Cost-effectiveness Analysis of Screening for Abdominal Aortic Aneurysms Based on Five Year Results from a Randomised Hospital Based Mass Screening Trial

J.S. Lindholt, S. Juul, H. Fasting and E.W. Henneberg

The Vascular Research Unit, Department of Vascular Surgery, Viborg Hospital, DK-8800 Viborg, and Department of Epidemiology, Institute of Public Health, Vennelyst Boulevard 6, University of Aarhus, DK-8000 Aarhus C, Denmark

Background. The aim of this study was to estimate the cost effectiveness of screening for abdominal aortic aneurysm (AAA). Material and methods. All 12,639 men born in the years 1921–1933 (aged 64–73) living in Viborg County, Denmark, were randomly allocated either to receive an invitation to abdominal ultrasound scanning for AAA or to be controls. Costs for screening and surveillance were assessed prospectively. Diagnosis Related Group (DRG) costs from 1999 were used concerning admissions with uncomplicated and complicated operations. Admissions for AAA surgery were retrospectively classified according to complications in patient records. Results. Mean follow-up time was 52 months. 76.6% of invited men attended screening, and 191 (4.0%) had an AAA. As previously reported, the cumulative 5-year AAA-specific mortality in the invited group was significantly reduced by 67% compared to the control group (P = 0.003). The costs were estimated to be €11.23 per scan. The costs per life-year saved were €9057 (€8572–20,063) after 5 years, and were expected to decrease to €2708 (€1758–6031) after 10 years and to €1825 (€1185–4063) after 15 years. Conclusion. Screening of 64–73 years old males in Denmark seems cost effective.

Keywords: Abdominal aortic aneurysm; Mass screening; Prevention; Randomised controlled trial.

Introduction

The elderly population is increasing in virtually all Western societies, and about 1–3% of men over the age of 64 will experience rupture of an abdominal aortic aneurysm (AAA), an event that carries a 70–95% mortality. AAAs seldom cause symptoms, but if an AAA is found before rupture, elective repair carries a much lower mortality of 4–6%, suggesting the benefit of screening.1–5 The cost effectiveness of ultrasound screening for AAA in older men is uncertain. Previous cost-effectiveness analyses have mostly been based on uncertain assumptions.6–9 Consequently, the results of these assessments have ranged from attractive cost effectiveness1,6,8,10 to the conclusion that screening was harmful and costly.8 The large-scale randomised multicentre aneurysm screening study (MASS) estimated the cost of AAA screening per life year saved to be £28,400,11 which probably is below £30,000 per quality adjusted life year saved.12 However, the costs were projected to decline to around £8000 per life year saved after 10 years.11 At about the same time as the MASS trial, our randomised screening trial was set up in the County of Viborg, Denmark. We previously reported its main finding: a significant 67% reduction of AAA mortality during the first 52 months after randomisation.13 These findings are used here to assess the cost effectiveness of screening for AAA in men. We also investigated the operative complications following screening. Previous reports, based upon non-randomised data, suggest elective operations on screen-detected AAA are associated with fewer complications and lower operative mortality compared to non-screen-detected cases.14,15

Material and Methods

The methods for this cost effectiveness analysis build on those of our clinical trial, which is described elsewhere.13 In brief, from 1994 to 1998, all 12,639
men aged 64–73 years resident in Viborg County in Denmark were randomly selected to be invited for screening (intervention arm) or not (control arm). Of these, 6306 became controls, while 6333 were invited to receive an abdominal ultrasonographic scan performed by a mobile screening team at their district hospital (Fig. 1).

An AAA was considered to be present if the infrarenal aortic diameter was 3 cm or greater. Patients with AAAs of 5 cm or more were referred to a vascular surgeon for consideration for elective repair. The remaining small AAAs were offered yearly surveillance to check for any expansion, and referred for surgical evaluation if the aneurysm became 5 cm or greater in diameter. Men who were found to have an initial ectatic aorta (diameter 2.5–2.9 cm) on the initial scan were offered rescreening after 3–5 years (Fig. 1).{footnote}16 Data were collected from both arms regarding vital status and elective or emergency aneurysm repairs (see details below). In the intervention arm, data were also collected concerning screening attendance, re-invitations, and follow-up surveillance of small AAAs.

