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Lifetime Risks of Cardiovascular Disease

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Abstract

BACKGROUND—The lifetime risks of cardiovascular disease have not been reported across the age spectrum in black adults and white adults.

METHODS—We conducted a meta-analysis at the individual level using data from 18 cohort studies involving a total of 257,384 black men and women and white men and women whose risk factors for cardiovascular disease were measured at the ages of 45, 55, 65, and 75 years. Blood pressure, cholesterol level, smoking status, and diabetes status were used to stratify participants according to risk factors into five mutually exclusive categories. The remaining lifetime risks of cardiovascular events were estimated for participants in each category at each age, with death free of cardiovascular disease treated as a competing event.

RESULTS—We observed marked differences in the lifetime risks of cardiovascular disease across risk-factor strata. Among participants who were 55 years of age, those with an optimal risk-factor profile (total cholesterol level, <180 mg per deciliter [4.7 mmol per liter]; blood pressure, <120 mm Hg systolic and 80 mm Hg diastolic; nonsmoking status; and nondiabetic status) had substantially lower risks of death from cardiovascular disease through the age of 80 years than participants with two or more major risk factors (4.7% vs. 29.6% among men, 6.4% vs. 20.5% among women). Those with an optimal risk-factor profile also had lower lifetime risks of fatal coronary heart disease or nonfatal myocardial infarction (3.6% vs. 37.5% among men, <1% vs. 18.3% among women) and fatal or nonfatal stroke (2.3% vs. 8.3% among men, 5.3% vs. 10.7% among women). Similar trends within risk-factor strata were observed among blacks and whites and across diverse birth cohorts.

CONCLUSIONS—Differences in risk-factor burden translate into marked differences in the lifetime risk of cardiovascular disease, and these differences are consistent across race and birth cohorts. (Funded by the National Heart, Lung, and Blood Institute.)

In recent decades, clinical and public health efforts to reduce the burden of cardiovascular disease have emphasized the importance of calculating global, short-term (generally 10-year) risk estimates.[1] However, the majority of adults in the United States who are

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considered to be at low risk for cardiovascular disease in the short term are actually at high risk across their remaining lifespan.[2,3] Estimates of the lifetime risk of cardiovascular disease provide a more comprehensive assessment of the overall burden of the disease in the general population, now and in the future, because they take into account both the risk of cardiovascular disease and competing risks (e.g., death from cancer) until participants reach an advanced age.[4,5] Such estimates can help guide public health policy, allowing projections of the overall burden of cardiovascular disease in the population.

Most estimates of the lifetime risk of cardiovascular disease have been derived from analyses restricted to risk factors measured at a single age in a predominantly white population.[6,7] These estimates do not account for the potential effects of birth cohort that may arise from secular changes in risk-factor levels[8,9] or for the widespread use of medical treatment, which has translated into marked reductions in rates of cardiovascular events in the United States.[10]

The Cardiovascular Lifetime Risk Pooling Project was designed to collect and pool data from numerous longitudinal epidemiologic cohort studies conducted in the United States over the past 50 years. This pooling approach provides an opportunity to calculate estimates of the lifetime risk of cardiovascular events according to age, sex, race, and other risk factors across multiple birth cohorts that would not be feasible within any one data set alone.

METHODS

STUDY SAMPLE

We included data sets in the Cardiovascular Lifetime Risk Pooling Project if they met the following criteria: they represented either community-based or population-based samples or large volunteer cohorts, they included at least one baseline examination with direct measurement of physiological and anthropometric (e.g., weight) variables, and they included 10 or more years of follow-up for fatal or nonfatal cardiovascular events or both. Data from 18 unique cohorts were included in the study, 17 of which were included in the pooled analysis[11–32] (all cohorts are listed in the Supplementary Appendix, available with the full text of this article at NEJM.org). Because of the large size of one study, the Multiple Risk Factor Intervention Trial (MRFIT), relative to the other 17 studies, this cohort was analyzed separately. All data were appropriately de-identified, and all study protocols and procedures were approved by the institutional review board at Northwestern University.

ASCERTAINMENT OF BASELINE MEASURES AND FOLLOW-UP EVENTS

The protocols used to obtain data on demographic characteristics, personal and medical history, physical examination, laboratory results, and follow-up procedures for ascertainment of vital status and events for all cohorts included in the study have been published elsewhere.[11–32] Blood pressure and serum cholesterol levels were measured directly in all participants; data on smoking status were self-reported, as were data on diabetes status, the latter derived from records of self-report, use of medication for diabetes, or both. Events were ascertained with the use of strategies selected by each cohort's investigator group and included death from cardiovascular disease, from coronary heart disease, or from any cause and nonfatal events of interest, including myocardial infarction and stroke. (Detailed descriptions of the approaches used in event ascertainment are provided in the Supplementary Appendix.)

