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Cardiometabolic Risk Factors Among US Adolescents and Young Adults and Risk of Early Mortality

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Abstract

OBJECTIVE—To determine the risk of mortality associated with cardiometabolic risk factors in a national sample of adolescents and young adults.

METHODS—Prospective study of participants in the third NHANES (1988–1994), aged 12 to 39 years at the time of the survey (*n* = 9245). Risk factors included 3 measures of adiposity, glycated hemoglobin (HbA1c) level, cholesterol levels, blood pressure, self-reported smoking status, and cotinine level. Death before age 55 (*n* = 298) was determined by linkage to the National Death Index through 2006. Proportional hazards models, with age as the time scale, were used to determine the risk of death before age 55 years after adjusting for gender, race/ethnicity, and presence of comorbid conditions.

RESULTS—After adjusting for age, gender, and race/ethnicity, results of categorical analyses showed that current smokers were at 86% greater risk for early death than those classified as never smokers; that those with a waist-to-height ratio >0.65 were at 139% greater risk than those with a WHR <0.5; and that those with an HbA1c level >6.5% were at 281% greater risk than those with an HbA1c level <5.7%. Neither high-density lipoprotein nor non–high-density lipoprotein cholesterol measures were associated with risk for early death.

CONCLUSIONS—Our finding that risk for death before age 55 among US adolescents and young adults was associated with central obesity, smoking, and hyperglycemia supports reducing the prevalence of these risk factors among younger US residents.

Keywords

adolescents; mortality; cardiometabolic risk factors; NHANES

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During the past 20 years, the prevalence of overweight and obesity in the United States has increased, particularly among adolescents and young adults.[1] At the same time, there have also been changes in blood pressure, lipids, smoking, and glucose levels among these groups,[2–6] whereas the prevalence of these cardiometabolic risk factors has generally declined among middle-aged and older adults. However, the implications of the increased prevalence of these risk factors in the young are unclear. Although these risk factors have been associated with earlier onset of many chronic diseases, including diabetes, hypertension, and cardiovascular disease,[7,8] most of the studies showing such associations have focused on adults 40 years or older, and relatively few have examined the relationship between these risk factors and risk for early death among adolescents and young adults.[9–11] In our analysis, we assessed the relationship between selected cardiometabolic risk factors and risk for death before 55 years of age among participants in the third NHANES (NHANES III) who were aged 12 to 39 years at the time of their participation in the survey (1988–1994).

METHODS

Data Sources

Our primary data source, NHANES III, used a stratified multistage sample design to produce a nationally representative sample of the noninstitutionalized US civilian population.[12] NHANES III data were collected from survey participants via a physical examination, laboratory tests, and questionnaires on health-related topics. The overall response rate among people selected to participate and who completed the examination was 77%.[13] Vital status for NHANES III participants from 1988 through 2006 was based on data from National Death Index (NDI). For our analysis, we excluded 452 participants whose race/ethnicity was classified as other than white, black, or Mexican American, and 6 whose vital status could not be determined. Our final analytic sample consisted of 9245 NHANES III participants who were aged 12 to 39 years when they participated in the survey.

Cardiometabolic Risk Factors

Cardiometabolic risk factors were obtained during the NHANES interview and examination and included measures of adiposity, serum lipid levels, glycated hemoglobin (HbA1c), blood pressure, and smoking status.[12]

Adiposity was measured by BMI, waist circumference, and waist-to-height ratio (WHR).[14] BMI was defined as normal (BMI<25 kg/m^2), overweight (BMI 25 to <30 kg/m^2), or obese (BMI≥30 kg/m^2). For participants 18 years or younger, overweight was defined as having age-and gender-specific BMI ≥85th and <95th percentile and obese was defined as having BMI ≥95th percentile based on the Centers for Disease Control and Prevention reference population.[15] Large waist circumference was defined as waist circumference ≥80 cm/>88 cm for adolescent/adult females, respectively, and ≥90 cm/≥102 cm for adolescent/adult males, respectively. WHR was categorized as <0.5, 0.5 to 0.64, or ≥0.65. HbA1c was categorized as <5.7%, 5.7% to 6.4%, or ≥6.5%.[16] For total cholesterol, the categories were <200 mg/dL, 200 to 239 mg/dL, or ≥240 mg/dL. High-density lipoprotein (HDL) cholesterol categories were <35 mg/dL, 35–59 mg/dl and ≥ 60 mg/dl for participants ≤18 years. For

