Adolescent dairy product consumption and risk of type 2 diabetes in middle-aged women[1–3]

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ABSTRACT

Background: Type 2 diabetes (T2D) prevention has generally focused on the identification of risk factors in adulthood. Dairy product consumption in adults has been associated with a lower risk of T2D.

Objective: The objective was to evaluate the relation between dairy product consumption during adolescence and risk of T2D in adulthood.

Design: We examined the incidence of T2D in relation to high school dairy product consumption within the Nurses' Health Study II cohort. A total of 37,038 women who completed a food-frequency questionnaire about their diet during high school were followed from the time of return of the questionnaire in 1998–2005. Cox proportional hazards regression was used to estimate RRs and 95% CIs.

Results: Compared with women in the lowest quintile of high school dairy product intake, those in the highest quintile (2 servings/d) had a 38% lower risk of T2D (RR: 0.62; 95% CI: 0.47, 0.83; *P*-trend = 0.0006), after adjustment for high school risk factors. After adjustment for adult risk factors, the association persisted (RR: 0.73; 95% CI: 0.54, 0.97; *P*-trend = 0.02) but was attenuated after adjustment for adult dairy product consumption. In a multivariate joint comparison of dairy product consumption by adults and high school adolescents, compared with women with consistently low intakes, those with consistently high intakes had the lowest risk of T2D (RR: 0.57; 95% CI: 0.39, 0.82).

Conclusions: Our data suggest that higher dairy product intake during adolescence is associated with a lower risk of T2D. Some of the benefits of dairy product intake during high school may be due to the persistence of the consumption pattern during adulthood. *Am J Clin Nutr* 2011;94:854–61.

INTRODUCTION

Over recent decades, the prevalence of T2D[4] has increased at an alarming rate in the United States and across the globe. Prevention efforts, which are paramount to abating this epidemic, have generally focused on the identification of risk factors that operate in adulthood. However, evidence is accumulating for a role of early-life exposures in chronic disease etiology, including maternal diet during pregnancy, postnatal growth, and childhood and adolescent diet (1). Such a life-course approach could enhance our understanding of disease etiology and make a significant contribution to primary prevention. There is some indication that risk of T2D may begin in early life. Low birth weight has been associated with an increased risk of T2D, CVD, and hypertension (1). In addition, greater adult height, which may represent adequate childhood nutrition, has been associated with a decreased risk of insulin resistance and T2D (2–4). Whether dietary habits during childhood or adolescence can affect risk of T2D in adulthood is unknown.

Many studies in adults have shown that dairy product intake is inversely associated with the metabolic syndrome and T2D (5, 6). It is of interest to know whether consuming greater amounts of dairy products at earlier points in the life course can influence T2D risk in later life. Therefore, we prospectively evaluated the relation between dairy consumption during adolescence and incident T2D in a large cohort of US women. We further evaluated the joint effect of current and adolescent dairy consumption on the risk of developing T2D.

SUBJECTS AND METHODS

Study population

The NHS II is a prospective cohort of 116,671 female registered nurses aged 24–42 y at study initiation in 1989. This cohort is followed by using biennial mailed questionnaires on lifestyle, diet, and medical history (7). In 1997, participants were asked whether they would complete a questionnaire about their diet during high school (HS-FFQ) at which time they were 34–53

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[4] Abbreviations used: ADA, American Diabetes Association; CVD, cardiovascular disease; FFQ, food-frequency questionnaire; GL, glycemic load; HS-FFQ, food-frequency questionnaire on diet during high school; IGF-I, insulin-like growth factor I; MET-h, metabolic equivalent task hours; NHS, Nurses' Health Study; T2D, type 2 diabetes.

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y of age. Approximately 55% of the cohort indicated a willingness to complete the questionnaire (n = 64,380). A comparison of these women with the entire cohort suggests that they do not differ with regard to baseline dairy product intake or T2D risk factors. This analysis was restricted to the 47,355 women who returned the HS-FFQ. We excluded participants if they reported implausible daily energy intakes of <500 or ≥3500 kcal/d for current intakes (n = 2920) and <500 or ≥5000 kcal/d for high school intakes (n = 1181) or left ≥10 items blank (n = 225). In addition we excluded participants if they had a confirmed diagnosis of diabetes (n = 502 T2D, n = 42 type 1 diabetes) or death (n = 1) before return of the HS-FFQ in 1998, were missing the date of diagnosis of diabetes (n = 616), or had a history of diabetes (n = 137), gestational diabetes (n = 1875), cancer (except non-melanoma skin cancer), or CVD (n = 2818) reported in 1999. After the exclusions, a total of 37,038 participants remained for the analysis. The procedures followed were in accordance with the ethical standards of Harvard University.

Assessment of dairy product intake during high school and in adulthood

Dairy product intake during high school was assessed by using the HS-FFQ—a 124-item FFQ that asked participants about their usual diet during high school (ages 13–17 y). The HS-FFQ was specifically designed to include foods that were commonly consumed between 1960 and 1980, when these women were in high school. Dairy products listed on the HS-FFQ included chocolate milk, milk, instant breakfast, yogurt, cottage/ricotta cheese, cheese, cream cheese, butter, ice cream, sherbet, and milkshakes. Responses were given by using commonly used portion sizes and 9 categories of intake ranging from "never or less than once per month" to "6 or more per day." Nutrient intakes on the HS-FFQ were computed by multiplying the frequency of consumption of each unit of food or beverage by the nutrient content of the specified portions and summing the contributions from all items. Nutrient values were obtained from the US Department of Agriculture, food manufacturers, and academic sources. Recall of adolescent diet by NHS II participants has been shown to be reproducible (8, 9). In addition, the HS-FFQ has been shown to have reasonable validity (9, 10).

