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# Inadequate fat or carbohydrate intake was associated with an increased incidence of type 2 diabetes mellitus in Korean adults: A 12-year community-based prospective cohort study

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## ABSTRACT

**Aims:** Few studies have focused on the relationship between long-term fat intake and type 2 diabetes mellitus (T2D) risk in Asia where fat intake is relatively lower than the Western countries. We examined association of dietary fat and carbohydrate intake with incidence of T2D among Korean adults.

**Methods:** Based on the data from the Korean Genome and Epidemiology Study, a total of 5595 adults aged 40–69 years without diabetes, cardiovascular diseases or any cancer at baseline were included. Dietary intake was measured by the validated semi-quantitative food frequency questionnaire. Cox proportional hazards regression analysis was used to calculate multivariable-adjusted relative risks (RRs) and 95% confidence intervals (CIs).

**Results:** During a median follow-up of 138-months, 1010 cases of T2D were newly determined. The proportion of participants with fat intake less than 15% of total energy and with carbohydrate intake more than 65% of total energy was 59.0% and 88.9%, respectively. After adjusting for confounders, a very-low-fat intake was associated with an increased risk of T2D (RR of Quartile 1 vs Quartile 4, 1.74; 95% CI, 1.18–2.57; p for trend = 0.0058) in women. A very-high-carbohydrate intake was associated with an increased risk of T2D in men (RR of Quartile 4 vs Quartile 1, 1.54; 95% CI, 1.03–2.30; p for trend = 0.0124) and women (RR of Quartile 4 vs Quartile 1, 1.69; 95% CI, 1.08–2.67; p for trend = 0.0376).

**Conclusions:** A very-low-fat or very-high-carbohydrate intake may increase the T2D risk and might be associated with lower intake of various nutrients and unbalanced macronutrient composition.

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## 1. Introduction

Type 2 diabetes mellitus (T2D) has emerged as a critical public health concern in Asia, where it is differentiated from the characteristics of T2D in Western countries by affecting people at a relatively young age and with a low body mass index (BMI) [1]. In Korea, nearly 1 in 7 adults aged 30 years or more has diabetes and approximately 30% of adults aged 65 years or more have diabetes [2]. Due to rapid economic development in Asia, nutrition transition and sedentary lifestyles are now listed among the risk factors for T2D [1,3,4].

In particular, the traditional Asian diet has become westernized, characterized by higher consumption of animal products including meat and milk and dairy products, which has resulted in increased fat intake [5]. The actual fat intake among Koreans has gradually increased from 17.9% of total energy in 1998 to 22.9% of total energy in 2016 [6]. Nevertheless, the fat intake of the Asian population is still relatively low compared with that in Western populations. The average fat intake among adults in Korea is 21.4% of energy [6] and 27.1% among adults in Japan [7], whereas average fat intake in adults in the United States is 34% of energy [8] and 33.2% for adults in the United Kingdom [9].

Recently, cross-sectional studies reported that a low intake of fat was associated with an increased risk of metabolic syndrome in Korean adults [10,11]. In addition, dietary fat and carbohydrates are reported to have differential associations with lipid abnormalities in the Korean population [12]. A very-low-fat diet contributes to inadequacy of nutrients other than carbohydrates in addition to other adverse effects [13].

With regard to dietary carbohydrate intake, many observational studies have been conducted to investigate the T2D risk. Several prospective studies in Asian populations have reported that dietary carbohydrates, glycemic index, and glycemic load are positively associated with T2D in Chinese women [14] and rice intake is positively associated with T2D in Japanese women [15]. However, few studies examined the relationship between long-term fat intake and incident T2D in Asian populations.

The relationship of low-fat or high-carbohydrate intakes with risk of T2D remains inconclusive and the evidence established for Asian population is limited [16]. Thus, this study aimed to investigate the relationship between long-term fat and carbohydrate intake and incident T2D among middle-aged Korean adults followed up for 12 years.

