

Clinical Study

Percentage of Deaths Attributable to Poor Cardiovascular Health Lifestyle Factors: Findings from the Aerobics Center Longitudinal Study

Xuemei Sui,¹ Hongjuan Li,² Jiajia Zhang,³ Li Chen,⁴ Ling Zhu,⁵ and Steven N. Blair^{1,3}

¹ Department of Exercise Science, Arnold School of Public Health, University of South Carolina, 921 Assembly Street, Columbia, SC 29208, USA

² Beijing Sport University, Beijing 100084, China

³ Department of Biostatistics and Epidemiology, Arnold School of Public Health, University of South Carolina, Columbia, SC 29208, USA

⁴ Markey Cancer Center, University of Kentucky, Lexington, KY 40536, USA

⁵ Department of Health Examination Center, Beijing Hospital, Beijing 100050, China

Correspondence should be addressed to Xuemei Sui; msui@mailbox.sc.edu

Received 2 April 2013; Accepted 2 July 2013

Academic Editor: Jaume Marrugat

Copyright © 2013 Xuemei Sui et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Purpose. We assessed the effects of the four newly defined American Heart Association (AHA) lifestyle factors on mortality by examining the associated population attributable fractions (PAFs) of these factors. **Methods.** Slightly modified AHA cardiovascular health factors (smoking, body mass index, cardiorespiratory fitness, and diet) were measured among 11,240 (24% women) participants from the Aerobics Center Longitudinal Study between 1987 and 1999. The cohort was followed to December 31, 2003, or death. PAFs were calculated as the proportionate reduction in death attributable to identified risk factors. **Results.** During an average 12 years of followup, 268 deaths occurred. Low fitness had the highest PAFs at the 5th, 10th, and 15th year of followup, respectively: 6.6%, 6.4%, and 5.5%. Current smokers had the second highest PAFs at the 5th, 10th, and 15th year of followup, respectively: 5.4%, 5.2%, and 5.0%. Additional adjusting for other confounders in the model did not change the above associations. The PAFs for overweight or obesity and unhealthy diet were not significant in the current analyses. **Conclusions.** Assuming a causal relationship between smoking, low fitness, and mortality, avoidance of both would have prevented 13% of the deaths in the current population. Preventive interventions to increase physical activity and stop smoking would most likely promote longevity.

1. Introduction

Cardiovascular disease (CVD) continues to be the leading cause of death in the United States with an average of 1 death every 39 seconds and an estimated direct and indirect cost of \$286.6 billion [1]. Recently, the American Heart Association (AHA) 2020 Impact Goal defined a new construct of cardiovascular health behavior for adults and children based on 4 lifestyle factors (smoking, body mass index (BMI), physical activity, and diet) and set national goals for promoting cardiovascular health and reducing CVD burden [2]. Previous studies consistently show an inverse association between

multiple low-risk lifestyle factors and all-cause mortality [3–7]; however, widely varying definitions of the lifestyle factors are applied in these studies. To date, only two studies have used AHA cardiovascular health behavior concept to define the 4 lifestyle factors [8, 9]. Bambs and colleagues addressed the prevalence of the new AHA metrics that define cardiovascular lifestyle factors and reported that 81% of all participants in the community-based Heart SCORE study presented ≤ 3 ideal lifestyle factors (nearly 60% presented zero or one ideal factor) [8]. In an ideal world with unlimited resources, targeting all 4 modifiable factors could result in substantial improvement in overall cardiovascular health;

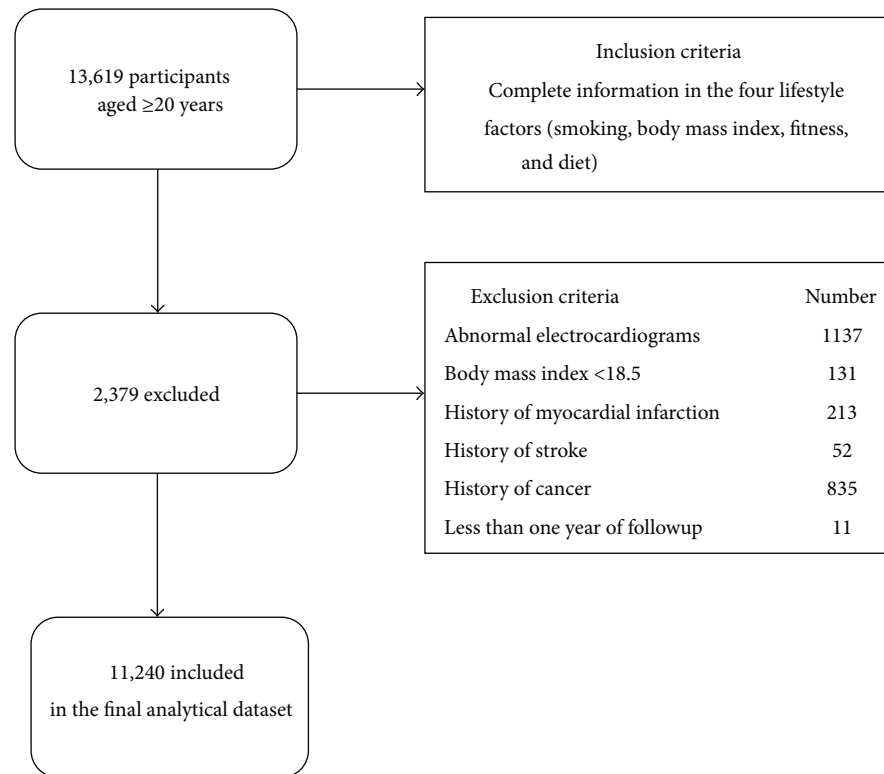


FIGURE 1: Participants flow diagram.

however, with the continuing financial crisis around the globe, it may be more cost-effective to choose the one or two most important lifestyle factors for intervention.

