

Ultrasonography Screening for Abdominal Aortic Aneurysms: A Systematic Evidence Review for the U.S. Preventive Services Task Force

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Background: Long-term follow-up of population-based randomized, controlled trials (RCTs) have demonstrated that screening for abdominal aortic aneurysms (AAAs) measuring 3 cm or greater decreases AAA-related mortality rates in men aged 65 years or older.

Purpose: To systematically review evidence about the benefits and harms of ultrasonography screening for AAAs in asymptomatic primary care patients.

Data Sources: MEDLINE, the Database of Abstracts of Reviews of Effects, the Cochrane Central Registry of Controlled Trials (January 2004 through January 2013), clinical trial registries, reference lists, experts, and a targeted bridge search for population-based screening RCTs through September 2013.

Study Selection: English-language, population-based fair- to good-quality RCTs and large cohort studies for AAA screening benefits as well as RCTs and cohort and registry studies for harms in adults with AAA.

Data Extraction: Dual quality assessment and abstraction of study details and results.

Data Synthesis: Reviews of 4 RCTs involving 137 214 participants demonstrated that 1-time invitation for AAA screening in men aged

65 years or older reduced AAA rupture and AAA-related mortality rates for up to 10 and 15 years, respectively, but had no statistically significant effect on all-cause mortality rates up to 15 years. Screening was associated with more overall and elective surgeries but fewer emergency operations and lower 30-day operative mortality rates at up to 10- to 15-year follow-up. One RCT involving 9342 women showed that screening had no benefit on AAA-related or all-cause mortality rates.

Limitations: Trials included mostly white men outside of the United States. Information for subgroups and about rescreening was limited.

Conclusion: One-time invitation for AAA screening in men aged 65 years or older was associated with decreased AAA rupture and AAA-related mortality rates but had little or no effect on all-cause mortality rates.

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An abdominal aortic aneurysm (AAA) is a weakening in the wall of the infrarenal aorta that results in an anteroposterior diameter of 3 cm or greater (1). Abdominal aortic aneurysms are often undiagnosed because a large proportion are asymptomatic until the development of rupture, which is generally acute and often fatal (59% to 83% of patients die before hospitalization) (2). Significant risk factors for the development of AAA include advanced age (3), male sex (4), smoking (1, 5, 6), and family history of AAAs (1, 7, 8). Other potential risk factors include a history of other vascular aneurysms (9), coronary artery disease (10), cerebrovascular disease (9), atherosclerosis (10), hypercholesterolemia (10), and hypertension (1, 10). Protective factors include black race, female sex, and diabetes mellitus (11). Smoking is the most important modifiable risk factor for AAA development (12–14) and aneurysm growth (15). Older age, female sex, smoking, and higher blood pressure are associated with increased risk for rupture in patients with small (3.0 to 5.4 cm) AAAs (15).

Although several screening methods exist, ultrasonography is accepted as the standard screening imaging method for AAA because it has a high sensitivity (94% to 100%) and specificity (98% to 100%) (1, 2, 16–19). Ultrasonography is noninvasive, can be conducted at a low

cost, and avoids radiation exposure. Computed tomography scans are highly sensitive and specific in detecting AAAs but are not recommended for first-line screening because of high cost and radiation exposure (1, 20).

In 2005, the U.S. Preventive Services Task Force (USPSTF) found good evidence to recommend 1-time screening for AAA by ultrasonography in men aged 65 to 75 years who have ever smoked (B recommendation). The USPSTF concluded that the benefits of screening did not clearly outweigh the harms and did not make a general recommendation for or against screening for AAA in men aged 65 to 75 years who have never smoked (C recommendation). The USPSTF recommended against routine screening for AAA in women (D recommendation) (21). This systematic review includes newly identified literature and all trials from the previous review that meet current inclusion criteria to provide updated evidence on the effectiveness of 1-time and repeated ultrasonography screening for AAAs (6).

METHODS

Detailed methods are publicly available in our full evidence report and its appendices (www.uspreventiveservices

taskforce.org) (22). This review addressed the following key questions: the effectiveness of 1-time screening for AAAs of all sizes (≥ 3.0 cm) and repeated screening for initially normal-sized aortas (< 3.0 cm) on affecting health outcomes and the harms related to 1-time and repeated screening for AAAs (**Appendix Figure**, available at www.annals.org). Of note, our detailed critique of treatment evidence for AAAs identified through screening that did not meet the currently accepted treatment threshold of 5 cm is presented in the full evidence report.

Data Sources and Searches

We searched MEDLINE, the Database of Abstracts of Reviews of Effects, and the Cochrane Central Registry of Controlled Trials for relevant English-language studies published between January 2004 and January 2013. We searched for screening trials through September 2013 in MEDLINE. We supplemented searches with suggestions from experts and considered all articles included in the previous review for the USPSTF. We also reviewed reference lists of relevant systematic reviews and meta-analyses.

