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Safety of Men with Small and Medium Abdominal Aortic Aneurysms Under Surveillance in the National Health Service Screening Programme

Running Title: *Oliver-Williams et al.; Safety in Abdominal Aortic Aneurysm Surveillance*

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Abstract

Background: Population screening for abdominal aortic aneurysm (AAA) has commenced in several countries, and has been shown to reduce AAA-related mortality by up to 50%. Most men who screen positive have an AAA below 5.5cm in diameter, the referral threshold for treatment, and are entered into an ultrasound surveillance programme. This study aimed to determine the risk of ruptured AAA (rAAA) in men under surveillance.

Methods: Men in the NHS AAA Screening Programme who initially had a small (3-4.4cm) or medium (4.5-5.4cm) AAA were followed-up. The screening programme's database collected data on ultrasound AAA diameter measurements and dates of referral and loss to follow-up. Local screening programmes recorded adverse outcomes, including rAAA and death. Rupture and mortality rates were calculated by initial and final known AAA diameter.

Results: A total of 18,652 men were included (50,103 men years of surveillance). Thirty-one men had rAAA in surveillance, of whom 29 died. Some 952 men died from other causes during surveillance, mainly cardiovascular complications (26.3%) and cancer (31.2%). The overall mortality rate was 1.96% per annum, similar for men with small and medium AAA. The rAAA risk was 0.03% per annum (95% confidence interval 0.02-0.05%) for men with small AAA, and 0.28% (0.17-0.44%) for medium AAA. The rAAA risk for men with AAA just below the referral threshold (5.0 to 5.4 cm) was 0.40% (0.22-0.73%).

Conclusions: The risk of rAAA in surveillance is below 0.5% per annum, even just below the present referral threshold of 5.5cm and only 0.4% of men in surveillance are estimated to rupture before referral. It can be concluded that men with small and medium screen-detected AAA are safe provided they are enrolled in an intensive surveillance program, and that there is no evidence that the current referral threshold of 5.5cm should be changed.

Key Words: Abdominal Aortic Aneurysm; Men; Surveillance; Screening; Ultrasonography

Clinical Perspective

What is new?

- There remains debate about when to intervene in patients with a large AAA.
- This study concerns men aged over 65 years with an AAA in surveillance detected either through population screening or self-referral.
- Using a standard surveillance schedule, the risk of rupture in AAA measured using the inner to inner ultrasound method was less than 0.5% per annum, even in men whose AAA was just below 5.5cm, the current referral threshold.

What are the clinical implications?

- Current surveillance procedures in the NHS AAA Screening Programme result in very low rupture risks.
- Men with small and medium screen-detected AAA are safe in an intensive surveillance program, and that there is no evidence that the current referral threshold of 5.5cm should be changed.

Introduction

Abdominal aortic aneurysm (AAA) ultrasound screening programmes are emerging worldwide[1,2]. The majority of programmes are based on a single scan in elderly men, who are reassured and discharged if an AAA is excluded (usually if the abdominal aorta is <3.0cm in diameter). A minority of screened individuals are diagnosed with large AAA (usually >5.4cm in diameter), and are referred to a vascular specialist for consideration of intervention. A further group has a small (3.0-4.4cm) or medium (4.5-5.4cm) AAA that is not immediately life-threatening, but warrants monitoring. These people are usually offered ultrasound surveillance with referral for treatment once the threshold for intervention (usually 5.5cm diameter) is reached.

After a population screening programme has become established, a substantial number of men will be under ultrasound surveillance. It is important to be able to show that AAA surveillance schedules are safe, and that men with small and medium AAA below the referral threshold are not at unacceptable risk of AAA rupture.

The NHS AAA Screening Programme (NAAASP) invites all men aged 65 in England for an abdominal ultrasound scan. Men aged over 65 who have never been screened may self-refer[3]. Men with small or medium AAA are offered surveillance: annually for small AAA, and every three months for medium AAA. This schedule is evidence-based from the results of previous randomised trials of AAA screening, and population programmes[4,5]. Details of the NAAASP standard operating procedure are recorded elsewhere[6]. Some 300,000 men each year reach the age of 65 and are invited for screening; in 2018 the two millionth man was invited.