The population attributable fraction (PAF) is an integrated measure that assesses the proportion of an outcome in a population that is attributable to exposure to 1 or more risk factors [10]. The aim of our study is to estimate the death burden that is attributable to nonideal or poor cardiovascular lifestyle factors using a slightly modified construct defined by the AHA, and to identify one or two factors which contribute to most of the deaths while accounting for age, gender, family history, and health status.

2. Methods

2.1. Study Population. The Aerobics Center Longitudinal Study (ACLS) began in 1970 as an observational epidemiological study to investigate health outcomes associated with physical activity and cardiorespiratory fitness [11, 12]. Participants came to the Cooper Clinic, Dallas, Texas for a preventive medical examination and for consultation regarding their unhealthy lifestyle behavior. They were unpaid volunteers, sent by their employers, healthcare providers, or self-referred and came from all 50 states. Participants were told the purpose of the study and provided their written informed consent to participate. The study protocol was approved annually by the Cooper Institute's institutional review board. All participants included in this study were from 20 to 82 years old at entry (23.5% women) and had an

extensive baseline health examination, normal electrocardiograms (ECGs), a BMI ≥ 18.5 kg/m², and complete data on the 4 lifestyle factors. Those who reported having a history of myocardial infarction, stroke, or cancer and those who had less than one year of followup were excluded. Based on these inclusion and exclusion criteria, the final analysis included 11240 individuals whose baseline examination took place between 1987 and 1999. Figure 1 shows the flow diagram of the study participants.

2.2. Data Collection. A medical history questionnaire at baseline provided age, sex, history of chronic diseases (myocardial infarction, stroke, cancer, hypertension, or diabetes), family history of CVD, cigarette smoking, and physical activity. Diet was assessed by a 3-day dietary record. Height and weight were measured. Blood samples were obtained after a fast of at least 12 hours and analyzed for lipids and glucose using automated bioassays in accordance with the Centers for Disease Control and Prevention Lipid Standardization Program. Diabetes was defined as glucose ≥ 7.0 mmol/L, a history of physician diagnosis, or use of insulin. Hypercholesterolemia was defined as serum cholesterol ≥ 6.2 mmol/L or a history of physician diagnosis. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, or a history of physician diagnosis.

2.3. Modified AHA Cardiovascular Lifestyle Factors. In accordance with AHA definition of cardiovascular health [2], we classified each ideal lifestyle factor in the ACLS at baseline.

Some factors from the definition of ideal cardiovascular health were slightly modified, according to the information available in the ACLS.

Smoking habits were determined from a standardized medical history questionnaire. Participants were classified as never, former, or current smokers, and ideal smoking behavior was defined as nonsmoker (never or former smoker).

Body mass index (BMI) was calculated as weight (kilograms)/the square of height (meters) which were measured using a stadiometer and balance beam scale, respectively. Ideal BMI was defined $<25 \text{ kg/m}^2$.

Physical Activity and Cardiorespiratory Fitness. Physical activity was measured through a self-report questionnaire over the previous 3 months. We do not have uniform collection of information on activity type, frequency, duration, and intensity over the entire duration of the ACLS. Therefore, for the purpose of this study, we used cardiorespiratory fitness (hereafter referred to as “fitness”) as an objective marker of physical activity [13]. Fitness was assessed by a symptom-limited maximal exercise treadmill test using a modified Balke protocol [14]. Total treadmill endurance time (minutes) was used as an index of aerobic power, with time on treadmill in this protocol correlated highly ($r \geq 0.92$) with maximal oxygen uptake ($\text{VO}_{2\text{max}}$) in both men [15] and women [16]. Participants were classified as “low fit” based on the lowest 20% of the age- and sex-specific distribution of treadmill exercise duration in the overall ACLS population. These cut-points are from previous reports on the relation between fitness and all-cause mortality in the ACLS [12]. Ideal fitness was defined as 80% of the age- and sex-specific distribution of treadmill duration in the overall ACLS population (moderate and high levels of fitness) and was considered as an indicator of ideal physical activity status because previous ACLS data have shown that a brisk walk of approximately 30 minutes on most days of the week was associated with moderate-to-high levels of fitness [17].

Diet assessment consisted of a 3-day diet record that required participants to keep detailed records of everything they ate over 2 preassigned weekdays and 1 weekend day. Participants were provided written instructions on how to accurately describe foods and estimate portion sizes. Participants kept an ongoing, real-time written record of foods consumed during and between meals, including assessing portion sizes in common household measures. Registered dietitians at the Cooper Clinic coded and analyzed the diet records using the Cooper Clinic Nutrition and Exercise Evaluation system [18]. This provided detailed dietary information on the overall diet such as the number of foods consumed from specific food groups and the volume of micronutrients (vitamins and minerals).