STATISTICAL ANALYSIS

All statistical analyses were performed with the use of SAS statistical software, version 9.1 (SAS Institute). For the calculation of lifetime risk, a modified version of survival analysis

was used.[4,5] In this type of analysis, the incidence of each end point and of death free of the end point for each age attained during follow-up is calculated. Age-specific hazards, incidence rates, cumulative incidence, and survival probabilities were calculated as they are in a Kaplan–Meier analysis.[33] Because the Kaplan–Meier cumulative incidence does not reflect the competing risk of death from causes other than cardiovascular disease before the occurrence of an end point (and therefore overestimates the remaining lifetime risk of cardiovascular disease when the competing risk is high[4,5,34]), adjustment was made for this competing risk to yield an accurate estimate of the remaining lifetime risk of cardiovascular disease.[5] Lifetime risk estimates reflect the sum of the adjusted, age-specific incidences from study entry to age at last observation.

Participant data were stratified according to risk-factor levels or status as assessed within 5 years of each index age. For example, risk factors measured for participants between 40 and 49 years of age were included in the analyses for the age of 45 years. Risk-factor level or status was classified in aggregate, in accordance with our previously published algorithm,[2,7] into five mutually exclusive categories (Table 1), one in which all risk factors were optimal, a second in which at least one risk factor was not optimal, a third in which at least one risk factor (cholesterol level or blood pressure) was elevated, a fourth in which one major risk factor was present, and a fifth in which two or more major risk factors were present.

Descriptions of secondary analyses are included in the Supplementary Appendix. All references to estimates of lifetime risk reflect those derived from the 17 studies in the pooled cohort, after the exclusion of data from participants in MRFIT, with the exception of race-specific estimates for men, which were derived from MRFIT.

RESULTS

BASELINE CHARACTERISTICS

A total of 67,890 participants (who underwent 117,557 in-person examinations) were included from the 17 studies in the pooled cohort; an additional 189,494 participants (each examined once) were included from MRFIT. In general, the older study participants in the pooled cohort had a higher prevalence of diabetes and higher systolic blood pressure, whereas the younger participants had a higher prevalence of smoking (Table 1). The percentage of participants in the lower-risk groups was small, with approximately 5% in the group in which all risk factors were optimal. In contrast, approximately two thirds of participants were in the two highest-risk groups (having at least one major risk factor).

When participants were stratified according to birth cohort, we observed significant but expected differences in the burden of risk factors between older and younger birth cohorts, for both men and women (Table 1 in the Supplementary Appendix). For example, as compared with 55-year-old men born before 1920, those born in or after 1920 had a higher prevalence of diabetes (8.8% vs. 4.2%), a lower prevalence of smoking (29.5% vs. 52.3%), and lower mean levels of total cholesterol (210 mg per deciliter vs. 216 mg per deciliter [5.4 mmol per liter vs. 5.6 mmol per liter]) and systolic blood pressure (124 mm Hg vs. 137 mm Hg). When participants were stratified according to race, the burden of risk factors was higher among blacks than among whites (Table 2 in the Supplementary Appendix).

EFFECTS OF AGGREGATE RISK-FACTOR BURDEN

In analyses of the pooled cohort at an index age of 55 years, during up to 731,615 person-years of follow-up, there were 5912 deaths from cardiovascular diseases, 5061 fatal or nonfatal myocardial infarctions, 2295 fatal or nonfatal strokes, and a total of 9391 events related to atherosclerotic cardiovascular disease. Among persons of the same index age in MRFIT, there were 14,199 deaths from cardiovascular disease, with 1,766,773 person-years

of follow-up. The lifetime risks of death from cardiovascular disease in the pooled cohort were higher among men than among women but were similar between blacks and whites (white men, 36.1%; black men, 33.0%; white women, 26.6%; black women, 27.1%).

Among men and women with an index age of 55 years, a higher burden of risk factors was associated with a higher lifetime risk of death from cardiovascular disease. (Fig. 1 and 2 provide the lifetime risks of death from cardiovascular disease according to aggregate levels of risk for men and women at 55 years of age in the pooled cohort [i.e., excluding persons from MRFIT].) The findings were similar at 45 years of age (Fig. 1A and 1B in the Supplementary Appendix). There were marked differences in the observed lifetime risks of death from cardiovascular disease according to the risk-factor burden, particularly at the age of 45 years. A similar pattern was noted for risk factors measured at other ages and for the additional end points of death from coronary heart disease or nonfatal myocardial infarction, fatal or nonfatal stroke, and total number of events related to atherosclerotic cardiovascular disease (Tables 2 and 3).

