



Changes in Overall Diet Quality and Subsequent Type 2 Diabetes Risk: Three U.S. Prospective Cohorts

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OBJECTIVE

Recent public health recommendations emphasize adopting a healthful dietary pattern, but evidence is scarce on whether incremental diet quality changes have an impact on long-term diabetes prevention. We aim to evaluate diet quality changes during a 4-year period and subsequent 4-year type 2 diabetes incidence.

RESEARCH DESIGN AND METHODS

Participants of prospective cohorts, the Nurses' Health Study (NHS), NHS II, and the Health Professionals Follow-up Study, who were free of diabetes at baseline ($n = 124,607$), were observed for ≥ 20 years. Diet quality, reflected by the Alternate Healthy Eating Index (AHEI) score, was assessed every 4 years to calculate changes.

RESULTS

We documented 9,361 cases of type 2 diabetes during 2,093,416 person-years of follow-up. A $>10\%$ decrease in AHEI score over 4 years was associated with a higher subsequent diabetes risk (pooled hazard ratio 1.34 [95% CI 1.23–1.46]) with multiple adjustment, whereas a $>10\%$ increase in AHEI score was associated with a lower risk (0.84 [0.78–0.90]). Greater improvement in diet quality was associated with lower diabetes risk across baseline diet quality status (P for trend ≤ 0.001 for low, medium, or high initial diet quality) and baseline BMI (P for trend ≤ 0.01 for BMI <25 , 25–29, or 30 kg/m²). Changes in body weight explained 32% (95% CI 24–41) of the association between AHEI changes (per 10% increase) and diabetes risk.

CONCLUSIONS

Improvement in overall diet quality is associated with a lower risk of type 2 diabetes, whereas deterioration in diet quality is associated with a higher risk. The association between diet quality changes and diabetes risk is only partly explained by body weight changes.

Evidence from prospective observational studies and clinical trials has demonstrated the importance of diet in the prevention of type 2 diabetes (1). In randomized controlled trials (RCTs), lifestyle changes, including individually tailored, macronutrient composition, focused dietary interventions, prevented or delayed type 2 diabetes among individuals at high risk (2,3). However, long-term maintenance of calorie-restricted and macronutrient-focused diets has been challenging (4). Further, these tailored therapeutic approaches are difficult to communicate in general populations.

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Therefore, improving the overall quality of diet, which allows flexibility in food choices, may be more practical for maintaining long-term compliance and sustainability for diabetes prevention.

Healthful dietary patterns, which have emerged from various target populations, have been associated with type 2 diabetes prevention (5–8). These dietary patterns are typically rich in whole grains, fruits and vegetables, nuts, and legumes; are moderate in alcohol consumption; and are lower in refined grains, red/processed meats, and sugar-sweetened beverages (1). In an RCT among participants who are at risk for cardiovascular disease (CVD), those assigned to a consume a high-quality diet with extra-virgin olive oil supplementation had a significant diabetes risk reduction after 4.1 years of follow-up (9).

In recent years, public health recommendations have increasingly focused on advocating the improvement of overall diet quality to prevent chronic disease (10–12), but scientific evidence is scarce on whether incremental improvement in the overall diet quality has a long-term preventive impact on type 2 diabetes in general populations. Healthful dietary patterns have been associated with type 2 diabetes prevention (1). However, the majority of these studies were conducted with a baseline measure of dietary variables only, and the impact of changes in dietary patterns has not been assessed in large population studies. Further, RCT evidence has shown that improvement in diet quality reduces type 2 diabetes risk (9,13), but it is unclear whether deterioration in diet quality can worsen the risk of the development of diabetes. Therefore, we investigated whether change in overall diet quality over a 4-year period was associated with type 2 diabetes risk in a subsequent 4-year follow-up in three large population-based cohorts of men and women with long-term follow-up and repeated measures of exposure (diet) and outcome (diabetes). To assess overall diet quality changes, we calculated changes in Alternate Healthy Eating Index (AHEI) scores every 4 years. This score was used to represent adherence to healthy eating for chronic disease prevention, as previously developed in the current study cohorts (8).

