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ASSOCIATION OF MARKERS OF OBESITY WITH SUDDEN CARDIAC DEATH

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ABSTRACT

Obesity has been identified as a risk factor for sudden cardiac death (SCD). The importance of central adiposity [waist-to-hip ratio (WHR)] and general obesity [body mass index (BMI)] in relationship to SCD has not been extensively studied. The objective of this thesis is to study how other markers of obesity such as WHR, along with BMI, affect the risk of SCD.

The baseline and follow-up data on SCD from the ongoing Atherosclerosis Risk in Communities (ARIC) study were used to examine the relationship between markers of obesity and SCD. ARIC is an ongoing biracial population based cohort of middle-aged Americans selected from four communities in 1987-1989. WHR and BMI for a total of 15,732 participants were measured at the baseline visit. Multivariable proportional hazards regression was used to model the association between each anthropometric variable and SCD.

In the model adjusted for age, gender, race, education level, smoking status, prevalent coronary heart disease, hypertension, diabetes, and total cholesterol, WHR (with a 1 SD increase) was associated with SCD within 1 hour of symptom onset (HR = 1.51, 95% CI = 1.22, 1.87; p= 0.0002). By examining the plots of the log hazard ratios versus the WHR quintile, there was no evidence of great deviation from a linear relationship between WHR and SCD. The association between BMI (with a 1 SD increase) and SCD within 1 hour of symptom onset was marginal (HR = 1.16, 95% CI = 1.00, 1.37; p= 0.082). Gender had a marginal interaction with BMI for SCD within 1 hour (p= 0.097). There was a significant association in women only (HR = 1.31, 95% CI = 1.06, 1.61; p= 0.013).

Additionally, in the model adjusted only for age, race, and gender, WHR and BMI (with a 1 SD increase) were associated with SCD within 1 hour of symptom onset for WHR (HR = 1.90, 95% CI = 1.59, 2.27; p= <0.0001) and for BMI (HR = 1.32, 95% CI = 1.15, 1.53; p= 0.0001). The increased HRs in the minimally adjusted model suggests that co-morbidity does play an

intermediate role in the obesity and SCD relationship. Analyses were also done using follow-up data for subjects who died within 24 hours of symptom onset. Although the identified cases were higher than those who died within 1 hour of symptom onset, the overall pattern of findings remained similar on the main effects.

These data suggest that the magnitude of WHR association with SCD within 1 hour of symptom onset is greater than that of BMI, thus supporting the use of measures of obesity such as WHR in addition to BMI in assessing the risk of cardiac death. Co-morbidities play an important intermediate role in the etiology of obesity and sudden cardiac death. Both models were used to examine the quintile-categorized and quadratic terms of the obesity measures, and they did not support significant deviation from the linear relationship.

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Chapter 1

Background and Objectives

The prevalence of obesity is rising in both developed and developing nations. Cited as an important risk factor for premature mortality [Geneva: World Health Organization (WHO), 1998], obesity has strong associations with all-cause mortality, cardiovascular disease (Stevens et al., 1998), stroke and coronary heart disease (Prospective Studies, 2009).

Body mass index, or BMI (weight in kilograms divided by the square of the height in meters), is promulgated by the World Health Organization as the most useful epidemiological measure of obesity (Geneva: WHO, 1998).

Abdominal obesity is more closely associated with the risk of several chronic diseases than is general obesity (Wang et al., 2005). Large studies have suggested the use of waist circumference or waist-to-hip ratio (WHR), as indicators of abdominal obesity, which may be better predictors of the risk of disease than BMI which is an indicator of general adiposity (Stevens et al., 2008). Current guidelines from the American Heart Association with respect to obesity recommend proposing cutoff points for WHR of 0.95 in men and 0.88 in women, to define abdominal obesity and to identify risk factors for disease. However, less is known about the association of WHR with the risk of death.

Most studies that have examined the association of both general and abdominal obesity with the risk of death have shown that abdominal adiposity is an important predictor of the risk of death (Folsom et al., 2000), but few such studies were conducted. Large studies did not assess waist circumference or WHR (Adams et al., 2006) or relied on self reports of anthropometric measurements (Zhang et al., 2008).

The objective of this thesis is to study (1) if there is any relationship between obesity measures and sudden cardiac death (SCD), (2) the shape of relationship if there is any, (3) whether co-morbidity plays an important intermediate role in the obesity and SCD relationships, and (4) gender differences in the relationships, if any.

Chapter 2

Methods

Sources of Data

A public-use data set from The Atherosclerosis Risk in Communities (ARIC) Study was used for this study. ARIC, sponsored by the National Heart, Lung and Blood Institute (NHLBI), is a prospective epidemiologic study conducted in four U.S. communities. The Cohort Component began in 1987, and each ARIC field center randomly selected and recruited a cohort sample of approximately 4,000 individuals aged 45-64 from a defined population in their community. A total of 15,732 participants received an extensive examination, including medical, social, and demographic data. These participants were reexamined every three years with the first screen (baseline) occurring in 1987-89, the second in 1990-92, the third in 1993-95, and the fourth exam in 1996-98. In 2009 the NHLBI funded a fifth exam, which is currently underway. Baseline data and the follow-up data on SCD to the end of 2002 were used for this study.

