Cost-effectiveness of screening women for abdominal aortic aneurysm

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Background: **Women are usually not considered for abdominal aortic aneurysm (AAA) screening because of their lower prevalence of disease. This position may, however, be questioned given the higher risk of rupture and the longer life expectancy among women. The purpose of this study was to assess the cost-effectiveness of screening 65-year-old women for AAA.**

Methods: **A systematic review of the literature was conducted to obtain data of importance to evaluate the effectiveness of screening women for AAA. Data were entered into a Markov simulation cohort model.**

Results: **The review suggested some main assumptions for women with AAA. Prevalence is 1.1%. In 6.8%, the AAA is of a size that merits surgery, and the patients are fit for a procedure. For patients with an AAA, the yearly risk for elective surgery and the rupture incidence was 3.1% and 2.4%, respectively, in the invited group and 1.1% and 5.7% in the noninvited group. The operative mortality for elective surgery was 3.5%, and the total mortality for ruptured AAA was 86.3%. The long-term mortality for AAA patients was 3.6 times higher than for an age-matched healthy population. Screening reduced the AAA rupture incidence by 33% and the AAA-related death rate by 35%. The cost per life year gained was estimated at $5911.**

Conclusion: **The incremental cost-effectiveness ratio was similar to that found for screening men, which reflects the fact that the lower AAA prevalence in women is balanced by a higher rupture rate. Screening women for AAA may be cost-effective, and future evaluations on screening for AAA should include women. (J Vasc Surg 2006;43:908-14.)**

Women are generally not considered a suitable target population for abdominal aortic aneurysm (AAA) screening. The main reason is not only the low prevalence of AAA[1-3] but also a development of the disease later in life[4] and an inferior relative long-term survival in women with AAA.[5,6] However, other aspects of the disease, such as the higher rupture rate, indicate that AAA in women may be more severe than in men.[7,8] Even though women with AAA have a higher mortality than disease-free women, the overall life-expectancy for women exceeds that of men.[9] The objective of this study was to assess the cost-effectiveness of screening women for AAA. A previously developed Markov simulation model was used, and data for the study were obtained by a systematic review of the literature.

METHODS

The Markov cohort simulation model was originally developed to evaluate the cost-effectiveness of different screening strategies for AAA in men. The model was described in detail previously[10] and is reviewed briefly. Two hypothetical groups of 65-year-old women were compared. One group was invited to ultrasound screening, but the other was not invited. The model follows a cohort of patients from the time of screening until death or 100 years of age. The lifetime is divided into 1-year cycles. Those not attending are assumed to be similar to the noninvited group regarding risk of the different events.

Patients with a detected AAA have yearly revisits to follow the expansion of the aneurysm. They are offered elective open surgery, if they are healthy enough, when the AAA has grown to >55 mm, has expanded rapidly, or has caused symptoms. Some patients with detected AAA fulfill the criteria for elective surgery at the time of screening and will be offered surgery as soon as possible. A proportion of the AAA in the nonscreened group will be detected opportunistically.

Each year, patients with AAA are at risk of rupture or death, either related to the AAA or due to other causes. False-negative AAAs or false-positive ultrasound measurements at screening were not explicitly included in the model. The model is graphically depicted in Fig 1.

In the previous publication, male-specific data were obtained by a systematic review of the literature.[10] These probabilities were adjusted when important differences between men and women were found in the literature review. In a Medline search through January 2005, the keyword *abdominal aortic aneurysm* was combined with *gender, sex, women,* and *female*. The following selection criteria were used:

1. Only population-based or multicenter studies were accepted.
2. The paper should be an original clinical research report published after 1990 and written in English or Scandinavian languages.
3. The definition of an AAA should be given, ≥30 mm being used in the present study.

