Screening for abdominal aortic aneurysms in men: a Canadian perspective using Monte Carlo–based estimates

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Objective: Recently generated randomized screening trial data have provided good evidence in favour of routine screening for abdominal aortic aneurysm (AAA) to reduce AAA-related deaths in men aged 65 years and older. We developed an economic model that assessed the incremental cost–utility of AAA screening to help decision makers judge the relevance of a national screening program in Canada. **Methods:** We constructed a 14 health state Markov model comparing 2 cohorts of 65-year-old men, where the first cohort was invited to attend screening for AAA using ultrasonography (US) and the second cohort followed the current practice of opportunistic detection. Lifetime outcomes included the life-years gained, AAA rupture avoided, AAA-related mortality, quality-adjusted life years (QALYs) and costs. Transition probabilities were derived from a systematic review of the literature, and a probabilistic sensitivity analysis was carried out to examine the effect of joint uncertainty in the variables of our analysis. The perspective adopted was that of the health care provider. **Results:** Invitations to attend screening produced an undiscounted gain in life expectancy of 0.049 years and a gain in discounted QALY of 0.019 for an estimated incremental lifetime cost of CAN$118. The estimated incremental cost–utility ratio was CAN$6194 per QALY gained (95% confidence interval [CI] 1892–10 837). The numbers needed to invite to attend screening, and the numbers needed to screen to prevent 1 AAA-related death were 187 (95% CI 130–292) and 137 (95% CI 85–213), respectively. The acceptability curve showed a greater than 95% probability of the program's being cost-effective, and the model was robust to changes in the values of key parameters within plausible ranges. **Conclusion:** Our results support the economic viability of a national screening program for men reaching 65 years of age in Canada. More clinical studies are needed to define the role of screening in subgroups at high risk, especially in the female population.

Objectif : Une étude de dépistage randomisée a produit de bonnes données probantes en faveur du dépistage de routine de l'anévrisme de l'aorte abdominale (AAA) afin de réduire les décès reliés à l'AAA chez les hommes de 65 ans et plus. Nous avons mis au point un modèle économique pour évaluer l'augmentation du facteur coût–utilité du dépistage de l'AAA afin d'aider les décideurs à juger de la pertinence d'un programme national de dépistage au Canada. **Méthodes :** Nous avons construit un modèle de Markov à 14 états de santé pour comparer deux cohortes d'hommes de 65 ans : le premier groupe a été invité à se soumettre à un dépistage de l'AAA par échographie (EG) et le deuxième groupe a suivi la pratique courante de détection opportuniste. Les résultats sur toute la vie ont inclus le nombre d'années de vie gagnées, la rupture évitée de l'AAA, la mortalité reliée à l'AAA, les années de vie pondérées par la qualité (QALY) et les coûts. Les probabilités de transition ont été dérivées d'une recension systématique des publications et on a effectué une analyse de sensibilité probabiliste pour déterminer l'effet de l'incertitude conjointe des variables de notre analyse. On a adopté le point de vue du fournisseur de soins de santé. **Résultats :** Les invitations au dépistage ont produit un gain non actualisé d'espérance de vie de 0,049 an et un gain de QALY actualisé de 0,019, pour une augmentation estimative du coût pour toute la vie de 118 $CAD. L'augmentation estimative du ratio coût–utilité s'est établie à 6194 $CAD par QALY gagnée (intervalle de confiance [IC] à 95 %, 1892–10 837). Le nombre de sujets qu'il a fallu inviter à se soumettre au dépistage et le nombre de sujets à soumettre à un

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dépistage pour éviter un décès relié à l'AAA se sont établis à 187 (IC à 95 %, 130–292) et 137 (IC à 95 %, 85–213), respectivement. La courbe d'acceptabilité a montré qu'il y avait plus de 95 % de chances que le programme soit rentable, et le modèle a résisté à la modification des valeurs des paramètres clés à l'intérieur des plages plausibles. **Conclusion :** Nos résultats appuient la viabilité économique d'un programme national de dépistage chez les hommes qui atteignent 65 ans au Canada. D'autres études cliniques s'imposent pour définir le rôle du dépistage dans des sous-groupes à risque élevé, en particulier dans la population féminine.

Abdominal aortic aneurysm (AAA) is the most common type of true aneurysm, affecting 4%–8% of men and 1.5% of women over age 60 years.[1] Because of its high propensity for rupture, AAA remains a serious health problem, especially in Western nations, where it accounts for about 2%–4% of all deaths in the male population.[2] Despite advances in general surgical care, the overall mortality rate from a ruptured AAA can be as high as 80%–90%.[3] Conversely, mortality rates are now less than 5% for elective surgical repair and appear to effect complete cure.[4]

Currently, only opportunistically detected cases are offered elective surgical treatment despite the availability of ultrasonography (US), a highly accurate, inexpensive and noninvasive screening tool.[5,6] Nevertheless, screening remains controversial because of the general uncertainty about the cost-effectiveness of population-based programs and the lack of agreement about which patients should be screened. In 1991, the Canadian Task Force on Periodic Health Examination reviewed available evidence and concluded:

> "there is poor evidence to support the inclusion or exclusion of screening by physical examination or US for abdominal aneurysm in the periodic health examination of asymptomatic individuals" (C recommendation based on grade II-2 and III-3 evidence).[7]

In the last decade, however, 2 prospective nonrandomized trials[8–10] and 4 randomized screening trials[11–15] have provided strong evidence in favour of routine AAA screening in men aged 65 years and older to reduce AAA rupture and AAA-related death.

Before any formal policy recommendations can be made, however, it is critical that results of international trials be interpreted in a Canadian context in terms of both cost and effectiveness. Randomized screening trials have provided an estimate of the efficacy of screening for AAAs (with efficacy meaning the performance of a program under highly controlled conditions). Whether similar results would occur in routine clinical practice depends on the context in which the program is implemented, the population involved, the level of compliance and the characteristics and performance of the health care system. In addition, published results of AAA screening trials are short-term with limited follow-up. For cost-effectiveness analysis to be valid, however, a much longer time horizon is required to include all the relevant lifetime costs and benefits resulting from the program under study.[16] Moreover, estimates of resource quantities and costs from trials conducted outside Canada are unlikely to be directly generalizable to the Canadian system because of major differences in the way health care is delivered internationally.[17]

In that perspective, mathematical models have been developed that combine the best available evidence from several sources in a model that mimics real-life situations as closely as possible.[18] Obviously, a long-term pragmatic trial would be ideal, but this is impractical because of time and fiscal constraints. Recommendations often have to be made despite this lack of perfect data. The following modelling exercise is therefore intended to aid decision makers in assessing the relevance of a screening program for AAAs in men reaching age 65 years in Canada.

Methods

Model

Decision analysis software (TreeAge Pro; TreeAge, Williamstown, Mass.) was used to construct a 14 health state Markov model comparing invitation to AAA screening with current practice for a hypothetical cohort of 65-year-old male patients. All subjects offered screening were assumed medically and anatomically suitable for AAA repair. The model portrayed screening at a point where the screening service had reached equilibrium, that is, when the annual intake of new subjects was constant after an initial build-up. Health states were mutually exclusive and collectively exhaustive; at a given time, each person in the hypothetical population was in one of the 14 possible health states but could not be in more than 1 state simultaneously. The health state of an individual could change between years according to predefined transition probabilities. The cycle length was 1 year, and each subject was followed until death. Outcome variables were the life-years gained, AAA rupture avoided, AAA-related death avoided, quality-adjusted life years (QALY) gained and costs. AAA-related death included death from rupture and death from elective or emergency surgical repair. A simplified version of the model is depicted in Figure 1.

