Fruits, Vegetables, and Adenomatous Polyps

The Minnesota Cancer Prevention Research Unit Case-Control Study


Although high vegetable intakes have been associated with a lower risk of colorectal cancer, this relation is less well established for the precursor lesions, adenomatous polyps. With a case-control design involving adenomatous polyp cases (n = 564), colonoscopy-negative controls who were polyp free at colonoscopy (n = 682), and community controls (n = 535), this 1991–1994 Minnesota Cancer Prevention Research Unit study investigated the relation between fruit and vegetable consumption and first incident adenomatous polyps. Dietary intake was assessed using a food frequency questionnaire. For women, adenoma risk was approximately halved in the highest versus lowest quintile of juice consumption (cases vs. colonoscopy-negative controls: odds ratio (OR) = 0.50, 95% confidence interval (CI): 0.27, 0.92; cases vs. community controls: OR = 0.56, 95% CI: 0.30, 1.06). The association was stronger for adenomas with moderate or severe dysplasia compared with mild dysplasia. Juice was not associated with adenoma risk in men. The results for fruits, vegetables, total fruits and vegetables, green leafy vegetables, and several botanically and phytochemically defined subgroups generally were not statistically significant. Because elevated vegetable consumption has been associated with a lower risk of colorectal cancer, vegetables may have a stronger role in preventing the progression of adenomas to carcinomas rather than in preventing the initial appearance of adenomas.

nonmelanoma skin cancer). An introductory letter, a consent form, and four study questionnaires were mailed to persons who met these criteria. The questionnaires were completed prior to the colonoscopy visit to minimize recall bias.

At the colonoscopy visit, the forms were collected and blood was drawn. To be eligible as either a case or colonoscopy-negative control, the participant received a complete colonoscopy reaching the cecum, had all identified polyps removed (if applicable), and did not have a new diagnosis of ulcerative colitis, Crohn's disease, or invasive cancer. The study participation rate was 68 percent among all patients receiving a colonoscopy. Colonoscopy-negative controls \( (n = 707) \) were polyp free at colonoscopy; cases \( (n = 574) \) had at least one adenoma (defined as either adenomatous or mixed pathology). Among the cases, polyp size was determined in vivo by comparison of the polyp with fully opened standard-sized flexible colonoscopy forceps. Polyps were removed and examined by the study pathologist using diagnostic criteria established for the National Polyp Study \( (27) \). If polyps were removed during a sigmoidoscopy prior to the colonoscopy, the relevant slides were evaluated by the study pathologist.

Because the colonoscopy-negative controls may represent a special group of persons who have undergone routine screening for colorectal cancer or who may have gastrointestinal disorders, signs, symptoms, or anxieties that prompted colonoscopy, they may have been too similar to the cases in lifestyle factors or family history. Therefore, we also recruited a community control group using the state of Minnesota Drivers' Registry. Community controls were frequency matched to estimates of the age (5-year intervals), sex, and zip code distribution of the cases to minimize differences in access to health care. University staff telephoned prospective community controls to determine eligibility using the same criteria specified for the colonoscopy patients. However, the current polyp status of the community controls was unknown, because receiving a colonoscopy was not a criterion for participation in this control group. A packet identical to that sent to the colonoscopy patients was mailed to eligible participants. Completed forms were returned by prepaid mail. The participation rate was 65 percent for the community controls \( (n = 550) \).

Data collection

Study participants provided information on personal medical history, family history of cancer and polyps, lifestyle factors, reproductive history (women only), and sociodemographic characteristics. Dietary intake over the previous year was assessed using a 153-item semiquantitative Willett food frequency questionnaire that was expanded and modified for the Minnesota Cancer Prevention Research Unit studies to include additional vegetables, fruits, and low-fat foods. The nine response categories for frequency of intake ranged from “never, or less than once per month” to “6+ per day.” The nutrient database and analysis program developed at Harvard University was used to estimate nutrient intake \( (\text{HarvardSSFQ.5/93}) \).

Fruit and vegetable consumption was estimated by summing the number of servings per week of the 59 fruits and vegetables included on the food frequency questionnaire. Portion sizes for fruits and vegetables were defined as one small can or 6 fluid ounces \( (0.18 \text{ liter}) \) for juices, 1 cup \( (0.24 \text{ liter}) \) for raw, green leafy vegetables, and one-half cup for most raw or cooked fruits and vegetables. Missing responses for items were coded as never consumed. The following fruit and vegetable categories were assessed: fruits without juice (referred to as fruits); vegetables without juice (vegetables); fruit and vegetable juice (juice); and fruits, vegetables, and juice (total fruits and vegetables). We also evaluated several fruit and vegetable groups on the basis of botanical taxonomy and phytochemical content to identify foods that may be potentially rich sources of bioactive phytochemicals \( (28) \). Correlations comparing the food frequency questionnaire with 15 days of diet records collected over 1 year were 0.67 for fruit, 0.32 for vegetable, and 0.82 for juice intakes \( (29) \).