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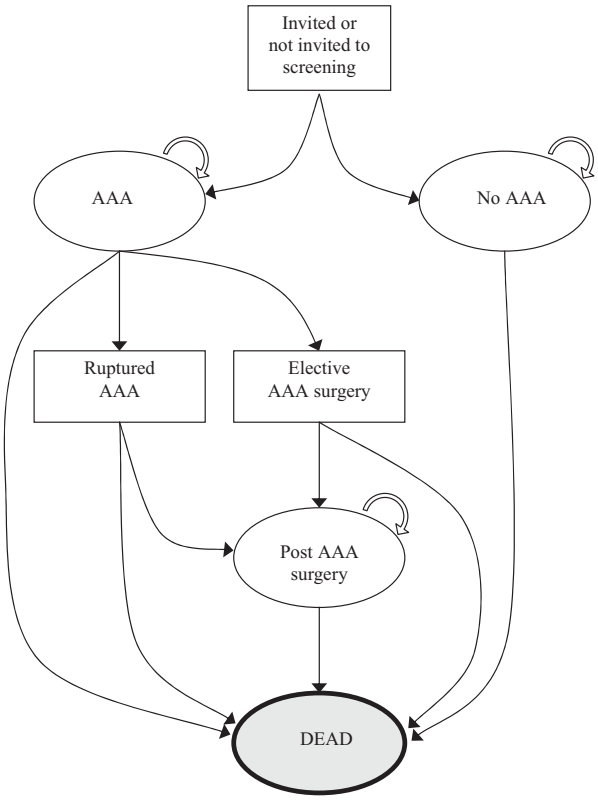

Fig 1. Model structure. Each circle represents a Markov state. The *shaded circle* labeled *DEAD* represents an absorbing state, from where a person cannot leave. *Arrows* indicate allowed transitions. The transition probabilities differ between the two groups; invited to ultrasound screening or not invited. Those not attending are assumed to be similar to the noninvited group regarding transition probabilities.

4. Female-specific data should be available.
5. Only open repair was assessed in the model, and a distinction between surgery for ruptured and nonruptured AAA should be possible.

Thirty-two studies with female-specific data were identified and read in full by the main investigator (A.W.). Of these reports, 18 contained suitable data to be extracted and used as basis for the parameter estimates in the model.

The cost per life year gained was the outcome measure. Costs and effects were discounted at 3% annually. All costs are presented in USD 2004 values, updated using the Swedish consumer price index.[9] One- and two-way sensitivity analyses were performed to assess how selected parameters affected the results.

RESULTS

Model probabilities. Table I presents the probabilities in the model and the related data for men. The age-adjusted male/female prevalence ratio was 5:1, based on four screening studies on both sexes.[2,3,11,12] With an assumed prevalence of 5.5% among 65-year-old men,[10] the probability of a positive screening result for women was estimated at 1.1%. Of these, 6.8% were assumed to be qualified and fit for immediate surgery.[10]

It was assumed that 72% of those invited would attend screening[3,13] and, based on the difference in rate of elective surgery between the screened and nonscreened groups in four prospective studies,[14-17] that 13% of the AAAs in the nonscreened patients would be opportunistically detected.

The rate of elective AAA surgery was lower for women than men with AAA.[18-20] It was estimated at 3.1% per year among women with AAA attending screening and at 1.1% among women with AAA not attending screening or not invited to screening compared with 3.9% and 1.4% in men with AAA.[10] Patients undergoing surgery for nonruptured AAA were assumed to have a perioperative mortality of 3.5%, based on the mortality of the Swedvasc database (the Swedish National Vascular Registry) for women operated on during 2000 through 2004.[21] Mortality data from the Swedvasc is 100% correct, given the unique personal identity code of each Swedish citizen and that the registry is cross-matched against the population registry once a month. The operative mortality was assumed to be the same in the invited and noninvited groups.

Among men, the rupture risk of an AAA was estimated at 0.8% per year among those with an AAA attending a screening and 1.9% among those with an AAA not attending a screening or not invited to a screening.[10] Women were estimated to have a threefold higher rupture risk than men.[8] Thus, the corresponding annual rupture risks were 2.4% and 5.7%, respectively, for women with AAA.

Sixty-five percent of men with ruptured AAA die before surgery, and an additional 14% die during surgery, corresponding to an operative mortality of 40%.[10] The rate of surgery for ruptured AAA was lower for women,[19,20,22] and the operative mortality was higher.[5,18,23] Thus, the total mortality for AAA rupture was estimated at 86.3% for women compared with 79% for men. Because of comorbidity, patients with AAA were assumed to have an increased relative mortality, unrelated to the AAA, compared with the general age- and sex-matched population. The increased relative mortality was higher for women with AAA than men with AAA[5,6] and was estimated to be 3.6 times the normal mortalities both before and after surgery for AAA. The estimate corresponds to a relative age- and sex-matched survival of 82.5% after 5 years for women compared with 90% for men.[10] Normal age- and sex-specific death rates were based on population mortality statistics for Swedish women.[9]

Costs. The cost for inviting persons to the screening is incurred by all invited patients, whereas the cost of the screening procedures only is incurred by those who attend. The cost of invitation was estimated at $5.60 and the cost of screening at $54.80.[24] The estimated cost for traveling to the screening was $5.60, based on an assumed cost for traveling within a Swedish city.