The clinical relevance of AAAs that develop after age 65 years is known to be negligible because they are very unlikely to reach critical diameter.[19–23] We assumed that freedom from AAAs at age 65 persists lifelong, and no rescreening policy was therefore added. In the model, US was considered 100% accurate, a

simplifying assumption that parallels current data.[5,6]

The only variable assigned a distinct value for each of the 2 model cohorts was the relative proportion of diagnosed and undiagnosed AAAs. In the screening group, this proportion reflected subjects' responsiveness to a request for screening. In the screened and nonscreened cohorts, undiagnosed AAAs could be detected opportunistically in each cycle. Diagnosed and undiagnosed AAAs were classified according to their largest diameter and assigned an annual risk of rupture and transition rate from one category to a higher category.

We assumed that screen-detected and nonscreen-detected aneurysms behaved in the same manner, although the latter were diagnosed later and followed a different size distribution at the time of diagnosis.

Subjects that did not require surgical treatment (aneurysm diameter < 5.5 cm) underwent annual US surveillance (if the aneurysm diameter was 3.0–4.4 cm) or semiannual surveillance (if the aneurysm diameter was 4.5–5.4 cm) and were assumed to be compliant. Because many of our variable estimates were data derived from intention-to-treat analyses of randomized screening trials, a certain level of noncompliance was implicit in the model; however, dropouts from US surveillance were tested in the sensitivity analysis.

Subjects with an aneurysm ≥ 5.5 cm in diameter were offered surgical repair. We assumed no patient older than age 85 years would be offered surgery. The threshold diameter for surgery was selected on the basis of level I evidence.[24–28] Open surgical repair of AAAs was selected as the standard treatment for nonruptured and ruptured AAAs, despite the increased worldwide use of endovascular aneurysm repair (EVAR) in the last decade. Results of randomized clinical trials of EVAR are only just beginning to emerge and have shown promising short- and mid-term results.[29–32] However, there is as yet no evidence of the long-term effectiveness of EVAR, and considerable uncertainty remains regarding long-term costs of surveillance and secondary interventions.[33,34] Moreover, current data show a relatively conservative dissemination of EVAR in Canada, compared with other countries.[35] We therefore chose to exclude EVAR from our base case analysis but tested the impact of the estimated incremental lifetime treatment cost of EVAR[31,34,36,37] (including costs associated with follow-up and readmission for procedure-related complications) in 1-way sensitivity analysis.

Major surgical complications incorporated into the model include stroke, dialysis-dependent renal failure, myocardial infarction and death.

Transition probabilities

Transition probabilities were derived from a systematic review of the literature with a top-down approach to data identification. Whenever possible, we selected only studies of the highest quality, such as randomized screening trials in men and prospective naturalistic trials. We computed weighted average probabilities and distributions, using sample size as the weighting factor (Table 1). Except for time-dependent probabilities such as age-specific annual mortality, extrapolation of short-term study results to long-term outcomes assumed an exponential function.

A base case attendance rate of 73.3% was derived from 19 population screening studies in men.[9,11–15,38–55] The prevalence of AAAs > 3.0 cm in diameter was estimated at 4.2%, derived

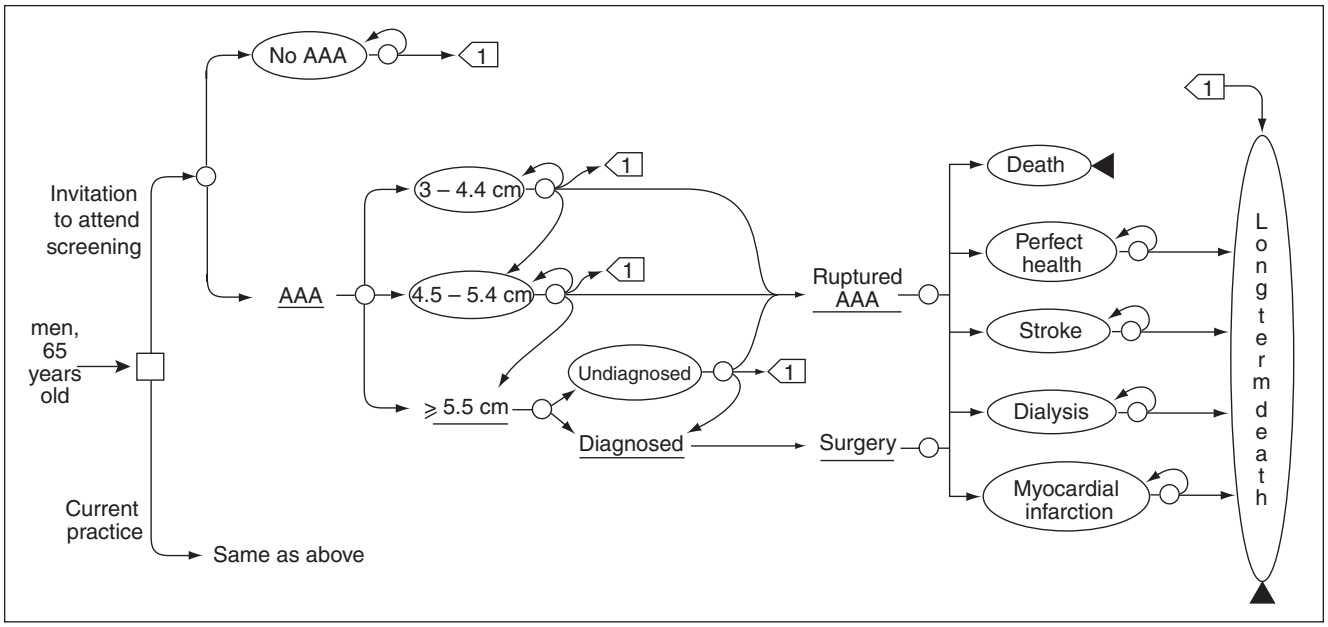

FIG. 1. Simplified Markov model. AAA = abdominal aortic aneurysm.

from age-specific combined data from the 4 randomized screening trials in men.[56]

There are no reliable data in the literature that can be used to estimate the potential for incidental detection of undiagnosed AAAs. From the ratio of elective surgeries in the nonscreened and screened cohorts in the 4 randomized screening trials, we assumed that 7% of undiagnosed AAAs would be discovered annually, regardless of their diameter.

Data related to the risk of rupture are scarce and difficult to interpret because patients with large aneurysms are usually offered surgery. Prospective follow-up data on patients with large AAAs are available only for those who either refused surgery or were considered unfit for surgery.[57–65] The risk of rupture for screen-detected AAAs ≥ 5.5 cm is therefore unknown; however, valuable information can be extracted from the 3 largest randomized screening trials[13–15] by assessing the number of AAA ruptures in the unscreened cohort relative to the assumed prevalence of undiagnosed large AAAs. This led us to assume a 16% rupture rate per year for the base case but with a wide range of plausible values.

