Antioxidant Supplement Use in Cancer Survivors and the General Population\textsuperscript{1,2}

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\textbf{EXPANDED ABSTRACT}

\textbf{KEY WORDS:} • antioxidants • dietary supplements • cancer

Results from national surveys suggest that dietary supplement use has been increasing in the U.S. over the past two decades (1), with \textasciitilde50\% of the general population currently reporting regular dietary supplement use. Micronutrients often categorized as antioxidants, such as vitamin C, vitamin E, and the carotenoids, comprise one subset of the ingredients in these products. Differential patterns of use of dietary supplements across population subgroups have been observed, and demographic and other characteristics appear to influence the pattern of use. Individuals with health concerns, including those who have been diagnosed with cancer (2,3), appear to be more likely to use dietary supplements than those in the general population. Concern has been expressed that antioxidant supplement use might pose a risk for adverse effects as well as provide possible benefits, especially in vulnerable populations such as individuals who have been diagnosed with cancer (4).

One of the challenges in comparing data on supplement use across population subgroups is that the approaches used to collect these data are highly variable (5). Supplement use is often examined as a dichotomous characteristic (user versus nonuser), although the frequency or regularity of use is an important determinant of the actual effect on status. Dosage is often not considered or verified by product label examination or other methods.

We examined the use of antioxidant dietary supplements in two populations: one that was fairly representative of adults in the general population, and another comprised of women who had been diagnosed with breast cancer. The time frame under study and the data collection methodology are important characteristics that would be expected to influence reported supplement usage, and these factors were similar for the two populations.

The general population group consists of participants in the Olestra Post-Marketing Surveillance Study (OPMSS) and details of the design and aims of the study have been previously described (6). The primary purpose of this study was to examine the influence of olestra consumption on serum carotenoids and fat-soluble vitamins. However, one aspect of the study involved examining dietary intakes and status for carotenoids and fat-soluble vitamins in a representative sample of the general population (not limited to olestra users). Cross-sectional samples were recruited from 1996 to 2000 at clinic sites in four regions of the U.S. (Baltimore, Indianapolis, Minneapolis, and San Diego). Data collection for dietary supplements involved in-person interviews with verification of frequency and dosage, including product label verification.

In adults in the OPMSS cross-sectional population sample (n = 6394), multivitamin use was reported by 41%, and use of single supplements was reported by \textasciitilde17\% for vitamin C, 10\% for vitamin E, and 2\% for \(\beta\)-carotene (the only carotenoid supplement reported in that study). Median supplemental intakes for those using supplements that contain these ingredients (including those from multivitamins and single supplements) were 500 mg/d for vitamin C, 34 mg/d for vitamin E, and 4.5 mg/d for \(\beta\)-carotene. Similar to other populations (1,2), several demographic factors were associated with use of these supplements: age, education, sex, and region of the U.S. For example, 12\% of the subjects aged 25–34 y reported use of vitamin C supplements vs. 27\% of those 55 y and older. In all regions and for all of the dietary supplements examined, frequency of use was associated with education (higher level being associated with increased likelihood of use) and sex (women being more likely than men to report use). Usage across the 4 regional sites can be generally ranked as: San Diego > Minnesota and Baltimore > Indianapolis.

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TABLE 1

Supplemental vitamin C intakes of users of vitamin C-containing supplements at enrollment in the WHEL Study

<table>
<thead>
<tr>
<th>Intake from supplements (mg/d)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>502 (17.8%)</td>
</tr>
<tr>
<td>0.1–249</td>
<td>930 (33.1%)</td>
</tr>
<tr>
<td>250–499</td>
<td>243 (8.6%)</td>
</tr>
<tr>
<td>500–999</td>
<td>467 (16.6%)</td>
</tr>
<tr>
<td>1000–1999</td>
<td>462 (16.4%)</td>
</tr>
<tr>
<td>2000–3999</td>
<td>151 (5.4%)</td>
</tr>
<tr>
<td>4000–5999</td>
<td>40 (1.4%)</td>
</tr>
<tr>
<td>6000–9999</td>
<td>15 (0.5%)</td>
</tr>
<tr>
<td>≥10,000</td>
<td>3 (0.1%)</td>
</tr>
</tbody>
</table>

n = 2813.