As part of the ongoing NHS II study, participants completed a 133-item semiquantitative FFQ estimating usual dietary intake during the past year, in 1991, 1995, 1999, and 2003. Dairy products and response categories included on these FFQs were similar to those on the HS-FFQ. The validity and reliability of FFQs similar to those used in the NHS II were described elsewhere (11).

Outcome assessment

Women reporting a new diagnosis of diabetes on any of the biennial questionnaires were sent supplementary questionnaires asking about diagnosis and treatment of their diabetes as well as ketoacidosis to confirm the self-report and to distinguish between type 1 diabetes and T2D. The diagnostic criteria for T2D were changed in 1997 to those recommended by the ADA, such that fasting glucose concentrations ≥7 mmol (126 mg/dL) are considered diagnostic (12). Cases in our analysis included new diagnoses of diabetes made from return of the HS-FFQ in 1998 to June 2005 and were therefore all ascertained by using the ADA criteria (12). In substudies of NHS I and the Health Professionals Follow-Up Study, 98% and 97% of the self-reported diabetes cases documented by the same supplementary questionnaire were confirmed by medical record review (13, 14).

Statistical analysis

Person-time of follow-up was calculated for each participant from 1997 until June 2005, from the date of diabetes mellitus diagnosis, or at the time of death, whichever came first. Responses to the individual dairy items were converted to average number of servings per day. Average daily intakes of individual items were combined to compute total dairy product intake (low-fat and high-fat items), low-fat dairy product intake (skim milk, skim chocolate milk, sherbet, yogurt, instant breakfast, and cottage/ricotta cheese), and high-fat dairy product intake (whole milk, whole chocolate milk, cream cheese, other cheese, ice cream, milkshakes, and butter). The average daily dairy product intake was categorized into quintiles. Cox proportional hazards regression was used to estimate the RR of incident T2D by comparing each quintile of dairy product intake with the lowest quintile. Tests for trends across quintiles of intake were conducted by modeling the median value for each category as a continuous variable. Because systematic overreporting and underreporting of dairy product intake may result in biased estimates, measurements were expressed as servings/1000 kcal (15). Multivariate models were adjusted for age in 5-y categories; BMI (in kg/m^2) at age 18 y (proxy for BMI during high school, <18.5, 18.5 to <22.5, 22.5 to <25, 25 to <30, or ≥ 30); total energy intake in high school (quintiles, servings/d); other high school dietary risk factors (quintiles, servings/d), including glycemic load and sugar-sweetened beverage, coffee, processed meat, *trans* fat, and alcohol intake (0, 0.1–4.9, 5.0–9.9, or ≥10 g/d); smoking between ages 15 and 19 y (0, 1–4, 5–14, or >15 cigarettes/d); and high school physical activity (MET-h/wk). In this cohort, recalled weight at age 18 y was highly correlated with measured weight from physical examination records (r = 0.87) (16). To assess whether current T2D risk factors mediated the association between adolescent dairy product intake and T2D, we evaluated additional adjustment for current smoking status (never, past, or current: 1–14 or ≥15 cigarettes/d), alcohol use (g/d), current physical activity (MET-h/wk), history of T2D in parents or siblings (yes or no), oral contraceptive use, hormone replacement therapy, and current dietary factors (quintiles, servings/d), including polyunsaturated:saturated fat ratio, glycemic load, and coffee, sugar-sweetened beverage, cereal fiber, *trans* fat, processed meat, and total energy intakes. Current dairy product intake, height [proxy for childhood IGF-I concentrations], and weight change since age 18 y were also evaluated as potential mediators (17). Current BMI was not added to the model because it is highly correlated with BMI at age 18 y. Quintiles of low-fat and high-fat dairy and individual dairy products were also evaluated separately in multivariate analyses. We conducted stratified analyses by BMI at age 18 y, physical activity during high school, glycemic load during high school, and dairy product consumption in adulthood. We also evaluated the association between dairy product consumption in adulthood and T2D, stratified by dairy product intake during high school. Tests for interaction were performed by including a product term with the respective stratification variable and the median score of dairy product intake quintiles during high school as a continuous variable in the model and evaluating Wald *P* values. To test for interaction between dairy product intake during high school and dairy product intake in adulthood, a cross-product term of median tertiles was evaluated. This method was selected for statistical efficiency because it evaluates only one interaction term.

To assess current dairy product intake on T2D risk, we conducted a similar analysis using categories based on quintiles of servings per 1000 kcal. To reduce random within-person variation and best reflect long-term dairy product intake, we calculated the cumulative average dairy product intake using FFQs from 1991, 1995, 1999, and 2003 (18). Multivariate models were fitted by using the same current risk factors that were examined in the high school analysis as well as current BMI. Hypertension and high school dairy product intake were evaluated as mediators in sensitivity analyses. We also examined the association by low- and high-fat dairy product intake. Linear effects for high school and dairy product intake in adulthood were evaluated by modeling these variables continuously.

