Abdominal aortic aneurysm ultrasound screening programme

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Role of the National Abdominal Aortic Aneurysm Ultrasound Screening Programme in Improving Health Outcomes: a systematic review

Abstract

Background: *Abdominal Aortic Aneurysm (AAA) is one of the common conditions that affect men aged 65 and older. Described as a 'ticking bomb' (1) , rupture of such an aneurysm results in fatal bleeding and death. Early detection allows appropriate treatment to be given to patients as an effort to reduce mortality rates. The National Abdominal Aortic Aneurysm Screening programme, an initiative of Public Health England, offers screening to men in the prevalence group by following its objective of reducing mortality rates of preventable illnesses (2) . Ultrasonography is the chosen imaging modality due to its high sensitivity and specificity (3) . The aim of this study is to examine current literature on AAA and to understand whether screening programmes are effective enough to reduce mortality rates of AAA. Quality of life (QoL) as a health outcome will also be examined and evidence analysed, to see whether screening programmes affect patients' quality of life.*

Method: *A thorough search of prominent databases was carried out and the search-results underwent application of inclusion and exclusion criteria developed for this review. Four major randomised controlled trials were identified. Following data extraction, quality assessment was carried out using the CASP tool. Risk of bias was checked using the Cochrane's tool for assessing risk of bias. All of these ensured a valid conclusion to be drawn.*

Results: *The four chosen RCTs were the MASS trial, the Chichester trial, the Viborg trial and the WA trial. The Mass and Chichester trials were conducted in the UK whereas the Viborg and WA trials were carried out in Denmark and Australia, respectively. The data pool of 125595 people added to the reliability of the findings of this review. A significant reduction in mortality rates of AAA was found in the intervention groups following an ultrasound screening of the abdominal aorta (4-7) . QoL was looked at as the secondary outcome in the MASS trial which concluded that there was no adverse effect on QoL (4) .*

Conclusion: *The review showed evidence on reduced AAA mortality rates in men aged 65 and older following ultrasound screening. No adverse effect in patients' QoL was found. The NAAASP is a commendable initiative of Public Health England and it is suggested that similar screening programmes be introduced through an evidence-based healthcare.*

Introduction

An aneurysm forms when a section of a weakened arterial wall dilates permanently. The walls of an artery can weaken and dilate due to cardiovascular diseases like arteriosclerosis, inflammation of the arterial wall or trauma. When this dilation occurs in the abdominal aorta, which runs from T12 to L5, it is considered to be an Abdominal Aortic Aneurysm (AAA)(8). Several studies have found smoking, hypertension and alcohol consumption to be the major risk factors of AAA(9). A family history of AAA is also considered to be a risk factor(10).

AAA is age and sex-dependent as concluded by a retrospective prevalence study that looked at a cohort of 100, 000 men and women each. The prevalence among men was found to increase rapidly after the age of 55 and that among women increases after the age of 70(11). Therefore, women are considered to be at low risk of developing AAA and hence screening programmes focus on a male population of 65 years or older(12).

Patients are mostly asymptomatic and where symptoms do present, these could be abdominal pain, flank pain, back pain, groin pain, or syncope. A palpable pulsating abdominal mass could also be found during examination. An aneurysm once formed, grows in size until it bursts, leading to fatal bleeding. Only 2 in 10 people with a ruptured aneurysm survive if not treated with emergency AAA repair surgery(13). The survival rate among those who receive surgery is 94%(14).

AAAs are detected using an ultrasound scan (US), which is considered to be the most effective screening modality with high sensitivity (98%) and specificity (99%) rates(15). The US is safe, cheap, quick, and non-invasive, and provides results immediately. It is widely accepted as a valid screening method and the aorta can be visualised in 99% of patients(15). Compared to CT scans which can sometimes overestimate the diameter of aneurysms in the oblique plane(15), ultrasound continues to be the choice of screening modality.

In 2014, around 2000 men died from ruptured AAA, accounting for around 1% of all registered deaths in men aged 65 and over(16). Past records show a reduction in mortality in England from 7. 5% in 2009 to 1. 6% in 2012(17).

This sheds light on the National AAA Screening Programme (NAAASP) offered by the NHS. Early detection via screening of a large aneurysm of above 5. 5cm, means that patients are given the choice of repair surgery thereby increasing their survival rate by 69%(8, 18). Surveillance is offered to patients with a small or medium aneurysm of 3-4. 4cm and 4. 5-5. 4cm, respectively(19, 20). This is through an ultrasound scan every twelve or three months for small and medium aneurysms, respectively.

