

Screening for Abdominal Aortic Aneurysm: A Best-Evidence Systematic Review for the U.S. Preventive Services Task Force

Craig Fleming, MD; Evelyn P. Whitlock, MD, MPH; Tracy L. Beil, MS; Frank A. Lederle, MD

An abdominal aortic aneurysm (AAA) occurs when the aorta below the renal arteries expands to a maximal diameter of 3.0 cm or greater. Abdominal aortic aneurysms are found in 4% to 8% of older men and 0.5% to 1.5% of older women.¹⁻⁵ Age, smoking, sex, and family history are the most significant AAA risk factors.¹ Aortic aneurysms account for about 15 000 deaths in the United States annually; of these, 9000 are AAA-related and the remainder are due to thoracic aortic aneurysms.^{6,7} Most AAA deaths occur in men 65 years of age and older.^{8,9}

Although AAAs may be asymptomatic for years, as many as 1 in 3 eventually rupture if left untreated.¹⁰ The prognosis for ruptured AAAs is grim. Since most patients with ruptured AAAs die out of the hospital or before surgery,¹¹ and since the operative mortality rate for emergent AAA repair is high,¹² only 10% to 25% of individuals with ruptured AAAs survive until hospital discharge.

Ultrasonography of the abdomen is accurate^{13,14} and reliable¹⁵ in detecting AAAs. Survival after elective surgical repair approaches that of the

general population.¹⁶ Elective AAA repair, however, may result in significant harms, such as operative mortality, myocardial infarction, respiratory and renal failure, and changes in functional status.^{17,18} In its 1996 recommendation, the U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to recommend for or against routine AAA screening of asymptomatic adults. The Task Force cited the need for data from population-based screening trials to determine whether the potential benefit from preventing ruptured AAAs justified the potential risks from increased surgery.¹⁹

Since 1996, results from 4 population-based randomized, controlled trials of AAA screening have been published.^{5,9,20-23} On the basis of this new evidence, the USPSTF sought to update its 1996 recommendation by reassessing the benefits and harms of population-based AAA screening. This systematic review was performed by investigators from the Oregon Evidence-based Practice Center, Portland, Oregon, in collaboration with the USPSTF and the Agency for Healthcare Research and Quality (AHRQ), Rockville, Maryland.

From the Oregon Evidence-based Practice Center and Center for Health Research, Kaiser Permanente (Fleming, Whitlock, Beil, Lederle), Portland, Oregon; and the Center for Epidemiological and Clinical Research, Veterans Affairs Medical Center (Lederle), Minneapolis, Minnesota.

This study was conducted by the Oregon Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ) Contract #290-02-0024, Task Order Number 2, Rockville, MD.

Address correspondence to Craig Fleming, MD, Center for Health Research, Kaiser Permanente, Northwest, 3800 North Interstate Avenue, Portland, OR 97227. E-mail: Craig.Fleming@kp.org.

Reprints are available from the AHRQ Web site (www.preventiveservices.ahrq.gov). Print copies of this article, along with other USPSTF summaries of evidence and recommendation statements, are available in print from the AHRQ Publications Clearinghouse (call 1-800-358-9295, or e-mail ahrqpubs@ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse™ (www.guideline.gov).

This first appeared in *Ann Intern Med.* 2005;142:203-211.

The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of AHRQ or the U.S. Department of Health and Human Services.

Descriptions of the analytic framework, key questions, literature search, inclusion criteria, data extraction methods, quality rating, and trial flow diagram are provided in the Appendix, Appendix Figures 1 and 2, and the Appendix Table.

The evidence review focused on the following key questions: 1a) Does AAA screening, in an asymptomatic average-risk or high-risk population, reduce AAA-related adverse health outcomes? 1b) For individuals who do not have AAAs on initial screening, does periodic repeated screening reduce AAA-related adverse health outcomes? 2) What are the harms associated with AAA screening? 3) For AAAs 3.0 to 5.4 cm detected through screening, does immediate repair or surveillance reduce AAA-related adverse health outcomes? 4) What are the harms associated with repair of AAAs 5.5 cm or greater? 5) What are the harms associated with immediate repair or surveillance of AAAs 3.0 to 5.4 cm?

This article focuses only on key questions 1a, 1b, 2, and 4, which are most relevant to determining the net benefit (benefit minus harms) of population-based screening for AAA. Key questions 3 and 5 address management strategies for AAAs 3.0 to 5.4 cm, which are at much lower risk for rupture than larger AAAs.^{24,25} A review of key questions 3 and 5 are in our full systematic evidence synthesis (available at www.preventiveservices.ahrq.gov).

Methods

We performed this review on the basis of methods previously established by the USPSTF.²⁶ We initially developed an analytic framework and key questions, in conjunction with USPSTF liaisons, to define the strategy used to perform this systematic review. Since direct evidence regarding population-based screening from randomized, controlled trials was available, we did not explicitly review the accuracy and reliability of ultrasonography in population-based AAA screening. The sensitivity of ultrasound scanning for an AAA is 95%, and the specificity approaches 100%; the examination is safe and reliable.^{14,15,27,28} Limited ultrasonography for AAA screening can be performed in less than 10 minutes.²⁹

To identify relevant studies, we searched MEDLINE® (January 1994 through July 2004), the Cochrane Database of Systematic Reviews (2004, Issue 1), and the Cochrane Controlled Trials Register (January 1994 through May 2004). Literature search strategies are summarized in the Appendix. We identified additional studies from the reference lists of retrieved articles, periodic hand searches of relevant journals, and suggestions from experts.

To evaluate the effectiveness of AAA screening (key question 1a), we searched for randomized, controlled trials of population-based screening for AAA. To evaluate the benefit of periodic repeated screening after a normal scan (key question 1b), we identified cohort or follow-up studies of patients without AAAs identified in population screening studies. To evaluate the potential harms associated with AAA screening and treatment (key questions 2 and 4), we examined data from the trials of population screening and searched for other relevant retrospective or prospective cohort studies.

Two authors reviewed 271 abstracts and 26 articles using defined inclusion criteria and abstracted relevant information about the population, setting, interventions, and outcomes of each included trial of screening and harms (see the Appendix and Appendix Figure 2, for inclusion criteria and the trial flow diagram). Predefined criteria from the USPSTF were used to assess the internal validity of each population-based screening trial and to assign quality ratings of “good,” “fair,” or “poor.”²⁶ We did not assign quality ratings for studies of repeated screening or harms of screening and treatment.

We used published data from the trials of population-based AAA screening to calculate estimates of unadjusted odds ratios (ORs) and 95% CIs for AAA-related mortality and all-cause mortality. We performed meta-analyses to calculate summary estimates for AAA-related mortality and all-cause mortality using the DerSimonian and Laird random-effects model.³⁰ When no heterogeneity is present, the DerSimonian and Laird random-effects estimate is identical to the fixed-effects estimate. We deemed the random-effects

model to be more appropriate than a fixed-effects model because the included studies differed in characteristics such as population, starting and stopping ages for screening, outcomes ascertainment, and duration of follow-up.³¹ We used graphs of trial outcomes and the Mantel-Haenszel chi-square test to assess heterogeneity. We used RevMan software (Reviewer Manager Version 4.2.2, 2003, The Cochrane Collaboration, Oxford, United Kingdom) to perform all statistical analyses.

