

A Prospective Study of Dairy Intake and the Risk of Type 2 Diabetes in Women

SIMIN LIU, MD, SCD^{1,2,3}
HYON K. CHOI, MD, DRPH^{4,5}
EARL FORD, MD⁶
YIQING SONG, MD, SCD¹

ANNA KLEVAK, PHD¹
JULIE E. BURING, SCD^{1,2,7}
JOANN E. MANSON, MD, DRPH^{1,2,4}

OBJECTIVE— Although studies have indicated that increased dairy intake may reduce risk of overweight and insulin resistance syndrome, data directly relating dairy intake to type 2 diabetes remain sparse.

RESEARCH DESIGN AND METHODS— We prospectively examined the associations between intake of dairy foods and calcium and incident type 2 diabetes in 37,183 women without a history of diabetes, cardiovascular disease, and/or cancer at baseline.

RESULTS— During an average of 10 years of follow-up, we documented 1,603 incident cases. After adjusting for potential confounders including BMI, smoking status, physical activity, family history of diabetes, alcohol consumption, history of hypertension, use of hormones, and high cholesterol, the relative risk for type 2 diabetes among women in the highest quintile of dairy intake was 0.79 (95% CI 0.67–0.94; *P* for trend = 0.007) compared with those in the lowest quintile. Each serving-per-day increase in dairy intake was associated with a 4% lower risk (0.96 [0.93–1.01]). The inverse association with type 2 diabetes appeared to be mainly attributed to low-fat dairy intake; the multivariate relative risks comparing the highest to the lowest quintiles was 0.79 (0.67–0.93; *P* for trend = 0.002) for low-fat dairy. The inverse relation between dairy intake and incident type 2 diabetes remained unchanged after further adjustment for dietary calcium, vitamin D, glycemic load, fat, fiber, and magnesium intake. These associations also did not vary significantly according to BMI.

CONCLUSIONS— A dietary pattern that incorporates higher low-fat dairy products may lower the risk of type 2 diabetes in middle-aged or older women.

Diabetes Care 29:1579–1584, 2006

Much remains to be learned about specific dietary factors that may affect type 2 diabetes risks in the general population. A series of recent metabolic and epidemiologic studies have suggested that dairy consumption may

have beneficial effects on body weight (2,3), blood pressure (5), insulin resistance syndrome (IRS) (5,6), and cardiovascular health (7,9). However, data directly relating dairy intake to risk of type 2 diabetes remain sparse, especially

From the ¹Division of Preventive Medicine, Brigham and Women's Hospital, Boston, Massachusetts; the ²Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; the ³Department of Epidemiology, University of California, Los Angeles, Los Angeles, California; the ⁴Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts; the ⁵Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; the ⁶Division of Adult and Community Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; and the ⁷Department of Ambulatory Care and Prevention, Harvard Medical School, Boston, Massachusetts.

Address correspondence and reprint requests to Simin Liu, MD, ScD, Department of Epidemiology, UCLA, 650 Charles E. Young Dr. South, 71-254 CHS Box 951772, Los Angeles, CA 90095-1772. E-mail: siminliu@ucla.edu.

Received for publication 31 January 2006 and accepted in revised form 20 March 2006.

H.K.C. is currently affiliated with the Division of Rheumatology, Department of Medicine, University of British Columbia, Arthritis Research Centre of Canada, Vancouver, Canada.

Abbreviations: ADA, American Diabetes Association; CARDIA, Coronary Artery Risk Development in Young Adults; IRS, insulin resistance syndrome; SFFQ, semiquantitative food frequency questionnaire; WHS, Women's Health Study.

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

DOI: 10.2337/dc06-0256

© 2006 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

in women. Moreover, previous studies have not specifically teased out the effects of dairy food intake from those of dietary calcium and vitamin D. Therefore, we evaluated the question of whether dairy intake may have additional effects on diabetes risk independent from that of calcium and vitamin D in a large prospective cohort of middle-aged women.