Study Selection

Two investigators independently reviewed abstracts and full-text articles for inclusion according to predetermined criteria. We resolved discrepancies through consensus with a third investigator. We considered randomized, controlled trials (RCTs) and large cohort studies (≥ 1000 participants) of asymptomatic adult populations for key questions examining the effectiveness of 1-time and repeated screening. For the key question examining the harms of screening for AAAs, we considered RCTs and observational studies. Ultrasonography was the only screening method we considered. For all bodies of evidence, we excluded studies that we rated as poor-quality on the basis of the USPSTF quality rating standards (23).

Data Extraction and Quality Assessment

One investigator extracted data, and a second investigator reviewed these data. Two investigators completed independent, critical appraisals of all relevant studies using the USPSTF's design-specific criteria (23), the National Institute for Health and Care Excellence method checklists (24), Quality Assessment of Diagnostic Accuracy Studies (25), and the Newcastle-Ottawa Scale (26). According to the USPSTF criteria, a good-quality study met all prespecified standards. A fair-quality study did not meet (or it was unclear whether it met) at least 1 criterion, but it also had no known limitation that could invalidate its results. A poor-quality study had a single fatal flaw or several important limitations that could likely bias results.

Data Synthesis and Analysis

We qualitatively synthesized data for each key question by summarizing relevant details and results for each included study. Although we decided a priori to pool studies for all outcomes using DerSimonian–Laird random-effects models, we report quantitative analyses only for all-

cause mortality. When we pooled AAA-related mortality and screening harms, the summary effects showed high statistical heterogeneity at the longest follow-up. Thus, we present forest plots with no pooled summaries. In addition, we did not pool studies examining the effectiveness of re-screening because of substantial differences in patient population, length of follow-up, and reported outcomes. For all pooled results using the DerSimonian–Laird random-effects models, see the full evidence report (22).

For all-cause mortality, we conducted planned random-effects analyses using the DerSimonian–Laird method (27). We conducted sensitivity analyses using a fixed-effect model as well as the profile likelihood method because there were only 3 trials and the DerSimonian–Laird method can underestimate uncertainty when the number of trials is small (27, 28). The 2 methods resulted in identical effect estimates and CIs. We examined heterogeneity across trials with the I^2 statistic and chi-square test for heterogeneity.

Role of the Funding Source

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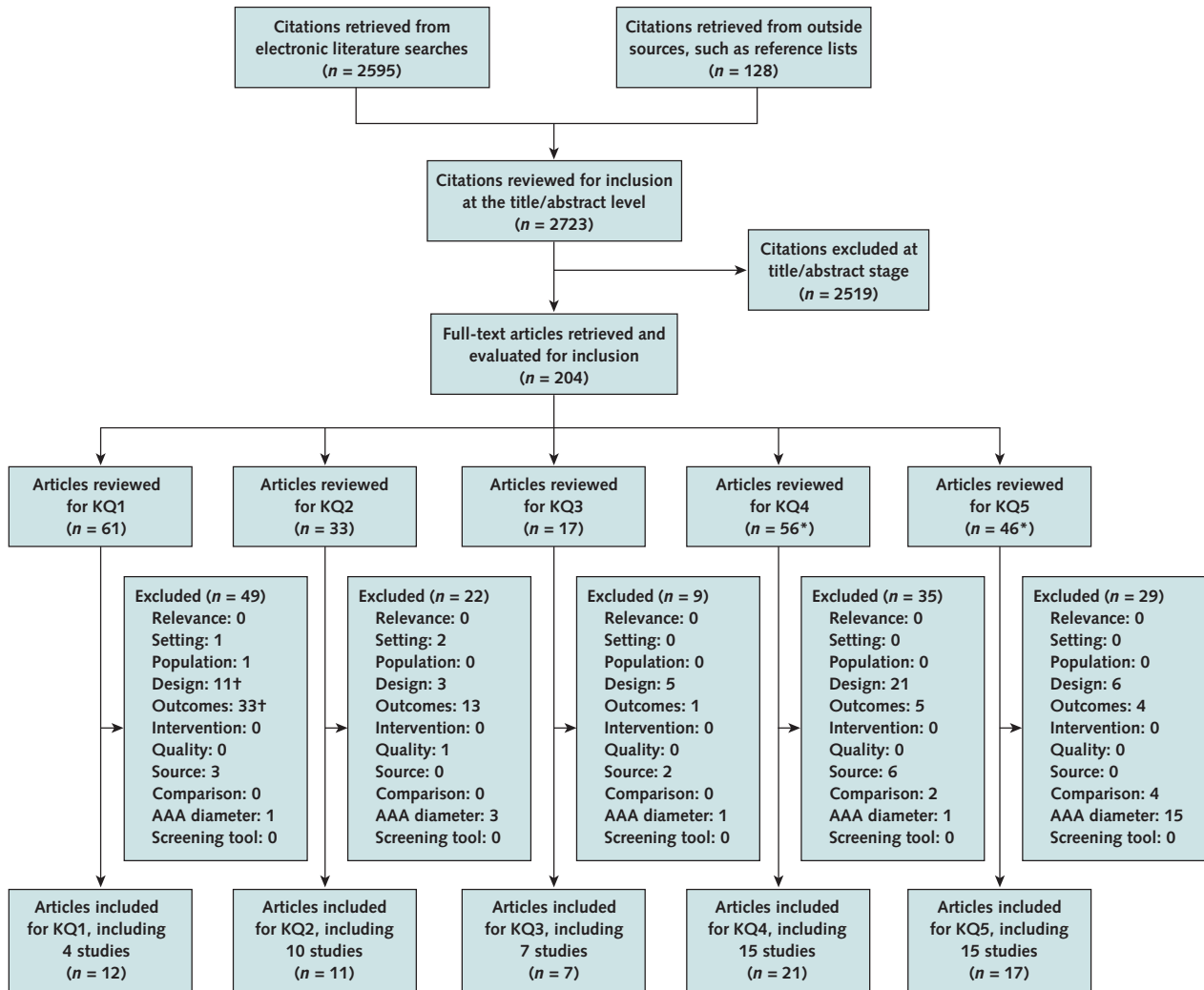
RESULTS