We modeled the impact of screening on AAA-related mortality over 5 years for 100 000 U.S. men age 65 to 74 years. We also examined how the modeled impact of screening would differ in those with a history of smoking and those who had never smoked within this same sample. This article is based on a full evidence synthesis, which is available at www.preventiveservices.ahrq.gov.

Role of the Funding Source

This research was funded by AHRQ under a contract to support the work of the USPSTF. Agency staff and Task Force members participated in the initial design of the study and reviewed interim analyses and the final manuscript. The full evidence report was distributed for review to content experts and was revised accordingly. Agency approval was required before this manuscript could be submitted for publication, but the authors are solely responsible for its content and the decision to submit it.

Data Synthesis

Trial Characteristics

We identified 4 randomized, controlled trials that evaluated population-based screening for AAA: the Multicentre Aneurysm Screening Study (MASS) from the United Kingdom;²² the Chichester, United Kingdom, screening study;^{5,9,20} the Viborg County, Denmark, screening study;²¹ and the Western Australia screening study.^{23,32,33} Table 1 shows the characteristics of the 4 screening trials. All trials identified potential participants age 65 years or older at average risk for AAA through population registries or regional health directories. The 4 trials

included more than 125 000 total participants. Different stopping ages were used for each trial and ranged from 73 years to 83 years. No data were provided on race or ethnicity. Only the Chichester trial included women.

In MASS and in the Chichester and Western Australia trials, participants were excluded before randomization if they resided in nursing homes. In MASS and in the Chichester trial, participants were also excluded before, and without knowledge of, randomization if their primary physician deemed them unfit for elective AAA repair. Participants were then randomly assigned to an intervention group that received an invitation to attend screening or to a control group that received “usual care.” All control group participants were followed passively and without contact. Across the 4 trials, 63% to 80% of invited participants attended ultrasound scanning. On an intention-to-treat basis, those who were invited to screening but did not attend were also included in the analysis.

In MASS and in the Chichester and Viborg County trials, patients with AAAs exceeding a threshold size of 5.0 to 6.0 cm on initial measurement were referred to a vascular surgeon. Patients with smaller AAAs periodically underwent repeated scanning and were referred to a vascular surgeon for AAAs that had expanded to or above the threshold size. In MASS and in the Chichester trial, patients were also referred if the AAA expanded rapidly (≥ 1.0 cm in 1 year) or became symptomatic. Participants with normal-size aortas (< 3.0 cm) on the initial scan received no further follow-up. In MASS, 31 of 322 patients in the invited group who had elective AAA repairs (9.6%) did not meet trial criteria for referral on the basis of AAA size. Crossover data were not available for other trials.

In the Western Australia trial, each patient attending screening received a letter with his results, as well as a letter for his physician with results and management guidelines suggesting yearly rescanning for AAAs 3.0 to 3.9 cm, twice yearly scanning or vascular surgery referral for AAAs 4.0 to 4.9 cm, and vascular surgery referral for AAAs 5.0 cm or greater. For patients with AAAs 4.5 cm or greater, a letter was also mailed to

Table 1. Characteristics of Screening Trials for Abdominal Aortic Aneurysm*

Characteristic	MASS ²²	Western Australia Study ^{23,32}	Viborg County Study ²¹	Chichester Study, Men ²⁰	Chichester Study, Women ²⁰
Location	United Kingdom	Australia	Denmark	United Kingdom	United Kingdom
Age, y	65–74	65–83	65–73	65–80	65–80
Total patients randomly assigned to treatment, <i>n</i>	67 800	38 704	12 658	6433	9342
Mean follow-up, y	4.1	3.6†	5.1	2.5	2.6
Invited for screening, <i>n</i>	33 839	19 352	6339	3205	4682
Attended screening, %	80	63	69	73	65
Uninvited controls, <i>n</i>	33 961	19 352	6319	3228	4660
Outcomes ascertained, %	99	99‡	100	NR	NR
Quality	Good	Fair	Fair	Fair	Fair

* Values in superscript are reference numbers. All studies except the Chichester study included only men. MASS= Multicentre Aneurysm Screening Study; NR= not reported.

† Median follow-up.

‡ Provided by the study investigators.

the patient's personal physician. Subsequent examinations and vascular surgery referral were left to the discretion of the patient and his physician. The investigators had no further contact with participants in either the group invited to screening, regardless of whether they were scanned, or the control group.

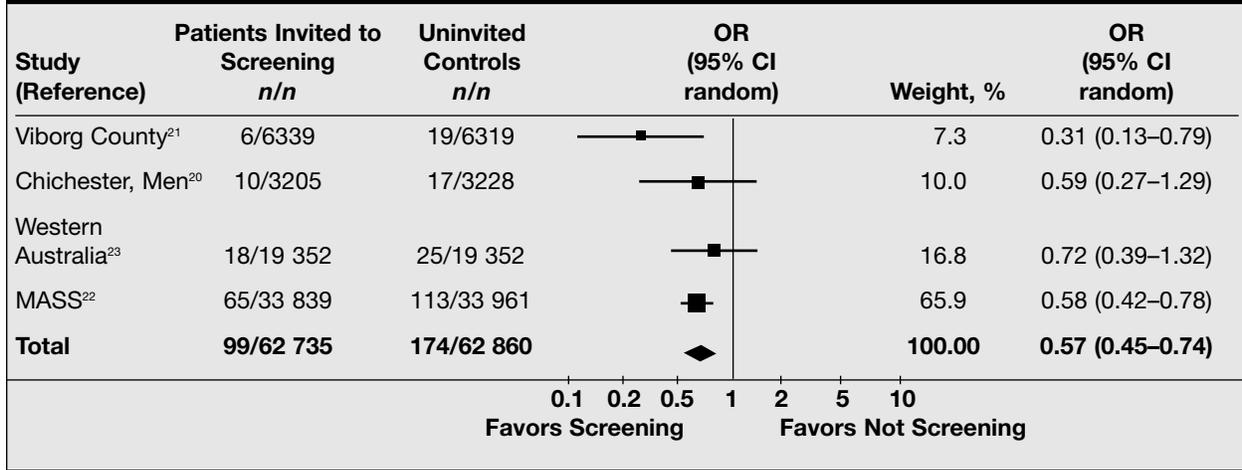
All 4 trials were rated as good or fair quality according to the USPSTF rating criteria (see Appendix).²⁶ We considered outcomes at 4 to 5 years of follow-up for all included trials. While the Chichester trial also reported outcomes for 10 years of follow-up,⁵ we did not include these data because the number of patients differed from the number of patients reportedly randomized in the paper detailing the 5-year results.²⁰

AAA Screening in Men

The results of the 4 AAA screening trials are shown in Figure 1 and Figure 2. All trials had ORs

