HHS Public Access
Author manuscript
Eur J Clin Nutr. Author manuscript; available in PMC 2019 May 03.

Published in final edited form as:
Eur J Clin Nutr. 2019 May ; 73(5): 703–713. doi:10.1038/s41430-018-0272-1.

Diet quality measured by four a priori-defined diet quality indices is associated with lipid-soluble micronutrients in the Multiethnic Cohort Study (MEC)

Nicole Aumueller[1,2], **Carol J. Boushey**[2], **Adrian A. Franke**[2], **Robert V. Cooney**[3], **Kristine R. Monroe**[4], **Christopher A. Haiman**[4], **Lynne R. Wilkens**[2], **Laurence N. Kolonel**[2], **Loic Le Marchand**[2], and **Gertraud Maskarinec**[2]

[1]Div. Metabolic and Nutritional Medicine, Dr. von Hauner Children's Hospital Munich

[2]Epidemiology Program, University of Hawaii Cancer Center, Honolulu, HI, USA

[3]Office of Public Health Studies, University of Hawaii, Honolulu, HI, USA

[4]Department of Preventive Medicine, Keck School of Medicine, and Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA

Abstract

Background/Objectives—This study examined the long-term relation of lipid-soluble micronutrients with diet quality as assessed by four *a priori*-defined dietary patterns.

Subjects/Methods—In a prospective design, nutritional biomarkers (carotenoids, tocopherols, retinol, and coenzyme Q10) were measured using a validated HPLC based assay. General linear models were applied to obtain covariate-adjusted means of biomarkers for tertiles of 4 *a priori* diet quality indices: Healthy Eating Index (HEI) 2010, Alternative HEI (AHEI) 2010, Alternate Mediterranean Diet Score (aMED), and Dietary Approaches to Stop Hypertension (DASH). For a subcohort of 8 367 participants within the Multiethnic Cohort (MEC), diet was assessed by a validated quantitative food frequency questionnaire in 1993–96 and serum was collected in 2001–06.

Results—Participants with the highest diet quality scores had significantly higher serum concentrations of all carotenoids, total tocopherols, and α-tocopherol, while γ-tocopherol was inversely associated with diet quality. Adjusted means for the lowest vs. highest tertile of HEI 2010 were 1.2 vs. 1.5 mg/L for total carotenoids, 11.4 vs. 12.3 mg/L for total tocopherols, and 1.9

Address for Correspondence: Nicole Aumüller, MSc, Div. Metabolic and Nutritional Medicine, Dr. von Hauner Children's Hospital, Ludwig-Maximilians University Munich, Lindwurmstr. 4, D-80337 Muenchen, Germany, Telefon +49 89 44005 - 57959, Nicole.Aumueller@med.uni-muenchen.de.

Conflict of interest
The authors have no conflicts of interest to declare.

Contribution statement
LNK, LLM, and LRW led the design and implementation of the prospective cohort; CJB provided nutritional support and developed the diet scores; AF provided analytical services for micronutrient quantitation; NA, GM analyzed the data and wrote the paper; NA, CJB, AF, RVC, CAH, LRW, LNK, KRM, and GM contributed to the interpretation of the data, the critical revision of the article for important intellectual content, and the final approval of the version to be published. NA had primary responsibility for final content.

vs. 1.6 mg/L for γ-tocopherol (p_{trend}<0.0001). The associations for the other dietary indices were similar; no indication for sex and ethnic differences was detected. Vegetable and fruit components were major predictors of most circulating micronutrients, but most other components were also associated.

Conclusions—Higher diet quality scores measured by four *a priori* diet quality indices were significantly associated higher serum concentrations of carotenoids and α-tocopherol, while γ-tocopherol was inversely associated with diet quality.

Introduction

As individuals consume foods not in isolation but in combination, nutritional epidemiologists have started to analyze dietary patterns, which are combinations of food components and represent an overall diet. *A priori*-defined dietary indices as indicators of diet quality measure the adherence to a predefined diet, such as the Mediterranean diet (MED) or the Dietary Approaches to Stop Hypertension (DASH), which are based on scientific evidence for healthy nutrition and dietary recommendations (1), whereas *a posteriori* dietary patterns reflect the correlation structure between foods in a specific data set. In general, dietary components such as vegetables, fruits, and fiber result score highly in *a priori*-defined dietary indices (Table 1) making them indicators of good diet quality. Dietary patterns have been associated with a reduced risk of type 2 diabetes, cardiovascular disease, cancer, and mortality (2–6). Understanding the biologic mechanisms underlying these risk reductions and their capacity for prevention is becoming more important to address increasing rates of chronic diseases (7). The relation between diet and disease may be mediated by intermediate markers measured in biological samples as a result of bioactive nutrients in food or representing metabolic pathways (8). For example, insulin resistance, triglycerides, and C-reactive protein (CRP) concentrations were lower among participants of the Multiethnic Cohort (MEC) study consuming a high quality diet (9). Lipid-soluble micronutrients, such as carotenoids, retinoids, tocopherols, and coenzyme Q10, are a result of higher vegetable and fruit intake as part of a high quality diet and may act as anti-oxidants (10, 11).

Only a few studies have reported on the association between *a priori*-defined dietary patterns and lipid-soluble micronutrients. In cross-sectional studies among Italian and Spanish populations, better adherence to the MED was associated with higher blood levels of lipid-soluble micronutrients including carotenoids (12, 13). Among Norwegian women, an *a posteriori* "Vegetarian" dietary pattern was positively associated with carotenoid levels, while a "Western" or "Continental" dietary pattern was inversely correlated with some plasma carotenoids (12–14). To our knowledge, no study has yet investigated the association of diet quality with lipid-soluble micronutrients over many years. On these grounds, we examined the long-term relation of nutritional biomarkers (carotenoids, retinoids, tocopherols and coenzyme Q10) with four *a priori*-defined dietary patterns, the Healthy Eating Index 2010 (HEI 2010), the Alternative HEI 2010 (AHEI 2010), the Alternate Mediterranean Diet Score (aMED), and the DASH, which were previously investigated within the MEC.

