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Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals

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Background: **Abdominal aortic aneurysm (AAA) disease is an insidious condition with an 85% chance of death after rupture. Ultrasound screening can reduce mortality, but its use is advocated only for a limited subset of the population at risk.**

Methods: **We used data from a retrospective cohort of 3.1 million patients who completed a medical and lifestyle questionnaire and were evaluated by ultrasound imaging for the presence of AAA by Life Line Screening in 2003 to 2008. Risk factors associated with AAA were identified using multivariable logistic regression analysis.**

Results: **We observed a positive association with increasing years of smoking and cigarettes smoked and a negative association with smoking cessation. Excess weight was associated with increased risk, whereas exercise and consumption of nuts, vegetables, and fruits were associated with reduced risk. Blacks, Hispanics, and Asians had lower risk of AAA than whites and Native Americans. Well-known risk factors were reaffirmed, including male gender, age, family history, and cardiovascular disease. A predictive scoring system was created that identifies aneurysms more efficiently than current criteria and includes women, nonsmokers, and individuals aged <65 years. Using this model on national statistics of risk factors prevalence, we estimated 1.1 million AAAs in the United States, of which 569,000 are among women, nonsmokers, and individuals aged <65 years.**

Conclusions: **Smoking cessation and a healthy lifestyle are associated with lower risk of AAA. We estimated that about half of the patients with AAA disease are not eligible for screening under current guidelines. We have created a high-yield screening algorithm that expands the target population for screening by including at-risk individuals not identified with existing screening criteria. (J Vasc Surg 2010;52:539-48.)**

Rupture of abdominal aortic aneurysm (AAA) is a high mortality event and usually the first and only clinical manifestation of aneurysmal dilatation of the abdominal aorta.[1] The in-hospital survival rate for treating a ruptured AAA (RAAA) is just above 50%, but many patients never have the opportunity for surgical intervention.[2] Aortic aneurysms result in at least 14,000 deaths per year in the United States.[3] This number is likely an underestimation, because approximately 5% of the 200,000 people who die of sudden death each year may have AAA as the cause.[4]

AAAs can be detected noninvasively and relatively inexpensively through ultrasound imaging, which has a sensitivity and specificity of nearly 100% for this disorder.[5] Early detection of AAA can be life-saving, giving patients the opportunity to undergo elective surgical repair, a much safer and effective intervention than emergency repair after rupture. The United States Preventive Services Task Force (USPSTF) has recommended AAA screening for men aged 65 to 75 years with a history of smoking[6] because of the high prevalence of AAA in this population and the demonstrated reduction in AAA-related mortality among those who have been screened.[7-10] However, at least 33% of ruptured AAA hospitalizations and 41% of aortic aneurysm deaths are among women, and 22% of AAA-related deaths occur in nonsmokers.[11-13] For these groups, screening has received a grade D (against) or C (neutral recommendation), respectively, by the USPSTF. Thus, current national guidelines for AAA screening fail to target some of the

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Competition of interest: Dr Manganaro is the Chief Medical Officer and a salaried employee of Life Line Screening, which is the source of the data used in this study, and reports no financial gain or any other material benefits from this publication.

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populations in which a large number of AAA ruptures and deaths occur.

Given the incidence of AAA deaths in women and nonsmokers, a reassessment of the benefits of screening is needed in these populations to determine whether high-risk subpopulations can be identified for targeted screening. Analyzing a cohort of 3.1 million men and women of different racial and ethnic backgrounds, we generated a robust multivariable model for risk stratification. We derived a scoring system from this model and applied it to a detailed independently collected representative national data set to estimate the prevalence of AAA nationwide and address the potential benefits of upgrading selection criteria for screening.

METHODS

Source of data. The AAA screening database was provided by Life Line Screening Inc (LLS, Independence, Ohio) to the Society for Vascular Surgery for purposes of research. The study cohort consists primarily of self-referred individuals who paid for the test out of pocket. Screenings were performed in >20,000 screening sites nationwide. Before screening, individuals complete a 36-item questionnaire including demographics, height and weight, coronary artery disease (previous myocardial infarction or a history of coronary revascularization), cerebrovascular disease (previous transient ischemic attack, stroke, or carotid artery revascularization), hypertension, hypercholesterolemia, diabetes, past revascularizations of coronary, carotid, and lower extremities arteries; and smoking, exercise, dietary habits, and family medical history (first-degree relative diagnosed with AAA, lower extremity arterial disease, cardiac, or cerebrovascular disease).

Hypertension, hypercholesterolemia, or diabetes were deemed present if diagnosed by a physician or controlled with medications, or both. Systolic blood pressure was measured in both upper extremities using Doppler technique. Hypertension was defined as a systolic pressure >140 mm Hg. When side-to-side measurements differed, the higher of the two was used. If an individual reported hypertension in the questionnaire and the measurement was lower or higher than 140 mm Hg, hypertension was defined as “controlled” or “uncontrolled,” respectively. Smoking history, defined as a lifetime use ≥100 cigarettes, was further subdivided by daily cigarette consumption (packs/day), years of smoking, and years from cessation. Height and weight were used to calculate body mass index. The greater of the anteroposterior or transverse ultrasound-based measurements of the infrarenal abdominal aorta was used to identify aortic size. AAA was defined by a diameter of the abdominal aorta ≥3 cm.