**Follow-up of subjects**

Subjects were followed from randomisation until death or 31.12.1999. Deaths were identified in the Danish Civil Registration System and the causes of death were obtained from the National Register of Causes of Death. Death certificates with AAA as the primary or a contributing cause of death were identified, and hospital and autopsy records were obtained. Two vascular surgeons, blind to the

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### Figure 1: Flow-chart concerning screening for abdominal aortic aneurysm.

**Assessed for eligibility:**
Males 64-73 years old, living in Viborg County
(N=12,639)

**Randomised**
(N=12,639)

- Randomised to screening offer
  (N=6,333)
  - Attended screening
    (N=4,852)
  - Did not attend screening
    (N=1,481)
- Randomised to no screening
  (N=6,306)
  - Operations
    - Acute (N=3)
    - Elective (N=46)
  - Deaths
    - AAA (N=7)
    - Total (N=601)

**Operations**
Acute (N=5)
Elective (N=48)

**Deaths**
AAA (N=9)
Total (N=939)

**Analysed**
(on intention to treat basis)
N = 6,333

**Operations**
Acute (N=20)
Elective (N=11)

**Deaths**
AAA (N=27)
Total (N=1,019)
randomisation group and to each other’s evaluations, assessed the available hospital records and autopsy records. Both surgeons assessed each death to be certainly, possibly, or not caused by AAA. Cases where both assessors evaluated the death to be certainly or possibly caused by AAA were classified as AAA deaths. No efforts were made to obtain agreement between the ratings.13

Estimation of costs

The costs for screening and surveillance were prospectively recorded during the first year of the trial. The data obtained were salaries and travel reimbursement (for doctor and nurse), portable ultrasound scanner, stamps, envelopes, printing costs of invitations, laptop computer, and various products such as ultrasonographic gel.17 AAA-operations were prospectively registered nationwide in the Danish Register of Vascular Surgery (‘Karbasen’). To assign costs of hospitalization for surgery, the existing Diagnosis Related Group (DRG) costs in 1999 were used (www.sum.dk, August 1999). The DRG costs are the mean hospital costs for the treatment of a patient with a specific diagnosis. These are based on independent cost studies from different hospitals in Denmark. In this study, the AAA-diagnosis group was that for patients admitted for major vessel surgery outside the heart. In 1999, the costs associated with the DRG differentiated between admissions for operation with, and without, complications. Consequently, medical records were reviewed in order to identify complications and assign costs accordingly. Medical and surgical complications consisted of the following: acute myocardial infarction, cardiac failure, severe pulmonary complication demanding treatment, artificial ventilation for more than 48 h, dialysis, intensive unit stay for more than 72 h, stroke, arrhythmia, wound complications including rupture, re-operation for bleeding, ileus, re-operation for thrombosis and peripheral embolisation requiring surgery. Costs were not discounted because of the short time period analysed, and indirect costs were not included. A previous study found that the costs to the participants and the indirect costs due to production loss were minor compared to the health care costs.18 All costs were originally calculated in Danish crowns (DKr), and transformed to Euro (€) and British pounds (£) based upon the exchange rate on the 1st of January 2006.