RESEARCH DESIGN AND METHODS

The Women's Health Study (WHS) is a randomized, double-blind, placebo-controlled trial originally designed to test the efficacy of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer among 39,876 female health professionals who were without heart disease, stroke, or cancer at baseline (10). Detailed information on dietary intake was provided by 37,183 (93%) of the randomized participants without previously diagnosed diabetes at baseline and who completed a 131-item validated semiquantitative food frequency questionnaire (SFFQ) (11). The study protocol was approved by the Brigham and Women's Hospital Institutional Review Board, and the protocol adhered to the guidelines put forth in the Helsinki declaration and Belmont Accord.

Assessment of diet

To assess dietary intake, we used a validated SFFQ that inquired about the average use of ~131 foods and beverages during the previous year (11). Nutrient intake was computed from the reported frequency of consumption of each specified unit of food or beverage and from published data on the nutrient content of the specified portions. 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 intake included skim or low-fat milk and whole milk.

Total calcium and vitamin D intakes were calculated from both dietary and

Table 1—Baseline characteristics according to dairy foods comparing the highest quintile (Q5) to the lowest quintile (Q1) among 37,183 women

Variable	Total dairy intake		High-fat dairy intake		Low-fat dairy intake	
	Quintile 1	Quintile 5	Quintile 1	Quintile 5	Quintile 1	Quintile 5
Age (year)	54 ± 7	55 ± 7	56 ± 7	54 ± 7	54 ± 7	55 ± 7
BMI (kg/m ²)	25.8 ± 5	26 ± 5	25 ± 4.6	26.1 ± 5.3	25.9 ± 5.2	25.8 ± 4.8
Physical activity (kcal/week)	856 ± 1,164	1,095 ± 1,345	1,114 ± 1,371	896 ± 1,188	786 ± 1,136	1,145 ± 1,323
Current smokers (%)	17.4	10.9	10.5	17.0	22.5	8.5
Alcohol intake (g/day)	4.7 ± 9	4.1 ± 8	3.4 ± 7	5.4 ± 10	5.3 ± 10.5	3.5 ± 6.8
Family history of diabetes (%)	25.2	24.4	25.4	23.6	25.2	24.7
Current postmenopausal hormone use (%)	42.0	40.5	45.2	36.9	38.8	42.4
Hypercholesterolemia (%)	30.9	26.5	36.1	24.0	27.6	28.4
History of hypertension (%)	25.4	24.0	25.6	24.8	26.1	24.0
Dietary variables						
Dietary fiber intake (g/day)*	19.1 ± 7	18.2 ± 5	21.5 ± 7	16.9 ± 4.9	17.6 ± 6.3	19.1 ± 5.8
Total fat (g)*	58.2 ± 13	57.2 ± 11.7	50.4 ± 12	64.3 ± 10.7	62.4 ± 13	53.2 ± 10.2
Dietary glycemic load*†	171 ± 35.6	161 ± 26.0	180 ± 33.5	156 ± 27.7	165 ± 36.3	167 ± 25.5
Dietary protein (g)*	78.6 ± 16.4	84 ± 13.2	83.7 ± 16.5	77.5 ± 12.9	76.4 ± 15.9	86.2 ± 12.5
Dietary magnesium (mg)*	307 ± 65	340 ± 58	349 ± 69	302 ± 52	292 ± 60.9	355 ± 54.9
Dietary calcium (mg)*	531 ± 126	1,081 ± 292	811 ± 325	777 ± 255	532 ± 150	1,160 ± 253
Dietary vitamin D (IU)*	163 ± 88	320 ± 116	261 ± 136	217 ± 98.9	155 ± 87	354 ± 108
Processed meat (servings/day)	0.08 ± 0.15	0.11 ± 0.2	0.05 ± 0.13	0.13 ± 0.21	0.10 ± 0.19	0.07 ± 0.15
Fruits and vegetables (servings/day)	5.03 ± 3.2	7.0 ± 3.4	6.0 ± 3.5	6.3 ± 3.3	5.0 ± 3.1	7.0 ± 3.4
Whole grains (servings/day)	1.05 ± 1.0	1.7 ± 1.3	1.5 ± 1.3	1.2 ± 1.3	0.96 ± 1.01	1.8 ± 1.4
Nuts (servings/day)	0.08 ± 0.19	0.11 ± 0.26	0.07 ± 0.2	0.13 ± 0.26	0.10 ± 0.23	0.10 ± 0.24
Coffee (servings/day)	1.8 ± 1.8	1.9 ± 1.9	1.6 ± 1.7	2.2 ± 1.9	2.0 ± 2.0	1.7 ± 1.8