RESEARCH DESIGN AND METHODS

Study Population

The Nurses' Health Study (NHS) is a prospective cohort study of 121,700 female

registered nurses (age range 30–55 years) living across the U.S. at the baseline data collection in 1976. The NHS II is another prospective cohort of 116,671 younger female registered nurses from the U.S. (age range 25–42 years) at baseline in 1989. The Health Professionals Follow-up Study (HPFS) is a prospective cohort study of 51,529 male health professionals from the U.S. who were 40–75 years of age at study enrollment in 1986. Participants underwent follow-up biennially using validated questionnaires on medical history and lifestyle. The study protocol was approved by the Institutional Review Board of the Brigham and Women's Hospital and the Human Subjects Committee Review Board of Harvard T.H. Chan School of Public Health.

The earliest year with detailed information available on diet and other lifestyle information, which was 1991 in the NHS II and 1986 in the NHS and HPFS, was used as the baseline in the current analysis. We excluded participants with a history of diabetes (i.e., type 1 diabetes, type 2 diabetes, and gestational diabetes mellitus) ($n = 7,295$ in NHS, $n = 2,109$ in NHS II, and $n = 2,340$ in HPFS), CVD ($n = 7,097$ in NHS, $n = 1,745$ in NHS II, and $n = 6,509$ in HPFS), or cancer ($n = 9,810$ in NHS, $n = 2,714$ in NHS II, and $n = 1,493$ in HPFS) at baseline, and incident cases during the first 4 years of follow-up (between 1986 and 1990 in the NHS and HPFS, and between 1991 and 1995 in the NHS II) because we were investigating 4-year changes in lifestyle exposures. We excluded deaths that occurred during that 4-year period ($n = 2,302$ in NHS, 193 in NHS II, and 686 in HPFS). The participants with missing food frequency questionnaires (FFQs) at the baseline of the current analysis follow-up period were excluded ($n = 31,314$ in NHS, $n = 29,577$ in NHS II, and $n = 1,160$ in HPFS). Participants who provided FFQ data had similar baseline characteristics such as age and BMI compared with those with missing FFQ data (Supplementary Table 1). Further, we excluded participants who left >10 items blank on the FFQ at baseline, who had a missing date of birth, who had missing BMI or physical activity variables at baseline, who were pregnant during the FFQ report cycle, or who reported unusual total energy intake on the baseline FFQ (i.e., <800 or >4,200 kcal/day for men and <500 or >3,500 kcal/day for women). A total

of 48,612 women in the NHS, 49,711 women in the NHS II, and 26,284 men in the HPFS were included in the current analysis.

Dietary Assessment

Dietary intake was assessed using a semiquantitative FFQ at baseline and was updated every 4 years (14–16). For each food item, participants were asked to report their usual intake of a standard portion of each food item from the previous year. The daily nutrient intake was estimated using the Harvard Food Composition Database derived from the U.S. Department of Agriculture nutrient data. The reproducibility and validity of nutrient, food, and dietary pattern measurements in the NHS and HPFS have been documented in detail (14–17).

Changes in diet quality were assessed by calculating changes in the AHEI 2010 score. The AHEI 2010 was based on a comprehensive review of the relevant literature to identify foods and nutrients that have been consistently associated with a lower risk of chronic disease (8). It was updated from the original AHEI (18). The AHEI was designed to provide quantitative scoring for adherence to dietary guidance (18). The rationale for variable selection and scoring criteria of the AHEI 2010 was described in detail previously (8). The score consisted of 11 components, which included higher intakes of vegetables, fruits, whole grains, nuts and legumes, long-chain n-3 fatty acids, and polyunsaturated fatty acids (excluding long-chain n-3 fatty acids); lower intakes of red/processed meat, sugar-sweetened beverages and fruit juice, transfat, and sodium; and moderate alcohol consumption, as being adherence to healthy eating. Each component score ranged from 0 (least healthy eating behavior) to 10 (maximum adherence), and the total AHEI 2010 score ranged from 0 to 110 (maximum adherence).

Other Exposure Assessment

Information on physical activity, body weight, other lifestyle information, and medical history was collected at baseline, and was updated through biennial questionnaires. BMI was calculated as weight (in kilograms) self-reported divided by the square of height (in meters). Based on the previous validation study, self-reported weights were highly correlated with measured weights

($r = 0.97$) (19). Information on cigarette smoking, family history of diabetes, postmenopausal hormone use, and history of hypertension or hypercholesterolemia was assessed from these questionnaires by self-report. The validity of these assessments has been documented previously (20,21).

