

A Prospective Study of Overall Diet Quality and Risk of Type 2 Diabetes in Women

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OBJECTIVE — The aim of this article was to assess the association between the Alternate Healthy Eating Index (AHEI) and risk of type 2 diabetes in women.

RESEARCH DESIGN AND METHODS — A total of 80,029 women aged 38–63 years in the Nurses' Health Study were followed from 1984 to 2002. The AHEI score was computed from dietary information collected from five repeated food frequency questionnaires administered between 1984 and 1998. Relative risks (RRs) for type 2 diabetes were calculated using Cox proportional hazards models and adjusted for known diabetes risk factors. We also examined how changes in score in 4, 6–8, and 10–12 years are associated with diabetes risk.

RESULTS — We ascertained 5,183 incident cases of type 2 diabetes during 18 years of follow-up. Women who scored high on the AHEI had a lower risk (RR comparing top to bottom score quintile 0.64 [95% CI 0.58–0.71], $P_{\text{trend}} < 0.0001$) for diabetes. Women with consistently high AHEI scores throughout follow-up, compared with those with consistently low scores, had the lowest risk for diabetes. In addition, women whose AHEI scores improved during follow-up, even during recent years, had a lower risk of diabetes than did women whose (low) score did not change.

CONCLUSIONS — A higher AHEI score is associated with a lower risk of type 2 diabetes in women. Therefore, the AHEI score may be a useful clinical tool to assess diet quality and to recommend for the prevention of diabetes.

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The prevalence of diabetes in the U.S. in 2005 was estimated to be 9.6% among adults aged 20 years and 20.9% among those aged ≥ 60 years (1). The vast majority of these cases are type 2 diabetes. Although obesity (2–4) and lack of physical activity (5,6) are the major risk factors, certain dietary factors may also modify the risk of developing type 2 diabetes. In particular, intake of whole grains and fiber (7), nuts (8,9), and magnesium (10,11) and moderate intake of alcohol (12,13) may reduce risk. On the other hand, intake of red and processed meats (14,15) and saturated fats (16) may in-

crease risk. Therefore, dietary modifications may play an important role in the prevention of type 2 diabetes.

The Alternate Healthy Eating Index (AHEI) was modified from the Healthy Eating Index developed by the U.S. Department of Agriculture (17). It measures diet quality using nine dietary components and can be used for providing dietary guidance for healthy eating. Several of the foods and nutrients included in the index have shown to be associated with risk of type 2 diabetes. The AHEI was previously shown to be inversely associated with risk of cardiovascular disease (18) and estrogen receptor-

negative breast cancer (19). However, it has not been evaluated in relation to type 2 diabetes. Therefore, we prospectively assessed the association between the AHEI and risk of type 2 diabetes in an ongoing cohort of U.S. women. Using repeated dietary measurement, we also examined the time period (i.e., recent versus distant diet) in which diet may have the greatest impact on diabetes risk.

RESEARCH DESIGN AND METHODS

The Nurses' Health Study (NHS) began in 1976 when 121,700 female nurses aged 30–55 years living in 11 U.S. states responded to a questionnaire regarding medical, lifestyle, and other health-related information (20). Since 1976, questionnaires have been sent biennially to update this information. Follow-up was complete for >95% of the potential person time up to 2002. In 1980, the participants completed a 61-item food frequency questionnaire (FFQ). In 1984, the FFQ was expanded to 116 items. Similar FFQs were sent in 1986, 1990, 1994, and 1998. We used 1984 as the baseline for the present analysis because the expanded number of items was critical for scoring the AHEI.

For this analysis, we included women who completed the 1984 FFQ with <70 missing items and total energy intake (as calculated from the FFQ) between 500 and 3,500 kcal/day. We excluded those with a history of cancer, cardiovascular disease, and diabetes at baseline, because these conditions may affect diet or reporting thereof. Thus, 80,029 women with follow-up from 1984 to 2002 were included. The NHS was approved by the Institutional Review Board of the Brigham and Women's Hospital, Boston, MA.

Dietary assessment

FFQs were designed to assess average food intake over the previous year. A standard portion size and nine possible frequencies of consumption responses, ranging from "never, or less than once per month" to "six or more times per day" were given for each food. Total energy and nutrient intake was calculated by summing up energy or nutrients from all foods. Previous validation studies among members of the NHS revealed good correlations between nutrients assessed by the FFQ and multiple weeks of

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Abbreviations: AHEI, Alternate Healthy Eating Index; FFQ, Food Frequency Questionnaire; NHS, Nurses' Health Study.

