Screening for Abdominal Aortic Aneurysm: Systematic Review and Meta-analysis

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Abstract

Background: This report was produced for the Canadian Task Force on Preventive Health Care (CTFPHC) to provide guidelines on screening for abdominal aortic aneurysm (AAA).

Purpose: The aim of this systematic review is to examine the evidence on benefits and harms of AAA screening in asymptomatic adults aged 50 years and older.

Data Sources: We searched Medline, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL). We also searched PubMed for any relevant publisher-supplied non-indexed citations from 2013 until April 2015. We conducted a targeted search for evidence on overdiagnosis/over-treatment in Medline, EMBASE and Cochrane Central from 2005 to April 2015. A separate search was conducted for the contextual questions in MEDLINE, Embase and PsychINFO (patient preferences question only) for the time period of 2005 to February/March. A focused web-based grey literature search was also undertaken.

Studies from the most recent systematic review from the United States Preventive Services Task Force (USPSTF) on AAA screening were included in our database and passed through the screening process with citations identified in our search.

Study Selection: Titles and abstracts of papers considered for the key questions were reviewed independently by two reviewers; any article marked for inclusion by either reviewer went on to full-text screening. Full text review was done independently by two people with consensus required for inclusion or exclusion.

Data Abstraction: Review team members extracted data about the population, study design, intervention, analysis and results for outcomes of interest. One team member completed full abstraction, followed by a second team member who verified all extracted data and ratings. We assessed study quality using Cochrane's Risk of Bias tool (randomized controlled trials) and the Newcastle-Ottawa Scale (observational studies). For outcomes ranked as critical, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to assess the strength and the quality of evidence.

Analysis: For binary outcomes we utilized the number of events; proportion or percentage data was used to generate the summary measures of effect in the form of risk ratio (RR) using a random effects model. The primary subgrouping in each meta-analysis was based on length of follow-up. The estimates of absolute risk reduction (ARR), absolute risk increase (ARI) and number needed to screen (NNS) were added. For the benefits of re-screening (observational studies), the rates/proportion across studies were calculated using Wilson score interval method and pooled.

For continuous outcomes of harms we utilized change from baseline data (means, standard deviations). For outcomes of harms of one-time AAA screening, further sensitivity analyses were conducted for rare events using Peto one-step odds ratio method to evaluate any significant changes in magnitude and direction of effect compared with the DerSimonian and Laird models.

Results:

For benefits of one-time AAA screening in men as compared to controls, pooled analyses from four population-based randomized controlled trials (MASS, Chichester, Viborg and Western Australia) with moderate quality evidence showed a significant reduction of 43% [RR = 0.57 (95% CI; 0.44 to 0.72), NNS = 796] in AAA-related mortality at an early follow-up of 3 to 5 years and this benefit was maintained at 13 to 15 years of follow-up with 42% reduction [RR = 0.58 (95% CI; 0.39 to 0.88), NNS = 212]. The effect of AAA screening on all-cause mortality was marginally significant for longer follow-up times and persisted up to 13 to 15 years of follow-up (3 trials; RR = 0.98, 95% CI 0.97 to 1.0; p=0.04). One-time screening of AAA in men was also associated with significant reductions in AAA rupture rate as compared to controls (38% to 53% reduction), which was maintained over a follow-up of up to 13 to 15 years (3 trials; RR = 0.62, 95% CI 0.45 to 0.86; ARR=0.50%, NNS= 200). The Chichester trial examined the benefits and harms of one-time AAA screening in women and found no significant differences between screening and control arms at 5 and 10 years of follow-up. We found no studies to answer the question on the effectiveness of one-time screening on other subgroups. The Viborg trial examined benefits of AAA screening on AAA related mortality in high risk groups and low risk groups. At 5.9 years of follow up, relative to no screening group, there was no difference in reduction for AAA-related mortality for the high risk group (RR = 0.22, 95% CI, 0.08 to 0.65) as compared with low risk group (RR = 0.24, 95% CI, 0.09 to 0.63). Thirteen years of follow up showed a reduced benefit from AAA screening in high risk group (RR = 0.42, 95% CI, 0.20 to 0.87) as compared with low risk group (RR = 0.29, 95% CI, 0.14 to 0.60) but difference remained statistically insignificant. High risk defined as men with chronic obstructive pulmonary disease (COPD) and cardiovascular conditions such as hypertension, ischemic heart disease, peripheral occlusive arterial disease, and history of acute myocardial infarction, transient ischemic attack and stroke.

For harms of one-time AAA screening in men as compared to controls, AAA screening using ultrasound was associated with a statistically significant increase in the total number of AAA-related operations performed and this effect was maintained over a follow-up of 13 to 15 years (range: 1.48 to 2.16 times more likely). One-time screening of AAA was associated with a statistically significant increase in the number of elective operations (range: 2.15 to 3.25 times more likely) and a statistically significant decrease in number of emergency procedures (range: 50% to 59% reduction) as compared to controls which persisted over a follow-up of 13 to 15 years. As compared to controls, one-time AAA screening was also associated with a statistically significant decrease in 30-day post-operative mortality due to overall AAA operations performed and this effect was maintained over a follow-up of 13 to 15 years (range: 54% to 69% reduction). However when 30-day post-operative mortality was looked at separately for elective and emergency operations the effects were not significant at all follow-up times.

The included evidence showed no significant difference in Health Related Quality of Life (HRQoL) measured with the Short Form Health Survey (SF-36) between screened positive and control groups (screened negative or no AAA). Evidence from the MASS trial using 13 year follow-up data showed that one-time AAA screening with ultrasound was potentially associated with an overdiagnosis of 45% (95% CI 42% to 47%) among screen-detected men.

For benefits of repeat screening, three studies were found. One uncontrolled observational cohort study reported that AAA mortality in the repeat screening arm was 0.56% (95% CI 0.38 to 0.83%); All-cause mortality was 1.53% (95% CI 1.21% to 1.94%) and AAA rupture rate was 0.70% (95% CI 0.49% to 0.99%) at a follow-up of ten years. Three uncontrolled cohort studies reported on AAA incidence and found that after a follow-up of 4 to 10 years, the AAA incidence in repeat screening arm was 2.26% (95% CI 0.41% to 4.10%).

Conclusion: Population based screening for AAA with ultrasound in asymptomatic men aged 50 years and older showed statistically significant reductions in AAA-related mortality and rupture and hence avoids unnecessary AAA-related deaths. Limited evidence is available on the benefits of repeat AAA screening and targeted screening approaches based on risk factors for AAA. Future research should explore the differential benefits of AAA screening based on risk factors that increase risk for developing AAA.

Table of Contents

List of Acronyms

AAA	Abdominal Aortic Aneurysm
AMSTAR	Assessing the Methodological Quality of Systematic Reviews
ARI	Absolute Risk Increase
ARR	Absolute Risk Reduction
ACC/AHA	American College of Cardiology/American Heart Association
CADTH	Canadian Agency for Drugs and Technologies in Health
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CQ	Contextual Question
CT	Computed tomography
CSVS	Canadian Society for Vascular Surgery
CTFPHC	Canadian Task Force on Preventive Health Care
ES	Evidence Set
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICER	Incremental cost-effectiveness ratio
KQ	Key Question
MRI	Magnetic resonance imaging
NHS	National Health Service
NNH	Number Needed to Harm
NNS	Number Needed to Screen
NR	Not Reported
PRESS	Peer Review Electronic Search Strategies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life years
SD	Standard Deviation
RR	Risk Ratio
RRR	Relative Risk Ratio
USPSTF	United States Preventive Services Task Force

Chapter 1: Introduction

Purpose and Background

In Canada, abdominal aortic aneurysm (AAA) is an important cause of death.[1] It is estimated that every year 20,000 Canadians are diagnosed with AAA with approximately 2,000 deaths resulting from ruptured aneurysms. [2] Risk of AAA increases for men over 60 years; with a history of atherosclerosis; people who have ever smoked; or the presence of a family history of AAA (higher if the person with AAA was female). [2] As the condition is often asymptomatic, ruptured AAA is often the first sign.[3] Without treatment, approximately 50% of the Canadians diagnosed each year have large AAA that may become fatal.[3]

The aim of this systematic review is to examine the evidence on benefits and harms of AAA screening. The findings of this review will be used by the Canadian Task Force on Preventive Health Care (CTFPHC) to update its previous recommendation on AAA screening.

Previous CTFPHC Recommendations and Other Guidelines

The last CTFPHC recommendation on screening for AAA was made in 1991.[4] The recommendation at that time was that screening through physical examination or ultrasonography for AAA neither be included in nor excluded from periodic health examinations due to "poor evidence".[4]

In 2014 the United States Preventive Services Task Force (USPSTF) recommended one-time ultrasound screening for men aged 65-75 who have ever smoked.[5] This recommendation is in keeping with a previous guideline (2005) from the American College of Cardiology/American Heart Association (ACC/AHA), that also recommended male relatives 60 years of age or older (siblings or children) of men and women with diagnosed AAA should undergo AAA screening.[6]

Scan of Changes in Clinical Practice since Previous Recommendation

In Canada, national and/or provincial screening programs do not currently exist, though their development has been recommended by the CSVS.[1]After an assessment of the randomized controlled trial (RCT) evidence from the United Kingdom (UK) as well as international evidence by the UK National Screening Committee,[7] the National Health Service (NHS) began implementation of an AAA Screening Programme in 2009 in the UK.[8] By 2013, the screening programme had been implemented throughout England. At the age of 65, all men are invited for ultrasound screening; after the age of 65 those who have not been screened can self-refer.[8]

Chapter 2: Methods

The protocol is registered with the International Prospective Registry of Systematic Reviews (PROSPERO CRD42015019047).

Analytic Framework, Key Questions and Contextual Questions

See Figure 1 for Analytic Framework.

Key Questions

KQ1. What is the effect of one-time AAA screening using ultrasound on health outcomes in asymptomatic adults aged 50 years and older?

> a. Does the effect of one-time screening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities?
>
> b. Does the effect of one-time screening vary between different screening approaches (i.e. high risk versus low risk status)?

KQ2. What is the effect of rescreening for AAA using ultrasound on health outcomes including AAA incidence in previously screened asymptomatic adults aged 50 years and older?

> a. Does the effect of rescreening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities?
>
> b. Does the effect of rescreening vary between different time intervals?

KQ3. What are the harms associated with one-time and repeated AAA screening using ultrasound?

Contextual Questions

CQ1. What are patients' preferences and values regarding AAA screening?

CQ2. What is the cost-effectiveness of screening for AAA?

CQ3. How well does ultrasound administered in a general practice setting or which can be administered in a general practice setting compare to standard US in a clinic or hospital setting for the detection of AAA?

Search Strategy

The literature search updated the search done for the 2014 USPSTF review on screening of AAA using the same search strategy[5] (Appendix A). The USPSTF also searched for treatment; however, as our review does not include treatment, we only updated their screening searches. The USPSTF review was rated as a high quality systematic review, using the Assessing the Methodological Quality of Systematic reviews (AMSTAR) tool[9] (Appendix B). Our librarian peer reviewed the search done by the USPSTF using the Peer Review Electronic Search Strategies (PRESS) methodology checklist[10] (Appendix C). We searched Medline, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL). We also searched PubMed for any relevant publisher-supplied non-indexed citations. The searches covered the time period since the last update of the USPSTF search, which was January 2013 until April 2015, and we

searched for both English and French studies. Reference lists of on-topic systematic reviews were reviewed in order to ensure all relevant articles had been captured by our electronic database search. We conducted a targeted search for evidence on overdiagnosis/over-treatment in Medline, EMBASE and Cochrane Central from 2005 to April 2015 (Appendix D).

A separate search was conducted for the contextual questions in MEDLINE, Embase and PsychINFO (patient preferences question only) for the time period of 2005 to February/March 2015 (Appendix E). A focused web-based grey literature search was also undertaken using Google advanced search (limited to Canada) and the Canadian section of Canadian Agency for Drugs and Technologies in Health (CADTH)'s Grey Matters[11] search to look for recent on-topic sources that provided Canadian specific information to help inform the contextual questions.

Citations were managed through the web-based systematic review platform DistillerSR.[12]

Study Selection

Two reviewers independently selected studies for possible inclusion. At the title and abstract level, any citation that was selected for inclusion by either reviewer moved to full text review. At that level any disagreement was discussed between reviewers and a third party was involved to help reach consensus, as necessary. The same process was followed for contextual questions.

Studies included in the USPSTF review were included in our database and passed through the screening process with citations identified in our search.

Inclusion and Exclusion Criteria

Population

The population of interest was asymptomatic adults aged 50 years and older.

Interventions

Interventions of interest were general or targeted screening with ultrasound.

Comparators

For KQ1 the comparison group was a no-screening comparison, or a comparison of different screening approaches (i.e. high risk vs. low risk groups).

For KQ2 the comparison was a no-screening or one-time screening using an ultrasound comparison group, different repeated screening approaches or no comparison/nonexposure.

For KQ3 no comparison group was required, however if a sufficient number of RCTs were found to answer the questions on harms we would not consider uncontrolled studies.

Outcomes

To answer the question on the effectiveness of screening outcomes of interest were AAA-related mortality, all-cause mortality, AAA rupture rate (KQ1 and KQ2) and AAA incidence (KQ2 only).

To answer the question on the harms of screening outcomes of interest were anxiety from risk labelling, anxiety of mortality, false-positive screening-related procedures, 30-day post-operative mortality, surgical procedures, quality of life and overdiagnosis/overtreatment (KQ3).

Study designs

For KQ1 and KQ2 we are interested in randomized controlled trials (RCTs), clinical controlled trials and large cohort studies (n>1000, KQ2 only). Although the USPSTF inclusion criteria also included cohort studies (n>1000) for KQ2, the number of participants analyzed was often <1000. We have included only cohort studies where the number analyzed was >1000.

For KQ3 we are interested in randomized controlled trials, cohort studies and case-control studies.

Settings

The settings of interest were primary care or other settings with primary care-comparable populations.

Language

We included English and French language studies (new search only).

Data Extraction and Quality Assessments

Full data extraction, including characteristics of included studies and risk of bias, was completed by one reviewer and verified by a second reviewer. Disagreements were resolved through consensus between the two reviewers. In the case of disagreements, a third review team member was asked to arbitrate. For key questions, data extraction was conducted using standardized forms by one person and independently verified by a second review member.

For outcomes ranked as critical, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system[13] was used to assess the strength and the quality of evidence using GRADEPro software.[14] The quality of outcome-based bodies of evidence was assessed for risk of bias due to limitations in design, indirectness, inconsistency of findings, imprecision, and reporting bias (such as publication bias). Meta-analyses were conducted where appropriate.

For contextual questions, data extraction was conducted by one reviewer. There was no assessment of the methodological quality of the studies used to answer the contextual questions.

Data Analysis

For the binary outcomes of benefit of one-time AAA screening (i.e. AAA-related mortality, all-cause mortality and AAA rupture rates); and binary outcomes of harms (i.e. increase in AAA-related procedures, 30-day post-operative mortality) we utilized the number of events; proportion or percentage data was used to generate the summary measures of effect in the form of risk ratio (RR) using DerSimonian and Laird random effects models with Mantel-Haenszel method.[15] The primary subgrouping in each meta-analysis was based on length of follow-up. The estimates of absolute risk reduction (ARR), absolute risk increase (ARI) and number needed to screen (NNS)

were added. The NNS were calculated using the absolute numbers presented in the GRADE tables estimated using the control group event rate and risk ratio with the 95% confidence interval obtained from the meta-analysis (see Chapter 12, Section 12.5.4.2 in the Cochrane Handbook for Systematic Reviews of Interventions).[16]

We also analyzed the benefits of repeat AAA screening for the outcomes of incidence of AAA, AAA-related mortality, AAA rupture rates, and all-cause mortality. As the data came from uncontrolled observational studies, the rates/proportion across studies were pooled using the DerSimonian and Laird random effects models with inverse variance method to generate the summary measures of effect.[17] The binomial confidence intervals for each proportion/rate were calculated using "Wilson score interval" method.[18]

For continuous outcomes of harms such as quality of life, we utilized change from baseline data (means, standard deviations). The DerSimonian and Laird random effects model[17] with inverse variance method were utilized to generate the summary measures of effect in the form of mean difference (MD).

For outcomes of harms of one-time AAA screening, further sensitivity analyses were conducted for rare events using Peto one-step odds ratio method to evaluate any significant changes in magnitude and direction of effect compared with the DerSimonian and Laird models.[19] The two methods showed similar effect estimates and confidence intervals (Evidence Set [ES] 3), see Chapter 16, Section 16.9.5 in the Cochrane Handbook for Systematic Reviews of Interventions.[20] The Cochran's Q (α=0.05) was employed to detect statistical heterogeneity and I^2 statistic to quantify the magnitude of statistical heterogeneity between studies where I^2 30% to 60% represents moderate and I^2 50% to 90% represents substantial heterogeneity across studies.[21]

Chapter 3: Results

Search Results

After removing duplicates, 186 citations from our search, as well as 15 citations included from the USPSTF review, were identified for screening.[12] At title and abstract screening, we excluded 167 studies, leaving 34 studies to be screened at full-text. Of those we identified 19 studies that did not meet our inclusion criteria, as well as 6 systematic reviews. References lists of the included systematic reviews were searched but no additional studies were added. We found 9 studies meeting our inclusion criteria. Please see PRISMA Flow Diagram – Screening Search Strategy for details (Figure 2a).

Overdiagnosis/overtreatment search results: After removing duplicates, 117 citations were identified for screening.[12] At title and abstract we excluded 103 studies, leaving 14 articles to be screened at full-text. We identified one study that met our inclusion criteria. Please see PRISMA Flow Diagram – Overdiagnosis/overtreatment Search Strategy for details (Figure 2b).

Summary of Included Studies

A total of 10 studies were included. See Tables 1 and 2 for details of the included studies. Four RCTs were found to answer KQ1 on the benefits of one-time screening using ultrasound; MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia.[36, 37] Three of these RCTs included men only, one study included a mixed gender population. The included ages ranged from 64 to 83 years of age. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. These studies took place in the UK (2 studies), Denmark and Western Australia and were published between 1995 and 2005. RCTs were assessed with the Cochrane Risk of Bias tool[38] (Table 3).

Three uncontrolled observational studies were found to answer KQ2 on the benefits of repeat screening using ultrasound.[39-41] These studies included men only, and ages ranged from 50 to 79 years. Repeat screening took place at various intervals (2, 4, and 5 years). These studies took place in the UK, the US and Sweden and were published between 2000 and 2014. Uncontrolled observational studies were assessed with the Newcastle Ottawa Scale[42] (Table 4).

All four RCTs (MASS, Chichester, Viborg and Western Australia) as well as three additional observational studies[37, 43, 44] (one using data from the Western Australia trial[37]) and one study, using data from the MASS trial,[45] were found to answer KQ3 on the harms of one-time screening using ultrasound. All four RCTs provided data on 30 day mortality from AAA operations, elective AAA operations and emergency AAA operations, as well as data on number of AAA operations, elective AAA operations and emergency AAA operations. Three observational studies[37, 43, 44] and one RCT (MASS)[22] provided data on quality of life. One additional study, using 13 year follow-up from the MASS trial provided data on overdiagnosis.[45]

One uncontrolled observational study was found to answer the question (KQ3) on the harms of repeat screening using ultrasound.[39]

KQ1. What is the effect of one-time AAA screening using ultrasound on health outcomes in asymptomatic adults aged 50 years and older?

See Evidence Set (ES) 1 for detailed results.

AAA Mortality

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on benefits of one-time AAA screening using ultrasound on AAA mortality in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: four RCTs reported a follow-up of 3 to 5 years;[22, 26, 33, 36] two RCTs (MASS and Viborg) reported a follow-up of 6 to 7 years;[23, 34] three RCTs (MASS, Chichester and Viborg) reported a follow-up of 10 to 11 years[25, 29, 30] and three RCTs (MASS, Chichester and Viborg) reported a follow-up of 13 to 15 years.[24, 27, 31] As compared to control group, the pooled estimate showed a significant reduction of 43% in AAA mortality for screening group at follow-up of 3 to 5 years (4 trials; RR = 0.57, 95% CI 0.44 to 0.72, ARR=0.13%, NNS= 796) and this effect persisted up to 13 to 15 years, with a 42% reduction (3 trials; RR = 0.58, 95% CI 0.39 to 0.88; ARR=0.47%, NNS= 212), (Forest Plot 1.1). The overall quality of this evidence was rated as MODERATE and downgraded for serious concerns regarding risk of bias.

All-Cause Mortality

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on benefits of one-time AAA screening using ultrasound on all-cause mortality in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: four RCTs reported a follow-up of 3 to 5 years;[22, 26, 33, 36] two RCTs (MASS and Viborg) reported a follow-up of 6 to 7 years;[23, 34] two RCTs (MASS and Viborg) reported a follow-up of 10 to 11 years[25, 30] and three RCTs (MASS, Chichester and Viborg) reported a follow-up of 13 to 15 years.[24, 27, 31] As compared to controls, AAA screening had no significant effect on all-cause mortality at 3 to 5 years of follow-up (4 trials; RR= 0.94, 95% CI 0.88 to 1.02, p=0.14) but the effect became marginally significant at longer follow-up times and persisted up to 13 to 15 years of follow-up (3 trials; RR = 0.98, 95% CI 0.97 to 1.0; p=0.04), (Forest Plot 1.2). The overall quality of this evidence was rated as LOW to MODERATE and downgraded due to serious concerns regarding risk of bias and imprecision.

AAA Rupture Rate

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on benefits of one-time AAA screening using ultrasound on AAA rupture rates in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: four RCTs reported a follow-up of 3 to 5 years;[22, 26, 33, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] two RCTs (MASS and Viborg) reported a follow-up of 10 to 11 years[25, 30] and three RCTs (MASS, Chichester and Viborg) reported a follow-up of 13 to 15 years.[24, 27, 31] As compared to control group, screening showed statistically significant reductions in AAA rupture rates at all follow-up times starting at 3 to 5 years with 48% reduction (4 trials; RR = 0.52, 95% CI 0.35 to 0.79; ARR=0.16%, NNS= 606) and persisted up to 13 to 15 years, 38% reduction (3 trials; RR = 0.62, 95% CI 0.45 to 0.86; ARR=0.50%, NNS= 200), (Forest Plot 1.3). The overall quality of this evidence was rated as MODERATE to HIGH and downgraded due to serious concerns regarding risk of bias.

KQ1a. Does the effect of one-time screening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities?

