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Mass Screening on Abdominal Aortic Aneurysm in Men Aged 60 to 65 Years in The Netherlands. Impact on Life Expectancy and Cost-effectiveness Using a Markov Model

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Objectives: *to predict the costs and effects on life expectancy of an AAA screening programme.*
Methods: *a Markov model was designed to compare the effects of a single screening for a cohort of men 60–65 years with the current no screening strategy. The following health states were distinguished: no AAA, unknown small AAA, follow-up small AAA, unknown large AAA, repaired AAA, rejected large AAA and death. Transition rates between the health states were simulated using cycle times of one year. Transition probabilities were derived from literature and a previous feasibility study. Incremental costs per life year saved were calculated. Sensitivity analyses and discounting for future effects were performed.*
Results: *the expected individual AAA costs for non-screening and AAA screening were €196 and €530 respectively. A difference of 3.5 months life expectancy was found in favour of screening leading to €1176/life-year gained. Costs increased as compliance fell. With a discount rate of 4% the costs are €2021/life-year gained.*
Conclusions: *one-time ultrasonographic screening for AAA in men aged 60–65 years appears to be cost-effective.*

Key Words: *Abdominal aortic aneurysm; Cost-effectiveness; Markov model; Screening; The Netherlands.*

Introduction

The incidence of ruptured abdominal aortic aneurysm (AAA) appears to be increasing in developed countries. Ruptured AAA is believed to be responsible for 2% of all male deaths over the age of 60 years, and rupture is associated with a community mortality of 80–90%.[1–5] In screening studies the prevalence of AAA in men over 60 years is estimated to be 4.3–8.3% although the definition of what is considered to be an AAA differs considerably between screens.[6–9] Several graphs have demonstrated that community screening for AAA reduces mortality from rupture.[10–13]

In the Netherlands study where all eligible male patients between 60–80 years were selected for screening by their family doctor.[9] The attendance rate was 83%. The prevalence of an AAA (defined as an aortic diameter >30 mm) was 8.1% (95% confidence interval 7.0–9.2%). Twenty percent of these patients had an AAA >50 mm and were referred for surgical repair.

The objective of our study is to establish the impact of a mass-screening program for AAA on life expectancy and cost. To achieve this objective, one can conduct a controlled clinical trial. A prospective study could produce data about added lifetime and economic consequences, but would be extensive, time consuming and costly. Only recently controlled clinical trials were started and it will take a considerable period of time before they can answer these long term matters. Another method to calculate costs and effects of screening on AAA over a long time frame is a modeling study. The model can be based on data from previous studies. The aim of the present study was to develop a Markov model to calculate the effects of a screening strategy for men aged 60–65 years in the Netherlands.[9,14]

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Material and Methods

The Markov model

The Markov model is represented in Figure 1. Seven possible health outcomes or Markov states were defined.

Health states and transitions

The following health states were distinguished: no AAA, unknown small AAA, follow-up small AAA, unknown large AAA, repaired AAA, rejected large AAA and death (see Fig. 1). Health states are mutually exclusive and collectively exhaustive, meaning that at any given time each person in the population being modeled must be in one of the possible health states, and each person cannot be in more than one state at the same time.

Health state "no AAA" includes men with an aortic diameter <30 mm, who have a life expectancy as is registered by the Dutch Central Bureau for Statistics. Compared with the health state "unknown small AAA", diameter between 30–50 mm, the state "unknown large AAA", diameter 50 mm or above, represents a significantly higher risk of rupture. A distinction between small AAA (30–50 mm diameter) versus a large AAA (>50 mm diameter) is made because of differences in natural history and subsequently different strategy in asymptomatic AAA.

When small AAA is detected follow-up is initiated until the chance of rupture justifies repair. This health state is called "follow-up small AAA". Subjects known to have large AAA are considered candidates for preventive repair. Elective treatment will be denied when the life extension due to the intervention is judged to be insignificant compared with the life expectancy. This judgment can be made by the patient, the medical staff or both. This health state is labeled as "rejected large AAA".

Repair of AAA is undertaken to exclude the life threatening condition of a rupture. At this moment the long-term durability, mortality and costs of the open repair of AAA are well known. In this model, intervention is assumed to be open repair. The condition after this operation is defined as a separate health state "repaired AAA", because in this state one will not undergo a transition to AAA developmen again.