Screening aims to reduce the risk of developing a disease in a healthy population who have no signs of illness with respect to the condition being screened. The NAAASP is based on the policies recommended by the UK National Screening Committee in 2005 following the results of the largest randomised controlled trial about AAA, the Multicentre Aneurysm Screening Study (MASS), which showed that screening reduces mortality by 40% after 10 years(21). Implemented in 2009, the programme achieved a nationwide coverage by the end of 2013.

The programme aims to 'reduce AAA mortality by providing a systematic population-based screening programme for the male population during their 65 th year and on request, for men over 65'(22). This falls under Domain 2 and 4 of the Public Health Outcomes Framework provided by the Department of Health, with the objectives to help people to live healthy lifestyles and, to reduce the number of people living with preventable ill health and people dying prematurely(22), respectively.

NAAASP Annual Data 2014/15 shows that a total of 280, 520 men were screened and 83. 2% had a conclusive screen(23). During the screening year

2013/14, this was 82% out of a total of 287, 126 men(24). Depending on the size of the aneurysm, either surveillance or surgery was offered.

Overall, the programme aims to achieve the health outcome of reduced mortality. Quality of life is also reported as a health outcome as shown by several retrospective, observational and cohort studies conducted on patients(25-27).

Knowledge on the success of screening programmes like NAAASP remains limited. The aim of this review, therefore, is to examine current evidence on whether a screening programme improves health outcomes, namely reduced mortality and improved quality of life, by critically and systematically reviewing literature using the quality assessment tools of the critical appraisal skills programme (CASP).

This will be achieved through the following objectives:

- Develop inclusion and exclusion criteria based on PICOS relating to AAA and ultrasound scanning
- Carry out a systematic search of databases- Medline, Web of Science, the Cochrane Database, OneSearch and the ISRCTN Registry (BioMed Central).
- Filter the search using the inclusion and exclusion criteria and carry out data-extraction using the Cochrane Data Collection form
- Carry out quality assessment using the CASP tool and use the Cochrane tool to assess risk of bias
- Conduct an analysis, focusing on mortality and quality of life as the health outcomes

Methods

Although evidence exists on the accuracy of using ultrasonography for detecting abdominal aortic aneurysms(3) and the validity of the scan results is widely accepted due to its high sensitivity and specificity(3), the process of abdominal aortic scanning was decided to be reviewed first(Appendix A).

Prior to conducting the search, inclusion and exclusion criteria were set (Table 1)(28). Following this, databases were chosen for the search-topic 'Abdominal Aortic Aneurysm'. These included PubMed/MEDLINE, ISRCTN Registry, Web of Science, Lancaster University/OneSearch and the Cochrane Database. Search strategies were developed for each source and search filters were decided (Table 3-7). Medical Subject Heading (MeSH) terms were used to further refine the results (Table 2).

Overall, seventy-four articles were found and after removing duplicates, forty-nine remained. These were subjected to the inclusion and exclusion criteria, thus narrowing down the results to seventeen relevant articles. The reference lists of the retrieved articles were further reviewed for any relevant cited papers. This process was repeated until no relevant articles were found. Four major randomised clinical trials were identified from these. These were reviewed after undergoing data extraction and quality assessment.

Data extraction was carried out using Cochrane's data extraction tool and this allowed for a full-text screening that removed any ineligible studies. Moreover, the use of a standardised form increased the validity and reliability of this review whilst also reducing any risk of bias(28). Finally, the

trials were critically appraised using the CASP tool. This enabled identifying risk of bias within the trials, particularly selection bias, performance bias and reporting bias.