## 2. Subjects and methods

### 2.1. Study design and participants

This study used data from the Korean Genome and Epidemiology Study (KoGES). The KoGES is a community-based prospective cohort study comprising 10,030 adults aged 40–69 years living in Ansan (an urban city) or Ansong (a rural city), both located in the Seoul metropolitan area, Korea. Participants were enrolled during 2001–2002 and have been followed up biennially through 2013–2014. Details of the KoGES can be found elsewhere [17].

Among the 10,030 participants, we excluded those who had diabetes at baseline or were missing variables required to define T2D ( $n = 1525$ ), refused to participate in the follow-up survey ( $n = 828$ ), and those who had cardiovascular diseases or any cancer at baseline ( $n = 1319$ ), did not participate in a food frequency questionnaire (FFQ) survey ( $n = 738$ ), and reported implausible energy intake ( $<500$  kcal/day or  $>5000$  kcal/day) ( $n = 25$ ). Thus, a total of 5595 participants were included in the final analysis.

The present study was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention and the Catholic University of Korea (1040395-201710-04). Written informed consent was received from every participant.

### 2.2. Assessment of dietary intake

Dietary intake was assessed using a 103-item validated semi-quantitative FFQ conducted at baseline (2001–2002) [18] and a revised version of the FFQ in the second follow-up period (2005–2006). Daily nutrient intake was calculated based on the seventh edition of Food Composition Table in Korea [19]. The cumulative average nutrient intake measured by the first and second FFQs was estimated for this analysis, to minimize measurement error and to represent long-term intake [20]. In order to evaluate the adequacy of energy and macronutrient intakes, the age-sex-specific estimated energy requirement (EER) and the acceptable macronutrient distribution range (AMDR) were used according to Dietary Reference Intakes for Koreans 2015 [21].

### 2.3. Measurement of sociodemographic information and health behaviors

Sociodemographic information such as age, sex, education, household income, and marital status as well as health behaviors including physical activity, alcohol consumption, and smoking status, were obtained using a self-administered questionnaire. Education level was categorized into elementary school or lower, middle school, high school, and college or higher. Household income level was classified into  $<1,000,000$ , 1 to  $<2,000,000$ , 2 to  $<4,000,000$ , and  $\geq 4,000,000$  Korean won (KRW) per month. Marital status was grouped into married and unmarried including divorced, separated, and the others. Physical activity was estimated using metabolic equivalents (METs)-hours per day. Study participants reported time spent on physical activities by intensities including sedentary, light, moderate, and vigorous. The METs-hours per day was calculated by multiplying the activity hours per day by MET value of each activity [22] and added up to total METs-hours per day. Alcohol consumption and smoking status were categorized into never, former, and current.

### 2.4. Measurement of biomarkers

Blood sample was collected for study participants who fasted for at least 8 h and measured at baseline and every two years of follow-up. A 2-h blood glucose was estimated by a 75-g oral

glucose tolerance test. Glucose levels were measured by an auto analyzer (ADVIA 1650; Siemens, Tarrytown, NY, USA). Fasting insulin was measured by a radioimmunoassay (Cobra gamma counter; Packard, Meriden, USA).

## 2.5. Ascertainment of type 2 diabetes mellitus

According to World Health Organization guidelines, T2D was defined as the existence of any one of following criteria during follow-up: (1) fasting blood glucose level  $\geq 126$  mg/dl, (2) 2-h blood glucose level  $\geq 200$  mg/dl, (3) physician's diagnosis of diabetes, and (4) treatment with oral hyperglycemic medication or insulin [23].

