Dietary Calcium, Vitamin D, and the Prevalence of Metabolic Syndrome in Middle-Aged and Older U.S. Women

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OBJECTIVE — To examine whether and to what extent intakes of calcium and vitamin D are related to the metabolic syndrome in middle-aged or older women.

RESEARCH DESIGN AND METHODS — We analyzed data from 10,066 women aged ≥45 years participating in the Women's Health Study who were free of cardiovascular disease, cancer, or diabetes and who never used postmenopausal hormones. We used multiple logistic regression models to estimate multivariable odds ratios (ORs) and 95% CIs comparing different dietary intake levels of calcium and vitamin D.

RESULTS — In age- and calorie-adjusted analyses, higher intakes of total, dietary, and supplemental calcium were significantly and inversely associated with the prevalence of metabolic syndrome. After further adjusting for smoking status, exercise, alcohol intake, multivitamin use, and parental history of myocardial infarction before age 60 years, the ORs of having the metabolic syndrome for increasing quintiles of total calcium intake were 1.00 (reference), 0.82 (95% CI 0.70–0.97), 0.84 (0.71–0.99), 0.70 (0.59–0.83), and 0.64 (0.54–0.77) (*P* for trend <0.0001). This association was not appreciably altered by additional adjustment for other dietary factors or total vitamin D intake. In contrast, neither total (*P* for trend = 0.13) nor supplemental (*P* for trend = 0.45) vitamin D was significantly associated with metabolic syndrome. Dietary vitamin D was inversely associated with prevalence of metabolic syndrome but was not independent of total calcium intake. Similar strong relations between intakes of dairy products and metabolic syndrome were also observed. After adjustment for lifestyle and dietary factors, the multivariable ORs comparing highest with lowest intake categories were 0.66 (0.55–0.80) (*P* for trend <0.0001) for total dairy products and 0.85 (0.71–1.02) (*P* for trend = 0.05) for total milk intake.

CONCLUSIONS — Our results indicate that intakes of calcium and dairy products may be associated with lower prevalence of the metabolic syndrome in middle-aged and older women.

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Recent studies (1–3) have shown that dairy consumption is inversely associated with body weight, hypertension, glucose homeostasis, and type 2 diabetes. Although the underlying mechanisms remain incomplete, calcium and vitamin D, two major components of dairy products, have been postulated to be primarily responsible for the beneficial effect of dairy consumption on body weight and insulin sensitivity (4–6). Intracellular calcium can act directly on adipocytes to regulate lipid metabolism and insulin-stimulated glucose uptake and storage (7). Some studies have indicated that dietary calcium intake may have favorable effects on body weight (2,5), hypertension (1), and coronary heart disease (8,9).

Vitamin D repletion improves insulin sensitivity and insulin secretion in animal studies (10,11). An association between vitamin D deficiency and β-cell dysfunction has been reported in healthy and glucose-tolerant subjects (4), nondiabetic people (6), and patients with type 2 diabetes (12). Several small cross-sectional studies reported an association between low circulating concentrations of vitamin D and the prevalence of diabetes (12–14) and impaired glucose tolerance (4,14–17). The metabolic syndrome defined by the clustering of impaired glucose tolerance, hypertension, adiposity, and abnormal lipid profiles is especially important for identification of those at especially high risk for type 2 diabetes and coronary heart disease. However, epidemiologic evidence relating calcium and vitamin D intakes to the metabolic syndrome is limited. Moreover, calcium and vitamin D are metabolically related since vitamin D is critical for maintenance of intracellular calcium homeostasis, but joint effects of calcium intake and vitamin D intake in relation to metabolic syndrome have not been evaluated. To provide additional information, we examine the relationship between dietary calcium and vitamin D intakes and the prevalence of metabolic syndrome in a large cohort of middle-aged and older U.S. women.

RESEARCH DESIGN AND METHODS

— Of 39,876 female health professionals aged ≥45 years in the Women's Health Study (18), ~98% of participants provided detailed information on their diet by completing a 131-item semiquantitative food frequency questionnaire (SFFQ), and 71% provided baseline blood samples collected in EDTA, which were stored in liquid nitrogen (19). To minimize the effects of postmenopausal hormone therapy on metabolic parameters, we excluded women who ever used postmenopausal hormones, leaving 10,066 women who

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Abbreviations: SFFQ, semiquantitative food frequency questionnaire.

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

were also free of diabetes at study entry and contributed complete data for all five components of the metabolic syndrome for this analysis.

Dietary intake assessment

Participants were asked how often on average they had consumed individual foods of commonly used portions during the previous year. Nutrient intakes were computed by multiplying the frequency of consumption of each unit of food from the SFFQ by the nutrient content of the specified portion size (20). The average daily intakes of individual dairy items were combined to compute dairy intake: low-fat dairy products, including skim or low-fat milk, sherbet, yogurt, and cottage/ricotta cheese; high-fat dairy foods, including whole milk, cream, sour cream, ice cream, cream cheese, and other cheese; and total dairy products, including all of the above. Total milk included skim or low-fat milk and whole milk.

