Dairy Product Consumption and Type 2 Diabetes among Korean Adults: A Prospective Cohort Study Based on the Health Examinees (HEXA) Study

Original article

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Competing Interests

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Abstract

Objectives: The consumption of dairy products has been suggested to help lower the prevalence of type 2 diabetes (T2D). We aimed to assess the association between the consumption of dairy products and T2D events in Korean middle-aged adults.

Methods: We followed up 53 288 participants (16 895 men and 36 393 women) in the Health Examinees (HEXA) study. The consumption of dairy products was assessed using the self-administered Food Frequency Questionnaire (FFQ), and T2D was defined according to the 2015 treatment guidelines of the Korean Diabetes Association (KDA). Hazard ratios (HRs) and 95% confidence interval (CIs) between the consumption of dairy product and the risk of T2D were calculated using Cox proportional hazards models after adjusting for potential confounders. Spline regression was used to better represent the association between the consumption of dairy products and the risk of T2D.

Results: Among men, those with a higher consumption of dairy products had significantly lower risk of T2D than those who consumed essentially no dairy products (HR=0.73; 95% CI=0.58, 0.91). Particularly, the consumptions of yogurt (HR=0.75; 95% CI=0.60, 0.93; p-trend=0.0351) and cheese (HR=0.66; 95% CI=0.49, 0.89; p-trend=0.0055) were negatively associated with the incidence of T2D in men. In women, daily consumption of one serving of yogurt decreased the risk of T2D by 11%.

22 Conclusions: The association between the consumption of dairy products and the risk of T2D
23 differed by gender and dairy product type. Further prospective studies are needed to confirm
24 these associations.

25 **Keywords:** dairy products, yogurt, type 2 diabetes, Korean adults, HEXA study

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Introduction

Type 2 diabetes (T2D) is one of the most prevalent chronic diseases worldwide, with 9.3% of adults (around 463 million) living with the condition [1], and its incidence increasing. The International Diabetes Federation (IDF) projects that approximately 578 million adults will have T2D by 2030 [2]. Diabetes is a disease of concern in Korea; in 2020, T2D was prevalent in 13.8% of adults (approximately 4.94 million) aged over 30 years [3]. T2D is a serious chronic disease caused by a complex combination of genetic and environmental interaction and other risk factors such as lifestyle [4]. Thus, it is important to understand the modifiable factors associated with the risk of T2D.

One of these modifiable risk factors is diet, in particular, dairy products. Dairy products contain saturated fat that is generally considered to have adverse effects on health [5]. Excessive intake of saturated fat increases the risk of cardiovascular disease [6]. Regular consumption of milk protein causes the insulin-like growth factor-1 (IGF-1) axis to permanently increase serum IGF-1 levels. Insulin/IGF-1 signaling is closely linked to the development of chronic diseases such as T2D, obesity, and cancer [7]. However, there is also increasing evidence supporting a possible benefit of dairy products in the management of T2D. Dairy products contain calcium, vitamin D, whey protein, and flavonoids, which have a favorable effect on glucose homeostasis and thus improve T2D [8, 9]. In addition, the lactic acid bacteria found in fermented dairy products, such as yogurt and cheese, contribute to intestinal microbial balance [10], which may improve T2D by reducing the risk of obesity [11].

In several studies, dairy products were divided into milk, yogurt, and cheese [12-14]. In a large cohort study of Chinese adults, daily milk intake was associated with a significant

reduction in the risk of T2D [15]. A study on yogurt intake and the risk of diabetes, which evaluated three cohorts of US adults, found that increased yogurt intake was associated with reduced risk of T2D [16]. In the European Prospective Investigation into Cancer and Nutrition study, a negative association between diabetes and cheese intake among dairy subtypes was found [17]. However, most of these studies were focused on the association between dairy product intake and the risk of T2D in Western countries. Furthermore, most current studies on dairy consumption and T2D in Korea are cross-sectional studies [18] with inadequate data [19]. The variety of dairy products and dairy product intake are lower in Korea than in Western countries [12, 13, 20]. Therefore, cohort studies on the association between the consumption of dairy products and the risk of T2D in Korea are limited.

