A Prospective Study of Fruit and Vegetable Intake and the Risk of Type 2 Diabetes in Women

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Fruits and vegetables contain many beneficial nutrients and phytochemicals that are thought to protect against cardiovascular disease (1,2) and diabetes (3–5). Further, different types of vegetables and fruits may differ in their contents of carbohydrates, antioxidants, vitamins, minerals, and other unidentified phytochemicals. However, epidemiologic data on fruit and vegetable intake and type 2 diabetes are very limited. To evaluate the hypothesis that a high intake of fruits and vegetables protects against the incidence of type 2 diabetes and to explore whether specific subgroups of fruits and vegetables differentially affect diabetes risk, we analyzed prospective data from the Women's Health Study (WHS) from 1993 to 2003.

RESEARCH DESIGN AND METHODS — The WHS comprised 39,876 female health professionals aged ≥45 years who were free of heart disease, stroke, or cancer at baseline. Detailed diet information was provided by 38,018 (95%) of the participants without previously diagnosed diabetes at baseline and who completed a 131-item semiquantitative food frequency questionnaire (6).

This semiquantitative food frequency questionnaire, including 28 vegetable and 16 fruit items, has demonstrated reasonably good validity as a measure of long-term dietary intakes in women (6). The average daily intakes of individual fruits and vegetables were calculated by multiplying the intake frequency by the portion size of the specific items. Intake of total fruits and vegetables was then computed by summing over the intake of individual items. We divided the vegetables into groups, including cruciferous (broccoli, cabbage, cauliflower, Brussels sprouts), dark yellow (carrots, yellow squash, yams, sweet potatoes), green leafy (spinach, kale, lettuce), and other (corn, mixed vegetables, celery, eggplant, mushrooms, and beets) (7).

Diagnosis of type 2 diabetes was based on self-report. As described in detail before (8), the validity of self-reported type 2 diabetes in the WHS has been confirmed according to the American Diabetes Association diagnostic criteria (9).

Statistical analysis was performed using SAS (version 8.0; SAS Institute, Cary, NC). Cox proportional hazards models were used to estimate the relative risk (RR) of developing type 2 diabetes, while adjusting for age, total calories, BMI, smoking status, alcohol consumption, exercise, history of hypertension, history of high cholesterol, and family history of diabetes. In stratified analyses, we sought to assess the potential effect modification by BMI (<25 or ≥25). The likelihood ratio test was used to assess the significance of interaction. Tests of linear trend were conducted by assigning the medians of intakes in quintiles treated as a continuous variable.

RESULTS — At baseline, mean daily intake in servings (±SD) was 2.2 ± 1.6 for fruits, 3.9 ± 2.6 for vegetables, and 6.1 ± 3.6 for total fruits and vegetables. Median intake of total fruits and vegetables ranged from 2.5 servings/day in the lowest quintile to >10 servings/day in the highest quintile. Women who consumed more fruits or vegetables tended to be older, exercised more, and had a lower BMI than those with lower intake.

During an average 8.8 years of follow-up (332,905 person-years), we documented 1,614 incident cases of type 2 diabetes. In models adjusted for age, total calories, and smoking, we observed significant inverse relationships with diabetes risk for total fruit and vegetable intake, fruits, citrus fruits, green leafy vegetables, dark yellow vegetables, and legumes and a significant positive association with intake of potatoes (Table 1). After adjusting for known diabetes risk factors, however, none of these associations remained statistically significant. Because BMI is an important risk factor for type 2 diabetes and has also been previously identified as an effect modifier of diet on diabetes risk (10), we performed subgroup analyses stratified by BMI (<25 and ≥25 kg/m^2). No significant findings were observed in the lower BMI group (~15% of case subjects) (data not shown). Among women with BMI ≥25 kg/m^2, higher intake of green leafy or dark yellow vegetables was significantly associated with reduced risk of type 2 diabetes (Table 2). Starchy vegetables such as potatoes did not appear to be beneficial. We observed a marginally significant interaction for BMI and intake of dark yellow vegetables ($P = 0.06$) but not for the interaction between BMI and

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Abbreviations: WHS, Women's Health Study.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*RRs of type 2 diabetes according to quintiles of total and specific subgroups of fruits and vegetables in the WHS*