Data on the use of individual and multivitamin supplements were used to assess intake of supplemental calcium and vitamin D. Total calcium and vitamin D intakes were calculated from both dietary and supplemental sources. In populations of nurses and health professionals, this SFFQ has demonstrated reasonably good validity as a measure of long-term average dietary intakes (20). Pearson's correlation coefficients between responses from the SFFQ and those from four 1-week dietary records spaced over a year were 0.56 for total calcium and 0.51 for dietary calcium (20). With respect to milk intake, the correlation coefficients between the SFFQ and dietary records were 0.69 for skim or low-fat milk and 0.56 for whole milk (21).

Definition of the metabolic syndrome

The metabolic syndrome was defined using a modification of the criteria proposed by the Adult Treatment Program III of the National Cholesterol Education Program, as previously described (22). Women with three or more of the following conditions were defined as having the metabolic syndrome: *1*) triglycerides ≥150 mg/dl, *2*) HDL cholesterol <50 mg/dl, *3*) blood pressure ≥135/85 mmHg, *4*) obesity as defined by a BMI ≥30 kg/m^2, and *5*) abnormal glucose metabolism as defined by incident type 2 diabetes. In the Women's Health Study, however, waist circumference was not reported until year 6 of follow-up. To assess the robustness of our definition for obesity, we performed sensitivity analysis using a definition of the metabolic syndrome based on a waist circumference of 88 cm (>35 inch). Because fasting glucose levels were not available, we instead used the diagnosis of incident type 2 diabetes during an average of 8.8 years of follow-up as an alternative measure of baseline abnormal glucose metabolism. The validity of self-reported type 2 diabetes has been confirmed by a validation study, as previously reported (23).

Biochemical measurements

Total, HDL, and LDL cholesterol and triglyceride levels were measured with direct measurement assays (Roche Diagnostics, Indianapolis, IN). All samples were identically handled and analyzed in random order to reduce systematic bias and interassay variation. Blinded quality control specimens were simultaneously analyzed with the study sample.

Data analysis

The age-adjusted (in 5-year groups) baseline characteristics according to quintiles of total calcium and vitamin D intake were compared. Proportions were tested with the stratified Mantel-Haenszel test, and mean values were compared using multiple linear regression. We applied a logistic regression model to examine the association between calcium and vitamin D intake and the risk of metabolic syndrome. The odds ratios (OR) and 95% CIs for the prevalence of the metabolic syndrome were calculated. The initial model was adjusted for age (continuous), total calorie intake (continuous), and randomized treatment. In multivariate models, we further adjusted for smoking status (current, past, and never), exercise (rarely/never, less than once per week, one to three times per week, and four or more times per week), alcohol intake (rarely/never, one to three drinks per month, one to six drinks per week, and one or more drinks per day), multivitamin use (never, past, and current), and parental history of myocardial infarction before age 60 years (yes/no). The second multivariable model added dietary factors, including intakes of total fat, cholesterol, protein, and glycemic load (all categorized as quintiles). In the final multivariable-adjusted model, we additionally adjusted for total calcium intake or total vitamin D intake. Tests of linear trend were conducted by assigning the medians of intakes in quintiles treated as a continuous variable. Furthermore, potential joint effects or effect modifications were evaluated by subgroup analyses stratified by the prespecified factors including age (>65 vs. ≤65 years) and smoking status (never, past, or current smokers). Likelihood ratio test was used to assess the significance of interaction. All statistical analyses were conducted using SAS (version 8.0; SAS Institute, Cary, NC). Statistical significance was set at $P <$ 0.05, using two-sided tests.

RESULTS — There was an approximately three- to fivefold difference in median intake of calcium or vitamin D between the highest and lowest quintiles of the study population (514 vs. 1,583 mg/day for total calcium and 120 vs. 667 IU/day for total vitamin D). The median intake was 857 mg/day (87.9% from diet and 12.1% from supplements) for total calcium and 266 IU/day (83.6% from diet and 16.4% from supplements) for vitamin D in these middle-aged women.

As shown in Table 1, women with high calcium intake were slightly older and leaner and less likely to smoke, drink alcohol, or have a history of hypertension and were more likely to exercise and use multivitamins than those with lower calcium intake. Calcium intake was also positively associated with dietary protein, fiber, and glycemic load and inversely associated with dietary fat and cholesterol. Similar associations were found for vitamin D intake, except that vitamin D intake was positively associated with cholesterol intake.

