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Is self-reported physical functioning associated with incident cardiometabolic abnormalities or the metabolic syndrome?

Kelly R. Ylitalo, PhD^{1,2}, Carrie Karvonen-Gutierrez, PhD¹, Candace McClure, PhD³, Samar R. El Khoudary, PhD³, Elizabeth A. Jackson, MD², Barbara Sternfeld, PhD⁴, and Siobán D. Harlow, PhD¹

¹School of Public Health, University of Michigan

²School of Medicine, University of Michigan

³Epidemiology Data Center, University of Pittsburgh

⁴Kaiser Permanente

Abstract

Background—Physical functioning may be an important pre-clinical marker of chronic disease, used as a tool to identify patients at risk for future cardiometabolic abnormalities. This study evaluated if self-reported physical functioning was associated with the development of cardiometabolic abnormalities or their clustering (metabolic syndrome) over time.

Methods—Participants (n=2,254) from the Study of Women’s Health Across the Nation who reported physical functioning on the Short Form health survey and had a metabolic syndrome assessment (elevated fasting glucose, blood pressure, triglycerides, and waist circumference; reduced HDL cholesterol) in 2000 were included. Discrete survival analysis was used to assess the 10 year risk of developing metabolic syndrome or a syndrome component through 2010.

Results—At baseline, the prevalence of metabolic syndrome was 22.0%. Women with substantial limitations (OR=1.60; 95% CI: 1.12, 2.29) in physical functioning were significantly more likely to develop the metabolic syndrome compared to women reporting no limitations. Self-reported physical functioning was significantly associated with incident hypertension and increased waist circumference.

Conclusions—Simple screening tools for cardiometabolic risk in clinical settings are needed. Self-reported physical functioning assessments are simple tools that may allow health care providers to more accurately predict the course of chronic conditions.

Keywords

Metabolic syndrome; physical functioning

Address for Correspondence: Kelly R. Ylitalo, 1415 Washington Heights, Ann Arbor, MI 48109-2029, Phone: 248-705-6449, kylitalo@umich.edu.

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Introduction

The steep rise in the prevalence of cardiovascular disease and diabetes mellitus during the late twentieth and early twenty-first centuries has focused attention on the identification of early disease markers in an effort to effectively time the initiation of prevention and treatment strategies. Abnormal cardiometabolic factors may be important in the pathogenesis of aging and are important predictors of overt cardiovascular disease and diabetes. The metabolic syndrome – a clustering of abnormal cardiometabolic risk factors including elevated fasting glucose, elevated blood pressure, dyslipidemia, and increased abdominal adiposity – is utilized clinically as a marker of cardiometabolic dysfunction. At least one in three adults have metabolic syndrome in the United States [1]. Individuals with metabolic syndrome have twice the risk of developing cardiovascular disease in the next decade, and five times the risk of developing type 2 diabetes [1]. Recent work has sought to identify predictors and correlates of the metabolic syndrome, including quality of life [2–4].

Several chronic conditions have been associated with poor physical functioning [5,6] and the association between cardiometabolic factors and physical functioning is established [7,8]. Thus, physical functioning has been suggested as an important pre-clinical marker of chronic disease [9]. While physical functioning has been shown to predict major health events including new disease onset [10], hospitalizations [11] and mortality [11,12], physical functioning would have greater clinical utility if it was also a predictor of the metabolic syndrome and could be used to identify patients at high risk for this collection of sub-clinical risk factors.

The purpose of this study was to evaluate if self-reported physical functioning was associated with the development of individual cardiometabolic abnormalities (elevated fasting glucose, elevated blood pressure, elevated triglycerides, reduced HDL cholesterol, and increased waist circumference) or their clustering (metabolic syndrome) over time in a multi-ethnic sample of mid-life women.

Materials and Methods

Subjects

The Study of Women's Health Across the Nation (SWAN) is a prospective, multicenter, multiethnic study of aging and the menopause transition. Sampling and recruitment methods have been described previously [13]. Briefly, a cross-sectional study of 16,065 women from seven locations (Boston, Chicago, Detroit, Los Angeles, New Jersey, Oakland, Pittsburgh) generated a longitudinal cohort of 3,302 women who at the 1996 baseline were aged 42–52 years, pre-menopausal, and self-identified with designated race/ethnic groups. Annual study visits provided clinical, behavioral, and functioning data. The analytic sample for the present manuscript included participants who reported physical functioning and had a metabolic syndrome assessment in 2000 (n=2254).