The original data set included 4,153,627 screening records obtained from 3,770,285 individuals. To distinguish an individual with multiple screenings, each individual was assigned a unique identifier. The investigators had access only to de-identified “coded” data. The code was not accessible to the investigators. When multiple screenings were performed on the same individual, only the most recent record with complete information was included. The analysis excluded individuals where gender, age, and smoking status were missing and those with past AAA repair. Also excluded were those aged ≥85 years because this is generally a frail group with reduced fitness for surgical intervention where only patients with very large aneurysms may benefit from screening. The final cohort included 3,056,455 screened individuals.

Statistical analysis. To construct a risk model, the screened individuals were allocated into two groups using simple randomization: a data set used for model development (50%) and a data set used for validation (50%). In deriving the model, we first analyzed the univariate associations between AAA and risk factors using χ^2 testing. Variables with a level of significance at $P < 0.2$ were included in logistic regression analysis. Only significant variables at $P < .05$ were left in the final model. The diagnostic properties of the final model obtained on the development data set were tested on the validation data set.

The area under the receiver operator curve (ROC) was calculated to assess predictive ability. From the best fitting model to predict AAA, we created a simplified scoring system based on the regression coefficients. To derive the score, the coefficient of each risk factor was divided by the absolute value of the lowest coefficient and then rounded to the nearest integer. For example, if we divide the coefficient of high cholesterol (0.29) for the coefficient of fruit and vegetable (0.1), we obtain 3 as the score for high cholesterol. The total risk score for a person is the sum of the scores for each individual risk factor. The AAA risk associated with the total risk score represents the average risk among all individuals having the same total score. The scoring system was validated by comparing the predicted AAA prevalence with the observed prevalence in the validation data set. The discriminative ability of the scoring system was evaluated by analysis of the ROC curve. All statistical analyses were performed using the SAS 9.1 software (SAS Institute Inc, Cary, NC).

Estimation of national AAA prevalence. The prevalence of risk factors in the general U.S. population was derived from the National Health and Nutrition Examination Survey (NHANES, 2003-2006), a cross-sectional survey of the civilian noninstitutionalized U.S. population performed by the National Center for Health Statistics. NHANES does not include a test for aortic aneurysms, making it impossible to estimate AAA prevalence based on NHANES alone. Common data elements in NHANES and the LLS data set allowed us to “crosswalk” between the two data sets. These elements include coronary artery disease, cerebrovascular history, smoking history (cigarettes/day, years of smoking, years since quitting), high blood pressure, high cholesterol, diabetes, family history of coronary artery disease or stroke, frequency of exercise, and demographic information. However, family history of AAA and carotid disease are recorded in the LLS cohort but not in NHANES, and peripheral arterial disease (ankle-brachial index <0.9) is not available for all years examined in this study.

These limitations required the development of a new risk model, based only on variables present in both NHANES and the LLS cohort. This new model was developed and validated using the development and validation subsets of the LLS cohort as described above. The discriminative ability of this model was excellent (C statistic = 0.886). A scoring system was then derived and applied to the NHANES database to calculate the score distribution in the U.S. population and to estimate the number of AAAs.

RESULTS

Characteristics of the study population. This analysis includes 3.1 million patients aged <85 and without previous AAA surgery that were screened by LLS throughout the United States between 2003 and 2008. The mean age of the screened cohort was 63.1 years, with 80% of individuals aged >55 years. Although most screenings were from people of white race (87%), there were also significant numbers of individuals from other racial and ethnic groups, including Hispanics, African Americans, Native Americans, and Asians.

Hypertension and high cholesterol were the most prevalent comorbidities, affecting more than half of the cohort, and 58% of those who had been diagnosed with hypertension or had been taking antihypertensive medications also had high blood pressure (HPB) at the screening visit (uncontrolled HBP group). More than half of the cohort exercised at least once weekly and consumed fruits and vegetables more than 3 times per week. Two-thirds of the cohort were overweight or obese (BMI >25). Smokers comprised 42.8% of the cohort. Most AAAs were in smokers and men; however, 19.8% of all AAAs were found in nonsmokers and 20.7% in women (Table I). The distribution of maximum aortic diameter by age among those with AAA was examined (Fig 1). There was no difference in age distribution between patients with different size aneurysms.

Risk of AAA. The effect of smoking history on the risk of AAA was analyzed in detail: it was higher for current smokers than past smokers, it increased with duration of smoking (Fig 2, *A*) and quantity of cigarettes smoked per day (Fig 2, *B*), and it declined over time after quitting (Fig 2, *C*). Consumption of fruit, vegetables, nuts, and fish showed a strong dose-dependent and inverse correlation with respect to AAA prevalence in an age-adjusted analysis (Fig 2, *D*), whereas red meat and processed or fast food were associated with increased AAA prevalence, although this effect did not remain significant in multivariable analysis. The multivariate logistic regression model for predicting AAA and the resultant scoring system are reported in Table II.