The Chichester trial examined the benefits and harms of one-time AAA screening in women and found no significant differences between screening and control arms. At 5-years of follow-up, the study reports AAA mortality (RR = 1.49, 95% CI: 0.25 to 8.93, p = 0.66); all-cause mortality (RR = 1.05, 95% CI: 0.93 to 1.18, p = 0.40); and AAA rupture (RR = 1.49, 95% CI: 0.25 to 8.93, p = 0.66).[26] At 10-years of follow-up, the Chichester trial reports AAA mortality (RR = 1.00, 95% CI: 0.37 to 2.65, p = 0.99); and AAA rupture (RR = 1.11, 95% CI: 0.45 to 2.72, p = 0.83).[28]

We found no studies to answer the question on the effectiveness of one-time screening on other subgroups, including smokers and non-smokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA and adults of different races/ethnicities.

KQ1b. Does the effect of one-time screening vary between different screening approaches (i.e. high risk vs low risk status)?

The Viborg trial examined benefits of AAA screening on AAA related mortality in high risk groups and low risk groups. The high risk group was defined as men with chronic obstructive pulmonary disease (COPD) and cardiovascular conditions such as hypertension, ischemic heart disease, peripheral occlusive arterial disease, and history of acute myocardial infarction, transient ischemic attack and stroke. At 5.9 years of follow up, relative to no screening group, there was no difference in reduction for AAA-related mortality for the high risk group (RR = 0.22, 95% CI, 0.08 to 0.65) as compared with low risk group (RR = 0.24, 95% CI, 0.09 to 0.63).[34] Thirteen years of follow up showed a reduced benefit from AAA screening in high risk group (RR = 0.42, 95% CI, 0.20 to 0.87) as compared with low risk group (RR = 0.29, 95% CI, 0.14 to 0.60) but difference remained statistically insignificant.[31] However, these subgroup analyses were subject to low statistical power and prone to classification bias as pointed out by USPSTF review,[5] therefore, should be considered with caution.

KQ2. What is the effect of rescreening for AAA using ultrasound on health outcomes including AAA incidence in previously screened asymptomatic adults aged 50 years and older?

See ES 2 for detailed results.

AAA Mortality

One uncontrolled observational cohort study (n>1000) with a total sample of 4,308 men reported on the effectiveness of rescreening for AAA using ultrasound on AAA mortality in adults aged 50 years and older at a follow-up of 10 years.[39] AAA mortality in the repeat screening arm was 0.56% (95% CI 0.38% to 0.83%). The overall quality of this evidence was rated as LOW due to study design (observational/uncontrolled).

All-cause Mortality

One uncontrolled observational cohort study (n>1000) with a total sample of 4,308 men reported on the effectiveness of rescreening for AAA using ultrasound on all-cause mortality in adults aged 50 years and older at a follow-up of 10 years.[39] All-cause mortality was 1.53% (95% CI 1.21% to 1.94%). The overall quality of this evidence was rated as LOW due to study design (observational/uncontrolled).

AAA Rupture Rates

One uncontrolled observational cohort study (n>1000) with a total sample of 4,308 men reported on the effectiveness of rescreening for AAA using ultrasound on AAA rupture rates in adults aged 50 years and older at a follow-up of 10 years.[39] AAA rupture rate was 0.70% (95% CI 0.49% to 0.99%). The overall quality of this evidence was rated as LOW due to study design (observational/uncontrolled).

AAA Incidence

Three uncontrolled observational cohort studies (n>1000) with a total sample of 8,971 reported on the effectiveness of rescreening for AAA using ultrasound on AAA incidence in adults aged 50 years and older at a follow-up of 4 to 10 years.[39-41] Patients with an aortic diameter <30 mm were invited to rescreening at intervals of 2 years or 5 years after the first interval (2-5 screens total). After a follow-up of 4 to 10 years, the AAA incidence in repeat screening arm was 2.26% (95% CI 0.41% to 4.10%), (Forest Plot 2.1). The overall quality of this evidence was rated as LOW due to study design (observational/uncontrolled).

KQ2a. Does the effect of rescreening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities?

We found no studies to answer the question on the effectiveness of repeat screening on subgroups, including men and women, smokers and non-smokers, adults ≥ or <65 years, adults with and without a family history of AAA and adults of different races/ethnicities.

KQ2b. Does the effect of rescreening vary between different time intervals?

Three uncontrolled observational cohort studies with an analyzed sample >1000 provided data on rescreening at different time intervals.[39-41] One study provided screens at two year intervals, or at 5 years after the first screen, over a period of 10 years (2-5 screens total).[39] The incidence of AAA in this study was 3.85% (95% CI 3.32 to 4.47). Another study examined the effect of offering two screens, 4 years apart.[40] The incidence of AAA in this study was 2.21% (95% CI 1.72 to 2.85). A final study examined the effect of two screenings, 5 years apart.[41] The incidence of AAA in this study was 0.74 % (95% CI 0.45% to 1.21%).

KQ3. What are the harms associated with one-time and repeated AAA screening using ultrasound?

See ES 3 and 4 for detailed results.

One-time AAA screening using ultrasound

30 day Mortality, AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on 30 day mortality from AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: three RCTs (MASS, Chichester and Western Australia) reported a follow-up of 3 to 5 years;[22, 26, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] two RCTs (MASS and Viborg) reported a follow-up of 10 to 11 years[25, 30] and two RCTs (MASS and Chichester) reported a follow-up of 13 to 15 years.[24, 27] As compared to control group, AAA screening was associated with significant reduction in 30-day post-operative mortality from overall AAA operations at all follow-up times and persisted up to 13 to 15 years with a 54% reduction (2 trials; RR=0.46, 95% CI 0.34 to 0.63), (Forest Plot 3.1). The overall quality of this evidence was rated as MODERATE to HIGH and downgraded due to serious concerns regarding risk of bias.

30 day Mortality, elective AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on 30 day mortality from elective AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: all four RCTs reported a follow-up of 3 to 5 years;[22, 26, 33, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] three RCTs (MASS, Chichester and Viborg) reported a follow-up of 10 to 11 years[25, 29, 30] and two RCTs (MASS and Chichester) reported a follow-up of 13 to 15 years.[24, 27] The effect of AAA screening on 30-day post-operative mortality from elective AAA operations was marginally significant at 3 to 5 years of follow-up (4 trials; RR=0.51, 95% CI 0.26 to 0.99, p=0.05) and became insignificant for longer follow-up times, (Forest Plot 3.2). The overall quality of this evidence was rated as LOW to MODERATE and downgraded due to serious concerns regarding risk of bias and imprecision.

30 day Mortality, emergency AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on 30 day mortality from emergency AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: three RCTs (MASS, Western Australia and Chichester) reported a follow-up of 3 to 5 years;[22, 26, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] two RCTs (MASS and Viborg) reported a follow-up of 10 to 11 years[25, 30] and two RCTs (MASS and Chichester) reported a follow-up of 13 to 15 years.[24, 27] There were no significant differences between AAA screening and control arms for 30-day post-operative mortality from emergency AAA operations at all follow-up time points, (Forest Plot 3.3). The overall quality of this evidence was rated as LOW to MODERATE and downgraded due to serious concerns regarding risk of bias and imprecision.

AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: all four RCTs reported a follow-up of 3 to 5 years;[22, 26, 33, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] three RCTs (MASS, Chichester and Viborg) reported a follow-up of 10 to 11 years[25, 29, 30] and two RCTs (MASS and Chichester) reported a follow-up of 13 to 15 years.[24, 27] As compared to control group, AAA screening was associated with significant increase in number of AAA operation performed at all follow-up times and persisted up to 13 to 15 years with 1.5 times more likely (RR = 1.48, 95% CI 1.33 to 1.65, NNH= 158), (Forest Plot 3.4). The overall quality of this evidence was rated as MODERATE to HIGH and downgraded due to serious concerns regarding risk of bias.

Elective AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on elective AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: all four RCTs (MASS, Western Australia, Viborg and Chichester) reported a follow-up of 3 to 5 years;[22, 26, 33, 36] one RCT (MASS) reported a follow-up

of 6 to 7 years;[23] three RCTs (MASS, Chichester and Viborg) reported a follow-up of 10 to 11 years[25, 29, 30] and three RCTs (MASS, Chichester and Viborg) reported a follow-up of 13 to 15 years.[24, 27, 31] As compared to control group, AAA screening was associated with significant increase in number of elective AAA operation performed at all follow-up times and persisted up to 13 to 15 years (3 trials; RR = 2.15, 95% CI 1.89 to 2.44, NNH= 111), (Forest Plot 3.5). The overall quality of this evidence was rated as MODERATE to HIGH and downgraded due to serious concerns regarding risk of bias.

Emergency AAA operations

Four RCTs, the MASS,[22-25] Chichester,[26-29] Viborg[30-35] and Western Australia[36, 37] trials, were identified to answer the question on harms of one-time AAA screening using ultrasound on emergency AAA operations in asymptomatic adults aged 50 years and older. Analysis was completed by length of follow-up: three RCTs (MASS, Western Australia and Chichester) reported a follow-up of 3 to 5 years;[22, 26, 33, 36] one RCT (MASS) reported a follow-up of 6 to 7 years;[23] three RCTs (MASS, Chichester and Viborg) reported a follow-up of 10 to 11 years[25, 29, 30] and three RCTs (MASS, Chichester and Viborg) reported a follow-up of 13 to 15 years.[24, 27, 46] As compared to control group, AAA screening was associated with significant reduction in number of emergency AAA operation performed at all follow-up times and persisted up to 13 to 15 years with 50% reduction (3 trials; RR = 0.50, 95% CI 0.40 to 0.63), (Forest Plot 3.6). The overall quality of this evidence was rated as MODERATE to HIGH and downgraded due to serious concerns regarding risk of bias.

Quality of Life

Four studies provided data on quality of life as a harm of one-time AAA screening.[22, 36, 43, 44]

Three studies provided meta-analyzable data (change from baseline) for quality of life as a harm due to one-time AAA screening.[36, 43, 44] All studies used the Short Form (36) Health Survey (SF-36) as an outcome measure for Health Related Quality of Life (HRQoL) and compared screened positive to control group (screened negative or no AAA). These results showed no significant differences between groups with a mean difference (MD) of -1.15 [-3.93, 1.63], (Forest Plot 3.7).

Data from the MASS trial, which could not be pooled, provided only post-screening data (SF-36) and reported no difference between screen positive and control groups; and at all times, and across quality of life measures were within the age-matched and sex-matched population normal range.[22]

Women

The Chichester trial examined the harms of one-time AAA screening in women and found no significant differences between screening and control arms: at 5-years of follow-up, total AAA operations (RR = 1.66, 95% CI: 0.40 to 6.94, p = 0.49); elective AAA operations (RR = 1.99, 95% CI: 0.36 to 10.86, p = 0.43); and emergency AAA operations (RR = 1.00, 95% CI: 0.06 to 15.91, p = 1.00).[26] One patient each in screening and control arms died within 30-days after emergency surgery and no patients died within 30-days after elective surgery.

Repeat AAA screening using ultrasound

One uncontrolled observational study with a total sample of 4,308 provided data on the harms of repeat screening using ultrasound, including 30 day mortality from AAA operations, elective AAA operations and emergency AAA operations, as well as data on AAA operations, elective AAA operations and emergency AAA operations.[39]

The proportion of people undergoing repeat screening; AAA operations performed was 0.69% (95% CI 0.49 to 0.99), elective operations was 0.53% (95% CI 0.36 to 0.80), and emergency operations was 0.16% (95% CI 0.08% to 0.34%).

The 30-day post-operative mortality due to any AAA operation was 20% (6 / 30) (95% CI 9.5% to 37%); from elective AAA surgery was 13% (3 / 23)(95% CI 4.5% to 32%); and from emergency AAA operations was 42.8% (3 / 7) (95% CI 15.8% to 75%).

Overdiagnosis

One study from our targeted search provided data on overdiagnosis as a result of screening.[45] Using 13 year follow-up data from the MASS trial, the study reports that 45% (95% CI 42% to 47%) of screen-detected men were overdiagnosed.

Contextual questions

CQ1. What are patients' preferences and values regarding AAA screening?

Our search located two studies that answered the question of patients' preferences and values regarding AAA screening.[47, 48]

An Australian study, in remote regional centre, invited 133 eligible men who participated in screening to answer a survey on their experiences with screening.[47] The screening program was a pilot program which brought trained sonographers and loaned ultrasound equipment to a region which was not able to offer population based screening. The study found that there were a variety of reasons for participating in the screening program: receiving a letter (52%); believing prevention is important (43%); wanting to know if they had AAA (36%); knowing a family member or friend with AAA (10%) and/or following government recommendations (4%).

One American study contacted 120 nonresponders in a screening program.[48] Of the 25 individuals who responded, reasons for nonparticipation included: no recollection of receiving the letter (28%), poor health (24%), lack of interest (24%), known AAA (8%), or recent abdominal imaging (4%); 8% who were initially not interested said they would reconsider after speaking with their primary-care physician.

CQ2. What is the cost-effectiveness of screening for AAA?

For the question regarding cost-effectiveness of screening for abdominal aortic aneurysms (AAA), two reviews were found,[49, 50] one randomized controlled trial[51] and three relevant modeling studies.[52-54]

The first review included eight cost-effectiveness modeling studies published up to 2009, comparing one-time screening in men over 65 years of age versus no screening.[49] The review

found one study that yielded a loss of life-years with an increased cost, whereas the other seven studies found gains in quality-adjusted life expectancy reports ranging from 0.015 to 0.059 quality adjusted life years (QALYs)[49] at a cost of 1,443 to 13,299 Euros per QALY gained. Overall, the findings of the modeling review looked favorably upon screening for AAA in men over the age of 65 at acceptable extra cost for likely additional life years gained.[49] The second review included 16 cost-effectiveness studies published up to 2008. Six of the included studies in this systematic review were also included in the first review mentioned above. Ten were modeling studies, comparing screening for AAA in males and females beginning at age 50 and older.[50] The costs considered in this review included invitations for screening, ultrasonography, surgery, hospital and community care, patient and family resources, and resources in other sectors (i.e. long term care homes). The review identified that most of the modeling studies used "optimistic" assumptions in favour of AAA screening and that most cost-effectiveness ratios related to screening for AAA have been too low. The review identifies that only two of the 16 studies carried out sensitivity analyses for quality of life assumptions, but further details were not provided.[50]

A large randomized trial of 12,639 men aged 64-73 in Viborg County, Denmark also examined cost-effectiveness of screening for AAA.[51] Screening included a 1-time ultrasound and annual follow up if the aneurysm was between 3-5 cm, or a referral to a vascular surgeon if the aneurysm was greater than 5 cm.[51] With mortality and AAA-related interventions recorded, the incremental cost-effectiveness ratio (ICER) was estimated as 157 Euros (95% CI -3292 to 4401) per life year gained and a cost of 179 Euros (95% CI -4083 to 4682) per QALY gained.[51]

Three relevant modeling studies were identified using European data.[52-54] The first study from England was based on the AAA screening programme in England, modeled to simulate 10 year follow up data from the MASS trial[25] for screening men aged 65 years of age and older. The model produced estimates of cost-effectiveness of one-time screening of 7,370 GBP per QALY gained.[52] The second study from Sweden modeled data to include one-time screening in men 65 years of age and older.[53] Using epidemiological data from trials, this study concluded that at 13 years follow-up, the incremental cost-efficiency ratio (ICER) was 14,706 Euros/QALY, concluding that screening for men for AAA remained cost-effective.[53] A third modelling study assessed the cost-effectiveness of ultrasound screening in men aged 65 years and older with no or varying levels of AAA.[54] The additional costs of screening compared to no screening in the Netherlands and Norway was 421 Euros (95% CI 33 to 806) and 562 Euros (95% CI 59 to 1,078) per person respectively, resulting in additional life years of 0.097 (95% CI -0.18 to 0.365) in the Netherlands and 0.057 (95% CI -0.135 to 0.253) in Norway.[54]

CQ3. How well does ultrasound administered in a general practice setting or which can be administered in a general practice setting compare to standard US in a clinic or hospital setting for the detection of AAA?

Five studies were located that addressed the use of portable or bedside ultrasound in the detection or measurement of AAA.[55-59]

Detection of AAA

One systematic review from 2013 was located that investigated whether emergency-performed ultrasound was sufficiently accurate to rule out a suspected AAA when compared to a reference standard of computed tomography (CT), magnetic resonance imaging (MRI), artography, emergency department ultrasound reviewed by radiology, or official ultrasound performed by radiology, exploratory laparotomy or autopsy results.[55] The systematic review found seven high-quality studies, with 655 included patients, to answer this question. Examining this body of evidence, the authors found that the sensitivity of the emergency department ultrasound for the detection of AAA was 99% (95% CI 96% to 100%) and specificity was 98% (95% CI 97% to 99%). Positive likelihood ratio was 10.8 to ∞ and negative likelihood ratio was -0.00 to 0.025. Statistical heterogeneity across the studies was moderate (chi-square >0.05 and I^2 <50%).

A Canadian observational study from 2012 examined the feasibility of point-of-care ultrasound technology for AAA screening in an office-based, family-physician administered setting.[57] Forty-five patients (mean age of 73 years) were screened by resident physician trained in emergency ultrasonography. The study found that this 4 minute scan had a sensitivity and specificity of 100% compared with the criterion standard scan. The study authors conclude that AAA screening using a point-of-care ultrasound by family physicians was safe and also could be done within the context of the time constraints of office visits.

One 2011 French study compared the performance of the bedside real pocket-ultrasound in 204 patients hospitalized in a cardiology institute to conventional approaches.[56] All examinations were conducted by two cardiologists certified and specialized in vascular Doppler investigations. The study found 100% agreement in AAA diagnosis.

Measurement of AAA

A French study from 2013 investigated the performance of a pocket-sized ultrasound system in 62 patients.[59] The study's aim was to determine whether novice operators (medical students) could measure abdominal aortic diameter using this system after a short period of training compared to experts using conventional machines (Vscan®; GE Healthcare, Wauwatosa, WI, USA). In 92% of cases, inter-operator variability in measuring abdominal aortic diameter was ≤ 4mm.

Another study from 2013 that took place in New Zealand examined measurement accuracy rather than detection of AAA. In this study five 'novices' (no experience or training in ultrasound) underwent 15 days of training by experienced vascular technologists on using a portable ultrasound system to detect AAA.[58] The novices used a portable laptop-based ultrasound system, Terason with the following features: 3.5 MHz curved array transducer, 25 cm penetration depth, time-gain-compensation, B-mode, real-time imaging, "cineloop" and depth control settings. These features are equivalent with the standard ultrasound system, Antares used by the experienced sonographers in a clinical setting. On average, the novice technicians performed 50 ultrasounds in people with and without AAA. This study found that the novices measured maximal aortic diameter accurately to within 0.46-0.52 cm of the true diameter; 85-97% of their coronal measurements were within 0.5 cm of the assessors.

Chapter 4: Discussion, Limitations, Conclusions

Summary of evidence

To our knowledge, this is the most up-to-date and comprehensive systematic review on the benefits and harms of AAA screening with ultrasound in asymptomatic adults aged 50 years and older.

Benefits of AAA screening using ultrasound

For benefits of one-time AAA screening as compared to controls, pooled analyses from four population-based randomized controlled trials (MASS[22, 23, 25, 60]; Chichester[26-29]; Viborg[30-35]; and Western Australia[36, 37]) with moderate quality evidence showed a statistically significant relative reduction of 43% [RR = 0.57 (95% CI; 0.44 to 0.72), NNS = 796] in AAA-related mortality at an early follow-up of 3 to 5 years and this benefit was maintained at 13 to 15 years of follow-up with 42% relative reduction [RR = 0.58 (95% CI; 0.39 to 0.88),NNS = 212]. The effect of AAA screening on all-cause mortality was not significant after 3 to 5 years but was marginally significant for longer follow-up. The clinical importance of this small long-term benefit observed in all-cause mortality is questionable considering the prevalence of AAA and limited ability of these relatively older patients with other competing causes of death and comorbidities to undergo AAA surgery. Consistent with expectations around the efficacy of screening in terms of earlier disease detection and management, one-time screening of AAA in men was associated with a statistically significant reduction in AAA rupture rate as compared to controls, which was maintained over a follow-up of up to 13 to 15 years (range: 38% to 53% reduction based on RR).

The evidence from three prospective cohort studies[39-41] with follow-up of 4 to 10 years showed AAA incidence of 2.26% in men who received repeat screening over a follow-up of 4 to 10 years; however the frequency of repeat screening varied across studies, therefore our ability to draw conclusions about the benefits of repeat AAA screening is limited.

Effect based on sub-groups

Evidence from one trial (Viborg[34]) showed a reduced benefit from AAA screening in a high risk group of men (previously defined - KQ1b - as men with chronic obstructive pulmonary disease (COPD) and cardiovascular conditions such as hypertension, ischemic heart disease, peripheral occlusive arterial disease, and history of acute myocardial infarction, transient ischemic attack and stroke) as compared with low risk group (58% vs 71% reduction in AAA-related mortality as compared to control group) over a follow-up of 13 years but the observed difference was statistically non-significant and subject to low statistical power.

The Chichester trial[26, 28] evaluating benefits of one-time AAA in women at 5 and 10-year of follow-up showed no significant differences between screening and control groups for AAA-related mortality, all-cause mortality and AAA rupture. This could primarily be attributed to low

incidence and prevalence of AAA in women; estimates from one study[28]showed AAA to be approximately 6 times less prevalent in women aged 65-80 years as compared to men (1.3% vs 7.6%).

Harms of AAA screening

As compared to controls, one-time AAA screening using ultrasound was associated with a statistically significant increase in the total number of AAA-related operations performed and this effect was maintained over a follow-up of 13 to 15 years (range: 1.48 to 2.16 times more likely). As expected, one-time screening of AAA with ultrasound was associated with a statistically significant increase in the number of elective operations (range: 2.15 to 3.25 times more likely) and a statistically significant decrease in number of emergency procedures (range: 50% to 59% reduction) as compared to controls which persisted over a follow-up of 13 to 15 years. One-time AAA screening using ultrasound was also associated with a statistically significant decrease in 30-day post-operative mortality as compared to control and this effect persisted over a follow-up of 13 to 15 years (range: 54% to 69% reduction). However when 30-day post-operative mortality was looked at separately for elective and emergency operations the effects were not significant as compared to controls.

The evidence from four studies[22, 36, 43, 44] showed no significant difference in Health Related Quality of Life (HRQoL) measured with the Short Form (36) Health Survey (SF-36) between screened positive and control groups (screened negative or no AAA).

Overdiagnosis

Evidence from the MASS trial[45] using 13 year follow-up data showed that one-time AAA screening with ultrasound was potentially associated with an overdiagnosis of 45% (95% CI 42% to 47%) among screen-detected men.

Cost-effectiveness of AAA screening

Evidence from recently published reviews and studies[49-54] evaluating cost-effectiveness of AAA screening showed that one-time screening of AAA with ultrasound in men aged 65 years and over is an extremely cost effective and economically viable approach with very low incremental cost-effectiveness ratios when compared with no screening (ICER range < $30,000 US per QALY or life year gained).

