

# How cost-effective is screening for abdominal aortic aneurysms?

L G Kim, S G Thompson, A H Briggs, M J Buxton and H E Campbell

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**Objective** To provide reliable estimates of the long-term cost-effectiveness of abdominal aortic aneurysm screening in men.

**Methods** A Markov health economic decision model for screening is described and extrapolated to 30 years. The strategy modelled involves a one-off scan at age 65 years, with annual and three-monthly follow-up scans for small and medium aneurysms, respectively. Referral for elective surgery occurs at an aortic diameter of 5.5 cm. Model parameters are estimated from patient-level data from the UK Multi-centre Aneurysm Screening Study. Model structure is validated on this trial's data, and input parameter uncertainty is addressed by probabilistic sensitivity analysis. Costs and life-years gained are obtained for both screening and no systematic screening strategies.

**Results** Cost-effectiveness improves dramatically when considered over longer timescales. Taking a 30-year perspective, screening for abdominal aortic aneurysms in men is highly cost-effective at £2320 per life-year gained (95% uncertainty interval: £1600 to £4240). Adjusting life-years for the age-specific health-related quality of life experienced in this population gave a figure of £2970 (95% uncertainty interval: £2030 to £5430) per quality-adjusted life-year gained. The additional cost of screening the UK male population is estimated to be £19 m per year.

**Conclusions** The long-term cost-effectiveness of screening for abdominal aortic aneurysms in men is highly attractive and this evidence provides further support for a national screening programme in the UK.

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## INTRODUCTION

Abdominal aortic aneurysms (AAAs) are a significant health problem for older men, accounting for 2.1% of deaths in men over 65 years.<sup>1</sup> In most cases, these aneurysms are asymptomatic and remain undetected until rupture, an event that carries a high risk of mortality; for the 40% of individuals with a ruptured AAA who survive to reach hospital,<sup>2,3</sup> there is a further 40% risk of postoperative mortality following emergency repair.<sup>3,4</sup> Ultrasound screening is a quick, inexpensive and non-invasive procedure that enables early detection of AAAs. Once detected, an AAA can be monitored for size, and surgical repair offered at a size threshold where the risk of rupture is considered high. Alternative imaging methods such as magnetic resonance imaging (MRI) and computerized tomography (CT) provide more accurate measurements of the aorta and are useful in preoperative evaluation, but due to increased costs compared with ultrasonography are not suitable for population screening.<sup>5</sup> Physical examination has limited sensitivity for identifying AAAs, particularly for smaller aneurysms.<sup>6</sup>

Ultrasound screening for abdominal aortic aneurysms (AAAs) has been investigated in a number of randomized trials<sup>3,7–9</sup> that have consistently reported an AAA-related mortality benefit in the group invited to screening. The largest of these trials, the Multi-centre Aneurysm Screening Study (MASS), randomized a population-based sample of 67,800 men aged 65–74 years in the UK, and after four years of follow-up reported a relative risk reduction of 42% (95% confidence interval [CI] 22–58%).<sup>3</sup> A recently published meta-analysis of all four AAA screening trials confirmed the

benefit of screening in terms of AAA-related mortality.<sup>10</sup> The case for a UK national screening programme is further supported by population-based studies of screening, which have provided evidence for the feasibility of screening in practice.<sup>11,12</sup> In the USA, it has recently been recommended that selective screening at age 65 years for male current or past smokers be undertaken.<sup>13</sup>

In addition to evidence of a mortality benefit and feasibility of implementation, a critical requirement for policy-making on screening programmes is cost-effectiveness. In MASS, cost-effectiveness at four years of follow-up was estimated to be £28,400 per life-year gained (£36,000 per quality-adjusted life-year gained),<sup>14</sup> on the borderline of acceptability in the UK for health interventions.<sup>15</sup> However, cost-effectiveness should improve considerably in the long term, as most costs occur in the early years of screening while life-years gained continue to accrue over a long period. A conservative estimate suggested that 10-year cost-effectiveness might be around £8000 per life-year gained.<sup>14</sup> Nevertheless, in order to inform a decision for a national screening programme, more reliable estimates of long-term cost-effectiveness are required.

