

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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Circulation 2008;117;754-761; originally published online Jan 22, 2008;

DOI: 10.1161/CIRCULATIONAHA.107.716159

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514

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Dietary Intake and the Development of the Metabolic Syndrome

The Atherosclerosis Risk in Communities Study

Pamela L. Lutsey, MPH; Lyn M. Steffen, PhD, MPH, RD; June Stevens, PhD, MS, RD

Background—The role of diet in the origin of metabolic syndrome (MetSyn) is not well understood; thus, we sought to evaluate the relationship between incident MetSyn and dietary intake using prospective data from 9514 participants (age, 45 to 64 years) enrolled in the Atherosclerosis Risk in Communities (ARIC) study.

Methods and Results—Dietary intake was assessed at baseline via a 66-item food frequency questionnaire. We used principal-components analysis to derive “Western” and “prudent” dietary patterns from 32 food groups and evaluated 10 food groups used in previous studies of the ARIC cohort. MetSyn was defined by American Heart Association guidelines. Proportional-hazards regression was used. Over 9 years of follow-up, 3782 incident cases of MetSyn were identified. After adjustment for demographic factors, smoking, physical activity, and energy intake, consumption of a Western dietary pattern ($P_{\text{trend}}=0.03$) was adversely associated with incident MetSyn. After further adjustment for intake of meat, dairy, fruits and vegetables, refined grains, and whole grains, analysis of individual food groups revealed that meat ($P_{\text{trend}}<0.001$), fried foods ($P_{\text{trend}}=0.02$), and diet soda ($P_{\text{trend}}=<0.001$) also were adversely associated with incident MetSyn, whereas dairy consumption ($P_{\text{trend}}=0.006$) was beneficial. No associations were observed between incident MetSyn and a prudent dietary pattern or intakes of whole grains, refined grains, fruits and vegetables, nuts, coffee, or sweetened beverages.

Conclusions—These prospective findings suggest that consumption of a Western dietary pattern, meat, and fried foods promotes the incidence of MetSyn, whereas dairy consumption provides some protection. The diet soda association was not hypothesized and deserves further study. (*Circulation*. 2008;117:754-761.)

Key Words: dairy products ■ diet ■ food habits ■ meat ■ metabolic syndrome X

Metabolic syndrome (MetSyn) is a cluster of cardiovascular risk factor abnormalities associated with increased risk of type 2 diabetes mellitus,^{1,2} cardiovascular disease,^{2,3} and all-cause mortality.⁴ Elevated measurements of ≥ 3 of the following cardiovascular risk factors define the syndrome: waist circumference, blood pressure, fasting glucose, high-density lipoprotein (HDL) cholesterol, and triglycerides.⁵ According to National Health and Nutrition Examination Survey (NHANES) III data, collected in 1988 to 1994, $\approx 24\%$ of adult Americans, or nearly 47 million US residents, have MetSyn.⁶ Given the present obesity epidemic in the United States,⁷ the current prevalence of MetSyn may be higher than that estimated from the 10- to 15-year-old NHANES III data.⁶

MetSyn is not well understood. Cross-sectionally, dietary intakes rich in whole-grain foods have been linked to a lower prevalence of MetSyn.^{19–21} The evidence is less consistent for refined-grain intake, with some cross-sectional studies reporting a positive association^{19,21} and others finding no relation.²⁰ Dairy intake has been inversely associated with MetSyn both cross-sectionally^{22,23} and prospectively.²⁴ Greater intakes of fruit and vegetables also have been associated with a lower prevalence of MetSyn.²⁵ No association has been found between MetSyn and intakes of meat and fish.²³ Intakes of regular and diet soda, however, have been positively associated with MetSyn both cross-sectionally and prospectively.²⁶ In cross-sectional dietary pattern analyses, a greater prevalence of MetSyn was found among consumers of “Western”²⁷ and “empty-calorie”²⁸ dietary patterns, whereas a lower prevalence was found among those consuming a “healthy” dietary pattern.²⁷ Associations between MetSyn and intakes of fried foods, coffee, and nuts have yet to be assessed among

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Although dietary intake has been linked to individual components of MetSyn,^{8–18} the role of diet in the origin of

Received May 18, 2007; accepted December 7, 2007.

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The online Data Supplement, which contains a table, can be found with this article at <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.107.716159/DC1>.

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Circulation is available at <http://circ.ahajournals.org>

DOI: 10.1161/CIRCULATIONAHA.107.716159

adults. With few exceptions,^{24,26} the relationship between dietary intake and incident MetSyn has not been explored.

The aim of the present article is to evaluate the relationship between dietary intake and the risk of developing MetSyn over 9 years of follow-up in men and women enrolled in the Atherosclerosis Risk in Communities (ARIC) study. We hypothesized that consumption of a “prudent” dietary pattern, dairy, whole grains, fruit and vegetables, and coffee would be inversely associated with incident MetSyn, whereas a positive association would be observed with consumption of a Western dietary pattern, meat, refined grains, fried foods, and sweetened beverages.