The discriminative ability of the risk model assessed by area under the ROC curve was excellent (C statistic = 0.893). The risk factors that remained significantly associated with AAA were age, gender, high blood pressure, coronary artery disease, family history of AAA, high cholesterol, lower extremity peripheral arterial disease, carotid disease, history of a cerebrovascular event, smoking, and being overweight or obese. A negative association with AAA was found for certain racial and ethnic groups, diabetes, exercise at least once per week, and consumption of fruit, vegetables, and nuts more than three times per week. The risk attributable to smoking varied over a wide range: the lowest risk was for individuals who smoked up to a half-pack/day for <10 years and quit >10 years ago, whereas the highest risk was for current smokers who had been smoking >1 pack/day for >35 years. Correspondingly, the risk score associated with smoking ranged from 1 to 26. Smoking was among the strongest predictors of AAA, along with age, gender, and family history of AAA.

Overall, the scores of different predictors ranged from −4 for Hispanics and Asians to 35 for individuals aged 80 to 84. The total risk score for an individual is obtained by summing the scores of all the individual risk factors; for example, a 65-year-old man, past smoker with no other risk factors, who quit smoking >10 years ago and smoked up to half a pack for no longer than 10 years, has a score of 42. The relationship between the probability of AAA and the score is shown in Fig 3, *A*. The agreement between predicted and observed AAA was very strong, as shown by the correlation coefficient ($r^2 = 0.98$; $P < .001$). The overall accuracy of the score is illustrated by the area under the ROC curve (C statistic = 0.842; Fig 3, *B*).

Prevalence of AAA in the United States. To estimate the prevalence of AAA in the adult population, we applied to the NHANES data a modified version of the scoring system including only the common variables between the LLS and NHANES data sets. Different cut points or scores for our new scoring system were compared with the current USPSTF recommendations, and we determined with each strategy (1) the total number of AAAs identified, (2) the number of screenings per AAA found, (3) the prevalence of AAA in the targeted group, and (4) the number of AAAs found in women, nonsmokers, and individuals aged <65 (Table III).

We estimated that there are about 1.1 million AAAs (prevalence, 1.4%) in the population aged 50 to 84. USPSTF selection criteria (men with smoking history, aged 65-75) capture 29.5% of these AAAs, targeting a cohort with AAA prevalence of 4.9%. None of the AAAs identified in this manner, by USPSTF definition, occur in women, nonsmokers, or people aged <65 years. Conversely, the use of the newly developed scoring system, with a cutoff of 42, where the system has the best discriminative ability (shortest distance from the point where sensitivity = 1 and specificity = 1), would identify 88.6% of all AAAs, if applied to a population aged 50 to 84 years, or 59%, if applied to people 50 to 75 years old. Such a cutoff would include not only the lowest-risk individuals captured by USPSTF recommendations (65-year-old male smokers, with no other risk factors, who smoked <0.5 pack/day and quit >10 years ago: score, 42) but also women, nonsmokers, and people aged <65.

Table I. Characteristics of the Life Line Screening cohort

	Screened population		
Variables	*Without AAA (N = 3,033,009)*	*With AAA (N = 23,446)*	P
Gender			
Females	65.07%	20.66%	<.0001
Males	34.93%	79.34%	<.0001
Mean age (95% CI)	62.98 (62.97-62.99)	71.10 (71.08-71.20)	<.0001
Age groups			
<55	20.24%	1.83%	<.0001
55-59	15.99%	4.87%	<.0001
60-64	19.19%	13.26%	<.0001
65-69	16.97%	20.14%	<.0001
70-74	13.24%	23.48%	<.0001
75-79	9.48%	22.07%	<.0001
80-84	4.88%	14.28%	<.0001
Race/ethnicity			
White	86.78%	90.73%	<.0001
Hispanics	2.37%	0.86%	<.0001
African-American	2.93%	1.48%	<.0001
Asian	1.92%	0.74%	<.0001
Native American	2.40%	2.93%	<.0001
Other race	3.59%	3.26%	.0060
Marital status			
Married	68.52%	69.53%	.0009
Single	8.08%	6.48%	<.0001
Divorced	8.75%	6.99%	<.0001
Widowed	11.83%	14.02%	<.0001
Status unknown	2.81%	2.96%	.1437
Smokers	42.47%	80.22%	<.0001
Current smokers	10.68%	28.09%	<.0001
Past smokers	31.79%	52.14%	<.0001
High blood pressure	65.02%	81.51%	<.0001
Controlled	19.49%	22.86%	<.0001
Uncontrolled	27.09%	38.61%	<.0001
Unaware	18.44%	20.05%	<.0001
High cholesterol	53.89%	68.06%	<.0001
Coronary artery disease	6.72%	26.69%	<.0001
Carotid disease	2.48%	9.76%	<.0001
Cerebrovascular history	5.47%	13.32%	<.0001
Peripheral arterial disease	2.96%	12.56%	<.0001
Diabetes	10.69%	13.83%	<.0001
Family history			
Coronary artery disease	17.66%	22.52%	<.0001
Stroke	9.38%	10.01%	.0009
AAA	2.48%	7.95%	<.0001
Peripheral arterial disease	2.91%	3.01%	.3550
Body mass index, kg/m^2			
Underweight, <20	1.18%	1.20%	.8260
Normal, 20-25	30.20%	23.87%	<.0001
Overweight, >25	66.73%	73.30%	<.0001
Unknown	1.89%	1.63%	.0039
Fast food, >3 times/wk	3.26%	2.75%	<.0001
Fruit & vegetables, >3 times/wk	56.00%	41.27%	<.0001
Fish, >3 times/wk	7.78%	7.04%	<.0001
Nuts, >3 times/wk	27.71%	23.32%	<.0001
Meats,[a] >3 times/wk	20.96%	22.90%	<.0001
Exercise, ≥ once/wk	56.00%	47.59%	<.0001

AAA, Abdominal aortic aneurysm.
Frequency distribution of demographics, comorbidities and life style variables among people diagnosed with and without AAA.
[a]Red and processed meat.