Participants were excluded from analyses if their reported energy intake was implausible (<600 or >5,000 kcal/day), if their total fruit and vegetable intake exceeded 175 servings/week, or if more than 10 percent of the items on the food frequency questionnaire were blank. On the basis of these criteria, 50 participants \( (10 \text{ cases}, 25 \text{ colonoscopy-negative controls}, 15 \text{ community controls}) \) were excluded from the analyses.

Statistical analysis

Analyses were conducted separately for women and men because the neoplastic potential of adenomas \( (30) \) and gastrointestinal function may differ between women and men \( (31–35) \). Associations between fruit and vegetable intake and adenomatous polyps were assessed using unconditional logistic regression in the Statistical Analysis System \( (\text{SAS Institute, Inc., Cary, North Carolina}) \); all tests of statistical significance were two sided. Participants were classified into sex-specific quantiles of fruit and vegetable intake by the combined distribution of cases and controls. Separate analyses were performed for comparisons of the cases versus the colonoscopy-negative controls and for the cases versus the community controls. Sex-specific odds ratios were adjusted for age, energy intake, fat intake, body mass index, smoking status, alcohol intake, multivitamin supplement use, nonsteroidal antiinflammatory drug use, and hormone replacement therapy use (women only). Tests for trend were conducted using the square root of the number of servings as a continuous regressor \( (36) \).

To investigate the association between fruit and vegetable intake and adenoma pathology, we classified cases into two subgroups: a mild dysplasia group and a moderate or severe dysplasia group. If a participant had more than one adenoma, the adenoma with the highest degree of dysplasia was used for classification. Logistic regression analyses compared each dysplasia subgroup with each control group.
RESULTS

Population characteristics

Study participants generally were White (97 percent), had an average age of 53–58 years, and had a mean body mass index of 27 kg/m² (table 1). Women made up a smaller proportion of cases than of either control group. The primary reason for receiving a colonoscopy among cases was a planned polyp excision (64 percent) and among the colonoscopy-negative controls, a strong family history of colorectal cancer (31 percent) or a positive fecal occult blood test (30 percent). Among the cases, the majority of adenomas were located in the distal colon and were smaller than 10 mm (table 2). Approximately half of the adenomas had mild dysplasia.

The mean fruit and vegetable intakes were similar across the three study groups. The mean total fruit and vegetable intakes (servings/week) were 45.8 (standard deviation (SD), 26.6) for female cases, 45.2 (SD, 24.4) for female colonoscopy-negative controls, 47.0 (SD, 23.0) for female community controls, 40.1 (SD, 23.0) for male cases, 40.2 (SD, 23.1) for male colonoscopy-negative controls, and 41.8 (SD, 20.9) for male community controls. The most commonly consumed fruits and vegetables were orange juice (2.9 servings/week), bananas (2.6 servings/week), potatoes (2.5 servings/week), iceberg lettuce (2.3 servings/week), and apples (1.8 servings/week).

Fruit and vegetable intake and adenoma risk

Most of the odds ratios for the four main fruit and vegetable groups did not reach statistical significance at the \( p < 0.05 \) level for either women or men (table 3). For women, only juice consumption showed a monotonic decrease in risk with increasing consumption. For both control group comparisons, women in the highest quintile of intake had at least a 40 percent lower adenoma risk than did women in the lowest quintile. Fruit, vegetable, and total fruit and vegetable intakes were not associated with adenoma risk.

TABLE 1. Selected demographic characteristics by group, Minnesota Cancer Prevention Research Unit case-control study, 1991–1994

