Cost-Effectiveness Analyses of Population-Based Screening for Abdominal Aortic Aneurysm: Evidence Synthesis

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Background

In 1996, the U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to recommend for or against routine screening of asymptomatic adults for abdominal aortic aneurysm (AAA) either with abdominal palpation or ultrasonography. The USPSTF did recognize that selective screening of high-risk patients might be beneficial, for example, in men with other risk factors such as peripheral vascular disease or a family history of AAA. However, the USPSTF stated clearly that there was no direct evidence that screening for AAA reduces mortality or morbidity in any population.

In 2002, the Research Triangle Institute-University of North Carolina (RTI-UNC) Evidence-based Practice Center (EPC) performed a topic review of AAA screening. The USPSTF used this review to prioritize AAA screening as a topic requiring an update. Two key developments were cited in prioritizing AAA screening as a topic to be updated in an evidence synthesis:

- Several population-based clinical trials of mass screening for AAA were completed.
- A new procedure, percutaneous endovascular repair (EVAR), was introduced, which may provide a less invasive alternative to surgical repair for certain individuals.

In 2003–2004, the Oregon EPC conducted an evidence synthesis of AAA screening, which was led by researchers at the Kaiser Permanente Center for Health Research in Portland, Oregon. Within the overall scope of this update, which was to focus primarily on effectiveness, the Oregon EPC was also charged with evaluating the feasibility of integrating published evidence on the cost-effectiveness of AAA screening. Many factors related to AAA screening will have differential effects on the costs and yields of screening asymptomatic adults for AAA. Economic evaluations and cost-effectiveness analyses (CEA), in particular, can summarize the expected benefits, harms, and costs of screening asymptomatic adults.

Therefore, in conjunction with the evidence synthesis,[1] we also conducted a systematic review of published CEAs to evaluate the costs and benefits of screening asymptomatic adults for AAA. This ancillary CEA review was intended to inform the

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deliberations of the USPSTF regarding the overall appropriateness of AAA screening.

Methods

Search Strategies

To guide our search, our first task was to develop a preliminary set of key questions around the cost-effectiveness of population-based AAA screening. Subsequent consultation with members of the USPSTF helped us refine the key questions into their final form.

1. Compared with usual care—ie, no screening—what is the cost-effectiveness of population-based screening of asymptomatic adults for AAA to reduce the risk for abdominal aortic rupture and AAA-specific morbidity and mortality?
2. What is the cost-effectiveness of selectively screening adults at higher risk for rupture—eg, those with a family history of AAA, peripheral vascular disease, and tobacco use—compared with routine screening and usual care?
3. Among individuals with 3.0 to 5.4 cm AAAs on initial screening exam, what is the cost-effectiveness of periodic surveillance compared with one-time screening?
4. Among individuals without AAA on initial screening exam, what is the cost-effectiveness of re-screening at varying intervals compared with one-time screening?
5. How will differences in treatment effectiveness affect cost-effectiveness estimates for AAA screening?

Our set of key questions initially included 2 questions on endovascular AAA repair (EVAR). However, discussions with experts on the USPSTF led us to conclude that data on the effectiveness of EVAR were too preliminary to meaningfully inform the cost-effectiveness issues surrounding population-based AAA screening.

In our literature search, we sought studies that reported both costs and health outcomes of population-based screening programs for AAA. We searched MEDLINE®, the Cochrane Central Register of Controlled Trials, and the National Health Service Economic Evaluation Database; we limited our search of each database to publication dates between 1994 and 2004. Search strategies were organized using a combination of controlled vocabulary terms, where available, and free text terms (Appendix 1). These strategies were subsequently combined with those designed for identification of effectiveness studies in each database. The final search was conducted in April 2004. To identify studies not captured in our database searches, we manually searched reference lists of retrieved articles and solicited input from experts on the USPSTF.