Using more stringent selection (higher scores), we calculated if the detection of AAA would be improved compared with USPSTF criteria. A cutoff at a score of 65 in the population aged 50 to 75, for example, would capture approximately the same number of AAAs as the USPSTF criteria (337,000 vs 334,000) but using fewer ultrasound studies (16 vs 20 per one AAA identified). Alternatively, a cutoff at a score of 58, which requires the same number of

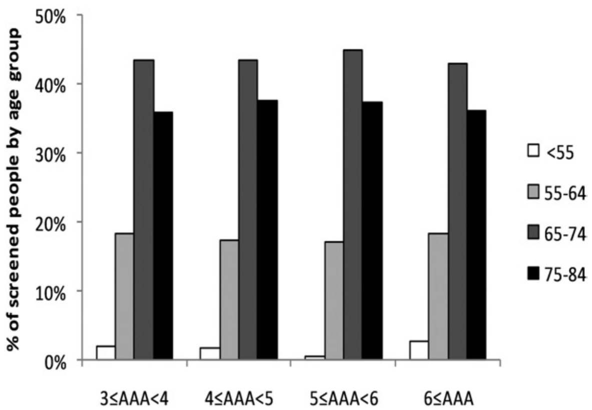

Fig 1. Distribution of screened people by age groups and abdominal aortic aneurysm *(AAA)* size. Number of people with AAA from 3 cm to <4 cm, 17,109; from 4 cm to <5 cm, 4093; from 5 cm to <6 cm, 1519; 6 cm and up, 725.

ultrasound studies to detect a AAA, as the USPSTF criteria in the population aged 50 to 75, would identify more AAA patients (480,000) and include women, nonsmokers, and people aged <65 years.

DISCUSSION

Screening for AAA, followed by surgery, saves lives, as has been demonstrated in four randomized clinical trials, with a decrease in AAA-related mortality of about 50%.[7-10] However, to design a screening program that is cost-effective, accurate risk stratification is critical to increase the likelihood of disease detection. Our study, which includes >3 million individuals, is the largest to date that stratifies risk for AAA (approximately 25 times the number of patients included in the next largest study).[14] The size of this cohort has allowed a detailed evaluation of all of the variables associated with AAA and the definition of a population that is truly high-risk.

Smoking is the major environmental risk factor for AAA, enhancing the chance of developing AAA as well as the risk of rupture.[14-16] With the current criteria for AAA screening, smoking is treated as a binary variable. However, we found that AAA had a strong positive association with quantity and duration of smoking and an inverse association with the years after smoking cessation. For example, the risk of AAA in a current smoker of <10 years is one-eighth the risk of a smoker of >35 years (Fig 2, *A*). Moreover, the risk of AAA in an individual who smokes ≤0.5 pack/day is one-third the risk of a smoker of >1 pack/day (Fig 2, *B*). Interestingly, the prevalence of AAA diminished with the years of abstinence from smoking. It is therefore not surprising that the inclusion of data regarding smoking patterns greatly enhanced the accuracy of our risk model for AAA.

Our findings reinforce the well-known fact that AAA prevalence is significantly lower in women than in men. However, despite having one-fifth the number of AAAs as men, women constitute approximately one-third of all AAA ruptures and almost as many deaths as men.[17] No doubt, screening programs directed exclusively at the male population contribute to this phenomenon. With application of our model to the U.S. population, we have identified a subset of women with multiple cardiovascular risk factors where the prevalence of AAA is high and screening is warranted.

We observed that the consumption of fruit, vegetables, and nuts, as well as regular exercise, reduced the risk of AAA. It remains possible that diet and exercise are surrogates for other important and unmeasured factors that contribute to a healthy lifestyle. Nevertheless, these are the first data available that demonstrate that lifestyle, independently from other risk factors, can affect the formation of AAA. Further reinforcing the role of lifestyle, we found that a BMI > 25 kg/m^2 increased the risk of AAA. It is important to note that the effects of BMI and lifestyle were small compared with those of age, gender, and smoking.

Our analysis confirms a significant association between AAA and hypertension, hypercholesterolemia, as well as pre-existing atherosclerotic occlusive disease in various vascular beds. The influence of elevated blood pressure and lipids on AAA is substantially less than the influence of these risk factors on atherosclerotic occlusive disease. This, along with the negative association of diabetes and AAA, suggests a very different pathophysiology for these two disease processes. Also worth noting is that blood pressure control was inadequate in 58% of individuals with known hypertension at the time of the screening event.