Methods

Study Population

The ARIC study is a multicenter population-based prospective cohort study designed to investigate the origin and natural history of atherosclerosis in middle-aged adults.²⁹ Participants were recruited from 4 US communities: Forsyth County, North Carolina; Jackson, Miss; suburbs of Minneapolis, Minn; and Washington County, Maryland. The study cohort included 15 972 white and black men and women 45 to 64 years of age at baseline in 1987 to 1989 (visit 1). Cohort reexaminations took place at 3-year intervals; response rates were 93%, 86%, and 81% at visits 2 (1990 to 1992), 3 (1993 to 1995), and 4 (1996 to 1998), respectively. Local institutional review boards approved the ARIC protocol, and all subjects gave informed consent.

All participants with MetSyn at baseline were excluded ($n=5879$), as were those with cardiovascular disease ($n=776$), missing diet data ($n=11$), or implausible energy intakes defined as <500 or >3500 kcal/d in women and <700 or >4500 kcal/d in men ($n=361$). The exclusion criteria were not mutually exclusive; thus, data from 9514 participants were included in the analyses.

Data Collection

ARIC participants underwent interviews, fasting venipuncture, and measurement of blood pressure and anthropometrics at each examination. Trained interviewers ascertained basic demographic data, medical history, and information about personal habits, including diet (2 exams only), smoking, physical activity (with the Baecke et al³⁰ questionnaire), and medication use.

Dietary Assessment

At baseline and examination 3 (6 years later), usual dietary intake was assessed by a 66-item interviewer-administered semiquantitative food-frequency questionnaire (FFQ). The questionnaire was a modified version of the 61-item instrument developed by Willett et al.³¹ Participants reported the frequency of consumption of each food on the basis of 9 levels of frequency, ranging from never or <1 time a month to ≥ 6 times a day. Standard serving sizes and food models were provided as a reference for intake estimation. Interviewers also obtained additional information, including the brand name of the breakfast cereal usually consumed.

Food and beverages from the FFQ were categorized into 29 food subgroups, which were used to derive dietary patterns via principal-components analysis. The subgroups were further collapsed into 5 major food groups: meat, dairy, fruits and vegetables, refined grains, and whole grains (see the online Data Supplement). Additionally, associations with the following individual food items were assessed: fried foods, sweetened beverages (regular soda and fruit drinks), diet soda, nuts, and coffee.

Metabolic Syndrome

MetSyn, defined according to current American Heart Association guidelines,³² was characterized by the presence of any 3 of the following risk factors: waist circumference >102 cm in men and >88 cm in women; triglycerides ≥ 150 mg/dL; HDL cholesterol

<40 mg/dL in men and <50 mg/dL in women; systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg, or current use of antihypertensive medication; and fasting glucose ≥ 100 mg/dL or current drug treatment for elevated glucose.

Waist circumference was measured with a cloth tape at the umbilicus. Fasting blood samples were drawn from an antecubital vein into tubes containing EDTA (lipids) or a serum separator gel (glucose). Total plasma cholesterol³³ and triglycerides³⁴ were determined by enzymatic methods. HDL cholesterol was measured after dextran-magnesium precipitation.³⁵ Serum glucose levels were assessed with a hexokinase/glucose-6-phosphate dehydrogenase method. Sitting blood pressure was measured by trained technicians 3 times on each participant with a random-zero sphygmomanometer after a 5-minute rest.^{36,37} Because of substantial intraindividual variation in blood pressure measurements, the first blood pressure reading was dropped and the second and third readings were averaged for use in this study.^{38,39} Study participants were asked to bring all medications, vitamins, and supplements taken in the 2 weeks before the examination. Information on pharmacological treatment of hypertension and elevated glucose was based on the participant's self-reported use of any medication to treat high blood pressure or elevated glucose and the transcription and coding of all medication names.

Statistical Analysis

All analyses were performed with SAS (version 9.1, SAS Institute Inc, Cary, NC). Principal-components analysis (PROC FACTOR) was used to derive dietary patterns and to determine factor loadings for each of the 29 food subgroups. Factors were rotated with varimax rotation to maintain uncorrelated factors and enhance interpretability.⁴⁰ After evaluation of the eigenvalues and interpretability, all values >2.0 were retained, resulting in a 2-factor solution, with factor 1 explaining 10.2% of the variability and factor 2 explaining 9.7%. Dietary patterns were named according to the nature of the food groups loading highest for each of the factors.

Interval-censored Cox proportional-hazards regression was used to assess the relation between diet and incident MetSyn. The dietary patterns and major food groups (meat, dairy, fruit and vegetables, whole grains, and refined grains) were categorized into quintiles; fried foods, nuts, sweetened beverages, diet soda, and coffee were classified into tertiles, given their low level of consumption. Hazard ratios (HRs) were obtained by entering the quintiles (or tertiles) into the model as indicator variables, whereas tests for trend across the quintiles were conducted by entering the median level of intake at each quintile (or tertile) into the model as a continuous variable. Cumulative average diet, which has been shown to increase the precision of dietary data,⁴¹ was used to create food groups and patterns. Specifically, the time-varying dietary covariates were modeled as follows: Between baseline and examination 3, dietary exposures were based on diet as measured at the baseline examination; after examination 3, dietary exposures were based on the mean of baseline diet and examination 3 diet. Spearman partial correlation coefficients, adjusted for age, sex, race, education, center, and total energy intake, were computed between examinations 1 and 3 for meat ($r=0.42$), dairy ($r=0.42$), fruit and vegetables ($r=0.50$), whole grains ($r=0.45$), and refined grains ($r=0.36$) ($P<0.001$ for all). Considering well-known within-person variation in response to diet questionnaires of the FFQ type, the correlations suggest considerable tracking (lack of change over time), although they also could represent some change in diet over 6 years.⁴¹