Lifetime risks tended to be very low among persons who had an optimal risk-factor profile at all index ages. Lifetime risks became substantially higher once any risk factor level or status was not considered to be optimal, with stepwise increases in remaining lifetime risk across groups with less favorable profiles for aggregate risk. In general, the lifetime risk of death from cardiovascular disease and coronary heart disease or of nonfatal myocardial infarction were about twice as high among men as they were among women, whereas the lifetime risks of fatal stroke and nonfatal stroke did not differ substantially according to sex.

For the comparison between blacks and whites of the same sex, the lifetime risks of death from cardiovascular disease were similar among participants with similar levels of aggregate risk. In the MRFIT cohort, at 55 years of age, both white men and black men with optimal risk-factor profiles had substantially lower lifetime risks of cardiovascular death than did men with two or more major risk factors (white men, 4.0% vs. 26.6%; black men, 9.9% vs. 27.9%) (Fig. 2 in the Supplementary Appendix). The results of race-stratified analyses were similar among women (data not shown).

EFFECTS OF BIRTH COHORT

At the age of 55 years, the 20-year adjusted risk of death from cardiovascular disease was lower in younger birth cohorts than it was in older birth cohorts. For example, as compared with men in the first National Health and Nutrition Examination Survey (NHANES I, examinations conducted from 1976 through 1980), the men in NHANES III (examinations conducted from 1988 through 1994) had a lower 20-year adjusted risk of death from cardiovascular disease (17.7% vs. 10.5%). The findings were similar for women (12.2% vs. 7.0%). These differences were observed when there were marked changes in the prevalence of two or more major risk factors, with the prevalence decreasing from 39.0% for older men to 21.2% for younger men and from 40.3% for older women to 23.0% for younger women (Table 1 in the Supplementary Appendix). Nevertheless, the 20-year adjusted risk of death from cardiovascular disease for each risk-factor profile remained quite similar across birth cohorts (Fig. 3 and 4 in the Supplementary Appendix).

COMPETING RISKS ACROSS THE LIFESPAN

With adjustment for competing causes of death, the lifetime risk of death from cardiovascular disease was reduced, as compared with the unadjusted risk, among all groups defined by age, sex, and risk-factor profile. The evidence for the effects of competing risks was most prominent at older ages and less favorable risk-factor profiles, which were associated with the highest rates of death from noncardiovascular causes. For example,

among men 55 years of age with two or more major risk factors for cardiovascular disease, the unadjusted, Kaplan–Meier estimate that excluded competing risks of death was substantially higher than the lifetime-risk estimate that accounted for competing risks (81.8% vs. 44.5%) (Fig. 5 in the Supplementary Appendix).

DISCUSSION

In this study, we calculated the lifetime risk of cardiovascular disease according to age, sex, race, and other risk factors across multiple birth cohorts. There were several important findings. First, our data strongly reinforce the influence of traditional risk factors on the lifetime risk of cardiovascular disease. Even a relatively low burden of these risk factors was associated with significant increases in the long-term risk of cardiovascular disease, and the absence of traditional risk factors was associated with a very low lifetime risk. Second, despite the development of notable secular trends in the prevalence of risk factors during the past 40 years, we observed that the effect of these factors, when present, remained remarkably consistent across birth cohorts. In addition, although the prevalence of risk factors overall was higher among blacks than among whites, the lifetime risks of end points related to cardiovascular disease were similar among blacks and whites when their risk-factor profiles were similar.

The presence or absence of traditional risk factors appears to represent a much more consistent determinant of the long-term risk of cardiovascular disease than race or birth cohort. For example, among 55-year-old men with two or more major risk factors, the 20-year adjusted risk of death from cardiovascular disease was only 4% lower among men born in or after 1920 than it was among those born before 1920 (16.8% vs. 20.7%), presumably reflecting the potential influences of subsequent treatment. In contrast with these modest effects related to birth cohort, the 20-year adjusted risk of death from cardiovascular disease was substantially greater across risk-factor strata. For example, among men born before 1920, those with only one risk factor had a 20-year adjusted risk of death from cardiovascular disease that was 13 percentage points lower than that among men with two or more major risk factors (7.5% vs. 20.7%). Thus, in the younger birth cohorts, the marked decrease in the proportion of cohort members who were classified in the highest risk group (persons with two or more major risk factors) appears to account for the majority of the decline in cardiovascular events.

We believe these findings have important implications for clinical disease prevention and public health practice. First, the effect of untreated risk factors has been fairly constant for decades. Therefore, the present estimates of lifetime risk, made on the basis of current or projected risk-factor levels, may be important in estimating the future burden of cardiovascular disease in the general population. Second, efforts to lower the burden of cardiovascular disease will require prevention of the development of risk factors (primordial prevention) rather than the sole reliance on the treatment of existing risk factors (primary prevention).

