Prospective study on long-term dietary patterns and incident depression in middle-aged and older women[1–4]

Patricia O Chocano-Bedoya, Eilis J O'Reilly, Michel Lucas, Fariba Mirzaei, Olivia I Okereke, Teresa T Fung, Frank B Hu, and Alberto Ascherio

ABSTRACT

Background: Although individual nutrients have been investigated in relation to depression risk, little is known about the overall role of diet in depression.

Objective: We examined whether long-term dietary patterns derived from a food-frequency questionnaire (FFQ) predict the development of depression in middle-aged and older women.

Design: We conducted a prospective study in 50,605 participants (age range: 50–77 y) without depression in the Nurses' Health Study at baseline (1996) who were followed until 2008. Long-term diet was assessed by using FFQs every 4 y since 1986. Prudent (high in vegetables) and Western (high in meats) patterns were identified by using a principal component analysis. We used 2 definitions for clinical depression as follows: a strict definition that required both a reported clinical diagnosis and use of antidepressants (3002 incident cases) and a broad definition that further included women who reported either a clinical diagnosis or antidepressant use (7413 incident cases).

Results: After adjustment for age, body mass index, and other potential confounders, no significant association was shown between the diet patterns and depression risk under the strict definition. Under the broad definition, women with the highest scores for the Western pattern had 15% higher risk of depression (95% CI: 1.04, 1.27; *P*-trend = 0.01) than did women with the lowest scores, but after additional adjustment for psychological scores at baseline, results were no longer significant (RR: 1.09; 95% CI: 0.99, 1.21; *P*-trend = 0.08).

Conclusion: Overall, results of this large prospective study do not support a clear association between dietary patterns from factor analysis and depression risk. *Am J Clin Nutr* 2013;98:813–20.

INTRODUCTION

According to the WHO, depression is the fourth leading cause of disease burden in the world (1). Depressive episodes may be recurrent or chronic and have a substantial impact on life functioning. In the United States, the lifetime prevalence of depression is 19.2%, and women are, on average, 1.7 times more likely to have depression than men (2).

Numerous studies have examined the relation between the intake of individual nutrients or foods and depression. Many of these studies have been cross-sectional, and results have been inconsistent (3). Some prospective studies have shown that fish (4), folate (5, 6), and caffeine (7) may each individually reduce risk of depression. Other studies have evaluated the role of polyunsaturated fatty acids (8–10), zinc (11), vitamin D (12), and other micronutrients with inconclusive results. But the study of the role of individual nutrients is challenging because many nutrients are highly correlated with each other because they may come from the same food sources, and some nutrients can affect the intestinal absorption of nutrients. Therefore, the study of an overall dietary pattern analysis has been recommended to examine the complex relation between diet and disease risk (13).

Previous studies on the role of diet patterns and depression have been scarce, and, in their majority, cross-sectional studies (14–17). To our knowledge, only 3 previous prospective studies have evaluated the role of dietary patterns and depressive symptoms in adulthood (18–20), and one previous prospective study evaluated the role of dietary patterns and depressive symptoms in adolescents (21). Although the study by Sanchez-Villegas et al (18) used the Mediterranean diet score, which is an a priori quality score selected on the basis of previous knowledge (13), the studies by Akbaraly et al (United Kingdom) (19) and Le Port et al (France) (20) have evaluated the associations between a posteriori dietary patterns and depression, in which diet patterns were selected from the dietary data collected in the specific population by using factor analysis (13). Overall, these prospective studies reported lower risk of depression with healthier diet patterns; however, all of the studies relied on a single measurement of diet over time.

In the Nurses' Health Study (NHS)[5] cohort, 2 dietary patterns have been selected by factor analysis by using dietary data from

[1] From the Departments of Nutrition (POC-B, EJO, FM, ML, FBH, and AA) and Epidemiology (OIO and AA), Harvard School of Public Health, Boston, MA; the Channing Division of Network Medicine, Department of Medicine (EJO, OIO, and AA) and the Department of Psychiatry (OIO), Brigham and Women's Hospital and Harvard Medical School, Boston, MA; the Department of Social and Preventive Medicine, University of Laval, Québec, Canada (ML); and the Department of Nutrition, Simmons College, Boston, MA (TTF).

[2] Funding sources were not involved in the collection, analysis, or interpretation of data.

[3] Supported by a grant from the National Alliance for Research on Schizophrenia & Depression (project 312 5048070-01; to TAA) and a Yerby Postdoctoral Fellowship at the Harvard School of Public Health (POC-B). The Nurses' Health Study is supported by the NIH (grant P01 CA87969).

[4] Address correspondence to PO Chocano-Bedoya, Department of Nutrition, Harvard School of Public Health, 655 Huntington Avenue, Boston, MA 02115. E-mail: pchocano@hsph.harvard.edu.

[5] Abbreviations used: FFQ, food-frequency questionnaire; MHI-5, 5-item Mental Health Inventory; NHS, Nurses' Health Study.

Received October 16, 2012. Accepted for publication June 7, 2013.