Data are means ± SD unless otherwise indicated. *Total energy adjusted. †Glycemic load 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.

supplemental sources. Intakes of dietary calcium and vitamin D were calculated from all dietary sources without supplements. Each nutrient was adjusted for total energy using the residual method (12). In similar cohorts of health professionals, this SFFQ has demonstrated reasonably good validity as a measure of long-term average dietary intakes. 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 (12). 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 (13). The validity of vitamin D intake was assessed by comparing it with the plasma concentrations of 25-hydroxyvitamin D among 323 healthy women (14).

Correlation coefficients between intake and plasma concentration of vitamin D were 0.35 for total vitamin D and 0.25 for dietary vitamin D.

Ascertainment of incident type 2 diabetes

Details regarding ascertainment of incident type 2 diabetes in the WHS have been reported previously (15,16). Using the diagnostic criteria recommended by the American Diabetes Association (ADA), we used three complementary approaches to validate self-reported incident cases of diabetes. Method 1 involved a telephone interview by a study physician of 473 women with self-reported diabetes who participated in a previous study (17). Method 2 used a supplemental questionnaire that contained detailed information mailed to a random sample of

147 women who self-reported diabetes. Method 3 involved contacting individual physicians for medical records of those women consenting for medical record review in method 2. Self-reported diagnoses of diabetes were confirmed in 406 of 446 women who responded via a physician-led telephone interview (positive predictive value 91.0% [95% CI 88.4–93.7]). Separately, among 136 responders to the supplemental questionnaire, 124 women were classified as diabetic using the ADA criteria (positive predictive value 91.2% [86.4–95.9]). Among 113 women who gave permission for study investigators to contact their primary care physician, 97 physicians responded, of whom 90 provided adequate medical record information to apply the ADA criteria. Of these 90 women, 89 were confirmed to have diabetes on the basis of

Table 2—RR (95% CI) of type 2 diabetes according to total dairy intake in the WHS, 1993–2004

	Total dairy intake (daily serving)					P for trend	RR per 1-serving/day increase
	Quintile 1 (<0.85)	Quintile 2 (0.89–1.35)	Quintile 3 (1.36–1.9)	Quintile 4 (1.9–2.9)	Quintile 5 (>2.9)		
Cases of type 2 diabetes	345	329	300	323	306	—	—
Person-years	73,096	71,698	73,793	73,413	73,260	—	—
Age, treatment, calorie adjusted	1.0	0.90 (0.78–1.05)	0.75 (0.64–0.88)	0.75 (0.64–0.88)	0.66 (0.56–0.78)	0.0001	0.93 (0.89–0.97)
Multivariate model 1*	1.0	0.94 (0.81–1.10)	0.85 (0.72–1.00)	0.87 (0.74–1.02)	0.79 (0.67–0.94)	0.007	0.96 (0.93–1.01)
Multivariate model 2†	1.0	0.94 (0.80–1.10)	0.85 (0.72–1.00)	0.88 (0.74–1.03)	0.80 (0.67–0.95)	0.011	0.97 (0.93–1.01)
Multivariate model 3‡	1.0	0.90 (0.76–1.01)	0.79 (0.65–0.96)	0.79 (0.64–0.99)	0.68 (0.52–0.89)	0.006	0.96 (0.90–1.02)

