Questionnaire Assessment of Intake of Specific Carotenoids

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Abstract
We determined whether estimation of intake of specific carotenoids with a standard food-frequency questionnaire (FFQ) could be improved by collection of additional data on the intake of carotenoid-rich food items. The foods included on an addendum to the standard FFQ were potentially important dietary contributors of α- and β-carotene, β-cryptoxanthin, lutein, zeaxanthin, or lycopene. Participants (n = 215), ages 50–74 years, provided fasting blood samples and completed the FFQ and the addendum. The participants were enrolled in a prepaid health plan and had undergone screening sigmoidoscopy for detection of colorectal polyps. Addendum foods were identified that accounted for variation in blood levels of specific carotenoids, conditional on intake of foods on the standard FFQ. Estimated carotenoid intakes from the standard FFQ, and from the modified FFQ with the selected addendum foods, were examined in relation to plasma carotenoid levels. The correlation coefficient between estimated carotenoid intake and plasma levels (adjusted for age, sex, serum cholesterol, alcohol intake, smoking status, and energy intake) were essentially the same for the standard and modified FFQs. The adjusted correlations for the standard FFQ only were 0.26 for α-carotene, 0.22 for β-carotene, 0.36 for β-cryptoxanthin, 0.32 for lutein + zeaxanthin, and 0.34 for lycopene. Adding carotenoid-rich foods to the FFQ did not improve estimation of intake for the carotenoids examined in this population. We conclude that assessment of intake of specific carotenoids with the FFQs currently in use may not necessarily be improved by a modified list of carotenoid-rich foods.

Introduction
The protective association of fruit and vegetable intake with the risk of cancer may be due to specific carotenoids found in these foods. High levels of dietary or plasma β-carotene have been associated with reduced risk of lung (1–9) and stomach (1, 3, 9, 10) cancers in numerous studies. A strong protective association of serum lycopene with risk of pancreatic cancer was found in one large prospective study (11). In the same cohort, serum lycopene had a statistically nonsignificant protective association with the risk of bladder cancer (12). In a population-based case-control study, dietary intakes of α-carotene and lutein showed inverse associations with lung cancer risk (6).

Two of the food-frequency questionnaires now in widespread use in epidemiological studies (13, 14) were developed when extensive data on the food content of β-carotene, but not other carotenoids, were available. These questionnaires were designed to assess intake of energy, macronutrients, and essential micronutrients, including vitamin A. Recently Mangels et al. (15) published an extensive nutrient data base with values for the carotenoids α-carotene, β-carotene, β-cryptoxanthin, lutein + zeaxanthin, and lycopene. We hypothesized that the addition of carotenoid-rich foods to the questionnaire that we were using in an epidemiological study (13) would improve dietary assessment for these five carotenoids. The hypothesis was examined using participants in a case-control study of adenomatous polyps conducted among subjects who had undergone screening sigmoidoscopy in Southern California.

Materials and Methods
Study Population. Subjects were recruited from the sigmoidoscopy screening clinics at two Southern California Kaiser-Permanente Medical centers (Bellflower and Sunset, CA). Cases were men and women, ages 50–74 years, diagnosed for the first time with at least one histologically confirmed adenomatous polyp. Controls were subjects free of polyps of any type. Subjects were excluded if they had a history of cancer, inflammatory bowel disease, or familial polyposis syndrome. Controls were matched to cases by gender, age (by 5-year age category), calendar date of sigmoidoscopy (by 3-month category), and Kaiser center. Of 1286 subjects screened for enrollment in the sigmoidoscopy study from January 1991 to December 1992, 140 (11%) refused to participate, 36 (3%) could not be located, and 160 (12%) did not provide blood specimens. The proportion of eligible subjects who provided blood specimens was 76% for cases and 72% for controls.

Demographic and other information on smoking, physical activity, and family history of colorectal polyps were collected with an interview questionnaire administered an average of 4.5 months (range, 1.2–17.5 months) after the sigmoidoscopy. The interviewer was blinded to the case or control status of the participant.

All case-control study participants enrolled from June 1992 through December 1992, were eligible for this analysis. Of the 281 eligible subjects who completed the 2-page dietary addendum (no one refused to complete the addendum) and the semi-quantitative food-frequency...
questionnaire (described below), 46 (16.4%) did not have plasma carotenoid determinations, 3 (1.1%) did not have demographic or smoking information, and 17 (6.0%) did not have cholesterol determinations, leaving 215 subjects for this analysis.