Given the increasing incidence of T2D among Koreans [3], it is crucial to understand the significance of the consumption of dairy products in the prevention of T2D. Thus, this study aimed to investigate the effect of consumption of dairy products including milk, yogurt, and cheese on the incidence of T2D among Korean adults aged 40-69 years, using data from a large Korean population.

Methods

Study population

The Health Examinees (HEXA) study was a part of the Korean Genome and Epidemiology study, a large, prospective, community-based genomic cohort study. The HEXA study was conducted to investigate the cause of major chronic diseases in Koreans [21]. The baseline survey for the HEXA study was conducted from 2004 to 2013 at 38 hospitals and local health screening centers following strict standardized study procedures. In

total, 65 642 participants completed the initial and follow-up surveys between 2012 and 2016 [21].

Among the 65 642 participants who completed the baseline and follow-up surveys, we excluded those aged <40 years and >69 years (n=983) and those who were diagnosed with T2D and complications at the baseline survey (n=9 129). Further, we excluded those without dietary intake records or those who reported unreasonable energy intake (<800 or $\geq$ 4 000 kcal/day in men and <500 or $\geq$ 3 500 kcal/day in women) (n=2 196). Participants with missing information on body mass index (BMI) (n=46) were also excluded. Finally, 53 288 participants (16 895 men and 36 393 women) were included in the final analysis (Figure 1).

All participants voluntarily signed an informed written consent form prior to enrollment. The current study was performed in accordance with the guidelines specified in the declaration of Helsinki, and the study protocol was approved by the local Institutional Review Board (IRB) of the Ethics Committee of the Korean Genome and Epidemiology Study of the Korea National Institute of Health (IRB no. 2014-08-02-3C_A).

Assessment of dairy product consumption

Food intake in the past year was assessed using a 106-item self-administered food frequency questionnaire (FFQ). The frequency of food consumption was classified into nine categories: never or almost never, once a month, two to three times a month, once or twice a week, three to four times a week, five to six times a week, once a day, twice a day, and three times a day. The portion sizes were categorized into three groups: half standard serving, one standard serving, and two standard servings. The dairy products in the FFQ included three types: milk, yogurt, and cheese. One serving size was equal to 200 ml for milk, 120 ml for

yogurt, and 20 g for cheese. The consumption of dairy products was converted to a weekly frequency and multiplied by the number of servings reported for each food. Based on their reported distribution of each target dairy product, the participants were categorized into three groups for consumption of cheese (non, <1/week, and ≥ 1 /week) or four groups for consumption of dairy products, milk, and yogurt (non, ≤ 2 /week, >2-<7/week, and ≥ 1 /day).

To verify the validity and 1-year repeatability of the FFQ, information was collected in each of the four seasons of the 1-year period using the 3-day diet record method. The correlation coefficients between the FFQ and 12-day diet record adjusted for attenuation, age, sex, and energy intake in the Korean population ranged between 0.23 and 0.64, with 0.45 being the value for nutrient intake and 0.39 for nutrient density [22].

Definition of T2D

T2D was defined according to the 2015 treatment guidelines of the Korean Diabetes Association (KDA) as a fasting blood glucose ≥ 126 mg/dL or active treatment with glucose-lowering medication (insulin or oral hypoglycemic agents), at a follow-up survey [23]. The person-year is calculated by multiplying the average number of participants by the number of years of observation.