First published online July 24, 2013; doi: 10.3945/ajcn.112.052761.

food-frequency questionnaires (FFQs) collected every 4 y and previously named prudent and Western patterns. Although the Western pattern, which is high in red and processed meats, has been associated with higher risk of diabetes, breast cancer, and other chronic diseases, the prudent pattern, which is high in vegetables and fruit, has been associated with lower risk of these disorders (22–26). To the best of our knowledge, no previous prospective studies of dietary patterns and depression have been conducted in the United States. Therefore, we conducted a prospective study of long-term diet patterns and depression risk in participants in the NHS for whom repeated assessments of both diet and clinical depression were compiled over a total follow-up of 12 y.

SUBJECTS AND METHODS

The NHS started in 1976 with 121,700 female US registered nurses who replied to a mailed questionnaire about lifestyle factors and medical conditions. This information has been updated every 2 y, with a response rate >90% for each questionnaire cycle. Although dietary information has been collected since 1980, questions regarding antidepressant use were first included in the questionnaires starting in 1996; therefore, we used 1996 as our baseline year. Of the 97,103 women who had completed the 1996, 1998, and 2000 questionnaires, we excluded women who reported antidepressant medication use in 1996 (n = 2052), had a history of physician diagnosed depression in 1996 or earlier (n = 3445), or had severe depressive symptoms on the basis of the 5-item Mental Health Inventory (MHI-5) questionnaires from 1992 or 1996 (MHI-5 score ≤52; n = 4645). In addition, we excluded women who did not report their depressive status in 1996, 1998, or 2000 (n = 20,587) or with an unknown date of onset of depression (n = 131) as well as participants who had incomplete information on depressive symptoms in 1992 or 1996 (n = 15,638). Thus, our baseline population comprised a total of 50,605 women with complete information from questionnaires from 1996 to 2000 and who were considered free of depression in 1996. The protocol was approved by the Institutional Review Board at Brigham and Women's Hospital.

Dietary assessment

In 1980, participants reported their usual food and beverage intake during the previous year on a 61-item semiquantitative FFQ. In 1984, 1986, and every 4 y since, a similar but expanded 131-item FFQ were sent to these participants. Women were asked to indicate how frequently they consumed a specific portion size of each food item, with 9 possible response options that ranged from never or <1 time/mo to ≥6 times/d.

Food items were aggregated into 38 predefined foods groups on the basis of similar nutrient compositions and biological origins. Foods that did not fit into any group or that may have represented distinctive dietary behaviors were left as individual categories (eg, pizza, beer, and tea). We included each type of alcoholic beverage (wine, liquor, and beer) separately as food groups in the factor analysis. Vitamin and mineral supplements were not included in the definition of patterns.

The validity and reproducibility of the FFQ has been evaluated before in a subgroup of participants by using four 1-wk-long diet records completed during the previous year and repeated FFQs 1 y apart (27–29). For example, correlation coefficients between the 1986 FFQ and the average intake from diet records in the same year were 0.68 for saturated fat and 0.73 for dietary cholesterol ($P < 0.001$) (27). The mean correlation coefficient between frequencies of intake of 55 foods from the 2 FFQs was 0.57 ($P < 0.001$) (28).

Prudent and Western dietary patterns

As previously described by Fung et al (22, 23), 2 major dietary patterns previously named prudent and Western were detectable by using factor analysis with principal components that were based on correlations between predefined food groups. The number of factors retained was determined by an eigenvalue >1 (ie, the factor explains more of the variance in correlations than is explained by a single variable) and the Scree test for each factor. To select uncorrelated factors and more-realistic diets, we used an orthogonal rotation procedure (varimax).

Factor loadings represented correlation coefficients between food groups and particular patterns, where positive loadings represented positive correlations, and negative loadings represented inverse correlations. The factor score for each pattern was calculated by summing observed frequencies of intakes of food groups weighted by their factor loadings. Factor scores for prudent and Western patterns were assigned to each woman according to their adherence to the respective diet pattern. A higher score suggested greater adherence to a certain dietary pattern. Factors scores were standardized to have a mean of 0 and SD of 1.

The validity and reproducibility of this method has been evaluated in a parallel cohort of men (Health Professionals Follow-Up Study) by using data collected with a FFQ and diet records (30). Correlations between scores for patterns generated from the FFQ and diet records were 0.52 for prudent and 0.74 for Western patterns, whereas reliability correlations between 2 FFQs (1 y apart) were 0.70 for prudent and 0.67 for Western patterns ($P < 0.001$).

Clinical depression assessment

Participants were first asked about their use of antidepressants in 1996. In 2000, participants were asked if they ever had a physician diagnosis of depression and the year of diagnosis (≥1996, 1997–1998, 1999, or 2000). Information on antidepressant use and physician-diagnosed depression was updated biennially thereafter.

We considered the following 2 definitions for cases with new onset of clinical depression: a strict definition and a broad definition. Under the strict definition, incident clinical depression cases were defined as women who first reported both a clinical diagnosis of depression and use of antidepressants after 1996. Under the broad definition, new cases were women who reported use of antidepressants or diagnosis of depression after 1996. The broad definition was more sensitive but less specific because it further included *1*) women who had been diagnosed with depression but do not take antidepressants and *2*) women who take antidepressants but did not report a depression diagnosis.