## 2.6. Statistical analyses

Energy and macronutrient intakes (percentage of total energy) were estimated using a generalized linear model (GLM) or chi-square test. Participants were stratified by sex and grouped into quartiles according to their percentage of energy from fat and carbohydrates. Differences in general characteristics according to quartile of fat and carbohydrate intake at baseline by sex were examined by chi-square test for categorical variables and a GLM for continuous variables with post-hoc Tukey's test. All continuous variables were log-transformed to normalize distribution and these values were used for statistical tests. For each participant, person-time was measured from the date of enrollment in the cohort to the date of T2D diagnosis or the date of joining the most recent follow-up survey. Cox proportional hazards regression analysis was carried out to estimate the relative risk (RR) and 95% confidence interval (CI) of T2D in quartiles of percentage of energy from fat and carbohydrates after adjusting for potential confounders such as BMI (continuous), education level, household income level, marital status, residence (Ansan or Ansong), physical activity, alcohol consumption, smoking status, parental history of diabetes (yes or no), energy intake (kcal/day), and protein intake (percentage of energy). Age at baseline (in 5-year categories) was used as stratification variable. Because fasting blood glucose level at baseline was different according to fat and carbohydrate intake, it was also included as confounding

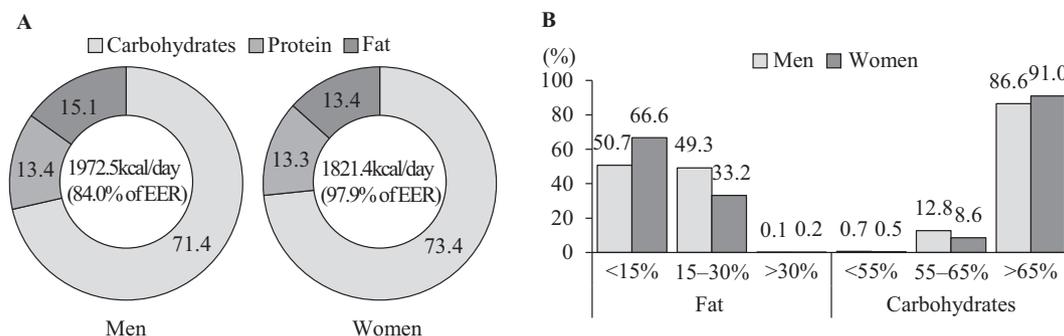
variables. We used the highest quartile for fat and the lowest quartile for carbohydrates as the reference group to examine the association between low-fat or high-carbohydrate intakes and incidence of T2D. We added cross-product terms between log-transformed time and dietary fat or carbohydrate intakes in the multivariable-adjusted model and observed no violation of the assumption of the proportional hazards. A linear trend was estimated using a median value of each quartile as a continuous variable.

Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA) and a two-sided  $p$ -value  $< 0.05$  was regarded as statistically significant.

## 3. Results

During a median follow-up of 138-months (range 5–152 months), 1010 participants (18.1%) were newly diagnosed with T2D. In this population, the average total energy intake was 1972.5 kcal in men and 1821.4 kcal in women, which was only 84.0% of EER for Koreans in men and 97.9% in women (Fig. 1A). In terms of macronutrient profile, the recommended ranges (AMDR) for Koreans are 15–30% of total energy for fat and 55–65% of total energy for carbohydrates (Fig. 1B). More than half of study participants consumed very-low-fat intake or very-high-carbohydrate intakes.

The general characteristics of study participants are presented in Table 1. At baseline, men and women with higher fat intake were more likely to be younger, live in urban area, have higher education and household income levels, and be current alcohol consumer. Men with a high intake of fat tended to have higher BMI and fasting blood glucose levels. The proportion of current smokers and parental history of diabetes was higher in women with higher fat intake than those with lower fat intake. With regard to carbohydrate intake, the baseline characteristics were mostly the opposite of fat intake (Supplementary Table 1). Men and women with higher carbohydrate intake tended to be older, live in rural area, and have lower education and household income level. In both sexes, current alcohol consumers and smokers were lower in those with higher carbohydrate intake than those with lower carbohydrate intake.