participants <18 years, the categories were <40 mg/dL for males and 50 mg/dL females, 40 to 59 mg/dL males and 50 to 59 mg/dL females, and ≥60 mg/dL. Non-HDL cholesterol categories were <130 mg/dL, 130 to 144 mg/dL, and ≥ 144 mg/dL.[17] Blood pressure categories were hypertension (defined as ≥140/90 or self-report of diagnosis), pre-hypertension (defined as blood pressure between 120/80 and 140/90 and no self-report of diagnosis), and normal. For participants ≤18 years, pre-hypertension was defined as the lower of 90th to 95th percentile for age, gender, and height or 120/80, and hypertension was defined as the lower of >95th percentile for age, gender, and height or 140/90.[18,19] Self-reported current smoker was based on report of smoking at least 100 cigarettes in a lifetime and currently smoking, past smoker as smoking at least 100 cigarettes in a lifetime but not currently smoking, and never smoker reporting <100 cigarettes in a lifetime. Enviromental exposure to tobacco was defined based on serum cotinine levels (limit of detection to 0.05, 0.05 to <10 ng/mL, 10–99 ng/mL, or ≥ 100 ng/mL).[20,21]

Outcomes

The 2 outcomes of interest in our study were death before age 55 from all causes and death before age 55 from endogenous causes only (ie, from diseases and self-inflicted injury but not from accidents or homicides). Because of the small number of deaths from exogenous causes, we were unable to report these results separately. Vital status was based on NDI data from January 1, 1988, through December 31, 2006, linked to NHANES III. A complete description of the methodology used to link NHANES III records to NDI data can be found at http://www.cdc.gov/nchs/data/datalinkage/matching_methodology_nhanes3_final.pdf (accessed October 24, 2011).

Other Covariates

In our analyses, we adjusted for subjects' gender, race/ethnicity, and chronic disease status (ie, any history of diabetes, cardiovascular disease, or cancer). All of these covariates were based on self-report of information provided by survey participants.

Analysis

We first calculated the number of person years (PYs) from the date of subjects' NHANES examination to the date of their death or the end of the follow-up period (December 31, 2006), whichever came first. We then estimated the number of deaths per 1000 PYs for each group based on the weighted number of deaths and PYs and used a loglinear Poisson model to calculate the 95% confidence intervals (CIs) for these estimates.

We used proportional hazards models separately for each cardiometabolic risk factor (with age as the time scale for analysis) to estimate the relative hazard (RH) for death before age 55 associated with the risk factors defined both as continuous variables and as categorical variables. We produced 2 sets of estimates: 1 adjusted only for gender and race/ethnicity (Model 1), and 1 adjusted for gender, race/ethnicity, and chronic disease status (Model 2). In our proportional hazards models for cotinine, we combined the 2 lower categories (limit of detection to 0.05ng/mL level and 0.05 to <10 ng/mL) because of the nonsignificant difference between these categories. We tested for interactions for each risk factor with

gender and race/ethnicity. Graphs of the log-log plot of the relative hazards by time showed that the assumption of proportional hazards was met.

All analyses used the sample weights and accounted for the multistage sampling within strata and Primary Sampling Units (PSUs).[13] We used SUDAAN statistical software, version 10.0 (Research Triangle Park, NC).

RESULTS

During NHANES III, 1988 to 1994, the meanage of our study subjects was 26.1 years; 49.6% were male subjects and 50.4% wre female subjects; and 77.2% were non-Hispanic white, 14.7% non-Hispanic black, and 8.1% Mexican American (Table 1). Although only 10% reported a history of chronic disease and few had elevated HbA1c or total cholesterol levels, more than 15% were classified as obese, 22% as having a large waist circumference, and 30% as being current smokers based on their self-reported smoking status. Participants who died were more likely to have higher levels of many cardiometabolic risk factors compared with those alive.