To illustrate the joint effect of current dietary product intake and dairy product intake during high school on T2D risk, dairy product intakes during high school and in adulthood were categorized into tertiles of high, medium, and low. These variables were cross-classified into a 9-level categorical variable, which was evaluated by using low-low as the reference. The correlation between adolescent and adult dairy product intake was evaluated by Spearman correlation coefficients. All statistical tests were 2-sided and performed by using SAS version 9 for UNIX (SAS Institute Inc, Cary, NC).

RESULTS

Characteristics of the study population during high school according to quintile of dairy product intake during high school are shown in **Table 1**. Those with higher dairy product intakes tended to be more physically active, gained less weight from age 18 y, were less likely to use oral contraceptives, were less likely to be younger than 12 y at first menarche, and were slightly taller. Frequent dairy consumers also had a lower glycemic load, a lower polyunsaturated fat:saturated fat ratio, higher intakes of

TABLE 1

Age-adjusted characteristics in participants in the Nurses' Health Study II during high school by quintile of total dairy product intake during high school[1]

	Quintile of dairy product intake				
	1	2	3	4	5
Median intake (daily servings/1000 kcal)	0.5	0.9	1.2	1.5	2.0
No. of subjects	7298	7407	7429	7450	7454
BMI at age 18 y (kg/m^2)	21.2 ± 1.8[2]	21.2 ± 1.7	21.1 ± 1.7	21.0 ± 1.6	21.0 ± 1.6
Weight gain from age 18 y (kg)[3]	13.2 ± 7.1	12.1 ± 6.8	11.8 ± 6.6	11.7 ± 6.6	11.6 ± 6.5
Current height (inches)[3]	64.7 ± 1.4	64.8 ± 1.4	64.9 ± 1.4	65.1 ± 1.4	65.1 ± 1.40
Birth weight (kg)	3.6 ± 0.56	3.6 ± 0.56	3.6 ± 0.55	3.6 ± 0.55	3.6 ± 0.56
Menarche at age <12 y (%)	25.0	24.6	24.0	23.2	22.9
Total physical activity (MET-h/wk)	49.8 ± 19.1	51.5 ± 19.0	53.0 ± 19.0	53.7 ± 19.4	54 ± 19.5
Strenuous physical activity (MET-h/wk)	28.2 ± 13.2	28.9 ± 13.2	30.2 ± 13.6	30.6 ± 13.6	30.3 ± 13.7
Moderate physical activity (MET-h/wk)	15.3 ± 7.1	16.0 ± 7.1	16.2 ± 7.1	16.3 ± 7.2	16.5 ± 7.4
Walking (MET-h/wk)	6.7 ± 4.5	7.1 ± 4.4	7.0 ± 4.3	7.2 ± 4.4	7.6 ± 4.6
Television viewing (h/wk)	3.8 ± 0.58	3.8 ± 0.56	3.8 ± 0.54	3.8 ± 0.55	3.7 ± 0.56
Smoking (%)	22.8	24.3	23.3	21.8	22.2
Smoking (cigarettes/wk)	2.9 ± 0.96	2.9 ± 0.94	2.9 ± 0.97	2.9 ± 0.94	2.9 ± 0.97[4]
OC use (%)	23.8	22.2	21.2	21.2	19.9
Dietary variables					
Total energy (kcal/d)	2592 ± 429	2721 ± 440	2868 ± 412	2792 ± 386	2687 ± 392
Sugar-sweetened beverage intake (servings/d)	2.6 ± 1.2	2.4 ± 1.1	2.3 ± 1.1	2.1 ± 1.1	1.8 ± 1.0
Coffee intake (servings/d)	1.3 ± 1.3	1.2 ± 1.2	1.1 ± 1.1	1.1 ± 1.2	1.0 ± 1.1
Alcohol (g/d)	1.0 ± 1.7	1.1 ± 1.7	1.0 ± 1.6	1.0 ± 1.6	1.0 ± 1.8
Glycemic load	182 ± 15	175 ± 12	171 ± 11	167 ± 11	160 ± 11
Cereal fiber (g/d)	6.1 ± 1.2	6.0 ± 1.1	5.8 ± 1.0	5.7 ± 1.1	5.4 ± 1.1
Polyunsaturated:saturated fat ratio	0.50 ± 0.06	0.46 ± 0.06	0.43 ± 0.05	0.40 ± 0.05	0.35 ± 0.05
trans Fat (g/d)	7.8 ± 1.3	7.5 ± 1.1	7.3 ± 1.1	7.1 ± 1.1	6.4 ± 1.0
Processed meat (servings/d)	0.30 ± 0.16	0.30 ± 0.16	0.30 ± 0.17	0.28 ± 0.16	0.25 ± 0.16
Red meat (servings/d)	1.6 ± 0.41	1.6 ± 0.38	1.6 ± 0.36	1.5 ± 0.33	1.3 ± 0.34
Fruit intake (servings/d)	2.0 ± 0.75	2.3 ± 0.75	2.4 ± 0.77	2.4 ± 0.73	2.2 ± 0.70
Vegetable intake (servings/d)	3.0 ± 1.0	3.1 ± 0.97	3.2 ± 0.92	3.0 ± 0.88	2.8 ± 0.87
Vitamin D from dairy products (IU/d)	81 ± 22	135 ± 29	197 ± 39	256 ± 50	328 ± 69
Baseline current dairy product intake (servings/1000 kcal per day)[3]	1.0 ± 0.31	1.2 ± 0.32	1.3 ± 0.31	1.5 ± 0.33	1.6 ± 0.37

[1] MET-h, metabolic equivalent task hours; OC, oral contraceptive. Linear and logistic regression analyses were used to assess linear trends of participant characteristics across quintiles and are significant ($P \leq 0.05$) unless noted otherwise.

