

Influence of using different sources of carotenoid data in epidemiologic studies

GINA M. VANDENLANGENBERG, MS, RD; WILLIAM E. BRADY, MS; LINDA C. NEBELING, PhD, MPH, RD; GLADYS BLOCK, PhD; MICHELE FORMAN, PhD; PHYLLIS E. BOWEN, PhD; MARIA STACEWICZ-SAPUNTZAKIS, PhD; JULIE A. MARES-PERLMAN, PhD, RD

ABSTRACT

Objective This study compared distributions of carotenoid intake and diet-serum correlations using two sources of carotenoid data: the US Department of Agriculture–National Cancer Institute (USDA–NCI) carotenoid food composition database and values accompanying the Block–NCI Health Habits and History Questionnaire (HHHQ).

Design and subjects A 100-item food frequency questionnaire was used to collect dietary data from 2,152 adults, aged 43 to 85 years, who were participating in the Nutritional Factors in Eye Disease Study, a population-based study designed to evaluate nutritional factors associated with age-related eye disease. Blood samples were collected from a random sample of 400 nonfasting participants in the study.

Results Median carotenoid intakes using HHHQ vs USDA–NCI data were alpha carotene (229 vs 223 $\mu\text{g}/\text{day}$), beta carotene (1,321 vs 1,325 $\mu\text{g}/\text{day}$), beta cryptoxanthin (72 vs 21 $\mu\text{g}/\text{day}$), lutein + zeaxanthin (653 vs 811 $\mu\text{g}/\text{day}$), and lycopene (593 vs 1,615 $\mu\text{g}/\text{day}$). All paired differences in carotenoid intake were significantly different from zero (Wilcoxon signed-rank, $P < .0001$). Despite these differences, the two databases similarly ranked individuals according to carotenoid intake: Spearman correlations ranged from .71 (lycopene) to .93 (alpha carotene). Differences between diet–serum correlations (adjusted for energy, body mass index, high density lipoprotein, and total cholesterol) using HHHQ vs USDA–NCI data were minor and not significant ($P > .05$): alpha carotene ($r = .33$ vs $.32$), beta carotene ($r = .27$ vs $.32$), beta cryptoxanthin ($r = .48$ vs $.53$), lutein + zeaxanthin ($r = .28$ vs $.24$), and lycopene ($r = .29$ vs $.25$).

Conclusions Although estimates of carotenoid intake differed significantly, only minor differences in carotenoid rankings and diet–serum correlations were observed using either data source in this population. *J Am Diet Assoc.* 1996; 96:1271-1275.

Carotenoids are brightly colored, fat-soluble plant pigments that are introduced into human beings and animals through the consumption of fruits and vegetables. Growing interest in the potential biological importance of these compounds has stimulated efforts to improve assessment of carotenoid intake. Cellular and animal studies have shown that carotenoids enhance immune response, inhibit mutagenesis, and protect against oxidative damage (1,2). Epidemiologic studies have consistently demonstrated a strong inverse association between consumption of carotenoid-rich foods and the incidence and mortality of certain chronic diseases (3-7).

Epidemiologic studies investigating diet–disease associations rely on food composition tables to translate food consumption data into estimates of nutrient intake. The integrity of food composition data is particularly vital to investigations because errors in food composition data can cause misclassification of dietary intake and limit the power of epidemiologic studies to detect potential diet–disease relationships (8).

Despite recognized limitations in current food composition tables (9), technologic advances are improving the accuracy and reliability of some nutrient estimates, including estimates of the carotenoid content of certain foods. Historically, carotenoid values in food tables were expressed in terms of their vitamin A activity because research focused primarily on their provitamin A capacity and analytic methods were unable to differentiate between individual carotenoids (10). A “caro-

G. M. VandenLangenberg is a doctoral candidate in the departments of Nutritional Sciences and Preventive Medicine/Epidemiology and W. E. Brady is a statistician and J. A. Mares-Perlman is an assistant professor in the Department of Ophthalmology and Visual Sciences at the University of Wisconsin-Madison. L. C. Nebeling is a Cancer Prevention Fellow and M. R. Forman is a senior nutritional epidemiologist at the National Cancer Institute, Bethesda, Md. G. Block is a professor of Public Health Nutrition at the University of California, Berkeley. P. E. Bowen is an associate professor and M. Stacewicz-Sapuntzakis is a senior research specialist in the Department of Nutrition and Medical Dietetics at the University of Illinois at Chicago.