Previous reports have shown an inverse association between African American race and prevalence of AAA.[18-20] We confirm this observation and additionally demonstrate that Hispanics and Asians have a lower prevalence of AAA than whites after adjusting for all other known risk factors. No significant differences were noted between Native American and whites. These findings would suggest that disparities in access to preventive care are not responsible for the observed differences of AAA prevalence among different racial and ethnic groups.

Knowledge of the risk factors for AAA is of little practical value unless this information can be formulated in a manner that helps the practicing physician determine which patients should be screened. Accordingly, we integrated our data into a scoring system to predict the likelihood of an individual having an AAA. Before being considered useful in clinical practice, the scoring system will need to be tested and validated in other well-defined populations. However, if validated, this prognostic tool could be used by programs that offer a one-time ultrasound screening benefit to qualified seniors to improve the selection of the target population. The criteria currently used by Medicare at the "Welcome to Medicare" physical examination are men with a smoking history or individuals with a family history of aneurysm disease.[21] The scoring system derived in this study could permit the inclusion of women and nonsmokers and extend the benefit of screening to individuals of various ages while excluding men who are not truly high-risk.

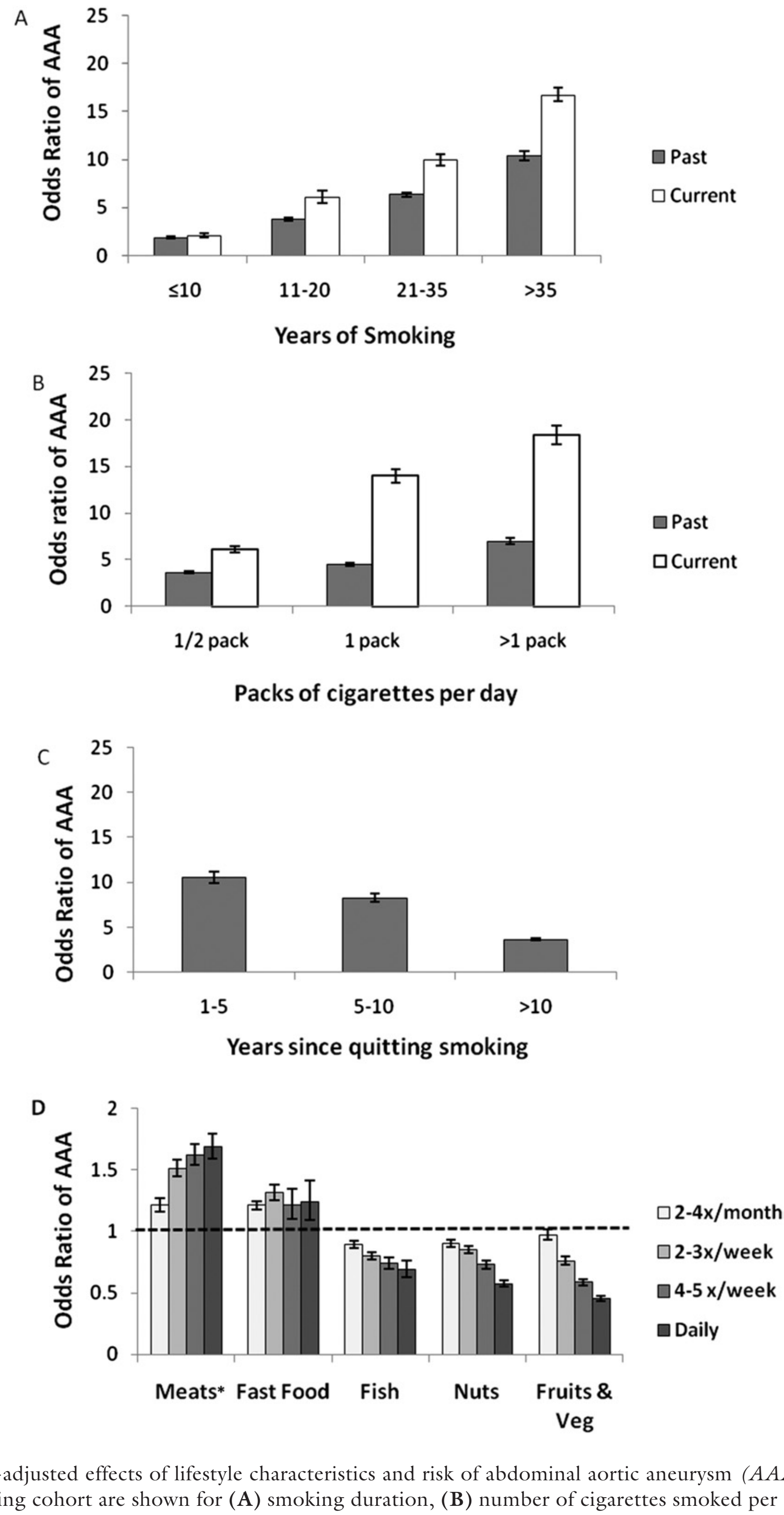

Fig 2. Age-adjusted effects of lifestyle characteristics and risk of abdominal aortic aneurysm *(AAA)* in the Life Line Screening cohort are shown for **(A)** smoking duration, **(B)** number of cigarettes smoked per day, **(C)** time elapsed since quitting, and **(D)** different dietary habits on the risk of AAA. Reference groups are once per month or less for food consumption and no smokers for all smoking variables. *Meats: Processed and red meats. The *vertical error bars* show 95% confidence intervals.

