Olestra Consumption Does Not Predict Serum Concentrations of Carotenoids and Fat-Soluble Vitamins in Free-Living Humans: Early Results from the Sentinel Site of the Olestra Post-Marketing Surveillance Study1,2

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ABSTRACT In 1996, the U.S. Food and Drug Administration approved olestra, a fat substitute, for use in snack foods. Previous studies had shown that olestra consumption could reduce absorption of carotenoids and fat-soluble vitamins. To determine the association between consumption of olestra-containing snack foods and serum concentrations of carotenoids and fat-soluble vitamins in a free-living population, we interviewed independent population-based cross-sectional samples of 1043 adults before olestra was available and 933 adults 9 mo after olestra snacks were introduced into the marketplace in Marion County, IN, the first major test market for olestra. A cohort composed of 403 adults from the first survey, oversampling those most frequently reporting olestra consumption during follow-up telephone interviews, completed a second survey. We assessed diet, lifestyle factors and olestra consumption, and collected blood for assays for the serum concentrations of six carotenoids, four fat-soluble vitamins and lipids. Nine months after the introduction of olestra into the marketplace, 15.5% of Marion County residents reported consuming an olestra-containing snack in the previous month, with a median frequency among consumers of 3.0 times per month. There were no significant associations or consistent trends for decreased serum carotenoids or fat-soluble vitamins associated with olestra consumption, although cohort members consuming ≥2 g/d of olestra had adjusted total serum carotenoids 15% lower compared with baseline. There were increases in serum vitamin K concentrations associated with olestra consumption (P = 0.03 in the cross section and P = 0.06 in the cohort). In summary, there was no statistically significant evidence in this free-living population of associations between olestra consumption and decreased serum concentrations of carotenoids and fat-soluble vitamins.


KEY WORDS: • olestra • carotenoids • fat-soluble vitamins • serum concentrations • humans

In 1996, the U.S. Food and Drug Administration (FDA)4 approved a new fat substitute, olestra (Olean®), for use in “savory snacks” (potato, tortilla and corn chips; crackers; and extruded snacks) (Federal Register 1996). Olestra has the taste and mouth feel of regular fat, but because it cannot be absorbed, it provides no energy (Daher et al. 1997). Despite its potential public health benefits as a nonenergy fat substitute, there is controversy concerning the effects of olestra (Blume 1995). Experimental studies in both humans and animals find that olestra can sequester fat-soluble nutrients in the gut and thereby reduce their absorption (Westrate and van het Hof 1999). The FDA therefore requires the addition of vitamins A, D, E and K to foods made with olestra (Federal Register 1996). Addition of carotenoids was not required because health effects of carotenoids, beyond their provitamin A activity, are not well understood (Rock 1997).

In approving olestra, the FDA made assumptions about the level of its consumption and its effects on serum micronutrient concentrations. As a condition for approval, the FDA mandated a program of active postmarketing surveillance to assess the accuracy of these assumptions. The Olestra Post-Marketing Surveillance Study (OPMSS) was designed to investigate whether consumption of olestra-containing foods, as part of self-selected mixed diets, will affect nutritional status (Kristal et al. 1998). The specific aim was to examine the association of olestra consumption with serum concentrations of six carotenoids (α- and β-carotene, lycopene, lutein, zeaxanthin, and β-cryptoxanthin) and four fat-soluble vitamins [retinol (vita-
min A), 25-hydroxyvitamin D, α-tocopherol (vitamin E) and vitamin K. The full study, with baseline data and 0 y of follow-up at four sites, will conclude data collection in October 2000.

At a public meeting in June 1998, the FDA reviewed the information about the potential health effects of olestra that had accumulated since the FDA’s approval of olestra in December 1996. This review included the early results from the OPMSS arising from the first major test market for olestra-containing snacks in Marion County (Indianapolis), IN. This paper presents the OPMSS data considered by the FDA during the deliberations leading to its continued approval of olestra.

This data represent the first findings of the associations between olestra consumption and serum levels of micronutrients in a free-living population.