Statistical analyses

The clinical trial estimates were conducted on an intention to treat basis from the date of randomisation. Using the life table for all Danish males in 1995–1996, the remaining life expectancy was calculated for two hypothetical cohorts: men invited to screening and controls, each containing 6333 67-year-old men. For controls, the number of remaining life-years was estimated directly from the life tables. The proportional hazards assumption for Cox regression was not confirmed, both by a graphical assessment and by test of the proportional-hazards assumption based on Schoenfeld residuals ($P = 0.03$) (STATA 8). Consequently, the follow up was split into two time periods, each with a separate analysis. During the first 18 months after randomisation the AAA mortality was quite similar between the two groups. Thereafter, however, the AAA-mortality in the intervention group was much lower than in the controls. In the cohort representing the screening group, the mortality for the period 1.5–5 years after randomisation was assumed to be reduced by the AAA-specific mortality difference found in the study (0.89 per 1000 years; 95% CI: 0.40–1.37); before and after that period mortality was assumed to be unaffected by screening. It should be noted that the observed age-specific mortality among controls was very close to that of all Danish males during 1995–1996, but because they were observed for less than 6 years their data could not be used for projections beyond that.13 In addition, Kaplan–Meier estimates of mortality from AAAs in the two groups were calculated for graphical illustration, and Chi square tests and t-tests were used to compare operative- and post-operative characteristics including complications between the two randomized groups. Two tailed p values less than 5% were considered statistically significant.

SPSS 10.0, and Stata 8.0 were used for the analyses.

Ethics

The trial was approved by the local scientific ethics committee and reported to the data protection authorities. All authors had no competing interest in the trial and were independent of the funding agency.

Results

In total, 12,639 men were included in the trial; the mean age was 67.7 years (range 64.3–73.8 years) (Fig. 1). Subjects were followed for 51.9 months on average, ranging from 0.1 to 69.0 months. No differences in length of follow-up and age at inclusion were observed between the invited group and the control group (data not shown). As previously
reported, within 5 years after randomization there were 9 AAA deaths in the invited group compared to 27 deaths in the controls.

### Resources use and unit costs

Table 1 shows pre-, per- and post-operative characteristics of operations for AAA. One AAA operation was conducted outside Viborg county. In the group invited to screening there were 53 AAA-related operations (five emergency and 48 planned) compared to 31 in controls (20 emergency and 11 planned). Thus the frequency of acute operations was reduced by 75% (95% CI: 34–91%) in the screening group compared to controls (Chi square, \( P < 0.003 \)). The planned operations in the screening group were shorter, tended to involve less blood loss and more often required an aortic–aortic tube graft. Nevertheless, the frequency of complications was similar in the two groups (25 versus 18%, Chi square, \( P = 0.931 \)).

Table 2 shows the overall number of events observed in each arm. The initial screening invitation to 6333 men generated 512 follow up scans after the initial scan. In the screening group, there were 40 uncomplicated and 13 complicated operations, while among controls, there were 17 and 14, respectively (\( P = 0.051 \)). Table 2 also summarises the unit costs estimated for these events. The excess costs in the screened group totalled €288,908, corresponding to €45.62 per invited person.

### Cost benefit and effectiveness

In the screening group nine died from AAA compared to 27 in the control group, corresponding to a 67% (95% CI: 46.0–83.5%) decrease in AAA-specific mortality (Fig. 2, \( P < 0.003 \)). Consequently, the estimated cost per prevented death of AAA was €16,050 (95% CI:}

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**Table 1. Pre-, per- and post-operative characteristics of operations for abdominal aortic aneurysms**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Planned (N of total)</th>
<th>Emergency (N of total)</th>
<th>Total (N of total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>48* (90.6)</td>
<td>5* (9.4)</td>
<td>53* (100.0)</td>
</tr>
<tr>
<td>Previous cardiovascular discharge diagnoses</td>
<td>19 (39.6)</td>
<td>2 (40.0)</td>
<td>21 (39.6)</td>
</tr>
<tr>
<td>Age (years (SD))</td>
<td>70.6 (3.0)</td>
<td>72.1 (2.4)</td>
<td>70.7 (2.9)</td>
</tr>
<tr>
<td>Pre-operative S-creatinine (µmol/l (SD))</td>
<td>99.6** (25.3)</td>
<td>–</td>
<td>121.0 (39.7)</td>
</tr>
<tr>
<td>Aortic tube graft (%)</td>
<td>35 (72.9)</td>
<td>3 (60.0)</td>
<td>38 (71.7)</td>
</tr>
<tr>
<td>Operation time (min (SD))</td>
<td>135** (46.1)</td>
<td>96.3 (62.1)</td>
<td>132** (47.9)</td>
</tr>
<tr>
<td>Wound complications (%)</td>
<td>6 (12.5)</td>
<td>1 (20.0)</td>
<td>7 (13.2)</td>
</tr>
<tr>
<td>Surgical complications (%)</td>
<td>6 (12.5)</td>
<td>1 (20.0)</td>
<td>7 (13.2)</td>
</tr>
<tr>
<td>Medical complications (%)</td>
<td>7 (14.6)</td>
<td>1 (20.0)</td>
<td>8 (15.1)</td>
</tr>
<tr>
<td>Total complications (%)</td>
<td>12 (25.0)</td>
<td>1 (20.0)</td>
<td>13 (24.5)</td>
</tr>
<tr>
<td>Admission time (days (SD))</td>
<td>10.0 (5.1)</td>
<td>12.8 (19.4)</td>
<td>10.2 (6.8)</td>
</tr>
</tbody>
</table>

