Effect of abdominal aortic aneurysm screening

Report from Kunnskapssenteret (Norwegian Knowledge Centre for the Health Services)
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Health Technology Assessment (Metodevurdering)

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Background: Abdominal aortic aneurysm (AAA) is a dilatation of the abdominal aortic artery. AAA rupture is a dramatic, lethal emergency condition with a high risk of death, even with treatment. The larger the dilation, the higher is the risk of rupture. Screening programs for AAA are used to identify aneurysms and individuals potentially at a high risk of AAA rupture or AAAs so-called suitable for repair. Those identified as suitable for repair, usually by ultrasound scan, are offered preventive (elective) surgery to reduce their individual risk of rupture. In Norway, the number of operations (urgent and elective) is approximately 800 per year. • The European Network for Health Technology Assessment (EUnetHTA) produces collaborative health technology assessments (HTAs) intended to be used by all countries to avoid duplication and waste of resources. The Norwegian Knowledge Centre for the Health Services (NOKC) has taken advantage of the HTA from EUnetHTA on the effect of AAA-screening published January 2013 to produce this systematic review. In terms of clinical effectiveness and safety, main conclusions are: • Evidence shows no reduction in overall morta- *(continued)*

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(continued from page one) lity, neither in men nor in women, resulting from AAA screening (moderate quality of evidence. • AAA screening can however be beneficial in men over 65 years of age, as it can reduce AAA-related mortality by nearly half in the mid- and long-term (low to moderate quality of evidence). • In women aged 65 years and more, however, data indicate no change in AAA-related mortality (very low quality of evidence). • Safety of AAA screening is mainly related to the subsequent surgical intervention that follows detection of an AAA with high risk of rupture (eligible for repair). • Hospital volume, surgeon volume, and surgeon's specialization in vascular surgery are factors associated with mortality when an AAA is eligible for repair.

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The Centre is organized under The Norwegian Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

We would like to thank Kirsten Krohg Sørensen and Anne Karin Lindahl for having contributed with their valuable expertise to this project.

Norwegian Knowledge Centre for the Health Services
Oslo, March 2014

Key messages

Abdominal aortic aneurysm (AAA) is a dilatation of the abdominal aortic artery. AAA rupture is a dramatic, lethal emergency condition with a high risk of death, even with treatment. The larger the dilation, the higher is the risk of rupture. Screening programs for AAA are used to identify aneurysms and individuals potentially at a high risk of AAA rupture or AAAs so-called suitable for repair. Those identified as suitable for repair, usually by ultrasound scan, are offered preventive (elective) surgery to reduce their individual risk of rupture. In Norway, the number of operations (urgent and elective) is approximately 800 per year.

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- Evidence shows no reduction in overall mortality, neither in men nor in women, resulting from AAA screening (moderate quality of evidence).
- AAA screening can however be beneficial in men over 65 years of age, as it can reduce AAA-related mortality by nearly half in the mid- and long-term (low to moderate quality of evidence).
- In women aged 65 years and more, however, data indicate no change in AAA-related mortality (very low quality of evidence).
- Safety of AAA screening is mainly related to the subsequent surgical intervention that follows detection of an AAA with high risk of rupture (eligible for repair).
- Hospital volume, surgeon volume, and surgeon's specialization in vascular surgery are factors associated with mortality when an AAA is eligible for repair.

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Effect of abdominal aortic aneurysm screening

Type of publication:
Health technology assessment (HTA) is a multidisciplinary process that summarizes information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the development of safe, effective health policies that are patient focused and that seek to achieve best value.

Doesn't answer everything:

- Excludes studies that fall outside of the inclusion criteria
- No recommendations

Publisher:

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Kirsten Krogh Sørensen og Anne Karin Lindahl

Executive summary

Background

Abdominal aortic aneurysm (AAA) is a dilatation of the abdominal aortic artery. AAA rupture is a dramatic, lethal emergency condition with a high risk of death even when treated, and the risk of rupture increases with the diameter of the dilatation. 1–2% of all deaths in the Western world are estimated to be caused by AAA ruptures. Although it varies across European countries, the percentage of men at high risk of AAA has been increasing steadily over the last 20 years. Screening programs to identify aneurysms and potential individuals at a high risk of AAA rupture have thus been considered as a potentially useful healthcare intervention in European countries, even if in most countries, including Norway, no systematic nationwide screening program has yet been implemented. Those individuals identified, usually through ultrasound scan examination, are offered preventive surgery (open or endovascular) to reduce the negative consequences of a spontaneous rupture if the aneurysm is large enough, or optimal medical treatment and follow-up if the aneurysm is less than the surgical treatment threshold (usually 50-55 mm).

Objective

In light of the increased interest in AAA screening in Norway (approximately 800 patients are operated per year in our country) and elsewhere, this report aims at assessing clinical effectiveness and safety of AAA screening using results from a HTA report carried out 2010-2012 by the European network for Health Technology Assessment (EUnetHTA).

Method

To produce the European HTA on the effect of AAA screening, the HTA Core Model® tool developed by EUnetHTA was used. The idea behind EUnetHTA's Core Model is to provide a framework for structuring relevant HTA information while at the same time facilitating use and adaptation of the information in different countries and settings. The Model is based on nine domains of evaluation: 1) Health problem and current use of the technology, 2) Description and technical characteristics of technology, 3) Clinical effectiveness, 4) Safety, 5) Costs and economic evaluation, 6) Eth-

ical analysis, 7) Organizational aspects, 8) Social aspects, and 9) Legal aspects. In this report, we have used all results from domains 3) and 4), while we have extracted the most relevant information from domains 1) and 2) for the background chapter.

In the common European HTA, a basic literature search was carried out for all domains (including the assessment of clinical effectiveness and safety used in this report). Additional searches were necessary for assessing safety. Criteria for inclusion of the population were all men and women aged 64 or more. The intervention was population-based systematic AAA screening, meaning detection of AAA in unruptured phase in order to treat those aneurysms with high risk of rupture (through one single invitation for the whole target population to do one ultrasound scan examination). The comparison was no population-based AAA screening which included incidental detection of AAA without age or sex limitation while performing abdominal ultrasound examinations due to other/unclear clinical indications and various opportunistic AAA-screening practices. Selection of literature was done according to these pre-defined inclusion criteria, and when appropriate, quality of evidence for the different outcomes was assessed using the GRADE instrument.

Results

Clinical effectiveness

Screening for AAA can result in a reduction of AAA-related mortality both in the long term (after 7 to 15 years) and in shorter term (after 3.5 to 5 years) in men, as evidence shows an approximately 50% significant reduction (low to moderate quality of evidence), whereas there appears to be no change in women. The evidence, however, does not support a reduction in long-term or shorter term overall mortality as a result of AAA screening neither in men nor in women. In terms of progression of the condition, evidence indicates that AAA screening possibly can reduce the incidence of ruptured AAA in men, but this does not seem to apply for women. For outcomes related to quality of life and patient satisfaction, evidence supports a possible reduction in anxiety and depression in AAA-screened individuals, but no change in quality of life. However, acceptance rates indicate that overall, patients are willing to be screened for AAA as evidence shows that acceptance of invitations to be screened is highest in men (81%) and women (73%) aged 65, and decreases with increasing age. Regarding outcomes related to change in management, there is no evidence on how use of the test may change physicians' management decisions or whether AAA screening detects other potential health conditions that may impact subsequent management decisions. However, AAA screening may modify the need for other technologies and resources in terms of planned and emergency operations as evidence shows that AAA-screened men both in the long-term (7 to 15 years) and in the medium term (3.5 to 5 years) have around 50% more planned operations and correspondingly fewer emergency operations than non-screened men (low quality of evidence). Intra- and inter-observer variation in ultrasound aorta diameter measure-

ments is the only outcome related to accuracy that has been assessed in the included literature, which indicates overall acceptable intra-observer repeatability and acceptable inter-observer reproducibility. However, the evidence is hampered by the fact that primary reliability and agreement studies cannot be assessed systematically across studies with regard to their quality. In addition, there are large variations in settings, examiner qualifications and training, sonography equipment and statistical analyses. Hence, the evidence does not allow any definite conclusions to be drawn regarding the importance of experience or background discipline.

Safety

AAA screening programs can cause harm to the screened subjects due to the expected increase in number of detected AAAs (increased incidence) and consequently the increased number of operations (subsequent surgical interventions that follow detection of AAAs with high risk of rupture) with potential risks for the patients. This is the main issue related to safety of AAA-screening. Hospital volume, surgeon volume, and surgeon's specialization in vascular surgery are associated with mortality when an AAA is detected and repaired. There may also be psychological consequences, as for instance anxiety related to detection of an AAA. In addition, unnecessary stress may be engendered by false-positive findings using AAA screening, but literature is scarce.

Discussion

While there is evidence for a benefit of AAA screening regarding clinical effectiveness, the evidence material on safety issues is poor. We should, however, bear in mind the importance of age, gender, preoperative morbidity, smoking and aneurysm size. These are relevant risk factors that may affect the outcome of surgical interventions following detection of an AAA suitable for repair (i.e. with high risk of rupture), hence the final outcome of an AAA screening program. In addition, detection of AAA would consequently lead to improved secondary prophylactic treatment of vascular risk factors, and thus reduce the risk of further enlargement of the AAA.

Conclusion

Evidence from the literature indicates that AAA screening can be beneficial in men over 65 years of age, as it can reduce AAA-related mortality by nearly 50% in the mid- and long-term. However, this is not likely to be the case in women, but here the evidence is poor. In terms of overall mortality, AAA-screening does not seem to have any effect neither in men nor in women. Moreover, AAA screening may result in a decrease of emergency operations for ruptured AAA, and an increase in elective AAA surgery. In terms of safety, serious harms are mainly related to the surgical intervention following detection of an AAA eligible for repair.

Hovedfunn (norsk)

Et abdominalt aortaaneurisme (AAA) er en svekkelse i åreveggen av bukdelen av hovedpulsåren som resulterer i en unormal utposning. Dersom utposningen sprekker (ruptur), er tilstanden livstruende og krever akutt operasjon / intervensjon. Jo større et AAA er, jo større er sjansene for ruptur. Screening for AAA har derfor som mål å identifisere individer med høy risiko for AAA-ruptur. De som får påvist slik AAA, vanligvis ved bruk av ultralyd, får tilbud om en preventiv operasjon for å redusere risikoen for ruptur. I Norge er antall operasjoner (akutte og elektive) ca. 800 per år. EUnetHTA, det europeiske nettverket for HTA (Health Technology Assessment - på norsk: metodevurdering) utarbeider felles metodevurderinger, som er ment å skulle brukes av alle land for å unngå dobbeltarbeid og sløsing av ressurser. I denne systematiske oversikten om effekt og sikkerhet av AAA-screening, har derfor Kunnskapssenteret benyttet seg av resultatene fra metodevurderingen om AAA-screening av EUnetHTA publisert i januar 2013. Hovedkonklusjonene er følgende:

- Dokumentasjonen viser ingen reduksjon i totaldødelighet hos menn eller kvinner som resultat av AAA-screening (moderat kvalitet på dokumentasjonen).

- AAA-screening kan ha god effekt hos menn over 65 år, siden forskningsdata viser at dødeligheten forårsaket av aneurismer nesten halveres både på kort og lang sikt (lav til moderat kvalitet på dokumentasjonen).

- Det er ingen endring i AAA-relatert dødelighet hos kvinner over 65 år, men det er usikkerhet knyttet dataene (svært lav kvalitet på dokumentasjonen).

- Sikkerhet rundt AAA screening er hovedsakelig knyttet til det kirurgiske inngrepet som eventuelt følger påvisning av et AAA når operasjonsindikasjon foreligger.

- Sykehusvolum og antall AAA-operasjoner en kirurg jevnlig utfører, i tillegg til kirurgens nivå av spesialisering innen karkirurgi, er faktorer som påvirker dødelighet som følge av AAA screening.

Tittel:
Effekt av abdominal aorta aneurisme screening

Publikasjonstype:
En metodevurdering er resultatet av å
- innhente
- kritisk vurdere og
- sammenfatte
relevante forskningsresultater ved hjelp av forhåndsdefinerte og eksplisitte metoder.

Minst ett av følgende tillegg er også med:
helseøkonomisk evaluering, vurdering av konsekvenser for etikk, jus, organisasjon eller sosiale forhold

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Svarer ikke på alt:

- Ingen studier utenfor de eksplisitte inklusjonskriteriene
- Ingen anbefalinger

Hvem står bak denne rapporten?

Nasjonalt kunnskapssenter for helsetjenesten

Fagfeller:

Kirsten Krogh Sørensen og Anne Karin Lindahl

Sammendrag (norsk)

Bakgrunn

Et abdominalt aortaaneurisme, også kalt AAA eller trippel A, er en svekkelse i åreveggen av bukaorta (bukdelen av hovedpulsåren) som resulterer i en unormal utposning av åren. Tilstanden er livstruende dersom utposningen sprekker (ruptur) og krever akutt operasjon. Risikoen for ruptur øker med utposningens diameter. Ruptur av AAA er årsak til 1–2 % av dødsfallene i den vestlige verden. Selv om det er variasjoner mellom de ulike europeiske landene, har prosenten av menn med høy risiko for AAA økt jevnlig de siste 20 årene. I enkelte europeiske land har man ansett AAA-screening som et gunstig tiltak i helsetjenesten og derfor iverksatt screeningprogrammer for å identifisere individer med høy risiko for AAA-ruptur. Men i de fleste land, deriblant Norge, er AAA-screening fortsatt ikke systematisk implementert. De som får påvist høy-risiko AAA, vanligvis ved bruk av ultralyd, blir tilbudt en preventiv operasjon for å redusere risikoen for ruptur. Operasjonen foregår enten ved åpen operasjon eller ved innvendig armering av åren (behandling med stentgraft).

Problemstilling

Målet med denne rapporten å vurdere klinisk effekt og sikkerhet av AAA-screening ved bruk av resultatene fra en felles europeisk metodevurdering eller Health Technology Assessment (HTA) utført av det europeiske nettverket for HTA (EUnetHTA) i perioden 2010-2012.

Metode

Verktøyet HTA Core Model® utviklet av EUnetHTA ble brukt for å produsere den europeiske metodevurderingen om AAA-screening. Ideen bak denne modellen er å danne et rammeverk for å strukturere informasjonen, samtidig som den tilrettelegger for bruk av resultatene og tilpasning av disse til ulike land og settinger. Modellen inndeler metodevurderingen i 9 såkalte domener: 1) helseproblemet og status for bruk av teknologien, 2) beskrivelse av teknologien og dens egenskaper, 3) klinisk effekt, 4) sikkerhet, 5) kostnadsevaluering, 6) etikk, 7) organiserings-, 8) sosiale-, og 9) juridiske aspekter. I denne systematiske oversikten har vi brukt alle resultatene

fra domenene 3) og 4), mens vi bare har brukt den mest relevante informasjonen fra domenene 1) og 2) for bakgrunnskapittelet.

I den europeiske metodevurderingen ble det utført et felles litteratursøk for alle domenene, (ekstrasøk trengtes for vurdering av sikkerhet). Inklusjonskriteriene for populasjonen var alle menn og kvinner i en alder av 64 eller mer. Intervensjonen var definert som populasjonsbasert systematisk AAA-screening, som innebar påvisning av AAA som ikke var sprukket (rumpert), for å kunne behandle de aneurismene med høy risiko for ruptur (ved å invitere hele målpopulasjonen til én ultralydundersøkelse). Dette skulle sammenlignes med ikke-populasjonsbasert AAA-screening, dvs. tilfeldig oppdagelse av AAA uten alders- eller kjønnsbegrensninger ved ultralydundersøkelse gjort på bakgrunn av en annen eller en ukjent indikasjon, eller tilfeldig AAA-screening undersøkelse. Relevant litteratur ble valgt ut på bakgrunn av inklusjonskriteriene, og når det var hensiktsmessig, ble kvaliteten på dokumentasjonen for utfallene vurdert ved hjelp av GRADE-verktøyet.

Resultat

Klinisk effekt

Screening for AAA kan medføre reduksjon i AAA-relatert dødelighet hos menn både på lang (etter 7 til 15 år) og kortere sikt (etter 3,5 til 5 år), da forskningsdata viser ca. 50 % signifikant reduksjon (lav til moderat kvalitet på dokumentasjonen); mens det ikke ser ut til å være noen effekt på dødelighet forårsaket av AAA hos kvinner. Den totale dødeligheten derimot er ikke redusert, verken på lang eller kort sikt. Med hensyn til videre utvikling av tilstanden viser resultatene at AAA-screening kan redusere forekomsten av AAA-ruptur hos menn, men dette er trolig ikke tilfellet hos kvinner. For utfall forbundet med livskvalitet og pasientenes tilfredshet støtter dokumentasjonen at AAA-screening kan redusere angst og depresjon, men uten å påvirke livskvaliteten. Derimot viser resultatene at pasientene stort sett er villige til å delta i AAA-screeningsprogrammer: de som godtar mest å delta er 65-år gamle menn (81 %) og kvinner (73 %), men tallene synker med økende alder. Det foreligger ingen dokumentasjon om hvordan AAA-screening eventuelt kan påvirke praksis, som f.eks. om hvordan bruk av ultralydtesting for AAA kan påvirke legens beslutninger eller om AAA-screening ved å muliggjøre påvisning av andre tilstander evt. kan påvirke behandlingsforløpet. Forskningsdata viser derimot at AAA-screening kan endre bruk av andre teknologier/helsetiltak og ressurser med tanke på planlagte versus akutte operasjoner: hos AAA-screenede menn både på lang sikt (etter 7 til 15 år) og kortere sikt (etter 3,5 til 5 år) er det 50 % flere planlagte operasjoner og tilsvarende færre akutte operasjoner enn hos ikke-screenede menn (lav kvalitet på dokumentasjonen). Intra- og inter-observatør variasjoner i målingene av aortadiameter ved ultralyd har vært det eneste utfallet i den inkluderte litteraturen, som kan si noen om nøyaktighet av AAA-screening. Generelt sett er repeterbarheten (intra-observatør) og reproduserbarheten (inter-observatør) akseptable, men det er usikkerhet rundt

resultatene, siden kvaliteten på disse reliabilitetsstudiene ikke har kunnet vurderes oppsummert på en systematisk og etterprøvbar måte. I tillegg er det stor variasjon i settinger, kvalifikasjon og erfaring blant dem som har gjort undersøkelsene, ultralydutstyr og de statistiske analysene som er utført. Derfor kan det ikke trekkes noen sikre konklusjoner med hensyn til betydning av f.eks. yrkesbakgrunn eller erfaring.

Sikkerhet

Et AAA-screening program kan være skadelig for den screenede populasjonen ved at man vil forvente økt antall påvisninger av AAA (økt insidens) og dermed økt antall operasjoner (altså kirurgiske inngrep som følger påvisning av et AAA med høy risiko for ruptur), som i sin tur innebærer risiko for pasientene. Det er dette sikkerheten rundt AAA screening hovedsakelig er knyttet til. Sykehusvolum, antall AAA-operasjoner per kirurg, i tillegg til kirurgenes nivå av spesialisering innen karkirurgi er knyttet til dødelighet som følge av påvisning og operasjon av et AAA. Konsekvensene av AAA-screening kan også ha negative psykologiske effekter, som for eksempel angst etter påvist AAA. I tillegg kan AAA-screeningen påføre unødvendig stress ved falskt positive funn, men det foreligger svært lite dokumentasjon om dette.

Diskusjon

Mens det foreligger dokumentasjon om gunstig klinisk effekt, er det lite informasjon om sikkerhet ved innføring av AAA-screening. Det er allikevel viktig å ta i betraktning alder, kjønn, pre-operativ morbiditet, røyking og AAA-størrelsen, da disse faktorene kan påvirke utfallet av det kirurgiske inngrepet som følger påvisningen av et høyrisiko AAA, og dermed også det endelige utfallet av innføring av et AAA-screeningprogram.

Konklusjon

Forskning viser at AAA-screening kan være gunstig for menn over 65 år, da AAA-relatert dødelighet reduseres med bortimot ca. 50 % både på kort og lang sikt. Dette er trolig ikke tilfellet hos kvinner, men her er det stor usikkerhet knyttet til resultatene. Derimot ser ikke AAA-screening ut til å ha noen effekt på totaldødelighet verken hos menn eller kvinner. Som følge av AAA-screening kan antall akutte operasjoner bli redusert, mens antall elektive operasjoner kan øke. Med hensyn til sikkerhet er de mest alvorlige effektene av AAA-screening knyttet til det kirurgiske inngrepet som følger påvisningen av et AAA med høy risiko for ruptur, altså i tilfellene der operasjonsindikasjon foreligger.

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Preface

The National Council for Priority Setting in Health Care in Norway has informed The Norwegian Knowledge Centre for the Health Services (NOKC) about the need of assessing the effect of abdominal aortic aneurysm screening (AAA) screening. In March 2013, NOKC decided to carry out a Health Technology Assessment (HTA) on the effect of AAA-screening based on a European assessment of AAA screening carried out 2010-2012 by EUnetHTA, the European network for HTA, a collaborative so-called Core HTA NOKC actively contributed to.

The Norwegian project group consisted of:

- Project leader: Senior Researcher, Katrine B. Frønsdal, Kunnskapssenteret (The Norwegian Knowledge Centre for the Health Services)
- Project collaborator: Senior Researcher, Ingvil Sæterdal, Kunnskapssenteret (The Norwegian Knowledge Centre for the Health Services)
- Project collaborator: Research Librarian, Ingrid harboe, Kunnskapssenteret (The Norwegain Knowledge Centre for Health Services)

The aim of this report is to support well-informed decisions in health care that lead to improved quality of health services. The evidence should be considered together with other relevant issues, such as clinical experience and patient preference.

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Objective

The aim of this HTA is to inform the Norwegian health care services on clinical effectiveness and safety issues of abdominal aortic aneurysm (AAA) screening.

Background

Definition and course of AAA

Abdominal aortic aneurysm (AAA or so called triple A) is a weakening of the aortic wall resulting in a focal pathological dilatation of the abdominal aortic artery. AAA usually forms at the level just beneath the departure of the renal arteries, i.e. infrarenal AAA (Figure 1). AAAs bears the risk of rupture, which is a dramatic emergency condition with a high risk of death. Of the patients with a ruptured AAA, about 50% reach hospital alive. Among those who reach hospital alive and have an operation, 50–70% survive the repair. 1–2% of all deaths in the Western world are estimated to be caused by AAA ruptures (Wilmink 1999; Vardulaki 1999). The risk of rupture increases with the diameter of the dilatation. The cut-off point for preventive surgery (elective repair) is 5.5 cm (UKSATP 2002) while aneurysms with sizes 4.0 – 5.5 cm should be followed up every sixth month (Moll 2011), however, the actual frequency of controls is poorly documented. An AAA screening program is aimed at identifying AAAs, and offering preventive surgery to individuals with high risk for rupture, in order to reduce their individual risk connected with a spontaneous rupture.

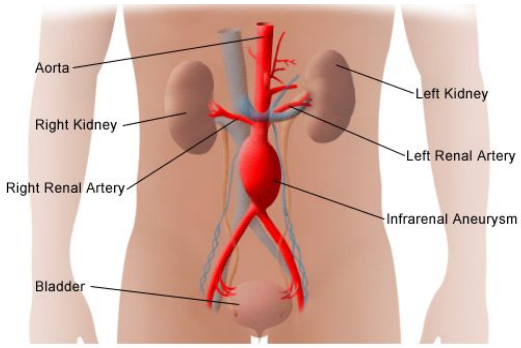
Prevalence of AAA

There is some variance in the prevalence of AAA found by screening programs. In the Western countries, the prevalence varies between 5 to 10% in 65–74 years old men. In Japan, the prevalence is 1% for the same age group of men. The prevalence increases with age. In England, the prevalence is 2% for men aged 50–64 years and 12% for men aged 80 years or older. In Denmark, the prevalence is 4% for men aged 65–69 and 6% for men aged 70–74 years. The prevalence for women is significantly lower than the prevalence for men. In a Swedish study, AAA was detected in 16.9% of men and 3.5% of women aged 65–75 years (Wanhainen 2001). A Norwegian study (the Tromsø Study from 2001) has shown lower percentages (8.9% for men and 2.2% for women), but in this study, younger people were included, i.e. 25–84 years (Singh 2001).

Symptoms of AAA

Unruptured AAA is usually asymptomatic. However, symptoms of back pain or abdominal pain, or symptoms due to peripheral embolism can be present. During general clinical examination a pulsatile abdominal mass may be present (Mohler 2011).