Covariates

Covariates included sociodemographic factors such as age, BMI, educational level, and health behavior. Education levels were divided into three categories: middle school or less, high school or college, and undergraduate school or higher. Smoking status was assessed using the question “Have you ever smoked 5 packs of cigarettes (100 cigarettes) in your

lifetime?” Participants who answered “no” were defined as non-smokers. Meanwhile, those who answered “yes” were categorized as current smokers and ever smokers when they were still and were no longer smoking at the time of the survey, respectively. Drinking status was determined by the question “Are you unable to drink alcohol or do you refuse to drink alcohol?” Participants who answered “no” were identified as non-drinkers. Meanwhile, those who answered “yes” were determined as current drinkers. Physical activity was assessed with the question “Do you regularly participate in any sport?” Participants who answered “yes” were assigned to the regular exercise group, while those who answered “no” were assigned to the non-regular exercise.

Statistical analysis

All analyses to investigate the association between the consumption of dairy products and the risk of T2D were conducted separately by sex. Categorical variables were analyzed using the chi-square test, while continuous variables were analyzed using general linear regression. The association between consumption of dairy products and the development of T2D was determined by calculating the hazard ratios (HRs) and 95% confidence intervals (CIs) using Cox proportional hazard models. We used multivariate models adjusted for age, BMI, educational level ($\leq$ middle school, high school or college, undergraduate school or higher), smoking status (never, ever, current, unknown), alcohol drinking status (never, ever, unknown), physical activity (yes, no, unknown), and total energy intake as covariates. To test for a linear trend between the consumption of dairy products and HR for T2D, participants were assigned a median for each category, and this variable was entered into the model as a continuous term. The coefficient was assessed using the Wald test. To assess the linearity of

the association between the consumption of dairy products and the risk of T2D, we used a spline regression analysis. Constrained cubic splines were fitted to logistic and proportional risk regression models to nonparametrically examine the relationship between the consumption of dairy products and the hazard ratio (HR) for T2D, with four knots at fixed percentiles (5%, 35%, 65%, 95%). We used the restricted maximum likelihood method in our analysis, combining the two regression coefficients and variance matrices estimated in this study. The pooled relative risk for a given exposure value was then estimated. P-values for nonlinearity were calculated by testing the null hypothesis that the coefficients of the second spline were equal to zero. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). $P \leq 0.05$ was considered statistically significant.

Results

The characteristics of the participants according to the consumption of dairy products are shown in Table 1. Compared with men who consumed no or less dairy products every week, those who consumed more than one dairy product per day were younger, with higher education levels, and were more likely to perform regular exercise. Similarly, women who consumed dairy products more than once a day were younger, had higher education levels, were less likely to be smokers, and were regular exercisers. Both men and women with a higher consumption of dairy products also consumed higher amounts of energy, carbohydrates, protein, and fat. The trends in the characteristics of the participants according to the consumption of milk, yogurt, and cheese categories were similar to those according to the total consumption of dairy products (Tables S1–S3).

Table 2 shows the multivariate HR (95% CI) for T2D according to the consumption of total

dairy products, milk, yogurt, and cheese. Among men, those who consume dairy products, including yogurt and cheese have a lower risk of T2D compared to those who do not consume dairy products. In the comparison between the highest and lowest (non) intake categories, the multivariate HRs (95% CIs) for the consumption of total dairy products, yogurt, and cheese were 0.73 (0.58, 0.91), 0.75 (0.60, 0.93), and 0.69 (0.51, 0.94), respectively. However, in dairy products p for trend were not shown to be significant. In women, there was no significant association for the consumption of total dairy products, milk, yogurt, and cheese. However, increasing the consumption of yogurt by one serving/day may reduce the risk of T2D by 11% (HR=0.89, 95% CI=0.79, 0.99).