Our data are also consistent with earlier observations suggesting that the decline in cardiovascular event rates in the general population reflects changes in the prevalence of risk factors rather than the effects of treatment alone.[10,35] For example, 44.3% of the overall decline in U.S. rates of death from coronary heart disease in 1980 and in 2000 was attributed to population changes in levels of serum total cholesterol (24.2%) and systolic blood pressure (20.1%). The effects of clinical treatment on these risk factors were more modest, with statin and antihypertensive therapy accounting for 4.9% and 7.0% of the decline, respectively.[10,35] We extend these observations to long-term risk estimates, showing that

changes in the prevalence of risk-factor profiles strongly influence estimates of lifetime risk in the general population.

Prior studies have consistently shown that a higher burden of risk factors, measured individually or in aggregate, is associated with a markedly higher lifetime risk of cardiovascular disease.[7,36,37] However, the majority of these earlier, smaller studies were confined to single cohorts with predominantly white participants. We believe that our analysis, which is based on pooled data from multiple birth cohorts, with both black participants and white participants and varied geographic origin, provides more representative estimates of the lifetime risks of cardiovascular disease.

Investigators in earlier studies, using standard methods, have observed that blacks and whites had similar magnitudes of relative risks for cardiovascular disease events associated with individual risk factors.[38–41] Thus, the higher prevalence of adverse risk factors among blacks translates into a higher observed risk of cardiovascular disease. In the present study, we also observed a higher prevalence of risk factors among blacks than among whites. However, because of the higher burden of competing risks among blacks, which our analytical approach accounted for, we observed similar lifetime risks of death from cardiovascular disease among blacks and whites, despite the higher burden of risk factors among blacks.

There are several limitations of the present study. First, our algorithm for aggregate risk-factor stratification included treated patients in the highest-risk groups. Although the inclusion of treated patients may have resulted in some misclassification, these participants represent a very small percentage of the overall cohort. The effect of this categorization, if anything, tends to underestimate future risk in the strata with the highest risk-factor burden. Furthermore, we have validated this algorithm in multiple and diverse cohorts, including the Framingham Heart Study,[7] the Chicago Heart Association Detection Project in Industry,[36] the Coronary Artery Risk Development in Young Adults (CARDIA) study,[2] the Multi-Ethnic Study of Atherosclerosis (MESA),[2] and the Dallas Heart Study,[42] using diverse clinical and subclinical end points. We have also observed that the association between risk-factor categories and risk of cardiovascular disease does not depend on the presence or absence of any one risk factor alone. Therefore, we believe that our classification of risk-factor burden provides a reliable, and conservative, projection of the risk of cardiovascular disease.

Second, we were not able to estimate lifetime risks of death from cardiovascular disease for persons with risk factors measured in the most recent decade included in the study because the estimation of lifetime risk ideally requires several decades of actual follow-up from the point at which the risk factor is measured. Nevertheless, because of the consistency of results across birth cohorts in which the prevalence of elevated risk factors varies, we believe that the present data are applicable to contemporary cohorts.