Figure 1. *Infrarenal abdominal aortic aneurysm*



(Image from: http://o.oolco.com/kategori/hjerte-blod-og-sirkulasjon/abdominal-aortaaneurisme)

Risk factors for acquiring AAA and risk of rupture

Age and sex are risk factors for AAA. The prevalence of AAAs increases with age. While it is uncommon in people below the age of 60 years, 1 person per 1000 develops an AAA in the 60–65 age group (Mohler 2011). AAA is four times more common in men than in women (Mohler 2011). Additional risk factors are smoking, cardiovascular disease and a family history of AAA.

The risk of rupture is mainly associated with the diameter of the AAA. The annual risk according to the diameter has been described as follows (Mohler 2011):

- Less than 4.0 cm in diameter = less than 0.5% chance of rupture
- Between 4.0 to 4.9 cm in diameter = 0.5 to 5% chance of rupture
- Between 5.0 to 5.9 cm in diameter = 3 to 15% chance of rupture
- Between 6.0 to 6.9 cm in diameter = 10 to 20% chance of rupture
- Between 7.0 to 7.9 cm in diameter = 20 to 40% chance of rupture
- Greater than or equal to 8.0 cm in diameter = 30 to 50% chance of rupture

Screening of AAA

Screening is a public health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test, to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of a disease or its complications. According to WHO, a set of criteria should be satisfied in order to initiate a screening program (Wilson 1968).

1. The condition being screened for should be an important health problem
2. The natural history of the condition should be well understood
3. There should be a detectable early stage
4. Treatment at an early stage should be of more benefit than at a later stage
5. A suitable test should be devised for the early stage
6. The test should be acceptable
7. Intervals for repeating the test should be determined
8. Adequate health service provision should be made for the extra clinical workload resulting from screening
9. The risks, both physical and psychological, should be less than the benefits
10. The costs should be balanced against the benefits

Although it varies across European countries, the percentage of men at high risk of AAA has been increasing steadily over the last 20 years. Screening programs for AAA have thus been considered as a potentially useful healthcare intervention in European countries, even if in most countries, including Norway, no systematic nationwide screening program has yet been implemented. A nationwide population-based screening program is performed only in the UK (Mitchel 2011; Lindholdt 2010), where men who turn 65 are automatically invited to the program (men who are older and have not been screened previously can opt in through self-referral). It has been reported that while hospital-based screening has an attendance rate of around 80%, the uptake in a general practice based screening is likely to be between 50% and 70% (Fowkes 2007).

Screening programs for AAA are used to identify individuals at a high risk of AAA rupture. Those identified are offered preventive surgery to reduce their individual risk of the negative consequences of a spontaneous rupture. In Norway 700–800 patients are operated each year (Haug 2005). There is around 5% 30-days mortality in those who are operated electively (either open surgery: 3-6% or endovascular, i.e. non-invasive: 0.5-1.5%), whereas mortality remains high (30-50%) in those who are operated due to ruptured aorta (Haug 2005; Bengtsson 1992). In addition, people die before they reach the hospital, which gives a total mortality of 60–90% for ruptured aneurysm (Bengtsson 1992).

AAA screening target population

In many organized screening programs, the target population (those who are invited) is around 65–80 years and males. In some screening programs, additional risk factors must be present to be included in screening.

In European countries, the percentage of men in the high-risk age group varies across countries and has tended to increase over the last 20 years. In 2010 Germany and France had the highest percentage (20%) of men aged 60–79. The lowest percentages reported were in Iceland and Ireland (13%). The average percentage of men

aged 60–79 (among all men) has raised in 31 European countries from 14% in 1990 to 17% in 2010. With the exception of Norway (1990: 16%, 2010: 16%), all the countries show trends towards an increasing percentage in this age group. In 31 European countries, there are ~43 millions of men aged 60–79.

Diagnosis of AAA and management of diagnosed AAA

Ultrasonography has been established worldwide as the gold standard technical device not only for screening, but also for monitoring potential size progression of AAAs. This non-invasive method is highly sensitive and specific, but the display of the images is not yet internationally standardized. Further strengths of this method include safety, portability and low costs. The investigation can be carried out not only by physicians, but also by medical technical assistants, however, intensive training and experience of the investigator is highly important to keep intra-observer reproducibility as low as possible.

Intervention depends on the diameter of the AAA. For smaller aneurysms (3.0–3.9 cm) with a lower risk of rupture, medical therapy and watchful waiting is recommended. For medium sized aneurysm (4.0–5.4 cm), checkups every 4-6 month is indicated, whereas AAAs that are 5.0 cm in diameter in women and 5.5 cm or more in men, the cut-off point of repair is reached (UKSATP 2002). Whether to use endovascular or an open surgical approach should be decided on an individual base. Open surgery is indicated for patients with a low preoperative risk (younger patients). Endovascular surgery is indicated in patients with favorable anatomy and who are at high surgical risk.

Burden of diagnosed AAA

The burden of AAA arises from the risk of AAA rupture and from harm that may arise from preventive actions against the risk of rupture. From a public health perspective the benefits and harms from organized preventive actions (and their consequences) must be compared with the benefits and harms from care that is not organized in the form of a public health program (individual care, opportunistic screening). The benefit and harm that may be introduced by a screening program depend on the prevalence of the disease (prevalence of AAAs, ruptured AAAs and deaths from ruptured AAAs), and on the effectiveness of the screening and of the preventive interventions.

The public health burden of AAA is increasing in developed countries because of its increasing prevalence in many populations (Blanchard 2000). This increase in prevalence can be explained, in part, by the increase in the number of people in the age groups at higher risk of developing AAA. In European countries, the number of people aged 60–79 has increased from 14% in 1990 to 17% in 2010. However, more re-

cent data indicate that the prevalence and incidence of ruptures are about to decrease (refs to be added).

Limitations and potential harms of AAA screening

In general, the implementation of screening practices has the potential to save lives or improve quality of life because of early diagnosis of serious diseases or conditions, but it cannot guarantee protection. In any screening practice, there is a potential for harms and adverse events for patients, e.g. during the screening test, during diagnosis or during treatment. There is, for example, the potential for false positive results in individual screening tests, which may be a considerable psychosocial burden for those concerned. Additionally, false positive results can result in unnecessary investigation and treatment. On the other hand, false negative results delay the detection and final diagnosis of a disease. During the screening test, patients could be exposed to radiation or chemicals or undergo discomfort, stress or anxiety, all of which could lead to adverse effects. Therefore, it is essential to establish whether, in practice, screening a healthy (risk) population leads to an improvement of relevant outcomes.

More specifically, the implementation of an AAA screening program can cause harm to the screened subjects due to the expected increase in the number of detected AAAs (increase of incidence) and consequently in the number of surgical interventions to repair intact or non-ruptured AAAs suitable for repair. These interventions, carried out by endovascular aneurysm repair (EVAR) or open aneurysm repair (OAR), can cause serious harms in terms of mortality, morbidity and psychological effects (Appendix 4, Section 1). Some subjects may suffer early harms, even though the natural history of their AAA might not cause clinical problems during their lifetime.

Method

Production of the European core HTA on AAA screening

To produce the HTA on the effect of abdominal aortic aneurysm (AAA) screening the EUnetHTA Core Model® was used (Lampe 2009). The idea behind this model is to provide a framework for structuring relevant HTA information while at the same time facilitating local use and adaptation of the information or guiding its production. The model is based on nine domains of evaluation: 1) health problem and current use of the technology, 2) description and technical characteristics of technology, 3) safety, 4) clinical effectiveness, 5) costs and economic evaluation 6) ethical analysis, 7) organizational aspects, 8) social aspects, 9) legal aspects. In this communication, we reported results from the safety and clinical effectiveness domains, and we have extracted the most relevant information from the two first descriptive domains for the background chapter. Of note, NOKC had the responsibility of assessing clinical effectiveness, i.e. domain 4, whereas other European HTA agencies were responsible for the other domains.

Systematic review on clinical effectiveness and safety

As guidance on how to assess clinical effectiveness, the Handbook for Summarizing Evidence from the Norwegian Knowledge Centre for the Health Services was used (NOKC 2011), as well as guidelines from the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011).

Information sources

A basic search strategy to identify systematic reviews (SRs) and randomized controlled trials (RCTs) to suit the overall project definition was developed by investigators from the different domains. This search strategy combined MeSH terms on the intervention exclusively (Appendix 1, Section 1). Searches for SRs and RCTs were performed by a research librarian from NOKC (IH) in the Cochrane Database, DARE and HTA databases via the Cochrane Library and CRD, as well as in Embase, Medline and ISI databases in October 2011, and later updated in February and in June 2012 (Appendix 1, Section 1). All references from these searches, updating searches, and an additional hand search performed in PubMed are listed in Appendix 3.

Criteria for literature selection

Selection of SRs and RCTs was done according to criteria for relevance (see *Inclusion criteria* and *Exclusion criteria* below) and criteria for quality. Quality had to be assessed as medium or high using validated checklists suited for SRs and RCTs (Appendix 1, Section 2). All outcomes relevant to selected assessment elements were included.

Inclusion criteria
Study design: systematic reviews (SR) and randomized controlled trials (RCT)
Population: Men and women from the age of 64
Intervention: Population-based AAA screening
Comparison: No population-based screening (this includes opportunistic screening and incidental AAA detection while performing abdominal ultrasound examination due to other indications)
Outcomes: All relevant to selected assessment elements

Exclusion criteria
Cost-effectiveness assessments
Languages other than English

Procedure for the literature selection

Titles and abstracts resulting from the literature searches were independently assessed by the two investigators KF and IS. Articles considered to meet the inclusion criteria were further examined in full text and assessed based on the inclusion criteria and quality requirements (see *Quality assessment tools and criteria* below). Discrepancies were resolved through discussion.

Quality assessment tools and criteria

Assessment of the methodological quality of selected SRs was done using the English version of the NOKC checklist for systematic reviews shown in Appendix 1 (NOKC 2011). Systematic reviews of high to moderate quality according to criteria set in the checklist were to be included. Quality of evidence for the different outcomes across the various studies was assessed using the GRADE instrument (GRADE Working Group 2004), and is shown as GRADE profiles in Section 4 of Appendix 2. Assessments of methodological quality and quality of evidence were performed by two investigators independently. Discrepancies were resolved through discussion. Of note, since no RCTs were included, no quality assessment was needed for RCTs.

Analysis and synthesis

All reporting of clinical effectiveness data was done according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA Statement 2012).

Safety

Information sources and inclusion criteria

In addition to the basic literature search, four searches in Medline using OVID and Embase were performed in June 2011, along with hand searches in the Cochrane Library and INAHTA databases. Searches were limited to publications after 1999.

The additional search sought articles about harms and risks of AAA screening, including psychological aspects. The second focused on effectiveness and adverse effects of AAA treatment, including open surgery and endovascular repair. The third sought clinical trials and systematic reviews about health-related effects of AAA screening. Finally, the fourth additional search sought articles about the relation between Health Centre's, surgeon's and surgery team characteristics and risks and benefits of AAA repair. Search strategy is described in Appendix 4, Section 2.

Literature selection

Information was retrieved from the basic literature search that was done for the whole project (i.e. as for assessing clinical effectiveness), and also from other searches in Cochrane, INAHTA databases, and from the references within the retrieved articles.

Articles that described health related outcomes of elective, eligible, intact, asymptomatic or non-ruptured AAA surgical repairs were selected. Main focus were large observational studies describing the long-term consequences of the surgical repair of asymptomatic AAA.

Quality assessments, data analysis and synthesis

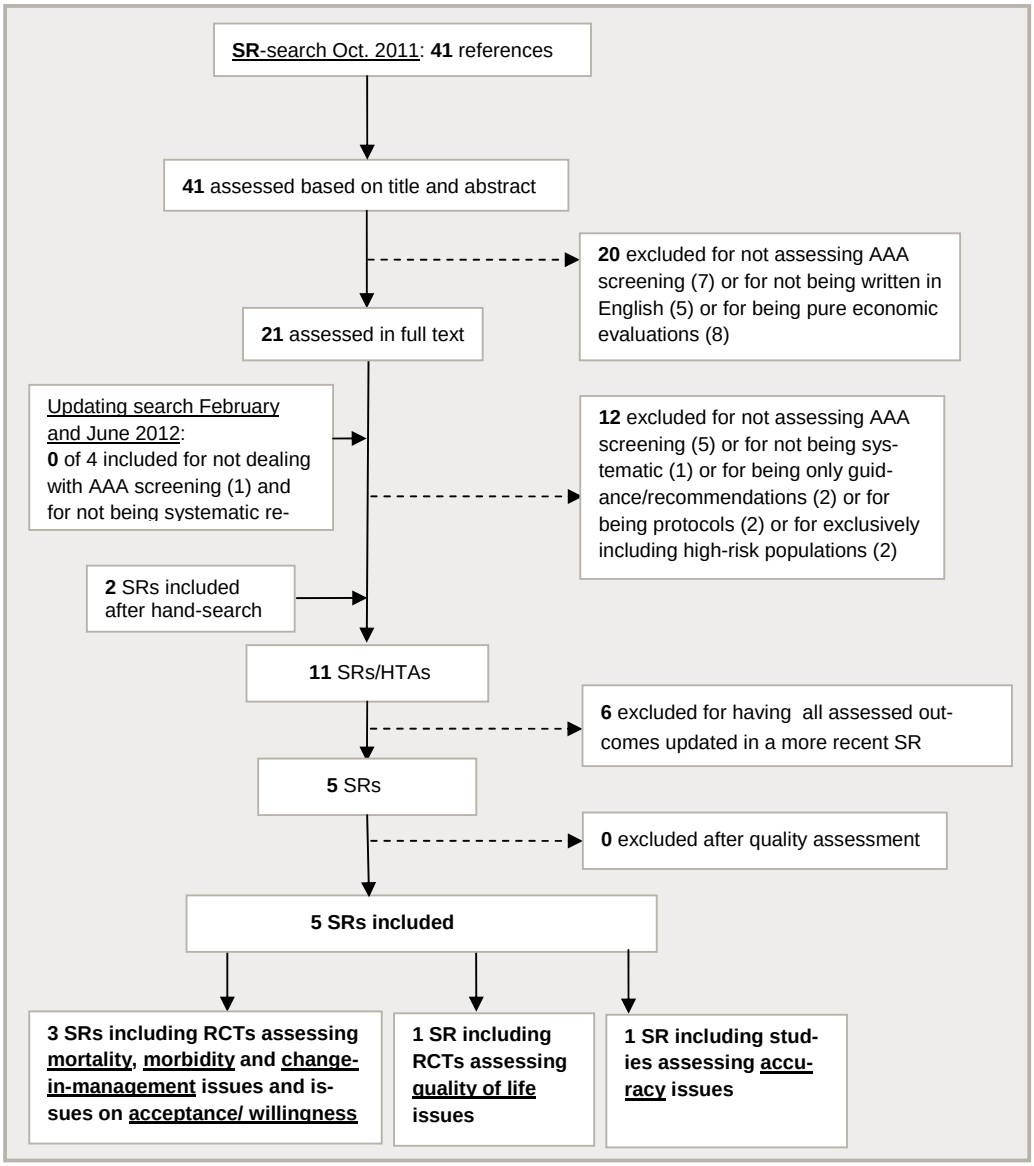
No formal quality assessment of included literature was done. No information on the methods used data analysis and synthesis was provided for the assessment of safety in this HTA.

Results

Clinical effectiveness

Included literature

Figure 3. *Flow chart showing the selection of systematic reviews (SR)*

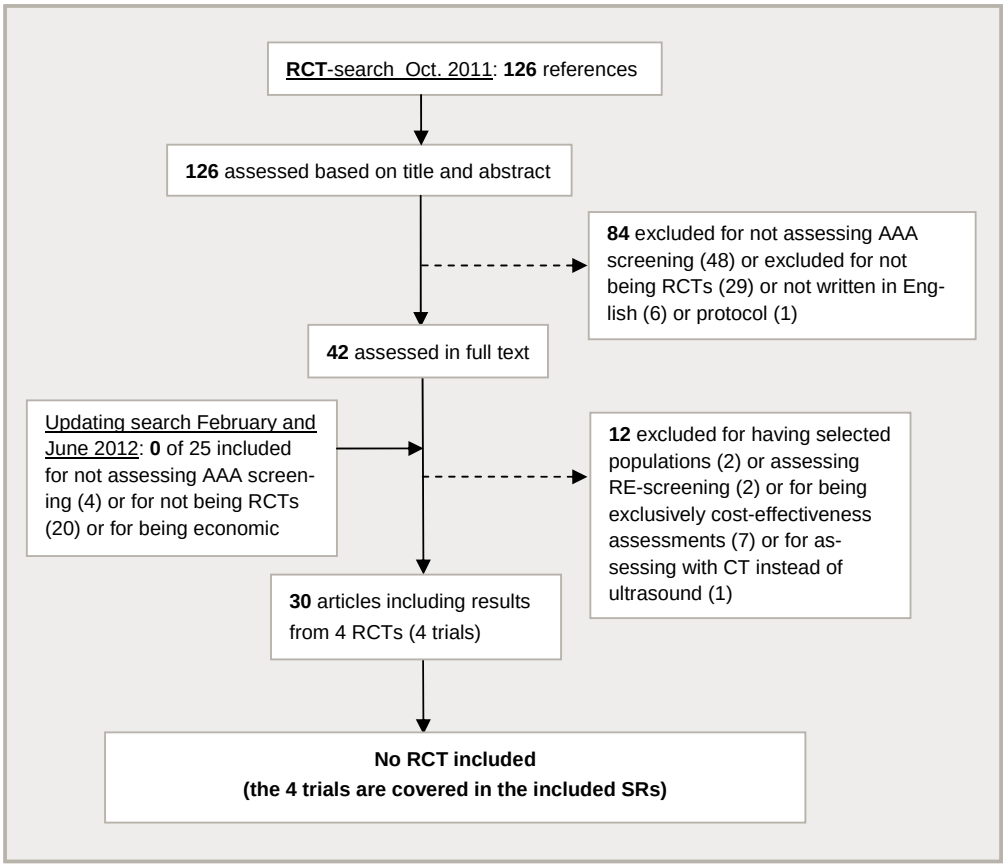


Selection of relevant SRs of highest quality (STEP 1)

Selection of SRs satisfying criteria for relevance and quality is shown in the flow chart above (Figure 3). An update literature search performed in February and June 2012 did not lead to further included articles. Assessment of relevant SRs that satisfied the inclusion criteria and quality requirements according to the checklist for SRs resulted in the inclusion of five SRs in total. In cases where the same outcome (e.g. mortality) was assessed in more than one SR, results from the most recent SRs were reported for that particular outcome.

Selection of RCTs not covered in included SRs and/or RCTs assessing additional relevant populations and/or outcomes other than those in the included SRs (STEP 2)

Figure 4. Flow chart showing the selection of randomized controlled trials (RCTs)



Selection of RCTs satisfying criteria for relevance and study design is shown in the flow chart above (Figure 4). The update literature search performed in February 2012 did not lead to further included articles. As shown in the flow chart, the last step in the selection process led to 30 articles that reported results from the four trials that were covered in the included SRs. These articles described updates of results from the RCTs or prospective studies (*not RCTs*) based on the population material taken from the four trials.

Hence no further results were assessed from the four RCTs since we did not include results from these trials for our research questions.

Overview of the 5 included SRs from the basic search

A brief description of the five included SRs is shown in the table below (Table 1). Abstracts, quality assessments and descriptions are provided in Appendix 2, Sections 1, 2 and 3.

Table 1. *Overview the five included SRs population(s) and outcome(s)*

Author	Year	Quality	Studies	Population	Selected outcomes
Beales	2011	Medium	9 observational studies	Some studies describe the population, others not. Large variability in number of measurements (10 to 112)	Intra- and inter-observer variability (repeatability and reproducibility)
Collins	2011	High	1 RCT*	Men 65-74 years	State anxiety, depression, QoL
Takagi	2010	Medium	4 RCTs	Men from 65 years	AAA-related (long-term) mortality Overall (long-term) mortality
Lindholt & Norman	2008	Medium	3 RCTs**	Men 64-83 years	AAA-related (mid-term) mortality Overall (mid-term) mortality Planned operations for AAA (mid-term) Emergency operations for AAA (mid-term) Planned operations for AAA (long-term) Emergency operations for AAA (long-term)
Cosford	2007	High	1 RCT***	Men and women 65-80 years	AAA-related mortality (in women only) Overall mortality (in women only) Progression to (incidence of) ruptured AAA

* One RCT out the 12 RCTs included in this SR involved screening of AAA (Ashton 2002)
** Three out of the four RCTs included in this SR assessed operations for AAA (long-term)
*** One out of the four RCTs included in this SR involved women and the outcome progression to (incidence) of ruptured AAA

As mentioned above, we chose to report the most recently reported effect estimates on relevant populations for relevant outcomes**.** Consequently, the review by Cosford et al. was included since it is the only SR that has included women and assessed incidence of ruptured AAA (Cosford 2007). Likewise, the Lindholt & Norman review was the most recent review assessing surgery of AAA as well as medium term mortality (i.e. after 3.5 to 5 years) both due to AAA and all causes (overall mortality) (Lindholt & Norman 2008). The review by Tagaki et al. was the most recent review on long-term (i.e. after 7 to 15 years) mortality, both AAA-related and overall (Takagi 2010). Collins et al. was the only review that dealt with emotional and quality of life outcomes related to screening programs (Collins 2011); however only one RCT within this review considers these outcomes in the context of AAA screening (Ashton 2002). Finally we included one SR assessing reproducibility of ultrasound measurement of the abdominal aorta (Beales 2011).

Excluded articles from the basic search

Excluded literature including reasons for exclusion are listed in Appendix 2, Section 3.

Results from included literature

Effect of AAA screening on overall mortality

Three SRs were included to assess the effect of AAA screening on the overall or 'all-cause' mortality outcomes (Takagi 2010; Lindholt & Norman 2008; Cosford 2007). While the SRs by Takagi et al. and Lindholt & Norman were assessed as being of medium quality, the SR by Cosford et al. was determined to be of high quality (Appendix 2, Section 2). GRADE Summary of findings (SoF) tables for these series of outcomes are shown in Appendix 2, Section 4.

Overall mortality in men (long-term)
The Takagi et al. SR was the most recent SR assessing long-term (i.e. after 7 to 15 years) overall mortality in men (Takagi 2010). Four RCTs included in total 114,376 men aged 65 years or more randomized to an invitation to attend screening for AAA (n=57,181) or no invitation (control; n=57,195). Pooled analysis of the four odds ratios (ORs) showed a non-significant reduction in overall mortality in the screened group. Fixed-effect OR = 0.98; 95% CI = 0.95-1.00 (moderate quality of evidence).

Overall mortality in men (medium term)
The Lindholt & Norman SR was the most recent SR assessing medium term (i.e. after 3½ to 5 years) overall mortality in men (Lindholt & Norman 2008). Four RCTs included in total 125,576 men aged between 64 and 83 years randomized to an invitation to attend screening for AAA (n=62,729) or no invitation (control; n=62,847). Pooled analysis of the four ORs showed a non-significant reduction in overall mortality in the screened group. Random-effect OR = 0.94; 95% CI = 0.86-1.20 (low quality of evidence).

Overall mortality in women
The Cosford et al. SR was the most recent SR assessing overall mortality in women (Cosford 2007). One RCT included in total 9,342 women aged between 65 and 80 years randomized to an invitation to attend screening for AAA (n=4,682) or no invitation (control; n=4,660). The ORs showed a non-significant increase in overall mortality in the screened group. Random-effect OR = 1.06; 95% CI = 0.93-1.21 (moderate quality of evidence).

Effect of AAA screening on the mortality caused by AAA

Three SRs were included to assess the effect of AAA screening on AAA-related mortality outcomes (Takagi 2010; Lindholt & Norman 2008; Cosford 2007). While the SRs by Takagi et al. and Lindholt & Norman were assessed to be of medium quality, the SR by Cosford et al. was determined to be of high quality (Appendix 2, Section 2). GRADE SoF tables for these series of outcomes are shown in Appendix 2, Section 4).

AAA-related mortality in men (long-term)
The Takagi et al. SR was the most recent SR assessing long-term (i.e. after 7 to 15 years) AAA-related mortality in men (Takagi 2010). Three RCTs included in total 86,449 men aged 65 years or more randomized to an invitation to attend screening for AAA (n=43,211) or no invitation (control; n=43,238). Pooled analysis of the three ORs showed a significant reduction in AAA-related mortality in the screened group. Random-effect OR = 0.55; 95% CI = 0.36-0.86 (low quality of evidence).

