REVIEW ARTICLE

SCREENING OF THE ABDOMINAL AORTIC ANEURYSM: COST-EFFECTIVENESS AND HEALTH BENEFITS

João Teles *[1], Nuno Teles [1], Hélder Sousa [1]

[1] General and Family Medicine, Unidade de Saúde Familiar de Fânzeres, Agrupamento de Centros de Saúde de Gondomar

* Corresponding author: joaosoaresteles.1993@gmail.com

Abstract

Introduction: *The abdominal aortic aneurysm (AAA) is a nosological entity whose main complication is rupture, being associated with a high mortality rate. The early identification of this pathology in groups at risk through an ultrasound screening program can have benefits based on elective surgical repair before the rupture occurs, preventing death. In Portugal, no screening program for this aneurysm is implemented. Our goal is to review the impact of screening among risk groups on the global and aneurysm-related mortality rates, quality of life, cost-effectiveness and its applicability in Portugal.*

Materials and methods: *We performed a narrative review of the literature on screening for AAA.*

Results: *There is evidence that screening is effective in reducing aneurysm-related mortality in men aged 65 and over, but not in reducing overall mortality. In addition, the implementation of a screening program in several countries appears to be cost-effective in at-risk populations.*

Discusssion and conclusion: *Data from epidemiological studies on AAA suggests that the implementation of an AAA screening program, based on ultrasound, in men aged 65 and over, can bring health benefits and be cost-effective. Even so, taking into account that all the studies took place outside Portugal, the possibility of generalizing the results to the portuguese population is not clear.*

Keywords: *Aortic Aneurysm, Abdominal; Prevalence; Mass Screening*

INTRODUCTION

An aneurysm is defined as a localized dilatation of an artery greater than or equal to 50% of its normal diameter.[1] The abdominal aortic aneurysm (AAA) can be found in any area of the abdominal aorta, but it occurs most often in the infrarenal aorta, close to the bifurcation of the iliac arteries. As the diameter of the infrarenal aorta is usually about 2 cm, AAA is considered to be a dilatation corresponding to a diameter greater than or equal to 3.0 cm in the antero-posterior or transverse planes, which corresponds to more than two standard deviations above average.[2]

The main risk factors for the development of this aneurysm are male gender, age ≥ 65 years, smoking at least 100 cigarettes throughout life, family history in 1st degree of AAA, existence of other arterial aneurysms, arterial hypertension and dyslipidemia.[3-6] The main independent risk factor for the occurrence of its rupture is the size of the aneurysm.[7] Based on epidemiological studies carried out in developed countries, it is estimated that the prevalence of AAA is 4-9% in men and 1% in women.[8,11] In Portugal, there are only two studies on its prevalence. The first, provided by the screening program "Aorta não avisa", developed by the Portuguese Society of Angiology and Vascular Surgery, estimated a prevalence of 2.2% for men over 60 years of age and 3.94% for men over the age of 65 years. This study was conducted in every district capitals of Portugal.[12] The other study was conducted in 2016 in a primary care setting in a northern Portugal city and estimated a prevalence of 2.1% in men aged 65 years and over.[13]

This disease is, in most cases, asymptomatic before rupture, being detected as an incidental imaging finding in more than 80% of cases.[14] Its main complication is rupture, which constitutes a medical emergency, as it is associated with a high mortality rate (80%), requiring immediate surgical correction.[15] Most patients who suffer AAA rupture die before arriving at the hospital and of those who arrive there and undergo emergent surgical correction, only 50% survive.[16,17] The implementation of screening programs in risk groups for AAA - men aged ≥ 65 years - may contribute to the reduction of related deaths, through early detection, follow-up and elective surgical correction.[12] In addition, AAA has a natural history that favors its screening, such as its prevalence, the fact that it is almost always asymptomatic before rupture, has a prolonged latency period from its onset to rupture and an elective surgical treatment with low mortality rate and complications.[16,17] Besides that, the screening test is abdominal ultrasound, which is an economical and safe diagnostic and screening tool, with a sensitivity and specificity close to 100% for AAA detection.[18-21]

The ratio between the number of AAAs treated and the total population in Portugal is among the lowest described in the literature. Bearing in mind that the criteria for surgical intervention are similar in different countries, the paucity in the treatment of this pathology could be justified by the deficit of diagnosis or by the low prevalence of the disease in the Portuguese population.[13] However, the two prevalence studies of AAA in Portugal have shown that this is apparently superior to the prevalence of AAA in other European countries where the screening is already implemented, like the United Kingdom, with a reported prevalence of AAA of 1.18%,[22] and Sweden where the screening detected an AAA prevalence of 1.7%.[23]

Bearing this in mind, it is probable that the deficit in diagnosis becomes the most likely answer for the low ratio between the number of treated aneurysms and the total population in Portugal.[12,13]

Bearing these facts in mind, the purpose of this work is to review the impact of AAA screening in risk groups, in terms of mortality rate due to AAA and global mortality, quality of life, cost-effectiveness and applicability in Portugal.