Participants and Methods

Study population

The MEC was established in Hawaii and Los Angeles to identify nutritional and genetic risk factors for cancer. Study protocols was approved by the institutional review boards of the University of Hawaii and the University of Southern California. Its design and implementation have been described elsewhere (15). Briefly, baseline data were collected in 1993–1996 within five ethnic groups (whites, Native Hawaiians, Japanese Americans, Latinos, and African Americans), aged 45 to 75 years and living in Hawaii or California. More than 215 000 men and women completed an extensive questionnaire containing a quantitative food frequency questionnaire (QFFQ) and questions related to demographics, health, anthropometric measurements, and lifestyle factors.

Dietary Assessment and Dietary Indices

Based on the data from the validated QFFQ and a large database of recipes, four *a priori* defined indices (Table 1) were calculated within the MEC as described elsewhere (4–6, 15). The HEI 2010 describes the adherence to the 2010 Dietary Guidelines for Americans (16), while the AHEI 2010, which is based on the HEI, takes additional food groups into account that are consistently associated with a lower risk of chronic diseases in clinical as well as epidemiologic investigations (3). The aMED as developed by Fung et al. (17) is based on the Mediterranean diet score developed earlier (18). The DASH focuses on adherence to the DASH diet designed to lower hypertension (19).

Blood Collection and Biomarker Assessment

During 2001–2006, a biospecimen subcohort of consenting cohort members was established (N=68 988). The majority of blood samples were collected after at least 8 hours of fasting. Within this subcohort, a panel of biochemical markers was assessed from blood of 12 583 participants, using standard assays, who had served as controls in several case-control studies. Lipid-soluble micronutrient measurements were assessed in 8 664 of these individuals during 2014–2016; this subset served as the basis for the current analysis. The micronutrients included 15 carotenoids, retinol, three tocopherols and two coenzyme Q10 forms that were analyzed by an isocratic heart-cut 2-dimensional HPLC assay with photo-diode array detection (20). This assay was continuously validated by participation in a quality assurance program organized by the National Institute for Standards and Technology. In this report, γ-tocopherol always refers to the sum of β- and γ-tocopherol.

Statistical Analysis

After excluding participants with invalid biomarker measurements and missing covariate data, the final cohort for analysis consisted of 8 367 participants (3 904 men and 4 463 women) (15). For each biomarker adjusted means across tertiles of dietary indices were calculated using linear regression. The biomarkers were log-transformed to meet model assumptions; means were back-transformed for presentation in the tables. Since a linear relation best fit the data, trends were analyzed by linear regression using standardized dietary pattern scores as the continuous exposure variables and log-transformed, standardized micronutrient variables as outcomes in order to obtain standardized slope parameters that can be compared across models. Potential covariates were tested for correlations with dietary intake and improvement of model fit. The final model included age at blood draw, sex, ethnicity, body mass index (BMI) calculated from self-reported weight and height and categorized by WHO standards, smoking status, education, total energy intake, cholesterol concentration, and blood draw season as covariates.

The models were repeated after stratification by sex and ethnicity. In addition, effect modification by sex-ethnic group was explored using interaction terms between sex-ethnic group and the dietary patterns. To examine long-term associations, we used dietary data from 1993–96 and biomarker data from 2001–06; a sensitivity analysis examined dietary data from 2003–08 to account for possible dietary changes. Separate models for participants reporting supplement intake at cohort entry were also conducted. To identify HEI 2010 components that are important predictors of lipid-soluble micronutrient concentrations, the individual component scores were examined in separate models. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary NC).

Results

Of the 8 367 participants in the analysis dataset, 53% were women and 47% men with a mean age of 68 years at blood draw and an ethnic distribution of 8% white, 28% African American, 26% Native Hawaiian, 30% Japanese American, and 8% Latino. Compared to the full cohort, participants of the Biospecimen Subcohort were better educated and less likely to smoke, but were similar in age, BMI, and total energy intake (data not shown). Whereas a large proportion of women were in the top tertile of the dietary indices, men were found more often in the lowest tertile (Table 2). Individuals in the highest tertiles were in general older, had lower BMIs, were less likely to be smokers, and reported higher total energy intake.

Participants with better diet quality had significantly higher serum concentrations of all measured carotenoids and α-tocopherol and significantly lower levels of γ-tocopherol (Table 3 and Figure 1). Only for retinol, δ-tocopherol, and coenzyme Q10, no relation with diet quality was detected. The differences across extreme tertiles for the HEI 2010, aMED and DASH were comparable but smaller for the AHEI 2010. For example, serum concentrations of total carotenoids increased from the lowest to the highest tertile by 25% for the HEI 2010, 24% for the aMED, 23% for the DASH, and 20% for the AHEI 2010.

When comparing standardized slope estimates across indices, the HEI 2010 tended to have the strongest association reflected in the largest regression coefficients in absolute value, while the AHEI 2010 had the weakest (smallest). In general, however, the patterns of the four indices across circulating micronutrients were similar. The biomarker models for total carotenoids, carotenes, and cryptoxanthins had the highest regression coefficients ($|\beta|>0.2$), models for luteins, α-tocopherol and γ-tocopherol (inverse) were intermediate ($|\beta|=0.1–0.2$), and models for lycopenes, zeaxanthin, and retinol had the lowest ($|\beta|<0.1$). Coenzyme Q10 and δ-tocopherol showed little relation with the dietary indices.

Stratified models and interaction terms did not suggest an influence of sex ($p_{interaction}$=0.69) or race/ethnicity ($p_{interaction}$=0.52) on the relation between the HEI 2010 and circulating micronutrients. Similar associations were observed for participants reporting supplement intake (Supplementary Figure 1), but regression coefficients were slightly higher in non-users than supplement users.