Assessment of other variables

Self-reported information about lifestyle factors including weight, smoking, menopause, use of hormone replacement therapy, education, marital and work status, multivitamin use, and medical events including cancer, high blood pressure, angina, hypercholesterolemia, and diabetes diagnosis was collected as part of the main questionnaires. BMI (in kg/m^2) was calculated as weight divided by height squared. In a validation study conducted in a subgroup of the NHS cohort, the correlation between self-reported weight and the average of 2 technician measurements was 0.98 ($P < 0.001$) (31). Physical activity information was collected by using a validated questionnaire (32), and metabolic equivalent task hours per week were calculated. Reported participation in community groups, including church, or volunteering was used as a proxy for social activity. Neighborhood socioeconomic status summary scores were estimated from addresses of participants on the basis of information from the US Census about wealth and income, educational levels, and occupation (33). Total calorie intake was derived from all items on the FFQ.

The MHI-5 score was included in the 1992 and 1996 questionnaires as part of the 36-Item Short-Form Health Survey. This 5-item score was designed to measure psychological stress compared with wellbeing (34), and included questions about how much of the time (from all of the time to never) over the previous month participants felt *1*) nervous, *2*) calm and peaceful, *3*) happy, *4*) down and blue, and *5*) so down that nothing could cheer them up. The total score ranged from 0 to 100, whereby a higher score denoted better mental health and a score ≤52 denoted severe depressive symptoms (33). Although we excluded participants with severe depressive symptoms in 1992 or 1996 from the baseline population, we further considered participants' MHI-5 scores in 1996 for additional adjustment in our analysis to minimize reverse causation (ie, the bias that would occur if subclinical symptoms of depression affected the participant diet).

Statistical analysis

Person-years of follow-up for each participant were computed from baseline to the date of diagnosis of first depression, date of reported start of antidepressant medication, death, end of total follow-up (June 2008) or the last questionnaire received, whichever came first. To assess long-term dietary intakes and reduce the random within-person variation, we used the cumulative average of the diet pattern scores starting in 1984 (ie, when the first expanded FFQ was administered) up to a 2–4-y lag period before the follow-up period ended. For example, dietary scores averaged from 1984 to 1994 were used to predict clinical depression reported on the 1996 questionnaire, and dietary scores averaged from 1984 to 2006 were used for cases reported in the 2008 questionnaire. Similarly, the cumulative average was used for potential confounders BMI, physical activity, and total calorie and caffeine intakes with a 2–4-y lag before the end of follow-up. For women who did not return the FFQ only in specific years, we created an indicator at every cycle of follow-up.

To evaluate the association between dietary patterns and depression risk, we categorized all women into quintiles according to their scores for prudent and Western patterns, whereby the lowest quintile was our reference group. We used Cox proportional hazard models to estimate RRs stratified by age in months and questionnaire cycle and with adjustment for total calorie intake (model 1). In a second model, we adjusted for BMI (quintiles), smoking status (never, 1–24 cigarettes in the past, >24 cigarettes in the past, 1–24 cigarettes currently, and >24 cigarettes currently), physical activity (quintiles), menopause status, use of hormonal replacement therapy (never, past, or current), marital status (married, widowed, separated or divorced, or single), multivitamin use (yes or no), retired (yes or no), participation in community groups (yes or no), caffeine intake (quintiles), and diagnosis of cancer, diabetes, hypertension, hypercholesterolemia, or heart disease (myocardial infarction or angina) as time-varying covariates during follow-up. Additional adjustment for neighborhood socioeconomic status, nurse education, and husband education level did not materially change our estimates, and thus, for parsimony, these variables were not retained in the models. Finally, in the third model, we adjusted for MHI-5 scores in 1996 to further adjust for levels of psychological stress or well-being at baseline (before depression diagnosis or antidepressant use). All models were adjusted for indicators for missing FFQ years. To estimate linear trends, we used Mantel's extension test, whereby the medians for each quintile were modeled as a continuous variable.

In additional analyses to further evaluate clinical depression by report of diagnosis or treatment, we used polytomous logistic regression across 3 mutually exclusive groups to compare *1*) women who had a diagnosis of depression and reported use of antidepressants, *2*) women who were taking antidepressants only or who had a diagnosis of depression only, and *3*) women who reported neither a diagnosis nor antidepressant use (reference).

In sensitivity analyses, we repeated our main analyses by using a longer latency (6–8 instead of 2–4 y) between cumulative intakes and the start of the follow-up period and by further excluding women with an MHI-5 score ≤65 (n = 7,875), which was a more strict cutoff recommended by Rumpf et al (35). Finally, we assessed whether the relation between diet patterns and depression varied by age (<60 compared with ≥60 y) BMI (<25 compared with ≥25), and smoking status (never compared with ever) by including their multiplicative terms in the multivariable Cox models and applying the likelihood ratio test with a cutoff of 0.05. All statistical analyses were conducted with the SAS statistical package (version 9.2; SAS Institute).

RESULTS

Correlations between food groups and dietary pattern factors in 1994 (ie, the last FFQ administered before the depression follow-up) are presented in **Table 1** for those food groups with correlation coefficients >0.30. In 1994, the prudent pattern had higher loadings from fruit (r = 0.62), vegetables (r = 0.69–0.59), fish (r = 0.43), whole-grain products (r = 0.43), and low-fat dairy (r = 0.35), whereas the Western pattern had higher loadings from red and processed meats (r = 0.61 and 0.57, respectively), French fries (r = 0.47), desserts (r = 0.45), high-fat dairy (r = 0.44), and refined grains (r = 0.43) ($P < 0.001$ for all). Similar loadings were observed for FFQs from 1984, 1986, 1990, 1998, 2002, and 2006 but were not identical. For example, nut intake had a correlation of 0.46 with the prudent pattern of 2006, but the correlation with the prudent pattern of 1994 was <0.15.