MATERIAL AND METHODS

We conducted a classic review on screening for AAA, through research and consultation of randomized clinical trials, guidelines, meta-analyzes and review articles published to date in the main databases and sites of evidence-based medicine, such as MEDLINE / PubMed, Web of Science and Cochrane, using the Mesh Terms "Abdominal Aortic Aneurysm", "Prevalence" and "Mass Screening".

RESULTS

Impact of screening on AAA mortality and global mortality

In the early 1990s, the first large-scale randomized clinical trials (RCT) were conducted to determine the benefits of implementing AAA population-based screening programs. Two studies took place in the United Kingdom (Chichester[11] and MASS[24]), one in Denmark (Viborg[25]) and another in Australia (Western Australia[26]). Abdominal ultrasound was the test used to screen for AAA in all these RCTs. All of these studies included men aged 65 and over, with the exception of the Chichester study[11] which included men and women over 65 years. Participants were randomized into two groups: a group invited to perform abdominal ultrasound to screen for AAA and a control group that was not invited for screening. All these clinical trials were non-blind. The primary outcome of all trials was the AAA-related mortality rate. The all-cause mortality rate was a secondary outcome. The cost-effectiveness of screening was a secondary outcome in two of the four RCTs (MASS[24] and Viborg[25]). No significant loss from follow-up was reported in any of these studies. Table 1 summarizes the conditions for implementing each study and its main results.

In the Chichester RCT[11], the prevalence of AAA in the group undergoing screening was 7.6% in men, 1.3% in women and 4% in total. At 5 years of study, there was a 42% reduction in ruptured AAA-related mortality in males in the intervention group, compared to males in the control group.[27] However, in the long term, there was a decrease in the benefits of the screening program, with a 21% reduction in AAA-related mortality at 10-years of follow-up[28] and only 11% at 15 years.[11] Thus, this RCT detected a significant reduction in AAA mortality in the male screening group compared to the control group at 5 and 10 years of follow-up, but not at 15 years. The decline over time in the difference in the AAA mortality rate between the groups was expected, justified by the aging of the patients selected at the beginning of the study (the youngest patients after 15 years of this study were 80 years old). Because of this, the majority of patients with criteria for elective surgical correction had a high surgical risk at the end of the study, so they did not undergo surgical repair. Consequently, there was a significant increase in the AAA mortality rate in the group screened after 15 years of follow-up. There were no statistically significant differences in the AAA mortality rate in females. The overall mortality rate was similar between groups, in both genders, both at the beginning and at the end of the study.[11,27]

In the MASS RCT,[24] the prevalence of AAA in the intervention group at the end of the study was 4.9%. The reduction in the AAA-related deaths was 53% at 4 years of follow-up, [8] 47% at 7 years, [29] 48% at 10 years[29] , and 42% at 13 years (end of follow-up).[24] Therefore, the effectiveness of screening in reducing mortality from AAA has remained similar over time in this RCT. As for the impact of

AAA screening on global mortality, there was only a slight, though not significant reduction of 3%, either at the beginning of the study,[8] or at the end of it.[24] The number needed to screen (NNS) was 216, that is, the number of men needed to screen to prevent one death from AAA was 216.[24]

In the Viborg RCT,[25] the prevalence of AAA in the screened group was 4.2%. There was also a significant reduction in mortality from AAA, with a reduction of 66% over the 14 years of follow-up. As at the end of the MASS study, there was a slight, though not significant reduction in the overall mortality rate - 2%.[25]

In the Western Australia RCT,[26] the prevalence of AAA in the screened group was 7.2%. At the end of the 13 years of follow-up, there was a no significant reduction of only 8% in mortality from AAA.[26] This can be explained by the age of the participants, with individuals up to 83 years of age, low acceptance rate of AAA screening compared to other studies, the fact that there was a high percentage of incidental diagnoses and elective treatment with success of AAA in the control group and the fact that there was a large number of individuals in the intervention group who refused the invitation to be screened and who ended up dying due to complications associated with AAA. At the end of the follow-up, there was a statistically non-significant 2% reduction in global mortality in the intervention group. The NNS was 4784.[26]

Several meta-analyzes that included the four aforementioned RCTs were carried out with the aim of assessing the impact of AAA screening on the global and AAA-related mortality rate and its cost-effectiveness. The Cochrane Review meta-analysis by Cosford et al [30] estimated a significant reduction in AAA-related mortality in men (OR 0.60; 95% CI 0.47-0.78), but not in women (OR 1.99; 95% CI 0.36-10.88), although only one of the trials included females. There were no statistically significant differences in the overall mortality rate in men (OR 0.95; 95% CI 0.85-1.07) and in women (OR 1.06; 95% CI 0.93-1.21). The authors of this meta-analysis concluded that screening for AAA in men over 65 years of age has strong evidence for reducing AAA-related mortal-

Table 1 **Summary of the characteristics and results of large-scale randomized clinical trials related to screening for abdominal aortic aneurysm**