Table 2 displays age-adjusted metabolic syndrome components according to quintiles of calcium and vitamin D intake at baseline. Overall, the prevalence of each of the five components was lower in women in the highest quintile of calcium and vitamin D intake than in those in the lowest quintile. All these associations reached statistical significance with several exceptions; hypertriglyceridemia was not associated with total intakes of calcium and vitamin and incident type 2 diabetes was not associated with dietary vitamin D intake. Similarly, there were inverse associations between calcium and vitamin D intakes and the prevalence of metabolic syndrome defined as the total number of components. Because the proportion of women with all five metabolic syndrome components was small, we may not have adequate statistical power to detect significant trends for both calcium and vitamin D intakes.

In the age- and total calorie–adjusted

Table 1—*Age-adjusted characteristics according to quintiles of dietary vitamin D or calcium intake among 10,066 apparently healthy women in the Women's Health Study

	Dietary calcium†				Dietary vitamin D†			
Characteristics	Q1 (223–561)	Q3 (684–805)	Q5 (1005–2596)	*P* for trend	Q1 (5.36–140)	Q3 (190–243)	Q5 (316–1058)	*P* for trend
n	2,013	2,013	2,013		2,013	2,014	2,013	
Median intake	486	740	1,168	—	111	215	377	—
Mean age (years)	52 ± 6.9	52 ± 6.7	53 ± 7.2	0.04	52 ± 6.7	52 ± 7.1	53 ± 7.3	<0.0001
Mean BMI (kg/m^2)	26.4	25.9	25.1	<0.0001	26.2	26.0	25.3	<0.0001
Current smoking (%)	17.7	10.1	7.2	<0.0001	15.0	9.3	8.2	<0.0001
Vigorous exercise (four or more times per week) (%)	7.6	11.4	14.1	<0.0001	8.9	10.8	14.5	<0.0001
Alcohol consumption (g/day)	5.5	4.5	4.2	<0.0001	5.1	4.6	4.5	0.003
Parental history of myocardial infarction before age 60 years (%)	15.3	14.4	12.8	0.19	15.9	15.4	14.2	0.68
History of hypertension (%)‡	23.4	22.1	17.7	<0.0001	22.8	19.7	19.8	0.02
History of hyperlipidemia (%)§	23.7	24.2	22.7	0.19	23.1	24.3	24.2	0.29
Multivitamin use (%)	12.9	25.4	45.7	<0.0001	7.6	11.9	75.2	<0.0001
Mean daily intake								
Total calorie (kcal)	1,653	1,757	1,662	0.002	1,647	1,821	1,636	0.05
Total fat (g)	62.3	57.0	53.7	<0.0001	61.1	57.5	55.1	<0.0001
Protein (g)	76.5	80.5	84.2	<0.0001	74.7	82.1	83.7	<0.0001
Cholesterol (mg)	235	221	214	<0.0001	218	225	224	0.12
Fiber (g)	16.8	19.2	19.3	<0.0001	17.9	18.6	19.2	<0.0001
Dietary glycemic load§	165	168	168	<0.0001	168	166	168	0.95
Calcium (mg)	501	863	1,695	<0.0001	686	947	1,289	<0.0001
Vitamin D (IU)	194	327	504	<0.0001	116	268	713	<0.0001
Total dairy products (servings)	0.99	2.01	2.61	<0.0001	1.21	2.16	2.17	<0.0001
Total fish intake (servings)	0.22	0.26	0.25	0.002	0.15	0.29	0.29	<0.0001
Red meat (servings)	0.88	0.67	0.54	<0.0001	0.80	0.74	0.58	<0.0001

Data are means ± SD, unless otherwise indicated. *All nutrient variables are energy adjusted. †Intake ranges are in parenthesis; mg/day for calcium and IU/day for vitamin D; history of hypertension is defined as a diagnosis of physician or self-reported blood pressure >140/90 mmHg. ‡History of high cholesterol is defined as having either any history of cholesterol-lowering medication use or a physician diagnosis of high cholesterol or a self-reported cholesterol ≥240 mg/dl. §Glycemic load was defined as an indicator of blood glucose induced by an individual's total carbohydrate intake. Each unit of glycemic load represents the equivalent of 1 g carbohydrate from white bread.

model, total calcium intake was significantly associated with the prevalence of metabolic syndrome (Table 3). Similar associations were observed for calcium intake from either diet or supplements; the multivariable ORs (model 1) for the highest relative to the lowest category were 0.69 (95% CI 0.58–0.82) (*P* for trend<0.0001) for dietary calcium and 0.84 (0.70–0.99) (*P* for trend = 0.005) for supplemental calcium. Further adjustment for dietary total fat, cholesterol, protein, and glycemic load (model 2) did not materially change these inverse associations. Neither did additional adjustment for total vitamin D (model 3). In contrast, a significant inverse association was consistently evident only for dietary vitamin D and the metabolic syndrome. However, this association appeared to be entirely explained by adding total calcium intake. In sensitivity analysis, we repeated statistical models using a waist circumference (>88 cm) and found similar results (data not shown).