TABLE 1
Correlations between food groups and dietary pattern from 1994, the Nurses' Health Study 1996–2008[1]

	Prudent pattern	Western pattern
Yellow vegetables	0.67	—
Cruciferous vegetables	0.63	—
Other vegetables[2]	0.69	—
Fruit	0.62	—
Legumes	0.62	—
Leafy green vegetables	0.59	—
Tomatoes	0.45	—
Whole grain	0.43	—
Fish	0.42	—
Low-fat dairy	0.35	—
Water	0.35	—
Poultry	0.31	—
Red meat	—	0.61
Processed meats	—	0.57
French fries	—	0.47
Desserts[3]	—	0.45
High-fat dairy	—	0.44
Refined grains	—	0.43
Eggs	—	0.44
Creamy soups	—	0.35
Margarine	—	0.33
Pizza	—	0.33
Sugared beverages	—	0.33
Snacks[4]	—	0.33
Potatoes	—	0.33

[1] With the orthogonal rotation used, correlations were identical to the factor loading matrix from the principal component analysis. Only items with correlation coefficients >0.30 are presented.
[2] Included corn, onion, eggplant, celery, green peppers, and mixed vegetables.
[3] Included chocolate, candy bars, cookies, brownies, cake, pie, and pastries.
[4] Included chips, popcorn, and crackers.

Age- and total calorie–adjusted characteristics of the population by quintiles of both patterns in 1994 are presented in **Table 2**. Women with high scores of the prudent pattern were older, were more physically active, were more frequent users of multivitamins and hormone replacement therapy, had a higher MHI-5 score at baseline, were more likely to be married and involved in a community group, were less likely to be current or ever smokers, and consumed less caffeine than did women with the lowest scores. In contrast, women with higher scores for the Western pattern were younger, had higher BMI, were less physically active, had a lower MHI-5 score at baseline, had higher caffeine intake per day, were less likely to use or have used hormone replacement therapy, and were more likely to be current smokers than were women in the lowest quintile. In addition, women in the highest quintile for the Western pattern were more likely to be widowed or retired and less likely to use multivitamins and participate in a community group.

At the end of follow-up, 3002 women (6% of the population at baseline) had newly reported a physician diagnosis of depression and the beginning use of antidepressant drugs (strict definition). Under the broad case definition (depression diagnosis or reported antidepressant use), 4411 additional potential cases were identified, for a total number of cases under the broad definition of 7413 women (15% of the population at baseline).

Overall, no significant association was shown between the prudent pattern and strict or the broad definitions of clinical depression after multivariate adjustment (**Table 3**). For the Western pattern (**Table 4**), a significant positive association with both the strict and the broad definition of depression was observed in analyses adjusted for age and total calories. However, results for the strict definition were strongly attenuated after additional adjustment for BMI, physical activity, smoking, caffeine intake, and other covariates (models 2 and 3). For the broad definition, significantly higher depression risk in women with the highest Western pattern score persisted after multivariate adjustment (model 2) but not after further controlling the analyses for the MHI-5 score at baseline (model 3).

Results were similar for the subanalysis with the exclusion of women with an MHI-5 score ≤65 but were slightly attenuated. For example, under the broad definition, women in the highest quintile of the Western pattern had 14% increased risk of depression (model 2: RR: 1.14; 95% CI: 1.00, 1.28; *P*-trend = 0.02) compared with that for women in the lowest quintile (results not shown in Table 4). For the analysis that used a 6–8-y period between dietary assessments and the follow-up period, there were no significant associations between the Western or prudent pattern and depression. Associations between both patterns and depression did not vary by age, BMI, or smoking.

We observed similar results when we used polytomous logistic regression to compare the following 3 mutually exclusive groups: *1*) women who reported a diagnosis of depression and antidepressant use (n = 3002), *2*) women who reported only a diagnosis of depression or only antidepressant use (n = 4411), and *3*) women who did not report a diagnosis of depression or antidepressant use as the reference group (*see* Table 1 under "Supplemental data" in the online issue**).** No significant associations were observed for the prudent pattern. For women in the highest quintile of the Western pattern score, there was 20% increased risk for the group who reported only a diagnosis of depression or only antidepressant use (RR: 1.18; 95% CI: 1.03, 1.34; *P*-trend = 0.01) compared with that for women in the lowest quintile after adjustment for age, total calories, BMI, physical activity, comorbidities, and other potential confounders (model 2). However, this association did not remain significant after adjustment for MHI-5 at baseline (RR: 1.13; 95% CI: 0.99, 1.29; *P*-trend = 0.07).

DISCUSSION

Over the 12 y of follow-up, we did not observe significant associations between prudent and Western pattern scores and depression risk. Under a broad depression definition, we showed that women who adhered more closely to the Western pattern had higher risk of developing depression after adjustment for BMI, physical activity, and other covariates. However, no association was observed after additional adjustment for psychological stress and well-being scores (MHI-5) at baseline.

