

# The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial

The Multicentre Aneurysm Screening Study Group\*

## Summary

**Background** Opposing views have been published on the importance of ultrasound screening for abdominal aortic aneurysms. The Multicentre Aneurysm Screening Study was designed to assess whether or not such screening is beneficial.

**Methods** A population-based sample of men (n=67 800) aged 65–74 years was enrolled, and each individual randomly allocated to either receive an invitation for an abdominal ultrasound scan (invited group, n=33 839) or not (control group, n=33 961). Men in whom abdominal aortic aneurysms ( $\geq 3$  cm in diameter) were detected were followed-up with repeat ultrasound scans for a mean of 4.1 years. Surgery was considered on specific criteria (diameter  $\geq 5.5$  cm, expansion  $\geq 1$  cm per year, symptoms). Mortality data were obtained from the Office of National Statistics, and an intention-to-treat analysis was based on cause of death. Quality of life was assessed with four standardised scales. The primary outcome measure was mortality related to abdominal aortic aneurysm.

**Findings** 27 147 of 33 839 (80%) men in the invited group accepted the invitation to screening, and 1333 aneurysms were detected. There were 65 aneurysm-related deaths (absolute risk 0.19%) in the invited group, and 113 (0.33%) in the control group (risk reduction 42%, 95% CI 22–58;  $p=0.0002$ ), with a 53% reduction (95% CI 30–64) in those who attended screening. 30-day mortality was 6% (24 of 414) after elective surgery for an aneurysm, and 37% (30 of 81) after emergency surgery.

**Interpretation** Our results provide reliable evidence of benefit from screening for abdominal aortic aneurysms.

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## Introduction

Rupture of abdominal aortic aneurysms caused about 6800 deaths in England and Wales in the year 2000. Most of these deaths occurred in men—the age-specific prevalence of the condition being six times greater in men than in women.<sup>1</sup> In men older than 65 years, ruptured abdominal aortic aneurysms are responsible for 2.1% of all deaths. Of the deaths attributed to ruptured aneurysms, about half take place before the patient reaches hospital.<sup>2,3</sup> For patients who reach hospital alive, the mortality rate for emergency treatment is 30–70%.<sup>3,4</sup> The overall mortality rate is, therefore, between 65% and 85%.<sup>4</sup>

Ultrasound can reliably visualise the aorta in 99% of people,<sup>5</sup> thus providing the possibility of detection of an abdominal aortic aneurysm at a size when rupture is unlikely to occur. Intervention at this stage could reduce the frequency of rupture, and so reduce mortality and the requirement for emergency hospital treatment. Elective surgery for an abdominal aortic aneurysm is, however, also associated with a mortality risk of about 2–6%.<sup>3,6,7</sup> Opposing views have, hence, been published on the potential importance of ultrasound screening for this condition.<sup>8,9</sup> Since ultrasound as a screening test is reasonably cheap and non-invasive, and the condition is a substantial cause of mortality, a randomised trial of sufficient size to detect realistic levels of effect was indicated.

Results of a pilot study indicated the feasibility of population screening by ultrasound, with participation rates of 68%.<sup>10</sup> The findings of the pilot study also suggested that a reduction of 30% in mortality from ruptured abdominal aortic aneurysms, on an intention-to-treat basis, would be a realistic basis for power calculations. Accordingly, plans for such a trial, the Multicentre Aneurysm Screening Study (MASS), were drawn up in 1995–96. Investigators acknowledged at the outset that no trial of realistic size could have appreciable power to detect an effect on total mortality. MASS was therefore designed to have acceptable power for detecting a 30% reduction in mortality from ruptured aneurysms. The investigators were aware when designing the trial that similar, although smaller, trials were being planned in Denmark<sup>5</sup> and Australia.<sup>7</sup> An additional combined analysis of the three trials was suggested as part of the study protocol.

As well as showing clinical benefits, screening has to be shown not to adversely affect quality of life among participants. Results of previous studies of the psychological effect of screening for abdominal aortic aneurysms show no significant effects of detecting the condition on mood,<sup>11,12</sup> but do indicate some impairment of quality of life, especially in those who do not undergo surgical repair of aneurysms.<sup>13,14</sup> The validity of these

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conclusions is, however, limited by small sample sizes in many of the studies. There is also uncertainty about the cost-effectiveness of screening.<sup>9,15</sup>

Here, we report the initial results from MASS on mortality, and the effect of screening on quality of life. A trial-based analysis of cost-effectiveness is being published elsewhere.<sup>16</sup>

## Methods

### Participants

Between January, 1997, and May, 1999, men aged 65–74 years from four centres (Portsmouth, Southampton, Winchester, and Oxford) in the UK were identified from family doctor lists and Health Authority lists, after obtaining the family doctor's permission. Before randomisation, doctors were asked to list patients they considered unfit to be screened. These were then excluded from the study. The study itself imposed no exclusion criteria other than sex and year of birth, but doctors typically informed the study investigators of recent deaths, and excluded men who were terminally ill, had other serious health problems, and had a previous abdominal aortic aneurysm repair. Ethics approval for the trial was obtained from the local ethics committees at each centre, and all patients provided signed informed consent.