Obesity Measures

Anthropometric indices were measured after an overnight fast with participants in standard scrub attire. Technicians measured height with participants barefoot using a wall mounted ruler. An anthropometric measuring tape was applied horizontally to measure hip and abdominal girth; participants stood upright with weight evenly distributed between both feet and breathing quietly. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2), waist and

hip girth were measured to the nearest cm, and waist-to-hip ratio (WHR) was the waist girth divided by the hip girth.

Statistical Analysis

Baseline measures and risk factors were included in a proportional hazards regression analysis for time to sudden cardiac death (SCD) within 1 hour and within 24 hours of symptom onset. Two sets of models were examined. In the first set of models (prefixed Model I) multivariable proportional hazards regression was used to model the association between each anthropometric variable (BMI and WHR) and sudden cardiac death, after adjusting for age, gender, race, education, smoking, prevalent CHD, hypertension, diabetes, and total cholesterol for significant association defined as ($p < 0.05$). In the minimally adjusted models (prefixed Model II), analyses were adjusted only for age, race, and gender to test if obesity is independently associated with SCD regardless of other risk factors. Standardized forms for the continuous measures of WHR and BMI were created to reflect a one standard deviation increase of WHR and BMI. Quadratic terms were created for both the standardized forms of WHR and BMI in addition to the linear terms to test if there is a j-shaped or u-shaped relationship with the outcome measure. To assess effect modification by gender, contrast terms were created to calculate hazard ratios for each gender if a significant interaction was identified (defined as $p < 0.10$). Similarly, WHR and BMI were divided into quintiles to examine if a nonlinear trend was present for the measures. The lowest group was considered as the referent category. Hazard ratios with 95% confidence intervals were calculated for the associations between potential risk factors and SCD. All analyses were performed with SAS statistical software, version 9.2 (SAS Institute Inc., Cary, NC).

Covariates

All covariates were collected from the baseline visit. Questionnaires were used to assess educational level, cigarette smoking, alcohol drinking, prevalent CHD, hypertension, diabetes, and total cholesterol. Race was categorized into black and non-black. Educational level was classified as those who had less than high school graduation, high school graduation, and some college education or more. Drinkers were divided into current, former, never, and unknown. Prevalent CHD at baseline was defined as a reported history of a physician-diagnosed myocardial infarction (MI) or prior MI detected by electrocardiography. Diabetes was measured as fasting glucose level with cut point < 126 mg/dl. Hypertension was defined by either a systolic blood pressure of ≥ 140 mm Hg or a diastolic blood pressure of ≥ 90 mm Hg and total cholesterol was measured in fasting state using standardized methods. SCD was defined as a fatal event such as death within 1 hour and 24 hours from onset of acute symptoms.

Chapter 3

Results

Population Characteristics

Table 3-1 summarizes the baseline characteristics of the study population. The total number of participants in the sample was 15,732. The cohort was 55% female and 73% non-black. Seventy-six percent had at least a high-school education. Only 26% were current smokers, while 56% were current drinkers. Thirty-five percent had a history of hypertension, 12% diabetes and 5% prevalent coronary heart disease. During the study period, there were 173 (1.1 %) sudden cardiac deaths within 1 hour of symptom onset and 323 (2.1%) sudden cardiac deaths within 24 hours of symptom onset.

During a mean follow-up of 13 years until death by 2002, the mean age of the study population was 54 with a mean BMI of 28, and mean WHR of 0.93.

Table 3-1-Characteristics of Study Cohort

Characteristic	**Frequency (Percent) or Mean (SD), where n = 15,732**
Female Gender	8677 (55.16)
Black Race	4256 (27.05)
Education Level Less than High School Graduation High School Graduation Some College Education or More	 3761 (23.95) 6393 (40.71) 5551 (35.35)
Current Smoker	4121 (26.22)
Drinker Status Current Drinker Former Drinker Never Drinker Unknown	 8726 (55.72) 2984 (19.05) 3942 (25.17) 8 (0.05)
Hypertension	5490 (35.07)
Diabetes	1864 (11.96)
Prevalent CHD	765 (4.97)
Sudden Cardiac Death within 1 hr	173 (1.10)
Sudden Cardiac Death within 24 hrs	323 (2.05)
Age	54.16 (5.74)
BMI ($kg/(m^2)$)	27.71 (5.38)
Waist Girth (cm)	97.03 (13.75)
Hip Girth (cm)	104.56 (10.18)
Waist-To-Hip Ratio	0.93 (0.08)
HDL (mg/dl)	51.58 (17.10)
LDL (mg/dl)	137.67 (39.36)
Total Cholesterol (mg/dl)	214.97 (42.08)
Total Triglycerides (mg/dl)	131.88 (90.46)
Glucose (mg/dl)	108.97 (40.62)
Leisure Index	2.36 (0.58)
Work Index	2.18 (0.95)
Sport Index	2.43 (0.79)
Total Calorie Intake (kcal/day)	1633.25 (714.60)
Follow-Up Time (days)	4907.48 (1021.81)

BMI denotes body mass index; CHD, coronary heart disease; HDL, re-calibrated high-density lipoprotein in mg/dl; LDL, re-calibrated low-density lipoprotein in mg/dl; SD, standard deviation.