We reviewed 2723 abstracts and 204 full-text articles and identified 4 trials addressing the benefits of 1-time screening, 10 studies on the effectiveness of rescreening, 7 studies addressing the harms of 1-time and repeated screening, 15 trials examining the benefits of treating small AAAs, and 15 studies on the harms associated with treating small AAAs (**Figure 1**). The evidence related to the treatment of small AAAs is discussed in our full evidence report (22), along with detailed study-level and summary results of the evidence related to AAA screening.

AAA Screening in Men

We identified 2 fair-quality and 2 good-quality population-based screening RCTs (137–214 participants) that assessed the efficacy of AAA screening in population-based settings: MASS (Multicentre Aneurysm Screening Study) (29–32); the Chichester, United Kingdom screening trial (33–36); the Viborg County, Denmark screening trial (37–41); and the western Australian screening trial (42) (**Table 1**). All trials used population registries or regional health directories to identify potential participants aged 64 or 65 years and older. The Chichester trial (33) was the only trial that included women (34). No trial reported outcomes by demographic characteristics other than age and sex. Three of the 4 trials described adequate randomization (30, 33, 37). Three had no trial exclusions,

Figure 1. Summary of evidence search and selection.



AAA = abdominal aortic aneurysm; KQ = key question.

* Evidence related to the treatment of small AAAs is included in the full evidence report (22).

† One study was excluded for study design and outcomes.

whereas the MASS trial excluded patients who were identified as being too high-risk to be screened by their primary care physicians, were terminally ill, or had other serious health problems or previous AAA repair (30). All trials randomly assigned participants to usual care or invitation for 1-time ultrasonography screening. Three specified post-screening ultrasonography surveillance protocols for AAAs measuring 3.0 cm or greater (30, 33, 39), whereas the MASS trial sent initial ultrasound results to primary care physicians for further management (30).

All trials used intention-to-treat analysis. Adherence to screening varied from the lowest in the western Australian trial (62.5% of invited attended screening) to the greatest in MASS (80.2% adherence). Less than 1% of the control group crossed over in any trial to receive elective surgery, even at the longest follow-up of 13 to 15 years.

The primary trial outcome was AAA-specific mortality (defined as all AAA deaths plus all deaths within 30 days of AAA surgical repair). Trials also reported AAA rupture and all-cause mortality rates. Deaths and their causes were ascertained from death certificates in all studies, and 3 used a blinded adjudication panel to assign causes of death using autopsy data and hospital records.