AAA-related mortality in men (medium term)
The Lindholt & Norman SR was the most recent SR assessing medium term (i.e. after 3½ to 5 years) AAA-related mortality in men (Lindholt & Norman 2008). Four RCTs included in total 125,576 men aged between 64 and 83 years randomized to an invitation to attend screening for AAA (n=62,729) or no invitation (control; n=62,847). Pooled analysis of the four ORs showed a significant reduction in AAA-related mortality. Fixed-effect OR = 0.56; 95% CI 0.44 - 0.72 (moderate quality of evidence).

AAA-related mortality in women
The Cosford et al. SR was the most recent systematic review assessing AAA-related mortality in women (Cosford 2007). One RCT included in total 9,342 women aged between 65 and 80 years randomized to an invitation to attend screening for AAA (n=4,682) or no invitation (control; n=4,660). The OR showed a non-significant increase in AAA-related mortality in the screened group. Random-effect OR = 1.99; 95% CI 0.36-10.88 (very low quality of evidence).

Effect AAA screening on the progression of AAA

One SR was included to assess the effect of AAA screening on the incidence of ruptured AAA (Cosford 2007). This SR was determined to be of high quality (Appendix 2, Section 2). GRADE Summaries of findings (SoF) tables for this outcome for men and women are shown in Appendix 2, Section 4.

Incidence of ruptured AAA in men
The Cosford et al. SR was the most recent SR assessing the incidence of ruptured AAA in men (Cosford 2007). One RCT included a total of 6,433 men aged between 65 and 80 years randomized to an invitation to attend screening for AAA (n=3,205) or no invitation (control; n=3,228). The ORs showed a significant reduction in the incidence of ruptured AAA in the screened group. Random-effect OR = 0.45; 95% CI 0.21-0.99 (very low quality of evidence).

Incidence of ruptured AAA in women

The Cosford et al. SR was the most recent SR assessing incidence of ruptured AAA in women (Cosford 2007). One RCT included in total 9,342 women aged between 65 and 80 years randomized to an invitation to attend screening for AAA (n=4,682) or no invitation

(control; n=4,660). The odds ratio (ORs) showed a non-significant increase in the incidence of ruptured AAA in the screened group. Random-effect OR = 1.49; 95% CI 0.25-8.94 (very low quality of evidence).

Effect on morbidity directly related to AAA screening

Morbidity was assessed by Cosford et al., but the SR did not find any RCTs for outcomes that, for instance, were associated with complications of surgery such as distal embolus, haemorrhage and graft failure, coronary and cerebrovascular events or renal complications (Cosford 2007).

Effect of AAA screening on return to work

Return to work was assessed by Cosford et al., but the SR did not find any RCTs for this outcome (Cosford 2007).

Effect of AAA screening on health-related quality of life

One SR was included to assess the effect of AAA screening on QoL in terms of state anxiety, depression and mental QoL (Collins 2011). This SR was determined to be of high quality (Appendix 2, Section 2). GRADE Summaries of findings (SoF) tables for these outcomes are shown in Appendix 2, Section 4. No information on gender or age distribution was provided. Outcomes assessed were anxiety, depression and mental QoL. Anxiety was measured using STAI, the state scale of the state-trait anxiety inventory (Spielberger 1970), depression was measured using HADS, the state Hospital Anxiety and Depression Scale (Zigmond & Snait 1983), whereas mental QoL was measured using Short Form Health Survey SF-36 (Ware & Sherbourne 1992).

Anxiety
In the SR by Collins et al., in the one RCT that assessed anxiety, a total of 1,956 participants were randomized to an invitation to attend screening for AAA (n=1,230) or no invitation (control; n=726). Anxiety was significantly reduced in the screened group: standard mean difference (Std.MD) = -0.12; 95% CI -0.21-(-0.02) (low quality of evidence).

Depression
In the Collins et al. SR, depression was assessed in the same RCT, which included a total of 1,956 participants randomized to an invitation to attend screening for AAA (n=1,230) or no invitation (control; n=726). Depression was significantly reduced in the screened group: Std.MD = -0.11; 95% CI -0.20-(-0.02) (low quality of evidence).

Quality of Life (QoL)
QoL was also assessed in the RCT included in the Collins et al. SR in which a total of 1,956 participants were randomized to an invitation to attend screening for AAA (n=1,230) or no invitation (control; n=726). QoL score was better in the screened group but not significantly so: Std.MD = 0.07; 95% CI -0.02-0.16 (low quality of evidence).

Patients' acceptance of AAA screening

The SR by Cosford et al. was the only SR to report patients' acceptance of AAA screening programs (Cosford 2007). Although this SR was determined to be of high quality, patients' willingness to join the AAA screening program was not a pre-defined outcome, thus the authors reported acceptance rates from the RCTs included in the SR in narrative form only.

Cosford et al. reported acceptance rates ranging between 63% (Norman 2004) and 80% (Ashton 2002). In one trial the acceptance rate increased from 63% to 70% when, after randomization, patients who were identified as too unwell or previously scanned were excluded (Norman 2004).

According to the SR, only one trial recorded acceptance rates by age (Scott 1995). In this trial, men and women aged 65 accepted the invitation to screen most often (81% and 73% respectively), but acceptance decreased with age and was lowest for men and women aged 76 to 80 years (66% and 58% respectively).

Effect of AAA screening on need for other technologies or resources

One SR was included to assess the effect of AAA screening on planned and emergency operations (Lindholt & Norman 2008). The SR was determined to be of medium quality (Appendix 2, Section 2). GRADE SoF tables for these outcomes are shown in Appendix 2, Section 4.

Planned operations in men (long-term)
The SR by Lindholt & Norman was the most recent SR assessing long-term (i.e. after 7 to 15 years) planned operations in men (Lindholt & Norman 2008). Three RCTs included in total 86,479 men aged between 64 and 83 years randomised to an invitation to attend screening for AAA (n=43,167) or no invitation (control; n=43,312). Pooled analysis of the three ORs showed a significant increase in planned operations (long-term) in the screened group. Fixed-effect OR = 2.81; 95% CI 2.40-3.30 (moderate quality of evidence).

Planned operations in men (medium term)

The SR by Lindholt & Norman was the most recent SR assessing medium term (i.e. after 3½ to 5 years) planned operations in men (Lindholt & Norman 2008). Four RCTs included a total of 125,576 men aged between 64 and 83 years randomised to an invitation to attend screening for AAA (n=62,729) or no invitation (control; n=62,847). Pooled analysis of the four ORs showed a significant increase in planned operations (medium term) in the screened group. Random-effect OR = 3.27; 95% CI 2.14-5.00 (low quality of evidence).

Emergency operations in men (long-term)

The SR by Lindholt & Norman was the most recent SR assessing long-term (i.e. after 7 to 15 years) emergency operations in men (Lindholt & Norman 2008). Three RCTs included a total of 86,479 men aged between 64 and 83 years randomised to an invitation to attend screening for AAA (n=43,167) or no invitation (control; n=43,312). Pooled analysis of the three ORs showed a significant reduction in emergency operations in the screened group. Random-effect OR = 0.48;95% CI 0.28-0.83 (low quality of evidence).

Emergency operations in men (medium term)
The SR by Lindholt & Norman was the most recent SR assessing medium term (i.e. after 3½ to 5 years) emergency operations in men (Lindholt & Norman 2008). Four RCTs included a total of 125,576 men aged between 64 and 83 years randomised to an invitation to attend screening for AAA (n=62,729) or no invitation (control; n=62,847). Pooled analysis of the four ORs showed a significant reduction in emergency operations in the screened group. Fixed-effect OR = 0.55; 95% CI 0.39-0.76 (low quality of evidence).

Intra- and inter-observer variation in test interpretation

As no tools are available at present for assessing the quality of reliability and agreement studies across all included studies, no grading to indicate quality of evidence has been performed for these outcomes.

One SR was included to assess the variation of AAA screening interpretation in terms of variation in intra-observer repeatability and inter-observer reproducibility of infra-renal aortic diameter measurements using ultrasound (Beales 2011). This SR was determined to be of medium quality (Appendix 2, Section 2).

Bland-Altman plots, a method based on the differences in observed values compared with the means of measured values was used to assess these outcomes in eight of the nine included studies (Bland & Altman 1986), whereas one study used a multilevel regression approach, i.e. generalized estimating equations (GEE) for the extraction of components of variation, separating intra-observer variation from inter-observer variation (GEE 2012). By using the GEE method, the number of assumptions for this analysis were reduced, which allowed variations to be reported in terms of standard deviations and appropriate definitions of measurement reliability derived from those standard deviations.

There were wide variations between the nine included studies in terms of numbers of measurements (from 10 to 112), participant demographics (age and gender) and types of ultrasound machine (all different). Various techniques of aortic diameter measurement techniques (calliper endpoints) were used, i.e. diameter measurement between aortic inner layers (ITI), between aortic inner and outer layers (ITO), or between aortic outer layers (OTO), and in both anteroposterior (AP) and transversal (TS) planes. Measurements were done on aneurysmal and normal aortas. In all studies, observers were blind to the results from the other observers, but they had different backgrounds in terms of discipline, grade or level of experience and training.

Intra-observer repeatability

The SR by Beales et al. was the only SR from the basic literature search that assessed intra-observer repeatability. Intra-observer repeatability was assessed using Bland-Altman plots by calculating repeatability coefficients in seven studies and using the GEE method in one study (Bland & Altman 1986; GEE 2012). Data for this outcome were not available for one of the nine included studies.

The intra-observer maximum AP mean difference ranged from 0.03 to 4.8 mm, and for TS from 0.2 to 1.9 mm. Beales et al. indicated diameter intra-observer repeatability coefficients, ranging from 1.6 to 7.5 mm for AP (and from 2.8 to 15.4 mm for TS). The National Health Service Abdominal Aneurysm Screening Programme (NAAASP 2009) suggested that 5 mm is an acceptable level of observer variation between aortic diameter ultrasound measurements. Authors suggested that aortic measurements by the same practitioner may vary significantly, but did not provide any statistical support for this statement, and the diameters (ITI, ITO or OTO) measured varied between studies. In addition, numbers of observers were few in eight of the nine included studies. It was difficult to draw a definitive conclusion from the review, but it indicated overall acceptable intra-observer repeatability.

In the studies included by Beales et al. numbers of observers ranged from 1 to 4, except for one study which had 24 observers (Hartshorne 2011). However, Hartshorne et al. included exclusively assessments of static images of aortas of different sizes, whereas the other eight studies included real-time examinations in which the relevant images to enable aortic diameter measurement were acquired. This study was nevertheless highlighted by the SR authors as being the only one that had used the GEE method. In this study, the intra-observer AP mean repeatability coefficients varied from 1.6 to 2.0 mm with individual repeatability coefficients ranging from 0.8 to 6.1 mm (TS measurements were not performed in this study), which are mainly below the acceptable level of variability of 5 mm (NAAASP 2009).

Intra-observer variability for ITI and OTO aorta diameter measurements

Hartshorne et al. was the only study that assessed possible differences in intra-observer variability according to different calliper endpoints of aortic diameter measurements (i.e. diameter measurements of ITI walls versus OTO walls), as well as according to differences in observers' background disciplines and experience (screening technicians versus vascular sonographers). In this study, 13 screening technicians and 11 vascular sonographers examined 60 aortic static images (not live). Among the sonographers, six had more than 10 years' experience and only one had less than 1 year of experience, whereas only two screeners had more than 10 years' experience and five had less than one year. While all 13 screeners routinely used ITI, five sonographers used OTO and six both ITI and OTO in their routine practice. When 15 images were each measured twice in random order by all 24 observers, there was no significant difference between the mean repeatability of ITI, 1.6 mm (range 0.8-5.2 mm) and that of OTO, 2.0 mm (range 0.5-6.1 mm).

For ITI, there was no significant difference between the mean repeatability of screeners, 1.7 mm (range 0.8-5.2 mm) and that of sonographers 1.4 mm (range 0.9-2.4 mm; *P*=0.27). For OTO, on the other hand, the mean repeatability was significantly better for sonographers at 1.4 mm (range 0.6-2.6 mm) compared with screeners, mean 2.5 mm (range 1.1-6.1 mm; *P*=0.037). It was, however, not possible to ascertain, using these data, the effect of the sonographers' longer experience since screeners, as opposed to sonographers, did not use OTO in their routine practice.

Inter-observer reproducibility

The SR by Beales et al. is the only SR from the basic literature search that assessed inter-observer reproducibility. Inter-observer reproducibility was assessed using Bland-Altman plots in eight studies and by the GEE method in one study (Bland & Altman 1986; GEE 2012).

For AP, the limits of agreement (reproducibility coefficients) for the diameter measurements ranged between -1.9 to +1.9 mm and -10.4 to +10.5 mm (all nine studies), whereas for TS, the largest limit of agreement was -5.6 to +5.2 mm (only two studies assessed TS diameters). According to Beales et al., five of the nine studies included had acceptable inter-observer reproducibility. For the study that involved 24 observers and used the GEE method (Hartshorne 2011), as opposed to the 1-4 observers in the eight others, the mean reproducibility coefficients were 3 mm; 95% CI 2.4-3.6 mm for ITI and 4.2 mm; 95% CI 3.5-4.9 mm, both of which were below the acceptable level of variability of 5 mm (NAAASP 2009). Although the authors of the SR do not draw any conclusions about inter-observer reproducibility, the results indicate overall acceptable inter-observer reproducibility regardless of whether diameters are measured as ITI, OTI or OTO.

Inter-observer variability for ITI and OTO aorta diameter measurements
Hartshorne et al. was the only study that assessed possible differences in inter-observer variability according to different calliper endpoints of aortic diameter measurements (i.e. diameter measurements of inner-to-inner walls [ITI] versus outer-to-outer walls [OTO]), as well as according to differences in observers' background disciplines and experience (screening technicians versus vascular sonographers) (Hartshorne 2011). In this study, in which 13 screening technicians and 11 vascular sonographers examined 60 images, mean reproducibility coefficient for ITI was significantly better than for OTO when measuring AP (TS was not measured in this study). Mean reproducibility coefficient was 3.0 mm; 95% CI 2.4-3.6 mm for ITI and 4.2 mm; 95% CI 3.5-4.9 for OTO, but both remained acceptable according to NAAASP, i.e. less than 5 mm (NAAASP 2009). Hartshorne and collaborators performed a corresponding analysis, excluding observers with less than 1 years' experience. In this group of 8 screening technicians and 10 sonographers, mean reproducibility coefficients were 3.2 mm; 95% CI 2.6-3.8 mm for ITI and 3.8 mm; 95% CI 3.1-4.5 mm for OTO. It was not possible, however, to ascertain that there was no effect of background discipline, because the screening technicians, as opposed to sonographers, did not use OTO in their routine practice.

Impact of ITI and OTO on the threshold for surveillance and referral for treatment
Hartshorne et al. grouped the 60 images into four categories to assess the impact of ITI versus OTO on the threshold for surveillance and referral for treatment. Results presented in the table below (Table 2) indicated that the ITI method would detect fewer aneurysms than using OTO.

Table 2. *Size categories using ITI vs size categories using OTO using 1440 measurements*

		Size categories using OTI			
		<30 mm	30-45 mm	45-55 mm	>55 mm
Size categories using ITI	<30 mm	348 (24%)	60 (4%)	0 (0%)	0 (0%)
	30-45 mm	0 (0%)	262 (18%)	124 (9%)	0 (0%)
	45-55 mm	0 (0%)	1 (0.1%)	418 (29%)	138 (10%)
	>55 mm	0 (0%)	0 (0%)	1 (0.1%)	88 (6%)

<30 mm is considered normal and requires no further surveillance (adapted from Hartshorne et al. 2011)
30-45 mm is considered a small aneurysm requiring yearly assessments
45-55 mm is considered a medium large aneurysm requiring 3-monthly assessments
>55 mm is considered a medium large aneurysm requiring immediate surgery

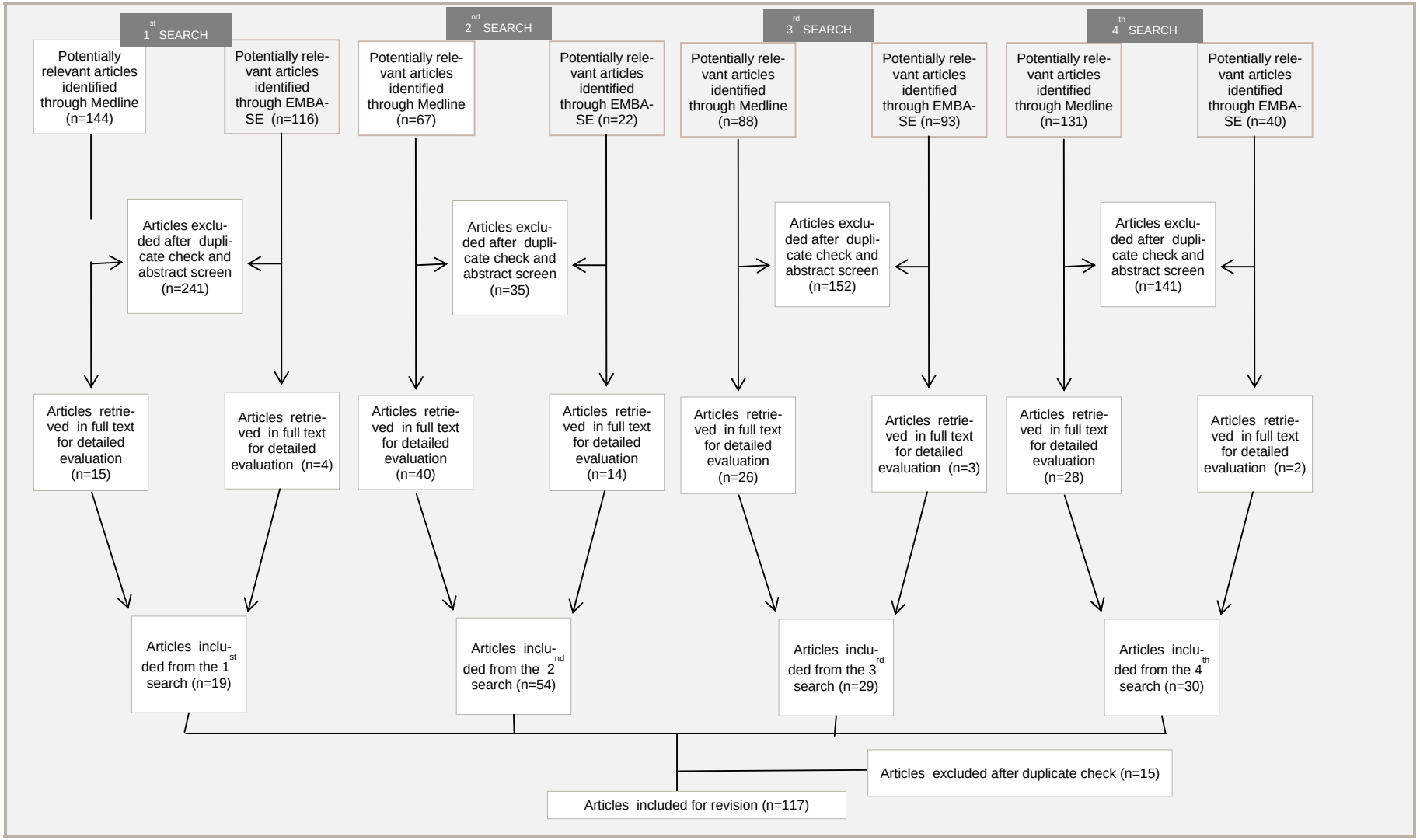
However, as indicated earlier, this study did not assess live images, and half of the observers were screening technicians who had less experience than vascular sonographers, and who used only ITI in their practice routine. These factors meant that a definite conclusion could not be drawn based on these data about the thresholds for surveillance and referral for treatment.

Safety

Included literature

After reading the abstracts, a list of 117 non-duplicated studies was available (see Appendix 4, Section 2 for references from each search). The full texts of all of these articles were read, and 52 of them were selected based on the inclusion criteria (see Figure 4 for selection of literature from the four searches performed).

Figure 4. *Flow chart showing the selection of included articles*


1st SEARCH
2nd SEARCH
3rd SEARCH
4th SEARCH
Potentially relevant articles identified through Medline (n=144)
Potentially relevant articles identified through EMBASE (n=116)
Potentially relevant articles identified through Medline (n=67)
Potentially relevant articles identified through EMBASE (n=22)
Potentially relevant articles identified through Medline (n=88)
Potentially relevant articles identified through EMBASE (n=93)
Potentially relevant articles identified through Medline (n=131)
Potentially relevant articles identified through EMBASE (n=40)
Articles excluded after duplicate check and abstract screen (n=241)
Articles excluded after duplicate check and abstract screen (n=35)
Articles excluded after duplicate check and abstract screen (n=152)
Articles excluded after duplicate check and abstract screen (n=141)
Articles retrieved in full text for detailed evaluation (n=15)
Articles retrieved in full text for detailed evaluation (n=4)
Articles retrieved in full text for detailed evaluation (n=40)
Articles retrieved in full text for detailed evaluation (n=14)
Articles retrieved in full text for detailed evaluation (n=26)
Articles retrieved in full text for detailed evaluation (n=3)
Articles retrieved in full text for detailed evaluation (n=28)
Articles retrieved in full text for detailed evaluation (n=2)
Articles included from the 1st search (n=19)
Articles included from the 2nd search (n=54)
Articles included from the 3rd search (n=29)
Articles included from the 4th search (n=30)
Articles excluded after duplicate check (n=15)
Articles included for revision (n=117)

Harms caused by AAA screening and characteristics of these

Important harms of the implementation of an AAA screening program derive from the expected increase in the number of detected AAAs (increase of incidence) and consequently in the increased number of surgical interventions to repair intact or non-ruptured AAAs suitable for repair. The surgical repair of an AAA, by EVAR or OAR, is a high-risk intervention. There are serious consequences, in terms of mortality, morbidity and psychological effects, for those in whom an AAA has been detected, which mainly are measured by quality of life (QoL) scales. Effect (reflecting safety of AAA screening) of the surgical interventions for AAA repair is described below.

Overall mortality

The European Society for Vascular Surgery reported data from 27,635 intact AAA surgical interventions performed in 386 hospitals in ten countries of Europe and Oceania between 2003 and 2007 (ESVS 2008). Most interventions were OAR (18,471), though EVAR accounted for 7,578, and the rest were unspecified. The mean age of patients was 72.1 years, and 13.5% of the patients were women. The overall mortality rate, which included in-hospital mortality or 30-day mortality, was 2.83%. The overall mortality rate for OAR was 3.5%, and for EVAR 1.15%. Schermerhorn et al. reported data from 45,660 Medicare beneficiaries undergoing elective AAA repair in the USA during the 2001–2004 period, and for whom the overall 30-day mortality was 1.2% with EVAR and 4.8% with OAR (Schermerhorn 2008). The probability of survival after 5 years was around 64% in this latter study, being similar between EVAR and OAR.

Related mortality

Among 5612 patients with intact AAA repaired by EVAR between June 1996 and February 2004, 589 had died within 8 years of follow-up and 24% of those deaths were procedure-related (141 patients) (Koning 2007). Of the 141 procedure-related deaths, 88 (14.9% of the 589 total deaths) were within the 30 days after surgery, 28 (4.8% of the 589 total deaths) due to AAA-rupture and 25 due to graft infection (4.2% of the 589 total deaths). The 'non'procedure-related deaths were caused by cancer (117 patients, 19.9%), other cardiovascular problems (27%), pulmonary problems (6.5%), renal problems (1.5%), multi-organ failure (1.4%), unknown reasons (10.7%) and other reasons (9.2%). According to the Committee for Standardized Reporting Practices in Vascular Surgery (Chaikof 2002), all deaths within 30 days after the surgical intervention were considered procedure-related deaths. The definition of "mortality related to AAA repair" varies so it must be borne in mind that published figures on procedure-related mortality could be inaccurate.

Morbidity

The Medicare database reported highly frequent complications from 45,660 elective AAA repairs performed by EVAR and OAR (Schermerhorn 2008). This Medicare

database reported, after 4 years follow-up, rupture rates of 1.8% and 0.5% after EVAR and OAR respectively. The re-intervention rates were 9% after EVAR and 1.7% after OAR.

