JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Primary Care Screening for Abdominal Aortic Aneurysm
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Ruptured abdominal aortic aneurysms (AAAs) have mortality estimated at 81%.

OBJECTIVE To systematically review the evidence on benefits and harms of AAA screening and small aneurysm treatment to inform the US Preventive Services Task Force.

DATA SOURCES MEDLINE, PubMed (publisher supplied only), Database of Abstracts of Reviews of Effects, and Cochrane Central Register of Controlled Trials for relevant English-language studies published through September 2018. Surveillance continued through July 2019.

STUDY SELECTION Trials of AAA screening benefits and harms; trials and cohort studies of small (3.0-5.4 cm) AAA treatment benefits and harms.

DATA EXTRACTION AND SYNTHESIS Two investigators independently reviewed abstracts and full-text articles and extracted data. The Peto method was used to pool odds ratios (ORs) for AAA-related mortality, rupture, and operations; the DerSimonian and Laird random-effects model was used to pool calculated risk ratios for all-cause mortality.

MAIN OUTCOMES AND MEASURES AAA and all-cause mortality; AAA rupture; treatment complications.

RESULTS Fifty studies (N = 323 279) met inclusion criteria. Meta-analysis of population-based randomized clinical trials (RCTs) estimated that a screening invitation to men 65 years or older was associated with a reduction in AAA-related mortality over 12 to 15 years (OR, 0.65 [95% CI, 0.57-0.74]; 4 RCTs [n = 124 926]), AAA-related ruptures over 12 to 15 years (OR, 0.62 [95% CI, 0.55-0.70]; 4 RCTs [n = 124 929]), and emergency surgical procedures over 4 to 15 years (OR, 0.57 [95% CI, 0.48-0.68]; 5 RCTS [n = 175 085]). In contrast, no significant association with all-cause mortality benefit was seen at 12- to 15-year follow-up (relative risk, 0.99 [95% CI 0.98-1.00]; 4 RCTs [n = 124 929]). One-time screening was associated with significantly more procedures over 4 to 15 years in the invited group compared with the control group (OR, 1.44 [95% CI, 1.34-1.55]; 5 RCTs [n = 175 085]). Four trials (n = 3314) of small aneurysm surgical treatment demonstrated no significant difference in AAA-related mortality or all-cause mortality compared with surveillance over 1.7 to 12 years. These 4 early surgery trials showed a substantial increase in procedures in the early surgery group. For small aneurysm treatment, registry data (3 studies [n = 14 424]) showed that women had higher surgical complications and postoperative mortality compared with men.

CONCLUSIONS AND RELEVANCE One-time AAA screening in men 65 years or older was associated with decreased AAA-related mortality and rupture rates but was not associated with all-cause mortality benefit. Higher rates of elective surgery but no long-term differences in quality of life resulted from screening.

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Abdominal aortic aneurysms (AAAs) are often asymptomatic, with slow expansion until rupture. AAA screening to identify and treat aneurysms before rupture can potentially prevent a fatal outcome. To prevent rupture, AAA, defined as an aneurysm 3.0 cm in diameter or larger, is most commonly surgically repaired via open repair or endovascular aneurysm repair (EVAR) when it reaches a diameter of 5.5 cm.[1-3] The role of pharmacotherapy to slow aneurysm expansion has been uncertain.[4]

Reported AAA prevalence rates in persons 60 years or older have declined from 3.9% to 7.2% in the 1990s[5,6] to more contemporary estimates that range from 1.2% to 3.3%.[7,8] The most important risk factors for the development of AAA include advanced age,[9,10] male sex,[10,11] smoking,[4,11-13] and family history of AAA.[12-14]

In 2014, the US Preventive Services Task Force (USPSTF) recommended 1-time screening for AAA by ultrasonography in asymptomatic men aged 65 to 75 years who have ever smoked (B recommendation).[15] The USPSTF concluded that the benefits of screening do not clearly outweigh the possible harms and recommended that clinicians selectively offer screening for AAA in men aged 65 to 75 years who have never smoked (C recommendation).[15] Also, the USPSTF recommended against routine screening for AAA in asymptomatic women who have never smoked (D recommendation) and determined that there was insufficient evidence for screening women aged 65 to 75 years who have ever smoked (I statement).[15] This review was prepared to inform an updated recommendation by the USPSTF on the evidence related to the effectiveness of 1-time and repeat screening for AAA and possible related harms, as well as the effectiveness and related harms of treatment (pharmacotherapy or surgery) of small AAAs (3.0-5.4 cm in diameter).

Methods

Scope of Review

Five key questions (KQs) (**Figure 1**) were developed to identify the benefits (KQ1) and harms (KQ3) of 1-time screening for AAA, the effects of rescreening for AAA on health outcomes or AAA incidence (KQ2), and the effectiveness (KQ4) and harms (KQ5) of treatment of small AAA (3.0-5.4 cm in diameter). Additional methodological details are publicly available in the full evidence report at http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/abdominal-aortic-aneurysm-screening1.

Data Sources and Searches

To identify studies published since the 2014 USPSTF review,[17] literature searches were conducted from January 2013 through September 4, 2018, in MEDLINE, PubMed (for publisher-supplied records only), the Database of Abstracts of Reviews of Effects, and the Cochrane Central Register of Controlled Trials (eMethods in the Supplement). Additional studies were located by reviewing reference lists of other systematic reviews and through suggestions by experts. Ongoing surveillance was conducted after September 2018 through July 26, 2019, to identify newly published studies that may affect the findings of the review. This was accomplished through targeted searches of journals with a high impact factor and journals relevant to the topic to identify major studies that might affect the conclusions or understanding of the evidence and therefore the related USPSTF recommendation. No additional articles were identified during the surveillance period.

Study Selection

Two reviewers independently evaluated articles from the previous review in addition to citations and full-text articles from the literature searches against specified inclusion criteria (eTable 1 in the Supplement). Eligible screening studies used ultrasound as the screening modality for identifying AAA in asymptomatic adults older than 50 years. Only randomized clinical trials (RCTs) comparing 1-time screening with no screening were used to evaluate the effectiveness of screening for AAA (KQ1). When assessing the benefits of repeated AAA screening and the harms of screening for AAA, RCTs and large cohort studies (n ≥1000) of asymptomatic adult populations were considered (KQ2 and KQ3). Studies of the effectiveness of treatment and related harms focused on individuals with small AAAs (3.0-5.4 cm in diameter) because the majority of screen-detected aneurysms are small. The effectiveness of treating small AAAs (KQ4) was examined through RCTs evaluating surgical intervention or pharmacotherapeutic treatment compared with surveillance, usual care, or placebo. The criteria for assessing harms of treating small AAAs (KQ5) included RCTs, observational studies, and registry data related to surgical harms. The results for pharmacotherapy interventions for KQ4 and KQ5 are not reported in depth in this article but are presented in the Supplement and available in the full report.

Data Extraction and Quality Assessment

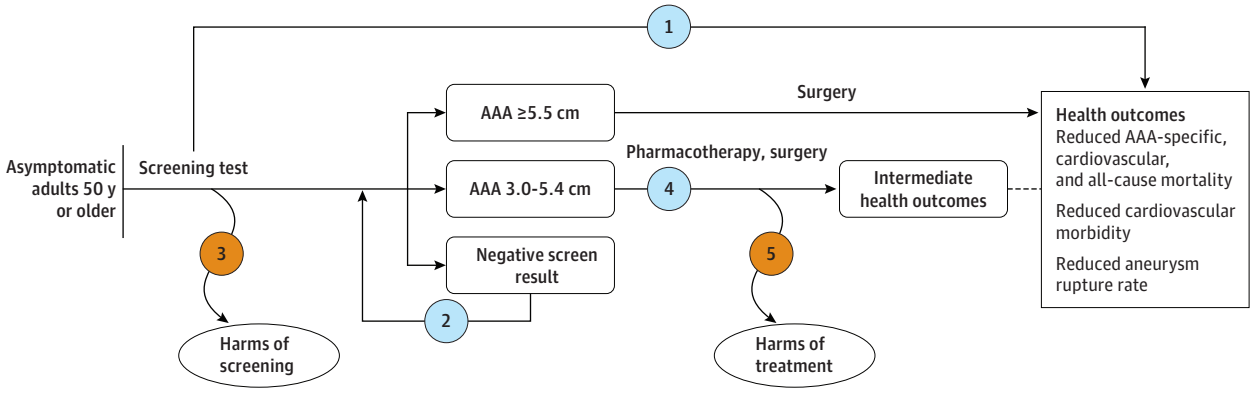
Two reviewers applied USPSTF design-specific criteria[16] to assess the methodological quality of all eligible studies, and studies were evaluated to be good or fair quality using items from the Newcastle-Ottawa Scale[18] and USPSTF quality rating standards.[16] Each study was assigned a quality rating of "good," "fair," or "poor." Discordant quality ratings were resolved by discussion or by a third reviewer and adjudicated as needed. Studies were rated as poor quality and excluded if there was a major flaw such as very high attrition (generally >40%); differential attrition between intervention groups (generally >20%); substantial lack of baseline comparability between groups without adjustment; or major concerns about the trial conduct, analysis, or reporting of results. Poor-quality observational studies had multiple threats to internal validity and were excluded from the review. One reviewer extracted data from all included studies rated as fair or good quality directly into summary tables, and a second reviewer checked the data for accuracy.

Subpopulations of interest were selected a priori based on the previous review and recommendation statement, established characteristics associated with the development of AAA, and feedback received from 3 key informants during the scoping phase. The subpopulation approach described in Whitlock et al[19] was followed to audit outcomes and rate the credibility of the subpopulation data provided by included studies.

Data Synthesis and Analysis

To evaluate the effectiveness of screening for AAA, all-cause mortality and AAA-related mortality, rupture, and emergency surgical procedures were examined in RCTs that compared screening vs no screening. The primary analysis for all-cause mortality pooled

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



Key questions

1 What are the effects of 1-time screening for abdominal aortic aneurysm (AAA) on health outcomes in an asymptomatic population 50 years or older?

a. Do the effects of 1-time screening for AAA vary among subpopulations (ie, by age, sex, smoking status, family history, or race/ethnicity)?

2 What are the effects of rescreening for AAA on health outcomes or AAA incidence in a previously screened, asymptomatic population without AAA on initial screening?

a. Do the effects of rescreening for AAA vary among subpopulations (ie, by age, sex, smoking status, family history, or race/ethnicity)?

b. Do the effects of rescreening for AAA vary by the time interval between screenings?

3 What are the harms of 1-time and repeated screening for AAA?

a. Do the harms of 1-time and repeated screening for AAA vary among subpopulations (ie, by age, sex, smoking status, family history, or race/ethnicity)?

4 What are the effects of treatment (pharmacotherapy or surgery) on intermediate and health outcomes in an asymptomatic, screen-detected population with small AAAs (ie, aortic diameter of 3.0-5.4 cm)?

a. Do the effects of treatment of small AAAs vary among subpopulations (ie, by age, sex, smoking status, family history, or race/ethnicity)?

5 What are the harms of treatment in an asymptomatic, screen-detected population with small AAAs (ie, aortic diameter of 3.0-5.4 cm)?

a. Do the harms of treatment of small AAAs vary among subpopulations (ie, by age, sex, smoking status, family history, or race/ethnicity)?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes. A dashed line depicts a health outcome that follows an intermediate outcome. Refer to USPSTF Procedure Manual for further details.[16] AAA indicates abdominal aortic aneurysm.

calculated risk ratios using the DerSimonian and Laird[20] random-effects model, since statistical heterogeneity was low (I^2 = 0%, τ^2 = 0.0). The Peto method was used to pool odds ratios (ORs) for AAA-related mortality, rupture, and emergency surgical procedures because events were rare and trials had a similar number of participants in both study groups.[21]

Meta-analyses of the rescreening studies included in KQ2 were not conducted because of substantial differences in patient population, length of follow-up, and outcomes reported.