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

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Table 1—Age-adjusted baseline (1984) lifestyle characteristics by quintiles of the AHEI

Quintiles of AHEI (mean score)	Quintiles of diet quality score								
	BMI	Current smoker (%)	Physical activity (MET/week)	Family history (%)	Alcohol (g/day)	Glycemic load*	Energy intake (kcal)	Hypertension (%)	High blood cholesterol (%)
Quintile 1 (24.2)	24.7	31.5	9.7	19.4	6	97	1,516	20	7
Quintile 2 (31.8)	24.5	27.4	11.9	19.3	7	98	1,663	20	7
Quintile 3 (37.3)	24.3	23.7	13.6	19.5	7	99	1,740	20	8
Quintile 4 (43.2)	24.1	20.8	15.8	18.9	8	100	1,826	21	9
Quintile 5 (53.5)	23.6	16.2	20.2	18.6	8	102	1,958	21	11

*Energy adjusted.

food records completed over the previous year (21). For example, correlation coefficients between 1986 FFQ and diet records obtained in 1986 were 0.68 for saturated fat, 0.48 for polyunsaturated fat, and 0.78 for crude fiber. The mean correlation coefficient between frequencies of intake of 55 foods assessed by two FFQs 12 months apart was 0.57 (22). For example, correlation coefficients between FFQ and diet records were 0.69 for broccoli, 0.17 for spinach, and 0.80 for apples.

Scoring for the AHEI was based on intake levels of nine components (18): fruits, vegetables, the ratio of white (seafood and poultry) to red meat, trans fat, the ratio of polyunsaturated to saturated fat, cereal fiber, nuts and soy, moderate alcohol consumption (0.5–1.5 servings/day), and long-term multivitamin use (<5 or 5+ years). These components were chosen on the basis of their association with disease and mortality risk in observational and experimental studies. Each component contributed 0 to 10 points, except for the multivitamin component, which was assigned either 2.5 or 7.5 to avoid overweighting of this binary variable. Summing up the scores for all components, the maximum possible AHEI score was 87.5.

Ascertainment of type 2 diabetes

Our end points included incident type 2 diabetes that occurred between the return of the 1984 questionnaire and June 1, 2002. When a participant reported a new diagnosis of diabetes in the biennial questionnaires, we mailed a supplementary questionnaire that assessed symptoms, diagnostic tests, and treatment to confirm the diagnosis. Diabetes was confirmed when one or more of the following criteria were met: 1) manifestation of classic symptoms (excessive thirst, polyuria, weight loss, and hunger) plus an elevated fasting glucose level (>140 mg/dl [7.8 mmol/l]) or elevated nonfasting level

(>200 mg/dl [11.1 mmol/l]); 2) asymptomatic but elevated plasma glucose level on at least two different occasions (as defined above) or abnormal oral glucose tolerance test (>200 mg/dl 2 h after glucose load); and 3) receipt of any hypoglycemic treatment for diabetes. These criteria for diabetes classification were consistent with those of the National Diabetes Data Group during our follow-up period (23). For follow-up after 1997, the fasting plasma glucose concentration indicative of type 2 diabetes was changed to 126 mg/dl (7.0 mmol/l) or higher consistent with the 1997 American Diabetes Association criteria (24). A validation study has shown a high level of accuracy in self-reporting of diabetes (25). Review of medical records by an endocrinologist blinded to the questionnaire information confirmed 61 (98%) of the 62 reports. Deaths were reported by family members, by the postal service, or through searches in the National Death Index.

Statistical analysis

We used Cox proportional hazards models to examine the associations between AHEI and diabetes risk. To reduce random within-person variation and best represent long-term dietary intake, we calculated cumulative averages of the AHEI score from our repeated FFQs (26). For example, AHEI score in 1984 was used to predict diabetes occurrence from 1984 to 1986, and the average score from 1984 to 1986 was used to predict diabetes risk from 1986 to 1990. We adjusted for age, family history of diabetes (yes or no), smoking (never, past, current with cigarette use of 1–14/day, 15–24/day, 25+ /day, or missing), postmenopausal hormone use (premenopausal or never, past, or current hormone use), energy intake (quintiles), leisure time physical activity (quintiles of MET hours), and BMI (in continuous and quadratic terms). To minimize confounding by adiposity, we