In the Women’s Healthy Eating and Living (WHEL) Study, detailed data on dietary supplement use, including dosage verification from the label or distributor, are collected at enrollment and at specific study intervals (2,7). The study participants are women with a history of early stage breast cancer (n = 3088), and the clinical trial is testing whether diet can affect risk for recurrence and overall survival. The WHEL Study protocol, including selection criteria, data collection, and intervention methodology, are provided elsewhere (8). Subjects were recruited and enrolled between 1995 and 2000 at 7 clinical sites in the southwestern and western U.S.

At enrollment into the WHEL Study, 58% of the participants reported use of multivitamins, and ~10% reported use of antioxidant mixtures. Additionally, 46% reported use of vitamin E supplements, 42% reported use of vitamin C supplements, and 11% reported use of vitamin A/carotenoid supplements (with the majority of these formulations containing carotenoids rather preformed vitamin A) as single supplement products. Median supplemental intakes for vitamin C and β-carotene were similar in the WHEL Study users of supplements containing these ingredients to those of the OPMSS supplement users: 453 mg/d and 1.5 mg/d, respectively. However, median supplemental vitamin E intake in users of supplements containing vitamin E was 268 mg/d in the WHEL Study population, which is considerably higher than that of the OPMSS supplement users at 34 mg/d. Also, the distribution of intakes from supplementation indicates that a considerable number of study participants consume very high amounts of dietary supplements. For example, ~24% of the WHEL Study supplement users reported intakes of vitamin C from dietary supplements that are ≥1000 mg/d, as shown in Table 1. Approximately 16% of supplement users reported intakes of ≥5 mg/d β-carotene from supplementation, and 17% reported intakes of ≥500 mg/d vitamin E from supplementation. Multivariate analysis revealed that the demographic characteristics that were significantly associated with supplement use among women who have been diagnosed with breast cancer are similar to those identified in the general population. Multivitamin use was marginally directly associated with education, physical activity, and stage at diagnosis. Use of both vitamin C and vitamin E single supplements showed a strong direct association with physical activity and age, particularly for age groups over 50 y. An inverse association with minority ethnic/racial group status and BMI of 30 kg/m² or more was shown for users of vitamin C, vitamin E, and vitamin A/carotenoids as single supplements, as well as for participants reporting use of multivitamins. In the WHEL Study, reasons for the use of specific dietary supplements also are being explored and preliminary data suggest a few interesting trends. Overall, general health and “to feel better” appear to be predominant reasons, as observed in other studies of individuals who have been diagnosed with cancer (3). Reasons uniquely cited for use of the various antioxidant dietary supplements include management of menopausal symptoms for vitamin E and improvement of immune function for vitamin C.

A notable trend that has emerged in the supplement usage patterns being monitored in the WHEL Study from 1995 to the present is that the products being reported are increasingly complex mixtures of ingredients. Another trend is that these products increasingly include non-nutrient ingredients, such as herbal and botanical compounds (including those that may have antioxidant properties), rather than being limited to nutrient constituents. A related challenge in terms of estimating influence on disease risk or recurrence is the identification and monitoring of non-nutrient constituents of new and fortified food products.

Results from this analysis and comparison highlight the importance of monitoring dietary supplement use in the general population and in observational and intervention studies. Differential usage occurs across various subgroups, and these groups may have differential risks or benefits associated with use. Availability of a regularly-updated national dietary supplement ingredient database will contribute to advances in monitoring and interpreting effects of antioxidant dietary supplements on health-related outcomes.

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LITERATURE CITED