Ascertainment of Type 2 Diabetes

In the baseline questionnaire and all biennial follow-up questionnaires, participants were asked about the incidence of physician-diagnosed diabetes. Participants who reported such a diagnosis completed a supplementary questionnaire asking about symptoms, diagnostic tests, and treatment to confirm diagnosis. The validity of the supplementary questionnaire for type 2 diabetes, in which self-reported diagnosis of diabetes was confirmed by medical records reviewed by an endocrinologist who was blinded to the supplementary questionnaire information for 61 of 62 (98%) randomly selected NHS participants and 57 of 59 (97%) HPFS participants, has been documented previously (22,23).

The diagnosis was confirmed if at least one of the following was reported according to the National Diabetes Data Group criteria (24): 1) at least one symptom (excessive thirst, polyuria, weight loss, or hunger) plus fasting glucose concentration of ≥ 7.8 mmol/L or random glucose concentration of ≥ 11.1 mmol/L; 2) in the absence of symptoms, at least two elevated glucose concentrations on different occasions (fasting glucose concentration > 7.8 mmol/L, random glucose concentration ≥ 11.1 mmol/L, and/or 2-h postload concentration ≥ 11.1 mmol/L at an oral glucose tolerance test); or 3) treatment with insulin or oral hypoglycemic medication. For the cases after 1998, the revised American Diabetes Association criteria were applied using the fasting glucose concentration cutoff of 7.0 mmol/L (25).

Statistical Analyses

Participants contributed person-time from the return of the baseline questionnaire until the date of diagnosis of type 2 diabetes, death, or the end of the follow-up (2011 for the NHS II, and 2010 for the NHS and HPFS), whichever came first. We used multivariable time-dependent Cox proportional hazards models to estimate hazard ratio (HR) and 95% CI. The HRs were pooled from the multivariable adjusted models in

each cohort to obtain summarized risk estimates. The time scale for the left truncated survival model was age, which was stratified by calendar time in 4-year groups, in addition to accounting for study cohorts in pooled analyses. We quantified a linear trend across AHEI change categories with a Wald test for linear trend by assigning the median value to each category and modeling this variable as a continuous variable. We assessed a potential nonlinear relation between the changes in the AHEI and incident type 2 diabetes by using restricted cubic spline transformations without prior specification of the risk function (26). We performed tests for nonlinearity by using the likelihood ratio test and compared the model with the linear term only with the model with both the linear and cubic spline terms.

To assess the associations between changes in diet quality and subsequent risk for type 2 diabetes, we used changes in AHEI scores updated every 4 years as a time-varying exposure for type 2 diabetes risk in the subsequent 4 years. In addition to accounting for age, regression models were adjusted for potential confounding factors including ethnicity (white/nonwhite); family history of diabetes (yes/no); baseline AHEI, physical activity, and total energy intake at the beginning of each 4-year period (all in quintiles); 4-year changes in smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator), physical activity, and total energy intake (all in quintiles); and a medical history of hypertension (yes/no) and hypercholesterolemia (yes/no) (model 1). In the NHS and NHS II, postmenopausal status and postmenopausal hormone use (never use, current use, past use, or missing) were also included. We additionally adjusted for baseline BMI at the beginning of each 4-year period (< 21 , 21–22.9, 23–24.9, 25–29.9, and ≥ 30 kg/m²) in a separate model (model 2) because the association under investigation might be mediated by body weight. Since changes in body weight may be a mediator of the association between changes in AHEI and risk of type 2 diabetes, we further adjusted model 2 with 4-year changes in body weight. To evaluate the contribution of body weight changes over the same period on the association

between changes in AHEI and the risk of type 2 diabetes, SAS macro %MEDIATE (publicly available at <https://www.hsph.harvard.edu/donna-spiegelman/software/mediate/>) was applied using $1 - (\beta_{\text{mediator model}} / \beta_{\text{base model}}) \times 100$ according to the methods described by Lin et al. (27). Trends of increases and decreases in AHEI scores were evaluated by modeling score changes in categories with “no change or less than $\pm 3\%$ ” as a reference.