Because intake of calcium was highly correlated to intake of vitamin D (correlation coefficient = 0.73), we further examined the joint association of dietary vitamin D and calcium together as a nine-category variable with risk of metabolic syndrome. An inverse association between dietary calcium intake and the metabolic syndrome was observed in women in each tertile of dietary vitamin D intake without significant interaction (*P* = 0.60) (data not shown). We also found no apparent modification of the relation between dietary vitamin D intake and the prevalence of metabolic syndrome by smoking status and age (data not shown).

To assess the internal consistency of our observations, we also examined the direct relations of major dairy products with the metabolic syndrome (Table 4). There were trends for lower prevalence of the metabolic syndrome associated with total diary products, high-fat dairy products, low-fat dairy products, and total milk intake.

CONCLUSIONS — In this large cohort of middle-aged and older U.S. women, we observed a significantly lower prevalence of the metabolic syndrome among those with higher calcium intake (both food and supplements). Similar inverse associations were also evident for intake of dairy products and the metabolic syndrome. There was a suggestion of an inverse association between vitamin D intake and metabolic syndrome, but this association was no longer apparent after adjustment for other major lifestyle risk factors including calcium intake.

Our findings are consistent with previous observations (1,2,5,24) of an inverse association between calcium intake and blood pressure and insulin sensitiv-

Table 2—*Age-adjusted characteristics of metabolic syndrome components according to quintiles of intakes of total and dietary calcium and vitamin D

	Total calcium				Dietary calcium			
	Q1 (210–610)	Q3 (771–979)	Q5 (1284–4211)	*P* for trend	Q1 (223–561)	Q3 (684–805)	Q5 (1005–2596)	*P* for trend
Metabolic abnormalities*								
Abdominal obesity (%)								
Waist circumference (>35 inches)	46.6	41.8	37.1	<0.0001	44.8	42.5	39.0	<0.0001
BMI ≥30 kg/m^2	21.0	17.0	13.1	<0.0001	20.0	18.1	14.1	<0.0001
Low HDL cholesterol (%)†	54.1	50.6	45.1	<0.0001	52.3	47.3	49.4	0.06
Hypertriglyceridemia (%)‡	28.3	26.5	26.3	0.16	28.8	27.5	25.6	0.03
High blood pressure (%)§	34.4	30.3	26.3	<0.0001	34.2	31.0	26.6	<0.0001
Incident type 2 diabetes (%)‖	5.6	3.5	2.7	<0.0001	4.9	3.7	3.3	0.0006
Metabolic syndrome#								
One or more components (%)	71.5	67.5	63.0	<0.0001	70.3	66.0	65.3	0.0001
Two or more components (%)	42.5	36.4	32.3	<0.0001	41.8	36.5	33.6	<0.0001
Three or more components (%)	20.7	17.4	13.3	<0.0001	20.3	17.2	14.3	<0.0001
Four or more components (%)	7.7	5.9	4.3	<0.0001	6.9	6.7	5.0	0.001
Five components (%)	1.1	0.7	0.6	0.07	1.0	1.0	0.9	0.29

	Total vitamin D				Dietary vitamin D			
	Q1 (6.0–159)	Q3 (225–319)	Q5 (511–2369)	*P* for trend	Q1 (5.36–140)	Q3 (190–243)	Q5 (316–1058)	*P* for trend
Metabolic abnormalities*								
Abdominal obesity (%)								
Waist circumference (>35 inches)	43.5	42.1	39.7	0.0004	43.1	45.9	38.9	0.003
BMI ≥30 kg/m^2	20.2	18.5	14.4	<0.0001	19.3	18.3	14.2	<0.0001
Low HDL cholesterol (%)†	51.9	50.2	45.6	<0.0001	51.1	50.0	47.8	0.05
Hypertriglyceridemia (%)‡	26.9	25.2	27.9	0.12	29.6	25.6	26.6	0.02
High blood pressure (%)§	33.0	29.1	27.6	<0.0001	32.7	31.1	27.4	<0.0001
Incident type 2 diabetes (%)‖	4.6	4.0	3.4	0.02	4.4	3.8	3.9	0.29
Metabolic syndrome(#)								
One or more components (%)	69.8	66.0	63.8	0.0001	69.9	66.9	65.2	0.001
Two or more components (%)	39.7	36.8	34.3	<0.0001	40.6	38.3	33.0	<0.0001
Three or more components (%)	18.7	17.6	15.2	0.0009	18.6	17.2	14.7	0.0003
Four or more components (%)	7.1	5.7	5.0	0.005	6.9	5.6	5.9	0.007
Five components (%)	1.2	0.8	0.6	0.09	1.1	0.9	1.0	0.40

*The metabolic abnormalities were defined following our modified National Cholesterol Education Program Adult Treatment Panel III criteria; intake ranges are in parenthesis; mg/day for calcium and IU/day for vitamin D. †HDL cholesterol <50 mg/dl. ‡Triglycerides ≥150 mg/dl. §Blood pressure ≥135/85 mmHg. ‖The diagnosis of incident type 2 diabetes during follow-up was used as an indicator of baseline abnormal glucose metabolism. #The metabolic syndrome was defined as having three or more components; adiposity was defined using BMI ≥30 kg/m^2.

