Risk Factors for the Metabolic Syndrome

The Coronary Artery Risk Development in Young Adults (CARDIA) study, 1985–2001

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OBJECTIVE — The aim of this study was to describe the association of the metabolic syndrome with demographic characteristics and to identify modifiable risk factors for development of the metabolic syndrome.

RESEARCH DESIGN AND METHODS — Men and women (55%) aged 18–30 years from the Coronary Artery Risk Development in Young Adults (CARDIA) study without the metabolic syndrome at baseline (n = 4,192, 49% black) were followed-up from 1985 to 2001. Incident metabolic syndrome, defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria, was ascertained 7, 10, and 15 years after baseline. Risk factors were measured via clinical examination and standardized questionnaires.

RESULTS — The age-adjusted rate of metabolic syndrome was 10 per 1,000 person-years (n = 575). Metabolic syndrome risk increased with age and was higher among black participants and those with less than a high school education. Higher baseline BMI, no alcohol intake (versus one to three drinks per day), higher intake of dietary carbohydrates, and lower intake of crude fiber were each associated with an increased risk for the metabolic syndrome (relative risk [RR] ranging from 1.3 to 1.9), and physical activity was protective (RR 0.84 [95% CI 0.76–0.92]). In models adjusting simultaneously for all factors, black participants and women were less likely to develop metabolic syndrome. Risk for metabolic syndrome increased 23% (20–27%) per 4.5 kg (10 lb) of weight gained, whereas regular physical activity over time versus low activity was protective (RR 0.49 [0.34–0.70]).

CONCLUSIONS — BMI and weight gain are important risk factors for the metabolic syndrome. Regular physical activity may counter this risk.

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Nearly one-quarter of adults in the U.S. have the metabolic syndrome (1), a clustering of abnormal lipid levels, glucose, blood pressure, and abdominal adiposity. Since 2001, when the National Cholesterol Education Program Adult Treatment Panel III (ATP III) proposed a definition of the syndrome that could be readily measured in clinical practice (2), a number of studies have investigated the cross-sectional and prospective association of the metabolic syndrome with type 2 diabetes and coronary heart disease (3–8). Determining who is at risk for the metabolic syndrome has been an equally high priority (9–14). However, relatively fewer studies have investigated this association prospectively using a comprehensive set of risk factors in a diverse population sample.

Although obesity has consistently been reported as a risk factor for the metabolic syndrome (14,15), the association of health behaviors and dietary composition with the development of metabolic syndrome is less well studied, particularly in young adults. Furthermore, these risk factors along with demographic characteristics have most often been evaluated individually instead of in a multivariable setting, which could more appropriately identify multifactorial origins of the syndrome. Thus, we investigated whether demographic characteristics and risk factors correlated with the metabolic syndrome in cross-sectional studies and based on a priori knowledge predicted development of the syndrome over 15 years.

RESEARCH DESIGN AND METHODS

— This investigation was conducted in the Coronary Artery Risk Development in Young Adults (CARDIA) study (16). Black and white men and women aged 18–30 years at baseline (n = 5,115) were selected via random sampling from Chicago, Illinois, Birmingham, Alabama, and Minneapolis, Minnesota, and from the Kaiser-Permanente health plan in Oakland, California. Participants were reexamined six times between baseline (1985–1986) and 2000 and 2001. After exclusions for missing measurements of metabolic syndrome components at baseline (n = 237), prevalent metabolic syndrome (n = 104), pregnancy (n = 6), and loss to follow-up (n = 576), 4,192 participants remained. The study was approved by the institutional review boards at all study sites.

Demographic characteristics (age, sex, and race) and education were collected via self-report on standardized questionnaires at each examination. Regular leisure time and work-related physi-

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Abbreviations: ATP III, Adult Treatment Panel III; CARDIA, Coronary Artery Risk Development in Young Adults.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Distribution of characteristics in the population*