Outcomes of elective and emergency surgical repair were derived from Canadian multicentre prospective data and are detailed in Table 1. The age-specific annual mortality is based on the 2000 Canadian life table

Table 1

Annual transition probabilities

Variable	Base case value, %	Distribution (SD)	References
Response rate, invitation to attend screening	73.3	Beta (9.42)	Heather et al,[9] Wilmink et al,[11] Vardulaki et al,[12] Ashton et al,[13] Lindholt et al,[14] Norman et al,[15] Loh et al,[38] O'Kelly and Heather,[39] Collin et al,[40] Bengtsson et al,[41] Krohn et al,[42] Grimshaw et al,[43] Smith et al,[44] Lucarotti et al,[45] Lucarotti et al,[46] Pleumeekers et al,[47] Simoni et al,[48] Scott et al,[49] Holdsworth,[50] Boll et al,[51] Vazquez et al,[52] Morris et al,[53] Wanhainen et al,[54] Jamrozik et al[55]
AAA prevalence			
Small (3–4.4 cm)	3.12	Beta (0.38)	CASS Group[56]
Medium (4.5–5.4 cm)	0.53	Beta (0.08)	CASS Group[56]
Large (> 5.5 cm)	0.44	Beta (0.13)	CASS Group[56]
Transition probabilities			
From small to medium	16.00	Beta (2.04)	Couto et al[109]
From medium to large	49.00	Beta (10.71)	Couto et al[109]
Incidental detection	7.00	Triangular (6–9)	Wilmink et al,[11] Vardulaki et al,[12] Ashton et al,[13] Lindholt et al,[14] Norman et al[15]
Rupture rate			
Small (3–4.4 cm)	0.20	Triangular (0–0.4)	Vardulaki et al[110]
Medium (4.5–5.4 cm)	2.00	Triangular (0.6–2.8)	Lederle et al,[28] Brown and Powell,[63] Vardulaki et al,[110]
Large (> 5.5 cm)	16.00	Triangular (10–22)	Wilmink et al,[11] Vardulaki et al,[12] Ashton et al,[13] Lindholt et al,[14] Norman et al,[15] Reed,[62] Brown and Powell,[63] Lederle[64]
Patient refusing surgery	5.00	Uniform (3–6)	Wilmink et al,[11] Vardulaki et al,[12] Lindholt et al[14]
Rupture in a patient scheduled for surgery	2.40	Beta (0.91)	Wilmink et al,[11] Vardulaki et al,[12] Ashton et al,[13] Lindholt et al[14]
Complications, elective AAA repair			
Death	4.50	Beta (0.18)	Dueck et al[111,112]
Stroke	0.60	Beta (0.29)	Johnston and Scobie,[113] Johnston[114]
Myocardial infarction	5.20	Beta (0.86)	Johnston and Scobie,[113] Johnston[114]
Long-term dialysis	0.60	Beta (0.29)	Johnston and Scobie,[113] Johnston[114]
Prehospital mortality of ruptured AAA	54.0	Triangular (34–68)	Wilmink et al,[11] Vardulaki et al,[12] Ashton et al,[13] Lindholt et al,[14] Norman et al[15]
Postoperative mortality of ruptured AAA	41.00	Beta (1.0)	Dueck et al[111]
Complications in patients surviving ruptured AAA			
Stroke	0.70	Beta (0.038)	Johnston[115]
Myocardial infarction	2.70	Beta (1.34)	Johnston[115]
Long-term dialysis	4.10	Beta (1.63)	Johnston[115]

SD = standard deviation; AAA = abdominal aortic aneurysm; CASS Group = Chichester Aneurysm Screening Study Group.

for males (www.bdlc.umontreal.ca). The overall survival of patients with AAAs is known to be reduced when compared with an age- and sex-matched population because of the greater associated comorbidities in patients with an aneurysm.[66] Their survival curve was therefore adjusted to account for an excess mortality of 2% yearly.[67,68] The reduction in life expectancy due to dialysis-dependant renal failure was adjusted with age- and sex-specific data from the 2004 US Renal Data System (www.usrds.org). An annual excess mortality of 2.25% was assigned for patients who survived myocardial infarction after AAA repair.[69,70] The annual mortality rate was assumed to be 2.3 times greater for patients who survived a stroke after AAA repair.[71,72]

Utilities

The quality adjustment factors of each state depicted in Figure 1 are derived from health state preference (utility) data. Current evidence suggests that screening has no significant adverse effect on quality of life.[13,73,74] Utility estimates were therefore calculated from published figures derived from the Health Utility Index values for men aged 65 and older from the 1994–1995 Canadian National Population Health Survey.[75] QALY weights are detailed in Table 2. Subjects undergoing elective or emergency surgical repair were only assigned a "disuse" because of current evidence suggesting the lack of significant long-term effect on quality of life.[78,79] Adjustments were also made for long-term complications.

Costs

Direct costs of health care resources were estimated from data on several Canadian published sources (Table 3). These included the cost of abdominal US, prehospitalization workup, inpatient care for surgical treatment of ruptured and nonruptured AAAs, professional fees and lifetime costs of complications. A cost for inviting people to screening was not included because we assumed that they would be identified during a regular health care visit. Given the age of the cohort, costs from lost productivity were not included, and a health care provider perspective was therefore adopted.

The cost of abdominal US was derived from our hospital costs accounting system and was estimated at CAN$69.75 (physician fees included). A cost for a vascular surgery consultation was added for those

Table 2

Health state preference (utility) estimates

Variable	QALY	References
Age, y		
65–69	0.82	Mittmann et al[75]
70–79	0.79	Mittmann et al[75]
> 80	0.72	Mittmann et al[75]
Adjustment factor for stroke	–0.25	Mo et al[76]
Adjustment factor for dialysis	–0.10	Kroeker et al[77]
Adjustment factor for myocardial infarction	–0.07	Mo et al[76]
Disuse of elective surgical repair	60 d	Assumption
Disuse of emergency repair	90 d	Assumption

QALY = quality-adjusted life years.

Table 3

Estimated direct costs of health care*

Category	Base case value, $	Distribution	References
Abdominal ultrasonography	70		
Abdominal CT scan	553		Forbes et al[80]
Inpatient care cost, elective AAA repair	17 991	Triangular ($16 482–$19 593)	Brox et al[107]
Ratio of inpatient care cost for ruptured v. elective AAA repair	2	Uniform (1.5–3.3)	Chew et al,[108] Katz and Cronenwett,[116] Ascher et al[117]
Cost of morbidity			
Stroke (lifetime cost)	102 119	Uniform ($57 759–$146 480)	Palmer et al[118]
Myocardial infarction			
First year	22 577		O'Brien et al[119]
Subsequent years	5734		
Dialysis (annual cost)	72 700		Kroeker et al[77]
Ratio of lifetime treatment cost of EVAR v. open repair	1.5 (discounted)		EVAR trial participants,[31] Michaels et al,[34] Birch et al,[36] Hayter et al[37]

AAA = abdominal aortic aneurysm; EVAR = endovascular aneurysm repair.
*CAN$ unless otherwise indicated.

who tested positive, and a cost was added for a physician visit after each US surveillance examination. Inpatient hospital care costs exclude overhead costs because these are unlikely to vary appreciably in response to small changes in the number of surgical procedures. The future health care costs of unrelated diseases were not included in the model.

Costs are displayed in 2005 Canadian dollars after adjustment by the health care component of the consumer price index. A discount rate of 5% per year was applied to costs and QALY in accordance with Canadian Coordinating Office for Health Technology Assessment guidelines.[81]

Sensitivity analysis

Probability distributions were used to characterize the uncertainty in the mean value of each parameter. We selected values at random from each distribution, using a second-order Monte Carlo simulation with 1000 iterations for each cohort. Probabilistic sensitivity analysis was selected as a means of examining the effect of joint uncertainty in the variables of our analysis.[82] Incremental cost-effectiveness ratios (ICERs) were calculated and the results presented as a scatter plot of ICER and the cost-effectiveness acceptability curve. Key variables and variables with the greatest level of uncertainty were also subjected to a 1-way sensitivity analysis and a threshold analysis.

Results

An invitation to attend screening produced an undiscounted gain in life expectancy of 0.0499 years (18 d). The survival advantage resulted from a reduced number of ruptured AAAs (risk ratio 0.43) and AAA-related deaths (risk ratio 0.50). The estimated risk differences were 0.83% (95% CI 0.52%–1.18%) for AAA rupture and 0.54% (95% CI 0.34%–0.77%) for AAA-related deaths. The numbers needed to invite to attend screening and the number needed to screen to prevent 1 AAA rupture were 121 (95% CI 85–193) and 89 (95% CI 63–142), respectively. Similarly, the numbers needed to invite to attend screening and the number needed to screen to prevent 1 AAA-related death were 187 (95% CI 130–292) and 137 (95% CI 85–213), respectively.