Quality of life

Inconsistent results have been found regarding the psychological effects of an AAA screening program. An appropriate design for measuring changes in QoL for participants versus non-participants has not been identified. Therefore, it is not possible to determine whether screening for AAA affects the health-related QoL among participants. However, other information can be highlighted from the literature related to QoL. The Viborg trial, which measured QoL using the Screen QL scale, found significantly lower scores, for those invited to an AAA screening when they compared scores before versus after the scan (Lindholt 2000). However, the Gloucestershire screening program reported a statistically significant fall in anxiety levels between before and 1 month after screening (Lucarotti 1997). A cross-sectional case-control study within the West Australia trial compared QoL before and after screening only for those who attended screening. They found increased self-perceived general health from before to after screening (Spencer 2004). The MASS trial found higher anxiety scores, no difference in depression scores, and lower scores on the SF-36 mental and physical scales at 6 weeks post-screening for those who had an AAA compared with those who had a negative screening (Ashton 2002). However, other studies found that poorer self-assessed health among those who have compared with those who do not have an aneurysm could be more predictive of an aneurysm rather than a consequence of an AAA screening program (Marteau 2004). The ADAM trial found QoL benefits for early repair using OAR compared with surveillance for small AAAs (Lederle 2003).

Sexual dysfunction

The ADAM trial compared immediate elective repair with surveillance for small AAAs (Lederle 2003). In the elective immediate OAR group more patients became impotent compared with the surveillance group.

Participant groups more likely to be harmed through AAA screening

The most important harms related to an AAA screening program derive from the surgical interventions to repair intact or non-ruptured AAAs. Across the studies, the most relevant risk factors that predict outcomes in elective non-ruptured AAA repairs were: gender, age, preoperative morbidity, smoking and aneurysm size.

Gender

There is no clear evidence about the effect of gender on the safety profile of the AAA screening. Chong et al. found higher long-term survival among women after open AAA repair (hazard ratio (HR) =0.72, 95% CI 0.55-0.93) (Chong 2009). The UK Small Aneurysm Trial, which included 40 to 55 mm AAAs, did not find significant

differences in death hazard between men and women (UKSATP 2002). In an observational study of 220,403 AAA patient-discharges in the USA, women had higher odds of both presenting with rupture and of in-hospital mortality compared with men, for both intact and ruptured AAA repairs (McPhee 2007). A systematic review that evaluated outcomes of 2387 EVARs, reported in 39 articles, found a significantly higher risk of complications after surgery among women (Walschot 2002). Women appear more likely to suffer AAA rupture at smaller aortic diameters than males. AAAs of equal diameter represented a greater proportional dilatation in females than in males in an observational study of elective AAA repairs. This led to the authors to recommend a smaller aneurysm diameter threshold of 52 mm for repair in females rather than the 55 mm threshold commonly used in males (Forbes 2006).

Age

Increasing age is an important adverse determinant of mortality for intact AAA repair. The 2008 Report of the European Society for Vascular Surgery, which reported data from 27,635 intact AAA surgical interventions (ESVS 2008), found a 1% mortality rate for patients between 51 and 55 years and nearly 5.2% mortality rate for those patients between 81 and 85 years old. Other studies have confirmed this (Chong 2009; Mastracci 2007; Brady 2000).

Smoking

The multivariate analysis of 1020 open non-rupture AAA repairs with a mean follow-up of 57.6 months found that smoking increased general morbidity in open AAA repairs (odds ratio (OR)=2.15, 95% CI 1.03-4.46) (Chong 2009). The UK Small Aneurysm Trial found that current smokers had a higher death risk than former smokers (UKSATP 2002).

Other factors

Long-term mortality after open AAA repair was associated with the presence of coronary artery disease (HR= 1.36; 95% CI 1.08-1.72), chronic obstructive pulmonary disease (HR = 1.59; 95%CI 1.21-2.09), chronic renal failure (HR = 2.87; 95% CI 1.90-4.33), and congestive cardiac failure (HR = 2.52; 95%CI 1.78-3.57) after a mean of 57.6 months of follow-up (Chong 2009). The same study found that preoperative renal failure increased postoperative renal decline and that increasing size of aneurysm increased peri-operative and long term mortality. The UK Small Aneurysm Trial found significant increases in mortality rates after intact AAA repair with older age, larger diameter of the aneurysm (higher hazard for those with 49 to 55 mm versus both 40 to 44 mm and 45 to48 mm), lower ankle brachial-pressure index, and worse lung function (lower FEV_1 [forced expiratory volume in 1 second]) (UKSATP 2002). Egorova et al. developed a model to define high risk patients when they are treated with elective EVAR of AAA. The model analysed the 30-day mortality of the 44,360 elective EVAR in USA. The regression model ordered the significant factors from the highest to the lowest predicted mortality as follows: renal failure with dialysis (highest score), clinically significant lower extremity ischemia, age > 85 years,

liver disease, congestive heart failure, renal failure without dialysis, 80-84 years age, female, neurological disorders, chronic pulmonary disease, surgeon experience in EVAR less than three procedures, hospital annual volume in EVAR less than seven procedures and 75-79 years age (Egorova 2009).

Consequences of false positive, false negative and incidental findings brought about AAA screening

Evidence about the consequences of false positive, false negative and incidental findings of using AAA screening from a safety perspective are scarce in the literature. However, the available data indicate that the magnitude of the estimates would be low. An evaluation of the screening program of Huntingdon (UK) found no false negatives when comparing ultrasound results with further ruptures. They also found no false positives when comparing ultrasound with computed tomography. They reported ultrasound sensitivity of 100% for detecting AAAs of 4.5 cm or more, specificity of 100% for AAAs of up to 3.0 cm, and therefore 100% for both positive and negative predictive values (Wilmink 2002).

Lindholt et al. estimated accuracy from the inter-observer values. Their estimated sensitivity, specificity and predictive values of a positive test for AAA in the distal part of the infrarenal aorta were 98.9%, 99.8% and 97.0%, respectively (Lindholt 1999). The sensitivity, specificity and predictive value of a positive test for AAA in the proximal part of the infrarenal aorta were estimated at 87.4%, 99.9%, and 94.7%. Based on these numbers, false positive and false negative rates were calculated (ratio of false positives to non-cases and ratio of false negatives to cases respectively). The false positive and false negative rates of AAA in the distal part of the infrarenal aorta using ultrasonography were 0.0013 and 0.0107 respectively (Lindholt 1999). The false positive and false negative rates of AAA in the proximal part of the infrarenal aorta, using ultrasonography, were 0.0006 and 0.1260 respectively (Lindholt 1999). The incidence of false positive scans is small and of little clinical consequence as they are likely to be detected on surveillance rescanning or confirmatory computed tomography (CT) scan. A false negative finding would result in the same outcomes as those occurring in subjects for whom screening was not performed.

Ultrasound has high accuracy values when used as the first diagnostic test in AAA screening program, however some difficulties with visualising the aorta may occur in some cases (1.2% in the MASS trial) (Ashton 2002). The MASS trial, which performed the screen in non-routine clinics using portable ultrasound machines, had 1.2% non-valid ultrasound tests. Therefore, it is advisable for some cases to be rescanned in a hospital setting by experienced sonographers.

The AAA screening clinical trials have not reported incidental discoveries of other pathologies. According to the clinical trials the frequency of incidental discovery of other pathologies in screening programs for AAA would be low.

Special features of AAA screening susceptible to increase safety risks

Intra- or interobserver variations
Beales et al. systematically reviewed studies on intra- or inter-observer variations in ultrasound measurements (Beales 2011). The acceptable level of observer variation between aortic diameter measurements was suggested to be 5 mm. Out of the nine studies evaluated, five presented coefficients lower that this limit. The most relevant factors they found that could affect reproducibility were: observer's experience level, patient's obesity and bowel gas, aortic diameter, and whether the machine was modern.

Singh et al. assessed the agreement between ultrasound and computed tomography (CT) measurements of normal and aneurysmatic aorta and the common iliac artery diameter (Singh 2004). After evaluating 3686 measurement pairs from 555 patients, they found considerable disagreement between the two techniques. Ultrasound underestimated aortic diameter in measurements of normal sized aortas (<30 mm) as compared with CT, whereas the opposite was true for aneurysmal aortas.

Singh et al. examined in an additional study the intra and inter-observer variability of CT measurements in 59 individuals. The authors found that approximately 95% of the CT measurements of the maximal infrarenal aortic diameter of the abdominal aorta could be performed with accuracy within the limit of 4 mm (Singh 2004). The intra-observer variability for both planes was less than inter-observer variability, was increased with increasing vessel diameter, and was influenced by the experience level of the radiologist.

Volume-outcome relationship
A systematic review that examined both open and endovascular repair of intact AAA found that hospital volume, surgeon volume, and surgeon's specialisation in vascular surgery were all significant and highly associated with mortality (Karthikesalingam 2010). Regarding hospital volume, a meta-analysis of 421,229 elective AAA repairs resulted in a pooled OR of mortality for high-volume institutions of 0.66 (95% CI = 0.65-0.67) (≥43 OAR per annum) as compared with low-volume institutions (<43 OAR per annum) (Holt 2007).

A meta-analysis evaluating 115,273 AAA repairs found that repairs by high-volume surgeons resulted in a decreased mortality compared with those by low-volume surgeons (pooled OR = 0.56; 95% CI 0.54-0.57), suggesting a threshold of 13 AAAs surgical repairs per year (Young 2007). Surgeon volume had more effect than did hospital volume in a study of 5972 OARs after adjusting for other patient and hospital

characteristics (McPhee 2011). However, neither surgeon nor hospital volumes were found to have a significant influence on mortality after EVARs (McPhee 2011).

Surgeon specialty, which implies subspecialty training and board certification, was also identified as influencing outcomes in AAA repair (Dimick 2003; Pearce 1999; Tu 2001). Operations performed by vascular specialist surgeons were associated with significant reductions in mortality compared with those done by general surgeons.

Increased burden on surgical services
There is evidence that AAA screening causes an increased burden on local vascular surgical services; however its consequence on health outcomes has not been assessed. Among the 67,770 men recruited in the MASS trial, and after 10 years of follow-up, 552 elective operations took place in the invited group (n=33,883) and 226 in the control group (n=33,887). Sixty-two men underwent emergency surgery in the invited group compared with 141 in the control group. These data show that the rate of elective repairs doubles with the advent of screening, and emergency ruptures are reduced by half (Thompson 2009).

How harms may influence the acceptability of AAA screening

There is scarce information on the impact of harms on acceptability or tolerability of AAA screening. However, some factors have been identified that influence AAA screening uptake. Three randomized clinical trials evaluating the efficacy of screening for AAA reported that increasing age is negatively associated with the rate of screening attendance (Jamrozik 2000; Lindholt 1998; Scott 1995). Lindholt et al. found from the "Viborg trial" that the age ranges 68-70 (OR = 0.82; 95% CI 0.69-0.97) and 71-73 (OR = 0.59; 95% CI 0.50-0.70) had significant lower attendance rates compared with the age range 65-67, when adjusting for all other predictors (Lindholt 1998). This is consistent with results from the "Chichester trial" (Scott 1995) and the "Western Australia Trial" (Jamrozik 2000). Compliances in the "Chichester trial" were 80%, 76%, 74%, and 66% for ages 65, 66-70, 71-75, and 76-80 years, respectively. Moreover, compliances for women were 73%, 69%, 66%, 58% for the same age ranges (Scott 1995). Lindholt et al. showed that attendance rates were above average among people with chronic pulmonary and cardiovascular conditions (OR = 1.40; 95% CI 1.12-1.77) compared with healthy individuals (Lindholt 1998). People with mobility-disabling diseases showed low rates of attendance compared with healthy individuals, although this was not statistically significant (Lindholt 1998).

There is also scarce information about the determinants of uptake for other screening program (Jepson 2000). A systematic review found only one study that measured the impact of information about benefit and risks on screening uptake. The study, a randomized controlled trial that measured women's uptake of Down's syn-

drome screening, found no increase in uptake when women received additional clinical information in different forms (detailed leaflet, audiovisual) (Michie 1997).

A recent systematic review of barriers to colorectal cancer screening uptake in participants over 65 years of age found that unpleasantness, discomfort, and perceived risks associated with performing the tests were the most commonly reported barriers related to screening tests (Guessous 2010). This would not apply to the AAA screening, however, because in AAA screening the perceived risk, unpleasantness and discomfort associated with the diagnostic test is low.

How safety risks can be reduced for screened subjects

Hospital volume, surgeon volume, and surgeon's specialization in vascular surgery have been found highly associated with mortality when an AAA is detected and repaired (Couto 2002), which makes advisable that both, open and endovascular repair of intact AAA be performed by high volume hospitals and high volume surgeons.

Discussion

Clinical effectiveness

Evidence from four high-quality RCTs included in several SRs indicates that AAA screening can be beneficial in men over 65 years of age, as it can reduce AAA-related mortality by nearly half in the mid- and long-term. The number needed to screen (NNS) to prevent one extra death in the male population over 65 years is 238 (Takagi 2010). Data also indicate that acceptance of screening sonography in the population under risk is high. AAA screening can result in decrease in emergency operations for ruptured AAA and increase in elective AAA surgery. Data on global function, activities of daily living and QoL is, however, poor, except for anxiety and depression, which appear to be reduced with AAA screening. No data on morbidity after screening were found. However, it is clear that morbidity will mainly consist of complications caused by the surgical intervention.

When establishing an AAA screening program, the qualification of the sonographers could be important. Inter-observer repeatability and intra-observer reproducibility appear to be acceptable, but the evidence is hampered by the fact that the quality of the primary studies on this topic could not be assessed systematically. As the included SR found the results of the primary studies to be heterogeneous, the need for careful selection and standard training of sonographers was emphasized. No data were found on diagnostic accuracy and the optimal threshold value. In the included RCTs, however, the usual threshold for referring men to a vascular surgeon ranged between 50 mm and 55 mm aortic diameter.

In contrast to men, there is no reliable clinical data to show that women benefit from AAA screening. Only one of the four RCTs included women in addition to men, but this did not detect a difference in AAA-related mortality in females. In this trial, the prevalence of AAA was six times lower in women than in men, so only very large trials would be able to detect a difference in this population. Recent data have shown a decline in AAA incidence in men (Anjum & Powell 2012, and references therein), which probably does not alter the relative effectiveness of screening measures, but clearly increases the NNS.

Safety

Adverse events are variably and sometimes poorly reported in randomized controlled trials (Ioannidis 2001; Pitrou 2009). Hence evidence reported here relies on identified real-world data from large observational studies describing the effect of the surgical repair of intact AAAs. This information has been useful for estimating what might happen in a hypothetic situation if a screening program was implemented in a European scenario. The implementation of an AAA screening program in Europe would result in a high number of high-risk surgical interventions done in different kinds of healthcare systems, in different hospitals with different surgeons and to different patients.

Ultrasonographic scanning is a highly accurate screening method for AAA. Close to 100% sensitivity and specificity values have been reported. The available information about harms indicates no relevant safety issues regarding the accuracy of the test used for AAA screening.

Inconsistent results have been found regarding psychological effects of an AAA screening program. An appropriate design for measurement of changes in quality of life for participants versus not participants was not identified. Therefore, it is not possible to determine whether screening for AAA affects the health related quality of life among participants.

The variability between methods and designs among our selected studies made it difficult to apply a systematic system for grading the evidence.

Conclusion

Summary of results

Evidence from the literature indicates that AAA screening does not affect overall mortality neither in men nor in women. However, AAA can be beneficial in men over 65 years of age, as it may reduce AAA-related mortality by nearly half in the mid- and long-term. In contrast to men, there are no reliable clinical data showing that women may benefit from AAA screening. Moreover, AAA screening can result in a decrease of emergency operations for ruptured AAA, and an increase in elective AAA surgery. In terms of safety, serious harms of AAA screening are mainly related to the surgical intervention following detection of an AAA with high risk of rupture, i.e. AAA suitable for repair.

Need for further research

Future research should probably focus on optimizing screening strategies in men. Also more research is needed before we can assess the benefit from screening of women. Screening intervals, risk-adjusted repeat screening, cut-off values for surgical procedures and training of sonographers could be valuable research topics.

Implications for practice

Since hospital volume, surgeon volume, and surgeons' specialization in vascular surgery have all been found to be associated with mortality when an AAA is detected and repaired, there are issues that should be taken into account in terms of safety when introducing an AAA screening program. Indeed, quality of screening could be guaranteed by applying several criteria including appropriate training of staff, standardized calibration of equipment, monitoring screening outcome and performance. All monitoring processes should be carried out using information technology (identification and collation of screening cohort; management of administration, screening and referral process; record-

ing of AAA surgery and outcomes). Human resources for AAA screening should include clinical staff (director/clinical lead, ultrasound clinician, consultants in vascular units), screening staff (ultrasound screening technicians, clinical skills trainer, nurse practitioner), management / administration / technical staff (coordinator, clerical officer, medical physicist, IT lead), governance (strategic health authorities, primary care trusts, primary care providers, local screening program, diagnostic and treatment services).

As a result of a decrease in the number of daily smokers in Western countries, the future incidence of AAA might be expected to fall, and, consequently, the need for an AAA screening program might also change within the next decade.

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Appendix 1

1. Basic literature search

Agreed overall approach for strategy for the basic literature search

1. aortic aneurysm, abdominal

2. mass screening

*3. screen**

4. 2 or 3

5. 1 and 4

Search log for the basic literature search

Databases: Cochrane Library: Cochrane Database of Systematic Reviews (CDSR), Database of Abstract of Reviews of Effects (DARE) (other Reviews), Health Technology Assessments D. (HTA), Central Register of Controlled Trials (CENTRAL). Centre for Reviews and Dissemination (CRD), EMBASE (Ovid), Ovid MEDLINE, Web of Knowledge (ISI)

Search date: 25.10.2011 Searched by: Ingrid Harboe, research librarian (NOKC)
Study design: Systematic Reviews, (Randomized) Controlled Trials
References: total: 167 total (243 including duplicates)
41 SRs or HTAs
126 RCTs

Database: Cochrane Library
Results: **Cochrane Reviews [2],** Other Reviews [2], Clinical Trials [63], Methods Studies [1], Technology Assessments [11]

Search strategy:

#1	MeSH descriptor Aortic Aneurysm, Abdominal, this term only	503
#2	(Abdominal Aort* Aneurysm*):ti,ab,kw	681
#3	(#1 OR #2)	681
#4	MeSH descriptor Mass Screening, this term only	3415
#5	screen*:ti,ab,kw	14943
#6	(#4 OR #5)	14943
#7	(#3 AND #6)	102

Database: Centre for Reviews and Dissemination

Results:12 SR/HTA

Search strategy:

#1	MeSH DESCRIPTOR Aortic Aneurysm, Abdominal EXPLODE ALL TREES	154
#2	("Abdominal Aortic Aneurysm") IN DARE, HTA	68
#3	#1 OR #2	174
#4	MeSH DESCRIPTOR Mass Screening EXPLODE ALL TREES	1704
#5	("Mass Screening") IN DARE, HTA	720
#6	#4 OR #5	1785
#7	#3 AND #6	32
#8	(#7) IN DARE, HTA	12

Databases: Embase 1980 to 2011 Week 42 & Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to Present
Results: 3

Search filters:
Systematic Reviews: reviews (maximizes specificity) & systematic* review*.ti,ab.
Randomized controlled trials: therapy (best balance of sensitivity and specificity)

Search strategy:

#1	abdominal aorta aneurysm/ use emez	15240
#2	Aortic Aneurysm, Abdominal/ use prmz	11591
#3	abdominal aort* aneurysm*.tw.	23463
#4	or/1-3	32698
#5	mass screening/	114617
#6	screen*.tw.	819044
#7	or/5-6	858256
#8	4 and 7	1925
#9	remove duplicates from 8	1148
#10	9 use emez [Embase]	1017
#11	9 use prmz [Medline]	131
#12	limit 11 to "reviews (maximizes specificity)"	3
#13	limit 10 to "reviews (maximizes specificity)"	25
#14	9 and systematic* review*.ti,ab.	22
#15	or/12-14	29
#16	limit 10 to "therapy (best balance of sensitivity and specificity)"	121
#17	limit 11 to "therapy (best balance of sensitivity and specificity)"	15
#18	or/16- 17	136
#19	15 use emez	26
#20	15 use prmz	3

2. Checklist for quality assessments

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?			
Comment:			
2. Are the comparison groups clearly stated?			
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the questions to be answered stated?			
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?			
Comment:			
5. Are explicit criteria used for deciding which studies to include in the review?			
Comment:			
6. Is bias in the selection of articles likely to be avoided?			
Comment:			
7. Are the reasons for excluding studies from the review reported?			
Comment:			
8. Are the criteria used for assessing the quality of the studies reported?			
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?			
Comment:			
10. Are the methods used to combine the findings of the relevant studies reported?			
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the questions to be answered by the review?			
Comment:			
Overall quality:			
Assessed by/date:			

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews (Grimshaw 2003). (http://www.uio.no/studier/emner/medisin/med/MF9000E/h09/lectures/kornoer-metaanalysis/EPOC%20checklist.pdf)

High quality: All or most criteria from the checklist are met. It is very unlikely that the study conclusions are affected.

Medium quality: Some criteria from the checklist are not met. It is unlikely that the study conclusions are affected.

Low quality: Few or no criteria in the checklist are met. It is likely that the study conclusions may be affected.

Appendix 2

1. List of included literature

Reference	*Abstract*
Beales L, Wolstenhulme S, Evans JA, West R, Scott DJA. Reproducibility of ultrasound measurement of the abdominal aorta. Br J Surg 2011;98(11):1517-25. **BASIC SEARCH OCT 2011**	Abdominal aortic aneurysm (AAA) screening and surveillance programmes use ultrasound imaging to measure the anteroposterior (AP) diameter of the infrarenal aorta. The aim of this study was to examine potential observer bias and variability in ultrasound measurements. METHODS: Studies were identified for review via a MEDLINE database search (1966-2009). References supplied in accessed papers were also checked for potential relevance. Consistent search terminology, and inclusion and exclusion criteria were used to ensure quality of data. Nine papers were available to review. RESULTS: Variation in intraobserver repeatability and interobserver reproducibility was identified. Six studies reported intraobserver repeatability coefficients for AP aortic diameter measurements of 1.6-4.4 mm. These were below the 5-mm level regarded as acceptable by the UK and USA AAA screening programmes. Five studies had interobserver reproducibility below the level of 5 mm. Four studies, however, reported poor reproducibility (range from - 2 to + 5.2 to - 10.5 to + 10.4); these differences may have had a significant clinical impact on screening and surveillance. CONCLUSION: The studies used different methodologies with no standardized measurement techniques. Measurements were taken by observers from different medical disciplines of varying grade and levels of training. Standard training and formal quality assurance of ultrasound measurements are important components of an effective AAA screening programme. Copyright Copyright 2011 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd. Copyright Copyright 2011 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd

Collins RE, Lopez LM, Marteau TM. Emotional impact of screening: a systematic review and meta-analysis. BMC Public Health 2011;11:603. **BASIC SEARCH OCT 2011**	BACKGROUND: There is a widely held expectation that screening for disease has adverse emotional impacts. The aim of the current review is to estimate the short (< 4 weeks) and longer term (> 4 weeks) emotional impact of such screening. METHODS: Studies selected for inclusion were (a) randomised controlled trials in which (b) participants in one arm underwent screening and received test results, and those in a control arm did not, and (c) emotional outcomes were assessed in both arms. MEDLINE via PubMed (1950 to present), EMBASE (1980 to present), PsycINFO (1985 to present) using OVID SP, and CINAHL (1982 to present) via EBSCO were searched, using strategies developed with keywords and medical subject headings. Data were extracted on emotional outcomes, type of screening test and test results. RESULTS: Of the 12 studies that met the inclusion criteria, six involved screening for cancer, two for diabetes, and one each for abdominal aortic aneurysms, peptic ulcer, coronary heart disease and osteoporosis. Five studies reported data on anxiety, four on depression, two on general distress and eight on quality of life assessed between one week and 13 years after screening (median = 1.3 years).Meta-analyses revealed no significant impact of screening on longer term anxiety (pooled SMD 0.01, 95% CI -0.10, 0.11), depression (pooled SMD -0.04, 95% CI -.12, 0.20), or quality of life subscales (mental and self-assessed health pooled SMDs, respectively: 0.03; -0.01, (95% CI -.02, 0.04; 0.00, 95% CI -.04, 0.03). CONCLUSION: Screening does not appear to have adverse emotional impacts in the longer term (> 4 weeks). Too few studies assessed outcomes before four weeks to comment on the shorter term emotional impact of screening.
Cosford PA, Leng GC, Thomas J. Screening for abdominal aortic aneurysm. Cochrane Database of Systematic Reviews 2007;(2):CD002945. **BASIC SEARCH OCT 2011**	BACKGROUND: Abdominal aortic aneurysm (AAA) is found in 5% to 10% of men aged 65 to 79 years. The major complication is rupture which presents as a surgical emergency. The mortality after rupture is high, 80% for patients reaching hospital and 50% for those undergoing surgery for emergency repair. Currently elective surgical repair is recommended for aneurysms discovered to be larger than 5.5 cm to prevent rupture. There is interest in population screening to detect, monitor and repair abdominal aortic aneurysms before rupture. OBJECTIVES: To determine the effects of screening asymptomatic individuals for AAA on mortality, subsequent treatment, quality of life and cost effectiveness of screening. SEARCH STRATEGY: The Cochrane Peripheral Vascular Diseases Group searched their Trials Register (last searched 27 July 2007)

	and CENTRAL (last searched 2007, Issue 3). SELECTION CRITERIA: Randomised controlled trials of population screening for AAA. DATA COLLECTION AND ANALYSIS: Two authors independently assessed trials and extracted data. MAIN RESULTS: Four studies involving 127,891 men and 9342 women were included in this review. Only one study included women. Results for men and women were analysed separately. Three to five years after screening there was no significant difference in all-cause mortality between screened and unscreened groups for men or women (men, odds ratio (OR) 0.95; 95% Confidence interval (CI) 0.85 to 1.07; for women OR 1.06; 95% CI 0.93 to 1.21).There was a significant decrease in mortality from AAA in men (OR 0.60; 95% CI 0.47 to 0.78), but not for women (OR 1.99; 95% CI 0.36 to 10.88). In this analysis mortality includes death from rupture and from emergency or elective surgery for aneurysm repair. There was also a decreased incidence of ruptured aneurysm in men (OR 0.45; 95% CI 0.21 to 0.99) but not in women (OR 1.49; 95% CI 0.25 to 8.94).There was a significant increase in surgery for AAA in men (OR 2.03; 95% CI 1.59 to 2.59). This was not reported in women. There were no data on life expectancy, complications of surgery or subjective quality of life. AUTHORS' CONCLUSIONS: There is evidence of a significant reduction in mortality from AAA in men aged 65 to 79 years who undergo ultrasound screening. There is insufficient evidence to demonstrate benefit in women. The cost effectiveness may be acceptable, but needs further expert analysis. These findings need careful consideration in judging whether a co-ordinated population-based screening programme should be introduced. SCREENING FOR ABDOMINAL AORTIC ANEURYSM: An aneurysm is a localised widening (dilation) of an artery. The blood vessel can burst (rupture) because the vessel wall is weakened. Some 5% to 10% of men aged between 65 and 79 years have an abdominal aneurysm in the area of the aorta, the main artery from the heart as it passes through the abdomen. Abdominal aortic aneurysms are often asymptomatic but a rupture is a surgical emergency and often leads to death. An aneurysm larger than 5 cm carries a high risk of rupture. Smaller aneurysms are monitored regularly using ultrasound to see if they are becoming larger. Elective surgical repair of aortic aneurysms aims to prevent death from rupture. The incidence of aortic aneurysm in women as they age is lower than for men. This review identified four controlled trials involving 127,891 men and 9342 women who were randomly assigned to aortic aneurysm screening using ultrasound or no screening. Only one

	trial included women. Two of the trials were conducted in the UK, one in Denmark and one in Australia. The results provide evidence of a benefit from screening in men with a strongly significant reduction in deaths from abdominal aortic aneurysm. The odds ratio (OR) for death was 0.60 (range 0.47 to 0.78, three trials) in men aged 65 to 83 years but was not reduced for women. From one trial there was also a decreased incidence of ruptured aneurysm in men but not women. All-cause mortality was not significantly different between screened and unscreened groups some three to five years after screening, which is to be expected given the relative infrequency of abdominal aortic aneurysm as a cause of death. Men who had been screened underwent more surgery for abdominal aortic aneurysm (OR 2.03; range 1.59 to 2.59, four trials) but resource analysis appears to demonstrate overall cost effectiveness of screening. There were no data on life expectancy, complications of surgery or quality of life.
Lindholt JS, Norman P. Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms. Eur J Vasc Endovasc Surg. 2008 (2):167-71. **HAND-SEARCH NOV 2011**	*BACKGROUND: Four randomised controlled trials of screening older men for abdominal aortic aneurysms (AAA) have been completed. A meta-analysis was performed to examine the pooled effects of screening on both mid- and long-term AAA-related and total mortality, and operations for AAA. METHODS: Pooled mid-term (3(1/2)-5 years) and long term (7-15 years) effects were calculated as odds-ratios (ORs) with 95% confidence intervals in fixed effect models. Long-term data from the West Australian trial were limited to all-cause deaths. Heterogeneity between the studies was assessed by the chi(2)-test. In cases of heterogeneity, random effect models were used. RESULTS: The pooled mid-term analysis showed the offer of screening caused a significant reduction in AAA related mortality (OR=0.56, 95% C.I. 0.44,0.72), and emergency operations (OR=0.55, 95% C.I.: 0.39; 0.76), while the number of elective operations increased significantly (OR=3.27, 95% C.I.: 2.14; 5.00). Overall mortality was reduced, but not significantly (OR=0.94, 95% C.I.: 0.86; 1.02). The long-term results also showed a significant reduction in AAA-related mortality (OR=0.47, 95% C.I.: 0.25; 0.90), overall mortality (OR=0.94, 95% C.I.: 0.92; 0.97) and emergency operations (OR=0.48, 95% C.I.: 0.28; 0.83), while the number of elective operations increased significantly (OR=2.81, 95% C.I.: 2.40; 3.30). CONCLUSION: Population screening for AAA reduces AAA-related and overall mortality, however local differences may exits which could influence cost effectiveness of screening.*

Takagi H, Goto SN, Matsui M, Manabe H, Umemoto T. A further meta-analysis of population-based screening for abdominal aortic aneurysm. J Vasc Surg. 2010 (4):1103-8. **HAND-SEARCH NOV 2011**	*PURPOSE: It remains unclear whether population-based screening for abdominal aortic aneurysm (AAA) in men reduces all-cause long-term mortality. We performed an updated meta-analysis of randomized controlled trials of AAA screening for prevention of long-term mortality in men. METHODS: To identify all randomized controlled trials of population-based AAA screening with long-term (≥ 10 year) follow-up in men, MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials were searched through June 2009. Data regarding AAA-related and all-cause mortality (including Cox regression hazard ratios [HRs] and 95% confidence intervals [CIs]) were abstracted from each individual study. For each study, data regarding mortality in both the screening and control groups were used to generate odds ratios (ORs) and 95% CIs. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic ORs or HRs (or risk ratios where no HR was reported) in both fixed- and random-effects models. RESULTS: Our search identified four randomized controlled trials of population-based AAA screening with long-term follow-up in men aged ≥ 65 years. Pooled analysis demonstrated a statistically significant reduction in AAA-related mortality (random-effects OR, 0.55; 95% CI, 0.36 to 0.86; P = .008; P for heterogeneity = .01; absolute risk reduction [ARR], 4 per 1000; number needed to screen [NNS], 238; random-effects HR, 0.55; 95% CI, 0.35 to 0.86; P = .009; P for heterogeneity = .009) and revealed a statistically non significant reduction (but a strong trend toward a significant reduction) in all-cause mortality (fixed-effects OR, 0.98; 95% CI, 0.95 to 1.00 [1.001]; P = .06; P for heterogeneity = .93; ARR, 5 per 1000; NNS, 217; fixed-effects HR, 0.98; 95% CI, 0.96 to 1.00 [1.0001]; P ≥ .05 [P = .052]; P for heterogeneity = .74) with AAA screening relative to control. CONCLUSION: The results of our analysis suggest that population-based screening for AAA reduces AAA-related long-term mortality by 4 per 1000 over control in men aged ≥ 65 years. Whereas, screening for AAA shows a strong trend toward a significant reduction in all-cause long-term mortality by 5 per 1000, which does not narrowly reach statistical significance.*

2. Quality assessment and description of included SRs

Cosford 2007

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?	X		
Comment:			
2. Are the comparison groups clearly stated?	X		
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the questions to be answered stated?	X		
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?	x		
Comment:			
5. Are explicit criteria used for deciding which studies to include in the review?	x		
Comment:			
6. Is bias in the selection of articles likely to be avoided?	x		
Comment:			
7. Are the reasons for excluding studies from the review reported?	x		
Comment:			
8. Are the criteria used for assessing the quality of the studies reported?	x		
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?	x		
Comment:			
10. Are the methods used to combine the findings of the relevant studies reported?	x		
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the questions to be answered by the review?	x		
Comment:			
Overall quality: High			
Assessed by/date: Ingvil Sæterdal, NOKC, 10 May 2012			

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews. Grimshaw et.al 2003.

Article	Full reference		Cosford PA, Leng GC, Thomas J. Screening for abdominal aortic aneurysm. *Cochrane Database of Systematic Reviews* 2007, Issue 2. Art. No.: CD002945.

	DOI		DOI: 10.1002/14651858.CD002945.pub2.
Project details	Reviewed by		Ingvil Sæterdal, NOKC
	Date of review		10 May 2012
	Project name		EUnetHTA WP4 pilot AAA
	Project ID		
Study type	Type of publication		Systematic review
	Country (area) Year		Authors from UK 2007
	Last updated search		July 2003
Research question		Overall question: To determine the effects of screening asymptomatic individuals for AAA on mortality, subsequent treatment, quality of life and cost effectiveness of screening.	
Included for		Domain: Clinical effectiveness Question/Result card: EFF1	
Study design		What study design(s) are included by the review: Randomized controlled trials	
Population		Patient characteristics: People asymptomatic of aortic aneurysm were eligible for this review.	
		Disease/condition: Asymptomatic of aortic aneurism	
Intervention		Any screening technique for abdominal aortic aneurysm	

Comparison		No screening
Outcomes/ Endpoints		Outcomes assessed for this domain-report: • mortality (overall mortality and mortality caused by abdominal aortic aneurysm; • progression to ruptured aortic aneurysm; Outcomes not assessed by this domain-report: • life expectancy; • complications of surgery including distal embolus, haemorrhage and graft failure, coronary and cerebrovascular • events and renal complications; • subjective measures including quality of life scores and impact on ability to work; • use of resources including hospital stay and use of intensive care facilities.
Sources of information		Databases: • The Cochrane Peripheral Vascular Diseases (PVD) Group Trials Register • Cochrane Central Register of Controlled Trials (CENTRAL) The PVD Group's Trials Register is compiled from backsearching and continued prospective searching of MEDLINE (1950 to date); EMBASE (1980 to date); CINAHL (1982 to date); LILACS (last searched July 2007); the Index to UK Thesis (searched May 2006); and the United States Department of Health & Human Services HRQ Agency for Healthcare Research And Quality Technology Assessments; and from handsearching journals and conference proceedings.
		Other sources of information: See above

Main Conclusion		Conclusion as stated by the review authors: There is evidence of a significant reduction in mortality from AAA in men aged 65 to 79 years who undergo ultra-sound screening. There is insufficient evidence to demonstrate benefit in women. The cost effectiveness may be acceptable, but needs further expert analysis. These findings need careful consideration in judging whether a co-ordinated popula-tion-based screening programme should be introduced.

			Quality assessment (Based on checklist for systematic reviews)								
1	2	3	4	5	6	7	8	9	10	11	Quality
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
			Comments:								

Takagi 2010

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?	X		
Comment:			
2. Are the comparison groups clearly stated?	X		
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the ques-tions to be answered stated?	X		
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?	x		
Comment:			
5. Are explicit criteria used for deciding which studies to include in the review?	x		
Comment:			
6. Is bias in the selection of articles likely to be avoided?	x		
Comment:			
7. Are the reasons for excluding studies from the review reported?			x
Comment: Excluded studies that did not meet the inclusion criteria. The excluded studies are not listed and an explanation for the exclusion is not provided.			
8. Are the criteria used for assessing the quality of the studies reported?	x		
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?	x		
Comment: Only a résumé of the quality of the studies is given. Detail on each quality assessment domain is missing			
10. Are the methods used to combine the findings of the relevant studies reported?	x		
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the ques-tions to be answered by the review?	x		

Comment:
Overall quality: low to medium
Assessed by/date: Ingvil Sæterdal, NOKC, 16 May 2012

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews. Grimshaw et.al 2003.

Article	Full reference		Takagi H, Goto Sn, Matsui M, Manabe H, Umemoto T. A further meta-analysis of population-based screening for abdominal aortic aneurysm. J Vasc Surg 2010;52:1103-8.
	DOI		
Project details	Reviewed by		Ingvil Sæterdal, NOKC
	Date of review		16 May 2012
	Project name		EUnetHTA WP4 pilot AAA
	Project ID		
Study type	Type of publication		Systematic review
	Country (area) Year		Authors from Japan 2010
	Last updated search		June 2009
Research question		Overall question: It remains unclear whether population-based screening for AAA in men reduces al-cause long-term mortality in men. We performed an updated meta-analysis of randomized controlled trials of AAA screening for prevention of long-term mortality in men.	
Included for		Domain: Clinical effectiveness Question/Result card: EFF1	
Study design		What study design(s) are included by the review: Randomized controlled trials	
Population		Patient characteristics: All randomized controlled trials of population-based	

		screening for AAA in men were included.
		Disease/condition: Asymptomatic of aortic aneurism
Intervention		Screening for AAA
Comparison		No intervention
Outcomes/ Endpoints		Outcomes assessed for this domain-report: • Long-term (≥ 10 years) mortality (overall mortality and mortality caused by abdominal aortic aneurysm; Outcomes not assessed by this domain-report: • None
Sources of information		Databases: • MEDLINE, EMBASE AND Cochrane Central Register of Controlled Trials
		Other sources of information: Relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries.
Main Conclusion		Conclusion as stated by the review authors: The results of our analysis suggest that population-based screening for AAA reduces AAA-related long-term mortality by 4 per 1000 over control in men aged >65 years. Whereas, screening for AAA shows a strong trend toward a significant reduction in all-cause long-term mortality by 5 per 1000, which does not narrowly reach statistical significance.

			Quality assessment (Based on checklist for systematic reviews)								
1	2	3	4	5	6	7	8	9	10	11	Quality

Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Medium
	Comments:										

Lindholt & Norman 2008

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?	x		
Comment:			
2. Are the comparison groups clearly stated?	x		
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the questions to be answered stated?	x		
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?			x
Comment: Should include more databases and not be language restricted. Search in additional sources is also missing.			
5. Are explicit criteria used for deciding which studies to include in the review?			x
Comment: Articles were retrieved based on search terms, population and intervention. However, this is not stated explicitly			
6. Is bias in the selection of articles likely to be avoided?		x	
Comment:			
7. Are the reasons for excluding studies from the review reported?			x
Comment: Excluded studies that did not meet the inclusion criteria. The excluded studies are not listed and an explanation for the exclusion is not provided.			
8. Are the criteria used for assessing the quality of the studies reported?		x	
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?		x	
Comment: Only a résumé of the quality of the studies is given. Detail on each quality assessment domain is missing			
10. Are the methods used to combine the findings of the relevant studies reported?	x		
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the questions to be answered by the review?	x		
Comment:			
Overall quality: medium			
Assessed by/date: Ingvil Sæterdal, NOKC, 7 June 2012			

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews (Grimshaw 2003)

Article	Full reference		Lindholt JS and Norman P. Overall Mortality in Men. A Meta-analysis of the Mid- and Long-term Effects of Screening for

			Abdominal Aortic Aneurysms. Eur J Vasc Endovasc Surg (2008) 36, 167e171.
	DOI		
Project details	Reviewed by		Ingvil Sæterdal, NOKC
	Date of review		6 June 2012
	Project name		EUnetHTA WP4 pilot AAA
	Project ID		
Study type	Type of publication		Systematic review
	Country (area) Year		Authors from Denmark and Australia 2008
	Last updated search		Not reported
Research question		Overall question: The aims of this study were to examine the updated pooled mid- and long-term effects of screening on AAA-related and total mortality, and operations	
Included for		Domain: Clinical effectiveness Question/Result card: EFF1	
Study design		What study design(s) are included by the review: Randomized controlled trials	
Population		Patient characteristics: Men and women, but women were excluded from the meta-analysis	
		Disease/condition: Asymptomatic of aortic aneurism	
Intervention		Screening for AAA	

Comparison		No intervention
Outcomes/ Endpoints		Outcomes assessed for this domain-report: • Mid-term (3-5 years) mortality (overall mortality and mortality caused by abdominal aortic aneurysm) • Planned and emergency operations Outcomes not assessed by this domain-report: • Long-term (7-15 years) mortality (overall mortality and mortality caused by abdominal aortic aneurysm)
Sources of information		Databases: • MEDLINE
		Other sources of information: Not reported
Main Conclusion		Conclusion as stated by the review authors: Population screening for AAA reduces AAA-related and overall mortality, however local differences may exits which could influence cost effectiveness of screening.

Quality assessment (Based on checklist for systematic reviews)											
1	2	3	4	5	6	7	8	9	10	11	Quality
Y	Y	Y	N	N	U	N	U	U	Y	Y	Low to medium

	Comments: We assess the SR to be of low to medium quality. However, according to our experience from our own search for literature, the relevant RCTs are included and we therefore include this SR.

Collins 2011

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?	x		

Comment:			
2. Are the comparison groups clearly stated?	x		
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the questions to be answered stated?	x		
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?	x		
Comment:			
5. Are explicit criteria used for deciding which studies to include in the review?	x		
Comment:			
6. Is bias in the selection of articles likely to be avoided?	x		
Comment:			
7. Are the reasons for excluding studies from the review reported?	x		
Comment: Excluded studies that did not meet the inclusion criteria. The excluded studies are not listed and an explanation for the exclusion is not provided.			
8. Are the criteria used for assessing the quality of the studies reported?			
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?	x		
Comment: Only a résumé of the quality of the studies is given. Detail on each quality assessment domain is missing			
10. Are the methods used to combine the findings of the relevant studies reported?	x		
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the questions to be answered by the review?	x		
Comment:			
Overall quality: High			
Assessed by/date: Ingvil Sæterdal, NOKC, 7 June 2012			

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews. Grimshaw et.al 2003.

Article	Full reference		Collins RE, Lopez LM and Marteau TM. Emotional impact of screening: a systematic review and meta-analysis. BMC Public Health 2011, 11:603
	DOI		
Project details	Reviewed by		Ingvil Sæterdal, NOKC
	Date of review		7 June 2012
	Project name		EUnetHTA WP4 pilot AAA
	Project ID		

Study type	Type of publication		Systematic review
	Country (area) Year		Authors from UK 2011
	Last updated search		Not reported
Research question		Overall question: The primary aim of this review is to estimate the immediate and longer term emotional impact of undergoing screening or risk assessment for disease.	
Included for		Domain: Clinical effectiveness Question/Result card: EFF1	
Study design		What study design(s) are included by the review: Randomized controlled trials	
Population		Patient characteristics: Adults that underwent screening for Abdominal Aortic Aneurisms, Type II diabetes, osteoporosis, colorectal cancer and ovarian cancer were identified through the search. All adults that underwent screening could be included.	
		Disease/condition: No limitations. The authors identified screening trials for AAA, type II diabetes, osteoporosis, colorectal cancer and ovarian cancer.	
Intervention		Adults that underwent screening or risk assessment. One measure of emotion should be reported on all participants. Emotion was defined broadly to include measures of general mood states as well as emotional well-being.	
Comparison		No screening or risk assessment	

Outcomes/ Endpoints		Outcomes assessed for this domain-report: • Short term (assessed within one month of receipt of test results) and longer term (assessed one month or longer after receipt of test results) emotional outcomes. Outcomes not assessed by this domain-report: • Emotional outcomes assessed for other screening interventions than AAA screening.
Sources of information		Databases: • MEDLINE via PubMed (1950 to present) • EMBASE (1980 to present) • PsycINFO (1985 to present) using OVID SP • CINAHL (1982 to present) via EBSCO
		Other sources of information: Cross-sectional and cited reference searches were conducted on all papers meeting the inclusion criteria.
Main Conclusion		Conclusion as stated by the review authors: Screening does not appear to have adverse emotional impacts in the longer term (> 4 weeks). Too few studies assessed outcomes before four weeks to comment on the shorter term emotional impact of screening

	Quality assessment (Based on checklist for systematic reviews)										
1	2	3	4	5	6	7	8	9	10	11	Quality
Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	High
	Comments:										

Beales 2011

	Yes	Unclear	No
1. Is the specific purpose (question to be answered) stated?	x		
Comment:			
2. Are the comparison groups clearly stated?		x	
Comment:			
3. Are the sources and search methods used to find evidence (primary studies) on the questions to be answered stated?	x		
Comment:			
4. Is the search strategy for evidence reasonably comprehensive?			x
Comment: Should include more databases.			
5. Are explicit criteria used for deciding which studies to include in the review?	x		
Comment:			
6. Is bias in the selection of articles likely to be avoided?	x		

Comment:			
7. Are the reasons for excluding studies from the review reported?			x
Comment: Excluded studies that did not meet the inclusion criteria. The excluded studies are not listed and an explanation for the exclusion is not provided.			
8. Are the criteria used for assessing the quality of the studies reported?			x
Comment:			
9. Is the quality of all the studies to be reviewed assessed using appropriate criteria?		x	
Comment: Only a résumé of the quality of the studies is given. Detail on each quality assessment domain is missing			
10. Are the methods used to combine the findings of the relevant studies reported?	x		
Comment:			
11. Are the methods used to combine the findings of the relevant studies appropriate to the questions to be answered by the review?	x		
Comment:			
Overall quality: Medium			
Assessed by/date: Ingvil Sæterdal, NOKC, 7 June 2012			

*Adapted from the Cochrane EPOC group appraisal list for systematic reviews. Grimshaw et.al 2003.

Article	Full reference		Beales L, Wolstenhulme S, Evans JA, West R and Scott DJA. Reproducibility of ultrasound measurement of the abdominal aorta. *British Journal of Surgery* 2011; **98**: 1517–1525.
	DOI		
Project details	Reviewed by		Ingvil Sæterdal, NOKC
	Date of review		7 June 2012
	Project name		EUnetHTA WP4 pilot AAA
	Project ID		
Study type	Type of publication		Systematic review
	Country (area) Year		Authors from UK 2011
	Last updated search		2009
Research question		Overall question: The aim of this systematic review was to determine the level of repeatability and reproducibility of aortic diameter measurements using ultrasound.	

Included for		Domain: Clinical effectiveness Question/Result card: EFF1
Study design		What study design(s) are included by the review: Not reported explicitly
Population		Patient characteristics: Participant demographics varied in the analyzed studies. The age range of the population was unknown in four studies. In the five papers that stated the demographics details, the age range was 24–82 years. Two studies recruited only men over 65 years of age and two studies recruited both men and women; in five studies the sex of the participants remained unknown.
		Disease/condition: AAA
Intervention		Different ultrasound measurements for AAA screening to measure intra and inter observer variability
Comparison		Different ultrasound measurements for AAA screening to measure intra and inter observer variability
Outcomes/ Endpoints		Outcomes assessed for this domain-report: • Intraobserver repeatability • Interobserver reproducibility Outcomes not assessed by this domain-report: • Repeatability and reproducibility of abdominal aortic diameter ultrasound measurement. • Time elapse between measurement examinations • Observer discipline, grade and experience • Clinical acceptability level • Variation between ultrasound machines

Sources of information		Databases: • MEDLINE (1966-2009)
		Other sources of information: References supplied in accesses papers were checked for potential relevance.
Main Conclusion		Conclusion as stated by the review authors: The studies used different methodologies with no standardized measurement techniques. Measurements were taken by observers from different medical disciplines of varying grade and levels of training. Standard training and formal quality assurance of ultrasound measurements are important components of an effective AAA screening program.

