Evidence Synthesis
Number 35

Primary Care Screening for Abdominal Aortic Aneurysm

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Primary Care Screening for Abdominal Aortic Aneurysm

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Preface

The Agency for Healthcare Research and Quality (AHRQ) sponsors the development of Systematic Evidence Reviews (SERs) and Evidence Syntheses through its Evidence-based Practice Program. With guidance from the U.S. Preventive Services Task Force* (USPSTF) and input from Federal partners and primary care specialty societies, the Oregon Evidence-based Practice Center systematically reviews the evidence of the effectiveness of a wide range of clinical preventive services, including screening, counseling, and chemoprevention, in the primary care setting. The SERs and Evidence Syntheses—comprehensive reviews of the scientific evidence on the effectiveness of particular clinical preventive services—serve as the foundation for the recommendations of the USPSTF, which provide age- and risk-factor-specific recommendations for the delivery of these services in the primary care setting. Details of the process of identifying and evaluating relevant scientific evidence are described in the "Methods" section of each SER and Evidence Synthesis.

The SERs and Evidence Syntheses document the evidence regarding the benefits, limitations, and cost-effectiveness of a broad range of clinical preventive services and will help further awareness, delivery, and coverage of preventive care as an integral part of quality primary health care.

AHRQ also disseminates the SERs and Evidence Syntheses on the AHRQ Web site (http://www.ahrq.gov/clinic/uspstfix.htm) and disseminates summaries of the evidence (summaries of the SERs and Evidence Syntheses) and recommendations of the USPSTF in print and on the Web. These are available through the AHRQ Web site and through the National Guideline Clearinghouse (http://www.ngc.gov).

We welcome written comments on this Evidence Synthesis. Comments may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 540 Gaither Road, Suite 3000, Rockville, MD 20850, or e-mail uspstf@ahrq.gov.

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*The USPSTF is an independent panel of experts in primary care and prevention first convened by the U.S. Public Health Service in 1984. The USPSTF systematically reviews the evidence on the effectiveness of providing clinical preventive services--including screening, counseling, and chemoprevention--in the primary care setting. AHRQ convened the current USPSTF in November 1998 to update existing Task Force recommendations and to address new topics.

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Structured Abstract

Background: While the prognosis for abdominal aortic aneurysm (AAA) rupture is poor, ultrasound imaging is an accurate and reliable test for detecting AAAs before rupture.

Purpose: To examine the benefits and harms of population-based AAA screening.

Data Sources: MEDLINE (1994 to July 2004) supplemented by the Cochrane Library, reference lists of retrieved articles, and expert suggestions.

Study Selection: We included English-language abstracts with original data about the effectiveness or harms of screening or treating AAA. Randomized trials were selected for AAA population screening or treatment of small AAAs. Population studies were reviewed for AAA risk factors and data on adverse screening or treatment events from randomized trials and cohort studies.

Data Extraction: We extracted study information regarding patient population, study design, and clinical outcomes including harms. Studies were quality rated using predefined criteria.

Data Synthesis: We identified four population-based randomized controlled trials of AAA screening in men 65 years and older. Based on meta-analysis, an invitation to attend screening was associated with a significant reduction in AAA-related mortality (OR 0.57; 95% CI, 0.45 to 0.74). A meta-analysis of three trials revealed no significant difference in all-cause mortality (OR 0.98; 95% CI, 0.95 to 1.02). No significant reduction in AAA-related mortality was found in one study of AAA screening in women. Screening does not appear to be associated with significant physical or psychological harms. For 4.0-5.4 cm AAAs, immediate surgical repair, compared to surveillance with delayed repair, does not appear to improve either AAA-related mortality or all-cause mortality. Major treatment harms include 2 to 6% operative mortality rate and significant risk of major complications.

Conclusions: For men age 65 years and older, an invitation to attend AAA screening reduces AAA-related mortality.

Chapter 1. Introduction

Primary Care Screening for Abdominal Aortic Aneurysm

An abnormal bulging of the abdominal aorta, called an abdominal aortic aneurysm (AAA), is a serious condition that often leads to death. The normal diameter of the aorta below the take-off of the renal arteries is approximately 2.0 cm. By consensus, an AAA is present when the infrarenal diameter exceeds 3.0 cm.[1] Based on US vital statistics data, aortic aneurysms accounted for approximately 15 000 deaths in the year 2000.[2] Abdominal aortic aneurysms account for approximately 9000 of these deaths, and the remainder are related to thoracic aneurysms.[3] These estimates also include operative mortality from elective AAA repair. These figures may underestimate the true mortality rate due to AAA. Since the majority of those with ruptured AAAs die before reaching a hospital, [4] these sudden deaths may be attributed to other causes.[5]

The prevalence of AAAs found in population-based ultrasound screening studies from various countries ranges from 4.2-8.8% in men, and 0.6-1.4% in women.[6-12]In a screening study of 126 696 US veterans, 97% of whom were male, the prevalence of AAAs rose 1.99% at 55-59 years to 4.75% at 65-69 years to 5.95 at 75-79 years.[13] The peak of the age-prevalence curve for AAAs in women occurs about ten years later than for men.[14]

Risk factors for an AAA include age, a history of regular smoking, family history, coronary artery disease, hypercholesterolemia, hypertension, and cerebrovascular disease.[13,15] Significant negative risk factors include female gender, diabetes mellitus, and black race. Although women with AAA are on average older than men with AAA, the increased risk associated with age, smoking, and family history are similar for women and men.

Almost all deaths from ruptured AAAs occur after the age of 65 years.[14,16] The highest mortality rates for AAA are found in white males over 65 years, and increase rapidly from 60 per 100 000 at ages 65-74 to 160 per 100 000 at age 85 and older.[3] AAA-related death rates in white females, black females, and black males are about one-third less at the same ages. Most AAA-related deaths in men occur before the age of 80 and most AAA-related deaths in women occur after the age of 80.[14]

Although age-adjusted death rates for AAA have remained stable in the US over the last several decades, studies based on hospital discharge data indicate an increasing rate of interventions for AAAs.[17] Based on US National Hospital Discharge Survey data,[3] the rate of hospital discharges for a first-listed AAA diagnosis in those aged 65 years or older rose from 11.2 per 100 000 in 1979 and to 20.5 per 100 000 in 1984, and remained steady from 1984 through 1992. The rate per 100 000 of surgical AAA repairs also rose by the same proportion over this period. Several retrospective population cohort studies from Europe have cited similar findings as support for a possible increase in the true incidence of AAA, but note that increasing use of diagnostic ultrasound over time, changes in coding of death registry data, and aging of the population may also contribute to this increase.[18-20]

The prognosis for ruptured AAAs is grim. In community-based studies, an estimated 59 to 83% of patients with ruptured AAAs die out-of-hospital or prior to surgery.[4] The operative mortality (in-hospital or 30-day) of those who survive to surgery was estimated to be 41% in the year 2000.[21] Thus, at most 10-25% of individuals with ruptured AAAs survive to hospital discharge.

The pathogenesis of AAA formation is complex and multifactorial.[22] The aorta is an elastic vessel, which primarily depends on elastin and collagen in the vessel wall for support. Physiological remodeling of the aortic wall maintains the integrity of the vessel wall over time. AAA seems to form after a breakdown in this process diminishes the elasticity of the aorta. The aorta becomes inflamed as macrophages and lymphocytes infiltrate the vessel wall, which then accelerates pathologic changes in the vessel wall. Proposed triggers for the inflammatory process include elastin degradation products in the vessel that attract macrophages, autoimmune responses, infectious agents, or damage from free-radicals. Familial clustering of AAAs suggests that their formation may also be influenced by genetics. Biomechanical forces may then expand the aorta to form an aneurysm.

The pathogenesis of AAA formation appears to differ from that of atherosclerosis in other vessels. From 1979 to 1990, age-adjusted death rates for AAA in the US remained unchanged.[3] By contrast, deaths rates for both cardiovascular and cerebrovascular disease have declined rapidly over the past several decades.[23,24] The finding that the association between smoking and AAA-related mortality is 2.5 times greater than for smoking and cardiovascular disease mortality also favors this hypothesis.[25]

The strongest predictor of rupture risk for AAAs is maximal diameter. [26,27] The natural history of AAAs ≥ 5.5 cm is difficult to determine since most large aneurysms are surgically repaired. In a 5-year prospective study of 198 male veterans with large AAAs who refused or were unfit for surgery, one-year incidence rates of rupture were 9.4% for 5.5-5.9 cm AAAs; 10.2% for 6.0-6.9 cm AAAs; and 32.5% for AAAs ≥ 7.0 cm.[28] A rapid rate of aneurysm expansion > 1 cm/year is also commonly used in decision making about elective repair of AAAs <5.5 cm, however, the predictive value of expansion as an index of rupture risk is less clear.[17]

Estimates of the rupture risk for AAAs < 5.5 cm from population and cohort studies range from 0.3% to 5.3% per year,[26,27,29,30] and may be related to current management practices. Two recent clinical trials compared immediate surgical repair to surveillance with delayed repair for individuals with 4.0-5.4 cm AAAs. The one year incidence rate of rupture was 0.6-1.0% for those undergoing surveillance, although over five years, two-thirds of patients being surveyed underwent surgical repair because of aneurysm expansion.[31,32] AAAs < 4.0 cm rarely rupture.[26,33,34]

In 1996, the United States Preventive Services Task Force found insufficient evidence to recommend for or against routine screening of asymptomatic adults for abdominal aortic aneurysm (AAA) either with abdominal palpation or ultrasound.[35] The USPSTF recognized that selective screening of high-risk patients might be beneficial, for example, in men with peripheral vascular disease or a family history of AAA. The USPSTF stated that at the time, however, no direct evidence showed that screening for AAA reduces mortality or morbidity in any population.

Since 1996, four large trials of population-based screening for AAA have been reported.[11,14,36,37] The purpose of this review is to update the evidence on the effectiveness of AAA screening since the second United States Preventive Services Task Force considered it in 1996.

Chapter 2. Methods

Analytic Framework and Key Questions

The analytic framework shown in Figure 1 was developed to guide our literature search strategy. We examined five key questions:

1) a) Does AAA screening, in an asymptomatic average-risk or high-risk population, reduce AAA-related adverse health outcomes? b) For individuals who do not have AAAs on initial screening, does periodic repeat screening reduce AAA-related adverse health outcomes?

2) What are the harms associated with AAA screening?

3) For 3.0-5.4 cm AAAs 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?

5) What are the harms associated with immediate repair or surveillance of 3.0-5.4 cm AAAs?

We focused our review of screening on the use of abdominal ultrasound scanning to detect AAAs in asymptomatic patients. The sensitivity of ultrasound scanning for an AAA is 95%, the specificity approaches 100%, and the examination is reliable and reproducible.[34] Limited ultrasonography for AAA screening can be performed in less than ten minutes, including time for training and unused appointments.[10]

Physical examination may also detect AAAs, particularly those large enough to warrant surgery. Physical examination may not be a suitable for population screening due to high false-positive and false-negative rates.[38,39] Other imaging modalities, such as computed tomography and magnetic resonance imaging, are also accurate and reliable for assessing aortic size, but are not as accessible as ultrasound imaging.[34] We found no population-based trials of AAA-screening using physical examination or imaging methods other than ultrasound scanning.

Literature Search Strategy

We searched MEDLINE® from January 1994 to May 2004 to identify studies about the following: the effectiveness of AAA screening in population-based settings, the effectiveness of repeat AAA screening, screening harms, effective management strategies for AAAs 3.0-5.4 cm, and harms of treatment for AAAs 3.0-5.4 cm and AAAs ≥ 5.5 cm. Search strategies for each key question are detailed in Appendix 1.