Address correspondence to: J. A. Mares-Perlman, PhD, RD, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, 610 N Walnut St, 405 WARF, Madison, WI 53705-2397.

Table 1
Characteristics of participants in the study sample and entire Nutritional Factors in Eye Disease Study (NFEDS) cohort

Characteristic	Study sample (n=400)		NFEDS cohort (n=2,152)	
	n	%	n	%
Gender				
Female	220	55	1,190	55
Male	180	45	962	45
Age				
43-54 y	69	17	693	32
55-64 y	144	36	580	27
65-74 y	119	30	575	27
75-86 y	68	17	304	14
Smoking status				
Never	186	47	961	45
Past	133	33	758	35
Current	81	20	432	20
Education				
<12 y	128	32	595	28
12 y	175	44	934	43
>12 y	97	24	623	29
Body mass index (kg/m²)				
<25	113	28	630	29
25-30	171	43	895	42
>30	116	29	627	29
Supplement use				
Current	126	32	705	33
Ever	204	51	1,160	54
Never	196	49	992	46

tene" estimate was used to represent the provitamin A carotenoid composition of foods (11).

Today, through the use of high-performance liquid chromatography, individual carotenoids in the food supply can be readily separated and quantified. These quantitative data were the basis for the US Department of Agriculture (USDA)-National Cancer Institute (NCI) carotenoid food composition database (USDA-NCI), which contains values for the five major carotenoids that occur in fruits, vegetables, and multi-component foods containing fruits and vegetables (12,13).

The primary purpose of this study was to compare the distribution and relative ranking of carotenoid intake for persons within a population-based cohort using two sources of carotenoid data: the USDA-NCI carotenoid food composition database and values obtained from the Block-NCI Health Habits and History Questionnaire (HHHQ). A second purpose was to examine the influence of using these different data sources by comparing the diet-serum relationships obtained using either data source. Although there are many physiologic and metabolic determinants of blood carotenoid levels, carotenoid concentrations in the blood reflect dietary intake, in part, and are not closely regulated by homeostatic mechanisms (14). Therefore, blood levels serve as a biomarker for dietary exposure, given a fairly consistent pattern of carotenoid intake throughout the period of dietary assessment. As such, blood levels provide an independent means to test the validity of various dietary assessment methods by circumventing errors in food composition data.

MATERIALS AND METHODS

Study Population

Beaver Dam is a mid-sized, primarily white community in south-central Wisconsin. Residents of this community over 43

years old were identified by a private census and invited to participate in the Beaver Dam Eye Study (BDES). Of the 5,924 persons identified, 4,926 (83%) agreed to participate. A 50% random sample of noninstitutionalized Beaver Dam Eye Study participants (n=2,429) was selected for inclusion in the Nutritional Factors in Eye Disease Study (NFEDS). Of these, 24 (1%) died, 6 (0.2%) could not be located, and 23 (0.9%) were physically or mentally incapable of responding to verbal interviews, and 2,152 persons (89%) participated in the NFEDS study. Blood specimens were obtained from 400 nonfasting persons who were randomly selected from NFEDS participants over the age of 50 years for a separate study of associations between serum carotenoids and cataracts.

Dietary Data and Nutrient Analyses

Dietary intake throughout the preceding year was assessed using a 100-item food frequency questionnaire (FFQ) (15), during in-home interviews conducted between May 15, 1988, and December 15, 1990. Usual daily nutrient intake was calculated from questionnaire responses using DIETSYS computer software (HHHQ-DIETSYS Analysis Software, version 3.4, 1995, National Cancer Institute, Bethesda, Md) and an accompanying nutrient database developed for the NCI diet history questionnaire (16). Later, the same food consumption data were linked to the recently developed USDA-NCI carotenoid database (12) and a composite of the two (described below).

Description of Carotenoid Data Sources

HHHQ carotenoid values were obtained from recent assay data as well as from literature values. When specific carotenoid data were unavailable for a particular food, beta carotene was estimated according to Handbook No. 8 vitamin A values (17). Content of other carotenoids was estimated according to the food's similarity to foods with known carotenoid content (18,19). The USDA-NCI food composition database was compiled from analytic data derived from critically evaluated published and unpublished sources (12). Because HHHQ and USDA-NCI carotenoid values may be derived from similar sources, these data should not be considered mutually exclusive.