[2] Mean ± SD (all such values).

[3] Denotes current risk factors assessed at baseline (1997).

[4] NS.

vitamin D from dairy products, and lower intakes of sugar-sweetened beverages, coffee, cereal fiber, processed meat, red meat, and *trans* fat. Individuals with higher dairy product intakes during high school also had higher current dairy product intakes. The correlation between dairy product intake during high school and current dairy product intake was 0.34. Baseline characteristics of the study population according to quintile of current dairy product intake are shown elsewhere (*see* Supplemental Table 1 under "Supplemental data" in the online issue).

During 7 y of follow-up, we ascertained 550 incident cases of T2D. After adjustment for age, dairy product intake during high school was significantly inversely associated with T2D (**Table 2**). The RR for individuals in the highest quintile of intake was 0.59 (95% CI: 0.46, 0.76; *P*-trend <0.0001) compared with those in the lowest quintile. After further adjustment for total energy intake during high school and BMI at age 18 y, the association persisted (RR: 0.62; 95% CI: 0.48, 0.81; *P*-trend = 0.0001). Additional adjustment for other high school risk factors did not change the estimate. When we adjusted for current risk factors, the association persisted (RR: 0.73; 95% CI: 0.54, 0.97; *P*-trend = 0.02), which suggested that the putative effect of dairy product intake during high school on T2D was not fully mediated through current risk factors. The addition of current dairy product intake to the model attenuated the association (RR: 0.78; 95% CI: 0.58, 1.06; *P*-trend = 0.09). The addition of height did not change the estimate (*P*-trend = 0.09). However, further adjustment for weight change since age 18 y attenuated the association (RR: 0.82; 95% CI: 0.61, 1.12; *P*-trend = 0.19). Similar results were observed in the analysis of linear effects (*see* Supplemental Table 2 under "Supplemental data" in the online issue).

When we examined the association of dairy product intake during high school by fat content, a significant inverse association was found in the multivariate analyses of high-fat, but not of low-fat, dairy product intake (**Table 3**). The results from the dose-response analysis, when the estimates were more comparable, suggested that there was less difference between low-fat (RR: 0.77; 95% CI: 0.58, 1.00; *P* = 0.05) and high-fat (RR: 0.77; 95% CI: 0.65, 0.92 *P* = 0.003) dairy product intake after adjustment for high school covariates (*see* Supplemental Table 3 under "Supplemental data" in the online issue). Our analyses of individual dairy foods found no significant associations, which suggests that the inverse association was not driven by any one dairy food but rather by a combination of foods (data not shown).

The results from stratified analyses suggest that the association between dairy product intake during high school and T2D varied by level of physical activity during high school and BMI at age 18 y (*see* Supplemental Table 4 under "Supplemental data" in the online issue), although tests for interaction were not significant (*P*-interaction = 0.19 and 0.52, respectively). There was no apparent effect modification by glycemic load during high school (*P*-interaction = 0.68). The test for interaction between dairy product intake during high school and dairy product intake in adulthood was marginally significant (*P*-interaction = 0.049). Stratified analyses suggested that the association between dairy product intake during high school and T2D was stronger in those with high intake of dairy products in adulthood and that the association between intake of dairy products in adulthood and T2D was stronger in those with high dairy product intakes during high school (*see* Supplemental Table 5 under "Supplemental data" in the online issue).

We also found a significant inverse association between current dairy product intake and T2D in the multivariate-adjusted model (RR: 0.75; 95% CI: 0.55, 1.02; *P*-trend = 0.03) (**Table 4**). This association was attenuated after adjustment for dairy product intake during high school (RR: 0.79; 95% CI: 0.57, 1.09; *P*-trend = 0.09). In our analysis by dairy fat, a moderate inverse assoiation was observed in multivariate-adjusted models of both low-fat and high-fat dairy product intake (**Table 5**). Additional adjustment for hypertension slightly attenuated the association for total dairy (RR: 0.78; 95% CI: 0.57, 1.06; *P*-trend = 0.06), low-fat dairy (RR: 0.76; 95% CI: 0.56, 1.03; *P*-trend = 0.04), and

TABLE 2

RRs and 95% CIs of type 2 diabetes in participants in the Nurses' Health Study by quintile of total dairy product intake during high school[1]