	Quality assessment (Based on checklist for systematic reviews)										
1	2	3	4	5	6	7	8	9	10	11	Quality
Y	U	Y	N	Y	Y	N	N	U	Y	Y	Medium
	Comments:										

3. Excluded literature

For SRs

References from search Oct 2011	Reason for exclusion
American Thoracic Society/European Respiratory Society statement: Standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. Am J Respir Crit Care Med 2003;168(7):818-900.	Does not assess AAA-screening
Ultrasound screening for abdominal aortic aneurysm: an evidence-based analysis. 2006.	HTA from Ontario updated in a more recent SR
Bockler D, Lang W, Debus ES, Flessenkamper I, Florek HJ, Noppeney T, et al. Randomised studies with EBM level 1 prove it : AA screening programme for abdominal aortic aneurysms makes sense. Gefasschirurgie 2009;14(5):350-61.	German
Center for Medical Technology Assessment. Screening for abdominal aortic aneurysm - a health economic assessment.: Center for Medical Technology Assessment (CMT); 2004.	Economic evaluation
Cornuz J, Pinto CS, Tevaearai H, Egger M. Risk factors for	Does not assess AAA-

asymptomatic abdominal aortic aneurysm: Sytematic review and meta-analysis of population-based screening studies. European Journal of Public Health 2004;14(4):343-9.	screening
Cote B, Lance JM, LeBrun M. Population ultrasound screening for abdominal aortic aneurysms.: Agence d'Evaluation des Technologies et des Modes d'Intervention en Sante (AETMIS); 2010.	French
Daly KJ, Torella F, Ashleigh R, McCollum CN. Screening, diagnosis and advances in aortic aneurysm surgery. Gerontology 2004;50(6):349-59.	Regular review on aortic aneurysm surgery
Eckstein H-H, Bockler D, Flessenkamper I, Schmitz-Rixen T, Debus S, Lang W. Ultrasonographic screening for the detection of abdominal aortic aneurysms. Deutsches Arzteblatt 2009;106(41):657-63.	German
Ehlers L, Sorensen J, Jensen LG, Bech M, Kjolby M. Is population screening for abdominal aortic aneurysm cost-effective? BMC cardiovascular disorders 2008;8(pp 32)	Economic evaluation
Fleming C, Whitlock E, Beil T, Lederle F. Primary care screening for abdominal aortic aneurysm.: Agency for Healthcare Research and Quality (AHRQ); 2005.	HTA from USA, but results updated in a more recent SR
Fleming C, Whitlock E, Beil T, Lederle F. Primary care screening for abdominal aortic aneurysm. 2005.	SR, but results updated in a more recent SR
Fleming C, Whitlock EP, Beil TL, Lederle FA. Screening for abdominal aortic aneurysm: A best-evidence systematic review for the U. Ann Intern Med 2005;142(3):203-11. Ref ID: 99	SR, but results updated in a more recent SR
Flynn K. Guidance for screening for abdominal aortic aneurysms in veterans health administration.: VA Technology Assessment Program (VATAP); 2005.	Guidance
Frame PS, Fryback DG, Patterson C. Screening for abdominal aortic aneurysm in men ages 60 to 80 years: A cost-effectiveness analysis. Ann Intern Med 1993;119(5):411-6.	Economic evaluation
Froehlich JB, Block PC. Abdominal aortic aneurysm Dx & Rx. ACC Cardiosource Review Journal 2006;15(11):73-7.	Does not assess AAA-screening
Galician Agency for Health Technology Assessment (AVALIA-. Efficacy and effectiveness of screening for abdominal aortic aneurysm in a population at risk. Cost-effectiveness analysis. Applicability inside the National Healthcare System.: Galician Agency for Health Technology Assessment (AVALIA-T); 2008.	Economic evaluation
Guessous I, Cornuz J. Abdominal aortic aneurysm screening: 2006 recommendations. Expert Review of Pharmacoeconomics and Outcomes Research 2006;6(5):555-61.	Recommendations only

Hamerlynck JVT, Legemate DA, Hooft L. From the Cochrane Library: Ultrasonographic screening for abdominal aortic aneurysm in men aged 65 years and older: Low risk of fatal aneurysm rupture.	Dutch
Health TA. The growth and rupture rate of small abdominal aortic aneurysms: implications for population re-screening intervals (Project record).: Health Technology Assessment; 2011.	Protocol
Henriksson M, Lundgren F. One-time screening for abdominal aortic aneurysm in 65-year-old men: a decision-analytic model with lifetime estimation of costs and health outcomes. 2005.	Economic evaluation
Lederle FA, Kane RL, MacDonald R, Wilt TJ. Systematic review: Repair of unruptured abdominal aortic aneurysm. Ann Intern Med 2007;146(10):735-41.	Does not assess AAA-screening
Leipala J. Cost-effectiveness and effectiveness of abdominal aortic aneurysm screening (Project record).: Finnish Office for Health Care Technology Assessment (FinOHTA); 2010.	Protocol
Lindholt JS, Norman PE. Meta-analysis of postoperative mortality after elective repair of abdominal aortic aneurysms detected by screening. Br J Surg 2011;98(5):619-22.	SR, but results updated in a more recent SR
Maceira-Rozas MC, Atienza-Merino G. Screening for abdominal aortic aneurysm in a population at risk: A systematic review. Angiologia 2008;60(3):165-76.	Only high risk population
Maceira Rozas MC, Atienza MG, Sampedro Morandeira JL. Efficacy and effectiveness of screening for abdominal aortic aneurysm in a high risk population. Cost-effectiveness analysis. Applicability in the National Health Care Service.: Galician Agency for Health	Only high risk population
Malkawi AH, Hinchliffe RJ, Xu Y, Holt PJ, Loftus IM, Thompson MM. Patient-specific biomechanical profiling in abdominal aortic aneurysm development and rupture. J Vasc Surg 2010;52(2):480-8.	Does not assess AAA-screening
Medical Advisory SecretariatOntario Ministry of Health and Long-Term Care (MAS). Ultrasound screening for abdominal aortic aneurysm: an evidence-based analysis.: Medical Advisory Secretariat, Ontario Ministry of Health and Long-Term Care (MAS); 2006.	HTA from Ontario, but results updated in a more recent SR
Montreuil B, Brophy J. Screening for abdominal aortic aneurysms in men: A Canadian perspective using Monte Carlo-based estimates. Can J Surg 2008;51(1):23-34.	Economic evaluation
Muszbek N, Thompson MM, Soong CV, Hutton J, Brasseur P, van Sambeek MRHM. Systematic Review of Utilities in Abdominal Aortic Aneurysm. Eur J Vasc Endovasc Surg 2008;36(3):283-9.	Does not assess AAA-screening
Powell JT, Sweeting MJ, Brown LC, Gotensparre SM, Fowkes FG, Thompson SG. Systematic review and meta-analysis of growth rates of small abdominal aortic aneurysms. Br J Surg 2011;98(5):609-18.	Does not assess AAA-screening

Swedish Council on Technology Assessment in Health Care. Screening for abdominal aortic aneurysm.: Swedish Council on Technology Assessment in Health Care (SBU); 2008. Ref ID: 66	SR, but with results updated in a more recent SR
Toomtong P, Suksompong S. Intravenous fluids for abdominal aortic surgery. Cochrane Database of Systematic Reviews 2010;(1):CD000991.	Does not assess AAA-screening
van Gils PF, de Wit GA, Schuit AJ, van den Berg M. Screening for abdominal aortic aneurysm; effectivity and cost-effectiveness. Ned Tijdschr Geneeskd 2009;153(pp B383)	Dutch
Van Vlijmen-Van Keulen CJ, Pals G, Rauwerda JA. Familial abdominal aortic aneurysm: A systematic review of a genetic background. Eur J Vasc Endovasc Surg 2002;24(2):105-16.	Does not assess AAA-screening
Wanhainen A, Lundkvist J, Bergqvist D, Bjorck M. Cost-effectiveness of different screening strategies for abdominal aortic aneurysm. J Vasc Surg 2005;41(5):741-51.	Economic evaluation
Wanhainen A, Lundkvist J, Bergqvist D, Bjorck M. Cost-effectiveness of screening women for abdominal aortic aneurysm. J Vasc Surg 2006;43(5):908-14.	Economic evaluation
References from search Feb 2012	**Reason for exclusion**
Andersen GN, Haugen BO, Graven T, Salvesen O, Mjolstad OC, Dalen H. Feasibility and reliability of point-of-care pocket-sized echocardiography. Eur J Echocardiogr 2011;12(9):665-70.	Does not assess AAA-screening
Bisoendial RJ, Tanck MW, Golledge J, Broekhuizen LN, Legemate DA, Stroes ESG, et al. The association between the gene encoding 5-lipoxygenase activating protein and abdominal aortic aneurysms. Atherosclerosis 2012;220(2):425-8.	Does not assess AAA-screening
Skroumpelos A, Pavi E, Kyriopoulos J. Discussing the introduction of national screening programs in Greece: A delphi study. Value in Health 2011;Conference(var.pagings):A462-A463.	Regular review: discussion from a conference
Sogaard R, Lindholt J. Evidence for the credibility of health economic models for health policy decision-making: A systematic literature review of screening for abdominal aortic aneurysms. J Health Serv Res Policy 2012;17(1):44-52.	Discussion of economic models

For RCTs

References from search Nov 2011	**Reason for exclusion**
Cost-effective screening test for abdominal aortic aneurysm. Expert Review of Pharmacoeconomics and Outcomes Research 2002	Not RCT

Aggarwal S, Qamar A, Sharma V, Sharma A. Abdominal aortic aneurysm: A comprehensive review. Experimental and Clinical Cardiology 2011	Not RCT
Ali ZA, Callaghan CJ, Ali AA, Sheikh AY, Akhtar A, Pavlovic A, et al. Perioperative myocardial injury after elective open abdominal aortic aneurysm repair predicts outcome. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2008	Not RCT
Ascher E, Scheinman M, DePippo P, Yorkovich W. Ruptured versus elective abdominal aortic aneurysm repair: Outcome and cost. Ann Vasc Surg 1999	Does not assess AAA-screening
Ashton HA, Gao L, Kim LG, Druce PS, Thompson SG, Scott RAP. Erratum: Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms (British Journal of Surgery (2007) 94 (696-701) Br J Surg 2007	Results from RCT covered in the included SRs (erratum)
Ashton HA, Gao L, Kim LG, Druce PS, Thompson SG, Scott RA. Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. The British journal of surgery 2007	Results from RCT covered in the included SRs
Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002	Results from RCT covered in the included SRs
Assar AN. Pharmacological therapy for patients with abdominal aortic aneurysm. Expert Review of Cardiovascular Therapy 2009	Does not assess AAA-screening
Barros FS, Pontes SM, Taylor MASA, Roelke LH, Sandri JL, De Melo JC, et al. Screening for abdominal aortic aneurysm in the population of the city of Vitoria, ES, Brazil. Jornal Vascular Brasileiro 2005	Not RCT
Baxter BT, Terrin MC, Dalman RL. Medical management of small abdominal aortic aneurysms. Circulation 2008	Does not assess AAA-screening
Bostom AG, Carpenter MA, Kusek JW, Hunsicker LG, Pfeffer MA, Levey AS, et al. Rationale and design of the Folic Acid for Vascular Outcome Reduction In Transplantation (FAVORIT) trial. Am Heart J 2006	Does not assess AAA-screening
Bown MJ, Fishwick G, Sayers RD, Bell PRF. Repair of Ruptured Abdominal Aortic Aneurysms by Endovascular Techniques. Adv Surg 2007	Does not assess AAA-screening
Brownsword R, Earnshaw JJ. The ethics of screening for abdominal aortic aneurysm in men. J Med Ethics 2010	Not RCT
Bryan S, Buxton M, McKenna M, Ashton H, Scott A. Private costs	Economic analysis

associated with abdominal aortic aneurysm screening: the importance of private travel and time costs. J Med Screen 1995	
Chew HF, You CK, Brown MG, Heisler BE, Andreou P. Mortality, morbidity, and costs of ruptured and elective abdominal aortic aneurysm repairs in Nova Scotia, Canada. Ann Vasc Surg 2003	Does not assess AAA-screening
Chichester Aneurysm Screening Group, Viborg Aneurysm SS, Western Australian Abdominal Aortic Aneurysm Program, Multicentre Aneurysm SS. A comparative study of the prevalence of abdominal aortic aneurysms in the United Kingdom, Denmark, and Australia. J Med Screen 2001	Does not assess AAA-screening
Chinien G, Waltham M, Saha P, Burnand KG, Smith A. Molecular genetics of abdominal aortic aneurysm: Therapeutic implications. Current Pharmacogenomics and Personalized Medicine 2008	Not RCT
Collin J. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. The British journal of surgery 1996	Results from RCT covered in the included SRs
Couto E, Duffy SW, Ashton HA, Walker NM, Myles JP, Scott RA, et al. Probabilities of progression of aortic aneurysms: estimates and implications for screening policy. J Med Screen 2002	Does not assess AAA-screening
d'Audiffret A, Santilli S, Tretinyak A, Roethle S. Fate of the ectatic infrarenal aorta: expansion rates and outcomes. Ann Vasc Surg 2002	Does not assess AAA-screening
Dale W, Hemmerich J, Ghini EA, Schwarze ML. Can induced anxiety from a negative earlier experience influence vascular surgeons' statistical decision-making? A randomized field experiment with an abdominal aortic aneurysm analog. J Am Coll Surg 2006	Does not assess AAA-screening
Dichgans M, Bevan S, Cole JW, Plourde A, Matarin M, Ross-Adams H, et al. Sequence variants on chromosome 9p21 confer risk of large vessel stroke. Stroke 2009	Does not assess AAA-screening
Dimick JB, Upchurch J, G.R. The quality of care for patients with abdominal aortic aneurysms. Cardiovasc Surg 2003	Not RCT
Ehlers L, Overvad K, Sorensen J, Christensen S, Bech M, Kjolby M. Analysis of cost effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm. BMJ (Clinical research ed 2009	Economic evaluation
Eugster T, Huber A, Obeid T, Schwegler I, Gurke L, Stierli P. Aminoterminal propeptide of type III procollagen and matrix metalloproteinases-2 and -9 failed to serve as serum markers for abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2005	Does not assess AAA-screening
Giardina S, Pane B, Spinella G, Cafueri G, Corbo M, Brasseur P, et al. An economic evaluation of an abdominal aortic aneurysm screening program in Italy. J Vasc Surg 2011	Economic evaluation

Golledge J, Dalman RL, Norman PE. Developments in non-surgical therapies for abdominal aortic aneurysm. Current Vascular Pharmacology 2009	Not RCT
Grøndal N, Søgaard R, Henneberg EW, Lindholt JS. The Viborg Vascular (VIVA) screening trial of 65-74 year old men in the central region of Denmark: study protocol. Trials 2010	Protocol
Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and aortic rupture: a population-based case-control study. Lancet 2006	Does not assess AAA-screening
Hartshorne TC, McCollum CN, Earnshaw JJ, Morris J, Nasim A. Ultrasound measurement of aortic diameter in a national screening programme. Eur J Vasc Endovasc Surg 2011	Accuracy study covered in included SRs
Heller JA, Weinberg A, Arons R, Krishnasastry KV, Lyon RT, Deitch JS, et al. Two decades of abdominal aortic aneurysm repair: Have we made any progress? J Vasc Surg 2000	Not RCT
Henderson RG, Smith GN. Screening for abdominal aneurysm. The Journal of family practice 1996	Not RCT
Hiller H, Ghauri ASK. Preventing Death from Abdominal Aortic Aneurysm Rupture. Vascular Disease Prevention 2005	Not RCT
Hoegh A, Lindholt JS. Basic science review. Vascular distensibility as a predictive tool in the management of small asymptomatic abdominal aortic aneurysms. Vascular and endovascular surgery 2009	Not RCT
Hoegh A, Lindholt JS. Basic science review. Vascular and endovascular surgery 2009	Not RCT
Hyhlik-Durr A, Debus S, Eckstein H-H, Lang W, Schmitz-Rixen T, Boeckler D. Ultrasoud screening in abdominal aortic aneurysm - Numbers, data, facts. Zentralblatt fur Chirurgie - Zeitschrift fur Allgemeine, Viszeral- und Gefasschirurgie 2010	Not RCT
Jacobs LA, Jamrozik K, Norman PE, Lawrence BM, Dickinson JA. A randomised trial of screening for abdominal aortic aneurysms [abstract]. AUSM1996: 26th Annual Scientific Meeting 1996	Meeting abstract of results from RCT covered in the included SRs
Jamrozik K, Norman PE, Spencer CA, Parsons RW, Tuohy R, Lawrence-Brown MM, et al. Screening for abdominal aortic aneurysm: lessons from a population-based study. Med J Aust 2000	Review on RCT included in included RCTs
Jelenska MM, Szmidt J, Bojakowski K, Grzela T, Palester-Chlebowczyk M. Compensated activation of coagulation in patients with abdominal aortic aneurysm: effects of heparin treatment prior to elective surgery. Thromb Haemost 2004	Does not assess AAA-screening
Judge JS, Low V, Gajraj H, House AK. The value of technetium-99M renography for the detection of renal artery stenosis in pa-	Does not assess AAA-screening

tients with aortic and lower limb vascular disease. The Australian and New Zealand journal of surgery 1992	
Kim JY, Jeon YS, Cho SG, Hong KC. Study for prevalence of peripheral vascular diseases by screening test for old male population in Korea. Cardiovasc Intervent Radiol 2010	Does not assess AAA-screening
Kim LG, Ra PS, Ashton HA, Thompson SG, Multicentre Aneurysm Screening Study Group. A sustained mortality benefit from screening for abdominal aortic aneurysm. Ann Intern Med 2007	Results from RCT covered in included SRs
Kim LG, Thompson SG. Estimation of life-years gained and cost effectiveness based on cause-specific mortality. Health Econ 2011	Economic evaluation
Kim LG, Scott RA, Thompson SG, Collin J, Morris GE, Sutton GL, et al. Implications of screening for abdominal aortic aneurysms on surgical workload. The British journal of surgery 2005	Results from RCT covered in included SRs
Kim LG, Thompson SG. Uncertainty and validation of health economic decision models. Health Econ 2010	Economic evaluation
Krausz MM, Dennis RC, Utsunomiya T. Cardiopulmonary function following transfusion of three red blood cell products in elective abdominal aortic aneurysmectomy. Ann Surg 1981	Does not assess AAA-screening
Lamont P. Screening for abdominal aortic aneurysm: headline is misleading. BMJ 2005	Not RCT
Lawrence-Brown MM, Norman PE, Jamrozik K, Semmens JB, Donnelly NJ, Spencer C, et al. Initial results of ultrasound screening for aneurysm of the abdominal aorta in Western Australia: relevance for endoluminal treatment of aneurysm disease. Cardiovascular surgery (London, England) 2001	Does not assess AAA-screening
Lederle FA. A summary of the contributions of the VA cooperative studies on abdominal aortic aneurysms. The Abdominal Aortic Aneurysm: Genetics, Pathophysiology, and Molecular Biology 2006	Does not assess AAA-screening
Lederle FA, Wilson SE, Johnson GR, Littooy FN, Acher C, Messina LM, et al. Design of the abdominal aortic Aneurysm Detection and Management Study. ADAM VA Cooperative Study Group. Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter 1994	Not ultrasound (CT)
Lederle FA. Screening for AAA in the USA. Scandinavian Journal of Surgery 2008	Does not assess AAA-screening
Lederle FA, Walker JM, Reinke DB. Selective screening for abdominal aortic aneurysms with physical examination and ultrasound. Arch Intern Med 1988	Not population screening
Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Maka-	Not RCT

roun MS, et al. The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med 2000	
Lederle FA. Ultrasonographic Screening for Abdominal Aortic Aneurysms. Ann Intern Med 2003	Not RCT
Lederle FA, Johnson GR, Wilson SE, Littooy FN, Krupski WC, Bandyk D, et al. Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval. Arch Intern Med 2000	Not RCT
Lindholt J, Juul S, Fasting H, Henneberg E. Costs, benefits, and effectiveness of screening for abdominal aortic aneurysms. Results from a randomised population screening trial. European Society for Vascular Surgery, Programme and Abstract Book, XVII Annual Meeting and Course on Vascular Surgical Techniques 2003	Abstract from a meeting on RCT covered in the included SRs
Lindholt J, Vammen S, Fasting H, Henneberg E, Heickendorff L. The plasma level of matrix metalloproteinase 9 may predict the natural history of small abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2000	Does not assess AAA-screening
Lindholt JS, Vammen S, Henneberg EW, Fasting H, Juul S. [Optimal interval screening and observation of abdominal aortic aneurysms]. Ugeskr Laeger 2001	Rescreening
Lindholt JS, Fasting H, Henneberg EW, Juul S. [Preliminary results of screening for abdominal aortic aneurysm in the county of Viborg]. Ugeskr Laeger 1997	Danish
Lindholt JS, Juul S, Fasting H, Henneberg EW. [Screening reduced abdominal aortic aneurysm mortality--secondary publication. Results from a Danish randomized screening trial]. Ugeskr Laeger 2005	Danish
Lindholt JS. Abdominal aortic aneurysms. Dan Med Bull 2010	Danish
Lindholt JS, Juul S, Fasting H, Henneberg EW. Cost-benefit analysis of population screening for abdominal aortic aneurism, based on five-year results of a randomised hospital-based screening trial. Ugeskr Laeger 2006	Economic evaluation
Lindholt JS, Juul S, Fasting H, Henneberg EW. Cost-effectiveness Analysis of Screening for Abdominal Aortic Aneurysms Based on Five Year Results from a Randomised Hospital Based Mass Screening Trial^{star, open}. Eur J Vasc Endovasc Surg 2006	Economic evaluation
Lindholt JS. Erratum: Screening for abdominal aortic aneurysms: Single centre randomised controlled trial (British Medical Journal (2005) 330 (750-752)). Br Med J 2005	Results from RCT covered in included SR

Lindholt JS, Sandermann J, Bruun-Petersen J, Nielsen JOD, Fasting H. Fatal late multiple emboli after endovascular treatment of abdominal aortic aneurysm. Int Angiol 1998	Does not assess AAA-screening
Lindholt JS, Juul S, Henneberg EW. High-risk and low-risk screening for abdominal aortic aneurysm both reduce aneurysm-related mortality. A stratified analysis from a single-centre randomised screening trial. European journal of vascular and endovascular surgery: the official journal of the European Society for Vascular Surgery 2007	Not whole population (stratified)
Lindholt JS, Henneberg EW, Fasting H, Juul S. Hospital based screening of 65-73 year old men for abdominal aortic aneurysms in the county of Viborg, Denmark. J Med Screen 1996	Results from RCT covered in included SR
Lindholt JS, Juul S, Fasting H, Henneberg EW. Hospital costs and benefits of screening for abdominal aortic aneurysms. Results from a randomised population screening trial. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2002	Results from RCT covered in included SR
Lindholt JS, Henneberg EW, Juul S, Fasting H. Impaired results of a randomised double blinded clinical trial of propranolol versus placebo on the expansion rate of small abdominal aortic aneurysms. International angiology : a journal of the International Union of Angiology 1999	Results from RCT covered in included SR
Lindholt JS, Juul S, Henneberg EW, Fasting H. Is screening for abdominal aortic aneurysm acceptable to the population? Selection and recruitment to hospital-based mass screening for abdominal aortic aneurysm. J Public Health Med 1998	Does not assess AAA-screening
Lindholt JS, Sørensen J, Søgaard R, Henneberg EW. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. The British journal of surgery 2010	Results from RCT covered in included SR
Lindholt JS, Sorensen HT, Michel JB, Thomsen HF, Henneberg EW. Low-dose aspirin may prevent growth and later surgical repair of medium-sized abdominal aortic aneurysms. Vascular and endovascular surgery 2008	Does not assess AAA-screening
Lindholt JS, Vammen S, Juul S, Fasting H, Henneberg EW. Optimal interval screening and surveillance of abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2000	Rescreening (does not assess one single invitation)
Lindholt JS, Jorgensen B, Fasting H, Henneberg EW. Plasma levels of plasmin-antiplasmin-complexes are predictive for small abdominal aortic aneurysms expanding to operation-recommendable sizes. Journal of vascular surgery : official publi-	Does not assess AAA-screening

cation, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter 2001	
Lindholt JS, Juul S, Fasting H, Henneberg EW. Preliminary ten year results from a randomised single centre mass screening trial for abdominal aortic aneurysm. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2006	Results from RCT covered in included SR
Lindholt JS, Vammen S, Fasting H, Henneberg EW. Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2000	Not RCT
Lindholt JS. Relatively high pulmonary and cardiovascular mortality rates in screening-detected aneurysmal patients without previous hospital admissions. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2007	Does not assess AAA-screening
Lindholt JS, Juul S, Henneberg EW, Fasting H. Screening for abdominal aortic aneurysm. Ugeskr Laeger 1997	Danish
Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. BMJ (Clinical research ed) 2005	Results from RCT covered in included SR
Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening reduced abdominal aortic aneurysm mortality--secondary publication. Ugeskr Laeger 2005	Danish
Lindholt JS, Vammen S, Juul S, Henneberg EW, Fasting H. The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 1999	Accuracy study covered in included SRs
Longo C, Upchurch J, G.R. Abdominal aortic aneurysm screening: Recommendations and controversies. Vascular and endovascular surgery 2005	Not RCT
McFalls EO, Ward HB, Moritz TE, Littooy F, Santilli S, Rapp J, et al. Clinical factors associated with long-term mortality following vascular surgery: Outcomes from The Coronary Artery Revascularization Prophylaxis (CARP) Trial. J Vasc Surg 2007	Does not assess AAA-screening
Multicentre Aneurysm Screening Study Group. Multicentre aneurysm screening study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. BMJ (Clinical research ed) 2002	Results from RCT covered in included SRs
Muntendam P, McCall C, Sanz J, Falk E, Fuster V, High-Risk P, I.	Does not assess AAA-