1. T

	Inclusion Criteria	Exclusion Criteria
Population	2. General population of males aged 65 years or older 3. Patients who are asymptomatic and symptomatic who were involved in AAA screening	6. Trials that include female s, younger children and males younger than 65 years since AAA is age

		4. Patients from all ethnicities and sex specific 5. Patients of all socioeconomic status
		7. Any other imaging modalities like CT, MRI or radiography
Intervention	Ultrasound Screening for AAA	
Comparison	Non-screened population	8. Aneurysm 9. Aortic Aneury

	sm	
	10. T horaci c Aneury sm	
Outc ome (s)	11. Mor tality 12. Qu ality of Life	
Stud y Desi gn	13. Ran domised Controlle d Trials (RCTs) 14. Tria ls that look at AAA detection using Ultrasono graphy	18. A ll other types of studies such as qualita tive studies , observ ational

15. Articles in the English language
16. Articles from the time period starting from approximately 20 years before the NAAASP programme came into effect, i.e., 1985 to present
17. Cohort or case-series studies.
19. Articles in foreign languages
20. Studies conducted outside this time period
21. Articles that

		are not
17.	Full articles	fully availab le

Table 2 Medical Search Headings (MeSH)

Abdominal Aortic Aneurysm

Mass Screening

Ultrasonography

Rupture

Table 3 PubMed

Search Strategy/Method	Results
Abdominal Aortic Aneurysm	23, 807
Mass Screening	128, 434
Ultrasonography	386, 798
Rupture	109,

	121
AAA + MS	599
AAA + MS + US	300
AAA + MS +US + Rupture	102
AAA + MS +US + RCTs	23
AAA + MS +US + Rupture + RCTs	11

Table 4 Web of Science

Search Strategy/Method	Results
Abdominal Aortic Aneurysm	18, 625
Mass Screening	43, 081
Ultrasonography	80, 257
Rupture	119, 830
AAA + MS	131
AAA + MS + US	23
AAA + MS +US + Rupture	12

Limit 'English'	11

Table 5 Cochrane Library (RCTs only)

Search Strategy/Method	Results
Abdominal Aortic Aneurysm	702
Mass Screening	3827
Ultrasonography	11, 318
Rupture	3097
AAA + MS	46
AAA + MS + US	23
AAA + MS +US + Rupture	10

Table 6 OneSearch

Search Strategy/Method	Results
Abdominal Aortic Aneurysm	27, 819

Mass Screening	73, 090
Ultrasonography	122, 460
Rupture	94738
AAA + MS	604
AAA + MS + US	123
AAA + MS +US + Rupture	42
Limit 'Articles'	39

Table 7 ISRCTN Registry/BioMed Central

Search Strategy/Method	Results
Abdominal Aortic Aneurysm	37
Mass Screening	328
Ultrasonography	88
Rupture	176
AAA + MS	3

Results

Four dominant randomised controlled trials (RCTs) were identified- the Multicentre Aneurysm Screening Study(4) (MASS) conducted between 1997 to 1999; the Chichester Study(5), 1988 to 1991; the Viborg County Trial(6), 1994 to 1998 and; the Western Australia (WA) Trial(7), 1996. These collectively showed that AAA mortality rate can be significantly reduced in the population following an ultrasound scan of the abdominal aorta (Table 8).

The Mass and Chichester trials were carried out in the UK and had a participant number of 67, 770 men aged 65 to 74 years and 6040 men aged 65-80 years, respectively. The Viborg Country trial was conducted in the Viborg county of Denmark with a participant number of 12, 639 men aged 65-73 years; the WA trial, carried out in the province of Western Australia included 41, 000 men aged 65-79.

All these trials used ultrasound screening of the abdomen to detect AAA and measured AAA-mortality as the primary outcome(4-7). The secondary outcomes of all trials were all-cause mortality. However the Mass trial also measured quality of life and cost-effectiveness as the secondary outcomes. Cost-effectiveness was also measured by the Viborg trial as the secondary outcome. Participants were randomly selected and randomisation was computer-generated(4-7).

Mass and Chichester trials recruited participants via GP registers based on gender and date of birth. In the Mass trial, some were excluded if the GP considered them to terminally ill, had other health problems or had

undergone AAA repair(4). In the Viborg trial, recruitment was through the county's health department and WA participants were selected from the electoral roll(6, 7). The WA trial excluded those men who were too far from the screening location; the Viborg trial had no such exclusions.

1. MASS Trial

The intervention group composed of 33839 men and the control group, 1333 men. Attendance was 80% and the median follow-up was ten years(4). 65 men died in the intervention group and 113 died in the control group, due to AAA. Mortality data was taken from death registry provided by the Office of National Statistics (ONS).

The study concluded that AAA mortality rate can be significantly reduced by up to half, following ultrasound screening. There was a 42% reduction in the intervention group, hazard ratio (HR) - 0. 58 95% CI (0. 42-0. 78)(4).