	Quintile of dairy product intake					
	1	2	3	4	5	*P*-trend
Median intake (daily servings/1000 kcal)	0.5	0.9	1.2	1.5	2.0	
No. of cases	149	108	110	88	95	
Person-years	57,134	58,181	58,352	58,512	58,524	
Model [RR (95% CI)][2]						
1	1.00	0.74 (0.58, 0.95)	0.73 (0.57, 0.93)	0.57 (0.44, 0.74)	0.59 (0.46, 0.76)	<0.0001
2	1.00	0.74 (0.58, 0.95)	0.75 (0.58, 0.96)	0.61 (0.47, 0.80)	0.62 (0.48, 0.81)	0.0001
3	1.00	0.75 (0.58, 0.97)	0.77 (0.59, 0.99)	0.63 (0.48, 0.83)	0.62 (0.47, 0.83)	0.0006
4	1.00	0.85 (0.65, 1.09)	0.89 (0.68, 1.16)	0.73 (0.55, 0.97)	0.73 (0.54, 0.97)	0.02
5	1.00	0.86 (0.66, 1.12)	0.93 (0.71, 1.21)	0.77 (0.58, 1.03)	0.78 (0.58, 1.06)	0.09
6	1.00	0.86 (0.66, 1.11)	0.96 (0.73, 1.25)	0.79 (0.59, 1.06)	0.82 (0.61, 1.12)	0.19

[1] Dairy products include skim/low-fat milk, skim chocolate milk, instant breakfast, sherbet, yogurt, cottage/ricotta cheese, whole milk, whole chocolate milk, cream cheese, other cheeses, ice cream, milkshakes, and butter.

[2] Model 1 was adjusted for age. Model 2 was adjusted for age, BMI at age 18 y, and total energy intake in high school. Model 3 was adjusted as for model 2 plus high school variables: sugar-sweetened beverage consumption, glycemic load, physical activity, smoking, alcohol use, and intakes of coffee, processed meat, and *trans* fat. Model 4 was adjusted as for model 3 plus adult risk factors: smoking status, alcohol use, physical activity, family history of type 2 diabetes, oral contraceptive use, hormone replacement therapy, polyunsaturated:saturated fat ratio, glycemic load, and intakes of coffee, sugar-sweetened beverages, cereal fiber, *trans* fat, processed meat, and total energy. Model 5 was adjusted as for model 4 plus dairy product intake as an adult. Model 6 was adjusted as for model 5 plus weight change since age 18 y.

TABLE 3
RRs and 95% CIs of type 2 diabetes in participants in the Nurses' Health Study II by quintile of low-fat and high-fat dairy product intake during high school

	Quintile of dairy product intake					
	1	2	3	4	5	*P*-trend
Low-fat dairy foods[1]						
Median intake (daily servings/1000 kcal)	0	0.04	0.09	0.28	0.94	
No. of cases	127	125	102	116	80	
Person-years	57,269	58,405	58,007	58,112	58,911	
Model [RR (95% CI)][2]						
1	1.00	0.98 (0.77, 1.26)	0.85 (0.65, 1.11)	1.08 (0.84, 1.40)	0.83 (0.62, 1.10)	0.28
2	1.00	0.96 (0.75, 1.23)	0.83 (0.63, 1.07)	0.96 (0.74, 1.24)	0.76 (0.57, 1.01)	0.09
3	1.00	1.01 (0.78, 1.29)	0.86 (0.66, 1.13)	0.99 (0.76, 1.29)	0.74 (0.54, 1.01)	0.05
4	1.00	1.04 (0.81, 1.35)	0.92 (0.70, 1.21)	1.16 (0.88, 1.52)	0.88 (0.64, 1.20)	0.39
5	1.00	1.04 (0.81, 1.35)	0.93 (0.71, 1.22)	1.17 (0.89, 1.53)	0.91 (0.66, 1.25)	0.55
6	1.00	1.03 (0.80, 1.34)	0.88 (0.67, 1.15)	1.14 (0.87, 1.50)	0.90 (0.65, 1.25)	0.61
High-fat dairy foods[3]						
Median intake (daily servings/1000 kcal)	0.24	0.47	0.76	1.15	1.74	
No. of cases	126	92	121	116	95	
Person-years	57,914	58,351	58,175	58,006	58,257	
Model [RR (95% CI)][2]						
1	1.00	0.73 (0.56, 0.96)	0.87 (0.68, 1.12)	0.78 (0.60, 1.00)	0.60 (0.46, 0.79)	0.001
2	1.00	0.76 (0.58, 0.99)	0.92 (0.71, 1.19)	0.85 (0.65, 1.10)	0.68 (0.52, 0.89)	0.02
3	1.00	0.73 (0.55, 0.96)	0.84 (0.64, 1.10)	0.77 (0.58, 1.02)	0.59 (0.43, 0.81)	0.005
4	1.00	0.74 (0.56, 0.98)	0.89 (0.68, 1.17)	0.88 (0.66, 1.17)	0.67 (0.49, 0.92)	0.06
5	1.00	0.75 (0.57, 0.99)	0.91 (0.69, 1.20)	0.90 (0.68, 1.20)	0.71 (0.51, 0.97)	0.12
6	1.00	0.79 (0.60, 1.05)	0.97 (0.73, 1.27)	0.97 (0.72, 1.29)	0.77 (0.56, 1.06)	0.28

[1] Includes skim/low-fat milk, skim chocolate milk, instant breakfast, sherbet, yogurt, cottage/ricotta cheese.

