A sustained mortality benefit from screening for abdominal aortic aneurysm

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined ultrasonography screening for abdominal aortic aneurysm (AAA) in men aged 65 to 74 years, compared with no screening. After screening, men with an aortic diameter of 3.0 cm or greater were defined as having an AAA and were subsequently invited for recall scans to monitor the growth of the aneurysm. Men with an aortic diameter of 3.0 to 4.4 cm were re-screened every year, while those with an aortic diameter of 4.5 to 5.4 cm were re-screened every 3 months. Men were considered for elective surgery when the aortic diameter reached 5.5 cm, aortic expansion was 1.0 cm or more in 1 year, or when they experienced symptoms attributable to the aneurysm. Finally, men with an aortic diameter of less than 3.0 cm on the initial scan were not re-screened.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised men aged 65 to 74 years. Men with known AAA, previous AAA surgery, or terminal illness were not included.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were gathered from 1997 to March 2005. The costs were measured in 2004/05 prices.

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
The design and results of the MASS are reported in a separate publication (see ‘Other Publications of Related Interest’ below for bibliographic details), thus limited information on the primary study was reported in the current paper. Overall, of the 70,495 patients who were initially identified, 2,725 were excluded because they did not meet the inclusion criteria. Thus, the final study sample included 67,770 men, of which 33,887 were in the control group and 33,883 in the screening group. The mean age at enrolment was 69.2 years in both groups.
Study design
This was a prospective, randomised controlled trial, which was carried out in four medical centres in the UK. Details of randomisation were not reported. The length of follow-up ranged from 5.9 to 8.2 years (mean 7.1 years). The loss to follow-up because of death was 2.1% overall (2.2% in the control group and 2.1% in the screening group). Loss to clinical follow-up (non-attendance at recall scans) was 19% at 4 years and 24% at 7 years. Blinding was not performed.

Analysis of effectiveness
The primary outcome measure was AAA-related mortality. This was defined as all deaths within 30 days of any AAA surgery (elective or emergency) plus all deaths coded as ruptured AAA, AAA without mention of rupture, ruptured aortic aneurysm at unspecified site, or aortic aneurysm at unspecified site without mention of rupture. The secondary clinical end point was all-cause mortality. Mortality data were obtained after flagging on the national database. The baseline comparability of the study groups was not reported, but the groups were likely to have been similar given the large sample size and the randomised design. However, the authors stated that patients who accepted an invitation to screening were more likely to be a less-fit group. The analysis of the clinical study was conducted on an intention to treat basis. Both measures of mortality were compared using unadjusted Cox regression.

Effectiveness results
The total AAA-related deaths per 1,000 person-years were 196 in the control group and 105 in the screening group, giving a hazard ratio of 0.53 (95% confidence interval, CI: 0.42 to 0.68).

When adjusted for baseline differences, the hazard ratio was reduced to 0.42 (95% CI: 0.33 to 0.55).

The total deaths per 1,000 person-years for all-cause mortality were 7,119 in the control group and 6,882 in the screening group, giving a hazard ratio of 0.96 (95% CI: 0.93 to 1.00).

Clinical conclusions
The effectiveness analysis showed that screening was effective in reducing AAA-related deaths and all-cause mortality in men aged 65 to 74 years.

Measure of benefits used in the economic analysis
The summary benefit measure used was the number of life-years (LYs) gained with screening over no screening. LYs were estimated as the area under the Kaplan-Meier curves for both groups, or calculated using two definitions of mortality (i.e. AAA-related deaths and all-cause deaths). An annual discount rate of 3% was applied.

Direct costs
The analysis of the costs was undertaken from the perspective of the health system. It included the costs of invitation to screening, re-invitation after nonresponse, initial scan, recall scan, consultation for elective surgery, elective AAA surgery and emergency AAA surgery. The unit costs were reported extensively, but quantities of resources used were given only for a few items. Resource use was determined prospectively from the sample of men included in the clinical trial. The source of the costs was not explicitly reported. Discounting was relevant given the time horizon of the analysis (7 years), and an annual rate of 3% was used. The costs were estimated using 2004/05 prices.

Statistical analysis of costs
The costs and quantities of resources used appear to have been treated deterministically.

Indirect Costs
Productivity costs were not considered in the economic analysis.
Currency
US dollars ($). The costs were initially measured in UK pounds sterling (£), then converted using a rate of 1.00 = $1.58.

Sensitivity analysis
The issue of uncertainty in the cost-effectiveness estimates was investigated in a deterministic sensitivity analysis in which the following scenarios were considered:

- the costs retained at the 2000/01 financial-year level for comparison with previous publications,
- quality-adjusted life-years based on age-related reductions,
- US-based unit cost estimates for scans and surgeries,
- an increase of 50% in the cost of a consultation, and
- scenarios 3 and 4 combined.