Low-fat dairy foods: skim/lowfat milk, sherbet, yogurt, and cottage/ricotta cheese. High-fat dairy foods: whole milk, cream, butter, sour cream, ice cream, cream cheese, and other cheese. Total dairy foods: low-fat dairy foods + high-fat dairy foods except for butter. Age-adjusted models adjusted for total energy intake, randomized-treatment assignment, and age. *Multivariate model 1 additionally adjusted for family history of diabetes (yes/no), smoking status (never smoked, former smoker, or current smoker), BMI (continuous), hypercholesterolemia (yes/no), hypertension (yes/no), physical activity (quintiles of METs), hormones (past, current, or never), and alcohol consumption (rarely/never, 1–3 drinks/month, 1–6 drinks/week, or >1 drink/day). †Multivariate model 2 adjusted for all covariates in model 1 + dietary intakes (quintiles) of fibers, total fat, and dietary glycemic load. ‡Multivariate model 3 adjusted for covariates in model 2 + quintiles of dietary calcium, vitamin D, and magnesium.

the combined information from the supplemental questionnaire and physician information. The follow-up for this cohort exceeded 99% during the study period.

Statistical analysis

We computed person-time of follow-up from the beginning of the trial to the date of diagnosis of type 2 diabetes, death from any cause, or the end of the study period (March 2005), whichever came first. The average daily dairy intake was categorized into quintiles of intake, and each quintile was compared with the lowest quintile. After testing the proportional hazard assumption, we used Cox proportional hazards modeling to estimate the rate ratios, or estimates of relative risk (RR), and 95% CIs for developing incident type 2 diabetes for each category of intake compared with the lowest category. The initial model was adjusted for age (continuous), treatment assignment (categorical), and total energy intake (continuous). In multivariate models, we additionally adjusted for BMI (continuous), smoking status (current, past, and never), exercise (quintiles in METs per week), alcohol intake (rarely/never, 1–3 drinks/month, 1–6 drinks/week, or ≥ 1 drink/day), use of postmenopausal hormone therapy (past, current, and never), high cholesterol, hypertension, and family history of diabetes (yes/no), as well as for dietary factors (all in quintiles) including intakes of dietary fiber, glycemic load, magnesium, calcium, total fat, and vitamin D.

The RR for the continuous measures indicates the change in risk associated

with an average increment of one serving per day of the standard portion size. To assess possible effect modification, we conducted analyses stratified by BMI (<25 vs. ≥ 25 kg/m²), physical activity (less than median versus more than median), and family history of diabetes (yes/no), which were determined a priori. We tested the significance of the interaction using the likelihood ratio test by comparing a model with the main effects of dairy intake and the stratifying variable and interaction term with a reduced model with only the main effects. All statistical analyses were conducted using SAS (version 8.0; SAS Institute, Cary, NC).

RESULTS

Baseline characteristics

The baseline characteristics of the cohort according to intake levels are shown in (Table 1). Women with higher dairy intake tended to have slightly lower alcohol consumption, a higher level of physical activity, lower prevalence of hypertension and hypercholesterolemia, a lower glycemic load, slightly higher caffeine intake, and higher intakes of whole grains, nuts, and fruits and vegetables. Women with higher intake of low-fat dairy had similar trends, whereas women with high intake of high-fat dairy tended to have less healthy lifestyle patterns.

Dairy product consumption and incident type 2 diabetes

During the 10-year follow-up, we documented 1,603 incident cases of type 2 diabetes. After adjusting for age, treatment

assignment, and total energy intake, the RR for women in the highest quintile of total dairy intake was 0.66 (95% CI 0.56–0.78; P for trend = 0.0001) compared with those in the lowest quintile (Table 2). After further adjustment for other risk factors, the association was attenuated but still statistically significant (RR 0.79 [0.67–0.94]; P for trend = 0.007). Each serving-per-day increase in dairy intake was associated with a 4% lower risk for type 2 diabetes (0.96 [0.93–1.01]).

The inverse association with type 2 diabetes appeared to be mainly attributed to low-fat dairy intake; the age-, calorie intake-, and treatment-adjusted RRs comparing the highest to the lowest quintiles were 0.64 (95% CI 0.54–0.75; P for trend = 0.0001) for low-fat dairy intake and 1.08 (0.92–1.28; P for trend = 0.20) for high-fat dairy intake (Table 3). Additional adjustment for BMI, family history of diabetes, smoking, alcohol intake, physical activity, postmenopausal hormone use, and history of hypercholesterolemia and hypertension did not appreciably change the results. The results also did not change after further adjustment for dietary intakes of calcium, vitamin D, fibers, total fat, glycemic load, and magnesium.