Characteristics	Total	Men		Women	
		Black	White	Black	White
n	4192	881	988	1185	1138
Baseline					
Age (years)	24.9 ± 3.6	24.2 (3.7	25.4 (3.3	24.4 (3.8	25.5 (3.4
Sex (% male)	44.6				
High school education or less (%)	66.7	81.8	53.7	80.4	51.9
BMI (kg/m^2)	24.2 ± 4.7	24.3 ± 3.9	24.0 ± 3.1	25.6 ± 6.2	22.9 ± 4.1
Baseline physical activity score (units)	421.3 ± 299.5	531.3 ± 344.4	513.0 ± 297.2	279.1 ± 229.4	404.6 ± 263.4
Smoking status (%)					
Never	58.1	56.0	59.6	61.2	55.4
Former	13.2	9.1	15.1	8.7	19.3
Current	28.7	34.9	25.3	30.1	25.4
Alcohol intake					
No drinks/day	22.9	23.7	14.9	34.4	17.2
One to three drinks/day	70.7	64.3	73.9	63.3	80.5
Three or more drinks/day	6.5	12.0	11.2	2.3	2.4
Energy from carbohydrates (%)	46.7 ± 7.3	45.9 ± 7.1	44.9 ± 6.8	48.3 ± 7.4	47.2 ± 7.3
Energy from total fat (%)	37.1 ± 5.8	37.9 ± 5.6	37.3 ± 5.4	37.3 ± 5.8	36.2 ± 6.3
Crude fiber (g)	5.6 ± 3.2	6.1 ± 3.5	6.5 ± 3.1	4.7 ± 3.0	5.4 ± 3.0
Metabolic syndrome components					
Waist circumference (cm)	77.1 ± 10.7	79.9 ± 9.1	82.3 ± 8.0	76.0 ± 12.5	71.4 ± 8.7
Glucose (mg/dl)	82.0 ± 12.7	83.3 ± 10.0	84.7 ± 10.9	80.1 ± 17.1	80.8 ± 10.1
HDL cholesterol (mg/dl)	53.6 ± 12.9	54.0 ± 13.3	47.5 ± 11.0	55.6 ± 12.6	56.5 ± 12.9
Triglycerides (mg/dl)	69.8 ± 41.9	67.8 ± 40.5	83.6 ± 57.2	61.8 ± 28.7	67.6 ± 35.6
Systolic blood pressure (mmHg)	110.0 ± 10.7	115.5 ± 10.4	113.9 ± 10.0	107.9 ± 9.6	104.6 ± 9.1
Diastolic blood pressure (mmHg)	68.4 ± 9.4	70.7 ± 10.0	70.4 ± 9.1	67.2 ± 9.3	66.1 ± 8.3
Change in weight and physical activity					
Weight change from baseline to year 15 (kg)	12.8 ± 12.1	14.1 ± 12.1	11.1 ± 9.4	16.2 ± 13.8	10.1 ± 11.7
Physical activity over time (%)*					
Regular	16.3	26.6	25.1	3.2	13.4
Moderate	53.3	54.5	56.7	47.6	54.7
Low	30.4	18.9	18.2	49.3	31.9

Data are means ±SD unless otherwise indicated. *Regular physical activity, a physical activity score above the median (364) at all four examinations; moderately active, activity fluctuated around the median; low activity, physical activity score below the median at all four examinations.

cal activities were assessed by a validated interview-administered questionnaire (17). Participants whose self-reported physical activity was above the median of the baseline sample distribution at all four examinations were classified as maintaining regular physical activity. Participants whose activity fluctuated were described as moderately active. Those whose activity was below the baseline median at all four examinations were classified as engaging in low activity. Usual dietary and alcohol intake (past 28 days) was estimated using the CARDIA Diet History (18). Based on previously reported findings of possible overestimation and underestimation of energy intake using the Diet History survey, participants with extremely high (men >8,000, women >6,000 kcal) or low (men <800, women <600 kcal) energy intakes were excluded (19). We evaluated total carbohydrates (percent energy), total fat (percent energy), and crude fiber (grams) because of previously reported associations between each component and type 2 diabetes and/or insulin resistance (13,20–23). Distributions of each were categorized into quintiles (sex specific for fiber) for analysis. One alcoholic drink was equivalent to 12.6 g ethanol according to the U.S. Department of Agriculture definition of a standard drink (24). Based on previous research (25), we compared participants who abstained (no drinks per day) and drank heavily (three or more drinks per day) with those who reported moderate consumption (one to three drinks per day).

Samples of glucose (26) and lipids (27,28) were collected according to standardized CARDIA procedures (16) and processed at central laboratories. After a 5-min rest, blood pressure was measured three times with participants seated; the average of the last two measurements was used. Height and weight were measured; BMI was calculated (weight in kilograms divided by the square of height in meters). Weight change over follow-up was calculated as the difference between weight at baseline and the final examination. Waist circumference was measured as the average of two waist circumference measures at the minimum abdominal girth (nearest 0.5 cm) from participants standing upright.