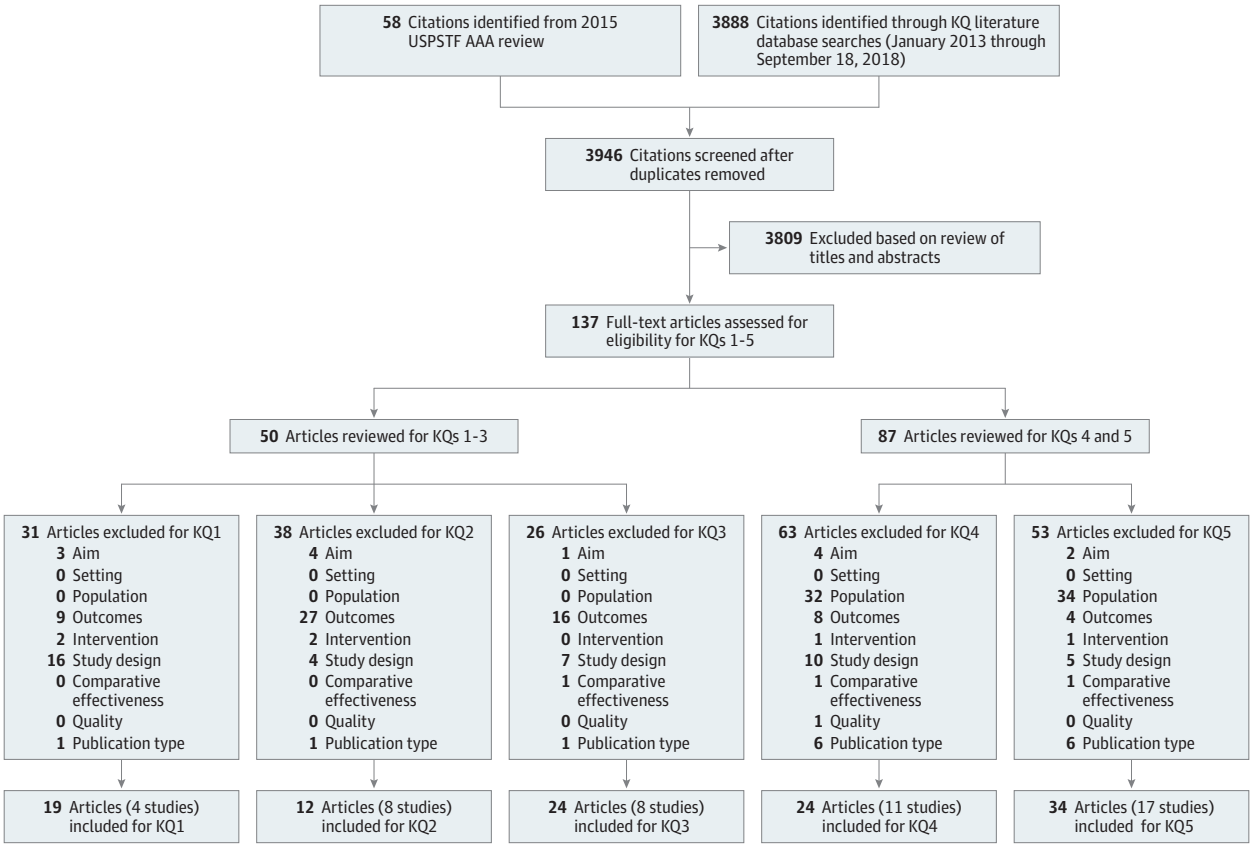
To analyze the harms of screening vs no screening in KQ3, 30-day mortality after elective surgery, 30-day mortality after emergency surgery, overall operations, elective operations, emergency operations, and quality of life (QOL) measures were examined. Only 2 trials reported 30-day mortality after elective surgery and 30-day mortality after emergency surgery outcomes; therefore, those trials were not pooled. The Peto method was used to pool overall operations, elective operations, and emergency operations, as described under KQ1. Because of the substantial difference in quality-of-life measurements and insufficient reporting of data (eg, lack of variation parameters), these data could not be pooled in the studies of screening vs no screening.

All statistical testing was 2-sided, and $P < .05$ was considered statistically significant. Statistical heterogeneity was examined across trials with the I^2 statistic and χ^2 test of heterogeneity. Stata version 15.1 (StataCorp) was used for all analyses.

The effectiveness of early intervention (KQ4) and associated harms of treating small AAAs (KQ5) was evaluated by capturing AAA growth, all-cause mortality, AAA-related mortality, and aneurysm ruptures. The data were narratively described and presented in data tables. Meta-analyses were not conducted because of the small number of studies of each intervention type.

The strength of evidence was rated for each key question based on consistency (similarity of effect direction and size), precision (degree of certainty around an estimate), reporting bias (potential for bias related to publication, selective outcome reporting, or selective analysis reporting), and study quality (ie, study limitations).

Figure 2. Literature Search Flow Diagram: Primary Care Screening for Abdominal Aortic Aneurysm



Reasons for exclusion: Aim: Study aim was not relevant. Setting: Study was not conducted in a country relevant to US practice, or not conducted in, recruited from, or feasible for primary care or a health system. Population: Study was not conducted in an included population. Outcomes: Study did not have relevant outcomes or had incomplete outcomes. Intervention: Intervention was out of scope. Study design: Study did not use an included design. Comparative effectiveness: Active comparator. Quality: Study was poor quality. Publication type: Abstract-only, non-English publication. AAA indicates abdominal aortic aneurysm; KQ, key question; USPSTF, US Preventive Services Task Force.

Results

Two reviewers evaluated 3946 citations and 137 full-text articles against inclusion criteria, and 33 studies (69 articles)[5,6,8,22-88] met inclusion criteria for this systematic review (**Figure 2**). Nine new studies were included (4 RCTs,[24,57,63,79] 2 cohort studies,[80,82] and 3 registry studies[27,60,70]) and 24 studies (13 RCTs, 8 cohort studies, 1 case-control study, and 2 registry studies) were carried forward from the previous USPSTF report.

Benefits of Screening

Key Question 1. What are the effects of 1-time screening for AAA on health outcomes in an asymptomatic population 50 years or older?

Two fair-[5,23] and 2 good-quality[6,83] population-based screening RCTs assessed AAA screening effectiveness on AAA-specific mortality and all-cause mortality (**Table 1**): the Multicenter Aneurysm Screening Study (MASS)[22,45,46,83,84]; the Chichester, United Kingdom, screening trial[23,76,78,86]; the Viborg County, Denmark, screening trial[6,54-56,58]; and the Western Australia screening trial.[5,65,66,81,88] The trials randomized participants to either an invitation to 1-time ultrasound screening or a usual care control group. All trials defined AAA as an aortic diameter of 3.0 cm or greater, and AAA prevalence varied from 4% to 7.6%; the majority of screen-detected AAAs were smaller than 4.5 cm in diameter. Mean or median follow-up in these 4 population-based screening trials ranged from 12.8 to 15 years, with short-term results published at 3- to 5-year intervals.

One additional new population-based screening trial in Denmark (Viborg Vascular [VIVA]) was included solely for the outcome of number of operations.[57] VIVA randomized participants to a multicomponent screening vs no screening for hypertension, peripheral artery disease, and AAA. Participants with confirmed AAA or peripheral artery disease were counseled to initiate preventive interventions, with aspirin and statin therapy prescribed to those meeting a total cholesterol threshold value.[57] The effects of AAA screening alone could not be independently assessed with respect to all-cause mortality or AAA mortality because multicomponent screening and cardiovascular disease (CVD)–prevention interventions were administered; however, the number of procedures was included in this review, as they would almost exclusively be expected to be attributable to AAA screening.

Table 1. Characteristics and Outcomes of Abdominal Aortic Aneurysm Screening Trials

Source (Quality)	Participants Randomized (Country)	Eligible Age (Mean), y	AAA Prevalence, %	Mean Follow-up, y	All-Cause Mortality, RR (95% CI)[a]	OR (95%CI)[a]					30-d Mortality After Surgery, RR (95% CI)	
						AAA		Surgery				
						Mortality	Rupture	All	Elective	Emergency	Elective	Emergency
Chichester Ashton et al,[23] 2007 (Fair)	15 382 (6040 men, 9342 women) (United Kingdom)	65-80 (72.0[b])	Men: 7.6 Women: 1.3	Men: 15.0 Women: 10.0[b]	Men: 1.0 (0.97-1.04)	Men: 0.88 (0.60-1.31)	Men: 0.87 (0.60-1.25)	Men: 1.45 (0.97-2.17)	Men: 2.13 (1.28-3.55)	Men: 0.77 (0.41-1.48)	NR	NR
Viborg Lindholt et al,[58] 2010 (Good)	12 639 men (Denmark)	64-73 (67.7)	3.9	13.0	0.98 (0.95-1.02)	0.37 (0.24-0.59)	0.46 (0.27-0.79)	1.24 (0.93-1.64)	1.97 (1.40-2.78)	0.47 (0.29-0.77)	NR	NR
MASS Thompson et al,[83] 2012 (Good)	67 800 men (United Kingdom)	65-74 (69.2)	4.9	13.1	0.98 (0.96-1.00)	0.59 (0.50-0.70)	0.58 (0.50-0.67)	1.54 (1.37-1.73)	2.11 (1.85-2.41)	0.50 (0.39-0.64)	0.76 (0.40-1.45)	0.98 (0.68-1.43)
Western Australia McCaul et al,[5] 2016 (Fair)	41 000 men (Australia)	64-83 (72.6)	7.2	12.8	0.99 (0.97-1.01)	0.92 (0.69-1.22)	0.73 (0.54-0.98)	1.23 (1.09-1.40)	1.30 (1.14-1.48)	0.60 (0.37-0.95)	0.82 (0.43-1.57)	1.43 (0.90-2.25)
VIVA Lindholt and Søgaard,[57] 2017 (Fair)	50 156 men (Denmark)	65-73 (69.0[b])	3.3	4.4[a]	NR[c]	NR[c]	NR	1.87 (1.54-2.26)	2.27 (1.84-2.81)	0.82 (0.53-1.27)	NR	NR
Pooled estimate					0.99 (0.98-1.0)	0.65 (0.57-0.74)	0.62 (0.55-0.70)	1.44 (1.34-1.55)	1.75 (1.61-1.90)	0.57 (0.48-0.68)	Not calculated	NA
I^2, %					0.0	79.7	53.3	74.1	88.5	26.7	Not calculated	NA

Abbreviations: AAA, abdominal aortic aneurysm; MASS, Multicenter Aneurysm Screening Study; NA, not applicable; NR, not reported; OR, odds ratio; RR, relative risk; VIVA, Viborg Vascular.

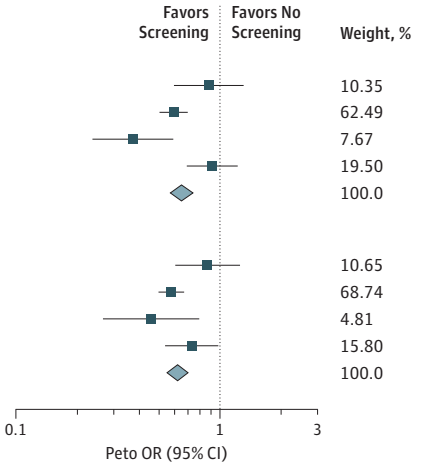
[a] Calculated.

[b] Median.

[c] Did not include the VIVA trial mortality data because of the inability to capture the independent contribution of AAA screening within the multicomponent screening program.

Figure 3. Pooled Analysis of Abdominal Aortic Aneurysm–Related Mortality and Ruptures (Men Only) for Rupture in 1-Time Screening Trials

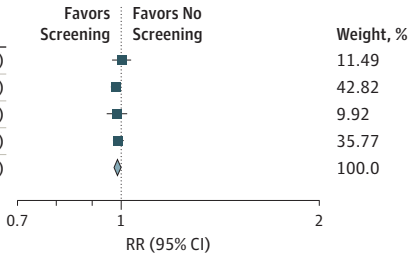
Source	Mean Follow-up, y	No. With Event/Total (%)		Peto OR (95% CI)	Weight, %
		Intervention	Control		
AAA mortality					
Chichester,[23] 2007	15	47/2995 (1.6)	54/3045 (1.8)	0.88 (0.60-1.31)	10.35
MASS,[83] 2012	13.1	224/33 883 (0.7)	381/33 887 (1.1)	0.59 (0.50-0.70)	62.49
Viborg,[58] 2010	13	19/6333 (0.3)	55/6303 (0.9)	0.37 (0.24- 0.59)	7.67
Western Australia,[5] 2016	12.8	90/19 249 (0.5)	98/19 231 (0.5)	0.92 (0.69-1.22)	19.50
Subtotal I^2 = 79.7%, P = .002				0.65 (0.57-0.74)	100.0
Rupture					
Chichester,[23] 2007	15	54/2995 (1.8)	63/3045 (2.1)	0.87 (0.60-1.25)	10.65
MASS,[83] 2012	13.1	273/33 883 (0.8)	476/33 887 (1.4)	0.58 (0.50-0.67)	68.74
Viborg,[58] 2010	13	16/6333 (0.3)	36/6306 (0.6)	0.46 (0.27-0.79)	4.81
Western Australia,[5] 2016	12.8	72/19 249 (0.4)	99/19 231 (0.5)	0.73 (0.54- 0.98)	15.80
Subtotal I^2 = 53.3%, P = .09				0.62 (0.55-0.70)	100.0



OR indicates odds ratio.