The present threshold for referral for treatment of 5.5cm in NAAASP is based on the Small Aneurysm[7] and Aneurysm Detection and Management[8] trials, where it was shown that it was as

safe to be in surveillance as it was to have early intervention for men with an AAA <5.5cm in diameter.

It is well known that men with small and medium AAA have coexisting medical conditions. They are often smokers, and many have smoking-related conditions including cancer[9,10]. Men with small and medium AAA benefit from the best medical therapy: usually secondary prevention with antiplatelet, and statins[11]. These medications, along with lifestyle improvements and smoking cessation, are recommended for men in surveillance in NAAASP. The main aim of the present study was to ensure the safety of men in surveillance in NAAASP. Since the aim of the programme is to prevent death from AAA rupture, the study examined fatal and non-fatal AAA ruptures in men with small and medium AAA in the surveillance programme. The risk of rupture during surveillance should be substantially less than the risk of in hospital death from elective AAA repair (1.4% for open and endovascular repair in the latest report from the UK National Vascular registry[12]). The secondary aim was to examine other causes of death in the surveillance cohort, with the long-term aim of designing medical interventions that might reduce the risk of any death in surveillance.

Methods

The study was approved by the NAAASP Research Committee and carried out as part of its programme evaluation. Men who accepted the invitation and attended for ultrasound imaging gave verbal consent to screening and to having their anonymised information stored and used for programme evaluation, which is recorded. The methods used for analysis and materials used to conduct the research are available to any researcher, but the original data are subject to current rules of Information Governance.

After screening, which was done using the inner to inner ultrasound measurement method[13], men with small (3.0-4.4cm) and medium (4.5-5.4cm) AAA detected in NAAASP were invited to join a surveillance programme; those who agreed and attended were included in the analysis. Data concerning their attendance and outcomes were collected within the programme on a bespoke IT system, AAA SMaRT (Screening Management and Referral Tracker). All men were offered an appointment with a nurse specialist on entering surveillance, where baseline data were obtained and advice was given about healthy lifestyle and best medical management. Management of men identified with an AAA after invitation at 65 years, and those who self-referred was identical.

Men were offered regular ultrasound scans using monitored standards. The reproducibility of the scan measurements has been demonstrated previously in this cohort[13]. Reasons for leaving surveillance were recorded. Also recorded on the database were details of surveillance scans (dates, aortic diameter), and outcomes including death, referral for surgery, declines, and loss to follow-up. Dates and causes of death during surveillance, and details concerning any men who had a ruptured AAA but survived, were obtained from local screening programmes as part of programme monitoring. Local screening programmes were advised to review death certificates, post-mortem results, hospital discharge summaries, or contact treating clinicians or family doctors directly to determine cause of death as accurately as possible.

Statistical analysis

Data from AAA SMaRT were extracted up to 18th August 2017. The first men were included in surveillance once the programme commenced in 2009. Follow-up was defined as from the time of first scan until either death, referral to a vascular surgeon, rupture, loss to follow-up, or the administrative censoring date of 18th August 2017, whichever came first. Loss to follow-up was

not always recorded and so patients were censored 18 months after the last scan if no further information was recorded.

Baseline characteristics and outcomes were tabulated by route of entry into the screening programme: either routinely invited or self-referred. Continuous variables were presented as median and interquartile ranges (IQR), and categorical variables were presented as number and percentage.

All analyses included self-referred and routinely invited men and were restricted to events that occurred before referral for surgery.

The number of person-years of follow-up, AAA ruptures, deaths, and the mortality and rupture rates per 100 person-years were calculated by referral status (self-referred or routinely invited), and aortic diameter, stratified by small and medium AAA categories, and also by 3.0-4.9cm and 5.0-5.4cm categories. The latter group had AAA just below the threshold for referral and might be considered to be at highest risk of rupture.

Analyses by aortic diameter were conducted using both the initial aortic diameter and a time-updated measurement (time--varying covariate). The latter split the time that individuals contributed before their censoring date into the relevant aorta diameter categories, as determined by the previous measurements. For example, men who initially had an aneurysm of less than 4.5cm, which increased to an aneurysm of more than 4.5cm during follow-up, contributed time to both the small and medium AAA categories.