**Fig. 1 – Energy and macronutrient intake (A) and distribution of study participants according to dietary fat and carbohydrate intake compared to Dietary Reference Intakes (B).** (A) EER, estimated energy requirement. Macronutrient intake is presented as percentage of total energy. (B) According to Dietary Reference Intakes for Koreans, the acceptable macronutrient distribution range is 15–30% of total energy for fat and 55–65% of total energy for carbohydrates among adults. All values were statistically significantly different between men and women by a generalized linear model or chi-square test ( $p < 0.05$ ).

**Table 1 – General characteristics of study participants according to quartile of dietary fat intake at baseline.**

	Dietary fat intake (% of energy)			
	Men (n = 2684)		Women (n = 2911)	
	Quartile 1 (n = 671)	Quartile 4 (n = 671)	Quartile 1 (n = 727)	Quartile 4 (n = 728)
Age (years)	54.2 ± 9.1	48.5 ± 7.5	56.0 ± 8.6	47.4 ± 7.2
Residence				
Rural (Ansung)	470 (70.0)	244 (36.4)	568 (78.1)	294 (40.4)
Urban (Ansan)	201 (30.0)	427 (63.6)	159 (21.9)	434 (59.6)
Education				
Elementary school or lower	224 (33.6)	77 (11.5)	481 (66.9)	154 (21.3)
Middle school	169 (25.3)	135 (20.2)	151 (21.0)	184 (25.4)
High school	191 (28.6)	286 (42.8)	73 (10.2)	291 (40.2)
College or higher	83 (12.4)	170 (25.5)	14 (2.0)	95 (13.1)
Household income (KRW/month)				
<1,000,000	300 (45.2)	105 (15.8)	454 (64.2)	155 (21.5)
1 to <2,000,000	209 (31.5)	207 (31.1)	159 (22.5)	209 (29.0)
2 to <4,000,000	134 (20.2)	254 (38.1)	82 (11.6)	267 (37.1)
≥4,000,000	21 (3.2)	100 (15.0)	12 (1.7)	89 (12.4)
Married, n (%)	637 (95.1)	643 (96.1) <sup>†</sup>	582 (80.6)	664 (91.6)
Physical activity (METs-hours/day)	27.3 ± 17.1	23.9 ± 15.8 <sup>†</sup>	26.4 ± 16.5	21.3 ± 13.3 <sup>†</sup>
Alcohol consumption				
Never	156 (23.3)	102 (15.2)	576 (79.8)	442 (60.9)
Former	76 (11.4)	44 (6.6)	25 (3.5)	16 (2.2)
Current	437 (65.3)	524 (78.2)	121 (16.8)	268 (36.9)
Smoking status				
Never	126 (18.8)	134 (20.0) <sup>†</sup>	683 (95.3)	666 (93.0)
Former	216 (32.2)	185 (27.7)	11 (1.5)	13 (1.8)
Current	328 (49.0)	350 (52.3)	23 (3.2)	37 (5.2)
Parental history of diabetes (yes)	76 (11.4)	44 (6.6) <sup>†</sup>	39 (5.4)	83 (11.4)
BMI (kg/m <sup>2</sup> )	23.7 ± 3.0 <sup>a</sup>	24.3 ± 2.9 <sup>b</sup>	24.6 ± 3.3	24.3 ± 3.1 <sup>†</sup>
Fasting blood glucose (mg/dl)	83.4 ± 9.3 <sup>a</sup>	85.4 ± 9.3 <sup>b</sup>	81.9 ± 8.2	81.3 ± 7.8
2-hour glucose (mg/dl)	109.8 ± 32.8	110.9 ± 32.7 <sup>†</sup>	117.1 ± 28.7	114.8 ± 28.4 <sup>†</sup>
Fasting insulin (μIU/ml)	6.7 ± 3.7	7.1 ± 4.5 <sup>†</sup>	8.5 ± 6.3	7.8 ± 4.2 <sup>†</sup>

BMI, body mass index; KRW, Korean won; MET, metabolic equivalent.

Data are presented as mean ± standard deviation or n (%).

