DASH diet was enhanced by its combination with a reduced sodium diet (100 and 50 mmol/day). The results of the present study support those of the DASH trials by showing similar, albeit somewhat weaker, results in a free-living, general population.

Further, Nowson *et al.* [28] conducted a cross-over dietary intervention study using a community-living subject. They reported a significant decrease in BP by a low-sodium, high-potassium diet and a DASH-type diet (DASH diet with moderate sodium reduction). The tendency of the results was similar to those of the present study, but the size of the effect was greater. However, the study population in their study was smaller ($n = 94$), the study period shorter (4 weeks), and the intervention more intensive (bi-weekly contact) than in the present study. Salt-free bread, salt-free margarine or both were provided to the intervention subjects. In contrast, no food was provided in the present study. The method used in the present study appears to be more practicable for use in community settings than that in the study of Nowson *et al.* [28].

Study limitations

Because this study was an open trial, the possibility of interaction between the intervention and control groups, such as information exchange, cannot be ruled out. In the control group, however, no statistically significant change in targeted nutrients and foods between the baseline and year 1 points was observed, suggesting that any interaction between the groups may have been negligible. Nevertheless, the possibility of some general information exchange remains, and the results should therefore be interpreted with caution.

To examine a practical model for population-based lifestyle improvement intervention, our present intervention study was performed in a primary health care setting rather than an academic center setting. Measurement of BP was conducted at the annual health check-up as a routine component of that check-up, and thus only a single measurement was done instead of multiple measurement. Nevertheless, conditions between the two groups were the same.

Because they had been previously exposed to various public health campaigns in the study area on the importance of decreasing salt intake, the present study subjects were relatively well-motivated to reduce their salt intake [29]. Moreover, they were provided further information about the unfavorable effect of dietary sodium on health prior to the start of the study. We therefore presume that they were more receptive to the message to decrease sodium given in this study. The decrease in sodium and consequent decrease in BP observed in this trial indicates the effectiveness of this intervention method for motivated persons. Further studies are necessary to determine whether this intervention method is equally effective on dietary and BP modification in other populations.

In conclusion, these findings indicate that the effects of dietary interventions undertaken to reduce the intake of sodium and increase that of fruit and vegetables may be expected to decrease BP level in free-living populations. The present randomized, controlled trial involved a relatively large number of free-living subjects and examined the change in dietary habits and BP over 1 year. The intervention method used here may represent an efficient and practicable model for population-based BP improvement in common primary care settings.

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Histidine Intake May Negatively Correlate with Energy Intake in Human: A Cross-Sectional Study in Japanese Female Students Aged 18 Years

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Summary L-Histidine (histidine), a precursor of neuronal histamine, has recently been hypothesized to suppress food intake. The association between dietary histidine and energy intake was examined among 1,689 Japanese female students of dietetic courses aged 18 y. Nutrient intakes were assessed over a 1-mo period with a validated, self-administered, diet history questionnaire. Both intake of histidine and the ratio of histidine to protein (histidine/protein) statistically and positively correlated with energy intake. After adjustment for potential non-dietary confounding factors, including body height, body weight, physical activity level, and rate of eating, both the histidine intake and histidine/protein ratio statistically and positively correlated with energy intake (Pearson's correlation coefficient, r=0.62 and 0.12, respectively, $p<0.001$). Moreover, when protein or protein excluding histidine was additionally included into the covariates in order to minimize the effect of dietary factors and other amino acids, both histidine intake and histidine/protein ratio turned out to show a statistically negative correlation with energy intake ($r=-0.22$ and -0.23, respectively, $p<0.001$). Considering the influence of unavoidable various covariates, we found an inverse association between histidine/protein ratio and energy intake among the young female Japanese students.

Key Words dietary histidine, energy intake, young Japanese women, epidemiology

Hypothalamus neuronal histamine has been shown to regulate food intake through the histamine H_1-receptor in the ventromedial hypothalamic nucleus and the paraventricular nucleus (*1–3*). Recently, it has been hypothesized that L-histidine (histidine), an essential amino acid, might also control food intake through its conversion into histamine (*4–6*). Histidine preloads delivered by intraperitoneal injection (IP) into rats reduced food intake (*7, 8*) and increased water intake (*8, 9*). Although histidine given by the intragastric route showed a low sensitivity to food intake suppression compared to IP, dietary histidine might also play a role in regulating food intake in the short-term, at least partially through the histaminergic pathway (*8*). However, its physiological importance has not been established.

On the other hand, in human studies, the effect of histidine on food intake was examined in respect to the alterations in zinc metabolism accompanied by anorexia in the 1970s (*10–13*). Administration of a large dose of histidine induced zinc deficiency, which led to functional losses of taste, smell, appetite, and food intake. Therefore, according to the previous points of view from human studies, feeding suppression has seemed to be caused by alteration of zinc metabolism rather than direct effects of histidine. However, pretreatment with alpha-fluoromethyl histidine (FMH), a specific suicide inhibitor of histamine-synthesizing histidine decarboxylase (HDC), attenuated histidine-induced feeding suppression in animal studies (*5, 6*). These results support the view that histidine-induced histamine rather than the histidine-induced zinc deficiency affects food intake. Although the available evidence in animal studies strongly suggests the effect of histidine on food intake, in human, only two small observational studies conducted in Japan examined this issue (*14, 15*).

To examine the association in more detail, we conducted a cross-sectional study using a large and homogenous sample consisting of 1,689 Japanese female dietetic students aged 18 y.

SUBJECTS AND METHODS

Subjects. The subjects were freshmen who entered dietetic courses at 22 colleges and technical schools in Japan in April 1997 (n=2,069). All the questionnaires were distributed between April 7 and 21, 1997. A total of 2,063 students (2,017 women and 46 men) returned the completed questionnaires within 1 wk (response rate, 99.7%). Faculty members of each school checked the submitted questionnaires. When missing replies and/or errors were found, the subjects were requested to answer the questions again. All question-

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naires were checked at least once by the local staff and once by the staff of the study center. The entire survey was completed before the end of May.

Assessment of dietary habits. We used a self-administered diet history questionnaire (DHQ). The DHQ is a validated 16-page questionnaire assessing dietary habits in the previous 1 mo. Intakes of 147 food items, 16 nutrients, and total energy intake were calculated using an ad-hoc computer algorithm developed to analyze the questionnaire. The 147 foods from the DHQ were grouped into 17 food groups, mainly according to the food composition tables of Japanese foods, 5th revised edition (*16*). The DHQ has been validated by comparison to 3-d dietary records. The Pearson's correlation coefficients were 0.48–0.55 for the macronutrients used in the study and 0.48 for energy. Moreover, the mean reported intakes of energy and three macronutrients assessed by the DHQ were close to the reported intakes assessed by dietary records, i.e., within a ±3% difference. A more detailed description of the questionnaire, the methods of calculating nutrients, and the validity are given elsewhere (*17, 18*). We estimated histidine intake using the DHQ attached with the amino acid food composition table (*19*) and supplemental food composition table of amino acid proposed by Todoriki et al. (*20*). We examined the validity of histidine intake from the DHQ by comparison with 16-d dietary records (16-d DRs) among Japanese men (n=92) and women (n=92) aged 30–78 y. The mean intake assessed by the DHQ was 2,192±774 mg/d for men and 2,144±628 mg/d for women. The mean intake assessed by 16-d DRs was 2,084±492 mg/d and 1,744±326 mg/d, respectively. Moreover, the Pearson's correlation coefficients were 0.37 and 0.32 for men and women, respectively.

Assessment of lifestyle variables. Lifestyle variables were obtained from the 4-page questionnaire designed for this survey. It included the frequency of sports club activity and smoking habits. The physical activity level was assessed by the monthly frequency of sports club activity without inquiring into the types of sports, their intensity or duration. The subjects who engaged in sports club activity at least once per week in the previous month were defined as 'physically active' and the others as 'sedentary.' Smoking habits were divided into three categories: never-, past-, and current smokers. Current smokers were defined as subjects who reported smoking cigarettes on a regular basis, whereas past-smokers were defined as subjects who quit smoking. Data on birthday, self-reported body weight, height, and rate of eating were obtained from the DHQ. Rate of eating was self-reported according to one of five qualitative categories: 'very slow,' 'relatively slow,' 'medium,' 'relatively fast,' and 'very fast.' The validity of this rating was described in the previous paper (*21*). BMI was calculated as body weight (kg) divided by the square of body height (m^2).

Statistical analysis. We included 1,689 subjects (83.3%) who satisfied the following two criteria in the analysis:

1) Women aged 18 y on the surveyed day (n=1,744);

2) Those with reported energy intake of more than or equal to half of the energy requirement of the lowest physical activity category and less than 1.5 times the energy requirement of the highest physical activity category (*22*), i.e., the subjects with reported energy intake of 3.0–14.4 MJ/d (n=1,980).

Macronutrient intakes were energy-adjusted using an energy density model, i.e., the percentage of energy intake (%E). Histidine was divided by the protein intake, i.e., histidine/protein (mg/g).

Differences in the means of energy intake between categories were tested by the Student's *t* test or ANOVA. Multiple regression analysis was performed to examine the effect of daily histidine intake on energy intake. Several confounding factors have been reported for energy intake, such as body height, body weight, physical activity level, and rate of eating (*21, 23–25*). In this analysis, these non-dietary variables were included in the models as covariates (Model 2). Furthermore, we additionally adjusted for dietary variables such as dietary fiber and protein as dietary confounding factors (Model 3). When histidine intake was used as an independent variable, protein excluding histidine (protein−histidine) was included as a dietary covariate to adjust for possible effects of other types of amino acids. We also computed the partial correlation coefficients between each independent variable and energy intake adjusting for other independent variables.

All statistical analyses were performed using version 8.2 of the SAS software package (SAS Institute, Inc., Cary, North Carolina, USA). A p-value of <0.05 was considered significant.

RESULTS

Table 1 shows the characteristics of the subjects and Pearson's correlation coefficients for each variable with energy intake. The mean BMI±SD for the subjects was 20.8±2.6 kg/m^2, and 95% of the subjects were classified into the non-obese group (25 kg/m^2 < BMI). In Pearson's correlation coefficient, a significant correlation with energy intake was observed for body height (p<0.001), sports club activity (p=0.04), and all nutrients described in Table 1, such as macronutrients, total dietary fiber, histidine, protein extracting histidine, and histidine/protein ratio (p<0.001 in all nutrients). As for categorical variables, the mean energy intake was significantly different between the two physical activity levels (p<0.001) and among the five categories of rate of eating (p<0.001).

Table 2 shows the results of multiple regression analysis with energy intake as a dependent variable. Histidine positively correlated with energy intake regardless of the adjustment of non-dietary factors (partial regression coefficient, β=0.002 in Model 1: β=0.002 in Model 2). However, after additional adjustment for dietary factors, such as total dietary fiber and protein excluding histidine, histidine intake turned out to show a negative correlation with energy intake (β=

Table 1. Physiological characteristics, lifestyle variables, and nutrient intakes of the subjects[a], and Pearson's correlation coefficients with energy intake.[b]

	Mean±SD (n=1,689)	Pearson's correlation coefficient with energy intake	p-value	t-value[e]	p-value
Body height (cm)	158.0±5.2	0.13	<0.001	—	—
Body weight (kg)	51.8±7.3	0.03	0.22	—	—
Body mass index (kg/m^2)	20.8±2.6	−0.03	0.17	—	—
Sports club activity (d/mo)	1.7±4.2	0.05[c]	0.04	—	—
Nutrient intake					
Energy intake (MJ/d)	7.2±2.0	—	—	—	—
Carbohydrate (g/d)	234.1±58.8	0.86	<0.001	—	—
Fat (g/d)	58.0±24.1	0.88	<0.001	—	—
Total protein (g/d)	63.3±21.0	0.86	<0.001	—	—
Total dietary fiber (g/d)	12.0±4.7	0.66	<0.001	—	—
Histidine (mg/d)	2081±785	0.79	<0.001	—	—
Protein excluding histidine (g/d)	61.2±20.3	0.86	<0.001	—	—
Histidine/protein ratio (mg/g)	32.6±3.2	0.12	<0.001	—	—
Percentage of subjects (%)					
Physical activity level					
Sedentary	88	—	—	−3.74	<0.001
Physically active[d]	12				
Rate of eating				6.65[f]	<0.001
Very slow	5				
Relatively slow	23				
Medium	36	—	—		
Relatively fast	32				
Very fast	4				
Experience of dieting[g]				−0.85	0.40
No	40				
Yes	60	—	—		
Smoking habits				2.75[f]	0.06
Current	3				
Past	3	—	—		
Never	94				
Alcohol intake[h]				0.60	0.55
Non-drinker	81				
Drinker	19	—	—		

[a] Unless otherwise specified, values are expressed as mean±SD.
[b] Pearson's correlation coefficient for numerical variable.
[c] Spearman's correlation coefficient for numerical variable because of the very skewed distribution.
[d] The subjects who took part in sports club activity at least once per week were defined as physically active.
[e] t-value for difference in energy intake between categories (t-test).
[f] F-value for difference in energy intake between categories (ANOVA).
[g] Dieting by intentional reduction of body weight within 1 mo by more than 2 kg.
[h] The subjects who did not drink alcohol during the previous 1 mo were defineds as non-drinkers and the others as drinkers.