Patients with a detected AAA were assumed to come for yearly revisits to control the expansion of the aneurysm with ultrasound scans. The estimated cost of these revisits was

Table I. Summary of model probabilities for women and for men as comparison

Assumption	*Probability*	
	Women	*Men*
Prevalence	1.10%	5.50%
Proportion of AAA qualified and fit for immediate surgery	6.80%	6.80%
Attendance rate	72%	80%
Proportion of opportunistically detected AAA	13%	13%
AAAs yearly risk for non-ruptured AAA surgery, screened group	3.12%	3.90%
AAAs yearly risk for non-ruptured AAA surgery, non-screened group	1.12%	1.40%
Mortality for non-rupture AAA surgery	3.50%	3.10%
Total mortality for ruptured AAA	86.30%	79%
Yearly risk of rupture among those with AAA, screened group	2.40%	0.80%
Yearly risk of rupture among those with AAA, non-screened group	5.70%	1.90%
AAA patient relative long term mortality	3.59	2.05
Cost of screening, including invitation and traveling	$66.10	$66.10
Cost of follow-up	$243.40	$243.40
Cost of elective AAA surgery	$16,898	$16,898
Cost of surgery for ruptured AAA	$32,310	$32,310
Discounting (annually)	3%	3%

AAA, Abdominal aortic aneurysm.

$243.40.[25] A cost of $188.20 for a physician visit was added at the time of detection for informing the patients about the AAA.[25] The estimated cost of elective AAA surgery was $16,898, and the estimated cost of surgery for a ruptured AAA was $32,310.[26] The consequences of including costs in added years of life were tested in sensitivity analysis.[27]

Model results. The estimated mean remaining life expectancies in the invited and noninvited groups were 19.83 and 19.81 years, respectively, and the base-case estimated cost per life year gained was $5911. The rupture incidence was 0.29% in the invited group and 0.43% in the noninvited group. The AAA-related death incidence was 0.26% for the invited group and 0.41% for the noninvited group, which corresponds to a 35% reduction. The base-case results are presented in Table II.

One-way sensitivity analyses are displayed in Figs 2, 3, and 4. A prevalence of 0.6% resulted in a cost per life year gained of $9253 (Fig 2). A relative rupture risk of 0.8% in the invited group and 1.9% in the noninvited group (same as for men)[10] resulted in a cost per life year gained of $17,099 (Fig 3). The cost per life saved year was $3422, with an assumed relative long-term mortality of 2.05 for patients with AAA (same as for men)[10] (Fig 4). Additional one- and two-way sensitivity analyses (Table III) indicate that the results were robust for variations in other model parameters.

Table II. Base case results (screening 65-year-old women once), per person

	Noninvited	*Invited for screening*	*Difference*
Cost*			
Invitation cost	0	5.60	5.60
Screening cost	0	39.50	39.50
Follow-up cost	2	13.70	11.70
Elective surgery cost	12.40	35.00	22.60
Rupture surgery cost	40.50	24.20	−16.30
Total cost	54.90	117.90	63.00
Effectiveness (life years)	14.402	14.412	0.011
Incremental cost-effectiveness ratio			5 911

*Cost in United States dollars.

DISCUSSION

The Chichester screening trial is the only published evaluation of screening for AAA in women. Some 9342 women aged 65 to 80 years (mean age, 72 years) were randomized, with no difference in rupture rate between the screened and the control groups after 10 years follow-up. The authors concluded that it was neither clinically indicated nor economically rational to screen women.[28] However, a possible limitation that is likely to counteract the possible benefits of screening women is the biased mortality data based on official statistics. With a low autopsy rate, the reliability is limited in determining mortality rate from ruptured AAA. The autopsy rate has decreased to an overall 11% in Sweden, and is almost nonexistent among women >80 years old.[29]

Our analyses showed that the cost-effectiveness was rather insensitive to variations in prevalence >1%. Below this level, however, the cost per life year gained increased rapidly (Fig 2). The prevalence of the disease is, however, highly dependent on the definition used.[12] In most population-based screening studies including women,[2,3,11,12] an AAA was defined as the maximum infrarenal aortic diameter being ≥30 mm, as proposed by McGregor.[30] Because the normal aortic diameter differs by gender,[31] a fixed diameter may not be an optimal definition of AAA and may partly explain the differences seen in prevalence between men and women.