One author (Meenan) reviewed identified abstracts for potentially eligible articles, which were then retrieved for full review. Based on information within the abstracts, we sought studies that addressed both the costs and health outcomes of population-based AAA screening. We excluded studies that were 1) not CEA, cost-utility analyses, or cost-benefit analyses; or 2) not relevant to any key question. For each included study, we extracted and summarized selected elements into 2 evidence tables (Tables 1 and 2): authors, publication date, screening intervention, screening interval, study time horizon, baseline group, AAA size motivating treatment, prevalence of AAA, AAA-specific mortality, operative mortality rates (elective and emergency), AAA rupture rate, analytic approach (trial-based vs non-trial-based), study perspective, data sources, utility measures (if any), discount rate, cost measures, cost-effectiveness results, and sensitivity analyses. We abstracted relevant data from each study into a Microsoft® Access database developed in 1997 for use by the Committee on Clinical Prevention Priorities.[2,3]

We then organized the included studies by key question (allowing studies to address more than 1 key question) and evaluated the quality of each against the following 13 criteria based on those presented in Saha,[4] and which themselves are based on recommendations of the Panel on Cost-Effectiveness in Health and Medicine.[5]

Framing

- Are the interventions and populations compared appropriate?
- Is the study conducted from the societal perspective?
- Is the time horizon clinically appropriate and relevant to the study question?

Effects

- Are all important drivers of effectiveness included—eg, AAA prevalence, AAA rupture rates, operative mortality rates (elective and emergency)?
- Are key harms included?
- Is the best available evidence used to estimate effectiveness?
- Are long-term outcomes used?
- Do effect measures capture preferences or utilities?

Costs

- Are all appropriate downstream costs included?
- Are charges converted to costs appropriately?
- Are the best available data used to estimate costs?

Results

- Are incremental cost-effectiveness ratios (ICERs) presented?
- Are appropriate sensitivity analyses performed?

We used these criteria to guide our categorization of studies as good, fair, or poor. Quality grades were assigned based on a subjective assessment of study design and quality of data inputs. The intent of our review was to focus on good quality studies, with fair quality studies also considered as appropriate. Poor quality studies were excluded from further review. (Our definition of fatal study flaws that would lead to a poor quality rating is provided in Appendix 2.) The goals of our systematic CEA review were to identify the best available evidence regarding a particular key question, and to critically review and synthesize that evidence to answer the question in an evidence-based way.

Results

We initially reviewed the abstracts of 241 studies and identified 25 definite or possible economic evaluations, for which we reviewed the full articles. We determined that 4 were relevant to 1 or more key questions. The other 21 articles were excluded from further analysis, either because they were not a CEA (or other form of economic evaluation such as a cost-benefit analysis) or were not relevant to any key question. Where necessary, we converted results reported in non-U.S. currency to U.S. dollars, and used the Medical Care component of the Consumer Price Index to convert all results to 2003 dollars.

Key Questions

1. Compared with usual care—ie, no screening—what is the cost-effectiveness of population-based screening of asymptomatic adults for AAA to reduce the risk for abdominal aortic rupture and AAA-specific morbidity and mortality?

We determined that 1 good-quality study (the Multicentre Aneurysm Screening Study[6] [MASS]) and 2 fair-quality studies[7,8] addressed the primary key question regarding the overall cost-effectiveness of population-based AAA screening. MASS[6] was trial-based; the others were based on published literature and/or data from a single hospital or health system. As will be discussed further, the superior quality of its effectiveness data distinguished MASS from "fair" studies such as those conducted by Lee, et al and Frame, et al. In addition, we believe that the detailed micro-costing approach used in the MASS CEA, as well as its use of probabilistic sensitivity analysis, mitigated its being set outside the United States (it was conducted in the United Kingdom) and justified a "good" quality rating. "Fair" quality ratings were assigned to studies based primarily on the uncertain quality of their effectiveness and/or cost data, even if most other favorable design characteristics were present. Poor studies combined lower-quality