Spline regression was used to better characterize the association between the consumption of dairy products and the risk of T2D. As shown in Figure 2, the four knots of the consumption of dairy products for men were 0.00, 1.44, 4.29, and 12.48, while those for women were 0.00, 2.54, 6.29, and 14.58. The four knots of the consumption of milk for men were 0.00, 0.40, 2.50, and 7.00, while those for women were 0.00, 0.86, 3.50, and 7.00. We divided the men in the yogurt intake category into three knots (0.00, 0.58, and 7.00) because of the uneven distribution of yogurt intake. The four knots of the consumption of yoghurt for women were 0.00, 0.23, 1.50, and 7.00. The models were adjusted for age, BMI, education level, smoking status, alcohol consumption status and physical activity, and we found that the consumption of dairy products and milk had no correlation with the risk of T2D. However, there was a linear inverse association between yogurt intake and the incidence of T2D in both men ($p=0.050$) and women ($p=0.025$).

Discussion

The association between the consumption of different types of dairy products and the risk of T2D remains controversial. This study found that consumption of dairy products has a lower risk of T2D than who do not consumption among men. In particular, the consumption of yogurt and cheese was inversely associated with the incidence of T2D in men. In women, increasing the daily consumption of one serving of yogurt decreased the risk of T2D by 11%.

Our findings regarding the association between the consumption of dairy products and the risk of T2D are consistent with those of other studies [5, 16, 24, 25]. A dose-response meta-analysis of observational study showed similar results to those of our study. The present study combined data from 22 prospective cohort studies and showed that the consumption of yogurt and dairy products was negatively and positively and non-linearly associated with the risk of T2D, while no significant association was observed for milk [26]. A meta-analysis of 14 prospective cohort studies showed that higher yogurt intake was associated with a reduce risk of T2D [16]. In a systematic evaluation and meta-analysis study, cheese and yogurt intake were found to be significantly and negatively associated with the risk of T2D, with no association between whole milk intake and the risk of T2D [10].

However, a recent study of 393 T2D patients from Rotterdam, the Netherlands, found no association between the consumption of dairy products and the risk of T2D [27]. Similarly, a European (EPIC-InterAct) study found no association between the total consumption of dairy products and the risk of T2D [17]. These conflicting findings may be due to the differences in the definition of T2D, the geographical study populations, and the analysis methods. In the current study, the consumption of dairy products, particularly yoghurt, was associated with a reduced risk of T2D in Korean adults. This finding may be related to the dairy intake pattern

of Koreans. Due to lactose intolerance, many Koreans prefer to consume yogurt, which is better for intestinal health than milk [28]. There were also significantly more people who consumed one serving/day of yogurt than those who consumed one serving/day of milk. In a narrative review of the latest evidence on the benefit of consumption of dairy products for the prevention of T2D, daily intake of three servings of dairy products, particularly yogurt and cheese, lowered the risk of T2D [29]. A cross-sectional study on the association between dairy subgroups and prediabetes and newly diagnosed T2D among Dutch adults found a negative association between the consumption of skim and fermented dairy products and the risk of T2D [30].

Although cheese is a fermented food like yogurt, the majority of participants in this study consumed less than one serving of cheese per week. This could explain the finding that cheese had lesser effect than yogurt. Nevertheless, cheese intake was found to be beneficial for preventing T2D in men. Cheese might be a good source of vitamin K2, which is responsible for protein carboxylation by osteocalcin [10]. Osteocalcin concentration may affect insulin sensitivity and T2D by regulating the expression of insulin genes and β -cell proliferation markers [31]. In the current study, the consumption of dairy products was higher in men than in women. This could be because Korean men are more concerned about their health, compared with Korean women [32, 33].

Certain components of dairy products, such as calcium, vitamin D, whey protein, and magnesium, have been suggested to be beneficial for T2D [34]. These components can positively affect glucose homeostasis [8]. The most active form of vitamin D is $1,25(\text{OH})_2\text{D}_3$ [9]. Ca^{2+} signaling induced by $1,25(\text{OH})_2\text{D}_3$ regulates insulin secretion from pancreatic beta cells [35]. Prospective studies have reported that calcium intake lowers the prevalence of T2D

[36]. Whey protein may also improve T2D, as it is composed of glycopeptides, β -lactoglobulin, α -lactalbumin, and lactoferrin, and improves glucose clearance through differential upregulation of glucoregulatory transcripts in the liver and skeletal muscle [37]. However, in our study who consumed dairy products had a reduced risk of T2D compared to who did not consume dairy products. This may be because the HR values have a trend of rising and falling, thus showing no significance.