We tested multiplicative interactions of changes in AHEI scores with age, hypertension, hypercholesterolemia, current smoking status, and BMI at the beginning of the 4-year period, using likelihood ratio tests. To consider the ceiling effect of the baseline diet quality, we stratified the analysis by the baseline AHEI scores (< 45 , 45–49, and ≥ 50). To assess the stability of the associations across simultaneously changing categories of physical activity, we assessed the associations stratified by changes in physical activity levels (decreased, stable as ± 2 MET-h/week change, and increased). Further, we performed a sensitivity analysis of calculating the AHEI score without the long-chain n-3 fatty acid component because of the small positive association between long-chain n-3 fatty acid intake and type 2 diabetes observed previously in the current study cohorts (28). AHEI score, physical activity, and weight change variables were assessed with the use of censoring of data at the 0.5 and 99.5 percentiles to minimize the influence of outliers. To minimize missing values during follow-up, missing variables were replaced with carried forward values for continuous variables, and a missing indicator was added for categorical variables. For all statistical analyses, a two-sided P value of < 0.05 was considered to be statistically significant. All data analyses were performed using SAS software, version 9.3 for UNIX (SAS Institute, Cary, NC).

RESULTS

We documented 9,361 incident type 2 diabetes cases (4,308 in the NHS, 3,136 in the NHS II, and 1,917 in the HPFS) during 2,093,416 person-years of follow-up. Baseline characteristics of study participants are presented across the 4-year changes in the percentage AHEI scores among U.S. women and men in three prospective cohorts (Table 1). Participants who had improved the diet quality generally had a lower AHEI score

Table 1—Baseline characteristics according to 4-year changes in percent diet quality scores among U.S. women and men in three prospective cohorts

	Change in diet quality (categories in % score change)				
	Decrease			Increase	
	Moderate to large (>10%)	Small to moderate (3–10%)	No change or stable ($\pm < 3\%$)	Small to moderate (3–10%)	Moderate to large (>10%)
NHS (1990)					
Participants, <i>n</i>	3,719	10,900	15,199	13,050	5,744
Age, years	56.2 \pm 7.2	55.9 \pm 7.1	55.9 \pm 7.1	55.8 \pm 7.0	56.0 \pm 7.0
BMI, kg/m ²	24.9 \pm 4.5	24.9 \pm 4.4	24.9 \pm 4.5	25.0 \pm 4.5	25.1 \pm 4.8
AHEI score	62.1 \pm 10.6	55.6 \pm 10.5	51.5 \pm 10.4	48.2 \pm 10.0	44.4 \pm 9.5
Physical activity, MET-h/week	16.0 \pm 21.3	14.4 \pm 20.9	14.4 \pm 21.6	13.8 \pm 19.4	13.8 \pm 20.1
White ethnicity, %	98.5	98.7	98.3	98.0	97.3
Current smoker, %	15.8	16.6	15.8	16.1	15.9
Hypertension, %	23.2	22.2	22.0	22.0	23.5
High cholesterol, %	30.9	32.3	33.4	35.4	38.4
Family history of diabetes, %	28.6	28.2	28.4	28.5	27.9
Total energy intake, kcal/day	1,794 \pm 542	1,800 \pm 527	1,786 \pm 519	1,739 \pm 503	1,717 \pm 486
Menopausal status and postmenopausal hormone use, %					
Premenopausal	29.2	31.2	31.1	31.2	29.7
Postmenopausal + never users	27.2	27.4	27.0	27.1	28.2
Postmenopausal + current users	26.4	26.0	25.8	26.0	26.2
Postmenopausal + past users	15.0	13.4	14.2	13.6	14.1
Missing information	2.3	2.0	2.0	2.2	1.8
NHS II (1995)					
Participants, <i>n</i>	4,379	11,245	15,266	13,110	5,711
Age, years	41.7 \pm 4.0	41.9 \pm 4.0	41.9 \pm 4.0	41.9 \pm 4.1	41.9 \pm 4.2
BMI, kg/m ²	25.4 \pm 5.6	24.8 \pm 5.3	24.6 \pm 5.2	24.6 \pm 5.4	24.7 \pm 5.5
AHEI score	59.5 \pm 9.7	52.8 \pm 9.9	48.4 \pm 10.1	45.4 \pm 10.0	42.2 \pm 9.5
Physical activity, MET-h/week	24.0 \pm 32.5	21.1 \pm 27.7	19.6 \pm 25.0	19.7 \pm 26.2	19.2 \pm 24.5
White ethnicity, %	97.1	96.7	97.0	97.0	96.6
Current smoker, %	12.3	11.4	11.3	11.5	11.9
Hypertension, %	13.4	10.6	10.4	10.0	10.7
High cholesterol, %	24.8	22.6	22.6	22.9	22.7
Family history of diabetes, %	37.1	36.8	36.5	35.5	36.8
Total energy intake, kcal/day	1,669 \pm 519	1,708 \pm 527	1,755 \pm 531	1,780 \pm 521	1,829 \pm 516
Menopausal status and postmenopausal hormone use, %					
Premenopausal	86.9	88.2	88.1	87.8	86.6
Postmenopausal + never users	0.6	0.6	0.7	0.7	0.7
Postmenopausal + past users	1.1	1.0	0.9	1.1	1.1
Postmenopausal + current users	8.8	7.6	7.8	7.7	8.7
Missing information	2.7	2.6	2.5	2.8	3.1
Oral contraceptive use, %					
Never user	14.8	14.1	14.6	14.5	14.3
Past user	78.1	79.4	79.0	78.0	78.3
Current user	7.1	6.5	6.4	7.4	7.4
Health Professionals Follow-up Study (1990)					
Participants, <i>n</i>	2,216	5,998	8,155	6,755	3,160
Age, years	56.0 \pm 9.2	56.0 \pm 9.2	56.1 \pm 9.1	56.1 \pm 9.0	56.8 \pm 9.1
BMI, kg/m ²	25.3 \pm 3.3	25.3 \pm 3.0	25.3 \pm 3.0	25.2 \pm 2.9	25.3 \pm 3.0
AHEI score	61.6 \pm 10.9	55.9 \pm 11.0	52.1 \pm 10.8	49.1 \pm 10.6	46.3 \pm 10.2
Physical activity, MET-h/week	23.7 \pm 38.8	22.4 \pm 30.0	21.3 \pm 28.0	21.4 \pm 30.6	21.1 \pm 28.9
White ethnicity, %	95.9	96.4	95.9	95.9	94.7
Current smoker, %	8.9	7.8	7.9	7.1	6.8
Hypertension, %	16.1	14.7	15.5	15.2	15.7
High cholesterol, %	15.7	17.2	18.9	21.6	27.6
Family history of diabetes, %	20.9	20.0	20.9	21.4	19.7
Total energy intake, kcal/day	2,011 \pm 603	2,032 \pm 608	2,030 \pm 603	1,996 \pm 585	1,943 \pm 569