The ideal cardiovascular health’ definition of the dietary goals included fruits and vegetables (≥ 4.5 cups per day, approximated as ≥ 4.5 servings/day in the ACLS study); fish (\geq two 3.5 oz servings/week, approximated as \geq two 3.5 oz servings/week of cooked lean meat equivalents from fish, shellfish, and other seafood); fiber-rich whole grains

($\geq 1.1 \text{ g}$ of fiber per 10 g of carbohydrate: three 1-oz-equivalent servings/day, approximated as ≥ 3 servings/day of whole grains); sodium ($<1500 \text{ mg}$ per day) and sugar-sweetened beverages ($\leq 450 \text{ kcal}$ (36 oz) per week). All these dietary components were included in this study, except sugar-sweetened beverages, due to a very low number of participants with this information. Ideal diet behavior was defined as meeting at least 3 of the above 4 diet components.

2.4. Mortality Surveillance. We followed participants for mortality from the baseline examination through the date of death for decedents or December 31, 2003 for survivors, using the National Death Index. We excluded participants with less than one year of followup to minimize potential bias due to serious underlying illness on mortality.

2.5. Statistical Analyses. The length of followup for each person was determined as the time from baseline to either death or censoring, whichever came first. Descriptive analyses summarized baseline characteristics of participants by survival status. The mean levels of continuous variables were compared using student *t*-test, while chi-square tests compared the distribution of categorical variables values. Univariate and multivariate Cox regressions were used to estimate the strength of the association (hazard ratios (HRs) and 95% confidence intervals (CIs)) between the selected potential nonmodifiable (age, gender, and family history of CVD) and modifiable lifestyle factors and all-cause mortality. With a score of 0 being allocated for each ideal lifestyle factor, nonideal or poor lifestyle factors were coded as 1. The PAFs for smoking (current smoking), fitness (low fitness), BMI (≥ 25), and diet (meeting 0 or 1 of the 4 diet components) on all-cause mortality were calculated. The PAF for the nonideal or poor lifestyle factor is defined as the proportionate reduction in death that would be achieved if the entire population had been unexposed to that risk factor or a combination of two lifestyle factors, compared with its current (actual) exposure pattern. Without considering confounders, the PAF can be defined by $\text{PAF}(t) = 1 - D_0(t)/D(t)$, where $D(t)$ is the probability of death during the time interval $(0, t)$ in the overall population and $D_0(t)$ is the death probability in the subgroup unexposed to the studied risk factor. When considering confounders we used the definition in Chen et al. [19] which has been shown to have a causal interpretation. For the special case of a categorical confounder and a fixed time point, the adjusted PAF in Chen et al. reduces to that defined in Whittemore [20] which replaced $D_0(t)$ in the above formula with the weighted average of confounder-stratum-specific unexposed death probability. The unadjusted/adjusted PAFs and 95% confidence intervals were estimated based on the univariate/multivariate Cox regression models and the methods developed by Chen et al. [19]. Data analyses were performed using SAS (version 9.2; SAS Institute, Cary, NC, USA) software, C and R 2.12.2. All *P* values are 2-sided with an alpha level of 0.05 established for significance.

TABLE 1: Baseline characteristics of study participants by survival status, Aerobics Center Longitudinal Study, 1987–1999.

	All	Survivor	Decedent	P value
N	11,240	10,972	268	
Age, years	45.7 (9.7)	45.5 (9.6)	53.5 (11.1)	<0.0001
Female, %	23.5	23.7	14.6	0.0005
BMI, kg/m ²	25.8 (4.1)	25.8 (4.0)	26.4 (4.7)	0.02
Treadmill time, minutes	18.1 (5.2)	18.1 (5.2)	16.5 (5.7)	<0.0001
Total cholesterol, mmol/L	5.4 (1.0)	5.4 (1.0)	5.6 (1.0)	0.0003
Fasting blood glucose, mmol/L	5.5 (0.9)	5.5 (0.9)	5.7 (1.3)	0.01
Blood pressure, mmHg				
Systolic	119 (14)	119 (14)	125 (16)	<0.0001
Diastolic	80 (10)	80 (10)	83 (10)	<0.0001
Hypertension ^a , %	26.4	26.1	41.0	<0.0001
Diabetes mellitus ^b , %	2.6	2.5	5.6	0.002
Hypercholesterolemia ^c , %	29.2	29.0	36.9	0.005
Family history of CVD, %	11.3	11.2	14.6	0.08
Ideal modifiable lifestyle factors, %				
Nonsmoker	88.6	88.6	84.7	0.045
18.5 ≤ BMI < 25	47.0	47.1	45.9	0.71
Moderate and high fit	91.3	91.4	86.9	0.01
Healthy diet (3-4 components)	37.6	37.5	43.3	0.05

Mean (standard deviation) for continuous variables; percentage for categorical variables.

CVD: cardiovascular disease; BMI: body mass index.

^aHypertension is defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or a history of physician diagnosis.

^bDiabetes mellitus is defined as a fasting plasma glucose concentration ≥7.0 mmol/L, a history of physician diagnosis, or insulin use.

^cHypercholesterolemia is defined as total cholesterol ≥6.20 mmol/L, or a history of physician diagnosis.

3. Results

There were 268 deaths during 130,584 person-years of followup. Compared with survivors, decedents were older, had lower fitness and higher BMI, had higher prevalence of major CVD risk factors, and had lower prevalence of ideal modifiable health factors other than body weight (Table 1).