Table 1. Clinical Components of Cost-Effectiveness Analyses

Author (Year)	Intervention	Interval	Time Horizon	Baseline Group	AAA Size
Key Question					
1. Compared with usual care—ie, no screening—what is the cost-effectiveness of population-based screening of asymptomatic adults for AAA to reduce the risk for abdominal aortic rupture and AAA-specific morbidity and mortality?					
Frame, et al (1993)	AAA screening by physical exam or U/S in males aged 60–80	One-time, repeated after 5 yrs	20 yrs	Hypothetical cohort of 10,000 males aged 60–79	4.0 cm, referral to surgery
Lee, et al (2002)	Quick-screen U/S vs full screen	NA	Lifetime	Hypothetical 70 yr old males	3.0–5.0 cm, surveillance 5.0 cm, referral to surgery
MASS (2002)	Trial-based CEA of U/S screening vs no screening	3.0–4.4 cm, annual; 4.5–5.4 cm, quarterly	4 yrs and 10 yrs	Population-based sample of 67,800 UK males aged 65–74	5.5 cm, symptoms or rapid expansion referred to surgery
2. What is the cost-effectiveness of selectively screening adults at higher risk for rupture—eg, those with a family history of AAA, peripheral vascular disease, and tobacco use—compared with routine screening and usual care?					
Lee, et al (2002)	See detail in key question 1				
Soisalon-Soininen, et al (2001)	Screening of first-degree male relatives > 50 of AAA patients vs no screening	6 mo (3.0–4.0 cm) Annual (2.1–2.9 cm)	Lifetime (17 yrs)	First-degree male relatives (aged > 50) of 150 consecutive AAA pts	5.0 cm, referred to surgery
3. Among individuals with 3.0 to 5.4 cm AAAs on initial screening exam, what is the cost-effectiveness of periodic surveillance compared with one-time screening?					
NA					
4. Among individuals without AAA on initial screening exam, what is the cost-effectiveness of re-screening at varying intervals compared with one-time screening?					
NA					
5. How will differences in treatment effectiveness affect cost-effectiveness estimates for AAA screening?					
MASS (2002)	See detail in key question 1				

AAA, abdominal aortic aneurysm; CEA, cost-effectiveness analyses; MASS, Multicentre Aneurysm Screening Study; mo, month; NA, not available; pts, patients; yrs, years; UK, United Kingdom; U/S, ultrasound.

Table 1. Clinical Components of Cost-Effectiveness Analyses (cont)

AAA Prevalence	Annual Rupture Rate	% Ruptures Surviving to Surgery	Elective Operative Mortality	Emergency Operative Mortality
3.1% < 4.0 cm 2.3% > 4.0 cm	4% > 4.0 cm 9% < 4.0 cm	38%	5%	50%
7%	0.1% 3.0 cm 0.6% 3.0–4.0 cm 2.3% 4.0–5.0 cm 7% > 5.0 cm	56%	4%	49%
5.50%	0.04% invitees 0.08% controls	40% for invitees 40% for controls	6%	37%
8.2% among relatives	0% > 5.0 cm 5% > 5.0 cm	13%	4%	64%

Table 2. Cost Components of Cost-Effectiveness Analyses

Key Question / Author (Year) and Overall Quality	Model Type Perspective	Data Source	Utility	Discount Rate	Screening Costs	Treatment Costs
1. Compared with usual care—ie, no screening—what is the cost-effectiveness of population-based screening of asymptomatic adults for AAA to reduce the risk for abdominal aortic rupture and AAA-specific morbidity and mortality?						
Frame, et al (1993) **Fair**	Decision model Health system	Systematic review by Canadian Task Force on the Periodic Health Examination; MEDLINE®, article bibliographies	None	5%	$260 U/S	$46K elective $90K ER
Lee, et al (2002) **Fair**	Markov Health system	Probabilities, costs, and quality adjustments: literature review and New York Presbyterian Hospital	Renal failure, 0.68; stroke, 0.40; major amputation, 0.80; MI, 0.80	3%	$350	Elective surgery, $22K; ruptured AAA, $39K; L/T cost of renal failure, stroke, MI, amputation included
MASS (2002) **Good**	Trial-based Health system	MASS trial	Assumes 0.8 for UK elderly men	LY 1.5% costs 6%	$1.58M total	Pre-operative consult, $433K; $4.26K, elective ($14K per); $516K, ER ($22K per)
2. What is the cost-effectiveness of selectively screening adults at higher risk for rupture—eg, those with a family history of AAA, peripheral vascular disease, and tobacco use—compared with routine screening and usual care?						
Lee, et al (2002) **Fair**	See detail in key question 1					
Soisalon-Soininen, et al (2001) **Fair**	Decision model Health system	Screening probabilities: sample of first-degree relatives of 150 surgery patients at Helsinki University Central Hospital (HUCH); effectiveness and costs: Finnish Hospital Discharge Register and survival analysis of 1,150 surgery HUCH patients	None	5%	$1M, total first screening; $261K total follow-up screenings	$6M
3. Among individuals with 3.0 to 5.4 cm AAAs on initial screening exam, what is the cost-effectiveness of periodic surveillance compared with one-time screening? **NA**						
4. Among individuals without AAA on initial screening exam, what is the cost-effectiveness of re-screening at varying intervals compared with one-time screening? **NA**						
5. How will differences in treatment effectiveness affect cost-effectiveness estimates for AAA screening?						
MASS (2002) **Good**	See detail in key question 1					

ER, emergency repair; ICER, incremental cost-effectiveness ratio; K, thousand; L/T, lifetime; LY, life year; LYS, life years saved; M, million; MI, myocardial infarction; QALY, quality-adjusted life-year; UK, United Kingdom; U/S, ultrasound; yrs, years.