Analysis of the HEI 2010 components (Figure 2), selected because the HEI 2010's strong association with micronutrients, indicated significant associations of circulating micronutrients to most of the index components although the regression coefficients were generally weaker. Among these components, 'total vegetables', 'greens and beans', 'total fruit', and 'whole fruit' showed stronger associations with the micronutrients (β=0.07–0.13) than the other components (β<0.05). In particular, higher scores in total vegetable consumption associated with higher regression estimates for total carotenoids (β=0.13, 95% CI: 0.11–0.15), carotenes (β=0.14, 95% CI: 0.12–0.15), and luteins (β=0.14, 95% CI: 0.12–0.16), whereas higher fruit intake scores were primarily associated with cryptoxanthins (β=0.22, 95% CI: 0.20–0.24). Although inversely correlated, the associations for γ-tocopherol with all food components (|β|=0.03–0.13) were equally strong; the highest regression coefficient estimate was observed for 'total fruit' (|β|=0.11, 95% CI: 0.13–0.08). Of the remaining components of the HEI 2010 index, 'whole grains', 'refined grains', and 'empty calories' had higher regression coefficient estimates than the protein and fat components, but all were distinctly lower than the coefficient estimates for vegetables and fruits. For the other diet quality indices, similar patterns were observed with the strongest associations for fruits and vegetables (data not shown).

Discussion

In a subset of MEC participants, diet quality as assessed by the HEI 2010, AHEI 2010, aMED, and DASH was significantly associated with most individual serum carotenoids and tocopherols except δ-tocopherol. Total carotenoids were higher by 20–25% and α-tocopherol by 8–13% across tertiles of diet quality, while γ-tocopherol was lower by 10–13%. No significant associations were observed for retinol and coenzyme Q10. In general, the four indices showed similar associations with serum markers although the influence of the AHEI 2010 appeared weaker than for the other three. Stratification by sex and race/ethnicity indicated little difference across groups, a novel finding as no previous reports for Japanese Americans, African Americans, Native Hawaiian, and Latinos have been reported.

The current findings are consistent with three previous studies reporting associations of micronutrients, including carotenoids, with versions of MED indices other than the aMED used here (17). Azzini et al. found the highest serum concentrations of lutein, zeaxanthin, cryptoxanthin, lycopene, and α- and β-carotene in 131 participants with the best diet quality although the differences were not statistically significant in the small study population (12). Two investigations observed significant associations of different MED indices with β-carotene (13, 21). Also, higher scores of the HEI were significantly associated with plasma concentration of several carotenoids but not lycopene in several reports (22–25). In a 3-month randomized feeding trial with 103 individuals (26), the DASH diet resulted in significantly higher serum lutein, cryptoxanthin, zeaxanthin, and β-carotene concentrations than in controls on a typical American diet. As carotenoids are mainly found in vegetables and fruits (27), common components of a high quality diet (3, 17, 19, 28), it is not surprising that carotenoids are associated with diet quality. On the other hand, results for lycopene are not as clear (12, 23–25), possibly due to its greater bioavailability from processed tomato products, such as pizza, marinara sauce, tomato soup or ketchup present in low quality diets (24, 27).

Inconsistent findings have been reported for vitamin A (12, 13, 24, 26). In the present analysis, retinol was not significantly associated with diet quality in the adjusted means analysis and only weakly in the trend analysis. Retinol is highly regulated homeostatically and is less dependent on retinol or provitamin A intake as long as enough vitamin A is stored (29). Consequently, the association is dependent on the concentration of stored vitamin A.

As α-tocopherol has the highest serum concentrations, it is the most frequently investigated tocopherol, but findings have been inconsistent (12, 24, 30). In the current analysis, the association of diet quality with α-tocopherol was statistically significant and stronger than for some other analytes, as also reported in two previous reports (30, 31), but was not observed among Finish smokers (32). Just as for δ-tocopherol in the current analysis, γ- and δ-tocopherol were not correlated with dietary intake in an earlier report (31). Previous investigations in the MEC and another study found inverse correlations of α- and γ-tocopherol levels in blood (33, 34). It appears that a high intake of α-tocopherol, primarily through α-tocopherol supplementation, influences concentration of circulating γ-tocopherol (33). This may be due to the enhanced metabolism of γ-tocopherol during increased α-tocopherol intake (35). Since γ-tocopherol is the only antioxidant elevated in smokers (36) and in patients with type 2 diabetes (37), a physiological regulation between the two micronutrients might explain the inverse association of γ-tocopherol with diet quality (24, 24, 30, 31, 31). Consistent with previous studies, coenzyme Q10 levels were not affected by diet quality; only supplementation appears to influence its plasma concentrations (38, 39). As supplement use was more frequent among participants with better diet quality, their serum concentrations were higher than in non-users resulting in smaller slope estimates. However, as we could not account for exact amount and type of supplementation, the associations might have been overestimated.

The association of component scores for vegetable consumption with higher concentrations of total carotenoids, carotenes, and luteins, and of fruit consumption with cryptoxanthins present in orange and red fruits, such as papayas and oranges (40), is well established. For example, specific vegetables and several fruits were good predictors of plasma carotenoids, while pizza was related to lycopene due to the high bioavailability from tomato sauce (41). Associations of the fruit and vegetable components of different MED scores with β-carotene have been reported repeatedly (13, 21). However, the association of circulating micronutrients with food groups was weaker than with the total score, as found in the present analysis, suggesting that the benefits of a high diet quality may not only be due to fruits and vegetables but the entire food pattern (13, 21). This idea is further supported by the associations, although weaker, of the ‘whole grains’, ‘refined grains’, and ‘empty calories’ HEI components with micronutrients. Whole grains contain several carotenoids, especially lutein, zeaxanthin, β-cryptoxanthin, α- and β-carotene, and tocopherols in the bran or germ fraction of the grain (42), although one has to keep in mind the strong correlation of all three components with the overall HEI 2010 score (r=0.47–0.64; p<0.0001). On the other hand, whole grains were not major predictors of circulating micronutrients in previous studies (13, 21, 41). As 'refined grains' and 'empty calories' were reverse coded and the models were energy adjusted, high scores in these components indicate consumption of other foods possibly vegetables (r=0.38) and fruits (r=0.28). In addition, correlations with the overall HEI 2010 score were relatively high for 'refined grains' (r=0.47) and 'empty calories' (r=0.57), which may explain the associations with circulating micronutrients. The nuts/legumes components in the other diet quality indices also showed moderate associations due to their tocopherol and carotenoid content, though lower than for fruits and vegetables (43) and possibly the correlation of nuts with overall diet quality (r=0.41–0.53; p-value <0.0001). The present analysis underlines the importance of investigating dietary patterns rather than single nutrients or foods in studies of nutrition and chronic disease risk and several of these biomarkers may be useful for assessing adherence to dietary patterns (10).