Model 1 adjusted for baseline age, sex, race, center, education (less than high school, high school or vocational, college and higher), and energy intake (kcal/d); model 2 further adjusted for behavioral characteristics, including smoking (current, former, never), pack-years (continuous), and physical activity (continuous). For analyses of individual food groups, a third model was considered that also adjusted for the major food groups: meat, dairy, fruit and vegetables, whole grains, and refined grains.

The authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table 1. Baseline Demographics, Behavioral Characteristics, and Dietary Intake of 9514 Male and Female ARIC Participants

	Men (n=4197)	Women (n=5317)
Demographic characteristics		
Age, mean (SD), y	54.4±5.8	53.1±5.7
Race, n (%)		
Black	1008 (24.0)	1388 (26.1)
White	3189 (76.0)	5317 (73.9)
Education, n (%)		
<High school	1001 (23.9)	968 (18.2)
High school or vocational	1467 (35.0)	2358 (44.4)
≥College	1723 (41.1)	1985 (37.4)
Behavioral characteristics		
Physical activity, mean (SD)*	2.61 (0.85)	2.37 (0.78)
Smoking status, n (%)		
Current	1212 (28.9)	1329 (25.0)
Former	1758 (41.9)	1217 (22.9)
Never	1227 (29.2)	2765 (52.1)
Dietary intake		
Dietary pattern scores, n (%) in highest quintile		
Western	1279 (30.5)	622 (11.7)
Prudent	697 (16.6)	1204 (22.7)
Food groups, baseline mean (SD) servings/d		
Whole grains	1.23 (1.33)	1.22 (1.09)
Refined grains	2.87 (1.98)	2.07 (1.44)
Fruit and vegetables	3.82 (2.19)	4.17 (2.21)
Dairy	1.70 (1.42)	1.58 (1.23)
Meat	1.22 (0.81)	0.87 (0.64)
Nuts	0.15 (0.29)	0.12 (0.26)
Sweetened beverages†	0.66 (0.97)	0.45 (0.83)
Diet soda	0.38 (0.82)	0.53 (0.96)
Coffee	2.08 (2.18)	1.79 (2.07)

Values are mean±SD unless indicated otherwise.

*Score on the sport index of the Baecke et al physical activity questionnaire.³⁰

†Regular soda and sweetened fruit-flavored punch or noncarbonated beverages.

Results

The cohort of 9514 ARIC participants had a mean age at baseline of 53.6 years, and 44.1% were male. Over 9 years of follow-up, 3782 participants (39.8%) developed incident MetSyn. On diagnosis, the most frequent contributor to MetSyn was abdominal obesity (79.8%), followed by elevated fasting glucose (77.5%), hypertension (62.4%), low HDL (58.5%), and high levels of triglycerides (48.5%). Sex-stratified baseline demographic, behavioral, and dietary variables are presented in Table 1.

Factor analysis revealed 2 main dietary patterns for the population under study; food groups and factor loadings for those with absolute values of ≥0.20 are presented in Table 2. Factor 1, identified as a Western dietary pattern, was characterized by high intakes of refined grains, processed meat, fried foods, and red meat, whereas factor 2, the prudent

Table 2. Principal Components Analysis Varimax-Rotated Food Group Factor Loading Scores* for Baseline Dietary Intake of 9514 Male and Female ARIC Participants

Food Item	Factor Loading
Western pattern	
Refined-grain bread, cereal, rice, and pasta	0.63
Processed meat	0.63
Fried foods	0.61
Red meat	0.57
Eggs	0.48
Refined-grain desserts	0.43
Soda and sweetened beverages	0.41
Cheese and whole milk	0.38
Legumes	0.35
Sweets/candy	0.30
Fat	0.30
Other vegetables	0.29
Potatoes	0.28
Ice cream	0.27
Yogurt	−0.21
Prudent pattern	
Cruciferous vegetables	0.62
Carotenoid vegetables	0.60
Fruit (no juice)	0.58
Other vegetables	0.52
Fish and seafood	0.46
Poultry	0.43
Dark leafy vegetables	0.43
Whole grains	0.40
Tomatoes	0.39
Legumes	0.34
Low-fat dairy	0.31
Yogurt	0.27
Nuts and peanut butter	0.26
Fruit juice	0.24
Potatoes	0.24
Fat	0.21

*For simplicity, only factor loading scores with absolute values of ≥0.20 are shown.

dietary pattern, was typified by greater consumption of cruciferous and carotenoid vegetables, fruit, fish, and poultry.