Comparison with other reviews

Most of our findings are consistent with the results reported in a recently published USPSTF review on ultrasonography screening for AAA, with a few noticeable differences.[5] First, we found a marginally significant benefit of one-time AAA screening on all-cause mortality for follow-up of 13 to 15 years as compared to controls whereas evidence from the USPSTF review showed no benefit on all-cause mortality for any length of follow-up. Second, we utilized a more

relevant dominator to estimate 30-day postoperative mortality related to elective and emergency procedures and found no differences between screening and control groups. In contrast, the USPSTF review showed a statistically significant reduction in 30-day postoperative mortality from emergency procedures for the screening group which could be a consequence of using overall number of AAA operations as denominator to estimate mortality due to emergency procedures. Third, unlike the USPSTF review, we also presented evidence on overdiagnosis associated with one-time AAA screening in men which has potential healthcare implications for patients as well as for healthcare providers and policy makers. Finally, to gain a more thorough understanding of the evidence we presented relative and absolute effects (RRR, ARR, ARI, and NNS/NNH) where possible for benefits and harms of AAA screening as compared to controls.

Implications for future research

Our review found limited evidence on the benefits of repeat AAA screening and high versus low risk screening approaches. In addition we found no direct evidence on the differential benefit of screening based on risk factors for AAA such age, gender, smoking status, and family history which warrants the need to evaluate the clinical benefit and cost-effectiveness of a multi-risk factor screening approach which would have implications in terms of costs, benefits and consequences in a resource constrained healthcare environment.

Limitations

First, the literature search was restricted to English and French language papers and it is possible that potentially relevant studies published in other languages were missed. Second, there was significant statistical heterogeneity across studies which could be attributed to differences in population, sample size and length of follow-up. Third, there was insufficient evidence to answer several questions of interest including how clinical benefits of screening differ for various high versus low risk screening approaches, or by subgroups that may influence the underlying risk of developing AAA. Fourth, we did not analyze the benefits of screening based on specific aortic diameter or baseline risk of rupture. Finally, there were insufficient studies reporting outcomes of interest to assess publication bias.

Conclusion

Population based screening for AAA with ultrasound in asymptomatic men aged 50 years and older showed statistically significant reductions in AAA-related mortality and rupture and hence avoids unnecessary AAA-related deaths. The current evidence does not support the use of population based AAA screening with ultrasound in women. Limited evidence is available on the benefits of repeat AAA screening and targeted screening approaches based on risk factors for AAA. Future research should explore the differential benefits of AAA screening based on risk factors that increase risk for developing AAA.

Evidence Set (ES) 1. Benefits of One-Time Screening

- ES Table 1.1 Overview of Key Results
- ES Table 1.2 GRADE Evidence Profile: Benefits of one-time screening
- ES Table 1.3 GRADE Summary of Findings Table: Benefits of one-time screening
- ES Forest Plots 1.1-1.3

ES Table 1.1 Overview of Key Results

Forest Plot	Outcome	Number of studies	Effect size (RR)
1.1	AAA Mortality – 3 to 5 years follow-up	4	0.57 (0.44 to 0.72)
1.1	AAA Mortality – 6 to 7 years follow-up	2	0.38 (0.17 to 0.86)
1.1	AAA Mortality – 10 to 11 years follow-up	3	0.50 (0.31 to 0.79)
1.1	AAA Mortality – 13 to 15 years follow-up	3	0.58 (0.39 to 0.88)
1.2	All-Cause Mortality – 3 to 5 years follow-up	4	0.94 (0.88 to 1.02)
1.2	All-Cause Mortality – 6 to 7 years follow-up	2	0.96 (0.94 to 0.99)
1.2	All-Cause Mortality – 10 to 11 years follow-up	2	0.98 (0.96 to 1.00)
1.2	All-Cause Mortality – 13 to 15 years follow-up	3	0.98 (0.97 to 1.00)
1.3	Rupture Rate – 3 to 5 years follow-up	4	0.52 (0.35 to 0.79)
1.3	Rupture Rate – 6 to 7 years follow-up	1	0.53 (0.43 to 0.65)
1.3	Rupture Rate – 10 to 11 years follow-up	2	0.47 (0.31 to 0.71)
1.3	Rupture Rate – 13 to 15 years follow-up	3	0.62 (0.45 to 0.86)

ES Table 1.2 GRADE Evidence Profile: Benefits of one-time screening

Quality assessment							No of patients		Effect				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Benefits of one-time screening	Control	Relative (95% CI)	Absolute per million	ARR	NNS (95% CI)		
AAA Mortality - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5.0 years; assessed with: Objectively)														
4[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	102/62,729 (0.16%)	182/62,847 (0.29%)	RR 0.5661 (0.4439 to 0.7221)	1,257 fewer (from 805 fewer to 1,610 fewer)	0.13%	796 (621 to 1,242)	⊕⊕⊕O MODERATE	CRITICAL
AAA Mortality - By length of Follow-up - 6 to 7 years of follow-up (follow-up 5.9 to 7 years; assessed with: Objectively)														
2[7]	randomised trials	serious[8]	no serious inconsistency[9]	no serious indirectness[10]	no serious imprecision[11]	none[6]	114/40,216 (0.28%)	235/40,193 (0.58%)	RR 0.3769 (0.166 to 0.8556)	3,643 fewer (from 844 fewer to 4,876 fewer)	0.36%	274 (205 to 1,185)	⊕⊕⊕O MODERATE	CRITICAL
AAA Mortality - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
3[12]	randomised trials	serious[13]	no serious inconsistency[14]	no serious indirectness[15]	no serious imprecision[16]	none[6]	193/43,216 (0.45%)	378/43,251 (0.87%)	RR 0.4960 (0.3121 to 0.7883)	4,405 fewer (from 1,850 fewer to 6,012 fewer)	0.44%	227 (166 to 541)	⊕⊕⊕O MODERATE	CRITICAL
AAA Mortality - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[17]	randomised trials	serious[18]	no serious inconsistency[19]	no serious indirectness[20]	no serious imprecision[21]	none[6]	290/43,211 (0.67%)	490/43,238 (1.1%)	RR 0.5831 (0.3882 to 0.8759)	4,725 fewer (from 1,406 fewer to 6,933 fewer)	0.47%	212 (144 to 711)	⊕⊕⊕O MODERATE	CRITICAL
All-cause Mortality - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5.0 years; assessed with: Objectively)														
4[22]	randomised trials	serious[23]	no serious inconsistency[24]	no serious indirectness[25]	serious[26]	none[6]	7,453/62,729 (11.9%)	7,953/62,847 (12.7%)	RR 0.9449 (0.8758 to 1.0195)	6,973 fewer (from 15,717 fewer to 2,468 more)	NS	-	⊕⊕⊕O LOW	CRITICAL
All-cause Mortality - By length of Follow-up - 6 to 7 years of follow-up (follow-up 5.9 to 7 years; assessed with: Objectively)														
2[27]	randomised trials	serious[28]	no serious inconsistency[29]	no serious indirectness[30]	no serious imprecision[31]	none[6]	8,258/40,216 (20.5%)	8,571/40,193 (21.3%)	RR 0.9628 (0.9373 to 0.989)	7,933 fewer (from 2,346 fewer to 13,371 fewer)	0.79%	126 (75 to 426)	⊕⊕⊕O MODERATE	CRITICAL
All-cause Mortality - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
2[51]	randomised trials	serious[32]	no serious inconsistency[33]	no serious indirectness[34]	no serious imprecision[35]	none[6]	12,458/ 40,216 (31%)	12,715/ 40,193 (31.6%)	RR 0.9791 (0.9593 to 0.9993)	6,612 fewer (from 221 fewer to 12,875 fewer)	0.66%	151 (78 to 4,525)	⊕⊕⊕O MODERATE	CRITICAL
All-cause Mortality - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[36]	randomised trials	serious[37]	no serious inconsistency[38]	no serious indirectness[39]	no serious imprecision[40]	none[6]	18,825/ 43,211 (43.6%)	19,165/ 43,238 (44.3%)	RR 0.9849 (0.9706 to 0.9995)	6,693 fewer (from 222 fewer to 13,031 fewer)	0.67%	149 (77 to 4,505)	⊕⊕⊕O MODERATE	CRITICAL

AAA Rupture - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5.0 years; assessed with: Objectively)														
4[41]	randomised trials	serious[42]	no serious inconsistency[43]	no serious indirectness[44]	no serious imprecision[45]	none[6]	117/62,729 (0.19%)	218/62,847 (0.35%)	RR 0.5247 (0.3475 to 0.7922)	1,649 fewer (from 721 fewer to 2,263 fewer)	0.16%	606 (442 to 1,387)	⊕⊕⊕O MODERATE	CRITICAL
AAA Rupture - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[46]	randomised trials	no serious risk of bias[47]	no serious inconsistency[48]	no serious indirectness[49]	no serious imprecision[50]	none[6]	135/33,883 (0.4%)	257/33,887 (0.76%)	RR 0.5254 (0.4268 to 0.6467)	3,599 fewer (from 2,679 fewer to 4,347 fewer)	0.36%	278 (230 to 373)	⊕⊕⊕⊕ HIGH	CRITICAL
AAA Rupture - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
2[51]	randomised trials	serious[52]	no serious inconsistency[53]	no serious indirectness[54]	no serious imprecision[55]	none[6]	207/40,216 (0.51%)	405/40,193 (1%)	RR 0.4663 (0.307 to 0.7083)	5,378 fewer (from 2,939 fewer to 6,983 fewer)	0.54%	186 (143 to 340)	⊕⊕⊕O MODERATE	CRITICAL
AAA Rupture - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[56]	randomised trials	serious[57]	no serious inconsistency[58]	no serious indirectness[59]	no serious imprecision[60]	none[6]	343/43,211 (0.79%)	575/43,238 (1.3%)	RR 0.6243 (0.4516 to 0.8631)	4,996 fewer (from 1,821 fewer to 7,293 fewer)	0.50%	200 (137 to 549)	⊕⊕⊕O MODERATE	CRITICAL

NOTE: The NNS was calculated from Absolute numbers presented in GRADE tables. The GRADE tables estimate the absolute numbers per million using control group event rate and risk ratio with 95 % CI obtained from meta-analysis. NS = non-significant.

ES Table 1.3 Benefits of one-time screening for AAA

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk per million	Corresponding risk per million				
	Control	**Benefits of one-time screening**				
AAA Mortality - By length of Follow-up - 3 to 5 years of follow-up Follow-up: 3.6 to 5.0 years	**Study population**		**RR 0.5661** (0.4439 to 0.7221)	125,576 (4 studies[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,6]	
	2,896	**1,639** (1,285 to 2,091)				
AAA Mortality - By length of Follow-up - 6 to 7 years of follow-up Follow-up: 5.9 to 7 years	**Study population**		**RR 0.3769** (0.166 to 0.8556)	80,409 (2 studies[7])	⊕⊕⊕⊖ **moderate**[6,8,9,10,11]	
	5,847	**2,204** (971 to 5,003)				
AAA Mortality - By length of Follow-up - 10 to 11 years of follow-up Follow-up: mean 10 years	**Study population**		**RR 0.4960** (0.3121 to 0.7883)	86,467 (3 studies[12])	⊕⊕⊕⊖ **moderate**[6,13,14,15,16]	
	8,740	**4,335** (2,728 to 6,889)				
AAA Mortality - By length of Follow-up - 13 to 15 years of follow-up Follow-up: 13 to 15 years	**Study population**		**RR 0.5831** (0.3882 to 0.8759)	86,449 (3 studies[17])	⊕⊕⊕⊖ **moderate**[6,18,19,20,21]	
	11,333	**6,608** (4,399 to 9,926)				
All-cause Mortality - By length of Follow-up - 3 to 5 years of follow-up Follow-up: 3.6 to 5.0 years	**Study population**		**RR 0.9449** (0.8758 to 1.0195)	125,576 (4 studies[22])	⊕⊕⊖⊖ **low**[6,23,24,25,26]	
	126,545	**119, 573** (110,828 to 129,013)				
All-cause Mortality - By length of Follow-up - 6 to 7 years of follow-up Follow-up: 5.9 to 7 years	**Study population**		**RR 0.9628** (0.9373 to 0.989)	80,409 (2 studies[27])	⊕⊕⊕⊖ **moderate**[6,28,29,30,31]	
	213,246	**205,313** (199,876 to 210,900)				
All-cause Mortality - By length of Follow-up - 10 to 11 years of follow-up Follow-up: mean 10 years	**Study population**		**RR 0.9791** (0.9593 to 0.9993)	80,409 (2 studies)	⊕⊕⊕⊖ **moderate**[6,32,33,34,35]	
	316, 349	**309,737** (303,473 to 316,127)				
All-cause Mortality - By length of Follow-up - 13 to 15 years of follow-up Follow-up: 13 to 15 years	**Study population**		**RR 0.9849** (0.9706 to 0.9995)	86,449 (3 studies[36])	⊕⊕⊕⊖ **moderate**[6,37,38,39,40]	
	443,244	**436,551** (430,213 to 443,023)				
AAA Rupture - By length of Follow-up - 3 to 5 years of follow-up Follow-up: 3.6 to 5.0 years	**Study population**		**RR 0.5247** (0.3475 to 0.7922)	125,576 (4 studies[41])	⊕⊕⊕⊖ **moderate**[6,42,43,44,45]	
	3,469	**1,820** (1,205 to 2,748)				

AAA Rupture - By length of Follow-up - 6 to 7 years of follow-up Follow-up: mean 7 years	**Study population**		**RR 0.5254** (0.4268 to 0.6467)	67,770 (1 study[46])	⊕⊕⊕⊕ **high**[6,47,48,49,50]
	7,584	**3,985** (3,237 to 4,905)			
AAA Rupture - By length of Follow-up - 10 to 11 years of follow-up Follow-up: mean 10 years	**Study population**		**RR 0.4663** (0.307 to 0.7083)	80,409 (2 studies[51])	⊕⊕⊕⊖ **moderate**[6,52,53,54,55]
	10,076	**4,699** (3,093 to 7,137)			
AAA Rupture - By length of Follow-up - 13 to 15 years of follow-up Follow-up: 13 to 15 years	**Study population**		**RR 0.6243** (0.4516 to 0.8631)	86,449 (3 studies[56])	⊕⊕⊕⊖ **moderate**[6,57,58,59,60]
	13,298	**8,302** (6,006 to 11,478)			

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Ashton et al. 2002 (MASS); 2) Lindholt et al. 2005 (Viborg); 3) Norman et al. 2004 (W. Australia); 4) Scott et al. 1995 (Chichester)

[2] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is minimal [Chi^2=2.57, df=3 (P=0.46); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[4] Four RCTs provided data for this outcome. Three studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 years to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[5] The sample size is adequate (62,729 screening arm, 62,847 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.5661 (0.4439, 0.7221)]. This body of evidence was not downgraded for imprecision.

[6] There were too few studies (n<10) to assess publication bias.

[7] 1) Kim 2007 (MASS); 2) Lindholt 2007 (Viborg)

[8] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[9] The statistical heterogeneity is high [Chi^2=4.77, df=1 (P=0.03); I^2=79%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[10] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64 to 74 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in the UK and one study was conducted in Denmark. Both studies were published in 2007. The length of follow-up across the two studies was 5.9 to 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[11] The sample size is adequate (40,216 screening arm, 40,193 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.3769 (0.1660, 0.8556)]. This body of evidence was not downgraded for imprecision.

[12] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS); 3) Vardulaki 2002 (Chichester)

[13] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power

calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[14] The statistical heterogeneity is moderate [Chi^2=6.95, df=2 (P=0.03); I^2=71%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[15] Three RCTs provided data for this outcome. Two studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 65-80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2002 and 2009. The length of follow-up across the three studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[16] The sample size is adequate (43,216 screening arm, 43,251 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4960 (0.3121, 0.7883)]. This body of evidence was not downgraded for imprecision.

[17] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); 3) Thompson 2012 (MASS)

[18] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[19] The statistical heterogeneity is high [Chi^2=8.31, df=2 (P=0.02); I^2=76%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[20] Three RCTs provided data for this outcome. Two studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 65-80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[21] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.5831 (0.3882, 0.8759)]. This body of evidence was not downgraded for imprecision.

[22] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)

[23] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[24] The statistical heterogeneity is high [Chi^2=16.13, df=3 (P=0.001); I^2=81%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

[25] Four RCTs provided data for this outcome. Three studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 64-83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 years to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[26] The sample size is adequate i.e. > 300 (62,729 screening arm, 62,847 control arm) but the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.9449 (0.8758, 1.0195)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[27] 1) Kim 2007 (MASS); Lindholt 2007 (Viborg)

[28] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[29] The statistical heterogeneity is minimal [Chi^2=0.45, df=1 (P=0.50); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[30] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64-74 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in the UK and one study was conducted in Denmark. Both studies were published in 2007. The length of follow-up across the two studies was 5.9 to 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[31] The sample size is adequate (40,216 screening arm, 40,193 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.9628 (0.9373, 0.9890)]. This body of evidence was not downgraded for imprecision.

[32] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[33] The statistical heterogeneity is minimal [Chi^2=0.07, df=1 (P=0.79); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[34] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64-83 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in in the UK and one study was conducted in Denmark. The studies were published in 2006 and 2009. The length of follow-up in both studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[35] The sample size is adequate (40,216 screening arm, 40,193 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.9791 (0.9593, 0.9993)]. This body of evidence was not downgraded for imprecision.
[36] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); Thompson 2012 (MASS)
[37] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[38] The statistical heterogeneity is minimal [Chi^2=1.16, df=2 (P=0.56); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[39] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[40] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.9849 (0.9706, 0.9995)]. This body of evidence was not downgraded for imprecision.
[41] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)
[42] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[43] The statistical heterogeneity is moderate [Chi^2=7.18, df=3 (P=0.07); I^2=58%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.
[44] Four RCTs provided data for this outcome. Three studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 years to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[45] The sample size is adequate (62,729 screening arm, 62,847 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.5247 (0.3475, 0.7922)]. This body of evidence was not downgraded for imprecision.
[46] 1) Kim 2007 (MASS)
[47] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.
[48] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[49] One RCT provided data for this outcome. The study included men aged 65-74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[50] The sample size is adequate (33,883 screening arm, 33,887 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.5254 (0.4268, 0.6467)]. This body of evidence was not downgraded for imprecision.
[51] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS)
[52] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence

generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[53] The statistical heterogeneity is minimal [Chi^2=1.75, df=1 (P=0.19); I^2=43%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[54] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64-83 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in in the UK and one study was conducted in Denmark. The studies were published in 2006 and 2009. The length of follow-up in both studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[55] The sample size is adequate (40,216 screening arm, 40,193 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4663 (0.3070, 0.7083)]. This body of evidence was not downgraded for imprecision.

[56] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); 3) Thompson 2012 (MASS)

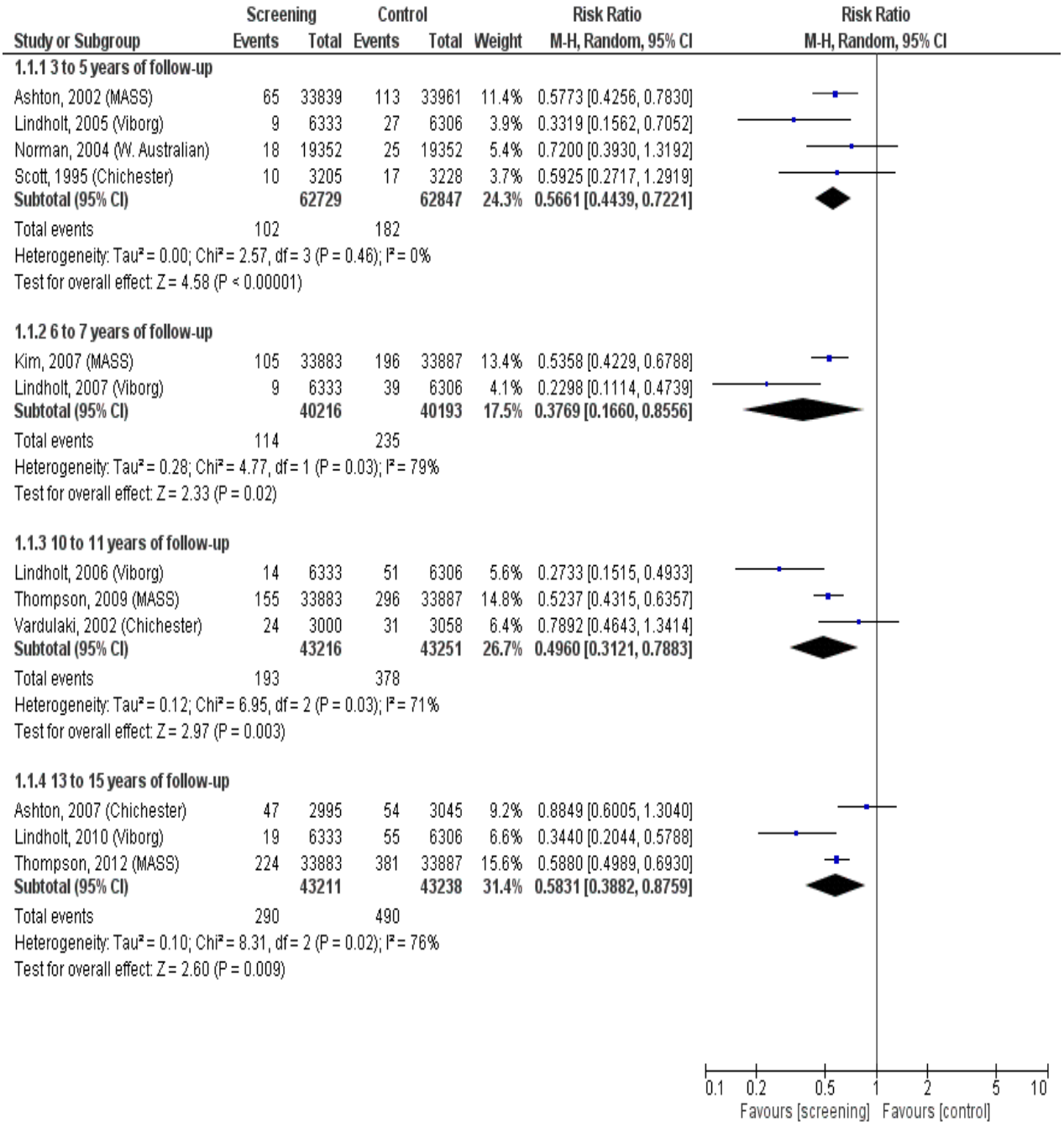
[57] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[58] The statistical heterogeneity is moderate [Chi^2=5.52, df=2 (P=0.06); I^2=64%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.