In the base case analysis, invitation to screening produced a gain in discounted QALYs of 0.019 for an estimated incremental lifetime cost of CAN$118, giving an ICER of CAN$6194 per QALY (95% CI $1892–$10 837). The result of the probabilistic sensitivity analysis is shown on the cost-effectiveness plane and acceptability curve (Fig. 2). Assuming a willingness to pay threshold of CAN$20 000 per QALY, the probability of a screening program being cost-effective is greater than 95%.

The results of 1-way sensitivity analysis are shown in Table 4. Our model is robust to variation in the value of key parameters within plausible ranges, although the prevalence of AAA, the risk of rupture for a large AAA and the age at initial screening were those that had the greatest impact on the cost–utility ratio.

Discussion

It is generally accepted that, for a disease to be considered a candidate for screening, it should pose an important health problem, the natural history should be well understood and there should be a recognizable early stage at which treatment is more beneficial than at a later time.[83] There should also be a suitable diagnostic

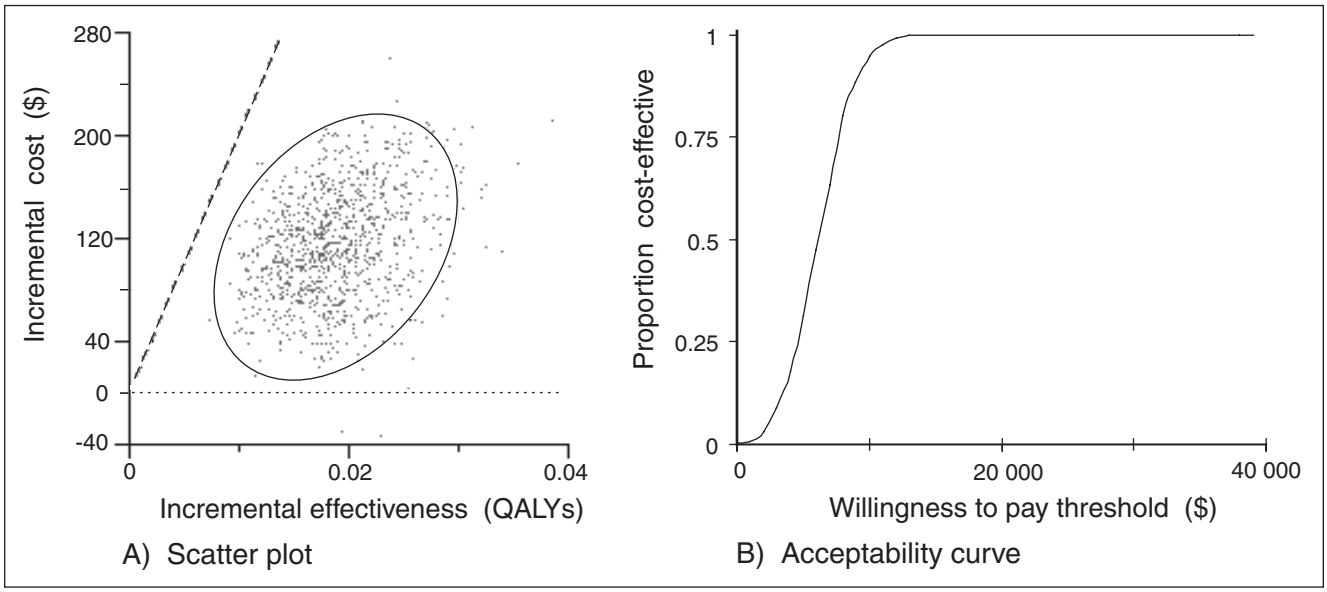

FIG. 2. (A) Scatter plot of the incremental cost-effectiveness ratio with 95% confidence interval ellipse derived from probabilistic sensitivity analysis. Dashed line represents a willingness-to-pay threshold of CAN$20 000 per QALY. (B) Cost-effectiveness acceptability curve. QALY = quality-adjusted life year.

test that is acceptable to the population and adequate existing facilities for the diagnosis and treatment of the condition. The costs of a screening program should also be balanced against potential benefits.

Table 4

Results of 1-way sensitivity analyses

Parameter	ICER per QALY gained*
Base case analysis	6194
Response rate	
30%	5679
90%	5943
AAA prevalence	
2%	9013
8%	4680
Age at initial screening	
75 y	10 912
80 y	18 649
Incidental detection (annually)	
20%	7495
40%	11 650
Risk of rupture for large aneurysms (annually)	
10%	11 001
22%	4140
Dropout from US surveillance (annually)	
10%	6462
50%	9275
Cost of US	
$50	5073
$150	9316
Cost of inpatient care	
Doubling	4611
Cost of morbidity	
Doubling	6607
Follow-up by serial CT scan	8777
Elective AAA repair by EVAR	
10%	6740
50%	8471
Discount rate (cost and QALY)	
0%	2445
3%	4493

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life years; AAA = abdominal aortic aneurysm; US = ultrasonography; EVAR = endovascular aneurysm repair.
*CAN$.

There is now good evidence that screening reduces the incidence of ruptured AAAs and AAA-related mortality. Studies that provided level I evidence were the Chichester trial[11,12] and the Multicentre Aneurysm Screening Study (MASS)[13] trial in the United Kingdom, the Viborg County study in Denmark[14] and the Western Australia study.[15] All trials identified potential participants who were 65 years old or older via population registries or regional health directories; collectively, the studies included more than 125 000 participants. Pooled results show an odds ratio of 0.56 (95%CI 0.44–0.72) for AAA-related deaths (Fig. 3). All-cause mortality was not significantly reduced, however, because AAA-related mortality accounted for only about 3% of all deaths in the control cohorts.

Concerns about the economic viability of a screening program promoted construction of several economic models.[84–94] Although these studies differed considerably in design and evaluated parameters, all but 1 study[86] concluded that screening of specific cohorts was economically appealing. Only 2 models, however, were developed from recently generated randomized screening trial data.[92,94]

Three economic analyses alongside clinical trials have also been conducted.[10,95,96] The largest of these, the MASS trial,[96] found screening to be only marginally cost-effective after 4 years of follow-up. On the basis of conservative assumptions, however, the authors projected a 10-year incremental cost-effectiveness ratio of about £8000 per life-year gained. This improvement was due largely to the accumulation of life-years gained by preventing the death of individuals during the first 4 years of the trial. In a recent systematic review of published cost-effectiveness analyses,[97] the authors concluded that existing evidence pointed to a cost-effectiveness ratio between US$14 000 and US$20 000 per QALY for population-based AAA screening in men, compared with non-screening.

Our own results also suggest that screening for AAA in 65-year-old men would be efficacious and cost-effective. The gain in undiscounted life expectancy appears modest (18 d), but in practice, this survival advantage would apply to only 4.2% of the cohort. The expected gain in patients with AAA is therefore 24 times 18 days, that is, 432 days. In the first 2 cycles (2 y), the reduction in AAA-related deaths is offset by increased deaths from elective surgical repair in the screened cohort, a finding consistent with the observations from the early years of randomized screening trials. Thereafter, mortality in the screened cohort separates from that of the control and reaches a plateau after about 15 years of follow-up. Although no clear consensus exists about our threshold value of willingness to pay for an additional QALY,[98] our estimated ICER (CAN$6194 per QALY) is below the value that is generally considered to be cost-effective. Model results are robust to changes in the value of key variables within the range of plausible values and the acceptability curve is steep, indicating a low level of uncertainty (variance) regarding our main estimate.