\( *P < 0.05 \) (Chi square test comparing the invited group with the control group). \( **P < 0.05 \) (t-test comparing the invited group with the control group).

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**Table 2. The overall number of events and their cumulated costs in the screening and control group**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Price per unit (Dkr)</th>
<th>Screening group (N)</th>
<th>Costs (Dkr)</th>
<th>Control group (N)</th>
<th>Costs (Dkr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>83.75</td>
<td>4843</td>
<td>405,601.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surveillance</td>
<td>83.75</td>
<td>512</td>
<td>42,880.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-screening</td>
<td>83.75</td>
<td>248</td>
<td>20,770.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAA admissions with uncomplicated operations</td>
<td>79,000</td>
<td>40</td>
<td>3160,000.00</td>
<td>17</td>
<td>1343,000.00</td>
</tr>
<tr>
<td>Total</td>
<td>131,000</td>
<td>13</td>
<td>1703,000.00</td>
<td>14</td>
<td>1834,000.00</td>
</tr>
<tr>
<td>Difference Danish Crowns (Dkr)</td>
<td></td>
<td></td>
<td>3177,000.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference Euro (€)</td>
<td>€288,907.68</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference Pounds (£)</td>
<td>£198,457.76</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
This is equivalent to £10,793 (95% CI: £8672–15,641). The overall mortality hazard ratio was 0.33 (95% CI: 0.16–0.71; \( P = 0.003 \)). However, as mentioned, the proportional hazards assumption for Cox regression was not met (\( P = 0.03 \)). Consequently, the follow up was split into two time periods, each with a separate analysis. During the first 18 months after randomisation the AAA mortality seemed similar between the two groups (hazard rate ratio 0.77; 95% CI: 0.29–2.07; \( P = 0.61 \)), but thereafter the AAA-mortality in the intervention group was much lower than in the control group (hazard ratio 0.11; 95% CI: 0.03–0.48; \( P = 0.003 \)).

Table 3 shows the estimated number of life years saved after 5, 10, and 15 years, and the corresponding costs per saved life-year. We estimated that the screening invitation to the 6333 men will save 32 life-years (95% CI: 14–49) during the first 5 years. Thus, the cost per year of life saved was €9057 (€5872–20,063). This is equivalent to £6221 (€4034–13,782).

If the prediction is extended to 10 and 15 years, 107 (95% CI: 48–164) and 158 (95% CI: 71–243) life-years will be saved, respectively. The costs per saved life-year would then be €2708 (€1758–6031) after 10 years and €1825 (€1185–4063) after 15 years. This is equivalent to £1860 after 10 years and £1254 after 15 years.

### Discussion

In this cost-effectiveness analysis, screening for AAA reduced the frequency of acute operations by 75%, and AAA-specific mortality by 67%. The cost per AAA death prevented was about €16,050 (€10,793), and €9057 (€6221) per saved life-year. In our previous report from 2002, the number of participants was believed to be 12,658, but when we analysed the newest mortality data, we realised that 19 actually had died, but not yet removed from the population register before the date of randomisation.