### Protocol

Eligible men were individually randomised either to be invited for screening (invited group) or not (control group). As each practice was recruited, lists of potential participants were obtained electronically. Doctors considered these lists for exclusions. Randomisation was done programmatically on each file in turn at the trial's statistical centre, using random sampling based on computer-generated pseudorandom numbers. The statistical centre had no clinical role in the study. All randomisations were done by the trial's database administrator, and uses of the randomisation tool logged. The local coordinator, who was supervised by the local clinical director, ran the screening trial at each centre. A clerk arranged the clinic bookings, and answered patients' queries. No contact was made with respect to screening the men in the control group. An invitation to come for ultrasound screening was sent on family doctor headed paper to the men in the invited group, together with an information booklet and questionnaire. Those who accepted the invitation and were scanned constituted the scanned group. Those who did not attend for whatever reason, despite a second invitation after non-attendance at a clinic, constituted the not scanned group.

A screening team made up of an ultrasonographer and a nurse or facilitator undertook the screening. Screening clinics were held in rooms at or near to the practice where men were being screened. On arrival, the facilitator explained the procedures to the individual, checked their questionnaire, and answered queries. Signed informed consent was obtained. Blood pressure and pulse were then taken three times in succession. The median blood pressure was reported to the family doctor.

The individual then had an ultrasound scan of the abdominal aorta, using a portable ultrasound machine (Hitachi ultrasound scanner EUB-405, Hitachi Medical Corporation, Tokyo, Japan). The maximum transverse diameter of the aorta in the transverse plane, and the maximum anterior-posterior diameter in the longitudinal plane were measured with callipers, and images were recorded on thermal paper. The largest diameter of these two readings was recorded as the maximum aortic diameter for each man. A hardcopy was kept of all scans.

After initial screening, the scanned group was subdivided into those who had an abdominal aortic aneurysm (maximum aortic diameter on ultrasound  $\geq 3$  cm), those in whom no aneurysm was detected, and those in whom the aorta could not be visualised. Arrangements were made to follow up patients who had an abdominal aortic aneurysm with repeat scans at intervals related to the aortic size.

Patients were not given their results at the clinic. A radiologist reviewed all abnormal scans and a subsample of normal scans. At the completion of screening of each practice, results were sent to the patients' family doctor, with letters for the doctors to send to the patients should they feel it appropriate.

Men who had a normal aorta (<3 cm diameter) and those whose aortas were not visualised were not rescanned. Patients with an aortic diameter of 3.0–4.4 cm were rescanned at yearly intervals, whereas those with an aortic diameter of 4.5–5.4 cm were rescanned at 3-monthly intervals. Urgent referral to a vascular consultant was recommended for patients with an aortic diameter of 5.5 cm or greater. Follow-up scans were done at recall clinics generally based in screening rooms at the local hospital. Follow-up was continued for up to 5 years in the trial. After which time further follow-up was arranged through the patient's doctor.

Family doctors were immediately informed about any patient whose aortic diameter was 5.5 cm or more on ultrasound measurement, whose aortic diameter expanded at a rate of 1 cm or more within 1 year, or whose symptoms were attributable to the aneurysm. In such instances, referral to a vascular surgeon was suggested.

When a patient was referred, the medical imaging department at the hospital did a further ultrasound scan, and the local clinical consultant attached to the trial centre assessed the patient for their fitness for surgical treatment. If the patient declined surgery, was unfit for surgery according to the criteria of Bernstein and Chan,<sup>17</sup> or the repeated scan did not confirm the need for surgery, the patient continued to be followed up at routine recall clinics.

Information on all surgical procedures for abdominal aortic aneurysms, in each centre, was obtained by a combination of monthly feedback from the local surgical team, review of operating theatre logbooks, hospital information systems, and patients' hospital notes. 30-day surgical mortality (emergency and elective) was based on date of operation combined with date of death.

The UK National Health Service number of every patient randomised to the trial was tagged via the Office of National Statistics mortality surveillance system. The Office of National Statistics provided a copy of the death certificate for any man who died during the course of the trial. The International Classification of Diseases, 9th edn (ICD 9), codes 441.3–441.6 were used to identify those patients certified as having died from a ruptured abdominal aortic aneurysm (code 441.3 abdominal aortic aneurysm, ruptured; code 441.4 abdominal aortic aneurysm without mention of rupture; code 441.5 aortic aneurysm of unspecified site, ruptured; code 441.6 aortic aneurysm of unspecified site without mention of rupture). Codes 441.5–441.6 are likely to include some deaths due to thoracic aneurysms (see discussion). Information was obtained on deaths up to March 31, 2002. Follow-up thus ranged from 2.9 to 5.2 years (mean 4.1 years).

An independent mortality working party was set up to review all death certificates, and to obtain additional