additionally adjusted for waist-to-hip ratio (collected in 1986) among women for whom these data were available. In separate analyses, we included only symptomatic cases, as these may represent rapidly progressing disease. Cases were considered symptomatic if women reported classic symptoms in a supplemental questionnaire for those who self-reported diabetes in the biennial questionnaire. To explore the critical period in which diet may have an influence on diabetes development, we assessed the association with diabetes risk using baseline and most recent AHEI scores. In addition, we used our multiple dietary assessments during follow-up to examine changes in AHEI score in 4, 6–8, and 10–12 years in relation to risk of diabetes. For example, in the analysis for the 4-year AHEI score change, we used differences in quintile change for the AHEI score between 1986 and 1990 to predict diabetes risk in 1990–1994, score change between 1990 and 1994 to predict diabetes risk in 1994–1998, and so forth.

RESULTS— During 18 years of follow-up, we ascertained 5,183 incident cases of type 2 diabetes. Mean AHEI scores in the entire cohort increased from 38.1 ± 10.5 points (mean \pm SD) in 1984 to 44.4 ± 11.7 points in 1998. Women who scored high on the AHEI tended to be leaner, more physically active, and less likely to be current smokers (Table 1). Using the cumulative AHEI score and adjusting for potential confounders, we found an inverse association between AHEI score and type 2 diabetes. Relative risk (RR) comparing top to bottom quintiles was 0.64 [95% CI 0.58–0.71] $P_{\text{trend}} < 0.0001$ (Table 2). This association was slightly stronger among the symptomatic individuals (RR comparing fifth to first quintile 0.56 [0.49–0.64] $P_{\text{trend}} < 0.0001$). Additional adjustment for waist-to-hip ratio somewhat attenuated the association, but it remained statistically sig-

Table 2—RRs (95% CI) for type 2 diabetes according to quintiles of the AHEI

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P_{trend}
Cases	1,273	1,202	1,052	946	710	
Age and energy adjusted	1	0.86 (0.79–0.93)	0.71 (0.65–0.77)	0.60 (0.55–0.65)	0.41 (0.37–0.45)	<0.0001
Multivariate*	1	0.93 (0.86–1.01)	0.84 (0.77–0.91)	0.78 (0.72–0.85)	0.64 (0.58–0.71)	<0.0001
Multivariate + WHR†	1	0.96 (0.85–1.08)	0.87 (0.77–0.99)	0.89 (0.78–1.01)	0.76 (0.66–0.88)	<0.0001

*Adjusted for age, energy intake, smoking, BMI (continuous and quadratic term), physical activity, family history, menopausal status, and postmenopausal hormone use. †Waist-to-hip ratio (WHR) analysis limited to those with waist and hip information in 1986. Cohort, $n = 46,412$; cases, $n = 2,482$.

nificant, indicating that diet composition apart from adiposity influences diabetes risk. In stratified analysis, the AHEI was associated with diabetes only among nonsmokers. RR comparing top to bottom quintiles among nonsmokers was 0.74 ([0.66–0.83] $P < 0.0001$, $P_{\text{interaction}}$ between smokers and nonsmokers 0.06). No sign of any association was observed with smokers. The inverse association remained strong among women with no hypertension (fifth vs. first quintile RR 0.60 [0.52–0.69], $P_{\text{trend}} < 0.0001$), but no association was observed among those with hypertension ($P_{\text{interaction}} = 0.0001$). Also, women who reported normal blood cholesterol level had a RR of 0.66 ([0.58–0.76] $P_{\text{trend}} < 0.0001$), but association for those reporting hypercholesterolemia was weaker (fifth vs. first quintile RR 0.88 [0.74–1.04], $P_{\text{trend}} = 0.07$, $P_{\text{interaction}} = 0.002$).

We then examined individual components in the AHEI for their contribution to the inverse association with type 2 diabetes risk and found a substantial inverse association with nuts and soy, cereal fiber, and the white-to-dark meat ratio. For every 5-point increase in the score of these components (maximum score for

each component is 10 points), the multivariate RR for diabetes was 0.56 (95% CI 0.50–0.63] $P_{\text{trend}} < 0.0001$) for cereal fiber, 0.86 ([0.81–0.91] $P_{\text{trend}} < 0.0001$) for nuts and soy, and 0.89 ([0.84–0.95] $P_{\text{trend}} = 0.0002$) for the white-to-red meat ratio. As alcohol has shown clear inverse association in epidemiological studies, we explored the importance of the alcohol component for diabetes risk by removing it from the AHEI score and adjusting for alcohol intake in the proportional hazards model. The AHEI remained inversely associated with diabetes, albeit weaker (RR comparing fifth with first quintile 0.81 [0.73–0.89], $P_{\text{trend}} < 0.0001$). The RR for alcohol consumption of 15 g/day (~1+ drink) compared with abstainers, after adjustment for the AHEI score (without the alcohol component) was 0.49 [0.43–0.55].