We found statistically significant differences in risk of death between categories of age, gender, family history of CVD, smoking, and low fitness (Table 2). Low fitness and smoking, in addition to age, showed the strongest associations with mortality. No statistically significant interactions between the variables in the model were found; therefore, we used a model with main effects only to study their effects on the risk of death. The fully adjusted model showed similar associations between age, gender, low fitness, and smoking and death as the unadjusted model.

Table 3 shows the unadjusted and adjusted PAFs and their CIs for the individual modifiable lifestyle factors and 6 possible combinations of two factors in each of the 5-year follow-up intervals. Of the 4 lifestyle factors, fitness had the strongest association with risk of death, reducing it by 7% if low fit individuals had become at least moderately fit (95% CI: 2.2%, 12%). A reduction in smoking would have led to a 6% reduction in mortality risk. However, reduction of BMI to the ideal level had the smallest effect, the PAF being −7% (95% CI: −14%, 8%). The unadjusted PAF estimates of fitness, smoking, and diet decreased at year 10 and year 15 compared with the estimates at year 5, respectively. However,

this pattern of associations disappeared after multivariate adjustment (Figure 2).

Finally, the cumulative PAF estimate is obtained from the full model including any of the 2 lifestyle factors (Table 3 and Figure 3). Of the 6 combination groups, smoking plus fitness had the greatest association with PAF, reducing it by 13% if all current smokers who also had low fitness had never started smoking and also became at least moderate fit (95% CI: 6%, 19%). Improving diet and reducing BMI had the least effect on PAF in this population of men and women.

4. Discussion

4.1. Summary of Main Findings. Attributable fractions are commonly used to measure the effect of risk factors on disease outcomes in a population. In this study, we extended these static measures to functions of time because we are interested in knowing if the PAFs will change with the event time. We found that fitness and smoking were the two most important factors for reducing risk of death in our population. The fraction of deaths attributable to low fitness equals 7% and to smoking equals 6% after accounting for other potential confounders. Considering the growing burden of CVD, this study provides some useful information for decision-makers by providing more information about identifying priority targets of modifiable health factors. Furthermore, by comparing the relative importance of these factors, we can focus policy debate on the opportunity of financing one intervention over another.

TABLE 2: Estimated hazard ratios of death in categories of potential risk factors, the Aerobics Center Longitudinal Study, 1987–2003.

	No. of deaths	Total no. of participants	Unadjusted HR (95% CI)	Multivariate-adjusted HR (95% CI) ^a
<i>Nonmodifiable variables</i>				
<i>Age group, years</i>				
20–39	30	2999	1	1
40–49	71	4453	1.62 (1.05–2.48)	1.58 (1.03–2.42)
50–59	83	2874	2.91 (1.92–4.42)	2.88 (1.88–4.41)
≥60	84	914	8.48 (5.59–12.86)	8.53 (5.55–13.13)
<i>Gender</i>				
Male	229	8598	1	1
Female	39	2642	0.59 (0.42–0.82)	0.66 (0.47–0.94)
<i>Family history of CVD</i>				
No	229	9974	1	1
Yes	39	1266	1.37 (0.98–1.93)	1.46 (1.04–2.05)
<i>Nonideal modifiable lifestyle factors</i>				
Current smoker	41	1287	1.50 (1.07–2.09)	1.62 (1.16–2.28)
BMI ≥ 25	145	5954	1.81 (0.93–1.50)	0.88 (0.68–1.14)
Unhealthy diet (<3 components)	152	7011	0.87 (0.68–1.11)	1.01 (0.79–1.29)
Low fitness	35	981	1.81 (1.27–2.59)	2.04 (1.40–2.99)

CVD: cardiovascular disease.

^aAdjusted for all the variables in the table plus hypertension, diabetes, and hypercholesterolemia.TABLE 3: Unadjusted and multivariable-adjusted PAF for each 5-year time interval^a using the Aerobics Center Longitudinal Study, 1987–2003.

	Unadjusted model						Multivariate-adjusted model ^c					
	PAF5	95% CI	PAF10	95% CI	PAF15	95% CI	PAF5	95% CI	PAF10	95% CI	PAF15	95% CI
<i>Individual factor^b</i>												
Smoking	5%	0.1%, 10%	5%	0.1%, 10%	5%	0.2%, 10%	6%	1%, 11%	6%	1%, 11%	6%	1%, 11%
BMI	9%	–5%, 20%	9%	–5%, 20%	8%	–4%, 19%	–7%	–14%, 8%	–7%	–24%, 8%	–7%	–23%, 8%
Diet	–9%	–26%, 6%	–9%	–25%, 5%	–8%	–24%, 5%	3%	–13%, 16%	3%	–13%, 16%	3%	–12%, 15%
CRF	7%	2%, 11%	6%	2%, 11%	6%	1%, 10%	7%	2%, 12%	7%	2%, 12%	7%	2%, 12%
<i>Multiple factors</i>												
Smoking + BMI	13%	–1%, 24%	12%	–1%, 24%	12%	–1%, 23%	–0.3%	–17%, 14%	–0.3%	–17%, 14%	–0.3%	–16%, 14%
Smoking + Diet	–4%	–22%, 11%	–4%	–21%, 10%	–4%	–20%, 10%	9%	–7%, 22%	9%	–7%, 22%	9%	–7%, 21%
Smoking + CRF	11%	4%, 17%	10%	4%, 16%	9%	3%, 15%	13%	6%, 19%	13%	6%, 19%	13%	6%, 18%
BMI + Diet	4%	–21%, 18%	0.4%	–21%, 18%	0.2%	–20%, 17%	–4%	–28%, 15%	–4%	–28%, 16%	–4%	–27%, 14%
BMI + CRF	11%	–2%, 22%	11%	–2%, 22%	10%	–3%, 20%	1%	–15%, 15%	0.9%	–15%, 14%	0.8%	–14%, 14%
Diet + CRF	–4%	–21%, 11%	–4%	–20%, 11%	–4%	–20%, 10%	10%	–5%, 23%	10%	–5%, 23%	9%	–5%, 22%

PAF: population attributable fraction; CI: confidence interval; BMI: body mass index; CRF: cardiorespiratory fitness; CVD: cardiovascular disease.