Previous cross-sectional studies have observed a significant association between patterns highly loaded with processed foods and depressive symptoms (14, 15). To our knowledge, only 2 previous prospective studies (19, 20) have evaluated associations between dietary patterns, derived from principal component analysis and resulting from a single dietary assessment, and depression symptoms [on the basis of the Center of Epidemiologic Depression Scale (36)]. In the study by Akbaraly et al (19) a whole food pattern was associated with a lower risk of

TABLE 2
Baseline characteristics of the population by prudent and Western pattern quintiles, the Nurses' Health Study 1996[1]

	Prudent pattern			Western pattern		
	Quintile 1	Quintile 3	Quintile 5	Quintile 1	Quintile 3	Quintile 5
Age (y)	60.8 ± 6.9[2]	62.4 ± 6.9	63.6 ± 6.8	63.0 ± 6.8	62.4 ± 6.9	61.5 ± 7.0
BMI (kg/m^2)	26.3 ± 0.02	26.2 ± 0.02	25.9 ± 0.02	24.9 ± 0.02	26.1 ± 0.02	27.6 ± 0.02
Physical activity (MET-h/wk)	13.2 ± 0.1	19.1 ± 0.1	26.9 ± 0.1	27.4 ± 0.1	19.4 ± 0.1	11.7 ± 0.1
Caffeine intake (mg/d)	303 ± 1.0	241 ± 0.9	191 ± 1.0	204 ± 1.0	239 ± 0.9	290 ± 1.0
Mental Health Index[3]	81.7 ± 0.05	83.3 ± 0.04	84.4 ± 0.05	84.2 ± 0.05	83.1 ± 0.04	82.2 ± 0.05
Menopause (%)	94	95	95	95	95	94
Current use of HRT[4]	40	48	49	49	47	40
Ever used HRT[4]	62	69	70	71	68	63
Current smokers (%)	19	8	4	4	9	17
Ever smokers (%)	59	52	50	56	53	52
Marital status (%)						
Married	76	82	81	80	82	78
Widowed	16	12	11	12	12	15
Separated, divorced, or single	8	6	7	8	6	6
Multivitamin use (%)	45	53	60	61	54	43
Retired (%)	47	49	49	47	49	49
Participates in community groups (%)	53	65	70	64	65	58

[1] Data are from the most recent measure of diet (1994) before baseline (1996). All variables were age- and total calorie–adjusted except for age. HRT, hormonal replacement therapy; MET-h/wk, metabolic equivalent task hours per week.
[2] Mean ± SD (all such values).
[3] Mental Health Index score measured in 1996. A higher score denotes a better mental health.
[4] With the exclusion of premenopausal women.

depressive symptoms whereas a processed food pattern was associated with higher risk ($n = 3486$). Le Port et al (20) reported healthy and traditional patterns associated with lower risk of depressive symptoms, low-fat and snacking patterns associated with higher risk, and no associations for animal protein and dessert patterns in 3132 women.

Both of the previous studies conducted sensitivity analyses to evaluate potential reverse causation (ie, an effect of early depression symptoms in the diet). In the study by Akbaraly et al (19), after exclusion of participants with depression symptoms or antidepressant use at baseline, the whole food diet pattern was no longer associated with lower risk of depressive symptoms. Similarly in the study by Le Port et al (20), no significant associations between the healthy pattern and depressive symptoms were observed after exclusion of participants with significant depressive symptoms at baseline.

TABLE 3
Association between the prudent diet pattern and clinical depression, the Nurses' Health Study 1996–2008[1]

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P*-trend
Strict definition of depression (diagnosis and antidepressant use)						
No. of events	624	623	602	575	578	—
Person-years	102,941	102,947	102,995	103,039	103,122	—
Model 1	1.00	1.00 (0.89, 1.12)	0.97 (0.87, 1.09)	0.92 (0.82, 1.04)	0.92 (0.81, 1.05)	0.11
Model 2	1.00	1.02 (0.91, 1.14)	1.00 (0.89, 1.13)	0.95 (0.84, 1.08)	0.96 (0.84, 1.10)	0.33
Model 3	1.00	1.05 (0.94, 1.18)	1.05 (0.93, 1.18)	1.02 (0.90, 1.15)	1.05 (0.91, 1.20)	0.73
Broad definition of depression (diagnosis and/or antidepressant use)						
No. of events	1552	1563	1441	1426	1431	—
Person-years	102,015	102,006	102,169	102,180	102,270	—
Model 1	1.00	1.01 (0.94, 1.08)	0.93 (0.86, 1.00)	0.92 (0.85, 0.99)	0.92 (0.85, 1.00)	0.01
Model 2	1.00	1.03 (0.96, 1.11)	0.96 (0.89, 1.04)	0.95 (0.88, 1.03)	0.97 (0.89, 1.06)	0.20
Model 3	1.00	1.06 (0.98, 1.14)	1.00 (0.92, 1.08)	1.00 (0.93, 1.09)	1.04 (0.95, 1.13)	0.79

[1] Cox proportional hazards models were used to calculate RRs (95% CIs). Model 1 was adjusted for age (mo) and total caloric intake (continuous). Model 2 was adjusted as for model 1 and for BMI (continuous), smoking, physical activity (quintiles), menopause status, use of hormonal replacement therapy [never (reference), past, or current], marital status, caffeine (quintiles), multivitamin use (yes or no), retired (yes or no), participation in a community group or volunteering (yes or no), and reported diagnosis of cancer, high blood pressure, hypercholesterolemia, heart disease (myocardial infarction or angina), or diabetes. Model 3 was adjusted as for model 2 and the 5-item Mental Health Inventory at baseline (continuous). All models were adjusted for indicators of missing dietary pattern information in the years 1986–2006.

