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Routine Screening for Abdominal Aortic Aneurysm: Is it for everyone?

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Abstract

Objective: Determine whether routine abdominal ultrasound screening in all men ages 65 and over, not just those who are symptomatic or at risk, would be beneficial in reducing the mortality rate from abdominal aortic aneurysms (AAA). **Design:** Systematic literature review. **Methods:** The clinical question investigated is whether routine ultrasound screening of AAA for men over age 65 reduces AAA-related mortality as compared to not routinely screening. Searches were done through PubMed using the keywords: screening, abdominal aortic aneurysm, reduce, and mortality. Citations used by the USPSTF AAA screening guidelines were also added to the literature search. In PubMed, further limitations were made by eliminating those that did not discuss screening and subsequent diagnosis of AAA, as well as full-text articles that did not discuss screening of males over 65 years old or if they were not clinical trials or systematic reviews. Eventually, only randomized controlled trials were included for analysis. **Results:** Randomized controlled trials conducted by Norman et al, Ashton et al, and Scott et al, were all chosen for analysis as they met the inclusion/exclusion criteria for the proposed clinical question. Studies by Norman et al, Ashton et al, and Scott et al estimated the numbers needed to screen at 1,393, 709, and 466 respectively. **Conclusion:** All of the studies clearly demonstrate a decrease in AAA-related mortality when routinely screening men greater than 65 years by ultrasound for AAA. However, the cost effectiveness of the suggested screening regimen as compared to the overall benefits of said screening warrants further investigation.