Several mechanisms could explain the negative association between yogurt intake and the risk of T2D. Obesity is one of the main causes of T2D [38]. The probiotics in yogurt reduce the risk of obesity, and this in turn may reduce the risk of T2D [11, 39]. Further, yogurt intake can improve glucose homeostasis and glucose metabolism by regulating hepatic gluconeogenesis [40]. Oxidative stress plays a major role in T2D [41], and probiotics in yogurt have antioxidative mechanisms, including scavenging of reactive oxygen species, inhibiting enzymes, and lowering the activity of lactic acid bacteria [42]. *Lactobacillus fermentum* ME-3 increases the total antioxidant status and decreases oxidative stress indicators [43]. *Lactobacillus acidophilus* and *Lactobacillus* have been shown to reduce oxidative stress and have anti-T2D effects [44].

This study had some limitations. First, information on the consumption of dairy products was obtained from a self-reported quantitative questionnaire, and thus, measurement error in dietary assessment is inevitable. Second, most Korean adults consume whole milk; as such, we were unable to obtain information from the FFQ on the effect of milk by its type (whole, low-fat, and skim) on the risk of T2D. Finally, the time of the T2D onset could not be accurately determined due to the limited follow-up period. Although we carefully adjusted for relevant confounders, some unmeasured and residual confounders related to the consumption

of dairy products and T2D may still occur.

Despite these limitations, our study has many strengths. The main advantage is that, to our best knowledge, this is the first large-scale prospective cohort study to evaluate the impact of the consumption of dairy products on the risk of T2D in Korea. Given that this study considered the pattern of consumption of dairy products among Koreans, the data can be used as evidence for establishing guidelines for the consumption of dairy products in Korea. In addition, we adjusted for potential key confounders to better analyze the independent association between the consumption of dairy product and the risk of T2D. More prospective studies are required to further determine the potential benefits of consumption of dairy products in the management of T2D.

In conclusion, the consumption of two servings of yogurt per week reduced the incidence of T2D among Korean adults compared with no or rare consumption of yoghurt. In contrast, no significant association was found between the consumption of milk and the risk of T2D. Therefore, further prospective studies and clinical trials are needed to test these findings.

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Figure legends

Figure 1. Participant inclusion flowchart.

Figure 2. Hazard ratio of T2D for dairy product consumption, calculated using spline regression.

Hazard ratios are shown as solid lines, and 95% confidence intervals are shown as dashed lines. A-C: Non-linear models of the association between the consumption of dairy products, milk, and yogurt and the risk of T2D. The four knots of dairy products for men: 0, 1.44, 4.29, and 12.48. The four knots of dairy products for women: 0, 2.54, 6.29, and 14.58. The four knots of milk for men: 0, 0.40, 2.50, and 7.00. The four knots of milk for women: 0, 0.86, 3.50, and 7.00. The three knots of yogurt for men: 0, 0.58, and 7.00. The four knots of yogurt for women: 0, 0.23, 1.50, and 7.00. The models are adjusted for age, BMI, educational level, smoking status, alcohol drinking status, and physical activity.

Key message

The study aimed to assess the association between the consumption of dairy products and type 2 diabetes events in Korean adults. Data was from the Health Examinees Study among 53 288 participants. Higher consumption of dairy products including yogurt and cheese was associated with a lower risk of developing type 2 diabetes in men. Increasing yogurt intake by one serving/day reduces the risk of type 2 diabetes in women. The association between the consumption of dairy products and the risk of type 2 diabetes differed by gender and dairy product type. Further studies are needed to confirm this.