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases</th>
<th>Colonoscopy-negative controls</th>
<th>Community controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>564</td>
<td>682</td>
<td>535</td>
</tr>
<tr>
<td>Age (years) (mean (SD))</td>
<td>58 (10)</td>
<td>53 (11)</td>
<td>58 (10)</td>
</tr>
<tr>
<td>Women (%)</td>
<td>38</td>
<td>62</td>
<td>45</td>
</tr>
<tr>
<td>Education (years) (mean (SD))</td>
<td>14 (3)</td>
<td>14 (3)</td>
<td>14 (3)</td>
</tr>
<tr>
<td>Drink alcohol (%)</td>
<td>73</td>
<td>72</td>
<td>74</td>
</tr>
<tr>
<td>No. of drinks/week (mean (SD))†</td>
<td>7 (9)</td>
<td>6 (9)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>Body mass index (kg/m²) (mean (SD))</td>
<td>Energy intake (kcal/day) (mean (SD))</td>
<td>Fat intake (% kcal) (mean (SD))</td>
</tr>
<tr>
<td>Cases</td>
<td>21</td>
<td>27 (5)</td>
<td>2,091 (776)</td>
</tr>
<tr>
<td>Colonoscopy-negative controls</td>
<td>15</td>
<td>27 (5)</td>
<td>2,011 (711)</td>
</tr>
<tr>
<td>Community controls</td>
<td>16</td>
<td>27 (4)</td>
<td>2,048 (712)</td>
</tr>
</tbody>
</table>

* SD, standard deviation.
† Among drinkers.

TABLE 2. Distribution of adenoma pathology in cases by sex, Minnesota Cancer Prevention Research Unit case-control study, 1991–1994

<table>
<thead>
<tr>
<th>Pathology*</th>
<th>Adenoma size (mm) (mean (SD))</th>
<th>Small (&lt;5 mm) (%)</th>
<th>Medium (5–9 mm) (%)</th>
<th>Large (≥10 mm) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of adenomas (mean (SD†))</td>
<td>9.0 (8.0)</td>
<td>30</td>
<td>33</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>1.5 (1.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>1.3 (0.6)</td>
<td>8.3 (6.8)</td>
<td>38</td>
<td>27</td>
</tr>
<tr>
<td>Men</td>
<td>1.6 (1.2)</td>
<td>9.4 (8.7)</td>
<td>25</td>
<td>36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Degree of dysplasia</th>
<th>Histology</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (%)</td>
<td>Medium or severe (%)</td>
<td>Tubular ( %)</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Women</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Men</td>
<td>48</td>
<td>52</td>
</tr>
</tbody>
</table>

* For those persons with more than one adenoma, the pathology of the largest adenoma is described.
† SD, standard deviation.
TABLE 3. Multivariate-adjusted odds ratios* for colorectal adenomas by quintile of fruit and vegetable intake for women and men, Minnesota Cancer Prevention Research Unit case-control study, 1991–1994

<table>
<thead>
<tr>
<th>Food group quintile</th>
<th>Mean intake (servings/week)</th>
<th>Cases vs. colonoscopy-negative controls</th>
<th>Cases vs. community controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>Fruits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.3</td>
<td>2.1</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>7.4</td>
<td>5.9</td>
<td>0.95 (0.52, 1.72)</td>
</tr>
<tr>
<td>3</td>
<td>11.2</td>
<td>9.6</td>
<td>0.91 (0.50, 1.63)</td>
</tr>
<tr>
<td>4</td>
<td>15.8</td>
<td>14.7</td>
<td>1.10 (0.59, 2.05)</td>
</tr>
<tr>
<td>5</td>
<td>27.5</td>
<td>26.9</td>
<td>1.34 (0.66, 2.69)</td>
</tr>
<tr>
<td>p trend</td>
<td></td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10.1</td>
<td>8.8</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>17.6</td>
<td>15.1</td>
<td>1.12 (0.62, 2.01)</td>
</tr>
<tr>
<td>3</td>
<td>23.8</td>
<td>20.2</td>
<td>1.16 (0.62, 2.16)</td>
</tr>
<tr>
<td>4</td>
<td>31.6</td>
<td>27.1</td>
<td>2.26 (1.23, 4.14)</td>
</tr>
<tr>
<td>5</td>
<td>51.4</td>
<td>44.7</td>
<td>1.70 (0.87, 3.34)</td>
</tr>
<tr>
<td>p trend</td>
<td></td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Juice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.5</td>
<td>0.5</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
<td>1.9</td>
<td>0.81 (0.48, 1.39)</td>
</tr>
<tr>
<td>3</td>
<td>4.8</td>
<td>4.2</td>
<td>0.72 (0.41, 1.27)</td>
</tr>
<tr>
<td>4</td>
<td>7.7</td>
<td>7.4</td>
<td>0.61 (0.34, 1.09)</td>
</tr>
<tr>
<td>5</td>
<td>14.2</td>
<td>15.1</td>
<td>0.50 (0.27, 0.92)</td>
</tr>
<tr>
<td>p trend</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Total fruits and vegetables</td>
<td>18.4</td>
<td>16.5</td>
<td>1.00</td>
</tr>
<tr>
<td>p trend</td>
<td></td>
<td></td>
<td>0.79</td>
</tr>
</tbody>
</table>

* Adjusted for age (continuous), energy intake (continuous), fat intake (continuous), body mass index (continuous), smoking status (never, current, former), alcohol status (nondrinker, former drinker, current drinkers consuming <1 drink/week, current drinkers consuming ≥1 drink/week), nonsteroidal antiinflammatory use (yes, no), multivitamin use (yes, no), and hormone replacement therapy use (yes, no in women only).
† OR, odds ratio; CI, confidence interval.