Table 3-2 summarizes the baseline characteristics of the study population by outcome. Of those who developed symptoms of SCD within 1 hour, 34% were female, and 40% were black. Fifty-six percent had at least a high school education. Only 38% were current smokers, while 46% were current drinkers. Sixty-four percent had a history of hypertension, 33% diabetes, and 35% prevalent coronary heart disease. The mean age of the study population was 56, with a mean BMI of 29, and mean WHR of 0.98.

Of those who developed symptoms of SCD within 24 hours, 38% were female, and 42% black. Fifty-seven percent had at least a high school education. Only 41% were current smokers, while 45% were current drinkers. Sixty-six percent had a history of hypertension, 34% diabetes, and 33% prevalent coronary heart disease. The mean age was 56, with a mean BMI of 29, and mean WHR of 0.97.

Table 3-2- Distribution of Characteristics of Study Cohort by Outcome

	Frequency (Percent) or Mean (SD)			
	SCD within 1 hour		SCD within 24 hours	
Characteristic	**Yes = 173**	**No = 15559**	**Yes = 323**	**No = 15409**
Female Gender	58 (33.53)	8619 (55.40)	124 (38.39)	8553 (55.51)
Black Race	69 (39.88)	4187 (26.91)	135 (41.80)	4121 (26.74)
Education Level Less than High School Graduation High School Graduation Some College Education or More	 76 (43.93) 59 (34.10) 38 (21.97)	 3685 (23.73) 6334 (40.78) 5513(35.49)	 138 (42.86) 109 (33.85) 75 (23.29)	 3623 (23.55) 6284 (40.85) 5476 (35.60)
Current Smoker	66 (38.15)	4055 (26.09)	133 (41.18)	3988 (25.91)
Drinker Status Current Drinker Former Drinker Never Drinker Unknown	 79 (45.93) 56 (32.56) 37 (21.51) 0	 8647 (55.83) 2928 (18.90) 3905 (25.21) 8 (0.05)	 143 (44.69) 102 (31.88) 75 (23.44) 0	 8513 (55.95) 2882 (18.79) 3867 (25.21) 8 (0.05)
Hypertension	110 (64.33)	5380 (34.75)	211 (65.73)	5279 (34.43)
Diabetes	56 (32.94)	1808 (11.73)	107 (33.54)	1757 (11.51)
Prevalent CHD	58 (34.94)	707 (4.64)	102(32.69)	663 (4.40)
Age	56.38 (5.61)	54.14 (5.74)	56.27 (5.60)	54.12 (5.74)
BMI ($kg/(m^2)$)	29.28 (6.20)	27.70 (5.37)	29.26 (6.19)	27.68 (5.35)
Waist Girth (cm)	102.39 (13.91)	96.97 (13.74)	102.51 (14.49)	96.91 (13.71)
Hip Girth (cm)	105.10 (11.67)	104.56 (10.16)	105.21 (11.95)	104.55 (10.14)
Waist-To-Hip Ratio	0.98 (0.06)	0.93 (0.08)	0.97 (0.07)	0.93 (0.08)
HDL (mg/dl)	45.64 (14.97)	51.65 (17.11)	44.60 (14.01)	51.73 (17.12)
LDL (mg/dl)	150.66 (41.17)	137.53 (39.32)	151.09 (40.92)	137.40 (39.28)
Total Cholesterol (mg/dl)	228.57 (47.47)	214.82 (42.00)	228.03 (46.93)	214.70 (41.93)
Total Triglycerides (mg/dl)	157.27 (110.56)	135.60 (90.18)	166.84 (128.28)	131.16 (89.38)
Glucose (mg/dl)	137.15 (80.56)	108.66 (39.85)	141.22 (84.30)	108.30 (38.91)
Leisure Index	2.23 (0.57)	2.36 (0.57)	2.18 (0.57)	2.36 (0.57)
Work Index	1.94 (1.01)	2.18 (0.95)	1.96 (1.01)	2.19 (0.95)
Sport Index	2.23 (0.75)	2.43 (0.79)	2.22 (0.76)	2.43 (0.79)
Total Calorie Intake (kcal/day)	1685.40 (723.76)	1632.67 (714.50)	1646.39 (762.85)	1632.97 (713.58)
Follow-Up Time (days)	2654.62 (1417.23)	4932.54 (988.14)	2608.20 (1479.60)	4955.69 (952.39)

BMI denotes body mass index; CHD, coronary heart disease; SCD within 1 hr, sudden cardiac death within 1 hour of symptom onset; SCD within 24 hrs, sudden cardiac death within 24 hours of symptom onset; HDL, re-calibrated high-density lipoprotein in mg/dl; LDL, re-calibrated low-density lipoprotein in mg/dl; SD, standard deviation.