As of December 31, 2006, 298 of the 9245 study subjects had died, and 222 of these deaths were from endogenous causes. Among NHANES participants aged 12 to 39 in 1988 to 1994, the all-cause mortality rate was 1.77 per 1000 PYs (95% CI 1.38–2.16), and the endogenous mortality rate was 1.31 per 1000 PYs (95% CI 1.02–1.60) (Table 2). Among participants 12 to 25 years in NHANES III, the top 3 causes of death were accidents, self-injury, and circulatory. The top 3 causes of death among participants 26 to 32 years in NHANES III were cancer, circulatory, and accidental. The top 3 causes of death among participants 33 to 39 years in NHANES III were cancer, circulatory, and genetic.

Results of categorical analyses adjusted only for gender and race/ethnicity (Model 1, Table 3) showed that WHR was the only measure of adiposity significantly associated with risk for death from all causes (RH 2.39, 95% CI 1.34–4.29 for risk among those with a WHR ≥0.65 versus risk among those with a WHR <0.50) but that all 3 measures of adiposity (BMI, waist circumference, and WHR) were associated with risk for death from endogenous causes. Results also showed that adolescents and young adults with HbA1c levels ≥6.5% were at significantly greater risk for death from all causes and from endogenous causes than were those with HbA1c levels <5.7% (all causes RH 3.81, 95% CI 1.98–7.31; endogenous causes RH 4.68, 95% CI 2.43–9.01); that those with hypertension were at significantly greater risk for death from endogenous causes than those with normal blood pressure (RH 1.84, 95% CI 1.02–3.32); that those classified as current smokers were at greater risk for death from all causes than those classified as never smokers (RH 1.86, 95% CI 1.25–2.76); and that those with cotinine levels ≥100 ng/mL were at greater risk for death from all causes and from endogenous causes than were those with cotinine levels<10 ng/mL (RH 1.70, 95% CI 1.02–2.82, and RH 1.89, 95% CI 1.17–3.08, respectively). No other factors were significantly associated with risk for early death.

Results of categorical analyses in which we also adjusted for survey respondents' self-reported history of chronic disease (Model 2, Table 3) generally showed a weaker relationship between the various risk factors and the likelihood of dying before age 55.

Although women had a higher risk of all-cause mortality from elevated total cholesterol, non-HDL cholesterol and blood pressure, there was no significant increased risk among men (Table 4). There were no significant interactions by race/ethnicity.

DISCUSSION

Among persons aged 12 to 39 in 1988 to 1994, smoking, adiposity, and an elevated HbA1c level were associated with an overall increased risk for death before age 55, and elevated blood pressure was associated with an increased risk for death from endogenous causes. Although the strength of the relationship between the various risk factors and risk for early death was reduced when we adjusted for study subjects' history of chronic diseases, this reduction was not surprising, given that diabetes is defined largely on the basis of elevated HbA1c levels and heart disease is associated with elevated blood pressure. Of the 4 factors we found to be associated with risk of dying before age 55, cotinine concentration and WHR had the strongest and most consistent associations, whereas only very high blood pressure and HbA1c levels were significantly associated with an increased risk. These findings underscore the importance of obesity prevention and tobacco control interventions for adolescents and young adults.

We found differences in risk of mortality for male and female subjects for total cholesterol, non-HDL cholesterol, blood pressure, and cotinine. These findings suggest that there may be a differential risk for male and female subjects. However, caution is urged in interpreting these findings because they are based on fewer than 90 deaths among female subjects.

Our findings for each individual risk factor largely support previous findings.[22–27] Although some previous studies have examined the impact of risk factors in youth on subsequent morbidity and mortality in adulthood, none have been conducted using nationally representative data. Elevated levels of various cardiometabolic risk factors among youth have been associated with an increased risk for early cardiovascular disease and diabetes in studies from Bogalusa[28] and Chicago,[29] in the Muscatine study,[30] in the National Heart, Lung, and Blood Institute Growth and Health Study,[31] and in various systematic reviews.[32,33] Results of one of these reviews showed an increased risk for both death and morbidity among adolescents who were overweight or obese.[31] Elevated BMI and glucose levels were associated with an increased risk for death before age 55 among children and young adults in the Gila River Indian Community in Arizona.[9] Elevated blood pressure in late adolescence was also recently found to be associated with increased risk for death before age 45 years in a cohort of Swedish men[11] and among young adults in China.[10] The association between risk for early death and smoking status (whether based on self-reports or cotinine levels) has been well documented[22,23]; however, our finding that smoking was less related to risk for early death from endogenous causes than to risk for early death from all causes suggests that, in addition to the risks from cigarette smoking itself, smoking may

also be a marker for additional risky behaviors that puts individuals at elevated risk for death (eg, by injury).