To date, a number of health economic decision models of AAA screening have been published. Inconsistency in model inputs, structure, and results, together with inadequate handling of uncertainty, have made the relevance of these models for decision-making unclear.<sup>16</sup> We have constructed a Markov model for AAA screening, based on the screening strategy and extensive patient-level data in the MASS trial, which addresses weaknesses of previous models and includes appropriate handling of parameter uncertainty.



**Table 1** Parameter estimates and uncertainty distributions for probabilistic sensitivity analysis

Parameter	Source	Estimate	Distribution
Parameters relating to starting states			
Reinvitation	MASS	0.136	Beta (4602, 29,237)
Attendance	MASS	0.802	Beta (27, 147, 6682)
Non-visualization of aorta	MASS	0.0121	Beta (329, 26,818)
Prevalence	MASS	0.0497	Beta (1333, 25,485)
Detected AAA is small (3–4.4 cm)	MASS	0.708	Dirichlet (944, 223, 166)
Detected AAA is medium (4.5–5.4 cm)	MASS	0.167	
Detected AAA is large ( $\geq 5.5$ cm)	MASS	0.125	
Parameters relating to three-month probability of transition			
Grow from normal to small AAA	Chichester <sup>18</sup>	0.00207	Gamma (27, $7.66 \times 10^{-5}$ )
Grow from small to medium AAA	MASS	0.0242	Gamma (258, $9.55 \times 10^{-5}$ )
Grow from medium to large AAA	MASS	0.0835	Gamma (273, $32.4 \times 10^{-5}$ )
Rupture if normal aorta	MASS	$1.49 \times 10^{-5}$	Gamma (6, $24.8 \times 10^{-5}$ )
Rupture if small AAA	MASS	$9.55 \times 10^{-5}$	Gamma (1, $9.55 \times 10^{-5}$ )
Rupture if medium AAA	MASS	0.00227	Gamma (7, $32.4 \times 10^{-5}$ )
Rupture if large detected AAA	MASS	0.0157	Gamma (14, 0.00114)
Rupture if large undetected AAA	Calibration*	0.024	Beta (21.6, 878) <sup>†</sup>
Rupture if contraindicated	MASS	0.0345	Gamma (9, 0.00391)
Dropout from recall monitoring	MASS	0.0203	Gamma (296, $6.92 \times 10^{-5}$ )
Incidental detection of AAA	MASS	0.0187	Beta (13.2, 691) <sup>†</sup>
Decision at consultation is elective operation	MASS	0.684	Dirichlet (295, 90, 46)
Decision at consultation is return to monitoring	MASS	0.107	
Decision at consultation is contraindication (refusal/unfit)	MASS	0.209	
Postoperative mortality following elective operation via screen detection of AAA	MASS	0.0373	Beta (11, 284)
Postoperative mortality following elective operation via incidental detection of AAA	MASS	0.0992	Beta (13, 118)
Emergency operation if rupture	MASS	0.441	Beta (90, 114)
Postoperative mortality following emergency operation	MASS	0.356	Beta (32, 58)
All-cause mortality if contraindicated	MASS	0.0569	Beta (15, 0.00391)

\*Cannot be directly observed; chosen parameter value produced outputs most similar to outputs observed in MASS at four years

<sup>†</sup>Based on assumption that 95% CI width is 0.02 (cannot be calculated directly)

invited arm) are incorporated by permitting transitions between the detected and undetected size states. Other key events in the model are aneurysm rupture, elective and emergency operations, AAA-related mortality (which includes deaths within 30 days of an AAA operation) and non-AAA-related mortality. Consultation with a vascular surgeon following achievement of the size threshold (i.e. entry into the large, detected AAA state) is also included for costing purposes. Outcomes following this consultation can be categorized into three groups: elective surgery, return to monitoring (where measurement  $\geq 5.5$  cm is not confirmed), and contraindication/refusal for elective surgery.