**Dietary Assessment.** Participants completed a 126-item version of a semi-quantitative, food-frequency questionnaire developed and validated by Willett et al. (16) and a 34-item addendum with the same format as the 126-item questionnaire.

The dietary addendum included as separate entries 19 food items that had been grouped into 7 food items on the standard questionnaire, and it included 15 foods rich in carotenoids that had not been included on the standard questionnaire. Grouped food items on the standard questionnaire were included as separate food items on the addendum when either the foods within a group varied widely in the content of one or more carotenoids or the pattern of consumption of the foods within the group potentially varied. Carotenoid-rich foods eaten rarely in a pilot study were eliminated from the addendum.

Food carotenoid values were obtained from a nutrient data base published recently by Mangels et al. (15).

**Laboratory Analyses.** Fasting blood samples were collected an average of 5 months (range, 1.5–22 months) after the sigmoidoscopy and within an average of 3 weeks (range, 1–12 months) of the date of the interview. The blood was collected in EDTA-coated tubes, placed in an ice bath, and shielded from light for up to 4 h. The plasma was then separated and stored at −70°C for up to 6 months. Total serum cholesterol and triglycerides were measured at the Kaiser-Permanente Clinical Laboratory (North Hollywood, CA), using enzymatic kits (Boehringer Mannheim Diagnostics, Indianapolis, IN), with between-assay coefficients of variation of less than 5%. Plasma α-carotene, β-carotene, β-cryptoxanthin, lutein, zeaxanthin, and lycopene were measured by HPLC after modification of a standard method (17) in the Vitamin and Trace Element Core Laboratory of the University of California at Los Angeles Clinical Nutrition Research Unit. All samples were processed under minimal lighting. Plasma β-carotene concentrations in samples from the Fat Soluble Vitamin Quality Assurance Program deviated less than 5% from the mean of the core laboratories participating in the program sponsored by the National Cancer Institute and the National Institute of Standards and Technology. The between-assay coefficients of variation for individual carotenoids were <5%.

**Statistical Analysis.** Dietary intakes of each carotenoid were computed for the standard questionnaire by first multiplying the frequency of food intake per day by the carotenoid content of the food, and then summing across all food items containing the carotenoid of interest. We examined the relation between the carotenoid intakes and plasma carotenoid levels using Pearson product-moment correlation coefficients. Normalizing transformations were used as needed.

For the standard questionnaire plus the addendum, we used a stepwise regression procedure (forward selection) to identify foods from the addendum that accounted for statistically significant between-person variation in plasma carotenoid levels ($p = 0.05$ for F-to-enter and F-to-remove). Average daily intake of foods (g/day) containing the carotenoid of interest was entered into the model. Foods from the standard questionnaire were forced into the model, except for the grouped food items on the standard questionnaire that corresponded to items separated on the addendum, to avoid redundancy of variables in the model. A list of foods was obtained for each carotenoid that included the standard questionnaire foods containing the carotenoid plus the addendum foods selected in the stepwise regression. Total carotenoid intake per subject was computed using this modified food list. We examined the relation between the carotenoid intakes determined from the modified food list and plasma carotenoid levels using Pearson product-moment correlation coefficients.

We used regression procedures to obtain partial correlation coefficients [a standard option in SAS statistical software (18)] for the associations of plasma levels with dietary intakes of carotenoids adjusted for other potential determinants of plasma levels. Partial correlation coefficients were determined from the model-regressing plasma carotenoid level on dietary carotenoid intake adjusting for age, sex, serum cholesterol, alcohol intake, current smoking status, and total calories. Previous studies have demonstrated associations between plasma carotenoid levels and alcohol intake (19–21), smoking (19–22), serum cholesterol (19, 20, 23), and gender (23, 24); and intakes of most nutrients are associated with total caloric intake (25). Energy intake is often a covariate in studies of the effects of dietary carotenoids. Thus, we controlled for energy in our analyses so that the dietary carotenoid measure would be evaluated after adjusting for the same factors included in epidemiological studies. All multivariate regressions were performed using SAS statistical software (18).