All values were statistically different according to quartiles by chi-square test for categorical variables and a generalized linear model for continuous variables ( $p < 0.05$ ) unless noted otherwise. Log-transformed values were used for statistical tests of continuous variables.

<sup>a,b</sup> Different superscript letters indicate significant differences according to quartiles by Tukey's test ( $p < 0.05$ ).

<sup>†</sup> Not statistically significant.

Higher fat intake was associated with higher total energy intake in both men and women (Table 2). Among the highest quartile of dietary fat, total energy intake of men and women was 96.0% and 111.8% of EER, respectively. Vitamin such as vitamin A, B, E, and folate and mineral such as calcium, potassium, and zinc intakes were positively associated with fat intake after adjusting for age and total energy intake. On the other hand, higher carbohydrate intake was related to lower intakes of vitamins and minerals (Supplementary Table 2).

In the multivariable-adjusted Cox proportional hazards model (Table 3), women in the lowest quartile of dietary fat intake showed a 1.70 times higher risk of T2D compared to those in the highest quartile (95% CI, 1.16–2.50;  $p$  for trend = 0.0105) after adjusting for confounding factors including total energy and protein intake. However, no significant association was observed in men. Since fasting blood glucose

level was different according to fat and carbohydrate intake at baseline in men (Table 1, Supplementary Table 1), fasting blood glucose level at baseline was additionally adjusted for. Further adjustment for fasting blood glucose level at baseline maintained a significant association among women and showed an increasing trend of T2D risk with decreased fat intake among men, although this was not statistically significant (RR, 1.40; 95% CI, 1.00–1.96;  $p$  for trend = 0.0374).

Association between dietary carbohydrate intake and the incidence of T2D was also examined in Table 4. Women in the highest quartile of dietary carbohydrate intake showed a 1.76 times increased risk of T2D compared to those in the lowest quartile (95% CI, 1.12–2.75;  $p$  for trend = 0.0314). Men also showed an increasing trend of T2D risk with increased carbohydrate intake, but this was not statistically significant. Additional adjustment for fasting blood glucose level at baseline strengthened positive associations in both men and

**Table 2 – Nutrient intake of study participants according to quartile of dietary fat intake.**

	Dietary fat intake (% of energy)					
	Men (n=2684)			Women (n=2911)		
	Quartile 1 (n=671)	Quartile 4 (n=671)	P for trend	Quartile 1 (n=727)	Quartile 4 (n=728)	P for trend
Energy (kcal/day)	1740.9 ± 17.6	2218.9 ± 18.7	<0.0001	1600.3 ± 18.2	2056.0 ± 19.8	<0.0001
EER/Energy (%)	76.7 ± 0.8	96.0 ± 0.8	<0.0001	88.1 ± 1.0	111.8 ± 1.1	<0.0001
<b>Macronutrients (% of energy)</b>						
Fat	9.9 ± 0.1	20.6 ± 0.1	<0.0001	8.1 ± 0.1	19.0 ± 0.1	<0.0001
Protein	11.8 ± 0.1	15.2 ± 0.1	<0.0001	11.4 ± 0.1	15.1 ± 0.1	<0.0001
Carbohydrates	78.3 ± 0.1	64.2 ± 0.1	<0.0001	80.5 ± 0.1	65.9 ± 0.1	<0.0001
<b>Vitamins</b>						
Vitamin A (ug RE/day)	479.1 ± 9.8	586.0 ± 10.4	<0.0001	432.0 ± 9.9	569.5 ± 10.7	<0.0001
Vitamin B <sub>1</sub> (mg/day)	1.1 ± 0.0	1.4 ± 0.0	<0.0001	1.0 ± 0.0	1.3 ± 0.0	<0.0001
Vitamin B <sub>2</sub> (mg/day)	0.8 ± 0.0	1.2 ± 0.0	<0.0001	0.7 ± 0.0	1.1 ± 0.0	<0.0001
Niacin (mg/day)	14.2 ± 0.1	17.8 ± 0.1	<0.0001	12.8 ± 0.1	16.0 ± 0.1	<0.0001
Vitamin C (mg/day)	113.1 ± 1.9	109.8 ± 2.0	0.0227	124.1 ± 2.3	122.9 ± 2.5	<0.0001
Vitamin E (mg/day)	8.3 ± 0.1	9.7 ± 0.1	<0.0001	7.6 ± 0.1	9.7 ± 0.1	<0.0001
Folate (ug/day)	228.5 ± 2.9	238.9 ± 3.1	<0.0001	223.2 ± 2.9	245.6 ± 3.1	<0.0001
<b>Minerals</b>						
Calcium (mg/day)	391.8 ± 5.8	514.6 ± 6.2	<0.0001	367.7 ± 5.8	562.7 ± 6.3	<0.0001
Potassium (mg/day)	2263.4 ± 21.8	2613.9 ± 23.2	<0.0001	2152.8 ± 22.5	2660.0 ± 24.5	<0.0001
Sodium (mg/day)	3094.6 ± 45.6	3351.8 ± 48.5	<0.0001	2703.2 ± 40.1	3045.7 ± 43.6	<0.0001
Zinc (mg/day)	8.2 ± 0.1	9.6 ± 0.1	<0.0001	7.3 ± 0.1	8.8 ± 0.1	<0.0001