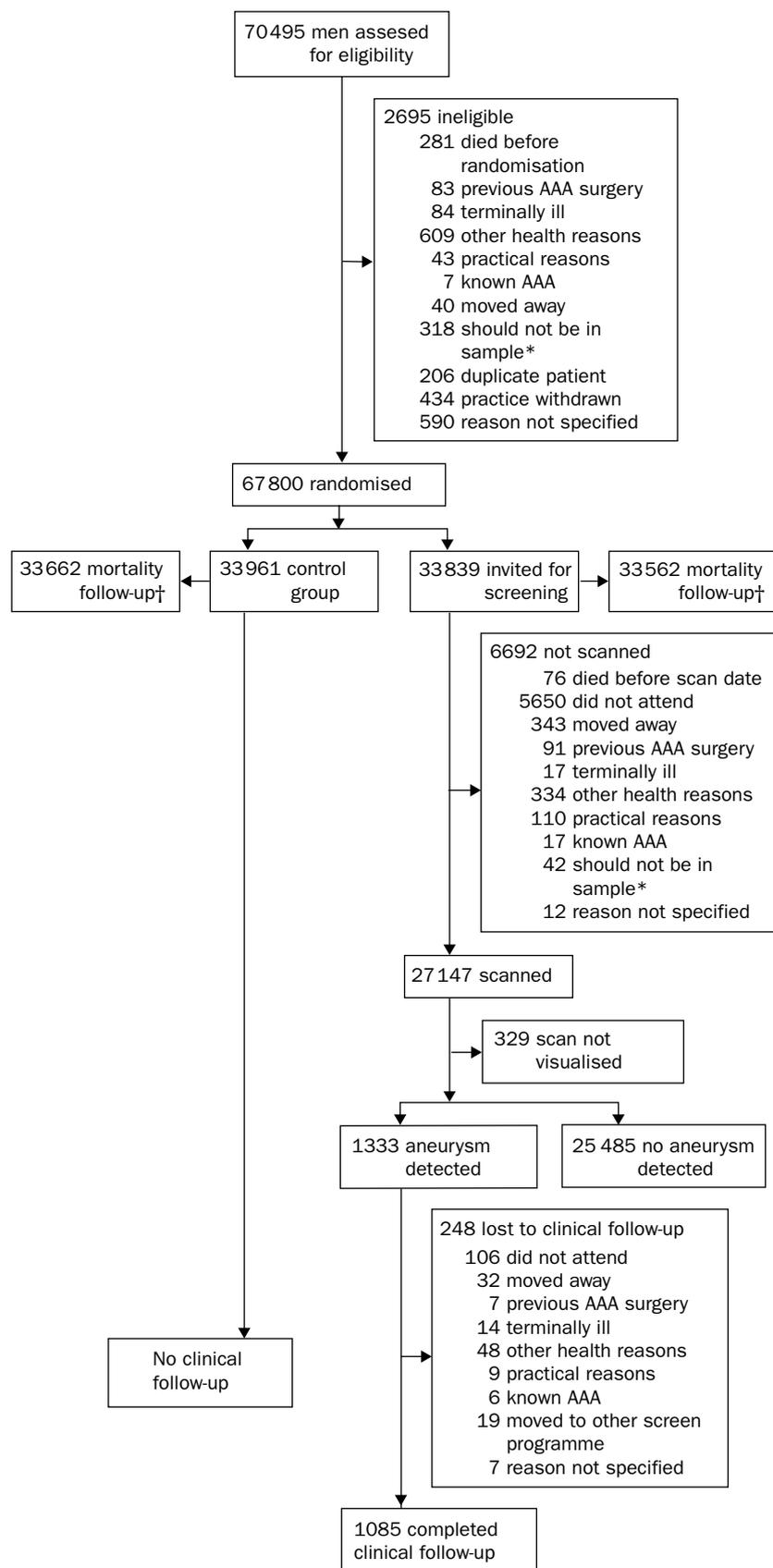


Figure 1: Trial profile

AAA=abdominal aortic aneurysm. \*Individuals did not meet inclusion criteria but were mistakenly included by either the health authority or the family doctor. †See text for explanation of participants lost to mortality follow-up.

information for all those in whom abdominal aortic aneurysm was a potential cause of death, or in whom the cause of death was unclear. This group included those deaths recorded as old age or involving postoperative complications, as well as those recorded as abdominal aortic aneurysm deaths or with aortic aneurysm mentioned on the certificate. Additional information with respect to the cause of death was obtained from coroners, hospital necropsy reports and, where appropriate, the hospital and family doctor clinical notes. The cause of death was then if necessary revised in the light of this information, and the effect of these revisions on the overall results of the trial assessed. An assessment was also made of the effect of additional information on the registered cause of death for 100 individuals categorised as having died suddenly (ICD 9 codes 410–412, 414, 415.1, 441.6, and 785.5).

Quality of life was assessed with four standardised scales: the depression scale of the hospital anxiety and depression scale (HADS),<sup>18</sup> the short-form state anxiety scale of the Spielberger state-trait anxiety scale,<sup>19</sup> the SF-36 health survey,<sup>20</sup> and the EuroQol EQ-5D.<sup>21</sup> All assessments were made with postal questionnaires sent to representative subsamples. 6 weeks after screening responses were collected from two groups; those receiving a negative result and those receiving a positive result (response rates 90% in both groups after up to two mailings). Scores from a control group, not invited to attend for screening, were collected at one time point (response rate 77%). Among those who received positive results, further comparisons were made between those who underwent surgery and those who underwent surveillance. These comparisons were made 3 months and 12 months after surgery or screening.