ity. Numerous epidemiologic studies have suggested that low calcium intake may be a risk factor for primary hypertension (25). Most trial data have shown that calcium supplementation led to a reduction in blood pressure among hypertensive patients (26). Recently, animal and human studies indicated that high calcium intake might decrease levels of parathyroid hormone and 1,25(OH) vitamin D and thus influence adipocyte metabolism by inhibiting lipogenesis and stimulating lipolysis (7). However, few studies have specifically examined the association between calcium intake and the metabolic syndrome, although it is plausible that a potential beneficial effect of calcium intake is partially mediated by its effects on blood pressure, insulin sensitivity, and body weight.

In contrast, our findings did not show an inverse association between vitamin D intake and the metabolic syndrome, although an inverse association between serum concentrations of vitamin D and the presence of metabolic syndrome has been observed in several studies (4,27). Vitamin D is an essential nutrient for calcium homeostasis, which is largely consumed as vitamin D2 (ergocalciferol) or D3 (cholecalciferol). Accumulating data indicate that people with impaired glucose tolerance (16,28) and diabetes (12,16,28) have lower concentrations of vitamin D compared with those with normal glucose tolerance. Also, low concentrations of vitamin D are associated with β-cell dysfunction and impaired insulin secretion and action (4,16). In a clinical study of 126 participants, those with hypovitaminosis D were nearly three times as likely to have the metabolic syndrome as participants with normal concentrations of vitamin D (30 vs. 11% of participants, $P < 0.001$) (4). More recently, we have

Table 3—*OR of metabolic syndrome according to quintiles of dietary vitamin D and calcium intakes

	Quintiles of intake					
	1 (lowest)	2	3	4	5 (highest)	*P* for trend
Total calcium						
Median intake (mg/day)	516	694	859	1,121	1,586	
Age (total calorie adjusted)†	1.00	0.81 (0.69–0.95)	0.78 (0.66–0.92)	0.67 (0.57–0.79)	0.59 (0.50–0.70)	<0.0001
Model 1‡	1.00	0.82 (0.70–0.97)	0.84 (0.71–0.99)	0.70 (0.59–0.83)	0.64 (0.54–0.77)	<0.0001
Model 2§	1.00	0.82 (0.70–0.97)	0.87 (0.73–1.03)	0.72 (0.61–0.87)	0.68 (0.56–0.82)	<0.0001
Model 3‖	1.00	0.82 (0.69–0.98)	0.86 (0.72–1.04)	0.73 (0.60–0.88)	0.68 (0.55–0.83)	0.0003
Dietary calcium						
Median intake (mg/day)	486	624	740	889	1,168	
Age (total calorie adjusted)†	1.00	0.85 (0.72–0.99)	0.80 (0.68–0.94)	0.72 (0.61–0.85)	0.65 (0.55–0.76)	<0.0001
Model 1‡	1.00	0.90 (0.76–1.06)	0.86 (0.73–1.01)	0.79 (0.66–0.93)	0.69 (0.58–0.82)	<0.0001
Model 2§	1.00	0.89 (0.76–1.05)	0.87 (0.74–1.03)	0.81 (0.68–0.97)	0.73 (0.61–0.88)	0.0009
Model 3‖	1.00	0.89 (0.75–1.06)	0.87 (0.73–1.04)	0.81 (0.67–0.98)	0.74 (0.60–0.92)	0.006
Supplemental calcium						
Median intake (range, mg/day)	0	17 (<37.9)	91 (37.9–<240.6)	597 (>240.6)		
Age (total calorie adjusted)†	1.00	1.05 (0.89–1.24)	0.96 (0.80–1.15)	0.77 (0.65–0.90)		<0.0001
Model 1‡	1.00	1.0 (0.90–1.26)	1.02 (0.84–1.23)	0.84 (0.70–0.99)		0.005
Model 2§	1.00	1.06 (0.89–1.25)	1.02 (0.84–1.24)	0.85 (0.71–1.01)		0.01
Model 3‖	1.00	1.06 (0.89–1.26)	1.04 (0.86–1.27)	0.86 (0.72–1.02)		0.01
Total vitamin D						
Median intake (IU/day)	121	192	267	390	667	
Age (total calorie adjusted)†	1.00	0.92 (0.78–1.08)	0.88 (0.74–1.03)	0.77 (0.65–0.91)	0.78 (0.66–0.93)	0.002
Model 1‡	1.00	0.97 (0.82–1.14)	0.93 (0.78–1.10)	0.82 (0.69–0.98)	0.88 (0.72–1.08)	0.13
Model 2§	1.00	0.95 (0.80–1.13)	0.92 (0.77–1.09)	0.83 (0.69–1.00)	0.89 (0.72–1.09)	0.22
Model 3‖	1.00	1.00 (0.84–1.20)	1.01 (0.84–1.22)	0.97 (0.79–1.19)	1.05 (0.84–1.32)	0.68
Dietary vitamin D						
Median intake (IU/day)	111	167	215	275	377	
Age (total calorie adjusted)†	1.00	0.98 (0.83–1.16)	0.89 (0.75–1.05)	0.85 (0.72–1.00)	0.77 (0.65–0.91)	0.0005
Model 1‡	1.00	1.03 (0.87–1.22)	0.96 (0.81–1.14)	0.92 (0.78–1.09)	0.84 (0.71–1.00)	0.02
Model 2§	1.00	1.00 (0.84–1.18)	0.92 (0.78–1.10)	0.90 (0.75–1.07)	0.85 (0.70–1.02)	0.05
Model 3‖	1.00	1.04 (0.88–1.24)	0.99 (0.83–1.19)	1.01 (0.83–1.22)	1.01 (0.82–1.24)	0.94
Supplemental vitamin D						
Median intake (range, IU/day)	0	5.34 (<12.23)	28.5 (12.23–<242.7)	403 (>242.7)		
Age (total calorie adjusted)†	1.00	1.02 (0.86–1.20)	0.87 (0.71–1.06)	0.92 (0.79–1.08)		0.42
Model 1‡	1.00	1.03 (0.86–1.22)	0.92 (0.75–1.13)	1.04 (0.86–1.27)		0.45
Model 2§	1.00	1.02 (0.86–1.22)	0.92 (0.75–1.13)	1.05 (0.86–1.28)		0.44
Model 3‖	1.00	1.03 (0.87–1.22)	0.97 (0.78–1.19)	1.00 (0.83–1.20)		0.16