We included only data published in full-article form. We also searched the online Cochrane Database of Systematic Reviews and Cochrane Controlled Trials Register. Additionally, we obtained articles from the reference lists of pertinent studies and reviews and from expert recommendations.

Inclusion/Exclusion Criteria

Two reviewers (Fleming and Beil) individually reviewed each abstract using the inclusion/exclusion criteria listed in Appendix 2. Excluded studies are listed in Appendix 3. For key question 1a, only randomized population-based trials of screening with unscreened controls were included. 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. For key question 3, only randomized clinical trials of immediate repair or ultrasound surveillance for AAAs 3.0-5.4 cm were included. For key questions related to harms of screening and treatment, we included studies of harms from randomized controlled trials, or retrospective or prospective cohort studies with comparative data. We resolved disagreements on inclusion/exclusion of individual studies by consensus by obtaining the source article and examining its relevance to the key question.

Data Extraction and Synthesis

We assessed the quality of included studies based on published USPSTF criteria (Appendix 4).[40] For each study rated "Good" or "Fair" quality, we abstracted study design, setting, population demographics, and results for primary and secondary outcomes.

To assess the benefit of population-based AAA screening, and immediate repair versus surveillance for moderate-sized AAAs, we pooled eligible studies to estimate the likelihood that screening reduces AAA-related death and all-cause mortality. We calculated estimates of unadjusted odds ratios with 95% confidence intervals. We assessed heterogeneity by using graphs of the outcomes and the Mantel–Haenszel chi-square test. We performed meta-analyses to calculate summary estimates for AAA-related mortality and all-cause mortality using the DerSimonian and Laird random-effects model.[41] 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.[42] Statistical analyses were performed with RevMan software.[43]

We used these pooled estimates to model the impact of AAA screening in a hypothetical population. These analyses also incorporated the rates of other AAA-related events obtained by averaging rates across all trials. We modeled upper and lower bounds for outcomes using the 95% confidence intervals from the meta-analyses and the average rates of other events.

Chapter 3. Results

Key Question 1a. Does AAA screening in an asymptomatic average-risk or high-risk population reduce AAA-related adverse health outcomes?

Our search strategy for question 1a identified four randomized, controlled trials that assessed the efficacy of AAA screening in population-based settings: the Multicentre Aneurysm Screening Study (MASS) from the United Kingdom;[11] the Chichester, United Kingdom screening trial;[14,44,45] the Viborg County, Denmark screening trial;[37] and the Western Australia screening trial.[12,36,46]

Trial Characteristics

Table 1 presents the characteristics of the four screening trials. All trials identified potential participants aged 65 years or older at average risk for AAA through population registries or regional health directories. Different stopping ages were used for each trial, ranging from 73-83 years. 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 the MASS, Chichester, and Viborg 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 were periodically re-scanned and referred to a vascular surgeon for AAAs that had expanded to or above the threshold size on follow-up scanning. In the MASS and Chichester trials, 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 initial scan received no further follow-up. In the MASS trial, 31 of 354 (18%) invited group patients undergoing elective AAA repairs did not meet trial criteria for referral based on size. Crossover data were not available for other trials. In the Western Australia trial, each patient attending screening was given a letter with his results, as well as a letter for his physician with results and management guidelines suggesting yearly rescanning for 3.0 to 3.9 cm AAAs, twice yearly scanning or vascular surgery

referral for 4.0 to 4.9cm AAAs, and vascular surgery referral for AAAs ≥ 5.0 cm. For patients with AAAs ≥ 4.5 cm, a letter was also mailed to 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, whether scanned or not, or the control group participants.

Each trial, except the Viborg study, used a combination of hospital records and death certificate registries to ascertain outcomes for both invited and control participants. The Viborg study ascertained outcomes using only hospital records from the regional hospital in Viborg County, Denmark. Use of death certificates to classify cause of death is prone to bias.[47] In these studies, this bias may be conservative. Private physicians were informed if patients invited to attend screening were diagnosed with AAAs, and thus may have been more likely to attribute more sudden death in these patients to AAAs than were physicians of uninvited controls. This ascertainment bias may make an advantage due to screening more difficult to detect.[5]

Assessment of Study Quality

Table 2 presents quality parameters for each trial based on defined USPSTF criteria.[40] In all trials, the individual participant was the unit of randomization and randomization methods were adequate. Due to the nature of the trials, blinding of participants and care providers to the screening results was not possible. MASS was assigned a "Good" quality rating based on USPSTF criteria. An independent working party that apparently was not aware of participant assignment, ascertained outcomes based on death registries. The Viborg study, the Chichester study, and Western Australia study were assigned "Fair" quality ratings. These trials did not report important information, such as baseline characteristics and whether outcomes assessors were blinded.

In MASS, the Western Australia study, and the Viborg study, outcomes were ascertained for 99% to 100% of all participants. These data were not reported for the Chichester study. In the Viborg study, only hospital records were available to assess these outcomes. In all studies, analyses were based on intent-to-treat. Outcomes for both attendees and non-attendees were included in the analyses for the invited for screening group.

While the Chichester trial also reported outcomes for 10 years of follow-up,[14,45] 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.[44]

Effect of Population Screening on AAA-Related Mortality

Table 3 presents the results of the four trials of AAA screening. 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; 95% 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 2). The pooled OR showed a reduction in AAA-related mortality favoring screening (OR, 0.57; 95% 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 the MASS trial 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;95% CI, 0.36 to 0.88).

Effect of Population Screening on All-Cause Mortality

All-cause mortality results for men were available for MASS and for the Western Australia and Chichester trials (Figure 3). 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; 95% CI, 0.95 to 1.02).

Population Screening for AAA in Women

The Chichester trial included 9342 women aged 65 to 80 years who were randomized to either an invitation-to-screening or control group (Table 3).[44] No other trials included women. Sixty-five percent of women attended screening compared to 73% of men ($p<0.0001$). The prevalence of AAA in the women who were scanned was 1.3% compared to 7.6% in men. At five 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; 95% CI, 0.14-7.07) or all-cause mortality (OR 1.05; 95% CI, 0.92-1.19). At ten years, the incidence of AAA rupture was the same for women in both the screening and control groups.[14] In men, the majority of deaths from AAA rupture occurred in those younger than 80 years of age. In contrast, for women, seventy percent of deaths from AAA rupture occurred after the age of 80.

Modeling of Outcomes for AAA Screening

Table 4 presents outcomes for population invited to attend AAA screening versus no invitation for a hypothetical cohort of 100 000 men age 65 to 74 years followed over five years (the mean follow-up interval for the four trials combined). Pooled estimates of odd ratios and event rates were taken from Table 3. Confidence intervals were used to estimate a lower and upper bound of benefit for each event. Life expectancy was calculated using life-table methods and assumes that AAA screening reduces all-cause mortality at a constant rate throughout the men's lives.

The prevalence of AAAs averaged across all four trials was 5.5%. Based on the average estimate across trials from Table 3, 72% of men invited for screening would attend and undergo ultrasound scanning. Sensitivity analyses on screening attendance rates could not be performed, however, since men who attend screening may be significantly different those who do not in terms of age, comorbidities, and socioeconomic status.[48,49] We used the summary odds ratios from the combined trials (Figures 2 and 3) to estimate the treatment effect arising from an invitation to screening. These estimates incorporate variability, both within and between trials, in a number of factors. Also note that these estimates do not reflect the benefit of ultrasound scanning of an AAA in a particular individual.

Among the 100 000 men in the hypothetical cohort, an expected 5500 men would have an AAA. If the cohort were invited for screening, 3960 of 5500 AAAs would be detected based on a 72% acceptance rate. Based on the combined AAA-mortality rate from Table 3 (0.72 deaths per 1000 person-years), 359 AAA-related deaths would be expected with no screening over five years. If the cohort were invited to screening, the number of AAA-related deaths would be

reduced to 205 over 5 years, and one AAA-related death would be prevented among every 648 men invited for screening. Based on the 95% confidence interval for the pooled odds ratio, 506 to 1072 men would need to be invited to screening to prevent one AAA-related death. For comparison, the number needed-to-invite to mammography to prevent one breast cancer death ranges from 345 to 3468.[50] The needed-to-invite to undergo screening to prevent one colorectal cancer death ranges from 345 to 1250.[51]

Without screening, 13 368 men would be expected to die from all causes over five years. At baseline, the summary odds ratio from the meta-analysis for all-cause mortality is 0.98 (95% CI, 0.95 to 1.02), and the screening program would result 249 excess all-cause deaths prevented. At the upper bound of the confidence interval, screening would result in 248 excess all-cause deaths and reduce average life expectancy by seven months per individual invited to screening. At the lower bound of the confidence interval, 624 additional lives would be saved as a result of screening with a gain in average life expectancy of seven months.

As expected, more AAA ruptures will occur if the cohort is not screened. The NNS to prevent one AAA rupture ranges from 435 to 500 men. More elective repairs than emergency repairs will be performed if the cohort is screened, and vice versa with no screening. Thus, screening results in more deaths from elective repair and fewer from emergency repair, and there are fewer deaths from elective repair and more from emergency repair without screening.

Screening for AAA in High-Risk Subgroups

Risk factors for AAA ≥ 4.0 cm, based on multivariate odds ratio from a screening study of 126 696 US veterans,[13] included a history of regular smoking (OR 5.07; 95% CI, 4.13-6.21); family history (OR 1.94; 95% CI, 1.63-2.32); age (OR 1.71 per 7-year age interval; 95% CI, 1.61-1.82); coronary artery disease (OR 1.52; 95% CI, 1.37-1.68); hypercholesterolemia (OR 1.44; 95% CI, 1.27-1.63); and cerebrovascular disease (OR 1.28; 95% CI, 1.11-1.47). Significant negative risk factors were female gender (OR 0.17; 95% CI, 0.07-0.48); diabetes mellitus (OR 0.52; 95% CI, 0.45-0.61); and black race (OR 0.53; 95% CI, 0.40-0.69).

A history of smoking is the most significant risk factor distinguishing populations at higher risk for AAA. Figure 4 shows the prevalence of AAAs by age and smoking history from the same screening study.[13] Ever-smokers are defined based on the CDC's definition as those who have smoked more than 100 cigarettes during their lifetime.[52] Overall, the prevalence of aneurysms ≥ 3.0 cm was 5.1% in ever-smokers versus 1.5% in never smokers (unadjusted OR 3.6; 95% CI 3.3, 4.0). In never-smokers, AAA prevalence was more strongly associated with age compared to ever-smokers; the mean age of those with AAA who never smoked was 73 years, compared to 69 years for ever-smokers. In a systematic review and meta-analysis, Lederle et al. also found a strong association between smoking history and the risk of AAA-related mortality.[25]

In Table 5, we model the impact of an invitation to attend screening based on smoking status in a hypothetical cohort of 100 000 US males aged 65 years. About 31% of men in the US aged 65-74 years have never smoked.[53] We use the average 5.5% prevalence of AAA derived from the four population-based screening trials (Table 3). Based on aneurysm prevalence data for 65-74 year old veterans from the veteran's screening study, the prevalence of AAA ≥ 3.0 cm is 6.4% for ever-smokers compared to 1.8% for never-smokers.[13] To model screening benefits, we use the combined odds ratios for reduction of AAA-related mortality from the four population screening trials (Figure 2). We assume that ever-smokers and never-smokers equally benefit from reduction in AAA-specific mortality. In this age cohort, inviting only those with a history

of smoking to screening will detect approximately 89% of prevalent AAAs. Without screening, AAA-related death over five years is expected in 320 of 69 000 (0.46%) of ever-smokers and 40 of 31 000 (0.13%) of never-smokers. Assuming that an invitation to screening reduces ever-smokers and never-smokers AAA-related mortality equally, the NNS to prevent one AAA-related death with screening is 645 men in the entire cohort, 500 in men who have ever smoked and 1783 in those with no smoking history. Based on 8 300 000 men 65-74 years in the US from the year 2000 census,[54] an invitation to screening would prevent an estimated 12 831 AAA-related deaths over five years, with a reduction of 11 392 AAA-related deaths (89%) attributable to screening men with a history of smoking.

