Surveillance Intervals for Small Abdominal Aortic Aneurysms
A Meta-analysis

The RESCAN Collaborators*

Importance Small abdominal aortic aneurysms (AAAs [3.0 cm-5.4 cm in diameter]) are monitored by ultrasound surveillance. The intervals between surveillance scans should be chosen to detect an expanding aneurysm prior to rupture.

Objective To limit risk of aneurysm rupture or excessive growth by optimizing ultrasound surveillance intervals.

Data Sources and Study Selection Individual patient data from studies of small AAA growth and rupture were assessed. Studies were identified for inclusion through a systematic literature search through December 2010. Study authors were contacted, which yielded 18 data sets providing repeated ultrasound measurements of AAA diameter over time in 15 471 patients.

Data Extraction AAA diameters were analyzed using a random-effects model that allowed for between-patient variability in size and growth rate. Rupture rates were analyzed by proportional hazards regression using the modeled AAA diameter as a time-varying covariate. Predictions of the risks of exceeding 5.5-cm diameter and of rupture within given time intervals were estimated and pooled across studies by random effects meta-analysis.

Results AAA growth and rupture rates varied considerably across studies. For each 0.5-cm increase in AAA diameter, growth rates increased on average by 0.59 mm per year (95% CI, 0.51-0.66) and rupture rates increased by a factor of 1.91 (95% CI, 1.61-2.25). For example, to control the AAA growth risk in men of exceeding 5.5 cm to below 10%, on average, a 7.4-year surveillance interval (95% CI, 6.7-8.1) is sufficient for a 3.0-cm AAA, while an 8-month interval (95% CI, 7-10) is necessary for a 5.0-cm AAA. To control the risk of rupture in men to below 1%, the corresponding estimated surveillance intervals are 8.5 years (95% CI, 7.0-10.5) and 17 months (95% CI, 14-22).

Conclusion and Relevance In contrast to the commonly adopted surveillance intervals in current AAA screening programs, surveillance intervals of several years may be clinically acceptable for the majority of patients with small AAA.

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THE SURVIVAL RATE FOLLOWING rupture of an abdominal aortic aneurysm (AAA) is only 20%,[1] making AAAs an important cause of mortality. In the United States in 2009, there were 6500 AAA–related deaths.[2] AAAs are usually asymptomatic until rupture occurs. A 10-year randomized trial of ultrasound screening in the United Kingdom reduced ruptured aneurysm–related death rates from 0.87% to 0.46% (relative risk reduction, 48%; 95% CI, 37%-57%).[3] Screening is recommended by the US Preventive Services Task Force for men aged 65 to 74 years who have ever smoked.[4] Following detection of AAA (aortic diameter ≥3.0 cm), the principal surgical strategy is to repair the AAA before rupture occurs. However, elective open AAA repair is associated with a 5% mortality rate.[3] Although the operative risk is lower than 2% for patients undergoing endovascular repair,[5] late complications make the long-term outcomes similar, irrespective of operative approach.[6]

In patients with small AAA (diameter <5.5 cm), the risk of rupture is lower than the risk of surgery and surveillance is indicated.[7] The majority of small AAAs grow slowly, but there is substantial variation in growth rates between different individuals.[8] The intervals between ultrasound surveillance examinations used in randomized trials of screening[3,9] depend on aneurysm size. However, no consensus exists regarding the optimal time intervals between ultrasounds.[10]

Heterogeneity exists in the literature describing AAA growth and rupture, resulting in an inability to aggregate studies.[11,12] Rarely is the variability in growth rates between patients reported, a factor that should be consid-

CME available online at www.jamanetworkcme.com and questions on p 830.

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ered when determining appropriate surveillance intervals.[13] Many studies overestimate growth rates by using statistical methods such as simple linear regression, which does not account for censoring of AAA growth rates at 5.5 cm, above which patients are referred to surgery.[8] The aim of this study was to determine the rates at which small AAAs progress to reach the surgery threshold diameter of 5.5 cm and the risk of AAA rupture over time, to better guide AAA surveillance efforts.