RE, retinol equivalent.

All values were presented as adjusted mean ± standard error after adjusting for age and total energy intake (except energy intake) by a generalized linear model and were statistically different between the lowest and highest quartile by Tukey's test ( $p < 0.0001$ ) except vitamin C intake of men. Log-transformed values were used for statistical tests.

women. The RRs for the highest quartile of dietary carbohydrate intake was 1.54 in men (95% CI, 1.03–2.30;  $p$  for trend = 0.0124) and 1.69 in women (95% CI, 1.08–2.67;  $p$  for trend = 0.0376).

#### 4. Discussion

In this prospective study of a 12-year follow-up, we found that a very-low-fat intake (less than 10% of total energy) or very-high-carbohydrate intake (more than 80% of total energy) was associated with an increased risk of incident T2D in middle-aged Korean adults.

This finding was not consistent with previous large prospective studies for Western population. Although the findings for total fat intake was inconclusive with no association of the risk of T2D in American [24–26] and Swedish [27] adults, and a positive association in Finnish adults [28], dietary fat has been reported to have different associations with cardiovascular diseases by their food source or subtypes [16]. Several prospective studies in Western countries reported that vegetable fat and polyunsaturated fat were associated with decreased risk of T2D [24,25], whereas animal fat and saturated fat were associated with increased risk of T2D [29]. In the present study, we could not examine the association of specific fatty acids with T2D because of a lack of database. However, our findings suggest that not excessive intake but inadequate intake was associated with an increased risk of T2D in Asians.

Riccardi et al. [30] suggested that if fat intake exceeds 35–40% of total energy, the amount of fat can have an influence on insulin sensitivity and the risk of T2D. Fat intakes were low among our study participants (an average 14.2% of total energy), and few participants had excessive fat compared to the AMDR. According to Misra et al. [31], appropriate fat intake over the minimum 15% of total energy is needed in Asians, for adequate intake of essential fatty acids. A cross-sectional study among Korean adults also found that very-low-fat intake was positively associated with the risk of metabolic syndrome [10]. In addition, a recent study in a Chinese population reported that a high-fat diet was only associated with an increased risk of T2D when participants had extra energy intakes [32].

Although mechanisms underlying the association between dietary fat and T2D remain unclear, it has been known that the quality of dietary fat affects glucose metabolism by changing cell membrane function, enzyme activity, insulin signaling and gene expression [33]. According to a meta-analysis of randomized controlled trials, replacing carbohydrate and saturated fat with an adequate intake of unsaturated fat was favorable for blood glucose control [34]. In particular, supplementation of polyunsaturated fatty acids might be beneficial treatment for T2D in Asian populations [35]. Therefore, sufficient unsaturated fatty acid intake with carbohydrate restriction is needed and further clinical trials are required to establish scientific evidences for substitution effect of carbohydrate with dietary fat among Koreans.