SUBJECTS AND METHODS

Design. The OPMSS has the following three principal aims: 1) to monitor the adoption and patterns of use of olestra-containing food products in representative samples of the U.S. population; 2) to assess the associations between introduction of olestra-containing foods into the marketplace and serum concentrations of carotenoids and fat-soluble vitamins in representative samples of the U.S. population; and 3) to assess the associations between consumption of olestra-containing foods and serum concentrations of carotenoids and fat-soluble vitamins in a cohort of olestra consumers.

The study was designed to have at least 80% power to test the following two null hypotheses: 1) changes in population-level total serum carotenoid concentrations that are attributable to olestra will be <10%, and 2) changes in serum concentrations of total carotenoids attributable to olestra, among olestra consumers, will be <10%.

Details of the design of the OPMSS, dietary assessment methods and baseline descriptive results have been reported previously (Kristal et al. 1998). Briefly, the OPMSS is a series of three related studies, each designed to address one of the three principal aims given above.

The first study, called the population cross section, uses annual, independent, random-digit dial (RDD) telephone surveys to collect population-level data on the prevalence and patterns of olestra consumption. The second study, called the clinic cross section, collects serum and extensive dietary and health-behavior information from volunteers drawn from each RDD survey. The third study, called the cohort, collects serum samples and dietary information annually from a subsample of the baseline clinic cross-section participants, chosen to target olestra consumers. In Marion County, the baseline cross-sectional survey was conducted from September 1996 to January 1997; marketing of olestra began February 1997, and the first follow-up survey and follow-up cohort visits were conducted from September 1997 to January 1998. The study populations include children aged 7–17 y. However, because of the small number of children in this preliminary analysis, we report data only for adults ≥18 y old.

The OPMSS is funded by The Procter & Gamble Company (Cincinnati, OH), the manufacturer of olestra. By contractual agreements, scientists at the coordinating center and the field sites are solely and independently responsible for data management, analysis and publication. All study activities were approved by the institutional review boards, and participants provided oral consent for the telephone surveys and written consent for clinic visit activities. To avoid biasing participants’ reports of olestra consumption, we did not tell them that the primary focus of the study was olestra. Participant selection. Participants in the two independent population cross sections were selected and interviewed using a list-assisted RDD sampling methodology, which screens out nonworking numbers but does not exclude nonresidential numbers. One adult (≥18 y old) was selected from random from each household. Of the 9170 numbers called in y 0 (baseline, before the marketing of olestra), interviews were completed on 2173, with an efficacy rate (completed interviews divided by the number of known eligibles plus estimated eligibles from the residential numbers on the list) of 64.2%. Of the 7300 calls made in y 1 (after introduction of olestra in the marketplace), interviews were completed on 1358, with an efficacy rate of 60.9%. These rates are similar to or better than those found in other RDD surveys (Kristal et al. 1993). Clinical cross-section participants were a random sample of persons who completed the telephone survey. We excluded persons with medical conditions such as hyperparathyroidism or short bowel syndrome that would confound interpretation of serum measures. In y 0, of those we invited, 72% agreed to participate and 58% completed the clinical visit. In y 1, 75% agreed to participate and 63% completed the visit. Participants received $100 as compensation for travel and their time.

Cohort participants were selected from the baseline clinic cross section for higher level of olestra consumption. On the basis of dietary information collected from telephone interviews that were conducted —3, 6 and 9 mo after the clinic visit and that assessed diet in the previous month, we recruited all adults who reported at least two occasions of eating olestra-containing foods, a random sample of 67% of those adults who reported a single eating occasion and a sample of 16% of those adults who did not report eating olestra. Of the 478 adults invited into the cohort, 88% completed the y 1 follow-up visit.

Measures. Nutrient intakes, with the exception of vitamin K, were measured with the use of a food-frequency questionnaire (FFQ) (Patterson et al. 1999) with a supplementary questionnaire on savory snack consumption (Neuhausser et al. 2000). The reference period for dietary assessment was “in the past month,” because serum carotenoid concentrations are sensitive to dietary changes in recent weeks (Rock et al. 1992). The nutrient database for these questionnaires was derived from the University of Minnesota Nutrition Coordinating Center nutrient database (Minneapolis, MN) (Schakel et al. 1998) and included the USDA-National Cancer Institute carotenoid database for foods (Mangels et al. 1993). Because serum vitamin K concentrations are most strongly influenced by recent diet (Shearer et al. 1974), vitamin K intake was estimated from a 24-h dietary recall collected at each clinic visit using the Nutrition Data System version 2.9 (Nutrition Coordinating Center, University of Minnesota) (Feskanich et al. 1989), with supplemental vitamin K food composition data provided by Tufts University (Boston, MA) (Booth et al. 1995).