We also evaluated type of dairy foods in relation to risk of type 2 diabetes (Table 4). Intake of yogurt was inversely associated with risk of type 2 diabetes. Additional adjustment for other factors including vitamin D, calcium, and magnesium did not attenuate the inverse association; the multivariate-adjusted RR was 0.82 (95% CI 0.70–0.97) for women

Table 3—RR (95% CI) of type 2 diabetes among men according to low-fat dairy foods vs. high-fat foods

Variables	≤0.27	0.28–0.64	0.70–1.07	1.13–2.00	>2.00	P for trend	RR per 1-serving/day increase*
Low-fat dairy foods	364/69,958	331/71,959	273/68,377	338/81,853	295/73,003	—	—
Cases/person-years	1.0	0.85 (0.74–0.99)	0.72 (0.61–0.84)	0.70 (0.60–0.82)	0.64 (0.54–0.75)	—	0.88 (0.84–0.93)
Age, calorie-adjusted	1.0	0.93 (0.80–1.09)	0.86 (0.73–1.01)	0.84 (0.72–0.98)	0.79 (0.67–0.93)	<0.0001	0.94 (0.89–0.99)
Multivariate model 1*	1.0	0.94 (0.81–1.10)	0.87 (0.74–1.02)	0.86 (0.74–1.02)	0.82 (0.68–0.98)	0.02	0.95 (0.90–1.01)
Multivariate model 2†	1.0	0.93 (0.79–1.09)	0.82 (0.68–0.99)	0.80 (0.65–0.99)	0.69 (0.52–0.91)	0.007	0.92 (0.84–1.01)
Multivariate model 3‡	<0.20	0.21–0.49	0.50–0.770	0.785–1.28	>1.329	—	—
High-fat dairy foods	261/65,616	309/77,027	334/76,712	338/72,868	361/72,841	—	—
Cases/person-years	1.0	0.99 (0.84–1.16)	1.03 (0.88–1.22)	1.07 (0.91–1.26)	1.08 (0.92–1.28)	0.20	1.04 (1.00–1.08)
Age, calorie-adjusted	1.0	0.98 (0.83–1.16)	0.99 (0.84–1.17)	1.03 (0.87–1.23)	1.05 (0.88–1.24)	0.44	1.02 (0.97–1.06)
Multivariate model 1*	1.0	0.96 (0.81–1.14)	0.96 (0.80–1.14)	0.9 (0.82–1.18)	0.97 (0.80–1.17)	0.88	1.00 (0.95–1.04)
Multivariate model 2†	1.0	0.96 (0.81–1.14)	0.97 (0.81–1.15)	1.00 (0.83–1.19)	0.99 (0.82–1.20)	0.90	1.00 (0.96–1.05)
Multivariate model 3‡	1.0	0.96 (0.81–1.14)	0.97 (0.81–1.15)	1.00 (0.83–1.19)	0.99 (0.82–1.20)	0.90	1.00 (0.96–1.05)

Age-adjusted models adjusted for total energy intake, randomized-treatment assignment, and age. *Multivariate model 1 additionally adjusted for family history of diabetes (yes/no), smoking status (never smoked, former smoker, or current smoker), BMI (continuous), hypercholesterolemia (yes/no), hypertension (yes/no), physical activity (quintiles of METs), hormones (past, current, or never), and alcohol consumption (rarely/never, 1–3 drinks/month, 4–6 drinks/week, or >1 drink/day). †Multivariate model 2 adjusted for all covariates in model 1 + dietary intakes (quintiles) of fibers, total fat, and dietary glyceemic load. ‡Multivariate model 3 adjusted for covariates in model 2 + quintiles of dietary calcium, vitamin D, and magnesium.

who consumed two servings/week yogurt compared with those who consumed less than one serving/day (*P* for trend = 0.03).