Figure 4. Pooled Analysis of All-Cause Mortality (Men Only) in 1-Time Abdominal Aortic Aneurysm Screening Trials

Source	Mean Follow-up, y	No. With Event/Total (%)		RR (95% CI)	Weight, %
		Intervention	Control		
Chichester,[23] 2007	15	2036/2995 (68.0)	2067/3045 (67.9)	1.00 (0.97-1.04)	11.49
MASS,[83] 2012	13.1	13 858/33 883 (40.9)	14 134/33 887 (41.7)	0.98 (0.96-1.00)	42.82
Viborg,[58] 2010	13	2931/6333 (46.3)	2964/6306 (47.0)	0.98 (0.95-1.02)	9.92
Western Australia,[5] 2016	12.8	9739/19 249 (50.6)	9832/19 231 (51.1)	0.99 (0.97-1.01)	35.77
Subtotal I^2 = 0.0%, P = .74				0.99 (0.98-1.00)	100.0



Weights are from random-effects analysis. RR indicates relative risk.

AAA-specific mortality in men was the primary outcome of the 4 screening trials. A meta-analysis of the trials[5,23,58,83] (n = 124 929) estimated a statistically significant lower AAA-specific mortality over 12 to 15 years of follow-up associated with an invitation to screening, with high heterogeneity (Peto OR, 0.65 [95% CI, 0.57-0.74]; I^2 = 80%; number needed to screen, 305 men [95% CI, 248-411]) (**Figure 3**). A meta-analysis of all-cause mortality in men from the 4 screening trials[5,23,58,83] (n = 124 929) did not reach statistical significance (relative risk [RR], 0.99 [95% CI, 0.98-1.00]; I^2 = 0%) (**Figure 4**). Only the MASS trial reported a statistically significant lower all-cause mortality (hazard ratio, 0.97 [95% CI, 0.95-0.99]).[83]

In addition to mortality outcomes, the screening trials reported ruptures and emergency operations among primarily male study populations. Pooled results of 4 trials[5,23,58,83] (n = 124 929) showed a statistically significant lower risk of AAA rupture associated with the invitation to screening (Peto OR, 0.62 [95% CI, 0.55-0.70]; I^2 = 53%; number needed to screen, 246 men [95% CI, 207-311]) (Figure 3). An invitation to screening in 5 trials[5,23,57,58,83] (n = 175 085) was also associated with a statistically significant lower risk of emergency operations in the screening group (Peto OR, 0.57 [95% CI, 0.48-0.68]; I^2 = 27%) (**Figure 5**). This would reduce the number of emergency procedures by 2 per 1000 men screened (95% CI, 2-2).

Patients invited to participate in the screening trials were predominantly men. Only the Chichester trial[23,76] examined AAA screening in women (59% of participants [n =9342] were women), showing that women had a lower AAA prevalence compared with men (1.3% vs 7.6%).[76,78] There was no significant difference between the invited and control groups for women in AAA-related or all-cause mortality at 5 years (AAA mortality: 0.06% vs 0.04%; all-cause mortality: 10.7% vs 10.2%) or AAA rupture rate at 10-year follow-up (0.2% in both groups), but the trial was underpowered.

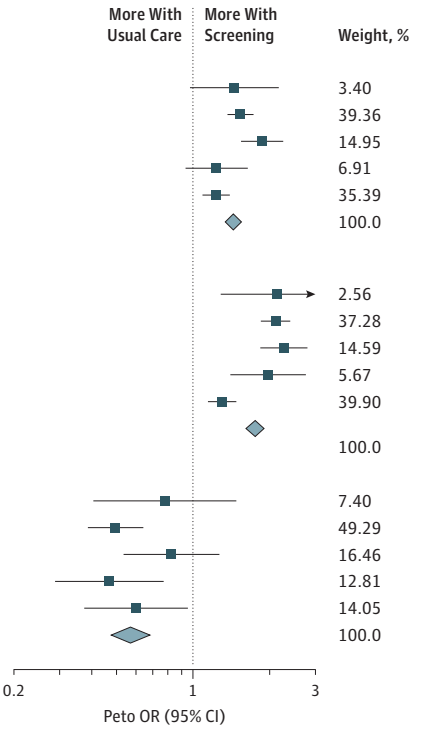
Benefits of Rescreening

Key Question 2. What are the effects of rescreening for AAA on health outcomes or AAA incidence in a previously screened, asymptomatic population without AAA on initial screening?

No trial-level evidence examined the effectiveness of 1-time screening plus rescreening compared with 1-time screening alone. Seven cohort studies (5 fair-quality,[32,34,77,80,82] 2 good-quality[30,31,36,49,62,67]) and 1 fair-quality case-control study[59] recruited screen-negative participants (AAA diameter 2.5-2.9 cm or 2.6-2.9 cm,[32,34,59,67,80] <2.5 cm,[82] or ≤3 cm[49,77]) and administered various rescreening protocols (rescreening every 1 to 5 years with 1 to 6 repeated scans), reporting the proportion of initially screen-negative aortas that reached 5.0 or 5.5 cm at the

Figure 5. Pooled Analysis of Operations (Men Only) in 1-Time Abdominal Aortic Aneurysm Screening Trials

Source	Mean Follow-up, y	No. With Event/Total (%) Intervention	Control	Peto OR (95% CI)	Weight, %
All operations					
Chichester,[23] 2007	15	57/2995 (1.9)	40/3045 (1.3)	1.45 (0.97-2.17)	3.40
MASS,[83] 2012	13.1	680/33 883 (2.0)	443/33 887 (1.3)	1.54 (1.37-1.73)	39.36
VIVA,[57] 2017	4.4	277/25 078 (1.1)	146/25 078 (0.6)	1.87 (1.54-2.26)	14.95
Viborg,[58] 2010	13	109/6333 (1.7)	88/6306 (1.4)	1.24 (0.93-1.64)	6.91
Western Australia,[5] 2016	12.8	562/19 249 (2.9)	458/19 231 (2.4)	1.23 (1.09-1.40)	35.39
Subtotal I^2 = 74.1%, P = .004				1.44 (1.34-1.55)	100.0
Elective operations					
Chichester,[23] 2007	15	41/2995 (1.4)	19/3045 (0.6)	2.13 (1.28-3.55)	2.56
MASS,[83] 2012	13.1	600/33 883 (1.8)	277/33 887 (0.8)	2.11 (1.85-2.41)	37.28
VIVA,[57] 2017	4.4	240/25 078 (1.0)	101/25 078 (0.4)	2.27 (1.84-2.81)	14.59
Viborg,[58] 2010	13	89/6333 (1.4)	44/6306 (0.7)	1.97 (1.40-2.78)	5.67
Western Australia,[5] 2016	12.8	536/19 249 (2.8)	414/19 231 (2.2)	1.30 (1.14-1.48)	39.90
Subtotal I^2 = 88.5%, P < .001				1.75 (1.61-1.90)	100.0
Emergency operations					
Chichester,[23] 2007	15	16/2995 (0.5)	21/3045 (0.7)	0.77 (0.41-1.48)	7.40
MASS,[83] 2012	13.1	80/33 883 (0.2)	166/33 887 (0.5)	0.50 (0.39-0.64)	49.29
VIVA,[57] 2017	4.4	37/25 078 (0.1)	45/25 078 (0.2)	0.82 (0.53-1.27)	16.46
Viborg,[58] 2010	13	20/6333 (0.3)	44/6306 (0.7)	0.47 (0.29-0.77)	12.81
Western Australia,[5] 2016	12.8	26/19 249 (0.1)	44/19 231 (0.2)	0.60 (0.37-0.95)	14.05
Subtotal I^2 = 26.7%, P = .24				0.57 (0.48-0.68)	100.0



OR indicates odds ratio.

repeat scan (eTables 2 and 3 in the Supplement). This group of heterogeneous studies reported that AAA-related mortality over 5 to 12 years was rare (<3%) among participants with normal aortas (<3 cm) on the initial scan. On rescreening, few aortas (0%-2%) grew to larger than 5 cm at 5 years,[32,34,49,59,80] and 0% to 15% had progressed at 10 years (eTable 2 in the Supplement).[31,77] Four studies reported no AAA ruptures or AAA-related deaths[32,49,80,82] at 4- to 5-year follow-up; 1 population screening program reported 2.4% ruptures at 7.9-year median follow-up (eTable 2 in the Supplement).[31] Overall, this heterogenous body of literature was too limited to make conclusions about the effectiveness of rescreening.

Harms of Screening

Key Question 3. What are the harms associated with 1-time and repeated screening?

Two population-based screening trials reported no statistically significant difference in 30-day operative mortality from elective surgical procedures (RR, 0.76 [95% CI, 0.40-1.45][83]; RR, 0.82 [95% CI, 0.43-1.57][5]) and emergency surgical procedures (RR, 1.43 [95% CI, 0.90-2.25][5]; RR, 0.98 [95% CI, 0.68-1.43][83]) among those invited to screening compared with those in the control group at 12.8- to 13.1-year follow-up (Table 1). All 5 screening trials reported more AAA-related operations in the invited group than in the control group, with 1.1% to 2.9% of the screened group undergoing surgical repair compared with 0.6% to 2.4% of the control group.[5,23,57,58,83] The pooled data estimated significantly more procedures in the invited group compared with the control group (Peto OR, 1.44 [95% CI, 1.34-1.55]; I^2 = 74%) (Figure 5). Implementing a screening program would increase the total number of operations per 1000 men by 6 (95% CI, 5-8). Elective operations were also consistently more common in the screened group (1.0%-2.8%) than in the control group (0.4%-2.2%) in all 5 trials[5,23,57,58,83] (Figure 5, Table 1). Pooled analysis of these trials confirmed a higher elective operation rate in the screened group than in the control group (Peto OR, 1.75 [95% CI, 1.61-1.90]; I^2 = 89%) (Figure 5, Table 1). This would increase the number of elective operations by 8 per 1000 men screened (95% CI, 6-9).

There were no RCTs assessing the harms of rescreening vs no rescreening in participants with normal-sized aortas (<3.0 cm) on initial screening. Six fair-quality cohort studies examined procedure rates in rescreened cohorts.[32,49,59,67,80,82] Five of these studies showed a low procedure rate (0%-4%) at up to 5-year follow-up[32,49,59,80,82]; a single screening program reported a higher procedure rate of 10.9% at 7.8-year mean follow-up (eTable 2 in the Supplement).[67]

Two subsamples of screening RCTs[5,22,81,83] and 3 small cohort studies[52,61,87] had mixed results but generally showed no substantial differences in QOL or mood scores between screen-positive and screen-negative participants at up to 12 months' follow-up; 1 of these RCTs (MASS) reported lower QOL scores at 6 weeks, but all scores were within age-matched population normal standards.[22,83]

Benefits of Early Treatment for Small AAAs

Key Question 4. What are the effects of treatment on intermediate and health outcomes in an asymptomatic, screen-detected population with small AAAs (ie, aortic diameter of 3.0-5.4 cm)?

Table 2. Characteristics and Outcomes of Open and EVAR Abdominal Aortic Aneurysm Surgical Trials

Source (Quality)	Participants Randomized (Country)	Eligible Age (Mean), y	Women, %	AAA Size for Inclusion and Surveillance, cm	Mean Follow-up, y	RR (95% CI)[a]			Participants Undergoing AAA Procedure, No. (%)	
						All-Cause Mortality	AAA Mortality	AAA Rupture	Intervention	Control
Open Repair										
ADAM Lederle et al,[51] 2002 (Good)	1136 (United States)	50-79 (68.1)	0.8	4.0-5.4	4.9	1.17 (0.95-1.44)	1.13 (0.57-2.24)	0.18 (0.04-0.81)	527 (92.6)	349 (61.6)
UKSAT Powell et al,[74] 2007 (Good)	1090 (United Kingdom)	60-76 (69.3)	17.5	4.0-5.5	12	0.96 (0.88-1.05)	0.67 (0.45-1.02)	0.51 (0.26-0.99)	528 (93.8)	401 (76.1)
Evar										
PIVOTAL Ouriel et al,[69] 2010 (Fair)	728 (United States)	40-90 (70.5)	13.4	4.0-5.0	1.7	0.99 (0.49-1.99)	1.98 (0.18-21.72)	Not calculated	326 (89.1)	112 (30.9)
CAESAR Cao et al,[29] 2011 (Fair)	360 (Europe and Asia)	50-80 (68.9)	4.2	4.1-5.4	2.7[b]	1.22 (0.49-3.03)	0.98 (0.06-15.52)	Not calculated	175 (96.2)	85 (47.8)

Abbreviations: AAA, abdominal aortic aneurysm; ADAM, Abdominal Aortic Aneurysm Detection and Management; CAESAR, Comparison of Surveillance vs Aortic Endografting for Small Aneurysm Repair; EVAR, endovascular aneurysm repair; NA, not applicable; NR, not reported; PIVOTAL, Positive Impact of Endovascular Options for Treating Aneurysms Early; RR, relative risk; UKSAT, UK Small Aneurysm Trial.