Paradoxical, "death" is defined as a separate health state. Death is the state wherein everybody ends after a certain time. Death is called the absorbing state.

At the start of the simulation, the subjects are divided over different health states according to

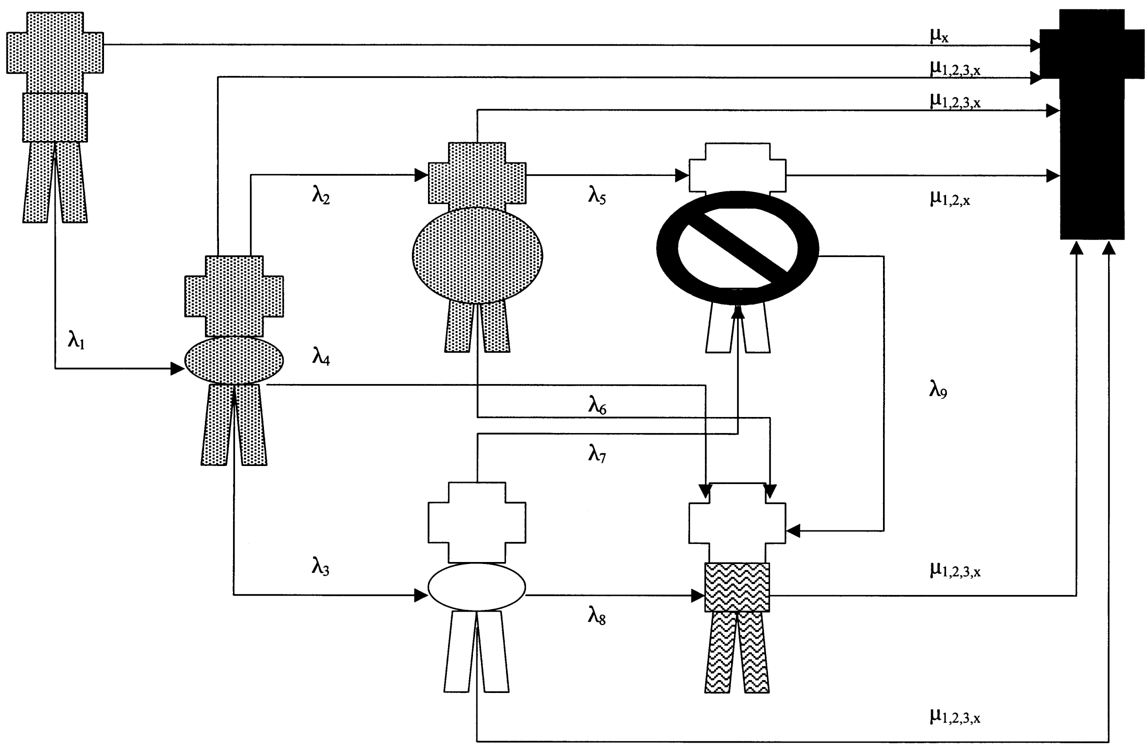

Fig. 1. Health states, definitions and transition possibilities in the Markov model.

known prevalence, except "death". The assumption is made that at the start no AAA is detected or operated on. The cycle time used in this model is a fixed interval of one year. Every year an individual can move to another health state with a certain transition probability. The so-called transitions can be caused by different events. The chance of a transition is defined by the risk of such an event to happen in this fixed time period. The members of the cohort were followed during their lifetime until 99% of simulated patients reached the death state. The difference in life expectancy and costs were calculated for both strategies.

Transition probabilities

The transition probabilities are different according to the health state of a virtual person. The chances of transition from one state to another are calculated based on demographic data from the Dutch Central Bureau for Statistics, data collected during a feasibility study in The Netherlands and published data.[9] A search of the Medline database was done for reports on Abdominal Aortic Aneurysm since 1966. The electronic database search was supplemented by manual search of bibliographic reference lists of these articles. In Table 1 the transition probabilities and the chance for each cycle time are displayed. The probabilities of some transitions are different for the two studied strategies.

Costs

Costs are displayed in Euro (€) and based on the year 1997. Cost calculations were based on the feasibility study performed. The design of that study is described elsewhere.[9] Fixed costs are incurred regardless of screening attendance as opposed to variable costs that are patient related. (Tables 2 and 3). Treatment costs are based on in hospital costs.

Sensitivity analysis

This Markov model is based on a broad set of determinants. As the figures are based on published results

Table 1. Transition probabilities of the health states in the Markov model.