Results from previous studies of the relationship between adiposity and mortality risk have been mixed, with some showing a direct association, some showing no association, and some showing a J-or U-shaped relationship.[24–26] However, many of these previous studies used BMI as the sole indicator of adiposity. Our findings suggest that WHR and waist circumference, both of which measure central adiposity more accurately than BMI, may also be better predictors of mortality risk.

Results from 1 previous study showed that>30% of US adolescents and young adults had HDL and non-HDL cholesterol levels associated with increased risk for cardiovascular disease.[34] Although we found no significant correlation between lipid levels and risk for early death among members of our study cohort, elevated lipid levels by age 50 were associated with an increased risk for cardiovascular disease events and with a lower mean survival time among members of the Framingham cohort.[35]

Our finding that an HbA1c level >6.5%, the cutoff used to define diabetes, was associated with a close to a twofold increased risk for early death, even after the exclusion of those in whom diabetes had been diagnosed, provides further evidence of the importance of identifying people with diabetes and providing appropriate treatment of those with elevated HbA1c levels.[27] Among older populations, HbA1c levels >6% have been associated with increased mortality.[36] Although we did not find HbA1c levels that were above normal but below the diagnostic threshold for diabetes to be associated with an increased risk of dying before age 55, our finding of a nonsignificantly higher relative risk for early death among adolescents and young adults with such prediabetic HbA1c levels than among those with normal HbA1c levels indicates a need for a study with larger samples to examine the health implications of prediabetic HbA1c levels in young adults.

The conveyance of information about risk factors for early death is an important component of health-promotion and disease-prevention efforts.[37–39] However, the definition of “early death” differs by country and is usually related to the mean life expectancy in the country and to the loss of what are perceived to be potentially productive years in which a person is expected to support other community members, including their children, and be a contributing member of their society’s work force.[40] Although it is well established that many early deaths, especially among teenagers and young adults, are caused by injuries,[41] the extent to which risk factors for disease are also associated with early deaths has not been well studied. Our findings suggest that, at least in the United States, certain cardiometabolic risk factors also contribute substantially to the overall risk for early death and to the social loss that such deaths entail.

There are 2 main limitations of our analysis. The first is that we had relatively few deaths from certain causes and were, therefore, unable to look at specific diseases. The second limitation is that the cardiometabolic risk factors were measured only during NHANES III and we have no information on how changes in any of the risk factors or on subsequent development of disease may or may not have influenced a participants’ risk of mortality.

On the other hand, this study has important strengths. This is the first time mortality follow-up has been provided for NHANES participants <20 years. To our knowledge, this is the first study to focus on risk factors and mortality among adolescents and young adults in a nationally representative US sample. Finally, there was little loss to follow-up for mortality with <3% of the sample missing vital status information.

Among US adolescents and young adults, high HbA1c levels, central obesity, and smoking were associated with an increased risk of dying before 55 years of age. These associations indicate a need for more effective community and clinical strategies for reducing the prevalence of these risk factors among US residents in these age groups.

ABBREVIATIONS

CI	confidence interval
HbA1c	glycated hemoglobin
HDL	high-density lipoprotein
NHANES III	third NHANES
NDI	National Death Index
PY	person years
RH	relative hazards
WHR	waist-to-height ratio

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WHAT'S KNOWN ON THIS SUBJECT

The presence of elevated cardiometabolic risk factors, such as obesity, high glucose or lipid levels, and smoking, in adolescents has been shown to be associated with earlier onset of chronic conditions, such as diabetes and heart disease.

WHAT THIS STUDY ADDS

Obesity, smoking, and elevated glucose increases the risk of dying before the age of 55 years. This is the first study to focus on risk factors and mortality among adolescents and young adults in a nationally representative US sample.