[a] Calculated.

[b] Median.

Four trials evaluated the effectiveness of immediate surgical repair of small aneurysms (4-5.4 cm) vs surveillance every 3 to 6 months until the aneurysm reached 5.5 cm, rapidly expanded (>1 cm/y), or became symptomatic. The Aneurysm Detection and Management trial (ADAM)[51] and the UK Small Aneurysm Trial (UKSAT)[74] evaluated the effectiveness of early open surgery, and the Comparison of Surveillance vs Aortic Endografting for Small Aneurysm Repair (CAESAR)[29] and Positive Impact of Endovascular Options for Treating Aneurysm Early (PIVOTAL) trial[69] evaluated EVAR interventions (**Table 2**).

The CAESAR[29] and PIVOTAL trials[69] terminated recruitment early because of interim analysis concluding intervention futility, but participants who had already been enrolled completed scheduled follow-up visits.

The 4 trials of early surgery found no significant differences in all-cause or AAA-specific mortality at any follow-up time between participants receiving early surgical repair vs those under surveillance (Table 2).[29,51,69,74] An individual patient data analysis (n = 2226) of the 2 trials of open repair additionally supported no survival benefit (adjusted hazard ratio, 0.99 [95% CI, 0.83-1.18]).[37] Ruptures were rare events in all surgical trials; however, participants who underwent early open repair had a significant reduction in the rate of rupture compared with those who underwent surveillance at each follow-up interval (RR, 0.18 [95% CI, 0.04-0.81] at 4.9 years [n = 1136]; RR, 0.33 [95% CI, 0.13-0.83] at 4.6 years [n = 1090]; RR, 0.51 [95% CI, 0.26-0.99] at 12 years [n = 1090]) (Table 2).[51,73,74] There were only 3 ruptures in the EVAR trials, making comparisons challenging. Overall, there were more surgical interventions in the early surgery groups than in the surveillance groups undergoing mostly elective surgical procedures (Table 2).

Seven short-term drug trials (n = 1553) of antibiotics, antihypertensive medications, and mast cell stabilizers showed no overall effect on AAA growth compared with placebo. Details are provided in the full evidence report and in eTable 4 in the Supplement.

Harms of Early Treatment for Small AAAs

Key Question 5. What are the harms of treatment in an asymptomatic, screen-detected population with small AAAs (ie, aortic diameter of 3.0-5.4 cm)?

The 4 trials of early surgery[29,51,69,74] and 5 registry publications reported complication rates for surgical patients with AAAs smaller than 5.5 cm[27,40,60,70,71] (**Table 3** and **Table 4**).

Both the ADAM trial and UKSAT reported no significant difference in 30-day postoperative mortality rates in the early open repair and surveillance groups (2.1% vs 1.8% in ADAM; 5.0% vs 6.3% in UKSAT) (Table 3).[51,74] The 2 largest and most contemporary registries (2011 to 2015; 2010 to 2013) capturing open repairs of small aneurysms reported a 30-day operative mortality rate within the range reported in these trials (3.1% and 3.5%) (Table 3).[27,70] Thirty-day operative mortality after EVAR in both the CAESAR and PIVOTAL trials was rare (Table 4).[29,69] The 2 largest and most contemporary registries (2011 to 2015 in the American College of Surgeons National Surgical Quality Improvement Program [ACS NSQIP]; 2010 to 2013 in Vascunet) capturing EVAR of small aneurysms reported a 30-day operative mortality rate for EVAR of 0.7%.[27,70] The 2 oldest registries reported slightly higher

Table 3. Harms Associated With Open Abdominal Aortic Aneurysm Repair, Randomized Clinical Trial and Registry Data

Source	Mean Follow-up, y	No. of Participants Analyzed	No. (%)			Major Complications
			30-d Mortality After Elective Repair	Reintervention Rates	Readmission Rates in 30 d	
Randomized Clinical Trial Data						
ADAM Lederle et al,[51] 2002	4.9	866 (526 intervention, 340 control)	Intervention: 11 (2.1)[a] Control: 6 (1.8)[a]	Intervention: 9 (1.7)[b] Control: 4 (1.2)[b]	Intervention: 108 (20.5)[b] Control: 56 (16.5)[b]	Intervention[b]: Any major complication: 24 (4.6) MI: 5 (1.0)[c] Stroke: 3 (0.6) Pulmonary embolism: 4 (0.8) Control[b]: Any major complication: 26 (7.6) MI: 13 (3.8)[c] Stroke: 2 (0.6) Pulmonary embolism: 1 (0.3)
UKSAT Powell et al,[74] 2007	12	915 (526 intervention, 389 control)	Intervention: 26 (5.0) Control: 25 (6.3)	NR	Intervention: 30 (6.3) Control: NR[d]	NR
Registry Data						
ACS NSQIP Overbey et al,[70] 2017	NR	705	25 (3.5)	64 (9.1)	44 (6.2)	MI: 24 (3.4) Stroke: 5 (0.7) Pulmonary embolism: 3 (0.4) Overall morbidity within 30 d of surgery: 69.4% Bleeding complications: 460 (65.2)
Vascunet Budtz-Lilly et al,[27] 2017	NR	12 610	391 (3.1)[e]	NR	NR	NR

Abbreviations: AAA, abdominal aortic aneurysm; ACS NSQIP: American College of Surgeons National Surgical Quality Improvement Program; ADAM, Abdominal Aortic Aneurysm Detection and Management study; MI, myocardial infarction; NR, not reported; UKSAT, UK Small Aneurysm Trial.

[a] Operative mortality associated with the repair of unruptured AAA.

[b] Follow-up timing NR.

[c] $P < .05$.

[d] Intervention group: From 1-year follow-up data; the use of bifurcated grafts (12/30 [40%]) was associated with a 2-fold increase in the risk of reoperation ($P = .03$).

[e] Defined as hospital death or death within 30 days of surgery.

mortality rates from EVAR (1.1% in Australian Safety and Efficacy Register of New Interventional Procedures–Surgical [ASERNIP-S]; 1.6% in European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair [EUROSTAR]) (Table 4).[40,71]

Only the ADAM trial reported adverse event rates for the open repair intervention and control groups, and results were mixed. The rate of 30-day readmissions was not significantly different between the surgery and surveillance groups, nor were the overall complication rates significantly different (Table 3).[51] Furthermore, the event rate for total major complications was higher in the surveillance group than the early treatment group (7.6% vs 4.6%, no statistical testing reported), with a significantly higher risk of surgery-related myocardial infarction reported in the surveillance group (1.0% vs 3.8%, $P = .004$). The ACS NSQIP registry reported overall 30-day morbidity for open repair as approximately 69.4% at 30 days after intervention, with the most common complication being bleeding (Table 3).[70]

Complications were variably reported in the 2 trials of EVAR.[29,69] In the CAESAR trial, the percentage of patients with any adverse events was significantly higher at 32.4-month follow-up in the early EVAR group compared with the surveillance group (19.1% vs 5.1%, $P < .01$). In addition, the percentage of patients with any morbidity related to repair at 30 days was also higher in the EVAR group compared with the surveillance group (17.7% vs 6.0%, $P = .01$).[29] Rates of any major morbidity (3.4% vs 4.7%) and 30-day endoleaks (16% vs 8.2%) were not significantly different in the early EVAR compared with the surveillance groups, but the early EVAR group had significantly more endoleaks at 1 year (12% vs 2.4%, $P = .03$) and significantly more reinterventions than the group undergoing surveillance (5.7% vs 0%, $P = .03$) (Table 4). The PIVOTAL trial reported rates of endoleaks in the early intervention and surveillance groups at 30 days after intervention (11.9% vs 10.3%) and at 1 year (26.1% vs 35.1%), but statistical testing was not reported (Table 4).

Two EVAR registries (ASERNIP-S[40] and EUROSTAR[71]) and the 1 registry of both open repair and EVAR (ACS NSQIP)[70] reported complication rates after EVAR intervention on small AAAs (Table 4). Registry data reported a composite of major or systemic complication rates for EVAR ranging from 12% to 29% at 30 days after intervention, which is consistent with trial data.[29,69-71] ASERNIP-S and ACS NSQIP reported reintervention rates within 30 days of EVAR of approximately 3%[40,70]; these rates are likewise comparable to trial data.[29,69] The ACS NSQIP reported readmission rates for small AAAs at 30-day postintervention as 6.8% after EVAR.[70] Readmission rates were not reported in the trials, so these data cannot be compared with trial findings. ASERNIP-S and EUROSTAR reported the occurrence of endoleaks at 20% and 31%, respectively, at 3- to 4-year follow-up.[40,71]

Eight short-term drug trials (n = 1598) reported high rates of adverse event–related discontinuation with propranolol (38% and 60% of the propranolol groups withdrew from the trials); other medications (including other antihypertensive medications [angiotensin-converting enzyme inhibitors, calcium channel blockers], antibiotics), apparently well tolerated based on few trial withdrawals, were reported in 1 to 2 studies per drug class (eTable 5 in the Supplement).

Table 4. Harms Associated With EVAR Abdominal Aortic Aneurysm Repair, Randomized Clinical Trial and Registry Data

Source	Mean Follow-up, y	No. of Participants Analyzed	No. (%)					
			30-d Mortality After Elective Repair	Rates		Endoleaks		Major Complications Within 30 d
				Reintervention	Readmission in 30 Days	At 30 d	At 1 y	
Randomized Clinical Trial Data								
CAESAR Cao et al,[29] 2011	2.6[a]	260 (175 intervention, 85 control)	Intervention: 1 (0.6) Control: 0	Intervention: 10 (5.7)[b] Control: 0 (0)[b]	Intervention: NR Control: NR	Intervention: 28 (16.0)[c] Control: 7 (8.2)[c]	Intervention: 21 (12.0)[c] Control: 2 (2.4)[c]	Intervention: Any major morbidity: 6 (3.4) Control: Any major morbidity: 4 (4.7)
PIVOTAL Ouriel et al,[69] 2010	1.7	431 (322 intervention, 109 control)	Intervention: 1 (0.3) Control: 1 (0.9)	Intervention: 12 (3.7)[d] Control: 5 (4.6)[d]	20 (4.6)[e]	Intervention: 36 (11.9) Control: 10 (10.3)	Intervention: 72 (26.1) Control: 30 (35.1)	Intervention: Serious cardiac event: 17 (5.3) Serious pulmonary event: 4 (1.2) Serious renal event: 6 (1.9) Control: Serious cardiac event: 9 (8.3) Serious pulmonary event: 1 (0.9) Serious renal event: 1 (0.9)
Registry Data								
ACS NSQIP Overbey et al,[70] 2017	NR	4471	31 (0.7)	150 (3.4)	304 (6.8)	NR	NR	Acute renal failure: 15 (0.3) Sepsis: 20 (0.4) Septic shock: 6 (0.1) Cardiac arrest: 14 (0.3) MI: 46 (1.0); Pulmonary embolism: 5 (0.1) Stroke: 12 (0.3) Overall morbidity within 30 d of surgery: 11.4% Bleeding complications: 296 (6.6)
ASERNIP-S Golledge et al,[40] 2007	3.2[a]	478	5 (1.1)	13 (3)[f]	NR	46 (9.6)	97 (20.3)[g]	Significant postoperative complications reported in 138 (29.0); 72 systemic complications noted in 64 (13.4) of patients
EUROSTAR Peppelenbosch et al,[71] 2004	1.7	1962	31 (1.6)	NR	NR	NR	NR[h]	30-d systemic complications combined: 235 (12.0) Cardiac: 55 (2.8)[d] Pulmonary: 31 (1.6)[d] Early procedure or device-related: 57 (2.9)[d]
Vascular Study Group of New England Lo et al,[60] 2013	1.0	1336	Men: 7 (0.7) Women: 4 (1.1)	NR	NR	NR	NR	NR
Vascunet Budtz-Lilly et al,[27] 2017	NR	12 610	88 (0.7)[i]	NR	NR	NR	NR	NR

Abbreviations: AAA, abdominal aortic aneurysm; ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ASERNIP-S, Australian Safety and Efficacy Register of New Interventional Procedures-Surgical; CAESAR, Comparison of Surveillance vs Aortic Endografting for Small Aneurysm Repair; EVAR, endovascular aneurysm repair; MI, myocardial infarction; NR, not reported; PIVOTAL, Positive Impact of Endovascular Options for Treating Aneurysms Early.

