

## **Intake of Fruit, Vegetables, and Fruit Juices and Risk of Diabetes in Women**

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*Running Head:* Intake of Fruit Juices and Diabetes

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**OBJECTIVE:** To examine the association between fruit, vegetable, and fruit juice intake and development of type 2 diabetes mellitus (DM).

**RESEARCH DESIGN AND METHODS:** A total of 71,346 female nurses ages 38-63 years, who were free of cardiovascular disease, cancer, and DM in 1984 were followed for 18 years and dietary information was collected using a semi-quantitative food frequency questionnaire every 4 years. Diagnosis of DM was self-reported.

**RESULTS:** During follow-up, 4,529 cases of DM were documented and cumulative incidence of DM was 7.4%. An increase of 3 servings/day in total fruit and vegetable consumption was not associated with development of DM (multivariate-adjusted hazard ratio [HR], 0.99; 95% Confidence Interval [CI], 0.94 to 1.05) while the same increase in whole fruit consumption was associated with a lower hazard of DM (HR, 0.82; 95% CI, 0.72 to 0.94). An increase of 1 serving/day in green leafy vegetable consumption was associated with a modestly lower hazard of DM (HR, 0.91; 95% CI, 0.84 to 0.98), whereas the same change in fruit juice intake was associated with an increased hazard of DM (HR, 1.18; 95% CI, 1.10 to 1.26).

**CONCLUSIONS:** Consumption of green leafy vegetables and fruit was associated with a lower hazard of DM, whereas consumption of fruit juices may be associated with an increased hazard among women.

The worldwide burden of type 2 diabetes mellitus (DM) has increased rapidly in tandem with increases in obesity. The most recent estimate for the number of people with DM worldwide, in 2000, was 171 million, and this number is projected to increase to at least 366 million by the year 2030 (1). Fruit and vegetable consumption has been associated with decreased incidence of and mortality from a variety of health outcomes including obesity, hypertension, and cardiovascular diseases in epidemiologic studies (2-4). However, few prospective studies have examined the relationship between fruit and vegetable intake and risk of DM, and their results are not entirely consistent (5-10).

Differences in the nutrient contents of fruits and vegetables by group could lead to differences in health effects. Furthermore, the role of fruit juices could be important and has not been well studied. While fruit juices may have antioxidant activity (11), they lack fiber, are less satiating, and tend to have high sugar content. To further explore the role of fruit and vegetable consumption in the development of DM, we examined the association between intake of all fruits and vegetables, specific groups of fruits and vegetables, and fruit juices among women enrolled in the Nurses' Health Study cohort.

## **RESEARCH DESIGN AND METHODS**

**Study Population:** The Nurses' Health Study was established in 1976 with response of 121,700 female registered nurses between the ages of 30 and 55 years from 11 different US states to an initial mailed questionnaire regarding medical history, lifestyle, diet and other health practices. Follow-up questionnaires were mailed every 2 years to update information on health-related behavior and determine incident disease, including DM and other chronic diseases. The diet cohort was established in 1980 with 98,462

participants. Of those, 81,757 completed the 1984 questionnaire, had a total energy intake that was between 600 and 3,500 kcal, and left fewer than 12 blank food items (n=16,705 excluded). We also excluded women who died prior to the return of the 1984 questionnaire (n=1), who had diagnosed cardiovascular disease (n=2,681), cancer (n=4,218) or DM (n=2,116) at the assessment in 1984, and those with missing date of diagnosis of DM (n= 1,395). After these exclusions, a total of 71,346 women (72.5% of the diet cohort) contributed to the analysis, with follow-up completed in June of 2002.

### **Dietary Assessment**

A semi-quantitative food-frequency questionnaire (FFQ) was included with the general health questionnaire in 1980, 1984, 1986, 1990, 1994, and 1998. The 1980 FFQ contained 61 items, with 6 questions regarding fruit consumption, 11 on vegetable consumption, and 3 on potato consumption. In 1984, the FFQ was substantially expanded to include 16 questions about fruit consumption, 28 on vegetable consumption, and 3 regarding potato consumption. In this analysis, we considered 1984 as the baseline since the FFQ remained consistent afterward. Participants were asked to report the frequencies of their consumption of fruit and vegetable items during the previous year. For each fruit or vegetable, a standard unit or portion size was specified. Nine responses were possible ranging from "never" to "six or more times per day" (12). The response to each food item was converted to average daily intakes and then summed to compute the total intake (fruit juices were not included in total fruit intake or total fruit and vegetable intake). Average daily intakes of foods in specific groups – green leafy vegetables, legumes, and fruit juices were assessed. Green leafy vegetables included spinach, kale, and lettuces; legumes included tofu, peas and beans; fruit juices included apple, orange,