For men, fruit, juice, and total fruit and vegetable intakes were not associated with adenoma risk in comparisons with either control group. However, high vegetable consumption was associated with a 45 percent reduced adenoma risk for men in comparison with the community controls but was not associated with adenoma risk in comparison with the colonoscopy-negative controls.

Because the glycemic index has been positively associated with the risk of colorectal cancer (37, 38), we repeated our analyses for fruits, vegetables, and total fruits and vegetables after excluding bananas and potatoes, two commonly consumed foods in our study population that have a high glycemic index (39). The results were essentially unchanged from those presented in table 2. For example, for comparisons with the colonoscopy-negative controls, the odds ratios for women comparing the highest versus lowest quintile of intake were 1.34 (95 percent confidence interval (CI): 0.57, 2.20) for fruits excluding bananas, 1.33 (95 percent CI: 0.70, 2.54) for vegetables excluding potatoes, and 0.84 (95 percent CI: 0.42, 1.67) for total fruits and vegetables excluding bananas and potatoes. For the same comparisons, the odds ratios for men were 0.61 (95 percent CI: 0.33, 1.14), 0.72 (95 percent CI: 0.38, 1.35), and 0.75 (95 percent CI: 0.33, 1.47), respectively.

Additional adjustment for dietary fiber intake did not materially change the results for fruits, vegetables, juice, and total fruits and vegetables (data not shown). Simultaneous adjustment for fruits, vegetables, and juice on a continuous scale (data not shown) also did not substantially change the results observed when each group was included in a separate model. Results restricted to cases with distal adenomas (data not shown) were similar to those reported for all cases.
We classified fruits and vegetables into botanically and phytochemically defined groups in an attempt to identify particular types of fruits and vegetables that have high cancer-preventive activity. For example, the fruits of the Rutaceae family (i.e., citrus fruits) are rich sources of vitamin C and monoterpenes (40). Tertiles were used to categorize persons because of the narrow range of intakes reported for these groups. Strong associations were not observed for most of the groups, and those observed were generally limited to comparisons with only one control group (table 4). For women, the Rutaceae family (citrus fruits, including juice) was the only botanical family for which an association was suggested. In the comparison with the community controls, adenoma risk was approximately 40 percent lower for the highest versus lowest tertile of intake of the Rutaceae family (odds ratio (OR) = 0.64, 95 percent CI: 0.38, 1.10; \( p \) trend = 0.07). No association was observed in the comparison with the colonoscopy-negative controls. In contrast, elevated consumption of the Solanacea family was associated with at least a 35 percent higher risk (not statistically significant) in comparisons with both control groups. For men, the strongest association was observed for fruits and vegetables with a high level of

Table continues
lycopene, with an odds ratio of 0.53 (95 percent CI: 0.34, 0.82; \( p \) trend = 0.002), in a comparison of the highest versus lowest tertile of intake in the comparison with the community controls. Inverse associations also were observed for men for the Cucurbitaceae and Solanaceae families and green leafy vegetables in comparison with the community controls but not in comparison with the colonoscopy-negative controls.

### Intakes of Fruits and Vegetables and Adenoma Pathology

Because cases with adenomas of moderate or severe dysplasia may have a higher risk of developing recurrent adenomas or colorectal cancer (26, 41), we examined associations separately for adenomas with mild dysplasia and adenomas with moderate or severe dysplasia (table 5). For women, in the comparison with the colonoscopy-negative controls, the odds ratios for juice were stronger for cases having adenomas of moderate or severe dysplasia than for cases having adenomas of mild dysplasia. A similar pattern of odds ratios was observed for comparisons with the community controls (for cases with moderate/severe dysplasia: OR = 0.48 for highest vs. lowest tertile, 95 percent CI: 0.25, 0.93; for cases with mild dysplasia: OR = 0.67, 95 percent CI: 0.35, 1.27). In contrast, a statistically significant, positive association was sug-