Values are reported as the mean \pm SD, unless otherwise indicated.

and physical activity levels at baseline compared with those who had a worsened diet quality.

Table 2 shows HRs of type 2 diabetes according to the 4-year changes in diet quality. A >10% decrease in AHEI scores over 4 years was associated with a higher subsequent risk of diabetes (pooled HR 1.34 [95% CI 1.23–1.46]) compared with participants who maintained relatively stable diet quality in each 4-year period with multiple adjustments in model 1, whereas an improvement of >10% in AHEI score was associated with a lower risk of diabetes (0.84 [0.78–0.90]). The association was attenuated slightly but remained significant with additional adjustment for baseline BMI at the beginning of each 4-year period in model 2 (pooled *P* value for trend <0.0001) (Table 2). The significance of the association remained when model 2 was further adjusted for changes in body weight over the same period: >10% decrease in AHEI scores over 4 years was associated with a higher subsequent diabetes risk (1.21 [1.11–1.32]), whereas an improvement of >10% in AHEI scores was associated with a lower risk (0.90 [0.84–0.96]). When the AHEI score was assessed as a continuous variable, each 10% incremental improvement in the score was associated with a 0.85 (0.83–0.88) risk of the development of type 2 diabetes over the subsequent 4-year period (0.89 [0.86–0.91]) in model 2, and a 0.91 (0.88–0.93) risk with additional adjustment for changes in body weight. Changes in body weight explained 32% (95% CI 24–41) of the association between changes in AHEI (per 10% increase) and the risk of type 2 diabetes with adjustment for model 2 variables (*P* value for contribution < 0.0001).

To assess the impact of baseline diet quality on the association between changes in diet quality and type 2 diabetes risk, the association was stratified by baseline diet quality in Table 3 (*P* value for interaction = 0.2). The significant association remained across low, medium, and high baseline diet quality (all *P* for trend ≤ 0.001) (Table 3). Similarly in Table 4, the association was stratified by baseline BMI (*P* for interaction = 0.001). The association between changes in diet quality and type 2 diabetes risk remained significant across categories of baseline BMI (*P* for trend ≤ 0.01 for BMI values of <25, 25–29, and 30 kg/m²) (Table 4).