Black race is a negative risk factor for AAAs. In the Veterans Affairs (VA) Aneurysm Detection and Management (ADAM) screening study, with adjustment for other factors, such as age and smoking, the odds ratio for AAAs ≥ 4.0 cm was 0.49 (95% CI 0.39-0.69) for blacks compared to whites.[15] Age-adjusted AAA death rates for black males are also less than one-half of those for white males, although death rates for dissecting aneurysms and thoracic aneurysms are similar.[3] The reason that black race appears protective for AAA is not clear. Blacks have a higher burden than whites of atherosclerotic risk factors, such as hypertension and diabetes.[55] The lower incidence of AAA in blacks may then be consistent with the hypothesis that atherosclerosis is not the primary pathogenic process in AAA formation.[22]

The potential for selective screening has been examined in the Viborg screening trial[10] and the Western Australia screening trial.[56] In the Viborg trial, 72 of 141 AAA (51.1%) were found in men who had one or more risk factors including a history of hypertension, acute myocardial infarction, angina pectoris, chronic obstructive pulmonary disease, cerebrovascular disease, or lower limb atherosclerosis. The Western Australia trial investigators gathered data on risk factors in the first 8995 men aged 65 to 83 years, who accepted an invitation for screening. Using this data, they developed a multivariate risk score with ten risk factors; this score was then applied in the next 2755 men who were scanned. Screening 50% of men in the second cohort based on the risk score would have missed 25% of AAAs present in the sample population. Using a history of smoking alone would identify most AAAs but would reduce those screened by only 34%, which may not greatly reduce the screening workload.[57]

Factors Influencing Attendance at Ultrasonography Screening for AAA

Investigators in the Viborg and MASS screening trials examined factors associated with attendance in those invited for ultrasound screening. In the Viborg study, age had a significant impact on screening attendance, which fell steadily from 81.1% in 65 year-old men to 65.1% in 73 year-old men.[49] The attendance rate was 80.5% in men with cardiac, pulmonary, or peripheral vascular disease versus 69% overall. When non-responders were re-invited or given the opportunity to revise appointment times, the overall attendance rate rose indicating that convenience of screening influences attendance. In MASS, advanced age was also associated with a small but significant decrease in attendance rates and an increase in AAA prevalence.[48] A socioeconomic deprivation score derived from census data also had a strong association with attendance. The attendance rate in the quartile with the lowest socioeconomic status was 75% compared to 85% in the quartile with the highest status (OR 0.44; 95% CI, 0.41-0.48). Lower socioeconomic status was also associated with an increased prevalence of AAAs in those scanned (OR 1.38 for the lowest vs. highest quartile; 95% CI, 1.16-1.63).

Key Question 1b. For individuals who do not have AAAs on initial screening, does periodic repeat screening reduce AAA-related adverse health outcomes?

Death from AAA rupture after a single negative ultrasound scan at 65 years of age is an infrequent occurrence. As part of a population screening program in Gloucestershire, UK, all men are offered ultrasonography at age 65.[58] A cohort of 223 65-year-old men with no AAAs on initial ultrasound had repeat ultrasounds 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 < 3.0 cm on initial screening at age 65 years.[16] Over 10 years of follow-up, the incident rate for new AAAs was 4%. None of the new AAAs identified exceeded 4.0 cm in diameter. Other studies from the UK and from the VA ADAM study reported similar findings over shorter time intervals.[59,60] Based on these studies, a single negative ultrasonography exam at age 65 appears to virtually exclude future risks of AAA rupture or death.

Key Question 2. What are the harms associated with AAA screening?

No significant physical harms appear to arise from ultrasound screening for AAA.[57] Table 6 addresses psychological harms that may result from AAA screening. As part of the MASS screening trial, a survey was mailed six weeks after screening to a sub sample of 599 of 25 485 (2.1%) participants with no aneurysm found on screening, and 631 of 1333 (47.3%) participants found to have aortic aneurysms ≥ 3.0 cm.[11] Responses to mailed surveys were 90% in both groups. Those participants with positive scans initially had slightly more anxiety, lower SF-36 mental physical health scores, and lower self-rated health status than those with negative scans; however, these differences were no longer apparent after six weeks. In all cases, however, results fell within population norms.

In the Viborg trial, a retrospective study was performed based on surveys of those attending ultrasound scanning, those invited but not attending, and uninvited controls.[61] One month after screening, participants with AAA ≥ 3.0 cm showed small but significant decreases on the survey measures of general health perception and self-estimated quality of life compared to non-invited controls. No differences were observed on other subscales measuring emotional health, psychosomatic distress, social and family, and marriage roles. Those attending screening who were not found to have AAAs, compared to those invited but not attending had significantly lower scores initially on measures of emotional health, psychosomatic distress, and self-estimated quality of life. One month after screening, however, these differences were no longer present, and scores on psychosomatic distress and self-estimated quality of life were significantly better in attendees versus non-attendees. These findings may reflect anxiety about attending screening or relief when no AAA was identified.

In a prospective case-control study of 161 participants from the Gloucestershire, UK aneurysm screening program, no initial differences in anxiety levels were found between men with normal aortas and those with aneurysms either before of after scanning.[62] Both groups, however, showed significant reductions in anxiety one month after screening.

Key Question 3. For 3.0-5.4 cm AAAs detected through screening, does immediate repair or surveillance reduce AAA-related adverse health outcomes?

Immediate repair of 3.0-3.9 cm AAAs is generally not considered since they rarely rupture, although periodic surveillance is a recommended practice.[26,33,34,63]

Management of 4.0-5.4 cm AAAs has been more controversial. At one time, vascular surgeons recommended elective repair of AAAs ≥ 4.0 cm in those with no medical contraindications.[64] The rationale underlying this recommendation was that patients undergoing early elective surgical repair of moderate-sized 4.0 to 5.4 cm AAAs will be younger and may have lower mortality rates and fewer surgical complications than if surgery were delayed until the AAA expanded to ≥ 5.5 cm. Patients may prefer this approach rather than face a small but definite risk of rupture with delayed repair.

On the other hand, elective AAA repair may be associated with operative mortality rates of 1-5% in referral centers and 4-8% in community settings.[65] On that basis, others recommended periodic surveillance with delayed surgical repair for AAAs that expanded over time to 5.0-6.0 cm.[26,27,66] To address this controversy, two randomized controlled trials were conducted comparing immediate surgical repair to periodic surveillance for 4.0-5.4 cm (Table 7).[31,32,67]

The characteristics and outcomes of these trials are shown in Table 7. The ADAM (ADAM) study was a multi-center trial conducted in 16 Veterans Affairs Medical Centers of 1136 veterans with 4.0-5.4 cm AAAs of whom 569 were randomized to immediate surgical repair and 567 to periodic surveillance with repair for AAAs expanding to ≥ 5.5 cm.[31] In the UK Small Aneurysm Trial (UKSAT), 563 individuals with 4.0-5.4 cm AAAs were randomized to immediate surgical repair and 527 individuals to periodic surveillance with delayed repair.[32,67] The quality of both trials was rated "Good" based on USPSTF quality rating methods.[40]

After eight years of follow-up, neither trial found a significant difference in AAA-related mortality between immediate repair and surveillance patients. Most patients undergoing periodic surveillance in both trials eventually had surgery based on aneurysm expansion (UKSAT 74%; ADAM 62%). The summary odds ratio from the meta-analysis of AAA-related mortality based on unadjusted data for the two trials was 0.77 (95% CI, 0.54-1.12) (Figure 5).

In the ADAM trial, no difference was found in all-cause mortality for immediate repair compared to surveillance. In the UKSAT trial, the hazard ratio for all-cause mortality was 0.83 (95% CI, 0.69-1.00) after adjustment for age, sex, smoking status, and other factors. This result was not attributable to fewer AAA-related deaths, but may have arisen from lifestyle changes in the immediate repair group, such as smoking cessation after surgery. Survival analyses, however, showed no evidence that patients in the immediate repair group had more life-years gained compared to those undergoing surveillance. The summary odds ratio from the meta-

analysis of all-cause mortality combining unadjusted data for the two trials was 0.97 (95% CI, 0.81-1.16) (Figure 6).

Key Question 4. What are the harms associated with repair of AAAs ≥ 5.5 cm?

Harms reported from AAA repair in the major screening trials have already been discussed. Known postoperative complications of elective aneurysm repair include myocardial infarction, respiratory failure, renal failure, ischemic colitis, and spinal cord ischemia. Prosthetic graft infections may also occur but are recognized much later. Reports of both morbidity and mortality rates after AAA repair, however, vary based on the study design.[68] Prospective population and hospital studies generally yield higher rates of complications than retrospective hospital studies. Cardiac complications are the most common with rates ranging from 10.6-11% in prospective population and hospital studies.

A retrospective analysis using data from the Nationwide Inpatient Sample database, a 20% sample of discharge data from all nonfederal US hospitals, examined mortality and complication rates for 16 450 intact AAA repairs from 1994 to 1996.[69] The overall in-hospital mortality rate was 4.2%, with a complication rate of 32.4%. Compared to younger age groups, the OR for in-hospital mortality was 1.8 (95% CI 1.4-2.3) in patients aged 70-79, and 3.8 (95% CI 2.9-4.9) in patients aged over 79 years. Increased in-hospital mortality was also associated with female gender (OR 1.6; 95% CI 1.3-1.9); preoperative renal failure (OR 9.5; 95% CI 7.7-11.7); and more than three preoperative comorbidities (OR 11.2; 95% CI 3.6-35.4).

In other retrospective analyses from the same database, significant variations for in-hospital mortality were associated with surgical specialty, surgeon volume, and hospital volume.[70] The lowest mortality rates were for AAA repairs performed by experienced vascular surgeons in hospitals with a high volume of AAA repairs.

Key Question 5. What are the harms associated with immediate repair or surveillance of 3.0-5.4 cm AAAs?

We found no studies that specifically addressed psychological harms from surveillance for 3.0-3.9 cm AAAs. Table 7 summarizes physical harms of immediate repair compared to surveillance for 4.0-5.4 cm from the ADAM study. Compared to the immediate repair group, the surveillance group only had a significantly increase risk of myocardial infarction. The total number of AAA-related hospitalizations was significantly lower in the surveillance group. Table 6 summarizes findings from the ADAM trial on psychological and functional harms of immediate repair versus surveillance.[71] The two randomized groups did not differ significantly for most Medical Outcomes Study short-form scales. The immediate repair group had higher scores for the general health subscale ($P < 0.0001$). Overall, more patients became impotent after randomization to immediate repair compared with surveillance ($P < 0.03$), but this difference did not become apparent until more than one year after randomization. Maximum

activity level did not differ significantly between the two groups at randomization, but decline over time was significantly greater in the immediate repair group ($P < 0.02$).