Abdominal aortic aneurysm prevalence varied from 4.0% to 7.7% (Table 1). Most (70% to 82%) screen-detected AAAs were small, measuring less than 4.0 to 4.5 cm. Abdominal aortic aneurysms measuring 5.5 cm or greater were detected in only 0.4% to 0.6% of the screened groups. The good-quality MASS and Viborg trials showed statistically significant reductions in AAA-related mortality rates with screening at all time points beginning at 3 years and persisted up to 15 years (30, 37) (Table 2). The

Table 1. Methodological and Intervention Characteristics of the 4 Included Population-Based AAA Screening Randomized, Controlled Trials

Variable	MASS (29–32)	Viborg Trial (37–41)	Western Australian Trial (42)	Chichester Trial (33–36)
Study quality	Good	Good	Fair	Fair
Participants randomly assigned, <i>n</i>	67 800 men	12 639 men	41 000 men	6433 men, 9342 women
Mortality follow-up, <i>n</i> (%)	65 834 (97.1)	12 639 (100.0)	38 704 (94.4)	6040 (93.9)*
Country	United Kingdom	Denmark	Australia	United Kingdom
Mean length of follow-up, <i>y</i>	13.1	13	3.6†	15.0
Mean age, <i>y</i>	69.2	67.7	72.6	72.0‡
AAA prevalence in screened group, %	4.9	4.0	7.2	Men: 7.6; women: 1.3
Intervention	Invitation to ultrasonography screening; follow-up of results by initial aortic diameters as follows: 3.0–4.4 cm: rescanned annually 4.5–5.4 cm: rescanned at 3-mo intervals ≥5.5 cm: referred to urgent vascular surgery	Invitation to ultrasonography screening; follow-up of results by initial aortic diameters as follows: 2.5–2.9 cm: rescanned after 5 y 3.0–4.9 cm: rescanned annually ≥5 cm: referred to vascular surgery	Invitation to ultrasonography screening; scan results sent to PCP for management or surveillance	Invitation to ultrasonography screening; follow-up of results by initial aortic diameters as follows: 3.0–4.4 cm: rescanned annually 4.5–5.9 cm: rescanned every 3 mo or until the patient died, had surgical intervention, or declined follow-up
Control	No invitation to screening	No invitation to screening	No invitation to screening	No invitation to screening

AAA = abdominal aortic aneurysm; MASS = Multicentre Aneurysm Screening Study; PCP = primary care physician.

* Men only.

† Median follow-up of 3.6 y.

‡ Median age.

Chichester and western Australian trials showed a tendency toward reductions in AAA-related mortality rates with screening that was not statistically significant (33, 42).

An invitation to AAA screening was not associated with a statistically significant all-cause mortality benefit in

any of the individual trials or in the pooled random-effects analysis at any time point up to 15 years (Table 2). Sensitivity analyses that were done using a fixed-effects model had similar findings (data not shown), and sensitivity analyses at the 13- to 15-year time point using the profile

Table 2. All-Cause and AAA-Related Mortality Data for 1-Time Screening Trials at the Initial and Longest Follow-up

Author, Year (Reference)	Study Quality	Mean Follow-up, <i>y</i>	Treatment Group	Participants Analyzed, <i>n</i>	All-Cause Mortality		AAA-Related Mortality	
					Deaths, <i>n</i> (%)	Risk Summary Measure (95% CI)	Deaths, <i>n</i> (%)	Risk Summary Measure (95% CI)
Ashton et al, 2002 (30) and Thompson et al, 2012 (29)	Good	4.1	IG	33 839	3750 (11.1)	0.97 (0.93–1.02)*	65 (0.2)†	0.58 (0.42–0.78)*‡
				CG	33 961		3855 (11.4)	
			CG	33 883	13 858 (40.9)	0.97 (0.95–0.99)*	224 (0.7)	0.58 (0.49–0.69)*
				CG	33 887		14 134 (41.7)	
Lindholt et al, 2002 (39) and Lindholt et al, 2010 (40)	Good	4.3§	IG	6333	NR	0.92 (0.84–1.00)*‡	9 (0.14)	0.33 (0.16–0.71)*‡
				CG	6306		NR	
			CG	6333	2931 (46.3)	0.98 (0.93–1.03)*	19 (0.3)	0.34 (0.20–0.57)*
				CG	6306		2964 (47.0)	
Scott et al, 1995 (33) and Ashton et al, 2007 (36)¶	Fair	5.0‡	IG	3205	532 (16.6)	1.05 (0.94–1.18) **	10 (0.3)	0.59 (0.27–1.29) **
				CG	3228		508 (15.7)	
			CG	2995††	2036 (68.0)	1.01 (0.95–1.07)*	47 (1.6)	0.88 (0.60–1.30)*
				CG	3045††		2067 (67.9)	
Norman et al, 2004 (42)‡‡	Fair	3.6‡	IG	19 352	1976 (10.2)	0.98 (0.92–1.04) **	18 (0.09)	0.61 (0.33–1.11) **
				CG	19 352		2020 (10.4)	

AAA = abdominal aortic aneurysm; CG = control group; IG = intervention group; MASS = Multicentre Aneurysm Screening Study; NR = not reported.

* Hazard ratio (95% CI).

† Defined as 30-d deaths plus deaths from ruptured AAA.