TABLE 1

Characteristics of Study Subjects (NHANES III Participants Aged 12–39 Years in 1988–1994)

Characteristics of Study Subjects	Mean Value, or % of Sample Population (SE)	Alive (SE)	Deceased Before Age 55 (SE)	*P* Value[a]
Sample size, *n*			8962	283
Population size, millions			93.9	2.5
Age, y, mean	26.1 (0.17)	26.1 (0.17)	27.6 (0.74)	.054
Male, %	49.6 (0.61)	49.3 (0.65)	61.7 (3.87)	<.01
Race/ethnicity, %				<.01
Non-Hispanic white	77.2 (1.19)	77.4 (1.21)	69.9 (3.43)	
Non-Hispanic black	14.7 (0.98)	14.5 (0.98)	22.7 (2.83)	
Mexican American	8.1 (0.76)	8.1 (0.76)	7.4 (1.26)	
Self-reported high blood pressure, %	9.5 (0.45)	9.2 (0.46)	20.0 (4.24)	<.01
Self-reported diabetes, %	1.0 (0.23)	0.9 (0.22)	4.0 (1.92)	<.01
Self-reported history of heart attack, %	0.3 (0.10)	0.3 (0.10)	—[b]	n/a
Self-reported history of chronic disease (heart disease, diabetes, or cancer), %	10.4 (0.52)	10.0 (0.54)	22.6 (4.53)	<.01
HbA1c level, mean	5.1 (0.02)	5.0 (0.02)	5.2 (0.07)	<.01
<5.7, %	95.7 (0.44)	95.9 (0.43)	88.9 (2.14)	<.01
5.7–6.4, %	3.4 (0.42)	3.3 (0.42)	6.7 (1.73)	
≥6.5, %	0.9 (0.18)	0.8 (0.18)	4.4 (1.14)	
Systolic BP, mean	111.6 (0.24)	111.5 (0.24)	114.2 (1.37)	.03
Diastolic BP, mean	69.0 (0.34)	68.9 (0.35)	72.5 (1.26)	.01
Normal blood pressure, %	71.6 (0.79)	72.1 (0.79)	58.3 (5.95)	<.01
Prehypertension,[c] %	23.2 (0.77)	23.4 (0.75)	31.8 (5.24)	
Hypertension,[d] %	5.2 (0.36)	4.5 (0.34)	9.9 (1.95)	
BMI, mean	24.8 (0.13)	24.8 (0.13)	26.4 (0.61)	<.01
Weight classification,[e] %				
Normal weight or underweight	60.3 (0.97)	59.5 (1.05)	50.5 (3.81)	.049
Overweight	24.3 (0.71)	24.4 (0.75)	27.6 (3.84)	
Obese	15.4 (0.67)	16.1 (0.68)	21.9 (3.53)	
Waist circumference in cm, mean	84.9 (0.26)	84.8 (0.28)	90.9 (1.67)	<.01
Large waist circumference,[f] %	22.4 (0.87)	22.2 (0.88)	28.6 (3.76)	.08
WHR, mean	0.50 (0.002)	0.50 (0.002)	0.53 (0.01)	<.01
<0.5, %	55.7 (0.95)	56.1 (0.96)	43.9 (3.51)	<.01
0.5–0.64, %	38.3 (0.79)	38.1 (0.78)	43.6 (4.20)	
≥0.65, %	6.0 (0.43)	5.8 (0.45)	12.5 (3.03)	
Total cholesterol level, mean	182.0 (0.82)	181.7 (0.85)	190.8 (3.56)	.01
<200, %	71.6 (1.03)	71.7 (1.02)	66.0 (3.80)	.12
200–239, %	20.9 (0.82)	20.8 (0.82)	22.5 (3.00)	
≥240, %	7.6 (0.53)	7.5 (0.53)	11.4 (2.42)	
HDL cholesterol level, mean	50.4 (0.37)	50.4 (0.39)	50.3 (1.29)	.96