^aPAF value at 5th, 10th, and 15th year was denoted by PAF5, PAF10, and PAF15, respectively.^bThe definition of smoking, BMI, diet, CRF is the same as in Table 2.^cAdjusted for age, gender, hypertension, diabetes, hypercholesterolemia, and family history of CVD.

4.2. Comparison with Other Studies. Previous studies have examined the 4 individual modifiable lifestyle factors, their association with mortality, and the PAF in different populations. Smoking has long been identified as a behavior that has an inverse association with longevity. Among developed Western countries, earlier reports show that 20% of all deaths are attributed to tobacco [21], and this number has varied in recent reports due to different populations studied

[22, 23]. In Asian countries there have been several reports on PAF due to smoking ranging from 25% in Japan [24] to 13% in China [25]. It is becoming more evident that physical activity and fitness have an important role in health outcomes. The Nurse's Health Study [26], a large cohort study of registered US nurses, assessed the PAFs of a wide range of risk factors, found that a total of 17% of deaths during followup could be attributed to lack of physical activity

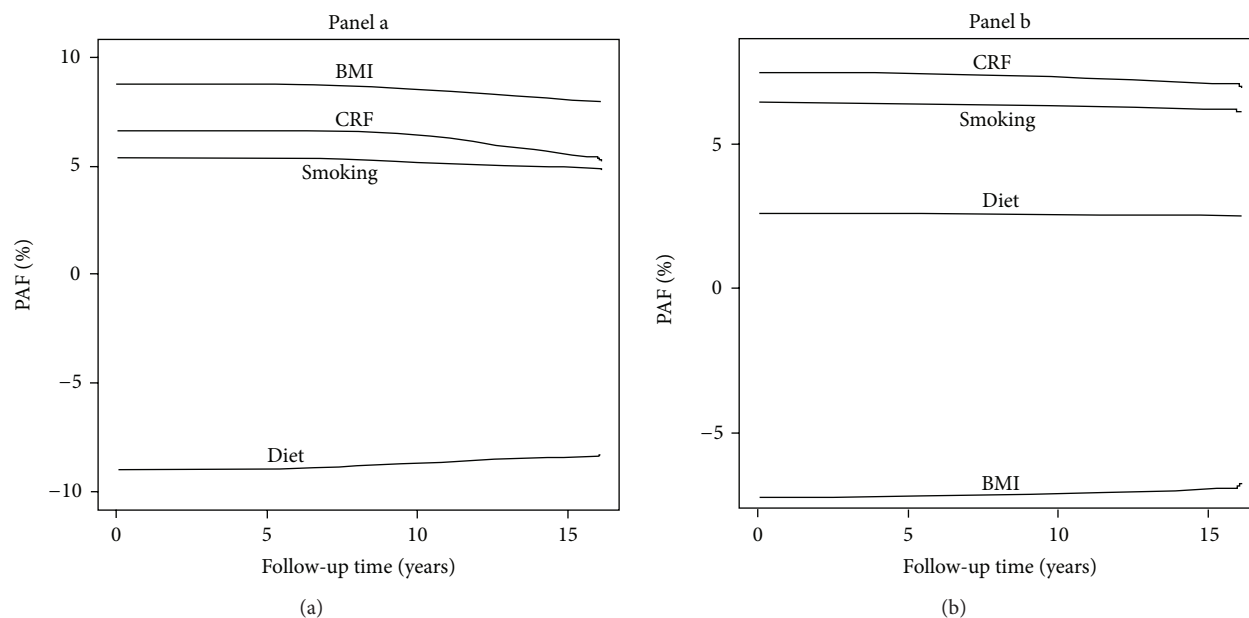


FIGURE 2: Estimates of the population attributable fraction (PAF) by assuming one of the four behavior factors are controlled at the ideal level: (a) unadjusted model; (b) multivariate-adjusted model (age, gender, hypertension, diabetes, hypercholesterolemia, and family history of CVD), the Aerobics Center Longitudinal Study, 1987–2003.