‡ *P* ≤ 0.05.

§ Median follow-up.

|| Relative risk (95% CI).

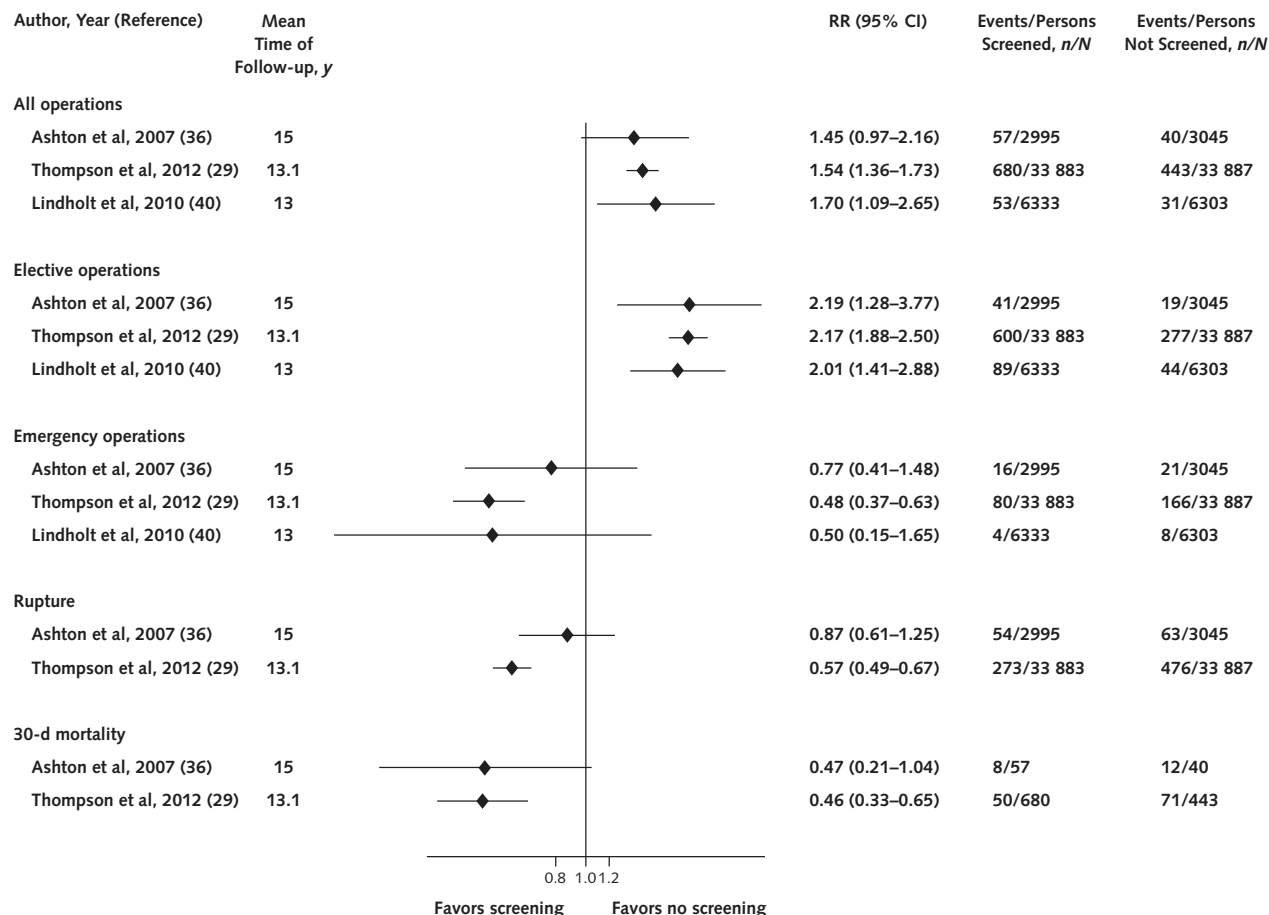
¶ Male subgroup only.

** Calculated value.

†† Because of updated computer systems and the correction of data, 391 men were excluded from the original data.

‡‡ A median of 3.6 y of follow-up is the only time point reported.

Figure 2. Downstream events in 1-time abdominal aortic aneurysm screening trials at longest follow-up.



RR = risk ratio.

likelihood estimation method yielded identical results (risk ratio, 0.98 [95% CI, 0.97 to 1.00]). Only MASS reported non-AAA causes of death, showing similar causes of death in the invited and control groups (ischemic heart disease [8.7% and 9.0%, respectively], stroke [2.7% for both], other cardiovascular cause [3.2% and 3.1%, respectively], and cancer [14.0% and 14.1%, respectively]) (29).