Data collection was halted mid-study at the New Jersey site (the only site to recruit Hispanic participants; n=284) which resulted in a lower participation, so these data were excluded from our analysis. Compared to the analytic sample, excluded women were more likely to be

younger ($p = 0.02$), have a higher body mass index ($p < 0.001$), and have less education ($p < 0.001$).

Measures

Cardiometabolic abnormalities and the metabolic syndrome were defined using established harmonized guidelines [1]. Possible cardiometabolic abnormalities included systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or current use of antihypertensive medications; fasting blood glucose ≥ 5.55 mmol/L or current use of diabetes medication; waist circumference >88 cm (or >80 cm for Chinese and Japanese women); HDL cholesterol <1.30 mmol/L; or triglycerides ≥ 1.70 mmol/L. Women taking fibrates or nicotinic acid were presumed to have the high triglyceride and low HDL-C components of the metabolic syndrome [1]. The presence of three out of five possible abnormalities qualified a woman for the metabolic syndrome. Metabolic syndrome and its components were assessed in 2000, 2001, 2002, 2003, and 2010.

Physical functioning was assessed by participant self-report from the ten-question physical functioning subscale from the Short Form health survey (SF-36) in 2000, 2002, 2004, 2006, and 2010. This ten-item questionnaire reflects the difficulty of performing physical activities, including vigorous and moderate activities, lifting/carrying groceries, climbing stairs, bending/kneeling/stooping, walking, and bathing/dressing. Responses were scored and transformed to a range of 0–100, with higher scores indicating better and lower scores indicating poorer perceived physical functioning [14]. Previously used cutpoints [15,16] were employed to identify no limitations (86–100), some limitations (51–85), or substantial limitations (0–50).

Additional covariates included age, race/ethnicity, body mass index, education, depressive symptoms, smoking status, alcohol consumption, and menopausal status. Age was centered at 50.5 years, the mean age of participants in 2000. Race/ethnicity was self-identified at baseline as Caucasian (reference group), African American, Japanese, or Chinese. Education was categorized as a high school diploma or less (reference group), some college, or a college degree or higher. At each visit, height was measured without shoes in centimeters by fixed stadiometer and weight was measured in light clothing in kilograms by balance beam scale. Body mass index was calculated as $\text{weight}[\text{kg}]/\text{height}[\text{m}^2]$ and categorized as underweight or normal weight (BMI <24.9 kg/m²), overweight (BMI 25–29.9 kg/m²) and obese (BMI ≥ 30 kg/m²) for Caucasian and African American women. We used Asian-specific cut points, categorized as underweight or normal weight (BMI <23 kg/m²), overweight (BMI 23–24.9 kg/m²), and obese (BMI ≥ 25 kg/m²), for Japanese and Chinese women [17–19]. For all race/ethnic groups, the under/normal weight group was used as the reference. Depressive symptoms was defined as a score ≥ 16 on the Center for Epidemiologic Studies Depression Scale [20]. Current smoking status was defined as smoking cigarettes regularly (at least one cigarette a day). Regular alcohol consumption was defined as an average of at least one glass of beer, wine, or liquor per week. Menopausal status was determined based on reports about regularity of menstrual bleeding and categorized as premenopausal (regular bleeding or women who were pregnant or breastfeeding), perimenopausal, and postmenopausal (including natural or surgical menopause).