Data on vitamin supplement use over the past month were obtained using a validated inventory procedure (Patterson et al. 2000), which was modified to collect precise dose information on vitamins A, D, E, and K and β-carotene (the only carotenoid available in supplements at the time). Interviewers collected extensive information on demographics, anthropometric factors, medical history, and health behaviors through the following standardized questionnaires:

1. Clinic staff collected anthropometric measures (weight, height and waist circumference) using a standardized protocol (ARI Investigators 1989, Friedman et al. 1988), and body mass index (BMI) was calculated as weight (kg)/height squared (m²).

Blood collection and processing. Details on blood collection, processing and analysis are given elsewhere (Rock et al. 1999). In brief, serum was protected from light, stored at −20°C for no longer than 4 d, shipped to the study’s coordinating center on dry ice and then stored at −70°C until analysis. Sera from y 0 and 1 were analyzed at different times. Carotenoids (α- and β-carotene, lycopene, lutein, zeaxanthin and β-cryptoxanthin), retinol and α-tocopherol were analyzed using HPLC methods. Interassay CV for individual analytes ranged from 1.9 to 9.8%. Minimal detectable concentrations were as follows (μmol/l): α-tocopherol, 1.163; α-carotene, 0.005; β-carotene, 0.011; lycopene, 0.011; lutein, 0.004; zeaxanthin, 0.011, and β-cryptoxanthin, 0.011. 25-Hydroxyvitamin D was analyzed using the INCSTAR (Stillwater, MN) 125I RIA kit. The interassay CV ranged between 5.7 and 9.2%. Serum vitamin K (phylloquinone) was analyzed by HPLC with vitamin K1 as an internal standard using the method of Davidson and Sadowski (1997). One low normal and one high normal concentration quality control sample was analyzed with each batch of samples with between-day variability of 9.7 and 5.3%, respectively. Total serum cholesterol and triacylglycerols were analyzed using enzymatic methods (Rock et al. 1999). Precision was evaluated using packaged reagents, pooled human serum and control sera; both interassay precision and bias were ≤3%.

Statistical analysis. We assigned individual weights to each observation in the clinic cross-sectional surveys, poststratified on age and sex, such that statistics calculated from these samples were
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representative of the Marion County adult population. We excluded from all analyses participants for whom sex (1<%) or age (1%) was unavailable. Because pregnancy has profound effects on serum lipid and nutrient concentrations (Lockitch, 1997), we excluded from analyses women who were pregnant (1%). After these exclusions, there were 1042 y-0 cross-section, 932 y-1 cross-section and 398 cohort participants available for our analyses. For participants whose FFQ or BMI was missing or unreliable, we completed the data set by assigning to them the mean of the variable among all participants with valid values and included dummy variables to indicate that values had been imputed. Unreliable values were defined as computed energy intake <3347 kJ/d or >20,920 kJ/d for men (11%) or <2510 kJ/d or >16,736 kJ/d for women (9%), and BMI <15 or >60 kg/m² (3%). For a small number of participants who had serum concentrations of carotenoids or vitamins that were undetectable by laboratory methods (4% undetectable for vitamin D, 3% for vitamin K, 7% for α-carotene, 1% for all other analytes), we replaced the missing values with the midpoint between zero and the laboratory’s minimum detectable value. Adults not fasting at both y 0 and 1 were excluded from the clinic cohort analyses; we used dummy variables to indicate nonfasting status at either y 0 or 1. Sensitivity analyses found that our conclusions were not changed by these analytic decisions.