Table 2—HRs of type 2 diabetes according to updated 4-year changes in dietary quality (categories in AHEI scores)

	Decrease			Increase			<i>P</i> for trend	HR per 10% score increase
	Moderate to large (>10%)	Small to moderate (3–10%)	No change or stable (±<3%)	Small to moderate (3–10%)	Moderate to large (>10%)			
NHS (1986–2010)								
Cases/person-years	358/61,075	870/176,310	1,477/300,169	1,074/226,534	529/109,284			
Model 1*	1.33 (1.18–1.50)	1.06 (0.97–1.15)	1.00	0.93 (0.85–1.00)	0.87 (0.78–0.96)	<0.0001	0.86 (0.83–0.90)	
Model 2†	1.27 (1.13–1.43)	1.04 (0.95–1.13)	1.00	0.95 (0.88–1.03)	0.89 (0.80–0.99)	<0.0001	0.89 (0.85–0.93)	
NHS II (1991–2011)								
Cases/person-years	258/47,760	539/127,070	1,143/265,994	705/189,609	491/129,739			
Model 1*	1.45 (1.25–1.67)	1.09 (0.97–1.21)	1.00	0.85 (0.77–0.94)	0.76 (0.67–0.85)	<0.0001	0.81 (0.78–0.85)	
Model 2†	1.31 (1.13–1.51)	1.03 (0.93–1.15)	1.00	0.88 (0.80–0.98)	0.77 (0.69–0.87)	<0.0001	0.85 (0.81–0.89)	
HPFS (1986–2010)								
Cases/person-years	118/27,668	340/83,582	734/176,678	470/116,985	255/54,959			
Model 1*	1.15 (0.93–1.41)	1.02 (0.89–1.17)	1.00	0.92 (0.81–1.04)	0.99 (0.85–1.16)	0.14	0.94 (0.87–1.00)	
Model 2†	1.05 (0.86–1.30)	0.98 (0.86–1.13)	1.00	0.94 (0.83–1.07)	1.01 (0.86–1.18)	0.67	0.97 (0.91–1.04)	
Pooled								
Model 1*	1.34 (1.23–1.46)	1.06 (1.00–1.13)	1.00	0.90 (0.85–0.94)	0.84 (0.78–0.90)	<0.0001	0.85 (0.83–0.88)	
Model 2†	1.25 (1.15–1.36)	1.03 (0.97–1.09)	1.00	0.93 (0.88–0.98)	0.86 (0.81–0.93)	<0.0001	0.89 (0.86–0.91)	

Values are reported as HR (95% CI), unless otherwise indicated. *Model 1 was adjusted for age, ethnicity (white/nonwhite), family history of diabetes (yes/no), baseline AHEI score, physical activity, and total energy intake at the beginning of each 4-year period (all in quintiles); 4-year changes in smoking status (never to never, never to current, past to current, current to past, current to current, or missing indicator), physical activity, and total energy intake (all in quintiles); and a medical history of hypertension (yes/no) and hypercholesterolemia (yes/no). In the NHS and NHS II, postmenopausal status and postmenopausal hormone use (never use, current use, past use, or missing) were also included. †Model 2 was adjusted for model 1 variables in addition to baseline BMI values at the beginning of each 4-year period (<21, 21–22.9, 23–24.9, 25–29.9, ≥30 kg/m²).

Table 3—HRs of type 2 diabetes according to 4-year changes in dietary quality (categories in AHEI scores) stratified by categories of AHEI scores at the beginning of the 4-year period, pooled results of NHS (1986–2010), NHS II (1991–2011), and HPFS (1986–2010)*

Initial diet quality scores	Diet quality change category 4 years later					P for trend	HR per 10% score increase
	Decrease		No change or stable ($\pm < 3\%$)	Increase			
	Moderate to large ($> 10\%$)	Small to moderate (3–10%)		Small to moderate (3–10%)	Moderate to large ($> 10\%$)		
Low (< 45)	1.56 (1.18–2.06)	1.05 (0.92–1.20)	1.00	0.95 (0.86–1.04)	0.83 (0.75–0.93)	< 0.0001	0.88 (0.84–0.93)
Medium (45–59)	1.13 (1.00–1.27)	0.99 (0.91–1.07)	1.00	0.93 (0.85–1.00)	0.90 (0.82–1.00)	0.001	0.93 (0.89–0.96)
High (≥ 60)	1.31 (1.14–1.50)	1.07 (0.94–1.21)	1.00	0.88 (0.76–1.02)	0.96 (0.78–1.18)	< 0.0001	0.87 (0.82–0.92)

Values are reported as HR (95% CI), unless otherwise indicated. *Adjusted for age; ethnicity (white/nonwhite); family history of diabetes (yes/no); baseline physical activity and total energy intake at the beginning of each 4-year period (all in quintiles); 4-year changes in smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator), physical activity, and total energy intake (all in quintiles); a medical history of hypertension (yes/no) and hypercholesterolemia (yes/no); and baseline BMI values at the beginning of each 4-year period. In the NHS and NHS II, postmenopausal status and postmenopausal hormone use (never use, current use, past use, or missing) were also included.