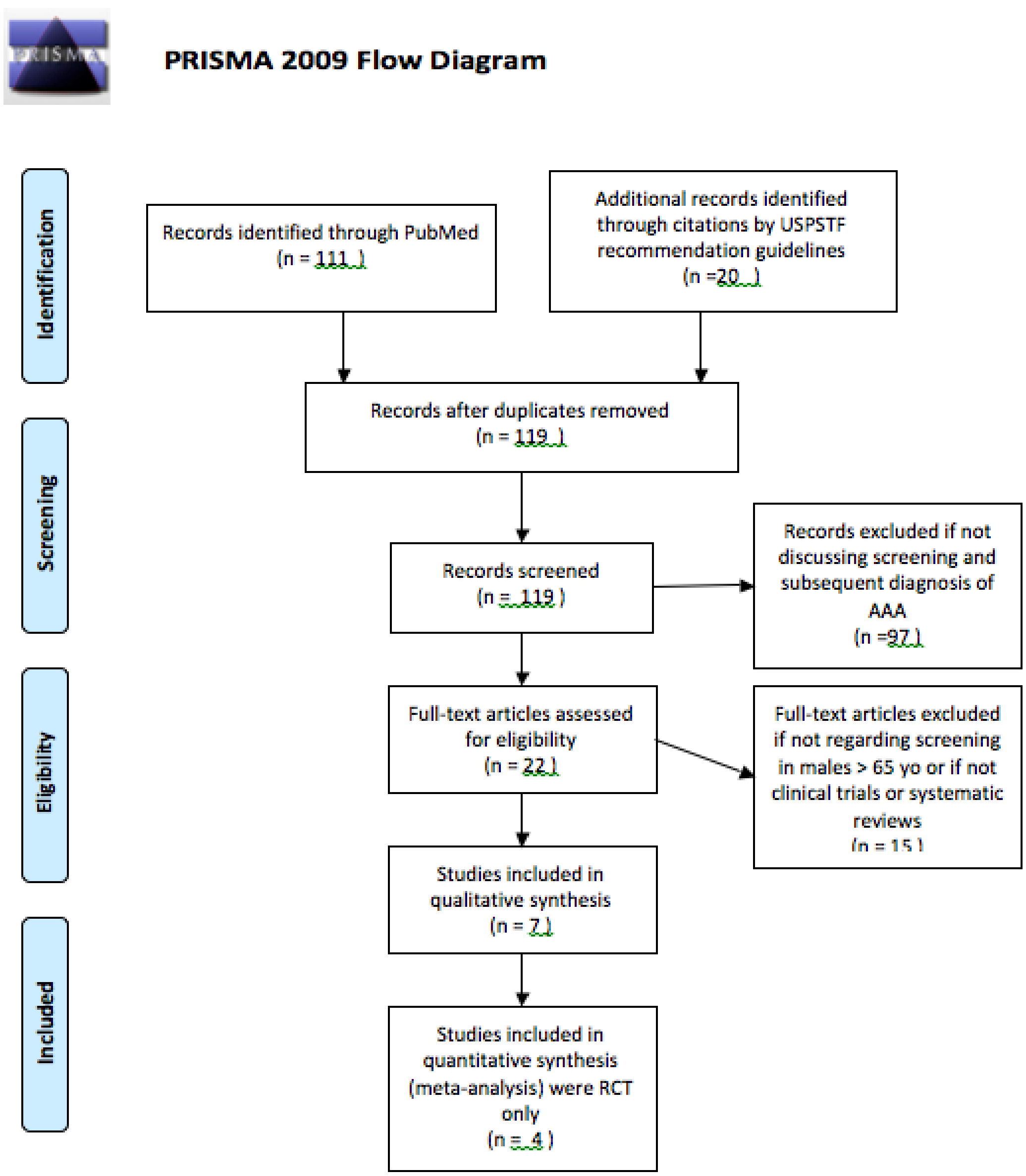
Introduction

Abdominal aortic aneurysm (AAA) is a prevalent severe medical condition in which the walls of the aorta become weakened and ballooning of the artery walls combined with blood pressure causes an enlargement of the artery. AAA are typically asymptomatic unless they rupture, an often fatal complication. Because they commonlyshow no signs or symptoms before rupture, the prevalence of AAA in the United States is unknown. However, according to the CDC, aortic aneurysms were the primary cause of approximately 11000 deaths in 2009.[1] About two thirds of people with aortic aneurysms are males but they are less common among black males than among white males.[2] Risk factors associated with AAA include: male gender, age > 65, hypertension, hypercholesterolemia, atherosclerosis and smoking, with tobacco use being the most significant modifiable risk. Patients with a history of smoking increase their likelihood of AAA 3 to 5 fold over the average nonsmoker.[3] As of 2005, the US Preventative Services Task Force (USPSTF) recommends a "1-time screening for AAA with ultrasonography in men aged 65 to 75 years who have ever smoked".[4] The USPSTF gives a grade C recommendation that health care providers use clinical judgment to offer AAA screening in 65 to 75 year old male nonsmokers with other known risk factors. USPSTF's grade C recommendation suggests that providers offer a given service depending upon individual patient circumstances rather than offering a service to all patients within a generalized population. The purpose of this paper is to determine whether all male nonsmokers should be screened using ultrasonography for AAA.

Methods

The generated PICO for the clinical question at hand is as follows:
Population—Men over the age of 65; Intervention—Routine screening for abdominal aortic aneurysms; Comparison—no routine screening; Outcome—AAA related mortality rate.

The clinical question investigated is whether routine ultrasound screening of AAA for men over age 65 reduces AAA-related mortality as compared to not routinely screening. Searches were done through PubMed using the keywords: screening, abdominal aortic aneurysm, reduce, and mortality. Citations used by the USPSTF AAA screening guidelines were also added to the literature search. Filters used included males and English. Upon manual analysis of articles found, additional exclusions were made by eliminating those that did not discuss screening and subsequent diagnosis of AAA, as well as full-text articles that did not discuss screening of males over 65 years old or if they were not clinical trials or systematic reviews. Eventually, only randomized controlled trials were included for analysis.



Results

Study #1

Population based randomized control trial on impact of screening on mortality from abdominal aortic aneurysm. Norman et al[5]

Objective: To determine whether a single ultrasound screen for abdominal aortic aneurysms (AAA) in men reduces mortality.

Study Design: This was a population based randomized control trial, administered in Western Australia, primarily Perth and the surrounding satellite towns. Participants were selected from an electronic copy of the voting registry of Australia. Initially, only men ages 65-74 years whom lived in or near the city of Perth, were pulled from the registry. However, this only provided less than 40000 men. As a result, the study opted to include men ages 75-79 in order to increase the potential participant number to 50,000 men. Figure 1 outlines the inclusion and exclusion criteria of the study.

