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

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OBJECTIVE — The purpose of this study was to examine the association between fruit, vegetable, and fruit juice intake and development of type 2 diabetes.

RESEARCH DESIGN AND METHODS — A total of 71,346 female nurses aged 38–63 years who were free of cardiovascular disease, cancer, and diabetes in 1984 were followed for 18 years, and dietary information was collected using a semiquantitative food frequency questionnaire every 4 years. Diagnosis of diabetes was self-reported.

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

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

The worldwide burden of type 2 diabetes has increased rapidly in tandem with increases in obesity. The most recent estimate for the number of people with diabetes 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 epidemiological studies (2–4). However, few prospective studies have examined the relationship between fruit and vegetable intake and risk of diabetes, and the 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. Although 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 diabetes, 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 diet cohort.

RESEARCH DESIGN AND METHODS

— The Nurses' Health Study was established in 1976 with responses of 121,700 female registered nurses between the ages of 30 and 55 years from 11 different U.S. 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 diabetes 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 food items blank (n = 16,705 excluded). We also excluded women who died before the return of the 1984 questionnaire (n = 1); who had diagnosed cardiovascular disease (n = 2,681), cancer (n = 4,218), or diabetes (n = 2,116) at the assessment in 1984; and who were missing date of diagnosis of diabetes (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 semiquantitative 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 on fruit consumption, 11 on vegetable consumption, and 3 on potato consumption. In 1984, the FFQ was substantially expanded to include 16 questions on fruit consumption, 28 on vegetable consumption, and 3 on potato consumption. In this analysis, we considered 1984 as the baseline because 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; and 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 nondietary covariates
Data on BMI, physical activity, smoking status, alcohol use, postmenopausal hormone therapy, family history of diabetes, 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 end point was development of type 2 diabetes. At each 2-year cycle, participants were asked whether they had a diagnosis of diabetes. For each self-reported diagnosis of diabetes, a supplemental questionnaire was sent, asking about diabetes symptoms, diagnostic tests, and treatments. A diagnosis of diabetes was accepted when any one of the following criteria was met: *1*) one or more classic symptoms of diabetes and reported elevated plasma glucose levels (fasting plasma glucose ≥ 7.8 mmol/l [140 mg/dl] or randomly measured plasma glucose ≥ 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 diabetes are consistent with those proposed by the National Diabetes Data Group (16) because most cases were diagnosed before 1997. For diagnoses of diabetes established after

1998, the American Diabetes Association criteria (reported fasting plasma glucose ≥ 7 mmol/l [126 mg/dl]) were used. We excluded women with type 1 diabetes or gestational diabetes mellitus. The diagnosis of type 2 diabetes 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 diabetes, 1 June 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 diabetes, smoking, postmenopausal hormone use, alcohol intake, and physical activity. We also adjusted for dietary variables that have been related to diabetes 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. 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 software (version 9.0; 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, were less likely to smoke cigarettes, and were 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, whereas 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 diabetes. No

association between total fruit and vegetable intake and risk of diabetes 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 diabetes. The multivariate-adjusted hazard ratio (HR) of diabetes by serving frequency for fruit juice is shown in Fig. 1.

To further investigate the association between fruit juice consumption and development of type 2 diabetes, 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/ month compared with those who consumed <1 cup of apple juice/month, the HR was 1.15 (95% CI 1.08–1.22; $P_{trend} < 0.001$). The corresponding HR for grapefruit juice consumers was 1.14 (1.05–1.23; $P_{trend} = 0.001$). Among participants consuming ≥ 1 cup of orange juice/day compared with those who consumed <1 cup of orange juice/month, the HR was 1.24 (1.10–1.39; $P_{trend} < 0.001$).

To situate our results for fruit juice intake in the context of results for 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 diabetes. After adjustment for BMI, family history of diabetes, 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 diabetes 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 kg/m^2, the HR (95% CI) for those in the highest quintile of fruit juice intake compared with those in the lowest was 1.33 (1.19–1.48); for participants with BMI <25 kg/m^2, the corresponding value was 1.60 (1.18–2.16). Among participants who performed ≤ 1.5 h of physical activity/week, the HR (95% CI) for those

Table 1—*Characteristics of the study population 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
n	14,573	14,408	14,337	14,118	13,910
Median intake fruits and vegetables (servings/day)*	2.1	3.2	4.2	5.3	7.5
Median intake fruit (servings/day)*	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 (years)	48.5 ± 7.1	49.4 ± 7.2	50.2 ± 7.1	50.8 ± 7.1	51.8 ± 7.0
BMI (kg/m^2)	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 (h/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
Premenopausal (%)	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