Table 2. Cost Components of Cost-Effectiveness Analyses (cont)

Outcomes	ICER (2003 U.S.$)	Sensitivity Analysis (2003 U.S.$)	Comments
ICER	$72K/LY, one-time U/S; $1.5M/LY, U/S 5 yrs after first screen; $50K/LY, physical exam + U/S for positives; $1.3M/LY, additional U/S at 5 yrs	Effect of changes in individual parameter estimates not known (parameter values varied simultaneously between best and worst estimates)	Not societal perspective; no quality adjustments; effectiveness data > 11 yrs old (much lower LYS estimate than other studies); uninformative sensitivity analysis; quality of cost data uncertain; assumes no relative mortality risk for surgery survivors
ICER	$14K/QALY	Influential (univariate), age (screening after 83 inefficient)	Not societal perspective; quality of effectiveness and cost data uncertain; single-hospital source of cost data
ICER	4 yrs $57K/LY; $72K/QALY; 10 yrs $16K/LY	Influential: all-cause mortality ($26K/LY)	Micro-costed interventions; effectiveness, reduction in AAA-related mortality up to 4 yrs; 10-yr horizon in sensitivity analysis; use of acceptability curves in sensitivity analysis
ICER	$8,900/LY, screening for male relatives	No influential variables in univariate analyses	Not societal perspective; no health state utilities; all data based on Finnish experience; generalizability of effectiveness and cost data uncertain

effectiveness and/or cost data with an absence of most other favorable design characteristics—eg, no downstream costs, no health state utilities. No study (including MASS) was conducted from the societal perspective.

Each study considered population-based screening of adult males by ultrasonography compared with no screening, although screening protocols differed: MASS[6]—initial screen of men aged 65 to 74 with quarterly surveillance of 4.5 to 5.4 cm AAAs and annual surveillance of 3.0 to 4.4 cm AAAs; Frame, et al[8]—screening of men aged 60 to 80 by ultrasonography or physical examination with 1 follow-up at 5 years; and Lee, et al[7]—one-time "quick screen" by ultrasonography of men aged 70. The studies also used different time horizons (MASS[6]—4 years (trial length) and 10 years; Frame, et al[8]—20 years; Lee, et al[7]—lifetime). Over 4 years in the MASS[6] trial, AAA screening generated an "incremental" cost-effectiveness ratio (ICER) of $57,000/life-years (LY), $72,000/QALY (quality-adjusted life-years) relative to no screening. (It must be emphasized that these ratios are not truly "incremental" because no study compared population-based screening with targeted screening, a more meaningful comparison, but rather only to the absence of screening.)

When life savings were projected out 6 years for a total 10-year time horizon, the ICER for screening dropped to $16,000/LY (approximately $20,000/QALY). This latter estimate is similar to Lee, et al's baseline ICER for screening of $14,000/QALY.[7] However, Frame, et al[8] obtained a significantly higher ICER of $72,000/LY for one-time ultrasonography screening ($50,000/LY for physical exam plus ultrasonography for positives).

Each study used a different base case discount rate: MASS[6] (6% for costs, 1.5% for benefits); Frame, et al[8] (5%); and Lee, et al[7] (3%). The use of different discount rates in MASS[6] is not currently recommended practice, although proponents argue that it is appropriate if one believes that the value of health increases over time.[9] In any case, it introduces bias in favor of screening—ie, lower ICERs—by raising the value of benefits relative to costs. In a sensitivity analysis, MASS[6] applied a 3% discount rate to both costs and benefits, which raised the ICER for AAA screening over 4 years to approximately $62,000/LY ($78,000/QALY).

Next, we discuss aspects of each model that we believe influenced their specific results.