This study had several limitations, foremost the lack of information on specific type of supplementation at the time of blood draw; exact type of supplementation may have led to attenuation of the associations presented. Nevertheless, a stratified analysis by supplement use showed similar results. However, changes in supplement use over time are likely and we were not able to take this into account. As MEC members were 45 years and older at cohort entry, results can only be generalized to this age group and to the five included ethnic groups. With the many comparisons, false positive findings due to multiple testing are possible. Our intention was to investigate the possible long-term effects of diet quality, but modifications in dietary habits over time may have led to inaccurate estimation of long-term dietary intake.

Despite these limitations, this study had several strengths, in particular the prospective design, which assured that exposure occurred before the outcome. The many years between diet assessment and blood draw allows the evaluation of potential long-term dietary effects and a strong correlation between diet in 1993–96 and 2003–08 was demonstrated (44) and the results for 2001–06 data were similar as for cohort entry. Due to the large size of the MEC, stratification by ethnicity and sex was possible, since only a few cohorts of this size and diversity exist. As the QFFQ was specifically designed for a multiethnic population, it was possible to compare heterogeneous dietary habits within one study population. Only a few previous studies have investigated diet quality and circulating micronutrients, especially for the DASH and AHEI 2010 indices and for δ-and γ-tocopherol and coenzyme Q10. Thus, this analysis adds new evidence to the body of nutrition research.

In conclusion, higher concentrations of carotenoids and α-tocopherol were significantly associated with higher scores of four *a priori* diet quality indices, while γ-tocopherol was inversely associated. Findings on retinol were inconsistent, while δ-tocopherol and coenzyme Q10 were not related to diet quality. The associations across sex and ethnic groups were very similar. The associations were mainly driven by index components containing vegetables or fruits, but all major components were related to serum concentrations to some extent indicating that an overall high-quality diet might be more important than the intake of individual foods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The Multiethnic Cohort has been supported by NCI grants R37 CA54281 (PI: L.N. Kolonel), U01 CA164973 (PI: L. Le Marchand/C.A. Haiman/L.R. Wilkens), and P30 CA71789 (PI: R. Holcombe). NA was supported by a student fellowship from the German Research Foundation (PROMOS) and from the Susanne Marie Sophie Haufen Foundation. None of the funders had a role in the design, analysis or writing of this article

List of abbreviations

AHEI	Alternative Healthy Eating Index
aMED	Alternate Mediterranean diet score
BMI	Body Mass Index
DASH	Dietary Approaches to Stop Hypertension
HEI	Healthy Eating Index
MEC	Multiethnic Cohort
MED	Mediterranean diet
QFFQ	Quantitative Food Frequency Questionnaire

References

1. Cespedes EM, Hu FB. Dietary patterns: from nutritional epidemiologic analysis to national guidelines. Am J Clin Nutr. 2015; doi: 10.3945/ajcn.115.110213
2. Jacobs S, Harmon BE, Boushey CJ, Morimoto Y, Wilkens LR, Le Marchand L, et al. A priori-defined diet quality indexes and risk of type 2 diabetes: the Multiethnic Cohort. Diabetologia. 2015; doi: 10.1007/s00125-014-3404-8
3. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, et al. Alternative dietary indices both strongly predict risk of chronic disease. J Nutr. 2012; doi: 10.3945/jn.111.157222
4. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, et al. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. J Nutr. 2014; doi: 10.3945/jn.113.189407
5. George SM, Ballard-Barbash R, Manson JE, Reedy J, Shikany JM, Subar AF, et al. Comparing indices of diet quality with chronic disease mortality risk in postmenopausal women in the Women's Health Initiative Observational Study. Evidence to inform national dietary guidance. Am J Epidemiol. 2014; doi: 10.1093/aje/kwu173
6. Harmon BE, Boushey CJ, Shvetsov YB, Ettienne R, Reedy J, Wilkens LR, et al. Associations of key diet-quality indexes with mortality in the Multiethnic Cohort: the Dietary Patterns Methods Project. Am J Clin Nutr. 2015; doi: 10.3945/ajcn.114.090688
7. World Health Organization. The global burden of chronic diseases. Internet: http://www.who.int/nutrition/topics/2_background/en/