Higher scores for the Western dietary pattern were associated with greater risk of developing MetSyn, even after adjustment for behavioral characteristics ($P_{\text{trend}}=0.03$) (Table 3). Participants in the highest quintile of Western dietary pattern scores had an 18% greater risk (HR, 1.18; 95% CI, 1.03 to 1.37) of developing MetSyn than those in the lowest quintile. Consumption of a prudent dietary pattern was not associated with incident MetSyn in either model.

In the analyses of major food groups, results from models 1 and 2 were similar; thus, only model 1 is shown in the tables. After adjustment for demographics, behaviors, and other food groups, greater consumption of meat was associ-

Table 3. Nine-Year Multivariable-Adjusted HRs (95% CIs) for 3782 Cases of Incident MetSyn by Quintile of Food Group Intake and Dietary Pattern Score in 9514 Male and Female Participants of the ARIC Study

	Q1	Q2	Q3	Q4	Q5	P_{trend}^*
Dietary pattern scores†						
Western diet‡	-1.10	-0.61	-0.16	0.37	1.34	
Model 1	1	1.15 (1.03-1.27)	1.16 (1.04-1.29)	1.20 (1.07-1.35)	1.25 (1.08-1.44)	0.004
Model 2	1	1.13 (1.02-1.25)	1.12 (1.01-1.25)	1.16 (1.03-1.31)	1.18 (1.03-1.37)	0.03
Prudent diet‡	-1.09	-0.59	-0.16	0.37	1.24	
Model 1	1	1.02 (0.92-1.14)	1.06 (0.96-1.18)	1.05 (0.94-1.16)	1.02 (0.91-1.14)	0.49
Model 2	1	1.04 (0.93-1.15)	1.09 (0.98-1.22)	1.09 (0.98-1.22)	1.07 (0.95-1.20)	0.11
Individual food groups†§						
Meat‡	0.25	0.56	0.86	1.29	1.94	
Model 1	1	1.14 (1.02-1.26)	1.20 (1.08-1.34)	1.27 (1.14-1.42)	1.31 (1.16-1.48)	<0.001
Model 3	1	1.11 (1.00-1.23)	1.17 (1.05-1.31)	1.25 (1.12-1.40)	1.26 (1.11-1.43)	<0.001
Dairy‡	0.28	0.93	1.29	1.94	3.30	
Model 1	1	0.97 (0.88-1.08)	0.99 (0.90-1.10)	0.94 (0.85-1.05)	0.85 (0.76-0.95)	0.003
Model 3	1	1.02 (0.92-1.13)	1.03 (0.93-1.14)	0.96 (0.86-1.06)	0.87 (0.77-0.98)	0.006
Fruits and vegetables‡	1.64	2.73	3.69	4.77	6.63	
Model 1	1	0.99 (0.89-1.10)	1.00 (0.91-1.11)	0.99 (0.89-1.11)	0.99 (0.88-1.10)	0.74
Model 3	1	1.02 (0.92-1.13)	1.07 (0.96-1.19)	1.08 (0.96-1.20)	1.10 (0.98-1.24)	0.09
Whole grains‡	0.07	0.43	1.00	1.43	2.64	
Model 1	1	0.96 (0.86-1.06)	1.07 (0.97-1.19)	0.96 (0.87-1.07)	1.00 (0.90-1.11)	0.89
Model 3	1	1.02 (0.92-1.13)	1.06 (0.96-1.18)	1.02 (0.92-1.14)	1.02 (0.92-1.14)	0.76
Refined grains‡	0.70	1.35	1.99	2.91	4.64	
Model 1	1	0.94 (0.85-1.04)	0.96 (0.86-1.06)	0.97 (0.88-1.08)	0.92 (0.81-1.03)	0.50
Model 3	1	0.92 (0.83-1.02)	0.95 (0.86-1.06)	0.95 (0.85-1.06)	0.89 (0.78-1.01)	0.15

Q indicates quintile. Model 1 was adjusted for age, sex, race, education, center, and total calories. Model 2 was adjusted for model 1 plus smoking status (current, former, never), pack-years, and physical activity. Model 3 was adjusted for model 2 plus intakes of meat, dairy, fruits and vegetables, whole grains, and refined grains (all as time-varying covariates).

*Trend across median quintile of intake.

†Analyzed as time-varying covariates using cumulative average diet.

‡Median score or servings per day as appropriate.

§For the individual food groups, estimates after model 1 and 2 adjustments were similar; thus, only model 1 adjustments are shown.

ated with higher incidence of MetSyn ($P_{\text{trend}} < 0.001$), whereas dairy consumption conferred some protection ($P_{\text{trend}} < 0.001$) (Table 3). There was no association between incident MetSyn and consumption of whole grains, refined grains, or fruits and vegetables.

The HR for the consumption of extreme quintiles of meat was 1.26 (95% CI, 1.11 to 1.43). Individual foods in the meat group also were adversely associated with MetSyn: hamburger ($P_{\text{trend}} = 0.002$), hot dogs ($P_{\text{trend}} = 0.002$), and processed meats ($P_{\text{trend}} = 0.03$). The HR for the extreme quintiles of dairy consumption was 0.87 (95% CI, 0.77 to 0.98); however, individual dairy foods were not associated with incident MetSyn.