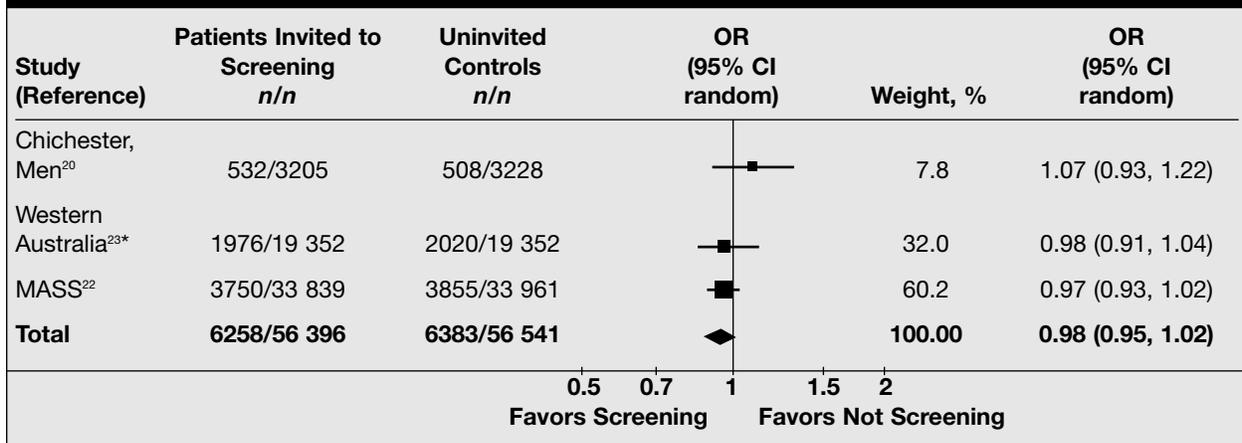
favoring an association between an invitation to attend screening and a reduction in AAA-related deaths. The association was significant in MASS (OR, 0.58 [95% CI, 0.42 to 0.78]) and in the Viborg County study (OR, 0.31 [CI, 0.13 to 0.79]). We examined the impact of an invitation to attend screening on AAA-related mortality for men by pooling trial results using meta-analysis (Figure 1). The pooled OR showed a reduction in AAA-related mortality favoring screening (OR, 0.57 [CI, 0.45 to 0.74]). The Multicentre Aneurysm Screening Study, the largest of the trials and the trial with the narrowest CI, contributed the most weight to the pooled OR. In sensitivity analyses, removing any of the other 3 studies, separately or in combination, had very little impact on the pooled OR and CI. When MASS was removed from the meta-analysis, however, the pooled meta-analysis based on the other 3 studies still showed a significant reduction in AAA-related mortality (OR, 0.56 [CI, 0.36 to 0.88]).

Figure 1. Meta-Analysis of Mortality Associated with Abdominal Aortic Aneurysms in the Abdominal Aortic Aneurysm Screening Trials



MASS= Multicentre Aneurysm Screening Study; OR= odds ratio.

Figure 2. Meta-Analysis of All-Cause Mortality in the Abdominal Aortic Aneurysm Screening Trials



MASS= Multicentre Aneurysm Screening Study; OR= odds ratio.

* Age-standardized numbers were used for the Western Australia trial because of an early age imbalance that was subsequently corrected.

Reference: Norman PE, Le M, Jamrozik K. Re: Questions about AAA screening trial. *BMJ Online Rapid Responses* 9 December, 2004. Accessed at www.bmj.com on 14 December 2004.

All-cause mortality results for men were available for MASS and for the Western Australia and Chichester trials (Figure 2). When the results of the 3 trials were pooled, an invitation to attend

screening was associated with a nonsignificant reduction in all-cause mortality (OR, 0.98 [CI, 0.95 to 1.02]).

AAA Screening in Women

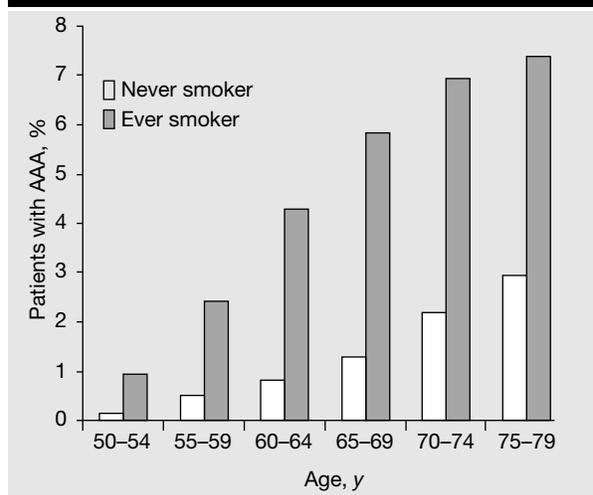
The Chichester trial included 9342 women age 65 to 80 years who were randomly assigned to either an invitation-to-screening group or a control group (Table 1).²⁰ Sixty-five percent of women attended screening, compared with 73% of men ($P<0.001$). The AAA prevalence in women was 1.3%, compared with 7.6% in men. At 5 years of follow-up, there were no differences between women invited for screening and the control group in either AAA-related mortality (OR, 1.0 [CI, 0.14 to 7.07]) or all-cause mortality (OR, 1.05 [CI, 0.92 to 1.19]). At 10 years, the incidence of AAA rupture was the same for women in the screening and control groups.⁹

AAA Screening in High-Risk Populations

Age is a significant AAA risk factor. The odds ratio of finding an AAA of at least 4.0 cm, adjusted for other risk factors, increases by 1.71 (CI, 1.61 to 1.82) for each 7-year age interval.¹ The Western Australia trial was the only study reporting AAA-related mortality for different age groups. Overall, there was no significant difference in AAA-related mortality between those invited to screening and uninvited controls (OR, 0.72 [CI, 0.39 to 1.32]) (Figure 1). In a post hoc analysis, an invitation to screening was associated with a significant reduction in AAA-related mortality for men age 65 to 75 years (OR, 0.19 [CI, 0.04 to 0.89]) and a trend toward increased mortality in older men.

