximately 1000 in order to avoid too long a time between randomisation and invitation to screening (Lindholt 1996; Lindholt 2002). Due to the nature of the intervention, patients were not blinded to the intervention in any of the studies. All four studies analysed results on an intention-to-treat basis.

Three of the trials (Chichester; MASS; Western Australia) sought information on deaths from all causes and from abdominal aortic aneurysm in the general population. The Western Australia trial randomised all men at the same time, but screening took place over a 32-month period for logistical reasons. Men were therefore not invited for screening until some months after randomisation. As a result, 2296 men died after randomisation but before the date of screening (screening group), or the equivalent "virtual" date of screening (control group). The virtual date of screening was the median scheduled date of examination for men from the same post code area randomised to be screened. Two sets of analyses were undertaken, one from the point of randomisation, and one from the point of invitation to screening. For the purpose of this review, analyses undertaken from the point of screening are included in the results, and the possible impact of analyses from the point of randomisation discussed.

The Viborg trial (Viborg) only identified deaths within hospital, and not deaths occurring in the community. Hence mortality could not be compared with the other trials. All four trials identified rates of surgery for abdominal aortic aneurysm as an outcome, and the Chichester trial identified incidence of ruptured aortic aneurysm (Chichester).

A subgroup of people with aneurysms between 3.0 cm and 4.9 cm identified in the Viborg trial was also invited to participate in a randomised double blind trial of the impact of propranolol versus placebo on the expansion rate of small abdominal aortic aneurysms (Lindholt 1999). This trial was stopped after two years because the propranolol group suffered significantly higher rates of dyspnoea (difficulty in breathing), decreased pulmonary function and death. Although only 30 of 122 patients identified as having a small abdominal aortic aneurysm were treated with propranolol, this could significantly alter the death rates in the screened group. This is a further reason for not comparing mortality in the Viborg study with the other trials.

In addition, 92 patients identified as having small aneurysms 2.5 cm to 2.9 cm were included in a trial of a macrolide antibiotic to decrease expansion. This had a small but significant effect decreasing the rate of expansion (Vammen 2001).

The methodological quality of cost effectiveness analyses was not assessed by the authors.

RESULTS

Acceptance rates

Overall the acceptance rates varied from 63.1% (Western Australia) to 80.2% (MASS). The acceptance rate in the Western Australia trial (Western Australia) increased to 70% if patients who were identified after randomisation to have been too unwell or had been previously scanned were excluded. Acceptance rates by age were published only for the Chichester trial (Chichester), with men and women aged 65 accepting the invitation to screen most often (80.5% and 72.7% respectively). Acceptance decreased with age and was lowest for men and women aged 76 to 80 years (66.2% and 58.3% respectively) (Scott 1995).

Mortality

The impact of screening on overall mortality is reported in the Chichester trial (Scott 1995), the MASS study (MASS) and the Western Australia trial (Norman 2004). Individually the Chichester and MASS trials do not identify an impact on overall mortality (Chichester, men: odds ratio (OR) 1.07; 95% Confidence intervals (CI) 0.93 to 1.22; Chichester, women: OR 1.06; 95% CI 0.93 to 1.21; MASS, men: OR 0.97; 95% CI 0.93 to 1.02). The Western Australia trial only reports all-cause mortality in its analysis from the point of screening and not from the point of randomisation. This identifies a significant reduction in all-cause mortality (OR 0.85; 95% CI 0.80 to 0.90). When all studies in men reporting all-cause mortality are analysed together, there is no significant reduction in all-cause mortality (OR 0.95; 95% CI 0.85 to 1.07). **Comparison 01/01**

Mortality from abdominal aortic aneurysm is reported in the Chichester; MASS and Western Australia trials. This includes deaths due to rupture and deaths associated with emergency and elective surgery for aneurysm repair. In men, the Chichester and Western Australia trials show a non-significant reduction (Chichester, OR 0.59; 95% CI 0.27 to 1.29 and Western Australia, OR 0.72; CI 0.39 to 1.32). The MASS study, however, demonstrated a strongly significant reduction (OR 0.58; 95% CI 0.42 to 0.78). The results of the Chichester trial in women show no benefit (OR 1.99; 95% CI 0.36 to 10.88). When all studies in men reporting death from abdominal aortic aneurysm are analysed together, there is a significant reduction in mortality (OR 0.60; 95%CI 0.47 to 0.78). **Comparison 01/02**

The Western Australia trial also presents data on mortality from abdominal aortic aneurysm analysed from the point of randomisation rather than from the point of screening. If this is combined with the Chichester and MASS trial data there is little difference in the outcomes and there remains a significant difference in mortality from abdominal aortic aneurysm (OR 0.64; 95% CI 0.50 to 0.81).