Alternative values of utility weights were obtained from a published study, while US cost estimates were based on Medicare reimbursement. CIs for cost-effectiveness ratios were also calculated, probably using a bootstrapping technique, and cost-effectiveness acceptability curves were generated.

Estimated benefits used in the economic analysis
When AAA-related deaths only were considered, the total LYs over the 7-year period were 2,143.30 in the control group and 2,145.82 in the screening group (difference 2.52).

When all-cause deaths were considered, the total LYs over the 7-year period were 2,124.96 in the control group and 2,131.48 in the screening group (difference 6.52).

In both cases, differences in LYs were much higher in years 5 to 7 than in the first four years.

Cost results
When only AAA-related deaths were considered, the total costs per patient over the 7-year period were $116.72 in the control group and $251.54 in the screening group (difference $134.82).

When all-cause deaths were considered, the total costs per patient over the 7-year period were $116.63 in the control group and $251.65 in the screening group (difference $135.02).

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the alternative strategies.

When AAA-related deaths only were considered, the incremental cost per LY gained with screening over no screening was $19,500 (95% CI: 12,400 to 39,800).

When all-cause deaths were considered, the incremental cost per LY gained with screening over no screening was $7,600 (95% CI: 3,300 to no limit).

The cost-effectiveness acceptability curve showed that, at a willingness-to-pay of $40,000 per LY gained, the probability that AAA ultrasonography screening would be cost-effective was 98%.

The results of the sensitivity analysis showed that the incremental cost-effectiveness ratio was:
$16,400 (95% CI: 10,400 to 33,400) when 2000/01 prices were used,
$24,600 (95% CI: 15,700 to 49,700) with quality of life adjustment (cost-utility analysis),
$29,600 (95% CI: 18,900 to 60,200) with US costs,
$20,700 (95% CI: 10,400 to 33,400) with consultation costs increased by 50%, and
$30,800 (95% CI: 19,700 to 62,600) with consultation costs increased by 50% and US costs.

Authors' conclusions
Screening ultrasonography for abdominal aortic aneurysm (AAA) was cost-effective and its value for money improved over time. Screening ultrasonography remained cost-effective even in the most unfavourable scenario.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear in that no screening represents the current pattern of care in most settings. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a large clinical trial, which was appropriate for the study question. Limited information on the design and other aspects of the study was provided as the trial itself was published in a companion paper. However, the length of follow-up, the use of intention to treat in the analysis of effectiveness, and the large sample of patients and institutions involved ensure a high internal validity of the clinical estimates.

Validity of estimate of measure of benefit
The summary benefit measure (LYs) was appropriate in that it reflected the most relevant dimension of health for patients at risk of developing an AAA. Discounting was performed, as recommended by UK guidelines. Two alternative sources of mortality data were considered. The impact of screening on quality of life was investigated in the sensitivity analysis.

Validity of estimate of costs
The analysis of the costs was consistent with the stated perspective, and all the relevant categories of costs appear to have been included. A breakdown of the cost items was given and the unit costs were reported. This might enable the analysis to be replicated in other settings. However, limited information on resource use was given. The source of the costs was not stated clearly, but it is likely to have reflected typical UK sources. The sensitivity analysis investigated the use of alternative sources of costs. The price year was reported, thus facilitating reflation exercises in other time periods.

Other issues
The authors did not compare their findings with those from other studies. They did not address the issue of the generalisability of the study results to other settings and limited sensitivity analyses were carried out. This reduces the external validity of the analysis. However, variability in the clinical and economic estimates was adequately addressed using a bootstrapping technique and by presenting cost-effectiveness acceptability curves. The authors noted some limitations to their analysis such as the inclusion of deaths from aortic aneurysm at an unexpected site, which might include some thoracic aortic aneurysm. This could have led to an underestimation of treatment effectiveness.

Implications of the study
The study results support the use of screening ultrasonography for AAA.
Source of funding
Supported by a grant from the UK Medical Research Council and a Raymond and Beverly Sackler Studentship Award.

Bibliographic details

PubMedID
17502630

Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Aortic Aneurysm, Abdominal /mortality /surgery /ultrasonography; Aortic Rupture /mortality /surgery /ultrasonography; Cost-Benefit Analysis; Follow-Up Studies; Humans; Male; Mass Screening /economics; Ultrasonography /economics; United States /epidemiology

AccessionNumber
22007008129

Date bibliographic record published
31/10/2007

Date abstract record published
31/10/2007