METHODS

Data Collection

Individual patient data were obtained from centers that had AAA surveillance programs or from clinical trials that had recorded these data. Data sets with more than 100 patients, either from randomized trials or from observational studies with consecutive patients, were identified for inclusion by a systematic literature search (MEDLINE, EMBASE on Ovid SP, CENTRAL, clinicaltrials.gov, and controlled-trials.com) through December 2010.[11,12] A manual search of abstracts from vascular surgical meetings held between 2007 and 2010 was also performed. Investigators from each institution or study were contacted. They provided 18 data sets containing repeated ultrasound measurements of AAA diameter over time.

Ultrasound AAA diameter measurement was classified as internal (inner to inner luminal surface) or external (outer to outer aortic wall). A few studies used computed tomography (CT) scans for some AAA measurements. When available, additional information regarding AAA rupture (including death due to rupture), surgical AAA repair, and non-AAA death was collected for each patient. The definition of AAA rupture was based on locally used criteria and reporting. Data sets were cleaned and harmonized by communicating with investigators contributing the data and then collated into a single database.

The Newcastle-Ottawa scale,[14] slightly adapted for our context (eAppendix, available at http://www.jama.com), was used to assess the quality of each study. We used this score and other relevant study characteristics to explain heterogeneity in growth or rupture rates between studies. Individual patient data were not available from 2 randomized controlled trials and 5 other studies totaling 2487 individuals (eTable 1) and data from these studies were not included in our analysis. The systematic literature review was updated to June 2012 to find any later studies for which individual data had not been obtained. All data sets were deidentified, resulting in an ethical waiver as determined by the health technology assessment program of the National Institute for Health Research (United Kingdom).

Patients were included if their abdominal aortic measurement was between 3.0 and 5.4 cm. Their first such measurement was considered as the baseline. Measurements taken prior to a patient reaching a threshold of 3.0 cm were not considered in this analysis. All measurements following the baseline measurement were used until either an aortic rupture or censoring event occurred. Censoring was defined as the first occurrence of: (1) a diameter measurement greater than or equal to 5.5 cm; (2) nonrupture-related death; (3) an elective AAA operation; or (4) the end of available follow-up in each data set. Aortic diameter measurements were not censored if they decreased to less than 3.0 cm. Consequently, some patients had negative growth rates.

Statistical Methods

Growth Rates. For each study, individual aortic growth rates were modeled using Bayesian linear random-effects models[13] (eAppendix). This method allows for individual variation in baseline diameters and growth rates, modeled as correlated random effects from a bivariate normal distribution, and independently normally distributed within-person variation (measurement error). For studies in which both ultrasound and CT scans were used to measure AAA diameter, an adjustment to the CT measurements was estimated within the analysis (noting that scanning modality did not affect the estimated rate of growth[15]). Interaction terms between baseline diameter, growth rate, and sex allowed for estimation of growth rates separately for men and women.

Rupture Rates. A Bayesian joint model of AAA rupture and growth was used[16] (eAppendix). The longitudinal AAA diameter measurements were fitted using a linear random-effects growth model while a proportional hazards model with constant baseline hazard was used for the time-to-event rupture data. A log-linear effect of underlying diameter on risk of rupture was assumed. At least 2 ruptures per study were required to fit these models. The risk of rupture was stratified by sex for studies that recruited both sexes. To account for possible unrecorded loss to follow-up in data sets in some of the studies, a sensitivity analysis was performed in which individuals were censored 2 years after their last AAA diameter measurement.

Meta-analysis. The following quantities were estimated from the growth and rupture models for each study: (1) mean growth rate given a baseline AAA diameter; (2) time taken to reach a 1% to 15% chance of crossing the 5.5-cm threshold for surgery given the baseline diameter; (3) the risk of rupture given the AAA diameter; and (4) time taken to reach a 0.25% to 5% chance of rupture given the AAA diameter (eAppendix). These outcomes were estimated for patients with AAAs between 3.0 cm and 5.4 cm at 0.1-cm intervals, ignoring the risk of competing mortality from non-AAA causes of death. The estimates from each study were combined using random-effects meta-analysis.[17] Overall means, 95% CIs, and 95% prediction intervals for each AAA diameter were calculated. The 95% CIs reflect uncertainty in the estimated mean across all the studies. The 95% prediction intervals encompass the heterogeneity of estimates among studies, and give the range within which values would be expected to lie if another study were done.[18] For AAAs with diameters of 3.0, 3.5, 4.0, 4.5, and 5.0 cm, between-study heterogeneity in growth and rupture rates was quantified using the I^2 measure[19] (the percentage of total variation across studies that is due to heterogeneity rather than chance), and potential study-level sources of heterogeneity were investigated by meta regression taking account of multiple comparisons.[20]