Characteristics of Study Subjects	Mean Value, or % of Sample Population (SE)	Alive (SE)	Deceased Before Age 55 (SE)	*P* Value[a]
Low,[g] %	29.2 (1.20)	29.1 (1.23)	30.6 (4.01)	.83
Middle,[g] %	48.4 (1.21)	48.4 (1.23)	45.6 (4.57)	
High,[g] %	22.5 (1.03)	22.5 (1.08)	23.8 (3.45)	
Non-HDL cholesterol, mean	131.6 (0.90)	131.4 (0.93)	140.3 (3.43)	.01
<130, %	53.1 (1.01)	53.4 (1.01)	40.2 (4.88)	.03
130–144, %	13.4 (0.64)	13.3 (0.64)	16.8 (3.79)	
≥144, %	33.5 (0.98)	33.2 (0.98)	43.0 (4.41)	
Self-reported smoking status, %				<.01
Current	33.6 (1.12)	33.2 (1.12)	48.1 (4.90)	
Former	13.5 (0.73)	13.6 (0.74)	12.6 (3.13)	
Never	52.9 (0.98)	53.2 (0.96)	39.3 (4.19)	
Cotinine levels, geometric mean	2.2 (0.22)	2.1 (0.22)	7.7 (2.73)	<.01
<0.05 (below limit of detection)	8.4 (0.72)	8.4 (0.74)	6.3 (2.31)	<.01
0.05–<10 (environmental tobacco smoke exposure)	57.6 (0.85)	58.0 (0.85)	42.5 (4.95)	
10–99 (moderate tobacco exposure)	7.8 (0.44)	7.6 (0.45)	12.2 (3.32)	
≥100 (heavy tobacco exposure)	26.3 (1.07)	25.9 (1.06)	39.1 (5.37)	

Population based on 9245 participants aged 12–39 y with complete data on early mortality. Data reported are percentages (SE) unless otherwise noted. BP, blood pressure.

[a]Difference between alive and deceased participants on selected characteristics estimated from design-corrected Wald *F* test.

[b]No cases reported.

[c]Prehypertension: for adults, as blood pressure between 120/80 and 140/90 and no self-report of a hypertension diagnosis. For adolescents, as blood pressure in the 90th to 95th percentile for one's age, gender, and height or by adult blood pressure criteria.

[d]Hypertension: For adults, hypertension was defined as blood pressure≥140/90 or a self-report of a hypertension diagnosis. For adolescents, as defined either as blood pressure above the 95th percentile for one's age, gender, and height or by adult blood pressure criteria.

[e]Weight classification: For adults, normal weight (BMI<25.0), overweight (BMI 25.0–29.9), or obese (BMI≥30.0). For adolescents, based on BMI percentiles relative to age- and gender-specific BMI distributions based on Centers for Disease Control and Prevention growth charts: normal weight (<85th percentile), overweight (85th–94th percentile), or obese (≥95th percentile).

[f]Large waist circumference was defined as ≥80 cm for adolescent females, >88 cm for adult females, ≥90 cm for adolescent males, and ≥102 cm for adult males.

[g]HDL cholesterol categories. For adolescents: low<35 mg/dL, middle 35–59 mg/dL, high≥60 mg/dL. For adults: low<40 mg/dL men and 50 mg/dL women, middle 40–59 mg/dL men and 50–59 mg/dL women, and high ≥ 60 mg/dL for both.

TABLE 2

Age-Specific Gender-Standardized Mortality Rates Among NHANES III Participants Aged 12 to 39 From 1988 Through 2006

NHANES III Age, y	Population Size per 100 000	No. of Deaths per 100 000	Mortality Rate per 1000 PY	Top 3 Causes of Death
Death from all causes				
Total	997.0	26.6	1.77 (1.38–2.16)	Cancer, circulatory, self-inflicted injury
12–18	224.9	4.8	1.38 (0.70–2.06)	Accidental, self-inflicted injury, circulatory
19–25	231.9	4.9	1.39 (0.70–2.09)	Self-inflicted injury, circulatory, accidental
26–32	273.0	9.3	2.25 (1.41–3.09)	Cancer, circulatory, accidental
33–39	267.2	7.7	1.94 (1.37–2.52)	Cancer, circulatory, genetic
Death from endogenous causes				
Total	997.0	19.7	1.31 (1.02–1.60)	Cancer, circulatory, self-inflicted injury
12–18	224.9	2.8	0.82 (0.27–1.37)	Circulatory, self-inflicted injury, cancer
19–25	231.9	3.0	0.84 (0.35–1.34)	Circulatory, self-inflicted injury, respiratory
26–32	273.0	7.5	1.81 (1.13–2.50)	Cancer, circulatory, self-inflicted injury
33–39	267.2	6.4	1.61 (1.09–2.13)	Cancer, circulatory, genetic

TABLE 3

Relationship Between Selected Characteristics and Risk for Death Before Age 55 From All Causes and From Endogenous Causes Among NHANES III Participants Aged 12 to 39 Years During NHANES III, With Follow-up From 1988 to 2006