In summary, the Cardiovascular Lifetime Risk Pooling Project represents a combined analysis of data from more than 250,000 participants derived from 18 cohorts during a period of more than 50 years. We found that the presence of elevated levels of risk factors at all ages translated into markedly higher lifetime risks of cardiovascular disease across the lifespan. These findings were consistent across risk-factor strata among both blacks and whites and across multiple birth cohorts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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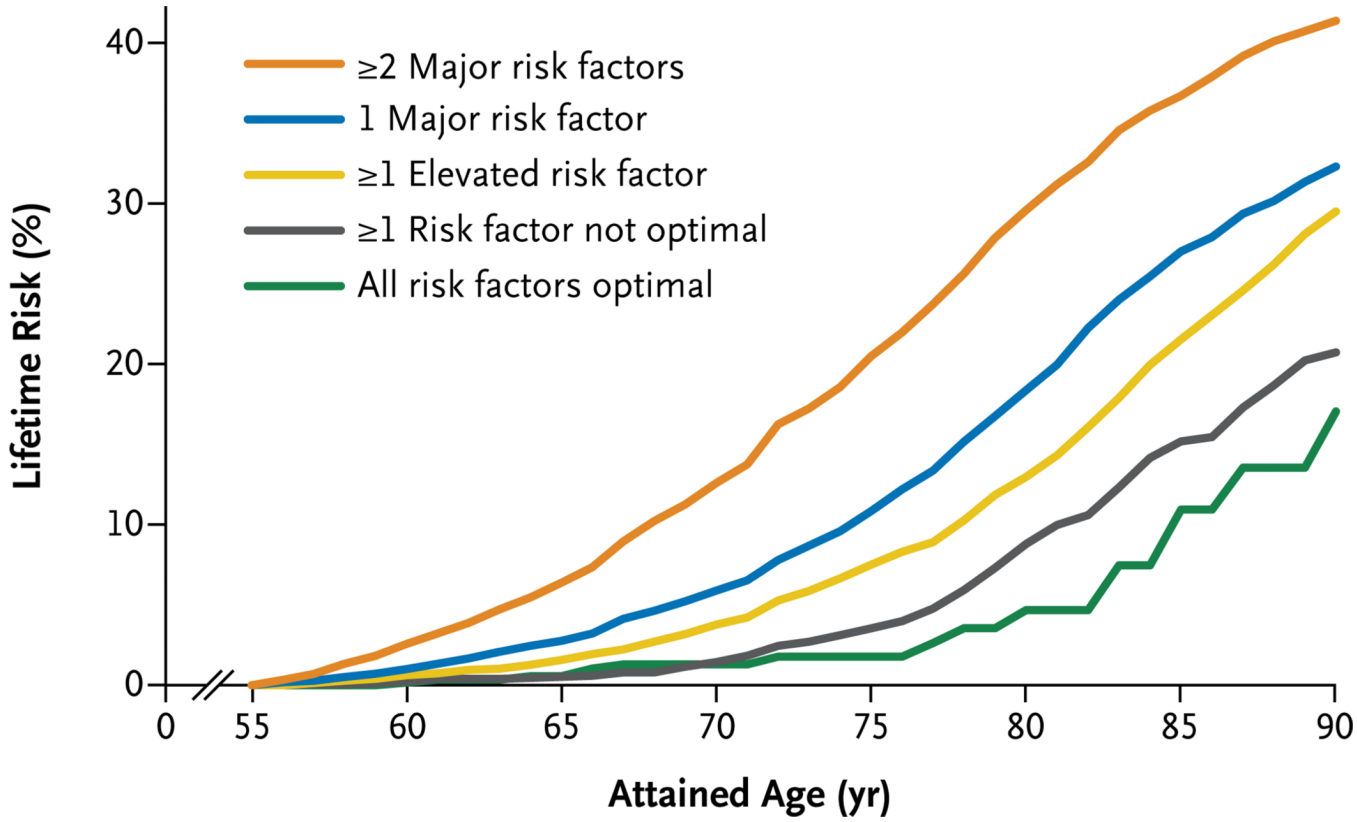

Figure 1. Lifetime Risk of Death from Cardiovascular Disease among Black Men and White Men at 55 Years of Age, According to the Aggregate Burden of Risk Factors and Adjusted for Competing Risks of Death

The risk-factor profile was considered optimal when a participant had a total cholesterol level of less than 180 mg per deciliter (4.7 mmol per liter) and untreated blood pressure of less than 120 mm Hg systolic and less than 80 mm Hg diastolic, was a nonsmoker, and did not have diabetes. It was considered not to be optimal for nonsmokers without diabetes who had a total cholesterol level of 180 to 199 mg per deciliter or untreated systolic blood pressure of 120 to 139 mm Hg or untreated diastolic blood pressure of 80 to 89 mm Hg. Levels of risk factors were viewed as elevated for nonsmokers without diabetes who had a total cholesterol level of 200 to 239 mg per deciliter (5.17 to 6.18 mmol per liter) or untreated systolic blood pressure of 140 to 159 mm Hg or untreated diastolic blood pressure of 90 to 99 mm Hg. Major risk factors were defined as current smoking, diabetes, treatment for hypercholesterolemia, an untreated total cholesterol level of at least 240 mg per deciliter (6.21 mmol per liter), and treatment for hypertension, untreated systolic blood pressure of at least 160 mm Hg, or untreated diastolic blood pressure of at least 100 mm Hg. The data were derived from the 17 studies in the pooled cohort; data from the Multiple Risk Factor Intervention Trial were not included.