Waist-to-Hip Ratio Relationship with Sudden Cardiac Death

In Model I a (Table 3-3), adjusted for age, gender, race, education, smoking, prevalent CHD, hypertension, diabetes, and total cholesterol, the standardized form of WHR reflecting an increase of 1 standard deviation was statistically significant for both SCD within 1 hour (HR = 1.51, 95% CI = 1.22, 1.87; p= 0.0002) and SCD within 24 hours (HR = 1.51, 95% CI = 1.30, 1.76; p= <0.0001) of symptom onset. The square of the standardized form of WHR, representing a quadratic effect, was not significant for either SCD within 1 hour (p = 0.842) or SCD within 24 hours (p = 0.838). In Model I c (Table 3-3), the quintile-categorized WHR showed a significant association for both SCD within 1 hour (p = 0.018) and SCD within 24 hours of symptom onset (p = <0.0001). By plotting the log hazard ratios against the quintile, there was no indication of significant deviation from linearity.

In Model II a (Table 3-3), adjusted only for age, race, and gender, the standardized form of WHR reflecting an increase of 1 standard deviation was significant for both SCD within 1 hour (HR = 1.90, 95% CI = 1.59, 2.27; p= <0.0001) and SCD within 24 hours (HR = 1.93, 95% CI = 1.70, 2.19; p= <0.0001) of symptom onset. In Model II c (Table 3-3), associations were significant between the quintile-categorized WHR and SCD within 1 hour (p = <0.0001) as well as within 24 hours (p = <0.0001) of symptom onset, and a linear relationship was observed.

BMI Relationship with Sudden Cardiac Death

In Model I b (Table 3-3), adjusted for age, gender, race, education, smoking, prevalent CHD, hypertension, diabetes, and total cholesterol, the standardized form of BMI reflecting a 1 standard deviation increment had a marginal association for SCD within 1 hour (HR = 1.16, 95% CI =

1.00, 1.37; p = 0.082), and a marginal association with SCD within 24 hours (HR = 1.12, 95% CI = 1.00, 1.27; p = 0.054) of symptom onset The square of the standardized form of BMI, representing a quadratic effect, was not significant for both SCD within 1 hour (p = 0.269) and SCD within 24 hours (p= 0.166). There were no significant associations between the quintile-categorized BMI and SCD within 1 hour (p = 0.474) as well as within 24 hours (p = 0.108) of symptom onset.

In Model II b (Table 3-3), adjusted only for age, race, and gender, the associations between the standardized form reflecting a 1 standard deviation increment of BMI and SCD were significant for both SCD within 1 hour (HR = 1.32, 95% CI = 1.15, 1.53; p = 0.0001) and within 24 hours (HR = 1.29, 95% CI = 1.16, 1.43; p = <0.0001) of symptom onset. In Model II d (Table 3-3), associations were significant between the quintile-categorized BMI and SCD within 1 hour (p = 0.019) as well as within 24 hours (p = <0.0001) of symptom onset. By looking at the log hazard ratios plotted versus quintile, the shape of the relationship between BMI and SCD appeared to be linear.

Interaction Terms between Measures of Obesity and Gender

In Model I e, adjusted for age, gender, race, education, smoking, prevalent CHD, hypertension, diabetes, and total cholesterol, no significant interactions were found between WHR and gender with respect to SCD within 1 hour (p= 0.159) and with respect to SCD within 24 hours (p = 0.264). Interactions between WHR quintiles and gender were not significant with respect to SCD within 1 hour (p = 0.801) and with respect to SCD within 24 hours (p = 0.276). Gender had a marginal interaction with BMI for SCD within 1 hour (p= 0.097). There was a significant association in women only (HR = 1.31, 95% CI = 1.06, 1.61; p= 0.013). Gender did not have an

interaction for SCD within 24 hours (p = 0.183). Interactions between BMI quintiles and gender were also not significant with respect to SCD within 1 hour (p = 0.212) and with respect to SCD within 24 hours (p = 0.737).

In Model II e, adjusted only for age, race, and gender, the interactions between WHR and gender with respect to both SCD within1 hour (p = 0.400) and within 24 hours (p = 0.504) were not significant. Similarly the interactions between WHR quintiles and gender were not significant with respect to both SCD within 1 hour (p = 0.996) and within 24 hours (p = 0.565). BMI and gender interaction with respect to both SCD within 1 hour (p = 0.458) and within 24 hours (p = 0.467) did not show significance. Also, the quintiles of BMI and gender did not show interaction with respect to SCD within 1 hour (p = 0.538) and with respect to SCD within 24 hours (p = 0.920).