Parameters	Transition probability (proportion/yr)	Health change	Source
λ_1	2×10^{-3}	Dilatation aorta over 29 mm	9,15,16
λ_2	2×10^{-1}	Small AAA growth to 50 mm or more	11,17–25
$\lambda_{3.1}$	3×10^{-4}	Small AAA detection current policy	12,26,27
$\lambda_{3.2}$	97×10^{-1}	Small AAA detection screening program	9,12,27
$\lambda_{3.3}$	12×10^{-5}	Small AAA detection after screening program	9,12,26,27
$\lambda_{4.1}$	83×10^{-2}	Small AAA surgery due to symptoms	27
$\lambda_{4.2}$	38×10^{-3}	Small AAA surgery due to rupture	1,3,28–30
$\lambda_{5.1}$	26×10^{-4}	Large AAA detected but unfit or refusing repair current policy	9,27
$\lambda_{5.2}$	62×10^{-1}	Large AAA detected but unfit or refusing repair screening program	9,27
$\lambda_{5.3}$	77×10^{-6}	Large AAA detected but unfit or refusing repair after screening program	9,27
$\lambda_{6.1}$	14×10^{-1}	Large AAA detected and surgical repair current policy	9,12,27
$\lambda_{6.2}$	35×10^{-1}	Large AAA detected and surgical repair screening program	9,12,27
$\lambda_{6.3}$	43×10^{-6}	Large AAA detected and surgical repair after screening program	9,12,27
$\lambda_{6.4}$	36×10^{-2}	Large AAA ruptured and emergency repair	1,11,29–33
λ_7	17×10^{-2}	Small AAA during follow-up growth to large AAA but unfit or refusing repair	9,11,17–25,27,34
$\lambda_{8.1}$	83×10^{-2}	Small AAA during follow-up surgical repair due to symptoms or growth > 1 cm/year	27
$\lambda_{8.2}$	38×10^{-3}	Small AAA during follow-up acute repair due to rupture	1,3,28–30
$\lambda_{8.3}$	72×10^{-2}	Small AAA during follow-up growth to large AAA and surgical repair	9,11,12,17–25,27
λ_9	36×10^{-2}	Large AAA unfit or refusing elective repair but acute repair due to rupture	1,11,29–33
μ_1	75×10^{-1}	Mortality of ruptured AAA	1,3,28–30
μ_2	50×10^{-1}	Mortality of emergency repair of ruptured AAA	1,3,28–30,35–37
μ_3	68×10^{-2}	Mortality of elective surgery for AAA	1,35
μ_x	Age specific	Registered life expectancy for Dutch inhabitants	Dutch Central Bureau for Statistics

Table 2. Fixed costs in €/year for ultrasound screening regardless attendance rate for capacity of 40 000 invitations/year (costs in 1997).

Costs	€/year
Ultrasound scanner	9100
Room rental	11 500
Administration	13 500
Manpower	29 500
Travel expenses	13 500
Telecommunication	20 000
Total expenses	97 700

Table 3. Variable costs for each patient in € (costs in 1997).

Costs	€
Administration of each examination	15
Inform patient about AAA detected	65
Follow-up program	90/year
Elective surgical repair	10 000
Acute operation ruptured AAA	14 000

from particular numbers of patients, the rates and probabilities used in the model have a certain accuracy. Some ranges of rates and probabilities are varied in a sensitivity analysis. Sensitivity analysis is a widely accepted method to explore the uncertainty of model results by varying its input parameters.[38] The sensitivity of the model is explored for different attendance rates in order to display the variation of outcomes. Both the influence on life expectancy and the extra costs are calculated for attendance rates ranging from 90% to a worst-case scenario of 10%.

There is a discrepancy between expenses for a preventive strategy towards AAA, which are merely made in advance, and effect on life expectancy, which in general is established years later.[39] In general it is accepted that we place greater value on an intervention that offers immediate rather than delayed health gains. Health economics introduced a method of discounting in order to compensate for this effect. The cost-effectiveness was calculated using discount rate of 0, 2 and 4%. The current discount rate according to Dutch guidelines is 4%.[40]

Results

Effect of screening on life expectancy

Implementation of a mass-screening program for AAA instead of the current policy of detection by chance increased the life expectancy according to the Markov model. The life expectancy for men 60–65 years without screening was estimated to be 16.99 years beyond their current age. Simulation of the same cohort in the model was based on the results with a single ultrasound screening for AAA with attendance of 83%. The model calculated an increased life expectancy of all individuals of this group of 17.27 years.[9,41] This is a prolongation of live for every man in the cohort of 0.28 year, 3.5 months or 104 days. Sensitivity analysis showed that life extensions differ depending on attendance rates, ranging from 112 days at an attendance rate of 90% to 12 days at a rate of 10% (Table 4).