### Parameter estimation

Transition parameters are estimated from the MASS patient-level data. Probabilities are calculated directly for starting state parameters and parameters relating to nodes passed through only once (e.g. postoperative mortality, decision following consultation). Rates calculated using person-years at risk of an event in MASS are converted to three-month probabilities for the model for events such as AAA growth and rupture.

There are a number of key assumptions in the structure and extrapolation of this model.<sup>17</sup> Parameters are based on men in MASS with starting ages of 65–74 years, and are applied here to a population with starting age 65 of years. While the majority of model parameters can be estimated from MASS, a small number cannot. These are estimated from systematic reviews where possible, or parameter values are chosen that best reproduce the observed MASS trial data at four years (Table 1). Although incidental detection of AAAs was not recorded in MASS, this parameter was derived from trial data relating to elective operations resulting from incidental detection and the probability of

receiving an elective operation in those with a screen-detected AAA. Non-AAA mortality is modelled using UK national mortality statistics,<sup>1</sup> and increases as the men age within the model. All other transition probabilities are assumed constant throughout the model, and so do not vary by age. A one-cycle (three month) delay is assumed before patients in the large detected AAA state can progress and receive an elective operation, broadly reflecting the median observed delay in MASS (130 days). Those contraindicated for elective surgery cannot later be declared fit for elective surgery in the model, as few such events occurred in the trial. All parameters relating to operations (both elective and emergency) refer to open surgical repair for AAA, and are assumed not to vary according to aneurysm size.

Costs in the model are taken from the costing exercise conducted alongside the MASS trial<sup>14</sup> and are expressed in UK £2000–2001 prices. Costed events in the model comprise invitation (£1.31) and a single re-invitation (£1.28) where necessary, ultrasound scans (both initial [£19.08] and recall [£46.04] monitoring scans), consultations for elective surgery (£309.88), and elective (£6908.75) and emergency (£11175.63) operations. The screening costs applied here represent scans taking place at a primary care location. The extrapolation of costs in the model proceeds by applying the costs estimated for events within the trial to those same events predicted as part of the extrapolation.

### Implementation

The decision model is implemented as a Markov model in MS Excel. The time horizon is 30 years, essentially a lifetime horizon for the 65 years olds at the start of the model. Principal outcomes from the model are costs and life-years accrued with and without invitation to screening. Both costs and life-years are discounted at the recommended rate of

3.5% per annum.<sup>19</sup> Life-years are adjusted for health-related quality of life using published population norms for the Euro Qol Instrument (EQ-5D<sup>20</sup>) to calculate quality-adjusted life-years (QALYs). No further adjustment is made to quality of life for those receiving positive screening results or undergoing AAA repair, as published evidence does not support long-term differences in quality-of-life outcomes in these groups.<sup>21,22</sup> Incremental life-years are estimated as life-years gained from a reduction in all-cause mortality.

The final results are summarized as an incremental cost-effectiveness ratio (ICER). The combined influence of input uncertainties on this result is investigated through probabilistic sensitivity analysis,<sup>23</sup> based on the statistical uncertainty of all the input parameters derived from the informing data. Table 1 summarizes the parameter values used together with their uncertainty distributions. Monte-Carlo simulation is used to make 1000 independent draws from each of the distributions, each simulation producing a set of parameter values and resulting costs and effects for each strategy. The quoted ICER is derived from the point estimates of the parameter values, with corresponding 95% uncertainty intervals calculated from the probabilistic sensitivity analysis simulations.