Smoking history has been suggested as a possible criterion for selective AAA screening.³⁴ A history of smoking has been associated with a 3- to 5-fold increase in AAA prevalence across all age groups and an increased risk for AAA-related mortality.^{35,36} Figure 3 shows the prevalence of AAAs 3.0 cm or larger in ever smokers and never smokers by age. Data were provided by 1 of the authors on the basis of a screening trial in 126 696 U.S. veterans.¹ Prevalence of AAAs increases more rapidly with age for ever smokers compared with never smokers ($P=0.004$). Among never smokers, the prevalence of AAAs 4.0 cm or larger, which are associated with a

Figure 3. Prevalence of Abdominal Aortic Aneurysms (AAAs) Greater Than 3.0 cm, According to Age and Smoking History



greater risk for rupture if not detected, is less than 1% for all ages.³⁵

To examine selective screening, we modeled the impact of an invitation to attend screening, based on smoking status, in a hypothetical cohort of 100 000 U.S. men age 65 to 74 years and extrapolated these results to the U.S. population of men in the same age group³⁷ (Table 2). Approximately 69% of men in the United States who are 65 to 74 years of age have a history of smoking, defined as lifetime consumption of more than 100 cigarettes.³⁸ The model estimates that inviting only those 69% of men with a history of smoking to attend screening would account for 89% of the expected reduction in AAA-related mortality from population-based screening of all men 65 to 74 years of age. Selective screening for AAAs only in current smokers, and not former smokers, is too restrictive, since most AAAs would be missed.³⁹

After adjustment for other risk factors, significant risk factors for AAAs of 4.0 cm or greater also include family history (OR, 1.94 [CI, 1.63 to 2.32]), coronary artery disease (OR, 1.52 [CI, 1.37 to 1.68]), hypercholesterolemia (OR, 1.44 [CI, 1.27 to 1.63]), and cerebrovascular disease (OR, 1.28 [CI, 1.11 to 1.47]). Risk for AAA is significantly lower for black persons (OR, 0.53 [CI, 0.40 to 0.69]) and patients with diabetes (OR, 0.52 [CI,

Table 2. Five-Year Outcomes of Abdominal Aortic Aneurysm Screening by Smoking History in a Cohort of 100 000 Men 65 to 74 Years of Age*

Variable Assumptions	Ever Smokers	Never Smokers	Total Cohort
History of smoking, %	-	-	69
AAA prevalence in men age 65–74 y, %			
Ever smokers	-	-	6.4
Never smokers	-	-	1.8
AAA-related deaths per 1000 person-years in uninvited controls	-	-	0.72
OR reduction in AAA-related death with screening	-	-	0.57
U.S. male population age 65–74 y (millions), <i>n</i>	-	-	8.3
Results			
AAAs in cohort, <i>n</i>	4416	558	4974
AAA-related deaths, <i>n</i>			
No screening	320	40	360
Invited for screening	182	23	205
AAA deaths prevented, <i>n</i>	138	17	155
Estimated 5-year AAA-related deaths in the U.S. male population age 65–74 y, <i>n</i>			
Not screened	26 521	3351	29 872
Invited for screening	15 129	1912	17 041
AAA deaths prevented by screening, <i>n</i>	11 392	1439	12 831
AAA-attributable deaths, %	89	11	-

* AAA= abdominal aortic aneurysm; OR= odds ratio. Approximately 69% of men in the United States age 65 to 74 years have a history of smoking (ever smokers), defined as lifetime consumption of more than 100 cigarettes.³⁸ One of the study authors provided the prevalence of AAAs in men age 65 to 74 years from a screening study of 126 696 U.S. veterans.¹ We estimated AAA-related deaths per 1000 person-years in uninvited controls by summing the number of AAA-related deaths in the control groups across the 4 trials (Figure 1) and dividing by the product of the number of control group participants multiplied by the mean follow-up for each trial in years (Table 1). We apportioned the expected number of AAA-related deaths without screening in ever smokers and never smokers on the basis of the relative prevalence of AAAs in each group. To model screening benefits, we used the pooled OR 0.57 for reduction of AAA-related mortality from the meta-analysis (Figure 1). We assumed that the screening attendance rate, operative mortality, and other factors were similar to those in the screening trials and that ever smokers and never smokers would receive equal benefit in reduction of AAA-specific mortality if invited to attend screening. The estimated number of men age 65 to 74 years in the U.S. population was obtained from U.S. Census data for the year 2000.³⁷ The Appendix Table shows the formulas used for calculations. The following caveats apply to these estimates:

- 1) In the veterans screening study cohort, 74% of veterans age 65 to 74 years had a history of smoking compared with 69% in the general population. As a result, the overall prevalence of AAAs in this cohort may also be higher than in the general population.
- 2) The key variable in this model is the relative prevalence of AAAs in ever smokers versus never smokers, which is determined by the relative burden of other AAA risk factors in each group. This model assumes that the burden of AAA-risk factors in the general population would not be greater in never smokers in relation to ever smokers than that seen in the veterans screening cohort.
- 3) This model assumes that the age-specific AAA-related mortality rate is similar for never smokers compared with ever smokers. This assumption appears to be conservative, since the prevalence of AAAs at a specific age is greater in ever smokers versus never smokers (Figure 2).
- 4) Since racial and ethnic data were not reported for the AAA screening trials, we cannot be sure that the AAA-related mortality reduction attributable to screening from the 4 screening trials would be applicable if applied to the racial and ethnic mix of the U.S. population.

0.45 to 0.61]).¹ However, although such risk factors may be important in managing individual patients, population screening strategies based on these factors have not been shown to perform better than strategies using age, sex, and smoking history in selecting high-risk populations for screening.^{29,39}

Repeated Screening for AAA after Negative Results on Ultrasonography

We identified 4 cohort studies of periodic repeated screening for AAA following negative results on ultrasonography. As part of a population screening program in Gloucestershire, United Kingdom, all men were offered ultrasonography at age 65 years.⁴⁰ A cohort of 223 men 65 years of age with no AAAs on initial ultrasonography had repeated ultrasonography at 5 and 12 years. Eight men were lost to follow-up, and 86 men died of causes unrelated to AAAs. None of the remaining 129 men experienced a clinically significant increase in aortic diameter over 12 years. Chichester study investigators prospectively followed 1011 men with aortic diameters less than 3.0 cm on initial screening at age 65 years.⁸ Over 10 years of follow-up, the incident rate for new AAAs was 4%. None of the new AAAs exceeded 4.0 cm in diameter. Since rupture is rare in AAAs less than 4.0 cm, and since the men in the cohort were in their mid- to late 70s at the time of follow-up, such aneurysms would probably not become clinically significant in their lifetimes. Another study from the United Kingdom⁴¹ and the Veterans Affairs Aneurysm Detection and Management (ADAM) study⁴² reported similar findings over shorter time periods.

Harms Associated with AAA Screening

No physical harms are known to arise from the use of ultrasonography in adults.²⁷ On the basis of surveys conducted by MASS trial investigators,²² invited participants with positive ultrasonography results initially had slightly more anxiety, lower Short Form-36 mental and physical health scores, and lower self-rated health status than did those with negative results. These differences, however,

were no longer apparent after 6 weeks, and all results fell within population norms. On the basis of surveys from the Viborg County trial,²¹ participants with AAAs 3.0 cm or greater showed small but significant decreases in 1-month survey measures of general health perception and self-estimated quality of life compared with noninvited controls. Another study examined psychological outcomes in 100 men with normal aortas and 61 men with AAAs participating in an aneurysm-screening program in Gloucestershire, United Kingdom.⁴³ No differences were found in general health measures or anxiety levels between men with normal aortas and those with aneurysms before or after screening.