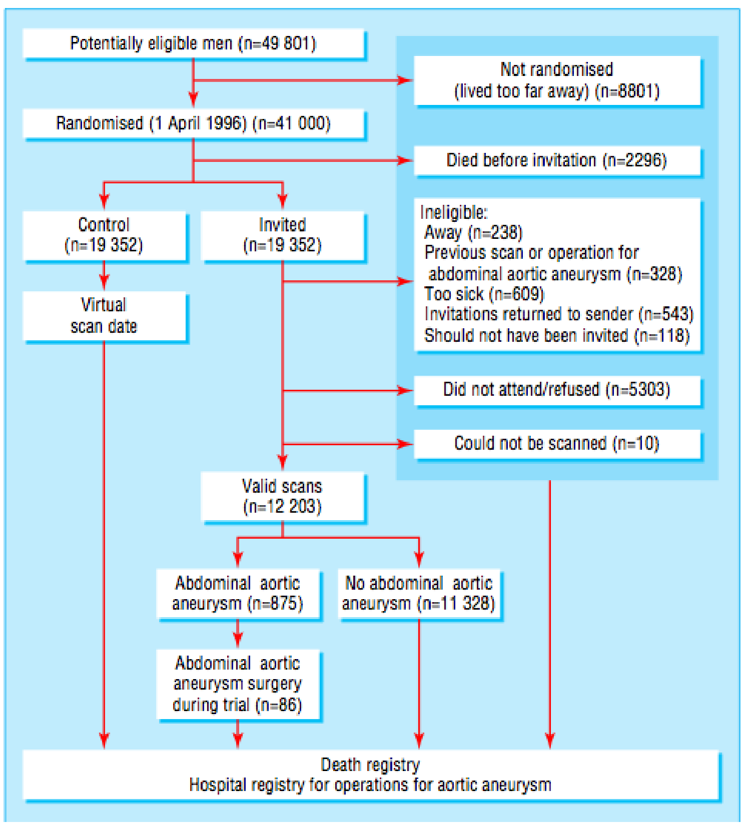


Figure 1: Inclusion and exclusion criteria of study by Norman et al[5]

In total, 41000 men were selected to participate in the study. From this group, participants were randomized equally into either the intervention group or the control group. Of those placed in the intervention group, only 12203 scans were actually obtained. Those in the control group were provided a hypothetical date for screening but never actually received the scan. Each actual screening was performed with a Toshiba Capasee ultrasound machine with a 3.75 MHz probe, at which time the greatest transverse and anteroposterior diameters were measured. The results of each exam were placed into an envelope with a copy for the participant's general practitioner, and handed to the participant. Any interventions following the scan were left completely up to the participant and their primary caregiver. The study coordinators made no attempt to influence any aspect of clinical measurement following the scan. Over the course of 5 years, participant deaths and hospital admissions were obtained via electronic records linked to a population based name identified records for death and hospital admissions in Western Australia. From this information, an individual blinded to the study and it's intentions, further confirmed or negated statements linking the participant's death or hospital admission to be caused by AAA.

Study Results: Of the 12203 men scanned for AAA, 875 (7.17%) were detected. Of the 875 detected, 699 (80%) aortas were 3.0-4.4 cm in diameter, 115 (13%) aortas were 4.5-5.4 cm in diameter, and 61 (7%) were ≥5.5 cm in diameter. The likelihood of detecting an AAA ≥3.0 cm in diameter increased with increasing age of participants. For the intervention group, it was reported that a total of 18 out of the 19352 invited (not the total screened) died of an apparent AAA complication from the time of screening until the conclusion of follow-up. Of the 12203 actually scanned, a total of 7 reportedly died from an AAA while 25 of the 19352 men in the control group died. In total, from the time of randomization to the end of follow up (5 years), there were 31 deaths from AAA in the intervention group and 37 deaths in the control group. The relative risk reduction calculated from this study is therefore only 0.07% from the control group to the group who had a one-time ultrasound screening. The calculated number needed to screen in order to save one life over a 5 year follow up period is 1393. Figure 2 shows that initially, men in the intervention group had a higher rate of mortality than those in the control group. However, after one year, the mortality curves crossed and revealed statistically significant difference in mortality rates between the two groups. The study determined a P value of 0.01 between the intervention group and the control group for men ages 64-75 years.