8. Bingham SA. Biomarkers in nutritional epidemiology. Public Health Nutr. 2002; 5:821–7. [PubMed: 12638591]
9. Jacobs S, Boushey CJ, Franke AA, Shvetsov YB, Monroe KR, Haiman CA, et al. A priori-defined diet quality indices, biomarkers and risk for type 2 diabetes in five ethnic groups. The Multiethnic Cohort. Br J Nutr. 2017; doi: 10.1017/S0007114517002033
10. Jenab M, Slimani N, Bictash M, Ferrari P, Bingham SA. Biomarkers in nutritional epidemiology: applications, needs and new horizons. Hum Genet. 2009; doi: 10.1007/s00439-009-0662-5
11. Rao AV, Rao LG. Carotenoids and human health. Pharmacol Res. 2007; doi: 10.1016/j.phrs.2007.01.012
12. Azzini E, Polito A, Fumagalli A, Intorre F, Venneria E, Durazzo A, et al. Mediterranean Diet Effect: an Italian picture. Nutr J. 2011; doi: 10.1186/1475-2891-10-125
13. Bach-Faig A, Geleva D, Carrasco JL, Ribas-Barba L, Serra-Majem L. Evaluating associations between Mediterranean diet adherence indexes and biomarkers of diet and disease. Public Health Nutr. 2006; doi: 10.1017/S1368980007668499
14. Markussen MS, Veierød MB, Sakhi AK, Ellingjord-Dale M, Blomhoff R, Ursin G, et al. Evaluation of dietary patterns among Norwegian postmenopausal women using plasma carotenoids as biomarkers. Br J Nutr. 2015; doi: 10.1017/S0007114514004103
15. Kolonel LN, Henderson BE, Hankin JH, Nomura AM, Wilkens LR, Pike MC, et al. A multiethnic cohort in Hawaii and Los Angeles. Baseline characteristics. Am J Epidemiol. 2000; 151:346–57. [PubMed: 10695593]
16. US Department of Health and Human Services and others. US Department of Agriculture. Dietary guidelines for Americans. Washington DC: US Department of Health and Human Services; 2010.
17. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, et al. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr. 2005; 82:163–73. [PubMed: 16002815]
18. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, Gnardellis C, Lagiou P, Polychronopoulos E, et al. Diet and overall survival in elderly people. BMJ. 1995; 311:1457–60. [PubMed: 8520331]
19. Fung TT, Chiuve SE, McCullough ML, Rexrode KM, Logroscino G, Hu FB. Adherence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med. 2008; doi: 10.1001/archinte.168.7.713
20. Franke AA, Morrison CM, Custer LJ, Li X, Lai JF. Simultaneous analysis of circulating 25-hydroxy-vitamin D3, 25-hydroxy-vitamin D2, retinol, tocopherols, carotenoids, and oxidized and reduced coenzyme Q10 by high performance liquid chromatography with photo diode-array detection using C18 and C30 columns alone or in combination. J Chromatogr A. 2013; doi: 10.1016/j.chroma.2013.05.027
21. Gerber M. Qualitative methods to evaluate Mediterranean diet in adults. Public Health Nutr. 2006; 9:147–51. [PubMed: 16512962]
22. Lipsky LM, Cheon K, Nansel TR, Albert PS. Candidate measures of whole plant food intake are related to biomarkers of nutrition and health in the US population (NHANES 1999–2002). Nutr Res. 2012; doi: 10.1016/j.nutres.2012.03.005
23. Hann CS, Rock CL, King I, Drewnowski A. Validation of the Healthy Eating Index with use of plasma biomarkers in a clinical sample of women. Am J Clin Nutr. 2001; 74:479–86. [PubMed: 11566646]
24. Weinstein SJ, Vogt TM, Gerrior SA. Healthy Eating Index scores are associated with blood nutrient concentrations in the third National Health And Nutrition Examination Survey. J Am Diet Assoc. 2004; doi: 10.1016/j.jada.2004.01.005
25. Kant AK, Graubard BI. A comparison of three dietary pattern indexes for predicting biomarkers of diet and disease. J Am Coll Nutr. 2005; 24:294–303. [PubMed: 16093407]
26. Miller ER3, Erlinger TP, Sacks FM, Svetkey LP, Charleston J, Lin P-H, et al. A dietary pattern that lowers oxidative stress increases antibodies to oxidized LDL. Results from a randomized controlled feeding study. Atherosclerosis. 2005; doi: 10.1016/j.atherosclerosis.2005.04.001
27. Maiani G, Castón MJP, Catasta G, Toti E, Cambrodón IG, Bysted A, et al. Carotenoids: actual knowledge on food sources, intakes, stability and bioavailability and their protective role in humans. Mol Nutr Food Res. 2009; doi: 10.1002/mnfr.200800053

28. Guenther PM, Reedy J, Krebs-Smith SM. Development of the Healthy Eating Index-2005. J Am Diet Assoc. 2008; doi: 10.1016/j.jada.2008.08.016
29. A report of the Panel on Micronutrients. National Acad. Press; Washington DC: 2001. DRI, Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc.
30. Guertin KA, Moore SC, Sampson JN, Huang W-Y, Xiao Q, Stolzenberg-Solomon RZ, et al. Metabolomics in nutritional epidemiology: identifying metabolites associated with diet and quantifying their potential to uncover diet-disease relations in populations. Am J Clin Nutr. 2014; doi: 10.3945/ajcn.113.078758
31. Talegawkar SA, Johnson EJ, Carithers T, Taylor HA, Bogle ML, Tucker KL. Total α-Tocopherol Intakes Are Associated with Serum α-Tocopherol Concentrations in African American Adults. J Nutr. 2007; 137:2297–303. [PubMed: 17885014]
32. Playdon MC, Moore SC, Derkach A, Reedy J, Subar AF, Sampson JN, et al. Identifying biomarkers of dietary patterns by using metabolomics. Am J Clin Nutr. 2017; doi: 10.3945/ajcn.116.144501
33. Cooney RV, Franke AA, Wilkens LR, Gill J, Kolonel LN. Elevated plasma gamma-tocopherol and decreased alpha-tocopherol in men are associated with inflammatory markers and decreased plasma 25-OH vitamin D. Nutr Cancer. 2008; doi: 10.1080/01635580802404162
34. Jiang Q, Christen S, Shigenaga MK, Ames BN. γ-Tocopherol, the major form of vitamin E in the US diet, deserves more attention. Am J Clin Nutr. 2001; 74:714–22. [PubMed: 11722951]
35. Wolf G. How an increased intake of alpha-tocopherol can suppress the bioavailability of gamma-tocopherol. Nutr Rev. 2006; 64:295–9. [PubMed: 16808116]
36. Bruno RS, Traber MG. Cigarette smoke alters human vitamin E requirements. J Nutr. 2005; doi: 10.1093/jn/135.4.671
37. Patel CJ, Bhattacharya J, Butte AJ. An Environment-Wide Association Study (EWAS) on type 2 diabetes mellitus. PLoS One. 2010; doi: 10.1371/journal.pone.0010746
38. Wajda R, Zirkel J, Schaffer T. Increase of bioavailability of coenzyme Q(10) and vitamin E. J Med Food. 2007; doi: 10.1089/jmf.2006.254
39. Bhagavan HN, Chopra RK. Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics. Free Radic Res. 2006; doi: 10.1080/10715760600617843
40. Higdon, J; Drake, VJ; Delage, B; Johnson, EJ; Mayer, J. Carotenoids. α-Carotene, β-Carotene, β-Cryptoxanthin, Lycopene, Lutein, and Zeaxanthin. Internet: http://lpi.oregonstate.edu/mic/dietary-factors/phytochemicals/carotenoids [cited 2017 Jun 21]
41. Hendrickson SJ, Willett WC, Rosner BA, Eliassen AH. Food predictors of plasma carotenoids. Nutrients. 2013; doi: 10.3390/nu5104051
42. Jonnalagadda SS, Harnack L, Liu RH, McKeown N, Seal C, Liu S, et al. Putting the whole grain puzzle together: health benefits associated with whole grains--summary of American Society for Nutrition 2010 Satellite Symposium. J Nutr. 2011; doi: 10.3945/jn.110.132944
43. Bolling BW, McKay DL, Blumberg JB. The phytochemical composition and antioxidant actions of tree nuts. Asia Pac J Clin Nutr. 2010; 19:117–23. [PubMed: 20199996]
44. Maskarinec G, Lim U, Jacobs S, Monroe KR, Ernst T, Buchthal SD, et al. Diet Quality in Midadulthood Predicts Visceral Adiposity and Liver Fatness in Older Ages. The Multiethnic Cohort Study. Obesity (Silver Spring). 2017; doi: 10.1002/oby.21868