−0.0011 in Model 3). The results were similar for histidine/protein (β=−0.079 in Model 3).

DISCUSSION

In this cross-sectional study of young Japanese women aged 18 y, both crude histidine intake and the ratio of histidine to protein (histidine/protein) negatively and significantly correlated with energy intake, independent of the other dietary factors and the currently known covariates (Pearson's correlation coefficient, r=−0.22, p<0.001 for histidine crude value; r=−0.23, p<0.001 for histidine/protein). One small-scale cross-sectional study with 26 male and 38 female students has also found a negative association between histidine/protein and energy intake, but it was statistically significant only in women (r=−0.18 in men and r=−0.34, p<0.05 in women) (*14*). Therefore, our findings on the basis of data from a large and homogenous sample suggested that dietary histidine might have a suppressive effect on energy intake in human.

Among previous animal studies, a number of approaches have been tried to clarify the roles of the histamine signaling pathway in the regulation of food intake (*5, 6, 26–28*). However, the routes of histidine

Table 2. Multiple regression analysis on association between dietary histidine intake, histidine/protein and energy intake (MJ/d).[a]

	Partial regression coefficient	R^2	*p*-value	Pearson's partial correlation coefficient
Histidine intake (mg/d)				
Model 1[b]	0.0020	0.62	<0.001	0.79
Model 2[c]	0.0020	0.63	<0.001	0.62
Model 3[d]	−0.0011	0.75	<0.001	−0.22
Histidine/protein (mg/g)				
Model 1[b]	0.076	0.01	<0.001	0.12
Model 2[c]	0.072	0.05	<0.001	0.12
Model 3[d]	−0.079	0.75	<0.001	−0.23

[a] Partial regression coefficient, adjusted R^2, and *p* values are for independent variables in multiple regression.
[b] Model 1: simple regression and correlation analyses.
[c] Model 2: adjusted for body height, body weight, sports club activity level (two categories), and rate of eating.
[d] Model 3: additionally adjusted for total dietary fiber and protein excluding histidine for histidine intake. When histidine/protein ratio was used as an independent variable, total dietary fiber and protein intake were included as a covariate.

administration were almost all intracerebroventricular infusion or intraperitoneal (IP) injection (*6–9, 28*). On the other hand, the intragastric route had been examined in rats by Vaziri et al. (*8*). Although the sensitivity to the suppression of food intake was low compared to that for IP, the results suggested that dietary histidine might play a role in regulating food and water intake. The suppressive effect of dietary histidine on energy intake observed in our human study was in agreement with the result reported by Vaziri et al.

To our knowledge, studies of the effects of histidine on feeding regulation in human were conducted mostly in the 1970s (*10–12*), except for one study (*14*). Most studies suggested that feeding suppression seemed to be caused by alteration of zinc metabolism rather than the direct effects of histidine. But a large dose of histidine such as more than 4 g/d was reported to produce anorexia even without alteration of the zinc metabolism (*11, 12*). Considering the above-mentioned reports, the possibility that histidine-induced zinc deficiency affects energy intake seemed to be quite low in our study because the mean intake of histidine was about 2.1 g/d (Table 1).

Several dietary and non-dietary variables have been reported to show an association with energy intake (*23–25*). However, the previous epidemiologic studies have not taken into consideration the confounding factors that are unavoidable in epidemiologic studies. Therefore, it was nearly impossible to accept the observed negative correlation between histidine and energy intake. On the other hand, we considered the confounding factors in this study (Models 2 and 3 in Table 2). After adjustment for non-dietary factors, both histidine and histidine/protein ratio positively correlated with energy intake (r=0.62 and 0.12, respectively, p<0.001). Since physical activity is known to be associated with energy intake, we also conducted the same analyses dividing the subjects into two groups by physical activity level, i.e., sedentary or physically active. However, the results did not materially change (data not shown). As for dietary factors, because both histidine and protein highly correlated with energy intake (r=0.79 and 0.86, respectively), we entered protein intake as a covariate into the multiple regression analyses in order to avoid multicolinearity as much as possible. Moreover, we adjusted for protein excluding dietary histidine in order to minimize a possible effect of other amino acids. Dietary histidine negatively correlated with energy intake after adjustment for dietary and non-dietary confounding factors in our study. These findings provide a new insight into a role of dietary histidine in energy intake in human, although it is not enough. However, we do not know whether this model was fully appropriate for examining the association between dietary histidine and energy intake.

It is most important to understand that self-reported dietary intakes are not entirely free from reporting errors such as underreporting of energy and food intakes (*29, 30*). In this population, when we examined the validity of energy intake to basal metabolic rate (EI/BMR) (*31, 32*), 37% of subjects tended to underreport energy intake because their EI/BMR level was below the minimum survival value of 1.27 (*33*). Few studies have examined the bias in reporting nutrients and types of foods consumed (*34, 35*). Inconsistent with our results (data not shown), Livingstone and Black revealed that energy from protein tended to be significantly higher in low energy reporters (*29*). Moreover, the low energy reporters tended to report a higher consumption of "socially desirable" foods such as meat, fish, and vegetables (*29*). Therefore, the results should be cautiously interpreted in respect to underreporting of energy intake.

Our data are limited by the possibility of error with respect to the measurement of diet and the calculation of dietary histidine intake because of the lack of a comprehensive food composition table of amino acids (*19*). Therefore, when histidine content of a particular food was unavailable, we used the reported value for a similar food, as proposed by Todoriki et al. (*20*). This procedure was used for the development of the food composition table of fatty acids, and the validity was examined (*36*). However, this procedure was far below the quality required for the study. Moreover, the validity of this procedure used for amino acids has not been reported. In addition, the food composition table of amino acid substitution used in this procedure is not available to the public. Nonetheless, we considered this method as the best available at the present time in Japan. The results should be interpreted very cautiously.

Some limitations of our study should be considered in interpreting the results. First, the subjects were not a randomly sampled general Japanese population but selected female dietetic students aged 18–20 y. Because they were freshmen who entered the dietetic course, the participants in this study might be highly health-conscious. In order to minimize the influence of nutritional education, we finished the survey within almost 1 mo after entrance into the course. Secondly, our findings came from a cross-sectional study. Therefore, it was impossible to evaluate causal association between histidine and energy intake. Moreover, epidemiologic studies can not clarify the mechanism of the effect of histidine intake on energy intake. Thirdly, the lists of food items in the DHQ, especially those of fishes, were made based on the conventional nutrients such as fats rather than histidine. The histidine intakes obtained by the DHQ in this study might have been less accurate than a direct observation by dietary record. Fourthly, the effective time, duration, and quantity of dietary histidine for regulating energy intake were not strictly clear in this study. In the case of animal studies, histidine was shown to be a regulator of short-term food intake, and the time interval for observation was designed within 24 h (*6, 8*). We might have misunderstood the relationship between histidine and energy intake observed in this study because habitual histidine intake for the previous 1 mo was assessed in our study. Fifthly, although we adjusted for possible confounding variables, unmeasured or unknown confounding dietary factors cannot be excluded.

In conclusion, we found an inverse association between histidine/protein ratio and energy intake among young female Japanese students. Although the central roles of mechanisms for regulation of energy intake have already been established in animal and in vitro studies, the contribution of daily histidine intake is not yet fully understood in humans. Future epidemiologic studies with better study designs are warranted to examine the role of dietary histidine in energy intake in human.

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Report

Effect of Dietary Factors on Incidence of Type 2 Diabetes: A Systematic Review of Cohort Studies

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Summary We systematically reviewed cohort studies on the effect of nutrient and food intake (except for alcohol) on the incidence of type 2 diabetes, which had been published in English as of May 2004. Using the MEDLINE (PubMed) database as well as reference lists of searched papers, 15 individual cohort studies (a total of 31 papers) were identified. The number of subjects (n=895–85,060), follow-up length (5.9–23 y), the number of diabetes cases (n=74–4,085), dietary assessment method used (simple food questionnaire, food frequency questionnaire, food frequency interview, diet history interview, and 24-h recall), and method of case ascertainment (questionnaire, oral glucose tolerance test, fasting glucose level, death certificate, and nationwide registry) varied among studies. For nutrients, intakes of vegetable fat, polyunsaturated fatty acid, dietary fiber (particularly cereal fiber), magnesium, and caffeine were significantly inversely correlated and intakes of trans fatty acid and heme-iron, glycemic index, and glycemic load were significantly positively correlated with the incidence of type 2 diabetes in several papers. For foods and food groups, several papers showed significantly decreased risk for type 2 diabetes with the higher consumption of grain (particularly whole grain) and coffee, and significantly increased risk with processed meat consumption. Because all the studies were carried out in Western countries, however, research in non-Western countries including Japan is needed.
Key Words nutrient, food, type 2 diabetes, cohort study, systematic review

It is estimated that in 2000 there were about 150 million people with type 2 diabetes all over the world and that this figure will double by 2025 (*1*). While type 2 diabetes and its complications such as cardiovascular disease, amputation, blindness, and renal failure adversely affect the quality of life, there is no currently available cure for diabetes. Thus, primary prevention of the disease is of paramount importance to public health. Although many lifestyle factors are associated with the development of type 2 diabetes (*2, 3*), food and nutrition may also play an important role in its cause (*4*). In Japan, a cohort study suggests decreased ratio of polyunsaturated to saturated fatty acids as a risk factor for glucose intolerance (*5*), although there is no cohort study where the endpoint is the incidence of diabetes.

In prevention and clinical settings, the findings in human studies are much more important than extrapolation of the results from animal studies. However, a report which systematically reviews human studies on the association between dietary factors and type 2 diabetes is not currently available. A systematic collection of previous publications (scientific papers) and its efficient application are essential for the evidence-based primary care and treatment of type 2 diabetes. We, therefore, systematically reviewed published cohort studies examining the effects of dietary factors on the incidence of type 2 diabetes. Alcohol was excluded in the present paper not only because assessment methods were quite different between alcohol and other dietary factors such as nutrient and food intake, but also because a systematic review of the relation between alcohol consumption and the risk of type 2 diabetes has been published very recently (*6*).

Materials and Methods

We searched the MEDLINE (PubMed) database for cohort studies on the relations of dietary variables including energy and nutrient intake, food consumption, and dietary score with the risk of developing type 2 diabetes using the following search strategy: ("diet" OR "dietary" OR "nutrient" OR "consumption" OR "intake") AND ("diabetes" OR "diabetic") AND ("prospective" OR "cohort" OR "follow-up"). The search was limited to English-language reports of apparently healthy persons 15 y of age or older, which were published by the end of May, 2004. We then identified papers (including review papers) on cohort studies assessing the effects of dietary factors on the incidence of type 2 diabetes by reading the abstract of each retrieved article. Of these articles and their reference lists, only articles that met all the following criteria

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were identified: 1) the endpoint was the incidence of diabetes; 2) follow-up procedure and length and the definition of the incidence of diabetes were clearly documented; 3) quantitative (including consumption frequency) assessment of food and/or nutrient was conducted; 4) results were shown using the relative risk (RR) (and 95% confidence interval (CI)); and 5) factors used when calculating multivariate RR were clearly indicated. As a result, 15 individual cohort studies (31 articles) of dietary factors and the risk of type 2 diabetes were examined in the present paper.

We retrieved from the 31 articles 1) the number of subjects, their sex, and age; 2) follow-up length; 3) procedure for ascertainment of the incidence of diabetes and the number of diabetes cases; 4) dietary assessment instrument used; 5) dietary factors examined; 6) variables used for adjustment; and 7) multivariate RR (and 95% CI) and p for trend. For dietary factors examined using more than one statistical analysis, the results of the analysis which included the largest number of factors for adjustment were retrieved. Although several articles performed stratified analyses according to several risk factors for diabetes, the analysis of all participants was retrieved whenever possible. When men and women or white and African-American were analyzed separately, we retrieved these separate analyses. The results were considered statistically significant when either of the following conditions was met: 1) the risk in the highest category was statistically significant ($p<0.05$) compared with that of the lowest category, or 2) p for trend between dietary factors and the risk of diabetes was statistically significant (<0.05).

Results

Table 1 shows all the results of the 15 cohort studies (31 articles) investigating the effect of dietary factors on the incidence of type 2 diabetes. All 15 studies were carried out in Western countries: 10 studies in the USA (studies 1–7, 9, 12, and 13 (*7–27, 29, 30, 34, 35*)); 3 in Finland (studies 10, 11, and 15 (*31–33, 37*)); 1 in the Netherlands (study 8 (*28*)); and 1 in Sweden (study 14 (*36*)). One study (study 3) investigated only male subjects, while five studies (studies 2, 5, 9, 13, and 14) examined only female subjects. Both sexes were investigated in the other nine studies; men and women were analyzed separately in three studies (studies 1, 6, and 15) while the remaining six studies (studies 4, 7, 8, 10, 11, and 12) analyzed the data of men and women combined. The age of subjects ranged from 15 to 98 y. The number of subjects examined (n=895–85,060), follow-up length (5.9–23 y), and number of cases (n=74–4,085) also varied considerably among articles.