grapefruit, and other fruit juices. These categories were modified from those used in a different cohort in an earlier report (13). Potato differs from all other commonly consumed vegetables in energy density, nutrient density, glycemic index and load, and the likelihood of its presence in fast food. Therefore, we did not include potatoes in any vegetable category. The validity of the FFQ has been evaluated in previous studies (14, 15).

**Assessment of Non-dietary Covariates:** Data on body mass index (BMI), physical activity, smoking status, alcohol use, post-menopausal hormone therapy, family history of DM, and physician-diagnosed hypertension and high cholesterol were self-reported on biennial questionnaires. BMI (measured as weight in kilograms divided by the square of height in meters) was calculated by using updated weight information for each time period.

**Ascertainment of Outcomes** The primary endpoint was development of type 2 DM. At each 2-year cycle, participants were asked whether they had a diagnosis of DM. For each self-reported diagnosis of DM, a supplemental questionnaire was sent, asking about DM symptoms, diagnostic tests, and treatments. A diagnosis of DM was accepted when any one of the following criteria were met: 1) one or more classic symptoms of DM and reported elevated plasma glucose levels (fasting plasma glucose  $\geq 7.8$  mmol/l [140 mg/dl] or randomly measured plasma glucose  $\geq 11.1$  mmol/l [200 mg/dl]), 2) reported elevated plasma glucose on at least two occasions in the absence of symptoms, or 3) treatment with oral hypoglycemic medication or insulin. These criteria for diagnosis of DM are consistent with those proposed by the National Diabetes Data Group (16) because most cases were diagnosed before 1997. For diagnoses of DM established after 1998, the American Diabetes Association criteria (reported fasting plasma glucose  $\geq 7$  mmol/l

[126 mg/dl]) were used. We excluded women with type 1 DM or gestational DM. The diagnosis of type 2 DM by the use of the supplemental questionnaire has been validated in this cohort (17).

**Statistical Analysis** Person-time of follow up was contributed by each eligible participant from the date of return of the 1984 questionnaire to the date of diagnosis of type 2 DM, June 1, 2002, or death from other causes. To reduce within-person variation and best represent long-term usual diet, the cumulative average frequency was calculated from all available questionnaires up to the start of each 2 year follow-up period (18). Participants were divided into quintiles by frequency of intake to avoid assumptions about the shape of the dose-response relationship. Cox proportional hazards models with time dependent variables were used to adjust for potential confounders, including BMI, family history of DM, smoking, postmenopausal hormone use, alcohol intake, and physical activity. We also adjusted for dietary variables which have been related to DM in this cohort, including intakes of processed meats, potatoes, nuts, coffee, sodas, and whole grains (19-24). The proportional hazards assumption was tested by modeling the interaction of time with fruit and vegetable intake. In order to assess the linearity of trends, median values of intake for quintiles were treated as continuous in Cox regression models. Statistical analyses were performed with SAS version 9.0 software (SAS Institute, Cary, NC).

## RESULTS

The baseline characteristics of the study participants by quintile of total fruit and vegetable intake are presented in **Table 1**. Women who consumed more fruits and vegetables were older, less likely to smoke cigarettes, and more likely to exercise regularly and use hormone replacement therapy than their counterparts who did not

consume fruits and vegetables as frequently. The median intake of fruit in this population throughout the follow-up period was 1.08 servings/day, while that for vegetables was 3.09 servings/day.

Over the 18 years of follow-up (1,203,994 person-years), we documented 4,529 cases of type 2 DM. No association between total fruit and vegetable intake and risk of DM was identified in age-adjusted or multivariate adjusted models (**Table 2**). Results were similar for intake of total vegetables. Intake of total fruit and green leafy vegetables was inversely associated with development of type 2 DM. The multivariate-adjusted HR of DM by serving frequency for fruit juice is shown in **Figure 1**.