Analyses were conducted using R version 2.15.0 and WinBUGS version 1.4 via user-written code. The rmeta package (version 2.16) was used for meta-analysis and ggplot2 (version 0.9.0) to generate the Figures.

RESULTS

A total of 18 studies containing records from 15 471 individual patients (13 728 men and 1743 women) under surveillance for small AAAs were included in the analyses (eTable 2). Most studies used 5.5 cm as the threshold for surgical intervention, used only ultrasound scans, and recorded external aortic diameters. The average follow-up ranged from 1 to 8 years. Data on ruptures were available in 14 studies. The updated literature review identified only 1 additional study, published in 2012, that included 453 patients with 12 months follow-up.[21]

AAA Growth

In male patients, a 3.0-cm AAA had an estimated mean growth rate of 1.28 mm per year (95% CI, 1.03-1.53; I^2=96%). When the aneurysm diameter was 5.0 cm, the mean estimated growth rate was 3.61 mm per year (95% CI, 3.34-3.88; I^2=89%; TABLE 1). Each 0.5-cm increase in baseline AAA diameter resulted in a 0.59-mm per year increase (95% CI, 0.51-0.66) in mean aortic growth rate (eFigure 1, eFigure 2). Overall, there was substantial heterogeneity in growth rates across studies (I^2 range, 89%-97%), resulting in wide 95% prediction intervals.

Much of the heterogeneity in aortic growth rates between studies is unexplained. Although smokers and nondiabetics have higher growth rates,[15] these factors did not explain the between-study heterogeneity, as adjustment for smoking and diabetes only reduced the overall percentage of variation due to heterogeneity from 97% to 94%. Excluding the 3 studies that measured internal aortic diameters (eTable 2), the pooled mean growth rates decreased by a range of 0.10 mm per year to 0.13 mm per year, depending on baseline diameter, but the percentage of variation due to heterogeneity only decreased by 1% to 3%. There were no significant differences ($P<.05$) in growth rates between studies according to the total Newcastle-Ottawa score (eTable 3), nor any convincing differences ($P<.005$) according to various study quality indicators (eTable 4; clearly specified imaging protocol, measurement variability documented, randomized trials vs observational studies, and an explicit intervention policy).

Table 1. Pooled (Meta-Analysis) Estimates of Abdominal Aortic Aneurysm Growth and Rupture for Men and Women