The study also measured mood and health status outcomes such as state anxiety, depression, and health-status measures such as mental and physical health, and self-rated health(4, 13). These were calculated at intervals of six weeks after screening and, 3 and 12 months after detection of aneurysm or surgery. There were no significant changes in anxiety and depression and these remained within the recommendations(4). However, those screened negative and undergoing surveillance scored higher in health-status measures. This trend continued until 3 months after screening(4). However at 12 months, those who had undergone surgery scored higher than those in surveillance. They also self-rated higher, similar

to those screened negative(4). Despite these results, the authors refrained from making a conclusive statement on quality of life.

In the intervention group, there was an increase in the number of elective surgeries, odds ratio (OR)- 2. 45 95% CI (2. 02-2. 97)(4). Nevertheless, there was no significant difference in the overall 30-day mortality after elective surgery in the intervention and control groups; this remained at 6%. However, 'unnecessary surgery and the risk of overdiagnosis' are seen as factors reducing the overall quality of life(29). So even though this increase in elective surgery in the intervention group and its effects could be used as a measure of quality of life, the authors did not make such a link.

2. Chichester Trial

The intervention group composed of 2995 men and the control group, 3045 men. The median follow-up was fifteen years and the attendance rate, 74%, decreased with age. About 33. 8% of men in the age range of 76-80 years declined compared to 19. 5% in the age group of 65 years(5). 10 men died in the intervention group and 17 died in the control group, due to AAA-related causes. Like the Mass trial, mortality data was taken from the ONS Death Registry.

The study found no differences in mortality rates in the two groups up to four years from screening. However, over 15 years, mortality was found to be reduced in the intervention group by 11%. This was not considered as a significant reduction, HR - 0. 89 95% CI (0. 60-1. 32) (5).

3. Viborg Trial

The intervention group composed of 6339 men and the control group, 6319 men. Attendance was 76% and the maximum follow-up was fourteen years(6). 6 men died in the intervention group, compared to 19 in the control group. Mortality data was taken from the national registry.

There was a significant reduction in AAA-related hospital mortality, OR-0. 31 95% CI (0. 13-0. 79)(6). The study recommends screening men aged 65 years to reduce AAA-mortality. However since the study only noted deaths from AAA in a hospital setting in the county of Viborg, this finding cannot be expanded to other countries.

4. Western Australia Trial

The intervention and control groups composed of 19352 men each. Attendance rate was 70% and the maximum follow-up was 43-months(7). 18 men died in the intervention group and 25 died in the control group. Mortality data was taken from the national death registry and the hospital registry.

The study found that there was no significant reduction in mortality following ultrasound scanning in the intervention group of men aged 65-83 years in Western Australia, OR- 0. 72 95% CI (0. 39-1. 32)(7). However the study noted that in the subgroup of men aged 65-75 years, mortality was found to be reduced(7).

Table 8 AAA mortality: raw data

Trial	Deaths in Screened	Deaths in Unscreened	Odds Ratio(95%

			CI)
MASS	65/33, 839	113/33, 961	0. 58 (0. 42 to 0. 78)
Chichester	10/3205	17/3228	0. 59 (0. 27 to 1. 29)
Viborg	6/6339	19/6319	0. 31 (0. 13 to 1. 79)
Western Australia (WA)	18/19352	25/19352	0. 72 (0. 39 to 1. 32)
Total *	93/56, 396	155/56, 541	0. 60 (0. 46 to 0. 78)

**Data from the Viborg trial is not included since the study noted deaths only in a hospital setting. Hence, results cannot be compared to the other studies (30)*

Discussion

The pooled data of 125595 participants shows that AAA mortality rate can be significantly reduced in the population following an ultrasound scan of the abdominal aorta. Data from the four RCTs show that the Absolute Risk Reduction (ARR) for the Mass trial, Chichester, Viborg and WA are 0. 14%, 0. 21%, 0. 21% and 0. 04%, respectively (See Table 9 for the full data processed by the review author). Although these may appear insignificant,

when applied over a population, the ARR is 140. 7, 214. 6, 206. 0 and 36. 2 per 100, 000 respectively. Hence, the Numbers Needed to Screen (NNS) are 711, 466, 485 and 2765 respectively. On an average, this is an ARR of 149. 4 out of every 100, 000 people for an NNS of 1107. This NNS is lower than other screening programmes like breast cancer screening which has an NNS of 1339(31). This confirms the benefits of a population-based screening programme such as the NAAASP.