Several checks for quality assurance were made. The local consultant radiologist linked to the trial reviewed all abnormal scans. In addition, scans generated from randomly selected clinics for each sonographer were reviewed at regular intervals to ensure that they were in line with the protocol and that standards were being maintained. An independent radiologist also reviewed scans and report sheets produced from all four centres over a randomly selected 1-month period at intervals during the trial, assessing the quality of image, accuracy of calliper placement, and accuracy of data transfer. To assess

interobserver and intraobserver variability, special crossover clinics were set up during the course of the trial. Two sonographers scanned patients independently, and the process was repeated after 1 h. An independent observer monitored the clinics. The ultrasound machines were checked with a range of commercial test objects at the start of the study and annually by the consultant physicist and a senior sonographer attached to the trial. Local centre sonographers also undertook checks at about monthly intervals, using standard test objects. Comparisons were made of the aortic image size recorded on the scan, on the report sheet, and the computer database. The accuracy of the patient questionnaire data entered on to the database for a subsample of individuals was also assessed, using double data entry.

The primary outcome measure was abdominal aortic aneurysm related mortality, and the secondary outcome measures were all cause mortality, frequency of ruptured abdominal aortic aneurysm, and effect of screening and surgery on quality of life.

#### Statistical analysis

A data monitoring committee reviewed information on the deaths from abdominal aortic aneurysms and other causes, as well as operative mortality after surgery for abdominal aortic aneurysms, throughout the trial. The trial coordinators were unaware of the results until data collection was completed in March, 2002.

The size of the trial was planned on the basis of having an 80% power to detect, as significant at the 5% level, a 30% reduction in deaths from ruptured abdominal aortic aneurysms. This level of power required around 115 deaths from ruptured aneurysms to have occurred in the control group. Based on UK mortality statistics, it was estimated that 66 000 men needed to be randomised and followed-up for an average of 4 years.

The statistical analysis was done in accord with a prespecified plan, considering the groups as randomised. The primary analysis compared the mortality from ruptured abdominal aortic aneurysms (ICD 9 codes 441.3–441.6) in the invited group and the control group, based on the cause of death as reported to the Office of National Statistics, including deaths from any cause within 30 days of surgery for abdominal aortic aneurysm (both elective and emergency). The aneurysm-related mortality was compared primarily in terms of the hazard ratio. As a measure of effect, it is likely to be less affected by the underlying risk in the study population, for example due to its age distribution, or by the length of follow-up than the difference in absolute risk between the two groups. We do, however, give results for the absolute risk as well. The analysis used Kaplan-Meier curves, log-rank test, and hazard ratio from a Cox proportional hazards regression analysis, censoring other causes of death. Adjustments for age at randomisation and screening centre, and a test of interaction by centre, were

done with Cox regression. Results of the primary and secondary outcome measures among those screened in the invited group were used to provide an unbiased estimate of the benefit of attending screening.<sup>22</sup> This estimate is obtained by subtracting, from the controls, a group, which is equivalent to the non-compliant group of those invited, to form a control group comparable to those compliant with screening in the invited group.

Mean scores on the four scales used to assess quality of life were compared, using *t* tests, between those who received a negative result on screening and those who received a positive result. Since there were no differences in the sub-sample on any of the outcome measures between those with small (3.0–4.4 cm, n=450), medium (4.5–5.4 cm, n=129), or large aneurysms ( $\geq 5.5$  cm, n=20), responses from these three groups were combined in the analyses.

#### Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, or in the decision to submit the paper for publication.

#### Results

Figure 1 shows the trial profile. 67 800 of 70 495 men considered for inclusion were randomised. The largest group excluded before randomisation were those whom family doctors considered unfit for screening (figure 1; other health reasons and other reasons not specified). One practice withdrew from the trial shortly after being included in the randomisation. The randomised groups were balanced at baseline in terms of screening centre (Portsmouth 33%, Southampton 28%, Oxford 26%, Winchester 13%), age (mean 69.2 years, SD 2.9), and social deprivation scores (mean at the 63rd percentile of the social deprivation distribution of 8414 wards in England, so less deprived than the median).<sup>23</sup>

Of the 33 839 men invited for screening, 80% accepted the invitation (77% after the first invitation, 3% after the second) and were scanned (figure 1). The predominant reason for not being scanned was that individuals did not attend their appointment. An aneurysm was detected in 1333 men (4.9% of those scanned). 71% (944) of detected abdominal aortic aneurysms were small (3–4.4 cm in aortic diameter), 17% (223) were medium (4.5–5.4 cm), and 12% (166) were large (5.5 cm or greater).

Mortality follow-up was available for 67 274 (99%) of the randomised men. Clinical follow-up in accordance with the trial protocol was complete in 81% (n=1085) of those with a detected aneurysm (figure 1). Table 1 shows the types of operation done for abdominal aortic aneurysm. More individuals in the invited group (n=322) had elective operations than in the control group (n=92). The overall 30-day mortality after elective surgery was 6%

	Control group		Invited group		Total	
	Operations (n=146)	Deaths (n=31)	Operations (n=354)	Deaths (n=23)	Operations (n=500)	Deaths (n=54)
<b>Elective surgery</b>	92	9 (10%)	322	15 (5%)	414	24 (6%)
By meeting criteria	0	0	291	11 (4%)	291	11 (4%)
Not by criteria	92	9 (10%)	31	4 (13%)	123	13 (11%)
<b>Emergency surgery</b>	54	22 (41%)	27	8 (30%)	81	30 (37%)
For ruptured AAA	49	22 (45%)	24	6 (25%)	73	28 (38%)
For emergency symptomatic AAA*	5	0	3	2 (67%)	8	2 (25%)
<b>Other†</b>	0	0	5	0	5	0

\*On day of admission. †Operations primarily for iliac aneurysm, with AAA surgery done at same time.