	AAA Diameter, cm									
	3.0		3.5		4.0		4.5		5.0	
	Mean (95% CI)	95% PI	Mean (95% CI)	95% PI	Mean (95% CI)	95% PI	Mean (95% CI)	95% PI	Mean (95% CI)	95% PI
Growth rate, mm/y										
Men	1.28 (1.03-1.53)	0.17-2.40	1.86 (1.64-2.08)	0.85-2.88	2.44 (2.22-2.65)	1.47-3.41	3.02 (2.79-3.25)	2.00-4.04	3.61 (3.34-3.88)	2.45-4.77
Women	1.46 (1.07-1.85)	0.03-2.89	1.98 (1.65-2.32)	0.75-3.22	2.51 (2.22-2.81)	1.47-3.56	3.06 (2.80-3.33)	2.18-3.95	3.62 (3.36-3.89)	2.79-4.45
Time to breach surgery threshold, y[a]										
Men	7.4 (6.7-8.1)	4.9-11.3	5.0 (4.6-5.4)	3.4-7.1	3.2 (3.0-3.4)	2.3-4.4	1.8 (1.7-2.0)	1.3-2.5	0.7 (0.6-0.8)	0.4-1.2
Women	6.9 (6.1-7.8)	4.5-10.6	4.8 (4.3-5.3)	3.3-6.8	3.1 (2.9-3.4)	2.3-4.3	1.8 (1.7-2.0)	1.3-2.5	0.7 (0.6-0.8)	0.4-1.3
Rate of rupture, per 1000 person-years										
Men	0.5 (0.3-0.7)	0.3-0.7	0.9 (0.6-1.3)	0.5-1.5	1.7 (1.1-2.4)	0.6-4.3	3.2 (2.2-4.6)	1.0-10.0	6.4 (4.3-9.5)	1.7-23.5
Women	2.2 (1.3-4.0)	0.9-5.7	4.5 (2.8-7.2)	2.1-9.7	7.9 (4.5-13.9)	1.7-36.1	14.7 (8.1-27.7)	2.3-95.1	29.7 (15.9-55.4)	3.9-222.9
Time to 1% chance of rupture, y[b]										
Men	8.5 (7.0-10.5)	5.1-14.2	5.5 (4.4-6.8)	2.8-10.7	3.5 (2.8-4.3)	1.8-6.9	2.2 (1.8-2.8)	1.1-4.4	1.4 (1.2-1.8)	0.7-2.8
Women	3.5 (1.9-6.4)	0.8-14.6	2.1 (1.2-3.6)	0.4-11.1	1.4 (0.9-2.1)	0.3-5.8	0.9 (0.6-1.4)	0.2-3.5	0.7 (0.5-1.1)	0.2-3.3

Abbreviation: AAA, aortic abdominal aneurysm; PI, prediction interval.
[a] Time taken to reach a 10% chance that the 5.5-cm threshold for surgery has been crossed.
[b] Time taken to reach a 1% chance of rupture.

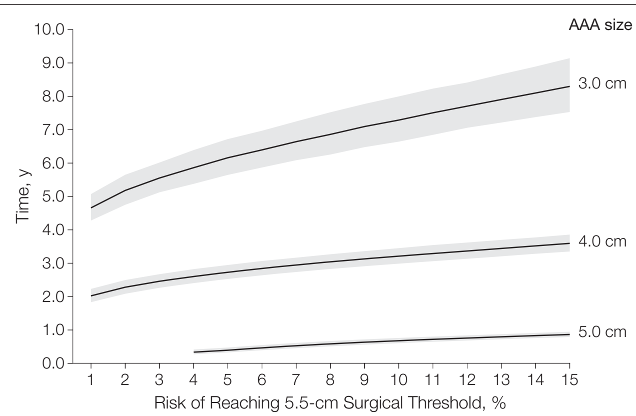
We examined the risk of an AAA growing to 5.5 cm (the commonly adopted threshold for surgery) during the interval between surveillance scans. FIGURE 1 shows the relationship between the time interval between surveillance examinations and the probability of attaining an aortic diameter of 5.5 cm in men, stratified by baseline AAA sizes of 3.0 cm, 4.0 cm, and 5.0 cm. For men with a 3.0-cm AAA, the estimated mean time taken to have a 10% chance of reaching 5.5 cm was 7.4 years (95% CI, 6.7-8.1; I^2=95%). The corresponding mean times for 4.0 cm- and 5.0 cm-AAAs were 3.2 years (95% CI, 3.0-3.4; I^2=96%) and 0.7 years (95% CI, 0.6-0.8 [8 months; 95% CI, 7-10]; I^2=96%), respectively (Table 1). FIGURE 2 shows the length of time taken to have a 10% probability of an aneurysm growing to 5.5 cm stratified by each of the studies contributing to this analysis.[8,22-36] The prediction intervals for the results in Figure 2 were substantially wider than the CIs because of the between-study heterogeneity.