Metabolic syndrome was defined according to ATP III guidelines (2) with the presence of at least three of the following:

Table 2—*RRs of baseline characteristics and incident metabolic syndrome*

		Men		Women	
	Total	Black	White	Black	White
Model 1					
Age (per 5 years)	1.32 (1.17–1.48)	1.31 (1.01–1.70)	1.19 (0.93–1.52)	1.40 (1.16–1.69)	1.29 (0.98–1.68)
Race					
Black	1.28 (1.08–1.51)				
White	1.00 (referent)				
Sex					
Men	1.12 (0.95–1.32)				
Women	1.00 (referent)				
Model 2 and model 1 + each variable individually					
Education					
High school or less	1.66 (1.36–2.03)	0.79 (0.50–1.24)	1.61 (1.15–2.25)	1.88 (1.25–2.83)	2.39 (1.60–3.57)
More than high school	1.00 (referent)	1.00	1.00	1.00	1.00
BMI (per 4.7 kg/m^2)	1.89 (1.79–2.00)	2.32 (2.03–2.65)	3.00 (2.46–3.65)	1.58 (1.46–1.72)	2.19 (1.96–2.44)
Physical activity (per 299.5 units)	0.84 (0.76–0.92)	0.86 (0.72–1.03)	0.87 (0.73–1.03)	1.01 (0.84–1.22)	0.64 (0.50–0.82)
Smoking status					
Current	1.16 (0.96–1.40)	0.85 (0.56–1.30)	1.11 (0.76–1.62)	1.31 (0.95–1.80)	1.36 (0.91–2.03)
Former	1.00 (0.77–1.29)	0.64 (0.29–1.40)	1.26 (0.81–1.96)	1.23 (0.77–1.98)	0.76 (0.45–1.28)
Never	1.00 (referent)	1.00	1.00	1.00	1.00
Alcohol intake					
No drinks/day	1.69 (1.41–2.03)	1.57 (1.03–2.41)	2.41 (1.67–3.49)	1.14 (0.84–1.54)	2.43 (1.65–3.58)
One to three drinks/day	1.00 (referent)	1.00	1.00	1.00	1.00
Three or more drinks/day	1.13 (0.79–1.60)	0.79 (0.39–1.59)	1.25 (0.74–2.09)	1.72 (0.76–3.92)	1.41 (0.45–4.47)
Carbohydrate intake (% energy)					
Q1 (25–41%)	1.00 (referent)	1.00	1.00	1.00	1.00
Q2 (41–45%)	1.03 (0.79–1.34)	1.83 (1.05–3.18)	0.77 (0.49–1.21)	1.09 (0.63–1.89)	0.85 (0.47–1.56)
Q3 (45–48%)	0.95 (0.73–1.25)	0.95 (0.50–1.79)	0.86 (0.54–1.38)	1.41 (0.83–2.38)	0.71 (0.38–1.33)
Q4 (48–52%)	1.32 (1.02–1.70)	1.46 (0.78–2.72)	1.23 (0.79–1.91)	1.68 (1.02–2.77)	1.04 (0.59–1.81)
Q5 (52–85%)	1.27 (0.98–1.64)	1.54 (0.85–2.81)	0.81 (0.46–1.43)	1.48 (0.91–2.41)	1.34 (0.79–2.27)
Crude fiber (g)					
Q1: F (0.3–2.7)/M (0.6–3.6)	1.41 (1.09–1.82)	2.02 (1.15–3.56)	1.08 (0.64–1.82)	1.08 (0.70–1.68)	2.07 (1.16–3.71)
Q2: F (2.8–3.8)/M (3.6–5.0)	1.32 (1.02–1.71)	1.58 (0.86–2.88)	1.24 (0.77–2.02)	1.13 (0.71–1.80)	1.48 (0.84–2.59)
Q3: F (3.8–5.0)/M (5.0–6.4)	1.26 (0.97–1.64)	0.85 (0.42–1.70)	1.33 (0.81–2.17)	1.36 (0.87–2.13)	1.37 (0.78,2.41)
Q4: F (5.0–6.9)/M (6.4–8.5)	0.99 (0.75–1.31)	0.93 (0.45–1.90)	0.82 (0.49–1.38)	1.14 (0.71–1.84)	1.05 (0.58–1.89)
Q5: F (6.9–33)/M (8.6–29.8)	1.00 (referent)	1.00	1.00	1.00	1.00
Total fat intake (% energy)					
Q1 (11–33%)	1.26 (0.97–1.64)	1.63 (0.85–3.11)	1.27 (0.74–2.18)	1.26 (0.80–2.00)	0.95 (0.57–1.58)
Q2 (33–36%)	1.31 (1.01, 1.70)	1.60 (0.83, 3.08)	1.24 (0.74, 2.10)	1.52 (0.98–2.37)	0.94 (0.56–1.59)
Q3 (36–39%)	1.00 (referent)	1.00	1.00	1.00	1.00
Q4 (39–42%)	0.97 (0.74–1.28)	1.36 (0.73–2.55)	1.19 (0.71–1.99)	0.98 (0.61–1.59)	0.44 (0.21–0.91)
Q5 (42–59%)	1.37 (1.06–1.77)	1.74 (0.95–3.18)	1.86 (1.15–3.01)	1.02 (0.63–1.63)	1.15 (0.67–2.00)

Data are RR (95% CI). Q, quintile.