Table 3-3- Multivariable Proportional Hazards Regression Models for the Main Effects

			SCD within 1 hour				SCD within 24 hours			
	Obesity measures		**HR**	**95% CI**		**P value**	**HR**	**95% CI**		**P value**
Model I a	WHR increment/1SD		1.51	1.22	1.87	0.0002	1.51	1.30	1.76	<0.0001
Model II a	WHR increment/1SD		1.90	1.59	2.27	<0.0001	1.93	1.70	2.19	<0.0001
Model I c	WHR quintiles	1	1.00				1.00			
		2	3.27	1.12	9.56	0.0301	2.46	1.29	4.67	0.0060
		3	2.60	0.88	7.66	0.0827	1.93	1.01	3.71	0.0472
		4	4.17	1.45	11.92	0.0078	2.59	1.37	4.88	0.0033
		5	4.55	1.59	13.03	0.0048	3.59	1.92	6.71	<0.0001
Model II c	WHR quintiles	1	1.00				1.00			
		2	2.95	1.19	7.27	0.0190	2.83	1.56	5.15	0.0007
		3	3.05	1.24	7.51	0.0151	2.72	1.49	4.97	0.0012
		4	5.13	2.15	12.27	0.0002	3.90	2.17	7.01	<0.0001
		5	7.08	2.99	16.76	<0.0001	6.91	3.91	12.22	<0.0001
Model I b	BMI increment/1SD		1.16	1.00	1.37	0.0817	1.12	1.00	1.27	0.0542
Model II b	BMI increment/1SD		1.32	1.15	1.53	0.0001	1.29	1.16	1.43	<0.0001
Model II d	BMI quintiles	1	1.00				1.00			
		2	1.12	0.65	1.91	0.6943	1.09	0.74	1.61	0.6615
		3	0.97	0.56	1.68	0.9212	0.98	0.67	1.45	0.9145
		4	1.24	0.74	2.08	0.4213	1.06	0.72	1.55	0.7851
		5	1.92	1.16	3.15	0.0110	1.91	1.34	2.72	0.0004

HR denotes hazard ratio; CI, confidence interval; SD, standard deviation; WHR, waist-to-hip ratio; BMI, body mass index; SCD within 1 hour, sudden cardiac death within 1 hour of symptom onset; SCD within 24 hours, sudden cardiac death within 24 hours of symptom onset.

Model I a, b and c: Adjusted for age, gender, race, education, smoking, prevalent CHD, hypertension, diabetes, and total cholesterol.

Model II a, b, c and d: Adjusted for age, race, and gender.

Chapter 4

Discussion

In this biracial cohort of 15,732 participants aged 45-64 years at baseline, 173 SCDs were documented within 1 hour of symptom onset and 323 SCDs were documented within 24 hours of symptom onset. After a mean 13 years of follow-up, abdominal adiposity defined as waist-to-hip ratio was associated with both sudden cardiac deaths within 1 hour as well as within 24 hours of symptom onset. The magnitude of WHR association with SCD was much greater than that of BMI. The relationship between the obesity measures and sudden cardiac death appeared to be linear from plots of the log hazard ratio with the quintile. The first model was adjusted for co-morbidities such as baseline CHD, diabetes, hypertension, and total cholesterol, in addition to age, race, gender, education, and smoking. If obesity measured by both WHR and BMI have significant positive associations with SCD largely explained by these conditions, the model could be over adjusted. Thus, the same results were compared with a model adjusted only for age, race, and gender. When comparing these two models, the hazard ratios were greatly attenuated with the adjustment of major cardiac and obesity related co-morbidity. These results are supportive of the important intermediate roles that these co-morbidities play in the etiology of obesity and sudden cardiac death. Indication of gender interaction was observed for BMI with respect to SCD within 1 hour for women only, in contrast to WHR, which was consistent for both genders. Women in general are ‘pear-shaped’ and have lower WHR, mainly because their weight is distributed on the lower trunk, the hips and thighs, while men have their body fat distributed mainly around their abdomen. This could be a reason why the risk of overall obesity measured by BMI is greater in women than WHR, which is only targeted towards the central area.

These results are consistent with some previous studies that have included both BMI and WHR or waist circumference in similar analyses. When studying both BMI and abdominal adiposity as

risk indicators, Folsom et al. (2000) demonstrated in the Iowa Women's Health Study that WHR was the best anthropometric predictor of total mortality compared to BMI and waist circumference, which is in accordance with the present study. The first longitudinal population studies from Gothenburg, Sweden, in 1984 showed that high waist-to-hip ratios were the strongest anthropometric predictors of CVD and death in women (Lapidus et al., 1985). In contrast, this study found evidence of an interaction between BMI and gender with respect to SCD.

There have been some inconsistent results concerning the relationships between WHR and BMI as predictors for sudden cardiac death. Few prospective studies have addressed these relationships. Some indicate a linear relationship, whereas others reported a j-shaped, a u-shaped, or no relationships (Manson et al., 1995). Most of these nonlinear relationship patterns may be attributed to several confounding factors (Willett et al., 1999).