Statistical Analysis

First, we used means and proportions to describe the sociodemographics, health, and prevalence of the metabolic syndrome and cardiometabolic abnormalities of our study population in 2000. Chi-square tests for categorical variables and ANOVA for continuous variables were used to describe the distribution of these factors by self-reported physical functioning status in visit 4. Next, women with prevalent metabolic syndrome in 2000 were removed from the analytic sample and we used discrete survival analysis [21] to assess the risk of developing incident metabolic syndrome given a previous report of physical functioning, adjusted for time-invariant sociodemographic factors (age, race/ethnicity, and education) and time-varying BMI. Discrete survival analysis was also used to assess the risk of developing each incident cardiometabolic abnormality given previous self-reported physical functioning, adjusted for age, race/ethnicity, and time-varying BMI. Additional covariates, including marital status, economic hardship, smoking, alcohol consumption, depressive symptoms, physical activity, menopause status, study site, and change in physical functioning since baseline were considered but excluded from the final models based on likelihood ratio tests. We also tested for heterogeneity in the association of physical functioning with metabolic syndrome by race/ethnicity, education, and BMI by evaluating the statistical significance of multiplicative interaction terms in our multivariate models. All analyses were conducted using SAS v9.3 (SAS Institute Inc., Cary, NC, USA) and statistical significance was defined at the two-sided $\alpha=0.05$ level.

Results

Approximately 50% of the population was Caucasian, 29% was African American, 10% was Chinese, and 11% was Japanese, by design. During study visit 4 when participants were aged 46–56 years, mean age was approximately 50 years, half of women did not have a college degree, and more than one-third were obese. Approximately 30% of women reported some limitations and 10% reported substantial limitations in physical functioning in 2000. By 2000, 8.3% of women were premenopausal, 63.3% were perimenopausal, and 28.4% were postmenopausal.

The prevalence of metabolic syndrome in 2000 was 22.0% (Table 1) and differed by self-reported physical functioning: 14.7% of women with no limitations in physical functioning had metabolic syndrome, 29.3% of women with some limitations in physical functioning had metabolic syndrome, and 41.4% of women with substantial limitations in physical functioning had metabolic syndrome ($p<0.001$). The most common abnormal cardiometabolic factor was elevated waist circumference (47.6%), and all component factors were disproportionately more prevalent among women with some or substantial limitations (Table 1).

In the bivariate analysis of women without the metabolic syndrome in 2000 (Table 2), women who reported some limitations in physical functioning had 60% higher odds of developing metabolic syndrome compared to women who reported no limitations (OR=1.57; 95% CI: 1.26, 1.96). Women who reported substantial limitations in physical functioning had 2.8 times the odds of developing metabolic syndrome compared to women who reported no limitations (OR=2.77; 95% CI: 2.02, 3.79). After adjusting for covariates (Table 2),

however, only women with substantial limitations (OR=1.60; 95% CI: 1.12, 2.29) in physical functioning were significantly more likely to develop the metabolic syndrome compared to women who reported no limitations.

In unadjusted analyses, African American women were more likely to develop the metabolic syndrome (OR=1.89; 95% CI: 1.52, 2.35) compared to Caucasian women, but this relationship did not persist in the multivariable models. Women who had a college degree or more were less likely to develop the metabolic syndrome, and overweight and obese women were more likely to develop the metabolic syndrome compared to under or normal weight women. The association between physical functioning and metabolic syndrome did not differ by race/ethnicity, education level, or BMI.

In the fully-adjusted multivariate analysis of individual cardiometabolic abnormalities (Table 3), self-reported physical functioning was significantly associated with incident hypertension and incident increased waist circumference. Compared to women with no limitations, women with some (OR=1.36; 95% CI: 1.08, 1.70) or substantial (OR=1.69; 95% CI: 1.20, 2.37) limitations were more likely to develop hypertension, adjusting for age, race/ethnicity, BMI, education, high glucose, high triglycerides, increased waist circumference, and low HDL. Similarly, compared to those with no limitations, the odds of developing increased waist circumference were greater among women with some (OR=1.55; 95% CI: 1.13, 2.13) or substantial (OR=2.28; 95% CI: 1.31, 3.94) limitations, adjusting for age, race/ethnicity, BMI, education, high glucose, high triglycerides, hypertension, and low HDL. The association between physical functioning and individual components of the metabolic syndrome did not differ by race/ethnicity, education level, or BMI.

Discussion

In this multiethnic longitudinal cohort of mid-life women, we observed a high prevalence and incidence of metabolic syndrome. In 2000, the prevalence of metabolic syndrome was 20%, and during 10 years of follow-up, substantial self-reported limitations in physical functioning were associated with incident metabolic syndrome. After evaluating the metabolic syndrome components individually, some and substantial limitations in physical functioning were associated with incident hypertension and waist adiposity.