The crude correlation coefficients obtained from the standard questionnaire were compared with the correlations obtained from the modified questionnaire using a paired r test of the equality of two correlation coefficients (26). To compare the adjusted correlation coefficients, we first calculated the residuals from the regression of plasma levels on age, sex, serum cholesterol, and smoking status and from the regression of dietary intakes on age, sex, total caloric intake, and alcohol intake. The correlation coefficients between residuals were then compared using the same procedure (26).

**Results**

The participants were predominantly nonsmokers and nearly two-thirds were male (Table 1). The average age was 62 years.

Plasma concentrations of the specific carotenoids were similar to those found in other studies (24, 27–32) (Table 2). The foods from the addendum that accounted for significant between-person variation in plasma carotenoid levels are shown in Table 3. Mango was a significant contributor to the between-person variation for β-carotene and was not included on the original questionnaire. Tomato sauce in mixed dishes (not including spaghetti) and catsup were selected for lycopene and also were not included on the original questionnaire. Catsup was also selected for α-carotene. Fresh peaches, selected for β-cryptoxanthin, and beet greens, selected for lutein + zeaxanthin, were included in grouped variables on the original questionnaire.

Table 4 shows the average daily carotenoid intakes for the standard food list and for the modified food list. The means calculated from the standard food list were similar to the means calculated from the modified food list for all carotenoids except lycopene, which increased
from zero at an α level of 0.05. The crude correlation
coefficients of plasma carotenoid levels with intakes for each of
the grouped food item on the standard questionnaire.

A stepwise regression procedure was used to select foods from the adden-
um food items than of the original
coefficients estimated from the standard questionnaire. Re-
striction to Whites did not affect the differences in the
coefficients estimated from the standard questionnaire. Re-
striction to males resulted in an average increase of only
0.01 (range, -0.04 to 0.00) in the partial correlation
coefficients between the standard and modified questionnaires.

Exclusion of smokers resulted in an average decrease of
0.03 of the partial correlation coefficient for lycopene, which increased by 0.06. After adjusting for po-
tential confounders, however, the increase in the partial
correlation coefficient for lycopene was reduced. When all
addendum foods were included on the modified food list
the results were unchanged. When the data were analyzed
separately for cases and controls, the results were no dif-
ferent. Exclusion of smokers resulted in an average decrease of
0.01 (range, -0.04 to 0.00) in the partial correlation
coefficients for the 5 carotenoids estimated from the stan-
dard questionnaire. Moreover, exclusion of the smokers did
not affect the differences in the partial correlation coeffi-
cients between the standard and modified questionnaires.
Restriction to Whites resulted in an average increase of only
0.01 (range, -0.01 to +0.07) for the partial correlation
coefficients estimated from the standard questionnaire. Re-
striction to Whites did not affect the differences in the
partial correlation coefficients between the standard and modified questionnaires. The numbers of non-White par-
ticipants were too small to permit analyses of other ethnic
groups.

When the data were analyzed separately for males and
females, the differences in the partial correlation coeffi-
cients between the standard and modified questionnaires
remained negligible. Restriction to males resulted in an
average change of +0.002 of the partial correlation coeffi-
cients estimated from the standard questionnaire; the
change varied according to carotenoid (range, -0.08 for
β-carotene to +0.07 for β-cryptoxanthin). Restriction to
females resulted in an average change of -0.03 of the
partial correlation coefficients estimated from the standard
questionnaire; again the change varied according to caro-

considerably. In some cases the mean intakes calculated
with the modified food list were smaller because the
respondents reported less frequent consumption of one
or more addendum food items than of the original
grouped food item on the standard questionnaire.

The crude and partial (adjusted) correlation coeffi-
cients of plasma carotenoid levels with intakes for each of
the carotenoids calculated from the standard food list and
from the modified food list are shown in Table 5. Coeffi-
cients in Table 5 were statistically significantly different
from zero at an α level of 0.05. The crude correlation
coefficients were essentially unchanged after including the
selected addendum foods for all the carotenoids except
lycopene, which increased by 0.06. After adjusting for po-
tential confounders, however, the increase in the partial
correlation coefficient for lycopene was reduced. When all
addendum foods were included on the modified food list
the results were unchanged. When the data were analyzed
separately for cases and controls, the results were no dif-
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females resulted in an average change of -0.03 of the
partial correlation coefficients estimated from the standard
questionnaire; again the change varied according to caro-