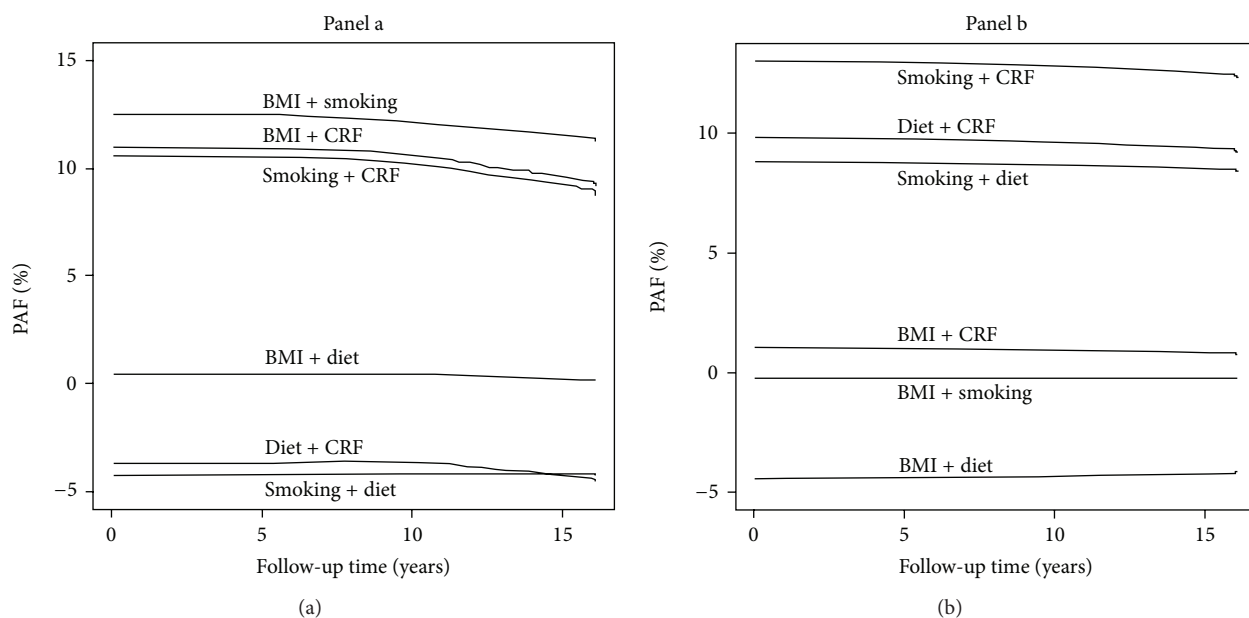


FIGURE 3: Estimates of the population attributable fraction (PAF) by assuming two of the four behavior factors are controlled at the ideal level: (a) unadjusted model; (b) multivariate-adjusted model (age, gender, hypertension, diabetes, hypercholesterolemia, and family history of CVD), the Aerobics Center Longitudinal Study, 1987–2003.

(<30 min of physical activity per day). Another study from the UK reported a higher PAF of 25% associated with physical inactivity among 10,059 middle-aged women under general practitioners' observation [23]. Poor diet is often commonly reported to be associated with a wide range of chronic conditions and therefore contributes to substantial burden of disease [22]. Due to the complex nature of the diet exposure

assessment, definitions of poor diet or unhealthy diet often vary significantly. The Nurse's Health Study developed a healthy eating score [26] that in the upper two fifths was defined as a low risk category. They found that a total 13% of deaths were attributed to low diet quality. A meta-analysis of US studies shows a 17% PAF for combined poor diet and physical inactivity, but the investigators did not provide

separate estimates for diet and inactivity [27]. Obesity has consistently been associated with higher risk of mortality [28]. Being overweight or obese had a higher PAF (14.2%, 95% CI = 11.6 to 16.9) in the US cohort [26], but there was no significantly higher mortality risk associated with overweight or obesity in the UK study [23].

Although there is an increasing literature on combinations of lifestyle factors with mortality [4, 23, 26, 29] few studies have estimated PAF for the individual factors [23, 26] and even fewer studies have reported the PAF for a combination of factors [23]; therefore, information is sparse on exactly which combination of lifestyle factors might be the best to target to reduce overall disease burden. Among studies estimating PAFs, most of them failed to identify which lifestyle factor(s) is (are) the most important one(s) contributing to overall mortality [4, 26, 29]. An important public health question is how to identify which lifestyle factor interventions might yield the greatest benefits in the population. The only current study that tried to answer this question is the UK study in middle-aged women [23]. Iversen and colleagues reported that among the four individual lifestyle factors (smoking, physical inactivity, BMI, and alcohol) smoking remains the leading cause of mortality and physical inactivity follows. When the investigators evaluated combinations of two factors, they found that smoking and physical inactivity are responsible for almost half of the deaths. They also report that a combination of three factors of smoking, physical inactivity, and alcohol consumption is responsible for about 60% of the deaths. Finally, avoidance of all four unhealthy lifestyle factors would also have prevented 60% of the deaths. These analyses indicate that avoidance of all four unhealthy lifestyle risk factors would only have prevented additional 10% of the deaths when compared with the combination of smoking and inactivity. However, this study did not assess the contribution of diet on mortality.

The changes observed in “diet” and “BMI” before and after the adjustment deserve further comment. We have compared overweight/obese participants with those who had normal BMI and found that overweight/obese participants had significantly higher prevalence of hypertension, diabetes, and hypercholesterolemia, but no differences in mean age. The PAF estimate changed direction which means that modifying BMI from nonideal to ideal level did not contribute significantly to mortality after adjusting these other risk factors. We postulate this might be due to the strong effects of these negative confounders and simply improving BMI without changing other risk factors is not sufficient to change the proportion of death at the population level. On the other hand, we found that ideal diet participants were not significantly different from those with nonideal diet regarding the abovementioned confounders except age. Those with nonideal diet were significantly younger than those with ideal diet. Based on Table 2, we can see that age had a significant and large effect on all-cause mortality. Therefore improving diet after adjusting other confounders especially age might influence the PAF estimate significantly.