We categorized olestra intake into the following four levels on the basis of daily intake (g) in the previous month: no intake (0 g/d), low intake (>0 to <0.4 g/d, approximately the median intake among users in the y-1 clinic cross section), moderate intake (0.4 to <2.0 g/d, from the median up to the 90th percentile of intake among users), and high intake (≥2.0 g/d, the 90th percentile of intake and higher). For regression modeling, we transformed serum and dietary distributions (except percentage of energy from fat, alcohol consumption and servings per day of fruits and vegetables) by the natural logarithm.

For the clinic cross-sectional analyses, we first used data from the y-0 clinic visit to develop models predicting serum nutrient concentrations, weighted to be representative of the Marion County population. All models included age, sex, race, total energy intake (except for the model for vitamin K) and dietary plus supplemental intake of the nutrient. Additional variables, such as serum cholesterol concentration, were added if they were significant at the 0.05 level. The variables considered for the models have been reported elsewhere (Rock et al. 1999). We then modeled serum nutrient concentrations at y 1 using the control variables identified from the y-0 data and added the olestra intake variable. This modeling strategy ensured that the associations between olestra intake and other control variables would not confound the y-1 analysis.

For the cohort analyses, we developed models to predict changes in serum nutrient concentrations without regard to olestra consumption. All models included age, sex, race, y-0 serum concentration, y-0 and change in total intake of the nutrient, and y-0 and change in energy intake, with additional variables included if they were significant at the 0.05 level. If a change variable (such as change in fat consumption) was included in the final model, we also included the baseline value regardless of statistical significance. Once the most parsimonious model was selected, we added olestra consumption to the model to assess its association with change in serum concentration. Details on the most parsimonious models found for the cross section and the cohort are available upon request.

In comparisons of the distributions of demographic characteristics, we used t tests for continuous measures and Pearson’s χ² test for unordered categorical measures. Geometric mean serum concentrations and 95% confidence limits (weighted to be representative of the Marion County population in the cross section, unweighted in the cohort) by level of olestra consumption were computed from the least-squares means for the log-transformed serum concentrations, back-transformed to the original units. Tests for olestra effects in the regression models used Type III sums of squares. The P-values reported are not adjusted for multiple tests. All analyses were performed using SAS version 6.12 (SAS Institute 1989).

Power. When completed, the national data from the OPMSS clinic cross section is projected to have 80% power to detect a 8.0% difference in serum total carotenoid concentration between olestra consumers and nonconsumers, assuming that 25% of participants report olestra consumption in the previous month. The cohort should be able to detect a 5% difference, assuming 80% reporting consumption. Under the same assumptions, the y-1 data from Marion County were projected to be able to detect differences of 13% in the clinic cross-sectional analyses and 20% in the cohort. However, the rate of olestra intake and the variance in serum measures differed from our assumptions. Post-hoc, the detectable differences actually achieved were slightly better (8.7% in the clinic cross section and 11% in the cohort) than the original projections.

RESULTS

Demographic characteristics of clinic cross-section participants were similar in y 0 and 1 (Table 1). We recruited relatively high percentages of minorities (23–25%) and less well-educated people (40–42% with no more than high school education), groups often underrepresented in research studies. Cohort participants (Table 2), who were selected to include the highest consumers of olestra-containing foods, were more likely to be Caucasian and overweight than the y-0 clinic cross section from which they were selected. The composition of the cohort is consistent with our previous report that Caucasian race, higher education, being overweight, lower fat intake and concerns about diet and health were predictors of early adoption of olestra-containing foods (Neu- mark-Sztainer et al. 2000).

High consumption of olestra-containing foods was rare. Only 24% of the clinic cross section reported eating any olestra in the month before the clinic visit, and only 3% reported consuming an average intake ≥2g/d. (There are ~15 g of olestra in a 2-oz average serving of olestra-containing potato chips.) After adjustment for sampling probability, we estimate that 15.5% of Marion County residents ate olestra-containing foods at least once a month ~9 mo after their initial availability in the marketplace, with a median intake of 3.0 servings in the previous month. Despite our selection of the most frequent olestra consumers for the cohort, only 36% reported eating olestra-containing foods in the month before their follow-up clinic visit. Table 3 gives the mean serum carotenoid and fat-soluble vitamin concentrations for the clinic cross section at y 1, for each category of olestra consumption. These results are adjusted for covariates and weighted to be representative of the Marion County population. There was no significant variation across levels of olestra consumption in the serum concentration of total carotenoids ($P = 0.83$ for heterogeneity, $P = 0.88$ for trend), any individual carotenoid or vitamins A, D or α-tocopherol. There was a significant trend for increased serum vitamin K concentration with increasing consumption of olestra, with an estimated 10.5% increase in serum concentration for each category of increasing olestra consumption. The test for heterogeneity for serum α-tocopherol had a P-value of 0.08 due to an anomalously high mean concentration among the highest consumers of olestra. There was, however, no consistent or significant trend for increasing serum α-tocopherol with increased olestra consumption.