1. MASS[6]: This CEA included few details about the MASS effectiveness model; however, the MASS study itself (Ashton, et al[10]) was assigned a "good" quality rating based on USPSTF criteria (Harris, et al[11]) in our associated evidence synthesis (Fleming, et al[1]). Combined with satisfaction of other CEA quality criteria, we used this rating to support our assignment of a good quality rating to the MASS CEA. This model apparently considered reduction in the intermediate outcome of AAA-related mortality as the basis for effectiveness (odds ratio [OR], 0.58; 95% confidence interval [CI], 0.42–0.78), which was then expressed in terms of life-years-saved. The MASS trial did not show that screening reduced all-cause mortality (OR, 0.97; 95% CI, 0.93–1.02).[10] Avoiding death from one cause (eg, AAA) compared with avoiding death from another cause (eg, coronary heart disease) would be cogent only if a much greater disutility were attached to AAA-related mortality. There is no evidence supporting this assertion. Expressed in terms of mean survival time, free from AAA-related mortality at 4 years, screening resulted in an incremental gain of 0.16 to 1.47 days of life for each man screened.

These authors applied detailed micro-costing to both the screening process itself and the surgical procedures, and included downstream costs related to post-surgical life expectancy. This was also the only study of those we reviewed to use probabilistic sensitivity analysis. The authors also acknowledged that the focus of the MASS trial was AAA-specific mortality; univariate sensitivity analysis suggested that focusing on all-cause mortality would lower the ICER of screening by over half ($26,000/LY) relative to the 4-year estimate of $57,000/LY. The authors did not explain their calculations; we inferred that the lower ICER using all-cause mortality results from the greater absolute number of deaths prevented over the 4-year trial period (105 [all-cause mortality] vs 48 [AAA-specific mortality]).

2. Lee, et al[7]: The screening and management protocol in this model was reasonable based on recent trial results. The sources of key parameter estimates were not presented in the published article, although the authors offered to make them available to readers; we were unable to obtain this information from the authors. Life-expectancy was modeled using all-cause mortality over the individual's lifetime. In the base-case analysis, screening compared with no screening in a cohort of 70-year-old men generated an expected incremental gain of 0.059 QALY or 22 days for each man screened. Based on our systematic review, the risk for rupture for 3.0 to 4.0 cm (0.6% per year) and 4.0 to 5.0 cm AAAs (2.3% per year) appear to be overstated. For example, in the UKSAT and ADAM trials, the annual rupture risk for 4.0 to 5.4 cm AAAs was 0.6% and 1.0%, respectively. Also the distribution of AAA size in screened patients was significantly skewed toward larger size AAAs than found in population screening studies.[12] The analysis also appears to assume 100% compliance with screening, although this is not stated. Taken together, these factors create a bias favoring screening that may lead to overestimation of its effectiveness.

Micro-cost estimates for screening and treatment (from the health system perspective) came from a literature review and a single hospital (New York Presbyterian). Disease-specific long-term cost and quality-of-life estimates were included for renal failure, stroke, major amputation (related to diabetes), and myocardial infarction. Univariate sensitivity analyses were conducted focusing on AAA prevalence in the screened population, annual incidental detection rate in the unscreened group, and age at initial screening.

3. Frame, et al[8]: The Frame, et al model compared one-time screening with elective repair of AAAs ≥ 4.0 cm with a usual care approach involving elective repair of incidentally discovered AAAs and emergency repair of ruptured AAAs. At the time of its 1993 publication, ADAM and UKSAT trial results comparing immediate repair of 4.0 to 5.4 cm AAAs vs surveillance with delayed repair of AAAs expanding to 5.5 cm were not available.[12,14] In the ADAM and UKSAT trials, however, there were no significant differences in either AAA-related or all-cause mortality between patients undergoing immediate repair of 4.0 to 5.4 cm AAA vs patients undergoing surveillance with delayed repair of AAAs expanding to 5.5 cm. Taking this into account, the Frame, et al model would be comparable to clinical strategies used in the population-based AAA screening trials, except that 3.0 to 3.9 cm AAAs would receive no further follow-up. Life-expectancy was modeled using all-cause mortality over a 20-year time horizon for a cohort of 10,000 males aged 60 to 79 years, adjusted to match the age distribution of the U.S. population. Screening resulted in an incremental gain of 57 life years in a cohort of 10,000 men screened, or approximately 2 days' average improvement in life expectancy for each man. The authors conclude that screening was of small benefit.