Our findings are consistent with results from other investigations. While others have reported a cross-sectional association of physical functioning and metabolic syndrome [2], ours is the first study to evaluate whether level of self-reported physical functioning is associated with the development of metabolic syndrome in a mid-life population. Related to our findings, a prospective population-based study of Australian adults found that physical functioning limitations at baseline were associated with 5 year incidence of impaired fasting glucose and diabetes [22], but they did not assess the full constellation of abnormalities associated with the metabolic syndrome. In an elderly cohort, the strongest associations between cardiometabolic risk and mobility limitations were observed for waist adiposity [23].

Physical functioning is a dynamic process, and the relationship between physical functioning and cardiometabolic abnormalities is likely complicated. Declines in physical functioning may be either age-related or as a result of increased sedentary behavior. The resulting decrease in muscle mass may enhance insulin resistance and its correlates [22,24], which suggests a possible mechanism by which limitations in physical functioning precede, rather than follow, metabolic syndrome.

Notably, we observed the association between self-reported physical functioning and metabolic syndrome to be independent of BMI. In contrast, a study of obese individuals seeking weight reduction found that the association between metabolic syndrome and physical functioning was eliminated after controlling for BMI [25]. Our findings highlight the importance of evaluating both body size and cardiometabolic health, since obese individuals may be metabolically healthy and non-obese individuals may be metabolically compromised [26].

While race/ethnicity is known to be associated with self-reported physical functioning [27], these differences have largely been explained by differences in sociodemographic and other health factors [27–29] including increased body size, diabetes, and hypertension. While our study did not find that race/ethnicity modified the association between physical functioning and metabolic syndrome or its components, it is notable that the association between physical functioning and incident metabolic syndrome components was statistically significant for hypertension and increased waist circumference. Previous studies have demonstrated the importance of the blood pressure criteria among African American women [30, 31]. Further, for a given BMI, there are known differences in body fat percentage among Chinese and Japanese individuals as compared to Caucasians [32], thereby motivating the race/ethnic-specific cut points for elevated waist circumference. Taken together, the observation of an independent association between self-reported physical functioning and hypertension and elevated waist circumference suggest that these factors may be critical reasons for the previously observed differences in physical functioning by race/ethnicity. Interventions to improve physical functioning among African American women may be most effective if blood pressure control is considered whereas among Chinese and Japanese women, reductions in visceral adiposity may be most beneficial.

There may be unmeasured confounders in our study, including dietary factors and family history of diseases including cardiovascular disease, which were unavailable for study participants. However, there are many notable strengths of our study. This is the first assessment of self-reported physical functioning limitations and incident metabolic syndrome and its components in a mid-life population. Our utilization of a longitudinal design allowed us to establish temporality and demonstrate that poor functioning preceded the development of metabolic syndrome. Further, the multiethnic cohort allowed us to contribute to existing scientific knowledge by adjusting for race/ethnicity as a covariate and extrapolating our findings to a diverse population of women.

Conclusions

Given the potential prognostic utility of our findings, future studies should determine if self-reported physical functioning is a proxy marker of overall health burden, or if improving physical functioning directly through interventions will result in better health outcomes and prevention of cardiovascular abnormalities. Nevertheless, the need for simple screening tools for future cardiometabolic risk in clinical settings cannot be overlooked, and physical functioning has been posited as the “sixth vital sign” [9,33]. We observed a significant association between self-reported physical functioning and incident metabolic syndrome, which suggests potential utility in evaluating self-reported physical functioning by clinicians. The SF-36 questionnaire is inexpensive and has a low respondent burden [34]. Self-reported physical functioning assessments are simple, cost-effective tools that may allow health care providers to more accurately predict the course of chronic conditions like the metabolic syndrome or the development of adverse cardiometabolic components.