## Validation

An internal validation exercise utilizing the MASS data has confirmed that the proposed structure adequately matches results from the trial at four years of follow-up in terms of overall numbers and timing of key events (ruptures, operations and deaths), and in terms of costs and benefits in total and over time. Further details of this validation exercise are provided in the Appendix, but the main results are summarized in Table 2. This evidence for internal validity of the model gives some confidence when extrapolating beyond the follow-up period of the trial. Consideration of alternative, simplified structures indicated that exclusion of events omitted from other published models, such as incidental detection, non-attendance and delays to surgery, resulted in an inaccurate representation of the MASS trial data.

## Role of the funding source

The providers of funding for this work had no involvement in study design; in the collection, analysis and interpretation of data; in the writing of the report or in the decision to submit the paper for publication.

## RESULTS

The absolute and incremental costs and effects for the two strategies are presented in Table 3. Figure 2 indicates that the ICER falls considerably in the long term, with an estimate of £2320 per life-year gained (95% uncertainty interval: £1600–£4240) over a 30-year period. This differs considerably from the model estimate at four years of £72,680 per life-year gained based on all-cause mortality. The estimated ICER with adjustment of life-years for the reduced health-related quality of life due to the age of this population is £2970 (£2050–£5430) per quality-adjusted life-year gained.

In addition to cost-effectiveness projections, this model also provides estimates of the long-term investment costs of a screening programme. The additional cost of screening the UK male population over a 30-year period (using population

**Table 2** Numbers of key events, as observed in MASS and as predicted by the model

	Observed in MASS	Predicted from model
No screening invitation		
Elective operation	100	83
Emergency operation	62	62
Rupture	138	141
Contraindicated for elective surgery	nk	14
AAA death	113	109
Non-AAA death	3750	3724
Invited to screening		
Elective operation		
Resulting from screen detection	295	282
Resulting from incidental detection	31	25
Emergency operation	28	34
Rupture	66	78
Contraindicated for elective surgery		
Resulting from screen detection	41	46
Resulting from incidental detection	nk	5
AAA death	65	69
Non-AAA death	3694	3724
Loss to recall follow-up	304	289

nk = not known (relevant data not recorded in MASS)

**Table 3** Incremental costs, effects and ICERs (95% uncertainty interval) resulting from model at 30 years

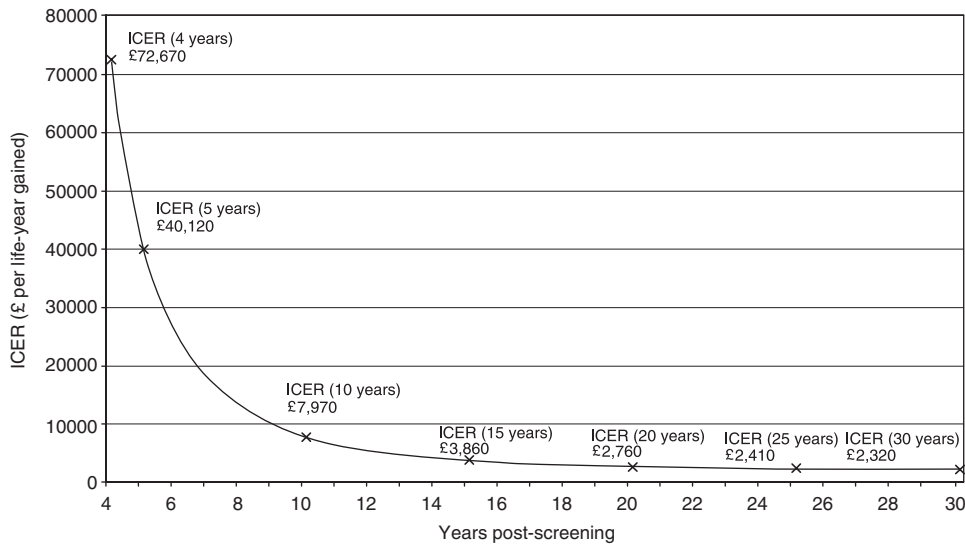
	Control arm	Invited arm
Life-years		
Undiscounted	16.157	16.148
Discounted	11.712	11.737
Discounted, quality adjusted	9.135	9.155
Costs		
Undiscounted	£419.11	£476.02
Discounted	£274.33	£333.20
ICER		
Discounted	£2320 (£1600, £4240)	
Discounted, quality adjusted	£2970 (£2050, £5430)	