Key Summary (Korean)

본 연구는 한국인 유전체역학조사사업의 도시코호트 기반조사와 추적조사에 참여한 40-69세 한국 성인 53 288명의 유제품 섭취와 제2형 당뇨병 발생 위험도를 분석하였다. 남자의 경우 요거트와 치즈를 포함하여 유제품 섭취자가 비섭취자에 비해 제2형 당뇨병의 위험도가 낮았다. 여자의 경우는 요거트 섭취가 하루 1회 증가할 때마다 제2형 당뇨병 위험도가 11% 감소하였다. 유제품 소비와 제2형 당뇨병의 위험도의 연관성은 성별과 유제품에 따라 다르다. 이를 확인하기 위해서는 추가 연구가 필요하다.

Table 1. Participant characteristics by total dairy product consumption by the HEXA study population

Variables ¹	Dairy product consumption (serving)				<i>p</i> -Value ²
	Non	≤2/week	>2-<7/week	≥1/day	
Men (n=16 895)	1 700	5 537	5 746	3 912	
Person-year	8 220.4	27 426.1	28 523.3	19 086.4	
Cases/Total participants (n)	136/1 700	323/5 537	364/5 746	222/3 912	
Age (years)	60.2 ± 8.1	59.0 ± 8.2	58.5 ± 8.4	59.4 ± 8.4	<0.0001
BMI (kg/m ²)	24.2 ± 2.8	24.4 ± 2.7	24.3 ± 2.7	24.3 ± 2.7	0.0470
Educational level					<0.0001
Middle school or less	503 (29.9)	1 257 (23.0)	1 012 (17.8)	641 (16.6)	
High school or college	684 (40.7)	2 248 (41.1)	2 322 (40.8)	1 510 (39.0)	
Undergraduate school or higher	494 (29.4)	1 967 (36.0)	2 356 (41.4)	1 718 (44.4)	
Smoking, n (%)					<0.0001
Non	409 (24.1)	1 603 (29.0)	1 873 (32.7)	1 365 (35.0)	
Ever	698 (41.2)	2 290 (41.5)	2 346 (41.0)	1 624 (41.7)	
Current	589 (34.7)	1 629 (29.5)	1 501 (26.2)	909 (23.3)	
Alcohol drinking, n (%)					0.0067
Non	322 (20.3)	1 085 (20.9)	1 117 (20.8)	852 (23.5)	
Current	1 266 (79.7)	4 098 (79.1)	4 253 (79.2)	2 779 (76.5)	
Regular exercise					<0.0001
No	816 (48.2)	2 464 (44.6)	2 235 (39.1)	1 311 (33.6)	
Yes	878 (51.8)	3 059 (55.4)	3 488 (61.0)	2 590 (66.4)	
Dietary intake					
Total energy intake (kcal/day)	1585.4±378.1	1651.9±403.5	1756.9±434.4	1850.6±488.0	<0.0001
Protein (g/day)	54.8±20.5	56.0±19.9	64.6±21.9	72.8±25.4	<0.0001
Protein (%)	13.0±2.6	13.0±2.3	13.6±2.3	14.1±2.4	<0.0001
Fat (g/day)	24.1±14.5	25.5±13.9	31.9±15.3	37.2±17.9	<0.0001
Fat (%)	12.6±5.3	13.0±4.9	14.9±4.8	16.0±5.0	<0.0001
Carbohydrate (g/day)	306.3±74.8	313.5±72.9	333.2±79.2	354.5±87.2	<0.0001
Carbohydrate (%)	74.3±7.5	74.0±6.8	71.4±6.6	69.9±6.8	<0.0001
Women (n=36 393)	2 056	8 751	13 768	11 818	
Person-year	9 977.1	43 661.2	69 322.1	59 393.6	
Cases/Total participant (n)	88/2 056	331/8 751	496/13 768	420/11 818	
Age (years)	58.7 ± 8.0	57.1 ± 7.8	56.8 ± 7.5	57.8 ± 7.3	<0.0001
BMI (kg/m ²)	23.8 ± 3.1	23.7 ± 3.1	23.6 ± 2.9	23.4 ± 2.9	<0.0001
Educational level					<0.0001
Middle school or less	958 (47.2)	3 359 (38.8)	4 533 (33.3)	3 555 (30.5)	
High school or college	811 (39.9)	3 794 (43.8)	6 215 (45.7)	5 387 (46.2)	
Undergraduate school or higher	263 (12.9)	1 507 (17.4)	2 866 (21.1)	2 728 (23.4)	
Smoking, n (%)					0.0039
Non	1 984 (96.8)	8 472 (97.3)	13 378 (97.7)	11 479 (97.5)	
Ever	21 (1.0)	71 (0.8)	113 (0.8)	129 (1.1)	
Current	44 (2.2)	161 (1.9)	205 (1.5)	160 (1.4)	
Alcohol drinking, n (%)					<0.0001