[a] Median.

[b] $P < .05$.

[c] Denominator is patients who received EVAR: 171 in intervention group (at 1 year, 19 [10.9%] with type 2, 1 [0.6%] with type 4, 1 [0.6%] unknown) and 71 in the control group (at 1 year, 2 [2.4%] with type 2).

[d] Follow-up timing NR.

[e] Group not specified for readmission rates.

[f] Reinterventions 30 or fewer days after surgery; for 30 or more days after surgery, 50 patients underwent 72 additional interventions by open repair (20 times in 16 patients [5 had an EVAR procedure]).

[g] Endoleak on follow-up imaging 30 or more days after procedure.

[h] At 4 years: 5.3% (type I proximal), 11.3% (type I distal), 14.4% (type III).

[i] Defined as hospital death or death within 30 days of surgery

Screening and Treatment Among Subpopulations

There was limited credible subpopulation information from the body of included studies. The Western Australia trial[5] showed that smoking was associated with a higher risk of all-cause mortality (OR, 1.59 [95% CI, 1.47-1.72]) and AAA-related mortality (OR, 2.95 [95% CI, 1.04-8.43]) in the screened group, but no included study examined differential screening benefits by smoking status or family history (KQ1a). Subgroup analyses in the Viborg and Western Australia trials suggested that there is no differential screening effect on mortality by age.[5,58] The Chichester trial[23,76] recruited 9342 women and showed a lower prevalence of AAA in women compared with men (1.3% vs 7.6%), with most screen-detected AAAs measuring 3.0 to 3.9 cm.[76,78] There was no significant difference in AAA rupture rates among women at 10-year follow-up (0.2% in both the screened and unscreened group) or in AAA-related mortality (0.06% vs 0.04%) or all-cause mortality (10.7% vs 10.2%) at 5 years between the invited and control groups; however, the trial was underpowered. Based on 2 trials of open repair, there was no differential treatment effect on all-cause mortality by sex (KQ4a).[51,73] Registry data, however, showed a higher rate of postoperative mortality after elective repair of small AAAs in women compared with men, regardless of the surgical technique (KQ5a).[27,40,60]

Discussion

This review, performed since the previous systematic review for the USPSTF in 2014,[17] included the following new data: (1) the final long-term follow-up from the Western Australia trial added to the meta-analysis confirmed prior AAA mortality benefits of screening[5]; (2) 2 new small rescreening cohort studies offered little additional information to a heterogeneous literature[80,82]; (3) 3 additional pharmacotherapy trials showed no benefit in halting AAA growth[24,63,79]; (4) 1 new population-based screening trial (VIVA) added to the meta-analysis on additional operations associated with screening confirmed previous results[57]; and (5) 3 contemporary registries[27,60,70] provided complication rates from EVAR and open repair generally comparable to those cited in the included trials.

A summary of the evidence by key question is provided in **Table 5**. The meta-analyses demonstrated that offering 1-time screening to men aged 65 to 75 years was associated with lower AAA-related mortality, AAA rupture, and emergency surgical procedures over 13 to 15 years of follow-up (KQ1) but do not resolve the question of all-cause mortality benefit. In terms of harms, screening for AAA was shown to expose patients to more procedures, which was primarily driven by elective operations. Overdiagnosis and overtreatment were not addressed in these trials but may be important considerations given that most screen-detected aneurysms are small.

The interest in a more targeted, high-risk approach to screening to enrich yield is particularly relevant given declines in AAA prevalence in men over the past 2 decades.[67,89-91] However, limiting screen-eligible populations to only "high-risk" populations inherently results in missed cases. Any attempt to expand screened populations (eg, extending to all men regardless of smoking history, increasing upper age threshold, adding women) would invariably increase detection of aneurysms smaller than 5.4 cm in diameter and would contribute to overdiagnosis and overtreatment. Based on US data showing that a substantial proportion of small aneurysms are repaired despite the lack of evidence of benefit over surveillance,[92] the number of procedures and consequent surgical harms that may ensue as a result of broadening the eligibility for screening remains a concern.

Because the population-based screening trials almost exclusively recruited white men aged 65 to 75 years and generally did not report outcomes by subpopulation, one critical question is whether these findings can be extrapolated to other populations. In the absence of trial data, assessing generalizability requires an understanding of contextual evidence about contemporary prevalence, natural history, and treatment effectiveness.

Indirect evidence in subpopulations (older age, female sex, smoking, and family history) reveal a set of complex issues. A large proportion of AAA burden (prevalence and ruptures) occurs in older age groups.[93,94] While AAA prevalence increases with age, so do surgical complications, including mortality.[95] The prevalence of AAA in women has consistently been reported to be less than in men.[96,97] However, small AAAs appear to have a higher risk of rupture[25,98-100] or rupture at a later age[76,99,101-106] and result in higher surgical complications—including 30-day postoperative mortality rates,[102-104,107,108] in-hospital mortality,[109] major complications,[104,108,110] and readmissions[103] after elective open repair or EVAR—in women than in men. A recent model examining the effectiveness of screening women 65 years or older using contemporary assumptions[111] estimated that 3900 screening invitations would be required to avoid 1 AAA-related death, which is higher than estimation in other models for men (the number needed to invite to screening was 700 for men).[112]

Smoking is the strongest predictor of AAA prevalence,[10,97,100,113,114] growth,[100] and rupture rates.[100] Even with substantial declines since 1995-2002 when the screening trials were conducted,[89] AAA prevalence in male smokers aged 65 to 75 years matches that of the population-based screening trials.[115] Family history is associated with an increased risk of developing AAA (OR, 2.2 [95% CI, 1.6-3.2]).[116] At this time, however, there is a lack of evidence to determine whether individuals with family histories exhibit differences in natural history or surgical success rates to alter the net screening benefits. Overall, because there is no direct trial evidence evaluating screening effectiveness in subpopulations and no externally validated risk assessment tools, decision analysis models populated with meta-analytic estimates of prevalence, yield, and surgical complication rates would be considered the best available evidence to date.

There are several limitations to the existing literature. The 4 large, population-based screening trials began recruiting participants during an era that predated the current widespread implementation of aggressive CVD risk-factor management and reductions in smoking. Thus, the contemporary AAA prevalence cited in Europe, and therefore the absolute benefit of screening, have declined over the intervening time. A general US population–based estimate of contemporary AAA prevalence is lacking, particularly for subpopulations, as a result of low AAA screening uptake in the United States. Furthermore, trial literature does not address the potential effect of AAA screening on CVD mortality through identification of individuals at increased CVD risk and provision of aggressive CVD risk

Table 5. Summary of Evidence

Subpopulation	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
KQ1: Benefits of Screening						
Entire study population	4 (124 929)	Invitation for 1-time screening in men ≥65 y was associated with a 35% reduction in AAA-related mortality, 38% reduction in AAA rupture rate, and a 43% reduction in the number of emergency operations but no statistically significant difference in all-cause mortality at 12- to 15-y follow-up	Reasonably consistent; reasonably precise	None	Moderate to high	These population-based screening trials were set in the 1990s in mostly white men aged 65 to 75 y; since that time, AAA prevalence has declined along with smoking prevalence, and medical management of CVD has changed
KQ1a: Benefits of Screening Among Subpopulations						
Age	2 (51 119)	The Viborg and Western Australia population-based screening trials reported subanalyses with substantial limitations suggesting no differential screening effect based on age	Consistent; imprecise	Subanalyses not prespecified, stratified at randomization to ensure baseline comparability, adjusted for confounders, or powered to detect subgroup differences; no heterogeneity testing was performed	Low	Both trials were conducted in mostly white older men
Sex	1 (9342)	There was no significant difference in AAA rupture rate at 10-y follow-up or in mortality (both AAA-related and all-cause) at 5 y between the invited and control groups Most AAA ruptures occur at ages ≥80 y in women	Consistency NA (1 study); imprecise	Underpowered for health outcomes	Low	Population was older white women in Chichester, United Kingdom
Smoking	1 (19 249)	Results showed that smoking was associated with a higher risk of all-cause mortality (OR, 1.59 [95% CI, 1.47-1.72]) and AAA-related mortality (OR, 2.95 [95% CI, 1.04-8.43]) in the screened group of men aged 64-83 y Trend was more pronounced in the group aged 65-74 y; however, no formal analysis was performed to explore if there is a differential screening effect based on smoking status	Consistency NA (1 study); imprecise	Subanalyses not prespecified or powered to detect subgroup differences; no heterogeneity testing performed to determine if there is modification in the effectiveness of screening among smokers	Low	Trial was conducted in mostly white older men
KQ2: Benefits of Rescreening						
Entire study population	8 (8018)	Studies rescreened participants with various rescreening protocols (rescreening annually to 5 y with 1 to 6 repeated scans), demonstrating that AAA-related mortality over 5 to 12 y is rare (<3%) among those with normal aortas (<3 cm) on the initial scan On rescreening, few aortas grew to >5 or ≥5.5 cm (0%-2.2% at 5 y; 0%-15% had progressed at 10 y) Four studies reported no AAA ruptures or AAA-related deaths at 4- to 5-y follow-up; 1 study reported 2.4% ruptures at 7.9-y median follow-up	Inconsistent; imprecise	Heterogeneous rescreening protocols A small number of participants with normal aortas were included in these studies; all but a single study was exclusively in men; there are no matched controls in most studies; the primary focus of most studies was growth rate, as the follow-up time for most studies was 5 y, a time frame too short to expect the development of AAA-related health outcomes	Low	Mostly men (only 1 trial conducted in women) All but 1 trial conducted outside of the United States

(continued)

Table 5. Summary of Evidence (continued)

Subpopulation	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
KQ2a: Benefits of Rescreening Among Subpopulations						
Sex	1 (33); remaining 7 KQ2 studies in men	One small study in women was too small to compare with other rescreening studies in men	Consistency NA; imprecise	Few studies reporting outcomes by subpopulation; most studies did not report if subgroup analyses were prespecified, and studies tested numerous risk factors Overall rescreening literature limited by lack of adequate reporting; heterogeneity of study rescreening protocols; short follow-up times with focus on growth rates rather than health outcomes	Low	Small study of women conducted outside of the United States
Smoking	3 (4706)	Two studies reported multiregression analyses suggesting that current smoking is an independent risk factor for the development of AAA at rescreening, and another univariate analysis in a study of solely women showed a similar trend for smoking; however, the number developing AAAs over the rescreening interval was small	Consistent; imprecise	None	Low	Studies conducted in mostly men
KQ3: Harms of Screening						
Entire study population	5 (175 085)	More procedures in the invited group compared with the control group (5 studies; Peto OR, 1.44 [95% CI, 1.34-1.55]), largely driven by elective operations (Peto OR, 1.75 [95% CI, 1.61-1.90]) There was no statistically significant difference in 30-d operational mortality rates in the invited vs control groups for either elective surgical procedures or emergency surgical procedures at 12- to 15-y follow-up	Consistent; reasonably precise	None	Moderate	Trials were conducted in mostly white older men
KQ3a: Harms of Screening Among Subpopulations						
Age	1 (19 571)	Single population-based screening trial reports no significant difference in the number of elective operations and lower 30-d operative mortality after elective and emergency surgery in the younger age subset (65-74 y) compared with entire trial population (64-83 y)	Consistent (1 trial NA); imprecise	Subanalyses not prespecified, stratified at randomization to ensure baseline comparability, adjusted for confounders, or powered to detect subgroup differences; no heterogeneity testing performed	Low	Trial was conducted in mostly white older men

(continued)

Table 5. Summary of Evidence (continued)