Data are OR (95% CI). *The metabolic syndrome was defined following our modified National Cholesterol Education Program Adult Treatment Panel III criteria (three or more components) and adiposity was defined using BMI (≥30 kg/m^2). †Randomized treatment assignment in the Women's Health Study was also included in all the models. ‡Model 1 additionally adjusted for smoking, exercise, total calories, alcohol use, multivitamin use, and parental history of myocardial infarction before age 60 years. §Model 2 included all covariates in model 1 and dietary intakes of total fat, cholesterol, protein, and glycemic load. ‖Model 3 included total vitamin D in the model 2 for calcium intake and included total calcium intake in the model 2 for vitamin D intake.

also reported an inverse relationship between serum concentrations of vitamin D and the prevalence of the metabolic syndrome in the Third National Health and Nutrition Examination Survey of the U.S. population (27). Our null results for vitamin D intake may be attributed to inadequate measures of overall vitamin D intake due to the lack of information on sun exposure, because the synthesis of vitamin D3 in the skin induced by the ultraviolet radiation from the sun is an important source of vitamin D. To date, serum concentrations of 25-(OH) vitamin D are considered as a reliable measure for vitamin D status in the human body, but the correlation between vitamin D intake assessed by the SFFQ and 25-(OH) vitamin D concentrations appeared to be relatively low (r^2 = 0.35 for total vitamin D and 0.25 for dietary vitamin D) (29).

It has been reported that supplementation with vitamin D improves insulin secretion (6,30). In our study, however, supplemental vitamin D contributed a relatively small proportion of total vitamin D intake (<15%) and did not significantly affect the metabolic syndrome. Moreover, the biological effects of vitamin D may well depend on the presence or absence of other highly correlated nutrients such as calcium. Both vitamin D and calcium are metabolically related and thereby contribute to the pathogenesis of metabolic abnormalities through common or different mechanisms. Given the strong evidence from both animal studies and human studies, a potential role of dietary vitamin D in the pathogenesis of metabolic disorders cannot be completely ruled out at present.

The 10th Recommended Dietary Al-

Table 4—*OR of metabolic syndrome according to quintiles of intakes of major dairy products