	Chichester[11]	MASS[24]	Viborg[25]	Western Austrália[26]
Number of participants	15 775	67 800	13 500	41 000
Gender	Men and women	Men	Men	Men
Age (years)	65-80	65-74	65-73	65-83
Date of study beginning (year)	1988-1990	1997-1999	1994-1998	1996-1998
Publication year	2007	2012	2010	2016
Number of years of follow-up	15	13	14	13
Acceptance rate in the screening group	68.4%	80.2%	76%	63.4%
Prevalence of AAA	4% (7.6% H; 1.3% M)	4.9%	4%	7.2%
Screening of AAA	Annual: 3-4.4 cm 3/3M: 4.5-6 cm	Annual: 3-4,4 cm 3/3 M: 4.5-5.5 cm	Annual: 3-5 cm	No indication for screeening
Elective AAA repair	≥ 6 cm	≥ 5,5 cm	≥ 5 cm	No indication for elective repair
Reduction of the relative risk of death related to AAA - Screened vs. Not Screened	11%	42%	66%	9%
Reduction of the relative risk of global death - Screened vs. Not Screened		3%	2%	2%

** AAA- Abdominal Aortic Aneurysm; M- Months.*

ity, but the same cannot be said for women. On the other hand, this screening has not been shown to cause a reduction in mortality from all causes, which may be an argument against its implementation.

The meta-analysis by Lindholt et al [31] analyzed the effects of AAA screening in the medium term (3.5-5 years) and long term (7-15 years). A significant decrease in the AAA-related mortality has been reported in the medium term (OR 0.56; 95% CI 0.44-0.72) and in the long term (OR 0.47; 95% CI 0.86-1, 02). A significant reduction in global mortality was demonstrated in the long term (OR 0.94; 95% CI 0.92-0.97), but not in the medium term (OR 0.94; 95% CI 0.86-1.02). The authors of this meta-analysis concluded that screening for AAA in men over the age of 65 years is effective in significantly reducing AAA-related mortality in the medium and long term, with the effects on global mortality being more tenuous and only significant in the long term.

Takagi et al 2010 and 2018 meta-analyzes analyzed the long-term impact of AAA screening (≥ 10 years).[32,33] The 2010 meta-analysis[32] demonstrated a significant reduction in AAA-related mortality in the screened group (HR 0.55 and OR 0.55; 95% CI 0.36-0.86), but failed to demonstrate a significant decrease in mortality from all causes. In this meta-analysis, the reduction in mortality from AAA was estimated at 4 per 1000 individuals, a value higher than that established in Cochrane's systematic reviews for screening programs already implemented, such as breast cancer (0.7 / 1000)[34] and colorectal cancer (1.5/1000).[35] In the 2010 meta-analysis, [32] the calculated NNS was 238, which is lower than that estimated in other screening programs already implemented, such as breast cancer (NNS= 1339)[34] and colorectal cancer (NNS= 671).[35] The 2018 meta-analysis assessed only the impact on all-cause mortality. Unlike 2010, the 2018 meta-analysis showed a significant, albeit slight, decrease in overall mortality (OR 0.973; 95% CI 0.95-0.997).[33]

Taking into account the promising results of RCTs and meta-analyzes, AAA population screening programs were implemented in Sweden, the United Kingdom and the United States of America (USA). Between 2006 and 2014, a AAA ultrasound screening program was gradually implemented in men aged ≥ 65 years in Sweden. The response rate to the call for screening was 84%, with the participation of more than 250 thousand people. The prevalence of AAA detected was 1.5%. The implementation of this program provided a significant reduction in the AAA-related mortality rate, more specifically a reduction of about 4% per year of screening. The NNS was 667, which for a population of 9.5 million corresponds to the prevention of 90 premature deaths from AAA per year and a gain of 557 years adjusted for quality of life (QALY).[36]

In the United Kingdom, in 2008, a national AAA screening program was implemented. This program was aimed at all men aged ≥ 65 years who were invited to perform AAA ultrasound screening. The response rate to the call in the first 5 years of screening was 78.1%, with the participation of more than 700 thousand individuals. The prevalence of AAA after 5 years of screening was 1.34%, well below the prevalence found in the MASS study, which was also carried out in the United Kingdom, but started in 1997. This decrease in prevalence may reflect important changes in lifestyle, such as changes in diet, regular physical exercise and decreased smoking habits, as well as better control of cardiovascular risk factors, such as hypertension and dyslipidemia. The number of screenings required to identify an aneurysm was 78 in caucasians, 154 in black people and 431 in asians.[22,37,28]

In 2007, Medicare® started an AAA screening program in the USA applied to beneficiaries of this insurer, offering a unique ultrasound screening to all 65-year-old men who have smoked at least 100 cigarettes throughout their lives and to all 65-year-old men and women with a family history of AAA. To assess the impact of this screening program, the intervention group was compared to three control groups that were not screened: a group of 70-year-old men, another group of 76-year-old men and, finally, a group of 65-year-old women. The variables under study were AAA surgical repair rates, AAA rupture rate, and all-cause mortality rate. The follow-up lasted one year. The program had a low performance, with only 1% of eligible users being screened. The impact of the program was modest, with no significant changes in the rate of repair of AAA, its rupture and overall mortality. This can be explained by the low adhesion of the eligible users to the screening program. [39,40]

