Dairy Consumption, Type 2 Diabetes, and Changes in Cardiometabolic Traits: A Prospective Cohort Study of Middle-Aged and Older Chinese in Beijing and Shanghai

Geng Zong,[1] Qi Sun,[2] Danxia Yu,[3] Jingwen Zhu,[1] Liang Sun,[1] Xingwang Ye,[1] Huaixing Li,[1] Qianlu Jin,[1] He Zheng,[1] Frank B. Hu,[2,4] and Xu Lin[1]

OBJECTIVE

To prospectively investigate associations of dairy consumption with risk of type 2 diabetes and changes of cardiometabolic traits.

RESEARCH DESIGN AND METHODS

In 2005, 2,091 middle-aged and older Chinese men and women were recruited and followed for 6 years. Baseline dairy consumption was assessed by a 74-item food frequency questionnaire. Erythrocyte fatty acids were analyzed by gas chromatography coupled with flame ion detector. Cardiometabolic traits were measured at both baseline and follow-up visits.

RESULTS

Only 1,202 (57.5%) participants reported any dairy consumption, with a median intake of 0.89 (interquartile range 0.19–1.03) serving/day. Compared with nonconsumers, the relative risks (RRs) of type 2 diabetes among those having 0.5–1 serving/day and >1 serving/day were 0.70 (95% CI 0.55–0.88) and 0.65 (0.49–0.85), respectively, after multivariate adjustment ($P_{trend} < 0.001$), which were attenuated by further adjusting for changes in glucose during follow-up ($P_{trend} = 0.07$). Total dairy consumption was associated with favorable changes in glucose, waist circumference, BMI, diastolic blood pressure (all $P_{trend} < 0.05$), and systolic blood pressure ($P_{trend} = 0.05$) after multivariate adjustment, including baseline values of dependent variables. Erythrocyte *trans*-18:1 isomers were significantly correlated with total dairy consumption ($r_s = 0.37$, $P_{trend} < 0.001$), and these dairy food biomarkers were associated with a lower risk of type 2 diabetes. The RR of type 2 diabetes comparing extreme quartiles of *trans*-18:1 isomers was 0.82 (0.65–1.04, $P_{trend} = 0.02$), which was attenuated after adjustment for dairy consumption ($P_{trend} = 0.15$).

CONCLUSIONS

Dairy consumption was associated with a significantly lower risk of type 2 diabetes and favorable changes of cardiometabolic traits in Chinese.

Diabetes Care 2014;37:56–63 | DOI: 10.2337/dc13-0975

[1]Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences and Graduate University of the Chinese Academy of Sciences, Shanghai, China

[2]Department of Nutrition, Harvard School of Public Health, and Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

[3]Division of Epidemiology, Vanderbilt University Medical Center, Nashville, TN

[4]Department of Epidemiology, Harvard School of Public Health, Boston, MA

Corresponding author: Xu Lin, xlin@sibs.ac.cn.

Received 24 April 2013 and accepted 4 September 2013.

This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc13-0975/-/DC1.

The epidemic of type 2 diabetes has emerged as a major global public health problem in the past several decades (1). In China, the prevalence of type 2 diabetes reached 9.7% in 2008, translating into 92.4 million diabetic patients (2). In this regard, effective methods are urgently needed for disease prevention.

Milk protein has been reported to be positively correlated with type 1 diabetes risk (3), although several bioactive components in dairy products may potentially lower risk of type 2 diabetes (4). However, only some prospective studies have observed inverse associations between dairy consumption and risk of diabetes (5–7), whereas others reported null findings (5,8–12). In this regard, prospectively investigating associations between dairy consumption and cardiometabolic traits related to diabetes may shed light onto the relationship between dairy consumption and risks of diabetes. Nevertheless, current findings in dairy consumption and cardiometabolic traits, such as glucose homeostasis and adiposity, remain inconclusive (12–15).

In most existing studies, dairy consumption was assessed by self-reported food frequency questionnaires (FFQs), which may be subject to measurement errors (16). Several circulating fatty acids (e.g., 15:0, 17:0) have been suggested as biomarkers of dairy consumption (17–19), and they were reported to be associated with lower risk of diabetes (20,21) or cardiovascular disease (22,23). Previously, we found that erythrocyte *trans*-18:1 isomers are associated with dairy product consumption and lower prevalence of metabolic syndrome and diabetes in middle-aged and older Chinese men and women (24). These findings indicate that dairy products could be an important source for *trans*-18:1 isomers in this population. However, the cross-sectional nature of the analysis limited causal inference.

In the current study, we aimed to prospectively investigate the associations of dairy consumption with risk of type 2 diabetes and changes of cardiometabolic traits during follow-up. We further evaluated whether erythrocyte *trans*-18:1 isomers, as biomarkers of dairy food intake, are also associated with risk of diabetes.