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Clinical Centers: *University of Michigan, Ann Arbor – Siobán Harlow, PI 2011 – present, MaryFran Sowers, PI 1994–2011; Massachusetts General Hospital, Boston, MA – Joel Finkelstein, PI 1999 – present, Robert Neer, PI 1994 – 1999; Rush University, Rush University Medical Center, Chicago, IL – Howard Kravitz, PI 2009 – present, Lynda Powell, PI 1994 – 2009; University of California, Davis/Kaiser – Ellen Gold, PI; University of California, Los Angeles – Gail Greendale, PI, Albert Einstein College of Medicine, Bronx, NY – Carol Derby, PI 2011 – present, Rachel Wildman, PI 2010 – 2011; Nanette Santoro, PI 2004 – 2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994 – 2004; and the University of Pittsburgh, Pittsburgh, PA – Karen Matthews, PI.*

NIH Program Office: *National Institute on Aging, Bethesda, MD – Winifred Rossi 2012 - present; Sherry Sherman 1994 – 2012; Marcia Ory 1994 – 2001; National Institute of Nursing Research, Bethesda, MD – Program Officers.*

Central Laboratory: *University of Michigan, Ann Arbor – Daniel McConnell (Central Ligand Assay Satellite Services).*

SWAN Repository: *University of Michigan, Ann Arbor – Dan McConnell 2011 - present; MaryFran Sowers 2000 – 2011.*

Coordinating Center: *University of Pittsburgh, Pittsburgh, PA – Maria Mori Brooks, PI 2012 - present; Kim Sutton-Tyrell, PI 2001 – 2012; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995 – 2001.*

Steering Committee: Susan Johnson, Current Chair

Chris Gallagher, Former Chair

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Frequency (%) of prevalent sociodemographic and health factors by perceived physical functioning status in 2000, Study of Women's Health Across the Nation.

Table 1

| | Total | No Limitation | Some Limitation | Substantial Limitation | P value |
|--------------------------------------|------------|---------------|-----------------|------------------------|---------|
| Demographics | | | | | |
| Age, years | 50.5 (2.7) | 50.4 (2.7) | 50.6 (2.6) | 50.6 (2.8) | 0.22 |
| Ethnicity | | | | | |
| Caucasian | 49.9 | 52.8 | 48.1 | 38.2 | |
| African American | 29.0 | 23.4 | 31.7 | 51.7 | <0.001 |
| Chinese | 10.1 | 10.5 | 10.4 | 6.3 | |
| Japanese | 11.2 | 13.3 | 9.7 | 3.8 | |
| Education | | | | | |
| High School or Less | 18.6 | 15.4 | 20.1 | 31.7 | |
| Some College | 33.2 | 30.4 | 37.2 | 36.7 | <0.001 |
| College Or More | 48.3 | 54.2 | 42.7 | 31.7 | |
| Health Factors | | | | | |
| Body Mass Index (kg/m ²) | | | | | |
| Under or Normal weight | 33.2 | 42.3 | 22.0 | 15.1 | |
| Overweight | 26.9 | 30.1 | 24.4 | 16.4 | <0.001 |
| Obese | 39.9 | 27.7 | 53.6 | 68.5 | |
| Smoking | 13.5 | 11.4 | 14.5 | 22.4 | <0.001 |
| Alcohol consumption | 47.8 | 52.3 | 42.5 | 39.0 | <0.001 |
| Depressive symptoms | 17.9 | 12.5 | 20.8 | 39.2 | <0.001 |
| Menopausal status | | | | | |
| Premenopausal | 8.3 | 10.1 | 6.2 | 3.9 | |
| Perimenopausal | 63.3 | 63.3 | 65.3 | 57.3 | <0.001 |
| Postmenopausal | 28.4 | 26.5 | 28.6 | 38.8 | |
| Metabolic Syndrome | 21.9 | 14.7 | 29.3 | 41.4 | <0.001 |
| Elevated waist circumference | 47.6 | 35.0 | 63.1 | 73.9 | <0.001 |
| Elevated triglycerides | 24.3 | 19.4 | 30.3 | 34.2 | <0.001 |

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| | Total | No Limitation | Some Limitation | Substantial Limitation | P value |
|--------------------------|-------|---------------|-----------------|------------------------|---------|
| Reduced HDL-C | 31.4 | 25.3 | 38.1 | 45.6 | <0.001 |
| Elevated fasting glucose | 16.4 | 11.8 | 19.2 | 33.5 | <0.001 |
| Elevated blood pressure | 25.0 | 20.2 | 29.1 | 39.7 | <0.001 |

Notes: Metabolic syndrome was defined using established guidelines (Alberti et al., 2009). The presence of 3 of 5 abnormalities qualified a woman for the metabolic syndrome.