Author Manuscript

Author Manuscript

Author Manuscript

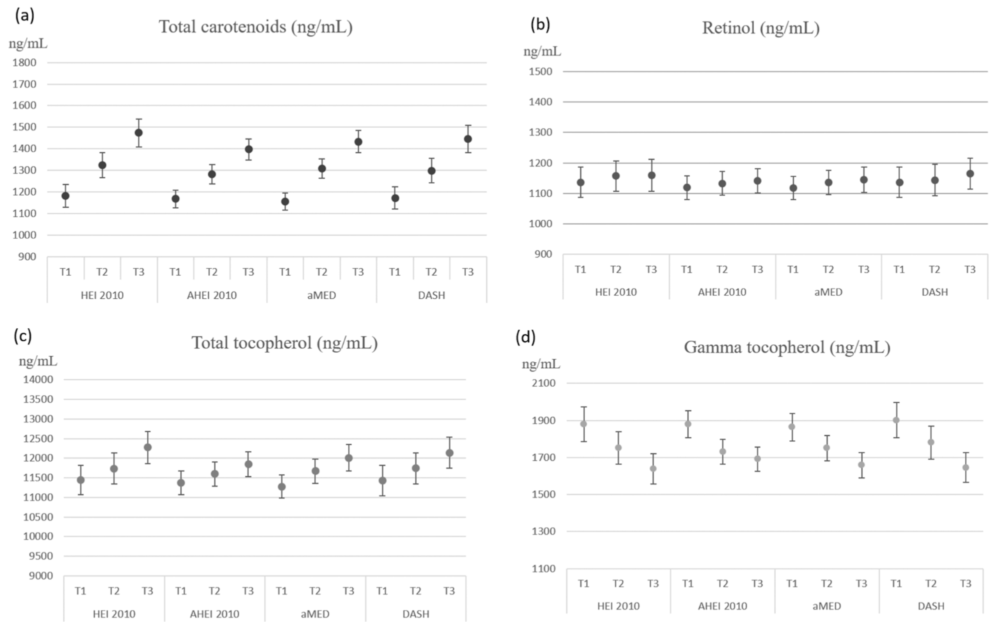

Fig. 1.

Adjusted Means of Circulating Micronutrients for Tertiles of Four Dietary Indices[1]

Abbreviations: Healthy Eating Index (HEI), alternative HEI (AHEI), alternate Mediterranean Diet Score (aMED), Dietary Approaches to Stop Hypertension (DASH), Tertile (T).

[1]Values are geometric means (95% CIs) for all measured circulating micronutrients in ng/mL across tertiles of dietary indices; adjusted for age at blood draw, sex, ethnicity, BMI, smoking status, education, blood draw season, total energy intake and cholesterol concentration. (a) Total carotenoids, (b) Retinol, (c) Total tocopherol, (d) Gamma tocopherol.

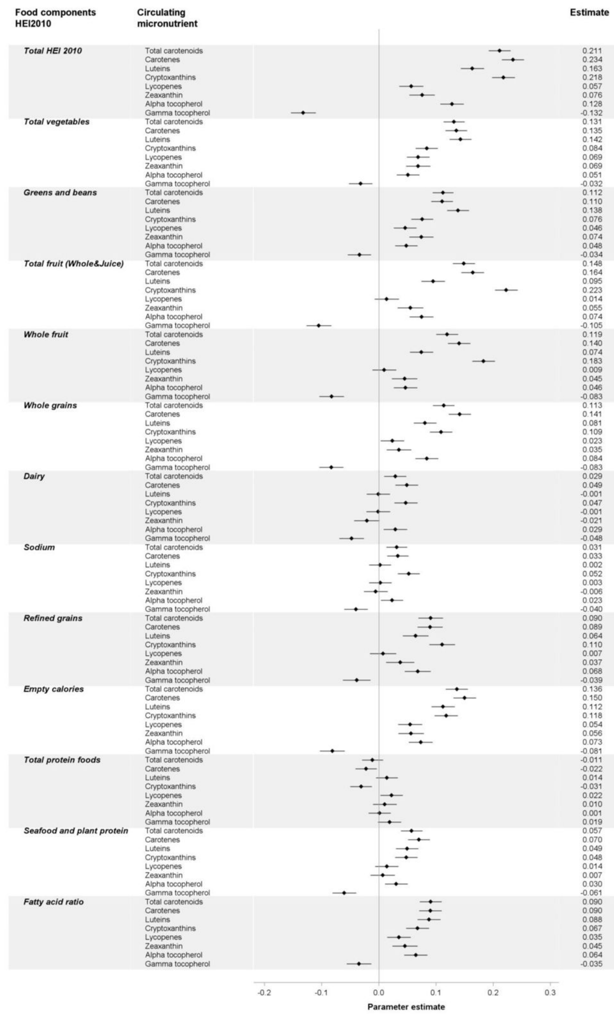

Fig. 2.