Non	1 495 (74.1)	6 043 (70.4)	8 999 (67.0)	7 980 (68.9)	
Current	524 (26.0)	2 538 (29.6)	4 442 (33.1)	3 611 (31.2)	
Regular exercise					<0.0001
No	1 171 (57.1)	4 591 (52.6)	6 433 (46.9)	4 690 (39.8)	
Yes	881 (42.9)	4 137 (47.4)	7 285 (53.1)	7 091 (60.2)	
Dietary intake					
Total energy intake (kcal/day)	1 411.4±384.7	1 450.0±412.9	1 539.1±436.0	1 621.3±470.5	<0.0001
Protein (g/day)	47.2±17.2	49.1±18.3	56.2±19.8	65.5±23.0	<0.0001
Protein (%)	12.7±2.4	12.9±2.4	13.5±2.4	14.2±2.5	<0.0001
Fat (g/day)	18.1±10.7	20.4±12.0	25.9±13.3	32.0±15.3	<0.0001
Fat (%)	10.8±4.8	11.8±4.9	13.9±4.9	15.4±5.1	<0.0001
Carbohydrate (g/day)	280.0±74.4	285.0±78.7	299.5±82.9	322.8±88.3	<0.0001
Carbohydrate (%)	76.5±6.7	75.4±6.8	72.6±6.8	70.4±7.0	<0.0001

¹ Values are presented as the mean±SD or as n (%). Continuous variables are reported as the mean±SD, while categorical variables are reported as n (%). Total energy intake is adjusted using the residual method.

² p values for categorical and continuous variables are calculated using the chi-square test and general linear regression, respectively.

Table 2. Hazard ratios (HRs) and 95% confidence interval (CIs) of T2D according to the dairy product consumed by the HEXA study population