As shown in Table 4, consumption of fried foods was associated with increased risk of MetSyn ($P_{\text{trend}} = 0.02$). The HR for the extreme tertiles was 1.25 (95% CI, 1.14 to 1.37). Sweetened beverages also were associated with incident MetSyn after base adjustments (HR, 1.17; 95% CI, 1.07 to 1.28; $P_{\text{trend}} = 0.02$), although the association became nonsignificant with additional adjustments. Diet soda intake was strongly associated with increased risk across all models (HR, 1.34; 95% CI, 1.11 to 1.29). No relations were observed between coffee or nut consumption and incident MetSyn.

In sensitivity analyses, similar results were observed when diet relations with MetSyn were examined even after exclusion of individuals with prevalent diabetes at baseline ($n = 1870$) and after omitting individuals diagnosed with incident MetSyn at 1 examination who reverted at a later examination ($n = 1161$). We also evaluated whether gender or baseline overweight status modified the relation between dietary intake and incident MetSyn, but no interactions were observed.

Discussion

Over 9 years of follow-up, nearly 40% of the 9514 middle-aged men and women included in this analysis developed MetSyn. Dietary consumption of a Western dietary pattern, meat, fried foods, and diet soda was adversely associated with incident MetSyn, whereas intake of dairy was protective. No association was observed between incident MetSyn and consumption of a prudent dietary pattern, fruit and vegetables, whole grains, refined grains, nuts, sweetened beverages, and coffee.

Consumption of a Western dietary pattern, characterized by high intakes of refined grains, processed meat, fried foods,

Table 4. Nine-Year Multivariable-Adjusted HRs (95% CIs) for 3782 Cases of Incident MetSyn by Tertile of Food Group* Intake in 9514 Male and Female Participants of the ARIC Study

	Q1	Q2	Q3	<i>P</i> _{trend} †
Fried foods‡§	0.00	0.21	0.80	
Model 1	1	1.12 (1.03–1.22)	1.25 (1.14–1.37)	0.02
Nuts§	0.00	0.07	0.14	
Model 1	1	0.85 (0.79–0.92)	0.78 (0.72–0.85)	0.31
Model 2	1	1.07 (0.98–1.16)	0.99 (0.91–1.08)	0.52
Coffee§	0.00	1.00	2.50	
Model 1	1	0.88 (0.82–0.96)	1.02 (0.95–1.11)	0.24
Model 2	1	0.93 (0.86–1.02)	0.93 (0.86–1.01)	0.11
Sweetened beverages §	0.00	0.14	1.00	
Model 1	1	1.16 (1.07–1.26)	1.17 (1.07–1.28)	0.02
Model 2	1	1.02 (0.94–1.11)	1.09 (0.99–1.19)	0.07
Diet soda§	0.00	0.07	0.80	
Model 1	1	0.79 (0.72–0.86)	1.20 (1.11–1.29)	<0.001
Model 2	1	1.05 (0.96–1.15)	1.34 (1.24–1.44)	<0.001

Q indicates quintile. Model 1 was adjusted for age, sex, race, education, center, and total calories. Model 2 was adjusted for model 1 plus smoking status (current, former, never), pack-years, physical activity, and intakes of meat, dairy, fruits and vegetables, whole grains, and refined grains.

*Analyzed as time-varying covariates using cumulative average diet.

†Trend across median tertile of intake.

‡Model 2 was not considered because of issues of overadjustment; the FFQ question queried for all fried foods except French fries.

§Median servings per day.

||Regular soda and sweetened fruit-flavored punch or noncarbonated beverages.

and red meat, was associated with a 18% greater risk of incident MetSyn for participants in the highest quintile of Western dietary pattern scores compared with those in the lowest quintile. In our study, the prudent dietary pattern, typified by consumption of cruciferous and carotenoid vegetables, fruit, fish, and poultry, was not associated with incident MetSyn. Prevalent MetSyn has previously been positively associated with consumption of Western²⁷ and empty-calorie²⁸ dietary patterns and inversely associated with consumption of a healthy dietary pattern.²⁷ In randomized controlled trials, the Dietary Approaches to Stop Hypertension (DASH) diet was shown to improve MetSyn component levels,⁴² and a Mediterranean-style diet reduced the prevalence of MetSyn among patients with MetSyn.⁴³

In this analysis, there was a positive monotonic trend between intake of meat and incident MetSyn, with individuals in the highest quintile of meat consumption being at 26% greater risk of developing MetSyn compared with individuals in the lowest quintile of meat consumption. Intake of hamburger, hot dogs, and processed meat appeared to promote the adverse association between meat and incident MetSyn. A previous cross-sectional study, however, found no relationship between intake of meat and MetSyn.²³ Meat is high in saturated fat, which has been adversely associated with cholesterol,⁸ blood pressure,⁹ obesity, and diabetes risk.¹⁰