Subpopulation	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
KQ4: Benefits of Early Treatment						
Open vs surveillance (entire study population)	2 (2226)	No significant difference in all-cause mortality, AAA-related mortality; reduction in rupture seen with early open surgery compared with surveillance for small AAAs	Consistent; imprecise	Only 2 studies No differentiation of sizes between 4-5.4 cm	Moderate	Trails primarily recruited male patients with small AAAs (4-5.4 cm)
EVAR vs surveillance (entire study population)	2 (1088)	No significant difference in all-cause or AAA-related mortality with early EVAR compared with surveillance for small AAAs	Consistent; imprecise	Both trials stopped early at interim analysis because of futility	Moderate	Trails primarily recruited male patients with small AAAs (4-5.4 cm)
Pharmacotherapy vs placebo (entire study population)	7 (1553)	Drug trials of antibiotics, antihypertensive medications, and a mast cell stabilizer showed no overall effect on AAA growth compared with placebo	Consistency NA (different drug classes); imprecise	One to 2 trials for each medication; follow-up times too short to expect development of AAA-related events or changes in health outcomes (all-cause mortality, AAA-related mortality, rupture)	Low	Studies were predominantly conducted in male patients with small AAAs All trials were conducted outside of the United States
KQ4a: Benefits of Early Treatment Among Subpopulations						
Open vs surveillance by age and sex	2 (2226)	Individual patient data meta-analysis available pooling the 2 early open vs surveillance trials (ADAM and UKSAT) with 5- to 8-y follow-up reported no differential all-cause mortality effect by sex The 2 trials reported no differential all-cause mortality treatment effect by age at 5- and 12-y follow-up; 1 of these trials (UKSAT) reported no significant difference in all-cause mortality by smoking status; this subanalysis did not address differential mortality effect of early surgery by smoking status No data on family history or race	Unknown consistency; imprecise	Subanalyses by age: 1 trial did not report interaction testing results Subanalyses by sex: both prespecified analyses, 1 trial did not adjust for confounders or report interaction testing	Low	Participants were men and women with small AAAs; analyses were separated by older and younger participants (reported in 5- to 10-y age strata), with and without a smoking history
EVAR vs surveillance	No studies	NA	NA	NA	NA	NA
Pharmacotherapy by age and smoking	Age: 1 (552) Smoking: 1 (32)	None of the pharmacotherapy trials report health outcomes by subgroup One small doxycycline trial and 1 propranolol trial performed limited subgroup analyses, which do not support a treatment effect modification by age or smoking history	Consistency NA (single trial for each medication); imprecise	Too few studies Available analyses would be considered exploratory at best, particularly given that the subgroup methodologies were of low quality (no prespecification of analysis, adjustment for confounders, or interaction testing), and overall trial results do not support a AAA growth benefit	Low	

(continued)

Table 5. Summary of Evidence (continued)

Subpopulation	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
KQ5: Harms of Early Treatment						
Open vs surveillance	5 (21 298)	Two trials of early open repair vs surveillance reported a 50% higher rate of procedures in the early intervention group with no significant difference in 30-d operative mortality Readmission rates at 30 d were not significantly different; major surgical complications were lower in the early intervention group QOL results were mixed but generally showed declines in both the early surgery and surveillance groups over time, with no statistically significant difference between the groups up to 1 to 2 y; only the ADAM trial showed higher general health scores in the early repair group in the first 2 y that did not persist over time One trial reported an increased incidence of impotence in the early repair group at up to 4 y Registry harms data were generally comparable to the 2 trials with the exception of reintervention rates, which were higher in the registries compared with the ADAM trial	Reasonably consistent for procedures and 30-d operative mortality; consistency NA for other complications (only reported in 1 trial) Reasonably precise for procedures; 30-d mortality and complications imprecise	Surgical morbidity complications not well reported	Moderate	Registry data from both national and international sources; contemporary
EVAR vs surveillance	7 (22 600)	Two trials of early EVAR vs surveillance reported approximately 100% more procedures in the early intervention group and rare 30-d operative mortality rates between the groups In the CAESAR trial, the early intervention group had a higher percentage of patients with any adverse events (19% vs 5%, $P < .01$), any morbidity related to repair at 30 d (18% vs 6%, $P = .01$), endoleaks at 1 y (12% vs 3%, $P = .028$), and reinterventions (6% vs 0%, $P = .03$), but rates of any major morbidity over the trial duration were not significantly different (3.3% vs 2.8%, $P = .99$) Conversely, PIVOTAL largely reported no significant difference in rates of adverse events at 30 d (12% vs 10%) and 1 y (26% vs 35%) and reinterventions (3.7% vs 4.6%) Reported complication rates from registry data were generally comparable with those rates reported in the above trials for 30-d operative mortality and reinterventions	Consistent for procedures, 30-d operative mortality, reinterventions, major morbidity; precise for procedures, 30-d mortality, reinterventions	Individual postoperative complications and major morbidities variably reported	Moderate	Registry data from both national and international sources; contemporary

(continued)

Table 5. Summary of Evidence (continued)

Subpopulation	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Pharmacotherapy vs placebo	8 (1598)	With the exception of the 2 propranolol trials reporting high adverse events–related discontinuation rates (38% and 60% of the propranolol groups withdrew from the trials), other medications (including other antihypertensive medications [ACE inhibitors, calcium channel blocker] and antibiotics) appear to be well tolerated based on few trial withdrawals reported from 1 to 2 studies per drug class	Propranolol: consistent, imprecise Doxycycline: consistent, imprecise Other drugs: NA for consistency (1 trial for each drug); imprecise	One to 2 trials per drug class with limited harms reporting	Low	Predominantly male population with small AAAs All trials conducted outside of the United States
KQ5a: Harms of Early Treatment Among Subpopulations						
Sex	3 (14 424)	Scant data on harms in subpopulations No trial data available to examine harms in subpopulations Existing evidence shows higher 30-d operative mortality and secondary complications in women compared with men for both EVAR and open repair No information available for other subpopulations	Consistent; imprecise	Few registries and nontrial data; few outcomes (mostly 30-d operative mortality)	Moderate	Registry data from both national and international sources; contemporary

Abbreviations: AAA, abdominal aortic aneurysm; ACE, angiotensin-converting enzyme; ADAM, Abdominal Aortic Aneurysm Detection and Management; CAESAR, Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair; CVD, cardiovascular disease; EVAR, endovascular aneurysm repair; KQ, key question; NA, not applicable; OR. odds ratio; PIVOTAL, Positive Impact of Endovascular Options for Treating Aneurysms Early; QOL, quality of life; UKSAT, UK Small Aneurysm Trial.

modification.[83,117,118] However, those identified with AAA would already be candidates for aggressive CVD risk management based on the Atherosclerotic Cardiovascular Disease Risk Algorithm's predicted 10-year risk of greater than or equal to 7.5% or 10%, as is standard contemporary guidance in the United States.[119,120]

Limitations

The current review and analysis included results limited to studies that met the USPSTF fair- or good-quality criteria, per USPSTF methods.[16] For 3 of the key questions (KQ2, KQ4, KQ5), there were too few studies or the studies were too clinically or statistically heterogeneous for pooling.[21]

Conclusions

One-time AAA screening in men 65 years or older was associated with decreased AAA-related mortality and rupture rates but was not associated with all-cause mortality benefit. Higher rates of elective surgery but no long-term differences in quality of life resulted from screening.

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Concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Guirguis-Blake, Beil, Coppola.
Critical revision of the manuscript for important intellectual content: Guirguis-Blake, Beil, Senger.
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REFERENCES

1. Society for Vascular Surgery (SVS). Abdominal aortic aneurysm. SVS website. https://vascular.org/patient-resources/vascular-conditions/abdominal-aortic-aneurysm. Published 2011. Accessed Jul 11, 2011.

2. Kent KC. Clinical practice: abdominal aortic aneurysms. *N Engl J Med*. 2014;371(22):2101-2108. doi:10.1056/NEJMcp1401430

3. Wanhainen A, Verzini F, Van Herzeele I, et al; ESVS Guidelines Committee. Editor's Choice—European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57(1):8-93. doi:10.1016/j.ejvs.2018.09.020

4. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg*. 2018;67(1):2-77. doi:10.1016/j.jvs.2017.10.044

5. McCaul KA, Lawrence-Brown M, Dickinson JA, Norman PE. Long-term outcomes of the Western Australian trial of screening for abdominal aortic aneurysms: secondary analysis of a randomized clinical trial. *JAMA Intern Med*. 2016;176(12):1761-1767. doi:10.1001/jamainternmed.2016.6633

6. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *BMJ*. 2005;330(7494):750. doi:10.1136/bmj.38369.620162.82

7. Benson RA, Poole R, Murray S, Moxey P, Loftus IM. Screening results from a large United Kingdom abdominal aortic aneurysm screening center in the context of optimizing United Kingdom National Abdominal Aortic Aneurysm Screening Programme protocols. *J Vasc Surg*. 2016;63(2):301-304. doi:10.1016/j.jvs.2015.08.091

8. Grøndal N, Søgaard R, Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65-74 years from a population screening study (VIVA trial). *Br J Surg*. 2015;102(8):902-906. doi:10.1002/bjs.9825

9. Wilmink AB, Hubbard CS, Day NE, Quick CR. The incidence of small abdominal aortic aneurysms and the change in normal infrarenal aortic diameter: implications for screening. *Eur J Vasc Endovasc Surg*. 2001;21(2):165-170. doi:10.1053/ejvs.2000.1285

10. Kent KC, Zwolak RM, Egorova NN, et al. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg*. 2010;52(3):539-548. doi:10.1016/j.jvs.2010.05.090

11. Vardulaki KA, Walker NM, Day NE, Duffy SW, Ashton HA, Scott RA. Quantifying the risks of hypertension, age, sex and smoking in patients with abdominal aortic aneurysm. *Br J Surg*. 2000;87(2):195-200. doi:10.1046/j.1365-2168.2000.01353.x

12. Moll FL, Powell JT, Fraedrich G, et al; European Society for Vascular Surgery. Management of abdominal aortic aneurysms: clinical practice guidelines of the European Society for Vascular Surgery. *Eur J Vasc Endovasc Surg*. 2011;41(suppl 1):S1-S58. doi:10.1016/j.ejvs.2010.09.011

13. van Vlijmen-van Keulen CJ, Pals G, Rauwerda JA. Familial abdominal aortic aneurysm: a systematic review of a genetic background. *Eur J Vasc Endovasc Surg*. 2002;24(2):105-116. doi:10.1053/ejvs.2002.1692

14. Larsson E, Granath F, Swedenborg J, Hultgren R. A population-based case-control study of the familial risk of abdominal aortic aneurysm. *J Vasc Surg*. 2009;49(1):47-50. doi:10.1016/j.jvs.2008.08.012

15. LeFevre ML; US Preventive Services Task Force. Screening for abdominal aortic aneurysm: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161(4):281-290. doi:10.7326/M14-1204

16. US Preventive Services Task Force. *U.S. Preventive Services Task Force Procedure Manual*. Rockville, MD: Agency for Healthcare Research and Quality; 2015.

17. Guirguis-Blake JM, Beil TL, Senger CA, Whitlock EP. Ultrasonography screening for abdominal aortic aneurysms: a systematic evidence review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2014;160(5):321-329. doi:10.7326/M13-1844

18. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. Ottawa Hospital Research Institute website. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2014. Accessed June 27, 2017.

19. Whitlock EP, Eder M, Thompson JH, et al. An approach to addressing subpopulation considerations in systematic reviews: the experience of reviewers supporting the U.S. Preventive Services Task Force. *Syst Rev*. 2017;6(1):41. doi:10.1186/s13643-017-0437-3

20. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2

21. Morton S, Murad M, O'Connor E, et al. *Quantitative Synthesis—An Update: Methods Guide for Comparative Effectiveness*. Rockville, MD: Agency for Healthcare Research and Quality; 2018. AHRQ publication 18-EHC007. doi:10.23970/AHRQEPCMETHGUIDE3

22. Ashton HA, Buxton MJ, Day NE, et al; Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet*. 2002;360(9345):1531-1539. doi:10.1016/S0140-6736(02)11522-4

23. Ashton HA, Gao L, Kim LG, Druce PS, Thompson SG, Scott RA. Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. *Br J Surg*. 2007;94(6):696-701. doi:10.1002/bjs.5780

24. Bicknell CD, Kiru G, Falaschetti E, Powell JT, Poulter NR; AARDVARK Collaborators. An evaluation of the effect of an angiotensin-converting enzyme inhibitor on the growth rate of small abdominal aortic aneurysms: a randomized placebo-controlled trial (AARDVARK). *Eur Heart J*. 2016;37(42):3213-3221. doi:10.1093/eurheartj/ehw257

25. Brown LC, Powell JT; UK Small Aneurysm Trial Participants. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. *Ann Surg*. 1999;230(3):289-296. doi:10.1097/00000658-199909000-00002

26. Brown LC, Thompson SG, Greenhalgh RM, Powell JT; UK Small Aneurysm Trial Participants. Fit patients with small abdominal aortic aneurysms (AAAs) do not benefit from early intervention. *J Vasc Surg*. 2008;48(6):1375-1381. doi:10.1016/j.jvs.2008.07.014