Life expectancy
This was not reported in any of the four trials.

Progression to ruptured aortic aneurysm
The Chichester trial (Chichester) is the only one to report progression to ruptured aortic aneurysm. Overall fewer ruptured aortic aneurysms were observed in the screened than in the control group (12/7887 versus 22/7888). Subgroup analyses by sex showed that the effect was again limited to males. Of the men who were screened, 9/3205 experienced ruptured abdominal aneurysm compared to 20/3228 in the unscreened group and this difference reached significance (OR 0.45; 95% CI 0.21 to 0.99). For females the rates were 3/4682 for those screened and 2/4660 for the unscreened (OR 1.49; 95% CI 0.25 to 8.94). **Comparison 01/03**

Surgery for abdominal aortic aneurysm
All four trials report rates of surgery for abdominal aortic aneurysm as a result of screening. When analysed individually, the Chichester, MASS and Western Australia trials identify a significant increase in rates of surgery. The Viborg trial identifies a non-significant trend to increased surgery. When the four trials are combined, the increased rate of surgery is highly significant (OR 2.03; 95%CI 1.59 to 2.59). **Comparison 01/04**

Complications of surgery
This was not reported in any of the four trials.

Patient subjective measures
No data are available from the study on the effects on patient quality of life of receiving the invitation to screen, undergoing the test, receiving results, being followed up or receiving surgery.

Resource use
The MASS study (MASS) has published a full cost effectiveness analysis of the benefits of abdominal aortic aneurysm screening at four years follow up, with projection of their data to estimate cost effectiveness at ten years. They identified 47 fewer deaths over four years due to abdominal aortic aneurysm, at an additional cost of £2.2 million. This equated to £28,400 per life year gained, and approximately £36,000 per QALY (Quality Adjusted Life Year). After ten years this is estimated to fall to about £8,000 per life year gained.

The Viborg trial (Viborg) identifies outline hospital costs with an estimate of costs outside hospital. They derive a figure of DKK 7540 per life year saved (£1 = 12 DKK).

DISCUSSION

This review identifies four randomised controlled trials of aortic aneurysm screening, and the results appear to identify evidence of significant benefit in men. Analysing data from the trials together shows a strongly significant reduction in mortality from abdominal aortic aneurysm. There is a highly significant increase in rates of surgery resulting from screening, but resource analysis appears to demonstrate overall cost effectiveness.

There are, however, a number of uncertainties in this review. Firstly, the study shows no significant impact on all-cause mortality, which is to be expected given the relative infrequency of abdominal aortic aneurysm as a cause of death. However, there is significant heterogeneity, with the Western Australia study showing a significant decrease in all-cause mortality. This study identified seven fewer deaths from abdominal aortic aneurysm in the screened group compared with controls, but there were 339 fewer deaths from all causes. This suggests that the reduction in overall mortality in this study may not be a genuine impact of screening. Instead, this may be related to the study design in which randomisation took place at the outset, but individuals were invited to screening over a 32 month period, in which 2296 of the intervention and control groups had died. The subsequent analysis of all-cause mortality took the point of screening rather than randomisation as the starting point, and this may have introduced an unrecognised bias in the design of this particular study

The second area of uncertainty is the cost effectiveness of screening. The results of the MASS and Viborg trials are very different, with a cost of £28,400 (MASS) per life year saved compared with DKK 7540 (Viborg). The authors did not assess the methodological quality of cost effectiveness calculations, but even the MASS study, demonstrating higher costs, gives a result at the margins of acceptable cost effectiveness. Projecting figures to ten years gives a considerably lower estimate of cost per life year saved. It is not possible from this analysis to be certain of the cost effectiveness of screening, but the published figures do suggest that cost effectiveness may be acceptable.

Thirdly is the paucity of information about the costs and benefits of screening in women. Only the Chichester study included women, and there were insufficient numbers to produce any meaningful results (Chichester).