Age-standardised mortality ratios (SMRs) were calculated, stratified by 5-year age group, using sex-specific combined English and Welsh data from the Office of National Statistics from 2011 to 2013[14]. The non-parametric cumulative incidence curve was calculated for the time to death under surveillance by initial aortic diameter categories and 95% confidence intervals (CI)

were based on the log-log transformation of the cumulative incidence[15]. Rupture and referral for consideration of intervention were treated as competing events in these analyses. Stacked cumulative incidence curves for each of the three competing events (rupture, referral for intervention and death without rupture or referral) were produced to assess the total risk of each event during surveillance for all men combined. The incidence of each outcome was also estimated by initial aortic diameter (3.0-3.4cm, 3.5-3.9cm, 4.0-4.4cm, 4.5-4.9cm and 5.0-5.4cm), with stacked cumulative incidence curves produced separately for each category.

All analyses were conducted using STATA release 14 (Stata Corp, College Station, Texas, USA).

Results

Between 2009 and 2017, a total of 18,652 men were found to have an initial AAA of 3.0cm or greater in NAAASP. The majority of the men (83.2%) were routinely invited for screening (they did not self-refer). Self-referred men were, on average, older (75.4 versus 65.0 years, P<0.001), and more likely to be non-smokers at nurse assessment (Table 1). There was no difference in the proportion of deaths, ruptures or loss to follow-up between the two groups.

During follow-up, 1,763 men had a scan measurement of 5.5cm or larger, of whom 1,742 were referred to a vascular service for consideration of treatment. A further 83 men were referred before their AAA size reached 5.5cm, usually because of an iliac aneurysm, tenderness, rapid aneurysm growth, or other finding. Of men whose aorta measured 5.5cm or over, 94.9% were referred to the vascular service within 1 day, which is the programme standard. Of the 21 men who were not referred, 16 declined referral, 2 left the surveillance programme, 2 died from non-AAA causes and 1 was referred after data collection ended on 18th August 2017.

AAA rupture

Thirty-one men had a ruptured AAA in surveillance: 25 routinely invited men and 6 self-referred men (Table 2). Twenty-nine (93.5%) of the men who had a ruptured AAA died. There was little difference in the incidence rate of rupture between routinely invited and self-referred men; 0.06 (95% CI 0.04-0.09), and 0.08 (95% CI 0.03-0.17) per 100 person-years, respectively (Table 2). Therefore, we combined the groups when calculating rupture rates by aortic diameter categories. The estimated rupture rate was below 1 per 100 person-years for all diameter categories, but was highest for men with an aortic measurement of 5.0-5.4cm; 0.40 (95% CI 0.13-1.25) per 100 person-years based on initial aortic measurement, and 0.40 (95% CI 0.22-0.73) per 100 person-years, based on time-updated aortic measurements (Table 2). Using time-updated measurements, there was strong evidence that the rupture rate was below 1 per 100 person-years for diameters 5.0-5.4cm ($p<0.001$). The cumulative incidence of rupture during surveillance reached 0.62% in men with medium aneurysms at baseline and 0.35% for men with small aneurysms at baseline (Figure 1). Overall, an estimated 0.4% of men are assumed to rupture whilst in surveillance.

Mortality

Of the initial cohort of 18,652 men, 980 (5.3%) died in surveillance, of which 29 (3.0%) died from ruptured AAAs (Table 1). Other deaths were due to cancer (31.2%), vascular or cardiac causes (26.3%), and non-cardiovascular and non-cancer causes (29.0%). The causes of death for 103 men (10.5%) were unknown. Individuals whose initial AAA diameter was in the range 4.5-5.4cm had a higher proportion of deaths from AAA rupture compared to individuals whose initial AAA diameter was 3.0-4.4cm (14.5% vs. 2.1%).

There was an estimated 1.96 deaths per 100 person-years (95% CI: 1.84-2.08) in men in surveillance before referral (Table 3). The mortality rate was similar for men who initially had a

medium sized aneurysm. When based on time-updated aortic measurements, mortality rates increased with AAA size, with the smallest rates for men with AAA of <3.0cm, and greatest for those with AAA of 5.5cm or more. A similar cumulative incidence of death was estimated for men with small and medium aneurysms within the first year of surveillance; 1.66% (95%CI: 1.47-1.87%) and 1.46% (1.01-2.05%), respectively (Figure 2). By the 3rd year, an estimated 5.42% (5.02-5.84%) of men who initially had a small aneurysm, and 3.16% (2.37-4.12%) of men with a medium aneurysm had died whilst in surveillance. The lower incidence for men with a medium aneurysm is due to accounting for greater referral rates in this group.