Cost-effectiveness of the AAA screening program

The MASS[24] and Viborg[25] were the first to demonstrate the cost-effectiveness of implementing the AAA population-based screening program. The MASS trial proved that this screening was cost-effective and with potential for improving cost-effectiveness over time, with a cost per year of life gained estimated by £41,000 in the fourth year of study, £14,000 in the 7th year and £7,600 after 10 years of study. [29] By the 7th year of the study, it had already a lower cost than the amount referred to as acceptable for health interventions in the UK (£25,000 per year of life gained). [41] Viborg study was equally cost-effective, with an estimated cost of €157 per year of life gained and €179 per QALY at the end of the study, which is markedly lower than what is generally considered cost-effective. [25]

The metanalysis of Cosford et al from Cochrane[30] demonstrated that the cost-effectiveness of screening in men aged 65 years and over seems to be acceptable. The authors of the meta-analysis by Lindholt et al[31] concluded that the AAA screening seems to be cost-effective; however they admit the existence of differences between populations from different geographical areas (such as the prevalence of AAA) , influencing the cost-effectiveness of this screening.

The national screening program implemented in

the UK was effective in the first 5 years of implementation and is expected to remain effective unless the prevalence of AAA in subsequent years drops below 0.35%. [22,37] More recently, the cost-effective ratio of this program was assessed again, 10 years after its implementation, remaining cost-effective over a long term, with an estimated cost of £5,758 per year gained and £7,370 per QALY, well below the limit recommended by the National Institute for Health and Care Excellence (NICE), which is £20,000-30,000 per QALY. [42] In addition to the United Kingdom, the AAA national screening program implemented in Sweden demonstrated to be cost-effective, with a cost-effectiveness ratio of €7770 per QALY. [36]

Recent studies have demonstrated changes in the epidemiology of AAA over time, namely a decrease in the prevalence, which can be explained by the reduction of smoking habits and a better control of cardiovascular risk factors. However, the basis for the current implementation of a cost-effective AAA screening program can be questioned by this epidemiological change. The AAA screening program implemented in the UK in 2008 confirmed that screening remains cost-effective, even with a much lower prevalence of AAA compared to the MASS study that was applied several years earlier in the same country (1.34% vs. 4.9%).[24,37] The AAA screening program was also cost-effective in Sweden, where the prevalence of registered AAA was much lower than the announced by large-scale RCTs.[36] Another study conducted by Svensjö et al in 2014 aimed to determine the efficacy and cost-effectiveness ratio of single screening of men aged 65 years and over taking into account recent epidemiological changes in the prevalence of AAA. In this study, a comparative analysis was performed between a group of men aged ≥ 65 years invited to screening the AAA (intervention group) and a group not invited to screening (control group) using the Markov model. The data used on the natural course of AAA (rate of surgical repair and rupture) were based on data from large-scale randomized clinical trials. The prevalence of AAA in the follow-up group (1.7%), the rate of endovascular surgical treatment (50%), the outcome of the repair and the costs were based on contemporary population data. In this simulation study with the Markov model, and using the NICE cut-off to consider a health intervention cost-effective in the UK (£25,000 per year of life gained), the unique ultrasound screening of AAA in men aged 65 and over continued to be cost-effective given, regarding contemporary epidemiological context of this pathology (prevalence of 1.7%). In fact, Svensjö et al found that single screening in men ≥ 65 years of age remains cost-effective up to a prevalence of 0.5%. For Svensjö et al, in addition to being economically viable, AAA screening in this at-risk population continues to show important health benefits, with an absolute risk of death from AAA of 15.1 per 10,000 screened individuals, a 42% reduction in relative risk of death related to AAA and an NNS of 530. [23]

Impact on quality of life and disadvantages of screening

The two main disadvantages of AAA screening are psychological stress and complications of elective surgical correction.

Psychological stress is an important disadvantage in individuals undergoing screening without AAA or with a small AAA that does not require elective surgical repair. This idea is supported by an RCT conducted in Denmark[43] which demonstrated that individuals undergoing AAA screening had a lower QOL (quality of life) score than the control group not screened. However, as soon as the individuals undergo screening, and found that they had no AAA, the QOL score value increased significantly, becoming higher than the value presented by controls, suggesting that this screening causes transient anxiety even in people without AAA. For individuals who underwent screening and found to have a small AAA without indication for elective treatment, they maintained a high and significantly higher QOL score than the control group. [43]

Complications of elective surgical treatment of AAA are common and may be severe. In addition, elective surgery may result in the need for prolonged hospitalization and death. Several RCTs estimated a perioperative mortality rate (30 days after surgical correction) between 0. 5 and 2. 0% for endovascular surgical repair and between 2. 4 and 5. 8% for open surgical repair, still well below the mortality rate caused by rupture of AAA. [43,48]

***Guidelines* recommendations**

There are several guidelines for AAA screening. The recommendations of the most recent guidelines are summarily presented in Table 2. All guidelines contain recommendations about surveillance intervals for aneurysms without indication for elective surgery, emphasizing the need for elective surgical correction for AAAs with a diameter ≥ 5.5 cm.