AAA Rupture Rates

Overall, there were relatively few AAA ruptures. There were 178 ruptures among 11 262 men under surveillance and 50 among 1314 women. Crude rupture rates in men in each study varied between 0 and 7.7 ruptures per 1000 person-years (eTable 2). There were 12 studies with at least 2 ruptures available, enabling assessment of the relationship between rupture rates and AAA diameter in men; this was the case for 5 studies in women (eTable 2). Rupture rates in men increased by a factor of 1.91 (95% CI, 1.61-2.25) for every 0.5-cm increase in baseline AAA diameter (eFigure 3 and eFigure 4). The degree of heterogeneity across studies also increased with baseline AAA diameter (I^2 ranged from 0%-82% for diameters 3.0-5.4 cm). There were no significant differences ($P<.05$) in rupture rates between studies as a function of the total Newcastle-Ottawa score (eTable 5), nor convincing differences ($P<.005$) according to various individual-study characteristics (eTable 4), with 1 exception. Rupture rates were lower in studies in which patient censorship was not systematically defined ($P<.001$ for 4.5- and 5.0-cm AAAs). The time taken for men to exceed varying probability thresholds for AAA rupture between scans is shown in FIGURE 3. The time to having a 1% probability of AAA rupture according to aortic diameter is shown in FIGURE 4.* For AAA diameters in the range of 3.0 cm to 4.5 cm, the average time to reach a rupture risk of 1% was at least 2 years (Table 1). For a 5.0-cm AAA, a 1% risk of rupture was reached in approximately 1.4 years (95% CI, 1.2-1.8; I^2=77%).

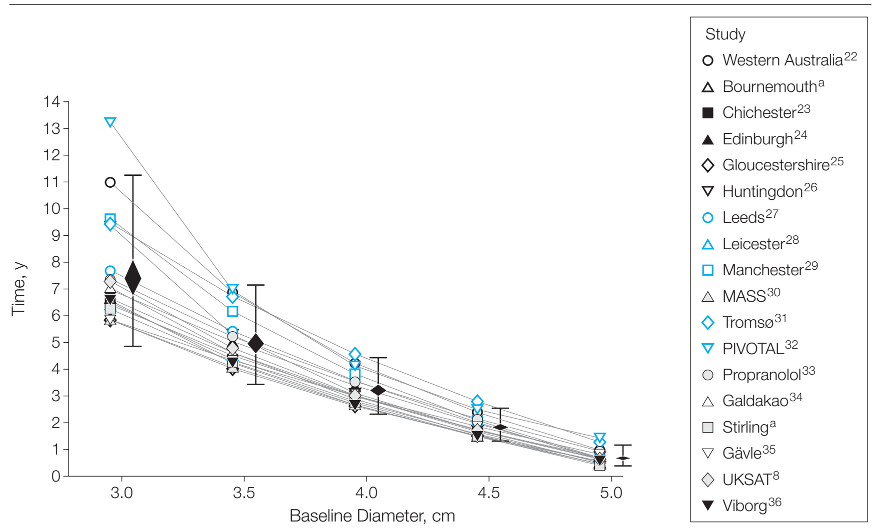
*References 8, 22, 23, 25, 26, 29-31, 33, 34, 36.

Figure 1. Time Intervals Between AAA Surveillance Scans and the Risk of Exceeding 5.5-cm Threshold for Surgery by Baseline AAA Diameter in Men



Time intervals required between abdominal aortic aneurysm (AAA) surveillance scans to limit the probability of reaching a 5.5-cm aortic diameter in men for 3 different baseline diameters (lines indicate meta-analysis estimate and shaded areas indicate 95% CIs).

Figure 2. Estimated Time for Reaching Threshold Diameter for Surgery in Men



Estimated time for which there is a 10% probability of reaching the threshold diameter for surgery (5.5 cm) as a function of baseline diameter and study of origin (in men). Overall results are shown by black diamonds representing 95% CIs and error bars showing 95% prediction intervals. References describe the study methods, with some studies being extended since these publications.

[a] For Bournemouth, patient data were according to S. Parvin, Royal Bournemouth Hospital (written communication, October 16, 2010); and for Stirling, according to R. J. Holdsworth, Stirling Royal Infirmary (written communication, January 27, 2010).