Linear Trend for the Change of Standardized Dietary Index Scores of the HEI 2010 Components for Circulating Micronutrients[1]

Abbreviation: Healthy Eating Index (HEI)

[1]Beta coefficients (95% CIs) of the HEI 2010 components for major circulating micronutrients. The HEI 2010 components as well as total the HEI 2010 score were included as continuous variables in the model and adjusted for age at blood draw, sex, ethnic, BMI, smoking status, education, blood draw season, total energy intake and cholesterol concentration. Circulating micronutrients were log-transformed and standardized.

Table 1

Components and Scoring System for Four Diet Quality Indices[1]

	HEI 2010	AHEI 2010	aMED	DASH
Total	**100 points total (12 components, 5–20 points each)**	**110 points total (11 components, 10 points each)**	**9 points total (9 components, 1 point each)**	**8–40 points total (8 components, 1–5 points each)**
Vegetables				
Total vegetables	↑			
Excluding potatoes		↑	↑	↑
Greens and beans	↑			
Fruits				
Total fruit	↑		↑	↑
Whole fruit	↑	↑		
Legumes and Nuts				
Legumes			↑	
Nuts, seeds and legumes				↑
Nuts and legumes		↑		
Nuts			↑	
Whole grains	↑	↑	↑	↑
Refined grains	↓			
Dairy	↑			↑
Total protein foods	↑			
Red and processed meat		↓	↓	↓
Fish			↑	
Seafood and plant proteins	↑			
Oils/ Fats				
PUFA + MUFA: SFA	↑			
MUFA: SFA			↑	
PUFA		↑		
EPA+DHA		↑		
Trans fat		↓		
Empty calories	↓			
Sodium	↓	↓		↓
Alcohol		↓	↓	
SSBs		↓		↓

Abbreviations: Healthy Eating Index (HEI), Alternative HEI (AHEI), alternate Mediterranean Diet Score (aMED), Dietary Approaches to Stop Hypertension (DASH), poly unsaturated fatty acids (PUFA), mono unsaturated fatty acids (MUFA), saturated fatty acids (SFA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), sugar-sweetened beverage (SSB).

[1]Components and scoring directions for every component of each diet quality index.

Table 2

Baseline Characteristics by Tertiles of Dietary Index, Multiethnic Cohort

Characteristics[1]	Categories	HEI 2010			AHEI 2010			aMED			DASH		
		T1 (0–64.5)	**T2 (64.6–74.4)**	**T3 (74.5–100)**	**T1 (0–61.1)**	**T2 (61.2–69.3)**	**T3 (69.4–110)**	**T1 (0–3)**	**T2 (4–5)**	**T3 (6–9)**	**T1 (10–21)**	**T2 (22–25)**	**T3 (26–40)**
Number		2789	2789	2789	2789	2789	2789	2879	3238	2250	2599	2674	3094
Index points	Mean (range)	56.9 (28.7–64.5)	69.5 (64.5–74.4)	81.0 (74.4–96.7)	54.7 (30.1–61.1)	65.2 (61.1–69.3)	75.4 (69.3–99.4)	2.3 (0.0–3.0)	4.5 (4.0–5.0)	6.5 (6.0–9.0)	18.7 (10.0–21.0)	23.5 (22.0–25.0)	28.4 (26.0–38.0)
Age at blood draw		66.1 (8.4)	68.8 (8.3)	70.1 (8.3)	66.5 (8.4)	68.6 (8.5)	69.9 (8.2)	67.2 (8.6)	68.5 (8.4)	69.6 (8.4)	65.7 (8.1)	68.3 (8.4)	70.6 (8.3)
Sex, N (%)	Male	1659 (60)	1279 (46)	966 (35)	1403 (50)	1274 (46)	1227 (44)	1319 (46)	1545 (48)	1040 (46)	1268 (49)	1260 (47)	1376 (45)
	Female	1130 (40)	1510 (54)	1823 (65)	1386 (50)	1515 (54)	1562 (56)	1560 (54)	1693 (52)	1210 (54)	1331 (51)	1414 (53)	1718 (55)
Ethnicity, N (%)	White	187 (7)	224 (8)	281 (10)	212 (8)	239 (8)	241 (9)	236 (9)	278 (9)	178 (78)	109 (4)	203 (8)	380 (12)
	Afr. Am.	588 (21)	742 (27)	968 (35)	839 (30)	750 (27)	709 (25)	844 (29)	859 (27)	595 (26)	649 (25)	746 (28)	903 (29)
	Nat. Haw.	826 (30)	709 (25)	600 (21)	750 (27)	727 (26)	658 (24)	720 (25)	819 (25)	596 (26)	788 (30)	680 (25)	667 (22)
	Jap. Am.	859 (31)	883 (32)	803 (29)	680 (24)	827 (30)	1038 (37)	785 (27)	1006 (31)	754 (34)	883 (34)	795 (30)	867 (28)
	Latinos	329 (11)	231 (8)	137 (5)	308 (11)	246 (9)	143 (5)	294 (10)	276 (8)	127 (6)	170 (7)	250 (9)	277 (9)
BMI, N (%)	<18.5	30 (1)	33 (1)	51 (2)	31 (1)	37 (1)	46 (2)	41 (1)	36 (1)	37 (2)	33 (1)	31 (1)	50 (2)
	18.5–24.5	943 (34)	1077 (39)	1246 (45)	937 (34)	1068 (38)	1261 (46)	1054 (37)	1258 (39)	954 (42)	917 (35)	1007 (38)	1342 (43)
	25.0–29.9	1161 (42)	1147 (41)	1011 (36)	1151 (41)	1144 (41)	1024 (36)	1174 (41)	1303 (40)	842 (37)	1057 (41)	1094 (41)	1168 (38)
	>=30	655 (23)	532 (19)	481 (17)	670 (24)	540 (20)	458 (16)	610 (21)	641 (20)	417 (19)	592 (23)	542 (20)	534 (17)
Smoking, N (%)[2]	Never	1039 (38)	1339 (49)	1498 (54)	1194 (43)	1351 (49)	1331 (48)	1277 (45)	1515 (47)	1084 (48)	1079 (42)	1249 (47)	1548 (50)
	Former	1177 (42)	1121 (40)	1091 (39)	1084 (39)	1082 (39)	1223 (44)	1126 (39)	1310 (41)	953 (43)	995 (38)	1097 (41)	1297 (42)
	Current	550 (20)	304 (11)	188 (7)	487 (18)	336 (12)	219 (8)	448 (16)	393 (12)	201 (9)	509 (20)	306 (12)	227 (8)
Total energy intake	kcal/day	2306 (1107)	2120 (985)	2000 (907)	2001 (995)	2174 (1046)	2251 (973)	1632 (698)	2189 (934)	2728 (1114)	1910 (857)	2131 (1015)	2346 (1082)