The major costs were due to operative admissions. As mentioned, specific DRG costs for admissions to AAA-surgery were not defined in 1999; only those for uncomplicated or complicated major heart or major vascular surgery including AAA surgery. Consequently, we did an analysis on a random sample of 100 admissions for elective and emergency AAA performed in Viborg Hospital from 1996 to 1998.Overhead for administration, heating, electricity, rent, discount, and depreciation of the equipment were incorporated. Other costs, such as indirect costs, salaries for the medical staff, and costs of transportation, were not included. Clinician and staff time in addition to the surgery was estimated by consensus between two representatives from each of the involved groups of staff, while the duration of surgery was

![Fig. 2. Kaplan–Meier estimates of mortality from abdominal aortic aneurysms. Screening group and control group.](image-url)
obtained from the patients’ records. Prices were given by the hospital administrations, and mean salaries were used.

The resulting costs were €9330 for uncomplicated operations compared to a DRG tariff of €10,590, and €17,292 for complicated operations compared to a DRG tariff of €17,560. Consequently, we believe the used DRG tariffs are representative for AAA operations. However, the costs for a planned operation were €12,321, and for emergency operation were €13,997, compared to €10,345 and €16,732 for planned and emergency operations in the similar but larger British MASS trial. If the operative costs from the MASS trial are used, the costs per saved life and costs per gained life-year would be €10,808 and €6099, respectively. In all, the DRG tariffs used resulted in the least attractive cost effectiveness of screening for AAA.

The benefits

Surprisingly, no deaths due to AAA were observed after 28 months in the group randomized to screening. Among those who attended screening, elective procedures rapidly became less common after the first 2 years. Therefore, the risk of death due to elective surgery was small, although from the experience of the control group four AAA-deaths were expected among those invited to screening who did not attend. The difference, however, was not statistically significant, and could merely be the result of chance. Alternatively, selection could be an explanation. We know from our earlier studies of this population that those with AAA-associated diseases attend screening more frequently than those without. Therefore, the prevalence of AAA among non-attenders could be expected to be lower than among attenders and so there would consequently be fewer ruptures than in the total population. The main results presented are limited by the relatively short observation period. This limitation is a conservative one because benefits are expected to increase with time without additional costs. We extrapolated the results to 10 and 15 years of follow-up, and the cost-effectiveness seems to become even more attractive by a factor of at least 5 after 10 years.

Comparison to the MASS trial

The results from the similar MASS-trial in the UK provide some contrast to this study. Their cost per life-year saved was £28,400 compared to £6221 per life-year saved in our present study, so the cost-effectiveness seems more attractive in our study. There are probably several reasons for this. First, the benefit of screening concerning reduced mortality tended to be higher in our study (67 versus 42%), although it was not statistically significantly different (Chi square, \( P=0.17 \)). Second, the total costs, frequency, and mortality, of emergency AAA surgery were higher in our study. Finally, the MASS trial’s screening costs were substantially higher than ours, and their sensitivity analyses reflected these costs. Our screening costs were approximately one third of theirs. This difference may relate to the fact that hospital based screening for AAA is much easier and more economically organized than screening at multiple general practitioners. The enthusiasm of the small mobile screening team in our study also could have played a role in the cost-effectiveness we observed, and the costs might be higher in a routine programme. If our screening costs had been similar to the MASS trial, our costs per life-year saved would be £8718 (95% CI: 5652–19,311) during the first 5 years, and would be expected to decrease to £2606 (95% CI: 1693–5806) after 10 years, which is still an acceptable cost effectiveness according to British guidelines.

Conclusion

Screening for AAA reduced the frequency of emergency operations by 75% and AAA-specific mortality by 67%. However, the frequency of elective operations with complications was not reduced by screening. In all, the costs were about €16,050 per AAA death prevented, and €9057 per life-year saved. The benefits are expected to increase further with time, and the costs per life-year saved to decrease. Consequently, screening of 64–73 year old men for AAA in Denmark seems cost effective.

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