In the Chichester trial, four of the 10 women from the screened group who had AAA rupture or emergency repair initially had a normal scan.[28] This may be the result of how an AAA was defined, where a fixed diameter may result in false-negative findings, or a consequence of the natural history of AAA development among women. Our study design did not including these possible effects. The prevalence also depends on the age of the screened population. However, the present lack of age-specific prevalence data in women makes a more precise analysis of the optimal screening age difficult.

In addition to the prevalence of the disease, the most striking epidemiologic difference between men and women is a higher rupture rate among women. Gender differences

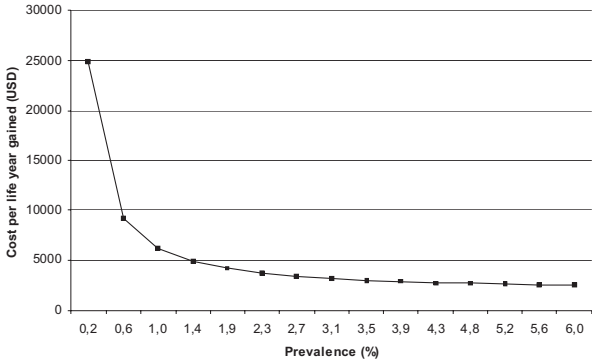

Fig 2. Cost-effectiveness at different prevalences of abdominal aortic aneurysm. *USD,* United States dollars.

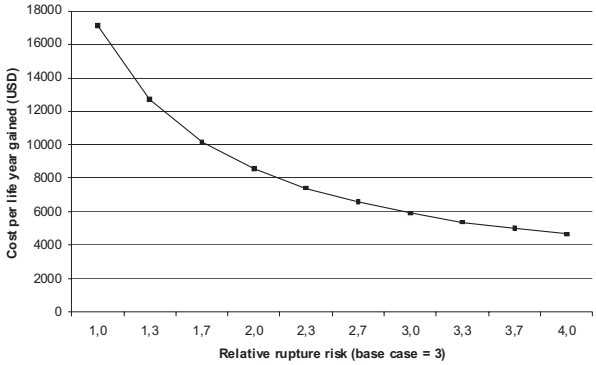

Fig 3. Cost-effectiveness at different relative rupture risk compared with those for men (relative rupture rate, 1.0). *USD,* United States dollars.

between prevalence ratio and rupture incidence ratio[32-34] and an observed increased growth rate of AAA in women[35] indicate gender differences in the natural course of the disease. In an observational study of AAA patients unfit for surgery, the annual rupture rate was 1% in men compared with 4% in women with AAA of 50 to 59 mm and 14.1% compared with 22.3% with AAA ≥60 mm.[7] Among 2257 AAA patients enrolled in the UK Small Aneurysm Trial (UKSAT) or Small Aneurysm Study, the risk of rupture was, independently of age and initial AAA diameter, associated with female sex. The rupture rate was three times higher in women compared with men.[8]

The rupture rate has a large impact on the cost-effectiveness of a screening program,[10] and the higher rupture rate among women compensates for the lower prevalence and reduces the cost per life year saved by 64% (Fig 3). Basing the assumed rupture rate among women on the results of only one study is surrounded by uncertainties. The sensitivity analysis showed, however, that the incremental cost per life year gained was lower than what is generally considered cost-effective, even if the rupture rate among women with AAA was assumed to be the same as for men (Table III, Fig 3).

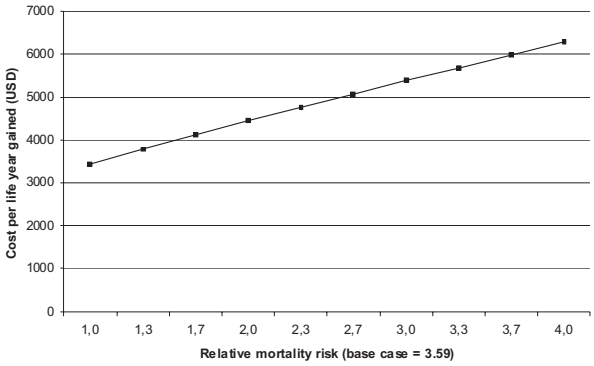

Fig 4. Cost-effectiveness at different relative mortality risk for abdominal aortic aneurysm patients compared with a general, age-matched population (relative mortality risk, 1.0). *USD,* United States dollars.