Harms Associated with AAA Repair

On the basis of an analysis of discharge data from a large U.S. hospital sample, the overall in-hospital mortality rate for elective AAA repair was 4.2%, with a complication rate of 32.4%.¹⁷ Complications include myocardial infarction, respiratory failure, renal failure, ischemic colitis, spinal cord ischemia, and prosthetic graft infection. Cardiac complications are most common, occurring in approximately 11% of patients.⁴⁴

The risk for death and complications from elective AAA repair increases with age. In a retrospective study of data from a large U.S. hospital database, after adjustment for sex, ethnicity, age, comorbid conditions, and hospital size, the OR for in-hospital death was 1.8 (CI, 1.4 to 2.3) for patients 70 to 79 years of age and 3.8 (CI, 2.9 to 4.9) for those 80 years of age and older compared with patients 60 to 69 years of age.¹⁷

Operative mortality for AAA repair also varies with hospital volume, surgical specialty, and surgeon volume. In a retrospective study using the same U.S. hospital database, in-hospital mortality after AAA repair was 4.2% overall after adjustment for age, sex, case mix, and urgency of the procedure.⁴⁵ In hospitals performing more than 35 AAA repairs per year, the mortality rate was 3.0%, compared with 5.5% at hospitals performing fewer than 35 procedures per year ($P < 0.001$). Lower mortality rates were associated with operations performed by

vascular surgeons (2.2%) compared with cardiac surgeons (4.0%) and general surgeons (5.5%) ($P < 0.001$). Similar results have been reported in studies of other large Canadian and U.S. hospital databases.^{46,47}

Discussion

On the basis of our systematic review and meta-analyses, an invitation to attend AAA screening may reduce AAA-related mortality by 43% in men age 65 to 75 years. The Western Australia screening study also included patients 75 to 83 years of age. In a post hoc analysis, a significant reduction of AAA-related mortality from screening was seen in men 65 to 74 years of age but not in older men. The absolute risk reduction for AAA-related deaths over 4 to 5 years ranged from 3.6 per 10 000 in the Western Australia trial to 21 per 10 000 in the Chichester and Viborg County trials. It is important to note that these estimates pertain to screening in populations and not to screening for individuals.

An invitation to screening did not appear to reduce all-cause mortality. This result is not unexpected, since AAA-related mortality accounts for only a small proportion of all deaths in older men. In MASS, for example, AAA-related mortality, including operative mortality for elective and emergency surgical repair, was the attributed cause of death in 2% of those invited to screening versus 3% of controls. As is true in screening for other diseases, the influence of competing causes of death makes it difficult to detect changes in all-cause mortality; to do so, substantially larger trials would be required.⁴⁸

Only the Chichester trial included women and showed no significant benefit of screening in reducing AAA-related mortality. An adequately powered trial of population-based screening for AAA, while desirable, would be challenging to perform. Abdominal aortic aneurysms are much less prevalent in women overall, occur on average 10 years later than in men, and are most likely to rupture after 80 years of age.⁹ While screening has been recommended for women older than 65 years of age with cardiac risk factors,⁴⁹ we found no controlled studies that support this recommendation.

After adjustment for other risk factors, a history of smoking is associated with a 5-fold increase in AAA risk.¹ Using a model of AAA screening in 65- to 74-year-old men, we estimated that 89% of AAA-related deaths prevented would be attributable to screening in 69% of those men with any history of smoking during their lifetime. Neither a current history of smoking nor consideration of other AAA risk factors appears to be more accurate than age, sex, and lifetime smoking history in selecting a high-risk screening population.

After at least 10 years of follow-up, periodic ultrasonography in men who had normal ultrasonography results at age 65 years found that the incidence of new AAAs was low. When AAAs were found, they were less than 4.0 cm and therefore were not likely to present a significant risk for rupture. On the basis of these findings, it appears unlikely that repeated screening of asymptomatic average-risk men older than age 65 years would be beneficial.

No significant physical harms were associated with ultrasonography screening. Changes in self-reported psychological and general health perception in those found to have AAA and those with normal results on ultrasonography were generally mild and did not persist over time. Our review of harms indicates that elective AAA repair may result in significant mortality and morbidity. The risk for death and complications increased with age and preoperative comorbid conditions. More favorable outcomes were seen when experienced vascular surgeons in high-volume hospitals performed the surgery.

Several limitations should be considered when interpreting our results. Because of the potential for misclassification of the cause of death from death certificates, the results of screening trials may be biased in favor of screening if deaths from disease, treatment, or screening among those screened are falsely attributed to other causes, that is, the so-called “slippery linkage” bias.⁵⁰ Data on causes of death from MASS argue against this; deaths from ischemic heart disease decreased slightly in those invited to screening compared with uninvited controls, while cancer-related deaths, which would

not be attributable to AAA screening or treatment, increased slightly.

Potential confounding of screening trial results may also have occurred because of improved management of cardiovascular risk factors in those invited to screening. In MASS, for example, those attending screening may have benefited from improved treatment of hypertension because blood pressure was measured at the screening visit and was reported to the general practitioner.³⁴ Hypertension treatment, however, is more effective in reducing stroke risk than in reducing coronary artery disease risk.⁵¹ In MASS, the percentage of deaths from ischemic heart disease was slightly lower in those invited to screening, but the percentage of deaths from strokes was the same in both groups, suggesting that improved hypertension treatment did not influence trial outcomes.

There were important differences in the design of the 4 population screening trials. The outcomes of the Viborg County study, in particular, were ascertained by using only hospital records, so an unknown number of AAA-related outcomes deaths occurring out of the hospital would have been missed. In the Western Australia study, patients found to have AAAs at screening were referred to their primary physicians for subsequent evaluation and management. In MASS and in the Viborg County and Chichester trials, follow-up scanning was performed periodically by study personnel. These factors had little impact on the meta-analysis of AAA-related mortality, however, because the pooled effect size was primarily determined by the MASS results.

Since all 4 AAA screening trials were conducted outside the United States and no data were provided on the race and ethnicity of the participants, the extent to which these findings can be generalized to the U.S. population is not clear. At this time, it is unlikely that a population-based trial would be performed in the United States, particularly given the strength of the evidence favoring screening in the trials reviewed here. We believe that these studies provide the best evidence available to support recommendations for AAA screening in the United States.

Finally, as previously noted, estimates of absolute risk reduction from the 4 trials are based on screening for AAA in populations and do not apply to screening of particular individuals. These population-based estimates incorporate variability in factors such as rate of participation in screening, accuracy and reliability of ultrasonography, selection factors in those who did and did not attend screening, and rates of operative mortality and complications. In shared decision making, estimating a patient's absolute risk for AAA depends on a variety of factors, such as age, sex, smoking history, family history, and cardiovascular risk factors, as well as the patient's willingness to accept the potential harms of screening and treatment if an AAA is found.

On the basis of our review, we conclude that population screening for AAA in men age 65 to 74 years appears to reduce deaths from AAA. Treatment is associated with significant risks for operative death and complications. These risks, however, may be acceptable to men with AAAs greater than 5.5 cm, which are most prone to rupture.