Key variables

The prevalence of screen-detected AAAs among Canadian men is unknown, and reported prevalence worldwide is highly variable owing to differences between studies in terms of how AAA is defined, the age and sex distribution of study populations and the prevalence of risk factors and preexisting morbidities. To avoid biasing our results in favour of screening, we used a very conservative estimate for the prevalence of screen-detected AAAs (4.2%),[56] the lowest in all models published to date. The extent to which this applies to the Canadian male population is unknown, but 1-way sensitivity analysis yielded a threshold prevalence of 0.67%, which is very unlikely.

The use of existing epidemiologic data to determine the risk of rupture for large aneurysms is highly problematic. For models that involve screening of the general population, published data are often unusable because of ill-defined or otherwise inappropriate denominator populations. The high level of uncertainty regarding the base case value is reflected in our choice of a wide triangular distribution. Not surprisingly, this variable accounts for 30% of the variance of the estimated ICER. In 1-way sensitivity analysis, the threshold value was about 6.7%, which is, again, very unlikely.

Age at initial screening has a significant impact on the cost–utility ratio, and its relevance is a result of the inverse relation between life expectancy after elective surgery and the cost per QALY gained. For example, studies including a high proportion of men older than 75 years at the time of randomization failed to show statistically significant reduction in AAA-related deaths.[15] These results are corroborated by our own findings, which show that screening after the age of 80 is not cost-effective and that the upper boundary of the 95% CI of the cost–utility ratio is above threshold after the age of 76. There is now a growing consensus that screening at age 65 years is probably the most appropriate strategy[99–101] because a single ultrasound at that age can rule out significant disease for life in 95% of men.[19–23] Reducing the screening age would pick up the few cases that would have ruptured before age 65 years; however, the need to repeat scanning at a later time would double the cost of screening overall.

Our model was robust in the face of changes to the cost of US; however, because that cost item applies to 100% of individuals attending screening, it accounted for 51.4% of the estimated incremental lifetime cost. Any strategy aimed at reducing the cost of US examination would therefore have a significant effect on the projected budgetary impact of a screening program. Options such as the use of portable US machines should be examined because the cost of a portable unit is 75%–80% less than that of a conventional duplex unit.[102] Moreover, portable units were used in several screening studies, including the MASS trial, which validates their use. A quick screen (single organ) examination can be performed in less than 5 minutes[89] and avoids unexpected findings in other intra-abdominal organs for which the value of screening is unknown.

Endovascular aneurysm repair (EVAR) is now considered a valid alternative to open repair. This new technology provides a clear reduction in 30-day mortality but no survival advantage over 1 year of follow-up.[31,32] More important, this short-term benefit comes at considerable additional cost, especially if follow-up costs are considered. The current status of use of EVAR in Canada (about 10% for nonruptured AAA)[35] is unlikely to affect the cost-effectiveness of a screening program. A trend toward increased use is to be expected and was tested in 1-way sensitivity analysis (Table 4). Those results should be interpreted cautiously, however, especially because of the lack of long-term cost data and the unproven long-term longevity of EVAR.

The costs of long-term complications accounted for only 4.5% of the incremental lifetime cost, demonstrating very little impact on the cost–utility ratio. Conversely, inpatient care cost (for elective and emergency surgical repair) accounted for

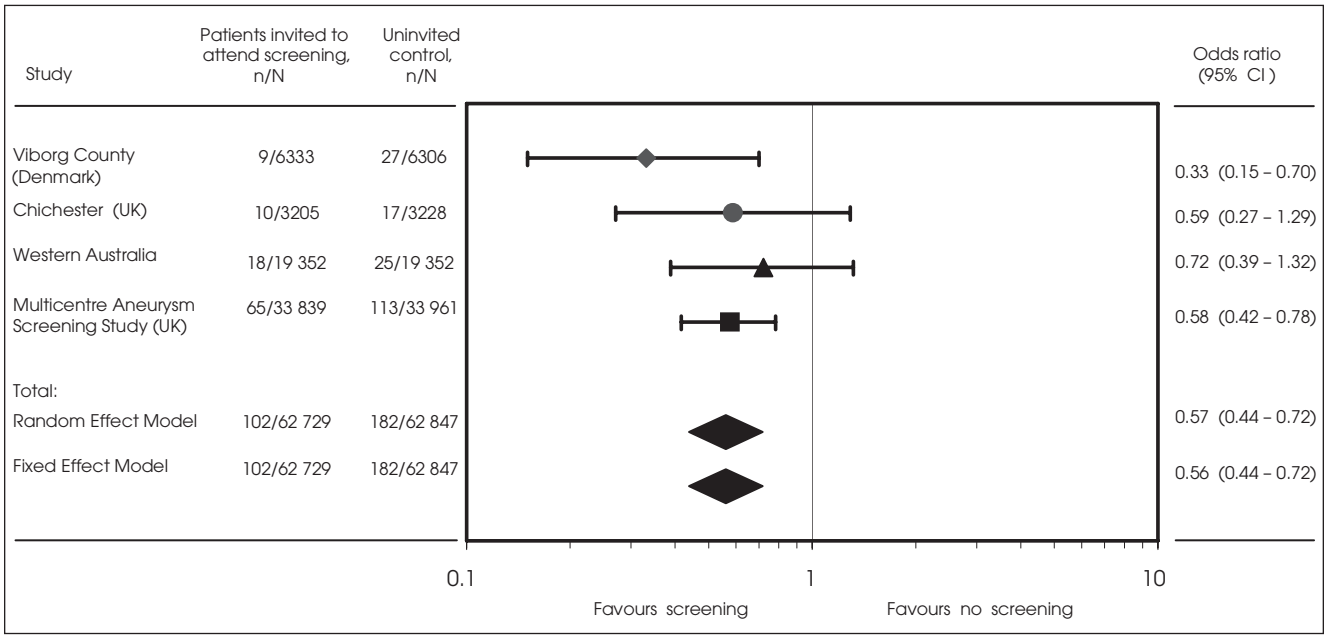

FIG. 3. Meta-analysis results of randomized screening trials for abdominal aortic aneurysm in men. CI = confidence interval.

40.2% of the incremental lifetime cost. Because screening changes the need for elective and emergency surgical repair in the opposite direction, varying the estimated cost of inpatient care had very little impact on the estimated ICER. The response rate to an invitation to attend screening also had very little impact on the estimated cost–utility ratio owing to the positive correlation between response rate and the numerator (incremental cost) and denominator (incremental QALY) of the ICER. The importance of response rate should not be neglected, however, because the overall cost and benefit will obviously depend on whether individuals attend screening or not.

The performance of a screening program in routine clinical practice depends largely on the level of compliance. In the randomized screening trials, 81%–88% of patients complied with surveillance US. Despite a certain level of noncompliance implicit in our model, we adjusted for a possible protocol-driven effect by testing additional dropouts from US surveillance in a 1-way sensitivity analysis. Unlikely values, such as 50% annually, did not result in an above-threshold estimated ICER.

Controversial issues

Selective screening

Cost-effective screening relies on the selection of a subpopulation at high risk for the disease in question. Documented risk factors for AAAs, in addition to age and sex, are smoking, cardiovascular disease, hypertension and familial clustering.[103] Today, most screening programs are targeted at men older than age 65 years and are nonselective to other risk factors.