To further investigate the association between fruit juice consumption and development of type 2 DM, we subdivided fruit juices into apple, grapefruit and orange juices and examined them individually in separate models. Among participants consuming >3 cups of apple juice per month compared to those who consumed <1 cup of apple juice per month, HR was 1.15 (95% CI, 1.08-1.22; P for trend <0.001). The corresponding HR for grapefruit juice consumers was 1.14 (95% CI, 1.05-1.23; P for trend=0.001). Among participants consuming ≥1 cup of orange juice per day as compared to those who consumed <1 cup of orange juice per month, the HR was 1.24 (95% CI, 1.10-1.39; P for trend<0.001).

In order to situate our results for fruit juice intake in the context of other beverages, we also examined intake of colas (sugar-sweetened and low-calorie), other carbonated beverages, and fruit punch in relation to hazard of type 2 DM. After adjustment for BMI, family history of DM, smoking, postmenopausal hormone use, alcohol intake, physical activity, smoking, total energy intake and consumption of whole grains, nuts, processed meats, coffee and potatoes, the HRs for an increase of 1 serving/day (95% CI)

were 1.08 (1.04-1.12), 1.11 (1.07-1.16), 1.04 (1.00-1.09) and 1.10 (1.06-1.15) for sugar-sweetened cola, low-calorie cola, other carbonated beverages, and fruit punch, respectively.

We also examined whether the relationship between fruit juice intake and DM was affected by BMI and physical activity. In multivariate adjusted models, we identified a modest ordinal interaction that was statistically significant (p<0.001 for BMI, and p=0.03 for physical activity). Among participants with a BMI≥25, HR (95% CI) for those in the highest quintile of fruit juice intake as compared to those in the lowest was 1.33 (1.19, 1.48); for participants with a BMI<25, the corresponding value was 1.60 (1.18, 2.16). Among participants who performed ≤1.5 hours of physical activity per week, HR (95% CI) for those in the highest quintile of fruit juice intake as compared to those in the lowest was 1.34 (1.18, 1.53); for participants who performed more than 1.5 hours of physical activity per day, the corresponding value was 1.42 (1.18, 1.73).

## **CONCLUSIONS**

In this large prospective cohort of middle-aged American women, overall fruit and vegetable intake was not associated with the development of type 2 DM. Intake of fruit juices was positively associated, while intake of whole fruits and green leafy vegetables was inversely associated with incidence of type 2 DM. These associations were independent of known risk factors for type 2 DM, including age, BMI, family history, smoking, postmenopausal hormone use, alcohol intake, physical activity, smoking, total energy intake and consumption of whole grains, nuts, processed meats, coffee and potatoes. This study is one of the first to prospectively examine fruit juice intake and the risk type 2 DM.

The positive association between fruit juice consumption and DM risk may relate to

the relative lack of fiber and other phytochemicals, liquid state, and high sugar load. The rapid delivery of a large sugar load, without many other components which are a part of whole fruits maybe an important mechanism by which fruit juices could contribute to the development of DM. Fructose consumption has also been implicated in the development of many manifestations of the insulin resistance syndrome (25, 26). Frequent consumption of fruit juices may contribute to a higher dietary glycemic load which has been positively associated with DM in this cohort (27). Fruit and green leafy vegetables may contribute to a decreased incidence of type 2 DM through their low energy density, low glycemic load, high fiber and micronutrient content (28). In particular, green leafy vegetables may supply magnesium which has been inversely linked to the development of type 2 DM in women (8).

We searched MEDLINE to January of 2008 to identify prospective studies of fruit and vegetable intake and risk of DM. In all, we identified 6 studies which are summarized in **Table 3** (5-10) Many of these studies had small sample sizes, combined fruit juice intake with whole fruit intake, and did not include updated measures of dietary intake during the study.

Other investigations have related the consumption of sugar-sweetened or non-diet colas, other sodas and fruit punches to development of type 2 DM (23). In the Nurses' Health Study II cohort, 91,249 women followed for eight years from 1991 to 1999, women consuming at least one sugar-sweetened soft drink per day were 1.83 times more likely (95% CI, 1.42 to 2.36; P for trend <0.001) to develop type 2 DM compared with those who consumed the beverages less than once per month, after adjustment for potential confounders. Consumption of fruit punches was also associated with increased DM risk (multivariate-adjusted HR, 2.00; 95% CI,

1.33-3.03; P=0.001). In that study, fruit juice consumption was not associated with DM risk, however increased consumption of fruit juices in the first 4 years from baseline was associated with a significantly greater weight gain among women over the course of follow-up (4.03 kg) compared with decreased fruit juice consumption (2.32 kg) during the same period (P<0.001). Possible reasons for the discrepancy between results in these two cohorts include misclassification of fruit juice intake in the Nurses' Health Study II, which incorporated only 2 dietary assessments (1991 and 1995). In the present study, 5 dietary assessments were available (1984, 1986, 1990, 1994, 1998) to classify fruit juice intake. In addition, the Nurses' Health Study II cohort is younger and over the course of 9 years of follow-up developed only 741 cases of incident type 2 DM. In the present study, 18 years of follow-up were available, with 4,529 cases of incident type 2 DM.