Table 1: Operations for abdominal aortic aneurysm (AAA) and subsequent 30-day mortality

(n=24), and did not differ much between the two groups (p=0.12). There were fewer emergency operations done in the invited group (n=27) than in the control group (n=54, table 1), but the overall 30-day mortality rate did not differ significantly (p=0.32). The in-hospital deaths after elective surgery (n=27, 7%) and emergency surgery (n=30, 37%) were similar to the 30-day mortalities. There were only four in-hospital deaths after 30 days post-surgery in the control group, and two in the invited group.

Table 2 shows mortality related to abdominal aortic aneurysm, the primary outcome. There were 65 (absolute risk 0.19%) such deaths in the invited group and 113 (0.33%) in the control group yielding a hazard ratio of 0.58 (95% CI 0.42–0.78; p=0.0002; table 2). This estimated 42% reduction in risk in the invited group was unaltered after adjustment for age and screening centre, and did not vary significantly by centre (p=0.71). The reduction in risk stemmed from a reduction in deaths from ruptured aneurysms, offset by a slight increase in deaths within 30 days of elective surgery. Since elective surgery tended to take place earlier after randomisation in the invited than in the control group, the reduction in overall aneurysm-related mortality in the invited group became more apparent after about 1 year of follow-up (figure 2).

The incidence of non-fatal ruptured abdominal aortic aneurysm was also lower in the invited than in the control group (table 2). This incidence combined with aneurysm-related mortality, 82 (absolute risk 0.24%) in the invited group versus 140 (0.41%) in the control group, gave a hazard ratio of 0.59 (p=0.00006; table 2); similar to that for aneurysm-related mortality alone.

Table 3 shows all-cause mortality. As expected, given the power of the study, there was no significant difference in all-cause mortality between the groups, around 11% of the men in each group had died by the end of the trial. Other than aneurysm-related mortality, which accounted for 2% of all deaths in the invited group and 3% in the control group, there was little difference between the randomised groups in any particular category of cause of death (table 3). However, ischaemic heart disease deaths were slightly lower in the invited group than in the control group (p=0.03).

In the invited group, 16 men died after elective surgery. Additionally, despite being invited for screening, 66 patients subsequently had a ruptured abdominal aortic

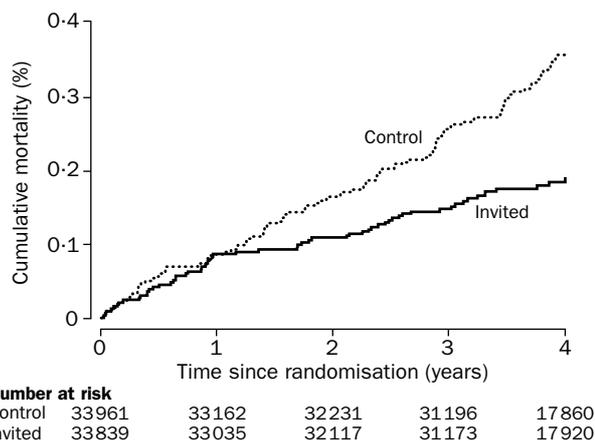


Figure 2: Aneurysm-related mortality over 4 years of follow-up by randomisation group

aneurysm (table 4). However, 20 of these did not attend for screening, and three died between randomisation and their first appointment. Of the remaining 43 who had a ruptured aneurysm despite being screened, four did not keep a subsequent clinic appointment, six did not attend the assessment for (or refused) surgery, and five were unfit for surgery, leaving 28 who were available for treatment. Of these, eight patients had a ruptured aneurysm between scans without reaching the criteria for surgery, five had normal scans at initial screening, and two had a non-visualised aorta at first scan. The remaining 13 had a ruptured aneurysm after being seen as outpatients (table 4).

Table 5 shows the aneurysm-related mortality, total ruptured aneurysm incidence, and all-cause mortality within the invited group, separated in accord with attendance at the initial scan. All three outcomes had a substantially greater frequency in the group who did not attend screening. The estimated hazard ratios for men who were scanned, as against a comparable group in the controls,<sup>22</sup> were 0.47 (95% CI 0.36–0.70, 53% risk reduction) for aneurysm-related mortality, and 0.49 (0.38–0.70, 51%) for total incidence of ruptured aneurysms.

After review of all available death certificates of patients, 8% (14 of 177) of those certified as having died from an abdominal aortic aneurysm were considered to have died from other causes, and 0.1% (nine of 7407) of

	Control group (n=33 961)	Invited group (n=33 839)
Person-years of observation (1000)	132.6	132.3
Deaths within 30 days of elective surgery*	9	15
Deaths from ruptured AAA†	91	37
Deaths from ruptured aortic aneurysm of unspecified site‡	13	13
<b>Total AAA-related deaths</b>	<b>113</b>	<b>65</b>
Rate per 1000 person-years (95% CI)	0.85 (0.71–1.02)	0.49 (0.39–0.63)
Hazard ratio (95% CI)	1.00 (reference)	0.58 (0.42–0.78)
<b>Non-fatal ruptured AAA</b>	<b>27</b>	<b>17</b>
Total§	140	82
Rate per 1000 person-years (95% CI)	1.06 (0.89–1.25)	0.62 (0.50–0.77)
Hazard ratio (95% CI)	1.00 (reference)	0.59 (0.45–0.77)

\*All-cause mortality, including any ICD codes 441.3–441.6 within 30 days of elective surgery. †ICD codes 441.3–441.4, and all deaths occurring within 30 days of emergency AAA surgery. ‡ICD codes 441.5 and 441.6. §AAA-related deaths plus non-fatal ruptured AAA incidence.