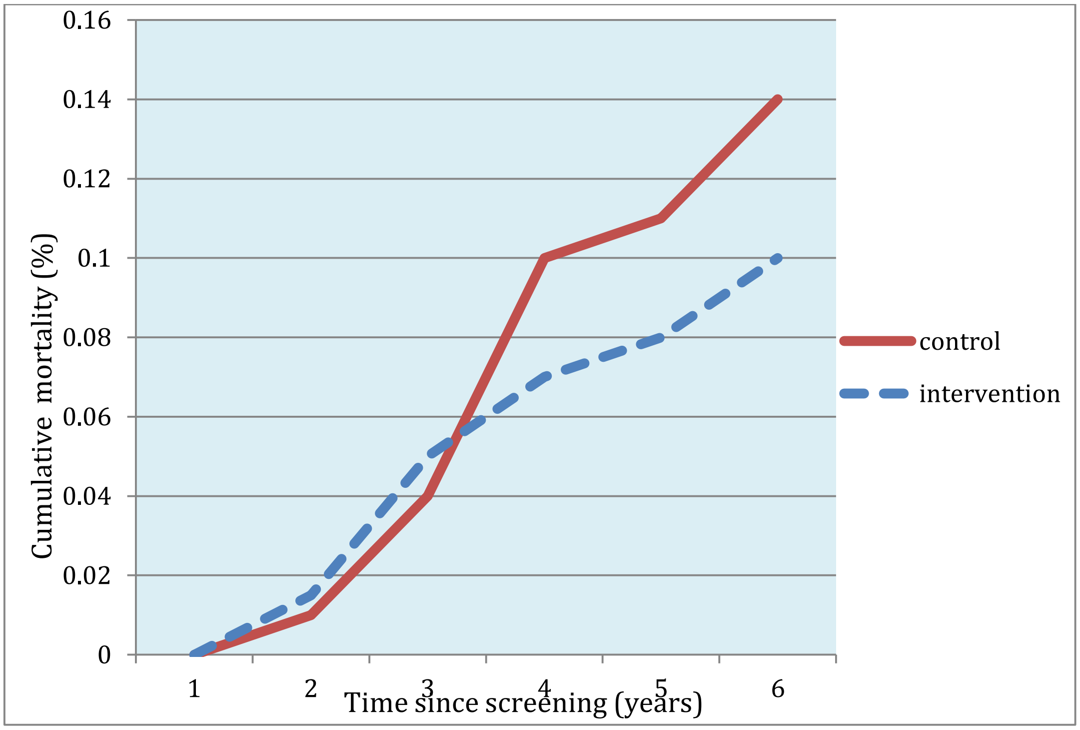


Figure 2: Cumulative mortality rate from time of screening to follow up from Norman et al[5]

Study Critique: The strongest points of the study include randomization, the large sample size, and the population perimeter. Men were invited from numerous cities surrounding Perth, which allowed for a more diverse population sample than would have been obtained if the participants had been recruited from Perth alone. However, these same perimeters also prevented the study recruiters from obtaining a large enough sample size initially. Consequently, they decided to include men up to 80 years old so that the sample size was more substantial. As a result, the total population did not necessarily represent the ideal targeted population consistent with the current recommendations of the USPSTF. In fact, the study even admitted that benefits were only seen in the men aged between 65 and 75. Additionally, the study was not able to exclude those who may be otherwise considered "ineligible" to participate in the study (i.e. those who have a history of AAA or have significant comorbidities).

The study is also greatly hampered by the lack of control with regards to any medical interventions. For every individual scanned, the results were presented to the participant with a copy to give their primary care physician. However, the results were not immediately disclosed, there was no way of determining if their physician ever received the results, and there was no way of ensuring that each participant received the same level of follow up care. Some men may have been more diligent about contacting their physician and being proactive in preventing or managing a AAA.

Perhaps one of the biggest problems with this study is the conclusions made regarding the study's results. The final assertion of the study results states, "at a whole population level, screening for abdominal aortic aneurysms was not effective in men aged 65-83 years and did not reduce overall death rates"[5]. However, the p-value of 0.01, which we calculated based on mortality rates between control and screened patient populations, suggests that the study is in fact statistically significant.

Study #2
The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomized controlled trial. Ashton et al[6]

Objective: To determine if screening for AAA affects AAA related mortality rates.

Study Design: This was a population based randomized control trial consisting of men aged 65-74 years old living in the United Kingdom. Men were selected from January 1997 through May 1999 from four different family medical centers located in Portsmouth, Southampton, Winchester, and Oxford. The personal physicians of the potential participants were asked to eliminate those they did not see fit for the study. In general, physicians excluded anyone who was terminally ill, had serious health problems, or had a previous AAA repair. Of the original 70495 men selected, only 67800 men were invited to participate. The exact inclusion and exclusion criteria are outlined in Figure 3.