The consistency of findings for the association of overweight with incident heart failure is in striking contrast with the inconsistencies regarding the association for obesity with coronary heart disease and mortality. Gelber et al. (2008), argues that BMI should be used as the single measure to predict cardiovascular deaths. There are patients in whom the BMI will give an inaccurate assessment of adiposity. However, those with large body frames and heavy muscle mass may be incorrectly classified as obese, but at the other end of the spectrum, those with muscle wasting, yet still replete with adipose tissue, could be classified as lean, particularly elderly subjects (Gallagher et al., 1996).

In the past 15 years, research has implicated abdominal visceral adiposity as the most hazardous to cardiovascular health. Yet, the number of prospective studies of CHD in relation to waist-to-hip ratio is relatively small (Larsson et al., 1984, Rimm et al., 1995). In these studies, WHR was positively associated with the occurrence of CHD more strongly than was BMI.

The risk differences between BMI and WHR as prognostic factors for cardiovascular disease may be explained by different baseline characteristics of the studied populations, including sex and age. Another explanation for these differences is related to the possibility that increased BMI may reflect obesity not only due to excessive fat, but also to high musculoskeletal mass or water retention, and that associations would be strengthened if different obesity measures were used (Romero-Corral et al., 2006).

The strengths of this study include a very large cohort of middle-aged adults, long duration of follow-up period, surveillance and confirmation of outcome events, and recording of multiple obesity measures. Since this is a biracial cohort study categorized as black and non-black, it limits the findings that cannot be generalized to other cultural and socio-economic contexts.

In conclusion, this study does not argue on the superiority of WHR as a measure of obesity, but supports the recommendation that WHR be measured along with weight and height as part of routine surveillance and monitoring of cardiovascular risk status in medical practice. Selecting the best anthropometric measure for the prediction of sudden cardiac death could have implications for the screening and prevention of cardiac deaths.