Table 2: Mortality related to abdominal aortic aneurysm (AAA) and incidence of ruptured AAA

	Control group (n=33 961)	Invited group (n=33 839)
Person-years of observation (1000)	132.6	132.3
<b>Cardiovascular deaths</b>	<b>1689 (44%)</b>	<b>1547 (41%)</b>
AAA-related	113 (3%)	65 (2%)
Ischaemic heart disease	1098 (28%)	999 (26%)
Stroke	212 (6%)	216 (6%)
Other	266 (7%)	267 (7%)
<b>Cancer deaths</b>	<b>1296 (34%)</b>	<b>1319 (35%)</b>
<b>Other deaths*</b>	<b>870 (22%)</b>	<b>884 (24%)</b>
<b>All deaths</b>	<b>3855 (100%)</b>	<b>3750 (100%)</b>
<b>Rate per 1000 person-years (95% CI)</b>	<b>29.1 (28.2–30.0)</b>	<b>28.3 (27.5–29.3)</b>
<b>Hazard ratio (95% CI)</b>	<b>1.00 (reference)</b>	<b>0.97 (0.93–1.02)</b>

Data are number (%) of all deaths unless otherwise indicated. AAA=abdominal aortic aneurysm. \*Includes 9 deaths of unknown cause.

Table 3: All-cause mortality

	Ruptured AAA incidence (n=82)	Deaths (n=65)
<b>AAA not known</b>		
Between randomisation and scan	3	3
Not scanned	20	17
After non-visualised first scan	2	2
After normal first scan	5	4
<b>AAA known</b>		
Aneurysm <55 mm detected		
Between recall scans	8	4
After non-attendance at recall scan	4	4
Aneurysm ≥55 mm detected		
After non-attendance at OPD appointment or refusal of operation	6	5
After declared unfit for surgery	5	5
Pending decision with respect to surgery	6	2
While awaiting operation	6	3
After returned to screening for reassessment	1	0
<30 days after elective surgery*	15	15
>30 days after elective surgery	1	1

OPD=outpatient department. \*Includes four opportunistic discovery operations after exit from screening procedure (one after normal scan, one after post-randomisation exclusion from study due to previously known AAA, one non-attendance at initial screening, one meeting criteria at a non-programme scan while still in recall cycle).

Table 4: **Timing of incidence of ruptured abdominal aortic aneurysm (AAA) and deaths for individuals invited for screening**

those certified as having died from other causes were considered to have died from an aneurysm. Applying these revisions of cause of death to the aneurysm-related mortality results made little difference to our findings, relative to the difference shown between the two randomised groups. It decreased the number of aneurysm-related deaths by two in the control group and by three in the invited group, yielding a hazard ratio of 0.62 (95% CI 0.43–0.88).

At all times, and across all groups, anxiety, depression, and health-status measures were within the age-matched and sex-matched population norms.<sup>19–21</sup> 6 weeks after screening, there were no differences in anxiety or depression between those who screened negative and those who screened positive (table 6). There were, however, small differences in health status measures, with those who screened positive having slightly lower scores on the physical and mental subscales of the SF-36, and lower self-rated health, as measured by the EQ-5D. 3 months later, those who underwent surgery differed from those with smaller aneurysms undergoing surveillance in having slightly lower scores on the mental subscale of SF-36 but slightly higher values for their self-rated health. 12 months after screening or surgery, there

	Not scanned (n=6692)	Scanned (n=27 147)
Observation person-years (1000)	25.0	107.3
<b>AAA-related deaths</b>		
Rate of AAA-related death per 1000 person-years (95% CI)	22 0.88 (0.58–1.34)	43 0.40 (0.30–0.54)
<b>Total ruptured AAA incidence</b>		
Incidence per 1000 person-years (95% CI)	25 1.00 (0.67–1.47)	57 0.53 (0.41–0.69)
<b>All deaths</b>		
Rate of death per 1000 person-years (95% CI)	1160 46.4 (43.8–49.1)	2590 24.1 (23.2–25.1)

Table 5: **Mortality related to abdominal aortic aneurysm (AAA), ruptured AAA incidence, and all-cause mortality, by attendance at screening**

were no differences between the groups in mood, the physical or mental subscale of SF-36, or the EQ-5D weighted health index. Those who had undergone surgery, however, rated their health more highly with the EQ-5D self-rating measure, at a degree similar to that of those screening negative.

No significant deterioration was detected in the performance of the ultrasound machines over the course of the study, and any faults were identified and repaired without problems. The intraobserver and interobserver variability was within acceptable limits; the mean intraobserver variability was 1.60 mm in the longitudinal plane and 2.60 mm in the transverse plane. The mean interobserver variability was 2.15 mm in the longitudinal plane and 3.27 mm in the transverse plane. Data quality validation checks indicated that errors were low; around 2% at the beginning of the trial, reducing to 1% at the end of initial screening.