Data are % categorical or means ± SD of continuous population characteristics adjusted for total energy intake unless otherwise indicated. Total *n* = 71,346 women. *Neither fruits nor fruit and vegetables include fruit juices.

in the highest quintile of fruit juice intake compared with those in the lowest was 1.34 (1.18–1.53); for participants who performed >1.5 h of physical activity/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 diabetes. Intake of fruit juices was positively associated with incidence of type 2 diabetes, whereas intake of whole fruits and green leafy vegetables was inversely associated. These associations were independent of known risk factors for type 2 diabetes, 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 of type 2 diabetes.

The positive association between fruit juice consumption and diabetes risk may relate to the relative lack of fiber and other phytochemicals, the liquid state, and the high sugar load. The rapid delivery of a large sugar load, without many other components that are a part of whole fruits, may be an important mechanism by which fruit juices could contribute to the development of diabetes. 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 diabetes in this cohort (27). Fruit and green leafy vegetables may contribute to a decreased incidence of type 2 diabetes through their low energy density, low glycemic load, and 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 diabetes in women (8).

We searched MEDLINE to January 2008 to identify prospective studies of fruit and vegetable intake and risk of type 2 diabetes. In all, we identified six studies that 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 diabetes (23). In the Nurses' Health Study II cohort, which comprised 91,249 women followed for 8 years from 1991–1999, women consuming at least 1 sugar-sweetened soft drink/day were 1.83 times more likely (95% CI 1.42–2.36; $P_{trend} < 0.001$) to develop type 2 diabetes compared with those who consumed this type of beverage less than once per month, after adjustment for potential confounders. Consumption of fruit punches was also associated with increased diabetes risk (multivariate-

Table 2—Age and multivariate-adjusted HRs (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_{trend}	3 servings/day and 1 serving/day increase in intake*	Median intake (quintile 1, 5) servings/day†
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5			
Vegetables								
n	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§	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)	
Fruit‖								
n	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§	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)	
Fruit and vegetables‖								
n	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§	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)	
Fruit juices								
n	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§	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)	
Legumes								
n	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§	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								
n	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§	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)	

*For vegetables, fruit, and fruit and vegetables combined, data for 3 servings/day increase are shown; for all other items, 1 serving/day increase is shown; data for 3 servings/day increase are shown; in parentheses. †Shown is overall median intake for the entire category and, in parentheses, the median intakes for the lowest and highest quintiles; data are in servings/day distribution based on the cumulative average of median values from questionnaires from 1984, 1986, 1990, 1994, and 1998. ‡Additionally adjusted for BMI, physical activity, family history of diabetes, postmenopausal hormone use, alcohol use, smoking, and total energy intake. §Adjusted for all variables in model 1 and additionally for whole grains, nuts, processed meats, coffee, potatoes, and sugar-sweetened soft drinks. ‖Neither fruit nor fruit and vegetables include fruit juices.

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

Author, year (reference)	Population	n	Age (years), sex	Exposure measure	Adjustments	Follow-up (years)	Case ascertainment	Events	Association (95% CI)	Notes
Colditz et al., 1992 (5)	U.S. nurses	84,360	34–59, F	61-item FFQ	Age, BMI, weight change, alcohol energy	6	Follow-up questionnaire	702 diabetes	HR Q5/1 0.76 (0.50–1.16) vegetable intake	Q5/1: ≥2.9 serving/day of vegetables vs. <1.2
Feskens et al., 1995 (6)	Finnish and Dutch	338	70–89, M	Cross-check diet history	Age, cohort, BMI, past BMI, past energy intake	30	OGTT	71 IGT, 26 diabetes	Inverse association of 2-h postload glucose and intake of vegetables and legumes	Multivariate regression predicting 2-h postload glucose
Meyer et al., 2000 (7)	Postmenopausal 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 diabetes	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/week fruit + vegetables vs. <23, Q5/1: >33.5 servings/week vegetable vs. <14, Q 5/1: >19 servings/week fruit vs. <6.25
Ford and Mokdad, 2001 (9)	NHEFS	9,665	25–74, M + F	Single 24-h dietary recall	Age, race, sex, smoking, BMI, alcohol, SBP, lipids, HTN, physical activity	19	Follow-up questionnaire, hospital records, death certificates	1,018 diabetes	HR fruit + vegetable intake 0.73 (0.54–0.98)	≥5 times/day vs. 0 times/day, no portion size included; also identified a sex interaction
Liu et al., 2004 (9)	WHS	38,018	≥45, F	131-item FFQ	Age, smoking, total energy, alcohol, BMI, physical activity, HTN, hyperlipidemia, FH	8.8	Follow-up questionnaire	1,614 diabetes	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 servings/day fruit + vegetables vs. 2.5, Q5/1: median 3.9 servings/day fruit vs. 0.62
Montonen et al., 2005 (10)	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 diabetes	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/day vegetables vs. <42, Q4/1: >43 g/day green vegetables vs. <11, Q4/1: >138 g/day fruit vs. <20