Acknowledgments

The authors thank Daphne Plaut, MLS, Paula Smith, RN, BSN, Rochelle Fu, PhD, and the reviewers of the full evidence synthesis for their contributions to this project. Ned Calonge, MD, MPH, Russ Harris, MD, MPH, Mark Johnson, MD, MPH, Diana Petitti, MD, MPH, and Steven Teutsch, MD, MPH, provided critical oversight and assistance for the USPSTF.

References

1. Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, et al. The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. *Arch Intern Med.* 2000;160:1425–30. [PMID: 10826454]
2. Lederle FA, Johnson GR, Wilson SE. Abdominal aortic aneurysm in women. *J Vasc Surg.* 2001;34:122–6. [PMID: 11436084]

3. Lindholt JS, Henneberg EW, Fasting H, Juul S. Hospital based screening of 65–73 year old men for abdominal aortic aneurysms in the county of Viborg, Denmark. *J Med Screen.* 1996;3:43–6. [PMID: 8861051]
4. Norman PE, Jamrozik K, Lawrence-Brown MM, Dickinson JA. Western Australian randomized controlled trial of screening for abdominal aortic aneurysm [Abstract]. *Br J Surg.* 2003;90:492.
5. Vardulaki KA, Walker NM, Couto E, Day NE, Thompson SG, Ashton HA, 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. [PMID: 12081734]
6. Table 1. Deaths, percent of total deaths, and death rates for the 10 leading causes of death in selected age groups, by race and sex: United States, 2000. National Center for Health Statistics. National Vital Statistics Report. 2002. Accessed at www.cdc.gov/nchs/fastats/pdf/nvsr50_16t1.pdf on 15 November 2004.
7. Gillum RF. Epidemiology of aortic aneurysm in the United States. *J Clin Epidemiol.* 1995;48:1289–98. [PMID: 7490591]
8. Scott RA, Vardulaki KA, Walker NM, Day NE, Duffy SW, Ashton HA. 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. [PMID: 11397028]
9. Scott RA, Bridgewater SG, Ashton HA. Randomized clinical trial of screening for abdominal aortic aneurysm in women. *Br J Surg.* 2002;89:283–5. [PMID: 11872050]
10. Darling RC, Messina CR, Brewster DC, Ottinger LW. Autopsy study of unoperated abdominal aortic aneurysms. The case for early resection. *Circulation.* 1977;56:II161–4. [PMID: 884821]
11. Adam DJ, Mohan IV, Stuart WP, Bain M, Bradbury AW. Community and hospital outcome from ruptured abdominal aortic aneurysm within the catchment area of a regional vascular surgical service. *J Vasc Surg.* 1999;30:922–8. [PMID: 10550191]
12. Bown MJ, Sutton AJ, Bell PR, Sayers RD. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg.* 2002;89:714–30. [PMID: 12027981]
13. Nusbaum JW, Freimanis AK, Thomford NR. Echography in the diagnosis of abdominal aortic aneurysm. *Arch Surg.* 1971;102:385–8. [PMID: 5553311]
14. Wilmink AB, Forshaw M, Quick CR, Hubbard CS, Day NE. Accuracy of serial screening for abdominal aortic aneurysms by ultrasound. *J Med Screen.* 2002;9:125–7. [PMID: 12370324]
15. Wilmink AB, Hubbard CS, Quick CR. Quality of the measurement of the infrarenal aortic diameter by ultrasound. *J Med Screen.* 1997;4:49–53. [PMID: 9200064]
16. Lederle FA, Walker JM, Reinke DB. Selective screening for abdominal aortic aneurysms with physical examination and ultrasound. *Arch Intern Med.* 1988;148:1753–6. [PMID: 3041938]
17. Huber TS, Wang JG, Derrow AE, Dame DA, Ozaki CK, Zelenock GB, et al. Experience in the United States with intact abdominal aortic aneurysm repair. *J Vasc Surg.* 2001;33:304–10. [PMID: 11174782]
18. Williamson WK, Nicoloff AD, Taylor LM Jr, Moneta GL, Landry GJ, Porter JM. Functional outcome after open repair of abdominal aortic aneurysm. *J Vasc Surg.* 2001;33:913–20. [PMID: 11331828]
19. U.S. Preventive Services Task Force. Guide to Clinical Preventive Services. 2nd ed. Washington, DC: Office of Disease Prevention and Health Promotion; 1996.
20. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysms: 5-year results of a randomized controlled study. *Br J Surg.* 1995;82:1066–70. [PMID: 7648155]
21. Lindholt JS, Juul S, Fasting H, Henneberg EW. 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. [PMID: 11748949]
22. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, 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. [PMID: 12443589]

23. Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ*. 2004;329:1259. [PMID: 15545293]
24. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med*. 2002;346:1437–44. [PMID: 12000813]
25. 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. [PMID: 12000814]
26. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med*. 2001;20:21–35. [PMID: 11306229]
27. Barnett SB, Ter Haar GR, Ziskin MC, Rott HD, Duck FA, Maeda K. International recommendations and guidelines for the safe use of diagnostic ultrasound in medicine. *Ultrasound Med Biol*. 2000;26:355–66. [PMID: 10773365]
28. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Variability in measurement of abdominal aortic aneurysms. Abdominal Aortic Aneurysm Detection and Management Veterans Administration Cooperative Study Group. *J Vasc Surg*. 1995;21:945–52. [PMID: 7776474]
29. Lindholt JS, Henneberg EW, Fasting H, Juul S. Mass or high-risk screening for abdominal aortic aneurysm. *Br J Surg*. 1997;84:40–2. [PMID: 9043447]
30. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177–88. [PMID: 3802833]
31. Normand SL. Meta-analysis: formulating, evaluating, combining, and reporting. *Stat Med*. 1999;18:321–59. [PMID: 10070677]
32. Lawrence-Brown MM, Norman PE, Jamrozik K, Semmens JB, Donnelly NJ, Spencer C, et al. Initial results of ultrasound screening for aneurysm of the abdominal aorta in Western Australia: relevance for endoluminal treatment of aneurysm disease. *Cardiovasc Surg*. 2001;9:234–40. [PMID: 11336846]
33. Jamrozik K, Norman PE, Spencer CA, Parsons RW, Tuohy R, Lawrence-Brown MM, et al. Screening for abdominal aortic aneurysm: lessons from a population-based study. *Med J Aust*. 2000; 173:345–50. [PMID: 11062788]
34. Lederle FA. Ultrasonographic screening for abdominal aortic aneurysms. *Ann Intern Med*. 2003;139:516–22. [PMID: 13679330]
35. Lederle FA, Johnson GR, Wilson SE, Chute EP, Littooy FN, Bandyk D, et al. Prevalence and associations of abdominal aortic aneurysm detected through screening. Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. *Ann Intern Med*. 1997;126:441–9. [PMID: 9072929]
36. Lederle FA, Nelson DB, Joseph AM. Smokers' relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg*. 2003;38:329–34. [PMID: 12891116]
37. Age Groups and Sex: 2000. Summary File 1 100-Percent Data. U.S. Census. 2001. Accessed at www.factfinder.census.gov on 15 November 2004.
38. Schoenborn CA, Adams PF, Barnes PM, Vickerie JL, Schiller JS. Health behaviors of adults: United States, 1999–2001. National Center for Health Statistics. Companion Table 4.1. Vital Health Statistics. 2004;10(219). Accessed at http://www.cdc.gov/nchs/data/series/sr_10/sr10_219companion.pdf on 15 November 2004.
39. Spencer CA, Jamrozik K, Norman PE, Lawrence-Brown MM. The potential for a selective screening strategy for abdominal aortic aneurysm. *J Med Screen*. 2000;7:209–11. [PMID: 11202589]
40. Crow P, Shaw E, Earnshaw JJ, Poskitt KR, Whyman MR, Heather BP. 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. [PMID: 11442524]
41. Emerton ME, Shaw E, Poskitt K, Heather BP. Screening for abdominal aortic aneurysm: a single scan is enough. *Br J Surg*. 1994;81:1112–3. [PMID: 7953333]
42. Lederle FA, Johnson GR, Wilson SE, Littooy FN, Krupski WC, Bandyk D, 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. [PMID: 10789604]
43. Lucarotti ME, Heather BP, Shaw E, Poskitt KR. Psychological morbidity associated with abdominal aortic aneurysm screening. *Eur J Vasc Endovasc Surg.* 1997;14:499–501. [PMID: 9467527]
 44. Blankensteijn JD, Lindenburg FP, Van der Graaf Y, Eikelboom BC. Influence of study design on reported mortality and morbidity rates after abdominal aortic aneurysm repair. *Br J Surg.* 1998;85:1624–30. [PMID: 9876063]
 45. Dimick JB, Cowan JA Jr, Stanley JC, Henke PK, Pronovost PJ, Upchurch GR Jr. Surgeon specialty and provider volumes are related to outcome of intact abdominal aortic aneurysm repair in the United States. *J Vasc Surg.* 2003;38:739–44. [PMID: 14560223]
 46. Tu JV, Austin PC, Johnston KW. The influence of surgical specialty training on the outcomes of elective abdominal aortic aneurysm surgery. *J Vasc Surg.* 2001;33:447–52. [PMID: 11241111]
 47. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. *N Engl J Med.* 2003;349:2117–27. [PMID: 14645640]
 48. Juffs HG, Tannock IF. Screening trials are even more difficult than we thought they were [Editorial]. *J Natl Cancer Inst.* 2002;94:156–7. [PMID: 11830599]
 49. Kent KC, Zwolak RM, Jaff MR, Hollenbeck ST, Thompson RW, Schermerhorn ML, et al. Screening for abdominal aortic aneurysm: a consensus statement. *J Vasc Surg.* 2004;39:267–9. [PMID: 14718853]
 50. Black WC, Haggstrom DA, Welch HG. All-cause mortality in randomized trials of cancer screening. *J Natl Cancer Inst.* 2002;94:167–73. [PMID: 11830606]
 51. Gueyffier F, Boutitie F, Boissel JP, Pocock S, Coope J, Cutler J, et al. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men. A meta-analysis of individual patient data from randomized, controlled trials. The INDANA Investigators. *Ann Intern Med.* 1997;126:761–7. [PMID: 9148648]

Appendix

Analytic Framework and Key Questions

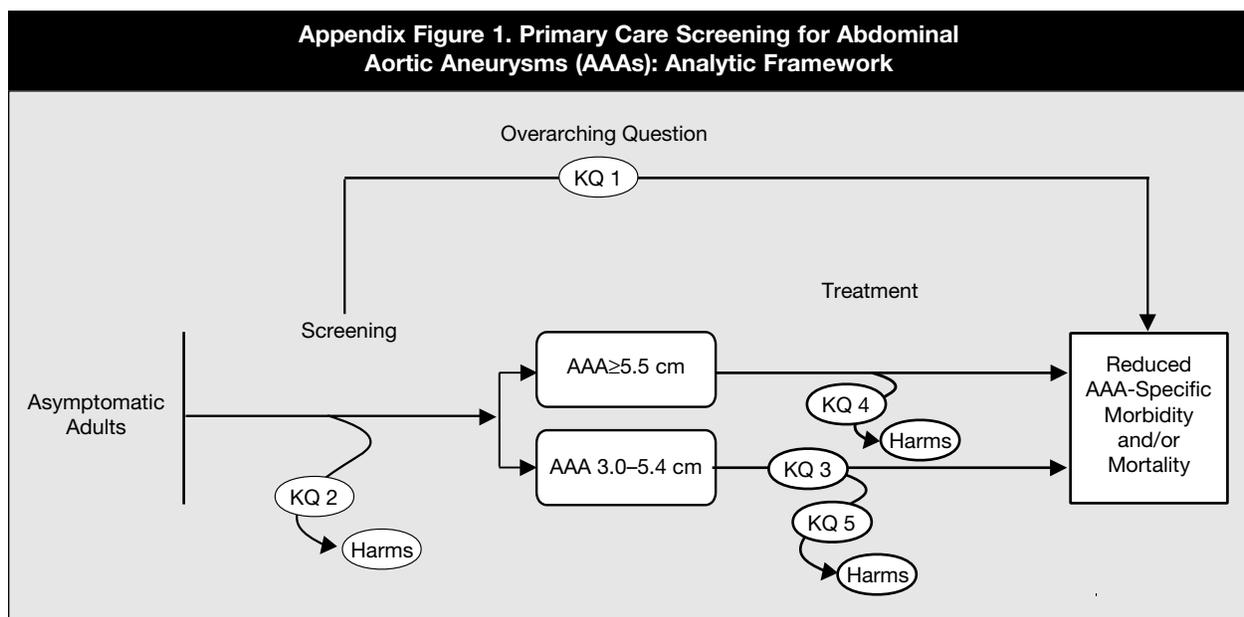
The analytic framework is a schematic outline used to define the population, preventive service, interventions, and health outcomes considered in the review (Appendix Figure 1). The arrows represent key questions that the evidence must answer to demonstrate the chain of logic from the preventive service (AAA screening) to improved health outcomes (reduced AAA-specific morbidity, mortality, or both). The key questions were determined in conjunction with the USPSTF liaisons.

Search Strategy

We searched the topic of AAA in MEDLINE® (January 1994 to May 2004), the Cochrane Database of Systematic Reviews (2004, Issue 1), and the Cochrane Controlled Trials Register (January 1994 to May 2004) to identify studies about the effectiveness of AAA screening in population-based settings, screening harms, and harms of treatment for AAAs at least 5.5 cm. We included only data published in full-

article form. In addition, we obtained articles from the reference lists of pertinent studies and reviews and from expert recommendations. The flow of articles is shown in Appendix Figure 2.