## Discussion

Our findings indicate that screening can significantly reduce mortality rates associated with abdominal aortic aneurysms, and show similar reductions in mortality rates to those reported from smaller randomised trials done in Chichester in the UK,<sup>10</sup> and Denmark,<sup>24</sup> and from two non-randomised population screening programmes in Huntingdon<sup>3</sup> and Gloucester, UK.<sup>25</sup> There was a similar aneurysm-related mortality among those in the invited group who did not attend for screening and those in the control group, thus reducing the benefit from the screening programme overall. For an individual, the relevant estimate of benefit is that associated with being screened, rather than being invited, obtained by comparison of those who attend screening with a subgroup of controls; a comparison that produces a greater reduction in abdominal aortic aneurysm mortality.<sup>22</sup> There was no significant difference between the invited and control groups with respect to all-cause mortality, as would be expected, since abdominal aortic aneurysms contributed to less than 3% of all deaths.

Because many aneurysms were detected in the screened group and required treatment in the first 1–2 years, we anticipated that the mortality in the invited group might exceed that of the control group over this period; a potential adverse effect of elective surgery. However, as can be seen from the mortality curves, this pattern did not arise, largely due to the sufficiently low postoperative mortality rate, and the elective surgery that occurred in patients with aneurysms diagnosed opportunistically in the control group.

Our study had several potential limitations. Mortality data were based on death certification provided by the Office of National Statistics. Death certification as a source of information can be criticised for its inaccuracy in the absence of a post-mortem. However, any bias in the certification is likely to be against screening, since the practitioner is aware of the presence of an aneurysm in the screened population when certification of sudden death is required. The accuracy of registration of cause of death is also limited by the quality of the information available to those completing death certificates. The mortality working party reviewed all death certificates and collected additional information to see whether these extra data suggested that the registered cause of death was inaccurate. Relative to the differences shown between the two randomised groups, the indicated revisions were very limited and did not alter the findings of the trial.

There is also a potential bias against screening associated with inclusion of ICD 9 codes 441.5 and 441.6

	6 weeks after screening				3 and 12 months after detection of aneurysm or surgery					
	Negative (n=631)	Positive (n=599)	p*	Controls (n=726)	3 months			12 months		
					Surveillance (n=426)	Surgery (n=129)	p	Surveillance (n=426)	Surgery (n=129)	p
State anxiety (20–80), clinical cutoff=42†	29.5	30.9	0.020	31.5	28.9	29.1	0.292	29.6	28.6	0.323
<b>Depression</b> (0–21), clinical cutoff=15‡	3.0	3.3	0.092	3.5	3.0	3.0	0.835	3.2	3.1	0.394
<b>SF-36</b> (0–100)‡										
Physical health	51.2	49.7*	0.003	50.0	51.0	50.0	0.295	49.8	51.1	0.086
Mental health	51.5	49.8	0.003	50.0	51.7	48.4	0.004	50.1	50.6	0.311
<b>EQ-5D‡</b>										
Weighted health index (0–1)	0.83	0.81	0.045	0.80	0.83	0.85	0.084	0.83	0.85	0.577
Self-rating (0–100)	80	76	0.0003	78	77	80	0.0003	76	81	0.0007

p values <0.010 were judged significant. \*Comparing men with negative and positive screening results. †Higher scores denote poorer states. ‡Higher scores denote better states.

Table 6: Mood and health status outcomes

(aortic aneurysm) as well as ICD 9 codes 441.3 and 441.4 (abdominal aortic aneurysms). The inclusion of 441.5 and 441.6 could have led to the inclusion of some patients with thoracic aneurysms that cannot be detected by routine ultrasound and therefore could not have elective treatment to prevent rupture. Deaths from aortic aneurysms were included because the male-to-female sex ratio in this group is two-to-one (similar to the ratio of abdominal aortic aneurysms of three-to-one, and dissimilar to death from thoracic aneurysms which is 1.5 times more common in women), suggesting that most of these deaths for aortic aneurysms were actually abdominal.

Finally, we might not have identified all deaths that arose within 30 days of elective repair for abdominal aortic aneurysms in some controls who moved away, further biasing our results against screening. Most deaths relating to surgery for ruptured aneurysms are correctly ascribed to rupture on the death certificate. The presence of previous elective surgery, however, is badly documented on death certificates. For this reason, operative deaths within 30 days of surgery were detected by comparison of the date of the operation and the date of death. Unlike the screened population, we had no record of the men in the control group who had moved away, and so no record of any operations undertaken or their outcome.

We estimate that in men aged 65–74 years invited to screening, the risk of dying from an abdominal aortic aneurysm over 4.1 years is reduced from 3.3 per 1000 to 1.9 per 1000. 710 men would therefore need to be screened to prevent one death in this timeframe. This reduction in absolute risk is likely to underestimate the full reduction achieved by a single screening test. First, the pattern of the two mortality curves in figure 2 strongly suggests that with further follow-up the gap will widen, indicating an increasing reduction in absolute risk, although the effect on the hazard ratio might only be slight. Second, we note a slight decrease in deaths attributed to ischaemic heart disease in the invited group. Since sudden deaths due to ruptured aneurysms could be incorrectly recorded as due to ischaemic heart disease on the death certificate (of the 100 we reviewed, we found two), part of the apparent deficit in deaths from ischaemic heart disease in the invited group might be due to misclassified deaths from aneurysms. This effect might not change the relative hazard of an aneurysm-related death appreciably, but could increase substantially the absolute reduction in risk.