Table II. Results of multivariable regression analysis for predictors of abdominal aortic aneurysm *(AAA)*

Variable	*Estimate*	P	*OR*	*95% CI*	*Score*
Male (vs female)	1.74	<.0001	5.71	5.57-5.85	18
Age (vs <55)					
55-59	1.01	<.0001	2.76	2.55-3.00	11
60-64	1.68	<.0001	5.35	4.97-5.76	17
65-69	2.24	<.0001	9.41	8.76-10.12	23
70-74	2.67	<.0001	14.46	13.45-15.55	28
75-79	3.02	<.0001	20.43	18.99-21.99	31
80-84	3.35	<.0001	28.37	26.31-30.59	35
Race/ethnicity (vs white)					
Hispanic	−0.37	<.0001	0.69	0.62-0.77	−4
African American	−0.33	<.0001	0.72	0.66-0.78	−3
Asian	−0.41	<.0001	0.72	0.59-0.75	−4
High blood pressure	0.22	<.0001	1.25	1.21-1.28	2
Coronary artery disease	0.54	<.0001	1.72	1.69-1.76	6
Family history of AAA	1.34	<.0001	3.80	3.66-3.95	14
High cholesterol	0.29	<.0001	1.34	1.31-1.37	3
Diabetes	−0.29	<.0001	0.75	0.73-0.77	−3
Peripheral arterial disease	0.47	<.0001	1.59	1.54-1.65	5
Carotid disease	0.41	<.0001	1.51	1.46-1.56	4
Cerebrovascular history	0.16	<.0001	1.18	1.14-1.21	2
Smoking, packs/day					
≤10 yrs					
<0.5	0.96	<.0001	2.61	2.47-2.74	10
0.5-1	1.16	<.0001	3.19	2.93-3.46	12
>1	1.16	<.0001	3.20	2.88-3.56	12
11-20 yrs					
<0.5	1.58	<.0001	4.87	4.63-5.12	16
0.5-1	1.76	<.0001	5.79	5.48-6.12	18
>1	1.79	<.0001	6.00	5.66-6.35	19
21-35 yrs					
<0.5	1.99	<.0001	7.29	6.97-7.64	21
0.5-1	2.08	<.0001	7.99	7.62-8.38	22
>1	2.13	<.0001	8.41	8.57-9.36	22
>35 yrs					
<0.5	2.19	<.0001	8.96	8.57-9.36	23
0.5-1	2.42	<.0001	11.19	10.76-11.64	25
>1	2.50	<.0001	12.13	11.66-12.61	26
Quit smoking					
<5 yrs ago	−0.14	<.0001	0.87	0.84-0.912	−1
5-10 yrs ago	−0.39	<.0001	0.68	0.65-0.71	−4
>10 yrs ago	−0.87	<.0001	0.42	0.41-0.43	−9
Fruit & veg, >3 times/wk	−0.10	<.0001	0.91	0.88-0.92	−1
Nuts, >3 times/wk	−0.11	<.0001	0.90	0.89-0.93	−1
Exercise, ≥1 time/wk	−0.15	<.0001	0.86	0.85-0.88	−2
BMI ≥25 kg/m^2	0.18	<.0001	1.20	1.17-1.22	2

BMI, Body mass index; *CI,* confidence interval; *OR,* odds ratio.
The model was developed on 50% of the Life Line Screening cohort and validated on the other 50%. The area under the receiver operator curve (ROC) of the model (C statistic) was 0.893. From this model a scoring system was derived as described in materials and methods. The overall accuracy of the scoring system as measured by the C statistic was 0.842.

Using the NHANEs data to integrate our model into the U.S. population, we estimate that there are approximately 1.1 million individuals aged between 50 and 85 with aneurysms. Importantly, a substantial number of women, nonsmokers, and people <65 with multiple comorbidities (approximately 569,000 of the 1.1 million) have a risk of AAA equivalent to or greater than that of 65-year-old male ever-smokers, the population currently recommended to have AAA screening by the USPSTF. Many of these at-risk individuals can be efficiently identified using the scoring system that has emanated from this analysis. As reported in Table III, the proposed system has the theoretic potential to identify a greater number of aneurysms in a broader group of individuals and achieve a more favorable ultrasound/aneurysm ratio than the existing criteria of men with a smoking history.