The UKSAT trial also used the Medical Outcomes Study short-form to analyze health-related quality of life for all 1090 study participants.[72] At baseline, reported measures of functional status and health were similar for the immediate repair and surveillance groups. After 12 months, patients in the immediate repair group reported significant improvement in perception of general health and lower bodily pain scores compared to the surveillance group.

Endovascular Aneurysm Repair

Endovascular repair of abdominal aortic aneurysms (EVAR) was first attempted in 1991.[73] The impetus for developing this procedure was the expectation that EVAR, as a less invasive procedure than open repair, may reduce procedural morbidity and mortality, speed recovery, decrease use of hospital resources, and reduce costs of AAA repair.[74] Over the last decade, at least 16 different devices have been tested, and as of 2004, the US Food and Drug Administration (FDA) has approved four devices, although one of these has been withdrawn.

We searched the literature from 1994 to 2004 for randomized clinical trials comparing EVAR with open aneurysm repair. The majority of trials identified were non-randomized Phase I or Phase II clinical trials, with either no controls or with matched controls undergoing open repair. Many of these trials were conducted to test investigational devices in support applications for FDA approval. Through our literature search and contacts with experts, we identified five randomized trials ongoing as of July 2004 that compare EVAR with open repair (Table 8).[75,76] All trials include patients with AAAs ≥ 5.0-5.5 cm on ultrasound or computed tomography scanning. Most use all-cause mortality as the primary endpoint. Publications of main results from these trials are expected in the next several years.

We also identified three multi-center registries that are prospectively following patents undergoing EVAR in participating clinical centers: The European EUROSTAR Registry, established in 1996[77]; the UK RETA registry, established in 1996[78]; and the US Lifeline Registry, established in 2001.[79]

One multi-center clinical trial recently reported 30-day mortality rates for 1047 patients age 60 years or older with intact AAAs ≥ 5.5 cm, who were deemed fit for surgery, randomized to EVAR or open surgical repair between September, 1999 and December, 2003.[80] The 30-day mortality rate was 1.7% for 531 patients randomized to EVAR compared to 4.7% for 516 patients assigned to open repair (OR 0.35; 95% CI, 0.16-0.77).

Short-term mortality rates for EVAR from reviews of uncontrolled trials and registry data range from 1.3% to 3.6%.[69,74,81-83] The EVAR 1 trial, however, included only those patients deemed fit for surgery from a larger group of patients with AAAs judged to be anatomically suitable for EVAR. Registry and early trial data include patients who may have been unfit for open repair based on the EVAR 1 inclusion criteria. Patients from the EVAR trial who were unfit for surgery were recruited to participate in a parallel EVAR 2 randomized trial.[76]

EVAR is associated with both short-term and long-term adverse events. In a report from the EUROSTAR registry, 27 of 1554 (2%) required immediate conversion to open repair; and 279 of 1554 patients (18%) experienced systemic cardiac, pulmonary, renal, cerebral, or infectious complications following EVAR,[84] compared to reported rates of 32% for similar complications following open repair of intact AAAs.[69] Long-term adverse events following EVAR may arise from device failure, which could cause bleeding into the aneurysmal sac either around the

device, or from retrograde flow into the aneurysmal sac through collateral blood vessels. These adverse events may require late conversion to open repair or aneurysmal rupture. In a report on four years of data from the EUROSTAR registry, conversion to open repair occurred at an average annual rate of 2.1% and was associated with a 24.4% 30-day operative mortality rate.[85]

Recommendations of Other Groups

In 2004, the Society for Vascular Surgery (SVS) recommended baseline ultrasound screening for AAA patients deemed fit for interventions among all men aged 60 to 85 years, women aged 60 to 85 years with cardiovascular risk factors, and men and women older than 50 years with a family history of AAA.[63] The SVS had previously recommended elective repair for AAA ≥ 5.5 cm for the average patient.[65] For patients with smaller AAAs, they recommend no further testing for aortic diameter less than 3.0 cm; annual ultrasound examinations for 3-3.9 cm AAAs; biannual examinations for 4.0 to 4.5 cm AAAs; and referral to a vascular specialist for AAA greater than 4.5 cm in diameter.

In 1994, the Canadian Preventive Services cited a lack of evidence for or against a recommendation to screen for AAA using ultrasound. This recommendation, like the 1996 USPSTF recommendation, preceded publication of the population-based screening studies reviewed here.

Chapter 4. Conclusion

Table 9 summarizes the overall strength and quality of evidence according to the USPSTF criteria (Appendix 4).[40] We reviewed four good or fair quality randomized, controlled trials of population-based AAA screening in 126 000 men that provide Level I evidence that screening significantly reduces AAA-related mortality in men age 65 to 80 years (summary OR from meta-analysis 0.57; 95% CI, 0.45-0.74). Data on all-cause mortality were available for two of the four trials reviewed. In meta-analysis of the three available trials, no significant reduction in all-cause mortality was evident with screening (summary OR 0.98; 95% CI, 0.95-1.02). We modeled expected outcomes of screening for AAA based on a hypothetical cohort of 65-74 year-old men. The NNS to prevent one AAA-related death was 648 (estimated upper and lower limits 506-1072). One study from the UK included 9342 women and showed no differences in AAA-related outcomes.

A history of smoking is the most significant risk factor distinguishing populations at higher risk for AAA (OR 5.07 for AAA ≥ 4.0 cm; 95% CI, 4.13-6.21). While it is likely that the benefit of population screening is related to prevalence as predicted by AAA risk factors such as smoking, we unfortunately have no direct trial evidence in this regard. We constructed a model to estimate benefits by smoking status for a hypothetical cohort of 65-74 year-old men using US data on lifetime smoking prevalence. Assuming that never-smokers and ever-smokers with AAAs experienced the same risk of AAA-related death and the same benefit of screening, we estimated that 89% of AAA-related deaths occur in ever-smokers. We estimated the NNS to prevent one AAA-related death to be 500 in ever-smokers compared to 1783 in never-smokers.

No significant physical harms were associated with screening. Those found to have AAAs ≥ 3.0 cm during screening initially had more anxiety, lower self-rated health status, and lower self-rated quality of life than those with negative scans. However, these changes tended to be within norms of ratings found in the general population and were no longer present after six weeks.

For individuals who are found to have an AAA ≥ 5.5 cm, immediate surgical repair is warranted provided the patient is fit for surgery. Periodic surveillance appears reasonable for those with 3.0-3.9 cm AAAs, which have a very low risk of rupture. For 4.0-5.4 cm AAAs, immediate surgical repair, compared to surveillance with delayed repair, does not appear to improve either AAA-related mortality or all-cause mortality. The yearly rupture rate of such AAAs with surveillance is 1% or less. In both trials, patients in the immediate repair group had higher scores for self-reported general health status compared to those undergoing surveillance. In the ADAM trial, those undergoing immediate repair reported significantly more impotence after one year, and a greater rate of decline in maximum activity level than did those in the surveillance group.

Open repair of AAAs may result in significant risk of operative mortality as well as such adverse outcomes as cardiac, pulmonary and other complications. Open repair is associated with better outcomes when performed by specialty surgeons in high-volume hospitals.

EVAR appears to reduce short-term morbidity and mortality compared to open repair and may be the preferred procedure for intact AAA repair in some patients. Long-term complications, including AAA rupture and the need of subsequent open repair, may result in significant long-term morbidity and mortality. Periodic surveillance with computed tomography to monitor for complications may also be required for the remainder of the patients' lifetime. Several randomized clinical trials are ongoing, comparing long-term outcomes of EVAR to open

repair for AAAs ≥ 5.5 cm. These trials may provide a better understanding of the balance of benefits and harms for patients undergoing EVAR.

We are not aware of ongoing clinical trials of EVAR for 4.0-5.4 cm AAAs, although more than 20% of EVAR procedures are currently performed in such patients.[86] In the ADAM trial, no significant difference was found in AAA-related or all-cause mortality at eight years for patients undergoing immediate repair compared to periodic surveillance. It is not clear what benefit EVAR may offer for individuals with small AAAs, since the 30-day operative mortality for immediate surgical repair in the ADAM trial of 1.8% was similar to the 30-day operative mortality rate of 1.7% for EVAR recently reported from the EVAR 1 trial.

The screening trials we evaluated compared outcomes of screening in populations. Because the screened group included both patients who were scanned and those who were not, these trials do not allow us to estimate an individual patient's benefit from attending screening and having an ultrasound scan for AAA. A variety of factors, such as fitness to undergo interventions smoking history, age, family history, and comorbidities are important in determining the individual benefit from screening. Primary care providers may need to consider such factors in discussions to inform a patient's screening decision.

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Table 1. Summary of AAA Screening Trials

Trial	MASS	Western Australia	Viborg	Chichester, Men	Chichester, Women
Reference	Ashton, 2002[11]	Norman, 2004[36]	Lindholt, 2002[37]	Scott, 1995[44]	Scott, 1995[44]
Location	UK	Australia	Denmark	UK	UK
Recruitment	Population screening	Population screening	Population screening	Population screening	Population screening
Age	65-74 years	65-83 years	65-73 years	65-80 years	65-80 years
Gender	Male	Male	Male	Male	Female
Ethnicity	Unknown	> 90% Caucasian	100% Caucasian	Unknown	Unknown
Total Randomized	67,800	38,704	12,658	6,433	9,342
Duration of Follow-up, Year	4.1	3.6	5.1	2.5	2.5
Invited for Screening	33,839	19,352	6339	3,205	4,682
Screened, %	80%	63%	69%	73%	65%
Uninvited Controls	33,961	19,352	6,319	3,228	4,660
Ascertainment of Outcomes					
Death Registry	Yes	Yes	No	Yes	Yes
Hospital Records	Yes	Yes	Yes	Yes	Yes
Outcomes ascertained, %	99%	99%§	100%	Not reported	Not reported
Quality	Good	Fair	Fair*	Fair	Fair

§ Provided by author.

* Only hospital records available to ascertain outcomes

Table 2. Quality of Randomized Trials of Screening for AAA

Trial	MASS	Western Australia	Viborg	Chichester
Reference	Ashton, 2002[11]	Norman, 2004[36]	Lindholt, 2002[37]	Scott, 1995[44]
Randomization	Yes, by individual	Yes, by individual	Yes, by individual	Yes, by individual
Allocation Concealed	Yes	Yes	Yes	Yes
Groups Similar at Baseline	Yes	Yes	Not stated	Not stated
Eligibility Criteria Specified	Yes	Yes	Yes	Yes
Outcomes Assessors Blinded	Yes	Not stated	Not stated	Not stated
Care Provider Blinded	Not possible due to type of study			
Patient Unaware of Treatment	Not possible due to type of study			
Maintenance of Comparable Groups	Follow-up data not available for control group			
Reporting of Loss to Follow-up	Yes	Yes	Yes	Yes
Differential Loss to Follow-up	Not possible due to type of study			
Intention-to-Treat Analysis	Yes	Yes	Yes	Yes
Statistical Analysis Appropriate	Yes	Yes	Yes	Yes
Score	Good	Fair	Fair	Fair
Comments		Fair: methods for outcomes assessment not reported	Fair: baseline characteristics and methods for outcomes assessment not reported; outcomes from hospital records only	Fair: baseline characteristics and methods for outcomes assessment not reported

MASS, Multicentre Aneurysm Screening Study.