There were no significant differences in change in total serum carotenoid concentration across levels of olestra consumption between y 0 and 1 (Table 4, $P = 0.13$ for heterogeneity, $P = 0.79$ for trend). Changes in serum lutein differed significantly across levels of olestra intake, but this was due to an increase among moderate olestra consumers and decreases in all other groups. Changes in other individual carotenoids were not significantly associated with level of olestra consumption. For most carotenoids, the pattern of change was for decreases among the nonusers and lightest consumers, an increase in moderate users, and a decrease in the heaviest
TABLE 1
Characteristics of the adult cross-section participants y 0 (n = 1042), and y 1 (n = 931) by olestra consumption

| Year 1 (n = 931) | Olestra consumption
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>0 (n = 714)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male, %</td>
</tr>
<tr>
<td></td>
<td>Female, %</td>
</tr>
<tr>
<td>Age, y</td>
<td>18-34 y, %</td>
</tr>
<tr>
<td></td>
<td>35-54 y, %</td>
</tr>
<tr>
<td></td>
<td>55+ y, %</td>
</tr>
<tr>
<td>Race</td>
<td>White, %</td>
</tr>
<tr>
<td></td>
<td>Black, %</td>
</tr>
<tr>
<td></td>
<td>Other, %</td>
</tr>
<tr>
<td>Education</td>
<td>≥12 y, %</td>
</tr>
<tr>
<td></td>
<td>13–15 y, %</td>
</tr>
<tr>
<td></td>
<td>≥16 y, %</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25–30, normal, %</td>
</tr>
<tr>
<td></td>
<td>30–40, overweight, %</td>
</tr>
<tr>
<td></td>
<td>40+, obese, %</td>
</tr>
<tr>
<td></td>
<td>Current smoker, %</td>
</tr>
</tbody>
</table>

1 Values are mean ± sd.
2 Body mass index (BMI) calculated as weight (kg) divided by height squared (m²). Normal = 15 to <25, overweight = 25 to <30, obese = 30+.

Twenty-four y-0 and 36 y-1 participants had missing or unreliable BMI.

...users. Although none was significant, point estimates of slopes were positive for three carotenoids (lutein, zeaxanthin and β-cryptoxanthin) and negative for three carotenoids (α-carotene, β-carotene and lycopene). The test for trend for serum vitamin K concentrations had a P-value of 0.06 and a point estimate for the slope of a 9.3% increase for each successive category of increasing olestra intake. Vitamin K concentrations decreased by 20% among nonconsumers and increased by 10% among heaviest users. There was no evidence of an association between olestra consumption and serum concentrations of other fat-soluble vitamins. Serum vitamin D was significantly lower during y 1 compared with y 0, independent of the level of olestra consumption.

DISCUSSION
There are two key findings from this early analysis of results from the first major test market monitored in the OPMSS. First, the associations of olestra consumption with serum carotenoids and fat-soluble vitamins were generally consistent and not significant. This result was seen in two independent study designs, one based on repeated cross-sectional surveys weighted to be representative of the Marion County, IN, population, and the other based on a cohort selected to include olestra consumers. Second, an increase in serum vitamin K concentration associated with olestra consumption was observed in both the clinic cross section and the cohort.