Bivariate and multivariate associations of physical functioning, demographic, and health variables with incident metabolic syndrome, Study of Women's Health Across the Nation.

Table 2

| | Bivariate model | | Multivariate model | |
|--------------------------------------|-----------------|-------------|--------------------|------------|
| | OR | 95% CI | OR | 95% CI |
| Physical Functioning | | | | |
| No Limitation | Ref | | Ref | |
| Some Limitation | 1.57 | 1.26, 1.96 | 1.19 | 0.93, 1.51 |
| Substantial Limitation | 2.77 | 2.02, 3.79 | 1.60 | 1.12, 2.29 |
| Demographics | | | | |
| Age, years | 1.01 | 0.97, 1.04 | 1.01 | 0.97, 1.05 |
| Ethnicity | | | | |
| Caucasian | Ref | | Ref | |
| African American | 1.89 | 1.52, 2.35 | 1.19 | 0.93, 1.53 |
| Chinese | 0.69 | 0.46, 1.02 | 0.89 | 0.59, 1.36 |
| Japanese | 0.81 | 0.57, 1.15 | 1.01 | 0.69, 1.47 |
| Education | | | | |
| High School or Less | Ref | | Ref | |
| Some College | 0.88 | 0.67, 1.17 | 0.88 | 0.64, 1.21 |
| College Or More | 0.67 | 0.52, 0.88 | 0.83 | 0.61, 1.12 |
| Health Factors | | | | |
| Body Mass Index (kg/m ²) | | | | |
| Under or Normal weight | Ref | | Ref | |
| Overweight | 3.95 | 2.86, 5.46 | 3.73 | 2.68, 5.19 |
| Obese | 8.44 | 6.20, 11.47 | 7.15 | 5.16, 9.92 |

Associations of physical functioning, demographic, and health variables with incident cardiometabolic abnormalities, Study of Women's Health Across the Nation.

Table 3

| | Glucose | | | Triglycerides | | | Hypertension | | | Waist | | | HDL | | |
|------------------------|---------|------------|--------|---------------|------------|------|--------------|------------|--------|-------|------------|-------|------|------------|-------|
| | OR | 95% CI | P | OR | 95% CI | P | OR | 95% CI | P | OR | 95% CI | P | OR | 95% CI | P |
| Model 1 | | | | | | | | | | | | | | | |
| No Limitation | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| Some Limitation | 1.44 | 1.14, 1.83 | 0.002 | 1.19 | 0.96, 1.48 | 0.11 | 1.62 | 1.32, 1.98 | <0.001 | 1.49 | 1.13, 1.97 | 0.005 | 1.18 | 0.92, 1.50 | 0.2 |
| Substantial Limitation | 1.93 | 1.37, 2.71 | <0.001 | 1.31 | 0.93, 1.82 | 0.12 | 2.34 | 1.73, 3.16 | <0.001 | 2.14 | 1.33, 3.44 | 0.002 | 1.72 | 0.19, 2.49 | 0.003 |
| Model 2 | | | | | | | | | | | | | | | |
| No Limitation | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| Some Limitation | 1.18 | 0.89, 1.47 | 0.3 | 1.09 | 0.85, 1.39 | 0.51 | 1.36 | 1.08, 1.70 | 0.01 | 1.55 | 1.13, 2.13 | 0.001 | 0.93 | 0.71, 1.23 | 0.61 |
| Substantial Limitation | 1.23 | 0.85, 1.80 | 0.28 | 1.21 | 0.83, 1.76 | 0.33 | 1.69 | 1.20, 2.37 | 0.003 | 2.28 | 1.31, 3.94 | 0.003 | 1.35 | 0.90, 2.04 | 0.15 |

* Model 1 adjusted for past physical functioning, age, race/ethnicity, past body mass index, and education (omitted from table presentation). Model 2 is adjusted for Model 1 variables, in addition to the four other cardiometabolic abnormalities. For example, the Model 2 physical functioning and glucose model is adjusted for past physical functioning, age, race/ethnicity, past body mass index, education, triglycerides, hypertension, waist circumference, and HDL.