RESEARCH DESIGN AND METHODS

The study population included male and female Chinese aged 50–70 years who participated in the Nutrition and Health of Aging Population in China study, a population-based, prospective study (25,26). In 2005, 3,289 participants were enrolled by multistage sampling from two urban districts and one rural district in Beijing and Shanghai, two representative municipals of northern and southern China. After 6 years of follow-up, 2,529 participants were revisited. For the current study, individuals with prevalent diabetes (n = 331) or implausible daily energy intake ($<$800 or $>$4,000 kcal/day for men and $<$500 or $>$3,500 kcal/day for women) (n = 107) at baseline were excluded, therefore the final analyses included 2,091 individuals. The study protocol was approved by the Institutional Review Board of the Institute for Nutritional Sciences, and all participants provided written informed consent at both baseline and follow-up.

Data Collection

Data on demographics, health status, lifestyle, and physical activities were collected by standardized questionnaires. Education attainment (0–6 years, 7–9 years, or $\geq$10 years), smoking (current, former, or never), physical activity (low, moderate, or high), and family history of chronic disease (yes or no) were defined as previously described (25). Alcohol drinking was classified into three groups: high ($>$30 g/day for men and $>$15 g for women), moderate (5–30 g/day for men and 5–15 g/day for women), and low ($<$5 g for both sexes). After overnight fasting, participants were invited to take a physical examination. Body weight, height, waist circumference, and blood pressure were measured by standard protocol (25).

Fasting venous blood samples were collected at both baseline and follow-up; EDTA was used as the anticoagulant. Plasma and erythrocytes were then stored at -80°C before analysis (25). Glucose, triglyceride, HDL cholesterol, LDL cholesterol, and total cholesterol were measured on an automatic analyzer (Hitachi 7080, Tokyo, Japan) with commercial reagents (Wako Pure Chemical Industries, Osaka, Japan). Baseline fasting insulin level was measured by radioimmunoassay (LINCO Research, St. Charles, MO) (27). Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated as insulin (μU/mL) $\times$ glucose (mmol/L) / 24. HbA_{1c} from resolved erythrocytes was measured with an automated immunoassay (Tina-Quant Hemoglobin A1C II; Roche Diagnostics, Indianapolis, IN) and was standardized according to the Diabetes Control and Complications Trial/National Glycohemoglobin Standardization Program (28). Erythrocyte fatty acids were measured by gas chromatography coupled with positive chemical ionization (Agilent 6890 GC-5975B) as previously described (27). The coefficient of variation for erythrocyte *trans*-18:1 isomers was 14.5%.

Assessment of Dairy and Other Food Intake

Diet was assessed with a 74-item FFQ modified from a validated questionnaire used in the 2002 National Nutrition and Health Survey in China (29). There were five items for dairy products, including milk, yogurt, ice cream, milk powder, and other products. Of them, milk (1,655 persons), yogurt (949 persons), and ice cream (561 persons) were recorded as serving, and their serving sizes were 250, 250, and 150 g, respectively. Milk powder and other products were recorded as gram, and their serving sizes were estimated according to the following: 40 g for milk powder (299 persons), 40 g for milk flake (5 persons), 30 g for cheese (7 persons), 30 g for cream (2 persons), 100 g for cream cake (3 persons), and 125 g for evaporated milk (1 person). Dietary glycemic index (GI) was estimated as the weighted average GIs for all carbohydrate-containing foods by the International Tables of Glycemic Index and Glycemic Load Values (30). Nutrients were estimated according to the Chinese Food Composition Tables (31).

Definition of Type 2 Diabetes

Incident type 2 diabetes was defined if one of the following criteria was met: *1*)

self-reported clinical diagnosis of diabetes, *2*) use of any oral hypoglycemic medication or insulin, or *3*) fasting glucose level ≥7.0 mmol/L.

Statistical Analysis

Participants were categorized into four groups (no consumption [0–0.5 serving/day], 0.5–1 serving/day, and >1 serving/day) on the basis of their intake of total dairy products. To evaluate the consumption of milk or other dairy products separately, the participants were classified as no consumption, 0–0.5 serving/day, and >0.5 serving/day.

Characteristics of the participants according to total dairy consumption groups were compared by ANOVA for continuous variables and χ^2 test for categorical variables. Because of the high incidence of type 2 diabetes in the study population, relative risks (RRs), CIs, and *P* for trend for type 2 diabetes were estimated with log-Poisson models, which provided consistent, but not fully efficient estimates of the RRs and CIs (32). Age, sex, region (Beijing, Shanghai), and residence (urban, rural) were adjusted in model 1. Smoking status, BMI, family history of diabetes, and dietary fiber intake were controlled in model 2 according to the results from backward stepwise regression based on model 1, which included education attainment, smoking status, drinking status, family history of diabetes, physical activity, total energy intake, BMI, dietary carbohydrate and fat (% of total energy) intake, dietary GI, and red meat, vegetable, fiber, and soymilk intake as potential confounding factors. We further adjusted for changes of cardiometabolic traits during follow-up based on model 2 to investigate whether these changes contributed to the dairy–diabetes association. Analysis was stratified by age (median <59 or ≥59 years), sex, BMI (<25 or ≥25 kg/m^2), and HOMA-IR (median <3.23 or ≥3.23). When modeling associations of erythrocyte *trans*-18:1 isomers and risk of type 2 diabetes, other erythrocyte *trans* fatty acids (*trans*-18:2n-6 9c12t and *trans*-18:2n-6 9t12c) were also adjusted in model 2, and total dairy intake was adjusted in model 3. Differences in changes of cardiometabolic traits according to total dairy consumption categories were compared in general linear models after multivariate adjustment, including the corresponding value of each metabolic trait at baseline. Spearman correlation coefficients between dairy intake and erythrocyte *trans* fatty acids were calculated after controlling for age, sex, region, residence, and total energy intake. All analyses were performed with Stata 9.2 (Stata Corp, College Station, TX). Two-sided $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of Study Population