The observed differences in surgery rates between women and men[18-20,22] were not explained by differences in AAA prevalence, hospitalization rate, age, or contraindications for surgery.[20] A possible reduced awareness of AAA in women,[22] or gender bias in the decision to operate[20] or when to operate may therefore exist, although the effect on the cost-effectiveness was only marginal in the present study. In men, an AAA diameter of 55 mm generally justifies elective repair,[36,37] whereas it has been suggested that women may benefit from a lower threshold for surgery.[7,8] A lower threshold diameter for surgical repair in women (≤50 mm) may reduce the difference in surgery rate and the likelihood of an AAA to rupture. In the UKSAT, the mean AAA diameter at rupture was 50 mm for women and 60 mm for men. They concluded that different thresholds should apply to women than men when AAA repair is being considered.[8] In the Chichester trial, however, a threshold diameter of 60 mm did not result in higher rupture rate.[28]

The reports on mortality differences between men and women for nonrupture AAA surgery are inconsistent. In several large population-based studies, no gender difference in mortality was found.[6,34,38,39] Using multiple logistic regression analysis, Heller et al[39] found no gender difference in mortality after elective AAA surgery in 360,000 patients over a 19-year period in the United States, but a significant difference in postoperative mortality after ruptured AAA was found (68,000). Others have found female gender to be a risk factor for death after surgery for nonruptured AAA, with an OR of 1.3 to 1.6.[18,40-42] Among 555 women operated on with intact AAA (elective or emergent nonruptured AAA) and reported to the Swedish Vascular Registry in 2000 through 2004, the 30-day mortality was 3.9%.[21] Excluding endovascular aneurysm repair (18% of the operations), the mortality decreased to 3.5%. The corresponding mortality for men was 3.1%. Mortality after surgery for nonruptured AAA is lower in Sweden compared with some previous reports but is well validated. Furthermore, an assumed 50%

Table III. Results from sensitivity analyses

Parameter	*Assumption*	*Cost difference ($)**	*Difference in life years**	*Cost per life year gained ($)**
Base case (screening 65-year-old women once)		63.00	0.011	5911
Elective surgery mortality	5.30%	63.00	0.010	6016
Ruptured AAA total mortality	79%	60.10	0.010	6183
Attendance rate	50%	45.50	0.007	6142
Yearly risk of rupture†	1.6%/3.8%	67.40	0.008	8551
Yearly risk of rupture†	0.8%/1.9%	73.30	0.004	17,099
Elective surgery costs	50%	74.30	0.011	6972
	−50%	51.70	0.011	4850
Ruptured surgery costs	50%	54.90	0.011	5145
	−50%	71.20	0.011	6677
Cost of screening	100%	102.50	0.011	9612
	−50%	43.30	0.011	4061
Including cost in added years of life‡		347.80	0.011	32,626
Discount rate	0%	65.70	0.014	4555
	6%	61.00	0.008	7573
Cost of screening +100% and elective surgery mortality 5.3%		102.5	0.010	9783
Cost of screening +100% and yearly risk of rupture† 1.6%/3.8%		106.9	0.008	13,554
Cost of screening +100% and yearly risk of rupture† 0.8%/ 1.9%		112.80	0.004	26,302

AAA, Abdominal aortic aneurysm.
*Compared to no invitation to screening.
†Among those with AAA, screened group/nonscreened group.
‡Using costs of $24,588 (65-74 years), $28,300 (75-84 years) and $40,199 (85+ years).

increased mortality (5.3%) had little impact on the cost-effectiveness (Table III).

We previously showed that the life expectancy of the screened individuals is a key variable for the cost-effectiveness ratio.[10] Because of comorbidity, men with AAA have an increased mortality, unrelated to the AAA, compared with a general aged-matched population.[10] The relative long-term survival after surgery for AAA was found to be better in men than in women,[5] although the crude long-term survival was similar between men and women, because women in general have a longer life expectancy.[6] The assumed additional relative mortality in women with AAA compared with men increased the cost per life years saved by 30% in our model (Fig 3).

Women seem to attend screening slightly less than men.[3,13] The attendance rate, however, has very little impact on the cost-effectiveness ratio.[10] This may, however, not be the case if the nonattenders are different from those attending screening. As stated previously, the life expectancy of the screened person is a key variable for the cost-effectiveness ratio. A paradoxical effect could thus occur: if people who attend screening are healthier than those who do not attend, the cost-effectiveness could increase with a decrease of the attendance rate.