Table 3. Results of AAA Screening Trials

Study	MASS	Western Australia	Viborg	Chichester, Men	Chichester, Women	Pooled Estimates for Men over 65
Reference	Ashton, 2002[11]	Norman, 2004[36]	Lindholt, 2002[37]	Scott, 1995[44]	Scott, 1995[44]	
Invited for Screening	33,839	19,352	6339	3,205	4,682	
Scanned	27,147	12,203	4843	2,342	3,052	
Accepted Screening, %	80%	63%	69%	73%	65%	72%
AAA in Scanned, n (%)	1330 (4.9%)	875 (7.2%)	191 (4.0%)	178 (7.6%)	40 (1.3%)	5.5%
Uninvited Controls	33,961	19,352	6,319	3,228	4,660	
Duration of Follow-up, Yr	5	2.5	5	5	5	
AAA-Specific Mortality						
Invited	65 (0.19%)	18 (0.09%)	6 (0.09%)	10 (0.31%)	2 (0.04%)	
Controls	113 (0.33%)	25 (0.13%)	19 (0.30%)	17 (0.36%)	2 (0.04%)	0.72 per 1000 person-years
OR* (95% CI)	0.58 (0.42, 0.78)	0.72 (0.39,1.32)	0.31 (0.13, 0.79)	0.59 (0.27,1.29)	1.00 (0.14, 7.07)	0.57 (0.45, 0.74)
All-cause Mortality						
Invited	3750 (11.1%)	1976 (10.2%)	-	532 (16.6%)	503 (10.7%)	
Controls	3855 (11.4%)	2020 (10.4%)	-	508 (15.7%)	476 (10.2%)	
OR* (95% CI)	0.97 (0.93, 1.02)	0.98 (0.91, 1.04)	-	1.07 (0.93, 1.22)	1.05 (0.92, 1.19)	0.98 (0.95, 1.02)
Elective Repair						
Invited	332 (0.98%)	107 (0.55%)	50 (0.79%)	28 (0.87%)	4 (0.08%)	0.96% (0.88%,1.06%)
Controls	92 (0.27%)	54 (0.28%)	14 (0.22%)	5 (0.15%)	2 (0.04%)	0.28% (0.24%, 0.34%)
Emergency Repair						
Invited	27 (0.08%)	9 (0.05%)	6 (0.09%)	3 (0.09%)	1 (0.02%)	0.11% (0.08%, 0.14%)
Controls	54 (0.16%)	8 (0.04%)	30 (0.47%)	8 (0.24%)	1 (0.01%)	0.23% (0.19%, 0.28%)
AAA Rupture						
Invited	67 (0.20%)	33 (0.17%)	4 (0.10%)	8 (0.25%)	3 (0.06%)	0.18% (0.15%, 0.23%)
Controls	134 (0.40%)	38 (0.20%)	20 (0.3%)	20 (0.62%)	2 (0.04%)	0.40% (0.35%, 0.46%)
Operative Mortality						
Elective Repair %	6%	4.3%	6%	0%	0%	6%
Urgent/Emergent Repair %	37%	50%	39%	25%	33%	37%

Table 4. 5-Year Outcomes of AAA Screening in a Cohort of 100,000 Men Aged 65-74 Years

Assumptions*	Baseline	Lower 95% CI	Upper 95% CI
AAA Prevalence	5.5%		
Screening Attendance	72.0%		
AAA-Related Deaths, 1000 person-years	0.72		
OR AAA-related death with screening	0.57	0.45	0.74
All-Cause Deaths, 1000 person-years	28.70		
OR deaths from all causes	0.98	0.95	1.02
AAA-ruptures			
No Screening Program	0.40%	0.35%	0.46%
With Screening Program	0.18%	0.15%	0.23%
Elective Surgery			
No Screening Program	0.28%	0.24%	0.34%
With Screening Program	0.96%	0.88%	1.06%
Emergency Surgery			
No Screening Program	0.23%	0.19%	0.28%
With Screening Program	0.11%	0.08%	0.14%
Operative Mortality			
Elective AAA repair	6%	6%	6%
Emergency AAA repair	37%	37%	37%
Results	Baseline	Lower bound	Upper bound
Total AAAs in Cohort	5,500	5,500	5,500
AAA-Related Deaths, n			
No Screening Program	359	359	359
With Screening Program	205	162	266
AAA Deaths Prevented	154	197	93
NNS to Prevent 1 Death from AAA	648	506	1,072
Deaths from All Causes, n			
No Screening Program	13,368	13,368	13,368
With Screening Program	13,119	12,744	13,616
All-Cause Deaths Prevented (Caused)	249	624	(248)
Elective Surgical Procedures, n			
Invited for Screening	960	880	1060
Not Screened	280	240	340
Emergency Surgical Procedures, n			
Not Screened	230	190	280
Invited for Screening	110	80	140
AAA Ruptures, n			
No Screening Program	400	350	460
With Screening Program	180	150	230
AAA Ruptures Prevented	220	200	230
NNS to Prevent 1 AAA Rupture	455	435	500
Deaths, Elective Surgery, n			
No Screening Program	17	14	20
With Screening Program	58	53	64
Deaths, Emergency Surgery, n			
No Screening Program	85	70	104
With Screening Program	41	30	52
Total Surgical Deaths, n			
No Screening Program	102	85	124
With Screening Program	98	82	115

CI, confidence interval, NNS, number needed to screen.

*OR = Odds ratio with screening program compared to no screening program. Estimates of event rates and relative risks incorporate variability across screening trials in prevalence, acceptance of screening, accuracy of screening, and adherence to clinical management protocols for surgery and surveillance.

Table 5. 5-Year Outcomes of AAA Screening by Smoking History in a Cohort of 100,000 Men Age 65-74 Years

Assumptions	Ever Smokers	Never Smokers	Total Cohort
Lifetime Smoking History, %			69%
AAA Prevalence in Men Age 65-74 years,%			
Ever Smokers			6.4%
Never Smokers			1.8%
AAA-Related Deaths Per 1000 Person-Years			0.72
OR AAA-Related Death with Screening			0.57
U.S. Male Population 65-74 (millions)*			8.3
Results			
Total AAAs in Cohort	4,416	558	4,974
AAA-Related Deaths, n			
Not Screened	320	40	360
Invited for Screening	182	23	205
AAA Deaths Prevented	138	17	155
NNS to Prevent 1 Death from AAA	500	1,783	645
Estimated 5-Year AAA-Related Deaths in the U.S. Male Population Aged 65-74 Years, n			
Not Screened	26,521	3,351	29,872
Invited for Screening	15,129	1,912	17,041
AAA deaths prevented by screening	11,392	1,439	12,831
% AAA-attributable deaths	89%	11%	

NNS, number needed to screen; OR, odds ratio.

*Source: Age Groups and Sex 2000. Summary File 1 100-Percent Data. U.S. Census Data. 2001. Accessed at www.factfinder.census.gov on 15 November 11/15/2004.

Table 6. Harms of AAA Screening and Treatment

Study	Population, n (% Response)	Measurements	Results
MASS Ashton, 2002[11]	6 weeks after screening Positive n=599 (90%) Negative n=631 (90%) Control n=726 (77%)	SF-36, HADS, Short-form state anxiety scale of the Spielberger state-trait anxiety scale, EuroQol EQ-5D	Those with a positive screen, compared to those with negative screens, had slightly higher anxiety scores (P=0.02) but no difference in depression scores (P=0.09) at 6 weeks after screening. Those with a positive screen also had showed lower scores on SF-36 mental (P=0.003) and physical (P=0.003) scales. Self-rated health was also lower in those with a positive screen (P=0.0003). In all cases, results for both groups within population norms. Results in control population were not reported.
	Total 555 with positive screen at 3 and 12 months after aneurysm detection or surgery Surveillance n=426 Surgery n=129)	Same	Those undergoing surgery, compared to surveillance, scored lower on the SF-36 mental health scale at 3 months (P=0.004), but not at 12 months. Surgery was associated with better self-rated health at 3 and 12 months (P=0.0003, P=0.0007 respectively. No significant differences on other measures.
VIBORG Lindholt, 2000[61]	Control n=231 (66%) At screening n=271 (81%) 1 month post screen n=286 (85%) With AAA n=127 (85%) Surgery after surveillance n=29 (81%)	ScreenQL	Those with positive screen significantly lower in health and over-all score. Scores were significantly lower in attendees pre-scan vs post-scan. Those under surveillance had significantly lower scores than those having immediate surgery No differences after surgery.
ADAM Lederle, 2003[71]	1,136 patients at 16 VA Medical Centers with AAAs 4.0-5.4 cm were randomized to immediate surgical repair or surveillance and followed up for 3.5 to 8 years (mean, 4.9 years).	SF-36	The two randomized groups did not differ significantly for most SF-36 scales at most times, but the immediate repair group scored higher overall in general health (P <.0001), which was particularly evident in the first 2 years after randomization, and slightly lower in vitality (P <.05). The baseline value of one SF-36 scale, physical functioning, was an independent predictor of mortality. Overall, more patients became impotent after randomization to immediate repair compared with surveillance (P <.03), but this difference did not become apparent until more than 1 year after randomization. Maximum activity level did not differ significantly between the two randomized groups, but decline over time was significantly greater in the immediate repair group (P <.02).

Table 6. Harms of AAA Screening and Treatment

Study	Population, n (% Response)	Measurements	Results
Lucarotti 1997[62]	161 men attending routine aneurysm screening in the Gloucestershire Aneurysm Screening Programme. 100 men with negative scans compared to 61 men with positive scans. One hundred men had a normal aorta and 61 were identified as having aneurysms.	GHQ-General Health Questionnaire; linear analogue anxiety scale	Tests administered just before screening and 1 month later. There was no difference in anxiety levels between those men with normal aortas and those with aneurysms either before or after screening. There was a statistically significant reduction in anxiety for both these groups 1 month after screening.

ADAM, VA Aneurysm Detection and Management (ADAM) Screening Study; HADS, Hospital Anxiety and Depression Scale; MASS, Multicentre Aneurysm Screening Study; SF-36, is a mental health survey questionnaire; VA, Veterans Affairs.

Table 7. Studies Comparing Surveillance vs Immediate Repair of 4.0-5.4 cm Abdominal Aortic Aneurysms

	UKSAT		ADAM	
Reference	UK Small Aneurysm Trial Participants, 2002[67]		Lederle, 2002[31]	
Population				
Age, Years	60-76 (mean 69.3 years)		50-79 (mean 68.1 years)	
Male	82.80%		99.2%	
Location	93 UK Hospitals		16 Veteran Affairs (VA) Medical Centers	
Interventions				
Surveillance	Repeat imaging every 6 months for diameters between 4.0-5.0 cm and every 3 months for 5.0-5.5 cm.		Repeat imaging every 6 months, repair upon reaching 5.5 cm, enlarged by at least 0.7 cm in 6 months or at least 1.0 cm in 1 year, or until symptomatic	
Immediate Repair	Repair within 3 months		Repair within 6 weeks	
Follow-up Period	8 years		8 years	
Recruitment	1,276 by referral or from screening		126,196 in multi-center VA screening program	
Randomized	1090		1136	
Quality Rating	Good		Good	
Results	**Immediate Repair**	**Surveillance**	**Immediate Repair**	**Surveillance**
N	563	527	569	567
Prevalence				
4.0-4.4 cm	214	213	174	197
4.5-4.9 cm	175	169	205	188
5.0-5.4 cm	174	145	190	182
Mortality Follow-up	100%	100%	85.3%	100%
Completed Surveillance Protocol		93%		87.0%
Elective/Emergency Repairs	526 (93%)	389 (74%)	527 (93%)	349 (62%)
30-day Surgical Mortality	5.5%	7.2%	2.6%	2.0%
Ruptured AAA	1.8%	4.0%	0.4%	1.9%
AAA-related mortality	37	49	19	19
OR* (95% CI)	0.69 (0.44-1.07)		1.0 (0.52-1.90)	
All-cause mortality	159	150	143	122
OR* (95% CI)	0.83 (0.69-1.00)		1.22 (0.93-1.61)	

Table 7. Studies Comparing Surveillance vs Immediate Repair of 4.0-5.4 cm Abdominal Aortic Aneurysms

	UKSAT		ADAM	
HARMS	**Immediate Repair**	**Surveillance**	**Immediate Repair**	**Surveillance**
Re-operation Required	-	-	9	4
Myocardial Infarction	-	-	5	13
Amputation	-	-	2	2
Paraplegia	-	-	0	2
Stroke	-	-	3	2
Pulmonary Embolism	-	-	4	1
Dialysis	-	-	1	2
Late Graft Failure	-	-	2	1
Re-hospitalization	-	-	108	56
Any complication	-	-	275	193

ADAM, VA Aneurysm Detection and Management Screening Study; CI, confidence interval; OR, odds ratio; UKSAT, UK Small Aneurysm Trial Participants.