[2] Model 1 was adjusted for age. Model 2 was adjusted for age, BMI at age 18 y, and total energy intake in high school. Model 3 was adjusted as for model 2 plus high school variables: sugar-sweetened beverage consumption, glycemic load, physical activity, smoking, alcohol use, and intakes of coffee, processed meat, and *trans* fat. Model 4 was adjusted as for model 3 plus adult risk factors: smoking status, alcohol use, physical activity, family history of type 2 diabetes, oral contraceptive use, hormone replacement therapy, polyunsaturated:saturated fat ratio, glycemic load, and intakes of coffee, sugar-sweetened beverages, cereal fiber, *trans* fat, processed meat, and total energy. Model 5 was adjusted as for model 4 plus low- or high-fat dairy product intake as an adult. Model 6 was adjusted as for model 5 plus weight change since age 18 y.

[3] Includes whole milk, whole chocolate milk, cream cheese, other cheeses, ice cream, milkshakes, and butter.

high-fat dairy (RR: 0.75; 95% CI: 0.55, 1.03; *P*-trend = 0.07) product intakes. Similar, though slightly less, robust results were observed in the dose-response analysis for total dairy (RR: 0.83; 95% CI: 0.70, 0.98; *P* = 0.03), low-fat dairy (RR: 0.84; 95% CI: 0.69, 1.03; *P* = 0.10), and high-fat dairy (RR: 0.79; 95% CI 0.62, 1.01; *P* = 0.06) product intakes in the fully adjusted models.

As shown in **Figure 1**, individuals who had both a high current dairy product intake and high dairy product intake during high school had the lowest risk of developing T2D compared with consistent low dairy product consumers (RR: 0.57; 95% CI: 0.40, 0.82) (*see* Supplemental Table 6 under "Supplemental data" in the online issue). There was a trend toward a decreasing risk of T2D in current high dairy product consumers with increasing

TABLE 4
RRs and 95% CIs of type 2 diabetes in participants in the Nurses' Health Study by current dairy product intake

	Quintile of total dairy product intake					
	1	2	3	4	5	*P*-trend
Median intake (daily servings/1000 kcal)	0.62	0.96	1.25	1.58	2.14	
No. of cases	141	118	119	89	83	
Person-years	57,622	57,957	58,152	58,382	58,590	
Model [RR (95% CI)][1]						
1	1.00	0.83 (0.65, 1.06)	0.85 (0.66, 1.09)	0.63 (0.48, 0.82)	0.62 (0.47, 0.81)	<0.0001
2	1.00	0.84 (0.65, 1.08)	0.90 (0.70, 1.15)	0.71 (0.54, 0.93)	0.72 (0.55, 0.95)	0.009
3	1.00	0.89 (0.69, 1.15)	0.97 (0.76, 1.25)	0.74 (0.56, 0.97)	0.76 (0.58, 1.01)	0.02
4	1.00	0.90 (0.70, 1.17)	0.98 (0.76, 1.28)	0.74 (0.55, 0.99)	0.75 (0.55, 1.02)	0.03

[1] Model 1 was adjusted for age. Model 2 was adjusted as for model 1 plus BMI and total energy intake. Model 3 was adjusted as for model 2 plus family history of diabetes, smoking status, physical activity, alcohol use, oral contraceptive use, and hormone replacement therapy. Model 4 was adjusted as for model 3 plus polyunsaturated:saturated fat ratio, glycemic load, and intakes of cereal fiber, *trans* fat, processed meat, carbonated soft drinks, fruit drinks, and coffee.

TABLE 5
RRs and 95% CIs of type 2 diabetes in participants in the Nurses' Health Study II by current low-fat and high-fat dairy product intake

	Quintile of dairy intake					
	1	2	3	4	5	*P*-trend
Low-fat dairy foods[1]						
Median intake (daily servings/1000 kcal)	0.18	0.44	0.66	0.96	1.44	
No. of cases	134	130	105	96	85	
Person-years	57,852	58,013	58,077	58,233	58,529	
Model [RR (95% CI)][2]						
1	1.00	0.97 (0.76, 1.24)	0.78 (0.61, 1.01)	0.74 (0.56, 0.96)	0.67 (0.51, 0.88)	0.0007
2	1.00	0.95 (0.74, 1.22)	0.80 (0.61, 1.03)	0.77 (0.59, 1.01)	0.76 (0.58, 1.01)	0.02
3	1.00	0.99 (0.77, 1.27)	0.85 (0.65, 1.11)	0.82 (0.62, 1.07)	0.78 (0.59, 1.03)	0.04
4	1.00	0.99 (0.76, 1.27)	0.86 (0.65, 1.13)	0.82 (0.61, 1.09)	0.74 (0.54, 1.01)	0.03
High-fat dairy foods[3]						
Median intake (daily servings/1000 kcal)	0.19	0.33	0.47	0.66	1.14	
No. of cases	114	126	105	111	88	
Person-years[4]	57,583	57,539	57,520	57,553	57,539	
Model [RR (95% CI)][2]						
1	1.00	1.10 (0.85, 1.42)	0.94 (0.72, 1.23)	1.00 (0.77, 1.30)	0.77 (0.58, 1.01)	0.03
2	1.00	1.01 (0.78, 1.31)	0.85 (0.65, 1.12)	0.95 (0.73, 1.24)	0.76 (0.57, 1.01)	0.04
3	1.00	1.02 (0.79, 1.33)	0.87 (0.66, 1.15)	0.99 (0.75, 1.29)	0.79 (0.59, 1.06)	0.08
4	1.00	0.99 (0.76, 1.29)	0.83 (0.62, 1.10)	0.91 (0.69, 1.20)	0.72 (0.53, 0.99)	0.03

[1] Includes skim/low-fat milk, sherbet, yogurt, and cottage/ricotta cheese.