Despite these uncertainties, there are now data on trials including over 122,000 men, using a similar method of screening, and approximately similar regimes for follow up and intervention. Uptake rates are high in all studies, and taken together they appear to demonstrate an overall benefit from ultrasound screening in men aged 65 to 79 years, in terms of reduced mortality from abdominal aortic aneurysm. There is also a suggestion that cost effectiveness may be acceptable. It is still the case, however, that even though the overall population benefit from screening appears to be established, there will still be a significant rate of mortality and morbidity from elective aneurysm repair in people who otherwise considered themselves healthy, and whose aneurysms detected by screening may not have ruptured in future. The mortality associated with elective surgical repair of an abdominal aortic aneurysm, though far lower than that following rupture, is not insignificant. Patients may therefore be asked to undergo this risk to repair a

large aneurysm which may not kill them. Conversely others will discover they have small aneurysms not yet needing surgery, but which could nonetheless expand and kill them in the future. There are limited data in these four trials on quality of life, surgical complications or overall life expectancy to further aid the analysis.

AUTHORS' CONCLUSIONS

Implications for practice

There is evidence from this study of a significant reduction in mortality from abdominal aortic aneurysm in men aged 65 to 79 years who undergo ultrasound screening. There is insufficient evidence to demonstrate benefit in women. The cost effectiveness may be acceptable, but needs further expert analysis. These findings need careful consideration in judging whether a co-ordinated population based screening programme should be introduced.

Implications for research

The most significant gap in the current research is the balance of benefits and harms in women. This should be a focus for any future research, and further work on the feasibility of implementation would also be helpful. This might include the most acceptable method of invitation to screening, ease and logistics of access to initial ultrasound and follow up, costs and workforce needs, and how to provide information on potential benefits and harms for individuals who are offered screening. The psychological effects of screening both on patients and their partners need detailed study. There is also the question of how far and how fast any positive effects of screening can be generalised outside of centres which have developed a special expertise in operating them over many years.

NOTES

The review author is currently updating this review as a result of a comment received from one of the trialists of an Included study. The update will include the results of new searches for studies. The comment and the review author's repsonse to comment have been added to the review.

FEEDBACK

Viborg and MASS Trials: Lindholt

Summary

The authors claim that the randomisation method is not described in The Viborg Trial, and that it is based on AAA deaths on hospitals. In addition, data on overall mortality is not included. This is true for the earliest publications, but the paper from BMJ in 2005 actually describes the randomisation method in blocks of approx. 1000 in order to avoid too long time between randomisation and invitation to screening, population based AAA mortality (AAA related deaths in and outside hospitals) on a national basis, and overall mortality on a national basis. These data ought to be used in the next update, which already seem needed after the publication of seven year results from the MASS trial.

Author's reply

1. The author has amended the sentence in the 'Methodological quality of studies' section to state the method of randomisation.
2. The author is currently updating the review to include the seven year results of the MASS trial.

Contributors

Jes S. Lindholt

POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

The authors would like to thank the contribution made to the Plain Language Summary by Dr Janet Wale of the Consumer Network.

SOURCES OF SUPPORT

External sources of support

- Chief Scientist Office, Health Department, The Scottish Executive UK

Internal sources of support

- No sources of support supplied

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Chichester
Methods	Study design: randomised, controlled unblinded clinical trial.
	Method of randomisation: computer.
	Concealment of allocation: none stated.
	Exclusions post randomisation:
	Losses to follow-up:
	Intention-to-treat analysis: yes.
Participants	Country: UK (Chichester).
	Setting: hospital outpatients.
	No: 15,775; screening group 7,887; control group 7,888.
	Age: 65 to 80 years.
	Sex: screening group males 3,205, females 4,682; control group males 3,228, females 4,660.
	Inclusion criteria: patients belonging to family medical practices in the area.
	Exclusion criteria: none given.
Interventions	7,887 were invited for screening and 5,394 accepted. (Overall acceptance 68.4%). Screening was by ultrasound to measure the aortic diameter diameter.
	Management of screening group: <3 cm diameter, no review; 3cm to 4.4 cm, annual rescan; 4.5 cm to 5.9 cm, 3-monthly rescan; >6 cm or >1 cm increase per year, or development of symptoms referral for surgery. After the third scan or if any abnormality was detected there was a surgical outpatient review and confirmatory scan.
	Control group of 7,888 received no intervention.
	Mean follow-up: 30.5 months, range 3 to 5 years.