Cost data came from a systematic review by the Canadian Task Force on the Periodic Health Examination, MEDLINE, and article bibliographies. Gross-cost values from the health system perspective for surgery, ultrasonography tests, and follow-up office visits were taken from earlier literature. This study's estimates of surgical costs ($46,000 for elective and $90,000 for emergency surgery in year 2003 dollars) were significantly larger than estimates in most subsequent studies. Downstream costs post-treatment were included. The only sensitivity analyses presented varied parameters simultaneously between their most and least favorable values for screening. Frame, et al[8] also found that for both screening protocols, a second screen 5 years after the first generated ICERs that were quite large ($1.5 million/LY relative to a single ultrasonography and $1.3 million/LY relative to abdominal palpation with an ultrasonography for positive results).

2. What is the cost-effectiveness of selectively screening adults at higher risk for rupture—eg, those with a family history of AAA, peripheral vascular disease, and tobacco use—compared with routine screening and usual care?

Two fair-quality studies, by Lee, et al[7] and Soisalon-Soininen, et al,[15] addressed the cost-effectiveness of selective screening for patients with higher rupture risk. Lee, et al[7] examined the effects

of age at initial screening and AAA prevalence at initial screening, which served as a proxy for specific risk factors: sex (7% males, 1% females, 4% females > age 60), circulatory disease (9%–12%), smoking history (17%), or family history of AAA (19%). Soisalon-Soininen, et al[15] examined selective screening of male relatives > age 50 of AAA patients. Life-expectancy was modeled using all-cause mortality over a 17-year time horizon. Both studies compared targeted screening with no screening; neither compared routine, but systematic, population-based screening with targeted screening.

Lee, et al[7] found that screening males beginning at age 60 (vs age 70 at baseline) lowers the ICER from $14,000/QALY to approximately $5,000/QALY. In generating the latter result, Lee, et al[7] maintained the baseline AAA prevalence estimate of 7%. By age 83, the ICER rises to $60,000/QALY. AAA prevalence at initial screening of 2% or higher generates an ICER of $10,000/QALY or below—eg, a 19% prevalence (proxy for family history of AAA) generates an ICER of $8,460/QALY. In Soisalon-Soininen, et al[15] screening male relatives > age 50 generates an ICER of $8,900/LY; note that their denominator does not include quality adjustments, so their ICER in terms of QALYs would be somewhat higher than reported. However, also note that Soisalon-Soininen et al's cohort is younger than Lee, et al's (age 50 vs 70), and has a much lower AAA prevalence than Lee et al's (8.2% based on their own data vs 19% from the literature). One might expect that using comparable ages would tend to widen the gap between the ICER estimates, but that using comparable prevalence values would tend to bring them closer together.

3. Among individuals with 3.0 to 5.4 cm AAAs on initial screening exam, what is the cost-effectiveness of periodic surveillance compared with one-time screening?

No identified study addressed the specific issue of periodic surveillance vs one-time screening.

4. Among individuals without AAA on initial screening exam, what is the cost-effectiveness of re-screening at varying intervals compared with one-time screening?

No identified study addressed the specific issue of targeting persons without AAA on initial screening for subsequent re-screening.

5. How will differences in treatment effectiveness affect cost-effectiveness estimates for AAA screening?

Only MASS[6] addressed differences in treatment effectiveness on the cost-effectiveness of AAA screening. MASS[6] focused on AAA-specific mortality—ie, "survival free from mortality related to abdominal aortic aneurysms for each individual up to 4 years," and including 30-day peri-operative mortality. In sensitivity analyses, the authors substituted all-cause mortality from the trial for AAA-related mortality, and found that the ICER for screening fell by roughly half ($26,000/LY). The authors acknowledged that the trial was not powered to detect changes in all-cause mortality, and the difference between screening and no screening for such mortality was not significant. Extending the time horizon from 4 to 10 years lowered the baseline ICER (again, in terms of AAA-specific mortality) from $57,000/LY to $16,000/LY.

Conclusions

Existing evidence—eg, MASS,[6] Lee, et al[7]—points to a cost-effectiveness ratio for population-based AAA screening (compared with no screening) that lies in the range of $14,000 to $20,000/QALY. The much higher ICER obtained by Frame, et al[8] is explained at least in part because of relatively higher surgical cost estimates, which are no longer appropriate. Applying current discounting practice to the MASS results would raise its estimated ICER above $20,000/QALY, although how much is uncertain. In any case, no study compared population-based screening with targeted screening, which would be a more appropriate comparison.