projections from 2006 onwards,<sup>24</sup> costs discounted at 3.5% per annum) compared with no systematic screening is estimated at £571 m. Steady-state additional costs (truncating costs and effects at age 95 years) are estimated at £18.6 m per year after discounting.

## DISCUSSION

Our model, based on extensive patient-level data from a well-conducted population-based randomized trial, indicates that screening for abdominal aortic aneurysms in men is highly cost-effective at £2320 per life-year gained over a 30-year perspective. This is substantially lower than the within-trial cost-effectiveness reported in MASS at four years (£28,400 per life-year gained<sup>14</sup>), since life-years gained continue to accrue over time at little additional cost. Even when adjusting for the lower health-related quality of life of this more elderly population, this intervention remains highly cost-effective at £2970 per quality-adjusted life-year gained over a 30-year perspective.

Early modelling studies produced a wide variety of long-term cost-effectiveness estimates, ranging from –£101,443 to £35,187 per life-year gained, but these have not adequately modelled the screening process or aneurysm development, or have not used reliable sources to obtain model parameter estimates.<sup>16</sup> Recently, more sophisticated



**Figure 2** Estimates of incremental cost-effectiveness ratio (ICER) over time, up to 30 years after invitation to screening

models of AAA screening have been proposed, providing estimates of €9700<sup>25</sup> (£6887; €1 = £0.71<sup>26</sup>), \$13,900<sup>27</sup> (£8757; \$1 = £0.63<sup>26</sup>) and \$15,723<sup>28</sup> (£9905; \$1 = £0.63<sup>26</sup>) per quality-adjusted life-year gained. Their use of published data from the randomized trials explains why their cost-effectiveness results are somewhat more similar to those presented in our model than the early modelling studies. However, the use of individual patient trial data to inform our model enables consistent estimation of parameters, including many of those for which there are little or no available published data. Furthermore, the other recent models still fail to account for a number of important factors, including the development of AAAs in those without an AAA at the initial scan, non-attendance at recall scans in those with a detected AAA, differential postoperative mortality rates in those undergoing elective surgery following incidental detection or screen detection,<sup>3</sup> and contraindication for elective surgery. Some key parameters also varied considerably between the models including, in the large AAA group, growth and rupture rates, and the probability of receiving elective surgery. Furthermore, although one of these models<sup>25</sup> was said to be validated at four years on published MASS data, outcomes at this time point did not reflect those observed in the trial; 149 and 105 AAA deaths were predicted from the model for the control and invited groups, respectively,<sup>29</sup> compared with 113 (32% fewer) and 65 (62% fewer) observed events in MASS.

Budget impact over time was also estimated from our model, with additional costs over a 30-year period for systematic screening of the UK male population at age 65 years estimated as £571 m. This reflects costs of £2.2b, compared with costs of £1.6b for no systematic screening, taking into account incidental detection and AAA surgery in the absence of a screening programme. The anticipated benefit for this outlay is 36,000 AAA-related deaths avoided over this 30-year period.