Although the intakes of olestra in this study may appear to be low, they are consistent with the premarket estimates of olestra intake (Webb et al. 1997). The highest level of intake is similar to that used in a controlled olestra feeding study that found effects of olestra on serum carotenoids. A previous controlled trial found that a daily dose of 3 g of sucrose polyester eaten as margarine with the main meal of the day reduced serum concentrations of β-carotene and lycopene by 20 and 38%, respectively (Westrate and van het Hof 1995). In the OPMSS clinic cross section at y 1, participants in the highest category of olestra consumption (≥2 g/d) had reductions in serum concentrations of 11% for β-carotene and 8% for lycopene, compared with nonconsumers. In the cohort, reductions between baseline and follow-up in the highest category of olestra consumption were 21% for β-carotene (compared with 7% for nonconsumers) and 7% for lycopene (compared with no change for nonconsumers). In contrast to the Westrate and van het Hof data, none of the effects of olestra in this analysis was significant and there were no ordered, dose-response relationships between olestra and serum carotenoids in either sample. For example, adults in the cohort with moderate consumption levels of olestra (0.4–2 g/d) had increased serum concentrations for all carotenoids except lycopene. Therefore, we interpret the results for analyses of olestra consumption and serum carotenoid concentrations as being consistent with random variability. The data are also consistent with lower serum carotenoid concentrations among the small subgroup of individuals (~3% of Marion County residents in Fall 1997) consuming ≥2 g/d of olestra, but not with a linear trend for decreasing serum carotenoid concentrations with increasing olestra consumption. Data from pigs (Cooper et al. 1997a) and humans (Schlagheck et al. 1997) do not suggest a threshold for effect of olestra; in fact, the greatest incremental effects are seen at the lowest consumption levels studied.

There are a number of reasons why results from an observational study of olestra consumption would be expected to differ from feeding studies. First, olestra intake is estimated...
from self-report and necessarily contains error. Second, from a biological perspective, there are many determinants of serum carotenoids in free-living persons eating a varied diet. For example, fiber reduces carotenoid absorption, whereas fat facilitates absorption (Rock 1997). This type of variation in nutrient absorption is a well-known aspect of a mixed diet and generally does not pose health risks. People who choose to consume olestra are likely to make different dietary choices than those who do not choose to consume olestra, and these differences can reduce the observed association between olestra consumption and serum levels. In feeding studies in which participants are unaware of whether they are consuming olestra, dietary choices are unlikely to confound the association between olestra consumption and serum levels. In feeding studies in which olestra was provided with every meal, 20 g/d olestra reduced serum β-carotene by 27% (Koonsvitsky et al. 1997). In a separate analysis of 489 24-h dietary recalls from study participants, we found that co-consumption of high carotenoid foods with savory snacks on any single day was low, i.e., on average, only 13–15% of total dietary carotenoids were consumed within 2 h of eating any type of savory snack; co-consumption with olestra was too small to be estimated reliably. Thus, it is not surprising that the effects of olestra consumption on serum micronutrient and carotenoid concentrations in free-living persons will be less than those in controlled studies.

The finding of increased serum vitamin K concentration with increased olestra consumption may be causal. The associations between olestra consumption and increased serum vitamin K were consistent in both the cross-section and cohort samples, and could be due to the level of vitamin K added to olestra. The FDA requires the addition of 8 μg vitamin K/g olestra (Federal Register 1996). At the time of approval, the manufacturer estimated, on the basis of animal and human studies, that the amount of vitamin K necessary to offset any olestra effect on absorption was 3.3 μg/g (Peters et al. 1997). Thus, those consuming 2.0 g/d olestra are consuming 9.4 μg/d vitamin K beyond that estimated to account for an olestra effect. This is 13% of the mean dietary intake of vitamin K in the y-0 cross section (70.1 μg/d). In its approval of olestra, the FDA considered the possibility that the mandated level of vitamin K supplementation would be greater than that required to correct for absorption effects of olestra and concluded that any excess did not pose a health risk (Federal Register 1996).
of Initiative, a multicenter clinical trial and observational study is the same questionnaire developed for the Women’s Health measurement error (Willett 1998). The FFQ used in this study are self-reported and therefore likely to contain significant including consumption of olestra-containing savory snacks, 1997–January 1998, a 36% decrease.