Dairy intake was found to be protective in this analysis, with individuals in the highest quintile of dairy consumption being at 13% lower risk of developing MetSyn. The protective effect of dairy in relation to MetSyn has been reported

previously, both cross-sectionally^{22,23} and prospectively.²⁴ In 1 cross-sectional study, however, the relationship was observed only in men,²³ whereas in the prospective study of insulin resistance syndrome (defined by ≥ 2 of 4 adverse risk factors), dairy intake was inversely associated with the incidence of MetSyn only among individuals who were overweight at baseline (body mass index ≥ 25 kg/m²).²⁴ Greater intake of dairy appeared to provide some protection against the development of MetSyn in the ARIC population across gender and body mass index categories. Dissimilar study methods may account for the different results in the 2 prospective studies, including differences in the definition of the outcome, population age, dietary assessment instrument, and statistical methods. Finally, dairy intake has been inversely associated with diabetes¹¹ and hypertension.¹²

Contrary to our a priori hypotheses, whole grains, refined grains, and fruit and vegetables were not associated with incident MetSyn. Cross-sectionally, diets rich in whole-grain foods have been linked to a lower prevalence of MetSyn,^{19–21} whereas the evidence for refined grains has been mixed, with positive associations reported in some cross-sectional studies^{19,21} and no relation in others.²⁰ Consumption of whole grains has been associated with reduced blood pressure, body mass index, triglycerides, and risk of diabetes and with increased HDL cholesterol.¹³ An inverse association between prevalent MetSyn and intakes of fruit and vegetables has been reported previously.²⁵ Consumption of diets high in fruit and vegetables has been associated with lower blood pressure⁹ and may be associated with a better lipid profile.¹⁴

Concordant with our a priori hypotheses, intake of fried food was positively associated with the development of incident MetSyn. Participants in the highest tertile of intake were at 25% greater risk of developing MetSyn compared with those in the lowest tertile.

In our study, consumption of sweetened beverages was not associated with incident MetSyn. Another recent prospective study reported a positive relation between sweetened beverage consumption and MetSyn risk.²⁶ Consumption of these beverages has been shown to promote the incidence of obesity¹⁵ and diabetes.¹⁶ Coffee intake, which is inversely related to diabetes,¹⁷ was not related to MetSyn in our study. Nut consumption also was unrelated to MetSyn incidence. Nut intake has been inversely related to dyslipidemia and may help regulate body weight by suppressing appetite and fat absorption.¹⁸

Diet soda also was positively associated with incident MetSyn, with those in the highest tertile of intake at 34% greater risk than those in the lowest tertile. The strength of this association was surprising. However, it is consistent with recent data from the Framingham Heart Study, which found a 56% increased risk of MetSyn among those consuming ≥ 1 serving of diet soda per day.²⁶ Furthermore, in a recent cross-sectional study, diabetics who consumed diet soda had poorer glucose control than those who consumed none.⁴⁴ A study in rats suggested that consumption of artificial sweeteners impairs the ability of the body to predict the caloric content of foods and may lead to increased intake and body weight.⁴⁵ Although prospective study designs establish temporal sequence, it is possible that reverse causality or residual confounding may explain this finding, especially because consumption of diet soda is higher among diabetics than among nondiabetics.⁴⁴ Additional research on the relation between diet soda and incident MetSyn is clearly warranted.

MetSyn is, by its very nature, a heterogeneous outcome. At present, no single pathogenesis has been elucidated, and it is possible that one does not exist.³² Regardless, MetSyn has been shown to be a good marker of future disease risk, and understanding how food intake or overall dietary pattern relates to MetSyn as an entity is valuable. In interpreting our results, however, it is important to keep this heterogeneity in mind.

An important limitation to consider in the interpretation of our results is the use of an FFQ containing only 66 items, thus restricting the number of food categories to characterize usual dietary intake and resulting in an underestimation of energy intake. Furthermore, dietary intake may be misclassified by this questionnaire, contributing to measurement error in the point estimates that may potentially result in large biases.⁴⁶ For example, the 66-item FFQ was not designed to differentiate whole-grain from refined-grain food items in the food list; thus, misclassification may have occurred.⁴⁷ Moreover, for some food groups (eg, nuts), low consumption and a narrow range of values among consumers may have prevented us from detecting a relationship if one was present. It is also possible that dietary intake may be confounded because eating behaviors tend to cluster.⁴⁸ To control for confounding, we adjusted our statistical models for the other food groups; however, it is possible that residual confounding

may remain. Furthermore, reporting biases may have occurred.⁴⁹ Although we acknowledge these limitations, the FFQ has been previously validated,³¹ and other studies have indicated that there is reasonable validity and reliability of food groups⁵⁰ and major dietary patterns⁵¹ obtained from FFQs. The use of cumulative average diet to increase the precision of our dietary measures is a strength of our study.⁴¹

Most previous studies relating MetSyn to diet have focused on a single food group, and all but 2 studies^{24,26} were cross-sectional. Thus, a major strength of this study is the prospective design, which overcomes a variety of limitations common to cross-sectional data. Another strength is the comprehensive exploration of the diet and MetSyn relationship as assessed by both dietary patterns and multiple food groups, especially in light of recent discussions concerning the benefits of whole-food approaches and possible limitations of single-nutrient approaches in assessing relationships between diet and complex diseases.⁵² Further strengths of this study are the 9 years of follow-up and the high participation rate.