To estimate carotenoid intake using the USDA-NCI carotenoid data, fruit and vegetable items from the FFQ were linked to identical foods in the USDA-NCI carotenoid food composition database. For single food items, the assigned carotenoid content was equivalent to the carotenoid profile for that food. For multiple food items, the assigned carotenoid value was the mean of the carotenoid values of each food in the item, weighted according to consumption frequency in the second National Health and Nutrition Examination Survey (20).

Whereas USDA-NCI carotenoid values are limited to fruits, vegetables, and multicomponent foods containing fruits and vegetables, HHHQ data include carotenoid estimates for additional foods such as dairy products, fats, and eggs. To determine the influence of assigning carotenoid values to these foods, we formed a composite database by combining USDA-NCI's carotenoid values for fruit and vegetables with HHHQ's carotenoid values for dairy products and fats (beta carotene), and eggs (lutein + zeaxanthin). The composite database used all available USDA-NCI carotenoid values, then incorporated HHHQ data for foods not described in the USDA-NCI database.

Serum Data

Blood specimens were obtained from 400 randomly selected nonfasting NFEDS participants approximately 1 month before the nutrition interviews. An aliquot of these specimens was used to determine total and high-density lipoprotein (HDL) cholesterol (21). The remaining serum was stored at -80°C in

Table 2

Daily carotenoid intakes ($\mu\text{g}/\text{day}$) and Spearman correlations between Block-NCI Health Habits and History Questionnaire (HHHQ) and US Department of Agriculture-National Cancer Institute (USDA-NCI) estimates ($n=2,152$)

Carotenoid	Data source	Mean \pm SD ^a	25th percentile	Median ^b	75th percentile
Alpha carotene	HHHQ	283 \pm 240	135	229	348
	USDA-NCI	267 \pm 186	148	223	331
	Composite	269 \pm 187	150	226	332
	Correlation	.93			
Beta carotene	HHHQ	1,553 \pm 1,005	926	1,321	1,904
	USDA-NCI	1,490 \pm 849	903	1,325	1,878
	Composite	1,619 \pm 860	1,026	1,452	2,015
	Correlation	.87			
Beta cryptoxanthin	HHHQ	80 \pm 53	41	72	105
	USDA-NCI	29 \pm 28	10	21	38
	Composite	30 \pm 29	11	22	39
	Correlation	.78			
Lutein+zeaxanthin	HHHQ	816 \pm 622	427	653	1,005
	USDA-NCI	962 \pm 642	545	811	1,180
	Composite	1,089 \pm 661	650	938	1,337
	Correlation	.77			
Lycopene	HHHQ	715 \pm 563	337	593	934
	USDA-NCI	1,889 \pm 1,239	1,041	1,615	2,439
	Composite	1,910 \pm 1,259	1,048	1,634	2,459
	Correlation	.71			
Total	HHHQ	3,446 \pm 1,890	2,179	3,088	4,220
	USDA-NCI	4,639 \pm 2,386	2,957	4,227	5,770
	Composite	4,919 \pm 2,434	3,212	4,485	6,078
	Correlation	.83			

^aSD=Standard deviation.

^bAll differences between HHHQ and USDA-NCI values are significantly different from zero, Wilcoxon signed-rank test ($P<.0001$).

cryogenic vials with O-rings for up to 4.5 years. Serum alpha carotene, beta carotene, beta cryptoxanthin, lutein + zeaxanthin, and lycopene were determined by high-performance liquid chromatography. The reproducibility and validity of this method have been described previously (22).

Statistical Analysis

The first step in our analytic approach was to compare distributions of individual and total carotenoids for each of the aforementioned data sources. We evaluated agreement between database estimates by comparing mean, median, and 25th and 75th percentile intakes. Because the distributions of the paired differences were not normally distributed, a non-parametric test, the Wilcoxon signed-rank test, was used to test whether the median difference of paired carotenoid estimates was significantly different from zero.

Because the primary objective of epidemiologic studies is to rank persons according to nutrient exposure, we assessed the level of concordance between nutrient rankings by calculating Spearman correlation coefficients between HHHQ and USDA-NCI estimates. Because persons are typically categorized into quintiles of nutrient intake to assess threshold effects and test dose-response relationships, we calculated the percentage of subjects who were jointly classified into identical quintiles by HHHQ and USDA-NCI carotenoid estimates.