	Quintiles of intake					
	1 (lowest)	2	3	4	5 (highest)	*P* for trend
Total dairy products	<0.91	~0.91–1.41	~1.42–1.99	~2.00–3.00	>3.00	
Model 1†	1.00	0.83 (0.71–0.98)	0.73 (0.62–0.87)	0.72 (0.61–0.86)	0.63 (0.52–0.75)	<0.0001
Model 2‡	1.00	0.85 (0.71–1.00)	0.77 (0.65–0.92)	0.76 (0.64–0.91)	0.66 (0.55–0.80)	<0.0001
Model 3§	1.00	0.85 (0.71–1.00)	0.76 (0.64–0.91)	0.77 (0.64–0.92)	0.66 (0.55–0.80)	<0.0001
High-fat dairy products	<0.27	~0.27–0.55	~0.56–0.91	~0.92–1.48	>1.48	
Model 1†	1.00	1.03 (0.87–1.22)	0.88 (0.74–1.05)	1.07 (0.90–1.27)	0.93 (0.78–1.10)	0.51
Model 2‡	1.00	1.04 (0.88–1.24)	0.89 (0.75–1.06)	1.10 (0.93–1.31)	0.94 (0.78–1.13)	0.56
Model 3§	1.00	0.95 (0.80–1.14)	0.78 (0.65–0.94)	0.91 (0.76–1.10)	0.71 (0.58–0.87)	0.002
Low-fat dairy products	<0.28	~0.28–0.78	~0.79–1.14	~1.15–2.13	>2.13	
Model 1†	1.00	0.75 (0.64–0.89)	0.79 (0.67–0.93)	0.79 (0.67–0.93)	0.66 (0.56–0.78)	<0.0001
Model 2‡	1.00	0.80 (0.67–0.94)	0.83 (0.70–0.98)	0.88 (0.74–1.05)	0.71 (0.59–0.84)	0.001
Model 3§	1.00	0.81 (0.68–0.96)	0.86 (0.72–1.02)	0.95 (0.79–1.14)	0.78 (0.64–0.95)	0.07
Total milk intake	<0.13	~0.13–0.43	~0.44–0.93	~0.94–1.07	>1.08	
Model 1†	1.00	0.95 (0.81–1.11)	1.03 (0.84–1.26)	0.99 (0.84–1.16)	0.81 (0.68–0.96)	0.01
Model 2‡	1.00	0.98 (0.83–1.15)	1.07 (0.87–1.31)	1.03 (0.88–1.22)	0.81 (0.68–0.96)	0.007
Model 3§	1.00	0.98 (0.84–1.16)	1.07 (0.87–1.32)	1.07 (0.90–1.27)	0.85 (0.71–1.02)	0.05

*The metabolic syndrome was defined following our modified National Cholesterol Education Program Adult Treatment Panel III criteria (three or more components) and adiposity was defined using BMI (≥30 kg/m^2); intakes of all dairy products are expressed as serving per day. †Model 1 adjusted for age, total calorie intake, and randomized treatment assignment. ‡Model 2 additionally adjusted for smoking, exercise, total calories, alcohol use, multivitamin use, and parental history of myocardial infarction before age 60 years. §Model 3 included all covariates in model 2 and dietary intakes of total fat, cholesterol, protein, and glycemic load.

lowances of calcium is 800 mg/day for adults aged ≥25 years; the recommended daily allowances of vitamin D is 200 IU/day up to the age of 50 years, 400 IU/day for people from age 51 to 70 years, and 600 IU/day for people aged >70 years (31). The median intake of total vitamin D is slightly higher than the 10th Recommended Daily Allowances. Recently, the Food and Nutrition Board raised the adequate daily intake of calcium intake to 1,200 mg/day for women aged >50 years (32).

Our findings that dairy products were significantly associated with risk of the metabolic syndrome were consistent with those reported previously from the Coronary Artery Risk Development in Young Adults study, where dairy consumption was inversely related to the development of the metabolic syndrome (3). Nevertheless, many major components in such foods are highly correlated so that it is difficult to completely separate the independent effects. Further research needs to determine what compounds are responsible for the potential beneficial effects of dairy products on metabolic syndrome components

Several limitations should be kept in mind when interpreting these findings. First, dietary assessment is not perfect and its associated measurement error may have biased findings toward the null. Second, our cross-sectional design cannot demonstrate the temporal relationship between calcium intake and risk of metabolic syndrome. Third, the Women's Health Study included mainly Caucasian women; our findings may not be directly generalized to the general U.S. population.

In conclusion, we found that high calcium intake and dairy product consumption are associated with lower prevalence of the metabolic syndrome in middle-aged and older women. There was no significant inverse association between vitamin D intake and metabolic syndrome. These findings warrant further examination in prospective studies including clinical trials.

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References

1. Ascherio A, Hennekens C, Willett WC, Sacks F, Rosner B, Manson J, Witteman J, Stampfer MJ: Prospective study of nutritional factors, blood pressure, and hypertension among US women. *Hypertension* 27:1065–1072, 1996
2. Lin YC, Lyle RM, McCabe LD, McCabe GP, Weaver CM, Teegarden D: Dairy calcium is related to changes in body composition during a two-year exercise intervention in young women. *J Am Coll Nutr* 19:754–760, 2000
3. 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* 287:2081–2089, 2002
4. Chiu KC, Chu A, Go VL, Saad MF: Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. *Am J Clin Nutr* 79:820–825, 2004
5. Davies KM, Heaney RP, Recker RR, Lappe JM, Barger-Lux MJ, Rafferty K, Hinders S: Calcium intake and body weight. *J Clin Endocrinol Metab* 85:4635–4638, 2000
6. Gedik O, Akalin S: Effects of vitamin D deficiency and repletion on insulin and glucagon secretion in man. *Diabetologia* 29:142–145, 1986
7. Zemel MB: Regulation of adiposity and obesity risk by dietary calcium: mechanisms and implications (Review). *J Am Coll Nutr* 21:146S–151S, 2002
8. Bostick RM, Kushi LH, Wu Y, Meyer KA, Sellers TA, Folsom AR: Relation of calcium, vitamin D, and dairy food intake to ischemic heart disease mortality among postmenopausal women. *Am J Epidemiol* 149:151–161, 1999
9. Ness AR, Smith GD, Hart C: Milk, coronary heart disease and mortality. *J Epidemiol Community Health* 55:379–382, 2001
10. Cade C, Norman AW: Vitamin D3 im-