The incidence of ruptured aneurysms (deaths from ruptured abdominal aortic aneurysms plus survivors of

surgery for ruptured abdominal aortic aneurysms) was lower in the screened group than in the controls. Although 66 patients in the invited group had a ruptured aneurysm, more than half of these (38 patients) were not available to benefit from treatment to prevent the rupture occurring, because they did not comply with the screening and intervention programme or because they were unfit for surgery. Of those who were available for treatment, eight patients died from rupture between scans without reaching the criteria for surgery. This represents 0.6% of all the detected abdominal aortic aneurysms. Although most ruptures arise in large aneurysms, inevitably some will occur in smaller aneurysms.<sup>26</sup> A review of the most recent scans of all these patients did not show any undermeasurement.

The incidence of ruptured abdominal aortic aneurysms in the group of men who did not attend, and so were never screened, reduced the benefit from screening overall. Keeping this group to a minimum is essential in a population-screening programme to maximise the benefit from screening.

Our findings indicate no adverse effects on the emotional states of men who had an aneurysm detected through population-based screening, or subsequent surgery. Degrees of anxiety and depression were within the population norms<sup>18,19</sup> at all assessment points in all the groups. In view of the high response rate, this finding is unlikely to reflect response bias. Detection of an aneurysm was associated in the short term with slightly more negative scores on some of the health-status measures. Men undergoing surgery, compared with those undergoing surveillance had, in the short term, poorer scores on the SF-36 mental-health scale, a difference that was no longer present at 12 months. Surgery was, however, associated with better self-rated health 3 months and 12 months after surgery, similar to the ratings made by those screening negative. These results indicate a similar pattern of findings to those reported in other studies of the effect of screening for aneurysms on quality of life.<sup>11–14</sup> They are also in agreement with the results of a systematic review of the adverse effects of screening, which shows that, 4 or more weeks after screening, adverse emotional effects are not apparent.<sup>27</sup>

Our results indicate that substantial reductions in aneurysm-related mortality could be achieved by the implementation of a population-screening programme. In view of the much higher frequency of the condition among men, and the absence of evidence of effect of screening on the incidence of ruptured aneurysms in

women,<sup>28</sup> it would be logical to screen only men. Our results show that minimum extra benefit would be gained by re-screening in the first 5 years, given the very low rupture rate among men with a normal aortic diameter at the initial screen. Longer-term follow-up is needed to ascertain whether the reduction in mortality associated with a single screening test continues in years 5–10 post-screening. From such a study, the value of supplementing a screen at age 65 with one at age 70 or 75 could be assessed. However, modelling the longitudinal data from the earlier Chichester and Huntingdon screening programmes indicates that few new aneurysms will develop and proceed to rupture within an interval of less than 10 years.<sup>29</sup> The suggestion in an earlier report<sup>30</sup> that a national screening programme could consist of a single aortic ultrasound scan at age 65 would be supported by our results. This trial has provided reliable evidence of benefit from abdominal aortic aneurysm screening which, taken in conjunction with our report on cost-effectiveness,<sup>16</sup> should provide the basis for an informed decision on population screening for abdominal aortic aneurysms.

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#### Conflict of interest statement

None declared.

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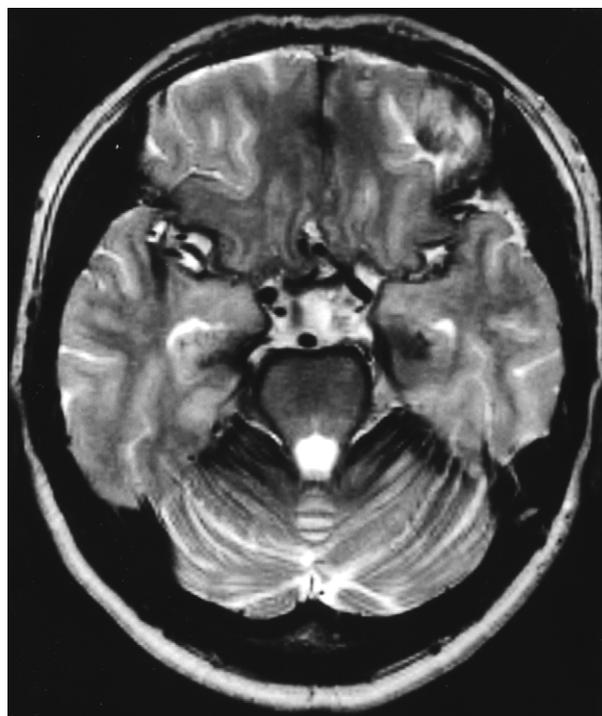
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## Clinical picture

### Superficial siderosis from spinal teratoma

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A 54-year-old woman presented with gradually progressive bilateral sensorineural hearing loss and gait ataxia. Cerebral magnetic resonance (MR) imaging showed a hypointense rim of the surface of the cerebellum and brainstem, indicating superficial siderosis (figure; T-2 weighted). However, the patient had no history of subarachnoid haemorrhage or cranial surgery. Magnetic resonance angiography showed no intracranial aneurysms or arteriovenous malformation. Further examination showed a spinal tumour with fatty components at the level of the lower cervical spine. Spinal teratoma was confirmed by surgical exploration. Superficial siderosis was probably due to rupture of the spinal teratoma into the subarachnoid space.



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