Various methods for ascertainment of the development of diabetes were used (see footnotes to Table 1): death certificate or nationwide registry (studies 1, 10, 11, 14, and 15); questionnaire to confirm whether the definitions of diabetes were met (studies 2, 3, 9, and 13); 2-h 75 g oral glucose tolerance testing (studies 7 and 12); self-report by subjects (studies 5 and 8); blood glucose level and self-report (study 4); and documents such as hospital record and death certificate and self-report (study 6). The criteria for diabetes were also slightly different among studies: the National Diabetes Data Group (NDDG) (*38*) and the World Health Organization (WHO) (*39*) in studies 2, 3, 7, 12, and 13 except for the article by Lopez-Ridaura et al. (*14*) and the American Diabetes Association (ADA) (*40*) in studies 4 and 9 and the article by Lopez-Ridaura et al. (*14*).

Different dietary assessment methods were also applied: non-validated questionnaire (studies 1, 11, 12, 14, and 15); validated questionnaire (study 8); validated food frequency questionnaire (studies 2, 3, 5, 7, 9, and 13); validated food frequency interview (study 4); diet history interview (study 10); and a single 24-h dietary recall (study 6). Repeated dietary assessments were made in 11 articles (study 13 and most of studies 2 and 3 (*10–15, 17–20, 35*)).

A total of 99 dietary factors were examined in the 31 articles. Different factors were used for adjustment in each article, although well-known factors associated with the development of type 2 diabetes such as age, body mass index (BMI: weight (kg)/height (m)^2), smoking, alcohol consumption, physical activity, family history of diabetes, and energy intake were used in many analyses.

A summary of the results of the association of energy and nutrient intake with the risk of type 2 diabetes is shown in Table 2. Although several studies investigated the relationship of energy and macronutrients (protein, fat, and carbohydrate) to the development of type 2 diabetes, no study has shown a significant relation to date. However, several studies indicated that several types of fat and sugar appeared to be more important. Vegetable fat and polyunsaturated fatty acid were inversely associated with the incidence of type 2 diabetes in several studies, while a positive association between trans fatty acid and the risk of type 2 diabetes was observed in several studies. One study showed an inverse association between the ratio of polyunsaturated to saturated fatty acid and the incidence of type 2 diabetes. For sugars, on the other hand, a beneficial effect of sucrose and adverse effects of glucose and fructose were observed in one study. In addition, positive relations of glycemic index (a qualitative indicator of carbohydrate's ability to raise blood glucose levels) and glycemic load (an indicator of a glucose response or insulin demand induced by the total carbohydrate intake) to the risk of type 2 diabetes were found in several studies.

Several studies indicated an inverse association between dietary fiber and the incidence of type 2 diabetes. Among various types of fiber, beneficial effects of cereal fiber (in several studies), soluble fiber (in one study), and insoluble noncellulose polysaccharides (in one study) were observed. One study showed a positive relationship between cholesterol and the risk of type 2 diabetes. For minerals, several studies indicated a beneficial effect of magnesium (both diet only and diet and supplement combined) and an adverse effect of heme iron. A positive relation between heme iron from red meat and the risk of type 2 diabetes was observed in one

Table 1. Cohort studies of dietary factors in relation to incidence of type 2 diabetes.