TABLE 4
Association between the Western diet pattern and clinical depression, Nurses' Health Study 1996–2008[1]

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	*P*-trend
Strict definition of depression (diagnosis and antidepressant use)						
No. of events	557	544	633	607	661	—
Person-years	103,056	103,092	102,949	103,039	102,908	—
Model 1	1.00	0.98 (0.87, 1.11)	1.15 (1.02, 1.30)	1.11 (0.97, 1.26)	1.23 (1.06, 1.43)	0.002
Model 2	1.00	0.95 (0.84, 1.08)	1.09 (0.97, 1.24)	1.04 (0.90, 1.18)	1.12 (0.95, 1.31)	0.12
Model 3	1.00	0.94 (0.83, 1.06)	1.05 (0.93, 1.19)	0.97 (0.85, 1.11)	1.05 (0.89, 1.23)	0.50
Broad definition of depression (diagnosis and/or antidepressant use)						
No. of events	1408	1422	1508	1503	1572	—
Person-years	102,202	102,222	102,074	102,148	101,993	—
Model 1	1.00	1.04 (0.96, 1.12)	1.13 (1.04, 1.22)	1.15 (1.06, 1.24)	1.26 (1.15, 1.39)	<0.001
Model 2	1.00	1.01 (0.94, 1.09)	1.07 (0.99, 1.16)	1.08 (0.99, 1.17)	1.15 (1.04, 1.27)	0.01
Model 3	1.00	1.00 (0.93, 1.08)	1.04 (0.96, 1.12)	1.03 (0.94, 1.12)	1.09 (0.99, 1.21)	0.08

[1] Cox proportional hazards models were used to calculate RRs (95% CIs). Model 1 was adjusted for age (mo) and total caloric intake (continuous). Model 2 was adjusted as for model 1 and for BMI (continuous), smoking, physical activity (quintiles), menopause status, use of hormonal replacement therapy [never (reference), past, or current], marital status, caffeine (quintiles), multivitamin use (yes or no), retired (yes or no), participation in a community group or volunteering (yes or no), and reported diagnosis of cancer, high blood pressure, hypercholesterolemia, heart disease (myocardial infarction or angina), or diabetes. Model 3 was adjusted as for model 2 and the 5-item Mental Health Inventory at baseline (continuous). All models were adjusted for indicators of missing dietary pattern information in the years 1986–2006.

In our study, all analyses were conducted in women without significant depressive symptoms, antidepressant use, or a diagnosis of depression at baseline. Moreover, to further address the potential effect of reverse causation, we adjusted our results for the MHI-5 score at baseline (model 3), which markedly attenuated our results. The Western pattern was no longer significantly associated with our broad definition of depression after this adjustment. In a previous study about diet quality and mental health in adolescents, results were also markedly attenuated after adjustment for depressive symptoms at baseline (21). In an additional sensitivity analysis, we used a stricter cutoff for depressive symptoms (MHI-5 score $\leq$65) and excluded 7875 women with moderate to severe depressive symptoms, and our results remained null.

To appropriately examine the association of long-term dietary patterns and development of depression later in life, we used the cumulative average of dietary intakes over a long period of time (10–20 y) and a latency period of 2–4 y between dietary (and covariate) assessments and the follow-up period. In addition, we conducted a sensitivity analysis with a longer latency period (4–8 y) in which no significant associations were observed.

Although we did not find an association between the prudent or Western pattern and depression risk, these patterns have been previously used to investigate the role of diet in several chronic diseases, including diabetes (22), breast cancer (23), and Parkinson's disease (26). Moreover, in a subset of the same cohort of women, the Western pattern has also been shown to be significantly associated with high plasma concentrations of inflammatory biomarkers (37) and homocysteine (38), which have been associated with late-life depression (39). Thus, a biological effect of both patterns in depression is plausible despite our observation of no association. An advantage of the use of dietary patterns is the potential to detect the combined effects of foods, especially if the individual components of a pattern contribute to only a small amount of risk, as seems to be the case for many of the nutrients associated with depression.

Some limitations in the dietary pattern selection warrant consideration. First, the statistical analysis used to derive dietary patterns involves several arbitrary decisions, including the construction of the food groups and the method of rotation (39). To address these issues, several sensitivity analyses have been conducted in a parallel cohort of men and similar patterns were identified by including individual food items instead of food groups, retaining 3 instead of 2 factors and using an oblique rotation instead of an orthogonal rotation (30, 40). Second, diet patterns may differ by sex, race, and geographical area; therefore, our results may not be generalizable to other populations. However similar patterns were shown in nationally representative samples (41).