Table 4. Sensitivity analysis for different attendance rates at mass screening and AAA related costs, life expectancy and costs/year saved compared with current policy of detection by chance (costs in 1997).

Attendance rate	90%	70%	50%	30%	10%	Current situation
Life-expectancy in years	17.30	17.23	17.16	17.09	17.02	16.99
Increase life-expectancy days	112	88	62	38	12	0
Costs for AAA treatment in € per individual	555	485	420	369	415	196
Extra costs for screening in € per individual	359	289	224	173	219	0
Costs per life year saved in €	1164	1204	1311	1683	6446	0

Cost of screening

When no screening for AAA is performed, the cost of detection and prevention by chance and the treatment attempts of ruptured AAA were estimated to be €196 per individual. The cost of mass screening for AAA were calculated to be €530 for each individual in the cohort. Sensitivity analysis showed that the cost per individual ranges from €415 at an attendance rate of 10% to €555 at an attendance rate of 90%.

Cost-effectiveness of screening for AAA

Results from the Markov model using data from the feasibility study indicate that a life extension of 104 days due to mass screening for AAA costs €334. This means that living one extra day costs €3.22 and one year extra costs €1176. Sensitivity analysis resulted in €6446 per year saved at a 10% attendance rate decreasing to €1164 per year extension when 90% takes their chance of AAA detection (Table 4).

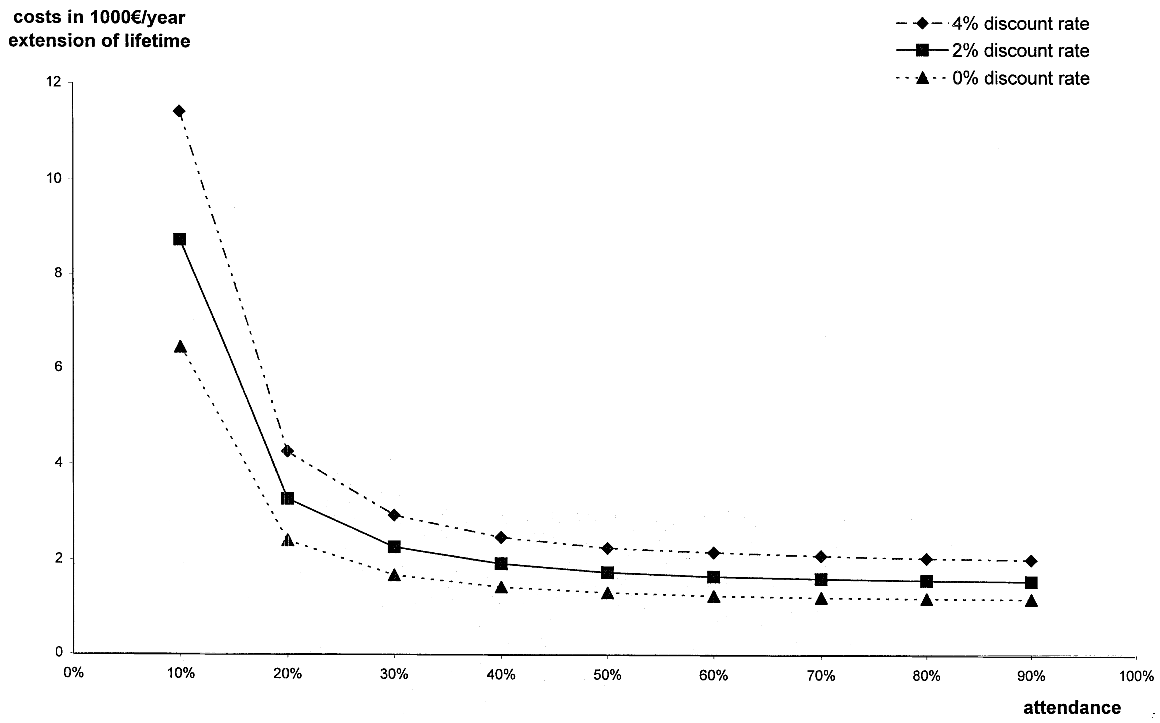

Fig. 2. Costs per life year gained for different attendance rates. Discount rate for immediate costs for later effect.