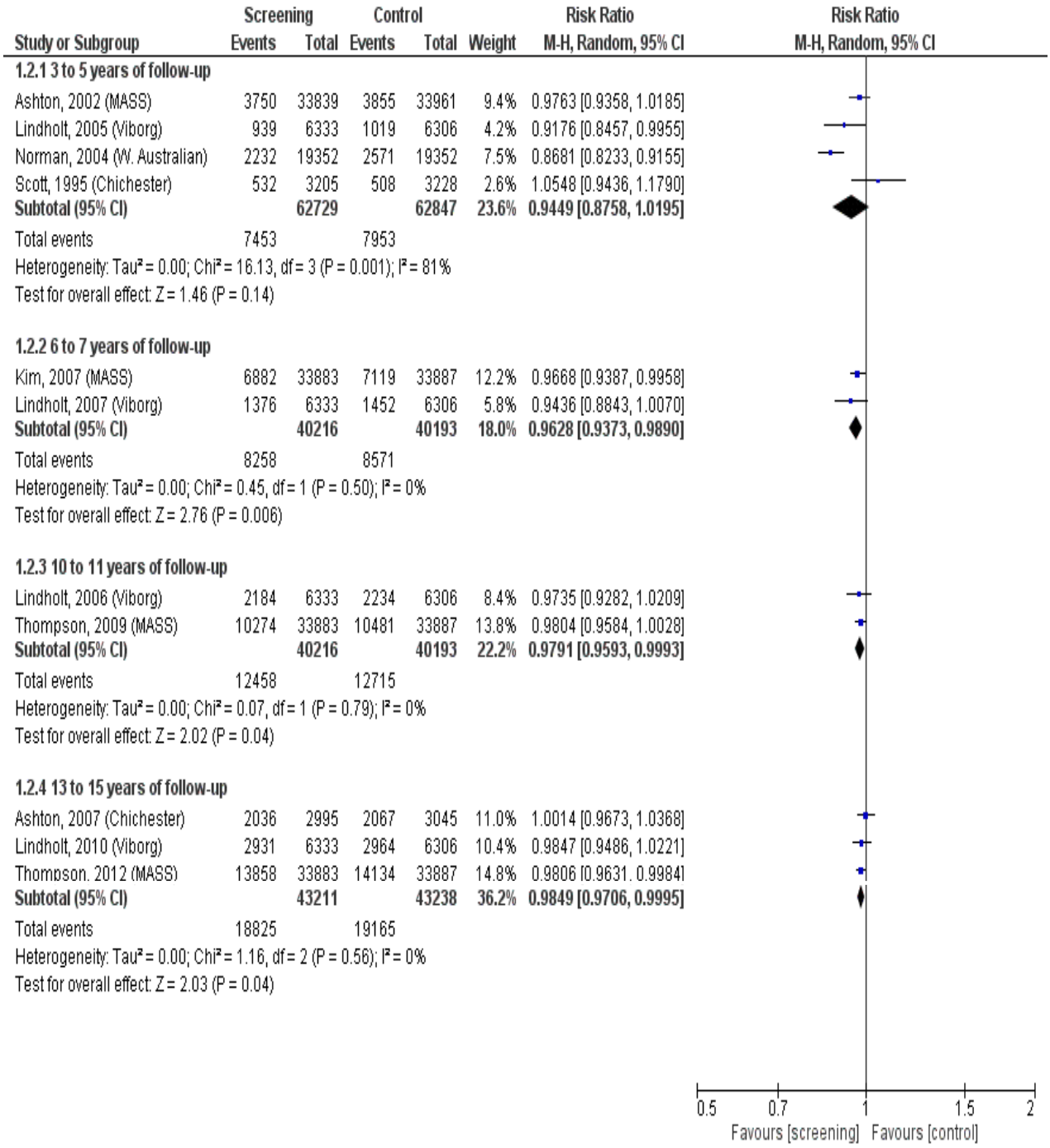
[59] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65-80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[60] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.6243 (0.4516, 0.8631)]. This body of evidence was not downgraded for imprecision.

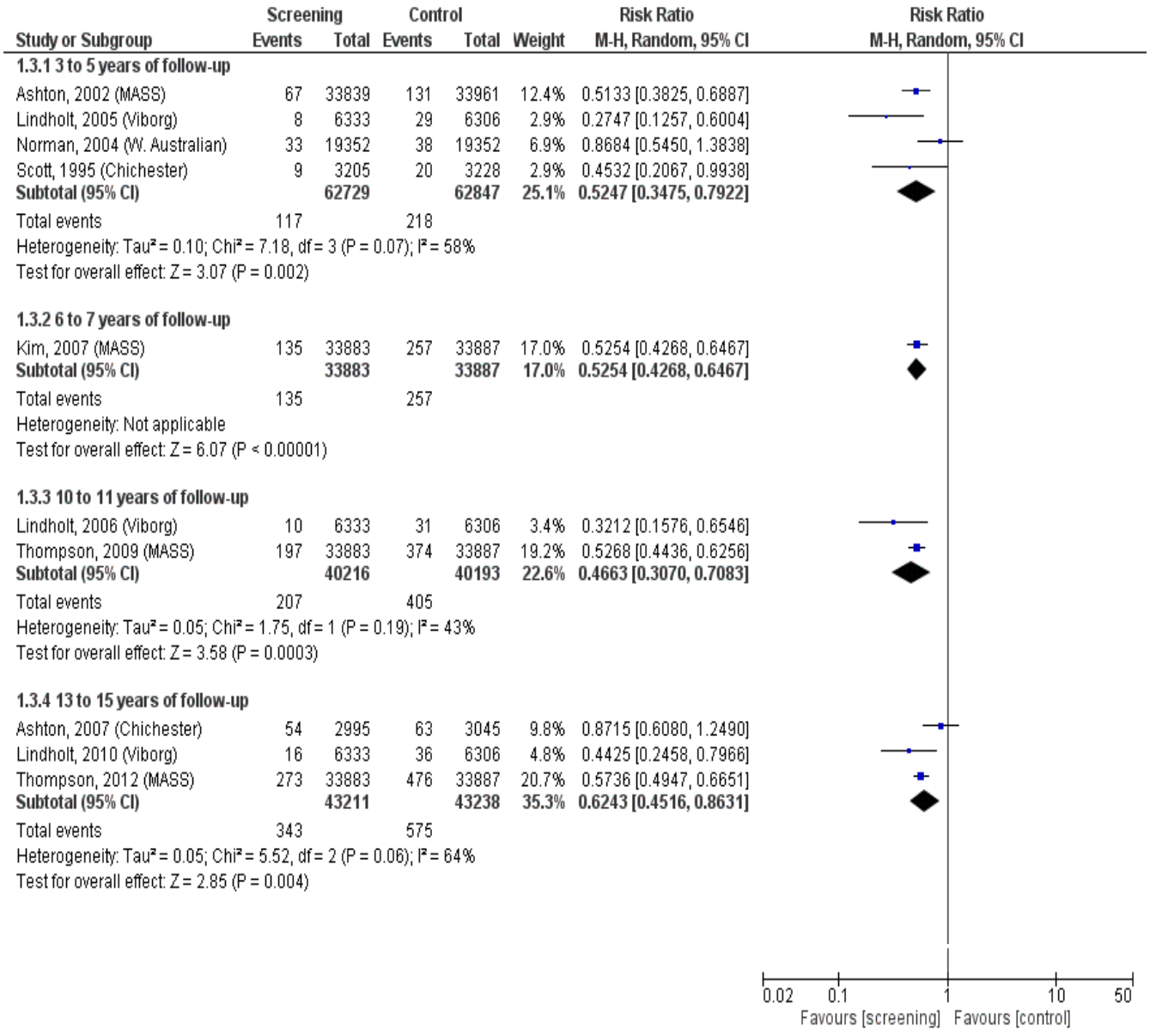
ES Forest Plot 1.1 Benefits of one-time AAA screening on AAA Mortality by Length of Follow-up



ES Forest Plot 1.2 Benefits of one-time AAA screening on All-Cause Mortality by Length of Follow-up



ES Forest Plot 1.3 Benefits of one-time AAA screening on AAA Rupture by Length of Follow-up



Evidence Set (ES) 2. Benefits of Repeat Screening

- ES Table 2.1 GRADE Evidence Profile: Benefits of Repeat Screening
- ES Forest Plot 2.1

ES Table 2.1 GRADE Evidence Profile: Benefits of repeat screening (uncontrolled observational studies)

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Benefits of repeat screening	Proportion (95% CI)	Absolute per million (95% CI)		
AAA incidence (follow-up 4 to 10 years; assessed with: Objectively)											
3[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	239/8,971 (2.6641%)	0.0226 (0.0041 to 0.0410)[7]	22,570 (4,120 to 41,020)	⊕⊕OO LOW	CRITICAL
AAA mortality (follow-up mean 10 years; assessed with: Objectively)											
1[8]	observational studies	no serious risk of bias[9]	no serious inconsistency[10]	no serious indirectness[11]	no serious imprecision[12]	none[6]	24/4,308 (0.5570%)	0.0056 (0.0038 to 0.0082)[7]	5,570 (3,750 to 8,280)	⊕⊕OO LOW	CRITICAL
All-cause mortality (follow-up mean 10 years; assessed with: Objectively)											
1[8]	observational studies	no serious risk of bias[9]	no serious inconsistency[10]	no serious indirectness[11]	no serious imprecision[13]	none[6]	66/4,308 (1.5320%)	0.0153 (0.0121 to 0.0194)[7]	15,320 (12,060 to 19,440)	⊕⊕OO LOW	CRITICAL
AAA Rupture (follow-up mean 10 years; assessed with: Objectively)											
1[8]	observational studies	no serious risk of bias[9]	no serious inconsistency[10]	no serious indirectness[11]	no serious imprecision[14]	none[6]	30/4,308 (0.6960%)	0.0070 (0.0049 to 0.0099)[7]	6,960 (4,880 to 9,920)	⊕⊕OO LOW	CRITICAL

[1] 1) Hafez et al. 2008; 2) Lederle et al. 2000; 3) Svensjö et al. 2013.

[2] Modified Ottawa Newcastle Tool (NOS) for cohort studies was used to assess risk of bias for these studies. Overall, one study had a concern regarding demonstration that the outcome of interest was not present at the beginning of the study and one study had a concern regarding the adequacy of follow-up. Given that most of the information is from studies at low risk of bias, this body of evidence was not downgraded for serious study limitations.

[3] The statistical heterogeneity is high [I^2=97.5%] but the direction of the effect is consistent across studies. The statistical heterogeneity is most likely due to small versus large screening effect observed across studies. This body of evidence was not downgraded for inconsistency.

[4] Three observational (cohort) studies provided data for this outcome. All studies included men only with a median age of 65 years. In all studies the intervention group received repeat screening with ultrasound. One study was conducted in the UK, one was conducted in Sweden and one was conducted in US. All studies were published between 2008 and 2013. The length of follow-up across the three studies was 4 years to 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[5] The sample size is adequate (8,971 screening arm) and the pooled effect estimate is precise with a narrow confidence interval [Proportion % = 2.257% (0.412%, 4.102%)]. This body of evidence was not downgraded for imprecision.

[6] There were too few studies (n<10) to assess publication bias.

[7] The estimates are based on number of events observed in repeat screening arm only with no comparison to control group.

[8] 1) Hafez et al. 2008

[9] Modified Ottawa Newcastle Tool (NOS) for cohort studies was used to access 6 domains of risk of bias. The study was rated as 5 stars with no statement provided on adequacy of follow-up. Given that most of the information is from low risk of bias, this body of evidence was not downgraded for serious study limitations.

[10] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.

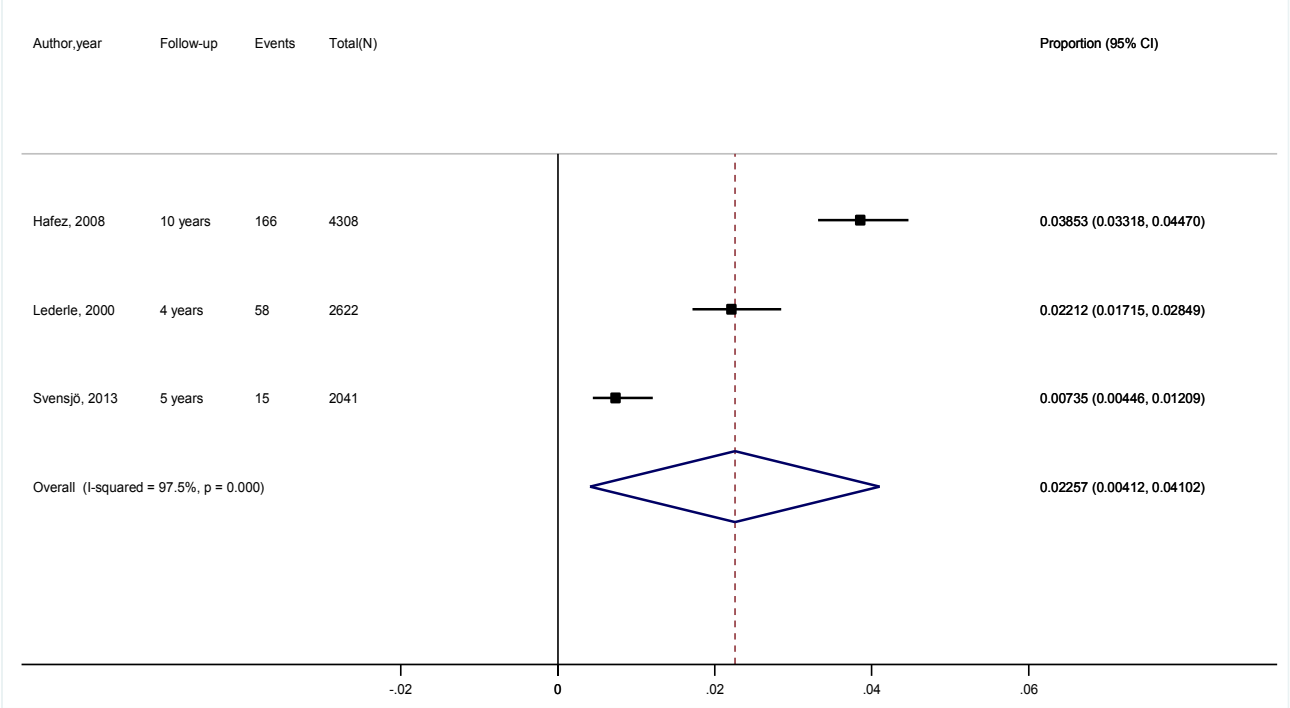
[11] One observational (cohort) study provided data for this outcome. The study included men only with a median age of 65 years. The intervention group received repeat screening with ultrasound. The study was conducted in the UK, and was published in 2008. The length of follow-up was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[12] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 0.557% (0.375%, 0.828%)]. This body of evidence was not downgraded for imprecision.

[13] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 1.5320% (1.2060%, 1.9440%)]. This body of evidence was not downgraded for imprecision.

[14] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 0.6960% (0.4880%, 0.9920%)]. This body of evidence was not downgraded for imprecision.

ES Forest Plot 2.1: AAA incidence in repeat screening



Evidence Set (ES) 3. Harms of One-Time Screening

- ES Table 3.1.1 Overview of Key Results: 30 day mortality and AAA operations
- ES Table 3.1.2 Overview of Key Results: Quality of Life
- ES Table 3.1.3 Overview of Key Results: Overdiagnosis
- ES Table 3.2 GRADE Evidence Profile: Harms of one-time screening
- ES Table 3.3 GRADE Summary of Findings Table: Harms of one-time screening
- ES Forest Plots 3.1-3.7
- ES Table 3.4 Sensitivity Analysis of Harms of one-time screening

ES Table 3.1.1 Overview of Key Results

Forest Plot	Outcome	Number of studies	Effect size (RR)
3.1	30 day mortality, AAA operations – 3 to 5 years follow-up	3	0.31 [0.20, 0.48]
3.1	30 day mortality, AAA operations – 6 to 7 years follow-up	1	0.32 [0.21, 0.48]
3.1	30 day mortality, AAA operations – 10 to 11 years follow-up	2	0.35 [0.25, 0.49]
3.1	30 day mortality, AAA operations – 13 to 15 years follow-up	2	0.46 [0.34, 0.63]
3.2	30 day mortality, elective AAA operations – 3 to 5 years follow-up	4	0.51 [0.26, 0.99]
3.2	30 day mortality, elective AAA operations – 6 to 7 years follow-up	1	0.52 [0.26, 1.05]
3.2	30 day mortality, elective AAA operations – 10 to 11 years follow-up	3	0.69 [0.36, 1.32]
3.2	30 day mortality, elective AAA operations – 13 to 15 years follow-up	2	0.78 [0.42, 1.46]
3.3	30 day mortality, emergency AAA operations – 3 to 5 years follow-up	3	0.67 [0.37, 1.21]
3.3	30 day mortality, emergency AAA operations – 6 to 7 years follow-up	1	0.78 [0.47, 1.31]
3.3	30 day mortality, emergency AAA operations – 10 to 11 years follow-up	2	0.83 [0.57, 1.19]
3.3	30 day mortality, emergency AAA operations – 13 to 15 years follow-up	2	0.95 [0.69, 1.31]
3.4	AAA operations – 3 to 5 years follow-up	4	2.16 [1.82, 2.57]

3.4	AAA operations – 6 to 7 years follow-up	1	1.85 [1.60, 2.15]
3.4	AAA operations – 10 to 11 years follow-up	3	1.57 [1.35, 1.83]
3.4	AAA operations – 13 to 15 years follow-up	3	1.48 [1.33, 1.65]
3.5	Elective AAA operations – 3 to 5 years follow-up	4	3.25 [2.13, 4.96]
3.5	Elective AAA operations – 6 to 7 years follow-up	1	2.88 [2.41, 3.46]
3.5	Elective AAA operations – 10 to 11 years follow-up	3	2.44 [2.12, 2.81]
3.5	Elective AAA operations – 13 to 15 years follow-up	3	2.15 [1.89, 2.44]
3.6	Emergency AAA operations – 3 to 5 years follow-up	4	0.50 [0.29, 0.86]
3.6	Emergency AAA operations – 6 to 7 years follow-up	1	0.41 [0.29, 0.57]
3.6	Emergency AAA operations – 10 to 11 years follow-up	3	0.42 [0.32, 0.54]
3.6	Emergency AAA operations – 13 to 15 years follow-up	3	0.50 [0.40, 0.63]

ES Table 3.1.2 Overview of Key Results: Quality of Life

Forest Plot	Outcome	Number of Studies	Results	GRADE Rating
3.7	Quality of Life	3	MD: -1.15 [-3.93, 1.63]	Very Low*

*Observational studies begin with a low GRADE rating; this evidence has been further downgraded due to Imprecision.

ES Table 3.1.3 Overview of Key Results: Overdiagnosis

Forest Plot	Outcome	Number of Studies	Results	GRADE Rating
-	Overdiagnosis	1	45% (95% CI 42% to 47%) overdiagnosed	Low*

*Observational studies begin with a low GRADE rating

ES Table 3.2 GRADE Evidence Profile: Harms of one-time screening for AAA

Quality assessment							No of patients		Effect				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Harms of	Control	Relative (95% CI)	Absolute per million	ARI	NNH (95% CI)		
30 day Mortality, AAA operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
3[1]	randomised trials	serious[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	29/501 (5.8%)	41/221 (18.6%)	RR 0.3086 (0.1967 to 0.4841)	128,269 fewer (from 95,710 fewer to 149,029 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, AAA operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[7]	randomised trials	no serious risk of bias[8]	no serious inconsistency[9]	no serious indirectness[10]	no serious imprecision[11]	none[6]	31/495 (6.3%)	53/267 (19.9%)	RR 0.3155 (0.2078 to 0.4789)	135,875 fewer (from 103,439 fewer to 157,253 fewer)	–	–	⊕⊕⊕⊕ HIGH	CRITICAL
30 day Mortality, AAA operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
2[12]	randomised trials	serious[13]	no serious inconsistency[14]	no serious indirectness[15]	no serious imprecision[16]	none[6]	48/703 (6.8%)	86/436 (19.7%)	RR 0.3539 (0.2537 to 0.4937)	127,442 fewer (from 99,867 fewer to 147,206 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, AAA operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13.1 to 15 years; assessed with: Objectively)														
2[17]	randomised trials	serious[18]	no serious inconsistency[19]	no serious indirectness[20]	no serious imprecision[21]	none[6]	58/737 (7.9%)	83/483 (17.2%)	RR 0.4602 (0.3362 to 0.6299)	92,761 fewer (from 63,599 fewer to 114,069 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, Elective AAA operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
4[22]	randomised trials	serious[23]	no serious inconsistency[24]	no serious indirectness[25]	no serious imprecision[26]	none[6]	21/505 (4.2%)	13/162 (8%)	RR 0.5102 (0.2618 to 0.9944)	39,305 fewer (from 449 fewer to 59,238 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, Elective AAA operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[27]	randomised trials	no serious risk of bias[28]	no serious inconsistency[9]	no serious indirectness[29]	serious[30]	none[6]	18/450 (4%)	12/156 (7.7%)	RR 0.5200 (0.2563 to 1.0549)	36,923 fewer (from 57,208 fewer to 4,223 more)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, Elective AAA operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
3[31]	randomised trials	serious[32]	no serious inconsistency[33]	no serious indirectness[34]	serious[35]	none[6]	24/664 (3.6%)	14/272 (5.1%)	RR 0.6927 (0.3634 to 1.3204)	15,817 fewer (from 32,766 fewer to 16,491 more)	–	–	⊕⊕OO LOW	CRITICAL
30 day Mortality, Elective AAA operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13.1 to 15 years; assessed with: Objectively)														
2[36]	randomised trials	serious[37]	no serious inconsistency[38]	no serious indirectness[39]	serious[40]	none[6]	26/676 (3.8%)	15/306 (4.9%)	RR 0.7834 (0.4202 to 1.4605)	10,618 fewer (from 28,422 fewer to 22,574 more)	–	–	⊕⊕OO LOW	CRITICAL
30 day Mortality, Emergency AAA operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
3[41]	randomised	serious[42]	no serious	no serious	serious[45]	none[6]	10/39	29/70	RR 0.6678	137,626 fewer	–	–	⊕⊕OO	CRITICAL