		Dairy product consumption (serving)				P-trend ¹	HR for each additional serving/day
		None	≤2/week	>2-<7/week	≥1/day		
Men (n=16 895)							
Total dairy product consumption							
Cases/Total	136/1 700	323/5 537	364/5 746	222/3 912			
participants (n)							
Person-year	8 220.4	2 7426.1	28 523.3	19 086.4			
Model 1 ²	1.00	0.66 (0.54, 0.80)	0.70 (0.57, 0.85)	0.65 (0.53, 0.81)	0.1007	0.90 (0.81, 0.99)	
Model 2 ³	1.00	0.66 (0.54, 0.82)	0.74 (0.60, 0.90)	0.73 (0.58, 0.91)	0.6943	0.94 (0.85, 1.04)	
Milk consumption							
Cases/Total	219/3 318	439/7 152	304/5 087	83/1 338			
participants (n)							
Person-year	16 042.3	35 867.4	25 108.9	6 237.6			
Model 1	1.00	0.81 (0.69, 0.96)	0.82 (0.69, 0.98)	1.05 (0.81, 1.35)	0.7089	1.00 (0.85, 1.18)	
Model 2	1.00	0.81 (0.68, 0.95)	0.84 (0.70, 1.00)	1.18 (0.91, 1.54)	0.1936	1.06 (0.90, 1.26)	
Yogurt consumption							
Cases/Total	422/6 276	404/6 826	114/1 882	105/1 911			
participants (n)							
Person-year	30 670.6	33 586.3	9 375.6	9 623.7			
Model 1	1.00	0.84 (0.74, 0.97)	0.83 (0.67, 1.02)	0.71 (0.57, 0.88)	0.0047	0.82 (0.70, 0.95)	
Model 2	1.00	0.85 (0.74, 0.98)	0.90 (0.72, 1.11)	0.75 (0.60, 0.93)	0.0351	0.86 (0.74, 1.01)	
	Non	<1/week	≥1/week				
Cheese consumption							
Cases/Total	715/10 850	280/4 941	50/1 104				
participants (n)							
Person-year	53 631.6	24 167.2	5 457.4				
Model 1	1.00	0.86 (0.75, 0.99)	0.66 (0.49, 0.88)		0.0028	0.37 (0.18, 0.77)	
Model 2	1.00	0.89 (0.76, 1.03)	0.69 (0.51, 0.94)		0.0157	0.44 (0.21, 0.94)	
Women (n=36 393)							
Total dairy product consumption							
Cases/Total	88/2 056	331/8 751	496/13 768	420/11 818			
participants (n)							
Person-year	9 977.1	43 661.2	69 322.1	59 393.6			
Model 1	1.00	0.83 (0.65, 1.04)	0.79 (0.63, 0.99)	0.76 (0.60, 0.96)	0.0855	0.91 (0.85, 0.98)	
Model 2	1.00	0.85 (0.67, 1.08)	0.87 (0.69, 1.10)	0.88 (0.70, 1.12)	0.9873	0.96 (0.89, 1.03)	
Milk consumption							
Cases/Total	201/5 277	495/13 011	489/13 900	150/4 205			

participants (n)						
Person-year	25 722.4	66 000.1	69 972.6	20 658.9		
Model 1	1.00	0.91 (0.77, 1.08)	0.87 (0.74, 1.03)	0.92 (0.74, 1.13)	0.3870	0.95 (0.84, 1.09)
Model 2	1.00	0.93 (0.78, 1.09)	0.91 (0.77, 1.08)	1.01 (0.81, 1.25)	0.8713	1.02 (0.90, 1.17)
Yogurt consumption						
Cases/Total	415/10 564	549/15 143	183/5 344	188/5 342		
participants (n)						
Person-year	51 965.4	75 878.0	27 352.3	27 158.3		
Model 1	1.00	0.91 (0.80, 1.04)	0.79 (0.67, 0.94)	0.81 (0.68, 0.96)	0.0084	0.85 (0.76, 0.95)
Model 2	1.00	0.94 (0.83, 1.08)	0.88 (0.74, 1.05)	0.87 (0.73, 1.04)	0.1147	0.89 (0.79, 0.99)
	Non	<1/week	≥1/week			
Cheese consumption						
Cases/Total	787/19 305	397/12 182	151/4 906			
participants (n)						
Person-year	97 340.2	60 771.0	24 242.8			
Model 1	1.00	0.88 (0.78, 0.99)	0.84 (0.70, 1.00)		0.0643	0.85 (0.61, 1.18)
Model 2	1.00	0.94 (0.83, 1.07)	0.96 (0.80, 1.15)		0.5837	1.03 (0.75, 1.43)

¹ p for trend is calculated by categories of milk consumption. Associations are tested using the median values for each category and is treated as a continuous variable.

² Model 1 is adjusted for age (continuous).

³ Model 2 is adjusted for age (continuous), BMI (continuous), educational level (≤middle school, high school or college, ≥undergraduate school), smoking status (never, ever, current, unknown), alcohol drinking status (never, ever, unknown), physical activity (yes, no, unknown), and total intake (continuous).

Figure 1

Figure 2