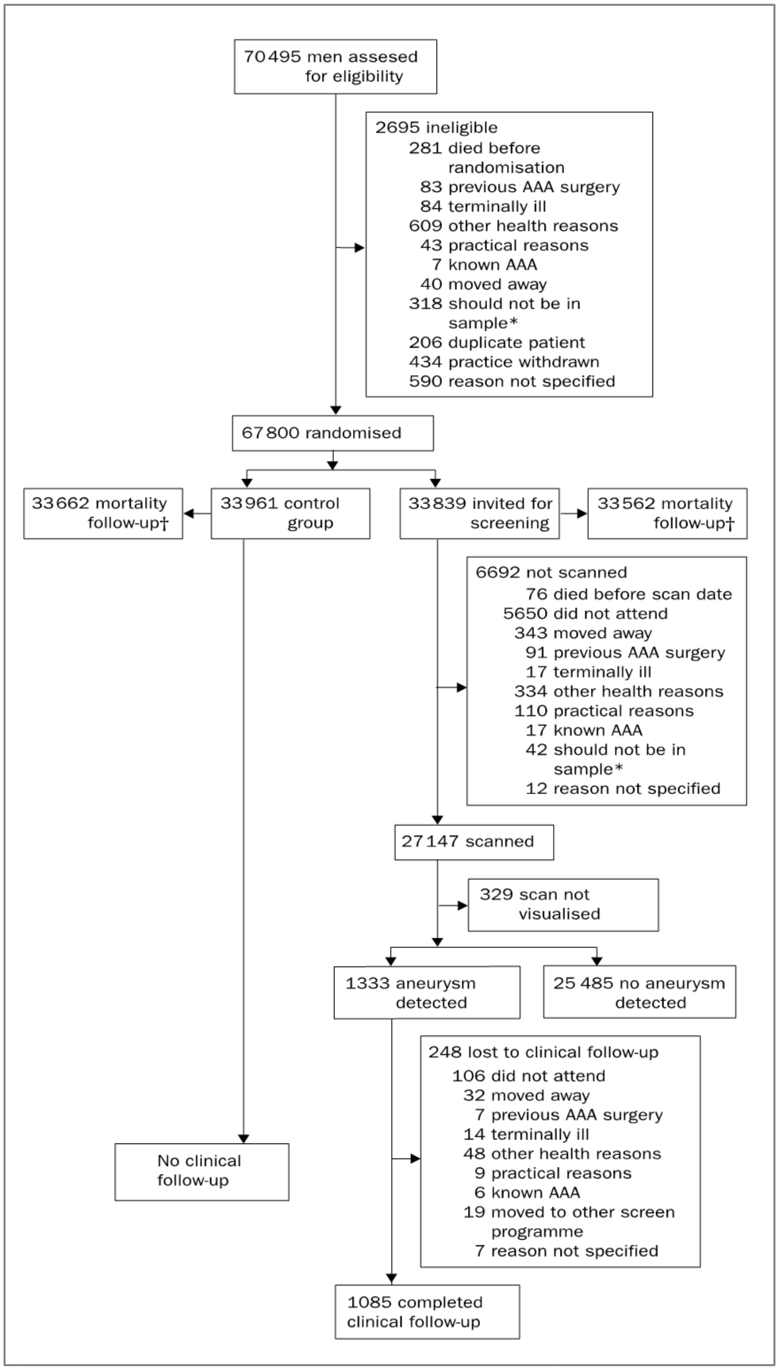


Figure 3: Inclusion and exclusion criteria of study by Ashton et al[6]

Of the 67800 men deemed eligible to participate and who were subsequently invited, 33961 men were randomly assigned into the control group, while 33839 were randomly assigned into the intervention group. Those in the intervention group were sent an invitation to receive an abdominal ultrasound. Of the 33839 men in this group, 27147 men were scanned. The machine used to scan for AAA was a Hitachi Ultrasound scanner EUB-405. The maximum transverse diameter of the aorta in the transverse plan and the maximum anterior-posterior diameter in the longitudinal plane were obtained. The largest diameter recorded became the maximum aortic diameter for each patient. All abnormal results were then reviewed by a radiologist and then were sent to the patient's family doctor. Patients who had an aortic diameter of 3.0-4.4 cm were rescanned at yearly intervals while those with aortic diameters of 4.5-5.4 cm were rescanned every 3 months. Participants with aortic diameters measuring 5.5 cm or greater were urgently referred for a vascular consult. All Participants were followed over the course of 5 years, after which additional follow up was conducted through the participant's family physicians.

In order to obtain mortality records for individuals participating in the study, every person was tagged via the Office of National Statistics mortality surveillance system. From this, the Office of National Statistics was able to provide a copy of the death certificate for any man who died during the course of the study. Each death certificate was then reviewed by an independent mortality working party. In some instances, additional information regarding the cause of death was obtained from other outside sources, i.e. coroners, hospital necropsy reports, and sometimes family physician notes. The primary outcome measured was AAA related mortality, while the secondary outcome measured was all cause mortality.

Results: Of the 33839 men invited, 27071 men accepted the invitation and received the screening. In this group, 1333 AAAs were detected. 944 (71%) were between 3.0 and 4.4 cm in diameter, 223 (17%) were 4.5-5.4 cm in diameter, and 166 (12%) measured 5.5 cm or greater. The study was able to follow up with 99% (67, 274) of the men enrolled in the study. Results showed that out of the control group, there were 113 (3%) AAA related deaths, while the total number of AAA related deaths among the invited group was only 65 (2%). These numbers show a relative risk reduction of 0.14%. The number needed to screen with a one-time abdominal ultrasound, in order to save one life over the course of a 5 year follow up, is approximately 709. Figure 4 shows that, while the mortality rate of the control group intersects the mortality rate of the intervention group at 3 years, at all other points in time, the control group has a higher rate of AAA related mortality. Overall, the study determined a P value of 0.0002 between the intervention group and the control group of men ages 65-74 years, making this study statistically and clinically significant.