With the exception of the Canadian Task Force on Preventive Health (CTFPHC),[49] all clinical guidance standards contain recommendations regarding surveillance intervals for aneurysms with diameters smaller than the threshold size for elective surgery. However, there is no consensus on the surveillance interval to be implemented in the follow-up of patients with AAA. These guidelines make different recommendations when compared to each other. Considering that aneurysms between 3 and 5.4 cm in diameter have a low risk of rupture, the indication for elective surgery defended by the European Society of Vascular Surgery (ESVS),[50] Society for Vascular Surgery (SVS) [7] and USA Preventive Services Task Force (USPSTF) [51] is for diameters equal to or greater than 5.5 cm, with the exception of the American College of Cardiology/American Heart Association (ACC/AHA), which considers a 5.0 cm of diameter the reference for surgical correction. [52] In addition, all these guidelines consider an annual growth rate greater than 1 cm as reference criteria for elective surgery. Despite this, the mean size of the aneurysm at the time of repair is not homogenous among

Table 2 **Summary of recommendations from the most recent guidelines on screening for abdominal aortic aneurysm and their strengths of recommendation and levels of evidence taking into account the respective taxonomy of each guideline**

Guideline	Country	Recommendations	Classes of recommendation	Evidence Level
ESVS 2019 [50]	Netherlands	Recommends single AAA screening through abdominal ultrasound to all men aged 65 and over	I	A
		Recommends against screening for AAA in women who do not have a family history in first-degree of AAA	III	B
		Men and women aged 50 years and over who have a family history in first-degree of AAA can be considered for screening at intervals of 10 years	IIb	C
		All men and women with a peripheral arterial aneurysm can be considered for screening every 5-10 years	IIb	C
SVS 2018 [7]	USA	Recommends single abdominal ultrasound screening for all men and women aged 65 to 75 who have smoked at least 100 cigarettes in their lifetime	1	A
		Suggests screening AAA for all men and women over 75 who have smoked at least 100 cigarettes in their lifetime, who are in good general health and who have never been previously screened	2	C
		Suggests screening AAA for all men and women with a family history in first-degree of AAA, and this screening should preferably be done between 65 and 75 years old or, if not possible, after 75 years old, as long as they have good general health state	2	C
CTFPHC 2017 [49]	Canada	Recommends single AAA screening by abdominal ultrasound in men aged 65 to 80	Weak	Moderate
		Recommends against screening in women of any age	Strong	Very Low
		Recommends against screening in men over the age of 80	Weak	Low
USPSTF 2014 [51]	USA	Recommends single AAA screening by abdominal ultrasound to all men aged 65 to 75 who have smoked at least 100 cigarettes in their lifetime	B	
		Recommends against screening in women, with no smoking history, family history of AAA and without other risk factors for AAA	C	
		Men and women between 65 and 75 years of age who have never smoked can be considered for screening, taking into account their medical and surgical history, family history of AAA and the presence of other risk factors for AAA	D	
ACC/AHA 2005 [52]	USA	Recommends single screening for AAA through physical examination and abdominal ultrasound in men aged 60 years and over who are brothers or children of patients with AAA	I	B
		All men aged between 65 and 75 years who have smoked at least 100 cigarettes in their lifetime should be considered for screening through physical examination and abdominal ultrasound.	IIa	B

** AAA- Abdominal Aortic Aneurysm; ACC/AHA- American College of Cardiology/American Heart Association; CTFPHC- Canadian Task Force on Preventive Health Care; ESVS- European Society of Vascular Surgery; USA- United States of America; SVS- Society for Vascular Surgey.*

all countries, in part due to their reimbursement systems, which are equally important for this decision in comparation with guidelines and clinical evidence in these countries.[53] The SSVS and ESVS agree on the surveillance intervals, recommending an ultrasound surveillance every three years for AAAs between 3.0 and 3.9 cm, annually for diameters between 4.0 and 4.9 cm and every three to six months for values between 5.0 and 5.4 cm. [7,50] The ACC/AHA recommends annual surveillance between 3.0 and 4.9 cm.[52] Finally, the USPSTF recommends ultrasound surveillance every three to twelve months for aneurysms between 3.0 and 5.4 cm in diameter. [51] None of the scientific societies recommend any kind of surveillance for diameters below 3 cm.

DISCUSSION AND CONCLUSION

The AAA is a potentially fatal disease if not diagnosed and treated early. Observing this, several studies have been developed in order to evaluate the health benefits and cost-effectiveness of a populational screening program for this pathology.

There seems to exist a robust evidence that AAA screening reduces aneurysm mortality in men ≥ 65 years of age, as demonstrated by three of the four RCTs and their respective meta-analyses. In addition, the analysis of the AAA screening program implemented in Sweden showed effectiveness in reducing AAA-related mortality by 4% per year of screening.