**Table 3 – Relative risks (RRs) and 95% confidence intervals (CIs) of type 2 diabetes mellitus according to quartile of dietary fat intake.**

	Dietary fat intake (% of total energy)				P for trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Men (n = 2684)					
Median (range)	10.2 (3.0–12.0)	13.5 (12.0–14.9)	16.3 (14.9–17.8)	20.2 (17.9–33.2)	
Cases (n)/person-months	129/71,413	142/73,415	125/74,707	137/69,763	
Model 1	1.35 (0.96–1.89)	1.22 (0.92–1.62)	0.94 (0.72–1.21)	1.00 (Ref.)	0.0521
RR (95% CI) <sup>a</sup>					
Model 2	1.40 (1.00–1.96)	1.22 (0.92–1.61)	0.96 (0.74–1.25)	1.00 (Ref.)	0.0374
RR (95% CI) <sup>b</sup>					
Women (n = 2911)					
Median (range)	8.2 (2.4–10.2)	11.6 (10.2–13.0)	14.4 (13.0–16.2)	18.6 (16.2–41.9)	
Cases (n)/person-months	132/81,624	116/85,131	113/83,950	116/81,877	
Model 1	1.70 (1.16–2.50)	1.20 (0.87–1.65)	1.09 (0.82–1.45)	1.00 (Ref.)	0.0105
RR (95% CI) <sup>a</sup>					
Model 2	1.74 (1.18–2.57)	1.31 (0.95–1.81)	1.14 (0.85–1.53)	1.00 (Ref.)	0.0058
RR (95% CI) <sup>b</sup>					

<sup>a</sup> Adjusted for alcohol consumption, body mass index, education level, household income level, marital status, smoking status, parental history of diabetes, physical activity, residence, protein intake (% of total energy), and total energy intake (kcal/day). Age at baseline was used as stratification variable.

<sup>b</sup> Additionally adjusted for fasting blood glucose at baseline.

**Table 4 – Relative risks (RRs) and 95% confidence intervals (CIs) of type 2 diabetes mellitus according to quartile of dietary carbohydrate intake.**

	Dietary carbohydrate intake (% of total energy)				P for trend
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Men (n = 2684)					
Median (range)	64.7 (46.7–67.7)	69.8 (67.7–71.7)	73.7 (71.7–75.6)	78.0 (75.6–88.2)	
Cases (n)/person-months	146/69,234	117/75,211	149/72,407	121/72,446	
Model 1	1.00 (Ref.)	0.90 (0.68–1.19)	1.39 (1.02–1.91)	1.38 (0.92–2.07)	0.0339
RR (95% CI) <sup>a</sup>					
Model 2	1.00 (Ref.)	0.92 (0.69–1.22)	1.40 (1.02–1.93)	1.54 (1.03–2.30)	0.0124
RR (95% CI) <sup>b</sup>					
Women (n = 2911)					
Median (range)	66.3 (37.9–69.6)	71.8 (69.6–73.7)	75.6 (73.7–77.6)	80.4 (77.6–88.6)	
Cases (n)/person-months	118/81,465	125/83,269	101/86,148	133/81,700	
Model 1	1.00 (Ref.)	1.14 (0.84–1.54)	1.05 (0.73–1.50)	1.76 (1.12–2.75)	0.0314
RR (95% CI) <sup>a</sup>					
Model 2	1.00 (Ref.)	1.11 (0.82–1.51)	1.09 (0.75–1.57)	1.69 (1.08–2.67)	0.0376
RR (95% CI) <sup>b</sup>					

<sup>a</sup> Adjusted for alcohol consumption, body mass index, education level, household income level, marital status, smoking status, parental history of diabetes, physical activity, residence, protein intake (% of total energy), and total energy intake (kcal/day). Age at baseline was used as stratification variable.