Table 5. Amount in € per year extension for different attendance rates and after correction by discounting for present-day cost and outcome in the future. (Costs in 1997)

Attendance rate	Discount rate		
%	0%	2%	4%
90	1164	1546	2005
80	1181	1569	2038
70	1204	1604	2087
60	1242	1656	2160
50	1311	1739	2255
40	1431	1919	2472
30	1683	2269	2938
20	2407	3276	4263
10	6446	8731	11 416

The cost per year of extended life can be converted to present day cost by discounting the immediate and ongoing costs for future effects. The cost per year extended life at a discount rate of 2 or 4% increase to €1559 or €2021 respectively. Reduction for present-day expenditure and outcome in the future for diverse attendance rates was calculated for discount rates of 2 and 4% (Table 5 and Fig. 2).

Discussion

As the Markov model used in this study to calculate the costs and effects of AAA screening is a simplification. Results are likely to be less precise than those from a randomised controlled trial.

Screening led to an increase in life expectancy of 3.5 months averaged across the whole cohort, which translates in to a 3.5 year survival advantage for the 8% of the patients who had an AAA.

While an increase in life expectancy of 104 days (or 3.5 months) seem as impressive, it has to be remembered. The reason is that these 3.5 months are added to the lives of all the men studied which greatly dilutes the effect of screening. In reality, however, only an 8% prevalence exists of AAA meaning that only a minor part of the cohort will benefit from a secondary prevention program. When we apply the beneficial consequences to a subpopulation including 8% of the cohort with AAA, then this fraction of the studied group with AAA will live roughly 3.5 years longer, which, indeed, is about 12 times more than when the benefit was spread over the whole group. Not only the effect of screening is concentrated on the subpopulation with AAA but also the majority of costs and efforts are intended for this group at risk.

The number of men attending for screening, too little influence on the cost per life-year saved. Even when discounting for immediate and ongoing costs for future effects at 4% the amount expended is between €2000 and €2500 per life-year gained for attendance rates of 40% or more.

In our Markov model for men 60–65 years of age the chances of transition (e.g., mortality and costs of treatment) were based on published data. These data for AAA treatment, however, concern patients who generally are older than the study group. Age is an independent risk factor for mortality.[36,42,43] Given the simulated effect of screening for AAA by our Markov model, the outcome of secondary prevention of AAA in practice can be expected to be even more favorable, both in terms of survival and cost.[44] Ironically, this argument also is supported by opponents of mass screening, who raise the issue of volunteer bias. Volunteer bias may be introduced because those who accept the invitation for screening may have a positive health attitude causing a better prognosis. While this volunteer bias highlights a potential discrepancy in prognosis between attendants and non-attendants, it will have little impact when compliance with mass screening for AAA is as good as reported in the majority of studies.[6–10] However, there is lack of data to estimate this favourable effect.

In our Markov model we assumed open repair of AAA as the accepted method of intervention to prevent rupture. The durability of the open surgical procedure has been established over the last 50 years. In the short term, this procedure involves a substantial mortality. Although implantation of a vascular prothesis for AAA repair can cause difficulties in the long run, complications occur infrequently. One retrospective study addressed this matter, describing 36 years of observation from a single institution with eight graft related deaths (2.6%) out of 304 repairs.[45] Therefore, the assumption was made in the design of the model that after successful elective or emergency aortic surgery, the AAA has vanished completely and the simulated patient comes in the repaired AAA state.

Although endovascular AAA management has been implemented widely all over the world during the last decade, the value of this experimental approach has yet to be assessed. The costs of AAA mass screening of about €2500 per life-year gained compares favorably with many other expenses. It is generally accepted is to spend €50 000 per year for life extension by heamodialysis. Breast cancer screening cost between €20 000 and €50 000 for each life year gained, depending on the screening method and age group. Preventive health interventions are considered cost-effective when costs per life year saved are less than €50 000.[46]

In conclusion, secondary prevention by mass screening for AAA appears worthwhile. The question shifts from "Do we need to initiate mass screening for AAA?" to "How should we introduce a mass screening program?"

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