Contrary to the apparent advantage of identifying aneurysms in patients aged <65, the value of screening for AAA in the elderly is less clear. For example, the discovery of a 3-cm aneurysm in an 83-year-old may be of little practical importance. One alternative might be to create screening criteria for individuals >75 years of age with the goal of identifying 5.5-cm rather than 3-cm aneurysms. Another alternative could be to avoid rigid age definitions

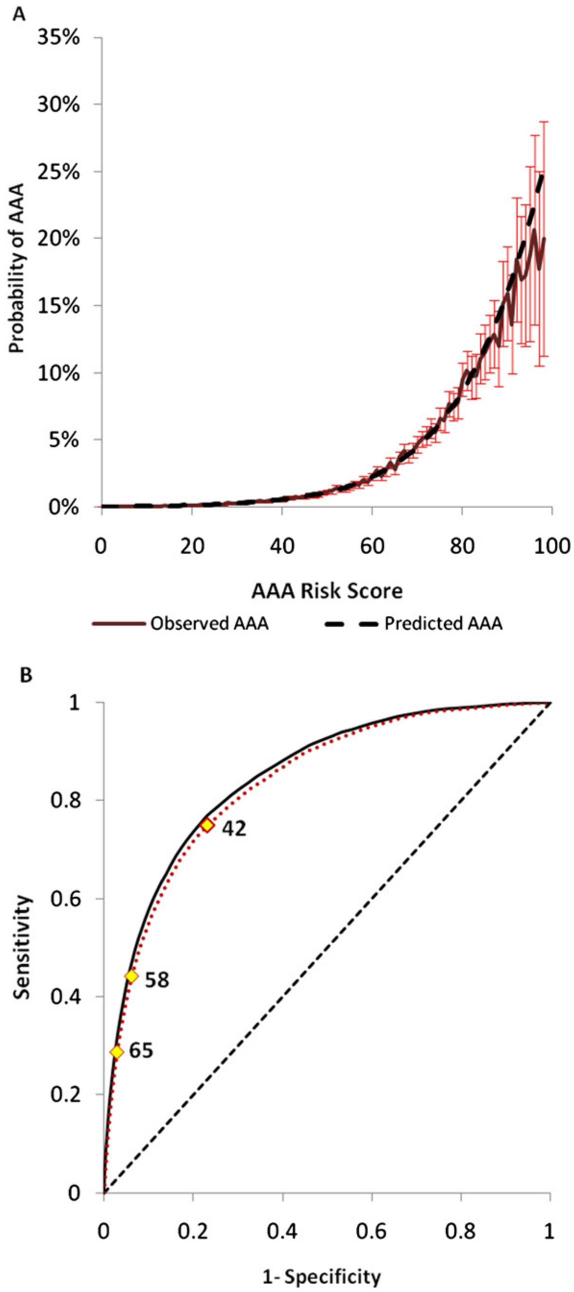

Fig 3. Validation and discriminative ability of the risk score to predict abdominal aortic aneurysm *(AAA)*. **(A)** Observed vs predicted probability of AAA as a function of total risk score. Predicted and observed probabilities were calculated using development and validation subsets (50% each) of the Life Line Screening cohort. The *vertical error bars* show 95% confidence intervals for the observed curve. **(B)** Receiver operating characteristic (ROC) curves of AAA risk score *(continuous line)* and risk score adapted for National Health and Nutrition Examination Survey (NHANES; *dotted red line)*. The performance of screening using cutoff points of 42, 58, and 65 is shown (NHANES version); 42 has the highest discriminative ability (closest point to sensitivity = 1 and specificity = 1). The *diagonal dashed line* represents a predictive accuracy no better than chance.

regarding who should be screened, but to allow primary care physicians to select patients who would benefit from identification of an aneurysm with the goal of excluding those with poor longevity or high operative mortality. Of note, gender is an important companion variable when considering age limits for screening. The average life expectancy for women is significantly longer than for men; thus, identifying aneurysms in a cohort of healthy elderly women may be of value.

A lower threshold score for screening will identify a greater number of aneurysms but will require a larger number of ultrasound studies as well as follow-up testing. For example, focusing only on the cost of the initial screening test, a score of ≥42 will allow identification of 680,000 aneurysms in the population aged 50 to 75 but at the expense of performing 24,907,000 ultrasound studies. Conversely a score of >65 will identify roughly half as many aneurysms but will require only one-fifth the number of ultrasound studies. The threshold score that is chosen will be a critical decision that will depend on many factors, with cost and ultimately cost-effectiveness leading the list.

Our study capitalizes on the unique size of the cohort of individuals screened by LLS to gain important insights about the risk of AAA; however, there are limitations. This cohort consists primarily of self-referred individuals. Individuals who are concerned with their health and engaged in taking preventive health measures, such as screening for vascular disease, typically tend to be from a higher socioeconomic status and may not be representative of the general population. Moreover, given that the cost of screening is generally not reimbursed by insurance, this population is also characterized by their willingness to pay out of pocket for the screening visit. The potential confounding due to self-selection of a specific class of individuals, however, may be reduced by controlling for a number of variables, such as dietary habits and level of exercise, that reflect individual socioeconomic status. We also estimated the prevalence of AAA using frequencies of risk factors extracted from the NHANES cohort, a sample designed to be nationally representative. This estimate rests on the assumption that the associations between AAA and risk factors found in the LLS cohort are applicable to the NHANES sample.

A second limitation is that this study relies on self-reporting of lifestyle variables and some risk factors, which may lead to misclassification. However, misclassification would likely bias results toward a lack of significance or toward elimination of dose-dependent effects, whereas we observed strong associations and dose responses for health promoting factors as well as for factors having a negative impact on health.