Smoking, which is associated with a 2- to 4-fold increase in AAA prevalence,[104] has been proposed as a possible criterion for selective screening. In a 2005 report, the US Preventive Services Task Force recommended 1-time screening only for men aged 65–75 years who have ever smoked (grade B recommendation)[100,101] but made no recommendation for or against screening the same age class of men who have never smoked (grade C recommendation). From a theoretical model, it was estimated that 89% of AAA-related deaths could be prevented by screening 69% of men; however, targeting high-risk patients for AAAs restricts screening to a cohort with an increased risk of long-term mortality. AAA prevalence and life expectancy are variables affecting the cost-effectiveness in the opposite direction. Not surprisingly, models that took into account the increased future mortality of high-risk groups found selective screening to be nonbeneficial.[90,105]

Screening in women

The Chichester study was the only randomized screening trial that included both men and women. A total of 9342 women aged 65–80 years were randomly assigned to an invitation to screening group or a control group.[106] The screened cohort had an AAA prevalence of 1.3%, and no benefit was observed after 10 years of follow-up. AAAs occurred on average a decade later in women than in men, and most ruptured after 80 years of age. The low prevalence of AAAs in the female population has been repeatedly documented and has resulted in the exclusion of women from subsequent large screening trials.

Because women share the same risk factors as men, targeted screening based on cardiovascular risk factors has been recommended,[99] although no clinical trial supports that recommendation. More studies using different screening strategies are therefore needed before any conclusions can be reached.

Limitations

A model can only be as good as the data it is based on. We therefore tried to structure our model to match the highest-quality data available. As discussed previously, the main limitations were the lack of good-quality data on the natural history of undetected large AAAs and the fact that we had to extrapolate long-term outcomes from studies with limited follow-ups. Another limitation arose from the lack of Canadian data on a screening program's generation and use of resources and their related costs. Although precise cost estimates are available from other countries, the trade-off between precision and relevance prompted us to adapt our model to the Canadian context by using what we considered to be the most locally relevant cost data. Head-to-head comparison of our results with that of published economic evaluations needs to be interpreted in light of known differences in approaches that have been adopted for the funding and delivery of health care services. In the United States for example, treatment of a given condition is known to be more resource-intensive when compared with Canada or the United Kingdom, and prices of medical supplies, labour and administrative infrastructure are also much higher.[107,108] Using currency conversion to compare results from one setting to another is therefore inappropriate.

Conclusion

Despite the limitations of the present model, it appears that screening for AAAs in men reaching 65 years of age is efficacious and cost-effective. Our model revealed that the incremental cost per QALY is lower than the value generally considered to be cost-effective and compares favourably with the estimates cited in other screening programs. AAA screening has many advantages, namely, its simplicity and reliance on a safe and highly accurate screening tool. For such a program to meet its goals, however, sufficient resources need to be made available for both the diagnosis and treatment of screen-detected AAAs. More clinical studies are also needed to define the

role of screening in subgroups at high risk, especially in the female population.

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Contributors: Drs. Montreuil and Brophy designed the study. Dr. Montreuil acquired the data, which both authors analyzed. Dr. Montreuil wrote the article, and both authors revised it. Both authors gave final approval for the article to be published.

References

1. Krupski WC, Rutherford RB. Update on open repair of abdominal aortic aneurysms: the challenges for endovascular repair. *J Am Coll Surg* 2004;199:946-60.
2. Earnshaw JJ, Shaw E, Whyman MR, et al. Screening for abdominal aortic aneurysms in men. *BMJ* 2004;328:1122-4.
3. Longo C, Upchurch G. Abdominal aortic aneurysm screening: recommendations and controversies. *Vasc Endovascular Surg* 2005;39:213-9.
4. Brewster DC, Cronenwett JL, Hallett JW Jr, et al. Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003;37:1106-17.
5. Shapira OM, Pasik S, Wassermann JP, et al. Ultrasound screening for abdominal aortic aneurysms in patients with atherosclerotic peripheral vascular disease. *J Cardiovasc Surg (Torino)* 1990;31:170-2.
6. Akkersdijk GJ, Puylaert JB, Coerkamp EG, et al. Accuracy of ultrasonographic measurement of infrarenal abdominal aortic aneurysm. *Br J Surg* 1994;81:376.
7. Periodic health examination, 1991 update: 5. Screening for abdominal aortic aneurysm. Canadian Task Force on the Periodic Health Examination. *CMAJ* 1991;145:783-9.
8. Heather BP, Poskitt KR, Earnshaw JJ, et al. Population screening reduces mortality rate from aortic aneurysm in men. *Br J Surg* 2000;87:750-3.
9. Wilmink TB, Quick CR, Hubbard CS, et al. The influence of screening on the incidence of ruptured abdominal aortic aneurysms. *J Vasc Surg* 1999;30:203-8.
10. Wilmink AB, Quick CR, Hubbard CS, et al. Effectiveness and cost of screening for abdominal aortic aneurysm: results of a population screening program. *J Vasc Surg* 2003;38:72-7.
11. Scott RA, Wilson NM, Ashton HA, et al. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg* 1995;82:1066-70.
12. Vardulaki KA, Walker NM, Couto E, et al. Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm. *Br J Surg* 2002;89:861-4.
13. Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet* 2002;360:1531-9.
14. Lindholt JS, Juul S, Fasting H, et al. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *BMJ* 2005;330:750.
15. Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ* 2004;329:1259.
16. Philips Z, Ginnelly L, Sculpher M, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;8:iii-iv, ix-xi, 1-158.
17. Drummond M, O'Brien BJ, Stoddart G, et al. *Methods for economic evaluation of health care programs.* New York: Oxford University Press; 1997.
18. Petitti DB. *Meta-Analysis, decision analysis and cost-effectiveness analysis. Methods for quantitative synthesis in medicine.* New York: Oxford University Press; 2000.
19. Scott RA, Vardulaki KA, Walker NM, et al. The long-term benefits of a single scan for abdominal aortic aneurysm (AAA) at age 65. *Eur J Vasc Endovasc Surg* 2001;21:535-40.
20. Emerton ME, Shaw E, Poskitt K, et al. Screening for abdominal aortic aneurysm: a single scan is enough. *Br J Surg* 1994;81:1112-3.
21. Crow P, Shaw E, Earnshaw JJ, et al. A single normal ultrasonographic scan at age 65 years rules out significant aneurysm disease for life in men. *Br J Surg* 2001;88:941-4.
22. Lederle FA, Johnson GR, Wilson SE, et al. Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. *Arch Intern Med* 2000;160:1117-21.
23. Lindholt JS, Vammen S, Juul S, et al. Optimal interval screening and surveillance of abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2000;20:369-73.
24. Brown PM, Pattenden R, Gutelius JR. The selective management of small abdominal aortic aneurysms: the Kingston study. *J Vasc Surg* 1992;15:21-5.
25. Brown PM, Sobolev B, Zelt DT. Selective management of abdominal aortic aneurysms smaller than 5.0 cm in a prospective sizing program with gender-specific analysis. *J Vasc Surg* 2003;38:762-5.
26. The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet* 1998;352:1649-55.
27. The United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1445-52.
28. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002;346:1437-44.
29. Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;364:843-8.
30. Prinssen M, Verhoeven E, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;351:1607-18.
31. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;365:2179-86.
32. Blankensteijn JD, de Jong S, Prinssen M, et al. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2005;352:2398-405.
33. Drury D, Michaels J, Jones L, et al. Systematic review of recent evidence for the safety and efficacy of elective endovascular repair in the management of infrarenal abdominal aortic aneurysm. *Br J Surg* 2005;92:937-46.
34. Michaels JA, Drury D, Thomas SM. Cost-effectiveness of endovascular abdominal aortic aneurysm repair. *Br J Surg* 2005;92:960-7.
35. Forbes TL, Lawlor DK, DeRose G, et al. National audit of the recent utilization of endovascular abdominal aortic aneurysm repair in Canada: 2003 to 2004. *J Vasc Surg* 2005;42:410-4.
36. Birch SE, Stary DR, Scott AR. Cost of endovascular versus open surgical repair of abdominal aortic aneurysms. *Aust N Z J Surg* 2000;70:660-6.
37. Hayter CL, Bradshaw SR, Allen RJ, et al. Follow-up costs increase the cost disparity between endovascular and open abdominal aortic aneurysm repair. *J Vasc Surg* 2005;42:912-8.
38. Loh CS, Stevenson IM, Wu AVO, et al. Ultrasound scan for abdominal aortic

