Dietary Intake and the Development of the Metabolic Syndrome
The Atherosclerosis Risk in Communities Study

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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 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 trend <0.001), fried foods (P trend =0.02), and diet soda (P trend = < 0.001) also were adversely associated with incident MetSyn, whereas dairy consumption (P 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, ≈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

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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 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 association19,21 and others finding no relation.20 Dairy intake has been inversely associated with MetSyn both cross-sectionally22,23 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...
adults. With few exceptions,\textsuperscript{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, and refined grains, 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.\textsuperscript{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 9512 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 al\textsuperscript{30} 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.\textsuperscript{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,\textsuperscript{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 cholesterol\textsuperscript{33} and triglycerides\textsuperscript{34} were determined by enzymatic methods. HDL cholesterol was measured after dextran-magnesium precipitation.\textsuperscript{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.\textsuperscript{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.\textsuperscript{36,37} 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.\textsuperscript{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,\textsuperscript{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.\textsuperscript{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.
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 dietary pattern, was typified by greater consumption of cruciferous and carotinoid 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-
associated 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: ham- burger ($P=0.002$), hot dogs ($P=0.002$), 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,
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 Western and empty-calorie dietary patterns and inversely associated with consumption of a healthy dietary pattern. In randomized controlled trials, the Dietary Approaches to Stop Hypertension (DASH) diet was shown to improve MetSyn component levels, and a Mediterranean-style diet reduced the prevalence of MetSyn among patients with MetSyn. 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 ham, 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. Meat is high in saturated fat, which has been adversely associated with cholesterol, blood pressure, obesity, and diabetes risk.

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 and prospectively. In a cross-sectional study, however, the relationship was observed only in men, 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). 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 diabetes and hypertension.

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, whereas the evidence for refined grains has been mixed, with positive associations reported in some cross-sectional studies and no relation in others. Consumption of whole grains has been associated with reduced blood pressure, body mass index, triglycerides, and risk of diabetes and with increased HDL cholesterol. An inverse association between prevalent MetSyn and intakes of fruit and vegetables has been reported previously. Consumption of diets high in fruit and vegetables has been associated with lower blood pressure and may be associated with a better lipid profile.
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. Consumption of these beverages has been shown to promote the incidence of obesity and diabetes. Coffee intake, which is inversely related to diabetes, 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.

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. Furthermore, in a recent cross-sectional study, diabetics who consumed diet soda had poorer glucose control than those who consumed none. 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. 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. 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. 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. 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. 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. 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. Although we acknowledge these limitations, the FFQ has been previously validated, and other studies have indicated that there is reasonable validity and reliability of food groups and major dietary patterns obtained from FFQs. The use of cumulative average diet to increase the precision of our dietary measures is a strength of our study.

Most previous studies relating MetSyn to diet have focused on a single food group, and all but 2 studies 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. 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. Taken collectively, the results of this study are supportive of the 2005 Dietary Guidelines for Americans.

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Disclosures
None.

References


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**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.