	Quintile of intake					
	1 (lowest)	2	3	4	5 (highest)	*P* for trend
All fruits and vegetables						
Servings per day (median)	2.54	4.13	5.49	7.09	10.16	—
Cases/person-years	342/66,799	318/66,595	296/66,946	303/66,388	355/66,178	—
Model A* [RR (95% CI)]	1.0	0.87 (0.74–1.01)	0.75 (0.64–0.88)	0.73 (0.62–0.86)	0.77 (0.65–0.92)	<0.001
Model B† [RR (95% CI)]	1.0	1.03 (0.88–1.20)	0.94 (0.79–1.11)	0.93 (0.78–1.10)	1.04 (0.87–1.25)	0.88
All fruits						
Servings per day (median)	0.62	1.32	1.91	2.62	3.91	—
Cases/person-years	365/66,554	308/65,015	297/68,317	307/66,974	337/65,951	—
Model A* [RR (95% CI)]	1.0	0.80 (0.69–0.94)	0.72 (0.61–0.84)	0.72 (0.61–0.85)	0.71 (0.60–0.84)	<0.0001
Model B† [RR (95% CI)]	1.0	0.93 (0.79–1.09)	0.87 (0.74–1.03)	0.94 (0.80–1.11)	0.97 (0.82–1.16)	0.79
All vegetables						
Servings per day (median)	1.47	2.49	3.40	4.58	6.84	—
Cases/person-years	322/66,706	320/66,892	306/66,636	306/66,709	360/65,891	—
Model A* [RR (95% CI)]	1.0	0.93 (0.79–1.08)	0.84 (0.71–0.99)	0.81 (0.69–0.96)	0.89 (0.75–1.05)	0.06
Model B† [RR (95% CI)]	1.0	1.01 (0.86–1.19)	0.98 (0.83–1.16)	0.99 (0.84–1.18)	1.03 (0.86–1.23)	0.83
Citrus fruits						
Servings per day (median)	0.07	0.28	0.57	1.00	1.57	—
Cases/person-years	338/66,654	326/64,992	268/63,382	359/71,437	321/66,101	—
Model A* [RR (95% CI)]	1.0	0.97 (0.83–1.14)	0.79 (0.67–0.93)	0.91 (0.78–1.06)	0.83 (0.70–0.98)	0.02
Model B† [RR (95% CI)]	1.0	1.06 (0.90–1.24)	0.90 (0.76–1.07)	1.14 (0.98–1.34)	1.07 (0.90–1.26)	0.26
Green leafy vegetables						
Servings per day (median)	0.14	0.35	0.56	0.92	1.42	—
Cases/person-years	398/68,240	320/62,247	306/68,294	308/73,119	282/60,572	—
Model A* [RR (95% CI)]	1.0	0.85 (0.73–0.98)	0.71 (0.61–0.83)	0.64 (0.55–0.74)	0.68 (0.57–0.79)	0.0001
Model B† [RR (95% CI)]	1.0	0.92 (0.79–1.08)	0.93 (0.79–1.09)	0.84 (0.72–0.99)	0.96 (0.81–1.13)	0.25
Cruciferous vegetables						
Servings per day (median)	0.13	0.21	0.35	0.57	1.00	—
Cases/person-years	290/60,264	229/50,189	436/90,548	279/61,179	380/70,599	—
Model A* [RR (95% CI)]	1.0	0.92 (0.77–1.10)	0.94 (0.81–1.10)	0.88 (0.75–1.05)	0.99 (0.84–1.17)	0.84
Model B† [RR (95% CI)]	1.0	0.91 (0.76–1.09)	0.98 (0.84–1.14)	0.96 (0.81–1.14)	0.95 (0.80–1.12)	0.71
Dark yellow vegetables						
Servings per day (median)	0.07	0.2	0.34	0.57	1.00	—
Cases/person-years	223/39,218	449/90,306	346/73,915	302/61,722	294/67,529	—
Model A* [RR (95% CI)]	1.0	0.83 (0.71–0.98)	0.75 (0.63–0.90)	0.76 (0.63–0.91)	0.63 (0.52–0.76)	0.0001
Model B† [RR (95% CI)]	1.0	0.90 (0.76–1.07)	0.89 (0.75–1.07)	0.92 (0.76–1.11)	0.81 (0.67–0.98)	0.08
Legumes						
Servings per day (median)	0.13	0.21	0.29	0.50	0.86	—
Cases/person-years	268/63,014	209/52,750	421/83,103	278/56,594	437/77,292	—
Model A* [RR (95% CI)]	1.0	0.91 (0.76–1.10)	1.14 (0.98–1.34)	1.08 (0.91–1.28)	1.16 (0.99–1.37)	0.02
Model B† [RR (95% CI)]	1.0	1.00 (0.83–1.20)	1.21 (1.03–1.42)	1.06 (0.89–1.26)	1.12 (0.95–1.33)	0.20
Potatoes						
Servings per day (median)	0.13	0.28	0.43	0.56	0.93	—
Cases/person-years	262/63,379	343/73,956	157/37,666	400/83,631	444/73,036	—
Model A* [RR (95% CI)]	1.0	1.15 (0.97–1.35)	0.97 (0.79–1.18)	1.11 (0.94–1.31)	1.31 (1.11–1.56)	0.009
Model B† [RR (95% CI)]	1.0	1.03 (0.87–1.22)	0.97 (0.79–1.19)	0.96 (0.81–1.13)	1.02 (0.86–1.22)	0.87

*Model A: adjusted for age, smoking, and total calories. †Model B: multivariate model adjusted for age, smoking, total calories, alcohol use, BMI, exercise, history of hypertension, history of high cholesterol, and family history of diabetes.