<sup>b</sup> Additionally adjusted for fasting blood glucose at baseline.

As dietary fat intake is reciprocally related to dietary carbohydrate intake, we also examined the association between carbohydrates and T2D after adjusting for confounding variables, including total energy and protein intakes. We found that a very-high-carbohydrate intake was related to an increased risk of T2D in Korean men and women. Several studies of dietary carbohydrates and T2D have been conducted in Asian populations [14,15]. In particular, white rice has been reported as increasing the risk of T2D in Chinese women [14] and Japanese women [15], as white rice is a staple food in these countries.

In the management of T2D, energy restriction is regarded as more crucial factor than the proportion of fat and carbohydrates [36]. However, our additional analyses showed no significant relationship between total energy intake and the risk of T2D (data now shown) and it might be explained that most of participants consumed less total energy than the EER.

The inverse association between fat intake and the risk of T2D in this study might be attributable to inadequate nutrient intake and unbalanced macronutrient composition. The current study showed that the very-low-fat intake group had lower energy and vitamin and mineral intakes than the

high-fat intake group, but the former group tended to depend on carbohydrates as the main energy source. Although the necessity for vitamin and mineral supplementation in the prevention or management of T2D is controversial [37], moderate intake of fruits or vegetables has been shown to be related to a decreased risk of T2D [38,39].

In recent years, nutrition transition which includes increasing fat intake due to adoption of the western dietary pattern has been paid attention in public in Asian countries [1,5]. Dietary fat appears to be the major dietary factor of cardiovascular disease, which misled the public that dietary fat intake is not benefited for health. A recent prospective study for Korean adults showed that processed red meat consumption was not associated with increased risk of T2D and cardiovascular diseases [40]. Moreover, Lee et al. [41] reported that a very-high-carbohydrate diet in Korea was attributable to a lower consumption of meat, fish, egg, and beans, as well as dairy products.

In Korea, a low socioeconomic status including education and income levels was associated with low-fat or high-carbohydrate intakes in this study and the other previous study [10]. Even though a low-fat intake group had relatively healthy lifestyles in terms of smoking, alcohol drinking, and physical activity, an increased risk of T2D was found. Moreover, older adults were likely to consume lower fat and their diet was mainly composed of white rice [42,43]. Since the age has also been reported as one of predictors for T2D in Koreans [44], specific dietary strategies would be necessary for older adults who have a lower socioeconomic status.

This is the first prospective study to examine the association between long-term fat intake and the risk of incident T2D in the Korean adult population. When total energy intake is within the recommended range, adequate amount of fat intake may be important for Koreans.

However, the present study has several limitations. First, we could not estimate specific fatty acid intake because of a lack of database. Second, because the study comprised middle-aged participants, it is difficult to generalize the study findings to younger populations. Third, even though we controlled for confounders after a review of previous studies and conducting step-wise regression, there may be unmeasured residual confounding. Fourth, due to the lack of biochemical and anthropometrical variables at follow-up, this study should be interpreted with caution along with other limitations. Lastly, there was no retesting to confirm the diagnosis in asymptomatic individuals that classification error may occur. However, it is not feasible to retest in a large-scale ongoing cohort study that physician's diagnosis of diabetes or treatment with medications was included in the diagnosis criteria.

In conclusion, our findings indicate that in Korean adults who maintain a low-fat diet along with inappropriate energy intake, very-low-fat intake may contribute to increased risk of T2D and might be associated with lower intake of various nutrients and unbalanced macronutrient composition. Dietary strategies that satisfy an optimal macronutrient profile should be appraised, to prevent or manage for T2D in Asian populations.

## Author contributions

KH analyzed the data and wrote the draft. HJ revised the manuscript and provided essential comments. YS supervised all the work and had primary responsibility for the final content. All authors read and approved the manuscript.

## Conflict of interest

The authors declare no potential conflicts of interest.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.diabres.2019.01.024>.

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