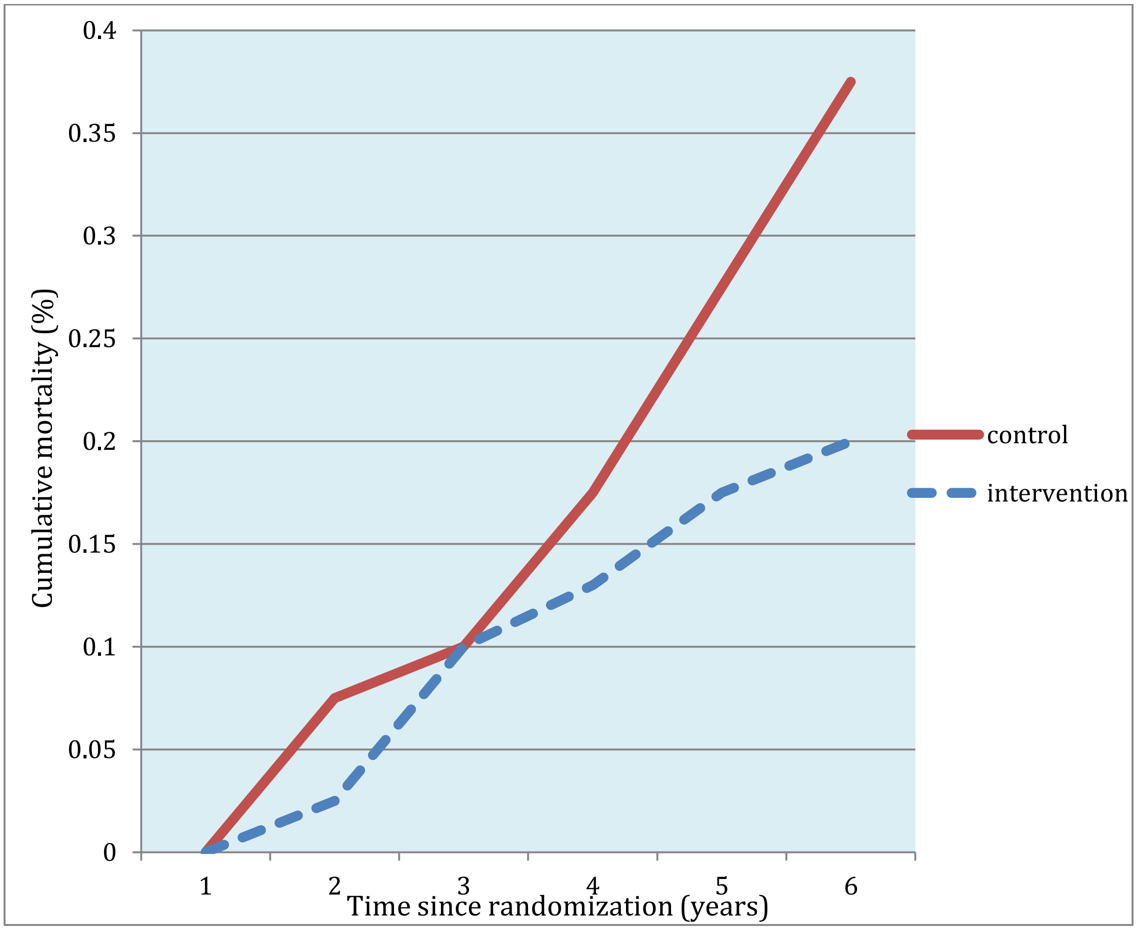


Figure 4: Cumulative mortality rate from time of randomization to follow up from Ashton et al[6]

Study Critique: One noticeable limitation of the study includes the multitude of codes that were used when inputting patient information. Because of this, it is possible that some participant's information was improperly entered into the database. Also, deaths identified as being due to simply "aortic aneurysm" were included in the data regardless of whether or not they were confirmed to be *abdominal* in origin. The study explains that this was done because AAAs occur more frequently than any other aortic aneurysm.

Although, one major strength of this particular study lies within the fact that they utilized a data monitoring committee, which determined that in order to successfully assess the effect of screening for AAA on mortality rates caused by AAA, the study population should be no less than 66000 and should be carried out over a 4 year period.

Also, the authors make a point to outwardly mention that the sponsors of the study had no involvement in the design, data collection, analysis, interpretation, or composition of the report. Additionally, they were able to obtain mortality follow up for 99% of the randomized participants. The methods of the study were clearly outlined and the results were easy to interpret. Additionally, the final conclusion and recommendation gathered from the study results accurately match and support the overall p-value of 0.0002 established for the study, confirming that the data collected is in fact statistically significant and that routine screening for AAA in men older than 65 years will decrease AAA related mortality

Study #3
Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study Scott et al[7]

Objective: In the article by Scott et al., the authors investigated the impact that ultrasound screening both males and females between ages 65 and 80 years old for abdominal aortic aneurysm (AAA) would have on the incidence of both AAA rupture and AAA related mortality.

Study Design: The study was conducted in the county of Chichester in the United Kingdom, where ruptured aortic aneurysm accounts for approximately 1.2% of all deaths in men older than 65 years. In the UK, the rupture of an AAA has a mortality rate of between 80 and 94 percent. On the other hand, elective surgery for repair of an AAA has a mortality rate of less than 5 percent. Therefore, the authors wanted to determine the efficacy of a screening program to maximize the number of patients receiving the much safer elective surgery rather than waiting for an aneurysm to rupture in order to be detected. The study was conducted as a randomized controlled trial. Participants were recruited from all general practice registers in the county of Chichester or from Family Health Service lists. A computer was used to randomize the participants into control and screening groups. Exclusion criteria was those patients who did not fall in an age range between 65 and 80 years.