1) fasting glucose ≥6.1 mmol/l, *2*) waist circumference >88 cm (women) or >102 cm (men), *3*) systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, *4*) triglycerides ≥1.7 mmol/l, and *5*) HDL cholesterol <1.3 mmol/l in women or <1.04 mmol/l in men. Participants who reported using medications for diabetes or hypertension control were classified as having met the criterion for elevated glucose or blood pressure, respectively. Incident metabolic syndrome was identified in participants who met the criterion for having metabolic syndrome at any follow-up examination.

Statistical methods

Person-time was calculated from the baseline examination until metabolic syndrome was identified or until the last examination, whichever came first. Age-adjusted event rates were calculated using Poisson regression. We estimated the relative risk (RR) and 95% CI of metabolic syndrome developing by each characteristic undergoing study using Cox proportional hazards regression. Continuous variables were investigated per SD increase above the mean.

In a secondary analysis, we tested the robustness of our findings by repeating the analysis after eliminating persons in

Table 3—*Multivariable RRs of baseline characteristics and incident metabolic syndrome*

		Men		Women	
	Total	Black	White	Black	White
Age (per 5 years)	1.26 (1.11–1.42)	1.18 (0.88–1.58)	1.09 (0.83–1.44)	1.31 (1.07–1.61)	1.53 (1.14–2.05)
Race					
Black	0.73 (0.60–0.87)				
White	1.00 (referent)				
Sex					
Men	1.55 (1.28–1.88)				
Women	1.00 (referent)				
Education					
High school or less	1.52 (1.24–1.87)	1.10 (0.67–1.83)	1.34 (0.94–1.93)	1.84 (1.20–2.82)	1.63 (1.05–2.52)
More than high school	1.00 (referent)	1.00	1.00	1.00	1.00
BMI (per 4.7 kg/m^2)	1.89 (1.77–2.00)	2.44 (2.06–2.88)	2.95 (2.37–3.67)	1.63 (1.50–1.77)	2.18 (1.89–2.51)
Physical activity (per 299.5 units)	0.95 (0.86–1.05)	0.99 (0.82–1.20)	0.92 (0.77–1.11)	1.08 (0.88–1.32)	0.93 (0.72–1.21)
Smoking status					
Current	1.18 (0.97–1.45)	1.52 (0.93–2.47)	1.14 (0.75–1.73)	1.28 (0.91–1.79)	0.99 (0.62–1.56)
Former	1.02 (0.79–1.33)	0.73 (0.33–1.64)	1.45 (0.91–2.31)	1.12 (0.69–1.82)	0.76 (0.44–1.31)
Never	1.00 (referent)	1.00	1.00	1.00	1.00
Alcohol intake					
No drinks/day	1.36 (1.11–1.66)	1.40 (0.88–2.23)	2.05 (1.34–3.13)	1.06 (0.76–1.48)	1.46 (0.92–2.30)
One to three drinks/day	1.00 (referent)	1.00	1.00	1.00	1.00
More than three drinks/day	1.24 (0.83–1.85)	1.04 (0.45–2.42)	1.26 (0.68–2.32)	2.10 (0.78–5.70)	1.58 (0.47–5.35)
Carbohydrate intake (% energy)					
Q1 (25–41%)	1.00 (referent)	1.00	1.00	1.00	1.00
Q2 (41–45%)	1.28 (0.96–1.70)	1.30 (0.69–2.45)	1.13 (0.67–1.89)	1.56 (0.87–2.82)	1.15 (0.57–2.29)
Q3 (45–48%)	1.30 (0.94–1.80)	1.25 (0.61–2.56)	1.10 (0.58–2.07)	2.10 (1.11–3.97)	0.79 (0.37–1.68)
Q4 (48–52%)	1.85 (1.30–2.65)	2.41 (1.09–5.32)	1.91 (0.95–3.86)	2.56 (1.28–5.12)	0.99 (0.46–2.13)
Q5 (52–85%)	1.63 (1.06–2.51)	1.98 (0.70–5.55)	1.22 (0.48–3.14)	2.17 (0.98–4.81)	1.16 (0.50–2.70)
Crude fiber (g)					
Q1: F (0.3–2.7)/M (0.6–3.6)	1.12 (0.86–1.47)	1.73 (0.90–3.33)	0.88 (0.50–1.53)	0.88 (0.55–1.40)	1.53 (0.81–2.88)
Q2: F (2.8–3.8)/M (3.6–5.0)	1.14 (0.87–1.49)	1.43 (0.74–2.78)	1.23 (0.73–2.07)	1.02 (0.63–1.66)	1.01 (0.55–1.88)
Q3: F (3.8–5.0)/M (5.0–6.4)	1.00 (0.76–1.32)	0.95 (0.45–1.97)	1.24 (0.74–2.08)	0.97 (0.60–1.57)	1.05 (0.57–1.90)
Q4: F (5.0–6.9)/M (6.4–8.5)	0.92 (0.69–1.22)	0.80 (0.37–1.75)	0.93 (0.54–1.59)	0.95 (0.58–1.55)	1.14 (0.61–2.11)
Q5: F (6.9–33)/M (8.6–29.8)	1.00 (referent)	1.00	1.00	1.00	1.00
Total fat intake (% energy)					
Q1 (11–33%)	1.00 (0.71–1.41)	1.37 (0.58–3.24)	1.23 (0.62–2.46)	0.96 (0.51–1.80)	0.85 (0.44–1.62)
Q2 (33–36%)	1.18 (0.89–1.57)	1.70 (0.83–3.46)	1.21 (0.67–2.18)	1.37 (0.84–2.25)	0.81 (0.44–1.47)
Q3 (36–39%)	1.00 (referent)	1.00	1.00	1.00	1.00
Q4 (39–42%)	1.04 (0.77–1.39)	1.19 (0.61–2.35)	1.18 (0.67–2.09)	1.17 (0.68–2.01)	0.32 (0.14–0.73)
Q5 (42–59%)	1.64 (1.19–2.25)	2.15 (1.08–4.31)	2.09 (1.12–3.87)	1.60 (0.86–2.99)	1.02 (0.51–2.04)