On the other hand, apparently, there is no evidence of this screening being effective in reducing overall mortality in this at-risk population. Thus, it is likely that the decrease in mortality from AAA observed with screening may not directly contribute to the reduction of overall mortality. The slight reduction in all-cause mortality found in some meta-analyses may be justified by a better control of cardiovascular risk factors associated with the lifestyle to which screening participants were subjected.

On the other hand, there also seems to exist evidence that this screening has greater health benefits than population screenings already implemented, such as breast cancer screening and colorectal cancer screening, taking into account the NNS and the reduction in the specific cause mortality rate estimated by multiple studies.

Regarding the cost-effectiveness of AAA screening in men ≥ 65 years of age, two of the RCTs demonstrated that screening programs implemented in the UK and Denmark were cost-effective. The meta-analyses by Cosford et al and Lindholt et al also demonstrated the cost-benefit of this screening. In the last decade, there has been a decrease in the prevalence of AAA, with a reduction to less than 2% in men aged ≥ 65 years, according to national screening programs in the United Kingdom and Sweden. Although the reduction in the prevalence of this disease may question the cost-effectiveness of the implementation of this screening program, several studies had shown that it has remained cost-effective in the UK and Sweden, even for lower prevalence values than those found in large-scale RCTs. [36,37] Thus, even considering this new epidemiological paradigm, AAA screening programs continue to be cost-effective and clinically relevant in men aged 65 years and more, up to a prevalence of 0.5%. [23]

There does not seem to be evidence to support AAA screening in women; however we must remember that only a large-scale RCT was performed on women and given the low prevalence of AAA in this sex, this trial may not achieved enough power to detect any benefit of screening in women. So, further studies are needed to assess the efficacy of screening in this gender.

Considering the effects on the overall mortality rate and cost-effectiveness, there seems to be robust evidence supporting the implementation of an AAA screening program in Portugal directed to men aged ≥ 65 years, since the prevalence of this nosological entity in men of this age group in this country is similar to the prevalence that was estimated in the studies that took place in other countries. [12,13] Thus, we consider that this screening program is likely to be viable, cost-effective and clinically relevant in Portugal. However, an important limitation of this conclusion is the fact that all data are obtained from studies that took place outside Portugal. In addition to the prevalence of the disease, many other factors may influence the health benefits and the cost-effectiveness ratio of the program, which also depends on the particularities of each health system. Thus, the possibility of generalizing the results for the Portuguese population is unclear, although the data seems to support its implementation in men aged ≥ 65 years. Considering the limitations identified, a cost-effectiveness analysis based in data from Portugal should be performed to confirm our assumptions and to substantiate the need of an AAA screening program implementation in Portugal, in men aged ≥ 65 years.

Conflicts of interest
We declare, as authors, that we do not have conflicts of interest.
Sources of funding
We do not request any source of funding.

REFERENCES

1. B. Desjardins, K.E. Dill, S.D. Flamm, C.J. Francois, M.D. Gerhard-Herman, S.P. Kalva, M.A. Mansour, E.R. Mohler, I.B. Oliva, M.P. Schenker, ACR Appropriateness Criteria® pulsatile abdominal mass, suspected abdominal aortic aneurysm, The international journal of cardiovascular imaging 29(1) (2013) 177-183.
2. A. Wanhainen, How to define an abdominal aortic aneurysm—influence on epidemiology and clinical practice, Scandinavian Journal of Surgery 97(2) (2008) 105-