The study included a total of 15775 people (6433 of whom were men) between the ages of 65 and 80 years. For the purpose of researching our PICO, the analysis of this paper analyzes only the male participants of Scott et al's study. The screening group was mailed a letter offering a free screening, non-respondents were sent a reminder and if the participant still didn't respond, they were considered to have refused the invitation for screening. 3205 men were invited for screening, 863 of whom declined screening. 2342 men accepted their invitation and participated in the screening group. The control group consisted of 3228 men.

For the study population, AAA screenings took place in primary care settings but abnormal ultrasounds were reviewed by a consulting radiologist. The study does not specify whether the consulting radiologist was consistent throughout all screenings, nor does the study specify the degree of experience or education of the consulting radiologist. The authors received mortality data from the Registry of Births and Deaths in Chichester district. The study includes those participants who lived locally but died outside the district. Neither participants nor researchers were blinded. Multiple outcomes were measured including acceptance rates for participants invited to screenings, prevalence of AAA (stratified by gender and age), number of participants with rupture over 5 year period, mortality from surgery, mortality from AAA rupture over 5 year period, size of aortic aneurysm and decrease in mortality from screening over 1 year period. The outcome most relevant to this paper is AAA related mortality rate over a 1 year period. The follow-up period was only 1 years, which is incomplete compared to the real world but seems likely to be a sufficiently accurate for evaluation of long term impact of screening protocol for AAA.

Results: Of the men invited for screening for AAA by ultrasound, 2342 men accepted the invitation and were screened. The number of men accepting the screening invitation varied by age, with men closer to age 65 more likely to accept the invitation and men at age 80 less likely to accept the invitation. The authors of this study theorized that this was due to immobility or comorbidity making participation more difficult at an older age. Average age of control group was 72.1 years. and average age of screened group was 71.8 years. The incidence of AAA in men was 7.6%. The prevalence of AAA in men aged 65 years was 5.9% but rose to 9.2% by age 80. Of the 863 men who declined screening, 4 men died from aneurysmal rupture. Of the men who were screened, 28 underwent elective surgery with no deaths at 1 year in that group. Of the men who were successfully screened, the AAA-related mortality rate was 0.73% (17 deaths related to AAA) at 1 year. Figure 5 elaborates on the distribution of AAA related deaths among the screened group and the control group, up to one year.

Group	No. of AAAs	Rupture and transient	Outcome
Control (n=3228)	25	20 ruptures	12 died without surgery 5 died after surgery 3 survived emergency surgery to 1 year
		5 elective surgery	No deaths to 1 year
Offered screening (n=3205)			
	35	28 elective surgery	29 survived to 1 year
Scanned group (n=2342)		3 emergency surgery (1 rupture 2 symptomatic)	2 deaths to 1 year
	4	4 ruptures	4 died without surgery
Refused screening (n-863)		4 ruptures	4 died without surgery

Figure 5: AAA mortality rate between control croup and intervention group up to one year from Scott et al[7]

Over a 5 year period, there was more than a 50% reduction of ruptured AAA in the intervention male population compared to the male control group even including men who declined the invitation for screening or did not meet criteria for elective AAA surgery. The absolute risk reduction for men between the control group and the screened group was 0.21% at a one year follow up. The results of this study suggest that in order to save one life, providers must offer 466 males between the ages of 65 and 80 the opportunity to undergo a one time ultrasound screening for AAA. Therefore, the number needed to screen for this study was found to be 466 over the course of a 1_year follow up.

Study Critique: All patients that were screened using ultrasound did not receive additional gold standard screening (computed tomographic angiography). Abnormal ultrasounds were reviewed by a consulting radiologist to determine the clinical accuracy of diagnosis. The authors of the study do not elaborate on the qualifications of the consulting radiologist nor do they discuss whether the same radiologist reviewed all the abnormal ultrasounds.

Authors did not discuss any protocol for blinding, leaving it unclear whether researchers were blinded prior to analysis of results but reasonably assumed that there was no blinding.

The tested population was representative of the population this paper explores because the population screened had no risk factors aside from gender and age which put them at risk for AAA. The population did not exclude nonsmokers and is therefore representative of the general population. However, while the population of the UK is likely generalizable to the USA, it cannot likely be applied worldwide due to differences in lifestyles (diet, exercise, weight, etc.), race and genetic makeup.