The major limitation of this study is that dietary data, including consumption of olestra-containing savory snacks, are self-reported and therefore likely to contain significant measurement error (Willett 1998). The FFQ used in this study is the same questionnaire developed for the Women’s Health Initiative, a multicenter clinical trial and observational study of ~164,500 women. In a validity study comparing nutrient estimates from this FFQ to 8 d of food records and recalls, correlation coefficients for some of the nutrients examined in this study were as follows: 0.62 for percentage of energy from fat, 0.57 for β-carotene, 0.56 for retinol, 0.73 for vitamin D and 0.83 for vitamin E (Patterson et al. 1999). The reliability of this instrument was good, with intraclass correlation coefficients ranging from 0.67 to 0.79 for these same nutrients. In a separate analysis, we compared fruit and vegetable intake with total carotenoids was 0.23, which is similar to estimates found in similar studies (Tucker et al. 1999). This study has several strengths. Our primary end point olestra exclusively affects the absorption of lipophilic substances (Cooper et al. 1997b), and carotenoids are considerably more lipophilic than fat-soluble vitamins or other polar substances (Cooper et al. 1997a), and carotenoids are considered to be representative of the Marion County population. Adjusted geometric mean levels and 95% confidence limits (CL) of serum concentrations of carotenoids and fat-soluble vitamins in the clinic cross-sectional samples

<table>
<thead>
<tr>
<th>Olestra intake</th>
<th>g/d</th>
<th>μmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 714)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td>1.33</td>
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<tr>
<td>&gt;0 to &lt;0.4</td>
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<td>1.29</td>
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<tr>
<td>≥0.4 to &lt;2.0</td>
<td></td>
<td>1.36</td>
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<tr>
<td>≥2.0</td>
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<td>1.32</td>
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</table>

1 Adjusted for age, sex, race, fasting status, energy intake (except for vitamin K) and intake of the nutrient (dietary plus supplemental for the four vitamins, dietary plus supplemental β-carotene for total carotenoids and β-carotene, and dietary alone for the other carotenoids). Individual analyses are adjusted for other covariates as noted in the footnotes. All analyses are weighted to be representative of the Marion County population.

2 Estimated percentage of change per category of olestra intake.

3 Sum of α-carotene, β-carotene, lycopene, lutein, zeaxanthin and β-cryptoxanthin.

4 Adjusted for body mass index.

5 Adjusted for smoking status.

6 Adjusted for serum cholesterol concentration.

7 Adjusted for alcohol intake.

8 Adjusted for daily servings of fruits and vegetables.

9 Adjusted for percent energy from fat.

10 Adjusted for serum triacylglycerol concentration.

11 Adjusted for an indicator variable of use of supplements containing the nutrient.

Factors that do not share a superscript differ at the 0.05 level.
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TABLE 4

Adjusted percentage of change from y0 to y1 with 95% confidence limits (CL) for serum concentrations of carotenoids and fat-soluble vitamins in the cohort1

<table>
<thead>
<tr>
<th>Olestra intake</th>
<th>g/d</th>
<th>(0 )</th>
<th>(&gt;0 &lt; 0.4)</th>
<th>(\geq 0.4 &lt; 2.0)</th>
<th>(\geq 2.0)</th>
<th>(P)-value for heterogeneity</th>
<th>Slope2</th>
<th>(P)-value for trend</th>
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<td>(n = 261)</td>
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<td>(n = 71)</td>
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<td>(n = 46)</td>
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<td>(n = 20)</td>
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</table>