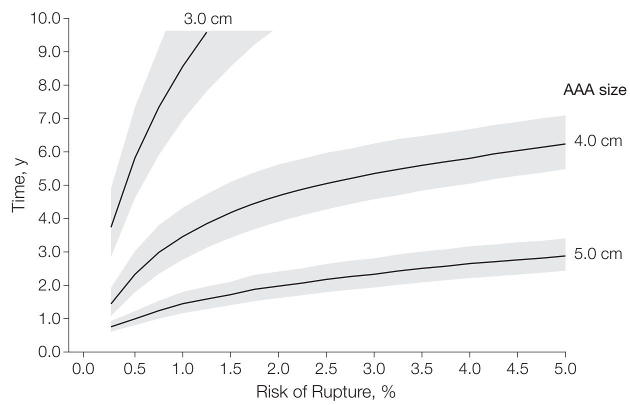
AAA Growth and Rupture in Women

The dependence of growth and rupture rates on AAA diameter was very similar in women and men (eFigure 5 and eFigure 6). Heterogeneity across studies was slightly less for women. However, while absolute growth rates were similar for women and men (particularly for larger baseline AAA diameters), there were marked differences in the absolute risks of rupture. Women had a 4-fold greater rupture risk for all AAA sizes and reached a rupture risk of greater than 1% in a much shorter time than men (Table 1).

Sensitivity Analysis to Length of Follow-up

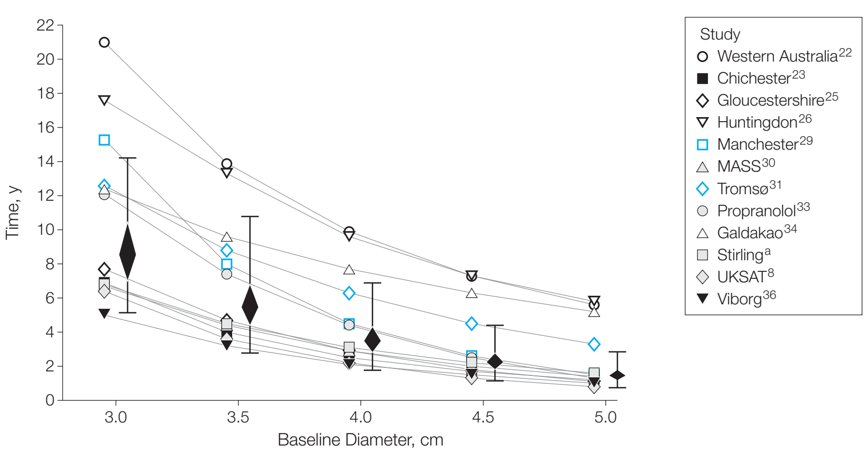
Sensitivity analyses restricting follow-up to a maximum of 2 years following the last AAA scan (eAppendix) did not substantially change the rupture rates reported previously.

Figure 3. Time Intervals Between AAA Surveillance Scans and the Risk of Rupture by Baseline AAA Diameter in Men



Time intervals required between abdominal aortic aneurysm (AAA) surveillance scans to limit the risk of AAA rupture in men for 3 different baseline AAA diameters (lines indicate meta-analysis estimate and shaded areas indicate 95% CIs).

Figure 4. Estimated Time for Reaching 1% Probability of Aneurysm Rupture in Men



Estimated time for which there is a 1% probability of aneurysm rupture as a function of baseline diameter and study of origin (in men). Overall results are shown by black diamonds representing 95% CIs and error bars showing 95% prediction intervals.

[a] For Stirling, patient data were according to R. J. Holdsworth, Stirling Royal Infirmary (written communication, January 27, 2010).

COMMENT

Currently, there is no consensus regarding appropriate surveillance intervals for patients with AAAs (TABLE 2). By pooling results from 18 studies, we quantified AAA growth rates and the AAA rupture risk as a function of aortic diameter. Our intent was to provide an objective basis for selecting surveillance intervals for patients with small AAA. For example, we have shown that the time taken for an AAA of 4.0 cm or less to have a 10% chance of growing to 5.5 cm is at least 3 years. For men with an AAA of 4.0 cm or smaller, it takes more than 3.5 years to have a risk of rupture greater than 1%. Based on these results, the risk of AAA rupture or the need for aortic repair can be objectively determined and guide surveillance interval decision making.