Because we relied on self-reported data, some misclassification of depression was possible. Therefore, we used 2 definitions for new cases of clinical depression. The stricter definition was more specific because it included only women who reported both a diagnosis of depression and antidepressant use. However, this definition was less sensitive because it excluded women who reported depression diagnosis but were not treated with antidepressants and women who took antidepressants without a physician diagnosis of depression. In contrast, we also analyzed data by using a broader definition that included women who reported antidepressant use or women who reported a diagnosis of depression only. This definition was more sensitive but also likely to have been affected by misclassification of the outcome because it could have included women who were taking antidepressants for reasons other than depression. Other indications for antidepressants in that age group (mean: 62 y at baseline) include chronic pain or pain disorders (42, 43), which are comorbid with depressive symptoms (44). Differences in results could have also been a result of the smaller number of cases under the strict definition compared with the broader definition. For both definitions, potential misclassifications were most likely to be independent of the dietary assessment.

Despite these limitations, the data allowed us to investigate the relation between dietary patterns and depression in a large

population with repeated measurement of diet collected over a long period of time before the beginning of the disease. In addition, tour our knowledge, this was one of the first studies to examine the association between dietary patterns and depression prospectively. Future studies should further evaluate the role of dietary behaviors and depression risk because they may affect the development of depression as well as the role of potential mediators of this association.

In conclusion, in this large prospective study, we observed no significant associations between long-term dietary patterns from a factor analysis and new onset of depression. Although the study was characterized by a 12-y follow-up period and multiple assessments of diet and depression, more studies are needed to understand these associations.

The authors' responsibilities were as follows—POC-B and AA: designed the research, had full access to all of the data in the study, and took responsibility for the integrity of the data and the accuracy of the data analysis; POC-B: wrote the first draft of the manuscript; EJO, FM, ML, OIO, TTF, FBH, and AA: critically reviewed the manuscript for important intellectual content; and all authors contributed to the data analysis and interpretation and read and approved the final manuscript. None of the authors had a conflict of interest.

REFERENCES

1. Ustün TB, Ayuso Mateos JL, Chatterji S, Mathers C, Murray CJL. Global burden of depressive disorders in the year 2000. Br J Psychiatry 2004;184:386–92.
2. Bromet E, Andrade L, Hwang I, Sampson N, Alonso J, de Girolamo G, de Graaf R, Demyttenaere K, Hu C, Iwata N, et al. Cross-national epidemiology of DSM-IV major depressive episode. BMC Med 2011; 9:90–105.
3. Murakami K, Sasaki S. Dietary intake and depressive symptoms: a systematic review of observational studies. Mol Nutr Food Res 2010; 54:471–88.
4. Sanchez-Villegas A, Henrquez P, Figueiras A, Ortuo F, Lahortiga F, Martnez-Gonzlez M. Long chain omega-3 fatty acids intake, fish consumption and mental disorders in the SUN cohort study. Eur J Nutr 2007;46:337–46.
5. Sánchez-Villegas A, Doreste J, Schlatter J, Pla J, Bes-Rastrollo M, Martnez-Gonzlez MA. Association between folate, vitamin B(6) and vitamin B(12) intake and depression in the SUN cohort study. J Hum Nutr Diet 2009;22:122–33.
6. Murakami K, Mizoue T, Sasaki S, Ohta M, Sato M, Matsushita Y, Mishima N. Dietary intake of folate, other B vitamins, and omega-3 polyunsaturated fatty acids in relation to depressive symptoms in Japanese adults. Nutrition 2008;24:140–7.
7. Lucas M, Mirzaei F, Pan A, Okereke O, Willett W, O'Reilly ÉJ, Koenen K, Ascherio A. Coffee, caffeine, and risk of depression among women. Arch Intern Med 2011;171:1571–8.
8. Appleton KM, Rogers P, Ness A. Updated systematic review and meta-analysis of the effects of n−3 long-chain polyunsaturated fatty acids on depressed mood. Am J Clin Nutr 2010;91:757–70.
9. Colangelo L, He K, Whooley M, Daviglus M, Liu K. Higher dietary intake of long-chain omega-3 polyunsaturated fatty acids is inversely associated with depressive symptoms in women. Nutrition 2009;25: 1011–9.
10. Lucas M, Mirzaei F, O'Reilly E, Pan A, Willett W, Kawachi I, Koenen K, Ascherio A. Dietary intake of n−3 and n−6 fatty acids and the risk of clinical depression in women: a 10-y prospective follow-up study. Am J Clin Nutr 2011;93:1337–43.
11. Lai J, Moxey A, Nowak G, Vashum K, Bailey K, McEvoy M. The efficacy of zinc supplementation in depression: systematic review of randomised controlled trials. J Affect Disord 2012;136:e31–9.
12. Bertone-Johnson E, Powers S, Spangler L, Brunner R, Michael Y, Larson J, Millen A, Bueche M, Salmoirago Blotcher E, Liu S, et al. Vitamin D intake from foods and supplements and depressive symptoms in a diverse population of older women. Am J Clin Nutr 2011;94: 1104–12.
13. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol 2002;13:3–9.
14. Jacka FN, Pasco J, Mykletun A, Williams L, Hodge A, O'Reilly S, Nicholson G, Kotowicz M, Berk M. Association of Western and traditional diets with depression and anxiety in women. Am J Psychiatry 2010;167:305–11.
15. Nanri A, Kimura Y, Matsushita Y, Ohta M, Sato M, Mishima N, Sasaki S, Mizoue T. Dietary patterns and depressive symptoms among Japanese men and women. Eur J Clin Nutr 2010;64:832–9.
16. Samieri C, Jutand M, Fart C, Capuron L, Letenneur L, Barberger Gateau P. Dietary patterns derived by hybrid clustering method in older people: association with cognition, mood, and self-rated health. J Am Diet Assoc 2008;108:1461–71.
17. Kuczmarski MF, Cremer Sees A, Hotchkiss L, Cotugna N, Evans M, Zonderman A. Higher Healthy Eating Index-2005 scores associated with reduced symptoms of depression in an urban population: findings from the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study. J Am Diet Assoc 2010;110:383–9.
18. Sánchez-Villegas A, Delgado-Rodriguez M, Alonso A, Schlatter J, Lahortiga F, Serra Majem L, Martinez-Gonzalez M. Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. Arch Gen Psychiatry 2009;66:1090–8.
19. Akbaraly TN, Brunner E, Ferrie J, Marmot M, Kivimaki M, Singh Manoux A. Dietary pattern and depressive symptoms in middle age. Br J Psychiatry 2009;195:408–13.
20. Le Port A, Gueguen A, Kesse Guyot E, Melchior M, Lemogne C, Nabi H, Goldberg M, Zins M, Czernichow S. Association between dietary patterns and depressive symptoms over time: a 10-year follow-up study of the GAZEL cohort. PLoS ONE 2012;7:e51593.
21. Jacka FN, Kremer P, Berk M, de Silva-Sanigorski AM, Moodie M, Leslie E, Pasco J, Swinburn B. A prospective study of diet quality and mental health in adolescents. PLoS ONE 2011;6:e24805.
22. Fung TT, Schulze M, Manson J, Willett W, Hu F. Dietary patterns, meat intake, and the risk of type 2 diabetes in women. Arch Intern Med 2004;164:2235–40.
23. Fung TT, Hu F, Holmes M, Rosner B, Hunter D, Colditz G, Willett W. Dietary patterns and the risk of postmenopausal breast cancer. Int J Cancer 2005;116:116–21.
24. Varraso R, Fung T, Barr RG, Hu F, Willett W, Camargo C. Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. Am J Clin Nutr 2007;86:488–95.
25. Fung T, Hu F, Fuchs C, Giovannucci E, Hunter D, Stampfer M, Colditz G, Willett W. Major dietary patterns and the risk of colorectal cancer in women. Arch Intern Med 2003;163:309–14.
26. Gao X, Chen H, Fung T, Logroscino G, Schwartzchild MA, Fu HB, Ascherio A. Prospective study of dietary pattern and risk of Parkinson disease. Am J Clin Nutr 2007;86:1486–94.
27. Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122: 51–65.
28. Salvini S, Hunter DJ, Sampson L, Stampfer MJ, Colditz GA, Rosner B, Willett WC. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18:858–67.
29. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992;135:1114–26; discussion 1127–36.
30. Hu FB, Rimm E, Smith Warner SA, Feskanich D, Stampfer MJ, Ascherio A, Sampson L, Willett WC. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. Am J Clin Nutr 1999;69:243–9.
31. Rimm EB, Stampfer MJ, Colditz GA, Chute CG, Litin LB, Willett WC. Validity of self-reported waist and hip circumferences in men and women. Epidemiology 1990;1:466–73.
32. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical activity questionnaire. Int J Epidemiol 1994;23:991–9.
33. Kim D, Masyn K, Kawachi I, Laden F, Colditz G. Neighborhood socioeconomic status and behavioral pathways to risks of colon and rectal cancer in women. Cancer 2010;116:4187–96.