109.
3. K. Singh, K. Bønaa, B. Jacobsen, L. Bjørk, S. Solberg, Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study, American journal of epidemiology 154(3) (2001) 236-244.
4. S.H. Forsdahl, K. Singh, S. Solberg, B.K. Jacobsen, Risk factors for abdominal aortic aneurysms, Circulation 119(16) (2009) 2202-2208.
5. S.C. Harrison, S.E. Humphries, Regarding "Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals", Journal of vascular surgery 53(1) (2011) 263-264.
6. D.H. Kim, G. Van Ginhoven, D.M. Milewicz, Familial aggregation of both aortic and cerebral aneurysms: evidence for a common genetic basis in a subset of families, Neurosurgery 56(4) (2005) 655-661.
7. E.L. Chaikof, R.L. Dalman, M.K. Eskandari, B.M. Jackson, W.A. Lee, M.A. Mansour, T.M. Mastracci, M. Mell, M.H. Murad, L.L. Nguyen, The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm, Journal of vascular surgery 67(1) (2018) 2-77. e2.
8. R. Scott, M.A.S.S. Group, The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial, The Lancet 360(9345) (2002) 1531-1539.
9. P.E. Norman, K. Jamrozik, M.M. Lawrence-Brown, M.T. Le, C.A. Spencer, R.J. Tuohy, R.W. Parsons, J.A. Dickinson, Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm, Bmj 329(7477) (2004) 1259.
10. J.S. Lindholt, S. Juul, H. Fasting, E.W. Henneberg, Screening for abdominal aortic aneurysms: single centre randomised controlled trial, Bmj 330(7494) (2005) 750.
11. H. Ashton, L. Gao, L. Kim, P. Druce, S. Thompson, R. Scott, Fifteen□year follow□up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms, British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery 94(6) (2007) 696-701.
12. J. Fernandes, A. Natário, A. Matos, Rede de Referenciação Hospitalar Angiologia e Cirurgia Vascular, SNS, ed: Republica Portuguesa (2017) 34-39.
13. R. Castro-Ferreira, P. Mendes, P. Couto, R. Barreira, F. Peixoto, M. Aguiar, M. Neto, D. Rolim, J. Pinto, A. Freitas, Rastreio populacional de aneurisma da aorta abdominal em Portugal–o imperativo da sua realização, Angiologia e Cirurgia Vascular 12(4) (2016) 267-270.
14. H.-H. Eckstein, D. Böckler, I. Flessenkämper, T. Schmitz-Rixen, S. Debus, W. Lang, Ultrasonographic screening for the detection of abdominal aortic aneurysms, Deutsches Ärzteblatt International 106(41) (2009) 657.
15. E.L. Chaikof, D.C. Brewster, R.L. Dalman, M.S. Makaroun, K.A. Illig, G.A. Sicard, C.H. Timaran, G.R. Upchurch, F.J. Veith, The care of patients with an abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines, Journal of vascular surgery 50(4) (2009) S2-S49.
16. P. Basnyat, A. Biffin, L. Moseley, A. Hedges, M. Lewis, Mortality from ruptured abdominal aortic aneurysm in Wales, British Journal of Surgery 86(6) (1999) 765-770.
17. K.W. Johnston, Ruptured abdominal aortic aneurysm: six-year follow-up results of a multicenter prospective study, Journal of vascular surgery 19(5) (1994) 888-900.
18. J.S. Lindholt, S. Vammen, S. Juul, E. Henneberg, H. Fasting, The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm, European journal of vascular and endovascular surgery 17(6) (1999) 472-475.
19. F.A. Lederle, J.M. Walker, D.B. Reinke, Selective screening for abdominal aortic aneurysms with physical examination and ultrasound, Archives of internal medicine 148(8) (1988) 1753-1756.
20. V.S. Tayal, C.D. Graf, M.A. Gibbs, Prospective study of accuracy and outcome of emergency ultrasound for abdominal aortic aneurysm over two years, Academic Emergency Medicine 10(8) (2003) 867-871.
21. T.G. Costantino, E.C. Bruno, N. Handly, A.J. Dean, Accuracy of emergency medicine ultrasound in the evaluation of abdominal aortic aneurysm, The Journal of emergency medicine 29(4) (2005) 455-460.
22. R.A. Benson, R. Poole, S. Murray, P. Moxey, I.M. Loftus, Screening results from a large United Kingdom abdominal aortic aneurysm screening center in the context of optimizing United Kingdom National Abdominal Aortic Aneurysm Screening Programme protocols, Journal of vascular surgery 63(2) (2016) 301-304.
23. S. Svensjö, K. Mani, M. Björck, J. Lundkvist, A. Wanhainen, Screening for abdominal aortic aneurysm in 65-year-old men remains cost-effective with contemporary epidemiology and management, European Journal of Vascular and Endovascular Surgery 47(4) (2014) 357-365.
24. S. Thompson, H. Ashton, L. Gao, M. Buxton, R. Scott, Multicentre Aneurysm Screening Study G. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening, Br J Surg 99(12) (2012) 1649-56.
25. J.S. Lindholt, J. Sørensen, R. Søgaard, E. Henneberg, Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial, British journal of surgery 97(6) (2010) 826-834.
26. K.A. McCaul, M. Lawrence-Brown, J.A. Dickinson, P.E. Norman, Long-term outcomes of the Western Australian trial of screening for abdominal aortic aneurysms: secondary analysis of a randomized clinical trial, JAMA internal medicine 176(12) (2016) 1761-1767.
27. R. Scott, N. Wilson, H. Ashton, D. Kay, Influence of screening on the incidence of ruptured abdominal aor-