[2] Model 1 was adjusted for age. Model 2 was adjusted as for model 1 plus BMI and total energy intake. Model 3 was adjusted as for model 2 plus family history of diabetes, smoking status, physical activity, alcohol use, oral contraceptive use, and hormone replacement therapy. Model 4 was adjusted as for model 3 plus polyunsaturated:saturated fat ratio, glycemic load, and intakes of cereal fiber, *trans* fat, processed meat, carbonated soft drinks, fruit drinks, coffee, and low- or high-fat dairy products.

[3] Includes whole milk, cream, sour cream, cream cheese, other cheeses, ice cream, and butter.

[4] Category for missing has 6 cases and 2969 person-years.

level of dairy product intake during high school. This trend was supported by our finding, that the association between current dairy product intake and T2D was stronger in those with high dairy product intakes during high school, from the test for interaction using 1 term representing median values of tertiles (*P*-interaction = 0.049).

DISCUSSION

In this large prospective cohort study of US women, greater dairy product intake during high school was significantly associated with a lower risk of T2D, but the association was attenuated after adjustment for current dairy product intake and weight change since age 18 y. This suggests that some of the benefit of dairy product intake during high school may be due to the persistence of the consumption pattern during adulthood, which was shown by the joint analysis. Current dairy product intake was moderately inversely associated with T2D, and women who had both high current intakes of dairy products and high intakes during high school had a markedly lower risk of T2D compared with women with consistent low intakes. This finding suggests that persistently high dairy product consumption during the life course may have potential benefits for T2D risk. To our knowledge, no other study has examined dairy consumption in adolescents in relation to risk of T2D in adulthood. Previous studies (5, 6) in adults have found inverse associations between dairy product intake and T2D, particularly for low-fat dairy product intakes. In our study, we observed inverse associations of the same magnitude for current low-fat and high-fat dairy product intakes, and the inverse association between dairy product intake during high school and T2D appeared to be driven by high-fat dairy product intake. One possible reason for this finding was the low availability and infrequent consumption of low-fat dairy products when these women were in high school.

The beneficial effect of dairy product intake on T2D risk may be mediated in part by the effect of dairy product intake on precursors of disease, including body weight (19), hypertension (20, 21), and glucose homeostasis (5). Certain components in dairy products, such as calcium, magnesium, lactose, and dairy protein may promote weight loss and reduce blood pressure (5). However findings from recent trials and prospective cohort studies do not support a role of dairy products in weight regulation (19, 22), which is consistent with our findings for current dairy product intakes, whereby the associations were independent of BMI. Conjugated linoleic acid, created by bacteria in the gut of ruminants, has been shown to reduce body weight in animals, but these effects have not been observed in humans consuming dairy foods (23). In the Dietary Approaches to Stop Hypertension (DASH) trial, dietary patterns containing 3 servings of low-fat milk and other dairy products daily resulted in blood pressure reductions that were nearly double those achieved with a diet high in fruit and vegetables but low in dairy products (21). Such effects may not be observed with high-fat dairy products because of the potential mitigating effects of saturated fat. Milk proteins such as whey may have insulinotropic properties with a relatively low GL, which may improve glucose tolerance (24). Whereas dairy product intake may also be associated with a low GL, some studies of the effects of dairy product intake on T2D, including ours, found independent associations after adjustment for GL (25, 26). In addition, other dairy product components,