Characteristic	Risk for Death From All Causes		Risk for Death From Endogenous Causes	
	Model 1 RH (95% CI)	Model 2 RH (95% CI)	Model 1 RH (95% CI)	Model 2 RH (95% CI)
Weight classification[a] normal (reference)				
Overweight	1.08 (0.71–1.64)	1.02 (0.65–1.58)	0.91 (0.53–1.54)	0.84 (0.48–1.46)
Obese	1.40 (0.92–2.13)	1.21 (0.80–1.81)	1.60 (1.06–2.43)	1.33 (0.87–2.04)
Waist circumference[b]				
Large	1.45 (0.97–2.17)	1.30 (0.88–1.94)	1.65 (1.06–2.57)	1.44 (0.92–2.25)
WHR <0.5 (reference)				
0.5–6.4	1.20 (0.88–1.64)	1.14 (0.81–1.60)	0.99 (0.68–1.46)	0.93 (0.61–1.41)
≥0.65	2.39 (1.34–4.29)	1.92 (1.09–3.40)	2.77 (1.52–5.07)	2.10 (1.14–3.87)
HbA1c <5.7% (reference)				
5.7%–6.4%	1.48 (0.86–2.55)	1.41 (0.83–2.40)	1.44 (0.66–3.41)	1.36 (0.63–2.93)
≥6.5%	3.81 (1.98–7.31)	2.52 (1.23–5.19)	4.68 (2.43–9.01)	2.92 (1.42–6.01)
Total cholesterol <200 mg/dL (reference)				
200–239 mg/dL	0.98 (0.70–1.38)	0.95 (0.67–1.34)	0.76 (0.47–1.22)	0.73 (0.45–1.19)
≥240 mg/dL	1.29 (0.78–2.16)	1.22 (0.74–2.03)	1.52 (0.88–2.60)	1.41 (0.82–2.43)
HDL cholesterol[c] high (reference)				
Middle	0.83 (0.52–1.34)	0.84 (0.51–1.36)	0.71 (0.39–1.30)	0.72 (0.39–1.32)
Low	0.95 (0.60–1.51)	0.93 (0.58–1.47)	0.87 (0.44–1.69)	0.84 (0.43–1.63)
Non-HDL cholesterol <130 mg/dL (reference)				
130–144	1.54 (0.85–2.80)	1.53 (0.85–2.75)	1.42 (0.66–3.08)	1.41 (0.66–3.02)
≥144	1.42 (0.92–2.17)	1.35 (0.88–2.08)	1.23 (0.76–1.98)	1.16 (0.72–1.89)
Blood pressure normal (reference)				
Prehypertension[d]	1.37 (0.80–2.34)	1.23 (0.73–2.05)	1.22 (0.66–2.27)	1.06 (0.60–1.88)
Hypertension[e]	1.73 (0.97–3.06)	1.29 (0.74–2.25)	1.84 (1.02–3.32)	1.25 (0.69–2.25)
Smoking self-report never (reference)				
Current	1.86 (1.25–2.76)	1.89 (1.27–2.81)	1.44 (0.99–2.09)	1.47 (1.01–2.16)
Former	1.14 (0.64–2.20)	1.13 (0.63–2.02)	0.76 (0.33–1.77)	0.75 (0.32–1.77)
Cotinine levels <10 (reference)				
10–99	2.18 (1.12–4.24)	2.21 (1.14–4.28)	1.23 (0.47–3.23)	1.25 (0.48–3.27)
≥100	1.89 (1.17–3.08)	1.91 (1.18–3.11)	1.70 (1.02–2.82)	1.72 (1.03–2.88)

For Models 1 and 2: Separate proportional hazards models for each risk factor. Model 1, with age as the time scale adjusted for gender, race/ethnicity. Model 2, with age as the time scale adjusted for gender, race/ethnicity, and history of chronic disease (self-report of cardiovascular disease, diabetes, and/or cancer).

[a]Weight classification: For adults, normal weight (BMI<25.0), overweight (BMI 25.0–29.9), or obese (BMI≥30.0). For adolescents, based on BMI percentiles relative to age- and gender-specific BMI distributions based on Centers for Disease Control and Prevention growth charts: normal weight (<85th percentile), overweight (85th–94th percentile), or obese (≥95th percentile).