	trials		inconsistency[43]	indirectness[44]			(25.6%)	(41.4%)	(0.3686 to 1.2098)	(from 261,580 fewer to 86,917 more)			LOW	
30 day Mortality, Emergency AAA operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[46]	randomised trials	no serious risk of bias[47]	no serious inconsistency[9]	no serious indirectness[48]	serious[49]	none[6]	13/45 (28.9%)	41/111 (36.9%)	RR 0.7821 (0.4655 to 1.314)	80,486 fewer (from 197,428 fewer to 115,982 more)	–	–	⊕⊕⊕O MODERATE	CRITICAL
30 day Mortality, Emergency AAA operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
2[50]	randomised trials	serious[51]	no serious inconsistency[52]	no serious indirectness[53]	serious[54]	none[6]	24/75 (32%)	72/181 (39.8%)	RR 0.8252 (0.5705 to 1.1938)	69,534 fewer (from 170,851 fewer to 77,092 more)	–	–	⊕⊕OO LOW	CRITICAL
30 day Mortality, Emergency AAA operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13.1 to 15 years; assessed with: Objectively)														
2[55]	randomised trials	serious[56]	no serious inconsistency[57]	no serious indirectness[58]	serious[59]	none[6]	35/96 (36.5%)	69/187 (36.9%)	RR 0.9527 (0.693 to 1.3097)	17,453 fewer (from 113,278 fewer to 114,274 more)	–	–	⊕⊕OO LOW	CRITICAL
AAA operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
4[60]	randomised trials	serious[61]	no serious inconsistency[62]	no serious indirectness[63]	no serious imprecision[64]	none[6]	554/62,729 (0.88%)	252/62,847 (0.4%)	RR 2.1600 (1.8179 to 2.5663)	4,651 more (from 3,280 more to 6,280 more)	0.47%	215 (159 to 305)	⊕⊕⊕O MODERATE	CRITICAL
AAA operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[65]	randomised trials	no serious risk of bias[66]	no serious inconsistency[9]	no serious indirectness[67]	no serious imprecision[68]	none[6]	495/33,883 (1.5%)	267/33,887 (0.79%)	RR 1.8542 (1.5990 to 2.1500)	6,730 more (from 4,720 more to 9,061 more)	0.67%	149 (110 to 212)	⊕⊕⊕⊕ HIGH	CRITICAL
AAA operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
3[69]	randomised trials	serious[70]	no serious inconsistency[71]	no serious indirectness[72]	no serious imprecision[73]	none[6]	752/43,216 (1.7%)	469/43,251 (1.1%)	RR 1.5700 (1.3502 to 1.8255)	6,181 more (from 3,797 more to 8,951 more)	0.62%	162 (112 to 263)	⊕⊕⊕O MODERATE	CRITICAL
AAA operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[74]	randomised trials	serious[75]	no serious inconsistency[76]	no serious indirectness[77]	no serious imprecision[78]	none[6]	846/43,211 (2%)	571/43,238 (1.3%)	RR 1.4805 (1.3300 to 1.6480)	6,345 more (from 4,358 more to 8,557 more)	0.63%	158 (117 to 229)	⊕⊕⊕O MODERATE	CRITICAL
Elective operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
4[79]	randomised trials	serious[80]	no serious inconsistency[81]	no serious indirectness[82]	no serious imprecision[83]	none[6]	505/62,729 (0.81%)	162/62,847 (0.26%)	RR 3.2535 (2.1341 to 4.9603)	5,809 more (from 2,923 more to 10,208 more)	0.58%	172 (98 to 342)	⊕⊕⊕O MODERATE	CRITICAL
Elective operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[84]	randomised trials	no serious risk of bias[85]	no serious inconsistency[9]	no serious indirectness[86]	no serious imprecision[87]	none[6]	450/33,883 (1.3%)	156/33,887 (0.46%)	RR 2.8850 (2.4062 to 3.4590)	8,678 more (from 6,473 more to 11,320 more)	0.87%	115 (88 to 154)	⊕⊕⊕⊕ HIGH	CRITICAL
Elective operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
3[88]	randomised	serious[89]	no serious	no serious	no serious	none[6]	664/43,216	272/43,251	RR 2.4422	9,070 more (from	0.91%	110	⊕⊕⊕O	CRITICAL

	trials		inconsistency[90]	indirectness[91]	imprecision[92]		(1.5%)	(0.63%)	(2.1221 to 2.8106)	7,057 more to 11,387 more)		(88 to 142)	MODERATE	
Elective operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[93]	randomised trials	serious[94]	no serious inconsistency[95]	no serious indirectness[96]	no serious imprecision[97]	none[6]	730/43,211 (1.7%)	340/43,238 (0.79%)	RR 2.1479 (1.8899 to 2.4412)	9,026 more (from 6,998 more to 11,333 more)	0.90%	111 (88 to 143)	⊕⊕⊕O MODERATE	CRITICAL
Emergency operations - By length of Follow-up - 3 to 5 years of follow-up (follow-up 3.6 to 5 years; assessed with: Objectively)														
4[98]	randomised trials	serious[99]	no serious inconsistency[100]	no serious indirectness[101]	no serious imprecision[102]	none[6]	44/62,729 (0.07%)	90/62,847 (0.14%)	RR 0.4971 (0.2875 to 0.8595)	720 fewer (from 201 fewer to 1,020 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
Emergency operations - By length of Follow-up - 6 to 7 years of follow-up (follow-up mean 7 years; assessed with: Objectively)														
1[103]	randomised trials	no serious risk of bias[104]	no serious inconsistency[9]	no serious indirectness[105]	no serious imprecision[106]	none[6]	45/33,883 (0.13%)	111/33,887 (0.33%)	RR 0.4055 (0.2869 to 0.5731)	1,947 fewer (from 1,398 fewer to 2,336 fewer)	–	–	⊕⊕⊕⊕ HIGH	CRITICAL
Emergency operations - By length of Follow-up - 10 to 11 years of follow-up (follow-up mean 10 years; assessed with: Objectively)														
3[88]	randomised trials	serious[107]	no serious inconsistency[108]	no serious indirectness[109]	no serious imprecision[110]	none[6]	81/43,216 (0.19%)	194/43,251 (0.45%)	RR 0.4192 (0.3234 to 0.5433)	2,605 fewer (from 2,049 fewer to 3,035 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL
Emergency operations - By length of Follow-up - 13 to 15 years of follow-up (follow-up 13 to 15 years; assessed with: Objectively)														
3[111]	randomised trials	serious[112]	no serious inconsistency[113]	no serious indirectness[114]	no serious imprecision[115]	none[6]	116/43,211 (0.27%)	231/43,238 (0.53%)	RR 0.5041 (0.4033 to 0.6302)	2,649 fewer (from 1,976 fewer to 3,188 fewer)	–	–	⊕⊕⊕O MODERATE	CRITICAL

NOTE: NNH were calculated from Absolute numbers presented in GRADE tables. The GRADE tables estimate the absolute numbers per million using control group event rate and risk ratio with 95 % CI obtained from meta-analysis. NS = non-significant. The NNH were not calculated for 30-day mortality AAA operations, 30 day Mortality Elective AAA operations, 30 day Mortality Emergency AAA operations, emergency operations and emergent repairs for ruptures because either the effect was non-significant or showed a risk reduction in screening arm as compared to control arm.

ES Table 3.3 GRADE Summary of Findings Table: Harms of one-time screening

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk per million **Control**	Corresponding risk per million **Harms of**				
30 day Mortality, AAA operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population** **185,520**	**57,252** (36,492 to 89,810)	**RR 0.3086** (0.1967 to 0.4841)	722 (3 studies[1])	⊕⊕⊕⊖ **moderate**[2,3,4,5,6]	
30 day Mortality, AAA operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population** **198,502**	**62,627** (41,249 to 95,063)	**RR 0.3155** (0.2078 to 0.4789)	762 (1 study[7])	⊕⊕⊕⊕ **high**[6,8,9,10,11]	
30 day Mortality, AAA operations - By length of Follow-up - 10 to 11 years of follow-up Objectively Follow-up: mean 10 years	**Study population** **197,248**	**69,806** (50,042 to 97,381)	**RR 0.3539** (0.2537 to 0.4937)	1,139 (2 studies[12])	⊕⊕⊕⊖ **moderate**[6,13,14,15,16]	
30 day Mortality, AAA operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13.1 to 15 years	**Study population** **171,843**	**79,082** (57,773 to 108,244)	**RR 0.4602** (0.3362 to 0.6299)	1,220 (2 studies[17])	⊕⊕⊕⊖ **moderate**[6,18,19,20,21]	
30 day Mortality, Elective AAA operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population** **80,247**	**40,942** (21,009 to 79,798)	**RR 0.5102** (0.2618 to 0.9944)	667 (4 studies[22])	⊕⊕⊕⊖ **moderate**[6,23,24,25,26]	
30 day Mortality, Elective AAA operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population** **76,923**	**40,000** (19,715 to 81,146)	**RR 0.5200** (0.2563 to 1.0549)	606 (1 study[27])	⊕⊕⊕⊖ **moderate**[6,9,28,29,30]	
30 day Mortality, Elective AAA operations - By length of Follow-up - 10 to 11 years of follow-up Objectively Follow-up: mean 10 years	**Study population** **51,471**	**35,654** (18,704 to 67,962)	**RR 0.6927** (0.3634 to 1.3204)	936 (3 studies[31])	⊕⊕⊖⊖ **low**[6,32,33,34,35]	
30 day Mortality, Elective AAA operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13.1 to 15 years	**Study population** **49,020**	**38,402** (20,598 to 71,593)	**RR 0.7834** (0.4202 to 1.4605)	982 (2 studies[36])	⊕⊕⊖⊖ **low**[6,37,38,39,40]	

30 day Mortality, Emergency AAA operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population**		**RR 0.6678** (0.3686 to 1.2098)	109 (3 studies[41])	⨁⨁⨀⨀ **low**[6,42,43,44,45]
	414,286	**276,660** (152,706 to 501,203)			
30 day Mortality, Emergency AAA operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population**		**RR 0.7821** (0.4655 to 1.314)	156 (1 study[46])	⨁⨁⨁⨀ **moderate**[6,9,47,48,49]
	369,369	**288,884** (171,941 to 485,351)			
30 day Mortality, Emergency AAA operations - By length of Follow-up - 10 to 11 years of follow-up Objectively Follow-up: mean 10 years	**Study population**		**RR 0.8252** (0.5705 to 1.1938)	256 (2 studies[50])	⨁⨁⨀⨀ **low**[6,51,52,53,54]
	397,790	**328,256** (226,939 to 474,882)			
30 day Mortality, Emergency AAA operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13.1 to 15 years	**Study population**		**RR 0.9527** (0.693 to 1.3097)	283 (2 studies[55])	⨁⨁⨀⨀ **low**[6,56,57,58,59]
	368,984	**351,531** (255,706 to 483,258)			
AAA operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population**		**RR 2.1600** (1.8179 to 2.5663)	125,576 (4 studies[60])	⨁⨁⨁⨀ **moderate**[6,61,62,63,64]
	4,010	**8,661** (7,289 to 10,290)			
AAA operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population**		**RR 1.8542** (1.599 to 2.15)	67,770 (1 study[65])	⨁⨁⨁⨁ **high**[6,9,66,67,68]
	7,879	**14,609** (12,599 to 16,940)			
AAA operations - By length of Follow-up - 10 to 11 years of follow-up Objectively Follow-up: mean 10 years	**Study population**		**RR 1.5700** (1.3502 to 1.8255)	86,467 (3 studies[69])	⨁⨁⨁⨀ **moderate**[6,70,71,72,73]
	10,844	**17,025** (14,641 to 19,795)			
AAA operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13 to 15 years	**Study population**		**RR 1.4805** (1.33 to 1.648)	86,449 (3 studies[74])	⨁⨁⨁⨀ **moderate**[6,75,76,77,78]
	13,206	**19,551** (17,564 to 21,763)			
Elective operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population**		**RR 3.2535** (2.1341 to 4.9603)	125,576 (4 studies[79])	⨁⨁⨁⨀ **moderate**[6,80,81,82,83]
	2,578	**8,387** (5,501 to 12,786)			
Elective operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population**		**RR 2.8850** (2.4062 to 3.459)	67,770 (1 study[84])	⨁⨁⨁⨁ **high**[6,9,85,86,87]
	4,604	**13,281** (11,077 to 15,924)			
Elective operations - By length of Follow-up - 10 to 11 years of follow-up Objectively	**Study population**		**RR 2.4422** (2.1221 to	86,467 (3 studies[88])	⨁⨁⨁⨀ **moderate**[6,89,90,91,92]
	6,289	**15,359**			

Follow-up: mean 10 years		(13,346 to 17,676)	2.8106)		
Elective operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13 to 15 years	**Study population**		**RR 2.1479** (1.8899 to 2.4412)	86,449 (3 studies[93])	⊕⊕⊕⊖ **moderate**[6,94,95,96,97]
	7,863	**16,890** (14,861 to 19,196)			
Emergency operations - By length of Follow-up - 3 to 5 years of follow-up Objectively Follow-up: 3.6 to 5 years	**Study population**		**RR 0.4971** (0.2875 to 0.8595)	12,5576 (4 studies[98])	⊕⊕⊕⊖ **moderate**[6,99,100,101,102]
	1,432	**712** (412 to 1,231)			
Emergency operations - By length of Follow-up - 6 to 7 years of follow-up Objectively Follow-up: mean 7 years	**Study population**		**RR 0.4055** (0.2869 to 0.5731)	67,770 (1 study[103])	⊕⊕⊕⊕ **high**[6,9,104,105,106]
	3,276	**1,328** (940 to 1,877)			
Emergency operations - By length of Follow-up - 10 to 11 years of follow-up Objectively Follow-up: mean 10 years	**Study population**		**RR 0.4192** (0.3234 to 0.5433)	86,467 (3 studies)	⊕⊕⊕⊖ **moderate**[6,107,108,109,110]
	4,485	**1,880** (1,451 to 2,437)			
Emergency operations - By length of Follow-up - 13 to 15 years of follow-up Objectively Follow-up: 13 to 15 years	**Study population**		**RR 0.5041** (0.4033 to 0.6302)	86,449 (3 studies[111])	⊕⊕⊕⊖ **moderate**[6,112,113,114,115]
	5,343	**2,693** (21,55 to 3,367)			

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] 1) Ashton et al. 2002 (MASS); 2) Norman 2004 (W. Australia); 3) Scott 1995 (Chichester)

[2] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (33%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[3] The statistical heterogeneity is minimal [Chi^2=1.42, df=2 (P=0.49); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[4] Three RCTs provided data for this outcome. Two RCTs included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Australia. All studies were published between 1995 and 2004. The length of follow-up across the three studies was 3.6 to 5 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[5] The sample size is adequate in screening arm and not adequate in control arm i.e. < 300 (501 screening arm, 221 control arm) but the pooled effect estimate is precise with a narrow confidence interval [RR= 0.3086 (0.1967, 0.4841)]. This body of evidence was not downgraded for imprecision.

[6] There were too few studies (n<10) to assess publication bias.

[7] Kim 2007 (MASS)

[8] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.
[9] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.
[10] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[11] The sample size is adequate in screening arm and not adequate in control arm i.e. < 300 (495 screening arm, 267 control arm) but the pooled effect estimate is precise with a narrow confidence interval [RR= 0.3155 (0.2078, 0.4789)]. This body of evidence was not downgraded for imprecision.
[12] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS)
[13] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[14] The statistical heterogeneity is minimal [Chi^2=0.24, df=1 (P=0.63); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[15] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64 to 83 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in the UK and one study was conducted in Denmark. The studies were published in 2006 and 2009. The length of follow-up in both studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[16] The sample size is adequate (703 screening arm, 436 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.3539 (0.2537, 0.4937)]. This body of evidence was not downgraded for imprecision.
[17] 1) Ashton 2007 (Chichester); 2) Thompson 2012 (MASS)
[18] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding allocation concealment (50%) and blinding (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[19] The statistical heterogeneity is minimal [Chi^2=0.00, df=1 (P=0.96); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[20] Two RCTs provided data for this outcome. One study included men only and one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Both studies were conducted in the UK. The studies were published between 2007 and 2012. The length of follow-up was 13.1 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[21] The sample size is adequate (737 screening arm, 483 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4602 (0.3362, 0.6299)]. This body of evidence was not downgraded for imprecision.
[22] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)
[23] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[24] The statistical heterogeneity is minimal [Chi^2=0.18, df=2 (P=0.92); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[25] Four RCTs provided data for this outcome. Three studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 to 5 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[26] The sample size is adequate in screening arm and not adequate in control arm i.e. < 300 (505 screening arm, 162 control arm) but the pooled effect estimate is precise and does not include the null value "0" [RR= 0.5102 (0.2618, 0.9944)]. This body of evidence was not downgraded for imprecision.
[27] 1) Kim 2007 (MASS)
[28] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.
[29] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The

study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[30] The sample size is adequate in screening arm but not adequate in control arm i.e. < 300 (450 screening arm, 156 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.5200 (0.2563, 1.0549)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[31] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS); 3) Vardulaki 2002 (Chichester)

[32] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[33] The statistical heterogeneity is minimal [Chi^2=0.21, df=1 (P=0.64); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[34] Three RCTs provided data for this outcome. Two studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2002 and 2009. The length of follow-up across the three studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[35] The sample size is adequate in screening arm but not adequate in control arm i.e. < 300 (664 screening arm, 272 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.6927 (0.3634, 1.3204)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[36] 1) Ashton 2007 (Chichester); 2) Thompson 2009 (MASS)

[37] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding allocation concealment (50%) and blinding (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[38] The statistical heterogeneity is minimal [Chi^2=0.12, df=1 (P=0.73); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[39] Two RCTs provided data for this outcome. One study included men only and one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Both studies were conducted in the UK. The studies were published between 2007 and 2012. The length of follow-up was 13.1 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[40] The sample size is adequate in screening arm and control arms i.e. => 300 (676 screening arm, 306 control arm) but the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.7834 (0.4202, 1.4605)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[41] 1) Ashton et al. 2002 (MASS); 2) Norman 2004 (W. Australia); 3) Scott 1995 (Chichester)

[42] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (33%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[43] The statistical heterogeneity is minimal [Chi^2=0.67, df=2 (P=0.71); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[44] Three RCTs provided data for this outcome. Two RCTs included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Australia. All studies were published between 1995 and 2004. The length of follow-up across the three studies was 3.6 to 5 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[45] The sample size is not adequate in screening arm and control arms i.e. < 300 (39 screening arm, 70 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.6678 (0.3686, 1.2098)]. This body of evidence was downgraded for serious concerns regarding imprecision.

[46] 1) Kim 2007 (MASS)

[47] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.

[48] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[49] The sample size is not adequate in screening arm and control arms i.e. < 300 (45 screening arm, 111 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.7821 (0.4655, 1.3140)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[50] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS)
[51] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[52] The statistical heterogeneity is minimal [Chi^2=0.00, df=1 (P=0.95); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[53] Two RCTs provided data for this outcome. Both studies included men only, with ages ranging from 64 to 83 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. One study was conducted in in the UK and one study was conducted in Denmark. The studies were published in 2006 and 2009. The length of follow-up in both studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[54] The sample size is not adequate in screening arm and control arms i.e. < 300 (75 screening arm, 181 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.8252 (0.5705, 1.1938)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[55] 1) Ashton 2007 (Chichester); 2) Thompson 2012 (MASS)
[56] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and one study was rated as unclear risk. In one study there was a lack of certainty (unclear ratings) regarding allocation concealment (50%) and blinding (50%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[57] The statistical heterogeneity is minimal [Chi^2=0.10, df=1 (P=0.75); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[58] Two RCTs provided data for this outcome. One study included men only and one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In both studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Both studies were conducted in the UK. The studies were published between 2007 and 2012. The length of follow-up was 13.1 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[59] The sample size is not adequate in screening arm and control arms i.e. < 300 (96 screening arm, 187 control arm) and the pooled effect estimate is not precise and confidence interval include the null value "1" [RR= 0.9527 (0.6930, 1.3097)]. This body of evidence was downgraded for serious concerns regarding imprecision.
[60] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)
[61] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[62] The statistical heterogeneity is minimal [Chi^2=3.49, df=3 (P=0.32); I^2=14%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[63] Four RCTs provided data for this outcome. Three studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[64] The sample size is adequate (62,729 screening arm, 62,847 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 2.1600 (1.8179, 2.5663)]. This body of evidence was not downgraded for imprecision.
[65] 1) Kim 2007 (MASS)
[66] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.
[67] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[68] The sample size is adequate (33,883 screening arm, 33,887 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 1.8542 (1.5990, 2.1500)]. This body of evidence was not downgraded for imprecision.
[69] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS); 3) Vardulaki 2002 (Chichester)

[70] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[71] The statistical heterogeneity is minimal [Chi^2=2.43, df=2 (P=0.30); I^2=18%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[72] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2002 and 2009. The length of follow-up across the three studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[73] The sample size is adequate (43,216 screening arm, 43,251 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 1.5700 (1.3502, 1.8255)]. This body of evidence was not downgraded for imprecision.
[74] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); 3) Thompson 2012 (MASS)
[75] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[76] The statistical heterogeneity is minimal [Chi^2=2.02, df=2 (P=0.36); I^2=1%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[77] Three RCTs provided data for this outcome. Two studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[78] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 1.4805 (1.3300, 1.6480)]. This body of evidence was not downgraded for imprecision.
[79] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)
[80] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[81] The statistical heterogeneity is moderate [Chi^2=10.92, df=3 (P=0.01); I^2=73%] but the direction of the effect is consistent across studies and the confidence intervals overlap across most studies. The statistical heterogeneity is most likely due to small versus large treatment effects observed across studies. This body of evidence was not downgraded for inconsistency.
[82] Four RCTs provided data for this outcome. Three studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 years to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[83] The sample size is adequate (62,729 screening arm, 62,847 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 3.2535 (2.1341, 4.9603)]. This body of evidence was not downgraded for imprecision.
[84] 1) Kim 2007 (MASS)
[85] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.
[86] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[87] The sample size is adequate (33,883 screening arm, 33,887 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 2.8850 (2.4062, 3.4590)]. This body of evidence was not downgraded for imprecision.
[88] 1) Lindholt 2006 (Viborg); 2) Thompson 2009 (MASS); 3) Vardulaki 2002 (Chichester)
[89] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding

sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[90] The statistical heterogeneity is minimal [Chi^2=0.27, df=2 (P=0.87); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[91] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2002 and 2009. The length of follow-up across the three studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[92] The sample size is adequate (43,216 screening arm, 43,251 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 2.4422 (2.1221, 2.8106)]. This body of evidence was not downgraded for imprecision.

[93] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); 3) Thompson 2012 (MASS)

[94] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[95] The statistical heterogeneity is minimal [Chi^2=0.14, df=2 (P=0.93); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[96] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[97] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 2.1479 (1.8899, 2.4412)]. This body of evidence was not downgraded for imprecision.

[98] 1) Ashton 2002 (MASS); 2) Lindholt 2005 (Viborg); 3) Norman 2004 (W. Australia); 4) Scott 1995 (Chichester)

[99] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and 3 studies were rated as unclear risk. Across studies, there was a lack of certainty (unclear ratings) regarding sequence generation (50%), allocation concealment (75%) and blinding (25%); and high risk of bias associated with other sources of bias (50%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[100] The statistical heterogeneity is minimal [Chi^2=4.92, df=3 (P=0.18); I^2=39%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.

[101] Four RCTs provided data for this outcome. Three studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 64 to 83 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK, one was conducted in Denmark and one was conducted in Western Australia. All studies were published between 1995 and 2005. The length of follow-up across the four studies was 3.6 to 5.0 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[102] The sample size is adequate (62,729 screening arm, 62,847 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4971 (0.2875, 0.8595)]. This body of evidence was not downgraded for imprecision.