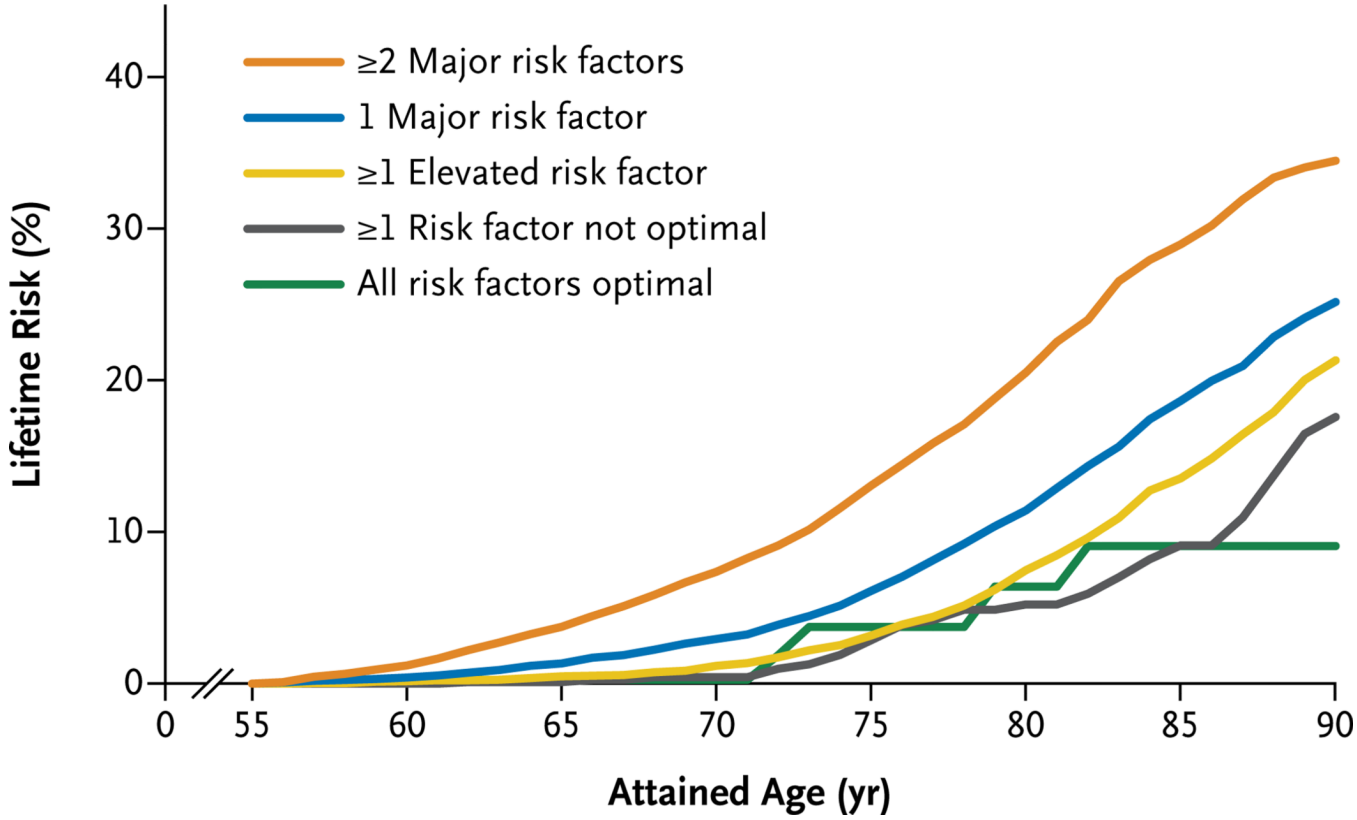

Figure 2. Lifetime Risk of Death from Cardiovascular Disease among Black Women and White Women at 55 Years of Age, According to the Aggregate Burden of Risk Factors and Adjusted for Competing Risks of Death

The data were derived from the 17 studies in the pooled cohort; data from the Multiple Risk Factor Intervention Trial were not included.

Table 1

Baseline Risk Factors and Risk-Factor Profile among Men and Women According to Age Group.*

Risk Factor	Age Group							
	45 Yr		55 Yr		65 Yr		75 Yr	
	men (N = 17,315)	*women (N = 12,679)*	*men (N = 25,595)*	*women (N = 17,222)*	*men (N = 16,845)*	*women (N = 14,250)*	*men (N = 6137)*	*women (N = 7514)*
Risk factors								
Diabetes (%)	2.8	3.0	5.6	6.2	9.2	9.7	11.7	9.7
Current smoking (%)	51.0	37.8	45.1	29.1	33.7	21.0	20.7	13.5
Mean total cholesterol (mg/dl)	214.3	208.5	214.6	226.7	211.7	232.2	203.1	224.7
Mean systolic blood pressure (mm Hg)	130.5	124.6	132.7	129.5	137.0	135.5	140.8	141.7
Risk-factor profile								
All risk factors optimal (%)	2.9	7.1	2.9	3.6	2.8	1.7	2.8	1.3
≥1 Risk factor not optimal (%)	9.5	14.4	8.2	8.4	8.8	6.6	10.0	6.4
≥1 Risk factor elevated (%)	19.1	22.0	18.8	21.5	19.2	18.8	20.4	18.2
1 Major risk factor (%)	46.5	40.1	45.9	40.7	44.2	41.6	43.3	43.3
≥2 Major risk factors (%)	22.0	16.4	24.2	25.8	25.0	31.3	23.5	30.8