27. Budtz-Lilly J, Venermo M, Debus S, et al. Editor's Choice—assessment of international outcomes of intact abdominal aortic aneurysm repair over 9 years. *Eur J Vasc Endovasc Surg*. 2017;54(1):13-20. doi:10.1016/j.ejvs.2017.03.003

28. Cao P; CAESAR Trial Collaborators. Comparison of Surveillance vs Aortic Endografting for Small Aneurysm Repair (CAESAR) trial: study design and progress. *Eur J Vasc Endovasc Surg*. 2005;30(3):245-251. doi:10.1016/j.ejvs.2005.05.043

29. Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E; CAESAR Trial Group. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial. *Eur J Vasc Endovasc Surg*. 2011;41(1):13-25. doi:10.1016/j.ejvs.2010.08.026

30. Crow P, Shaw E, Earnshaw JJ, Poskitt KR, Whyman MR, Heather BP. A single normal ultrasonographic scan at age 65 years rules out significant aneurysm disease for life in men. *Br J Surg*. 2001;88(7):941-944. doi:10.1046/j.0007-1323.2001.01822.x

31. Darwood R, Earnshaw JJ, Turton G, et al. Twenty-year review of abdominal aortic aneurysm screening in men in the county of Gloucestershire, United Kingdom. *J Vasc Surg*. 2012;56(1):8-13. doi:10.1016/j.jvs.2011.12.069

32. d'Audiffret A, Santilli S, Tretinyak A, Roethle S. Fate of the ectatic infrarenal aorta: expansion rates and outcomes. *Ann Vasc Surg*. 2002;16(5):534-536. doi:10.1007/s10016-001-0283-5

33. De Rango P, Verzini F, Parlani G, et al; Comparison of Surveillance vs. Aortic Endografting for Small Aneurysm Repair (CAESAR) Investigators. Quality of life in patients with small abdominal aortic aneurysm: the effect of early endovascular repair versus surveillance in the CAESAR trial. *Eur J Vasc Endovasc Surg*. 2011;41(3):324-331. doi:10.1016/j.ejvs.2010.11.005

34. Devaraj S, Dodds SR. Ultrasound surveillance of ectatic abdominal aortas. *Ann R Coll Surg Engl*. 2008;90(6):477-482. doi:10.1308/003588408X301064

35. Eisenstein EL, Davidson-Ray L, Edwards R, Anstrom KJ, Ouriel K. Economic analysis of endovascular repair versus surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg*. 2013;58(2):302-310. doi:10.1016/j.jvs.2013.01.038

36. Emerton ME, Shaw E, Poskitt K, Heather BP. Screening for abdominal aortic aneurysm: a single scan is enough. *Br J Surg*. 1994;81(8):1112-1113. doi:10.1002/bjs.1800810810

37. Filardo G, Lederle FA, Ballard DJ, et al. Immediate open repair vs surveillance in patients with small abdominal aortic aneurysms: survival differences by aneurysm size. *Mayo Clin Proc*. 2013;88(9):910-919. doi:10.1016/j.mayocp.2013.05.014

38. Forbes JF, Brady AR, Brown LC, Fowkes FG; UK Small Aneurysm Trial Participants. Health service costs and quality of life for early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*. 1998;352(9141):1656-1660. doi:10.1016/S0140-6736(98)10284-2

39. Fowkes FG, Greenhalgh RM, Powell JT, Ruckley CV; U.K. Small Aneurysm Trial Participants. Length of hospital stay following elective abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg*. 1998;16(3):185-191. doi:10.1016/S1078-5884(98)80218-9

40. Golledge J, Parr A, Boult M, Maddern G, Fitridge R. The outcome of endovascular repair of small abdominal aortic aneurysms. *Ann Surg*. 2007;245(2):326-333. doi:10.1097/01.sla.0000253965.95368.52

41. Greenhalgh RM, Forbes JF, Fowkes FG, Powell JT, Ruckley CV; UK Small Aneurysm Trial Participants. The UK Small Aneurysm Trial: design, methods and progress. *Eur J Vasc Endovasc Surg*. 1995;9(1):42-48. doi:10.1016/S1078-5884(05)80223-0

42. Høgh A, Vammen S, Joensen J, et al. Intermittent roxithromycin treatment for preventing small abdominal aortic aneurysms progression: long term results from a small randomised double-blinded clinical controlled trial. Abstract presented at: European Society for Vascular Surgery Annual Meeting 2008; September 4-7, 2008; Nice, France.

43. Høgh A, Vammen S, Ostergaard L, Joensen JB, Henneberg EW, Lindholt JS. Intermittent roxithromycin for preventing progression of small abdominal aortic aneurysms: long-term results of a small clinical trial. *Vasc Endovascular Surg*. 2009;43(5):452-456. doi:10.1177/1538574409335037

44. Karlsson L, Gnarpe J, Bergqvist D, Lindbäck J, Pärsson H. The effect of azithromycin and *Chlamydophilia pneumonia* infection on expansion of small abdominal aortic aneurysms—a prospective randomized double-blind trial. *J Vasc Surg*. 2009;50(1):23-29. doi:10.1016/j.jvs.2008.12.048

45. Kim LG, P Scott RA, Ashton HA, Thompson SG; Multicentre Aneurysm Screening Study Group. A sustained mortality benefit from screening for abdominal aortic aneurysm. *Ann Intern Med*. 2007;146(10):699-706. doi:10.7326/0003-4819-146-10-200705150-00003

46. Kim LG, Scott RAP, Ashton HA, Thompson SG. A prolonged mortality benefit from screening for abdominal aortic aneurysm: seven-year follow-up of the MASS trial. *Br J Surg*. 2007;94(suppl 1):8. doi:10.1002/bjs.5765

47. Kiru G, Bicknell C, Falaschetti E, Powell J, Poulter N. An evaluation of the effect of an angiotensin-converting enzyme inhibitor on the growth rate of small abdominal aortic aneurysms: a randomised placebo-controlled trial (AARDVARK). *Health Technol Assess*. 2016;20(59):1-180. doi:10.3310/hta20590

48. Lederle FA, Johnson GR, Wilson SE, et al; Aneurysm Detection and Management Veterans Affairs Cooperative Study. Quality of life, impotence, and activity level in a randomized trial of immediate repair versus surveillance of small abdominal aortic aneurysm. *J Vasc Surg*. 2003;38(4):745-752. doi:10.1016/S0741-5214(03)00423-3

49. Lederle FA, Johnson GR, Wilson SE, et al; Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval. *Arch Intern Med*. 2000;160(8):1117-1121. doi:10.1001/archinte.160.8.1117

50. Lederle FA, Wilson SE, Johnson GR, et al; ADAM VA Cooperative Study Group. Design of the abdominal aortic Aneurysm Detection and Management Study. *J Vasc Surg*. 1994;20(2):296-303. doi:10.1016/0741-5214(94)90019-1

51. Lederle FA, Wilson SE, Johnson GR, et al; Aneurysm Detection and Management Veterans Affairs Cooperative Study Group. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med*. 2002;346(19):1437-1444. doi:10.1056/NEJMoa012573

52. Lesjak M, Boreland F, Lyle D, Sidford J, Flecknoe-Brown S, Fletcher J. Screening for abdominal aortic aneurysm: does it affect men's quality of life? *Aust J Prim Health*. 2012;18(4):284-288. doi:10.1071/PY11131

53. Lindholt JS, Henneberg EW, Juul S, Fasting H. Impaired results of a randomised double blinded clinical trial of propranolol versus placebo on the expansion rate of small abdominal aortic aneurysms. *Int Angiol*. 1999;18(1):52-57.

54. Lindholt JS, Juul S, Fasting H, Henneberg EW. Hospital costs and benefits of screening for abdominal aortic aneurysms: results from a randomised population screening trial. *Eur J Vasc Endovasc Surg*. 2002;23(1):55-60. doi:10.1053/ejvs.2001.1534

55. Lindholt JS, Juul S, Fasting H, Henneberg EW. Preliminary ten year results from a randomised single centre mass screening trial for abdominal

aortic aneurysm. *Eur J Vasc Endovasc Surg*. 2006; 32(6):608-614. doi:10.1016/j.ejvs.2006.06.008

56. Lindholt JS, Juul S, Henneberg EW. High-risk and low-risk screening for abdominal aortic aneurysm both reduce aneurysm-related mortality: a stratified analysis from a single-centre randomised screening trial. *Eur J Vasc Endovasc Surg*. 2007;34(1):53-58. doi:10.1016/j.ejvs.2006.12.031

57. Lindholt JS, Søgaard R. Population screening and intervention for vascular disease in Danish men (VIVA): a randomised controlled trial. *Lancet*. 2017; 390(10109):2256-2265. doi:10.1016/S0140-6736(17) 32250-X

58. Lindholt JS, Sørensen J, Søgaard R, Henneberg EW. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *Br J Surg*. 2010;97(6):826-834. doi: 10.1002/bjs.7001

59. Lindholt JS, Vammen S, Juul S, Fasting H, Henneberg EW. Optimal interval screening and surveillance of abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg*. 2000;20(4):369-373. doi:10. 1016/S1078-5884(00)91191-2

60. Lo RC, Bensley RP, Hamdan AD, Wyers M, Adams JE, Schermerhorn ML; Vascular Study Group of New England. Gender differences in abdominal aortic aneurysm presentation, repair, and mortality in the Vascular Study Group of New England. *J Vasc Surg*. 2013;57(5):1261-1268. doi:10.1016/j.jvs.2012. 11.039

61. Lucarotti ME, Heather BP, Shaw E, Poskitt KR. Psychological morbidity associated with abdominal aortic aneurysm screening. *Eur J Vasc Endovasc Surg*. 1997;14(6):499-501. doi:10.1016/S1078-5884(97) 80131-1

62. McCarthy RJ, Shaw E, Whyman MR, Earnshaw JJ, Poskitt KR, Heather BP. Recommendations for screening intervals for small aortic aneurysms. *Br J Surg*. 2003;90(7):821-826. doi:10.1002/bjs.4216

63. Meijer CA, Stijnen T, Wasser MN, Hamming JF, van Bockel JH, Lindeman JH; Pharmaceutical Aneurysm Stabilisation Trial Study Group. Doxycycline for stabilization of abdominal aortic aneurysms: a randomized trial. *Ann Intern Med*. 2013;159(12):815-823. doi:10.7326/0003-4819-159-12-201312170-00007

64. Mosorin M, Juvonen J, Biancari F, et al. Use of doxycycline to decrease the growth rate of abdominal aortic aneurysms: a randomized, double-blind, placebo-controlled pilot study. *J Vasc Surg*. 2001;34(4):606-610. doi:10.1067/mva. 2001.117891

65. Norman PE, Jamrozik K, Lawrence-Brown MM, Dickinson JA. Western Australian randomized controlled trial of screening for abdominal aortic aneurysm. *Br J Surg*. 2003;90(4):492. doi:10.1002/ bjs.4108

66. Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ*. 2004;329(7477): 1259. doi:10.1136/bmj.329.7477.1259

67. Oliver-Williams C, Sweeting MJ, Turton G, et al; Gloucestershire and Swindon Abdominal Aortic Aneurysm Screening Programme. Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. *Br J Surg*. 2018; 105(1):68-74. doi:10.1002/bjs.10715

68. Ouriel K. The PIVOTAL study: a randomized comparison of endovascular repair versus surveillance in patients with smaller abdominal aortic aneurysms. *J Vasc Surg*. 2009;49(1):266-269. doi:10.1016/j.jvs.2008.11.048

69. Ouriel K, Clair DG, Kent KC, Zarins CK; Positive Impact of Endovascular Options for Treating Aneurysms Early (PIVOTAL) Investigators. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg*. 2010;51(5):1081-1087. doi:10.1016/j.jvs. 2009.10.113

70. Overbey DM, Glebova NO, Chapman BC, Hosokawa PW, Eun JC, Nehler MR. Morbidity of endovascular abdominal aortic aneurysm repair is directly related to diameter. *J Vasc Surg*. 2017;66 (4):1037-1047.e7. doi:10.1016/j.jvs.2017.01.058

71. Peppelenbosch N, Buth J, Harris PL, van Marrewijk C, Fransen G; EUROSTAR Collaborators. Diameter of abdominal aortic aneurysm and outcome of endovascular aneurysm repair: does size matter? a report from EUROSTAR. *J Vasc Surg*. 2004;39(2):288-297. doi:10.1016/j.jvs.2003.09.047

72. Powell JT, Brady AR, Brown LC, et al; United Kingdom Small Aneurysm Trial Participants. Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med*. 2002;346(19): 1445-1452. doi:10.1056/NEJMoa013527

73. Powell JT, Brady AR, Brown LC, Forbes JF; UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet*. 1998; 352(9141):1649-1655. doi:10.1016/S0140-6736(98) 10137-X