All searches included only English-language abstracts. Full search strategies may be found in the full review at www.preventiveservices.ahrq.gov. The search for key question 1a crossed terms for randomized, controlled trials with the terms *abdominal aortic aneurysm* and *mass screening or screen*. Terms for cohort, cross-sectional, epidemiologic, or longitudinal studies were crossed with mass screening and abdominal aortic aneurysm for the search for key question 1b. The search for key question 2 crossed psychological harms terms; false-positive or false-negative reactions; and the terms *risk assessment*, *predictive value of tests*, *attitude to health*, *psychiatric status rating scales*, *health status*, *health status indicators*, *severity of illness index*, and *quality of life* with the terms *abdominal aortic aneurysm* and *mass screening or screen* to locate articles pertaining to the harms of screening for AAA. The search for key question



KQ= key question. KQ 1a= Does AAA screening, in an asymptomatic average-risk or high-risk population, reduce AAA-related adverse health outcomes? KQ 1b= For individuals who do not have AAAs on initial screening, does periodic repeated screening reduce AAA-related adverse health outcomes? KQ 2= What are the harms associated with AAA screening? KQ 3= For AAAs 3.0 to 5.4 cm detected through screening, does immediate repair or surveillance reduce AAA-related adverse health outcomes? KQ 4= What are the harms associated with repair of AAAs 5.5 cm or greater? KQ 5= What are the harms associated with immediate repair or surveillance of AAAs 3.0 to 5.4 cm?

Appendix Table. Formulas for Calculations in Outcomes Table 2*

AAAs in cohort

$n \times [(smoking\ prevalence) \times (AAA\ prevalence\ in\ ever\ smokers) + (1 - smoking\ prevalence) \times (AAA\ prevalence\ in\ never\ smokers)]$

Ever smokers

AAAs in ever smokers:

$n \times (smoking\ prevalence) \times (AAA\ prevalence\ in\ ever\ smokers)$

AAA-related deaths at 5 years with no screening:

$n \times (AAAs\ in\ ever\ smokers / AAAs\ in\ cohort) \times (1 - e^{-(AAA\ mortality\ rate \times 5)})$

AAA-related deaths at 5 years if invited for screening:

$n \times (AAAs\ in\ ever\ smokers / AAAs\ in\ cohort) \times (1 - e^{-(AAA\ mortality\ rate \times 5) \times OR\ reduction\ in\ AAA-related\ death\ with\ screening})$

Never smokers

AAAs in never smokers:

$n \times (AAA\ prevalence\ in\ never\ smokers) \times (1 - smoking\ prevalence)$

AAA-related deaths at 5 years with no screening:

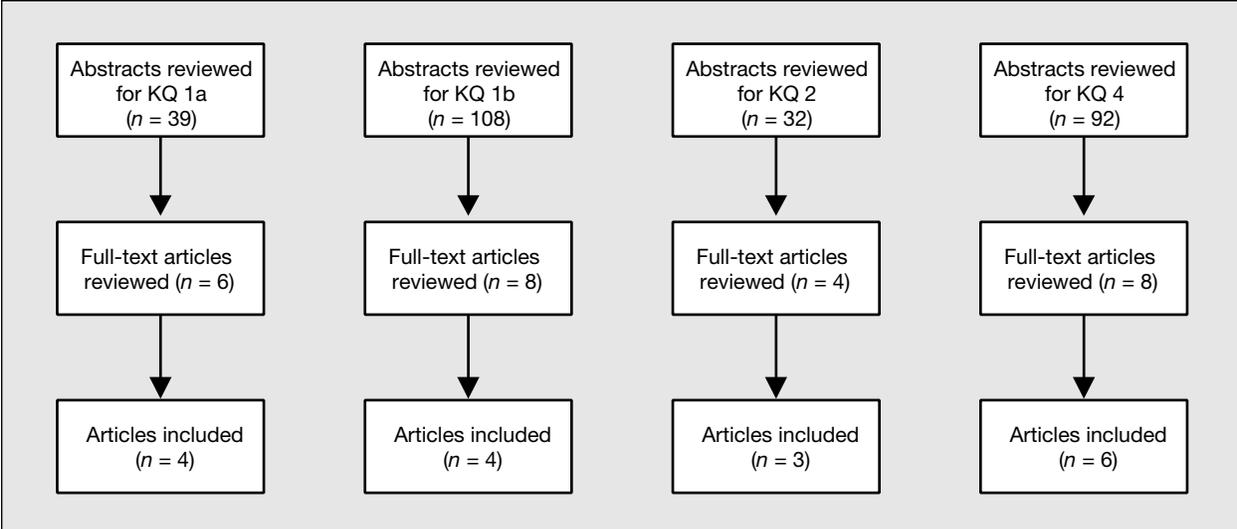
$n \times (AAAs\ in\ never\ smokers / AAAs\ in\ cohort) \times (1 - e^{-(AAA\ mortality\ rate \times 5)})$

AAA-related deaths at 5 years if invited for screening:

$n \times (AAAs\ in\ never\ smokers / AAAs\ in\ cohort) \times (1 - e^{-(AAA\ mortality\ rate \times 5) \times OR\ reduction\ in\ AAA-related\ death\ with\ screening})$

* AAA= abdominal aortic aneurysm; OR= odds ratio.

Appendix Figure 2. Trial Flow Diagram of Studies Evaluated for Inclusion in Each Key Question (KQ)



All abstracts were reviewed for relevance to other KQs. Articles from experts or reference lists were also reviewed if relevant.

4 used the randomized, controlled trial or review terms and the term *abdominal aortic aneurysm* with surgical terms, prognosis terms, or treatment outcome terms to locate articles relating to harms of AAA repair.

Inclusion Criteria

Two reviewers individually reviewed each abstract using the inclusion and exclusion criteria. A subset of full-text articles was selected for further review. We resolved disagreements on inclusion or exclusion of individual studies by consensus and by examining each study's relevance to the key question. One reviewer abstracted relevant information into an evidence table, and another reviewer checked the tables for accuracy.

The common inclusion criteria used for all key questions were English-language publication, presentation of original data, and use of human subjects. For key question 1a, only randomized population-based trials that compared screening with unscreened controls and reported AAA-related mortality were included. For key question 1b, we included follow-up or cohort studies that involved repeated scanning of a representative population. For key questions 2 and 4, we included studies of harms from randomized, controlled trials, or

retrospective or prospective cohort studies with comparative data.

Quality Rating and Data Extraction

We assessed the quality of studies on the basis of USPSTF criteria²⁶ to rate studies as “good,” “fair,” or “poor.” Quality criteria for randomized, controlled trials included assembly of comparable groups, maintenance of comparable groups, important differential loss to follow-up or overall high loss to follow-up, valid and reliable measurements, clear definition of interventions, all important outcomes considered, and intention-to-treat analysis. In general, a good study meets all criteria, a fair study does not meet all criteria but is judged to have no fatal flaw, and a poor study contains a fatal flaw. The final quality rating was assigned by the consensus of the investigator team.

Data were abstracted from each study considered for inclusion in the review. Information abstracted fell into 3 categories: study quality criteria as listed earlier; study characteristics, such as study identification, participants, and intervention and control conditions; and study outcomes, including harms. Only studies receiving a fair or good rating were included in the evidence synthesis.