To explore the period during follow-up at which diet may have an influence on diabetes development, we used the baseline and the most recent AHEI score to predict diabetes risk and found associations of a magnitude similar to that for the cumulative updated AHEI score in the main analysis (data not shown). Most women did not

change their diet drastically during follow-up. Women who consistently had a high AHEI score (fourth or fifth quintile) during the follow-up period had a substantially lower risk for diabetes than those who consistently had a low score (first or second quintile) (Table 3). We then examined the association between a change in the AHEI score according to different time intervals of dietary change. When women scored high in the beginning of a score change period but dropped to low scores at the end of that period, there was no significant reduction of risk. On the other hand, changes in score from low to high conferred a substantial risk reduction, even when changes occurred in the last 4 years (RR comparing low-to-high versus low-to-low in 4 years 0.78 [95% CI 0.66–0.92], $P_{\text{trend}} = 0.003$). This result suggests that recent changes in diet may still have a substantial influence on diabetes development.

CONCLUSIONS— In this prospective analysis of overall diet and risk of type 2 diabetes in >80,000 U.S. women, we found that a higher AHEI score was associated with a substantially lower risk of type 2 diabetes during 18 years of follow-

Table 3—Multivariate RRs (95% CI) for change in the AHEI over 4, 6–8, and 10–12 years and risk for type 2 diabetes during subsequent period of follow-up (1990–2002 or 1994–2002)

AHEI	Low-low	High-low	Low-high	High-high
4 years change*				
Case	1,031	161	126	621
Multivariate RR†	1	0.85 (0.73–1.00), $P = 0.04$	0.78 (0.66–0.92), $P = 0.003$	0.73 (0.67–0.80), $P < 0.0001$
6–8 years change‡				
Case	1,011	221	173	600
Multivariate RR	1	0.89 (0.78–1.02), $P = 0.10$	0.81 (0.70–0.93), $P = 0.004$	0.71 (0.65–0.79), $P < 0.0001$
10–12 years change§				
Case	756	189	130	457
Multivariate RR	1	0.95 (0.82–1.10), $P = 0.50$	0.83 (0.70–0.98), $P = 0.03$	0.78 (0.70–0.87), $P = 0.0001$

Low-low, AHEI score in quintile 1 or 2 at the start and end of change period. High-low, AHEI score in quintile 4 or 5 at the start of change period and 1 or 2 at the end of change period; Low-high, reverse of High-low; High-high, AHEI score in quintile 4 or 5 at the start and end of change period. Results for women with a small amount of change (i.e., remainder of the cohort who were in the third quintile and did not change during the score-change period or did not move to the extreme or were in one extreme and moved to the third quintile at the end of the score change period) are not presented. *AHEI score change between 1986 and 1990, 1990 and 1994, and 1994 and 1998 was used to model diabetes incidence in 1990–1994, 1994–1998, and 1998–2002, respectively. †Adjusted for the same covariates as the multivariate model in Table 2. ‡AHEI score change between 1984 and 1990, 1986 and 1994, and 1990 and 1998 was used to model diabetes incidence in 1990–1994, 1994–1998, and 1998–2002, respectively. §Follow-up duration: 1994–2002. AHEI score change between 1984 and 1994 and 1986 and 1998 was used to model diabetes incidence in 1994–1998 and 1998–2002, respectively.

up. Although diabetes risk appeared to be more strongly related to a consistently high AHEI score, recent improvement in diet may still have substantial risk reduction potential. However, the AHEI did not appear to benefit current smokers or women with hypertension.

In the Diabetes Prevention Program, high-risk individuals in the treatment group following a healthy low-calorie, low-fat weight loss diet in combination with exercise had a lower incidence of type 2 diabetes compared with the control group within 4 years of follow-up (27). Similarly, a Finnish trial on weight reduction, reduced saturated fat intake, and increased fiber intake and physical activity showed a reduction of diabetes risk within a mean follow-up of 3.2 years (28). These studies show that lifestyle changes may affect incidence of type 2 diabetes quickly. In our study, the AHEI was associated with lower risk of incident diabetes independent of BMI, suggesting that changes in dietary composition play an important role in diabetes etiology.