*Odds ratios were obtained from the random effects meta-analyses based on unadjusted data for each trial.

Table 8. Ongoing Studies of Endovascular Repair of Abdominal Aortic Aneurysms (EVAR)

	DREAM	Open vs Endovascular Repair Trial (OVER)	EVAR 1	EVAR 2
Reference	Prinssen, 2002[75]	Unpublished, Lederle	Brown, 2004[76]	
Location	Holland	U.S.	UK	UK
Protocol	EVAR or open repair	EVAR or open repair	EVAR or open repair	EVAR with best medical management or best medical management
Centers	Required to have performed >20 EVAR, may refer to another center for procedure	40 VA sites that are prepared to perform open and EVAR with at least one approved device	Required to have performed > 20 EVAR procedures	Required to have performed > 20 EVAR procedures
EVAR Device	European Conformité Européenne-Mark Approval or preliminary Market Approval or investigational device exemption of the FDA	Any FDA approved device, including any new devices approved during study	In-house devices or commercially available devices with CE mark, which is favored	In-house devices or commercially available devices with CE mark, which is favored
Inclusion Criteria	Asymptomatic AAA > 5.0 cm, adequate infrarenal neck, life expectation > 2 years, cleared for transabdominal intervention	AAA $\geq$ 5.0 cm or $\geq$ 4.5 cm if expanded more than 0.7 cm in 6 months or 1.0 cm in 1 year, eligible for either procedure	$\geq$ 60 yrs, $\geq$ 5.5 cm, $\geq$ 5.0 cm ultrasound referred for CT scan due to under sizing with U/S, anatomical suitability for EVAR, fitness for surgery	$\geq$ 60 years, $\geq$ 5.5 cm, $\geq$ 5.0 cm ultrasound referred for CT scan due to under sizing with ultrasound, anatomical suitability for EVAR
Exclusion Criteria	Juxtarenal or suprarenal AAA, inflammatory AAA, infrarenal neck unsuitable for EVAR, active infection, transplantation patients, non-iatrogenic bleeding diathesis, connective tissue disease	Previous AAA surgery, urgent need for surgery, or evidence of AAA rupture	Myocardial infarction (MI) or angina onset within last 3 months, unstable angina, severe valve disease, significant arrhythmia, uncontrolled CHF, Severe COPD, Renal Failure FEV1 < 1.0 L	MI within last 3 months, onset of angina within last 3 months, unstable angina at night or at rest

Table 8. Ongoing Studies of Endovascular Repair of Abdominal Aortic Aneurysms (EVAR)

	DREAM	Open vs Endovascular Repair Trial (OVER)	EVAR 1	EVAR 2
Randomization	Stratified by center to either open or EVAR	Equal chance of open or EVAR	Stratified by center to either open or EVAR	Stratified by center to either open or EVAR
Sample Size	400; 200 in each arm. Based on a 10% reduction in mortality and morbidity with a statistical power of 80%	1260; 85% power to detect a 25% difference in mortality.	900 in EVAR Trial 1, with 80% power to detect a reduction in 2.5% mortality for EVAR	280 patients in EVAR Trial 2 with 93% power to detect a difference of 10% between the two treatment regimes
Primary Outcome	Combined perioperative mortality and morbidity	All-cause mortality	All-cause mortality	All-cause mortality
Secondary Measures	QoL with SF-36, EQ-5D, and questionnaire about sexual function, cost-effectiveness	Morbidity, secondary procedures, cost, health-related quality of life	QoL through SF-36, EQ-5D, State-trait Anxiety questionnaire, and the patient generated index; cost-effectiveness of EVAR vs open repair quality-adjusted life-years (QALY)	QoL through SF-36, EQ-5D, State-trait Anxiety questionnaire, and the patient generated index. Cost-effectiveness of best medical management versus EVAR plus best medical management (QALY)
Adverse Events	Complications of remote/systemic and local/vascular	Operative AAA mortality and all AAA repair complications	Tender AAA, ruptured AAA, conversion to open repair, MI, stroke, renal failure and amputation, growth rates, endoleaks	Tender AAA, ruptured AAA, conversion to open repair, MI, stroke, renal failure and amputation, growth rates, endoleaks
Duration	2 years of follow-up	8 years of follow-up	3.33 years/patient	3.33 years/patient
Results Anticipated	Early 2004	12 month data for all participants-early 2007, complete results 2010	Mid 2005	Mid 2005

Anévrisme de l'aorte abdominale: Chirurgie versus Endoprothèse (ACE)

Unpublished
France
Not able to obtain any further information

CHF, congested heart failure; CT, computed tomography; FDA, Food and Drug Administration;MI, myocardial infarction; QALY, quality-adjusted life-years; QoL, quality of life; VA, Veterans Affairs.

Anévrisme de l'aorte abdominale: Chirurgie versus Endoprothèse (ACE)

Table 9. Summary of Evidence Quality for Screening for Abdominal Aortic Aneurysm

Key Question	Study Hierarchy	Overall USPSTF Quality
1a. AAA screening	I	Fair-to-good
1b. Repeat screening	II-2	
2. Screening harms	II-2	
3. Harms of treatment ≥ 5.5 cm	II-2	Good
4. Treatment 4.0-5.4 cm AAA	I	
5. Harms treatment 3.0-5.4 cm AAA	II-2	

Figure 1. Primary Care Screening for Abdominal Aortic Aneurysm: Analytic Framework

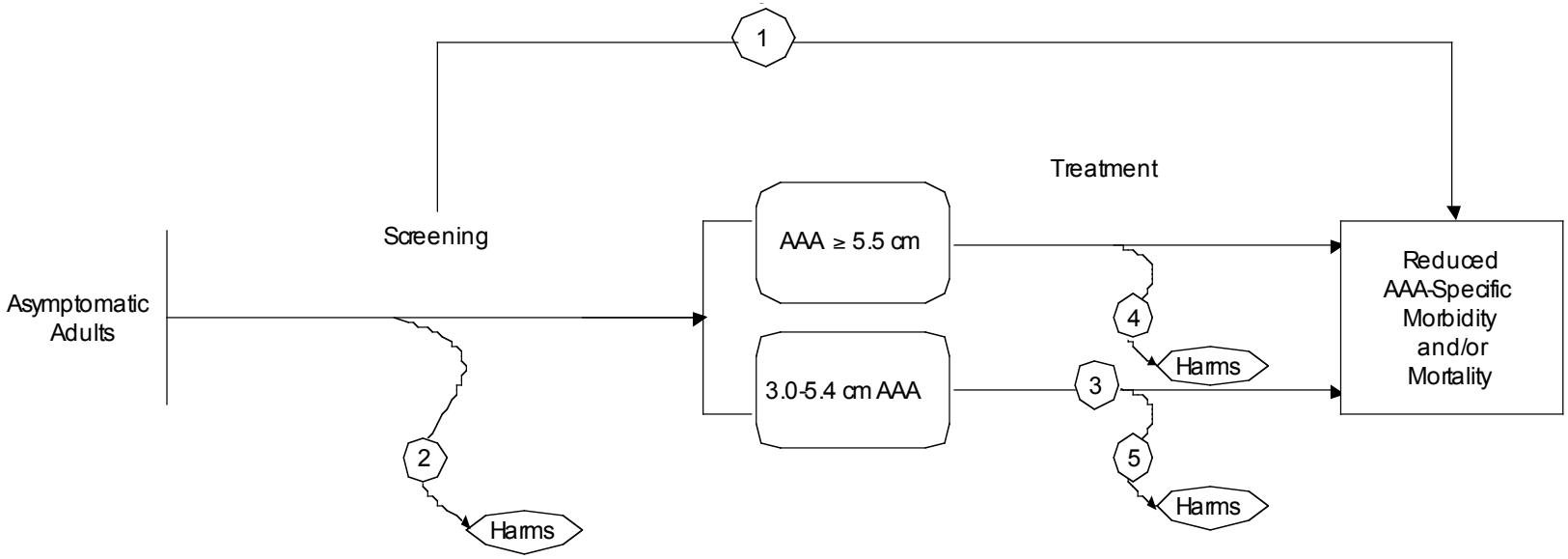
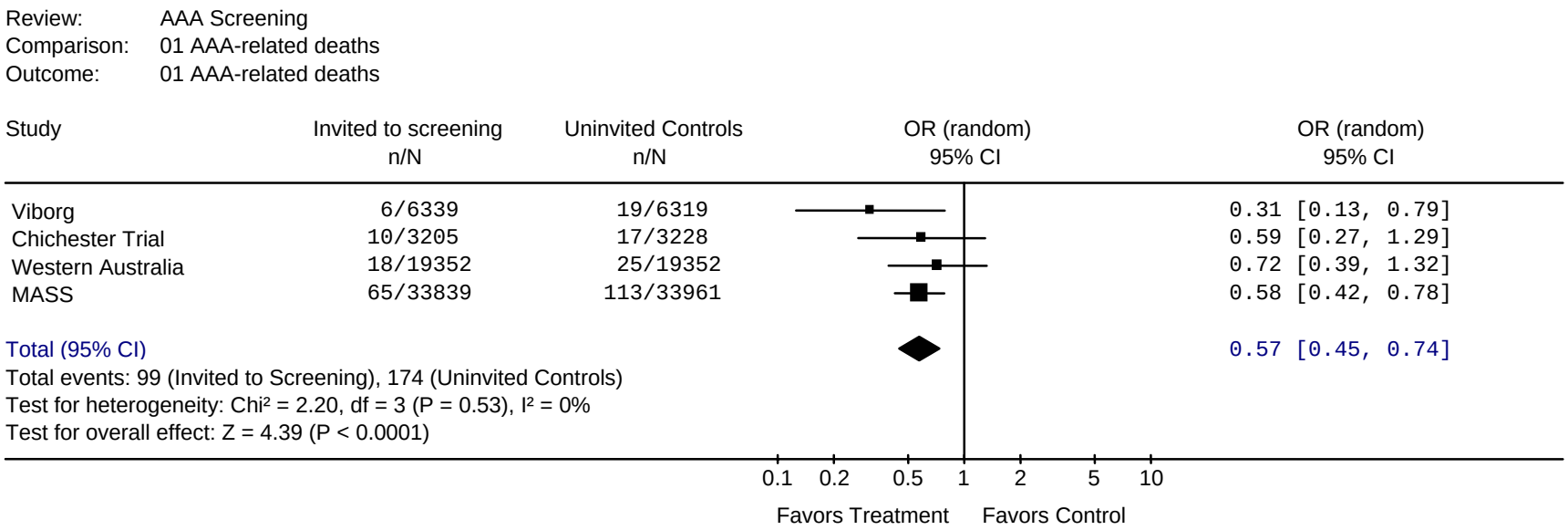