*The risk-factor profile was considered to be optimal when a participant had a total cholesterol level of less than 180 mg per deciliter and untreated blood pressure of less than 120 mm Hg systolic and less than 80 mm Hg diastolic, was a nonsmoker, and did not have diabetes. Risk factors were viewed as not being optimal for nonsmokers without diabetes who had a total cholesterol level of 180 to 199 mg per deciliter or untreated systolic blood pressure of 120 to 139 mm Hg or untreated diastolic blood pressure of 80 to 89 mm Hg. Risk factors were viewed as elevated for nonsmokers without diabetes who had a total cholesterol level of 200 to 239 mg per deciliter or untreated systolic blood pressure of 140 to 159 mm Hg or untreated diastolic blood pressure of 90 to 99 mm Hg. Major risk factors included being a current smoker or having diabetes, having treated hypercholesterolemia, having an untreated total cholesterol level of at least 240 mg per deciliter, or having treated hypertension, untreated systolic blood pressure of at least 160 mm Hg, or untreated diastolic blood pressure of at least 100 mm Hg. These data were derived from the 17 studies in the pooled cohort; data from the Multiple Risk Factor Intervention Trial were not included. To convert the values for total cholesterol to millimoles per liter, multiply by 0.02586.

Table 2

Lifetime Risks of Fatal and Nonfatal Events among Men According to Aggregate Burden of Risk Factors.*

Variable	Risk-Factor Status				
	All Risk Factors Optimal	≥1 Risk Factor Not Optimal	≥1 Elevated Risk Factor	1 Major Risk Factor	≥2 Major Risk Factors
	percent (95% confidence interval)				
Risk at 45 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	1.7 (0–4.3)	27.5 (15.7–39.3)	32.7 (24.5–41.0)	34.0 (30.4–37.6)	42.0 (37.6–46.5)
Fatal or nonfatal stroke	6.7 (1.4–11.9)	7.7 (5.0–10.4)	8.5 (6.9–15.6)	8.4 (7.5–9.4)	10.3 (9.0–11.7)
Death from cardiovascular disease	9.1 (0–18.6)	13.1 (9.9–16.3)	15.3 (13.3–17.3)	20.7 (19.4–22.2)	32.5 (30.5–34.5)
Total events related to atherosclerotic cardiovascular disease	1.4 (0–3.4)	31.2 (17.6–44.7)	35.0 (26.8–43.2)	39.6 (35.7–43.6)	49.5 (45.0–53.9)
Risk at 55 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	3.6 (0.7–6.5)	15.6 (7.9–23.2)	24.7 (19.5–29.9)	26.8 (24.0–29.6)	37.5 (33.9–41.1)
Fatal or nonfatal stroke	2.3 (0–4.8)	3.7 (2.3–5.0)	5.5 (4.6–6.4)	6.1 (5.5–6.7)	8.3 (7.4–9.2)
Death from cardiovascular disease	4.7 (1.2–8.2)	8.8 (6.7–10.9)	13.0 (11.6–14.3)	18.4 (17.4–19.4)	29.6 (28.1–31.1)
Total events related to atherosclerotic cardiovascular disease	14.6 (1.0–28.3)	19.7 (11.9–27.4)	33.9 (27.9–39.8)	32.2 (29.1–35.2)	46.8 (43.0–50.7)
Risk at 65 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	9.6 (0–21.6)	21.6 (12.5–30.6)	26.6 (21.5–31.8)	29.5 (26.1–32.8)	43.0 (38.6–47.4)
Fatal or nonfatal stroke		6.7 (4.4–9.1)	9.2 (7.7–10.8)	8.1 (7.1–9.0)	9.1 (7.9–10.3)
Death from cardiovascular disease		18.4 (14.5–22.0)	27.7 (25.3–30.2)	33.6 (31.9–35.3)	42.2 (40.0–44.4)
Total events related to atherosclerotic cardiovascular disease	29.5 (17.0–42.0)	29.4 (20.7–38.1)	38.2 (32.4–43.9)	37.2 (33.7–40.8)	49.5 (45.2–53.8)
Risk at 75 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	9.2 (0–21.8)	12.5 (5.0–20.0)	22.1 (17.1–27.1)	29.3 (25.5–33.0)	34.6 (29.2–40.0)

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Variable	Risk-Factor Status				
	All Risk Factors Optimal	**≥1 Risk Factor Not Optimal**	**≥1 Elevated Risk Factor**	**1 Major Risk Factor**	**≥2 Major Risk Factors**
	percent (95% confidence interval)				
Fatal or nonfatal stroke		9.1 (5.9–12.3)	10.6 (8.4–12.8)	9.1 (7.7–10.5)	9.6 (7.6–11.6)
Death from cardiovascular disease	20.7 (11.1–30.3)	18.7 (13.9–23.5)	28.1 (24.6–31.6)	32.2 (29.6–34.7)	39.3 (35.8–42.9)
Total events related to atherosclerotic cardiovascular disease	17.5 (3.0–32.0)	22.8 (14.4–31.2)	28.9 (22.7–35.2)	36.1 (31.6–40.5)	38.5 (32.0–45.0)

[*] Lifetime risks are reported as percentages, with 95% confidence intervals, to the age of 80 years for participants 45 or 55 years of age and to the age of 90 years for participants 65 or 75 years of age. Empty cells represent strata for which no reliable estimates of lifetime risks could be calculated because of small sample sizes or incomplete follow-up to the oldest age. The data were derived from the 17 studies in the pooled cohort; data from the Multiple Risk Factor Intervention Trial were not included.