No.	Year	Authors (reference No.)	Subjects n	Subjects Sex	Subjects Age (y)	Follow-up (y)	Cases[1] (n)	Dietary method (times)	Dietary factor examined	Range or median Multivariate relative risk 95% confidence interval					p for trend	Factors used for adjustment	Association
1	1985	Snowdon and Phillips (7)	22,632	M/W	30–89	21	434	NVQ (1)									
			8,295	M			143		Meat (d/wk)	<1 1 Ref	1–2 1.6 0.9–2.9	3–5 1.6 0.8–3.0	>6 3.6 1.9–7.1		—	Age, desirable weight, PA, frequency of use (meat, eggs, milk, FT, sweet desserts, candy, soft drinks)	Y
			14,337	W			291		Meat (d/wk)	<1 1.0 Ref	1–2 1.3 0.9–2.0	3–5 1.2 0.7–1.8	>6 0.6 0.3–1.2		—	Age, desirable weight, PA, frequency of use (meat, eggs, milk, FT, sweet desserts, candy, soft drinks)	N
2	1992	Colditz et al. (8)	84,360	W	34–59	6	702	VFFQ (1)									
			Women with BMI<29						Energy	—(Low) 1.00 Ref	— 0.90 —	— 1.09 —	— 1.04 —	—(High) 1.24 0.84–1.82	0.24	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Protein	—(Low) 1.00 Ref	— 1.14 —	— 1.03 —	— 1.06 —	—(High) 0.83 0.55–1.25	0.24	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Animal fat	—(Low) 1.00 Ref	— 0.93 —	— 1.06 —	— 1.34 —	—(High) 0.92 0.60–1.42	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (VF)	N
									*Vegetable fat	—(Low) 1.00 Ref	— 0.85 —	— 1.06 —	— 0.78 —	—(High) 0.62 0.40–0.97	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (AF)	Y
									*SFA	—(Low) 1.00 Ref	— 0.92 —	— 1.08 —	— 1.00 —	—(High) 1.12 0.76–1.65	0.50	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*MUFA	—(Low) 1.00 Ref	— 0.80 —	— 1.04 —	— 0.90 —	—(High) 0.91 0.62–1.35	0.83	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*PUFA	—(Low) 1.00 Ref	— 0.84 —	— 0.85 —	— 0.59 —	—(High) 0.79 0.54–1.17	0.07	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Linoleic acid	—(Low) 1.00 Ref	— 0.86 —	— 0.86 —	— 0.63 —	—(High) 0.77 0.52–1.14	0.06	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*P/S	—(Low) 1.00 Ref	— 1.05 —	— 0.99 —	— 0.92 —	—(High) 0.67 0.44–1.03	0.07	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*CHO	—(Low) 1.00 Ref	— 1.29 —	— 1.08 —	— 1.14 —	—(High) 1.31 0.86–1.98	0.42	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Dietary fiber	—(Low) 1.00 Ref	— 0.89 —	— 0.82 —	— 1.19 —	—(High) 0.75 0.50–1.13	0.60	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Cereal fiber	—(Low) 1.00 Ref	— 0.77 —	— 0.83 —	— 0.84 —	—(High) 0.98 0.62–1.55	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (FDF, VDF)	N
									*Fruit fiber	—(Low) 1.00 Ref	— 0.90 —	— 0.82 —	— 0.73 —	—(High) 0.95 0.60–1.50	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (CDF, VDF)	N
									*Vegetable fiber	—(Low) 1.00 Ref	— 1.07 —	— 0.82 —	— 1.35 —	—(High) 1.06 0.67–1.66	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (CDF, FDF)	N
									*Sucrose	—(Low) 1.00 Ref	— 1.18 —	— 0.94 —	— 1.03 —	—(High) 1.16 0.77–1.76	0.76	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Potassium	—(Low) 1.00 Ref	— 0.98 —	— 1.04 —	— 0.85 —	—(High) 0.76 0.44–1.30	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (Mg, Ca)	N
									*Magnesium	—(Low) 1.00 Ref	— 1.01 —	— 1.04 —	— 0.92 —	—(High) 0.95 0.56–1.61	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (K, Ca)	N
									*Calcium	—(Low) 1.00 Ref	— 1.19 —	— 0.71 —	— 0.77 —	—(High) 0.85 0.53–1.37	—	Age, BMI, AL, FH, prior weight change (1976–1980), time period, IT (K, Mg)	N
									Vegetable (servings/d)	<1.2 1.00 Ref	— — —	≥2.9 0.76 0.50–1.16			0.21	BMI, AL, IT (E), prior weight change (1976–1980)	N
									Fruit (servings/d)	<0.6 1.00 Ref	— — —	≥ 3 1.15 0.72–1.84			0.88	BMI, AL, IT (E), prior weight change (1976–1980)	N
			Women with BMI ≥29						Energy	—(Low) 1.00 Ref	— 1.03 —	— 1.04 —	— 1.04 —	—(High) 1.35 1.00–1.82	0.29	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Protein	—(Low) 1.00 Ref	— 0.95 —	— 1.11 —	— 1.18 —	—(High) 0.92 0.68–1.25	0.88	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Animal fat	—(Low) 1.00 Ref	— 1.78 —	— 0.90 —	— 1.11 —	—(High) 0.99 0.74–1.36	0.83	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Vegetable fat	—(Low) 1.00 Ref	— 1.03 —	— 0.93 —	— 1.08 —	—(High) 0.92 0.68–1.25	0.77	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*SFA	—(Low) 1.00 Ref	— 0.95 —	— 1.08 —	— 0.85 —	—(High) 0.88 0.63–1.24	0.56	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*MUFA	—(Low) 1.00 Ref	— 0.94 —	— 1.27 —	— 1.24 —	—(High) 1.01 0.73–1.41	0.23	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects n	Sex	Age (y)	Follow-up (y)	Cases[1] (n)	Dietary method (times)	Dietary factor examined	Range or median / Multivariate relative risk / 95% confidence interval					p for trend	Factors used for adjustment	Association
									*PUFA	—(Low) 1.00 Ref	— 1.07 —	— 1.08 —	— 1.12 —	—(High) 1.26 0.91–1.75	0.17	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Linoleic acid	—(Low) 1.00 Ref	— 1.10 —	— 1.07 —	— 1.06 —	—(High) 1.02 0.73–1.46	0.81	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*P/S	—(Low) 1.00 Ref	— 1.15 —	— 1.24 —	— 1.14 —	—(High) 1.16 0.85–1.59	0.39	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*CHO	—(Low) 1.00 Ref	— 1.01 —	— 1.29 —	— 1.04 —	—(High) 1.13 0.84–1.55	0.39	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Dietary fiber	—(Low) 1.00 Ref	— 1.21 —	— 1.21 —	— 1.04 —	—(High) 1.08 0.78–1.48	0.97	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Sucrose	—(Low) 1.00 Ref	— 1.21 —	— 0.99 —	— 0.90 —	—(High) 0.90 0.64–1.28	0.20	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Potassium	—(Low) 1.00 Ref	— 0.97 —	— 1.01 —	— 0.88 —	—(High) 0.92 0.68–1.23	0.42	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Magnesium	—(Low) 1.00 Ref	— 1.25 —	— 1.03 —	— 0.81 —	—(High) 0.73 0.53–1.02	0.008	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
									*Calcium	—(Low) 1.00 Ref	— 0.95 —	— 0.92 —	— 0.91 —	—(High) 0.84 0.59–1.18	0.260	Age, BMI, AL, FH, prior weight change (1976–1980), time period	N
2	1997	Salmerón et al. (9)	65,173	W	40–65	6	915	VFFQ (1)	Energy (kJ/d)	4710 1.00 Ref	6100 1.24 1.00–1.53	7172 1.20 0.96–1.49	8374 1.12 0.90–1.39	10367 1.24 1.00–1.53	0.16	Age, BMI, AL, SM, PA, FH	N
									*Vegetable fat (g/d)	15.8 1.00 Ref	20.8 0.92 0.75–1.13	24.6 0.97 0.79–1.20	28.6 0.89 0.72–1.09	35.3 0.85 0.68–1.04	0.12	Age, BMI, AL, SM, PA, FH	N
									*Animal fat (g/d)	21.8 1.00 Ref	27.8 1.21 0.97–1.52	32.0 1.24 0.99–1.54	36.7 1.07 0.85–1.35	44.2 1.09 0.87–1.37	0.76	Age, BMI, AL, SM, PA, FH	N
									*SFA (g/d)	15.1 1.00 Ref	18.3 1.21 0.98–1.50	20.4 0.99 0.79–1.24	22.7 0.98 0.79–1.22	26.4 0.95 0.76–1.18	0.20	Age, BMI, AL, SM, PA, FH	N
									*PUFA (g/d)	7.6 1.00 Ref	9.3 0.93 0.76–1.15	10.6 0.91 0.74–1.12	12.1 0.91 0.74–1.13	14.5 0.97 0.79–1.19	0.81	Age, BMI, AL, SM, PA, FH	N
									*MUFA (g/d)	15.9 1.00 Ref	19.1 0.98 0.78–1.21	21.3 0.99 0.80–1.23	23.4 0.99 0.80–1.23	26.7 0.91 0.73–1.13	0.42	Age, BMI, AL, SM, PA, FH	N
									*CHO (g/d)	155 1.00 Ref	178 0.94 0.76–1.17	189 1.14 0.92–1.41	208 0.95 0.76–1.19	231 1.04 0.83–1.30	0.83	Age, BMI, AL, SM, PA, FH	N
									*Dietary fiber (g/d)	11.8 1.00 Ref	14.7 1.01 0.83–1.24	17.0 0.90 0.73–1.11	19.6 0.91 0.74–1.13	24.1 0.78 0.62–0.98	0.02	Age, BMI, AL, SM, PA, FH	Y
									*Fruit fiber (g/d)	1.4 1.00 Ref	2.6 0.87 0.70–1.07	3.7 0.95 0.77–1.18	5.1 0.94 0.76–1.16	7.6 0.87 0.70–1.08	0.39	Age, BMI, AL, SM, PA, FH	N
									*Vegetable fiber (g/d)	3.4 1.00 Ref	4.8 1.40 1.13–1.73	5.9 1.23 0.99–1.53	7.2 1.29 1.04–1.61	9.6 1.17 0.93–1.46	0.54	Age, BMI, AL, SM, PA, FH	N
									*Cereal fiber (g/d)	2 1.00 Ref	2.9 1.01 0.83–1.23	3.7 0.85 0.69–1.04	4.9 0.82 0.66–1.01	7.5 0.72 0.58–0.90	0.001	Age, BMI, AL, SM, PA, FH	Y
									*Magnesium (mg/d)	222 1.00 Ref	261 0.91 0.74–1.10	292 0.84 0.69–1.03	327 0.82 0.67–1.01	338 0.62 0.50–0.78	<0.001	Age, BMI, AL, SM, PA, FH	Y
									*Glycemic index	64 1.00 Ref	68 1.21 0.96–1.52	71 1.37 1.10–1.72	73 1.37 1.09–1.71	77 1.37 1.09–1.71	0.005	Age, BMI, AL, SM, PA, FH, IT (CDF)	Y
									*Glycemic load	111 1.00 Ref	131 1.24 0.99–1.55	144 1.22 0.97–1.54	157 1.25 0.99–1.59	178 1.47 1.16–1.86	0.003	Age, BMI, AL, SM, PA, FH, IT (CDF)	Y
2	2000	Liu et al. (10)	75,521	W	38–63	9.6	1,879	VFFQ (3)	Total grain	—(Low) 1.00 Ref	— 0.84 0.72–0.97	— 0.82 0.70–0.96	— 0.72 0.61–0.85	—(High) 0.75 0.63–0.89	0.005	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
									Whole grain (servings/d)	0–0.26 1.00 Ref	0.27–0.56 0.91 0.79–1.05	0.57–1.06 0.94 0.82–1.08	1.07–1.76 0.74 0.64–0.86	1.77–15.93 0.73 0.63–0.85	<0.0001	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
									Refined grain	—(Low) 1.00 Ref	— 1.09 0.94–1.26	— 1.01 0.86–1.17	— 1.09 0.92–1.27	—(High) 1.11 0.94–1.30	0.26	Age, BMI, PA, SM, AL, FH, SP, IT (E)	N
									Ratio of refined to whole grain	—(Low) 1.00 Ref	— 1.09 0.93–1.27	— 1.15 0.99–1.33	— 1.27 1.09–1.47	—(High) 1.26 1.08–1.46	0.01	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
									Dark bread (servings/wk)	AN 1.00 Ref	<1 0.90 0.77–1.04	2–4 0.87 0.75–1.01	5–6 0.79 0.66–0.94	≥7 0.77 0.66–0.90	0.002	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
									Whole-grain breakfast cereal (servings/wk)	AN 1.00 Ref	<1 0.81 0.71–0.93	2–4 0.70 0.60–0.81	5–6 0.71 0.62–0.82	≥7 0.66 0.55–0.80	<0.0001	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects n	Subjects Sex	Subjects Age (y)	Follow-up (y)	Cases[1] (n)	Dietary method (times)	Dietary factor examined	Range or median / Multivariate relative risk / 95% confidence interval					p for trend	Factors used for adjustment	Association
									Popcorn (servings/wk)	AN	<1	2–4	5–6	≥7			
										1.00	0.89	1.00	0.84	0.88	0.47	Age, BMI, PA, SM, AL, FH, SP, IT (E)	N
										Ref	0.81–0.99	0.85–1.17	0.62–1.15	0.59–1.31			
									Cooked oatmeal (servings/wk)	AN	<1	2–4	5–6	≥7			
										1.00	0.97	0.84	0.61	0.73	0.08	Age, BMI, PA, SM, AL, FH, SP, IT (E)	N
										Ref	0.88–1.07	0.69–1.03	0.32–1.15	0.35–1.54			
									Brown rice (servings/wk)	AN	<1	2–4	5–6				
										1.00	0.77	0.64	0.47		<0.0001	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
										Ref	0.69–0.86	0.44–0.91	0.15–1.45				
									Wheat germ (servings/wk)	AN	<1	2–4	5–6				
										1.00	0.64	0.79	0.85		0.003	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
										Ref	0.51–0.80	0.51–1.22	0.52–1.37				
									Bran (servings/wk)	AN	<1	2–4	5–6				
										1.00	0.66	0.63	0.54		<0.0001	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
										Ref	0.56–0.78	0.48–0.83	0.41–0.72				
									Other whole grains (servings/wk)	AN	<1						
										1.00	0.77				0.02	Age, BMI, PA, SM, AL, FH, SP, IT (E)	Y
										Ref	0.63–0.94						
2	2001	Hu et al. (77)	84,941	W	34–59	15.3	3,300	VFFQ (4)	Cereal fiber	—(Low)	—	—	—	—(High)			
										1.00	0.97#	0.79#	0.76#	0.60#	<0.001	P/S, IT (TF), GL, age, time, FH, MS, HRT, SM, BMI, PA, AL	Y
										Ref	0.87–1.07#	0.69–0.89#	0.66–0.86#	0.50–0.70#			
									P/S	—(Low)	—	—	—	—(High)			
										1.00	0.92#	0.83#	0.81#	0.80#	<0.001	IT (CDF, TF), GL, age, time, FH, MS, HRT, SM, BMI, PA, AL	Y
										Ref	0.82–1.02#	0.73–0.93#	0.71–0.91#	0.70–0.90#			
									Trans fatty acid	—(Low)	—	—	—	—(High)			
										1.00	1.05#	1.19#	1.19#	1.40#	<0.001	IT (CDF), P/S, GL, age, time, FH, MS, HRT, SM, BMI, PA, AL	Y
										Ref	0.95–1.15#	1.09–1.29#	1.09–1.29#	1.30–1.50#			
									Glycemic load	—(Low)	—	—	—	—(High)			
										1.00	1.00#	1.12#	1.18#	1.40#	<0.001	IT (CDF, TF), P/S, age, time, FH, MS, HRT, SM, BMI, PA, AL	Y
										Ref	0.87–1.130#	0.98–1.26#	1.02–1.34#	1.22–1.58#			
									Dietary score[2]	1(Low)	2	3	4	5(High)			
										1.00	0.86	0.77	0.67	0.49	—	Age, time, FH, MS, HRT, PA, BMI, SM, AL	Y
										Ref	0.78–0.95	0.68–0.86	0.60–0.74	0.42–0.56			
2	2001	Salmerón et al. (72)	84,204	W	34–59	14	2,507	VFFQ (4)	Total fat (%E)	28.9	33.9	37.2	40.6	46.1			
										1.00	0.87	1.01	0.97	0.97	0.96	Age, time period, BMI, SM, PH, AL, PA, IT (P, E, CL)	N
										Ref	0.77–1.00	0388–1.15	0.85–1.10	0.85–1.11			
									Animal fat (%E)	17.3	21.6	25.0	29.2	36.4			
										1.00	0.88	1.00	1.02	0.97	0.71	Age, time period, BMI, SM, PH, AL, PA, IT (P, E, CL, VF, TF)	N
										Ref	0.76–1.02	0.86–1.15	0.88–1.19	0.82–1.15			
									Vegetable fat (%E)	5.3	8.7	11.1	13.5	17.2			
										1.00	0.85	0.67	0.65	0.60	<0.0001	Age, time period, BMI, SM, PH, AL, PA, IT (P, E, CL, AF, TF)	Y
										Ref	0.75–0.96	0.59–0.77	0.56–0.76	0.51–0.71			
									SFA (%E)	10.7	12.8	14.3	16.0	18.8			
										1.00	0.97	0.96	1.03	0.99	0.98	Age, time period, BMI, SM, FH, AL, PA, IT (P, E, CL, MUFA, PUFA, TF)	N
										Ref	0.83–1.12	0.81–1.14	0.86–1.24	0.80–1.21			
									MUFA (%E)	10.9	13.1	14.6	16.3	19.3			
										1.00	1.07	1.05	1.02	1.06	0.51	Age, time period, BMI, SM, FH, AL, PA, IT (P, E, CL, SFA, PUFA, TF)	N
										Ref	0.91–1.25	0.88–1.26	0.83–1.25	0.84–1.33			
									PUFA (%E)	2.9	3.4	4.1	4.8	6.2			
										1.00	0.86	0.77	0.75	0.75	0.0002	Age, time period, BMI, SM, FH, AL, PA, IT (P, E, CL, SFA, MUFA, TF)	Y
										Ref	0.76–0.97	0.67–0.88	0.65–0.86	0.65–0.88			
									Trans fatty acid (%E)	1.3	1.7	2.0	2.4	2.9			
										1.00	1.12	1.18	1.14	1.31	0.02	Age, time period, BMI, SM, FH, AL, PA, IT (P, E, CL, SFA, MUFA, PUF)	Y
										Ref	0.97–1.29	1.02–1.37	0.97–1.34	1.10–1.56			
									*Cholesterol (mg/d)	131	163	188	217	273			
										1.00	1.02	1.16	1.25	1.36	<0.0001	Age, time period, BMI, SM, FH, AL, PA, IT (P, E, SFA, MUFA, PUFA, TF)	Y
										Ref	0.88–1.18	1.00–1.34	1.08–1.45	1.17–1.59			
2	2002	Jiang et al. (73)	83,818	W	34–59	16	3,206	VFFQ (5)	Nuts (times/wk)	NV/AN	<1	1–4	≥5				
										1.00	0.91	0.81	0.71			Age, BMI, FH, PA, SM, AL, GL, SP, IT (E, PUFA, SFA, TF, CDF, Mg, VG, FT, WG, fish)	Y
										Ref	0.84–0.99	0.74–0.90	0.57–0.87				
									Peanut butter (times/wk)	AN	<1	1–4	≥5		<0.001		
										1.00	0.98	0.91	0.81		0.002	Age, BMI, FH, PA, SM, AL, GL, SP, IT (E, PUFA, SFA, TF, CDF, Mg, VG, FT, WG, fish)	Y
										Ref	0.90–1.07	0.84–1.00	0.69–0.94				
2	2004	Lopez-Ridaura et al. (14)	85,060	W	34–59	18	4,085	VFFQ (6)	*Magnesium (diet & SP) (mg/d)	222	261	290	321	373			
										1.00	0.92	0.88	0.76	0.73	<0.001	FH, BMI, PA, SM, AL, HPTS, HPCL, GL, IT (E, CDF, PUFA, TF, processed meat)	Y
										Ref	0.84–1.01	0.80–0.98	0.69–0.85	0.65–0.82			
2	2004	Salazar-Martínez et al. (15)	84,276	W	34–59	18	4,085	VFFQ (5)	Coffee (cups/d)	0	<1	1–3	4–5	≥6			
										1.00	1.16	0.99	0.70	0.71	<0.001	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA, MS, HRT	Y
										Ref	1.05–1.29	0.90–1.08	0.60–0.82	0.56–0.89			
									Tea (cups/d)	0	<1	1–3	≥4				
										1.00	1.05	1.01	0.91		>0.20	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA, MS, HRT	N
										Ref	0.97–1.15	0.92–1.11	0.72–1.16				
									Decaffeinated coffee (cups/d)	0	<1	1–3	≥4				
										1.00	0.96	0.88	0.85		0.008	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA, MS, HRT	N
										Ref	0.88–1.05	0.80–0.97	0.61–1.17				
									Caffeine (mg/d)	69	193	328	432	708			
										1.00	1.02	0.90	0.85	0.70	<0.001	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA, MS, HRT	Y
										Ref	0.93–1.11	0.82–0.99	0.77–0.94	0.63–0.79			
3	1997	Salmerón et al. (76)	42,759	M	40–75	6	523	VFFQ (1)	Energy (kcal/d)	1249	1606	1902	2245	2831			
										1.00	1.00	1.24	1.12	1.22	0.13	Age, BMI, AL, SM, PA, FH	N
										Ref	0.75–1.33	0.94–1.64	0.84–1.49	0.92–1.61			
									*Vegetable fat (g/d)	18.5	24.5	29.1	34.0	42.6			
										1.00	0.95	0.95	0.99	0.83	0.28	Age, BMI, AL, SM, PA, FH	N
										Ref	0.73–1.24	0.72–1.25	0.75–1.30	0.62–1.11			
									*Animal Fat (g/d)	26.5	34.5	49.5	47.0	57.3			
										1.00	0.89	1.19	1.19	1.11	0.26	Age, BMI, AL, SM, PA, FH	N
										Ref	0.64–1.25	0.87–1.62	0.88–1.62	0.82–1.50			