Only 1,202 (57.5%) participants consumed any dairy product at baseline, and their median consumption was 0.89 (interquartile range 0.19–1.03) serving/day. The baseline characteristics of participants according to total dairy consumption are shown in Table 1. Participants with higher dairy consumption at study entry were younger and more likely to be women, nonsmokers, and northern and urban residents and had education ≥10 year and family history of diabetes. Moreover, they had lower physical activity and higher BMI. Dairy consumers also had lower carbohydrate and dietary GI but higher intakes of fat, red meat, vegetables, dietary fiber, and soymilk.

Dairy Consumption and Risk of Type 2 Diabetes

After 6 years of follow-up, 24.1% (*n* = 504) of the study participants had type 2 diabetes. Compared with individuals without dairy consumption, RR (95% CI) of type 2 diabetes was 0.73 (0.58–0.92) for those consuming 0.5–1 serving/day and 0.67 (0.52–0.88) for those consuming >1 serving/day, after adjustment for age, sex, region, and residence (*P* for trend < 0.001) (Table 2). The associations were not changed after multivariate adjustment in model 2. Those who had 0.5–1.0 serving/day and >1 serving/day of total dairy consumption showed a 29% (0.71 [0.57–0.89]) and 35% (0.65 [0.50–0.85]) lower risk of type 2 diabetes (*P* for trend < 0.001), respectively. The dairy–diabetes association did not change by including

Table 1—Characteristics of participants according to total dairy product consumption (*n* = 2,091)

	Total dairy product consumption (serving/day)			
	None	≤0.5	0.5–1.0	>1
No. participants	889	470	399	333
Age (years)	58.7 (6.0)	58.4 (5.8)	59.0 (6.4)	57.7 (6.3)
Male	433 (48.7)	194 (41.3)	146 (36.6)	86 (25.8)
Northern residents	280 (31.5)	236 (50.2)	219 (54.9)	218 (65.5)
Urban residents	160 (18.0)	182 (38.7)	252 (63.2)	282 (84.7)
Family history of diabetes	67 (7.5)	44 (9.4)	48 (12.0)	52 (15.6)
Current smoking	294 (33.1)	137 (29.2)	83 (20.8)	46 (13.8)
Moderate drinking	86 (9.7)	43 (9.2)	40 (10.0)	26 (7.8)
Education attainment ≥10 years	62 (7.0)	80 (17.0)	126 (31.6)	127 (38.1)
Physical activity, high	521 (58.6)	256 (54.5)	180 (45.1)	142 (42.6)
BMI (kg/m^2)	23.8 (3.5)	24.3 (3.5)	24.8 (3.6)	24.9 (3.6)
Erythrocyte *trans*-18:1 isomers (%)*	0.18 (0.06)	0.19 (0.05)	0.23 (0.06)	0.23 (0.07)
Total energy intake (kcal/day)	2,264 (666)	2,237 (652)	2,170 (584)	2,298 (580)
Carbohydrate (% in energy)	63.9 (9.4)	60.9 (9.6)	56.9 (7.8)	54.6 (7.1)
Fat (% in energy)	24.8 (7.9)	27.6 (8.3)	31.1 (7.2)	32.7 (6.5)
Red meat intake (g/day)	34.5 (40.2)	41.0 (44.7)	44.3 (51.9)	51.2 (49.7)
Vegetable intake (g/day)	323.2 (211.8)	350.2 (216.3)	390.1 (203.5)	425.4 (257.9)
Fiber intake (g/day)	11.1 (4.9)	12.9 (5.9)	13.6 (5.6)	15.8 (6.5)
Soymilk intake (g/day)	13.6 (47.5)	26.2 (54.2)	35.2 (64.9)	47.2 (75.2)
Glycemic index	77.7 (4.4)	75.4 (5.1)	71.0 (5.2)	67.0 (6.0)

Data are mean (SD) or *n* (%) unless otherwise indicated. *Data missing for 25 participants.