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**Table 1** Characteristics of the study population (n = 215)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean or % (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62.0 (6.8)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.3 (4.5)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.3 (14.7)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 (0.1)</td>
</tr>
<tr>
<td>Total calories (kcal/day)</td>
<td>1970.0 (840.0)</td>
</tr>
<tr>
<td>Plasma cholesterol (mg/dl)</td>
<td>224.0 (39.5)</td>
</tr>
<tr>
<td>Alcohol intake (g/day)</td>
<td>6.4 (12.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>37.2</td>
</tr>
<tr>
<td>Male</td>
<td>62.8</td>
</tr>
<tr>
<td>Current smoking status</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>13.0</td>
</tr>
<tr>
<td>Nonsmokers</td>
<td>87.0</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>61.9</td>
</tr>
<tr>
<td>Black</td>
<td>9.3</td>
</tr>
<tr>
<td>Latino</td>
<td>15.3</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>8.8</td>
</tr>
<tr>
<td>Other</td>
<td>4.7</td>
</tr>
</tbody>
</table>

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**Table 2** Plasma concentrations of specific carotenoids (n = 215)

<table>
<thead>
<tr>
<th>Carotenoid (μmol/liter)</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Carotene</td>
<td>0.138</td>
<td>0.123</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.571</td>
<td>0.423</td>
</tr>
<tr>
<td>β-Cryptoxanthin</td>
<td>0.367</td>
<td>0.231</td>
</tr>
<tr>
<td>Lutein + zeaxanthin</td>
<td>0.324</td>
<td>0.136</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.742</td>
<td>0.380</td>
</tr>
</tbody>
</table>

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**Table 3** Addendum foods selected in stepwise regression that accounted for a significant portion of the between-person variation in plasma carotenoid levels for each of the specific carotenoids

<table>
<thead>
<tr>
<th>Carotenoid</th>
<th>Foods selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Carotene</td>
<td>Catup</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>Mango</td>
</tr>
<tr>
<td>β-Cryptoxanthin</td>
<td>Peach, fresh</td>
</tr>
<tr>
<td>Lutein + zeaxanthin</td>
<td>Beet greens</td>
</tr>
<tr>
<td>Lycopene</td>
<td>Catup, tomato sauce, in mixed dishes (not spaghetti), e.g., lasagne, and sloppy joes, Hamburger Helper</td>
</tr>
</tbody>
</table>

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**Table 4** Average daily dietary intakes of specific carotenoids calculated from the standard Willett FFQ and from the modified FFQ (n = 215)

<table>
<thead>
<tr>
<th>Carotenoid (μg)</th>
<th>Standard FFQ</th>
<th>Modified FFQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>α-Carotene</td>
<td>940.0 (790.0)</td>
<td>940.0 (790.0)</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>4770.0 (3220.0)</td>
<td>4800.0 (3230.0)</td>
</tr>
<tr>
<td>β-Cryptoxanthin</td>
<td>69.5 (68.2)</td>
<td>70.1 (66.3)</td>
</tr>
<tr>
<td>Lutein + zeaxanthin</td>
<td>3270.0 (2500.0)</td>
<td>3230.0 (2290.0)</td>
</tr>
<tr>
<td>Lycopene</td>
<td>4280.0 (3520.0)</td>
<td>5180.0 (3860.0)</td>
</tr>
</tbody>
</table>

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**Table 5** Unadjusted and adjusted correlations of plasma carotenoid levels with dietary carotenoids calculated from the standard questionnaire and from the modified questionnaire (n = 215)

<table>
<thead>
<tr>
<th>Carotenoid</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>Modified</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>Modified</td>
<td></td>
</tr>
<tr>
<td>α-Carotene</td>
<td>0.26</td>
<td>0.27</td>
</tr>
<tr>
<td>β-Carotene</td>
<td>0.20</td>
<td>0.22</td>
</tr>
<tr>
<td>β-Cryptoxanthin</td>
<td>0.35</td>
<td>0.35</td>
</tr>
<tr>
<td>Lutein + zeaxanthin</td>
<td>0.31</td>
<td>0.33</td>
</tr>
<tr>
<td>Lycopene</td>
<td>0.21</td>
<td>0.34</td>
</tr>
</tbody>
</table>

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*Note:* *a* p < 0.01 for difference from standard questionnaire estimate.