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects *n*	Sex	Age (y)	Follow-up (y)	Cases[1] (*n*)	Dietary method (times)	Dietary factor examined	Range or median / Multivariate relative risk / 95% confidence interval					*p* for trend	Factors used for adjustment	Association
										16.7	21.3	24.3	27.3	32.1			
									*SFA (g/d)	1.00	1.20	1.31	1.17	1.03	0.75	Age, BMI, AL, SM, PA, FH	N
										Ref	0.87–1.65	0.96–1.78	0.85–1.59	0.75–1.41			
										9.2	11.3	12.8	14.5	17.4			
									*PUFA (g/d)	1.00	1.00	1.00	1.16	1.01	0.70	Age, BMI, AL, SM, PA, FH	N
										Ref	0.76–1.34	0.76–1.34	0.89–1.54	0.77–1.35			
										19.5	24.2	27.3	30.2	36.6			
									*MUFA (g/d)	1.00	1.04	1.26	1.16	1.01	0.96	Age, BMI, AL, SM, PA, FH	N
										Ref	0.76–1.42	0.93–1.69	0.85–1.56	0.74–1.37			
										182	213	234	255	288			
									*CHO (g/d)	1.00	0.88	0.93	0.88	0.85	0.33	Age, BMI, AL, SM, PA, FH	N
										Ref	0.67–1.14	0.71–1.22	0.66–1.17	0.62–1.15			
										13.4	17.1	20.0	23.5	29.7			
									*Dietary fiber (g/d)	1.00	0.98	1.08	0.87	0.98	0.70	Age, BMI, AL, SM, PA, FH	N
										Ref	0.75–1.29	0.83–1.42	0.65–1.17	0.73–1.33			
										2.5	3.8	5.0	6.8	10.2			
									*Cereal fiber (g/d)	1.00	1.14	0.95	0.91	0.70	0.007	Age, BMI, AL, SM, PA, FH	Y
										Ref	0.89–1.46	0.73–1.25	0.69–1.20	0.51–0.96			
										1.2	2.8	3.8	5.3	8.3			
									*Fruit fiber (g/d)	1.00	1.01	0.89	1.14	1.01	0.68	Age, BMI, AL, SM, PA, FH	N
										Ref	0.76–1.34	0.67–1.19	0.86–1.51	0.76–1.36			
										3.5	4.9	6.3	7.9	11.3			
									*Vegetable fiber (g/d)	1.00	1.12	1.22	1.10	1.12	0.65	Age, BMI, AL, SM, PA, FH	N
										Ref	0.85–1.49	0.93–1.61	0.83–1.46	0.84–1.49			
										262	307	343	385	461			
									*Magnesium (mg/d)	1.00	0.92	0.83	0.66	0.72	0.004	Age, BMI, AL, SM, PA, FH	Y
										Ref	0.72–1.19	0.64–1.08	0.49–0.88	0.54–0.96			
										65	70	73	75	79			
									*Glycemic index	1.00	1.16	1.19	1.20	1.37	0.03	Age, BMI, AL, SM, PA, FH, IT (CDF)	Y
										Ref	0.88–1.50	0.89–1.58	0.90–1.60	1.02–1.83			
										119	144	160	177	203			
									*Glycemic load	1.00	1.07	1.04	1.13	1.25	0.17	Age, BMI, AL, SM, PA, FH, IT (CDF)	N
										Ref	0.82–1.14	0.78–1.39	0.83–1.54	0.90–1.73			
3	2002	Fung et al. (17)	42,898	M	40–75	10.3	1,197	VFFQ (3)		0.4	0.8	1.3	1.9	3.2			
									Whole grain (servings/d)	1.00	0.88	0.77	0.79	0.70	0.0006	Age, period, PA, missing FFQ, SM, FH, AL, IT (E, FT, VG), BMI	Y
										Ref	0.74–1.04	0.65–0.92	0.66–0.95	0.57–0.85			
										0.8	1.3	1.9	2.6	4.1			
									Refined grain (servings/d)	1.00	1.07	1.08	1.00	1.08	0.69	Age, period, PA, missing FFQ, SM, FH, AL, IT (E, FT, VG), BMI	N
										Ref	0.89–1.29	0.90–1.30	0.82–1.22	0.87–1.33			
3	2002	van Dam et al. (18)	42,504	M	40–75	12	1,321	VFFQ (3)		1(Low)	2	3	4	5(High)			
									Prudent pattern score[1]	1.00	0.77	0.96	0.89	0.84	0.20	Age, BMI, IT (E), PA, SM, AL, ancestry, HPCL, HPTS, FH	N
										Ref	0.65–0.92	0.81–1.14	0.75–1.06	0.70–1.00			
										1(Low)	2	3	4	5(High)			
									Western pattern score[4]	1.00	1.22	1.34	1.34	1.59	<0.001	Age, BMI, IT (E), PA, SM, AL, ancestry, HPCL, HPTS, FH	Y
										Ref	1.00–1.48	1.10–1.63	1.10–1.63	1.32–1.93			
3	2002	van Dam et al. (19)	42,504	M	40–75	12	1,321	VFFQ (3)		24	29	32	35	39			
									Total fat (%E)	1.00	0.99	1.14	1.00	0.97	0.63	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT(E, CDF, Mg), BMI	N
										Ref	0.81–1.21	0.94–1.39	0.82–1.22	0.79–1.18			
										7.6	9.6	11	12	14			
									SFA (%E)	1.00	1.20	1.12	1.22	0.97	0.47	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.98–1.46	0.92–1.38	1.00–1.49	0.79–1.20			
										8	10	11	12	14			
									Oleic acid (%E)	1.00	1.02	1.09	1.09	0.93	0.53	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.84–1.24	0.90–1.32	0.90–1.33	0.76–1.14			
										3.5	4.4	4.9	5.6	6.8			
									Linoleic acid (%E)	1.00	0.99	1.03	1.06	0.89	0.27	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.83–1.18	0.86–1.23	0.89–1.26	0.74–1.06			
										0.7	1.0	1.3	1.5	2.0			
									Trans fatty acid (%E)	1.00	0.95	0.93	0.91	0.90	0.33	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.79–1.15	0.77–1.12	0.75–1.11	0.74–1.10			
										321	396	458	533	671			
									*α-Linolenic acid (mg/d)	1.00	1.03	1.10	1.00	0.93	0.27	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.86–1.23	0.92–1.31	0.84–1.20	0.78–1.11			
										80	155	250	350	570			
									*Long-chain *n*-3 fatty acid (mg/d)	1.00	1.01	0.95	1.05	1.01	0.81	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.85–1.19	0.79–1.13	0.88–1.25	0.84–1.21			
										<1/mo	1–3/mo	1/wk	2–4/wk	≥5/wk			
									Total processed meat	1.00	1.13	1.04	1.35	1.46	<0.0001	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	Y
										Ref	0.90–1.41	0.82–1.30	1.08–1.68	1.14–1.86			
										<1/mo	1–3/mo	1/wk	≥2/wk				
									Bacon	1.00	0.96	1.19	1.33		0.0002	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	Y
										Ref	0.83–1.10	1.01–1.40	1.11–1.58				
										<1/mo	1–3/mo	1/wk	≥2/wk				
									Hot dogs	1.00	1.14	1.27	1.26		0.03	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	1.00–1.30	1.07–1.51	1.00–1.60				
										<1/mo	1–3/mo	1/wk	≥2/wk				
									Sausage, salami, bologna, other processed meats	1.00	0.95	1.12	1.18		0.01	Age, time period, PA, SM, AL, HPCL, HPTS, FH, IT (E, CDF, Mg), BMI	N
										Ref	0.81–1.12	0.94–1.34	0.99–1.41				
3	2004	Jiang et al. (20)	38,394	M	40–75	12	1,168	VFFQ (3)		11.1	13.1	15.2	19.7	34.2			
									*Iron (diet & SP) (mg/d)	1.00	1.10	1.36	1.23	1.16	0.67	BMI, FH, PA, SM, AL, IT (E, TF, CDF, Mg, WG, VG, FT), P/S, GL, SP	N
										Ref	0.91–1.33	1.11–1.66	0.99–1.53	0.92–1.47			
										0.80	1.05	1.27	1.50	1.90			
									*Heme iron (diet only) (mg/d)	1.00	1.09	1.28	1.22	1.28	0.045	BMI, FH, PA, SM, AL, IT (E, TF, CDF, Mg, WG, VG, FT), P/S, GL, SP	Y
										Ref	0.87–1.36	1.03–1.58	1.22–1.53	1.28–1.61			
										0.20	0.45	0.63	0.90	1.30			
									*Heme iron from red meat (mg/d)	1.00	1.24	1.26	1.43	1.63	<0.001	BMI, FH, PA, SM, AL, IT (E, TF, CDF, Mg, WG, VG, FT), P/S, GL, SP	Y
										Ref	0.98–1.55#	1.00–1.60#	1.15–1.80#	1.26–2.10			