aneurysm [Abstract]. *Br J Surg* 1989;76: 417.
39. O'Kelly TJ, Heather BP. General practice-based population screening for abdominal aortic aneurysms: a pilot study. *Br J Surg* 1989;76:479-80.
40. Collin J, Araujo L, Walton J. A community detection program for abdominal aortic aneurysm. *Angiology* 1990;41:53-8.
41. Bengtsson H, Bergqvist D, Ekberg O, et al. A population based screening of abdominal aortic aneurysms (AAA). *Eur J Vasc Surg* 1991;5:53-7.
42. Krohn CD, Kullmann G, Kvernebo K, et al. Ultrasonographic screening for abdominal aortic aneurysm. *Eur J Surg* 1992;158:527-30.
43. Grimshaw GM, Thompson JM, Hamer JD. Prevalence of abdominal aortic aneurysm associated with hypertension in an urban population. *J Med Screen* 1994; 1:226-8.
44. Smith FC, Grimshaw GM, Paterson IS, et al. Ultrasonographic screening for abdominal aortic aneurysm in an urban community. *Br J Surg* 1993;80:1406-9.
45. Lucarotti ME, Shaw E, Heather B. Distribution of aortic diameter in a screened male population. *Br J Surg* 1992;79:641-2.
46. Lucarotti M, Shaw E, Poskitt K, et al. The Gloucestershire Aneurysm Screening Programme: the first 2 years' experience. *Eur J Vasc Surg* 1993;7:397-401.
47. Pleumeekers HJ, Hoes AW. van der DE et al. Aneurysms of the abdominal aorta in older adults. The Rotterdam Study. *Am J Epidemiol* 1995;142:1291-9.
48. Simoni G, Pastorino C, Perrone R, et al. Screening for abdominal aortic aneurysms and associated risk factors in a general population. *Eur J Vasc Endovasc Surg* 1995;10:207-10.
49. Scott RA, Ashton HA, Kay DN. Abdominal aortic aneurysm in 4237 screened patients: prevalence, development and management over 6 years. *Br J Surg* 1991;78: 1122-5.
50. Holdsworth JD. Screening for abdominal aortic aneurysm in Northumberland. *Br J Surg* 1994;81:710-2.
51. Boll AP, Verbeek AL, van de Lisdonk EH. van d, V. High prevalence of abdominal aortic aneurysm in a primary care screening programme. *Br J Surg* 1998;85:1090-4.
52. Vazquez C, Sakalihasan N, D'Harcour JB, et al. Routine ultrasound screening for abdominal aortic aneurysm among 65- and 75-year-old men in a city of 200,000 inhabitants. *Ann Vasc Surg* 1998;12:544-9.
53. Morris GE, Hubbard CS, Quick CR. An abdominal aortic aneurysm screening programme for all males over the age of 50 years. *Eur J Vasc Surg* 1994;8:156-60.
54. Wanhainen A, Bjorck M, Boman K, et al. Influence of diagnostic criteria on the prevalence of abdominal aortic aneurysm. *J Vasc Surg* 2001;34:229-35.
55. Jamrozik K, Norman PE, Spencer CA, et al. Screening for abdominal aortic aneurysm: lessons from a population-based study. *Med J Aust* 2000;173:345-50.
56. Chichester Aneurysm Screening Group (CASS Group). A comparative study of the prevalence of abdominal aortic aneurysms in the United Kindom, Denmark, and Australia. *J Med Screen* 2001;8:46-50.
57. Nevitt MP, Ballard DJ, Hallett JW Jr. Prognosis of abdominal aortic aneurysms. A population-based study. *N Engl J Med* 1989;321:1009-14.
58. Guirguis EM, Barber GG. The natural history of abdominal aortic aneurysms. *Am J Surg* 1991;162:481-3.
59. Glimaker H, Holmberg L, Elvin A, et al. Natural history of patients with abdominal aortic aneurysm. *Eur J Vasc Surg* 1991;5:125-30.
60. Limet R, Sakalihassan N, Albert A. Determination of the expansion rate and incidence of rupture of abdominal aortic aneurysms. *J Vasc Surg* 1991;14:540-8.
61. Perko MJ, Schroeder TV, Olsen PS, et al. Natural history of abdominal aortic aneurysm: a survey of 63 patients treated nonoperatively. *Ann Vasc Surg* 1993;7: 113-6.
62. Reed WW, Hallett JW Jr, Damiano MA, et al. Learning from the last ultrasound. A population-based study of patients with abdominal aortic aneurysm. *Arch Intern Med* 1997;157:2064-8.
63. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK Small Aneurysm Trial Participants. *Ann Surg* 1999;230:289-96.
64. Lederle FA, Johnson GR, Wilson SE, et al. Rupture rate of large abdominal aortic aneurysms in patients refusing or unfit for elective repair. *JAMA* 2002;287:2968-72.
65. Brown PM, Zelt DT, Sobolev B. The risk of rupture in untreated aneurysms: the impact of size, gender, and expansion rate. *J Vasc Surg* 2003;37:280-4.
66. Hollier LH, Plate G, O'Brien PC, et al. Late survival after abdominal aortic aneurysm repair: influence of coronary artery disease. *J Vasc Surg* 1984;1:290-9.
67. Norman PE, Semmens JB, Lawrence-Brown MM. Long-term relative survival following surgery for abdominal aortic aneurysm: a review. *Cardiovasc Surg* 2001;9:219-24.
68. Johnston KW. Nonruptured abdominal aortic aneurysm: six-year follow-up results from the multicenter prospective Canadian aneurysm study. Canadian Society for Vascular Surgery Aneurysm Study Group. *J Vasc Surg* 1994;20:163-70.
69. Yeager RA, Moneta GL, Edward JM, et al. Late survival after perioperative myocardial infarction complicating vascular surgery. *J Vasc Surg* 1994;20:598-604.
70. McFalls EO, Ward HB, Santilli S, et al. The influence of perioperative myocardial infarction on long-term prognosis following elective vascular surgery. *Chest* 1998; 113:681-6.
71. Hardie K, Hankey GL, Jamrozik K, et al. Ten-year survival after first-ever stroke in the Perth Community Stroke Study. *Stroke* 2003;34:1842-6.
72. Bronnum-Hansen H, Davidsen M, Thorvaldsen P; Danish MONICA Study Group. Long-term survival and causes of death after stroke. *Stroke* 2001;32:2131-6.
73. Lindholt JS, Vammen S, Fasting H, et al. Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2000;20:79-83.
74. Lucarotti ME, Heather BP, Shaw E, et al. Psychological morbidity associated with abdominal aortic aneurysm screening. *Eur J Vasc Endovasc Surg* 1997;14: 499-501.
75. Mittmann N, Trakas K, Risebrough N, et al. Utility scores for chronic conditions in a community-dwelling population. *Pharmacoeconomics* 1999;15:369-76.
76. Mo F, Choi B, Li F, et al. Using Health Utility Index (HUI) for measuring the impact on health-related quality of life (HRQL) among individuals with chronic diseases. *ScientificWorldJournal* 2004;4: 746-57.
77. Kroeker A, Clark WF, Heidenheim AP, et al. An operating cost comparison between conventional and home quotidian hemodialysis. *Am J Kidney Dis* 2003; 42(Suppl 1):49-55.
78. Magee TR, Scott DJ, Dunkley A, et al. Quality of life following surgery for abdominal aortic aneurysm. *Br J Surg* 1992; 79:1014-6.
79. Korhonen SJ, Kantonen I, Pettila V, et al. Long-term survival and health-related quality of life of patients with ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2003;25:350-3.
80. Forbes TL, DeRose G, Kribs S, et al. A cost-effectiveness analysis of standard versus endovascular abdominal aortic aneurysm repair. *Can J Surg* 2002;45: 420-4.
81. Canadian Coordinating Office for Health Technology Assessment (CCOHTA). *Guidelines for the economic evaluation of pharmaceutical: Canada*. Ottawa (ON): CCOHTA; 1994.
82. Briggs A, Gray A. Handling uncertainty when performing economic evaluation of healthcare intervention. *Health Technol Assess* 1999;3.
83. Wilson J, Jungner G. *Principles and prac-*