The Mass trial, which looked at the effects of ultrasound screening on the quality of life found its measures to be within normal standards. Since the NAAASP is based on the results of this trial, it can be said that ultrasound screening has no adverse effects on the quality of life of the screened population. However, a limitation acts on the trial- quality of life was measured only up to twelve months after scan; no data is available for the period after that. If quality of life was continued to be measured during follow-ups or even separately via postal questionnaires or GP appointments, a more valid inference could have been drawn. It would also have provided a fuller picture on the long-term effects on quality of life.

One other limitation acting on this review is the possibility of selection bias as a result of excluding some articles in foreign languages. Despite this, the findings of this review remain unaffected and can be considered valid since an exhaustive search of the major databases was carried out systematically. Although the inclusion criteria of 'free-articles' was applied after this search, Lancaster University's subscription service ensured access to all available articles and a complete retrieval of the selected search was possible. The pooled study population consisted of 125, 595 men and the MASS trial alone

had a sample of 67800 people. So, conclusions on quality of life and AAA mortality can be considered reliable.

However, there are inconsistencies present in the four RCTs due to the different methods used. For example, the Viborg trial noted mortality only in a hospital setting. This makes its results incomparable to the other trials. Also, the source of mortality data varies in the four studies. All the trials looked at the national death registries but the Chichester and WA trials also looked at other sources(5, 7). This may have resulted in possible over-estimation or duplication of data. Similarly, the cause of death was re-checked by a clinician and two random vascular surgeons in the Chichester and WA trials, respectively. Whilst expert opinion regarding the cause of death could lead to precise and accurate mortality data, there could also be false-positives when opinions are formed on complex cases with multiple causes of mortality.

This subject of human error was also noted whilst carrying out the preparatory ultrasound screening (Appendix A). Individual measurements of the same abdominal aortic diameter were varied. Although this points to the possibility of human error that may adversely affect the accuracy the diagnosis, the NAAASP identifies staff training as a significant aspect of the programme to overcome this. Staffs are well-trained in the use of ultrasonography for AAA screening and in the overall delivery of the programme(8). Also, the programme itself has several failsafe procedures incorporated within all phases of the programme so that the performance thresholds are constantly maintained(8).

The result of this review can be applied to patient care in the UK. The NAAASP is successfully running its seventh year. Since its implementation in 2009, one million men have been screened(32). Accumulating evidence shows it is feasible to reduce AAA-mortality by ultrasound screening, thereby making it possible to achieve the programme's aim.

Public Health England could implement similar screening interventions in other disease areas. There is currently a long of list of conditions like atrial fibrillation, thyroid disease and lung cancer where a population-based screening is not offered (but privately available) due to the absence of 'enough evidence to inform a screening programme'(33). Evidence-based healthcare could be further expanded to diseases like these.

It is not just new and untreatable diseases that prove to be a challenge to 21st century medicine; it is the phenomenon of the disease-iceberg that proves most challenging. By detecting and treating early onset of illnesses, people live a longer and healthier life.

Table 9 Data processed by the review author using the results from the four RCTs

Trial	Experimental Event Rate (EER)	Control Event Rate (CER)	Absolute Risk Reduction	Relative Risk Reduction	Number(s) Needed to Screen	Odds Ratio/Relative Risk

						(NNS)
MASS	0.00192086	0.003327 35	0.0014064 9	0.422705	710.992	1.73222
Chichester	0.00312012	0.005266 42	0.0021462 9	0.407543	465.919	1.68789
Viborg	0.00094652 2	0.003006 80	0.0020602 8	0.685207	485.370	3.17669
Western Australia	0.00093013 6	0.001291 86	0.0003617 20	0.280000	2764.57	1.38889
Overall	0.00157807	0.002768 06	0.0011899 9	0.429901	840.344	1.75408
Overall *	0.00164905	0.002741 37	0.0010923 2	0.398457	915.482	1.66239

**Data from the Viborg trial is not included since the study noted deaths only in a hospital setting. Hence, results cannot*

be compared to the other studies (30)

Conclusion

Following critical appraisal of the current available evidence provided by four major RCTs, it was found that mortality from AAA can be significantly reduced in males aged 65 years and older, through a population-based screening programme. Ultrasonography continues to be the chosen imaging modality due to its accuracy and ease-of-use. It was also found that such a screen