Although the strategy modelled demonstrates considerable cost-effectiveness in the long term, it may not be optimal. Our model provides the opportunity to investigate the cost-effectiveness of different screening strategies, such as the potential impact of new endovascular techniques for AAA repair.<sup>30</sup> Furthermore, although screening for AAA in women has previously been ruled out,<sup>31</sup> the very favourable cost-effectiveness reported here over a life-time horizon for

men supports suggestions that screening in women should be reconsidered over a longer perspective.<sup>32</sup>

Many previously published models of AAA screening have not addressed the issue of model and parameter uncertainty. The propriety of our model structure has been investigated by internal validation on the MASS trial data, but uncertainty in input parameters must also be considered. The results of the probabilistic sensitivity analysis indicate that the long-term conclusions from this model are robust to the uncertainty in the parameter input values. The use of constant parameters over the 30-year time period covered by the model, however, remains an area that requires further investigation.

In summary, this model provides strong evidence for the long-term cost-effectiveness of AAA screening in men at age 65 years, with an estimate of £2320 per life-year gained. This compares favourably with other screening programmes already in place.<sup>33–35</sup> The mortality benefit of AAA screening in men has been demonstrated,<sup>3,7–9</sup> the feasibility of population screening has been shown,<sup>11,12</sup> and we have provided evidence here of its attractive long-term cost-effectiveness. The body of evidence in favour of AAA screening in men is now substantial, and introducing a national screening programme in the UK is a health service priority.

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## APPENDIX

Further details regarding the internal validation of the Markov model are presented in this appendix. The validation compared key outputs from the model at four years with the MASS trial after four years of follow-up. In order to make this comparison, a small number of changes from the model intended for long-term extrapolation were necessary. Firstly, since the men randomized into MASS are known to be less deprived than the median for England and Wales,<sup>3</sup> it was not appropriate to use national mortality statistics in the comparison with the trial. Instead, the probability of non-AAA death in each three-month period was modelled directly from non-AAA mortality observed in the trial. Secondly, data on scans following incidental detection of an AAA were not collected in the trial (only data regarding operations resulting from incidental detection), hence the costs relating to these events are excluded from the model used for validation. Finally, in order to compare key events, it is necessary to mimic the censoring pattern observed in the trial (arising from staggered randomization) in the model. This ensures the numbers at risk at each time point, and hence numbers of key events are comparable.

Three key areas for validation were identified: total numbers of key events over four years, the timing of these events within the four-year period, and total costs and effects in each arm. Key events considered are loss to recall follow-up, reaching large AAA size (eligibility for consultation), contraindication for elective intervention, elective operation, rupture, emergency operation, AAA death and non-AAA death. Overall numbers of the key events in each arm are presented in Table 2. Although the results from the model and the trial are broadly similar, in the model ruptures in the invited arm are overestimated and elective operations are underestimated in both arms. The difference in ruptures arises from an overestimation primarily in those with a large undetected AAA. The parameter for ruptures in large undetected AAAs cannot be observed, and was calibrated based on events in the control arm as well as events in the invited arm (a 3-month probability of rupture of 0.024). Reducing this value further also further reduces AAA deaths in the control arm in the model, which are already slightly underestimated. These differences suggest that the probability of

**Table A1**

	MASS	Model
Costs*		
Controls	£38.22	£36.05
Invited	£103.67	£104.06
Difference	£65.45	£68.01
Life-years*		
Controls	3.9933	3.9944
Invited	3.9956	3.9961
Difference	0.0023	0.0017
ICER†	£28,400	£37,700

\*No discounting Based on AAA mortality alone, censored for other causes of death