Abbreviations: Healthy Eating Index (HEI), Alternative HEI (AHEI), alternate Mediterranean Diet Score (aMED), Dietary Approaches to Stop Hypertension (DASH), Tertile (T).

[1] Unadjusted means and standard deviations unless noted otherwise;

[2] Missing values in women: smoking status n=35; men: smoking status n=25.

Table 3

Adjusted Means for Tertiles of Four Dietary Indices and slope of a linear trend

Circulating micronutrient	Adjusted Means[1]												Trend estimates[2]			
	HEI 2010			AHEI 2010			aMED			DASH			HEI 2010	AHEI 2010	aMED	DASH
	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3				
Total carotenoids	1181*	1323*	1474**	1167*	1281*	1397**	1155*	1307*	1433**	1172*	1298*	1445**	0.211 (0.000)	0.166 (0.000)	0.199 (0.000)	0.198 (0.000)
Carotenes	253*	314*	380**	248*	298*	342**	246*	305*	356**	249*	299*	371**	0.234 (0.000)	0.186 (0.000)	0.209 (0.000)	0.235 (0.000)
Luteins	306*	327*	355**	301*	322*	348**	300*	326*	355**	304*	325*	348**	0.163 (0.000)	0.149 (0.000)	0.171 (0.000)	0.145 (0.000)
Cryptoxanthins	185*	221*	256**	189*	214*	239**	184*	218*	253**	182*	214*	250**	0.218 (0.000)	0.154 (0.000)	0.202 (0.000)	0.211 (0.000)
Lycopenes	283*	296	301**	284	294	296**	282*	296	299**	286	294	297**	0.057 (0.000)	0.032 (0.002)	0.057 (0.000)	0.025 (0.024)
Zeaxanthin	54.4*	56.8*	59.2**	54.3	55.8*	59.0**	53.4*	57.0*	59.9**	54.8*	56.6	58.2**	0.076 (0.000)	0.068 (0.000)	0.097 (0.000)	0.057 (0.000)
Retinol	1137	1157	1160	1119	1133	1141	1118	1136	1145	1137	1144	1165	0.035 (0.003)	0.024 (0.030)	0.028 (0.025)	0.025 (0.035)
Total tocopherols	11444*	11738*	12277*	11370	11598*	11849*	11278*	11669*	12012*	11431*	11740*	12141*	0.091 (0.000)	0.065 (0.000)	0.080 (0.000)	0.079 (0.000)
α tocopherol	8474*	8919*	9566*	8414*	8813*	9096*	8347*	8856*	9298*	8443*	8876*	9428*	0.128 (0.000)	0.090 (0.000)	0.107 (0.000)	0.118 (0.000)
δ tocopherol	685	677	692	689*	671*	689	682	679	692	680	684	689	0.003 (0.768)	0.007 (0.548)	0.024 (0.052)	0.007 (0.552)
γ tocopherol	1879*	1752*	1638*	1880*	1730	1691*	1863*	1750*	1658*	1901*	1780*	1645*	−0.132 (0.000)	−0.093 (0.000)	−0.103 (0.000)	−0.145 (0.000)
Coenzyme Q10	419	418	426	415	408	421	409	417	419	429	418	419	0.008 (0.502)	0.015 (0.019)	0.030 (0.013)	−0.020 (0.082)

Abbreviations: Healthy Eating Index (HEI), alternative HEI (AHEI), alternate Mediterranean Diet Score (aMED), Dietary Approaches to Stop Hypertension (DASH), Tertile (T).

[1] Values are geometric means for all measured circulating micronutrients in ng/mL across tertiles of dietary indices; adjusted for age at blood draw, sex, ethnicity, BMI, smoking status, education, blood draw season, total energy intake and cholesterol concentration.

[2] Beta coefficients (p-value) for circulating micronutrients. The dietary indices were included as continuous variables in the model, standardized and adjusted for age at blood draw, sex, ethnicity, BMI, smoking status, education, blood draw season, total energy intake and cholesterol concentration. Biomarkers were log-transformed and standardized. Due to the standardization, a comparison across diet quality indices and biomarkers is possible.

* Statistically significant trends to the higher tertile (P<0.05).

** Statistically significant trends from the lowest to the highest tertile (P<0.05).