tic aneurysm: 5-year results of a randomized controlled study, British Journal of Surgery 82(8) (1995) 1066-1070.
28. K. Vardulaki, N. Walker, E. Couto, N. Day, S. Thompson, H. Ashton, R. Scott, Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm, British journal of surgery 89(7) (2002) 861-864.
29. S. Thompson, H. Ashton, L. Gao, R. Scott, Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study, Bmj 338 (2009) b2307.
30. P.A. Cosford, G.C. Leng, J. Thomas, Screening for abdominal aortic aneurysm, Cochrane database of systematic reviews (2) (2007).
31. J.S. Lindholt, P. Norman, 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, European Journal of Vascular and Endovascular Surgery 36(2) (2008) 167-171.
32. H. Takagi, S.-n. Goto, M. Matsui, H. Manabe, T. Umemoto, A further meta-analysis of population-based screening for abdominal aortic aneurysm, Journal of vascular surgery 52(4) (2010) 1103-1108.
33. H. Takagi, T. Ando, T. Umemoto, Abdominal aortic aneurysm screening reduces all-cause mortality: make screening great again, Angiology 69(3) (2018) 205-211.
34. P.C. Gøtzsche, Relation between breast cancer mortality and screening effectiveness: systematic review of the mammography trials, Dan Med Bull 58(3) (2011) A4246.
35. P. Hewitson, P. Glasziou, E. Watson, B. Towler, L. Irwig, Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update, American Journal of Gastroenterology 103(6) (2008) 1541-1549.
36. A. Wanhainen, R. Hultgren, A. Linné, J. Holst, A. Gottsäter, M. Langenskiöld, K. Smidfelt, M. Björck, S. Svensjö, S.A.S.S. Group, Outcome of the Swedish nationwide abdominal aortic aneurysm screening program, Circulation 134(16) (2016) 1141-1148.
37. J. Jacomelli, L. Summers, A. Stevenson, T. Lees, J. Earnshaw, Impact of the first 5 years of a national abdominal aortic aneurysm screening programme, British Journal of Surgery 103(9) (2016) 1125-1131.
38. M. Davis, M. Harris, J.J. Earnshaw, Implementation of the national health service abdominal aortic aneurysm screening program in England, Journal of vascular surgery 57(5) (2013) 1440-1445.
39. N. Olchanski, A. Winn, J. Cohen, P. Neumann, Abdominal aortic aneurysm screening: how many life years lost from underuse of the medicare screening benefit?, Journal of general internal medicine 29(8) (2014) 1155-1161.
40. J.B. Shreibati, L.C. Baker, M.A. Hlatky, M.W. Mell, Impact of the Screening Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act on abdominal ultrasonography use among medicare beneficiaries, Archives of internal medicine 172(19) (2012) 1456-1462.
41. M.D. Rawlins, A.J. Culyer, National Institute for Clinical Excellence and its value judgments, Bmj 329(7459) (2004) 224-227.
42. M. Glover, L. Kim, M. Sweeting, S. Thompson, M. Buxton, Cost-effectiveness of the National Health Service abdominal aortic aneurysm screening programme in England, British Journal of Surgery 101(8) (2014) 976-982.
43. J.S. Lindholt, S. Vammen, H. Fasting, E. Henneberg, Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms, European Journal of Vascular and Endovascular Surgery 20(1) (2000) 79-83.
44. F.A. Lederle, R.L. Kane, R. MacDonald, T.J. Wilt, Systematic review: repair of unruptured abdominal aortic aneurysm, Annals of internal medicine 146(10) (2007) 735-741.
45. M.L. Schermerhorn, D.B. Buck, A.J. O'Malley, T. Curran, J.C. McCallum, J. Darling, B.E. Landon, Long-term outcomes of abdominal aortic aneurysm in the Medicare population, New england journal of medicine 373(4) (2015) 328-338.
46. P. Cao, P. De Rango, F. Verzini, G. Parlani, L. Romano, E. Cieri, C.T. Group, Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): results from a randomised trial, European Journal of Vascular and Endovascular Surgery 41(1) (2011) 13-25.
47. K. Ouriel, D.G. Clair, K.C. Kent, C.K. Zarins, P.I.o.E.O.f.t.A.E. Investigators, Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms, Journal of vascular surgery 51(5) (2010) 1081-1087.
48. F.A. Lederle, S.E. Wilson, G.R. Johnson, D.B. Reinke, F.N. Littooy, C.W. Acher, D.J. Ballard, L.M. Messina, I.L. Gordon, E.P. Chute, Immediate repair compared with surveillance of small abdominal aortic aneurysms, New England Journal of Medicine 346(19) (2002) 1437-1444.
49. C.T.F.o.P.H. Care, Recommendations on screening for abdominal aortic aneurysm in primary care, CMAJ 189(36) (2017) E1137-E1145.
50. A. Wanhainen, F. Verzini, I. Van Herzeele, E. Allaire, M. Bown, T. Cohnert, F. Dick, J. van Herwaarden, C. Karkos, M. Koelemay, European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms (vol 57, pg 8, 2019), European Journal of Vascular and Endovascular Surgery 59(3) (2020) 494-494.
51. M.L. LeFevre, Screening for abdominal aortic aneurysm: US Preventive Services Task Force recommendation statement, Annals of internal medicine 161(4) (2014) 281-290.
52. A.T. Hirsch, Z.J. Haskal, N.R. Hertzer, C.W. Bakal, M.A. Creager, J.L. Halperin, L.F. Hiratzka, W.R. Murphy, J.W.

Olin, J.B. Puschett, ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic) a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery,* Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (writing committee to develop guidelines for the management of patients with peripheral arterial disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation, circulation 113(11) (2006) e463-e654.

53. A.W. Beck, A. Sedrakyan, J. Mao, M. Venermo, R. Faizer, S. Debus, C.-A. Behrendt, S. Scali, M. Altreuther, M. Schermerhorn, Variations in abdominal aortic aneurysm care: a report from the International Consortium of Vascular Registries, Circulation 134(24) (2016) 1948-1958.