When we examined whether the association of total dairy intake and type 2 diabetes were modified by BMI, physical activity, and family history of diabetes (Table 5), significant inverse association was stronger in women who had no family history of diabetes than in those with family history (*P* for interaction = 0.03), but we found no significant interactions of dairy intake with BMI (*P* for interaction = 0.06) and physical activity (*P* for interaction = 0.29) in relation to type 2 diabetes risk.

CONCLUSIONS — In this large prospective cohort study of women, we found a moderate inverse association between dairy consumption, especially low-fat dairy consumption, and incidence of type 2 diabetes that was independent of age, BMI, family history of diabetes, history of hypertension, hypercholesterolemia, smoking history, physical activity, and some dietary factors related to type 2 diabetes.

Previous studies have suggested favorable effects of dairy intake on body weight (2,3,6), hypertension (4), and glucose homeostasis (5,6). A strong inverse association between dairy intake and risk of IRS was observed in the Coronary Artery Risk Development in Young Adults (CARDIA) study of young adults who were overweight (BMI ≥25 kg/m²) but not among leaner individuals (6). In our study, however, we did not find a significant effect modification by BMI, and the overall magnitude of the association with type 2 diabetes (4% reduction per serving increase in dairy foods) was notably smaller than that with IRS shown among those who were overweight in the CARDIA study (21%). Further, the association in the CARDIA study was present with both high- and low-fat dairy products but in our study was limited to low-fat dairy intake. It is possible that a strong inverse association between dairy intake and risk of IRS in young adulthood in the CARDIA study may not directly relate to risk of type 2 diabetes later in life observed in these middle-aged or older women. Aside from the fact that type 2 diabetes and IRS are two related but different end points, age differences (at the time of dairy exposure or outcome measurement) and dilution of effect in the later phases of the causal pathway toward type 2 diabetes

Table 4—Multivariate RR of type 2 diabetes among women according to servings of dairy foods

Variables	<1/month	1–3/month	1/week	≥2/week	P for trend
Skim milk					
Cases/person-years	275/58,525	178/34,395	97/24,590	1032/244,200	
RR (95% CI)	1.0	1.05 (0.86–1.27)	0.87 (0.69–1.10)	0.92 (0.78–1.09)	0.22
Whole milk					
Cases/person-years	1301/308,188	121/21,309	47/8,286	95/16,191	
RR (95% CI)	1.0	1.06 (0.88–1.28)	1.32 (0.98–1.79)	1.04 (0.84–1.30)	0.30
Yogurt					
Cases/person-years	744/149,622	429/96,568	156/40,301	243/71,452	
RR (95% CI)	1.0	0.98 (0.86–1.14)	0.94 (0.78–1.13)	0.82 (0.70–0.97)	0.03
Sherbet					
Cases/person-years	584/129,055	552/124,390	197/46,102	243/59,929	
RR (95% CI)	1.0	0.98 (0.87–1.10)	0.97 (0.82–1.15)	0.92 (0.77–1.05)	0.22
Cottage cheese					
Cases/person-years	653/146,681	624/140,910	168/41,461	131/30,802	
RR (95% CI)	1.0	1.01 (0.91–1.14)	0.91 (0.76–1.08)	0.86 (0.71–1.05)	0.12
Ice cream					
Cases/person-years	581/146,447	589/131,214	207/43,008	194/38,391	
RR (95% CI)	1.0	0.93 (0.83–1.05)	0.94 (0.80–1.11)	0.88 (0.74–1.05)	0.17
Other cheese					
Cases/person-years	104/22,345	336/85,052	397/89,623	752/165,231	
RR (95% CI)	1.0	0.78 (0.62–0.98)	0.83 (0.66–1.04)	0.80 (0.64–1.01)	0.45
Cream cheese					
Cases/person-years	807/187,531	506/119,370	132/29,055	112/20,099	
RR (95% CI)	1.0	0.99 (0.88–1.11)	1.03 (0.85–1.25)	1.19 (0.97–1.47)	0.21
Cream					
Cases/person-years	1219/267,599	176/48,043	38/10,143	128/28,818	
RR (95% CI)	1.0	0.81 (0.69–0.95)	0.91 (0.66–1.26)	1.03 (0.86–1.25)	0.60
Sour cream					
Cases/person-years	701/162,051	613/141,780	168/34,299	87/19,249	
RR (95% CI)	1.0	0.97 (0.86–1.08)	1.11 (0.93–1.32)	0.93 (0.74–1.18)	0.97