An invitation for screening was associated with lower AAA rupture rates at all-time points in the MASS and Viborg trials than no invitation. In addition, a nonstatistically significant tendency toward a reduction in ruptures was seen in the Chichester trial at 13 years, and no difference was reported in the western Australian trial at 3.6 years (Figure 2). Two of the 4 trials (Viborg and MASS) showed fewer emergency surgeries in the invited group up to 10 to 13 years. Chichester showed a nonsignificant tendency toward fewer emergency surgeries in the invited group up to 15 years, and the western Australian trial showed a nonstatistically significant increase in emergency surgery in the invited group at 3.6 years.

Screening for AAA in Women

Only the Chichester study recruited female participants, and these women were aged 65 to 80 years (9342 women [59% of participants]) (34). Abdominal aortic aneurysm prevalence in women was 6 times lower than in men (1.3% vs. 7.6%). Most (30 out of 40) AAAs were small (3.0 to 3.9 cm), and AAA-specific mortality rates were low in both groups (<0.2%; no statistical analysis). All-cause mortality rates at 5 years and rupture rates at 5 and 10 years were similar in the invited and control groups. Because of the low prevalence of AAA in women, the trial was underpowered to detect differences in health outcomes. A separate analysis that considered the entire unscreened population in the Chichester trial showed that more than one half of the AAA deaths in men occurred before age 80 years, whereas most (70%) AAA deaths in women occurred in women aged 80 years and older (34).

Screening for AAA in High-Risk Populations

In addition to male sex, strong risk factors for AAA include age, smoking, and family history (12–14). The old-

est participants in the 4 major screening trials ranged from age 73 to 80 years. Two trials reported no differences in AAA-related mortality outcomes when stratified by age (40, 42). In a simulation analysis after randomization from the Viborg trial, selective high-risk screening (only patients with chronic obstructive pulmonary disorder or other cardiovascular conditions) would have prevented nearly one half (14 out of 30) of all reported deaths at 5 years and required 72.9% fewer screening invitations compared with mass screening (41). However, these are likely underestimates because researchers only identified high-risk status through hospital discharge codes. No trial reported participants' smoking history, AAA family history, or race or ethnicity. All studies were conducted in mostly white populations.

Repeated Screening for AAA After Negative Results From Initial Ultrasound

We identified 1 good-quality and 6 fair-quality prospective cohort studies that examined various rescreening protocols (43–49). Studies showed that AAA-related death over 5 to 12 years was rare (<3%) among those with normal aortas (<3.0 cm) on the initial scan (43–49) (data not shown). Few of those with aortas measuring less than 3.0 cm developed any AAA over the following 5 to 12 years, which was particularly true for aortas less than 2.5 cm. Although some aortas (19% to 88%) with initial diameters of 2.5 to 2.9 cm progressed to a small AAA (diameter >3.0 cm) after 5 to 6 years, very few increased to greater than 5.0 cm (0.0% to 2.4%) at 5 years (48–50) and 15% had progressed to greater than 5.4 cm at 10 years (51). We identified 1 fair-quality meta-analysis of individual patient data that confirmed that AAA rupture was rare (<1%) in patients with subaneurysmal aortic dilatation (2.5 to 2.9 cm) over a mean of 13.2 years (52). Overall, this rescreening literature was limited by studies with small numbers of participants with normal aortas, no matched control participants, and primary outcomes of expansion rates rather than health outcomes (52).

One good-quality cohort study (2622 participants) that analyzed AAA detection and AAA-related mortality rates with rescreening at 4 years using multilogistic regression models showed that current smoking, coronary artery disease, and any atherosclerosis were associated with AAA detection at rescreening (44). In addition, no AAA ruptures or AAA deaths were identified during 4 years of follow-up. One fair-quality cohort examined the association of age with aortic size less than 3.0 cm at initial scan for development of an AAA and found no association between age group and subsequent AAA-related death (47). This cohort study (47) was an analysis of a single center that was included in the aforementioned good-quality cohort study (44). These conclusions about the yield of rescreening in subgroups are limited by very few nonwhite or female participants and by using only national death certificate information for mortality data.

Harms Associated With Screening

All 4 large population-based screening RCTs reported results on operative death and number of AAA surgeries (30, 33, 53, 54) (Figure 2). The risk for any AAA-related operation in the invited group was approximately double that of the noninvited group at 3 to 5 years in all trials (hazard ratio of 2.4 in MASS and Viborg; hazard ratio of 1.70 and 1.87 in Chichester and western Australian), which was driven by more elective surgeries in the invited group in all trials at all time points. Chichester and MASS trials showed some attenuation over time: by 13 to 15 years, there were 50% more AAA-related operations in the invited group compared with the control group. An unchanged risk over time was reported in Viborg. Thirty-day postoperative mortality rates after elective surgery in the only trial reporting this outcome at various time points (MASS) was similar between groups but was significantly reduced after emergency surgery in the screened group for all periods up to 10-year follow-up compared with the control group.