ACLS participants were mainly white and of middle-to-upper socioeconomic status. Although participants are

similar in many respects to other US cohorts that have provided important information on disease prevention [11], the prevalences of smoking and low fitness were low (11% and 8%, resp.). However, even with such low prevalences, they were still responsible for the largest number of deaths in this population. From this point of view, our results are in fact consistent with previous cohort studies and suggest that smoking cessation programs and physical activity promotion have the greatest potential for reducing the total number of deaths.

4.3. Limitations. As mentioned previously, the ACLS population was mainly white and of middle-to-upper socioeconomic status. The prevalence of the four behavior factors was lower than in the US general population. Thus, these factors might have a larger population effect if they were studied in a representative sample. We used fitness instead of physical activity in the current study. Although fitness and physical activity are not interchangeable because physical activity is a behavior, whereas fitness is a functional attribute that can be influenced by other factors, physical activity is the primary determinant of fitness. Fitness is less prone to misclassification and may better reflect the adverse health consequences of a sedentary lifestyle than does self-reported physical activity exposure [13]. We were unable to evaluate the effect of changes in the factors over time on all-cause mortality because we only had baseline assessments. The PAF estimates depend on the prevalence of the studied factors and the magnitude of the association between them and the outcomes. During this long follow-up period, both the prevalence of the lifestyle factors and the observed associations between these factors and all-cause mortality are likely to change and therefore influence the PAF estimates. Future studies are needed with repeat assessment of the behavior. In addition, the measurement of fitness and diet might not be feasible for clinical practice. Finally, the estimates presented here assume that changes in the behavior would affect the number of deaths. Our ability to change lifestyle factors in large populations is largely untested. However, we do know that it is possible to produce lifestyle changes in clinical trials [30].

5. Conclusions

In conclusion, low fitness was responsible for the highest proportion of deaths in this sample of men and women, and smoking had the second highest PAF among the four cardiovascular lifestyle factors. Preventive targeted interventions to decrease the prevalence of low fitness and smoking would most likely promote reduced mortality rates. Therefore the major public health gain in the coming years will come from getting sedentary individuals to start moving as well as getting smokers to stop smoking.

Conflict of Interests

The authors declare that they have no conflict of interests.

Acknowledgments

This study was supported by National Institutes of Health Grants AG06945, HL62508, and R21DK088195. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors thank the Cooper Clinic physicians and technicians for collecting the baseline data and staff at the Cooper Institute for data entry and data management.