No significant effect modification was observed for the association between changes in AHEI score and incidence of type 2 diabetes by comorbidity of hypertension, hypercholesterolemia, or current smoking status. When the association was stratified by age-groups (P for interaction = 0.02), the inverse associations were more pronounced in younger than in older participants: HR 0.83 (95% CI 0.78–0.89) in participants < 50 years of age, 0.89 (0.85–0.92) in participants 50–64 years of age, and 0.93 (0.89–0.98) in participants ≥ 65 years of age per 10% AHEI score increase (Supplementary Table 2).

To test the stability of the associations simultaneously across the categories of changes in physical activity, the association between changes in diet quality and type 2 diabetes risk was assessed according to changes in physical activity (P for interaction = 0.8). The association remained significant across physical activity

change categories (P for trend ≤ 0.0005 for participants whose physical activity decreased, remained stable, or increased) (Supplementary Table 3). The significance and direction of association remained when AHEI scores were calculated without the long-chain n-3 fatty acid component (Supplementary Table 4).

CONCLUSIONS

In three large prospective cohorts of U.S. men and women, improvement in overall diet quality over a 4-year period was associated with a lower risk of the development of type 2 diabetes in the subsequent 4 years, whereas deterioration in diet quality was associated with a higher risk. This association was only partly explained by concurrent changes in body weight, and remained across the categories of baseline diet quality and baseline BMI.

Previously, several healthful dietary patterns, developed in various study populations, have been associated with the

risk of type 2 diabetes (1). Prospective data using exploratory methods to define patterns that supported dietary patterns favoring fruits, vegetables, and whole grains are beneficial for diabetes prevention, whereas patterns high in red meats, refined grains, and sugar-sweetened beverages are harmful (29–34). Mediterranean-style diets have been consistently associated with lower incident type 2 diabetes in the context of both prospective cohort studies (5,6) and RCTs (9,13). Adherence to the Dietary Approaches to Stop Hypertension diet, which is rich in vegetables, fruits, and low-fat dairy products, was also associated with a lower diabetes risk (7,35). In the current study cohorts, adherence to a high-quality diet assessed by the cumulative AHEI scores was associated with a lower diabetes risk (8). The current study extends previous evidence by demonstrating that changing overall diet quality, assessed by changes in AHEI scores, has

Table 4—HRs of type 2 diabetes according to 4-year changes in dietary quality (categories in AHEI scores) stratified by BMI at the beginning of the 4-year period, pooled results of NHS (1986–2010), NHS II (1991–2011), and HPFS (1986–2010)*

Initial BMI (kg/m ²)	Diet quality change category 4 years later					P for trend	HR per 10% score increase
	Decrease		No change or stable ($\pm < 3\%$)	Increase			
	Moderate to large ($> 10\%$)	Small to moderate (3–10%)		Small to moderate (3–10%)	Moderate to large ($> 10\%$)		
< 25	1.12 (0.89–1.42)	1.01 (0.85–1.18)	1	0.91 (0.78–1.06)	0.84 (0.69–1.01)	0.01	0.89 (0.82–0.96)
25–29	1.37 (1.20–1.58)	0.99 (0.90–1.10)	1	0.98 (0.89–1.07)	0.94 (0.84–1.05)	0.0006	0.90 (0.86–0.94)
≥ 30	1.21 (1.07–1.37)	1.06 (0.97–1.16)	1	0.89 (0.82–0.97)	0.82 (0.75–0.90)	< 0.0001	0.88 (0.84–0.91)

Values are reported as HR (95% CI), unless otherwise indicated. *Adjusted for age; ethnicity (white/nonwhite); family history of diabetes (yes/no); baseline AHEI, physical activity, and total energy intake at the beginning of each 4-year period (all in quintiles); 4-year changes in smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator), physical activity, and total energy intake (all in quintiles); and a medical history of hypertension (yes/no) and hypercholesterolemia (yes/no). In the NHS and NHS II, postmenopausal status and postmenopausal hormone use (never use, current use, past use, or missing) were also included.