Several studies have shown associations between certain eating patterns and risk of type 2 diabetes. We have previously reported for the same group of women that a dietary pattern with some similarity to the AHEI was associated with a lower risk of type 2 diabetes (29). This “prudent” pattern was characterized by higher intakes of fruits and vegetables, whole grains, and poultry. However, this pattern did not emphasize moderate alcohol intake or consumption of nuts or soy. In contrast, a dietary pattern (“Western”) high in red and processed meats, refined grains, and sweets and desserts was associated with a higher diabetes risk. Similar results were observed for these dietary patterns in a cohort of men (30). Inflammation is believed to play an important role in diabetes development (31,32). The prudent pattern was associated with a lower fasting insulin level (33) and lower C-reactive protein levels (34) in a subsample of our cohort, and a dietary pattern similar to the Western pattern was associated with higher levels for markers of inflammation and insulin resistance (35). Therefore, the association between the AHEI and type 2 diabetes may also be mediated by increased insulin sensitivity and reduced inflammation. However, unlike the AHEI, the prudent and Western dietary patterns were population-specific as they were identified from existing eating habits in our cohort. The a priori scoring criteria used for the AHEI may

facilitate use by clinicians in individual settings as well as public health guidelines for the prevention of type 2 diabetes and cardiovascular disease (18).

Several components of the AHEI score have been linked to diabetes risk in other populations. Whole grains and fiber were associated with reduced diabetes risk in several cohorts, including African-American women (36–38), a reduction that may be mediated through their favorable association with insulin sensitivity (39,40). Short-term clinical trials in overweight subjects have also shown that consumption of whole grains can lower the fasting insulin level (41) and improve insulin sensitivity (41,42). The AHEI favors low intake of red meat including processed meats, as reflected in awarding points for a high white-to-red meat ratio, which has been linked to a lower risk of diabetes (14,15,29). Moderate alcohol intake may enhance insulin sensitivity (13) and has also been associated with lower diabetes risk in several cohorts (12,13).

In our analysis of change in AHEI score, we do not know when the score changed in each score period we considered (e.g., 1984–1994 for a 10-year change), or how rapidly the change occurred. However, the results of dietary changes over various periods (4, 6–8, and 10–12 years) consistently suggested that more recent diet maybe a stronger predictor for type 2 diabetes than distant diet. Although diabetes is usually diagnosed some time after glucose abnormality, this timing would only have led to an overestimation of the time it takes for dietary changes to have an effect. However, women may respond to detection of mild hyperglycemia by adopting an AHEI-like diet. The cumulatively updated AHEI score used in our analysis would not be affected strongly by any short-term changes in diet that have no effect on diabetes. On the other hand, if the timing of the FFQs did not capture short-term diet improvement that reduced diabetes risk, our results would underestimate the strength of the inverse association between AHEI score and diabetes risk.

The association between AHEI score and type 2 diabetes was slightly weaker after additional adjustment for waist-to-hip ratio. This is probably due to the analytic sample being a subset of the entire cohort and residual confounding by abdominal obesity that is reflected by waist-to-hip ratio. Nevertheless, a clear inverse association remained. On the other hand, the prospective design of this study renders recall bias unlikely. Because of the

study participants’ ready access to health care, under-reporting of diabetes is expected to be less than that in the general population. The long follow-up and multiple dietary measurements allowed us to evaluate temporality of dietary influence during adult life by exploring different durations of latency and change in diet. We used repeated measurements of various potential confounders and statistically controlled for BMI and waist-to-hip ratio. Women with a high AHEI score tended to have other healthy lifestyle habits that may reduce the risk of diabetes. We have adjusted for the major diabetes risk factors in detail. However, it is conceivable that there are other confounders that we did not completely account for, and this may have led us to overestimate the strength of the association. The AHEI was not developed specifically for diabetes prevention; therefore, a dietary pattern may exist that is more strongly associated with the prevention of type 2 diabetes. However, promotion of a dietary pattern that can contribute to the prevention of various major diseases may be preferable for public health efforts.

In summary, a higher AHEI score, independent of adiposity, was associated with a lower risk of type 2 diabetes in women. The AHEI may be a useful tool in both clinical and public health settings for providing dietary advice for the prevention of diabetes in addition to other chronic diseases (18,19). In addition, our findings suggest that dietary change may have an impact on diabetes risk even within a few years.

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