Data are RR (95% CI). Q, quintile.

whom diabetes developed based on a fasting glucose ≥7.0 mmol/l or the use of hypoglycemic medications or insulin. Next, we repeated the primary analysis after removing waist circumference from the definition because of the high correlation between BMI and waist, and we tested the association between each risk factor and the risk of metabolic syndrome developing without abdominal adiposity (three of the remaining four components). Statistical significance is denoted by $P < 0.05$. All analyses were conducted using the SAS System (version 8.1; SAS Institute, Cary, NC).

RESULTS — On average, participants had cardiovascular risk factor profiles below conventional treatment levels at baseline (Table 1). These values varied slightly by sex and race groups.

During an average of 13.6 years of follow-up, the metabolic syndrome developed in 575 participants. The age-adjusted rate per 1,000 person-years was 10.3 for men and 9.7 for women ($P = 0.48$); the rate was higher among black (11.0) versus white (8.5) participants ($P = 0.02$). Black women had the highest rate (12.2, $P < 0.0001$), followed by white men (11.0, $P < 0.001$), black men (9.4, $P = 0.07$), and white women (7.4) (significance testing compared with white women).

The risk of metabolic syndrome increased with age and was higher among black participants and those with the least education (Table 2). After adjustment for

Table 4—*Association of weight change and physical activity change with incident metabolic syndrome*

	Total	Men		Women	
		Black	White	Black	White
Model 1*					
Weight gain (per 4.54 kg/10 lb)	1.24 (1.21–1.27)	1.34 (1.27–1.42)	1.39 (1.31–1.47)	1.11 (1.05–1.16)	1.26 (1.20–1.31)
Model 2†					
Physical activity over time‡					
Regular vs. no activity	0.40 (0.28–0.57)	0.47 (0.25–0.88)	0.45 (0.27–0.75)	0.22 (0.03–1.60)	0.19 (0.06–0.59)
Moderate vs. no activity	0.82 (0.69–0.97)	0.82 (0.55–1.24)	0.76 (0.54–1.08)	0.96 (0.71–1.31)	0.75 (0.52–1.08)
Model 3§					
Weight gain (per 4.54 kg/10 lb)	1.23 (1.20–1.27)	1.35 (1.27–1.42)	1.38 (1.30–1.46)	1.10 (1.05–1.16)	1.24 (1.19–1.30)
Physical activity over time					
Regular vs. no activity	0.49 (0.34–0.70)	0.50 (0.26–0.96)	0.61 (0.36–1.04)	0.28 (0.04–2.03)	0.22 (0.05–0.91)
Moderate vs. no activity	0.89 (0.74–1.07)	0.72 (0.46–1.12)	0.82 (0.57–1.18)	1.03 (0.75–1.42)	0.90 (0.62–1.32)
Model 4‖					
Weight gain (per 4.54 kg/10 lb)	1.17 (1.14–1.20)	1.26 (1.17–1.35)	1.26 (1.18–1.35)	1.10 (1.05–1.15)	1.17 (1.11–1.24)
Physical activity over time					
Regular vs. no activity	0.65 (0.43–0.98)	0.76 (0.35–1.66)	0.74 (0.39–1.41)	0.50 (0.07–3.80)	0.38 (0.08–1.76)
Moderate vs. no activity	0.93 (0.76–1.14)	0.94 (0.56–1.59)	0.85 (0.56–1.30)	0.93 (0.64–1.35)	1.14 (0.70–1.87)