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects			Follow-up (y)	Cases[1] (n)	Dietary method (times)	Dietary factor examined	Range or median Multivariate relative risk 95% confidence interval					p for trend	Factors used for adjustment	Association
			n	Sex	Age (y)												
									*Heme iron from sources other than red meat (mg/d)	0.21 1.00 Ref	0.40 0.98 0.80–1.20#	0.55 0.92 0.75–1.10#	0.70 0.96 0.80–1.15#	1.00 0.98 0.80–1.21	0.87	BMI, FH, PA, SM, AL, IT (E, TF, CDF, Mg, WG, VG, FT), P/S, GL, SP	N
3	2004	Lopez-Ridaura et al. (14)	42.872	M	40–75	12	1.333	VFFQ (4)	*Magnesium (diet & SP) (mg/d)	270 1.00 Ref	314 0.83 0.70–0.98	348.5 0.89 0.75–1.05	388 0.66 0.55–0.80	457 0.72 0.58–0.89	<0.001	FH, BMI, PA, SM, AL, HPTS, HPCL, GL, IT (E, CDF, PUFA, TF, processed meat)	Y
3	2004	Salazar-Martinez et al. (15)	41.934	M	40–75	12	1.333	VFFQ (3)	Coffee (cups/d)	0 1.00 Ref	<1 0.98 0.84–1.15	1–3 0.93 0.80–1.08	4–5 0.71 0.53–0.94	≥6 0.46 0.26–0.82	0.007	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA	Y
									Tea (cups/d)	0 1.00 Ref	<1 0.92 0.81–1.04	1–3 0.97 0.82–1.14	≥4 1.02 0.59–1.78		>0.20	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA	N
									Decaffeinated coffee (cups/d)	0 1.00 Ref	<1 0.95 0.84–1.08	1–3 0.91 0.76–1.03	≥4 0.74 0.48–1.12		0.048	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA	N
									Caffeine (mg/d)	13 1.00 Ref	74 1.06 0.89–1.26	172 1.01 0.85–1.20	323 0.94 0.78–1.12	566 0.80 0.66–0.97	0.002	Age, FH, AL, SM, GL, IT (E, TF, PUFA, CDF, Mg), BMI, PA	Y
4	1999	Kao et al. (21)	11.896	M/W	45–64	6	1.106	VFFI (1)									
			Black (n=2.548)						Magnesium (mg/4.2 kJ)	<0.12 0.95 0.52–1.74	0.12–0.14 1.19 0.72–1.96	0.14–0.17 1.11 0.74–1.67	>0.17 1.00 Ref		0.47	Age, sex, ED, FH, BMI, W/H, PA, AL, diuretic use, IT (Ca, K), FIL, FGL	N
			White (n=9.348)						Magnesium (mg/4.2 kJ)	<0.14 0.80 0.56–1.14	0.14–0.16 0.96 0.70–1.31	0.16–0.19 0.98 0.75–1.29	>0.19 1.00 Ref		0.49	Age, sex, ED, FH, BMI, W/H, PA, AL, diuretic use, IT (Ca, K), FIL, FGL	N
4	2002	Stevens et al. (22)	12.251	M/W	45–64	9	1.447	VFFI (1)									
			White						Cereal fiber	—(Low) 1.00 Ref	— — —	— — —	— — —	—(High) 0.75 0.60–0.92	—	Age, BMI, sex, field center, ED, SM, PA	Y
			African-American						Cereal fiber	—(Low) 1.00 Ref	— — —	— — —	— — —	—(High) 0.86 0.65–1.15	—	Age, BMI, sex, field center, ED, SM, PA	N
5	2000	Meyer et al. (23)	35.988	W	55–69	6	1.141	VFFQ (1)	*CHO (g/d)	<192.1 1.00 Ref	192.1–210.6 1.05 0.87–1.26	210.7–225.6 0.98 0.81–1.19	225.7–243.8 0.90 0.74–1.09	>243.8 0.93 0.76–1.13	0.22	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Starch (g/d)	<50.5 1.00 Ref	50.5–59.3 0.79 0.65–0.96	59.4–67.0 0.86 0.71–1.03	67.1–76.8 0.82 0.68–1.00	>76.8 0.83 0.69–1.00	0.12	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Glucose (g/d)	<13.9 1.00 Ref	13.9–17.6 0.95 0.78–1.17	17.7–21.1 1.11 0.91–1.35	21.2–25.8 1.18 0.97–1.44	>25.8 1.30 1.08–1.57	0.0007	Age, IT (E), BMI, W/H, ED, SM, AL, PA	Y
									*Sucrose (g/d)	<31.2 1.00 Ref	31.2–38.0 0.98 0.82–1.19	38.1–43.6 0.96 0.79–1.16	43.7–51.0 0.93 0.76–1.13	>51.0 0.81 0.67–0.99	0.027	Age, IT (E), BMI, W/H, ED, SM, AL, PA	Y
									*Fructose (g/d)	<15.9 1.00 Ref	15.9–20.3 0.95 0.77–1.16	20.4–24.5 1.17 0.96–1.42	24.6–30.0 1.18 0.97–1.43	>30.0 1.27 1.06–1.54	0.0015	Age, IT (E), BMI, W/H, ED, SM, AL, PA	Y
									*Lactose (g/d)	<11.9 1.00 Ref	11.9–16.7 1.16 0.96–1.41	16.8–29.5 1.02 0.84–1.24	29.6–101.8 1.09 0.90–1.32	>101.8 0.94 0.77–1.14	0.24	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Maltose (g/d)	<0.92 1.00 Ref	0.92–1.19 0.86 0.71–1.05	1.20–1.45 1.11 0.92–1.34	1.46–1.85 1.07 0.88–1.30	>1.85 0.98 0.81–1.19	0.60	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Glycemic index	<58 1.00 Ref	59–65 1.19 0.98–1.43	66–71 1.26 1.05–1.53	72–80 0.96 0.78–1.17	>80 0.89 0.72–1.10	0.0507	Age, IT (E, DF), BMI, W/H, ED, SM, AL, PA	N
									*Glycemic load	<103 1.00 Ref	104–114 0.96 0.79–1.15	115–124 0.86 0.71–1.05	125–136 0.92 0.75–1.12	>136 0.95 0.78–1.16	0.53	Age, IT (E, DF), BMI, W/H, ED, SM, AL, PA	N
									*Dietary fiber (g/d)	<15.3 1.00 Ref	15.3–17.8 1.09 0.91–1.31	17.9–20.3 1.00 0.83–1.21	20.4–23.6 0.94 0.78–1.15	>23.6 0.78 0.64–0.96	0.005	Age, IT (E), BMI, W/H, ED, SM, AL, PA	Y
									*Soluble fiber (g/d)	<4.8 1.00 Ref	4.8–5.5 1.00 0.83–1.21	5.6–6.2 1.02 0.84–1.23	6.3–7.2 0.99 0.82–1.20	>7.2 0.89 0.73–1.08	0.23	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Insoluble fiber (g/d)	<11.4 1.00 Ref	11.4–13.4 0.96 0.80–1.15	13.5–15.2 0.92 0.77–1.11	15.3–17.7 0.81 0.67–0.99	>17.7 0.75 0.61–0.91	0.0012	Age, IT (E), BMI, W/H, ED, SM, AL, PA	Y
									*Cereal fiber (g/d)	<3.4 1.00 Ref	3.4–4.3 0.93 0.78–1.12	4.4–5.5 0.90 0.74–1.09	5.6–7.5 0.80 0.65–0.99	>7.5 0.71 0.56–0.89	0.0017	Age, IT (E, WG, Mg), BMI, W/H, ED, SM, AL, PA	Y
									*Fruit fiber (g/d)	<2.55 1.00 Ref	2.55–3.85 0.98 0.81–1.20	3.86–5.19 1.14 0.94–1.38	5.20–7.02 1.06 0.87–1.29	>7.02 1.17 0.96–1.42	0.081	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Vegetable fiber (g/d)	<5.75 1.00 Ref	5.75–7.11 1.07 0.88–1.30	7.12–8.38 1.12 0.92–1.35	8.39–10.14 1.12 0.92–1.36	>10.14 0.97 0.80–1.18	0.77	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Legume fiber (g/d)	<0.31 1.00 Ref	0.31–0.56 0.97 0.80–1.18	0.57–0.83 0.95 0.78–1.16	0.84–1.21 1.04 0.85–1.27	>1.21 1.10 0.91–1.33	0.17	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									*Magnesium (mg/d)	<242 1.00 Ref	242–270 0.82 0.69–0.99	271–297 0.86 0.71–1.03	298–332 0.88 0.73–1.06	>332 0.76 0.62–0.95	0.048	Age, IT (E, WG, CDF), BMI, W/H, ED, SM, AL, PA	Y
									Total grain (servings/wk)	<13.0 1.00 Ref	13–18.5 0.90 0.74–1.10	19–24.5 0.96 0.79–1.17	25–33 0.84 0.67–1.04	>33 0.73 0.56–0.96	0.022	Age, IT (E, CDF, Mg), BMI, W/H, ED, SM, AL, PA	Y