We identified 5 small observational studies (3 cohort and 2 cross-sectional) that reported conflicting results of AAA screening's influence on quality of life (QOL) and anxiety or depression measures (data not shown) (30, 44, 53–57). One study reported short-term decreases in QOL at 12 months in those who screened positive for AAA (55). Four studies showed no clinically important decrease in QOL measures in those who screen positive for AAA compared with unscreened control participants (30, 54, 56, 57). Of note, no trial used AAA-specific QOL instruments.

DISCUSSION

Our systematic review of 4 population-based screening trials (30, 33, 37, 42) found convincing direct evidence that screening men aged 65 and older decreased AAA-related mortality rates by approximately 50% over 13 to 15 years (58–60). Abdominal aortic aneurysm-related mortality benefits occurred relatively early (by roughly 4 years) and were maintained for at least another decade. In contrast to the previous review for the USPSTF (6), we do not present pooled estimates of effect on AAA-related mortality rates because of high statistical heterogeneity, although they are available in the full report (22). Subsequent to this previous review (6), some work also suggests that certain random-effects models (such as DerSimonian–Laird) may significantly underestimate statistical heterogeneity (27) and that, particularly when there are small study numbers, alternate statistical methods may provide more appropriate variance estimates (27, 28, 61, 62). Therefore, for the presentation of AAA-related mortality benefits, we emphasized the findings from the largest, good-quality study (MASS). In previous years, the estimates of treatment benefit on AAA-related mortality in MASS were very similar to the overall pooled effects used for screening recommendations. This is not surprising given its disproportionately large

sample size. Moreover, relying on MASS alone to estimate AAA-related mortality benefit at 13 to 15 years provides data that is essentially consistent with previous reviews done for the USPSTF that used a slightly different method.

Because of the lack of apparent heterogeneity, we pooled the longer-term all-cause mortality data using our prespecified (a priori) random-effects model on the basis of the DerSimonian–Laird model. We repeated the analysis using an alternative statistical approach, the profile likelihood method. Both methods produced the same pooled estimate of a nonstatistically significant reduction in all-cause mortality rates, which stands in contrast to authors' conclusions from a fixed-effects meta-analysis (63). Deaths due to AAA represented less than 3% of all deaths. We do not believe that the available data firmly support a reduction in all-cause mortality rates with AAA screening. It is important to note that although age is the strongest risk factor for AAA (12, 13), competing causes of death and limited surgical candidacy due to comorbid conditions diminish the effectiveness of AAA screening.

Although we found minimal direct evidence addressing subgroups in our systematic review, determining the most effective and efficient approaches to population-based AAA screening remains an important issue. In response to the 2005 USPSTF recommendation for a selective screening approach targeting men aged 65 to 75 years who have ever smoked, concerns have been voiced about missed opportunities to prevent AAA rupture, particularly in women, younger nonsmoking males, and those with a family history of AAA. Critics note the substantial rupture rates and AAA-related deaths that occur in women (at least 33% of ruptured AAA hospitalizations and 41% of AAA-related deaths), and nonsmokers account for approximately 22% of AAA-related deaths (64–68). A different high-risk approach using a validated multifactorial risk calculator that considers family history, cardiovascular disease, race, body mass index, and other factors could possibly identify a group with increased prevalence of AAA and thereby could more effectively identify AAAs and be equally efficient. However, many higher-risk persons have known comorbid conditions that could affect either eligibility or complications associated with surgical treatment and could compromise the ability to attend surveillance.

As an example of a high-risk approach, screening programs targeting current smoking women could increase screening yield, but one must weigh these possible benefits against the greater surgical complication rate and older age at time of rupture when compared with men (34, 67). Some current screening strategies have targeted persons with family history who have a reported AAA prevalence of 4% to 11%, particularly siblings of patients with AAA (68–70); however, no direct evidence exists for screening benefits in those with a family history of AAA. Recently, investigators have developed and internally validated a novel scoring tool to predict prevalent AAA using demo-

graphic and medical history data from 3.1 million persons who volunteered for community-based ultrasonography screening. Although promising, this risk scoring must be validated in the general population (12).