proves impaired glucose tolerance and insulin secretion in the vitamin D-deficient rat in vivo. *Endocrinology* 119:84–90, 1986
11. Norman AW, Frankel JB, Heldt AM, Grodsky GM: Vitamin D deficiency inhibits pancreatic secretion of insulin. *Science* 209:823–825, 1980
12. Isaia G, Giorgino R, Adami S: High prevalence of hypovitaminosis D in female type 2 diabetic population (Letter). *Diabetes Care* 24:1496, 2001
13. Pietschmann P, Schernthaner G, Woloszczuk W: Serum osteocalcin levels in diabetes mellitus: analysis of the type of diabetes and microvascular complications. *Diabetologia* 31:892–895, 1988
14. Scragg R, Sowers M, Bell C: Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the third National Health and Nutrition Examination Survey. *Diabetes Care* 27:2813–2818, 2004
15. Baynes KC, Boucher BJ, Feskens EJ, Kromhout D: Vitamin D, glucose tolerance and insulinaemia in elderly men. *Diabetologia* 40:344–347, 1997
16. Boucher BJ, Mannan N, Noonan K, Hales CN, Evans SJ: Glucose intolerance and impairment of insulin secretion in relation to vitamin D deficiency in east London Asians. *Diabetologia* 38:1239–1245, 1995
17. Lind L, Hanni A, Lithell H, Hvarfner A, Sorensen OH, Ljunghall S: Vitamin D is related to blood pressure and other cardiovascular risk factors in middle-aged men. *Am J Hypertens* 8:894–901, 1995
18. Rexrode KM, Lee IM, Cook NR, Hennekens CH, Buring JE: Baseline characteristics of participants in the Women's Health Study. *J Womens Health Gend Based Med* 9:19–27, 2000
19. Liu S, Buring JE, Sesso HD, Rimm EB, Willett WC, Manson JE: A prospective study of dietary fiber intake and risk of cardiovascular disease among women. *J Am Coll Cardiol* 39:49–56, 2002
20. Willett WC, Sampson L, Browne ML, Stampfer MJ, Rosner B, Hennekens CH, Speizer FE: The use of a self-administered questionnaire to assess diet four years in the past. *Am J Epidemiol* 127:188–199, 1988
21. Salvini S, Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, Willett WC: Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. *Int J Epidemiol* 18:858–867, 1989
22. Ridker PM, Buring JE, Cook NR, Rifai N: C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14,719 initially healthy American women. *Circulation* 107:391–397, 2003
23. Song Y, Manson JE, Buring JE, Liu S: A prospective study of red meat consumption and type 2 diabetes in middle-aged and elderly women: the women's health study. *Diabetes Care* 27:2108–2115, 2004
24. Sanchez M, de la Sierra A, Coca A, Poch E, Giner V, Urbano-Marquez A: Oral calcium supplementation reduces intraplatelet free calcium concentration and insulin resistance in essential hypertensive patients. *Hypertension* 29:531–536, 1997
25. McCarron DA, Reusser ME: Finding consensus in the dietary calcium-blood pressure debate. *J Am Coll Nutr* 18 (Suppl. 5): 398S–405S, 1999
26. Bucher HC, Cook RJ, Guyatt GH, Lang JD, Cook DJ, Hatala R, Hunt DL: Effects of dietary calcium supplementation on blood pressure: a meta-analysis of randomized controlled trials. *JAMA* 275:1016–1022, 1996
27. Ford ES, Ajani UA, McGuire LC, Liu S: Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. *Diabetes Care* 28:1228–1230, 2005
28. Scragg R, Holdaway I, Singh V, Metcalf P, Baker J, Dryson E: Serum 25-hydroxyvitamin D3 is related to physical activity and ethnicity but not obesity in a multicultural workforce. *Aust N Z J Med* 25: 218–223, 1995
29. Feskanich D, Willett WC, Colditz GA: Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. *Am J Clin Nutr* 77:504–511, 2003
30. Borissova AM, Tankova T, Kirilov G, Dakovska L, Kovacheva R: The effect of vitamin D3 on insulin secretion and peripheral insulin sensitivity in type 2 diabetic patients. *Int J Clin Pract* 57:258–261, 2003
31. National Research Council: *Recommended Dietary Allowances*. Washington, DC, National Academy Press, 1989
32. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Institute of Medicine, National Academy of Sciences: *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. Washington, DC, National Academy Press, 2000