The BioImage Study: novel approaches to risk assessment in the primary prevention of atherosclerotic cardiovascular disease--study design and objectives. Am Heart J 2010	screening
Nordon IM, Hinchliffe RJ, Loftus IM, Thompson MM. Pathophysiology and epidemiology of abdominal aortic aneurysms. Nature Reviews Cardiology 2011	Does not assess AAA-screening
Norman PE. Erratum: Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm (British Medical Journal (2004) 329 (1259-1262)). Br Med J 2005	Results from RCT covered in included SRs (erratum)
Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. BMJ (Clinical research ed) 2004	Results from RCT covered in included SRs
Norman PE, Jamrozik K, Lawrence BM, Le MM. Results of the Western Australian trial of screening for abdominal aortic aneurysms. ANZ Journal of Surgery 2005	Results from RCT covered in included SRs
Ogata T, Arrington S, Davis J, P.M, Sam II AD, Hollier LH, et al. Community-based, nonprofit organization-sponsored ultrasonography screening program for abdominal aortic aneurysms is effective at identifying occult aneurysms. Ann Vasc Surg 2006	Not RCT
Ogren M, Bengtsson H, Bergqvist D, Ekberg O, Hedblad B, Janzon L. Prognosis in elderly men with screening-detected abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 1996	Not RCT
Padberg J, F.T, Hauck K, Mercer RG, Lal BK, Pappas PJ. Screening for abdominal aortic aneurysm with electronic clinical reminders. Am J Surg 2009	Does not assess AAA-screening
Pfeiffer T, Muller BT, Huber R, Reiher L, Hafele S, Sandmann W. Management of Patients with Renal Artery Stenosis. Herz 2004	Does not assess AAA-screening
Rentschler ME, Baxter BT. Screening aortic drug treatments through arterial compliance measurements. Current Vascular Pharmacology 2008	Does not assess AAA-screening
Riegert-Johnson DL, Bruce CJ, Montori VM, Cook RJ, Spittell PC. Residents can be trained to detect abdominal aortic aneurysms using personal ultrasound imagers: A pilot study. J Am Soc Echocardiogr 2005	Not RCT
Rizzo M, Berneis K. An update on the role of the quality of LDL in cardiovascular risk: The contribution of the universities of Palermo and Zurich. Recent Patents on Cardiovascular Drug Discovery 2007	Does not assess AAA-screening
Santilli SM. The Coronary Artery Revascularization Prophylaxis	Does not assess AAA-

(CARP) Trial: results and remaining controversies. Perspectives in vascular surgery and endovascular therapy 2006	screening
Schermerhorn M, Zwolak R, Velazquez O, Makaroun M, Fairman R, Cronenwett J. Ultrasound Screening for Abdominal Aortic Aneurysm in Medicare Beneficiaries. Ann Vasc Surg 2008	Not RCT
Schlotzer-Schrehardt U, Naumann GOH. Ocular and Systemic Pseudoexfoliation Syndrome. Am J Ophthalmol 2006	Does not assess AAA-screening
Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. The British journal of surgery 1995	Results from RCT covered in included SRs
Scott RA, Bridgewater SG, Ashton HA. Randomized clinical trial of screening for abdominal aortic aneurysm in women. The British journal of surgery 2002	Results from RCT covered in included SRs
Scott RA, Vardulaki KA, Walker NM, Day NE, Duffy SW, Ashton HA. The long-term benefits of a single scan for abdominal aortic aneurysm (AAA) at age 65. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2001	Results from RCT covered in included SRs
Settembrini P, Ronchetti E, Galli G, Codemo R, Roveri S, Olivari N, et al. General population based screening for abdominal aortic aneurysms: Randomized ultrasound study in Italy ('Asola'). <ORIGINAL> PREVALENZA DEGLI ANEURISMI DELL'AORTA ADDOMINALE NELLA POPOLAZIONE GENERALE. STUDIO RANDOMIZZATO 'ASOLA'. Chirurgia (Turin) 1992	Italian
Silverstein MD, Pitts SR, Chaikof EL, Ballard DJ. Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. Proceedings (Baylor University 2005	Not RCT
Singh K, Bonaa KH, Solberg S, Sorlie DG, Bjork L. Intra- and interobserver variability in ultrasound measurements of abdominal aortic diameter. Eur J Vasc Endovasc Surg 1998	Accuracy study covered in included SRs
Smallwood L, Allcock R, Van BF, Warrington N, Palmer LJ, Iacopetta B, et al. Polymorphisms of the matrix metalloproteinase 9 gene and abdominal aortic aneurysm. Br J Surg 2008	Does not assess AAA-screening
Spencer CA, Jamrozik K, Lawrence-Brown M, Norman PE. Lifestyle still predicts mortality in older men with established vascular disease. Prev Med 2005	Does not assess AAA-screening
Spencer CA, Jamrozik K, Norman PE, Lawrence-Brown MM. The potential for a selective screening strategy for abdominal aortic aneurysm. J Med Screen 2000	Not RCT

Svensson LG, Hess KR, D'Agostino RS, Entrup MH, Hreib K, Kimmel WA, et al. Reduction of neurologic injury after high-risk thoracoabdominal aortic operation. The Annals of thoracic surgery 1998	Does not assess AAA-screening
Symons NRA, Gibbs RGJ. The management of abdominal aortic aneurysms. Br J Hosp Med 2009	Does not assess AAA-screening
Takagi H, Tanabashi T, Kawai N, Kato T, Umemoto T. Abdominal Aortic Aneurysm Screening Reduces Mortality: Meta-analyses of Randomized, Controlled Trials. Eur J Vasc Endovasc Surg 2007	Not RCT
Thompson A, Cooper JA, Fabricius M, Humphries SE, Ashton HA, Hafez H. An analysis of drug modulation of abdominal aortic aneurysm growth through 25 years of surveillance. J Vasc Surg 2010	Does not assess AAA-screening
Thompson SG, Ashton HA, Gao L, Scott RA, Multicentre Aneurysm Screening Study Group. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. BMJ (Clinical research ed) 2009	Results from RCT covered in included SRs
Thompson S, Kim L, Scott A. Screening for abdominal aortic aneurysm: screening reduces deaths related to aneurysm. BMJ 2005	Results from RCT covered in included SRs (editorial)
Treiman GS, Lawrence PF, Edwards WH, Galt SW, Kraiss LW, Bhirangi K. An assessment of the current applicability of the EVT endovascular graft for treatment of patients with an infrarenal abdominal aortic aneurysm. Journal of vascular surgery : official publication, the Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter 1999	Does not assess AAA-screening
Upchurch J, G.R, Schaub TA. Abdominal aortic aneurysm. Am Fam Physician 2006	Not RCT
Vammen S, Lindholt JS, Østergaard LJ, Fasting H, Henneberg EW. [Reduction of the expansion rate of small abdominal aortic aneurysms with roxithromycin. Results from a randomized controlled trial]. Ugeskr Laeger 2002	Does not assess AAA-screening
Vammen S, Lindholt JS, Ostergaard L, Fasting H, Henneberg EW. Randomized double-blind controlled trial of roxithromycin for prevention of abdominal aortic aneurysm expansion. The British journal of surgery 2001	Does not assess AAA-screening
Vammen S, Lindholt JS, Juul S, Henneberg EW, Fasting H. Screening for abdominal aortic aneurysms: An analysis of the private and indirect costs in a hospital-based screening program. International Journal of Angiology 2001	Economic evaluation
van Keulen CJ, van den Akker E, van den Berg FG, Pals G, Rauwerda JA. The role of type III collagen in family members of	Does not assess AAA-screening

patients with abdominal aortic aneurysms. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2000	
Van Sambeek MRH. Different guidelines are needed for men and women with AAA. Vascular 2010	Not RCT
Van WC, Wong J, Morant K, Jennings A, Jetty P, Forster AJ. Incidence, follow-up, and outcomes of incidental abdominal aortic aneurysms. J Vasc Surg 2010	Does not assess AAA-screening
Vardulaki KA, Prevost TC, Walker NM, Day NE, Wilmink AB, Quick CR, et al. Incidence among men of asymptomatic abdominal aortic aneurysms: estimates from 500 screen detected cases. J Med Screen 1999	Does not assess AAA-screening
Vardulaki KA, Walker NM, Couto E, Day NE, Thompson SG, Ashton HA, et al. Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm. The British journal of surgery 2002	Results from RCT covered in included SRs
Vardulaki KA, Walker NM, Day NE, Duffy SW, Ashton HA, Scott RA. Quantifying the risks of hypertension, age, sex and smoking in patients with abdominal aortic aneurysm. The British journal of surgery 2000	Does not assess AAA-screening
Vidakovic R, Feringa HH, Kuiper RJ, Karagiannis SE, Schouten O, Dunkelgrun M, et al. Comparison with computed tomography of two ultrasound devices for diagnosis of abdominal aortic aneurysm. The American journal of cardiology 2007	Does not assess AAA-screening
References from search Feb 2012	**Reason for exclusion**
Badger SA, Jones C, Murray A, Lau LL, Young IS. Implications of Attendance Patterns in Northern Ireland for Abdominal Aortic Aneurysm Screening. Eur J Vasc Endovasc Surg 2011	Not RCT
Badger SA, O'Donnell ME, Sharif MA, Boyd CS, Hannon RJ, Lau LL, et al. Risk Factors for Abdominal Aortic Aneurysm and the Influence of Social Deprivation. Angiology 2008	Not RCT
Badger SA, O'Donnell ME, Boyd CS, Hannon RJ, Lau LL, Lee B, et al. The low prevalence of abdominal aortic aneurysm in relatives in northern Ireland. Eur J Vasc Endovasc Surg 2007	Not RCT
Bekkers SCAM, Habets JHM, Cheriex EC, Palmans A, Pinto Y, Hofstra L, et al. Abdominal aortic aneurysm screening during transthoracic echocardiography in an unselected population. J Am Soc Echocardiogr 2005	Not RCT
Criqui MH, Alberts MJ, Fowkes GR, Hirsch AT, O'Gara PT, Olin JW. Atherosclerotic Peripheral Vascular Disease Symposium II Screening for Atherosclerotic Vascular Diseases: Should Nation-	Does not assess AAA-screening

wide Programs Be Instituted? Circulation 2008	
Duncan JL, Wolf B, Nichols DM, Lindsay SM, Cairns J, Godden DJ. Screening for abdominal aortic aneurysm in a geographically isolated area. Br J Surg 2005	Not RCT
Dynda DI, Andrews JA, Chiou AC, Debord JR. Project PROMIS: Peoria Regional Outpatient Medical Imaging Study. Am J Surg 2008	Not RCT
Earnshaw JJ, Shaw E, Whyman MR, Poskitt KR, Heather BP. Screening for abdominal aortic aneurysms in men. Br Med J 2004	Not RCT
Flessenkamper I, Kendzia A, Stalke J. Multicenter Aortic Aneurysm Screening Trial in an Arterial Sick Cohort. BARE - Berlin Aneurysm Recurrence Evaluation. Gefasschirurgie 2009	Not RCT
Hafez H, Druce PS, Ashton HA. Abdominal Aortic Aneurysm Development in Men Following a "normal" Aortic Ultrasound Scan. Eur J Vasc Endovasc Surg 2008	Not RCT
Harris DA, Al-Allak A, Thomas J, Hedges AR. Influence of presentation on outcome in abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 2006	Does not assess AAA-screening
Hobbs S, Claridge M, Drage M, Quick C, Bradbury A, Wilmink A. Strategies to improve the effectiveness of abdominal aortic aneurysm screening programmes. J Med Screen 2004	Not RCT
Kim LG, Thompson SG, Marteau TM, Scott RAP. Screening for abdominal aortic aneurysms: the effects of age and social deprivation on screening uptake, prevalence and attendance at follow-up in the MASS trial. J Med Screen 2004	Not RCT
Lindholt JS, Norman P. Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2008	Not RCT (meta-analysis)
Lindsay SM, Duncan JL, Cairns J, Godden DJ. Geography, private costs and uptake of screening for abdominal aortic aneurysm in a remote rural area. BMC Public Health 2006	Not RCT
Lippi G, Franchini M, Targher G. Screening and therapeutic management of lipoprotein(a) excess: Review of the epidemiological evidence, guidelines and recommendations. Clin Chim Acta 2011	Does not assess AAA-screening
McPhail I. Abdominal Aortic Aneurysm and Diastasis Recti. Angiology 2008	Does not assess AAA-screening
Palombo D, Lucertini G, Pane B, Mazzei R, Spinella G, Brasesoo PC. District-based abdominal aortic aneurysm screening in population aged 65 years and older. J Cardiovasc Surg (Torino) 2010	Not RCT
Rothberg AD, McLeod H, Walters L, Veller M. Screening for ab-	Not RCT

dominal aortic aneurysm - a pilot study in six medical schemes. Samj South African Medical Journal 2007	
Schmidt T, Muhlberger N, Chemelli-Steingruber IE, Strasak A, Kofler B, Chemelli A, et al. Benefit, Risks and Cost-Effectiveness of Screening for Abdominal Aortic Aneurysm. Rofo-Fortschritte Auf dem Gebiet der Rontgenstrahlen und der Bildgebenden Verfahren 2010	Economic evaluation
Scott RAP, Kim LG, Ashton HA. Assessment of the criteria for elective surgery in screen-detected abdominal aortic aneurysms. J Med Screen 2005	Not RCT
Taylor JC, Shaw E, Whyman MR, Poskitt KR, Heather BP, Earnshaw JJ. Late survival after elective repair of aortic aneurysms detected by screening. Eur J Vasc Endovasc Surg 2004	Not RCT
Venkatasubramaniam AK, Mehta T, Chetter IC, Bryce J, Renwick P, Johnson B, et al. The value of abdominal examination in the diagnosis of abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2004	Not RCT
Waterhouse DF, Cahill RA, Sheehan F, Sheehan SJ. Concomitant detection of systemic atherosclerotic disease while screening for abdominal aortic aneurysm. World J Surg 2006	Not RCT
Wilmink T, Claridge MWC, Fries A, Will O, Hubbard CS, Adam DJ, et al. A comparison between the short term and long term benefits of screening for abdominal aortic aneurysms from the huntingdon aneurysm screening programme. Eur J Vasc Endovasc Surg 2006	Not RCT

4. GRADE profiles

Table 1. Overall mortality, AAA-related mortality (long- and mid-term), and planned and emergency operations (long- and mid-term) in men

screening compared to no screening for men

Patient or population: men
Settings:
Intervention: screening
Comparison: no screening

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				

	No screening	Screening			
Overall mortality, long-term Follow-up: mean > 10 years	**355 per 1000**	**350 per 1000** (343 to 355)	**OR 0.98** (0.95 to 1)	114376 (4 studies)	⊕⊕⊕⊖ **moderate**[1]
Death from abdominal aortic aneurysm, long-term Follow-up: mean >10 years	**9 per 1000**	**5 per 1000** (3 to 8)	**OR 0.55** (0.36 to 0.86)	86449 (3 studies)	⊕⊕⊖⊖ **low**[2,3]
Overall mortality, mid-term Follow-up: 3-5 years	**127 per 1000**	**120 per 1000** (111 to 129)	**OR 0.94** (0.86 to 1.02)	125576 (4 studies)	⊕⊕⊖⊖ **low**[3,4]
Death from abdominal aortic aneurysm, mid-term Follow-up: 3-5 years	**3 per 1000**	**2 per 1000** (1 to 2)	**OR 0.56** (0.44 to 0.72)	125576 (4 studies)	⊕⊕⊕⊖ **moderate**[4]
Incidence of ruptured AAA Follow-up: 2-5 years	**6 per 1000**	**3 per 1000** (1 to 6)	**OR 0.45** (0.21 to 0.99)	6433 (1 study)	⊕⊖⊖⊖ **very low**[5,6]
Planned operations, long-term Follow-up: 7-15 years	**5 per 1000**	**13 per 1000** (11 to 15)	**OR 2.81** (2.40 to 3.30)	86479 (3 studies)	⊕⊕⊕⊖ **moderate**[4]
Emergency operations, long-term Follow-up: 7-15 years	**4 per 1000**	**2 per 1000** (1 to 3)	**OR 0.48** (0.28 to 0.83)	86479 (3 studies)	⊕⊕⊖⊖ **low**[3,4]
Planned operations, mid-term Follow-up: 3-5 years	**3 per 1000**	**8 per 1000** (6 to 13)	**OR 3.27** (2.14 to 5.00)	125576 (4 studies)	⊕⊕⊖⊖ **low**[3,4]
Emergency operations, mid-term Follow-up: 3-5 years	**2 per 1000**	**1 per 1000** (1 to 1)	**OR 0.55** (0.39 to 0.76)	125576 (4 studies)	⊕⊕⊖⊖ **low**[4,7]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds 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] One study was rated as good quality and the three others as fair quality according to USPSTF rating criteria.
[2] One study was rated as good quality and the two others as fair quality according to USPSTF rating criteria.
[3] I-square > 60 %
[4] Unclear Risk of Bias, however, the studies included are the same as for long term mortality follow up so we assess them similar.
[5] Unclear description of risk of bias. Allocation concealment was not reported.
[6] Few events and wide confidence interval
[7] Few events

Table 2. Overall mortality, AAA-related mortality, and incidence of AAA rupture in women

screening compared to no screening for women asymptomatic of aortic aneurysm

Patient or population: women asymptomatic of aortic aneurysm
Settings: hospital outpatients
Intervention: screening
Comparison: no screening

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **No screening**	Corresponding risk **Screening**				
Overall mortality Follow-up: 3-5 years	**102 per 1000**	**108 per 1000** (96 to 120)	**OR 1.06** (0.93 to 1.2)	9342 (1 study)	⊕⊕⊕⊖ **moderate**[1,2]	
Death from abdominal		**1 per 1000**	**OR 1.99**	9342	⊕⊖⊖⊖	

aortic aneurysm Follow-up: 3-5 years		(0 to 5)	(0.36 to 10.88)	(1 study)	**very low**[1,3]
Incidence of ruptured AAA Follow-up: 2-5 years		**1 per 1000** (0 to 4)	**OR 1.49** (0.25 to 8.94)	9343 (1 study)	⊕⊖⊖⊖ **very low**[1,3]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds 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] Unclear description of risk of bias. Allocation concealment was not reported.
[2] Only one trial reported this outcome for women
[3] Few events and very wide confidence interval

Table 3. Anxiety, depression, and mental quality of life

screening compared to no screening for asymptomatic aortic aneurism

Patient or population: patients with asymptomatic aortic aneurism
Settings:
Intervention: screening
Comparison: no screening

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **No screening**	Corresponding risk **Screening**				
Anxiety the state scale of the state-trait anxiety inventory		The mean anxiety in the intervention groups was **0.12 standard deviations lower** (0.21 to 0.02 lower)		1956 (1 study)	⊕⊕⊖⊖ **low**[1,2]	
Depression The state Hospital Anxiety and depression Scale		The mean depression in the intervention groups was **0.11 standard deviations lower** (0.20 to 0.02 lower)		1956 (1 study)	⊕⊕⊖⊖ **low**[1,2]	
Mental QoL Short for health survey SF-36		The mean mental qol in the intervention groups was **0.07 standard deviations higher** (0.02 lower to 0.16 higher)		1956 (1 study)	⊕⊕⊖⊖ **low**[1,2]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval;

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] The study met three of five criteria for risk of bias assessment.
[2] Only one study included

Appendix 3

List of all references from the basic search for SRs and HTAs (clinical effectiveness) – 41 references

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Appendix 4

1. Medicare reported complications

Medicare reported complications data from 45,660 elective AAA repairs performed by EVAR and OAR* (safety)

	EVAR (N=22,830)	OAR (N=22,830)
Medical Complications (% of patients)		
Myocardial infarction	7	9.4
Pneumonia	9.3	17.4
Acute renal failure	5.5	10.9
Renal failure requiring dialysis	0.4	0.5
Deep-vein thrombosis or pulmonary embolism	1.1	1.7
Surgical complications (% of patients)		
Conversion to open repair	1.6	-
Acute mesenteric ischemia	1.0	2.1
Reintervention for bleeding	0.8	1.2
Tracheostomy	0.2	1.5
Thrombectomy	0.4	0.2
Embolectomy	1.3	1.7
Repair of infected graft of graft-enteric fistula	0.01	0.09
Major amputation	0.04	0.13
Complications related to laparatomy		
Lysis of adhesions without resection	0.1	1.2
Bowel resection	0.6	1.3
Ileus of bowel obstruction without resection of lysis of adhesions	5.1	16.7
Mean length of hospital stay (nº of days)	3.4 ± 4.7	9.3 ± 8.1
Discharge home (% of survivors)	94.5	81.6

* Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F, Landon BE. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. N Engl J Med 2008; 358(5):464-474.

2. Safety specific literature searches and references

The following searches have been performed:

1. FIRST SEARCH

Search about harms and risks of AAA screening, including psychological aspects.

2. SECOND SEARCH

Search about effectiveness and adverse effects of AAA treatment, including open surgery and endovascular repair.

3. THIRD SEARCH

Search of clinical trials and systematic reviews about health related effects of AAA screening

4. FOURTH SEARCH

Search about the relation between Health Centre's, surgeon's and surgery team characteristics and risks and benefits of AAA repair.

The attached flow chart explains the literature screen and selection process we have done.

The first Medline search retrieved 144 references, 15 of them were selected after abstract screening and deletion of duplicates. The first Embase search retrieved 116 references, 4 of them were selected after abstract screening and deletion of duplicates.

The second Medline search retrieved 67 references, 40 of them were selected after abstract screening and deletion of duplicates. The second Embase search retrieved 22 references, 14 of them were selected after abstract screening and deletion of duplicates.

The third Medline search retrieved 88 references, 26 of them were selected after abstract screening and deletion of duplicates. The third Embase search retrieved 93 references, 3 of them were selected after abstract screening and deletion of duplicates.

The fourth Medline search retrieved 131 references, 28 of them were selected after abstract screening and deletion of duplicates. The fourth Embase search retrieved 40 references, 2 of them were selected after abstract screening and deletion of duplicates.

After merging these four searches a list of non-duplicated 117 studies was available.

More references retrieved and selected from other sources of information through searches on Cochrane, INAHTA databases, references from the articles retrieved and others sources.

FIRST SEARCH

Search about harms and risks of AAA screening, including psychological aspects.

Name of the database or link/reference to other source: MEDLINE via OVID

Search string or search terms:

1. Stress, psychological.sh .
2. Anxiety.sh .
3. (anxiety or anxious*) .ab.ti.
4. Depression.sh .
5. Depressive disorder .sh .
6. depress*.ab.ti.
7. harm* .ab.ti.
8. adverse effect* .ab.ti .
9. “Risk Assessment”
10. “Predictive Value of Tests”
11. “Attitude to Health”
12. “Psychiatric Status Rating Scales”
13. “Health Status”
14. “Health Status Indicators”
15. “Severity of Illness Index”
16. “Quality of Life”
17. false positive reactions.sh .
18. false negative reactions .sh .
19. or/1–18
20. aortic aneurysm, abdominal .sh .
21. mass screening.sh .
22. screen* .ab.ti
23. or/21–22
24. 20 and 23
25. 24 and 19
26. Limits: Humans, Publication Date from 2000-current

Date of search 15/06/2011

Name and affiliation of person who performed the search: Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 144

Abstract screen:

Number of included 15

References of the included studies

(1) Alonso-Perez M, Segura RJ, Sanchez J, Sicard G, Barreiro A, Garcia M, et al. Factors increasing the mortality rate for patients with ruptured abdominal aortic aneurysms. Ann Vasc Surg 2001 Nov;15(6):601-7.

(2) Cosford PA, Leng GC, Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. [Review] [26 refs]. Cochrane Database Syst Rev 2007;(2):CD002945.

(3) Flu WJ, van Kuijk JP, Merks EJ, Kuiper R, Verhagen HJ, Bosch JG, et al. Screening for abdominal aortic aneurysms using a dedicated portable ultrasound system: early results. Eur J Echocardiogr 2009 Jul;10(5):602-6.

(4) Lederle FA, Johnson GR, Wilson SE, Acher CW, Ballard DJ, Littooy FN, et al. Quality of life, impotence, and activity level in a randomized trial of immediate repair versus surveillance of small abdominal aortic aneurysm
14. J Vasc Surg 2003 Oct;38(4):745-52.