an impact on diabetes prevention in the subsequent years. In the randomized controlled PREDIMED (Prevención con Dieta Mediterránea) trial, participants assigned to a Mediterranean diet without calorie restriction had a significant 40% diabetes risk reduction with extra-virgin olive oil supplementation and a nonsignificant 18% risk reduction with mixed nut supplementation compared with a low-fat control diet after 4.1 years of follow-up (9). Here we reported that incremental changes in diet quality (per 10% improvement in AHEI score) were associated with an 11% reduction in diabetes risk. The effect sizes were smaller in the current study, likely because the PREDIMED trial selected participants who were at risk for CVD (9), whereas the current investigation represented a general population. The current study provides evidence for the incremental benefits of improving diet quality by following public health recommendations in a general population. In addition, we provide evidence, for the first time to our knowledge, that deterioration in diet quality is associated with a higher risk of the development of diabetes, independent of baseline BMI and concurrent changes in physical activity.

The potential mechanisms explaining the lower risk with improvement in overall diet quality are multifactorial because healthful dietary patterns include multiple food components. Changes in the consumption of individual food items that are known to be associated with type 2 diabetes risk have been also associated with long-term weight gain (36). Increased adipose mass may influence the pathogenesis of type 2 diabetes through mechanisms such as alterations in proinflammatory and anti-inflammatory proteins contributing to reduced sensitivity to insulin (37). However, concurrent changes in body weight only partly explained the association between changes in diet quality and diabetes risk in the current study. In addition, we tested using stratified analysis whether the benefits of diet quality changes remained throughout the categories of initial body weight and confirmed that the associations remained. This may be explained by multiple food components in overall diet contributing to multiple pathways to diabetes prevention. For example, moderate alcohol consumption has been associated with improved insulin sensitivity (38), whereas red/process

meat intakes have been associated with weight gain (36). Previously in the current study cohorts, changes in the consumption of individual food items, such as of red meat (39) and alcohol (40), were associated with subsequent risk of the development of type 2 diabetes. Therefore, investigating the overall dietary quality accounting for food and nutrient interactions is helpful in understanding the overall role of dietary changes. In addition, communicating overall diet quality improvement offers a clearer message to the public as food items are consumed in combinations in the daily diet.

The strengths of the current study design, which include a large sample size with high long-term follow-up rates and repeated assessments of dietary and lifestyle variables, provided the unique ability to investigate changes in diet quality on the subsequent risk of type 2 diabetes. The current study also has several limitations. Our study participants were health professionals of primarily European ancestry, and, therefore, the observed associations may not be generalizable to other populations. Although AHEI score is useful to measure overall diet quality changes in the current study populations, it will be important to confirm our findings in other populations accounting for culturally suitable dietary patterns and potential confounding factors and practices specific to the population. Because of a ceiling effect among participants who start with a high AHEI score, the current results may underestimate the role of a healthful diet. However, in our stratified analysis by baseline diet quality, the reported association remained across the categories of baseline AHEI score. The observed beneficial effect of diet quality changes may have been confounded by other healthful behaviors, although we attempted to account for these confounders through statistical adjustment of regression models. The stratified analysis by changes in physical activity with adjustment for baseline BMI at the beginning of each 4-year period further demonstrates the beneficial effects of diet quality improvement both in groups that had improved and worsened physical activity levels. This confounding seemed to have a greater influence on older participants, especially among older men, since we observed that the associations were more pronounced in younger women. However, the current study was limited

by its study design to understand the underlying behavioral and biological mechanisms. Investigations using longer-term trials controlled for potential confounders including caloric intakes, physical activity, and clinically measured covariates, such as blood pressure, will be needed to further understand the causality of the presently reported associations.

In conclusion, improving the overall diet quality over a 4-year period was associated with a lower risk of the development of type 2 diabetes in the subsequent 4 years in these prospective cohorts of U.S. adults, whereas deterioration in diet quality was associated with a higher risk of the development of type 2 diabetes, and the association between changes in diet quality and diabetes risk was only partly explained by changes in body weight. Expanding from previous RCT evidence that demonstrated that individually tailored dietary interventions can prevent or delay type 2 diabetes among those at high risk (1), we provide evidence that changing overall diet quality may have a significant impact on long-term diabetes risk. Further, our findings provide scientific evidence supporting the current public health recommendation (10–12), which is to adopt healthful dietary patterns for long-term type 2 diabetes prevention.

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