<table>
<thead>
<tr>
<th>Carotenoids</th>
<th>Total3 carotenoids4,5,6</th>
<th>(-4.5, b)</th>
<th>(-7.9, b)</th>
<th>(2.5a)</th>
<th>(-14.5b)</th>
<th>0.13</th>
<th>(-0.5)</th>
<th>0.79</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\alpha)-Carotene7</td>
<td>(-0.6)</td>
<td>(-19.1)</td>
<td>(6.9)</td>
<td>(-17.9)</td>
<td>0.16</td>
<td>(-3.5)</td>
<td>0.45</td>
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<tr>
<td>(\beta)-Carotene4,5,6</td>
<td>(-7.0)</td>
<td>(-13.3)</td>
<td>(-11.4, 28.9)</td>
<td>0.25</td>
<td>(-0.2)</td>
<td>0.96</td>
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<tr>
<td>Lycopene4</td>
<td>(-0.3)</td>
<td>(-4.9)</td>
<td>(-4.1)</td>
<td>(-7.1)</td>
<td>0.78</td>
<td>(-2.4)</td>
<td>0.34</td>
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<tr>
<td>Lutein4,6</td>
<td>(-12.4a)</td>
<td>(-14.2a)</td>
<td>(-15.9, 9.4)</td>
<td>(-23.5, 12.9)</td>
<td>0.05</td>
<td>2.3</td>
<td>0.31</td>
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<tr>
<td>Zeaxanthin4,6</td>
<td>(-16.4, 8.2)</td>
<td>(-21.7, 6.0)</td>
<td>(-8.3, 15.1)</td>
<td>(-31.3, 18)</td>
<td>0.47</td>
<td>(-2.1, 7.0)</td>
<td>0.21</td>
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<tr>
<td>(\beta)-Cryptoxanthin5,6,7</td>
<td>(16.6)</td>
<td>(10.2)</td>
<td>(27.0)</td>
<td>(13.6)</td>
<td>0.55</td>
<td>0.9</td>
<td>0.77</td>
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<td>Fat-soluble vitamins</td>
<td>Retinol7</td>
<td>(-3.6)</td>
<td>(0.2)</td>
<td>(-3.3)</td>
<td>(-6.3)</td>
<td>0.36</td>
<td>0.0</td>
<td>0.98</td>
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<tr>
<td>25-Hydroxyvitamin D</td>
<td>(-5.7, 1.4)</td>
<td>(-4.0, 4.6)</td>
<td>(-8.5, 2.3)</td>
<td>(-13.6, 1.6)</td>
<td>0.95</td>
<td>(-2.1, 2.2)</td>
<td>0.5</td>
<td>0.84</td>
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<tr>
<td>(\alpha)-Tocopherol4</td>
<td>(-22.9, 14.1)</td>
<td>(-24.2, 16.6)</td>
<td>(-28.9, 7.2)</td>
<td>(-32.3, 0.3)</td>
<td>0.79</td>
<td>0.2</td>
<td>0.87</td>
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<tr>
<td>Vitamin K8</td>
<td>(-20.3)</td>
<td>(-6.7)</td>
<td>(-12.4)</td>
<td>10.9</td>
<td>0.19</td>
<td>9.3</td>
<td>0.06</td>
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</tbody>
</table>

1 Adjusted for y0 serum concentration of the nutrient, age, sex, race, y0 and y1 fasting status, y0 and change in energy intake (except for vitamin K), and y0 and change in intake of the nutrient (dietary plus supplemental for the four vitamins, dietary plus supplemental \(\beta\)-carotene for total carotenoids and \(\beta\)-carotene, and dietary alone for the other carotenoids). Individual analyses are adjusted for other covariates as noted in the footnotes.

2 Estimated percentage of change per category of olestra intake.

3 Sum of \(\alpha\)-carotene, \(\beta\)-carotene, lycopene, lutein, zeaxanthin and \(\beta\)-cryptoxanthin.

4 Adjusted for y0 and change in serum cholesterol concentration.

5 Adjusted for y0 smoking status.

6 Adjusted for y0 body mass index.

7 Adjusted for y0 and change in alcohol intake.

8 Adjusted for y0 and change in serum triacylglycerol concentration.

\(a, b\) Factors that do not share a superscript differ at the 0.05 level.

Continued monitoring of olestra consumption and its effects on nutritional status is warranted. At the conclusion of the Olestra Post Marketing Surveillance Study in October 2000, we will have analyzed serum from \(\approx 4800\) individuals before olestra availability and 2500 individuals in three cross-sectional surveys after the introduction of olestra to the market. In addition, we will have followed a cohort of over 2000 individuals from baseline for up to 2.5 y after the introduction of olestra. The total sample size gives the OPMSS good power to detect even small changes in serum concentrations of carotenoids and fat-soluble vitamins attributable to the consumption of olestra-containing foods.

ACKNOWLEDGMENTS

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LITERATURE CITED