Table 3

Lifetime Risks of Fatal and Nonfatal Events among Women According to Aggregate Burden of Risk Factors.*

Variable	Risk-Factor Status				
	All Risk Factors Optimal	≥Risk Factor Not Optimal	≥1 Elevated Risk Factor	1 Major Risk Factor	≥2 Major Risk Factors
	percent (95% confidence interval)				
Risk at 45 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	1.6 (0–4.3)	9.3 (3.0–15.6)	9.3 (5.0–13.7)	12.7 (10.3–15.0)	21.5 (17.5–25.5)
Fatal or nonfatal stroke	8.3 (3.8–12.8)	8.9 (6.5–11.3)	9.1 (7.5–10.9)	9.1 (7.9–15.9)	11.5 (9.5–13.5)
Death from cardiovascular disease	4.8 (0.8–8.7)	4.9 (3.1–6.7)	6.9 (5.4–8.3)	11.2 (9.9–12.5)	21.9 (19.4–24.5)
Total events related to atherosclerotic cardiovascular disease	4.1 (0–8.2)	12.2 (4.6–19.7)	15.6 (10.3–20.9)	20.2 (17.2–23.2)	30.7 (26.3–35.0)
Risk at 55 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	0	6.5 (0.7–12.2)	6.3 (3.7–8.9)	10.1 (8.4–11.9)	18.3 (15.9–20.8)
Fatal or nonfatal stroke	5.3 (0–11.3)	8.3 (5.3–11.4)	6.0 (4.8–7.2)	7.2 (6.3–8.1)	10.7 (9.5–11.9)
Death from cardiovascular disease	6.4 (0–13.3)	5.2 (2.8–7.6)	7.5 (6.1–8.8)	11.4 (10.3–12.5)	20.5 (18.9–22.2)
Total events related to atherosclerotic cardiovascular disease	10.1 (0–25.0)	13.3 (5.5–21.1)	15.3 (11.3–19.3)	16.7 (14.5–19.0)	29.2 (26.2–32.3)
Risk at 65 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction	0.9 (0–2.7)	1.9 (0–4.1)	10.6 (7.1–14.1)	19.7 (17.1–22.3)	27.0 (24.7–30.9)
Fatal or nonfatal stroke		11.2 (6.0–16.4)	12.5 (10.1–14.9)	11.8 (10.4–13.3)	14.2 (12.6–15.9)
Death from cardiovascular disease		17.6 (11.3–23.9)	20.7 (17.7–23.7)	27.1 (25.1–29.1)	35.2 (32.9–37.5)
Total events related to atherosclerotic cardiovascular disease	12.4 (2.8–22.0)	25.0 (15.4–34.5)	29.3 (23.8–34.7)	31.9 (28.8–34.9)	38.7 (35.3–42.1)
Risk at 75 yr of age					
Fatal coronary heart disease or nonfatal myocardial infarction		10.8 (2.6–19.0)	14.3 (10.5–18.2)	17.3 (14.8–19.9)	27.8 (24.4–31.2)

Variable	Risk-Factor Status				
	All Risk Factors Optimal	≥Risk Factor Not Optimal	≥1 Elevated Risk Factor	1 Major Risk Factor	≥2 Major Risk Factors
	percent (95% confidence interval)				
Fatal or nonfatal stroke		7.8 (4.6–11.1)	10.8 (8.5–13.1)	11.7 (10.3–13.2)	13.7 (11.9–15.5)
Death from cardiovascular disease		19.2 (13.4–25.0)	20.5 (17.4–23.6)	24.3 (22.2–26.3)	33.6 (31.0–36.2)
Total events related to atherosclerotic cardiovascular disease	12.4 (0–25.6)	19.9 (10.9–29.0)	21.8 (16.8–26.8)	29.4 (26.1–32.7)	36.3 (32.2–40.4)

[*] Lifetime risks are reported as percentages, with 95% confidence intervals, to the age of 80 years for participants 45 or 55 years of age and to the age of 90 years for participants 65 or 75 years of age. Empty cells represent strata for which no reliable estimates of lifetime risks could be calculated because of small sample sizes or incomplete follow-up to the oldest age. Zero reflects the fact that there were no events despite adequate person-years of follow-up. The data were derived from the 17 studies in the pooled cohort; data from the Multiple Risk Factor Intervention Trial were not included.