The mortality rate increased with age for both routinely invited (Table 4) and self-referred men (Table 5). For routinely invited men, the mortality rate was approximately 60% higher than in the male, age-matched English and Welsh population, but for self-referred men it was approximately 40% lower. However, as self-referred men were on average older this led to overall mortality rates similar to routinely invited men.

Figure 3 shows the cumulative incidence functions for each competing outcome (rupture, referral and death without rupture) stacked on top of each other. The estimated probability of each outcome increases over the 8 year period of follow-up, with referral the most prevalent outcome. Approximately half of the population are estimated to remain under surveillance after 8 years.

Figure 4 displays the cumulative incidence of the same outcomes by initial aortic diameter. The estimated probability of referral within 8 years is high for men with initial diameters 4.0cm and above, whilst the probability of rupture remains low for all diameter groups.

Discussion

This study has shown that the suggested referral threshold of 5.5cm measured by ultrasound imaging using the inner to inner method results in AAA rupture rates consistently below 0.5% in men in surveillance. The present UK in hospital mortality rate for elective AAA repair is around 1.4%[12]. After 8 years of surveillance, approximately 50% of men had died or were referred for surgery. The cumulative incidence of rupture over 8 years was very low (0.4%). Therefore, it is considered that men enrolled in an intensive surveillance program such as NAAASP are safe, and that there is no evidence that current NAAASP referral threshold of 5.5cm should be changed. The risk of rupture is related to aortic diameter, but even in men with an AAA 5.0-5.4cm, just below the threshold for referral, the rate was less than 0.5% per annum. This study examined only men with screen-detected AAA, but it would be expected these findings would be generalizable to men in surveillance with small and medium AAA detected incidentally.

A small number of men in surveillance do rupture their AAA, including small AAAs of less than 4.5cm diameter. Some of these men may have developed an infection in their AAA (mycotic aneurysm) to account for early rupture. The majority of men who rupture do not survive, despite knowledge of their condition. It had been thought that men known to have an AAA might be treated quicker if their AAA ruptures, but this is not supported by the present report.

The second conclusion is that the overall mortality rate in men in surveillance is higher than age-matched men in the general population, but only in the invited cohort. Self-referred men have a lower mortality. They have a lower BMI and are less likely to be smokers, suggesting they are health-conscious, and possibly already medically well managed. Men with an AAA are known to have a higher risk of cardiovascular disease and to be at risk of premature death,

mainly from smoking related conditions[10]. It has been shown previously that the risk of death from any cause is associated with increasing AAA diameter[16]. The main causes of death in the men reported here were cardiovascular disease and cancer. Men in NAAASP are given advice about their health, in particular smoking cessation, and prescription of antiplatelets and statins is recommended. It has been shown that compliance with these medications improves the chances of survival[11]. Optimising the medical management of these men, possibly with regular monitoring, offers the best chance of reducing mortality in this cohort. The reduced mortality rate in self-referred men supports the expectation that good medical care can reduce mortality.

This study has a number of implications for practice. Patient referral thresholds for treatment of AAA are largely derived from RCTs done in the 1990s[7,8]. There has been argument that a single referral threshold for all people with an AAA is dated, in the current era of personalised medicine. Scoring systems have been developed to identify subjects with an AAA for whom operation below the current threshold may be safe, and improve cost efficacy[17]. In Sweden, the perioperative risk of death after elective endovascular repair for AAA is 0.3%[1]. It might be argued that where intervention risks are small, a lower referral threshold is appropriate. Yet controlled trials, such as the CAESAR Study that compared early endovascular treatment with conservative treatment of small AAA failed to show the superiority of early intervention[18]. An alternative use of personalised scoring systems might be to delay intervention in men with a 5.5cm AAA at low risk of rupture. There are a number of new biological and radiological imaging methods that could be employed in this way[19,20].