Characteristics of included studies (*Continued*)

Outcomes	Primary: acceptance rates by age; prevalence of AAA by age; death from all causes; death from AAA; incidence of ruptured AAA and subsequent treatment.
Notes	Mortality data for all patients in the trial was obtained weekly from the Register of births and deaths.
Allocation concealment	A – Adequate

Study	**MASS**
Methods	Study design: randomised, controlled, unblinded clinical trial. Method of randomisation: computer. Concealment of allocation: none stated. Exclusions post randomisation: none. Losses to follow up: less than 1%. Intention-to-treat analysis: yes
Participants	Country: UK (Portsmouth, Southampton, Oxford, Winchester). Setting: outpatients in community settings. No: 67,800; screening group 33,839; control group 33,961. Age: 65 to 74 years. Sex: males. Inclusion criteria: men identified from family medical practices in Oxford, Portsmouth, Winchester and Southampton, UK. Exclusion criteria: those family doctor considered unfit for screening.
Interventions	33,839 were invited for screening and 27,147 were screened (overall uptake 80.2%). Screening was by ultrasound to measure aortic diameter. Management of screening group: <3 cm, no review; 3.0 cm to 4.4 cm, annual rescan; 4.5 cm to 5.4 cm, 3-monthly rescan; >5.5 cm or >1 cm increase per year, or development of symptoms, referral for surgery. Control group of 33,961 received no intervention. Mean follow up: 4.1 years, range 2.9 to 5.2 years.
Outcomes	Primary: mortality due to AAA. Secondary: prevalence and natural history of AAA; mortality from all causes; impact of screening on quality of life; health service costs; impact on surgical workload.
Notes	Mortality data for all patients was obtained from the Office for National Statistics mortality surveillance system.
Allocation concealment	D – Not used

Study	**Viborg**
Methods	Study design: randomised, controlled, unblinded clinical trial. Method of randomisation: computer. Concealment of allocation: none stated. Exclusions post randomisation: none.

Characteristics of included studies (*Continued*)

	Losses to follow up: not commented on, but only hospital treatment and deaths in hospital identified during follow up. Intention-to-treat analysis: yes.
Participants	Country: Denmark (Viborg). Setting: hospital out-patients. Number: 12,682; screening group 6,339; control group 6,319. Age: 65 to 73. Sex: male. Inclusion crieria: men identified from health department records for Viborg County, Denmark. Exclusion criteria: none.
Interventions	6,339 were invited for screening, and 4,843 attended (acceptance rate of 76%). Screening was by ultrasound to measure abdominal aortic diameter. Management of screening group: <3.0 cm, no review; 3.1 cm to 4.9 cm, offered annual rescan; 5.0 cm or more, referred to vascular surgeon. Control group of 6,319 received no intervention. Mean follow up 5.1 years. Range not stated.
Outcomes	Primary: acceptance rates; prevalence of AAA; surgery for AAA ; hospital diagnosis of AAA; hospital deaths from AAA; costs per prevented hospital death.
Notes	Trial only reports on outcomes identified in hospital, and therefore not on deaths in the community. Therefore comparison with other studies can only be made on rates of surgery for abdominal aortic aneurysm.
Allocation concealment	D – Not used

Study	**Western Australia**
Methods	Study design: randomised, controlled, unblinded clinical trial. Method of randomisation: not stated. Concealment of allocation: none stated. Exclusions post randomisation: 2,296 individuals died after randomisation and before invited for screening. Losses to follow up: not commented upon. Intention-to-treat analysis: yes.
Participants	Country: Australia (Perth). Setting: Outpatient screening clinics. Number: 41,000 men were randomised; 38,704 identified as controls or invited to screening (2,296 died between randomisation and invitation to screening). Screening group 19,352, control group 19,352. Age: Those expected to be 65 to 79 at midpoint of screening programme were subject to initial randomisation. Sex: Male Inclusion criteria: Men on the electoral role for Perth area, Australia. Exclusion criteria: Nursing home residents and inhabitants of furthest satellite town from Perth were excluded.
Interventions	19,352 were invited to screening and 12,213 accepted (overall uptake 63.1%). Screening was by ultrasound to measure aortic diameter.