The primary limitation of our study is the potential for bias due to measurement error. We attempted to reduce measurement error in assessing long-term diet by using the average of all available measurements of diet up to the start of each 2 year follow-up interval (18). In addition, although our results for fruit juice consumption and type 2 DM are a relatively new finding, those for green leafy vegetable consumption have been replicated in at least one large study using different dietary assessment methods which should have differently structured measurement errors (10). The possibility of unknown confounding, which cannot be ruled out in any observational study, must also be acknowledged. The FFQ used in this study does not distinguish between canned and fresh fruits which have different nutrient profiles and may be associated with different food habits. Moreover, the food supply has changed significantly over the past decades while our FFQ has not; nevertheless, the most common foods eaten in the US population are

encompassed in our instrument. There may be underestimation of type 2 DM by self-report; however, our population is highly educated about medical conditions, so self-report error should be substantially less than in a general population. Fasting glucose criteria for DM were lowered in 1997, possibly contributing to underestimation in this study. Also, it is possible that women may have misreported fruit punches as juices. Fruit punches have been associated with an increased incidence of DM in US women (23). Due to the homogeneity of our population, generalizability of these results to women of other race and ethnicity bears further examination.

Our findings of a positive association of fruit juice intake with hazard of DM suggest that caution should be observed in replacing some beverages with fruit juices in an effort to provide healthier options. Moreover, the same caution applies to the recommendation that 100% fruit juice be considered a serving of fruit as it is in the present national dietary guidelines (30). In general, the observed associations between fruits and vegetables are weaker than those for cardiovascular disease (31). However, if fruits and vegetables are used to replace refined grains and white potatoes, both of which have been shown to be associated with increased risk of DM (20, 32), the benefits of regular consumption of fruits and vegetables should be substantial.

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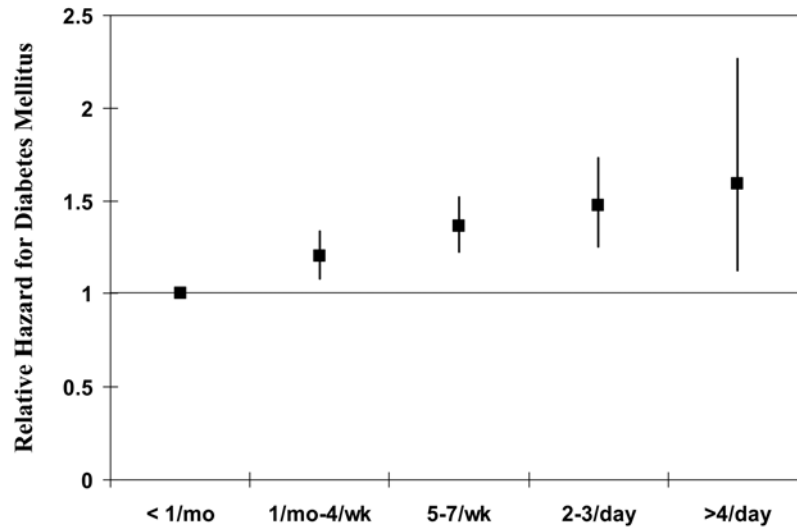
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FIGURE LEGEND

Figure 1. Multivariate-adjusted\* Relative Hazard of Diabetes Mellitus by Category of Cumulative-updated Fruit Juice Intake.



**Fruit Juice Intake, No. of 1 cup (8 oz) servings/time**

\* adjusted for cumulatively updated body mass index, physical activity, family history of diabetes, post-menopausal hormone use, alcohol use, smoking, and total energy intake. For an increase of 1 serving/day of fruit juice, multivariate adjusted RR was 1.18 (95% CI, 1.10 to 1.26; P<0.0001).