34. Berwick DM, Murphy JM, Goldman PA, Ware JE, Barsky AJ, Weinstein MC. Performance of a five-item mental health screening test. Med Care 1991;29:169–76.
35. Rumpf HJ, Meyer C, Hapke U, John U. Screening for mental health: validity of the MHI-5 using DSM-IV Axis I psychiatric disorders as gold standard. Psychiatry Res 2001;105:243–53.
36. Radloff LS. The CES-D Scale. Appl Psychol Meas 1977;1:385–401.
37. Lopez-Garcia E, Schulze M, Fung T, Meigs J, Rifai N, Manson J, Hu F. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr 2004;80: 1029–35.
38. Fung TT, Rimm EB, Spiegelman D, Rifai N, Tofler GH, Willett WC, Hu FB. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. Am J Clin Nutr 2001;73: 61–7.
39. Almeida OP, McCaul K, Hankey G, Norman P, Jamrozik K, Flicker L. Homocysteine and depression in later life. Arch Gen Psychiatry 2008; 65:1286–94.
40. van Dam RM, Rimm E, Willett W, Stampfer M, Hu F. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. Ann Intern Med 2002;136:201–9.
41. Tseng M, DeVillis R. Correlates of the "western" and "prudent" diet patterns in the us. Ann Epidemiol 2000;10:481–2.
42. Mease PJ, Dundon K, Sarzi Puttini P. Pharmacotherapy of fibromyalgia. Best Pract Res Clin Rheumatol 2011;25:285–97.
43. Olfson M, Marcus S. National patterns in antidepressant medication treatment. Arch Gen Psychiatry 2009;66:848–56.
44. Mohr P, Bitter I, Svestka J, Seifritz E, Karamustafalioglu O, Koponen H, Sartorius N. Management of depression in the presence of pain symptoms. Psychiatr Danub 2010;22:4–13.