F, female; FH, family history of diabetes; HTN, hypertension; IGT, impaired glucose tolerance; M, male; NHEFS, First National Health and Nutrition Examination Study Epidemiologic Follow-up Study; OGTT, oral glucose tolerance test; Q, quantile; SBP, systolic blood pressure; WHR, waist-to-hip ratio; WHS, Women's Health Study.
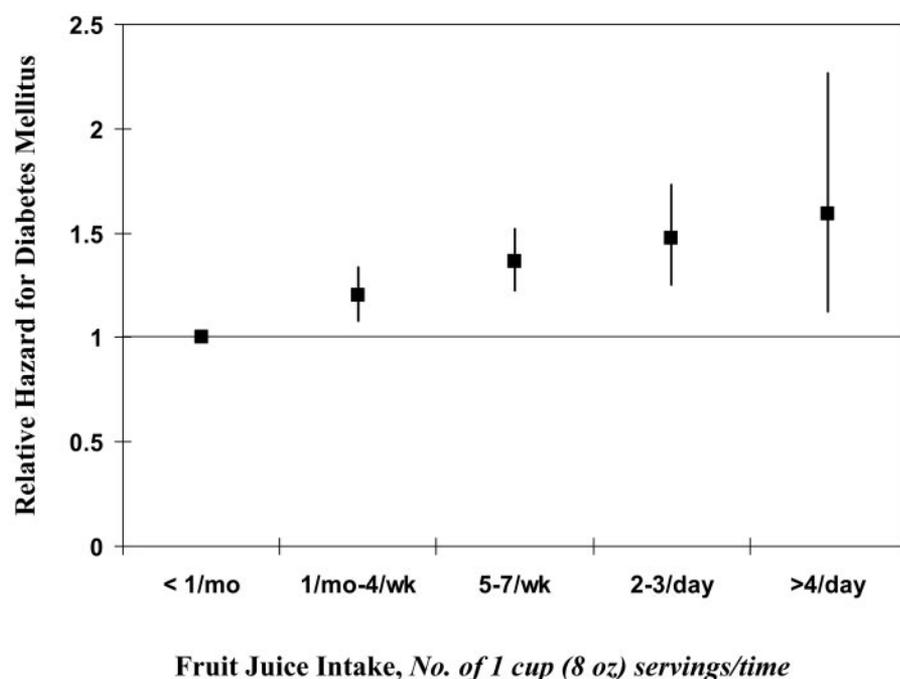
Figure 1—*Multivariate-adjusted relative hazard of diabetes by category of cumulatively updated fruit juice intake. Values were adjusted for cumulatively updated BMI, physical activity, family history of diabetes, postmenopausal hormone use, alcohol use, smoking, and total energy intake. For an increase of 1 serving/day of fruit juice, the multivariate-adjusted relative risk was 1.18 (95% CI 1.10–1.26;* P < 0.0001).

adjusted HR 2.00 [95% CI 1.33–3.03]; $P = 0.001$). In that study, fruit juice consumption was not associated with diabetes 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 two dietary assessments (1991 and 1995). In the present study, five dietary assessments were available (1984, 1986, 1990, 1994, and 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 diabetes. In the present study, 18 years of follow-up were available, with 4,529 cases of incident type 2 diabetes.

The primary limitation of our study was 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 diabetes 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 that 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, whereas our FFQ has not; nevertheless, the most common foods eaten in the U.S. population are encompassed in our instrument. There may be underestimation of type 2 diabetes by self-report; however, our population is highly educated about medical conditions, so self-report error should be substantially less than that in a general population. Fasting glucose criteria for diabetes 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 diabetes in U.S. women (23). Because of 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 diabetes 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 diabetes (20,32), the benefits of regular consumption of fruits and vegetables should be substantial.

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