Data are RR (95% CI). *Model 1: age, race, sex, and weight gain. †Model 2: age, race, sex, and physical activity over time. ‡Regular physical activity, physical activity score above the median (364) at all four examinations; moderately active, activity fluctuated around the median; low activity, physical activity score below the median at all four examinations. §Model 3: age, race, sex, weight gain, and physical activity over time. ‖ Model 4: Model 3 plus education, baseline BMI, baseline physical activity, smoking status, drinking status, crude fiber (quintiles), total dietary fat intake (quintiles), and carbohydrate intake (quintiles).

age, race, and sex, the RR was significantly elevated among participants with higher BMI, those who reported no alcohol intake in the previous month (versus one to three drinks), a higher proportion of total energy from carbohydrates, and lower intake of crude fiber. Both high (quintile 5) and low (quintiles 2 and 3) fat intakes (percent energy) were associated with a significantly elevated risk of metabolic syndrome relative to moderate fat intake (quintile 3). Physical activity was inversely associated with metabolic syndrome risk. BMI was the only characteristic that was a significant predictor of metabolic syndrome across race-sex groups, but trends for risk factors were generally in a similar direction.

In models that simultaneously adjusted for all risk factors, the metabolic syndrome was less likely to develop in black participants, whereas risk was increased in men versus women (Table 3). Most of the same risk factors remained predictive of metabolic syndrome, with the exceptions that the inverse association of metabolic syndrome with physical activity and fiber intake attenuated to nonsignificance, and high levels of dietary fat were associated with metabolic syndrome risk. Again, higher BMI was the only factor that remained significantly associated with metabolic syndrome in all race and sex groups.

Weight gain was associated with an increased risk for metabolic syndrome in the total sample and in each race and sex group (Table 4). This association persisted independent of all risk factors. Regular physical activity over time was inversely associated with the metabolic syndrome risk independent of weight gain, demographic characteristics, and other risk factors in the total population.

Because the association of demographic characteristics and risk factors with metabolic syndrome remained the same when we excluded persons in whom diabetes developed ($n = 54$), we do not present the results separately. The metabolic syndrome without abdominal adiposity developed in 223 participants (Table 5). In models adjusted for age and sex, there was no difference in risk by race group, but in multivariable models, risk among black participants was approximately half that of their white counterparts. Men were 2.5–3.9 times more likely than women to have the metabolic syndrome without abdominal adiposity as a component. The association between other risk factors and metabolic syndrome without abdominal adiposity was similar to that seen in previous analyses of the complete metabolic syndrome.

CONCLUSIONS — Our most robust finding, that higher body mass in young adulthood and weight gain over 15 years predicts development of the metabolic syndrome, confirms previous reports but does so for the first time in a diverse cohort of young adults using the new ATP III definition. We also present evidence that young adults who consume no alcohol relative to moderate drinkers and those who consume a higher proportion of their calories from carbohydrates and less crude fiber may be at increased risk. Despite the presence of other risk factors, young adults who maintained regular physical activity over time appeared to be at reduced risk. The association among race, sex, education, and metabolic syndrome risk is complex and varies depending on the presence of other risk factors and the composition of the syndrome.

Obesity and weight gain

Obesity is an important, easily observed, and measurable risk factor for the metabolic syndrome. Other longitudinal studies, including the Bogolusa Heart Study, Amsterdam Growth and Health Study, Framingham Offspring Cohort, and IRAS (Insulin Resistance Atherosclerosis Study)