	Management of screening group: letter with result of scan provided to patient with copy of family doctor. No attempt to influence or recommend subsequent management. Control group of 19,352 received no intervention. Median follow up 43 months, range 27 to 61 months.
Outcomes	Primary: Acceptance rates for screening, prevalence of AAA, surgey for AAA, mortality from AAA, deaths from all causes.
Notes	Because of method of age recording in electoral role, 5.9% of attendees for screening were aged 80 and over at screening. Subanalyses of 65 to 74 years and 75 years and over are reported.
Allocation concealment	D – Not used

AAA = Abdominal aortic aneurysm

Characteristics of excluded studies

Study	Reason for exclusion
Lindholt 1999	This a randomised controlled trial on a subgroup of 122 patients with small abdominal aortic aneurysm from the Viborg trial already considered. Patients discovered to have aneurysms at screening were randomised to receive propanolol to prevent expansion but the trial was closed early because of adverse effects. The trial is relevant to the management of screened populations but is not a trial of screening.
Lindholt 2000	This study sent quality of life questionnaires to samples of patients in the Viborg trial. It included non-responders to screening, some before and after screening, some with small abdominal aneursyms discovered and some control subjects. The study considers psychological consequences of screening using a case control rather than randomised controlled design.
Vammen 2001	This is a randomised controlled trial of a subgroup of 92 patients with small abdominal aneursym from the Viborg trial. Patients discovered at screening to have small abdominal aneurysm were randomised to receive roxithromycin to prevent expansion. The trial is relevant to the managment of screened populations but is not a trial of screening.
Vammen 2002	Duplicate reference (Vammen 2001).

ADDITIONAL TABLES

Table 01. Search strategy used to search CENTRAL

Search terms

#1 MeSH descriptor AORTIC ANEURYSM ABDOMINAL this term only
#2 (aortic in All Text near/6 aneurysm in All Text near/6 abdominal in All Text)
#3 aortic next aneurysm in All Text
#4 (abdominal in All Text near/6 aneurysm in All Text)
#5 (aneurysm in All Text near/6 ruptured in All Text)
#6 (#1 or #2 or #3 or #4 or #5)
#7 screening in All Text
#8 (#6 and #7)

ANALYSES

Comparison 01. Screening vs no screening for abdominal aortic aneurysm

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Death from all causes			Odds Ratio (Random) 95% CI	Subtotals only
02 Death from abdominal aortic aneurysm			Odds Ratio (Random) 95% CI	Subtotals only
03 Incidence of ruptured AAA			Odds Ratio (Random) 95% CI	Subtotals only
04 Surgery for abdominal aortic aneurysm	4	125595	Odds Ratio (Random) 95% CI	2.03 [1.59, 2.59]

INDEX TERMS

Medical Subject Headings (MeSH)

Aortic Aneurysm, Abdominal [*diagnosis; mortality; surgery]; Cost-Benefit Analysis; Life Expectancy; *Mass Screening [economics]; Randomized Controlled Trials; Sex Factors

MeSH check words

Aged; Aged, 80 and over; Female; Humans; Male

COVER SHEET

Title	Screening for abdominal aortic aneurysm
Authors	Cosford PA, Leng GC
Contribution of author(s)	Paul Cosford identified possible trials for inclusion, contacted authors for further information on trials, assessed trial quality, extracted data, and wrote the review. Gillian Leng assessed unblinded trial reports to confirm eligibility, assessed trial quality, extracted data, and contributed to the text of the review.
Issue protocol first published	2001/1
Review first published	2007/2
Date of most recent amendment	17 August 2007
Date of most recent SUBSTANTIVE amendment	26 January 2007
What's New	August 2007: Minor update. Comment and review author's repsonse to comment added. The review author is currently updating this review in the light of this comment and the results of new searches for studies. Citations of new publications added to 'Classification pending'.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	27 July 2007
Date new studies found and included/excluded	26 January 2007
Date authors' conclusions section amended	Information not supplied by author

Contact address Dr Paul Cosford
East of England Strategic Health Authority
Victoria House
Capital Park
Fulbourn
Cambridge
CB1 5XB
UK
E-mail: Paul.Cosford@eoe.nhs.uk
Tel: +44 01223 597533

DOI 10.1002/14651858.CD002945.pub2

Cochrane Library number CD002945

Editorial group Cochrane Peripheral Vascular Diseases Group

Editorial group code HM-PVD

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Screening vs no screening for abdominal aortic aneurysm, Outcome 01 Death from all causes