Table 1. Characteristics of the Study Population (N=71,346 women) by Quintile of Total Intake of Fruit and Vegetables in 1984.\*

	Total Intake of Fruit and Vegetables in 1984				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Participants	14,573	14,408	14 337	14 118	13 910
Median intake fruits and vegetables, servings/day <sup>†</sup>	2.1	3.2	4.2	5.3	7.5
Median intake fruit, servings/day <sup>†</sup>	0.5	0.9	1.2	1.7	2.5
Median intake vegetables, servings/day	1.5	2.3	3.0	3.7	5.2
Median intake fruit juices, servings/day	0.2	0.4	0.5	0.6	0.7
Age, y	48.5 (7.1)	49.4 (7.2)	50.2 (7.1)	50.8 (7.1)	51.8 (7.0)
Body mass index, kg/m <sup>2</sup>	23.5 (7.1)	23.6 (7.0)	23.6 (6.9)	23.7 (6.9)	23.6 (7.0)
Alcohol, g	7.4 (12.7)	7.2 (11.6)	7.1 (11.0)	6.9 (10.6)	6.6 (10.5)
Physical activity, hours/week	2.1 (2.0)	2.2 (2.1)	2.4 (2.1)	2.5 (2.2)	2.8 (2.3)
Current smoker, %	34	27	23	20	17
Hypertension, %	19	20	19	20	21
Hypercholesterolemia, %	7	7	7	8	8
Current use of hormone replacement, %	22	23	24	26	26
Pre-menopausal, %	47	47	47	46	45
Family history of diabetes, %	25	25	25	25	26
Dietary intake					
Total energy, kcal	1,457 (465)	1,621 (474)	1,744 (486)	1,859 (501)	2,061 (537)
Carbohydrate, g	176 (35)	181 (31)	184 (30)	187 (29)	195 (31)
Glycemic load, g	98 (22)	98 (20)	98 (19)	99 (18)	101 (19)
Protein, g	67 (13)	69 (12)	71 (12)	73 (12)	76 (14)
Polyunsaturated fat, g	11.7 (3.3)	11.9 (3.1)	11.9 (3.0)	11.8 (3.0)	11.6 (3.2)
Monounsaturated fat, g	24.0 (4.6)	23.3 (4.1)	22.7 (3.9)	21.8 (3.8)	20.3 (4.0)
Saturated fat, g	23.9 (5.0)	23.0 (4.4)	22.3 (4.2)	21.5 (4.0)	20.0 (4.2)
Trans-unsaturated fat, g	3.8 (1.2)	3.6 (1.1)	3.4 (1.0)	3.2 (1.0)	2.9 (0.9)
Cholesterol, mg	284 (108)	286 (94)	287 (90)	287 (90)	281 (95)
Fiber, g	12.1 (3.2)	14.4 (3.1)	16.0 (3.3)	17.8 (3.6)	21.3 (4.9)

\* Percentage of categorical or mean (standard deviation) of continuous population characteristics adjusted for total energy intake.

† Neither all fruits nor all fruit and vegetables include fruit juices

Table 2. Age and Multivariate-Adjusted Hazard Ratios (95% CI) for Incident Type 2 Diabetes According to Quintile of Cumulative Averaged Intake of Fruit and Vegetables.