Multivariate model adjusted for total energy intake, randomized-treatment assignment, age, family history of diabetes (yes/no), smoking status (never smoked, former smoker, or current smoker), BMI (continuous), hypercholesterolemia (yes/no), hypertension (yes/no), hormones (past, current, or never), physical activity (quintiles of METs), alcohol consumption (rarely/never, 1–3 drinks/month, 1–6 drinks/week, or >1 drink/day), dietary intakes (quintiles) of fibers, total fat, dietary glycemic load, dietary calcium, vitamin D, and magnesium.

may potentially explain these different observations.

The exact mechanisms underlying the inverse association between dairy in-

take and risk of type 2 diabetes remain unclear. Milk proteins appear to have insulinotropic properties with a relatively low glycemic load (6). Milk proteins ap-

pear to induce rapid release of insulinotropic amino acids and incretin hormones (insulinotropic peptide hormones from the gut including glucose-dependent in-

Table 5—Multivariate RR (95% CI) of type 2 diabetes according to total dairy food consumption, stratified by major risk factors

	Cases (n)	Total dairy intake (daily serving)					P for trend
		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
BMI (kg/m ²)							
<25	209	1.0	1.16 (0.75–1.81)	0.70 (0.41–1.20)	0.66 (0.36–1.22)	0.46 (0.22–1.00)	0.02
≥25	1,347	1.0	0.87 (0.72–1.05)	0.79 (0.64–0.97)	0.82 (0.65–1.03)	0.70 (0.52–0.94)	0.03
Family history of diabetes							
Yes	733	1.0	0.90 (0.69–1.17)	0.96 (0.72–1.29)	1.04 (0.75–1.44)	0.82 (0.55–1.23)	0.82
No	870	1.0	0.95 (0.76–1.19)	0.67 (0.51–0.87)	0.64 (0.47–0.85)	0.57 (0.39–0.83)	0.0003
Physical activity							
High	608	1.0	0.81 (0.60–1.08)	0.73 (0.53–1.01)	0.67 (0.47–0.96)	0.58 (0.37–0.91)	0.02
Low	971	1.0	0.97 (0.78–1.20)	0.84 (0.65–1.07)	0.90 (0.68–1.18)	0.76 (0.54–1.07)	0.14

Multivariate model adjusted for total energy intake, randomized-treatment assignment, age, family history of diabetes (yes/no), smoking status (never smoked, former smoker, or current smoker), BMI (continuous), hypercholesterolemia (yes/no), hypertension (yes/no), hormones (past, current, or never), physical activity (quintiles of METs), alcohol consumption (rarely/never, 1–3 drinks/month, 1–6 drinks/week, or >1 drink/day), dietary intakes (quintiles) of fibers, total fat, dietary glycemic load, dietary calcium, vitamin D, and magnesium.

sulinotropic polypeptide and glucagon-like peptide) (18). Whey appears to be a particularly potent stimulus for the secretion of glucagonlike peptide (18). The ability of milk to enhance the secretion of insulinotropic amino acids and incretin hormone may help reduce the incidence of type 2 diabetes in those with high intakes of dairy foods. While a lower glycaemic index or load associated with dairy intake may also contribute to the reduced risk, our results showed independent associations after adjusting for glycaemic load. These data are consistent with the possibility that milk seems to influence glucose tolerance more through its insulinotropic effect than its relatively lower glycaemic load. However, saturated fat contained in dairy foods may mitigate these potential benefits, which may explain a weaker or null association with high-dairy foods observed in our study.