[103] 1) Kim 2007 (MASS)

[104] Using Cochrane's Risk of Bias tool, for this outcome this study was rated as low. Given that this study has low risk of bias, this body of evidence was not downgraded for serious study limitations.

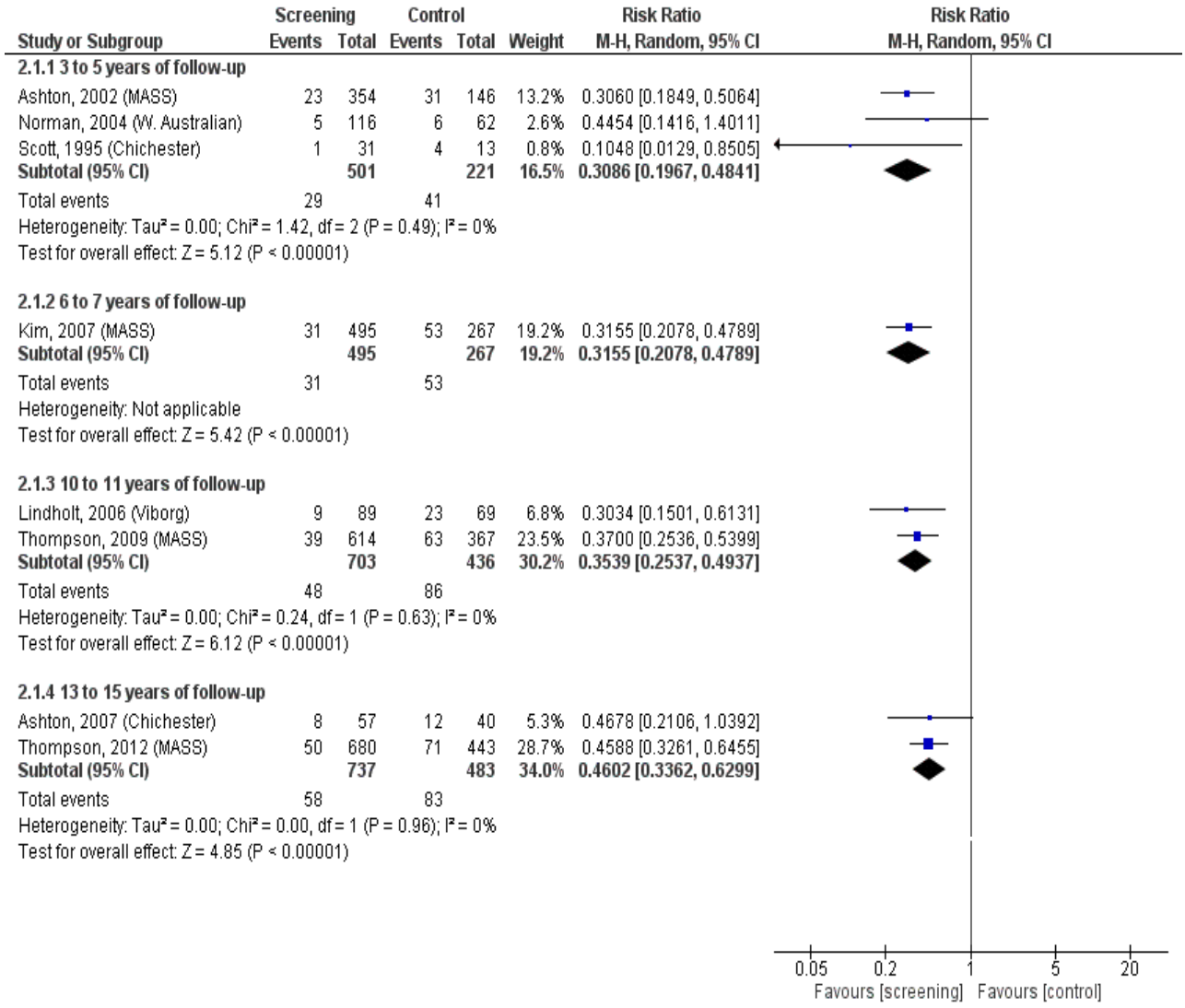
[105] One RCT provided data for this outcome. The study included men aged 65 to 74 years. The intervention group received one screen with ultrasound and the control group received no screening. The study was conducted in the UK. The study was published in 2007. The length of follow-up was 7 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[106] The sample size is adequate (33,883 screening arm, 33,887 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4055 (0.2869, 0.5731)]. This body of evidence was not downgraded for imprecision.

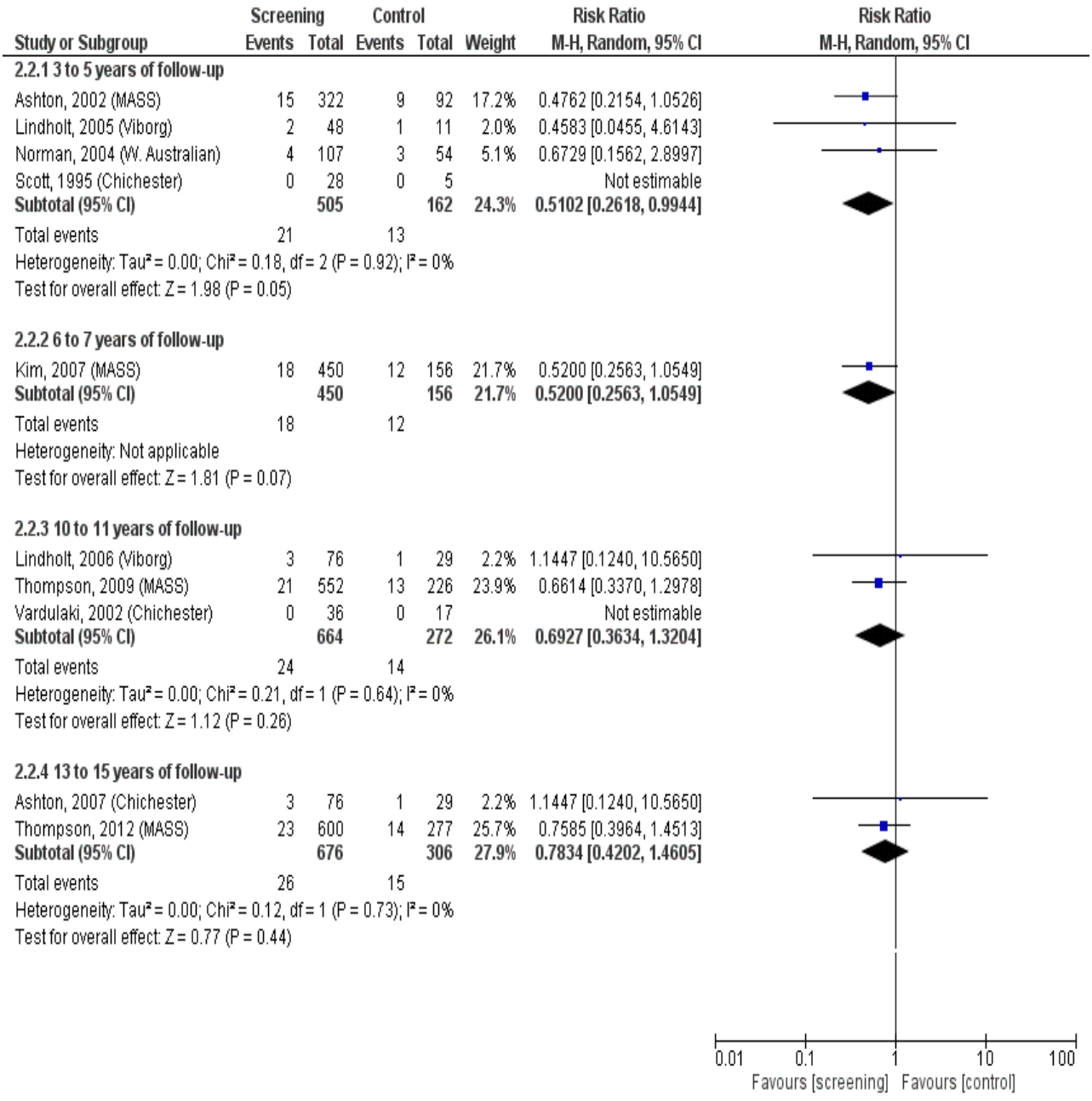
[107] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.

[108] The statistical heterogeneity is minimal [Chi^2=0.81, df=2 (P=0.67); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[109] Three RCTs provided data for this outcome. Two studies included men only, one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2002 and 2009. The length of follow-up across the three studies was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[110] The sample size is adequate (43,216 screening arm, 43,251 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.4192 (0.3234, 0.5433)]. This body of evidence was not downgraded for imprecision.
[111] 1) Ashton 2007 (Chichester); 2) Lindholt 2010 (Viborg); 3) Thompson 2012 (MASS)
[112] Using Cochrane's Risk of Bias tool, for this outcome one study was rated as low and two studies were rated as unclear risk. Across studies there was a lack of certainty (unclear ratings) regarding sequence generation (33%), allocation concealment (66%) and blinding (33%); and high risk of bias associated with other sources of bias (66%; i.e., baseline differences between groups, power calculations and contamination). Given that most of the information is from studies at moderate risk of bias, this body of evidence was downgraded for serious study limitations.
[113] The statistical heterogeneity is minimal [Chi^2=1.96, df=2 (P=0.38); I^2=0%] and the direction of the effect is consistent across studies with overlapping confidence intervals. This body of evidence was not downgraded for inconsistency.
[114] Three RCTs provided data for this outcome. Two studies included men only; one study included a mixed gender population though only data for men was considered. Included ages ranged from 65 to 80 years. In all studies the intervention group received one screen with ultrasound and the control group received no screening/usual care. Two studies were conducted in the UK and one was conducted in Denmark. All studies were published between 2007 and 2012. The length of follow-up across the three studies was 13 to 15 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.
[115] The sample size is adequate (43,211 screening arm, 43,238 control arm) and the pooled effect estimate is precise with a narrow confidence interval [RR= 0.5041 (0.4033, 0.6302)]. This body of evidence was not downgraded for imprecision.

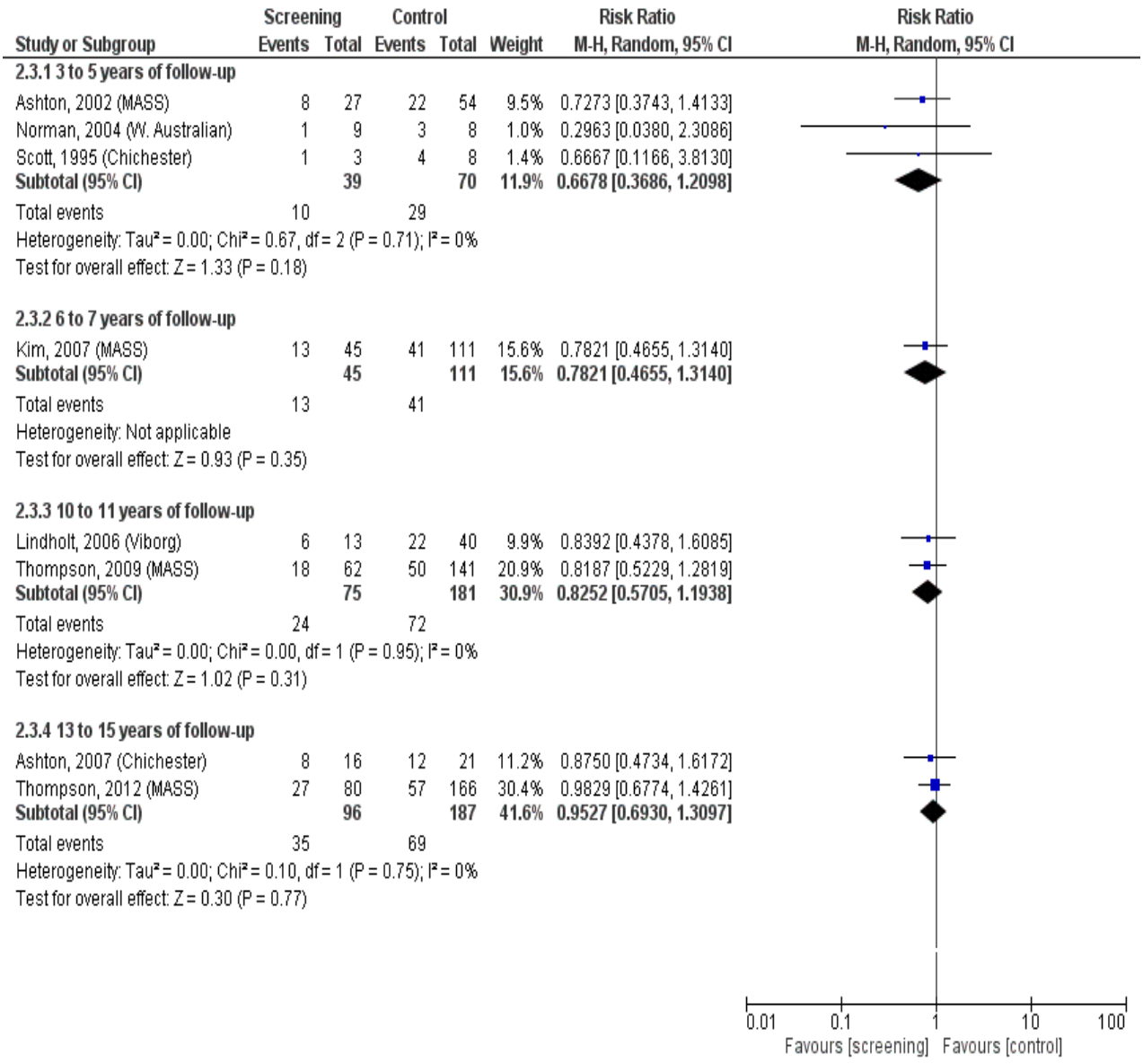
ES Forest Plot 3.1: Harms of one-time AAA screening: 30 day Mortality, AAA operations – By length of follow-up



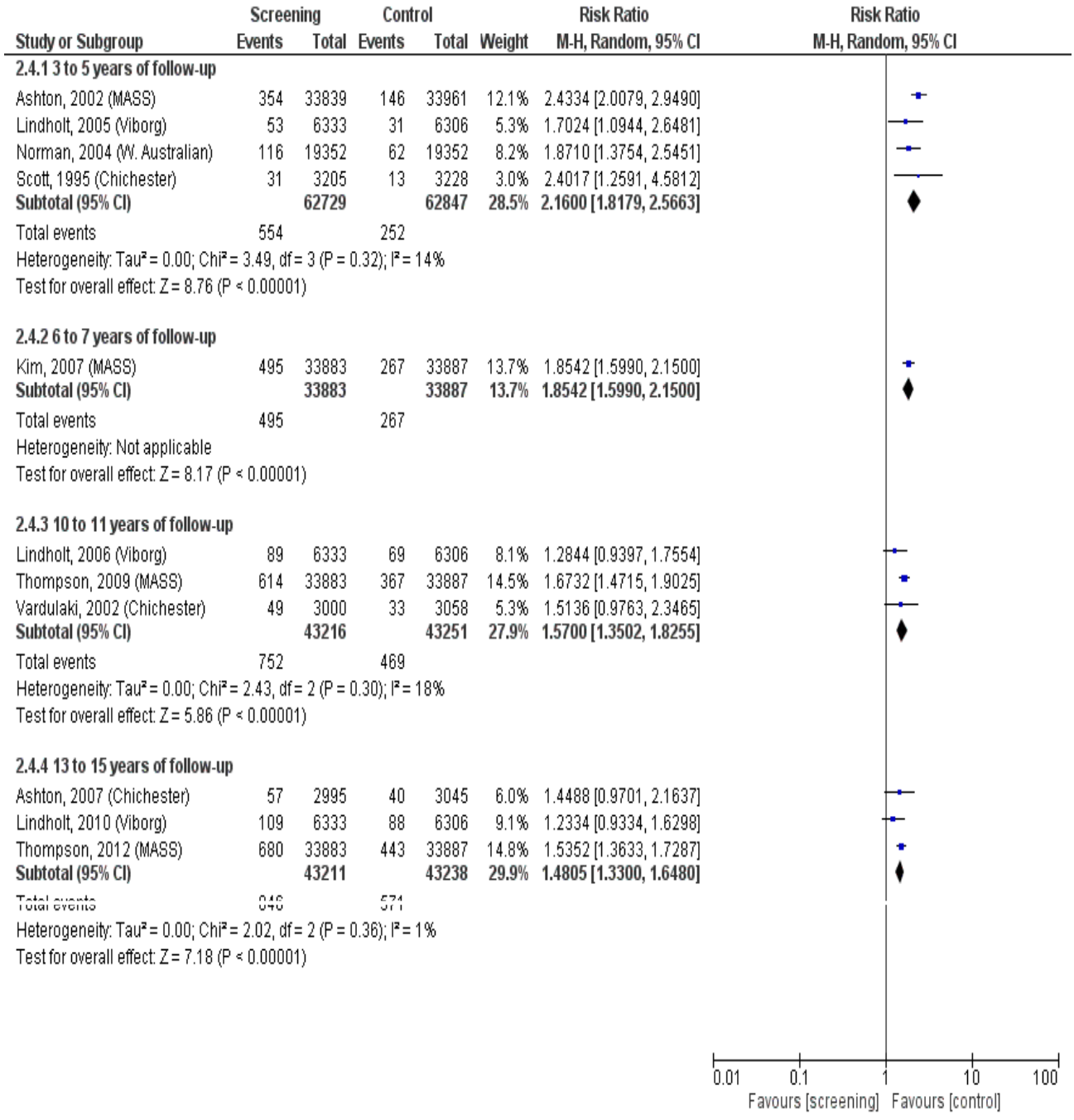
ES Forest Plot 3.2: Harms of one-time AAA screening: 30 day Mortality, elective AAA operations – By length of follow-up



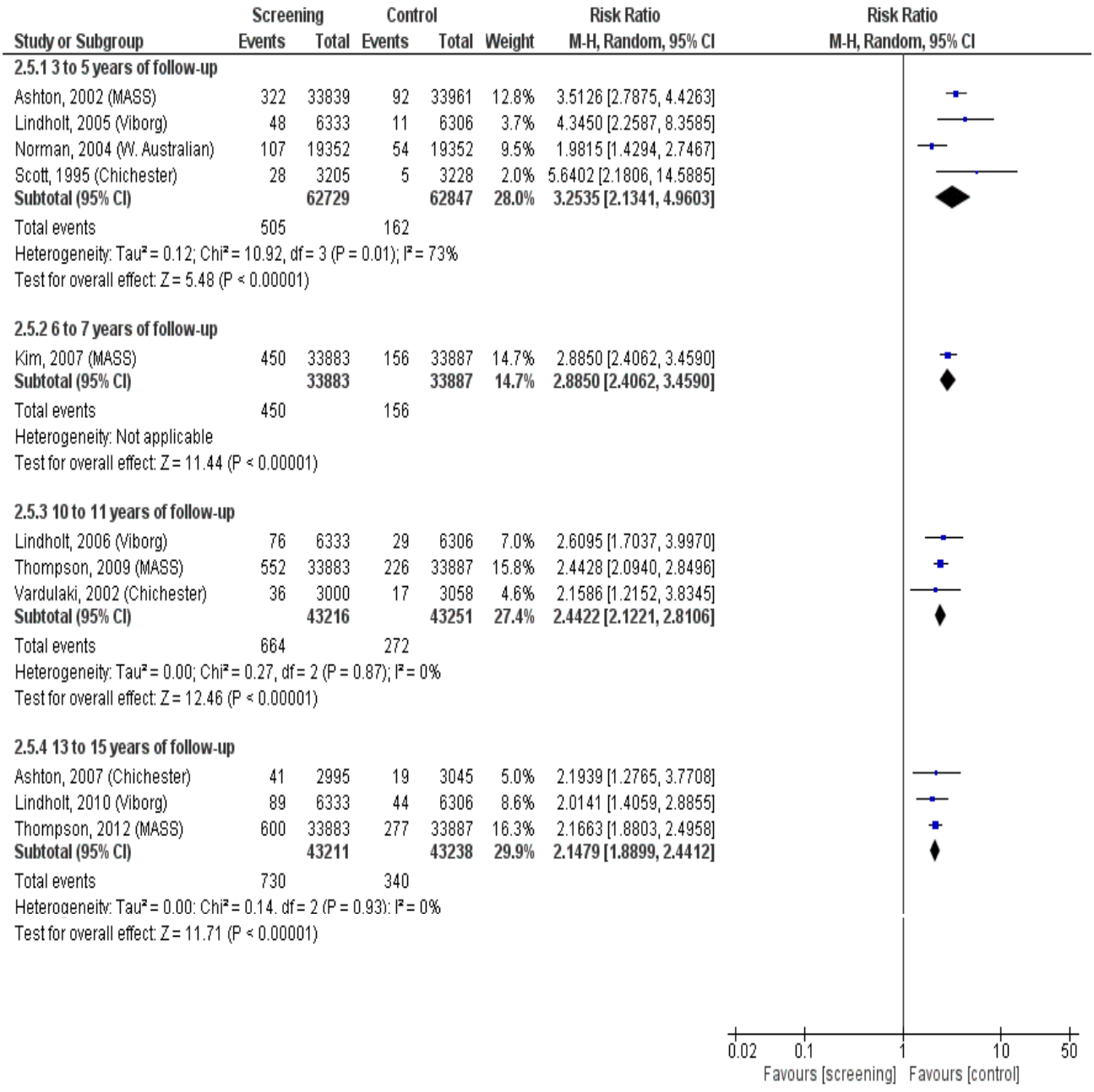
ES Forest Plot 3.3: Harms of one-time AAA screening: 30 day Mortality, emergency AAA operations – By length of follow-up