CONCLUSIONS

This study provides new and important insights into the epidemiology of AAA. Our results confirm the importance of previously known risk factors and identify new positive and negative predictors such as weight, diet, and race. Importantly, we integrate this information into a

Table III. Comparative efficacy of differing abdominal aortic aneurysm *(AAA)* screening strategies

Screening strategy	*AAA prevalence*	*People requiring screening (×1000)*	*Screens per AAA found*	*AAAs detected (×1000)*			
				All	*Females*	*No smokers*	*Age ≤64*
1. All people Age 50-84	1.40%	81,024 (100%)	71	1134 [963-1304] (100%)	234 [195-272] (20.60%)	147 [120-174] (13.00%)	329 [270-388] (29.00%)
2. USPSTF Age 65-75	4.90%	6846 [5711-7980] (8.40%)	20	334 [282-387] (29.5%)	0	0	0
3. Score ≥42 Age 50-75	2.70%	24,907 [21,026-28,789] (30.70%)	37	680 [575-785] (59.90%)	88 [71-104] (7.70%)	37 [27-46] (3.20%)	247 [197-296] (21.70%)
4. Score ≥58 Age 50-75	4.90%	9770 [8276-11,265] (12.10%)	20	480 [405-555] (42.3%))	21 [17-24] (1.80%)	2 (0.20%)	143 [110-177] (12.60%)
5. Score≥65 Age 50-75	6.40%	5241 [4333-6149] (6.50%)	16	337 [278-397] (29.8%)	5 [4-6] (0.40%)	0	84 [58-109] (7.40%)
6. Score ≥42 Age 50-84	3.10%	32,553 [27,562-37,544] (40.20%)	32	1005 [850-1,159] (88.6%)	154 [124-183] (13.50%)	74 [57-90] (6.50%)	247 [197-296] (21.70%)
7. Score ≥58 Age 50-84	5.40%	14,070 [12,030-16,109] (17.40%)	19	754 [639-869] (66.5%)	55 [47-64] (4.9%)	15 [12-17] (1.30%)	143 [110-177] (12.60%)
8. Score ≥65 Age 50-84	7.00%	8109 [6893-9324] (10.00%)	14	566 [476-656] (49.9%)	22 [19-24] (1.9%)	2 (0.20%)	84 [58-109] (7.40%)

USPSTF, United States Preventive Services Task Force.
The first column identifies the various AAA screening strategies, including all adult U.S. population ages 50-84 (row 1), the USPSTF recommendations of men ages 65-75 with smoking history (row 2), varying threshold scores on people age 50-75 (rows 3-5) or age 50-84 (rows 6-8). For these various strategies we have determined AAA prevalence, number of people requiring screening, number of ultrasound screens per one AAA found, and the number of people with AAA detected overall and in specific subgroups. The 95% confidence intervals are shown in brackets. Percentages in columns "People requiring screening" and "AAAs detected" are reported vs total population and total AAAs, respectively. The total number of females, nosmokers, and patients aged 50-64 with AAA was calculated at 569,000 (95% CI, 476,000-663,000).

scoring system that may permit clinicians to perform tailored risk estimations in a primary care setting. When we extrapolated our results to the general population, our projections showed that a substantial group of high-risk individuals, including subsets of women, nonsmokers, and patients aged <65, are excluded from screening using current criteria. These data offer critical evidence to support the refinement of AAA screening strategies to more accurately target individuals at risk and motivates validation of this new screening tool using prospective methods.

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AUTHOR CONTRIBUTIONS

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Statistical analysis: NE
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INVITED COMMENTARY

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This is an important article. These results will expand our knowledge, inform future study, and drive government policy. Critics will point out that the data set is flawed and that the application of the scoring system to the National Health and Nutrition Examination Survey (NHANES) data is speculative. They are correct on both counts, but these criticisms do not negate the value of this report.

The demographic and lifestyle data reported here consist of unconfirmed, nonvalidated, self-reported information provided to a third party by a self-selected population of people sufficiently motivated by health concerns to pay out of pocket for a heath screening. Nevertheless, the shear size of this data set provides the authors with significant statistical power to confirm known associations, to refine our understanding of specific relationships, and to identify potential new factors that will benefit from additional study. The interaction of the quantity and duration of tobacco use with abdominal aortic aneurysm (AAA) risk could certainly have been hypothesized, but these effects have not been demonstrated in multiple, smaller, well-designed studies published previously. In particular, the negative association of AAA risk with the duration of smoking abstinence is both welcome and unexpected.

The application of the new scoring scheme to the NHANES data is indeed a formal exercise and somewhat of a stretch. However, this "exercise" clearly illustrates the tremendous impact that initial conditions and selection criteria can have on the costs and effectiveness of a preventative health service such as AAA screening. Prospective studies will be needed to confirm the assertions of the authors' report, but this analysis will influence the direction of current government-supported screening programs for AAA as well as the health promotion activities of private organizations and payers. There are simply no comparable alternative data available today to inform public policy in this area.

The reader is correct to be somewhat skeptical of drawing broad conclusions from an analysis of large data sets collected for payment or other purposes, but these data and this report clearly point out the power of large numbers when properly analyzed. Vascular experts should embrace the appropriate conclusions of this study and look to creative analysis of other large data sets with relevance to vascular disease. Personal, institutional, and regional experiences, although informative, are simply inadequate in a time when health policy will be driven by cost-benefit and outcomes analysis applied across populations at risk.