Major components in dairy products such as magnesium, calcium, lactose, and dairy protein may enhance satiety and reduce the risk of overweight and obesity compared with other high-carbohydrate foods and beverages. There was no evidence in this study that BMI varied with milk intake, and adjusting for BMI did not alter the dairy food–type 2 diabetes relation. Low-fat dairy foods have been one of the main components of the Dietary Approaches to Stop Hypertension (DASH) diet that has been shown to substantially lower blood pressure (19) and were included in a randomized trial for type 2 diabetes prevention (1).

Our study findings may be affected by unmeasured confounding factors, although our study minimized the possibility of biases due to recall and/or loss of follow-up. We have also adjusted for the known risk factors of type 2 diabetes in our multivariate analyses. Thus, our results were independent of these factors that are correlated with dairy consumption at baseline. Underdiagnosis of type 2 diabetes may be a concern because the study population was not screened for glucose tolerance and the diagnosis was self-reported. However, our validation study of self-reported diabetes in the WHS indicated a high rate of agreement with medical record review. All participants in this study are health professionals, who are likely to have more robust and valid self-reported diagnostic information. The relatively high screening rate of WHS health professionals (85–90% for

blood glucose screening) also reduces the likelihood of underdiagnosis. Thus, as compared with the general population, the degree of underdiagnosis was probably smaller in this cohort of health professionals with ready access to medical care.

In conclusion, higher intake of dairy foods was prospectively associated with lower risk of type 2 diabetes in women. These data indicate that a diet that incorporates higher dairy intake, especially low-fat dairy intake, may lower the risk of type 2 diabetes among middle-aged or elderly women. Further confirmation of these findings and comprehensive risk-benefit assessments, however, are required before public health measures to increase dairy consumption can be recommended for prevention of type 2 diabetes.

Acknowledgments— This study was supported by grants DK66401, CA-47988, and HL-43851 from the National Institutes of Health, Bethesda, MD.

We are indebted to the 39,876 dedicated and committed participants of the WHS.

References

1. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM, the Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
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. Zemel MB: Mechanisms of dairy modulation of adiposity. *J Nutr* 133:252S–256S, 2003
4. 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
5. Mennen LI, Balkau B, Vol S: Tissue-type plasminogen activator antigen and consumption of dairy products: the DESIR study: data from an Epidemiological Study on Insulin Resistance Syndrome. *Thromb Res* 94:381–388, 1999
6. 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
7. 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
8. Elwood PC, Strain JJ, Robson PJ, Fehily AM, Hughes J, Pickering J, Ness A: Milk consumption, stroke, and heart attack risk: evidence from the Caerphilly cohort of older men. *J Epidemiol Community Health* 59:502–505, 2005
9. Ness AR, Smith GD, Hart C: Milk, coronary heart disease and mortality. *J Epidemiol Community Health* 55:379–382, 2001
10. Buring JE, the Women's Health Study Research Group: The Women's Health Study: summary of the study design. *J Myocardial Ischemia* 4:27–29, 1992
11. Liu S, Manson J, Lee I, Cole S, Willett W, Buring J: Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. *Am J Clin Nutr* 72:922–928, 2000
12. Willett WC: *Nutritional Epidemiology*, 2nd ed. New York, Oxford University Press, 1998
13. 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
14. 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
15. Janket SJ, Manson JE, Sesso H, Buring JE, Liu S: A prospective study of sugar intake and risk of type 2 diabetes in women. *Diabetes Care* 26:1008–1015, 2003
16. 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
17. Pradhan A, Manson J, Rifai N, Buring J, Ridker P: C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 286:327–334, 2001
18. King JC: The milk debate. *Arch Intern Med* 165:975–976, 2005
19. Sacks FM, Obarzanek E, Windhauser MM, Svetkey LP, Vollmer WM, McCullough M, Karanja N, Lin PH, Steele P, Proschan MA, et al.: Rationale and design of the Dietary Approaches to Stop Hypertension trial (DASH): a multicenter controlled-feeding study of dietary patterns to lower blood pressure. *Ann Epidemiol* 5:108–118, 1995