Table 5—*RRs of developing the metabolic syndrome without abdominal adiposity

	Model 1†	Model 2‡	Model 3§
Age (per 5 years)	1.36 (1.12–1.65)	1.34 (1.09–1.65)	1.42 (1.14–1.77)
Race			
Black	0.87 (0.67–1.14)	0.54 (0.40–0.73)	0.51 (0.37–0.70)
White	1 (referent)	1.00	1.00
Sex			
Men	2.54 (1.93–3.35)	3.52 (2.55–4.88)	3.89 (2.77–5.47)
Women	1 (referent)	1.00	1.00
Education			
High school or less	1.73 (1.26–2.36)	1.55 (1.12–2.15)	1.52 (1.07–2.14)
More than high school	1 (referent)	1.00	1.00
BMI (per 4.7 kg/m^2)	1.79 (1.62–1.97)	1.76 (1.58–1.96)	1.66 (1.46–1.88)
Physical activity (per 299.5 units)	0.89 (0.78–1.03)	1.00 (0.86–1.16)	1.01 (0.84–1.20)
Smoking status			
Current	1.06 (0.79–1.44)	1.08 (0.77–1.50)	1.01 (0.71–1.44)
Former	0.86 (0.56–1.31)	0.86 (0.55–1.32)	0.86 (0.54–1.36)
Never	1 (referent)	1.00	1.00
Alcohol intake			
No drinks/day	2.22 (1.66–2.97)	1.83 (1.32–2.53)	1.56 (1.10–2.22)
One to three drinks/day	1 (referent)	1.00	1.00
Three or more drinks/day	1.04 (0.60–1.77)	1.01 (0.54–1.87)	1.04 (0.55–1.98)
Carbohydrate intake (% energy)			
Q1 (25–41%)	1 (referent)	1.00	1.00
Q2 (41–45%)	1.19 (0.80–1.77)	1.31 (0.85–2.02)	1.25 (0.80–1.96)
Q3 (45–48%)	0.88 (0.57–1.37)	0.96 (0.56–1.64)	0.82 (0.46–1.46)
Q4 (48–52%)	1.22 (0.80–1.84)	1.26 (0.70–2.28)	1.25 (0.67–2.32)
Q5 (52–85%)	1.43 (0.95–2.14)	1.45 (0.72–2.94)	1.41 (0.67–2.98)
Crude fiber (g)			
Q1: F (0.3–2.7)/M (0.6–3.6)	1.25 (0.81–1.93)	1.06 (0.67–1.68)	1.06 (0.65–1.74)
Q2: F (2.8–3.8)/M (3.6–5.0)	1.44 (0.95–2.18)	1.22 (0.79–1.89)	1.20 (0.75–1.92)
Q3: F (3.8–5.0)/M (5.0–6.4)	1.36 (0.89–2.08)	1.13 (0.72–1.76)	1.32 (0.82–2.12)
Q4: F (5.0–6.9)/M (6.4–8.5)	1.11 (0.72–1.73)	1.10 (0.70–1.73)	1.24 (0.77–2.00)
Q5: F (6.9–33)/M (8.6–29.8)	1 (referent)	1.00	1.00
Total fat intake (% energy)			
Q1 (11–33%)	1.56 (0.98–2.49)	1.50 (0.82–2.75)	1.37 (0.72–2.62)
Q2 (33–36%)	1.99 (1.28–3.10)	2.12 (1.28–3.53)	2.06 (1.21–3.49)
Q3 (36–39%)	1 (referent)	1.00	1.00
Q4 (39–42%)	1.48 (0.94–2.35)	1.79 (1.08–2.99)	1.75 (1.02–2.99)
Q5 (42–59%)	1.83 (1.17–2.86)	1.94 (1.11–3.39)	1.82 (1.02–3.25)
Weight change from baseline to year 15 per 4.54 kg (10 lb)	1.23 (1.17–1.28)		1.16 (1.11–1.21)
Physical activity over time‖			
Regular	0.49 (0.30–0.81)		0.72 (0.40–1.30)
Moderate	0.97 (0.73–1.29)		1.10 (0.79–1.54)
Low	1 (referent)	1.00	1.00

Data are RR (95% CI). *Metabolic syndrome components without large waist: high blood pressure and high triglyceride level, low HDL cholesterol, and high glucose levels (cumulative incidence = 223). †All variables adjusted for age, race, and sex. Estimates for age, race, and sex are generated from one model with each of those three characteristics. All variables are from the baseline examination only except for weight change and physical activity change. ‡Multivariable 1 model with all variables listed in the model. §Multivariable 2 model with all variables listed in the model including weight gain and physical activity over time. ‖Regular physical activity, physical activity score above the median (364) at all four examinations; moderately active, activity fluctuated around the median; low activity, physical activity score below the median at all four examinations. Q, quintile.

reported this association (14,15,29–31). When we evaluated risk factors for the metabolic syndrome without abdominal adiposity in the definition, BMI and weight gain remained strong significant predictors of the syndrome. This is not surprising given evidence from longitudinal observational studies that higher BMI and weight gain over time are associated with poorer blood pressure, higher fasting glucose, and dyslipidemia—the remaining components of the syndrome (32,33).

Who is at risk?