In addition, it is unlikely that the risk of AAA rupture suddenly becomes acute once an AAA reaches 5.5cm in diameter. A controlled trial, randomizing men with AAA 5.5-6.5cm to treatment or continued surveillance, was never done, due to lack of equipoise among vascular

surgeons. The positive effects of elective AAA repair are a balance of risk against benefit, accounting for postoperative quality of life as well as life-expectancy; clearly the balance for a fit 65 year old man with a 5.5cm AAA are different from those of an 85 year old man with the same sized AAA[21].

The method used to assess aortic diameter in NAAASP is the inner to inner ultrasound method[13], which excludes the thickness of the aortic wall and is usually around 0.5cm less than aortic diameter measured on CT. It could be argued that men in the NAAASP surveillance programme may well be safe up to a diameter of 6.0cm on CT. This is a direct challenge to the use of 5.5cm diameter on CT as the threshold for intervention; thresholds should be different for each imaging modality. It is also in direct contrast to a recent publication criticising surgeons in the UK for having a higher threshold for intervention than surgeons in the US[22]. This difference in threshold was used as an explanation for death from ruptured AAA (rAAA) being more common in the UK. The present results suggest the explanation for this variation could be more complex.

The main limitation of this study is the fact that some of the causes of death were unknown. It is possible that some were due to rAAA. The local screening programmes have close ties with the vascular centres, and record any patient admitted with a rAAA, so that can information be linked back. It is possible that some men who die suddenly at home, and do not have a post mortem could have died from rAAA. The study also concerns only men with AAA in surveillance. Population screening for AAA in women is not cost effective[23], yet there will be women with small and medium AAA who need surveillance. It is probably not appropriate to extrapolate the results of the present study to women, since there is some evidence the referral threshold should be lower[24,25]. Similarly, the findings may only be generalizable among

populations with similar ethnic composition as England[26]. The prevalence of AAA is known to vary among ethnic groups, though little is known about growth rate and rupture risks in various ethnicities.

The NAAASP has now been implemented for 5 years, and its outcomes are starting to be recorded[2,26]. The present study is reassuring for current surveillance standards. It is possible that with more data on men just below the threshold for referral, that surveillance intervals could be relaxed, as recommended[4]. It will take a decade before it will be possible to be sure to what extent the introduction of screening programmes has had on the rate of AAA-related deaths. Although preliminary data from Sweden on the effectiveness of screening are conflicting[3,27], early signs are more encouraging in England[27].

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Disclosures

None of the authors have any competing interests to declare, or any financial interests connected with this manuscript.

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Table 1. Characteristics of participants with initial diameter ≥3.0cm in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017