	Cumulative Averaged Intake of Fruit and Vegetables					P-value for Trend	3 serving/d and 1 serving/d Increase in Intake <sup>§</sup>	Median Intake (Quintile 1, 5) servings/d <sup>  </sup>
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5			
<b>Vegetables</b>								
Cases	845	877	930	976	901			
Person-years	233,945	247,049	249,343	246,076	227,581			
age-adjusted	1.00	0.96 (0.88-1.06)	1.00 (0.91-1.10)	1.05 (0.96-1.15)	1.04 (0.95-1.15)	0.13	1.06 (0.98-1.13)	3.09 (1.61 5.40)
model 1*	1.00	0.98 (0.89-1.08)	0.98 (0.89-1.08)	1.03 (0.93-1.13)	0.98 (0.88-1.09)	0.92	1.00 (0.92-1.08)	
model 2 <sup>†</sup>	1.00	1.00 (0.91-1.10)	1.02 (0.93-1.12)	1.08 (0.98-1.19)	1.05 (0.94-1.16)	0.22	1.04 (0.97-1.13)	
<b>Fruit<sup>‡</sup></b>								
Cases	862	988	948	914	817			
Person-years	237,964	249,649	247,769	241,595	227,017			
age-adjusted	1.00	1.06 (0.97-1.16)	1.00 (0.91-1.10)	0.97 (0.88-1.06)	0.90 (0.82-0.99)	0.003	0.84 (0.74-0.94)	1.08 (0.46, 2.64)
model 1*	1.00	1.01 (0.92-1.11)	0.94 (0.86-1.04)	0.89 (0.81-0.98)	0.81 (0.73-0.91)	<0.001	0.74 (0.65-0.84)	
model 2 <sup>†</sup>	1.00	1.04 (0.94-1.14)	0.99 (0.90-1.09)	0.96 (0.86-1.06)	0.90 (0.80-1.00)	0.008	0.82 (0.72-0.94)	
<b>Fruit and Vegetables<sup>‡</sup></b>								
Cases	870	900	945	924	890			
Person-years	237,727	248,219	247,926	244,157	225,964			
age-adjusted	1.00	0.96 (0.88-1.06)	0.99 (0.90-1.09)	0.97 (0.88-1.07)	1.00 (0.91-1.10)	0.91	1.00 (0.96-1.05)	4.47 (2.35, 7.66)
model 1*	1.00	0.98 (0.89-1.07)	0.95 (0.87-1.05)	0.92 (0.84-1.02)	0.92 (0.82-1.02)	0.06	0.95 (0.90-1.00)	
model 2 <sup>†</sup>	1.00	1.01 (0.92-1.11)	1.00 (0.91-1.10)	0.99 (0.89-1.09)	1.01 (0.90-1.12)	0.99	0.99 (0.94-1.05)	
<b>Fruit Juices</b>								
Cases	749	946	1032	920	882			
Person-years	239,408	241,268	250,260	241,633	231,425			
age-adjusted	1.00	1.21 (1.10-1.34)	1.28 (1.17-1.41)	1.17 (1.06-1.28)	1.17 (1.06-1.29)	0.10	1.05 (0.99-1.12)	0.54 (0.04, 1.33)
model 1*	1.00	1.20 (1.09-1.32)	1.28 (1.16-1.40)	1.25 (1.13-1.38)	1.33 (1.20-1.48)	<0.001	1.17 (1.10-1.25)	
model 2 <sup>†</sup>	1.00	1.21 (1.10-1.33)	1.29 (1.17-1.42)	1.25 (1.14-1.38)	1.35 (1.22-1.50)	<0.001	1.18 (1.10-1.26)	
<b>Legumes</b>								
Cases	825	874	951	968	911			
Person-years	248,849	216,815	248,202	259,566	230,563			
age-adjusted	1.00	1.12 (1.02-1.23)	1.09 (0.99-1.20)	1.08 (0.99-1.19)	1.12 (1.02-1.23)	0.11	1.20 (0.96, 1.50)	0.17 (0.07, 0.45)
model 1*	1.00	1.13 (1.03-1.25)	1.10 (1.00-1.21)	1.10 (1.00-1.21)	1.09 (0.99-1.21)	0.40	1.11 (0.87-1.40)	

model 2 <sup>†</sup>	1.00	1.14 (1.03-1.25)	1.12 (1.02-1.23)	1.13 (1.02-1.24)	1.14 (1.03-1.25)	0.09	1.23 (0.97-1.56)	
Green Leafy Vegetables								
Cases	921	957	995	837	819			
Person-years	223,958	239,419	256,196	241,036	243,385			
age-adjusted	1.00	0.96 (0.88-1.05)	0.92 (0.84-1.00)	0.81 (0.74-0.89)	0.78 (0.71-0.86)	<0.001	0.80 (0.75-0.86)	0.72 (0.25, 1.48)
model 1*	1.00	0.99 (0.90-1.08)	0.99 (0.90-1.09)	0.90 (0.82-0.99)	0.87 (0.78-0.96)	<0.001	0.88 (0.82-0.95)	
model 2 <sup>†</sup>	1.00	1.00 (0.91-1.10)	1.02 (0.93-1.11)	0.93 (0.85-1.03)	0.90 (0.82-1.00)	0.010	0.91 (0.84-0.98)	

\* Additionally adjusted for body mass index, physical activity, family history of diabetes, post-menopausal hormone use, alcohol use, smoking, and total energy intake.