The study is not always clearly defined, making it difficult to reproduce. There remain certain details which are unclear including: the qualifications of the consulting radiologist, the blinding or lack thereof, program used to randomize study groups, etc. Additionally, very few mathematical calculations were performed to determine the significance of the study, making it difficult to evaluate the validity of the study. No likelihood ratios, p-values, sensitivity or specificity were given for the screening of AAA by ultrasound.

The control group was not treated similarly to the study group because they had no additional medical care. The participants in the control group did not visit any doctors or have any appointments with any medical professionals to discuss risk factors and potential modifications for AAA. On the other hand, participants in the screening protocol went to appointments to have ultrasonography performed and were made aware of the risk involved with AAA. This difference in protocols likely introduced bias by making study group participants more aware of AAA and potential lifestyle modifications to minimize its risk.

The study is relatively weak in a number of areas. The most concerning area is the date of the study. This paper was published in 1995. Because more than 20 years have passed since the research was conducted, it is impossible to trust that statistics haven't changed. Technology has improved dramatically since that time. It is reasonable to assume that the surgery to save a life following AAA rupture has improved but it is also likely to assume that the accuracy of ultrasound screening is better able to detect the presence of an aneurysm and accurately estimate its size. There is no way of knowing whether the conclusions of this study is still relevant without more recent research (of which there is very little).

Another concern regarding the validity of this study is the lack of statistical analysis by authors. The study does not address p-values, leaving the reliability of their conclusion recommending ultrasound screening for AAA in men aged 65-80 in question because they have no quantifiable evidence to show that screening reduced mortality.

However, the study's strength includes complete randomization of a sizable sample size. Even when accounting for those participants who declined to participate in screening and those patients who declined elective surgery, there was a lower percentage of AAA related mortality among the screened population than among the control group. This makes the study more externally valid because in clinical scenarios, not all patients will accept screening and not all patients will desire elective surgery.

Discussion

These studies clearly demonstrate a decrease in AAA-related mortality when routinely screening men greater than 65 years by ultrasound for AAA. Less clear is the benefit of routine screening as compared to the cost of such screenings.

Each of the studies found different numbers needed to screen (NNS) in order to save a life. The follow up times on these studies varied from 1 to 5 years of follow up in measuring AAA related mortality. The most conservative estimate suggests that, in order to save a single life over the course of 5 years, 1393 males over age 65 must be screened by ultrasound[5]. The other studies suggest a lower NNS. Ashton et al has a number needed to screen of 709 in order to save one life within a 5 year timeframe, and Scott et al estimates a NNS of 466 to save one life within a 1 year timeframe. While there is a large range of calculations between each of the studies, all studies conclude that, in order to save one life over the course of a 5 year followup, fewer than 1500 males older than 65 must undergo a one time ultrasound screening. For comparison, the number needed to screen for colorectal cancer is 1250 people and the number needed to screen for breast cancer is 781 women. Screenings for both colorectal cancer and breast cancer are considered standard care. Because the NNS to prevent an AAA-related mortality is comparable to other routine screening recommendations, it seems logical to implement routine AAA screening in men older than 65 years, if the costs of screening are reasonable.

Unfortunately, almost all studies regarding both the efficacy and the cost of routine AAA ultrasound screening are outdated. Though pricing has undoubtedly changed since the time of the study, Vazquez estimates the cost of AAA ultrasound screening to be $551 each.[8] At that price, the cost per life saved ranges between $256,766 and $767,543. For comparison, the estimated cost of a colonoscopy is $681.39.[10] The estimated cost of a colonoscopy[10] multiplied by the estimated NNS[9] results in an approximate cost of $852,737.50 per life saved. When considering whether the value of screening for AAAs is worth the financial cost, one must also consider that, to loved ones, the financial cost is irrelevant and the value of a life is immeasurable. However, it is crucial to consider costs beyond the financial as well.

More difficult to quantify but also invaluable to analyze is the potential risks of morbidity and mortality associated with screening. For patients who are identified as having an AAA, there is a risk of anxiety and emotional damage inflicted by the knowledge of their diagnosis. For those patients who have an AAA of operable size, there is inherent risk to the elective surgery to repair an AAA. However, it is important to note that the risk of an elective surgery, <5%,[7] is much less than the risk of a rupture outside of a hospital, 30-50%.[7]

Because recent studies are lacking, recommendations rely primarily upon outdated studies. Since the publication of the studies analyzing in this paper, technological advances have occurred in both ultrasound machines and surgical technique and equipment. Therefore, it is reasonable to predict that an increased number of lives can be saved by routine screening than the outdated publications would estimate. More recent studies are needed to accurately reflect the efficacy of ultrasound screening for AAA in modern times.

In conclusion, more updated research is necessary to definitively determine whether routine screenings for AAA in men greater than 65 years old should be recommended. Available data, though outdated, suggests strongly that the use of one time ultrasound to routinely screen men older than 65 years should be recommended in order to save lives that would otherwise be lost due to an AAA rupture.

Great job!

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