Table 2—RR of type 2 diabetes according to dairy product consumption (n = 2,091)

		Dairy product consumption (serving/day)			*P* value
Total dairy products	None	≤0.5	0.5–1.0	>1	
Cases/participants	215/889	127/470	89/399	76/333	
Model 1	1	0.96 (0.79–1.16)	0.73 (0.58–0.92)	0.67 (0.52–0.88)	0.001
Model 2	1	0.95 (0.79–1.15)	0.71 (0.57–0.89)	0.65 (0.50–0.85)	<0.001
Model 3	1	0.92 (0.76–1.11)	0.73 (0.58–0.92)	0.66 (0.51–0.85)	<0.001
Model 4	1	0.86 (0.71–1.06)	0.83 (0.67–1.02)	0.81 (0.63–1.05)	0.07
Milk	None	≤0.5	>0.5	—	
Cases/participants	283/1,179	95/333	129/579	—	
Model 1	1	1.00 (0.82–1.23)	0.73 (0.60–0.89)	—	0.003
Model 2	1	1.00 (0.82–1.22)	0.72 (0.59–0.87)	—	0.002
Model 3	1	0.97 (0.80–1.19)	0.75 (0.62–0.91)	—	0.005
Model 4	1	1.03 (0.82–1.29)	0.92 (0.77–1.12)	—	0.45
Total dairy products except milk	None	≤0.5	>0.5	—	
Cases/participants	315/1,315	152/582	40/194	—	
Model 1	1	1.00 (0.84–1.20)	0.72 (0.53–0.98)	—	0.11
Model 2	1	0.99 (0.83–1.19)	0.69 (0.51–0.94)	—	0.06
Model 3	1	0.97 (0.81–1.15)	0.65 (0.48–0.89)	—	0.02
Model 4	1	0.94 (0.78–1.13)	0.77 (0.58–1.03)	—	0.11

RR (95% CI) and *P* for trend of type 2 diabetes were calculated by log-Poisson model with multivariate adjustment as follows: model 1, age, sex, region, and residence; model 2, further adjusted for smoking (current, past, never), family history of diabetes, BMI, and dietary fiber intake based on model 1; model 3, further adjusted for changes in BMI and waist circumference based on model 2 (n = 1,903); and model 4, further adjusted for changes in glucose based on model 3 (n = 1,894).

changes in BMI and waist circumference during follow-up as covariates (model 3) but attenuated after further adjustment for changes in glucose over time (model 4) (*P* for trend = 0.07). Similarly, milk consumption and total dairy products except milk were both independently associated with a lower risk of diabetes, and the RR (95% CI) in those with >0.5 serving/day was 0.75 (0.61–0.93, *P* for trend < 0.001) and 0.69 (0.51–0.94; *P* for trend = 0.02), respectively, compared with nonconsumers after multivariate adjustment in model 2. Further adjustment for changes in fasting glucose attenuated these associations (model 4) (*P* for trend > 0.11). In stratified analysis, age, sex, BMI, and HOMA-IR did not significantly modify the associations between total dairy intake and risk of type 2 diabetes (all *P* for interaction > 0.05) (Supplementary Table 1).

Dairy Product Consumption and Changes in Cardiometabolic Traits

We further calculated changes in cardiometabolic traits during 6 years of follow-up according to total dairy consumption at baseline (Table 3), after

Table 3—Changes of cardiometabolic traits after 6 years of follow-up

	Dairy product consumption (serving/day)				
	None	<0.5	0.5–1.0	>1	*P* value
Glucose (mmol/L)	1.21 ± 0.05	1.28 ± 0.06	1.04 ± 0.06	0.90 ± 0.07	<0.001
HbA_{1c} (%)	0.81 ± 0.03	0.78 ± 0.03	0.72 ± 0.03	0.72 ± 0.04	0.12
HbA_{1c} (mmol/mol)	8.8 ± 0.3	8.5 ± 0.3	7.9 ± 0.5	7.8 ± 0.4	0.12
Waist circumference (cm)†	1.76 ± 0.25	1.49 ± 0.29	2.01 ± 0.32	0.83 ± 0.37	0.045
BMI (kg/m^2)†	0.29 ± 0.07	0.21 ± 0.08	0.47 ± 0.09	−0.01 ± 0.11	0.001
Systolic blood pressure (mmHg)‡	−0.62 ± 0.74	−1.92 ± 0.84	−1.98 ± 0.93	−4.15 ± 1.08	0.054
Diastolic blood pressure (mmHg)‡	2.37 ± 0.40	1.47 ± 0.46	1.77 ± 0.51	0.29 ± 0.59	0.02
Triglycerides (mmol/L)§	0.37 ± 0.05	0.33 ± 0.06	0.38 ± 0.06	0.29 ± 0.07	0.66
Total cholesterol (mmol/L)§	0.92 ± 0.05	0.90 ± 0.06	0.85 ± 0.07	0.83 ± 0.08	0.80
HDL cholesterol (mmol/L)§	0.13 ± 0.02	0.15 ± 0.03	0.10 ± 0.03	0.13 ± 0.03	0.37
LDL cholesterol (mmol/L)§	0.63 ± 0.05	0.59 ± 0.06	0.55 ± 0.06	0.54 ± 0.07	0.64