Characteristics		**Routinely Invited (N=15,527)**		**Self-referral (N=3,125)**		**Total (N=18,652)**		**p-value†**
Age, years		65.0	(0.004)	75.4	(0.10)	66.8	(0.03)	<0.001
Systolic Blood Pressure, mmHg		142.4	(0.20)	141.5	(0.43)	142.3	(0.18)	0.070
Diastolic Blood Pressure, mmHg		83.8	(0.11)	79.2	(0.24)	83.0	(0.10)	<0.001
Height, metres		176.3	(0.07)	175.5	(0.14)	176.1	(0.06)	<0.001
Weight, Kg		90.3	(0.15)	85.4	(0.28)	89.4	(0.14)	<0.001
BMI, kg/m^2		29.0	(0.04)	27.7	(0.08)	28.8	(0.04)	<0.001
Number of scans*		3	(2-5)	3	(2-5)	3	(2-5)	0.024
Follow-up duration, years*		2.5	(1.5-4.0)	2.5	(1.4-3.7)	2.5	(1.4-3.9)	<0.001
Smoking Status	Never	1,042	(8.4%)	498	(18.9%)	1,540	(10.2%)	<0.001
	Previous	6,502	(52.1%)	1,778	(67.7%)	8,280	(54.8%)	
	Current	4,928	(39.5%)	350	(13.3%)	5,278	(35.0%)	
Statins		7,347	(61.4%)	1,686	(67.0%)	9,033	(62.4%)	<0.001
Aspirin		4,686	(38.9%)	1,079	(42.5%)	5,765	(39.5%)	0.001
Initial AAA size	3.0-4.4cm	13,747	(88.5%)	2,683	(85.9%)	16,430	(88.1%)	<0.001
	4.5-5.4cm	1,780	(11.5%)	442	(14.1%)	2,222	(11.9%)	
Last AAA size	<3.0cm	673	(4.3%)	120	(3.8%)	793	(4.3%)	0.046
	3.0-4.4cm	11,131	(71.7%)	2,229	(71.3%)	13,360	(71.6%)	
	4.5-5.4cm	2,235	(14.4%)	501	(16.0%)	2,736	(14.7%)	
	5.5cm+	1,488	(9.6%)	275	(8.8%)	1,763	(9.5%)	
Outcomes								
Deaths before referral		801	(5.2%)	179	(5.7%)	980	(5.3%)	0.193
Cause of Death	AAA rupture	24	(3.0%)	5	(2.8%)	29	(3.0%)	0.046
	Vascular/cardiac	212	(26.5%)	46	(25.7%)	258	(26.3%)	
	Cancer	264	(33.0%)	42	(23.5%)	306	(31.2%)	
	Other	217	(27.1%)	67	(37.4%)	284	(29.0%)	
	Unknown	84	(10.5%)	19	(10.6%)	103	(10.5%)	
Referral		1,545	(10.0%)	280	(9.0%)	1,825	(9.8%)	0.089
Surgery		1,126	(7.3%)	188	(6.0%)	1,314	(7.0%)	0.014
Ruptures under surveillance		25	(0.2%)	6	(0.2%)	31	(0.2%)	0.698
Lost to follow-up		1,416	(9.1%)	261	(8.4%)	1,677	(9.0%)	0.171

Data presented are mean (standard deviation), median (IQR) or number of patients (%).

* Median (IQR)

† p-values comparing routinely invited and self-referred men. A Kruskal Wallis test was used to calculate P-values for number of scans, follow-up duration and initial AAA size. All other continuous variables compared with t-tests; categorical variables compared with Pearson's X^2 tests.

BMI = body mass index.

* Missing Data: weight – 4,836 (25.9%), height – 4,857 (26.0%), diastolic blood pressure – 5,756 (30.9%), systolic blood pressure – 5,745 (30.8%), BMI – 4,974 (26.7%), Smoking status – 3,555 (19.1%), Statins – 4,174 (22.4%), Aspirin – 4,068 (21.8%)

Table 2. Rates of ruptures that occurred in the NHS Abdominal Aortic Aneurysm Screening Programme during surveillance, 2009-2017.

	Number of men	**Ruptures (N)**	**Follow-up (person-years)**	**Incidence rate per 100 person-years (95% CI)**	
Overall	18,652	31	50,095	0.06	(0.04, 0.09)
Routinely invited	15,527	25	42,220	0.06	(0.04, 0.09)
Self-referred	3,125	6	7,876	0.08	(0.03, 0.17)
Initial aortic measurement Grouping 1					
3.0-4.4cm	16,430	20	46,576	0.04	(0.03, 0.07)
4.5-5.4cm	2,222	11	3,519	0.31	(0.17, 0.56)
Grouping 2					
3.0-4.9cm	17,883	28	49,349	0.06	(0.04, 0.08)
5.0-5.4cm	769	3	746	0.40	(0.13, 1.25)
Time-updated aortic measurement (time-varying categories)*Grouping 1					
<3.0cm	-	0	1,713	0	-
3.0-4.4cm	-	13	41,788	0.03	(0.02, 0.05)
4.5-5.4cm	-	18	6,532	0.28	(0.17, 0.44)
5.5cm+	-	0	32	0	-
Grouping 2					
<3.0cm	-	0	1,713	0	-
3.0-4.9cm	-	20	45,594	0.04	(0.03, 0.07)
5.0-5.4cm	-	11	2,726	0.40	(0.22, 0.73)
5.5cm+	-	0	32	0	

* time-updated aortic measurement (time--varying covariate) was calculated by splitting the time that individuals contributed before their censoring date into the relevant aorta diameter categories, as determined by the previous measurements

Table 3. Mortality rates during surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017, by initial aortic measurement and last known aortic measurement.