We were rather surprised by the finding that the decrease in AAA-specific mortality among women invited to screening was only 32% compared with 50% among men. The explanation lies in the complex relations between mortality, risk of rupture, and risk of elective surgery. If women had an identical compliance and rupture rate as men, the model would generate a decrease in AAA-specific mortality of 43%.

In a consensus statement by Kent et al,[43] women aged 60 to 85 years with cardiovascular risk factors and women >50 years with a family history of AAA, who appear fit for any intervention, were considered a suitable screening population.[43] A recent systematic review for the United States Preventive Service Task Force by Fleming et al[44] found no evidence in the literature of the benefit of screening women regardless of risk factors. In a previous report on men, we demonstrated a trade-off between high prevalence of AAA and lower life expectancy, eliminating the expected benefits of screening high-risk groups such as smokers or cardiovascular patients.[10] Whether this is true also for women remains to be shown.

The present study showed that the incremental cost per life year gained for screening all 65-year-old women for AAA was lower than what is generally considered cost-effective[27,45,46] and was similar to that for screening men at the same age.[10,24] This reflects the fact that in women, a low prevalence is balanced by a high rupture rate.

CONCLUSION

Although the results should be interpreted with some caution because women-specific epidemiologic data are scarce, the findings in this study do not justify the exclusion of women in future evaluations of the pros and cons of screening for AAA. Screening women for AAA may be cost-effective, and future prospective evaluations on screening for AAA should include women.

AUTHOR CONTRIBUTIONS

Conception and design: AW, JL, DB, MB
Analysis and interpretation: AW, JL, DB, MB
Data collection: AW
Writing the article: AW, JL
Critical revision of the article: JL, DB, MB
Final approval of the article: AW, JL, DB, MB
Statistical analysis: Not applicable
Obtained funding: Not applicable
Overall responsibility: AW

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INVITED COMMENTARY

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In the current issue of *Journal of Vascular Surgery*, Wanhainen et al address the controversial but timely question of whether women should be screened for abdominal aortic aneurysms (AAAs). The publication of this manuscript coincides temporally with a landmark accomplishment in the United States, as legislation mandating reimbursement for AAA screening for >65-year-old ever-smoking men has now passed the Senate and House of Representatives and, with luck, will soon be signed into law. Although, there now appears to be relatively uniform consensus that AAA screening is useful in men, for women, the controversy continues on.

It has long been understood that AAAs are less prevalent in women than in men, and there is little doubt that disease prevalence is a critical contributor to the cost-effectiveness of screening. Moreover, the Chichester Aneurysm Study, a small but randomized study, did not demonstrate an advantage of AAA screening in women. But as clearly established by the authors of this article, prevalence is not the only factor of importance when evaluating the cost-effectiveness of aneurysm screening.

When it comes to aneurysms, there is little dispute that women behave differently than men. Yes, prevalence is less in women; however, aneurysms in women rupture at an increased rate and at a smaller size. Paraphrased, fewer aneurysms are found by screening women, but the ones that are found are more dangerous. Although the ratio of prevalence is fairly well established at approximately 5:1, men vs women, the increased propensity for aneurysm rupture in women is less well documented. The authors, in their base case analysis, use a ratio of 3:1, women vs men, based upon data from the United Kingdom Small Aneurysm Study.

Wanhainen et al also point out that in addition to prevalence and rupture rate, multiple other factors are essential to this analysis, including patient longevity, which appears to be less in women with AAA than in men, and death after rupture, which is greater in women than in men. The outcome of all of these factors, when introduced into a detailed Markov model, is that screening for AAA in women is extremely cost-effective. Moreover, in sensitivity analyses, the cost-effectiveness of screening remains robust despite a number of variations in assumptions, including prevalence.

Cost-effective analyses are only as good as the data that are introduced into the model, and as Wanhainen et al clearly state, there are a paucity of data regarding the natural history of aneurysms in women. However, until more data become available, it seems prudent to be inclusive of women in screening programs. In light of this analysis, the recent opinion rendered by the United States Preventative Service Task Force, that "screening in women is harmful," seems unwarranted.

One fact that we can all agree on is that aneurysms behave differently in women than in men. The responsibility is ours to better understand these differences. Until more data becomes available it seems best to be inclusive rather than exclusive and include high risk women in our screening programs.