Data are least squares mean ± SE calculated in the general linear model after adjustment for age, sex, region, residence, smoking status, family history of diabetes, BMI (not for BMI and waist circumference), dietary fiber intake, and baseline values of respective variables. Total numbers of participants in each analysis was 1,807 for glucose and HbA_{1c}, 1,903 for BMI and waist circumference, 1,902 for systolic blood pressure and diastolic blood pressure, and 1,525 for triglyceride, total cholesterol, HDL cholesterol, and LDL cholesterol levels. †BMI not adjusted. ‡For participants taking medications for hypertension at baseline or follow-up, systolic blood pressure + 10 mmHg and diastolic blood pressure + 5 mmHg. §Participants with self-reported dyslipidemia or related medication use at baseline or follow-up were excluded.

adjustment for age, sex, region, residence, smoking status, family history of diabetes, BMI, dietary fiber intake, and baseline values of respective variables. Comparing participants with >1 serving/day of consumption to nonconsumers, the absolute differences in changes were −0.31 (95% CI −0.49 to −0.14) mmol/L for glucose (*P* for trend < 0.001), −0.93 (−1.79 to −0.07) cm for waist circumference (*P* for trend = 0.045), −0.30 (−0.54 to −0.05) kg/m^2 for BMI (*P* for trend = 0.001) , −3.54 (−6.06 to −1.02) mmHg for systolic blood pressure (*P* for trend = 0.054), and −2.08 (−3.45 to −0.71) mmHg for diastolic blood pressure (*P* for trend = 0.02).

Erythrocyte *Trans*-18:1 Isomers and Risk of Type 2 Diabetes

Spearman correlation coefficients of erythrocyte *trans*-18:1 isomers were 0.37 (*P* < 0.001) for intake of total dairy products and 0.35 (*P* < 0.001) for milk after adjustment for age, sex, and total energy intake (Supplementary Table 2). There was an inverse association between erythrocyte *trans*-18:1 isomers and risk of type 2 diabetes (Table 4). RR in the fourth quartile was 0.81 (0.65–1.02, *P* for trend = 0.01); however, further adjustment for total dairy consumption attenuated the association (0.91 [0.72–1.16], *P* for trend = 0.15).

Sensitivity Analysis on Risk of Diabetes

In a sensitivity analysis, we further included HbA_{1c} ≥6.5% in diabetes diagnostic criteria and subsequently identified a total of 879 diabetic patients with the new criteria among 2,003 participants who were free of diabetes at baseline. In this analysis, the inverse associations for dairy and milk consumption remained (Supplementary Table 3). The associations between *trans*-18:1 isomers and diabetes risk were somewhat attenuated after further adjustment for lifestyle factors and BMI (Supplementary Table 4).

CONCLUSIONS

We found that total dairy consumption was associated with a lower risk of diabetes and favorable changes in fasting glucose, waist circumference, BMI, and blood pressure in middle-aged and older Chinese during 6 years of follow-up. These associations were independent of established diabetes risk factors. In addition, erythrocyte *trans*-18:1 isomers were associated with a lower risk of diabetes, which appeared to be explained by dairy product consumption. All these findings suggest potential benefits of dairy consumption on metabolic disorders.

According to a Medline search of English-language publications through March 2013, few studies have investigated associations of dairy products with the risk of diabetes among populations with low overall dairy consumption. Chinese National Nutrition and Health Survey (2002) data showed that mean dairy consumption was 27 g/day for Chinese, whereas this number was >240 g/day for Americans during the same period (33). Despite the low level of intake, dairy is associated with a significantly reduced risk of diabetes in the current study. Similarly, Villegas et al. (34) reported that compared with nonconsumers, the RR (95% CI) for type 2 diabetes was 0.61 (0.54–0.69) for women consuming <100 g/day of milk and 0.74 (0.67–0.82) for women consuming powdered milk in the Shanghai Women's Health Study. These associations among Chinese populations seemed stronger than those from a previous meta-analysis, which showed that the risk of type 2 diabetes was 14% lower in the highest quintile of total dairy consumption compared with the lowest quintile (5,35). Several recent studies, on the other hand, did not find significant associations between dairy product consumption and diabetes (8–12). For example, Sluijs et al. (10) showed that the RR (95% CI) for type 2 diabetes comparing extreme quintiles of total dairy consumption was 0.97 (0.82–1.15, *P* = 0.69) by pooling case–cohort samples from eight countries in the European Prospective Investigation into Cancer and Nutrition study (10,694 participants with incident type 2 diabetes and 13,780 in the subcohort). It is worth noting that the reference group participants in these studies often consumed considerable amounts of dairy products (up to 1 serving/day). Such a consumption level might already exhibit protective effects according to findings from the current study. Thus, this observation could partly explain the reason for the lack of benefit from higher dairy consumption in previous studies.