Review: Screening for abdominal aortic aneurysm

Comparison: 01 Screening vs no screening for abdominal aortic aneurysm

Outcome: 01 Death from all causes

Study	Screened n/N	Unscreened n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
01 Male					
Chichester	532/3205	508/3228		26.2	1.07 [0.93, 1.22]
MASS	3750/33839	3855/33961		37.6	0.97 [0.93, 1.02]
Western Australia	2232/19352	2571/19352		36.2	0.85 [0.80, 0.90]
Subtotal (95% CI)	56396	56541		100.0	0.95 [0.85, 1.07]
Total events: 6514 (Screened), 6934 (Unscreened)					
Test for heterogeneity chi-square=15.74 df=2 p=0.0004 I^2 =87.3%					
Test for overall effect z=0.88 p=0.4					
02 Female					
Chichester	503/4682	476/4660		100.0	1.06 [0.93, 1.21]
Subtotal (95% CI)	4682	4660		100.0	1.06 [0.93, 1.21]
Total events: 503 (Screened), 476 (Unscreened)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.83 p=0.4					

Analysis 01.02. Comparison 01 Screening vs no screening for abdominal aortic aneurysm, Outcome 02 Death from abdominal aortic aneurysm

Review: Screening for abdominal aortic aneurysm

Comparison: 01 Screening vs no screening for abdominal aortic aneurysm

Outcome: 02 Death from abdominal aortic aneurysm

Study	Screened n/N	Unscreened n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
01 Male					
Chichester	10/3205	17/3228		10.8	0.59 [0.27, 1.29]
MASS	65/33839	113/33961		71.1	0.58 [0.42, 0.78]
Western Australia	18/19352	25/19352		18.1	0.72 [0.39, 1.32]
Subtotal (95% CI)	56396	56541		100.0	0.60 [0.47, 0.78]
Total events: 93 (Screened), 155 (Unscreened)					
Test for heterogeneity chi-square=0.41 df=2 p=0.81 I^2 =0.0%					
Test for overall effect z=3.87 p=0.0001					
02 Female					
Chichester	4/4682	2/4660		100.0	1.99 [0.36, 10.88]
Subtotal (95% CI)	4682	4660		100.0	1.99 [0.36, 10.88]
Total events: 4 (Screened), 2 (Unscreened)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.80 p=0.4					

Analysis 01.03. Comparison 01 Screening vs no screening for abdominal aortic aneurysm, Outcome 03 Incidence of ruptured AAA

Review: Screening for abdominal aortic aneurysm

Comparison: 01 Screening vs no screening for abdominal aortic aneurysm

Outcome: 03 Incidence of ruptured AAA

Study	Screened n/N	Unscreened n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
01 Male					
Chichester	9/3205	20/3228		100.0	0.45 [0.21, 0.99]
Subtotal (95% CI)	3205	3228		100.0	0.45 [0.21, 0.99]
Total events: 9 (Screened), 20 (Unscreened)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.98 p=0.05					
02 Female					
Chichester	3/4682	2/4660		100.0	1.49 [0.25, 8.94]
Subtotal (95% CI)	4682	4660		100.0	1.49 [0.25, 8.94]
Total events: 3 (Screened), 2 (Unscreened)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.44 p=0.7					

Analysis 01.04. Comparison 01 Screening vs no screening for abdominal aortic aneurysm, Outcome 04 Surgery for abdominal aortic aneurysm

Review: Screening for abdominal aortic aneurysm

Comparison: 01 Screening vs no screening for abdominal aortic aneurysm

Outcome: 04 Surgery for abdominal aortic aneurysm

Study	Treatment n/N	Control n/N	Odds Ratio (Random) 95% CI	Weight (%)	Odds Ratio (Random) 95% CI
Chichester	31/3205	13/3228		11.2	2.42 [1.26, 4.62]
MASS	354/33839	146/33961		38.8	2.45 [2.02, 2.97]
Viborg	60/6339	41/6319		21.8	1.46 [0.98, 2.18]
Western Australia	116/19352	62/19352		28.3	1.88 [1.38, 2.56]
Total (95% CI)	62735	62860		100.0	2.03 [1.59, 2.59]
Total events: 561 (Treatment), 262 (Control)					
Test for heterogeneity chi-square=6.19 df=3 p=0.10 I^2 =51.5%					
Test for overall effect z=5.63 p<0.00001