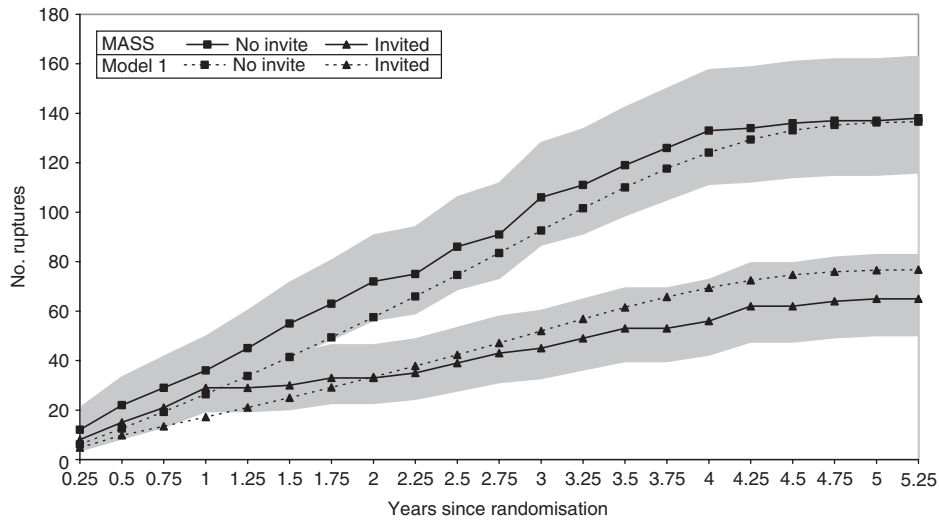
†Costs discounted at 6%, effects at 1.5%

rupture among large undetected AAAs was higher in the control arm than the invited arm of the trial, although the reasons for this are unclear. This can be further investigated in terms of the timing of ruptures.

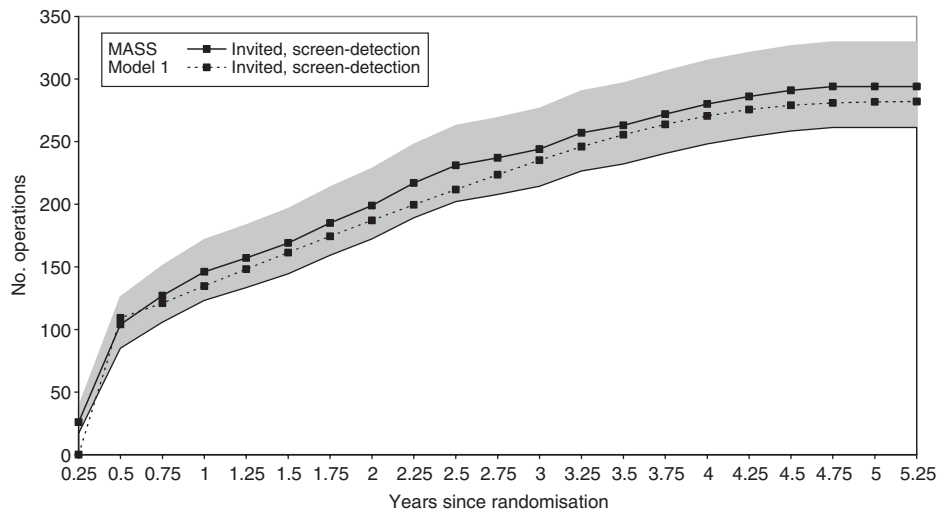
The majority of events are well matched in terms of overall numbers in the trial and the model. However, it is also of interest whether these events are accrued at similar time points. In the case of ruptures, a consistent underestimation is observed in the control arm of the model, while ruptures are initially underestimated in the invited group, but are overestimated after two years (Figure A1). Although the parameter for rupture in the model is constant over time, the occurrence of ruptures

may not be uniform over time. For example, it may be expected that in the invited arm at the start of the model, more very large aneurysms would be present, thus increasing the number of ruptures early on. The timing of other key events are similar in the trial and the model (for example, elective operations via the screening programme in the invited arm, Figure A2).

Finally, overall costs and effects in each arm are compared (Table A1). As the published four-year MASS results were adjusted for censoring, the comparable model results are taken from a model without censoring. Life-years are slightly overestimated in both arms, although the difference is similar to that observed in the trial.



**Figure A1** Cumulative ruptures over time for MASS and the model, showing 95% CIs for observed data



**Figure A2** Cumulative elective operations via the screening programme in the invited arm over time for MASS and the model, showing 95% CIs for observed data