References

- [1] V. L. Roger, A. S. Go, D. M. Lloyd-Jones et al., "Heart disease and stroke statistics—2011 update: a report from the American Heart Association," *Circulation*, vol. 123, no. 4, pp. e18–e209, 2011.
- [2] D. M. Lloyd-Jones, Y. Hong, D. Labarthe et al., "Defining and setting national goals for cardiovascular health promotion and disease reduction: the American heart association's strategic impact goal through 2020 and beyond," *Circulation*, vol. 121, no. 4, pp. 586–613, 2010.
- [3] K.-T. Khaw, N. Wareham, S. Bingham, A. Welch, R. Luben, and N. Day, "Combined impact of health behaviours and mortality in men and women: the EPIC-Norfolk prospective population study," *PLoS Medicine*, vol. 5, no. 1, article e12, 2008.
- [4] K. T. B. Knuys, L. C. P. G. M. de Groot, D. Kromhout et al., "Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project," *Journal of the American Medical Association*, vol. 292, no. 12, pp. 1433–1439, 2004.
- [5] A. C. Carlsson, H. Theobald, and P. E. Wändell, "Health factors and longevity in men and women: a 26-year follow-up study," *European Journal of Epidemiology*, vol. 25, no. 8, pp. 547–551, 2010.
- [6] U. Nöthlings, E. S. Ford, J. Kröger, and H. Boeing, "Lifestyle factors and mortality among adults with diabetes: findings from the European Prospective Investigation into Cancer and Nutrition-Potsdam study," *Journal of Diabetes*, vol. 2, no. 2, pp. 112–117, 2010.
- [7] E. Kvaavik, G. D. Batty, G. Ursin, R. Huxley, and C. R. Gale, "Influence of individual and combined health behaviors on total and cause-specific mortality in men and women: the United Kingdom Health and Lifestyle Survey," *Archives of Internal Medicine*, vol. 170, no. 8, pp. 711–718, 2010.
- [8] C. Bambs, K. E. Kip, A. Dinga, S. R. Mulukutla, A. N. Aiyer, and S. E. Reis, "Low prevalence of ideal cardiovascular health in a community-based population: the heart strategies concentrating on risk evaluation (Heart SCORE) study," *Circulation*, vol. 123, no. 8, pp. 850–857, 2011.
- [9] A. R. Folsom, H. Yatsuya, J. A. Nettleton, P. L. Lutsey, M. Cushman, and W. D. Rosamond, "Community prevalence of ideal cardiovascular health, by the American heart association definition, and relationship with cardiovascular disease incidence," *Journal of the American College of Cardiology*, vol. 57, no. 16, pp. 1690–1696, 2011.
- [10] M. A. Laaksonen, P. Knekt, T. Härkänen, E. Virtala, and H. Oja, "Estimation of the population attributable fraction for mortality in a cohort study using a piecewise constant hazards model," *American Journal of Epidemiology*, vol. 171, no. 7, pp. 837–847, 2010.
- [11] S. N. Blair, W. B. Kannel, H. W. Kohl, N. Goodyear, and P. W. F. Wilson, "Surrogate measures of physical activity and physical fitness. Evidence for sedentary traits of resting tachycardia, obesity, and low vital capacity," *American Journal of Epidemiology*, vol. 129, no. 6, pp. 1145–1156, 1989.
- [12] S. N. Blair, J. B. Kampert, H. W. Kohl III et al., "Influences of cardiorespiratory fitness and other precursors on cardiovascular disease and all-cause mortality in men and women," *Journal of the American Medical Association*, vol. 276, no. 3, pp. 205–210, 1996.
- [13] M. Aadahl, M. Kjær, J. H. Kristensen, B. Møllerup, and T. Jørgensen, "Self-reported physical activity compared with maximal oxygen uptake in adults," *European Journal of Cardiovascular Prevention and Rehabilitation*, vol. 14, no. 3, pp. 422–428, 2007.
- [14] B. Balke and R. W. Ware, "An experimental study of physical fitness in Air Force personnel," *United States Armed Forces Medical Journal*, vol. 10, pp. 675–688, 1959.
- [15] M. L. Pollock, R. L. Bohannon, K. H. Cooper et al., "A comparative analysis of four protocols for maximal treadmill stress testing," *American Heart Journal*, vol. 92, no. 1, pp. 39–46, 1976.
- [16] M. L. Pollock, C. Foster, D. Schmidt, C. Hellman, A. C. Linnerud, and A. Ward, "Comparative analysis of physiologic responses to three different maximal graded exercise test protocols in healthy women," *American Heart Journal*, vol. 103, no. 3, pp. 363–373, 1982.
- [17] J. R. Stofan, L. DiPietro, D. Davis, H. W. Kohl III, and S. N. Blair, "Physical activity patterns associated with cardiorespiratory fitness and reduced mortality: the Aerobics Center Longitudinal Study," *American Journal of Public Health*, vol. 88, no. 12, pp. 1807–1813, 1998.
- [18] S. Brodney, R. S. McPherson, R. A. Carpenter, D. Welten, and S. N. Blair, "Nutrient intake of physically fit and unfit men and women," *Medicine and Science in Sports and Exercise*, vol. 33, no. 3, pp. 459–467, 2001.
- [19] L. Chen, D. Y. Lin, and D. Zeng, "Attributable fraction functions for censored event times," *Biometrika*, vol. 97, no. 3, pp. 713–726, 2010.
- [20] A. S. Whittemore, "Statistical methods for estimating attributable risk from retrospective data," *Statistics in Medicine*, vol. 1, no. 3, pp. 229–243, 1982.
- [21] R. Peto, A. D. Lopez, J. Boreham, M. Thun, and C. Heath Jr., "Mortality from tobacco in developed countries: indirect estimation from national vital statistics," *The Lancet*, vol. 339, no. 8804, pp. 1268–1278, 1992.
- [22] G. Danaei, E. L. Ding, D. Mozaffarian et al., "The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors," *PLoS Medicine*, vol. 6, no. 4, Article ID e1000058, 2009.
- [23] L. Iversen, P. C. Hannaford, A. J. Lee, A. M. Elliott, and S. Fielding, "Impact of lifestyle in middle-aged women on mortality: evidence from the Royal College of general practitioners' oral contraception study," *British Journal of General Practice*, vol. 60, no. 577, pp. 563–569, 2010.
- [24] Y. Murakami, K. Miura, T. Okamura, and H. Ueshima, "Population attributable numbers and fractions of deaths due to smoking: a pooled analysis of 180,000 Japanese," *Preventive Medicine*, vol. 52, no. 1, pp. 60–65, 2011.
- [25] J. Jiang, B. Liu, F. Sitas et al., "Smoking-attributable deaths and potential years of life lost from a large, representative study in China," *Tobacco Control*, vol. 19, no. 1, pp. 7–12, 2010.
- [26] R. M. van Dam, T. Li, D. Spiegelman, O. H. Franco, and F. B. Hu, "Combined impact of lifestyle factors on mortality: prospective

- cohort study in US women,” *British Medical Journal*, vol. 337, article a1440, 2008.
- [27] A. H. Mokdad, J. S. Marks, D. F. Stroup, and J. L. Gerberding, “Actual causes of death in the United States, 2000,” *Journal of the American Medical Association*, vol. 291, no. 10, pp. 1238–1245, 2004.
- [28] K. M. Flegal, B. I. Graubard, D. F. Williamson, and M. H. Gail, “Excess deaths associated with underweight, overweight, and obesity,” *Journal of the American Medical Association*, vol. 293, no. 15, pp. 1861–1867, 2005.
- [29] A. Tamakoshi, K. Tamakoshi, Y. Lin, K. Yagyu, and S. Kikuchi, “Healthy lifestyle and preventable death: findings from the Japan Collaborative Cohort (JACC) Study,” *Preventive Medicine*, vol. 48, no. 5, pp. 486–492, 2009.
- [30] J. L. Unick, D. Beavers, J. M. Jakicic et al., “Effectiveness of lifestyle interventions for individuals with severe obesity and type 2 diabetes: results from the Look AHEAD trial,” *Diabetes Care*, vol. 34, no. 10, pp. 2152–2157, 2011.