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects *n*	Subjects Sex	Subjects Age (y)	Follow-up (y)	Cases[1] (*n*)	Dietary method (times)	Dietary factor examined	Range or median Multivariate relative risk 95% confidence interval					*p* for trend	Factors used for adjustment	Association
									Whole grain (servings/wk)	<3.0 1.00 Ref	3.0–5.5 1.03 0.86–1.24	6.0–8.0 1.05 0.87–1.27	8.5–17.5 0.97 0.86–1.29	>17.5 0.82 0.78–1.21	0.69	Age, IT (E, CDF, Mg), BMI, W/H, ED, SM, AL, PA	N
									Refined grain (servings/wk)	<6.0 1.00 Ref	6.0–9.5 0.96 0.79–1.16	10–13.5 0.81 0.66–0.99	14–22 0.98 0.81–1.19	>22 0.87 0.70–1.08	0.36	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									Fruit & vegetables (servings/wk)	<23 1.00 Ref	23–30 1.00 0.82–1.22	31–39 1.12 0.92–1.36	40–51 1.21 0.99–1.49	>51 1.05 0.84–1.31	0.41	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									Fruit (servings/wk)	<6.25 1.00 Ref	6.5–10 1.05 0.87–1.26	10.1–13.5 1.00 0.82–1.22	13.6–19 1.08 0.88–1.32	>19 1.14 0.93–1.39	0.20	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									Vegetable (servings/wk)	<14 1.00 Ref	14–19.4 1.03 0.85–1.24	19.5–25 0.99 0.82–1.21	25.1–33.5 1.09 0.90–1.34	>33.5 1.07 0.86–1.32	0.45	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
									Mature beans (servings/wk)	<1.5 1.00 Ref	1.5–2 1.01 0.82–1.23	2.25–3 1.06 0.85–1.31	3.5–4.5 1.10 0.89–1.36	>4.5 0.96 0.76–1.20	0.85	Age, IT (E), BMI, W/H, ED, SM, AL, PA	N
5	2001	Meyer et al. (24)	35,988	W	55–69	11	1,890	VFFQ (1)	*Total fat (g/d)	55.7 1.00 Ref	56.1 1.00 0.85–1.17	60.1 0.95 0.81–1.11	66.8 0.93 0.79–1.10	86.6 0.89 0.75–1.05	0.11	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF)	N
									*SFA (g/d)	19.3 1.00 Ref	19.2 1.06 0.89–1.27	20.4 1.07 0.89–1.29	23.2 1.11 0.91–1.36	31.8 0.95 0.76–1.19	0.71	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, PUFA, MUFA, TF, n-3 fatty acid, CL)	N
									*PUFA (g/d)	8.9 1.00 Ref	9.2 0.94 0.81–1.09	10.4 0.93 0.79–1.08	12.2 0.88 0.74–1.03	16.6 0.90 0.75–1.07	0.19	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, SFA, MUFA, TF, n-3 fatty acid, CL)	N
									*MUFA (g/d)	20.4 1.00 Ref	20.9 0.99 0.83–1.19	22.7 1.03 0.84–1.27	25.7 0.93 0.74–1.18	33.8 1.02 0.78–1.34	0.93	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, SFA, PUFA, TF, n-3 fatty acid, CL)	N
									*Long-chain n-3 fatty acid (g/d)	0.03 1.00 Ref	0.09 0.97 0.83–1.12	0.13 0.99 0.84–1.15	0.20 0.94 0.80–1.10	0.39 1.11 0.94–1.30	0.14	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, PUFA, MUFA, TF, CL)	N
									*Trans fatty acid (g/d)	2.2 1.00 Ref	2.4 1.01 0.86–1.19	2.8 0.94 0.79–1.12	3.5 0.88 0.73–1.06	5.2 0.92 0.75–1.11	0.20	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, SFA, PUFA, MUFA, TF, n-3 fatty acid, CL)	N
									*Cholesterol (mg/d)	185 1.00 Ref	201 0.84 0.71–1.00	237 1.02 0.86–1.22	281 1.03 0.87–1.23	382 1.11 0.92–1.33	0.07	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, Mg, CDF, P, SFA, PUFA, MUFA, TF, n-3 fatty acid)	N
									*Animal fat (g/d)	29.1 1.00 Ref	29.8 1.04 0.88–1.22	33.7 0.97 0.82–1.15	40.4 0.99 0.83–1.18	56.8 0.89 0.73–1.07	0.18	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT(E, Mg, CDF, P, VF)	N
									*Vegetable fat (g/d)	18.6 1.00 Ref	20.2 0.90 0.78–1.04	23.7 0.87 0.75–1.01	29.2 0.84 0.72–0.98	41.7 0.82 0.82–0.97	0.02	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT(E, Mg, CDF, P, AF)	Y
5	2004	Lee et al. (25)	35,698	W	55–69	11	1,921	VFFQ (1)	*Non-heme iron (diet only) (mg/d)	6.5 1.00 Ref	8.9 0.96 —	11.1 0.99 —	14.1 0.90 —	20.8 0.80 0.64–1.01	0.08	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, AF, VF, CDF, Mg, heme Fe, Fe (SP))	N
									*Heme iron (diet only) (mg/d)	0.5 1.00 Ref	0.8 1.07 —	1.2 1.12 —	1.5 1.14 —	2.2 1.28 1.04–1.58	0.02	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, AF, VF, CDF, Mg, non-heme Fe, Fe (SP))	Y
									*Iron (SP only) (mg/d)	0 1.00 Ref	1–29 0.94 —	≥30 1.16 0.92–1.46			0.79	Age, W/H, BMI, PA, SM, AL, ED, marital status, residential area, HRT, IT (E, AF, VF, CDF, Mg, non-heme Fe, heme Fe)	N
6	2001	Ford and Mokdad (26)	9,665	M/W	25–74	20	1,018	24HR (1)									
			3,874	M			416		Fruit & vegetables (servings/d)	0 1.00 Ref	1–4 1.23 0.76–1.99	≥5 1.14 0.67–1.93			—	Age, SM, SBP, CL concentration, use of antihypertensive medication, PA, AL, BMI, ED	N
			5,791	W			602		Fruit & vegetables (servings/d)	0 1.00 Ref	1–4 0.85 0.62–1.16	≥5 0.61 0.42–0.88			—	Age, SM, SBP, CL concentration, use of antihypertensive medication, PA, AL, BMI, ED	Y
7	2002	Mayer-Davis et al. (27)	895	M/W	40–69	5	146	VFFI (1)									
			577	VitE SP nonusers			87		Vitamin E (mg/d)	1–4.9 1.00 Ref	5–9.9 1.00 0.43–2.31	10–19.9 0.61 0.21–1.84	≥20 0.80 0.13–5.06		>0.05	GT, age, ethnicity, clinic, sex, general health, FH, BMI, waist circumference, SM, PA, IT(E, F, DF, Mg, VitC), AL	N
			318	VitE SP users			59		Vitamin E (diet & SP) (mg/d)	1–23.7 1.00 Ref	23.7–37.1 0.94 0.22–3.96	37.1–278.3 1.34 0.29–6.19	≥278.3 0.70 0.17–3.51		>0.05	GT, age, ethnicity, clinic, sex, general health, FH, BMI, waist circumference, SM, PA, IT(E, F, DF, Mg, VitC), AL	N
8	2002	van Dam and Feskens (28)	17,111	M/W	30–60	7.4	306	VQ (1)	Coffee (cups/d)	≤2 1.00 Ref	3–4 0.79 0.57–1.10	5–6 0.73 0.53–1.01	≥7 0.50 0.35–0.72		0.0002	Age, sex, town, BMI, ED, PA, AL, SM, history of cardiovascular disease, known HPTS, known HPCL	Y
9	2003	Janket et al. (29)	38,480	W	≥45	5.8	918	VFFQ (1)	*Total sugar (g/d)	—(Low) 1.00 Ref	— 0.94 0.77–1.15	— 0.88 0.72–1.08	— 0.92 0.74–1.14	—(High) 0.86 0.69–1.06	0.17	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N
									*Sucrose (g/d)	25.8 1.00 Ref	33.6 1.00 0.81–1.23	39.3 0.98 0.79–1.22	45.8 1.00 0.81–1.24	57.2 0.84 0.67–1.04	0.16	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N
									*Fructose (g/d)	—(Low) 1.00 Ref	— 0.99 0.81–1.22	— 1.04 0.85–1.29	— 1.03 0.83–1.27	—(High) 0.96 0.78–1.19	0.86	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N
									*Glucose (g/d)	—(Low) 1.00 Ref	— 1.08 0.88–1.33	— 1.02 0.82–1.26	— 0.96 0.77–1.19	—(High) 1.04 0.85–1.28	0.91	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N
									*Lactose (g/d)	—(Low) 1.00 Ref	— 1.08 0.88–1.32	— 1.03 0.83–1.26	— 0.86 0.69–1.07	—(High) 0.99 0.80–1.22	0.33	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects *n*	Subjects Sex	Subjects Age (y)	Follow-up (y)	Cases[1] (*n*)	Dietary method (times)	Dietary factor examined	Range or median Multivariate relative risk 95% confidence interval					*p* for trend	Factors used for adjustment	Association
										—(Low)	—	—	—	—(High)			
									*Starch (g/d)	1.00 Ref	0.95 0.77–1.17	1.05 0.85–1.28	1.06 0.86–1.30	0.88 0.71–1.09	0.61	Age, SM, BMI, vigorous PA, AL, HRT, SP, history of HPTS, history of high CL, FH	N
9	2004	Song et al. (30)	38,025	W	≥45	5.9	918	VFFQ (1)	*Magnesium (diet & SP) (mg/d)	255 1.00 Ref	296 1.06 0.88–1.28	328 0.81 0.66–1.00	365 0.86 0.70–1.06	433 0.89 0.71–1.10	0.05	Age, SM, BMI, PA, AL, FH, IT (E)	N
									*Magnesium (diet only) (mg/d)	252 1.00 Ref	291 1.00 0.83–1.22	319 0.96 0.79–1.18	349 0.84 0.68–1.04	399 0.88 0.71–1.10	0.09	Age, SM, BMI, PA, AL, FH, IT (E)	N
10	2003	Montonen et al. (31)	4,316	M/W	40–69	10	156	DH (1)	Total grain (g/d)	10–181 1.00 Ref	182–248 0.80 0.54–1.20	249–339 0.48 0.28–0.81	340–1535 0.38 0.19–0.77		0.001	Age, sex, residential area, SM, BMI, IT (E, FT & BR, VG)	Y
									Whole grain (g/d)	0–109 1.00 Ref	110–162 1.05 0.71–1.55	163–237 0.52 0.31–0.88	238–1321 0.65 0.36–1.18		0.02	Age, sex, residential area, SM, BMI, IT (E, FT & BR, VG)	N
									Rye (g/d)	0–58 1.00 Ref	59–112 0.99 0.66–1.48	113–181 1.00 0.65–1.54	182–1026 0.65 0.36–1.18		0.30	Age, sex, residential area, SM, BMI, IT (E, FT & BR, VG)	N
									Other whole grain (g/d)	0–5 1.00 Ref	6–23 1.20 0.77–1.88	24–75 1.12 0.71–1.79	76–632 1.14 0.69–1.87		0.69	Age, sex, residential area, SM, BMI, IT (E, FT & BR, VG)	N
									Refined grain (g/d)	0–45 1.00 Ref	46–73 0.70 0.47–1.07	74–110 0.68 0.43–1.06	111–567 0.62 0.36–1.06		0.05	Age, sex, residential area, SM, BMI, IT (E, FT & BR, VG)	N
									Refined grain from wheat (g/d)	0–33 1.00 Ref	34–58 0.81 0.53–1.22	59–90 0.70 0.45–1.10	91–389 0.69 0.41–1.14		0.11	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									Dietary fiber (g/d)	2.6–19.2 1.00 Ref	19.3–25.3 0.70 0.46–1.07	25.4–33.1 0.67 0.40–1.11	33.2–118 0.51 0.26–1.00		0.04	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									Soluble fiber (g/d)	0.53–4.5 1.00 Ref	4.6–5.8 0.50 0.31–0.81	5.9–7.3 0.74 0.44–1.25	7.4–22.7 0.57 0.29–1.12		0.21	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									INCP (g/d)	1.1–8.7 1.00 Ref	8.8–12.0 0.75 0.50–1.12	12.1–16.5 0.72 0.45–1.17	16.6–69.3 0.47 0.25–0.91		0.03	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	Y
									Cellulose (g/d)	0.48–3.2 1.00 Ref	3.3–4.2 0.53 0.32–0.85	4.3–5.3 0.67 0.39–1.14	5.4–15.2 0.60 0.29–1.21		0.19	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									Lignin (g/d)	0.48–2.3 1.00 Ref	2.4–3.1 0.79 0.52–1.20	3.2–4.1 0.69 0.42–1.15	4.2–14.5 0.68 0.36–1.30		0.16	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									Cereal fiber (g/d)	0.47–12.0 1.00 Ref	12.1–17.3 0.81 0.54–1.21	17.4–24.4 0.74 0.46–1.18	24.5–111 0.39 0.20–0.77		0.01	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	Y
									Fruit fiber (g/d)	0–0.99 1.00 Ref	1.0–2.0 0.68 0.39–1.20	2.1–3.3 0.79 0.39–1.60	3.4–36.8 0.92 0.40–2.13		0.87	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
									Vegetable fiber (g/d)	0.11–3.7 1.00 Ref	3.8–5.0 1.02 0.58–1.79	5.1–6.7 0.89 0.43–1.85	6.8–26.5 1.19 0.46–3.04		0.86	Age, sex, geographic area, SM, BMI, IT (E, FT & BR, VG)	N
10	2004	Montonen et al. (32)	4,304	M/W	40–69	23	383	DH (1)	*Vitamin E (diet only) (mg/d)	<5.51 1.00 Ref	5.51–6.26 0.79 0.60–1.04	6.27–7.31 0.78 0.58–1.06	>7.31 0.69 0.51–0.94		0.02	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	Y
									*α-Tocopherol (diet only) (mg/d)	<4.66 1.00 Ref	4.66–5.30 0.72 0.54–0.96	5.31–6.20 0.80 0.59–1.08	>6.20 0.66 0.49–0.90		0.02	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	Y
									*β-Tocopherol (diet only) (mg/d)	<0.38 1.00 Ref	0.38–0.49 0.97 0.73–1.29	0.50–0.64 1.09 0.82–1.43	>0.64 0.76 0.56–1.03		0.18	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*γ-Tocopherol (diet only) (mg/d)	<0.79 1.00 Ref	0.79–1.23 0.91 0.69–1.20	1.24–2.06 0.75 0.56–1.01	>2.06 0.77 0.57–1.03		0.04	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*δ-Tocopherol (diet only) (mg/d)	<0.09 1.00 Ref	0.09–0.15 0.85 0.64–1.13	0.16–0.28 0.81 0.60–1.08	>0.28 0.69 0.51–0.93		0.02	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	Y
									*α-Tocotrienol (diet only) (mg/d)	<1.07 1.00 Ref	1.07–1.54 0.95 0.72–1.25	1.55–2.05 0.91 0.68–1.21	>2.05 0.91 0.67–1.23		0.47	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*β-Tocotrienol (diet only) (mg/d)	<1.69 1.00 Ref	1.69–2.15 0.97 0.74–1.28	2.16–2.67 0.77 0.58–1.03	>2.67 0.76 0.56–1.03		0.03	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*γ-Tocotrienol (diet only) (mg/d)	<0.04 1.00 Ref	0.04–0.07 0.95 0.72–1.26	0.08–0.12 0.88 0.65–1.18	>0.12 0.79 0.59–1.07		0.11	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*δ-Tocotrienol (diet only) (mg/d)	<0.002 1.00 Ref	0.002–0.006 1.01 0.77–1.32	0.007–0.01 0.69 0.51–0.93	>0.01 0.84 0.63–1.13		0.06	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*Vitamin C (diet only) (mg/d)	<49.7 1.00 Ref	49.7–66.2 0.97 0.73–1.29	66.3–87.9 0.91 0.68–1.22	>87.9 0.97 0.72–1.32		0.77	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
									*Total carotenoids (diet only) (μg/d)	<1862 1.00 Ref	1863–2865 0.71 0.53–0.96	2867–4519 0.97 0.71–1.27	>4519 0.71 0.52–0.96		0.07	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	Y
									*α-Carotene (diet only) (μg/d)	<9.4 1.00 Ref	9.4–34.4 1.11 0.83–1.49	34.5–103 1.02 0.75–1.38	>103 0.94 0.69–1.28		0.55	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N

Table 1. (Continued)

No.	Year	Authors (reference No.)	Subjects: n	Subjects: Sex	Subjects: Age (y)	Follow-up (y)	Cases[1] (n)	Dietary method (times)	Dietary factor examined	Range or median / Multivariate relative risk / 95% confidence interval					p for trend	Factors used for adjustment	Association
									*β-Carotene (diet only) (μg/d)	<698	698–1104	1105–2121	>2121				
										1.00	0.83	1.14	0.74		0.25	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
										Ref	0.62–1.11	0.87–1.51	0.54–1.01				
									*γ-Carotene (diet only) (μg/d)	<6.3	6.4–28.5	28.6–60.3	>60.3				
										1.00	0.78	0.88	0.82		0.29	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
										Ref	0.59–1.04	0.67–1.18	0.61–1.10				
									*Lycopene (diet only) (μg/d)	<112	113–494	495–1064	>1064				
										1.00	0.79	0.86	0.81		0.23	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	N
										Ref	0.59–1.05	0.65–1.14	0.60–1.09				
									*β-Cryptoxanthin (diet only) (μg/d)	<0.24	0.24–1.36	1.37–4.18	>4.18				
										1.00	0.54	0.57	0.58		<0.001	Age, sex, geographic area, occupation, SM, BMI, FH, IT (E)	Y
										Ref	0.40–0.73	0.43–0.76	0.44–0.78				
									*Lutein & zeaxanthin (diet only) (mg/d)	<749	749–935	936–1156	>1156				
										1.00	0.91	0.95	0.74		0.09	Age, sex, geographic area, occupation, SM, BMI, PH, IT (E)	N
										Ref	0.69–1.21	0.71–1.26	0.55–1.01				
11	2003	Reunanen et al. (33)	19,518	M/W	20–98	15.6	855	NVQ (1)		≤2	3–4	5–6	≥7				
									Coffee (cups/d)	1.00	1.01	0.98	0.92		—	Age, sex, BMI, SM, leisure time PA	N
										Ref	0.81–1.27	0.79–1.21	0.73–1.16				
12	2003	Saremi et al. (34)	2,680	M/W	≥15	11	824	NVQ (1)		NV	<1	1–2	≥3	OH			
									Coffee (cups/d)	1.00	1.09	0.92	1.01	0.81	0.60	Age, sex, BMI	N
										Ref	0.89–1.34	0.74–1.13	0.82–1.26	0.55–1.03			
13	2003	Schulze et al. (35)	91,246	W	26–46	7.8	741	VFFQ (2)	Total processed meat (servings/wk)	<1	1	2–4	≥5				
										1.00	1.09	1.31	1.72		<0.001	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDR CL, fatty acid)	Y
										Ref	0.90–1.32	1.02–1.68	1.26–2.36				
									Bacon (servings/wk)	<1	1	≥2					
										1.00	1.28	1.65			<0.001	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	Y
										Ref	1.03–1.59	1.20–2.27					
									Hot dogs (servings/wk)	<1	1	≥2					
										1.00	1.01	1.48			0.051	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	Y
										Ref	0.83–1.23	1.04–2.11					
									Sausage, salami, bologna, other processed meats	<1/wk	1/wk	≥2/wk					
										1.00	1.08	1.30			0.019	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	Y
										Ref	0.89–1.30	1.04–1.62					
									Total red meat (servings/wk)	<1	1	2–4	≥5				
										1.00	1.11	1.19	1.26		0.269	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, fatty acid)	N
										Ref	0.72–1.70	0.76–1.86	0.78–2.04				
									Beef or lamb as MD (servings/wk)	<1	1	≥2					
										1.00	1.03	1.11			0.41	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	N
										Ref	0.86–1.24	0.87–1.42					
									Pork as MD (servings/wk)	<1	1	≥2					
										1.00	0.95	1.01			0.91	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	N
										Ref	0.80–1.13	0.69–1.48					
									Hamburgers (servings/wk)	<1	1	≥2					
										1.00	1.12	1.34			0.026	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	Y
										Ref	0.94–1.34	1.05–1.70					
									Beef, pork, or lamb as SW or XD (servings/wk)	<1	1	≥2					
										1.00	0.97	0.89			0.31	Age, BMI, AL, PA, FH, SM, history of high blood pressure, history of high blood CL, HRT, OC, GI, IT (E, Mg, CF, CDF, CL, SFA, MUFA, PUFA, TF)	N
										Ref	0.81–1.15	0.71–1.11					
14	2004	Rosengren et al. (36)	1,361	W	39–65	18	74	NVQ (1)		≤2	3–4	5–6	≥7				
									Coffee (cups/d)	1.00	0.56	0.45	0.57		—	Age, SM, PA, ED, BMI, serum CL, serum triglycerides	N
										Ref	0.32–0.98	0.23–0.90	0.26–1.29				
15	2004	Tuomilehto et al. (37)	14,629	M/W	35–64	12	381	NVQ									
			6,974	M			203			≤2	3–4	5–6	7–9	≥10			
									Coffee (cups/d)	1.00	0.73	0.70	0.67	0.45	0.12	Age, study year, BMI, SBP, ED, occupational PA, commuting PA, leisure-time PA, SM, AL, tea drinking	Y
										Ref	0.47–1.13	0.45–1.05	0.40–1.12	0.25–0.81			
			7,655	W			178			≤2	3–4	5–6	7–9	≥10			
									Coffee (cups/d)	1.00	0.71	0.39	0.39	0.21	<0.001	Age, study year, BMI, SBP, ED, occupational PA, commuting PA, leisure-time PA, SM, AL, tea drinking	Y
										Ref	0.48–1.05	0.25–0.60	0.20–0.74	0.06–0.69			