[b]Large waist circumference was defined as ≥80 cm for adolescent girls, >88 cm for adult women, ≥90 cm for adolescent boys, and ≥102 cm for adult men.

[c]HDL cholesterol categories: for adolescents, low<35 mg/dL, middle 35–59 mg/dL, high≥60 mg/dL. For adults, low<40 mg/dL for men and 50 mg/dL for women, middle 40–59 mg/dL for men and 50–59 mg/dL for women, and high ≥60 mg/dL for both.

[d]Prehypertension: For adults, as blood pressure between 120/80 and 140/90 and no self-report of a hypertension diagnosis. For adolescents, as blood pressure in the 90th to 95th percentile for one's age, gender, and height or by adult blood pressure criteria.

[e]Hypertension: For adults, hypertension was defined as blood pressure≥140/90 or a self-report of a hypertension diagnosis. For adolescents, as defined either as blood pressure above the 95th percentile for one's age, gender, and height or by adult blood pressure criteria.

TABLE 4

Male and Female Relationship Between Selected Characteristics and Risk for Death Before Age 55 From All Causes and From Endogenous Causes Among NHANES III Participants Aged 12 to 39 Years During NHANES III, With Follow-up From 1988 to 2006

Characteristic	Male Individuals				Female Individuals			
	Death From All Causes		Death From Endogenous Causes		Death From All Causes		Death From Endogenous Causes	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Total cholesterol								
<200								
200–239	0.79 (0.44–1.40)	0.75 (0.42–1.37)	0.75 (0.36–1.53)	0.71 (0.34–1.51)	1.44 (0.75–2.75)	1.39 (0.71–2.70)	0.80 (0.38–1.68)	0.77 (0.36–1.62)
≥240	0.89 (0.34–2.32)	0.83 (0.32–2.14)	1.08 (0.38–3.10)	1.01 (0.36–2.85)	2.61 (1.42–4.81)	2.46 (1.31–4.65)	2.82 (1.48–5.37)	2.58 (1.31–5.08)
Non–HDL cholesterol								
<130								
130–143	2.06 (0.97–4.36)	2.03 (0.98–4.23)	2.01 (0.80–5.04)	2.00 (0.81–4.92)	0.73 (0.21–2.57)	0.72 (0.20–2.59)	0.47 (0.10–2.16)	0.46 (0.10–2.14)
≥144	1.17 (0.67–2.04)	1.10 (0.64–1.91)	0.90 (0.44–1.84)	0.85 (0.42–1.71)	2.07 (1.17–3.66)	2.00 (1.11–3.62)	2.05 (1.05–4.01)	1.95 (0.97–3.90)
BP								
Normal BP								
pre–HTN	1.55 (0.84–2.87)	1.41 (0.79–2.54)	1.24 (0.62–2.47)	1.10 (0.58–2.08)	0.79 (0.35–1.79)	0.71 (0.30–1.65)	1.01 (0.39–2.62)	0.85 (0.31–2.32)
HTN	1.29 (0.62–2.68)	0.96 (0.47–1.96)	1.16 (0.56–2.40)	0.81 (0.40–1.67)	3.30 (1.68–6.47)	2.43 (1.05–5.62)	4.22 (1.94–9.16)	2.72 (1.00–7.39)
Cotinine								
<10								
10–99	0.76 (0.29–1.95)	0.79 (0.31–2.02)	0.73 (0.22–2.46)	0.77 (0.23–2.58)	6.29 (2.43–16.29)	6.11 (2.38–15.68)	2.39 (0.57–9.95)	2.27 (0.57–9.14)
≥100	1.64 (0.96–2.80)	1.67 (0.98–2.87)	1.51 (0.87–2.64)	1.55 (0.88–2.75)	2.46 (1.21–4.99)	2.43 (1.19–4.97)	2.08 (1.03–4.19)	2.03 (0.99–4.16)

For Models 1 and 2: Separate proportional hazards models for each risk factor. Model 1, with age as the time scale adjusted for race/ethnicity. Model 2, with age as the time scale adjusted for race/ethnicity and history of chronic disease (self-report of cardiovascular disease, diabetes, and/or cancer). BP, blood pressure; HTN, hypertension.