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*a* = 0.05 for F-to-enter and F-to-remove.

*b* A stepwise regression procedure was used to select foods from the adden-
um food items than of the original
grouped food item on the standard questionnaire.

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Intake of Specific Carotenoids

tenoid (range, −0.16 for lycopene to +0.09 for lutein plus zeaxanthin). When the stepwise regression procedures to select foods were run separately for males and females, the same results were obtained for males as for all subjects combined but the data were insufficient to obtain reliable results for females.

Discussion

Adding extra food items to the standard food-frequency questionnaire did not improve its effectiveness for estimating intake of specific carotenoids in this population. The standard questionnaire includes 36 fruit and vegetable items that contain one or more of the five carotenoids examined in this study. The marginal gain in the ability of the questionnaire to discriminate between individuals with respect to carotenoid intake by adding foods beyond this number may be relatively small.

The crude and partial correlation coefficients of dietary and plasma levels of β-carotene are slightly lower than those found in other studies (20, 32–34). Compared to serum α-carotene, 3-cryptoxanthin, lutein + zeaxanthin, or lycopene, the crude and partial correlations found in this study are generally the same or higher (33, 34).

Willett (35) indicated that improvements in the food-frequency questionnaire estimation of nutrient intake will likely occur by adding foods to the questionnaire, separating multiple food items currently included on the questionnaire, or including more information about portion size or frequency of intake. We assessed improvement in the food-frequency questionnaire estimation of carotenoid intake by adding foods to the questionnaire and separating food items that were grouped on the original questionnaire. These changes did not improve estimation of carotenoids, similar to the findings of Pietinen et al. (36, 37). Pietinen et al. (36, 37) found that increasing the number of food items on a food-frequency questionnaire from 44 to 276 items resulted in small or negligible improvements in the assessment of various nutrients. In contrast, Coates et al. (34) found that the addition of 19 food items to the Block questionnaire improved the adjusted diet-plasma correlation coefficients for α-carotene and β-carotene, but not for cryptoxanthin, lutein, or lycopene. Differences in design, content, and number of food items among the various food-frequency questionnaires and the populations evaluated make generalizations about the effects of questionnaire changes tenuous.

Further improvements in food-frequency questionnaire estimation of carotenoid intake may be achieved by the addition of mixed dishes to the standard questionnaire. The recently published nutrient data base by Mangels et al. (15, 38) contains carotenoid values for more than 2300 food items, including many regional and ethnic dishes. Addition of mixed dishes to the questionnaire may improve questionnaire estimation of carotenoid intake in more ethnically diverse populations or in populations in different regions of the United States.

Our ability to demonstrate improvement in questionnaire assessment of carotenoid intake through the addition of food items may have been constrained by our study design. The increased length of the questionnaire with the addendum items may have reduced respondent motivation to answer accurately. Additionally, estimates of carotenoid intake calculated from the standard questionnaire were compared to estimates calculated from the standard questionnaire plus an addendum rather than an actual, modified questionnaire, resulting in redundancy due to the separated food items. The participants may have checked the consistency of their responses for the redundant items or they may have been confused by the redundant items. These problems may have resulted in more similar estimates of carotenoid intake from the two food lists which may have led to reduced differences in the diet-plasma correlation coefficients for the two lists. We used plasma carotenoid levels as the gold standard in this study. Plasma levels are affected by absorption and metabolism, which vary among individuals, as well as other dietary factors, such as fat intake (39).

Also, plasma levels reflect carotenoid intake over the previous 2–3 weeks (39), whereas the food-frequency questionnaire estimates dietary intake over the previous 12 months. This incomplete overlap may also have made an improvement in assessment with the modified questionnaire more difficult to detect.

The causal role of carotenoids, if any, in the prevention of cancer is under active investigation. Reducing instrument error in diet assessment would improve the ability to assess the carotenoid-cancer relationship in observational studies. Modifying the Willett questionnaire food list in this population, however, did not reduce instrument error in the estimation of intakes of the specific carotenoids examined. The assessment of intake of specific carotenoids with the food-frequency questionnaires currently in use may not necessarily be improved by a modified list of carotenoid-rich foods.

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