[1] Ascertainment of cases was carried out using the following procedures:

Study 1: death certificates which mentioned diabetes as a contributing or underlying cause of death reviewed by a medically trained clerk;

Studies 2, 3, and 13: the definition of diabetes by the National Diabetes Data Group (*38*) and/or the World Health Organization (WHO) (*39*) [1) 1 or more classic symptoms (thirst, polyuria, weight loss, pruritus), plus a fasting plasma glucose concentration of ≥7.8 mmol/L (140 mg/dL) or a random plasma glucose concentration of ≥11.1 mmol/L (200 mg/dL); 2) at least 2 elevated plasma glucose concentrations on different occasions (fasting ≥7.8 mmol/L (140 mg/dL) and/or random ≥11.1 mmol/L (200 mg/dL) and/or ≥11.1 mmol/L (200 mg/dL) after 2 h or more on oral glucose tolerance testing) in the absence of symptoms; or 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agents)], which was confirmed by a validated questionnaire that was mailed every 2 y. In a study by Lopez-Ridaura et al.(*14*), however, the new guideline from the American Diabetes Association (ADA) (*40*) (fasting plasma glucose ≥7.0 mmol/L (126 mg/dL)) was incorporated in 1997;

Study 4: presence of any of the following: 1) fasting glucose level of ≥7.0 mmol/L (126 mg/dL); 2) nonfasting glucose level of ≥11.1 mmol/L (200 mg/dL); 3) current use of diabetic medication (self-report); or 4) a positive response to the question: Has a doctor ever told you that you had diabetes (sugar in the blood)?;

Study 5: affirmative response to the following question on one of the follow-up surveys: Since baseline (or respective follow-up), were you diagnosed for the first time by a doctor as having sugar diabetes?;

Study 6: at least one or more following criteria met: 1) he or she confirmed that he or she had been told by a doctor that he or she had diabetes during any of the four follow-up contacts; 2) a hospitalization record listed the International Classification of Diseases-9-Clinical modification (ICD-9-CM) code 250 on any one of 10 diagnoses on the hospital discharge sheet; or 3) death certificate included the ICD-9 code 250;

Studies 7 and 12: 2-h 75 g oral glucose tolerance test using the WHO criteria (≥11.1 mmol/L (200 mg/dL)) (*39*);

Study 8: presence of diabetes, use of drugs for diabetes, or use of insulin injections assessed using a self-administered questionnaire;

Study 9: the definition of diabetes by ADA (*40*) confirmed by a validated questionnaire that was mailed annually;

Studies 10, 11, and 15: a nationwide register of patients receiving drug reimbursement (in Finland, all diabetic persons needing drug therapy are entitled to reimbursement of drug costs.);

Study 14: at least one or more following criteria met: 1) a doctor's diagnosis of diabetes according to a questionnaire; 2) fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL); or 3) having been hospitalized at least once with a principal or secondary diagnosis of diabetes.

[2] The intakes of trans fat and cereal fiber, the glycemic load, and the ratio of polyunsaturated fat intake to saturated fat intake were categorized in quintiles. Each woman was assigned a score for each variable on the basis of her quintile of intake (a higher score represented a lower risk), then the four scores were summed, and the total score was categorized into quintiles.

[3] A dietary pattern characterized by high consumption of vegetables, legumes, fruit, whole grains, fish, and poultry.
[4] A dietary pattern characterized by high consumption of red meat, processed meat, refined grains, French fries, high-fat dairy products, sweets and desserts, high-sugar drinks, and eggs.

Abbreviations:

[Study No.] 1, Study among White Seventh-Day Adventists (1960–, USA); 2, Nurses' Health Study (1976–, USA); 3, Health Professional Follow-up Study (1986–, USA); 4, Atherosclerosis Risk in Communities Study (1987–, USA); 5, Iowa Women's Health Study (1986–, USA); 6, First National Health and Nutrition Examination Survey (1971–, USA); 7, Insulin Resistance and Atherosclerosis Study (1992–, USA); 8, Study among randomly selected adults from the civil resister (1987–, Netherlands); 9, Women's Health Study (1993–, USA); 10, Finnish Mobile Clinic Health Examination Survey (1966–); 11, Mobile Clinic Health Examination Survey (1973–, Finland); 12, Study among the Pima Indians (1978–, USA); 13, Nurse's Health Study II (1989–, USA); 14, Study among randomly selected women in Göteborg (1979–, Sweden); 15, Study in 2 eastern provinces and a southwestern region in Finland (1982–).

[Subjects] M, men; W, women; BMI, body mass index; VitE, vitamin E; SP, dietary supplement.

[Dietary method] NVQ, not-validated questionnaire; VFFQ, validated food frequency questionnaire; VFFI, validated food frequency interview; 24HR, a single 24-h dietary recall; VQ, validated questionnaire; DH, diet history interview.

[Dietary factor examined] *, energy-adjusted intake; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; P/S, ratio of polyunsaturated to saturated fatty acid; CHO, carbohydrate; %E, percentage of energy intake; SP, dietary supplement; INCP, insoluble noncellulose polysaccharides; MD, main dish; SW, sandwich; XD, mixed dish.

[Range or median]—, not available; NV, never; AN, almost never; OH, occasionally heavy.

[Multivariate relative risk]—, not available; #, value estimated from figure.

[95% confidence interval] Ref, referent;—, not available; #, value estimated from figure.

[*p* for trend]—, not available.

[Factors used for adjustment] PA, physical activity; FT, fruit; BMI, body mass index; AL, alcohol consumption; FH, family history of diabetes; IT, intake; VF, vegetable fat; AF, animal fat; FDF, fruit fiber; VDF, vegetable fiber; CDF, cereal fiber; Mg, magnesium; Ca, calcium; K, potassium; E, energy; SM, smoking; SP, dietary spplement; P/S, ratio of polyunsaturated to saturated fatty acid; TF, trans fatty acid; GL, glycemic load; MS, menstrual status; HRT, hormone replacement therapy; P, protein; CL, cholesterol; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; VG, vegetable; WG, whole grain; HPTS, hypertension; HPCL, hypercholesterolemia; FFQ, food frequency questionnaire; ED, education; W/H, ratio of waist to hip; FIL, fasting insulin level; FGL, fasting glucose level; DF, dietary fiber; Fe, iron; SBP, systolic blood pressure; GT, glucose tolerance; F, fat; VitC, vitamin C; FT & BR, fruit and berry; OC, oral contraceptive use; GI, glycemic index; CF, caffeine.

[Association] Y, yes; N, no.

study. Another study investigating the effects of antioxidant vitamins indicated the decreased risk of type 2 diabetes by vitamin E, α-tocopherol, γ-tocopherol, δ-tocopherol, β-tocotrienol, carotenoid, and β-cryptoxanthin. The decreased risk of type 2 diabetes was also observed in both studies examining the effect of caffeine.

Table 3 summarizes the results of association of intakes of foods and food groups with the risk of type 2 diabetes. Three studies assessed the effect of grain on the incidence of type 2 diabetes. All three indicated a favorable effect of grain consumption. A beneficial effect of whole grain was also observed in several studies. Furthermore, the risk of type 2 diabetes was positively associated with the ratio of refined to whole grain and inversely associated with several types of whole grain products such as dark bread, whole-grain breakfast cereal, brown rice, wheat germ, bran, and other whole grains in one study. Although the association between meat and type 2 diabetes was investigated in only a few studies, the results appeared to be consistent. Not only did several studies show an increased risk of type 2 diabetes by higher consumption of processed meat, bacon, and hot dogs, but one study showed an increased risk from higher consumption of meat, hamburger, sausage, salami, bologna, and other processed meats. The effects of vegetables, fruits, and beans were also investigated in only a small number of studies, but one study indicated an inverse association of vegetable and fruit consumption to the risk of type 2 diabetes. Additionally, one study investigated the association of nut and peanut butter consumption with the incidence of type 2 diabetes. The beneficial effects of both nuts and peanut butter were observed.

An inverse relation of coffee to the incidence of type 2 diabetes was shown in five out of eight analyses. A beneficial effect of decaffeinated coffee was also observed in several studies. On the other hand, no significant association between tea consumption and type 2 diabetes was indicated in any study. Finally, for dietary pattern, an inverse association between the risk of type 2 diabetes and dietary score (characterized by low intake of trans fatty acid, high intake of cereal fiber, high ratio of polyunsaturated to saturated fatty acid, and low glycemic load) was observed in one study, whereas another indicated a positive association between the risk of type 2 diabetes and the Western pattern score (characterized by high consumption of red meat, processed meat, French fries, high-fat dairy products, refined grains, sweets and desserts, high-sugar drinks, and eggs).

Discussion

In the present paper, we systematically reviewed 15 individual cohort studies (31 articles) on the association between dietary factors and the risk of type 2 diabetes. Because there is no publication of systematic review of cohort studies on diet and type 2 diabetes, this paper may be useful for future research on this area.

It is important to note that the interpretation and application of the findings should be conducted with great caution not only because the results are not necessarily consistent, but also because only a relatively small number of cohort studies are available at present. However, the following findings may be considered as low-to-medium level evidence: for nutrients, decreased risk by vegetable fat, polyunsaturated fatty acid, dietary fiber (particularly cereal fiber), magnesium and caffeine, and increased risk by trans fatty acid, heme iron, glycemic index, and glycemic load; for foods and food groups, decreased risk by grain (particularly whole grain) and coffee, and increased risk by processed meat. In addition, antioxidant vitamins and nuts might reduce the risk of type 2 diabetes. However, all 15 studies reviewed in the present paper were conducted in Western countries; thus, given the large differences of dietary habits among countries and/or societies, it may

Table 2. Summary of association between dietary factors and incidence of type 2 diabetes: energy and nutrients.

Dietary factors examined	Study (n)	Significant positive association (n)		Significant inverse association (n)	
		Highest vs. lowest categories	Trend	Highest vs. lowest categories	Trend
Energy	4				
Protein	2				
Fat	3				
Vegetable fat	6			3	2
Animal fat	6				
Saturated fatty acid	7				
Monounsaturated fatty acid	6				
Polyunsaturated fatty acid	6			1	1
P/S	3			1	1
Trans fatty acid	4	2	2		
Linoleic acid	3				
Oleic acid	1				
α-Linolenic acid	1				
Long-chain n-3 fatty acid	2				
Carbohydrate	5				
Sugar	1				
Starch	2				
Glucose	2	1	1		
Sucrose	3			1	1
Fructose	2	1	1		
Lactose	2				
Maltose	1				
Glycemic index	3	2	2		
Glycemic load	4	2	2		
Dietary fiber	6			2	3
Fruit fiber	5				
Vegetable fiber	5				
Cereal fiber	8			6	5
Legume fiber	1				
Soluble fiber	2				
Insoluble fiber	1			1	1
INCP	1			1	1
Cellulose	1				
Lignin	1				
Cholesterol	2	1	1		
Magnesium (diet only)	8			3	4
Magnesium (diet and supplement)	3			2	2
Potassium	2				
Calcium	2				
Iron	1				
Heme iron	2	2	2		
Heme iron from red meat	1	1	1		
Heme iron from other sources	1				
Non-heme iron	1				
Iron from supplement	1				
Vitamin E	3			1	1
Tocopherol					
α-Tocopherol	1			1	1
β-Tocopherol	1				
γ-Tocopherol	1				1
δ-Tocopherol	1			1	1
Tocotrienol					
α-Tocotrienol	1				
β-Tocotrienol	1				1
γ-Tocotrienol	1				
δ-Tocotrienol	1				
Vitamin C	1				
Carotenoid	1			1	
α-Carotene	1				
β-Carotene	1				
γ-Carotene	1				
Lycopene	1				
β-Cryptoxanthin	1			1	1
Lutein and zeaxanthin	1				
Caffeine	2			2	2

Abbreviations: P/S, ratio of polyunsaturated to saturated fatty acid; INCP, insoluble noncellulose polysaccharides.