	Number of men	**Deaths (N)**	**Follow-up (person-years)**	**Mortality rate per 100 person-years (95% CI)**	
Overall	18,652	980	50,103	1.96	(1.84-2.08)
Routinely invited	15,527	801	42,226	1.90	(1.77-2.03)
Self-referred	3,125	179	7,877	2.27	(1.96-2.63)
Initial AAA measurement					
Grouping 1					
3.0-4.4cm	16,430	912	46,581	1.96	(1.83-2.09)
4.5-5.4cm	2,222	68	3,522	1.93	(1.52-2.45)
Grouping 2					
3.0-4.9cm	17,883	965	49,354	1.96	(1.84-2.08)
5.0-5.4cm	769	15	749	2.00	(1.21-3.32)
Time-updated aortic measurement (time-varying categories)*					
Grouping 1					
<3.0cm		19	1,713	1.11	(0.71-1.74)
3.0-4.4cm		826	41,791	1.98	(1.85-2.12)
4.5-5.4cm		133	6,535	2.04	(1.72-2.41)
5.5cm+		2	33	6.02	(1.51-24.08)
Grouping 2					
<3.0cm		19	1,713	1.11	(0.71-1.74)
3.0-4.9cm		895	45,597	1.96	(1.84-2.10)
5.0-5.4cm		64	2,729	2.35	(1.84-3.00)
5.5cm+		2	33	6.02	(1.51-24.08)

* time-updated aortic measurement (time--varying covariate) was calculated by splitting the time that individuals contributed before their censoring date into the relevant aorta diameter categories, as determined by the previous measurements

Table 4. Standardised Mortality Ratios for routinely invited men whilst under surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017, stratified by age

Age group	Person-years	Deaths	Mortality Rate per 100 person-years (95% CI)		Expected number of deaths	SMR (95% CI)	
55 - 60	2.5	0	0	-	0	0	-
60 - 65	2,057	21	1.02	(0.67, 1.57)	16	1.28	(0.84, 1.97)
65 - 70	38,407	732	1.91	(1.77, 2.05)	457	1.60	(1.49, 1.72)
70 - 75	1,759	48	2.73	(2.06, 3.62)	36	1.35	(1.02, 1.79)
Total	42,226	801	1.90	(1.77, 2.03)	509	1.57	(1.47, 1.69)

SMR = Standardised Mortality Ratio

Table 5. Standardised Mortality Ratios for self-referred men whilst under surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017, stratified by age

Age group	Person-years	Deaths	Mortality Rate per 100 person-years (95% CI)		Expected number of deaths	SMR (95% CI)	
55 - 60	1.5	0	0	-	0	0	-
60 - 65	0.6	0	0	-	0	0	-
65 - 70	759	4	0.53	(0.20, 1.40)	9	0.44	(0.17, 1.18)
70 - 75	2,727	39	1.43	(1.04, 1.96)	55	0.71	(0.52, 0.97)
75 - 80	2,449	56	2.29	(1.76, 2.97)	80	0.70	(0.54, 0.91)
80 - 85	1,321	55	4.19	(3.22, 5.46)	74	0.75	(0.57, 0.97)
> 85	629	25	3.98	(2.69, 5.89)	63	0.40	(0.27, 0.59)
Total	7,877	179	2.27	(1.96, 2.63)	281	0.64	(0.55, 0.74)

SMR = Standardised Mortality Ratio

Figure Legends

Figure 1. Cumulative incidence of rupture during surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017, by initial diameter (3.0-4.4cm / 4.5-5.4cm) Incidence of rupture was estimated with referral and mortality as competiting risks

Figure 2. Cumulative incidence of death during surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017, by initial diameter (3.0-4.4cm / 4.5-5.4cm) Incidence of death was estimated with referral and mortality as competiting risks

Figure 3. Stacked cumulative incidence function plot for men under surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009-2017

Figure 4. Stacked cumulative incidence function plots for men under surveillance in the NHS Abdominal Aortic Aneurysm Screening Programme, 2009, 2017, by initial diameter: A) 3.0-3.4cm, B) 3.5-3.9cm, C) 4.0-4.4cm, D) 4.5-4.9cm and E) 5.0-5.4cm.