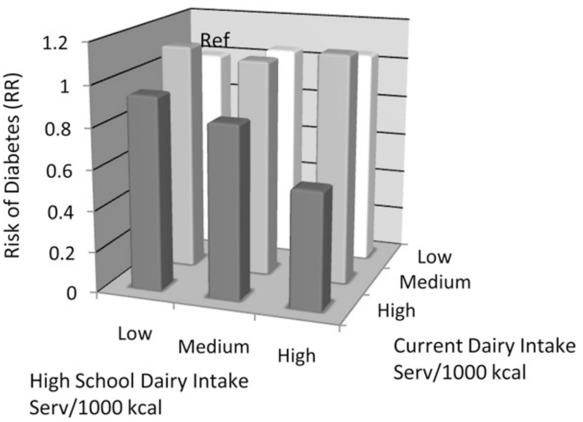

FIGURE 1. Joint analysis between current dairy product intake and dairy product intake during high school in relation to type 2 diabetes (T2D) risk. Tertiles (low, medium, or high) of dairy product intake in high school and adulthood were cross-classified into a single categorical variable and evaluated for risk of T2D by using the low-low category as the reference (Ref). High current dairy product intakes are depicted by dark gray bars, medium intakes by light gray bars, and low intakes by white bars. Models were adjusted for age, current BMI, total energy intake, family history of diabetes, smoking status, physical activity, alcohol use, oral contraceptive use, hormone replacement therapy, polyunsaturated:saturated fat ratio, glycemic load, and intakes of cereal fiber, *trans* fat, processed meat, carbonated soft drinks, fruit drinks, and coffee. RRs (95% CI) for current intake–intake during high school: Low-Low (reference), 1.00; Medium-Low, 1.11 (0.81, 1.52); High-Low, 0.94 (0.63, 1.41); Low-Medium, 1.05 (0.76, 1.46); Medium-Medium, 1.06 (0.78, 1.45); High-Medium, 0.84 (0.59, 1.21); Low-High, 1.05 (0.72, 1.52); Medium-High, 1.12 (0.81, 1.55); and High-High, 0.57 (0.39, 0.82). Median current dairy product intake (servings/1000 kcal): Low = 0.76, Medium = 1.25, and High = 1.89. Median dairy product intake during high school (servings/1000 kcal): Low = 0.65; Medium = 1.16; and High = 1.78. *P*-interaction = 0.049 based on the cross-product of median values of tertiles. Serv, servings.

including medium-chain fatty acids, calcium, vitamin D, and magnesium, may reduce insulin resistance or inflammation (5, 6, 27). Recently, Mozaffarian et al (28) found that circulating *trans*-palmitoleate, which is a *trans* fatty acid derived primarily from dairy foods and other ruminant *trans* fat, was associated with lower insulin resistance, presence of atherogenic dyslipidemia, and incident diabetes Whole-fat dairy product consumption was most strongly associated with higher *trans*-palmitoleate concentrations (28), which may partially explain the inverse associations observed between high-fat dairy product intake and T2D in our analyses. Additional exploration of this potential mechanism is warranted. The effect of dairy product intake on T2D risk may also be mediated by the ability of dairy products to increase circulating concentrations of IGF-I (29, 30). IGF-1 is thought to enhance glucose uptake and has been associated with impaired glucose tolerance and T2D (31), although more studies are needed to fully understand the role of IGF-I and other components of the IGF axis in T2D risk.

Little is known about how diet during early periods of life affect the risk of T2D in later years. Findings from the Bogalusa Heart Study indicate that risk factors for T2D, such as high blood pressure, hyperinsulinemia, and dyslipidemia, can start to increase in childhood and are able predict the risk of cardiometabolic dysfunction in adulthood (32, 33). It is possible that the beneficial effect of dairy product intake on T2D exists during adolescence to modulate concentrations of these risk factors and provide additional protection from T2D over that imparted by current dairy product consumption, which agrees with the findings from our joint analysis.

Because greater adult height has been associated with a reduced risk of insulin resistance and T2D (2–4) and because adult height and leg length are thought to be markers of childhood nutritional status, growth, and IGF-I concentrations (34, 35), childhood IGF-I may underpin the height-T2D association. Because we did not have blood measurements of IGF-I that corresponded to dairy product intake data during high school, we were not able to directly evaluate this hypothesis. However, adjustment for height, a potential proxy for childhood IGF-I, did not change our estimates, which suggests that childhood IGF-I may not be a mediator, although this finding is limited by height not being a perfect marker. It is also possible that higher IGF-I concentrations during adolescence may carry over into adulthood. Whether the effect of dairy product intake in adolescence on T2D risk is mediated by IGF-I or other components in dairy products is unknown.

It may also be possible that higher dairy product consumption is associated with an overall healthy diet and lifestyle, which may track through the life course and ultimately lowers the risk of T2D. In our analysis, adjustment for weight change since age 18 y attenuated the association between dairy product intake during high school and T2D, and those with higher dairy product intakes during high school had less weight gain from age 18 y than did those with lower intakes, which suggests possible confounding by other factors associated with weight change. Despite the adjustment for potential confounding by many high school and current risk factors, residual confounding remains a potential limitation. The HS-FFQ has been shown to be reasonably valid and reproducible (9, 10) when administered several decades later; however, recall of dairy product intake during high school likely includes some random measurement error, which may have attenuated our results. The prospective design, in which cases were ascertained after return of the HS-FFQ, limited the possibility of recall bias; however, some participants may have developed higher BMIs—a precursor to T2D—before the collection of data on dairy product intake during high school.

For the public health application of our findings, other potential benefits and risks associated with dairy product intake should be considered. Consumption of milk has been displaced by sugar-sweetened beverages, which are associated with obesity (36) and T2D (37). Therefore, replacement of sugary beverages with low-fat milk may be advantageous. In addition, low-fat dairy product intake is associated with a reduced risk of coronary heart disease (38), colon cancer (39), and gout (40); however, inconsistent findings have been reported for breast cancer (41), and dairy product intake may increase the risk of prostate cancer (42). Additional confirmation of these findings and a risk-benefit assessment including consideration of the environmental impact of dairy farming—including the use of corn-based animal feeds and the health effects of consuming dairy products from cows treated with recombinant bovine somatotropin or kept lactating for extended periods—are needed before clear public health recommendations for dairy product intakes can be made.

In conclusion, higher consumption of dairy products during adolescence is associated with a reduced risk of T2D in adulthood and appears to provide additional benefit to that observed with current dairy product intakes, possibly because of the persistence of the consumption pattern. These findings are novel and warrant further evaluation, including examination of the potential mechanisms.

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