tice of screening for disease. Geneva: World Health Organisation; 1968.
84. Bengtsson H, Bergqvist D, Jendteg S, et al. Ultrasonographic screening for abdominal aortic aneurysm: analysis of surgical decisions for cost-effectiveness. *World J Surg* 1989;13:266-71.
85. Frame PS, Fryback DG, Patterson C. Screening for abdominal aortic aneurysm in men ages 60 to 80 years. A cost-effectiveness analysis. *Ann Intern Med* 1993;119:411-6.
86. Mason JM, Wakeman AP, Drummond MF, et al. Population screening for abdominal aortic aneurysm: do the benefits outweigh the costs? *J Public Health Med* 1993;15:154-60.
87. St Leger AS, Spencely M, McCollum CN, et al. Screening for abdominal aortic aneurysm: a computer assisted cost-utility analysis. *Eur J Vasc Endovasc Surg* 1996; 11:183-90.
88. Pentikainen TJ, Sipila T, Rissanen P, et al. Cost-effectiveness of targeted screening for abdominal aortic aneurysm. Monte Carlo-based estimates. *Int J Technol Assess Health Care* 2000;16:22-34.
89. Lee TY, Korn P, Heller JA, et al. The cost-effectiveness of a "quick-screen" program for abdominal aortic aneurysms. *Surgery* 2002;132:399-407.
90. Connelly JB, Hill GB, Millar WJ. The detection and management of abdominal aortic aneurysm: a cost-effectiveness analysis. *Clin Invest Med* 2002;25:127-33.
91. Boll AP, Severens JL, Verbeek AL. et al. 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. *Eur J Vasc Endovasc Surg* 2003;26:74-80.
92. Wanhainen A, Lundkvist J, Bergqvist D, et al. Cost-effectiveness of different screening strategies for abdominal aortic aneurysm. *J Vasc Surg* 2005;41:741-51.
93. Henriksson M, Lundgren F. Decision-analytical model with lifetime estimation of costs and health outcomes for one-time screening for abdominal aortic aneurysm in 65-year-old men. *Br J Surg* 2005;92:976-83.
94. Silverstein MD, Pitts SR, Chaikof EL, et al. Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. *Proc (Bayl Univ Med Cent)* 2005;18:345-67.
95. Lindholt JS, Juul S, Fasting H, et al. Hospital costs and benefits of screening for abdominal aortic aneurysms. Results from a randomised population screening trial. *Eur J Vasc Endovasc Surg* 2002;23: 55-60.
96. Multicentre aneurysm screening study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. *BMJ* 2002;325:1135.
97. Meenan RT, Fleming C, Whitlock EP, et al. Cost-effectiveness analyses of population-based screening for abdominal aortic aneurysm: evidence synthesis; 2005. p. 1-14. Available: www ahrq gov/clinic/uspstf /uspstopics.htm (Accessed 2005 Dec.)
98. Laupacis A, Feeny D, Detsky AS, et al. How attractive does a new technology have to be to warrant adoption and utilisation? Tentative guidelines for using clinical and economic evaluations? *CMAJ* 1992;146:473-81.
99. Kent KC, Zwolak RM, Jaff MR, et al. Screening for abdominal aortic aneurysm: a consensus statement. *J Vasc Surg* 2004; 39:267-9.
100. U.S.Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. *Ann Intern Med* 2005;142:198-202.
101. Fleming C, Whitlock EP, Beil TL, et al. Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Task Force. *Ann Intern Med* 2005;142:203-11.
102. Bruce CJ, Spittell PC, Montgomery SC, et al. Personal ultrasound imager: abdominal aortic aneurysm screening. *J Am Soc Echocardiogr* 2000;13:674-9.
103. Cornuz J, Sidoti Pinto C, Tevaearai H, et al. Risk factors for asymptomatic abdominal aortic aneurysm. Systematic review and meta-analysis of population-based screening studies. Eur J Public Health 2004;14:343-9.
104. Lederle FA, Nelson DB, Joseph AM. Smoker's relative risk for aortic aneurysm compared with other smoking-related disease: A systematic review. *J Vasc Surg* 2003;38:329-34.
105. Wanhainen A, Lundkvist J, Bergqvist D, et al. Cost-effectiveness of different screening strategies for abdominal aortic aneurysms. *J Vasc Surg* 2005;41:741-50.
106. Scott RA, Bridgewater SG, Ashton HA. Randomized clinical trial of screening for abdominal aortic aneurysm in women. *Br J Surg* 2002;89:283-5.
107. Brox AC, Filion KB, Zhang X, et al. In-hospital cost of abdominal aortic aneurysm repair in Canada and the United States. *Arch Intern Med* 2003;163:2500-4.
108. Chew HF, You CK, Brown MG, et al. Mortality, morbidity, and costs of ruptured and elective abdominal aortic aneurysm repairs in Nova Scotia, Canada. *Ann Vasc Surg* 2003;17:171-9.
109. Couto E, Duffy SW, Ashton HA, et al. Probabilities of progression of aortic aneurysms: estimates and implications for screening policy. *J Med Screen* 2002;9: 40-2.
110. Vardulaki KA, Prevost TC, Walker NM, et al. Growth rates and risk of rupture of abdominal aortic aneurysms. *Br J Surg* 1998;85:1674-80.
111. Dueck AD, Kucey DS, Johnston KW, et al. Survival after ruptured abdominal aortic aneurysm: effect of patient, surgeon, and hospital factors. *J Vasc Surg* 2004;39: 1253-60.
112. Dueck AD, Kucey DS, Johnston KW, et al. Long-term survival and temporal trends in patient and surgeon factors after elective and ruptured abdominal aortic aneurysm surgery. *J Vasc Surg* 2004;39: 1261-7.
113. Johnston KW, Scobie TK. Multicenter prospective study of nonruptured abdominal aortic aneurysms. I. Population and operative management. *J Vasc Surg* 1988;7:69-81.
114. Johnston KW. Multicenter prospective study of nonruptured abdominal aortic aneurysm. Part II. Variables predicting morbidity and mortality. *J Vasc Surg* 1989;9:437-47.
115. Johnston KW. Ruptured abdominal aortic aneurysm: six-year follow-up results of a multicenter prospective study. Canadian Society for Vascular Surgery Aneurysm Study Group. *J Vasc Surg* 1994;19:888900.
116. Katz DA, Cronenwett JL. The cost-effectiveness of early surgery versus watchful waiting in the management of small abdominal aortic aneurysms. *J Vasc Surg* 1994;19:980-90.
117. Ascher E, Scheinman M, DePippo P, et al. Ruptured versus elective abdominal aortic aneurysm repair: outcome and cost. *Ann Vasc Surg* 1999;13:613-7.
118. Palmer AJ, Valentine WJ, Roze S, et al. Overview of costs of stroke from published, incidence-based studies spanning 16 industrialized countries. *Curr Med Res Opin* 2005;21:19-26.
119. O'Brien BJ, Willan A, Blackhouse G, et al. Will the use of low-molecular-weight heparin (enoxaparin) in patients with acute coronary syndrome save costs in Canada? *Am Heart J* 2000;139:423-9.