(5) Lee ES, Pickett E, Hedayati N, Dawson DL, Pevec WC, Lee ES, et al. Implementation of an aortic screening program in clinical practice: implications for the Screen For Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act. J Vasc Surg 2009 May;49(5):1107-11.

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(7) Lindholt JS, Vammen S, Fasting H, Henneberg EW, Lindholt JS, Vammen S, et al. Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2000 Jul;20(1):79-83.

(8) Marteau TM, Kim LG, Upton J, Thompson SG, Scott AP, Marteau TM, et al. Poorer self assessed health in a prospective study of men with screen detected abdominal aortic aneurysm: a predictor or a consequence of screening outcome? J Epidemiol Community Health 2004 Dec;58(12):1042-6.

(9) Prinssen M, Buskens E, Nolthenius RP, van Sterkenburg SM, Teijink JA, Blankensteijn JD. Sexual dysfunction after conventional and endovascular AAA repair: results of the DREAM trial. J Endovasc Ther 2004 Dec;11(6):613-20.

(10) Roshanali F, Mandegar MH, Yousefnia MA, Mohammadi A, Baharvand B, Roshanali F, et al. Abdominal aorta screening during transthoracic echocardiography. Echocardiography 2007 Aug;24(7):685-8.

(11) Schmidt T, Muhlberger N, Chemelli-Steingruber IE, Strasak A, Kofler B, Chemelli A, et al. Benefit, risks and cost-effectiveness of screening for abdominal aortic aneurysm. [Review] [50 refs]. ROFO Fortschr Geb Rontgenstr Nuklearmed 2010 Jul;182(7):573-80.

(12) Spencer CA, Norman PE, Jamrozik K, Tuohy R, Lawrence-Brown M, Spencer CA, et al. Is screening for abdominal aortic aneurysm bad for your health and well-being? ANZ J Surg 2004 Dec;74(12):1069-75.

(13) van Walraven C, Wong J, Morant K, Jennings A, Jetty P, Forster AJ, et al. Incidence, follow-up, and outcomes of incidental abdominal aortic aneurysms. J Vasc Surg 2010 Aug;52(2):282-9.

(14) Wanhainen A, Rosen C, Rutegard J, Bergqvist D, Bjorck M, Wanhainen A, et al. Low quality of life prior to screening for abdominal aortic aneurysm: a possible risk factor for negative mental effects. Ann Vasc Surg 2004 May;18(3):287-93.

(15) Wilmink AB, Forshaw M, Quick CR, Hubbard CS, Day NE, Wilmink ABM, et al. Accuracy of serial screening for abdominal aortic aneurysms by ultrasound. J Med Screen 2002;9(3):125-7.

Name of the database or link/reference to other source: EMBASE

Search string or search terms

1. stress/
2. anxiety/
3. (anxiety or anxious*).ti,ab.
4. depression/
5. "depress*".ti,ab.
6. "adverse effect*".ti,ab.
7. risk assessment/
8. predictive value/
9. attitude to health/
10. psychological rating scale/
11. health status/
12. hospitalization/
13. "quality of life"/
14. laboratory diagnosis/
15. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. abdominal aorta aneurysm/
17. mass screening/
18. "screen*".ti,ab.
19. 17 or 18
20. 16 and 19
21. 15 and 20
22. limit 21 to (human and yr="2000 -Current")

Date of search 23/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 116

Abstract screen:

Number of included 4

References of the included studies

(1) Fassiadis NR. Is screening of abdominal aortic aneurysm effective in a general practice setting? International Angiology 2005;24(2):185-8.

(2) Hobbs S.Claridge. Strategies to improve the effectiveness of abdominal aortic aneurysm screening programmes. Journal of Medical Screening 2004;11(2):93-6.

(3) Hogh AG. False-positive findings in screening for abdominal aortic aneurysm. Ugeskrift for laeger 2009;171(43):3101-2.

(4) Irvine CDS. A comparison of the mortality rate after elective repair of aortic aneurysms detected either by screening or incidentally. European Journal of Vascular and Endovascular Surgery 2000;20(4):374-8.

Total selection for the first search after deletion of duplicates: 19 studies

SECOND SEARCH

Search about effectiveness and adverse effects of AAA treatment, including open surgery and endovascular repair.

Name of the database or link/reference to other source MEDLINE via OVID.

Search string or search terms

1. safety management (MeSH) OR adverse effects.fs.
2. "safety".ab.ti.tw.
3. "adverse events".ab.ti.tw.
4. 1 AND (2 or 3)
5. ((Blood vessel prosthesis/ OR Blood vessel prosthesis implantation/ OR (endovascular repair.mp. OR evar.mp. OR Stents/) OR (vascular surgical procedures/ OR open surgery.mp.))
6. (aortic aneurysm, abdominal).sh.
7. 4 AND 5
8. 7 AND 6
9. limit 8 to humans and published 2000-current,

(case reports or classical article or clinical trial, all or comparative study or controlled clinical trial or "corrected and republished article" or evaluation studies or introductory journal article or journal article or meta analysis or multicenter study or randomized controlled trial or "review" or "scientific integrity review" or technical report or validation studies)

Date of search 23/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 67

Abstract screen:

Number of included 40

References of the included studies

(1) Abbruzzese TA, Kwolek CJ, Brewster DC, Chung TK, Kang J, Conrad MF, et al. Outcomes following endovascular abdominal aortic aneurysm repair (EVAR): an anatomic and device-specific analysis. J Vasc Surg 2008 Jul;48(1):19-28.

(2) Alonso-Perez M, Segura RJ, Sanchez J, Sicard G, Barreiro A, Garcia M, et al. Factors increasing the mortality rate for patients with ruptured abdominal aortic aneurysms. Ann Vasc Surg 2001 Nov;15(6):601-7.

(3) Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. J Vasc Surg 2011 May;53(5):1167-73.

(4) Becquemin JP, Allaire E, Desgranges P, Kobeiter H, Becquemin JP, Allaire E, et al. Delayed complications following EVAR. [Review] [23 refs]. Tech Vasc Interv Radiol 2005 Mar;8(1):30-40.

(5) Blankensteijn JD, de Jong SE, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SM, et al. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. N Engl J Med 2005 Jun 9;352(23):2398-405.

(6) Buth J, Laheij RJ, Buth J, Laheij RJ. Early complications and endoleaks after endovascular abdominal aortic aneurysm repair: report of a multicenter study. J Vasc Surg 2000 Jan;31(1 Pt 1):134-46.

(7) Chong T, Nguyen L, Owens CD, Conte MS, Belkin M, Chong T, et al. Suprarenal aortic cross-clamp position: a reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. J Vasc Surg 2009 Apr;49(4):873-80.

(8) Coselli JS, Bozinovski J, LeMaire SA, Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. Ann Thorac Surg 2007 Feb;83(2):S862-S864.

(9) Cuypers PW, Gardien M, Buth J, Charbon J, Peels CH, Hop W, et al. Cardiac response and complications during endovascular repair of abdominal aortic aneurysms: a concurrent comparison with open surgery. J Vasc Surg 2001 Feb;33(2):353-60.

(10) Davenport DL, O'Keeffe SD, Minion DJ, Sorial EE, Endean ED, Xenos ES, et al. Thirty-day NSQIP database outcomes of open versus endoluminal repair of ruptured abdominal aortic aneurysms. J Vasc Surg 2010 Feb;51(2):305-9.

(11) Egorova N, Giacovelli J, Greco G, Gelijns A, Kent CK, McKinsey JF, et al. National outcomes for the treatment of ruptured abdominal aortic aneurysm: comparison of open versus endovascular repairs. J Vasc Surg 1100 Nov;48(5):1092-100.

(12) Enzler MA, van Marrewijk CJ, Buth J, Harris PL, Enzler MA, van Marrewijk CJ, et al. [Endovascular therapy of aneurysms of the abdominal aorta: report of 4,291 patients of the Eurostar Register]. [German]. Vasa 2002 Aug;31(3):167-72.

(13) Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE, Schermerhorn ML, et al. Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. J Endovasc Ther 2009 Oct;16(5):554-64.

(14) Greenberg R, Zenith I, Greenberg R, Zenith I. The Zenith AAA endovascular graft for abdominal aortic aneurysms: clinical update. Semin Vasc Surg 2003 Jun;16(2):151-7.

(15) Harris PL, Vallabhaneni SR, Desgranges P, Becquemin JP, van Marrewijk C, Laheij RJ, et al. Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: the EUROSTAR experience. European Collaborators on Stent/graft techniques for aortic aneurysm repair. J Vasc Surg 2000 Oct;32(4):739-49.

(16) Holt PJ, Poloniecki JD, Hofman D, Hinchliffe RJ, Loftus IM, Thompson MM, et al. Re-interventions, readmissions and discharge destination: modern metrics for the assessment of the quality of care. Eur J Vasc Endovasc Surg 2010 Jan;39(1):49-54.

(17) Jetty P, Hebert P, van Walraven C, Jetty P, Hebert P, van Walraven C. Long-term outcomes and resource utilization of endovascular versus open repair of abdominal aortic aneurysms in Ontario. J Vasc Surg 583 Mar;51(3):577-83.

(18) Jim J, Rubin BG, Geraghty PJ, Criado FJ, Fajardo A, Sanchez LA, et al. A 5-year comparison of EVAR for large and small aortic necks. J Endovasc Ther 2010 Oct;17(5):575-84.

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(20) Jordan WD, Jr., Moore WM, Jr., Melton JG, Brown OW, Carpenter JP, Endologix I, et al. Secure fixation following EVAR with the Powerlink XL System in wide aortic necks: results of a prospective, multicenter trial. J Vasc Surg 2009 Nov;50(5):979-86.

(21) Kibbe MR, Matsumura JS, Excluder I, Kibbe MR, Matsumura JS, Excluder I. The Gore Excluder US multi-center trial: analysis of adverse events at 2 years. Semin Vasc Surg 2003 Jun;16(2):144-50.

(22) Kim LG, RA PS, Ashton HA, Thompson SG, Multicentre Aneurysm Screening Study Group., Kim LG, et al. A sustained mortality benefit from screening for abdominal aortic aneurysm.[Erratum appears in Ann Intern Med. 2007 Aug 7;147(3):216]. Ann Intern Med 2007 May 15;146(10):699-706.

(23) Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT, Jr., Matsumura JS, Kohler TR, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009 Oct 14;302(14):1535-42.

(24) Lederle FA, Johnson GR, Wilson SE, Acher CW, Ballard DJ, Littooy FN, et al. Quality of life, impotence, and activity level in a randomized trial of immediate repair versus surveillance of small abdominal aortic aneurysm. J Vasc Surg 2003 Oct;38(4):745-52.

(25) Lederle FA, Kane RL, MacDonald R, Wilt TJ, Lederle FA, Kane RL, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. Ann Intern Med 2007 May 15;146(10):735-41.

(26) Lindholt JS, Norman PE, Lindholt JS, Norman PE. Meta-analysis of postoperative mortality after elective repair of abdominal aortic aneurysms detected by screening. [Review]. Br J Surg 2011 May;98(5):619-22.

(27) Londero H, Lev G, Bertoni H, Mendaro E, Santaera O, Martinez RL, et al. Safety and feasibility of balloon-expandable stent implantation for the treatment of type I endoleaks following endovascular aortic abdominal aneurysm repair. Eurointervention 2011 Jan;6(6):740-3.

(28) Lottman PE, Laheij RJ, Cuypers PW, Bender M, Buth J, Lottman PEM, et al. Health-related quality of life outcomes following elective open or endovascular AAA repair: a randomized controlled trial. J Endovasc Ther 2004 Jun;11(3):323-9.

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vascular repair of abdominal aortic aneurysms in Spain. Int Angiol 2009 Jun;28(3):181-91.

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(31) Ricco JB, InterGard Silver Study Group., Ricco JB, InterGard Silver Study Group. InterGard silver bifurcated graft: features and results of a multicenter clinical study. J Vasc Surg 2006 Aug;44(2):339-46.

(32) Rosenthal R, von Kanel O, Eugster T, Stierli P, Gurke L, Rosenthal R, et al. Does specialization improve outcome in abdominal aortic aneurysm surgery?.[Erratum appears in Vascular. 2006 Jan-Feb;14(1):54]. Vascular 2005 Mar;13(2):107-13.

(33) Schmiedt W, Duber C, Pitton M, Neufang A, Dorweiler B, Herber S, et al. [Endovascular aneurysm therapy--long-term treatment outcomes after 7 years]. [German]. Med Klin 2002 Apr 15;97(4):204-8.

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(35) Stella A, Freyrie A, Gargiulo M, Faggioli GL, Stella A, Freyrie A, et al. The advantages of Anaconda endograft for AAA. J Cardiovasc Surg (Torino) 2009 Apr;50(2):145-52.

(36) Subramanian K, Woodburn KR, Travis SJ, Hancock J, Subramanian K, Woodburn KR, et al. Secondary interventions following endovascular repair of abdominal aortic aneurysm. Diagn Interv Radiol 2006 Jun;12(2):99-104.

(37) Sultan S, Hynes N, Sultan S, Hynes N. Clinical efficacy and cost per quality-adjusted life years of pararenal endovascular aortic aneurysm repair compared with open surgical repair. J Endovasc Ther 2011 Apr;18(2):181-96.

(38) Thomas SM, Beard JD, Ireland M, Ayers S, Vascular Society of Great Britain and Ireland, British Society of Interventional Radiology., et al. Results from the prospective registry of endovascular treatment of abdominal aortic aneurysms (RETA): mid term results to five years. Eur J Vasc Endovasc Surg 2005 Jun;29(6):563-70.

(39) Turnbull IC, Criado FJ, Sanchez L, Sadek M, Malik R, Ellozy SH, et al. Five-year results for the Talent enhanced Low Profile System abdominal stent graft pivotal trial including early and long-term safety and efficacy. J Vasc Surg 544 Mar;51(3):537-44.

(40) van Marrewijk CJ, Leurs LJ, Vallabhaneni SR, Harris PL, Buth J, Laheij RJ, et al. Risk-adjusted outcome analysis of endovascular abdominal aortic aneurysm repair in a large population: how do stent-grafts compare? J Endovasc Ther 2005 Aug;12(4):417-29.

Name of the database or link/reference to other source EMBASE

Search string or search terms

1. safety/
2. adverse drug reaction/ or adverse outcome/
3. 1 or 2
4. blood vessel prosthesis/ or blood vessel transplantation/
5. interventional cardiovascular procedure/
6. vascular surgery/
7. abdominal aorta aneurysm/
8. 3 or 4 or 5 or 6
9. 7 and 8
10. limit 9 to (human and (evidence based medicine or meta analysis or outcomes research or "systematic review") and (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) and yr="2000 -Current" and (article or journal or report or "review" or short survey))

Date of search 23/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 22

Abstract screen:

Number of included 14

References of the included studies

(1) Bosch JLK. Abdominal aortic aneurysms: Cost-effectiveness of elective endovascular and open surgical repair. Radiology 2002;225(2):337-44.

(2) Bown MJS. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair
38. Br J Surg 2002;89(6):714-30.

(3) Cau JR. Total Laparoscopic Aortic Repair for Occlusive and Aneurysmal Disease: First 95 Cases. European Journal of Vascular and Endovascular Surgery 2006;31(6):567-74.

(4) De Rango PC. Outcome after Endografting in Small and Large Abdominal Aortic Aneurysms: A Metanalysis. European Journal of Vascular and Endovascular Surgery 2008;35(2):162-72.

(5) Lovegrove REJ. A meta-analysis of 21,178 patients undergoing open or endovascular repair of abdominal aortic aneurysm. The British journal of surgery 2008;95(6):677-84.

(6) Maher MMM. Abdominal aortic aneurysms: Elective endovascular repair versus conventional surgery - Evaluation with evidence-based medicine techniques 35. Radiology 2003;228(3):647-58.

(7) Mastracci TMG. Endovascular repair of ruptured abdominal aortic aneurysms: A systematic review and meta-analysis. J Vasc Surg 2008;47(1):214-21.

(8) Matsumoto AH. What Randomized Controlled Trials Tell Us About Endovascular Repair of Abdominal Aortic Aneurysms. Journal of Vascular and Interventional Radiology 2008;19(6 SUPPL.):S18-S21.

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(10) Ouriel K. Randomized clinical trials of endovascular repair versus surveillance for treatment of small abdominal aortic aneurysms. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 2009 Feb;16 Suppl 1(pp I94-105):Feb.

(11) Reilly LM. Pro: Endovascular Repair of Abdominal Aortic Aneurysms Reduces Perioperative Morbidity and Mortality. Journal of Cardiothoracic and Vascular Anesthesia 2003;17(5):655-8.

(12) Sadat UB. Endovascular vs open repair of acute abdominal aortic aneurysms-A systematic review and meta-analysis. J Vasc Surg 2008;48(1):227-36.

(13) Stolberg HO. Treatment of abdominal aortic aneurysms: Review with evidence-based methods. Radiology 2003;228(3):614-6.

(14) Walschot LHB. Outcome after endovascular abdominal aortic aneurysm repair: A meta-analysis. J Endovasc Ther 2002;9(1):82-9.

Total selection for the second search after deletion of duplicates: 54 studies

THIRD SEARCH

Search of clinical trials and systematic reviews about health related effects of AAA screening

Name of the database or link/reference to other source : MEDLINE via OVID

Search string or search terms

1. controlled clinical trials.sh .
2. randomized controlled trials.sh.
3. multicenter studies.sh.
4. double-blind method .sh.
5. meta-analysis.sh.
6. random allocation .sh.
7. single-blind method.sh .
8. controlled clinical trial. pt.
9. meta analysis.pt .
10. randomized controlled trial. pt.
11. (meta analy* OR metaanaly*) .ab.ti
12. (systematic* review* OR systematic* overview*).ab.ti.
13. (quantitative* review* OR quantitative* overview*).ab.ti.
14. evidence based review*.ab.ti.
15. or/1-14
16. Aortic aneurysm, abdominal .sh.
17. 15 AND 16
18. mass screening.sh.
19. screen*.ab.ti.
20. 17 AND (18 OR 19)
21. Limits: Humans, Publication Date from 2000-current

Date of search 13/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 88

Abstract screen:

Number of included 26

References of the included studies

(1) Lindholt JS, Norman PE, Lindholt JS, Norman PE. Meta-analysis of postoperative mortality after elective repair of abdominal aortic aneurysms detected by screening. [Review]. Br J Surg 2011; 98(5):619-622.

(2) Takagi H, Goto SN, Matsui M, Manabe H, Umemoto T, Takagi H et al. A further meta-analysis of population-based screening for abdominal aortic aneurysm. J Vasc Surg 2010; 52(4):1103-1108.

(3) Lindholt JS, Sorensen J, Sogaard R, Henneberg EW, Lindholt JS, Sorensen J et al. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. Br J Surg 2010; 97(6):826-834.

(4) Eckstein HH, Bockler D, Flessenkamper I, Schmitz-Rixen T, Debus S, Lang W et al. Ultrasonographic screening for the detection of abdominal aortic aneurysms. [Review] [29 refs]. Dtsch 2009; 106(41):657-663.

(5) van Gils PF, de Wit GA, Schuit AJ, van den BM, van Gils PF, de Wit GA et al. [Screening for abdominal aortic aneurysm; effectivity and cost-effectiveness]. [Review] [27 refs] [Dutch]. Ned Tijdschr Geneeskd 2009; 153:B383.

(6) Thompson SG, Ashton HA, Gao L, Scott RA, Multicentre Aneurysm Screening Study Group., Thompson SG et al. Screening men for abdominal aortic aneurysm: 10 year mortality and

cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. BMJ 2009; 338:b2307.

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(8) Hamerlynck JV, Legemate DA, Hooft L, Hamerlynck JVTH, Legemate DA, Hooft L. [From the Cochrane Library: ultrasonographic screening for abdominal aortic aneurysm in men aged 65 years and older: low risk of fatal aneurysm rupture]. [Dutch]. Ned Tijdschr Geneeskd 2008; 152(13):747-749.

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

(11) Lederle FA, Kane RL, MacDonald R, Wilt TJ, Lederle FA, Kane RL et al. Systematic review: repair of unruptured abdominal aortic aneurysm. [Review] [35 refs]. Ann Intern Med 2007; 146(10):735-741.

(12) Kim LG, RA PS, Ashton HA, Thompson SG, Multicentre Aneurysm Screening Study Group., Kim LG et al. A sustained mortality benefit from screening for abdominal aortic aneurysm.[Erratum appears in Ann Intern Med. 2007 Aug 7;147(3):216]. Ann Intern Med 2007; 146(10):699-706.

(13) Cosford PA, Leng GC, Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. [Review] [26 refs]. Cochrane Database Syst Rev 2007;(2):CD002945.

(14) Lindholt JS, Juul S, Fasting H, Henneberg EW, Lindholt JS, Juul S et al. Preliminary ten year results from a randomised single centre mass screening trial for abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 2006; 32(6):608-614.

(15) Lindholt JS, Juul S, Fasting H, Henneberg EW, Lindholt JS, Juul S et al. [Screening reduced abdominal aortic aneurysm mortality--secondary publication. Results from a Danish randomized screening trial]. [Danish]. Ugeskr Laeger 2005; 167(15):1641-1644.

(16) Lindholt JS, Juul S, Fasting H, Henneberg EW, Lindholt JS, Juul S et al. Screening for abdominal aortic aneurysms: single centre randomised controlled trial.[Erratum appears in BMJ. 2005 Oct 15;331(7521):876]. BMJ 2005; 330(7494):750.

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Name of the database or link/reference to other source: EMBASE

Search string or search terms

1. controlled clinical trial/
2. randomized controlled trial/
3. multicenter study/
4. double blind procedure/
5. meta analysis/
6. randomization/
7. single blind procedure/
8. (meta analy* or mataanaly*).ti,ab.
9. (systematic* review* or systematic* overview*).ti,ab.
10. (quantitative* review* or quantitative* overview*).ti,ab.
11. "evidence based review*".ti,ab.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. abdominal aorta aneurysm/
14. 12 and 13
15. mass screening/
16. "scree*".ti,ab.
17. 15 or 16
18. 14 and 17
19.limit 18 to (human and yr="2000 -Current")

Date of search 13/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 93

Abstract screen:

Number of included 3

References of the included studies

(1) Maceira-Rozas MCA. Screening for abdominal aortic aneurysm in a population at risk: A systematic review. Angiologia 2008;60(3):165-76.

(2) Muszbek NT. Systematic Review of Utilities in Abdominal Aortic Aneurysm. European Journal of Vascular and Endovascular Surgery 2008;36(3):283-9.

(3) Pande RLB. Abdominal Aortic Aneurysm: Populations at Risk and How to Screen. Journal of Vascular and Interventional Radiology 2008;19(6 SUPPL.):S2-S8.

Total selection for the third search after deletion of duplicates: 29

FOURTH SEARCH

Search about the relation between Health Centre's, surgeon's and surgery team characteristics and risks and benefits of AAA repair.

Name of the database or link/reference to other source MEDLINE via OVID

Search string or search terms

1. learning curve.sh.
2. "outcome and process assessment health care" .sh.
3. clinical competence.sh.
4. "standard of care".sh.
5. health resources.sh.
6. aortic aneurysm, abdominal.sh.
7. 1 or 2 or 3 or 4 or 5
8. 6 and 7
9. limit 8 to humans and published 2000-current,

(case reports or classical article or clinical trial, all or comparative study or controlled clinical trial or "corrected and republished article" or evaluation studies or introductory journal article or journal article or meta analysis or multicenter study or randomized controlled trial or "review" or "scientific integrity review" or technical report or validation studies)

Date of search 23/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 131

Abstract screen:

Number of included 28

References of the included studies

(1) Abularrage CJ, Sheridan MJ, Mukherjee D, Abularrage CJ, Sheridan MJ, Mukherjee D. Endovascular versus "fast-track" abdominal aortic aneurysm repair. Vasc Endovascular Surg 2005 May;39(3):229-36.

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Name of the database or link/reference to other source EMBASE

Search string or search terms

1. learning curve/
2. treatment outcome/
3. clinical competence/
4. health care planning/
5. abdominal aorta aneurysm/
6. 1 or 2 or 3 or 4
7. 5 and 6
8. limit 7 to (human and (evidence based medicine or meta analysis or outcomes research or "systematic review") and (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) and yr="2000 -Current" and (article or journal or report or "review" or short survey))

Date of search 23/06/2011

Name and affiliation of person who performed the search Javiera Valdés. AETS ISCIII.

Selection of studies

Number of references retrieved: 40

Abstract screen:

Number of included 2

References of the included studies

(1) Holt PJE. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. British Journal of Surgery 2007;94(4):395-403.

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Total selection for the third search after deletion of duplicates: 30