Recent epidemiologic evidence from population-based screening programs in Europe and New Zealand demonstrate a substantial decrease in AAA prevalence in men aged 65 years or older over the past 2 decades, with current AAA prevalence reported at 1.5% to 1.7% (51, 71–73). The United States lacks similar prevalence reporting, probably because of low screening uptake, which makes it difficult to estimate true AAA prevalence (74). Decreasing smoking rates could largely account for this decline abroad (75, 76), although decreasing atherosclerotic disease due to aggressive management of hypertension and hyperlipidemia probably also contributes to this decline (72, 76). One recent study suggests that the risk for AAA in persons who have ever smoked may remain high with a shift toward smaller aneurysms, even if the overall prevalence of AAA were declining in the United States as it is in other countries (77). This decrease in prevalence must be carefully considered when estimating the yield from mass versus targeted screening approaches and certainly favors a more targeted approach (that is, persons who have ever smoked). No single risk factor other than age, sex, or smoking history is as strong of a predictor of AAA, which makes developing a multiple risk factor approach appealing once a validated risk score is available.

Limitations of this review include only evaluating English-language literature and RCTs or large cohort studies and a requirement that studies meet the USPSTF's fair-or good-quality criteria (23). In addition, the benefits realized in the trials with populations with access to universal health care may be optimistic to directly apply to the U.S. population. Because this review was conducted to update a previous USPSTF review (6), some issues, such as risk assessment, incidental AAA detection on computed tomography screening for other purposes, and possible sex differences in the risk for rupture at a specific aortic diameter, were not systematically reviewed.

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Current author addresses and author contributions are available at www.annals.org.

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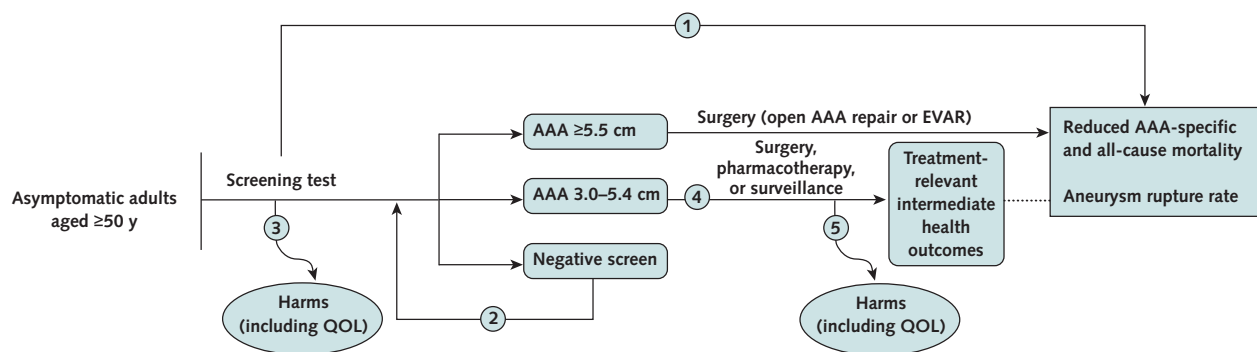
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Appendix Figure. Analytic framework and key questions.



Key Questions

1. What is the effect of 1-time AAA screening on health outcomes in an asymptomatic population aged ≥ 50 y?
 - a. Does the effect of 1-time screening vary between men and women, smokers and nonsmokers, older (≥ 65 y) and younger (> 65 y) patients, patients with a family history of AAA and those without a family history of AAA, and patients of different races/ethnicities?
 - b. Does the effect of 1-time screening vary between different screening approaches?
2. In a previously screened, asymptomatic population without an AAA on an initial screen, what is the effect of rescreening for AAAs on health outcomes or AAA incidence?
 - a. Does the effect of rescreening vary between men and women, sizes of AAA, smokers and nonsmokers, older (≥ 65 y) versus younger (< 65 y) patients, patients with a family history of AAA and those without a family history of AAA, and patients of different races/ethnicities?
 - b. Does the effect of rescreening vary between different time intervals?
3. What are the harms associated with 1-time and repeated AAA screening?
4. What is the effect of pharmacotherapy versus placebo or surgery (open AAA repair and EVAR) versus surveillance on treatment-relevant intermediate health outcomes in an asymptomatic population with small AAAs (3.0–5.4 cm) identified by screening?
 - a. Does the effect of pharmacotherapy, surgery, and surveillance differ between men and women, smaller (3.0–4.0 cm) and larger aneurysms (4.1–5.4 cm), smokers and nonsmokers, older (≥ 65 y) and younger (< 65 y) patients, patients with a family history of AAA and those without a family history of AAA, patients with diabetes and without diabetes, patients with COPD and without COPD, or patients of different races/ethnicities?
5. What harms are associated with pharmacotherapy, EVAR and open AAA repair surgery, and surveillance in an asymptomatic population with small AAAs (3.0–5.4 cm) identified by screening?

AAA = abdominal aortic aneurysm; COPD = chronic obstructive pulmonary disease; EVAR = endovascular aneurysm repair; QOL = quality of life.