To understand why intake estimates and quintile classifications differed for the two data sources, we constructed multiple regression models. The difference between database estimates was designated as the dependent variable and foods that were major contributors to carotenoid intake (using either database) were entered as potential explanatory variables. The maximum R^2 approach was used to obtain the one-variable model, two-variable model, and so on, that yielded the highest

R^2 (ie, best explained the variation in the difference between carotenoid estimates).

The next step was to examine diet-serum relationships for the five major carotenoids (alpha carotene, beta carotene, beta cryptoxanthin, lutein + zeaxanthin, and lycopene). Both crude and energy-adjusted Pearson correlation coefficients were calculated. The nutrient density method of energy-adjustment (nutrient per 1,000 kcal) was chosen as a means to reduce extraneous variation in nutrient intake due primarily to differences in body size (14).

Although a number of factors have been previously identified as potential confounders of the diet-serum carotenoid relationship, our primary purpose was to compare the correlations obtained using either data source. Therefore, we simplified our approach by limiting the adjustment of diet-serum correlations to those factors found to be related to serum carotenoid levels independent of carotenoid intake in this population: total cholesterol, HDL cholesterol, and body mass index (23). Adjustment for these factors served to reduce extraneous variation in the measurement of serum carotenoids. This was accomplished by regressing serum carotenoids on HDL cholesterol, total cholesterol, and body mass index, and using the residuals for correlations with diet. Nutrient estimates and serum levels were skewed toward higher values, therefore, natural logarithmic transformations were used to normalize their distributions. SAS software (version 6.09, 1993, SAS Institute, Cary, NC) was used to perform all statistical computations. Two-tailed P values $<.05$ were considered statistically significant.

RESULTS

Characteristics of participants from whom blood specimens were obtained and of the entire NFEDS cohort are shown in

Table 3
Mean serum carotenoid levels (nmol/L) and Pearson correlations between carotenoid levels in the serum and the diet (n=400)^{a,b}

	Alpha carotene		Beta carotene		Beta cryptoxanthin		Lutein+zeaxanthin		Lycopene	
Serum level (mean±SD)	87±61		334±227		182±129		287±126		496±245	
Correlations	r	95%CI^c	r	95%CI	r	95%CI	r	95%CI	r	95%CI
HHHQ	.33	(.24,.41)	.27	(.18,.36)	.48	(.40,.55)	.28	(.19,.37)	.29	(.20,.38)
USDA-NCI	.32	(.23,.41)	.32	(.23,.41)	.53	(.46,.60)	.24	(.15,.33)	.25	(.16,.34)
Composite	.33	(.24,.41)	.33	(.24,.41)	.51	(.43,.58)	.25	(.16,.34)	.25	(.16,.34)

^aDietary carotenoid intake expressed as nutrient densities (nutrient/1,000 kcal). Serum carotenoids were adjusted for body mass index, high-density lipoproteins, and total cholesterol. Log_e-transformed values used for serum and dietary carotenoids.

^bAll correlation coefficients were significantly different from zero ($P < .05$). No significant differences between correlations were obtained using the above data sources ($P > .05$).

^cCI=confidence interval.

Table 1. With the exception of age, the distributions of characteristics were similar for the two groups.

Table 2 presents population mean (\pm standard deviation), median, and quartile estimates of daily carotenoid intake using HHHQ, USDA-NCI, and composite carotenoid data. Although distributions for alpha carotene and beta carotene were similar using either data source, HHHQ estimates of beta cryptoxanthin intake were higher than USDA-NCI estimates, whereas HHHQ estimates of lutein + zeaxanthin and lycopene intake were lower. Use of USDA-NCI carotenoid values increased estimates of total daily carotenoid intake by 35%.

Agreement between HHHQ and USDA-NCI estimates in terms of comparable rank assignment is described in Table 2. Spearman correlation coefficients between HHHQ and USDA-NCI estimates ranged from .71 for lycopene to .93 for alpha carotene. Likewise, the percentage of persons jointly classified into the exact quintile ranged from 43% for lycopene to 66% for alpha carotene (data not shown).