74. Powell JT, Brown LC, Forbes JF, et al. Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg*. 2007;94(6): 702-708. doi:10.1002/bjs.5778

75. Propanolol Aneurysm Trial Investigators. Propranolol for small abdominal aortic aneurysms: results of a randomized trial. *J Vasc Surg*. 2002;35 (1):72-79. doi:10.1067/mva.2002.121308

76. Scott RA, Bridgewater SG, Ashton HA. Randomized clinical trial of screening for abdominal aortic aneurysm in women. *Br J Surg*. 2002;89(3): 283-285. doi:10.1046/j.0007-1323.2001.02014.x

77. Scott RA, Vardulaki KA, Walker NM, Day NE, Duffy SW, Ashton HA. The long-term benefits of a single scan for abdominal aortic aneurysm (AAA) at age 65. *Eur J Vasc Endovasc Surg*. 2001;21(6):535-540. doi:10.1053/ejvs.2001.1368

78. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg*. 1995;82(8): 1066-1070. doi:10.1002/bjs.1800820821

79. Sillesen H, Eldrup N, Hultgren R, et al; AORTA Trial Investigators. Randomized clinical trial of mast cell inhibition in patients with a medium-sized abdominal aortic aneurysm. *Br J Surg*. 2015;102(8): 894-901. doi:10.1002/bjs.9824

80. Söderberg P, Wanhainen A, Svensjö S. Five year natural history of screening detected sub-aneurysms and abdominal aortic aneurysms in 70 year old women and systematic review of repair rate in women. *Eur J Vasc Endovasc Surg*. 2017;53 (6):802-809. doi:10.1016/j.ejvs.2017.02.024

81. Spencer CA, Norman PE, Jamrozik K, Tuohy R, Lawrence-Brown M. Is screening for abdominal aortic aneurysm bad for your health and well-being? *ANZ J Surg*. 2004;74(12):1069-1075. doi:10.1111/j.1445-1433.2004.03270.x

82. Svensjö S, Björck M, Wanhainen A. Editor's choice: five-year outcomes in men screened for abdominal aortic aneurysm at 65 years of age: a population-based cohort study. *Eur J Vasc Endovasc Surg*. 2014;47(1):37-44. doi:10.1016/j.ejvs. 2013.10.007

83. Thompson SG, Ashton HA, Gao L, Buxton MJ, Scott RA; Multicentre Aneurysm Screening Study (MASS) Group. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. *Br J Surg*. 2012;99(12):1649-1656. doi:10.1002/bjs.8897

84. Thompson SG, Ashton HA, Gao L, Scott RA; Multicentre Aneurysm Screening Study Group. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. *BMJ*. 2009;338:b2307. doi:10.1136/bmj.b2307

85. Vammen S, Lindholt JS, Ostergaard L, Fasting H, Henneberg EW. Randomized double-blind controlled trial of roxithromycin for prevention of abdominal aortic aneurysm expansion. *Br J Surg*. 2001;88(8):1066-1072. doi:10.1046/j.0007-1323. 2001.01845.x

86. Vardulaki KA, Walker NM, Couto E, et al. Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm. *Br J Surg*. 2002;89(7): 861-864. doi:10.1046/j.1365-2168.2002.02133.x

87. Wanhainen A, Rosén C, Rutegård J, Bergqvist D, Björck M. Low quality of life prior to screening for abdominal aortic aneurysm: a possible risk factor for negative mental effects. *Ann Vasc Surg*. 2004;18 (3):287-293. doi:10.1007/s10016-004-0021-x

88. Jamrozik K, Norman PE, Spencer CA, et al. Screening for abdominal aortic aneurysm: lessons from a population-based study. *Med J Aust*. 2000; 173(7):345-350. doi:10.5694/j.1326-5377.2000. tb125684.x

89. Mani K, Alund M, Björck M, Lundkvist J, Wanhainen A. Screening for abdominal aortic aneurysm among patients referred to the vascular laboratory is cost-effective. *Eur J Vasc Endovasc Surg*. 2010;39(2):208-216. doi:10.1016/j.ejvs.2009.11.004

90. Public Health England. Abdominal aortic aneurysm screening: 2015 to 2016 data. Gov.UK website. https://www.gov.uk/government/ publications/abdominal-aortic-aneurysm-screening-2015-to-2016-data. Published 2016. Accessed June 9, 2019.

91. Public Health England. Abdominal aortic aneurysm screening: 2016 to 2017 data (1 April 2016 to 31 March 2017). Gov.UK website. https://www.gov.uk/government/publications/ abdominal-aortic-aneurysm-screening-2016-to-2017-data. Published 2018. Accessed June 9, 2019.

92. Karthikesalingam A, Vidal-Diez A, Holt PJ, et al. Thresholds for abdominal aortic aneurysm repair in England and the United States. *N Engl J Med*. 2016;375(21):2051-2059. doi:10.1056/ NEJMoa1600931

93. Savji N, Rockman CB, Skolnick AH, et al. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. *J Am Coll Cardiol*. 2013;61(16):1736-1743. doi:10.1016/j.jacc.2013.01.054

94. Greco G, Egorova NN, Gelijns AC, et al. Development of a novel scoring tool for the identification of large ≥5 cm abdominal aortic aneurysms. *Ann Surg*. 2010;252(4):675-682.

95. Han Y, Zhang S, Zhang J, Ji C, Eckstein HH. Outcomes of endovascular abdominal aortic aneurysm repair in octogenarians: meta-analysis and systematic review. *Eur J Vasc Endovasc Surg*. 2017;54(4):454-463. doi:10.1016/j.ejvs.2017.06.027

96. Ulug P, Powell JT, Sweeting MJ, Bown MJ, Thompson SG; SWAN Collaborative Group. Meta-analysis of the current prevalence of screen-detected abdominal aortic aneurysm in women. *Br J Surg*. 2016;103(9):1097-1104. doi:10.1002/bjs.10225

97. Tang W, Yao L, Roetker NS, et al. Lifetime risk and risk factors for abdominal aortic aneurysm in a 24-year prospective study: the ARIC study (Atherosclerosis Risk in Communities). *Arterioscler Thromb Vasc Biol*. 2016;36(12):2468-2477. doi:10.1161/ATVBAHA.116.308147

98. Brown PM, Zelt DT, Sobolev B. The risk of rupture in untreated aneurysms: the impact of size, gender, and expansion rate. *J Vasc Surg*. 2003;37(2):280-284. doi:10.1067/mva.2003.119

99. Skibba AA, Evans JR, Hopkins SP, et al. Reconsidering gender relative to risk of rupture in the contemporary management of abdominal aortic aneurysms. *J Vasc Surg*. 2015;62(6):1429-1436. doi:10.1016/j.jvs.2015.07.079

100. Sweeting MJ, Thompson SG, Brown LC, Powell JT; RESCAN Collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg*. 2012;99(5):655-665. doi:10.1002/bjs.8707

101. Laine MT, Vänttinen T, Kantonen I, et al. Rupture of abdominal aortic aneurysms in patients under screening age and elective repair threshold. *Eur J Vasc Endovasc Surg*. 2016;51(4):511-516. doi:10.1016/j.ejvs.2015.12.011

102. Tomee SM, Lijftogt N, Vahl A, Hamming JF, Lindeman JHN. A registry-based rationale for discrete intervention thresholds for open and endovascular elective abdominal aortic aneurysm repair in female patients. *J Vasc Surg*. 2018;67(3):735-739. doi:10.1016/j.jvs.2017.07.123

103. Lowry D, Singh J, Mytton J, Tiwari A. Sex-related outcome inequalities in endovascular aneurysm repair. *Eur J Vasc Endovasc Surg*. 2016;52(4):518-525. doi:10.1016/j.ejvs.2016.07.083

104. Deery SE, Lancaster RT, Baril DT, et al. Contemporary outcomes of open complex abdominal aortic aneurysm repair. *J Vasc Surg*. 2016;63(5):1195-1200. doi:10.1016/j.jvs.2015.12.038

105. Desai M, Choke E, Sayers RD, Nath M, Bown MJ. Sex-related trends in mortality after elective abdominal aortic aneurysm surgery between 2002 and 2013 at National Health Service hospitals in England: less benefit for women compared with men. *Eur Heart J*. 2016;37(46):3452-3460. doi:10.1093/eurheartj/ehw335

106. Heikkinen M, Salenius JP, Auvinen O. Ruptured abdominal aortic aneurysm in a well-defined geographic area. *J Vasc Surg*. 2002;36(2):291-296. doi:10.1067/mva.2002.125479

107. Ulug P, Sweeting MJ, von Allmen RS, Thompson SG, Powell JT, SWAN Collaborators. Morphological suitability for endovascular repair, non-intervention rates, and operative mortality in women and men assessed for intact abdominal aortic aneurysm repair: systematic reviews with meta-analysis. *Lancet*. 2017;389(10088):2482-2491. doi:10.1016/S0140-6736(17)30639-6

108. Mehta M, Byrne WJ, Robinson H, et al. Women derive less benefit from elective endovascular aneurysm repair than men. *J Vasc Surg*. 2012;55(4):906-913. doi:10.1016/j.jvs.2011.11.047

109. Sidloff DA, Saratzis A, Sweeting MJ, et al. Sex differences in mortality after abdominal aortic aneurysm repair in the UK. *Br J Surg*. 2017;104(12):1656-1664. doi:10.1002/bjs.10600

110. Grootenboer N, Hunink MG, Hendriks JM, van Sambeek MR, Buth J; EUROSTAR Collaborators. Sex differences in 30-day and 5-year outcomes after endovascular repair of abdominal aortic aneurysms in the EUROSTAR study. *J Vasc Surg*. 2013;58(1):42-49. doi:10.1016/j.jvs.2013.01.028

111. Sweeting MJ, Masconi KL, Jones E, et al. Analysis of clinical benefit, harms, and cost-effectiveness of screening women for abdominal aortic aneurysm. *Lancet*. 2018;392(10146):487-495. doi:10.1016/S0140-6736(18)31222-4

112. Wanhainen A, Hultgren R, Linné A, et al; Swedish Aneurysm Screening Study Group (SASS). Outcome of the Swedish nationwide abdominal aortic aneurysm screening program. *Circulation*. 2016;134(16):1141-1148. doi:10.1161/CIRCULATIONAHA.116.022305

113. Jahangir E, Lipworth L, Edwards TL, et al. Smoking, sex, risk factors and abdominal aortic aneurysms: a prospective study of 18 782 persons aged above 65 years in the Southern Community Cohort Study. *J Epidemiol Community Health*. 2015;69(5):481-488. doi:10.1136/jech-2014-204920

114. Howard DP, Banerjee A, Fairhead JF, Handa A, Silver LE, Rothwell PM; Oxford Vascular Study. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *Br J Surg*. 2015;102(8):907-915. doi:10.1002/bjs.9838

115. Chun KC, Teng KY, Van Spyk EN, Carson JG, Lee ES. Outcomes of an abdominal aortic aneurysm screening program. *J Vasc Surg*. 2013;57(2):376-381. doi:10.1016/j.jvs.2012.08.038

116. Joergensen TM, Houlind K, Green A, Lindholt JS. Abdominal aortic diameter is increased in males with a family history of abdominal aortic aneurysms: results from the Danish VIVA trial. *Eur J Vasc Endovasc Surg*. 2014;48(6):669-675. doi:10.1016/j.ejvs.2014.09.005

117. Forsdahl SH, Solberg S, Singh K, Jacobsen BK. Abdominal aortic aneurysms, or a relatively large diameter of non-aneurysmal aortas, increase total and cardiovascular mortality: the Tromsø study. *Int J Epidemiol*. 2010;39(1):225-232. doi:10.1093/ije/dyp320

118. Freiberg MS, Arnold AM, Newman AB, Edwards MS, Kraemer KL, Kuller LH. Abdominal aortic aneurysms, increasing infrarenal aortic diameter, and risk of total mortality and incident cardiovascular disease events: 10-year follow-up data from the Cardiovascular Health Study. *Circulation*. 2008;117(8):1010-1017. doi:10.1161/CIRCULATIONAHA.107.720219

119. Stone NJ, Robinson JG, Lichtenstein AH, et al; 2013 ACC/AHA Cholesterol Guideline Panel. Treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease risk in adults: synopsis of the 2013 American College of Cardiology/American Heart Association cholesterol guideline. *Ann Intern Med*. 2014;160(5):339-343. doi:10.7326/M14-0126

120. Bibbins-Domingo K, Grossman DC, Curry SJ, et al; US Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;316(19):1997-2007. doi:10.1001/jama.2016.15450