Accumulating evidence from human studies has shown inverse associations between dairy consumption and blood pressure and body fat (11,14,15). In contrast, findings on glucose homeostasis are rather limited, and potentially beneficial effects have been found only in certain subgroups. For example, Pereira et al. (36) showed that dairy consumption was associated with lower fasting glucose and blood pressure and smaller waist

Table 4—RR of type 2 diabetes according to quartiles of erythrocyte *trans*-18:1 isomers

	Quartile				
	1	2	3	4	*P* value
Trans-18:1 isomers (%)	0.13 ± 0.02	0.17 ± 0.01	0.21 ± 0.01	0.28 ± 0.05	
Cases/participants	127/516	147/517	111/517	119/516	
Model 1	1	1.05 (0.86–1.29)	0.78 (0.62–0.98)	0.81 (0.65–1.02)	0.01
Model 2	1	1.03 (0.84–1.25)	0.79 (0.63–0.99)	0.82 (0.65–1.04)	0.02
Model 3	1	1.04 (0.85–1.27)	0.82 (0.66–1.03)	0.91 (0.72–1.16)	0.15

RR (95% CI) and *P* for trend were calculated by log-Poisson model, and covariates adjusted for included the following: model 1, age, sex, region, and residence; model 2, further adjusted by smoking status (current, former, never), family history of diabetes, BMI, dietary fiber intake, and erythrocyte *trans* 18:2n-6 9c12t and *trans* 18:2n-6 9t12c based on model 1; and model 3, further adjusted for total dairy product consumption based on model 2.

circumference during 10 years of follow-up among overweight participants. Moreover, Samara et al. (13) reported that milk, yogurt, and cottage cheese consumption was associated with 5-year favorable changes of fasting glucose in men (n = 288) but not in women. Among 40,000 Danish subjects aged 50–64 years, a high-fat dairy consumption was also found to be inversely associated with 5-year changes in waist circumference for women but not for men (37). In the current study of Chinese participants, dairy consumption was associated with favorable changes in glucose level, waist circumference, BMI, and blood pressure in the total population, regardless of obesity status and sex. We also found that the beneficial effects of dairy food on fasting glucose may partly account for the inverse association between dairy food and diabetes risk. These observations deserve replication in future studies among populations with relatively low dairy consumption levels.

In the current study, dairy products were likely to be an important source for *trans*-18:1 isomers (4). The observed correlation coefficient of *trans*-18:1 isomers with total dairy consumption (r = 0.37, $P < 0.001$) was comparable to previous studies investigating associations of dairy intake measured by FFQ, with 15:0 and 17:0 in plasma, erythrocyte, or adipose tissue (18,19). However, the finding was distinct from a previous study in the U.S. that showed *trans*-18:1 isomers in plasma phospholipids were mainly associated with intakes of food high in industrialized *trans* fatty acids, such as biscuits, chips and popcorn, margarines, fried food, and bakery food (38). This may be attributable to our participants being middle-aged and older Chinese who were less influenced by a westernized diet and had low *trans* fatty acids in their diet. This conclusion is further supported by two observations. First, Spearman correlation coefficients of *trans*-18:1 isomers and *trans*-18:2 isomers (r = 0.23–0.33) were weak compared with the intercorrelation of two *trans*-18:2 isomers (r = 0.83), suggesting that *trans*-18:1 isomers and *trans*-18:2 isomers may have different dietary sources. Second, we found an inverse association between *trans*-18:1 isomers and risk of type 2 diabetes, which was abolished after adjustment for total dairy consumption. Similarly, Lemaitre et al. (39) reported that *trans*-18:1 isomers were inversely associated with risk of fatal ischemic heart disease and sudden cardiac death in the U.S., indicating that *trans*-18:1 isomers may also reflect dietary items other than industrial *trans* fat, even in western countries. Whether *trans*-18:1 isomers could serve as biomarkers for dairy consumption in people with relatively low or no consumption of *trans* fat needs to be clarified in further studies.

Although mechanisms linking dairy consumption and risk of metabolic disorders are not entirely clear, some nutrients, such as minerals (calcium, magnesium, and potassium), vitamin D, and proteins (casein and whey protein) in dairy products may play protective roles (4). For instance, calcium and magnesium have been shown to improve blood pressure, weight control, and possibly glucose metabolism, whereas vitamin D has been reported to maintain calcium homeostasis, stimulate insulin synthesis and secretion, and improve blood pressure control by regulating the renin-angiotensin-aldosterone system (4). In addition, dairy proteins, particularly whey protein, have been inversely associated with insulin sensitivity, blood pressure, weight control, and body composition (4). However, milk is not a major source of calcium and magnesium for Chinese (33), and it is not fortified with vitamin D in China. Consistent with this, we did not observe a significant mediating effect of vitamin D, calcium, and magnesium on the association between dairy consumption and type 2 diabetes (data not shown). Thus, more mechanistic studies are warranted.

The current study has several strengths. First, we used both FFQ and dairy fat markers to assess dairy consumption and analyzed their associations not only with risk of diabetes but also with changes in several cardiometabolic traits. These data consistently showed an inverse association between dairy consumption and risk of diabetes. Second, the low dairy consumption in the study population enabled us to include participants without any dairy consumption as the reference group and to investigate the potential benefits of dairy consumption at a low level.