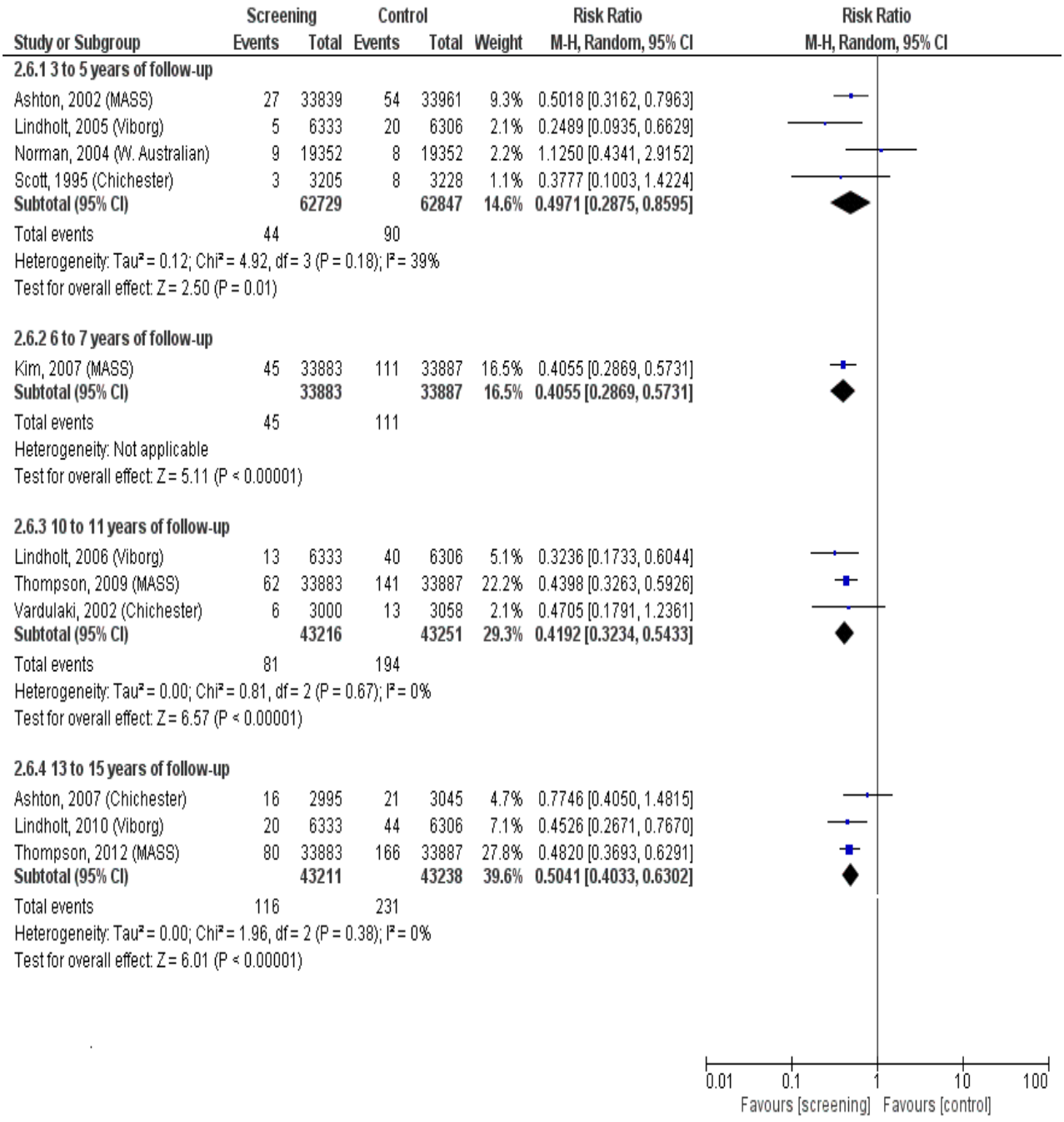
ES Forest Plot 3.4: Harms of one-time AAA screening: AAA operations – By length of follow-up



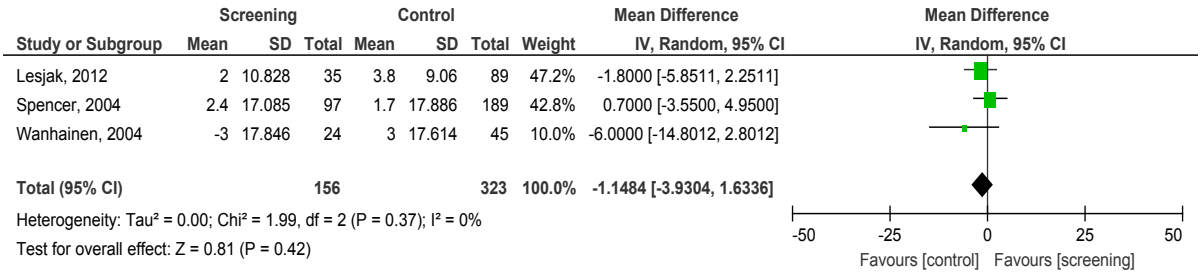
ES Forest Plot 3.5: Harms of one-time AAA screening: elective AAA operations – By length of follow-up



ES Forest Plot 3.6: Harms of one-time AAA screening: emergency AAA operations – By length of follow-up



ES Forest Plot 3.7: Harms of one-time screening: Quality of Life



ES Table 3.4 Sensitivity Analysis for rare events: Harms of one-time screening

Outcome	Risk Ratio	Peto's Odd Ratio
30 day mortality, AAA operations – by length of follow-up		
3 to 5 years follow-up	0.31 [0.20, 0.48]	0.22 [0.13, 0.38]
6 to 7 years follow-up	0.31 [0.20, 0.48]	0.25 [0.16, 0.40]
10 to 11 years follow-up	0.35 [0.25, 0.49]	0.29 [0.20, 0.43]
13 to 15 years follow-up	0.46 [0.34, 0.63]	0.40 [0.28, 0.58]
30 day mortality, elective AAA operations – by length of follow-up		
3 to 5 years follow-up	0.51 [0.26, 0.99]	0.44 [0.20, 1.00]
6 to 7 years follow-up	0.52 [0.26, 1.05]	0.46 [0.20, 1.06]
10 to 11 years follow-up	0.69 [0.36, 1.32]	0.67 [0.33, 1.37]
13 to 15 years follow-up	0.78 [0.42, 1.46]	0.77 [0.39, 1.51]
30 day mortality, emergency AAA operations – by length of follow-up		
3 to 5 years follow-up	0.67 [0.37, 1.21]	0.54 [0.24, 1.23]
6 to 7 years follow-up	0.78 [0.47, 1.31]	0.70 [0.34, 1.45]
10 to 11 years follow-up	0.83 [0.57, 1.19]	0.74 [0.42, 1.30]
13 to 15 years follow-up	0.95 [0.69, 1.31]	0.94 [0.56, 1.57]
AAA operations – by length of follow-up		
3 to 5 years follow-up	2.16 [1.82, 2.57]	2.13 [1.86, 2.45]
6 to 7 years follow-up	1.85 [1.60, 2.15]	1.83 [1.59, 2.11]
10 to 11 years follow-up	1.57 [1.35, 1.83]	1.60 [1.43, 1.79]
13 to 15 years follow-up	1.48 [1.33, 1.65]	1.48 [1.34, 1.65]
Elective operations – by length of follow-up		
3 to 5 years follow-up	3.25 [2.13, 4.96]	2.82 [2.42, 3.28]
6 to 7 years follow-up	2.88 [2.41, 3.46]	2.66 [2.27, 3.12]
10 to 11 years follow-up	2.44 [2.12, 2.81]	2.33 [2.05, 2.65]
13 to 15 years follow-up	2.15 [1.89, 2.44]	2.09 [1.86, 2.36]
Emergency operations - by length of follow-up		
3 to 5 years follow-up	0.50 [0.29, 0.86]	0.50 [0.36, 0.71]
6 to 7 years follow-up	0.41 [0.29, 0.57]	0.43 [0.31, 0.59]
10 to 11 years follow-up	0.42 [0.32, 0.54]	0.44 [0.35, 0.56]
13 to 15 years follow-up	0.50 [0.40, 0.63]	0.51 [0.42, 0.64]

Evidence Set (ES) 4. Harms of Repeat Screening

- ES Table 4.1 GRADE Evidence Profile: Harms of repeat screening

ES Table 4.1 GRADE Evidence Profile: Harms of repeat AAA screening (uncontrolled cohort studies)

Quality assessment							No of patients	Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Harms of repeat AAA screening	Proportion (95% CI)	Absolute per million (95% CI)		
AAA operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[5]	none[6]	30/4,308 (0.6960%)	0.0070 (0.0049 to 0.0099)[7]	6,960 (4,880 to 9,920)	⊕⊕OO LOW	CRITICAL
Elective operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[8]	none[6]	23/4,308 (0.5340%)	0.0053 (0.0036 to 0.0080)[7]	5,340 (3,560 to 8,000)	⊕⊕OO LOW	CRITICAL
Emergency operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	no serious imprecision[9]	none[6]	7/4,308 (0.1620%)	0.0016 (0.0008 to 0.0034)[7]	1,620 (790 to 3,350)	⊕⊕OO LOW	CRITICAL
30 day Mortality, AAA operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[10]	none[6]	6/30 (20.00%)	0.2000 (0.0951 to 0.3731)[7]	200,000 (95,050 to 373,060)	⊕OOO VERY LOW	CRITICAL
30 day Mortality, Elective AAA operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[11]	none[6]	3/23 (13.04%)	0.1304 (0.0454 to 0.3213)[7]	130,430 (45,380 to 321,270)	⊕OOO VERY LOW	CRITICAL
30 day Mortality, Emergency AAA operations (follow-up mean 10 years; assessed with: Objectively)											
1[1]	observational studies	no serious risk of bias[2]	no serious inconsistency[3]	no serious indirectness[4]	serious[12]	none[6]	3/7 (42.85%)	0.4286 (0.1582 to 0.7495)[7]	428,570 (158,220 to 749,540)	⊕OOO VERY LOW	CRITICAL

[1] 1) Hafez et al. 2008

[2] Modified Ottawa Newcastle Tool (NOS) for cohort studies was used to access 6 domains of risk of bias. The study was rated as 5 stars with no statement provided on adequacy of follow-up. Given that most of the information is from low risk of bias, this body of evidence was not downgraded for serious study limitations.

[3] The statistical heterogeneity across studies could not be assessed due to only one study providing data for this outcome.

[4] One observational (cohort) study provided data for this outcome. The study included men only with a median age of 65 years. The intervention group received repeat screening with ultrasound. The study was conducted in the UK, and was published in 2008. The length of follow-up was 10 years. There were no serious concerns regarding indirectness for this body of evidence and it was not downgraded.

[5] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 0.6960% (0.4880%, 0.9920%)]. This body of evidence was not downgraded for imprecision.

[6] There were too few studies (n<10) to assess publication bias.

[7] The estimates are based on number of events observed in repeat screening arm only with no comparison to control group.

[8] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 0.5340% (0.3560%, 0.8000%)]. This body of evidence was not downgraded for imprecision.

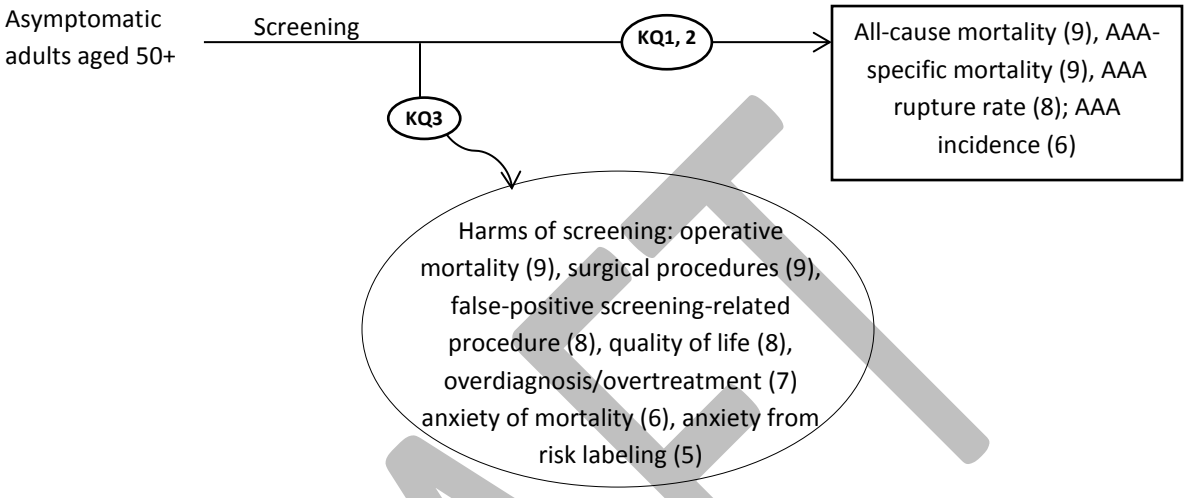
[9] The sample size is adequate (4,308 screening arm) and the effect estimate is precise with a narrow confidence interval [Proportion % = 0.1620% (0.0790%, 0.3350%)]. This body of evidence was not downgraded for imprecision.

[10] The sample size is not adequate (30 screening arm) and the effect estimate is not precise with a wide confidence interval [Proportion % = 20.0% (9.50%, 37.3%)]. This body of evidence was downgraded for imprecision.

[11] The sample size is not adequate (23 screening arm) and the effect estimate is not precise with a wide confidence interval [Proportion % = 13.0430% (4.5380%, 32.1270%)]. This body of evidence was downgraded for imprecision.
[12] The sample size is not adequate (7 screening arm) and the effect estimate is not precise with a wide confidence interval [Proportion % = 42.8570%(15.8220%, 74.9540%)]. This body of evidence was downgraded for imprecision.

Figure 1. Analytic Framework for Screening for Abdominal Aortic Aneurysm

(#) Numbers in brackets: indicate the CTFPHC's GRADE[13] rankings for each outcome (7-9=critical; 4-6=important; 1-3 not important and therefore not included here)



Key Questions

KQ1. What is the effect of one-time AAA screening using ultrasound on health outcomes in asymptomatic adults aged 50 years and older?

a. Does the effect of one-time screening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities.

b. Does the effect of one-time screening vary between different screening approaches (i.e. high risk versus low risk status)?

KQ2. What is the effect of rescreening for AAA using ultrasound on health outcomes including AAA incidence in previously screened asymptomatic adults aged 50 years and older?

a. Does the effect of rescreening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities.

b. Does the effect of rescreening vary between different time intervals?

KQ3. What are the harms associated with one-time and repeated AAA screening using ultrasound?

Figure 2a. PRISMA Flow Diagram: Screening Search Strategy

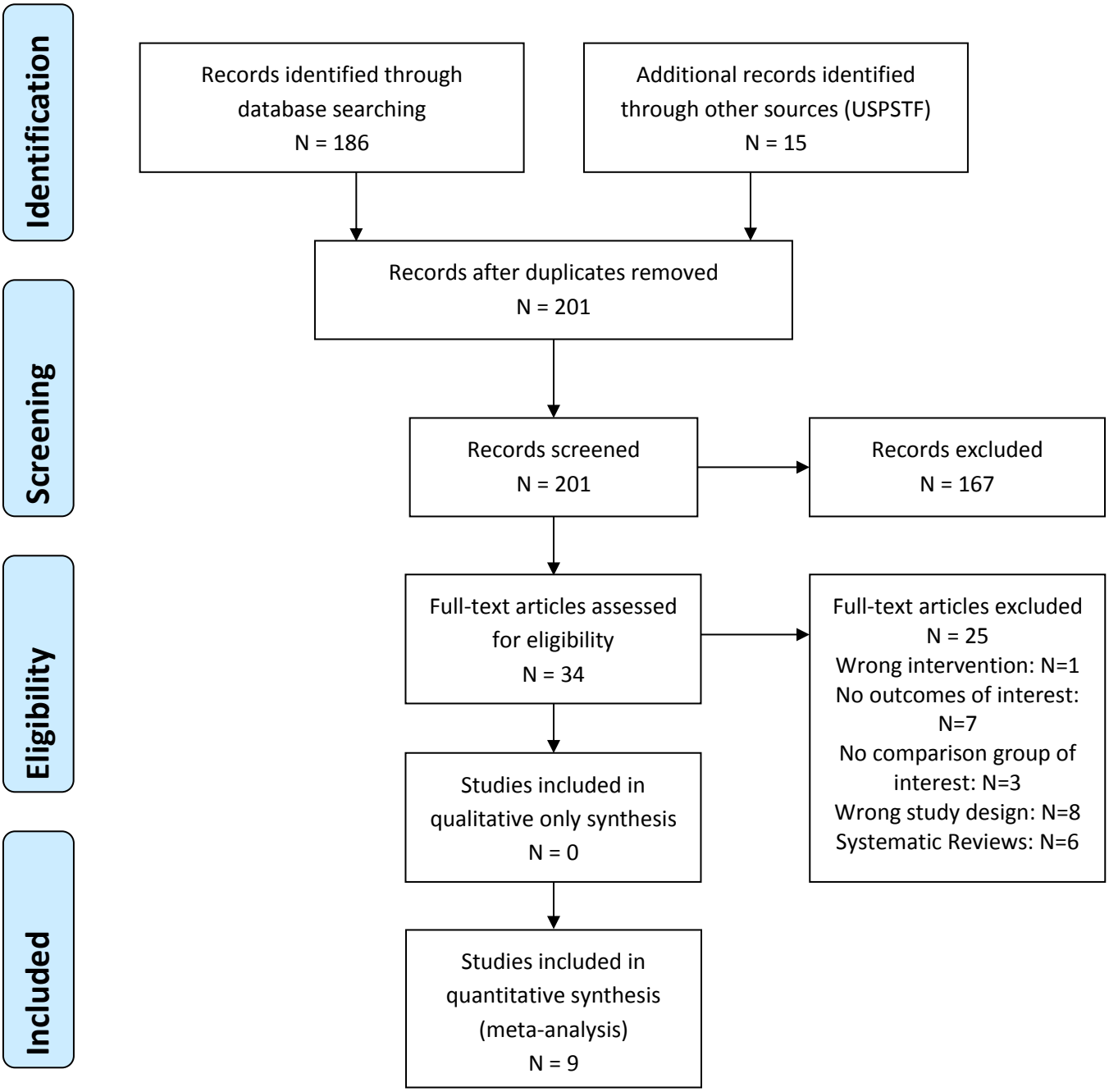


Figure 2b. PRISMA Flow Diagram: Overdiagnosis/ overtreatment Search Strategy

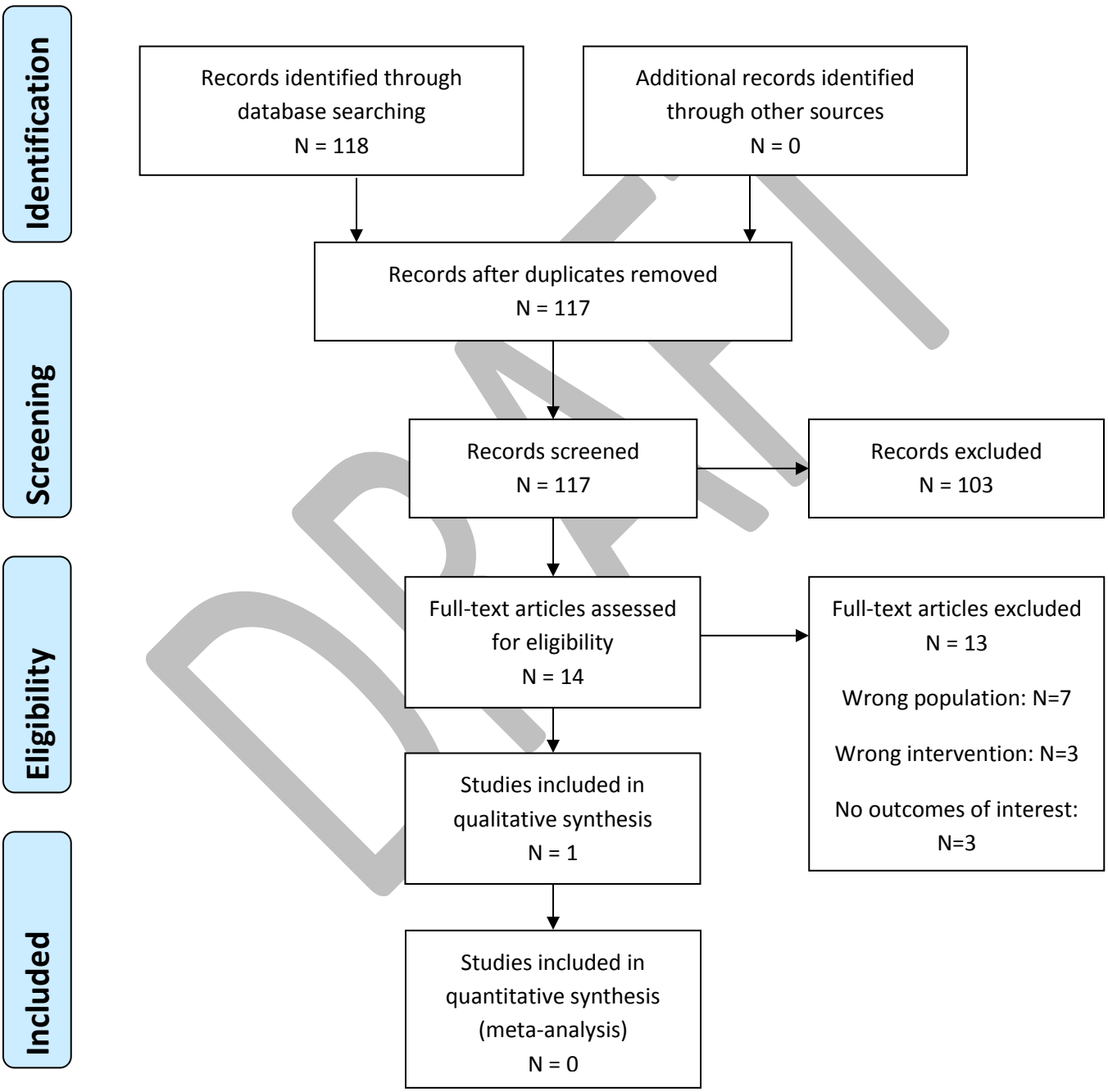


Table 1: Characteristics of Included Studies

STUDY/LOCATION	MASS[22-25]; UK
OBJECTIVE	The Multicentre Aneurysm Screening Study was designed to assess whether or not ultrasound screening for abdominal aortic aneurysms is beneficial
METHODS	**Design:** RCT **Recruitment:** men from 4 centres (Portsmouth, Southampton, Winchester, and Oxford) identified from family doctor lists and Health Authority lists, after obtaining the family doctor's permission **Exclusion Criteria:** study imposed no exclusion criteria other than sex and year of birth, but doctors informed investigators of recent deaths, and excluded: men who were terminally ill, had other serious health problems, and had a previous abdominal aortic aneurysm repair **Funding:** UK Medical Research Council and the Department of Health (G9533930; ISRCTN 37381646). T M Marteau was supported by the Welcome Trust.
PARTICIPANTS	**Sample:** n= 67,700, Intervention: n= 33,883, Control: n=33,887 **Loss to Follow-up:** Intervention: n=6, 679 did not attend screening; 322 were lost to clinical follow-up; Control: n=0 **Age:** Mean Age Overall (SD) 69.2 years (2.9); Ages ranged from 65-74 years **Sex:** 100% male *Mortality outcome data available for 97.9% of patients who were randomly assigned (n=66, 328)
INTERVENTION	**Description of Intervention:** ultrasound screening **Description of Control:** no screening **Frequency of Intervention:** one screen **Length of Follow-up:** 13.1 years