These results rely on the quality of the effectiveness estimates, which is an open question based on our associated systematic review. Each effectiveness model review showed, at best, modest

gains in life expectancy ranging from 2 days to 4 months favoring screening vs no screening, and immediate repair vs surveillance for moderate-sized AAAs. In each case, concerns regarding the structure or assumptions of the models indicate that even these modest gains may be overstated. Our assessment is supported by the results of clinical trials examining both screening and management of moderate-sized AAAs that show no differences in all-cause mortality.

In any case, current evidence addressing the cost-effectiveness of population-based AAA screening is extremely limited. Although more recent trial data on mass screening have been generated, to date only MASS has produced a CEA based on such data. Also, our evidence synthesis[1] concluded that evidence of the effectiveness of EVAR, especially over the longer term, did not yet exist; therefore, we chose early on to exclude EVAR from our review process. Evidence that addresses important economic dimensions of screening—eg, effectiveness (and appropriate targets) of selective screening, surveillance of small AAAs, re-screening of individuals without AAA, appropriate effectiveness measures—is nearly non-existent. The quality of cost data varies significantly. All analyses reviewed were conducted from the health system perspective. None considered patient-incurred burdens of time and money related to AAA screening and treatment. It is unknown whether their inclusion would alter policy implications about the cost-effectiveness of AAA screening, but valid measures of them would be helpful.

CEA of AAA screening would benefit considerably from more extensive sensitivity analyses. A general limitation across studies is a focus on univariate sensitivity analysis without consideration of plausible connections between parameters—eg, age and rupture risk. MASS[6] provides a framework for the future application of probabilistic sensitivity analysis, which could inform CEA users of the likely robustness of ICER estimates based on changes in AAA-related mortality.

Also, most studies took the design of the screening program as given, especially the screening interval. Future analyses should explore implications of variations in the interval of screening—eg, semi-annual vs annual vs bi-annual. Furthermore, as we have noted, comparisons were made between a screening program and usual care (no screening), which tends to bias results toward screening. In cases where a targeted screening program is of interest, it would be useful to compare the targeted program with a systematic population-based program as well as, or in lieu of, usual care.

In conclusion, currently available evidence suggests that population-based AAA screening may have the potential to produce a year of life at reasonable cost, but new CEAs based on recently completed screening trials are needed before formal policy recommendations will be appropriate.

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Appendix 1. Search Strategy

MEDLINE®, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database
Search dates: Publication date between January 1994 and April 2004

1. Aortic Aneurysm, Abdominal
2. (aortic and aneurysm$ and abdom$).ti,ab
3. 1 or 2
4. Economics
5. Economics, Nursing
6. Economics, Pharmaceutical
7. ec.fs.
8. (econom$ or cost or costs or costing or pharmacoeconomic$).ti,ab.
9. (expenditure$ not energy).ti,ab
10. "costs and cost analysis"/ or cost allocation/ or cost-benefit analysis/ or cost control/ or cost savings/ or cost of illness/ or cost sharing/ or "deductibles and coinsurance"/ or medical savings accounts/ or health care costs/ or direct service costs/ or drug costs/ or employer health costs/ or hospital costs/ or health expenditures/ or capital expenditures
11. economics, hospital/ or hospital charges/ or hospital costs
12. economics, medical/ or fees, medical
13. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
14. 3 and 13
15. limit 14 to English language

Appendix 2. Fatal Flaws

Fatal Flaws:

1) "General" or "Methodological"—any single flaw is fatal
   - a) No (incremental) comparison of costs and benefits
   - b) No sensitivity analysis
   - c) Focus on intermediate outcomes, rather than final health outcomes
   - d) Inappropriate focus on short-term outcomes only
2) "Topic-specific"—evaluated in the context of other analysis characteristics
   - a) Exclusion of relevant cost category
   - b) Inappropriate cost sources and/or measurement
   - c) Exclusion of important harms
   - d) Inappropriate interventions and/or populations
   - e) Inappropriate comparators—eg, comparing only with usual care (or doing nothing) when a current alternative is well known to be more cost-effective than usual care
   - f) Inappropriate time horizon
   - g) Not conducted from a societal perspective and not representing a valid perspective clinically relevant to the topic
   - h) Not using best evidence to estimate effectiveness
   - i) Not capturing important utilities or preferences in effect measures
   - j) No discount rate or different discount rates for costs and health benefits

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