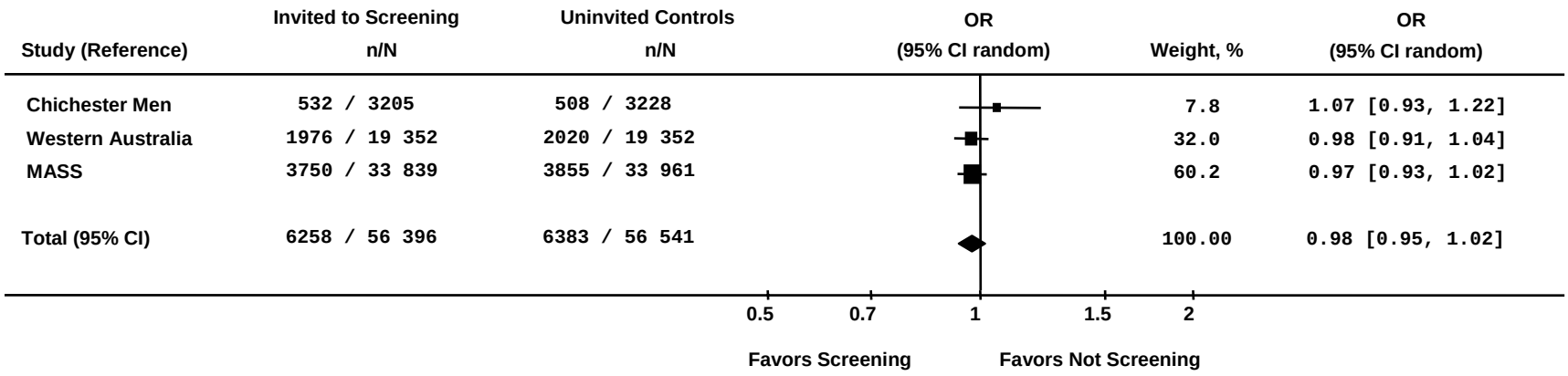
Figure 2. Meta-Analysis of AAA-Related Deaths in Population Screening Trials



CI, confidence interval; MASS, Multicentre Aneurysm Screening Study; OR, odds ratio.

Figure 3. Meta-Analysis of All-Cause Mortality in Population Screening Trials

Review: AAA Screening
Comparison: 04 All-Cause Deaths
Outcome: 01 All-Cause Mortality



CI, confidence interval; MASS, Multicentre Aneurysm Screening Study; OR, odds ratio.

Figure 3. Meta-Analysis of All-Cause Mortality in Population Screening Trials (continued)

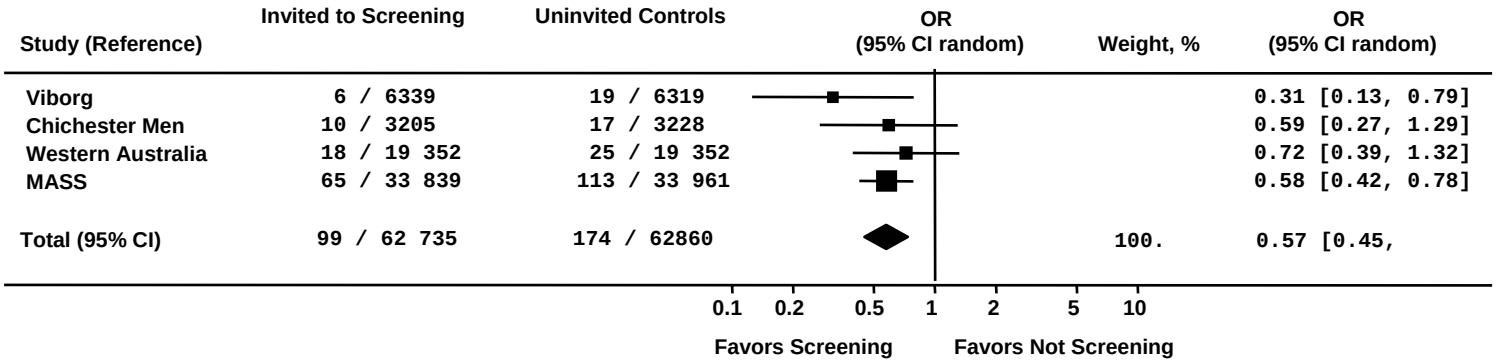


Figure 4. Prevalence of AAAs > 3.0 cm by Age and Smoking History

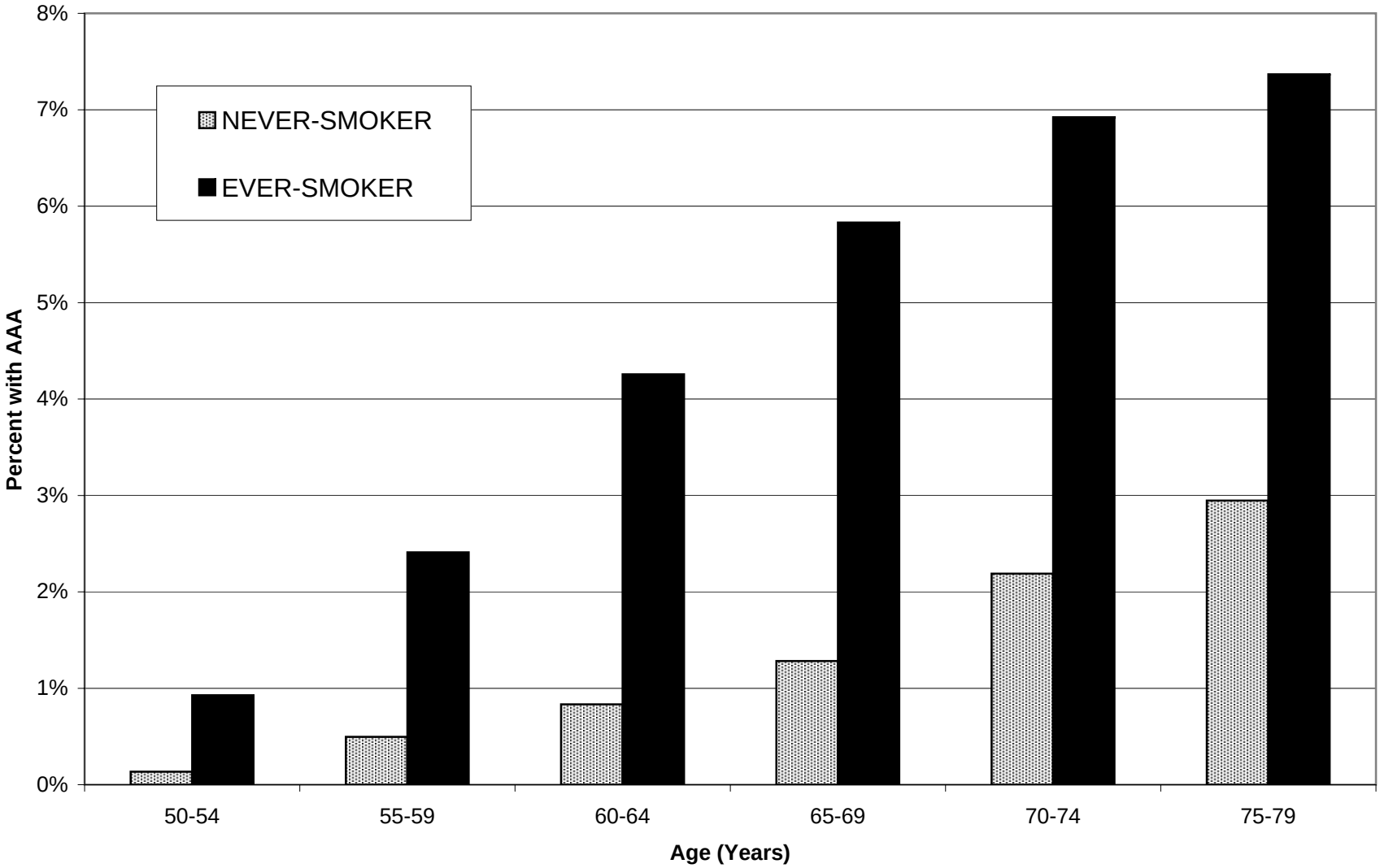
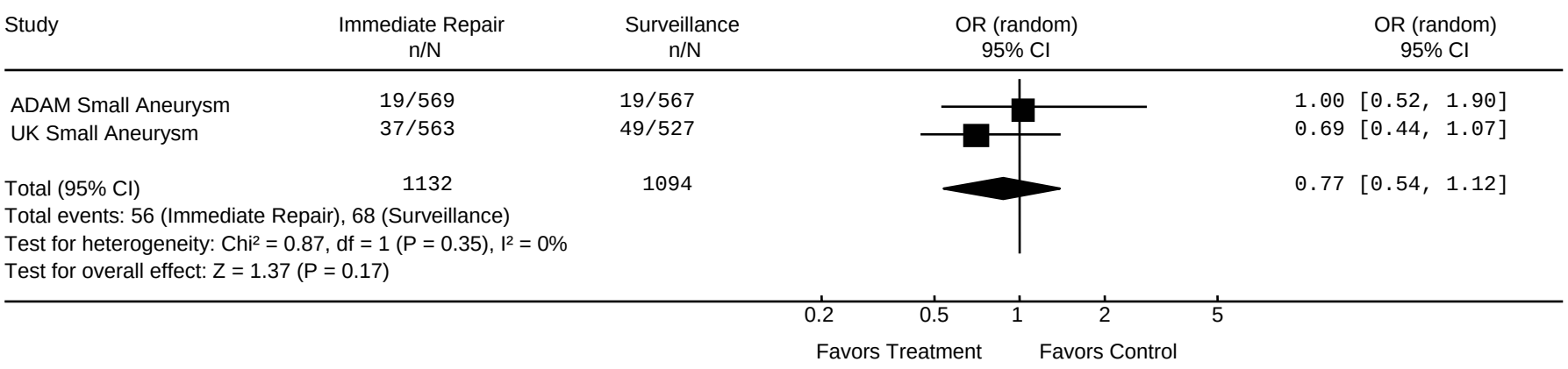


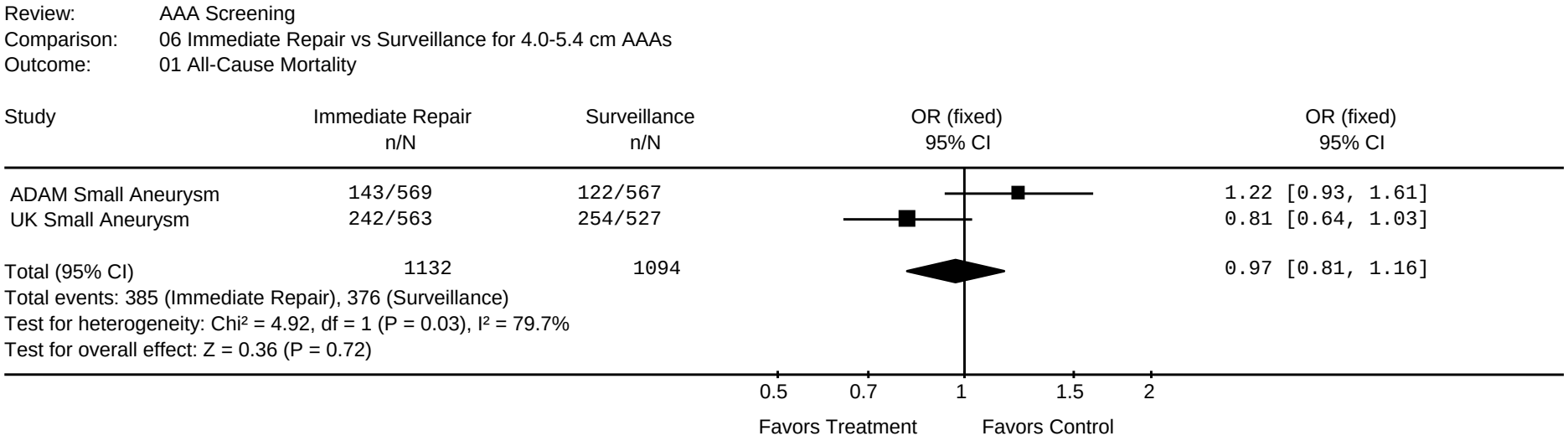
Figure 5. Meta-Analysis of AAA-related Mortality in Small Aneurysm Trials

Review: AAA Screening
Comparison: 06 Immediate Repair vs Surveillance for 4.0-5.4 cm AAAs
Outcome: 03 AAA-related Mortality



ADAM, Aneurysm Detection and Management screening study; CI, confidence interval; OR, odds ratio.