STUDY/LOCATION	Chichester [26-29]; UK
OBJECTIVE	To determine the effect of screening on the incidence of rupture abdominal aortic aneurysm
METHODS	**Design:** RCT **Recruitment:** participants were obtained for each general practice through the use of the practice register and Family Health Service lists. Participants in each practice were then randomized to control and screening groups. **Inclusion Criteria:** men and women aged 65 and older **Funding:** grants from the Department of Health, SWT Regional Health authority and local charities
PARTICIPANTS	**Sample:** n= 15,775, Intervention: n=7,887, Control n=7,888 **Loss to Follow-up:** Intervention n=2,493 did not attend screening; n=35 did not attend clinical follow-up*; Control: n=0

	Age: Mean Age (SD): NR; Aged 65-80 years **Sex (Female):** Intervention: n=4,682, Control: n=4,660 *Outcomes are presented for all patients lost
INTERVENTION	**Description of Intervention:** ultrasonographic screening **Description of Control:** no screening **Frequency of Intervention:** one screen **Length of Follow-up:** 15 years

STUDY/LOCATION	Viborg[30-33, 35]; Denmark
OBJECTIVE	To ascertain whether screening for AAA in men >65 years old reduces mortality
METHODS	**Design:** RCT **Recruitment:** all men born between 1921-1929 who lived in Viborg County, Denmark were randomized in blocks of 1000. In 1995-98, all participants who were 65 were randomized to either screening or control groups **Inclusion Criteria:** men >65 years of age living in Viborg County, Denmark **Funding:** National Health and Medical Research Council and the National Heart Foundation of Australia
PARTICIPANTS	**Sample:** n= 12,639, Intervention: n=6,333, Control n=6,306 **Loss to Follow-up:** Intervention: n=1,481 did not attend screening*; C=0 **Age:** Mean Age Overall 67.7 years (range: 64.3 to 73.8 years) **Sex:** 100% male *Outcomes are presented for all patients who did not attend screening
INTERVENTION	**Description of Intervention:** screening by abdominal ultrasonography **Description of Control:** usual care **Duration of Intervention:** one screen **Length of Follow-up:** 10 years

STUDY/LOCATION	Western Australia [36, 37]; Australia
OBJECTIVE	To assess whether screening for abdominal aortic aneurysms in men reduces mortality
METHODS	**Design:** RCT **Recruitment:** men identified from an electronic copy of the electoral roll, enrolment to vote being compulsory for all Australian adults **Exclusion Criteria:** too far away (35 km from Perth) **Funding:** National Health and Medical Research Council and the National Heart Foundation of Australia
PARTICIPANTS	**Sample:** n= 38,704, Intervention: n=19,352, Control n= 19,352 **Loss to Follow-up:** Intervention: n=5,303 did not attend screening; n=1,836 were ineligible; n=10 could not be scanned; Control: n=0

	Age: Mean Age (SD) Intervention 72.6 (4.7) years, Control: 72.6 (4.7) years; Ages ranged from 65-83 years **Sex:** 100% male
INTERVENTION	**Description of Intervention:** single ultrasound screen **Description of Control:** no screening **Duration of Intervention:** one screen **Length of Follow-up:** median follow-up: 43 months (27-61)

STUDY/LOCATION	Hafez [39]
OBJECTIVE	To determine predictors related to abdominal aortic aneurysm (AAA) development following a "normal" aortic ultrasound scan
METHODS	**Design:** Cohort **Recruitment:** the General Practitioners and the Local Health Authority provided lists of men selected on year of birth; patient details were cross-matched and individuals were then invited to attend an abdominal aortic ultrasound scan **Inclusion/ Exclusion Criteria:** NR **Funding:** NHS R&D support funding and local charitable donations
PARTICIPANTS	**Sample:** n= 22, 961 (first screen); n= 4, 308 (second screen) **Loss to Follow-up:** none **Age:** Median age 65.6 years **Sex:** 100% male
INTERVENTION	**Description of Intervention:** ultrasound screening **Frequency of Intervention:** repeat scans at 2 year intervals **Length of Follow-up:** 10 years

STUDY/LOCATION	Lederle[40]; US
OBJECTIVE	To determine the result of repeated screening for AAA after a 4 year interval
METHODS	**Design:** Cohort **Recruitment:** a subgroup of participants who had been screened for AAA as part of another study were invited to a second screening 4 years after first screen **Inclusion Criteria:** participants had to be participants in the original study; had infrarenal and suprarenal aortic diameter of 3.0 cm or less on first screen; no previous history of AAA **Funding:** Cooperative Studies Program of the Department of Veterans Affairs Office of Research and Development
PARTICIPANTS	**Sample:** n= 16, 643 (first screen); n=5,151 (selected for re-screening); n=2,622 (second screen) **Loss to Follow-up:** n=2,529 **Age:** Mean age (SD) of re-screening population With AAA 67.3 years (6.2 SD),

	No AAA: 66.0 years (6.7 SD); Ages ranged from 50-79 years **Sex:** 100% male
INTERVENTION	**Description of Intervention:** screening with ultrasound **Frequency of Intervention:** 2 screens; second screen at 4 years **Length of Follow-up:** 4 years

STUDY/LOCATION	Svensjö[41]; Sweden
OBJECTIVE	To determine the fate of a 65-year-old male population 5 years following an invitation to an aortic ultrasound (US) examination
METHODS	**Design:** Cohort **Recruitment:** all men born 1941 and 1942 in county of Uppsala identified in the National Population Registry were invited to screening for AAA with ultrasound at age 65 years during the years 2006 and 2007 **Exclusion Criteria:** individuals with a history of AAA repair **Funding:** Financial support provided by the Swedish Research Council (grant 2012-1978), the Swedish Heart-Lung Foundation, and the Centre for Clinical Research (CKF), Dalarna, Sweden.
PARTICIPANTS	**Sample:** n= 3, 268 (invited to first screen); n= 2,739 (first screen); n= 2,811 (invited for re-screening); n=2, 094 (repeat screen) **Loss to Follow-up:** n=717 did not attend re-screening **Age:** all participants were 65 years at first screen **Sex:** 100% male
INTERVENTION	**Description of Intervention:** screening with ultrasound **Frequency of Intervention:** 2 screens; second screen at 5 years **Length of Follow-up:** 5 years

Table 2: Summary of Included Studies

Study	Recruitment dates	Country	Age	Sex (% Male)	Intervention	Comparator	Benefits Outcomes	Harms Outcomes
RCTs (KQ1 and KQ3)								
MASS[22-25]	1997-1999	UK	Range: 65-74 years Mean age overall: 69.2 (2.9 SD)	100% male	One time screening with ultrasound	No screening	AAA mortality All cause mortality AAA rupture rates	30 day mortality – AAA operations 30 day mortality – elective AAA operations 30 day mortality – emergency AAA operations AAA operations Elective AAA operations Emergency AAA operations HRQoL
Chichester[26-29]	1989	UK	Range: 65-80 years Mean age: NR	Intervention: 41% male; Control: 41% male	One time screening with ultrasound	No screening	AAA mortality All cause mortality AAA rupture	30 day mortality – AAA operations 30 day mortality – elective AAA operations 30 day mortality – emergency AAA operations AAA operations Elective AAA operations Emergency AAA operations
Viborg[30-35]	1994	Denmark	Range: 64.3-73.8 years Mean age: 67.7 years	100% male	One time screening with ultrasound	Usual care	AAA mortality All cause mortality AAA rupture	30 day mortality – AAA operations 30 day mortality – elective AAA operations 30 day mortality – emergency AAA operations AAA operations Elective AAA operations Emergency AAA operations
Western Australia[36, 37]	2004 (publication date)	Australia	Range: 65-83 years Mean age: Intervention 72.6 (4.7 SD) years; Control: 72.6 (4.7	100% male	One time screening with ultrasound	No screening	AAA mortality All cause mortality AAA rupture	30 day mortality – AAA operations 30 day mortality – elective AAA operations 30 day mortality – emergency AAA operations

Study	Recruitment dates	Country	Age	Sex (% Male)	Intervention	Comparator	Benefits Outcomes	Harms Outcomes
			SD) years					AAA operations Elective AAA operations Emergency AAA operations HRQoL
Uncontrolled observational studies (KQ2 and KQ3)								
Hafez[39]	1983	UK	Range: 64.4-76.6 years Median age: 65.5 years	100% male	Ultrasound screening with repeat scan at 2 yearly intervals or 5 years after the first scan	-	AAA incidence AAA mortality All cause mortality AAA rupture	30 day mortality – AAA operations 30 day mortality – elective AAA operations 30 day mortality – emergency AAA operations
Lederle[40]	1992	US	Range: 50-79 years Mean age: with AAA 67.3 years (6.2SD); no AAA: 66.0 years (6.7 SD)	100% male	Two screens with ultrasound; 4 years apart	-	AAA incidence	-
Svensjö[41]	2006-2007	Sweden	65 years at first screen	100% male	Two screens with ultrasound; 5 years apart	-	AAA incidence	-
Uncontrolled observational studies (KQ3)								
Wanhainen[43]	NR	Sweden	Range: 65-75 years	With AAA: 84% male; No AAA: 78% male	Screening with ultrasound; completion of Short-Form 56 (SF-36)	-	-	HRQoL
Lesjack[44]	NR	Australia	Range: 65-74 years	100% male	Screening with ultrasound; completion of MOSF36	-	-	HRQoL

Table 3: Cochrane Risk of Bias (RCTs)

Study	Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Reporting	Selective Outcome Reporting	Other Risk of Bias	Overall
MASS[22-25]	L	L	L	L	L	L	L
Chichester[26-29]	L	U	U	L	L	H	U
Viborg[30-35]	U	U	L	L	L	H	U
Western Australia[36, 37]	U	U	L	L	L	L	U

Table 4: Newcastle-Ottawa Scale (Cohort Studies)

Study	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Comparability of cohorts	Assessment of outcome	Was follow-up long enough	Adequacy of follow up cohorts
Hafez[39]	truly representative	n/a*	secure record (eg. surgical records)	yes	n/a	independent blind assessment	yes	no statement
Lederle[40]	truly representative	n/a	secure record (eg. surgical records)	no	n/a	independent blind assessment	yes	subjects lost to follow up unlikely to introduce bias
Svensjö[41]	truly representative	n/a	secure record (eg. surgical records)	yes	n/a	independent blind assessment	yes	subjects lost to follow up unlikely to introduce bias

*n/a: not applicable

Appendix A: Screening Search Strategy

Abdominal Aortic Aneurysm Detailed Search Strategies

Medline, Cochrane Central-OVID
April 20, 2015
1. Aortic Aneurysm, Abdominal/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. mass screening/
5. screen*.ti,ab.
6. 4 or 5
7. 3 and 6
8. limit 7 to (english or french)
9. limit 8 to ed=20130131-20141030
10. limit 8 to ed=20130131-20150420
11. limit 10 to (case reports or comment or editorial)
12. 10 not 11

EMBASE-Screening
April 20 2015
1. abdominal aorta aneurysm/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. screening/ or mass screening/ or screening test/
5. screen*.ti,ab.
6. 4 or 5
7. 3 and 6
8. limit 7 to (english or french)
9. limit 8 to em=201304-201444
10. limit 8 to (book or book series or conference paper or editorial or letter or note)
11. 8 not 10
12. limit 11 to em=201304-2015016

Appendix B: AMSTAR

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	✓ Yes □ No □ Can't answer □ Not applicable
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	✓ Yes □ No □ Can't answer □ Not applicable
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	✓Yes □ No □ Can't answer □ Not applicable
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	□ Yes ✓ No □ Can't answer □ Not applicable

5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	✓ Yes □ No □ Can't answer □ Not applicable
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	✓ Yes □ No □ Can't answer □ Not applicable
7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	✓ Yes □ No □ Can't answer □ Not applicable
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	✓ Yes □ No □ Can't answer □ Not applicable

9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).	✓ Yes □ No □ Can't answer □ Not applicable
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	✓ Yes □ No □ Can't answer □ Not applicable
11. Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	✓ Yes □ No □ Can't answer □ Not applicable

Appendix C: PRESS

The following document is a peer review of the search strategy used by the USPSTF in their review Primary Care Screening for Abdominal Aortic Aneurysm: A Systematic Evidence Review for the U.S. Preventive Services Task Force.[5] The assessment of this strategy is to evaluate whether or not it is suitable for the purposes of our update. As such, the detailed search strategy on the form is the relevant part of the strategy used by the USPSTF in their review while the key questions are those from our update. The evaluation on page 3 of the form is what changes/adaptations, if any, are necessary for the search to find the literature needed/required address our questions.

PRESS EBC Search Submission

Searcher's Name: USPSTF **E-mail:**

Date submitted: **Date needed by:**

Note to peer reviewers – please enter your information in the Peer Review Assessment area

Remember: this peer review only pertains to your MEDLINE search strategy.

Search question (Describe the purpose of the search)

KQ1. What is the effect of one-time AAA screening using ultrasound on health outcomes in asymptomatic adults aged 50 years and older?

a. Does the effect of one-time screening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities.

b. Does the effect of one-time screening vary between different screening approaches (i.e. high risk vs low risk status)?

KQ2. What is the effect of rescreening for AAA using ultrasound on health outcomes including AAA incidence in previously screened asymptomatic adults aged 50 years and older?

a. Does the effect of rescreening vary between men and women, smokers and nonsmokers, older (≥65 years) and younger (<65 years) adults, adults with and without a family history of AAA, and adults of different races/ethnicities.

b. Does the effect of rescreening vary between different time intervals?

KQ3. What are the harms associated with one-time and repeated AAA screening using ultrasound?

PICO format (Outline the PICO for your question, i.e., the Patient, Intervention, Comparison and Outcome)

P: asymptomatic adults aged 50 years and older

I: General or targeted screening with ultrasound

C: KQ1: no screening, comparison of difference screening approaches (i.e. high risk vs low risk groups)

KQ2: no screening or one-time AAA screening using ultrasound, different repeated screening approaches, or no comparison/nonexposure

KQ3: no comparison group required

O: KQ1 and KQ2: All-cause mortality (9), AAA-related mortality (9), AAA rupture rate (8), AAA incidence (KQ2 only) (6)

KQ3: anxiety from risk labeling (5), anxiety of mortality (6), false-positive screening-related procedure (8), 30 day post-operative mortality (9), surgical procedure (9)s, and quality of life (8)

Inclusion criteria (List criteria such as age groups, study designs, to be included)

Exclusion criteria (List criteria such as study designs, to be excluded)

-case reports, comments, editorials

Was a search filter applied? (Remember this pertains only to the MEDLINE strategy)

Yes ☐ **No** X

If yes, which one?

Cochrane hedge: PUBMED clinical query:

Haynes/McKibbon et al: SIGN (Scottish):

CRD (UK): Robinson and Dickerson:

Other:

MEDLINE search interface used

EBSCO ☐ **OVID** X *PubMED* ☐ *Other* _____

Has the search strategy been adapted (i.e., subject heading and terms reviewed) for other databases? Please check all that apply.

Ageline	☐
AMED	☐
C2-SPCTRE	☐
CINAHL	☐
Cochrane Database of Systematic Reviews (CDSR; Cochrane Reviews)	☐
Cochrane Central Register of Controlled Trials (CENTRAL; Clinical Trials)	X
Cochrane Methodology Register (CMR; Methods Studies)	☐
Cochrane Library (all databases)	☐
Database of Abstracts of Reviews of Effects (DARE; Other Reviews)	☐
Embase	X
ERIC	☐
ICTRP (International Clinical Trials Registry Platform)	☐
LILACS (Latin American and Caribbean Health Sciences Literature)	☐
MEDLINE	☐
PreMEDLINE	☐
PsycINFO	☐
Other PubMed (limited search)	X
Other	☐

Other notes or comments that you feel would be useful for the peer reviewer?

The PubMed search is for any relevant publisher-supplied non-indexed citations

Please paste your MEDLINE strategy here:

1. Aortic Aneurysm, Abdominal/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. mass screening/
5. screen*.ti,ab.
6. 4 or 5
7. 3 and 6
8. limit 7 to (english or french)
9. limit 8 to ed=20130131-current
10. limit 9 to (case reports or comment or editorial)
11. 9 not 10

Peer Review Assessment

[For peer reviewers only]

Peer reviewer's name: Maureen Rice—(MERSC librarian)

E-mail:

Date completed: March 10, 2015

Please select the one most appropriate answer for each element

	Adequate	Adequate with revisions*	Needs revision*
1. Translation of the research question	x		
2. Boolean and proximity operators	x		
3. Subject headings	x		
4. Natural language / free-text	x		
5. Spelling, syntax and line numbers	x		
6. Limits and filters		x	
7. Search strategy adaptations	x		

* Provide an explanation or example for "Adequate with revisions" and "needs revision":

We will be including both French and English citations

Other Comments (please limit to 3-5 sentences):

Appendix D:

Overdiagnosis Search Strategies

Medline-OVID

April 14 2015

1. Aortic Aneurysm, Abdominal/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. overdiagnos*.mp.
5. over diagnos*.mp.
6. False Positive Reactions/
7. false positive.mp.
8. ((over or unnecessary or excessive) adj (diagnosis or testing or procedures)).tw.
9. diagnostic error/
10. or/4-9
11. 3 and 10
12. animals/ not (animals/ and humans/)
13. 11 not 12
14. limit 13 to (english or french)
15. limit 14 to yr="2004 -Current"

EMBASE-OVID

April 14, 2015

1. abdominal aorta aneurysm/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. overdiagnos*.mp.
5. over diagnos*.mp.
6. false positive result/
7. false positive.mp.
8. ((over or unnecessary or excessive) adj (diagnosis or testing or procedures)).tw.
9. diagnostic error/
10. or/4-9
11. 3 and 10
12. limit 11 to (english or french)
13. limit 12 to yr="2004 -Current"

Cochrane Central-OVID

April 14, 2015

1. Aortic Aneurysm, Abdominal/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. overdiagnos*.mp.
5. over diagnos*.mp.
6. False Positive Reactions/
7. false positive.mp.
8. ((over or unnecessary or excessive) adj (diagnosis or testing or procedures)).tw.
9. diagnostic error/
10. or/4-9
11. 3 and 10
12. limit 11 to yr="2004 -Current"

Appendix E:

Contextual Question Search

Patient Preferences

Medline-OVID
March 11 2015
1."patient acceptance of health care"/
2. patient compliance/
3. exp patient participation/
4. patient satisfaction/
5. patient preference/
6. "treatment refusal"/
7. consumer satisfaction/
8. ((parent? or guardian*) adj3 (acceptance or preference? or satisfaction or experience?)).tw.
9. (consumer? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
10. (patient? adj3 (acceptance or perference? or satisfaction or experience?)).tw.
11. willingness to pay.tw.
12. ((conjoint or contingent) adj3 (valuation or analysis)).tw.
13. Choice Behavior/
14. standard gamble.ti.
15. standard gamble.tw.
16. time trade off.tw.
17. choice model?ing.mp.
18. survey preferences.mp.
19. preference?.tw.
20. or/1-19
21. Aortic Aneurysm, Abdominal/
22. abdominal aortic aneurysm*.ti,ab.
23. 21 or 22
24. 20 and 23
25. limit 24 to (english)
26. limit 25 to yr="2004 - 2015"

EMBASE-OVID
March 11, 2015
1. patient attitude/
2. exp patient compliance/
3. patient participation/
4. patient preference/
5. patient satisfaction/
6. refusal to participate/
7. treatment refusal/
8. decision making/ or patient decision making/
9. decision making/

10. consumer attitude/
11. ((parent? or guardian*) adj3 (acceptance or preference? or satisfaction or experience?)).tw.
12. (consumer? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
13. (patient? adj3 (acceptance or perference? or satisfaction or experience?)).tw.
14. (patient? adj3 (acceptance or perference? or satisfaction)).tw.
15. willingness to pay.tw.
16. ((conjoint or contingent) adj3 (valuation or analysis)).tw.
17. standard gamble.tw.
18. time trade off.tw.
19. choice model?ing.mp.
20. preference?.tw.
21. or/1-20
22. abdominal aorta aneurysm/
23. abdominal aortic aneurysm*.ti,ab.
24. 22 or 23
25. screening/ or mass screening/ or screening test/
26. screen*.ti,ab.
27. 25 or 26
28. 24 and 27
29. 21 and 28
30. limit 29 to english language
31. limit 30 to yr="2004 -Current

PsycINFO-OVID
March 11 2015
1. client attitudes/
2. client satisfaction/
3. exp preference measures/
4. preferences/
5. "patient preferences".id.
6. decision making/ or choice behavior/
7. ((parent? or guardian*) adj3 (acceptance or preference? or satisfaction or experience?)).tw.
8. (consumer? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
9. (client? adj3 (acceptance or preference? or satisfaction or experience?)).tw.
10. (patient? adj3 (acceptance or perference? or satisfaction or experience?)).tw.
11. willingness to pay.tw.
12. ((conjoint or contingent) adj3 (valuation or analysis)).tw.
13. standard gamble.tw.
14. time trade off.tw.
15. choice model?ing.mp.
16. preference?.tw.
17. or/1-6
18. abdominal aortic aneurysm*.mp.
19. 17 and 18
20. limit 19 to yr=2004-Curent

Cost of Screening

Medline-OVID
March 11, 2015
1. Aortic Aneurysm, Abdominal/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. mass screening/
5. screen*.ti,ab.
6. 4 or 5
7. 3 and 6
8. limit 7 to (english)
9. limit 8 to "costs (maximizes sensitivity)"
10.. limit 14 to yr="2004 - 2015"

EMBASE-OVID
March 11, 2015
1. abdominal aorta aneurysm/
2. abdominal aortic aneurysm*.ti,ab.
3. 1 or 2
4. screening/ or mass screening/ or screening test/
5. screen*.ti,ab.
6. 4 or 5
7. 3 and 6
8. limit 7 to (english or french)
9. limit 8 to em=201304-201444
10. limit 8 to (book or book series or conference paper or editorial or letter or note)
11. 8 not 10
12. limit 11 to yr=2004-Curent
13. limit 8 to "economics (best balance of sensitivity and specificity)"

Hand Held Ultra Sound
Medline-OVID
February 5, 2015
1. Aortic Aneurysm, Abdominal/us [Ultrasonography]
2. "Point-of-Care Systems"/
3. ((portable or hand held or office based or point of care) adj3 ultrasound).tw.
4. 2 or 3
5. 1 and 4
6. limit 5 to yr="2011 -Current"
7. limit 6 to (english)
8. limit 7 to (comment or editorial or letter or news)
9. 7 not 8

EMBASE-OVID
February 5, 2015
1. "point of care testing"/
2. *"abdominal aorta aneurysm"/
3. 1 and 2
4. ((portable or hand held or office based or point of care) adj3 ultrasound).tw.
5. 2 and 4
6. 3 or 5
7. limit 6 to yr="2011 - current"
8. limit 7 to (english or french)
9. limit 8 to (book or book series or conference abstract or editorial or letter or note)
10. 8 not 9

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