The principal strength of this study is the large volume of individual patient data that were aggregated into a single analysis. Using aortic growth data from a single study of 250 patients, previous authors made recommendations regarding the safety of small AAA surveillance programs.[40] The results we report have the advantage of greater generalizability resulting from pooling of results from many studies. We also used robust statistical techniques, addressing both growth and rupture, that take into account the systematic and random error of differing measurement modalities (ultrasound, computed tomography), the varying growth rates in different individuals, and the differences between studies. From all the studies originally identified, we collated data from 84% of all included patients. The remaining 2500 patients were from studies in which published results appeared generally similar to the studies we assessed. One additional study has been published since the literature search that identified the studies for this meta-analysis was completed[21]; it included 453 patients with 12 months follow-up and would be unlikely to alter our findings, which are based on 15 471 patients with longer follow-up.

Table 2. Abdominal Aortic Aneurysm Surveillance Intervals by Country

Source	Country	Diameter Bands, cm	Surveillance Interval, mo
Stather et al,[37] 2013[a]	Denmark	3.0-5.5	12
National Health Service,[9b]	England	3.0-4.4 4.5-5.4	12 3
Giardina et al,[38] 2011[c]	Italy	3.0-3.9 4.0-4.9	12[c] 6
Stather et al,[37] 2013[a]	New Zealand	3.0-5.5	12
Stather et al,[37] 2013[a]	Norway	3.0-3.9 4.0-4.5 4.5-5.5	24 12 3-6
Stather et al,[37] 2013[a]	Sweden	2.5-2.9 3.0-3.9 4.0-4.4 4.5-5.0 5.1-5.5	60 24 12 6 3
Chaikof et al,[39] 2009[d]	United States[e]	2.5-2.9 3.0-3.4 3.5-4.4 4.5-5.4	60 36 12 6

Abbreviation: CX34, Charing Cross International Symposium.
[a] Data source was CX34. Data were also reported at the Satellite AAA screening meeting, April 15, 2012, 34th Charing Cross International Symposium, London, England.
[b] Same intervals proposed for Northern Ireland, Scotland, and Wales.
[c] CX34 indicated that all surveillance intervals were 6 mo.
[d] Society for Vascular Surgery guidelines were an additional source for this study.
[e] The US Preventive Services Task Force report[4] did not make surveillance interval recommendations.

The current findings have implications for AAA surveillance programs worldwide. Because screening for AAA is becoming established in many countries, there will soon be large numbers of individuals under surveillance for AAA with the large majority having aneurysm diameters between 3.0 and 4.5 cm.[9] Current recommendations for surveillance intervals vary widely (Table 2) although the intervals usually decrease with increasing AAA diameter (for example, 1 year for AAAs measuring 3.0-4.4 cm and 3 months for those measuring 4.5-5.4 cm in the current screening program in England). Based on the lower 95% confidence limits for rupture risk in men from our study, these surveillance intervals could be extended to 3 years for AAAs measuring 3.0 to 3.9 cm, 2 years for 4.0 to 4.4 cm, and yearly for 4.5 to 5.4 cm; the risk of rupture would be maintained at less than 1%. For a US patient with a 3.0-cm AAA detected by screening, this would reduce the average number of surveillance scans from approximately 15 to 7. If the lower 95% prediction limits of the estimates are applied (to acknowledge that the populations in each study may have different growth and rupture rates), surveillance intervals for men could be reduced to once every 2 years for AAAs measuring 3.0 to 3.9 cm, once yearly for 4.0 to 4.9 cm, and every 6 months for 5.0 to 5.4 cm. Using the previous example, this would reduce the average number of surveillance scans required for an AAA measuring 3.0 cm from approximately 15 to 10.