Figure 6. Meta-Analysis of All-Cause Mortality in Small Aneurysm Trials



ADAM, Aneurysm Detection and Management screening study; CI, confidence interval; OR, odds ratio.

Appendix A. Search Strategies

Databases: MEDLINE®, Cochrane database of systematic reviews, Cochrane central register of controlled trials.

Dates searched: 1994-2004

Key Question 1a

1. controlled clinical trials
2. randomized controlled trials
3. multicenter studies
4. double-blind method
5. meta-analysis
6. random allocation
7. single-blind method
8. controlled clinical trial.pt
9. meta analysis.pt
10. randomized controlled trial.pt
11. (meta analy$ or metaanaly$).ti, ab
12. (systematic$ review$ or systematic$ overview$).ti,a b
13. (quantitative$ review$ or quantitative$ overview$).ti, ab
14. evidence based review$.ti, ab
15. or/1-14
16. aortic aneurysm, abdominal
17. 15 and 16
18. mass screening
19. screen$.ti, ab
20. 17 and (18 or 19)
21. limit 20 to yr=1994-2004
22. limit 21 to English language

Key Question 1b

1. Epidemiologic studies/ Epidemiologic studies
2. exp cohort studies
3. Case control.tw
4. (cohort adj (study or studies)).tw
5. Cohort analy$.tw
6. (Follow up adj (study or studies)).tw
7. (observational adj (study or studies)).tw
8. Longitudinal.tw
9. Retrospective.tw
10. Cross sectional.tw
11. Cross-sectional studies
12. or/1-11
13. mass screening/ or screen$.ti,ab
14. 12 and 13
15. aortic aneurysm, abdominal
16. 14 and 15
17. limit 16 to (English language and yr=1994-2004)

Key Question 2

1. Stress, psychological
2. Anxiety

Appendix A. Search Strategies (continued)

3. (anxiety or anxious$).ti,ab.
4. Depression
5. Depressive disorder
6. depress$.ti,ab.
7. harm$.ti,ab.
8. adverse effect$.ti,ab.
9. *"Risk Assessment"
10. "Predictive Value of Tests"
11. "Attitude to Health"
12. "Psychiatric Status Rating Scales"
13. "Health Status"
14. *"Health Status Indicators"
15. "Severity of Illness Index"
16. "Quality of Life"
17. false positive reactions
18. false negative reactions
19. or/1-18
20. aortic aneurysm, abdominal
21. mass screening
22. screen$.ti,ab.
23. or/21-22
24. 20 and 23
25. 24 and 19
26. limit 25 to yr=1994-2004
27. limit 26 to (human and English language)

Key Question 3

1. exp clinical trials/ or clinical trials.mp
2. controlled clinical trials/ or controlled clinical trials.mp
3. randomized controlled trials/ or randomized controlled trials.mp
4. multicenter studies/ or multicenter studies.mp
5. Double-Blind Method/ or double blind.mp
6. Single-Blind Method/ or Single Blind.mp
7. Meta-Analysis/ or Meta-Analysis.mp
8. Random Allocation/ or Random Allocation.mp
9. or/1-8
10. RANDOMIZED-CONTROLLED-TRIAL.pt
11. META-ANALYSIS.pt
12. CONTROLLED-CLINICAL-TRIAL.pt
13. CLINICAL-TRIAL.pt
14. or/10-13
15. (meta analy$ or metaanaly$).ti,ab
16. (systematic$ review$ or systematic$ overview$).ti,ab
17. evidence based review$.ti,ab
18. random$.ti,ab
19. ((doubl$ or singl$) and blind$).ti,ab
20. (meta-anal$ or metaanaly$ or meta analy$).ti,ab
21. or/15-20
22. 9 or 14 or 21
23. vascular surgical procedures
24. surgical procedures, elective
25. surgery
26. surg$.ti,ab
27. "open repair".ti,ab
28. aortic aneurysm, abdominal/su

29. or/23-28
30. blood vessel prosthesis implantation
31. (endo$ or endovascular or pevr or evar).ti,ab
32. or/30-31
33. aortic aneurysm, abdominal
34. 29 or 32
35. 33 and 34 and 22
36. limit 35 to yr=1994-2004
37. limit 36 to (human and English language)

Key Question 4 and 5

1. treatment outcome
2. cause of death
3. mortality
4. morbidity
5. postoperative complications
6. or/1-5
7. "Prognosis"
8. "Survival Rate"
9. "Survival Analysis"
10. "Risk Factors"
11. or/7-10
12. vascular surgical procedures
13. surgical procedures, elective
14. surgery
15. surg$.ti,ab
16. "open repair".ti,ab
17. or/12-16
18. blood vessel prosthesis implantation
19. (endo$ or endovascular or pevr or evar).ti,ab
20. or/19-20
21. controlled clinical trials
22. randomized controlled trials
23. multicenter studies
24. Double-Blind Method
25. Meta-Analysis
26. Random Allocation
27. Single-Blind Method
28. controlled clinical trial.pt
29. meta analysis.pt
30. randomized controlled trial.pt
31. (meta analy$ or metaanaly$).ti,ab
32. (systematic$ review$ or systematic$ overview$).ti,ab
33. (quantitative$ review$ or quantitative$ overview$).ti,ab
34. evidence based review$.ti,ab
35. or/21-34
36. 6 or 11
37. 17 or 20
38. 35 and (36 and 37)
39. aortic aneurysm, abdominal
40. 38 and 39
41. limit 40 to yr=1994-2004
42. limit 41 to (human and English language)

Appendix B. Inclusion Criteria and Search Results

Key Question (KQ)	Inclusion Criteria	# Abstracts Reviewed*	# Articles Reviewed	Included Articles
KQ 1: a. Does AAA screening in an asymptomatic average-risk population reduce AAA-related adverse health outcomes?	Unselected population relevant to primary care, reported health outcome reduction of AAA specific morbidity/mortality/rupture rate, randomized controlled trial, USPSTF quality of fair or good, English.	39	7	5
KQ 1: b. For individuals who do not have AAAs on initial screening, does periodic repeat screening reduce AAA-related adverse health outcomes?	Follow-up or cohort study that included repeat scanning of a representative population, USPSTF quality of fair or good, English.	108	8	4
KQ 2: What are the harms associated with AAA screening?	RCT (or cohort study if no RCT available) screening for AAA, which explicitly evaluates or discusses harms, USPSTF quality of fair or good, English.	32	4	4
KQ 3: For 3.0-5.5 cm AAAs detected through screening, does immediate repair or surveillance reduce AAA-specific adverse health outcomes?	Population relevant to primary care, reported AAA-specific adverse health outcome, randomized controlled trial, USPSTF quality of fair or good, English.	387	5	2
KQ 4: What are the harms associated with repair of AAAs $\geq$ 5.5 cm?	RCT (or cohort study if no RCT available) of treatment of AAA, which explicitly evaluates or discusses harms, USPSTF quality of fair or good, English.	92	8	6
KQ 5: What are the harms associated with immediate repair or surveillance of 3.0-5.4 cm AAAs?			4	2

RCT, randomized controlled trial; USPSTF, U.S. Preventive Services Task Force

* All abstracts were reviewed for relevance to other key questions.

Appendix C. Excluded Studies

Key Question 1a Does AAA screening, in an asymptomatic average-risk or high-risk population, reduce AAA-related adverse health outcomes?

Study	Reason for Exclusion
Heather BP, Poskitt KR, Earnshaw JJ, Whyman M, Shaw E. Population screening reduces mortality rate from aortic aneurysm in men. Br J Surg. 2000; 87(6):750-753.	Not a randomized controlled trial.
Wilmink TB, Quick CR, Hubbard C, Day NE. The influence of screening on the incidence of ruptured abdominal aortic aneurysms. J Vasc Surg. 1999;30(2):203-208.	Not a randomized controlled trial.

Design-Specific Criteria and Quality Category Definitions

Systematic Reviews

Criteria:

- Comprehensiveness of sources considered/search strategy used.
- Standard appraisal of included studies.
- Validity of conclusions.
- Recency and relevance are especially important for systematic reviews.

Definition of ratings from above criteria:

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.

Fair: Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies.

Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

Case-Control Studies

Criteria:

- Accurate ascertainment of cases.
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both.
- Response rate.
- Diagnostic testing procedures applied equally to each group.
- Measurement of exposure accurate and applied equally to each group.
- Measurement of exposure accurate and applied equally to each group.
- Appropriate attention to potential confounding variables.

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; respo9nse rate equally to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rates less than 80 percent or attention to some but not all important confounding variables.

Poor: Major section or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

Randomized Controlled Trials and Cohort Studies

Criteria:

- Initial assembly of comparable groups:
    - -for randomized controlled trials (RCTs): adequate randomization, including first concealment and whether potential confounders were distributed equally among groups.
    - -for cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts.
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination).
- Important differential loss to follow-up or overall high loss to follow-up.
- Measurements: equal, reliable, and valid (includes masking of outcome assessment).
- Clear definition of the interventions.
- All important outcomes considered.

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening tests; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100 broad-spectrum of patients.

Fair: Evaluates relevant available screening tests; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a “medium” spectrum of patients.

Poor: Has fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum of patients.

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primacy care, adequately described.
- Study uses a credible reference standard, performed regardless of test results.
- Reference standard interpreted independently of screening test.
- Handles indeterminate result in a reasonable manner.
- Spectrum of patients included in study.
- Sample size.
- Administration of reliable screening test.

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner;
includes large number (more than 100) broad-spectrum patients with and without disease.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50-100 subjects) and a “medium” spectrum of patients.

Poor: Has fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum patients.

Hierarchy of Research Design

I	Properly conducted randomized controlled trial (RCT).
II-1:	Well-designed controlled trial without randomization.
II-2:	Well-designed cohort or case-control analytic study.
II-3:	Multiple time series with or without the intervention; dramatic results from uncontrolled experiments.
III:	Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees.

Reference

1. Saha S, Hoerger TJ, Pignone MP, Teutsch SM, Helfand M, Mandelblatt JS; Cost Work Group, Third U.S. Preventive Services Task Force. *Am J Prev Med*. 2001;20(3):36-43.

2. 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. *American Journal of Preventive Medicine* 2001; 20(3:Suppl):Suppl-35.