Although previous reports of the prevalence of the metabolic syndrome defined by ATP III showed no differences between black and white women and a lower prevalence among black compared with white

men (9), we report the highest age-adjusted incidence of the metabolic syndrome among black women. One explanation for the increased incidence in black women versus other race-sex groups may be the high prevalence of overweight in this subgroup. To evaluate which single variable had the largest influence on the reversal of the RR between race and metabolic syndrome, we entered single variables into a multivariable model in a forward selection procedure. We found that when BMI is statistically controlled, the risk for metabolic syndrome is lower in black versus white participants. Furthermore, we report that black adults are less likely to have the metabolic syndrome in the absence of abdominal adiposity. These findings suggest, but do not confirm, that adiposity may be a central feature of the metabolic syndrome in black versus white adults.

Despite the initial hypothesis that insulin resistance is the underlying factor in the metabolic syndrome (34), Liao et al. (35) reported that ATP III criteria have a low sensitivity for predicting insulin resistance. Previous research indicates that black adults are routinely more insulin resistant than white adults (36,37) but paradoxically have more favorable values for triglyceride and HDL cholesterol, two components that define the syndrome. The use of uniform cut points to define dyslipidemia are less likely to include black adults, which may result in missed identification of black adults who remain at high risk for diabetes and coronary heart disease. This finding should not be interpreted as a lower risk for the health consequences of the metabolic syndrome in black adults but rather possibly as a misclassification of risk that warrants further research on syndrome components in diverse populations.

Participants with less education were at increased risk for the metabolic syndrome in this cohort. Although education is closely associated with race/ethnicity in this country, both factors remained significant predictors of the metabolic syndrome in our multivariable models. Low education may be a marker for characteristics associated with increased risk for the metabolic syndrome, such as limited access to health care, higher personal and physical stress, and differences in body image that influence motivation to lose weight.

Health behaviors

Evidence for the role of specific dietary components on the metabolic syndrome remains unclear. Previous reports in this cohort suggested that dietary fiber (21) and dairy intake (among overweight persons [39]) were inversely associated with insulin levels and an insulin resistance syndrome, respectively. Our finding that crude fiber was inversely associated with the metabolic syndrome in minimally adjusted models is consistent with previous reports (13) and plausible because fiber slows absorption of foods in the gut, resulting in a measured release of insulin from the pancreas and better control of glucose levels. However, in multivariable models, the fiber association was no longer significant, but higher carbohydrate and fat intakes were stronger risk factors. It is plausible that carbohydrates alone, regardless of their fiber quality, are associated with metabolic syndrome risk through the role on insulin resistance (40). Given the significant effects we report regarding fat intake, moderating fat intake may be equally important.

Elevated risk for the metabolic syndrome among participants who abstained from alcohol relative to moderate drinkers is the first such prospective finding. However, these results are consistent with cross-sectional research (9) and plausible because light and moderate alcohol consumption may boost HDL levels (41,42) and increase insulin sensitivity (43,44), both of which may be factors in the pathogenesis of the metabolic syndrome.

In this same study population, we previously reported an inverse association between cardiorespiratory fitness and development of the metabolic syndrome (11). This study advances beyond those findings to demonstrate that physical activity, a health behavior as opposed to a physiological characteristic, is associated with metabolic syndrome risk independent of other risk factors. We confirm findings from two previous studies in largely (>70%) male cohorts (12,45). It is plausible that the absence of an association between regular physical activity and metabolic syndrome risk in black women is attributable to the small percentage of women (3.2%) who maintained regular physical activity and not a distinct biological mechanism.

Limitations

Given the large number of statistical tests that we conducted, there is a high likelihood that some observations were derived from chance alone. Thus, the importance of our findings should instead be evaluated in light of the biological plausibility, magnitude, and precision of the effect estimate. Because of our measurement tool for physical activity, we cannot relate metabolic syndrome risk to current physical activity recommendations that suggest days per week to improve cardiovascular health. Instead, we can only report a strong trend toward risk reduction with increased activity. We restricted our analysis of diet to the baseline measurement, because dietary history was not repeated at the end of follow-up. Although macronutrient intakes did not appear to change markedly over 7 years, diet may have changed over 15 years.

The metabolic syndrome may be another important consequence of the current obesity epidemic. The high prevalence of overweight and obesity among black adults and in lower socioeconomic groups, as reported in national surveys (46), may play an important role in excess metabolic syndrome incidence in those subpopulations. This report confirms that obesity and physical inactivity, in addition to other health behaviors such as alcohol intake and dietary composition, are important determinants of metabolic syndrome risk in young adulthood. Lifestyle modification, specifically weight loss and physical activity, cited as first-line therapies for managing the metabolic syndrome (47), should be encouraged for everyone and specifically targeted toward at-risk subpopulations.

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