intake of green leafy vegetables (P = 0.19). After fully adjusting for BMI, the inverse associations of green leafy and deep yellow vegetables were still observed among overweight women, although the trends were not statistically significant; the multivariate RRs across quintiles were 1.00, 0.94, 0.92, 0.85 and 0.90 (95% CI 0.76–1.08) for green leafy vegetables (P for trend = 0.09) and 1.00, 0.87, 0.90, 0.91 and 0.79 (0.65–0.97) for dark yellow vegetables (P for trend = 0.13). Since BMI may also reflect the impact of long-term fruit and vegetable intake, the addition of BMI into the model may be an

Table 2—*RRs of type 2 diabetes according to quintiles of fruit and vegetable intake in overweight women (BMI ≥25) in the WHS*

	Cases/person-years	RR (95% CI)*		Cases/person-years	RR (95% CI)*
Fruits and vegetables			Green leafy vegetables		
Q1 (lowest)	278/30,850	1.0	Q1 (lowest)	341/34056	1.0
Q2	268/30,923	0.97 (0.82–1.16)	Q2	270/29481	0.92 (0.78–1.08)
Q3	256/31,016	0.89 (0.75–1.07)	Q3	258/31034	0.85 (0.72–1.01)
Q4	260/30,759	0.89 (0.74–1.07)	Q4	236/29234	0.80 (0.68–0.96)
Q5 (highest)	299/30,654	0.98 (0.80–1.19)	Q5 (highest)	256/30211	0.86 (0.72–1.02)
P for trend		*P* = 0.54	*P* for trend		*P* = 0.02
All fruits			Dark yellow vegetables		
Q1 (lowest)	300 /31,002	1.0	Q1 (lowest)	193/18654	1.0
Q2	266/30,706	0.88 (0.74–1.04)	Q2	366/42608	0.83 (0.70–1.00)
Q3	239 /31,171	0.79 (0.66–0.94)	Q3	300/34,539	0.83 (0.69–1.00)
Q4	260 /30,720	0.86 (0.72–1.03)	Q4	244/26,959	0.86 (0.70–1.05)
Q5 (highest)	296 /30,569	0.91 (0.75–1.09)	Q5 (highest)	258/31,316	0.73 (0.60–0.90)
P for trend		*P* = 0.31	*P* for trend		*P* = 0.02
Vegetables			Potatoes		
Q1 (lowest)	272 /30,660	1.0	Q1 (lowest)	322/41,317	1.0
Q2	273 /31,109	1.00 (0.84–1.18)	Q2	293/35,125	1.06 (0.90–1.24)
Q3	251 /30,998	0.87 (0.73–1.05)	Q3	187/22,718	1.00 (0.83–1.20)
Q4	268 /30,772	0.96 (0.80–1.15)	Q4	235/24,697	1.14 (0.95–1.36)
Q5 (highest)	297 /30,628	1.00 (0.82–1.21)	Q5 (highest)	316/29,745	1.14 (0.95–1.36)
P for trend		*P* = 0.83	*P* for trend		*P* = 0.12

*Based on model B: multivariate model adjusted for age, smoking, total calories, alcohol use, exercise, history of hypertension, history of high cholesterol, and family history of diabetes.

overadjustment that could distort the underlying temporal relationship between fruit and vegetable intake and diabetes risk.

CONCLUSIONS— Overall, we found no inverse association between total intake of fruits and vegetables and risk of incident type 2 diabetes after adjustment for known risk factors, whereas a high intake of green leafy or dark yellow vegetables was associated with reduced risk of type 2 diabetes among overweight women.

Although cross-sectional studies (11,12) support beneficial effects of a high intake of fruits and vegetables on type 2 diabetes and glucose metabolism, the results of prospective cohort studies are inconsistent. Fruit and vegetable consumption was inversely related to incident type 2 diabetes in some (3–5,13) but not all cohort studies (14). Our study provided further evidence for benefits from specifically consuming green leafy vegetables and dark yellow vegetables. This result is supported by the report from the EPIC-Norfolk Study (12), which observed a significantly inverse association between green leafy vegetable consumption and HbA_{1c} levels. Our findings also suggest that BMI might be an effect measure modifier on the relation of leafy green or dark yellow vegetable intake and the risk of type 2 diabetes, although additional prospective studies are warranted to confirm these findings. Relevant data from clinical trials are scarce. In a small randomized trial (15) examining a comprehensive dietary intervention among 577 adults with impaired glucose tolerance, a diet high in fruits and vegetables appeared to reduce 6-year incidence of type 2 diabetes by 24%.

The biological mechanisms responsible for the beneficial effects of fruits and vegetables on diabetes risk are likely to be multiple. Besides their contribution to low energy intake, high fiber content, and low glycemic load, fruits and vegetables are also rich in antioxidant vitamins, magnesium, potassium, plant proteins, and other individual phytochemicals, which could be beneficial in reducing risk of type 2 diabetes (2).

In conclusion, our results suggest that higher intake of dark yellow and green leafy vegetables may be beneficial for preventing type 2 diabetes among overweight women.

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