Multiple regression analyses revealed that specific FFQ items could account for discrepancies in carotenoid intake estimates due to their frequency of consumption and/or disparate carotenoid assignments. For example, two foods, grapefruit and chili with beans, accounted for 65% of the variance in the difference between lycopene estimates: the lycopene concentration of grapefruit is 1,546 $\mu\text{g}/100\text{ g}$ (USDA-NCI, average of pink and white varieties) vs 0 $\mu\text{g}/100\text{ g}$ (HHHQ), and the lycopene concentration of chili with beans is 2,118 $\mu\text{g}/100\text{ g}$ (USDA-NCI) vs 130 $\mu\text{g}/100\text{ g}$ (HHHQ). Corn and orange juice explained 85% of the variability in the difference between beta cryptoxanthin estimates: the beta cryptoxanthin concentration assigned to corn is 0 $\mu\text{g}/100\text{ g}$ (USDA-NCI) vs 200 $\mu\text{g}/100\text{ g}$ (HHHQ), whereas the beta cryptoxanthin concentration assigned to orange juice is 11.6 $\mu\text{g}/100\text{ g}$ (USDA-NCI) vs 48 $\mu\text{g}/100\text{ g}$ (HHHQ).

Carotenoid intakes were significantly correlated with their respective serum concentrations (Table 3) for both databases ($P < .01$). Only small differences were observed (ranging from .01 to .05) between energy-adjusted correlations (crude correlations not shown) using different databases (Table 3). The only significant difference between correlations for the two data sources was for beta cryptoxanthin (crude correlations: .42 HHHQ vs .52 USDA-NCI). Formation of a composite carotenoid database failed to improve diet-serum correlations.

DISCUSSION

In this population-based cohort, estimations of carotenoid intake sometimes differed when different databases were used to assess intake. Intakes of lutein + zeaxanthin and lycopene

were higher using the USDA-NCI carotenoid database, whereas beta cryptoxanthin intake was higher using HHHQ carotenoid values.

Despite differences in intake estimates, the two databases similarly ranked people according to carotenoid intake, (Spearman correlations, Table 2). Thus, these results indicate that the observed differences in carotenoid estimates are not likely to markedly influence diet-disease relationships in this population. However, in populations consuming greater or more varied quantities of foods with disparate carotenoid values, differences in nutrient exposure classification could be more extreme.

The magnitude of diet-serum correlations, with the exception of beta cryptoxanthin, was also similar using either database. This finding could imply that physiologic factors influence diet-serum correlations to a greater extent than does the accuracy with which specific quantities of carotenoids are assigned to the foods that are consumed. This finding may also suggest that the database discrepancies described in this study are insufficient to influence diet-serum correlations in populations whose consumption of foods with disparate carotenoid values is neither greater nor more diverse than this population.

The formation of a composite database had little influence on diet-serum correlations. One explanation may be that fruits, vegetables, and multicomponent foods containing fruits and vegetables are the primary sources of carotenoids in the diet, whereas the carotenoids in foods added to the composite database accounted for only a small percentage of carotenoid intake.

Although the diet-serum correlations measured in this study were modest, they are similar in magnitude to those obtained using FFQs in other populations (18,24,25). There are several explanations for the rather low correlations measured in this and other studies. First, there are many physiologic and metabolic determinants of blood carotenoid levels, the random effects of which tend to dilute correlations with diet (26). Thus, while blood carotenoid levels serve as an independent marker of carotenoid intake, diet-serum correlations should be viewed primarily as a benchmark by which to assess the validity of carotenoid data, rather than as a gold standard. Second, although the FFQ assessed usual carotenoid intake over the preceding year, it is generally assumed that serum levels reflect more recent intake (during the preceding weeks or months) (27). This explanation is supported by higher correlations achieved when dietary data are based on food records and serum carotenoids are measured upon completion of the recording period (24). Third, because within-person variation exists in serum carotenoid levels and our results were

based on a single determination per subject, large intrasubject relative to intersubject variability in serum carotenoids could mask important relationships. Finally, because the correlation coefficient is a function of between-person variation, the generalizability of our correlation coefficients may be limited to populations with similar demographic and behavioral characteristics as well as to populations with similar between-person variations in carotenoid intake (14).

In this population-based cohort, estimations of carotenoid intake sometimes differed when different databases were used to assess intake; however, only minor differences in carotenoid rankings and diet-serum correlations were observed

APPLICATIONS

These results indicate that although differences in database values exist, the influence of choice of database on the classification or ranking of persons according to carotenoid intake may be modest. As the linkage of USDA-NCI data to the HHHQ becomes available for public use, investigators will have the opportunity to test for themselves whether the choice of carotenoid data influences estimates of diet-serum and diet-disease relations in their populations.

Continued research efforts aimed at optimizing assessment of carotenoid intake will enhance our ability to test hypotheses regarding the role that carotenoids may play in the prevention of certain degenerative diseases. ■

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