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Appendix

SAS Code

```
libname aric '\\fs.hes.hmc.psu.edu\saravanad\ARIC Pub Data';

data temp_antaps12;
set aric.antaps12;
proc sort data=temp_antaps12;
by ID_C;
run;

data temp_derps12;
set aric.derps12;
proc sort data=temp_derps12;
by ID_C;
run;

data temp_lipaps12;
set aric.lipaps12;
proc sort data=temp_lipaps12;
by ID_C;
run;

data temp_scd;
set aric.scd;
if SUDTH1=1 or SUDTH24=1;

proc sort data=temp_scd;
by ID_C;
run;

data temp_all;
merge temp_antaps12 temp_derps12 (in=incohort) temp_lipaps12 temp_scd;
by ID_C;
keep BMI01 ANTZ07A ANTZ07B WSTHPR01 V1AGEZ1 RACEGRP1 GENDER ELEVEL02
LISR_I01 WORK_I02 SPRT_I02 TOTCAL03 CURSMK01 DRNKR01 HYPERT05
DIABTS03 HDL01 LDL02 LIPA01 LIPA02 GLUCOS01 PRVCHD05 FUDTH02
SUDTH1 SUDTH24 DEAD02 ID_C;
if incohort;
if SUDTH1 NE 1 then SUDTH1=0;
if SUDTH24 NE 1 then SUDTH24=0;
run;

proc freq data=temp_all;
tables SUDTH1 SUDTH24;
run;

proc contents data=temp_all;
run;
```

```
title "Deepa's Thesis Analysis";
title2 'Frequencies of outcomes';
proc freq data=temp_all;
tables DEAD02 SUDTH1 SUDTH24;
run;

proc means data = temp_all mean std nonobs clm alpha=0.05 t probt;
var BMI01 ANTZ07A ANTZ07B WSTHPR01 V1AGEZ1 ELEVEL02
LISR_I01 WORK_I02 SPRT_I02 TOTCAL03 CURSMK01 DRNKR01 HYPERT05
DIABTS03 HDL01 LDL02 LIPA01 LIPA02 GLUCOS01 PRVCHD05 FUDTH02
SUDTH1 SUDTH24 DEAD02;
run;

title2 'Descriptive statistics of continuous variables';
proc means data = temp_all n nmiss mean std median qrange min max maxdec=3;
var BMI01 ANTZ07A ANTZ07B WSTHPR01 V1AGEZ1
LISR_I01 WORK_I02 SPRT_I02 TOTCAL03
HDL01 LDL02 LIPA01 LIPA02 GLUCOS01 FUDTH02;
run;

title2 'Descriptive statistics of categorical variables';
proc freq data = temp_all;
tables ELEVEL02 CURSMK01 DRNKR01 HYPERT05 DIABTS03 PRVCHD05 GENDER RACEGRP1;
run;

data temp_analysis;
set temp_all;
if SUDTH1 = 1 then new_SUDTH1=1;
else new_SUDTH1=0;

if SUDTH24 = 1 then new_SUDTH24=1;
else new_SUDTH24=0;

WSTHPR01_STD=WSTHPR01/0.078;
BMI01_STD=BMI01/5.378;

BMI01_SQ=BMI01_STD**2;
WSTHPR01_SQ=WSTHPR01_STD**2;
run;

title2 'Frequencies of newly defined outcomes';
proc freq data=temp_analysis;
tables new_SUDTH1 new_SUDTH24;
run;

title2 'Bivariate analysies of SCD1';
* Categorical example for SCD1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0');
model FUDTH02*new_SUDTH1(0) = CURSMK01 / risklimits;
run;
proc phreg data=temp_analysis;
class ELEVEL02(ref='1');
model FUDTH02*new_SUDTH1(0) = ELEVEL02 / risklimits;
run;
proc phreg data=temp_analysis;
class DRNKR01(ref='1');
model FUDTH02*new_SUDTH1(0) = DRNKR01 / risklimits;
run;
proc phreg data=temp_analysis;
```

```
class HYPERT05(ref='0');
model FUDTH02*new_SUDTH1(0) = HYPERT05 / risklimits;
run;
proc phreg data=temp_analysis;
class DIABTS03(ref='0');
model FUDTH02*new_SUDTH1(0) = DIABTS03 / risklimits;
run;
proc phreg data=temp_analysis;
class PRVCHD05(ref='0');
model FUDTH02*new_SUDTH1(0) = PRVCHD05 / risklimits;
run;

* Continuous example for SCD1;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = BMI01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = ANTZ07A / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = ANTZ07B / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = WSTHPR01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = LISR_I01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = WORK_I02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = SPRT_I02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = TOTCAL03 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = HDL01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = LDL02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) =  LIPA01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) =  LIPA02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH1(0) = GLUCOS01  / risklimits;
run;

title2 'Bivariate analysies of SCD24';
*Categorical example for SCD24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0');
```

```
model FUDTH02*new_SUDTH24(0) = CURSMK01 / risklimits;
run;
proc phreg data=temp_analysis;
class ELEVEL02(ref='1');
model FUDTH02*new_SUDTH24(0) = ELEVEL02 / risklimits;
run;
proc phreg data=temp_analysis;
class DRNKR01(ref='1');
model FUDTH02*new_SUDTH24(0) = DRNKR01 / risklimits;
run;
proc phreg data=temp_analysis;
class HYPERT05(ref='0');
model FUDTH02*new_SUDTH24(0) = HYPERT05 / risklimits;
run;
proc phreg data=temp_analysis;
class DIABTS03(ref='0');
model FUDTH02*new_SUDTH24(0) = DIABTS03 / risklimits;
run;
proc phreg data=temp_analysis;
class PRVCHD05(ref='0');
model FUDTH02*new_SUDTH24(0) = PRVCHD05 / risklimits;
run;

* Continuous example for SCD 24;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = BMI01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = ANTZ07A / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = ANTZ07B / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = WSTHPR01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = LISR_I01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = WORK_I02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = SPRT_I02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = TOTCAL03 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = HDL01 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = LDL02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) =  LIPA01 / risklimits;
run;
```

```
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) =  LIPA02 / risklimits;
run;
proc phreg data=temp_analysis;
model FUDTH02*new_SUDTH24(0) = GLUCOS01  / risklimits;
run;

title2 'Multivariable modeling of SCD24 with WHR (standardized)';
* Multivariable modeling for WHR on SCD 24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01_STD / risklimits;
run;

* Multivariable modeling for WHR on SCD 24 for few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01_STD / risklimits;
run;

*quadratic terms for WHR on SCD24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01  WSTHPR01_STD WSTHPR01_SQ / risklimits;
run;

*interactions for WHR on SCD24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01_STD GENDER*WSTHPR01_STD / risklimits;
run;

*interactions for WHR on SCD24 for few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01_STD
GENDER*WSTHPR01_STD / risklimits;
run;

title2 'Multivariable modeling of SCD1 with WHR (standardized)';