The fact that 60.5% of the ARIC population either had MetSyn at baseline or developed MetSyn over the 9 years of follow-up foreshadows a worrisome trend for the burden of MetSyn in the United States. Elucidation of how diet contributes to the development of this syndrome is valuable. A dietary strategy aimed at this multicomponent syndrome may provide a less confusing message to the public to support positive changes than attempting to address the individual abnormalities of this syndrome. Consistent with this approach, experts are increasingly calling for research on overall dietary patterns to improve our understanding of the numerous modifiable determinants of disease risk that may guide the development of innovative, focused, and individualized preventative strategies.^{28,53,54} Taken collectively, the results of this study are supportive of the 2005 *Dietary Guidelines for Americans*.⁵⁵

Acknowledgment

We thank the staff and participants of the ARIC study for their important contributions.

Sources of Funding

The ARIC study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022. P.L. Lutsey was supported by the NIH Training Grant in Cardiovascular Disease Epidemiology T32 HL007779.

Disclosures

None.

References

1. Resnick HE, Jones K, Ruotolo G, Jain AK, Henderson J, Lu W, Howard BV. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians: the Strong Heart Study. *Diabetes Care*. 2003;26:861–867.
2. Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DSJ, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation*. 2003;108:414–419.

3. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, Ballantyne CM, Heiss G. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities Study. *Diabetes Care*. 2005;28:385–390.
4. Lakka H-M, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288:2709–2716.
5. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106:3143–3421.
6. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002;287:356–359.
7. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. *JAMA*. 2002;288:1723–1727.
8. Schaefer EJ. Lipoproteins, nutrition, and heart disease. *Am J Clin Nutr*. 2002;75:191–212.
9. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. *Hypertension*. 2006;47:296–308.
10. Parillo M, Riccardi G. Diet composition and the risk of type 2 diabetes: epidemiological and clinical evidence. *Br J Nutr*. 2004;92:7–19.
11. Choi HK, Willett WC, Stampfer MJ, Rimm E, Hu FB. Dairy consumption and risk of type 2 diabetes mellitus in men: a prospective study. *Arch Intern Med*. 2005;165:997–1003.
12. Ascherio A, Hennekens C, Willett WC, Sacks F, Rosner B, Manson J, Willett WC, Stampfer MJ. Prospective study of nutritional factors, blood pressure, and hypertension among US women. *Hypertension*. 1996;27:1065–1072.
13. Jacobs DR Jr, Gallaher DD. Whole grain intake and cardiovascular disease: a review. *Curr Atheroscler Rep*. 2004;6:415–423.
14. Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, Franklin B, Kris-Etherton P, Harris WS, Howard B, Karanja N, Lefevre M, Rudel L, Sacks F, Van Horn L, Winston M, Wylie-Rosett J. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation*. 2006;114:82–96.
15. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr*. 2006;84:274–288.
16. Schulze MB, Manson JE, Ludwig DS, Colditz GA, Stampfer MJ, Willett WC, Hu FB. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. *JAMA*. 2004;292:927–934.
17. van Dam RM, Hu FB. Coffee consumption and risk of type 2 diabetes: a systematic review. *JAMA*. 2005;294:97–104.
18. Coates AM, Howe PR. Edible nuts and metabolic health. *Curr Opin Lipidol*. 2007;18:25–30.
19. Sahyoun NR, Jacques PF, Zhang XL, Juan W, McKeown NM. Whole-grain intake is inversely associated with the metabolic syndrome and mortality in older adults. *Am J Clin Nutr*. 2006;83:124–131.
20. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. *Diabetes Care*. 2004;27:538–546.
21. Esmailzadeh A, Mirmiran P, Azizi F. Whole-grain consumption and the metabolic syndrome: a favorable association in Tehranian adults. *Eur J Clin Nutr*. 2005;59:353–362.
22. Azadbakht L, Mirmiran P, Esmailzadeh A, Azizi F. Dairy consumption is inversely associated with the prevalence of the metabolic syndrome in Tehranian adults. *Am J Clin Nutr*. 2005;82:523–530.
23. Mennen LI, Lafay L, Feskens EJM, Novak M, Lepinay P, Balkau B. Possible protective effect of bread and dairy products on the risk of metabolic syndrome. *Nutr Res*. 2000;20:335–347.
24. Pereira MA, Jacobs DR Jr, Van Horn L, Slattery ML, Kartashov AI, Ludwig DS. Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study. *JAMA*. 2002;287:2081–2089.
25. Esmailzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. *Am J Clin Nutr*. 2006;84:1489–1497.
26. Dhingra R, Sullivan L, Jacques PF, Wang TJ, Fox CS, Meigs JB, D'Agostino RB, Gaziano JM, Vasan RS. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. *Circulation*. 2007;116:480–488.
27. Esmailzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. *Am J Clin Nutr*. 2007;85:910–918.
28. Sonnenberg L, Pencina M, Kimokoti R, Quattromoni P, Nam BH, D'Agostino R, Meigs JB, Ordovas J, Cobain M, Millen B. Dietary patterns and the metabolic syndrome in obese and non-obese Framingham women. *Obes Res*. 2005;13:153–162.
29. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives: the ARIC Investigators. *Am J Epidemiol*. 1989;129:687–702.
30. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr*. 1982;36:936–942.
31. Willett WC SL, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol*. 1985;122:51–65.
32. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F, for the American Heart Association and National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Circulation*. 2005;112:2735–2752.
33. Siedel J, Hagele EO, Ziegenhorn J, Wahlefeld AW. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. *Clin Chem*. 1983;29:1075–1080.
34. Nagele U, Hagele EO, Sauer G, Wiedemann E, Lehmann P, Wahlefeld AW, Gruber W. Reagent for the enzymatic determination of serum total triglycerides with improved lipolytic efficiency. *J Clin Chem Clin Biochem*. 1984;22:165–174.
35. Warnick GR, Benderson J, Albers JJ. Dextran sulfate-Mg²⁺ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. *Clin Chem*. 1982;28:1379–1388.
36. ARIC Investigators. Seated blood pressure and postural changes in blood pressure and heart rate. In: *Atherosclerosis Risk in Communities Study Protocol, Manual 11*. Available at: www.csc.unc.edu/aric/visit/Sitting_Blood_Pressure_and_Postural_Changes_in_Blood_Pressure_and_Heart_Rate. Accessed September 28, 2007.
37. Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: the Atherosclerosis Risk in Communities (ARIC) study. *Hypertension*. 2003;42:1106–1111.
38. Campbell NR, Myers MG, McKay DW. Is usual measurement of blood pressure meaningful? *Blood Press Monit*. 1999;4:71–76.
39. Beevers G, Lip GY, O'Brien E. ABC of hypertension: blood pressure measurement: part I: sphygmomanometry: factors common to all techniques. *BMJ*. 2001;322:981–985.
40. Kim J. *Factor Analysis: Statistical Methods and Practical Issues*. Beverly Hills, Calif: Sage Publications; 1978.
41. Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D, Willett WC. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *Am J Epidemiol*. 1999;149:531–540.
42. Azadbakht L, Mirmiran P, Esmailzadeh A, Azizi T, Azizi F. Beneficial effects of a Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome. *Diabetes Care*. 2005;28:2823–2831.
43. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA*. 2004;292:1440–1446.
44. Mackenzie T, Brooks B, O'Connor G. Beverage intake, diabetes, and glucose control of adults in America. *Ann Epidemiol*. 2006;16:688–691.
45. Davidson TL, Swithers SE. A Pavlovian approach to the problem of obesity. *Int J Obes Relat Metab Disord*. 2004;28:933–935.
46. Kipnis V, Subar AF, Midthune D, Freedman LS, Ballard-Barbash R, Troiano RP, Bingham S, Schoeller DA, Schatzkin A, Carroll RJ. Structure of dietary measurement error: results of the OPEN Biomarker Study. *Am J Epidemiol*. 2003;158:14–21.
47. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. *Am J Clin Nutr*. 1998;68:248–257.

48. Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR. Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr.* 2003;78:383–390.
49. Willett W. *Nutritional Epidemiology*. 2nd ed. New York, NY: Oxford University Press; 1998.
50. Bohlscheid-Thomas S, Hoting I, Boeing H, Wahrendorf J. Reproducibility and relative validity of energy and macronutrient intake of a food frequency questionnaire developed for the German part of the EPIC project: European Prospective Investigation Into Cancer and Nutrition. *Int J Epidemiol.* 1997;26(suppl 1):S71–S81.
51. Hu FB, Rimm E, Smith-Warner SA, Feskanich D, Stampfer MJ, Ascherio A, Sampson L, Willett WC. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr.* 1999;69:243–249.
52. Jacobs DR Jr, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. *Am J Clin Nutr.* 2003;78(suppl):508S–513S.
53. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med.* 2000;343:16–22.
54. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol.* 2002;13:3–9.
55. US Department of Health and Human Services and US Department of Agriculture. *Dietary Guidelines for Americans, 2005*. 6th ed. Washington, DC: US Government Printing Office; 2005.

CLINICAL PERSPECTIVE

Metabolic syndrome (MetSyn) is a cluster of cardiovascular disease risk factor abnormalities associated with increased risk of type 2 diabetes mellitus, cardiovascular disease, and all-cause mortality. The role of diet in the development of MetSyn is not well understood. In a prospective study of almost 15 000 middle-aged black and white adults, we observed a 13% to 18% higher risk of incident MetSyn among those eating a “Western diet” pattern, a diet characterized by high intakes of red and processed meat, fried food, regular soda, and refined-grain products and low intakes of fruit and vegetables, fish, and whole-grain products. To support this result, we found that eating 1 to 2 servings per day of meat was associated with 17% to 26% higher risk of incident MetSyn compared with one-fourth serving per day, and eating fried foods everyday also was associated with higher risk. Risk of MetSyn was lower among adults consuming >3 daily servings of dairy products compared with one-fourth serving. Interestingly, adults who consumed 1 serving of diet soda a day had a 34% higher risk of MetSyn compared with nonconsumers. These prospective findings suggest that consumption of a Western dietary pattern, meat, and fried foods promotes the incidence of MetSyn, whereas dairy consumption provides some protection. The diet soda association was not hypothesized and deserves further study.