The 4-fold higher rupture rate found for women compared with men is notable, particularly given that both sexes have similar growth rates. The imbalance between sexes in the risk of rupture has been noted previously.[2,15] Differences in anatomy, structure, sex steroids, and smoking habits have all been suggested to play a role in the increased risk of rupture in women.[41] The clinical implication is that a lower AAA diameter threshold for surgery should be adopted for women, a recommendation already made by the joint council of the American Association for Vascular Surgery and Society for Vascular Surgery,[42] but one not yet supported by randomized trial evidence. Since the rupture rate for women with a 4.5-cm AAA is approximately the same as that for a man with a 5.5-cm AAA, a threshold for surgery of 4.5 cm might seem appropriate in women. However, the prescribing of cardioprotective drugs,[43] as well as operative mortality and discharge outcome, appears to be worse in women than men. For instance, the US Medicare database shows that operative mortality after endovascular repair (now the majority procedure) is 3.2% in women vs 1.8% in men, and similar findings have been reported in other studies.[44-46] Further work is therefore required to assess the competing risks of surgery and rupture in women with small AAA before specific recommendations based on patient sex can be made.

The lower heterogeneity across studies in women compared with men might relate to differences in the distribution of body fat and the performance of certain ultrasound probes.[47,48] Other characteristics have been shown to influence growth or rupture rates: smokers and nondiabetics have higher growth rates, while smoking, older age, and higher blood pressure increase rupture risk.[15] In theory, such individual characteristics could be taken into account to tailor surveillance intervals for each individual. However, the effects of such variables are not substantial enough to justify the organizational difficulty that such individualized surveillance strategies would involve. Similarly, AAA measurements preceding the most recent measurement are informative about an individual's rate of AAA growth.[13] However, growth rates can be sporadic and obscured by measurement error.[8] Therefore, taking previous AAA measurements into account appropriately to refine surveillance intervals would be complex, and perhaps impractical in the usual clinical settings of AAA surveillance. Further work is required to determine if there is benefit from adopting a more individualized clinical approach to both surveillance of small AAAs and screening for AAAs.

There are some limitations to this study. First, there was substantial heterogeneity between studies in growth and rupture rates. Despite adjusting for known risk factors for growth and rupture, modality of measurement, and available study-level quality indicators, the majority of this heterogeneity remained unexplained. This heterogeneity is likely due to undefined or unmeasured differences in study methodology or to differences between populations. Although this heterogeneity makes interpretation more difficult, it reveals that analyses based on single data sets may be misleading. If the underlying causes for the differences between studies are biological rather than simply methodological, these may yield insights for developing interventions to lower growth rates in patients with small AAA. Such treatments are not as yet available.[49,50]

A second limitation is the difficulty in ensuring that all rupture events are captured in the data sets used for this analysis. Complete recording of ruptures relies on accurate diagnosis and cause of death information. Precise diagnostic criteria for aneurysm rupture were not provided for any of the contributing data sets, the methods used to determine this outcome were only reported in 2 studies, and only 3 studies had any independent audit of deaths.[12] This may have resulted in underreporting of aneurysm ruptures in some studies. This problem is exacerbated by loss to follow-up implied by lower rupture rates in studies in which patient censorship was not systematically defined. Although a sensitivity analysis restricting follow-up to 2 years following the final AAA scan did not substantially change the results of this study, the surveillance intervals based on aneurysm growth may be more robust than the ones based on rupture risk.

There is a need for more research regarding women with aneurysms in the diameter range of 4.5 to 5.4 cm. Since national rates of AAA rupture are declining, recommended surveillance intervals may need to be reassessed.[15,51-53] There is also a need to establish the cost effectiveness of different surveillance policies. Decreasing surveillance frequency would reduce surveillance costs. However, it may also slightly increase rupture rates and increase patient anxiety. This would decrease overall life expectancy and quality of life in AAA patients under surveillance and increase costs attributable to emergency surgery.

In conclusion, we have demonstrated that most of the smallest AAAs remain quiescent over many years. Our findings suggest that surveillance strategies for small AAAs could be refined to reduce the number and frequency of surveillance scans required.

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Author Contributions: Dr Thompson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Acquisition of data: Bown, Brown, Powell, Thompson.
Analysis and interpretation of data: Bown, Sweeting, Brown, Powell, Thompson.
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Critical revision of the manuscript for important intellectual content: Bown, Sweeting, Brown, Powell, Thompson.
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