* Multivariable modeling for WHR on SCD1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01_STD / risklimits;
run;

* Multivariable modeling for WHR on SCD1 for few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01_STD / risklimits;
run;
```

```
*quadratic terms for WHR on SCD1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01  WSTHPR01_STD WSTHPR01_SQ / risklimits;
run;

*interactions for WHR with SCD1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01_STD GENDER*WSTHPR01_STD / risklimits;
run;

*interactions for WHR with SCD1 for few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01_STD
GENDER*WSTHPR01_STD / risklimits;
run;

* How to obtain quintiles for a variable;
proc rank data=temp_analysis out=bmi_ranks groups=5;
var WSTHPR01;
run;

title2 'Frequency of WHR quintiles';
proc freq data=bmi_ranks;
tables WSTHPR01;
run;

title2 'Multivariable modeling of SCD24 with WHR quintiles';
* Multivariable modeling for WHR quintiles with SCD24;
proc phreg data=bmi_ranks;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01 / risklimits;
run;

* Multivariable modeling for WHR quintiles with SCD24 for few adjustments;
proc phreg data=bmi_ranks;
class GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01 / RISKLIMITS;
run;

*interactions for WHR quintiles with SCD 24;
proc phreg data=bmi_ranks;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01 GENDER*WSTHPR01 / risklimits;
run;

*interactions for WHR quintiles with SCD 24 for few adjustments;
proc phreg data=bmi_ranks;
class GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
```

```
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01 GENDER*WSTHPR01 /
risklimits;
run;

title2 'Multivariable modeling of SCD1 with WHR quintiles';
*Multivariable modeling for SUDTH1;
proc phreg data=bmi_ranks;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01 / risklimits;
run;

*Multivariable modeling for SUDTH1 for few adjustments;
proc phreg data=bmi_ranks;
class GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01 / risklimits;
run;

*interactions for WHR quintiles with SCD1;
proc phreg data=bmi_ranks;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 WSTHPR01 GENDER*WSTHPR01 / risklimits;
run;

*interactions for WHR quintiles with SCD1 for few adjustments;
proc phreg data=bmi_ranks;
class GENDER (ref='F') RACEGRP1 (ref='N') WSTHPR01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 WSTHPR01 GENDER*WSTHPR01 /
risklimits;
run;

title2 'Multivariable modeling of SCD24 with BMI';
* Multivariable modeling for BMI with SCD 24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD / risklimits;
run;

*Multivariable modeling for BMI with SCD 24 with few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 BMI01_STD / risklimits;
run;

*quadratic term for BMI with SCD 24;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD BMI01_SQ / risklimits;
run;

*interactions for BMI with SCD 24;
proc phreg data=temp_analysis;
```

```
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD GENDER*BMI01_STD / risklimits;
run;

*interactions for BMI with SCD 24 with few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 BMI01_STD GENDER*BMI01_STD /
risklimits;
run;

title2 'Multivariable modeling of SCD1 with BMI';
* Multivariable modeling for BMI with SCD 1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD / risklimits;
run;

*Multivariable modeling for BMI with SCD 1 with few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 BMI01_STD / risklimits;
run;

*quadratic term for BMI with SCD 1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD BMI01_SQ / risklimits;
run;

*interactions for BMI with SCD 1;
proc phreg data=temp_analysis;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01_STD GENDER*BMI01_STD / RISKLIMITS;
CONTRAST 'Hazard ratio for BMI01 for males' BMI01_STD 1 GENDER*BMI01_STD 1  / ESTIMATE=BOTH E;
CONTRAST 'Hazard ratio for BMI01 for females' BMI01_STD 1 GENDER*BMI01_STD 0  / ESTIMATE=BOTH E;
run;

*interactions for BMI with SCD 1 with few adjustments;
proc phreg data=temp_analysis;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 BMI01_STD GENDER*BMI01_STD /
risklimits;
run;

* How to obtain quintiles for a variable;
proc rank data=temp_analysis out=bmi_ranks1 groups=5;
var BMI01;
run;

proc univariate data=temp_analysis;
var BMI01;
```

```
output out=cutpoints pctlpts=20 40 60 80 pctlpre=P;
run;

proc print data=cutpoints;
run;

title2 'Frequency of BMI quintiles';
proc freq data=bmi_ranks1;
tables BMI01;
run;

title2 'Multivariable modeling of SCD24 with BMI quintiles';
* Multivariable modeling for bmi ranks for SCD24;
proc phreg data=bmi_ranks1;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01 / risklimits;
run;

* Multivariable modeling for bmi ranks for SCD24 for few adjustments;
proc phreg data=bmi_ranks1;
class GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1  BMI01 / risklimits;
run;

*Testing interactions for bmi ranks for SCD24;
proc phreg data=bmi_ranks1;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01 GENDER*BMI01 / risklimits;
run;

*Testing interactions for bmi ranks for SCD24 for few adjustments;
proc phreg data=bmi_ranks1;
class GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH24(0) = V1AGEZ1 GENDER RACEGRP1 BMI01 GENDER*BMI01 / risklimits;
run;

title2 'Multivariable modeling of SCD1 with BMI quintiles';
*Multivariable modeling for bmi ranks for SUDTH1;
proc phreg data=bmi_ranks1;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01 / risklimits;
run;

*Multivariable modeling for bmi ranks for SUDTH1 for few adjustments;
proc phreg data=bmi_ranks1;
class GENDER (ref='F') RACEGRP1 (ref='N') BMI01(ref='0');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 BMI01 / risklimits;
run;

*Testing interactions for BMI ranks with SCD1;
proc phreg data=bmi_ranks1;
class CURSMK01(ref='0') ELEVEL02(ref='1') HYPERT05(ref='0') DIABTS03(ref='0') PRVCHD05(ref='0')
GENDER (ref='F') RACEGRP1 (ref='N');
```

```
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 ELEVEL02 CURSMK01 PRVCHD05
HYPERT05 DIABTS03 LIPA01 BMI01 GENDER*BMI01 / risklimits;
run;

*Testing interactions for BMI ranks with SCD1 for few adjustments;
proc phreg data=bmi_ranks1;
class GENDER (ref='F') RACEGRP1 (ref='N');
model FUDTH02*new_SUDTH1(0) = V1AGEZ1 GENDER RACEGRP1 BMI01 GENDER*BMI01 / risklimits;
run;
```