The study also has several limitations. First, 23.1% of participants were lost to follow-up and were more likely to be male urban participants with a high education level and high income (40). They also had higher baseline dairy consumption compared with other participants (0.65 vs. 0.46 serving/day). This differential loss of follow-up may bias the true association to the null because dairy consumption is inversely associated with diabetes risk. Second, most of the incident diabetes cases were diagnosed on the basis of fasting glucose; therefore, the misclassification of incident diabetes was inevitable. Nevertheless, we believe that participants with different dairy food intake levels had similar proportions of misclassification, which would likely nullify the associations under investigation. Third, most incident diabetes cases were diagnosed at the follow-up visit, and exact person-years of follow-up could not be obtained. Finally, although we extensively controlled for lifestyle and dietary factors, there is still a possibility of residual confounding. The participants who consumed dairy products were more likely to be female, younger, well-educated, and nonsmokers and to have a higher consumption of vegetables and dietary fibers, indicating that they may be more health conscious and have an overall higher quality diet (41). However, these variables were not associated with risk of diabetes according to the results of stepwise regression, and controlling for these variables did not alter the association between dairy consumption and diabetes (data not shown).

In conclusion, the findings suggest that dairy consumption, even at a moderate level, is associated with a lower risk of type 2 diabetes and favorable changes of cardiometabolic traits. The association between *trans*-18:1 isomers and diabetes was largely explained by dairy consumption, suggesting a beneficial role of dairy consumption in cardiometabolic health.

Acknowledgments. The authors thank Geng Zhang, Xin Liu, Gang Liu, Yunhua Zhou, Shaojie Ma, Yiqin Wang, and Ling Lu of Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences and Graduate University of the Chinese Academy of Sciences, Shanghai, China.

Funding. This study was supported by the National Natural Science Foundation of China (30930081 and 81021002), the National Basic Research 973 Program (2012CB524900), the Chinese Academy of Sciences (KSCX2-EW-R-10 and SIBS2008006), and Key Discipline of Shanghai Public Health-Food and Nutritional Sciences (12GWZX0702).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. G.Z. collected and researched data and wrote the manuscript. Q.S. researched data, contributed to the discussion, and reviewed and edited the manuscript. D.Y. and J.Z. collected and researched data and reviewed and edited the manuscript. L.S., X.Y., H.L., Q.J., and H.Z. collected data. F.B.H. contributed to the discussion and reviewed and edited the manuscript. X.L. designed the study, collected and researched data, contributed to the discussion, and reviewed and edited the manuscript. X.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998;21:1414–1431
2. Yang W, Lu J, Weng J, et al.; China National Diabetes and Metabolic Disorders Study Group. Prevalence of diabetes among men and women in China. N Engl J Med 2010; 362:1090–1101
3. Elliott RB, Harris DP, Hill JP, Bibby NJ, Wasmuth HE. Type I (insulin-dependent) diabetes mellitus and cow milk: casein variant consumption. Diabetologia 1999; 42:292–296
4. Rice BH, Cifelli CJ, Pikosky MA, Miller GD. Dairy components and risk factors for cardiometabolic syndrome: recent evidence and opportunities for future research. Adv Nutr 2011;2:396–407
5. Tong X, Dong JY, Wu ZW, Li W, Qin LQ. Dairy consumption and risk of type 2 diabetes mellitus: a meta-analysis of cohort studies. Eur J Clin Nutr 2011;65:1027–1031
6. Fumeron F, Lamri A, Abi Khalil C, et al.; Data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR) Study Group. Dairy consumption and the incidence of hyperglycemia and the metabolic syndrome: results from a french prospective study, Data from the Epidemiological Study on the Insulin Resistance Syndrome (DESIR). Diabetes Care 2011;34:813–817
7. Malik VS, Sun Q, van Dam RM, et al. Adolescent dairy product consumption and risk of type 2 diabetes in middle-aged women. Am J Clin Nutr 2011;94:854–861
8. Grantham NM, Magliano DJ, Hodge A, Jowett J, Meikle P, Shaw JE. The association between dairy food intake and the incidence of diabetes in Australia: the Australian Diabetes Obesity and Lifestyle Study (AusDiab). Public Health Nutr 2013; 16:339–345
9. Louie JC, Flood VM, Rangan AM, et al. Higher regular fat dairy consumption is associated with lower incidence of metabolic syndrome but not type 2 diabetes. Nutr Metab Cardiovasc Dis. 27 September 2012 [Epub ahead of print]
10. Sluijs I, Forouhi NG, Beulens JW, et al.; InterAct Consortium. The amount and type of dairy product intake and incident type 2 diabetes: results from the EPIC-InterAct Study. Am J Clin Nutr 2012;96: 382–390
11. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, Brunner EJ. Consumption of dairy products and associations with incident diabetes, CHD and mortality in the Whitehall II study. Br J Nutr 2012;109:1–9
12. Struijk EA, Heraclides A, Witte DR, et al. Dairy product intake in relation to glucose regulation indices and risk of type 2 diabetes. Nutr Metab Cardiovasc Dis. 23 July 2012 [Epub ahead of print]
13. Samara A, Herbeth B, Ndiaye NC, et al. Dairy product consumption, calcium intakes, and metabolic syndrome-related factors over 5 years in the STANISLAS study. Nutrition 2013;29:519–524
14. Louie JC, Flood VM, Hector DJ, Rangan AM, Gill TP. Dairy consumption and overweight and obesity: a systematic review of prospective cohort studies. Obes Rev 2011; 12:e582–e592
15. Chen M, Pan A, Malik VS, Hu FB. Effects of dairy intake on body weight and fat: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2012;96:735–747
16. Hodson L, Skeaff CM, Fielding BA. Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. Prog Lipid Res 2008;47:348–380
17. Brevik A, Veierød MB, Drevon CA, Andersen LF. Evaluation of the odd fatty acids 15:0 and 17:0 in serum and adipose tissue as markers of intake of milk and dairy fat. Eur J Clin Nutr 2005;59:1417–1422
18. Sun Q, Ma J, Campos H, Hu FB. Plasma and erythrocyte biomarkers of dairy fat intake and risk of ischemic heart disease. Am J Clin Nutr 2007;86:929–937
19. Aslibekyan S, Campos H, Baylin A. Biomarkers of dairy intake and the risk of heart disease. Nutr Metab Cardiovasc Dis 2012;22:1039–1045
20. Hodge AM, English DR, O'Dea K, et al. Plasma phospholipid and dietary fatty acids as predictors of type 2 diabetes: interpreting the role of linoleic acid. Am J Clin Nutr 2007;86:189–197
21. Patel PS, Sharp SJ, Jansen E, et al. Fatty acids measured in plasma and erythrocyte-membrane phospholipids and derived by food-frequency questionnaire and the risk of new-onset type 2 diabetes: a pilot study in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk cohort. Am J Clin Nutr 2010;92:1214–1222
22. Warensjö E, Jansson JH, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study. Am J Clin Nutr 2010;92:194–202
23. Mozaffarian D, Cao H, King IB, et al. Trans-palmitoleic acid, metabolic risk factors, and new-onset diabetes in U.S. adults: a cohort study. Ann Intern Med 2010;153: 790–799
24. Yu DX, Sun Q, Ye XW, et al. Erythrocyte trans-fatty acids, type 2 diabetes and cardiovascular risk factors in middle-aged and older Chinese individuals. Diabetologia 2012;55:2954–2962
25. Ye X, Yu Z, Li H, Franco OH, Liu Y, Lin X. Distributions of C-reactive protein and its association with metabolic syndrome in middle-aged and older Chinese people. J Am Coll Cardiol 2007;49:1798–1805
26. Yu Z, Ye X, Wang J, et al. Associations of physical activity with inflammatory factors, adipocytokines, and metabolic syndrome in middle-aged and older Chinese people. Circulation 2009;119:2969–2977
27. Zong G, Ye X, Sun L, et al. Associations of erythrocyte palmitoleic acid with adipokines, inflammatory markers, and the metabolic syndrome in middle-aged and older Chinese. Am J Clin Nutr 2012;96:970–976
28. Lu L, Yu Z, Pan A, et al. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. Diabetes Care 2009;32:1278–1283
29. Zhao W, Hasegawa K, Chen J. The use of food-frequency questionnaires for various purposes in China. Public Health Nutr 2002; 5:829–833
30. Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. Diabetes Care 2008;31:2281–2283
31. Yang YX, Wang GY, Pan XC (Eds.). *China Food Composition Tables 2002*. Beijing, China, Beijing University Medical Press, 2002
32. Skov T, Deddens J, Petersen MR, Endahl L. Prevalence proportion ratios: estimation