<sup>†</sup> Adjusted for all variables in model 1 and additionally for whole grains, nuts, processed meats, coffee, potatoes, and sugar-sweetened soft drinks.

<sup>‡</sup> Neither fruit nor fruit and vegetables include fruit juices

<sup>§</sup> 3 serving/day increase shown for Vegetables, Fruit, and Fruit and Vegetables combined, 1 serving/day increase shown for all other items

<sup>||</sup> Overall median intake for the entire category, and in parentheses the median intakes for the lowest and highest quintiles, in servings/day Distribution based on the cumulative average of median values from questionnaires from 1984, 1986, 1990, 1994, and 1998.

Table 3. Prospective cohort studies reporting measures of association between intake of fruits and vegetables and diabetes mellitus.

Author, year	Population	N	Age, sex	Exposure measure	Adjustments	Follow-up (years)	Case Ascertainment	Events	Association	Notes
Colditz, 1992	US Nurses	84,360	34-59, F	61 item FFQ	Age, BMI, weight change, alcohol intake, total energy	6	Follow-up questionnaire	702 DM	HR Q5/1 0.76 (0.50-1.16) vegetable intake	Q5/1: $\geq 2.9$ serving/d of vegetables vs. $< 1.2$
Feskens, 1995	Finnish and Dutch	338	70-89, M	Cross-check diet history	Age, cohort, BMI, past BMI, past energy intake	30	OGTT	71 IGT, 26 DM	Inverse association of 2-hr post load glucose and intake of vegetables and legumes	Multivariate regression predicting 2 hr post load glucose
Meyer, 2000	Post-menopausal Iowa women	35,988	55-69, F	127 item FFQ	Age, smoking, total energy, BMI, alcohol, WHR, education, physical activity	6	Iowa death register, Biennial questionnaire and NDI	1,141 DM	HR Q5/1 fruit+ vegetables 1.05 (0.84-1.31) HR vegetables 1.07 (0.86-1.32) HR fruit 1.14 (0.93-1.39)	Q5/1: $> 51$ servings/wk fruit +vegetables vs. $< 23$ Q5/1: $> 33.5$ serving/wk vegetable vs. $< 14$ Q 5/1: $> 19$ servings/wk fruit vs. $< 6.25$
Ford, 2001	NHEFS	9,665	25-74, M+F	Single 24 hour dietary recall	Age, race, sex, smoking, BMI, alcohol, SBP, lipids, HTN, physical activity	19	Follow up questionnaire and hospital records, death certificates	1,018 DM	HR fruit+ vegetable intake 0.73 (0.54-0.98)	5 or more times/d vs. 0 times/d, no portion size included, also identified a sex interaction
Liu, 2004	WHS	38,018	$\geq 45$ , F	131 item FFQ	Age, smoking, total energy, alcohol, BMI, physical activity, HTN, hyperlipidemia, FH	8.8	Follow-up questionnaire	1,614 DM	HR Q5/1 fruit+ vegetables 1.04 (0.87-1.25) HR fruit 0.97 (0.82-1.23) HR vegetables 1.03 (0.86-1.23)	Q5/1: median 10.1 serving/d fruit+ vegetables vs. 2.5 Q5/1: median 3.9 serving/d fruit vs. 0.62
Montonen, 2005	Finnish	4,304	40-69, M+F	Diet history	Age, sex, smoking, total energy, BMI, FH, geographic area	23	Finnish Social Insurance Institution's National database	383 DM	HR Q4/1 vegetables 0.77 (0.57-1.03) HR green vegetables 0.69 (0.50-0.93) HR fruit 0.82 (0.61-1.11) HR berries 0.63 (0.47-0.85)	Q4/1: $> 130$ g/d vegetables vs. $< 42$ Q4/1: $> 43$ g/d green vegetables vs. $< 11$ Q4/1: $> 138$ g/d fruit vs. $< 20$

NHEFS: First National Health and Nutrition Examination Study Epidemiologic Follow-up Study; WHS: Women's Health Study; M: male; F: female; IHD: ischemic heart disease; CVA: cerebrovascular accident; FFQ: food frequency; SBP: systolic blood pressure; BMI: body mass index; SBP: systolic blood pressure; DM: diabetes mellitus; WHR: waist to hip ratio; FH: family history of diabetes; HTN: hypertension; OGTT: oral glucose tolerance test; NDI: National Death Index; HR: hazard ratio; Q: quantile