and hypothesis testing. Int J Epidemiol 1998;27:91–95

33. Wang Y, Li S. Worldwide trends in dairy production and consumption and calcium intake: is promoting consumption of dairy products a sustainable solution for inadequate calcium intake? Food Nutr Bull 2008;29:172–185
34. Villegas R, Gao YT, Dai Q, et al. Dietary calcium and magnesium intakes and the risk of type 2 diabetes: the Shanghai Women's Health Study. Am J Clin Nutr 2009;89:1059–1067
35. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab 2007;92:2017–2029
36. Pereira MA, Jacobs DR Jr, Van Horn L, Slattery ML, Kartashov AI, Ludwig DS. Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study. JAMA 2002;287:2081–2089
37. Halkjaer J, Tjønneland A, Overvad K, Sørensen TI. Dietary predictors of 5-year changes in waist circumference. J Am Diet Assoc 2009;109:1356–1366
38. Micha R, King IB, Lemaitre RN, et al. Food sources of individual plasma phospholipid trans fatty acid isomers: the Cardiovascular Health Study. Am J Clin Nutr 2010;91:883–893
39. Lemaitre RN, King IB, Mozaffarian D, et al. Plasma phospholipid trans fatty acids, fatal ischemic heart disease, and sudden cardiac death in older adults: the cardiovascular health study. Circulation 2006;114:209–215
40. Zong G, Zhu J, Sun L, et al. Associations of erythrocyte fatty acids in the de novo lipogenesis pathway with risk of metabolic syndrome in a cohort study of middle-aged and older Chinese. Am J Clin Nutr 2013;98:319–326
41. Holmes BA, Kaffa N, Campbell K, Sanders TA. The contribution of breakfast cereals to the nutritional intake of the materially deprived UK population. Eur J Clin Nutr 2012;66:10–17