### TABLE 4. Continued

<table>
<thead>
<tr>
<th>Food group tertile</th>
<th>Mean intake (servings/week)</th>
<th>Cases vs. colonoscopy-negative controls</th>
<th>Cases vs. community controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
<td>OR</td>
</tr>
<tr>
<td>Solanaceae (peppers, potatoes, tomatoes)</td>
<td>1</td>
<td>2.7</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>5.6</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10.6</td>
<td>10.7</td>
</tr>
<tr>
<td>( p ) trend</td>
<td>0.17</td>
<td>0.98</td>
<td>0.08</td>
</tr>
<tr>
<td>Green leafy vegetables (lettuce, spinach, collard greens)</td>
<td>1</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3.9</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9.1</td>
<td>7.1</td>
</tr>
<tr>
<td>( p ) trend</td>
<td>0.30</td>
<td>0.22</td>
<td>0.97</td>
</tr>
<tr>
<td>High ( \beta )-carotene (apricots, carrots, sweet potatoes)</td>
<td>1</td>
<td>1.6</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>4.4</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>11.3</td>
<td>8.2</td>
</tr>
<tr>
<td>( p ) trend</td>
<td>0.36</td>
<td>0.70</td>
<td>0.77</td>
</tr>
<tr>
<td>High lutein (broccoli, peas, spinach)</td>
<td>1</td>
<td>2.8</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>6.9</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>14.8</td>
<td>10.9</td>
</tr>
<tr>
<td>( p ) trend</td>
<td>0.10</td>
<td>0.55</td>
<td>0.76</td>
</tr>
<tr>
<td>High lycopene (tomatoes, tomato paste, watermelons)</td>
<td>1</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>5.0</td>
<td>4.7</td>
</tr>
<tr>
<td>( p ) trend</td>
<td>0.71</td>
<td>0.82</td>
<td>0.32</td>
</tr>
</tbody>
</table>

* Adjusted for age (continuous), energy intake (continuous), fat intake (continuous), body mass index (continuous), smoking status (never, current, former), alcohol status (nondrinker, former drinker, current drinkers consuming <1 drink/week, current drinkers consuming ≥1 drink/week), nonsteroidal antiinflammatory use (yes, no), multivitamin use (yes, no), and hormone replacement therapy use (yes, no in women only).

† OR, odds ratio; CI, confidence interval.

‡ Three fruits and vegetables from each botanical and phytochemical group are given as examples. For more detailed descriptions, see Smith et al. (Cancer Causes Control 1995;6:292–302).
suggested for vegetable consumption in both groups of cases in comparisons with the colonoscopy-negative controls. Weaker, nonsignificant associations were observed in comparisons with the community controls. For men, stronger associations with fruit and juice consumption were suggested for cases having adenomas with moderate or severe dysplasia in comparisons with both control groups (data not shown for comparisons with the community controls).

**DISCUSSION**

Although fruits and vegetables contain a multitude of compounds that have been shown to have potential cancer-preventive activity (40), our study adds to the evidence suggesting that fruits and vegetables are not strongly associated with the risk of adenomatous polyps. In comparisons with each control group, a statistically significant reduction in the risk of adenomas was observed only for juice intake in women. The association was stronger among cases with moderate or severe dysplasia versus mild dysplasia. Because orange juice (the most commonly consumed fruit and vegetable in this population) is a primary contributor to folate intake in the United States (42), the inverse association observed for juice is consistent with our previous report that higher levels of dietary folate are associated with a lower risk of adenomas (43). Results for fruits, vegetables, total fruits and vegetables, green leafy vegetables, and the botanically and phytochemically defined subgroups generally were not statistically significant. If significant associations were observed for these groups, they were restricted to either women or men in comparison with only one of the control groups; thus, it is likely they may be chance findings.

As in our study, most studies of adenomatous polyps have reported that fruit and vegetable consumption is not associated with the risk of adenomas, although the risk estimates generally have been in the protective direction (4, 7). For fruit intake, only two (12, 20) of 12 (8–10, 12–15, 18–22) studies have reported statistically significant inverse associations. In one study, women in the highest quartile of fruit consumption had about half the risk of adenomas as did women in the lowest quartile (OR \(0.44, 95\) percent CI: 0.20, 0.95) (12). A somewhat weaker, but statistically nonsignificant association was observed for men in this study.
A cohort of 51,529 male health professionals (relative risk was associated with a modest reduction in adenoma risk in the OR between women and men is believed to be greater than the risk difference in colorectal cancer incidence (30). Other studies examining fruit and vegetable intakes have indicated differences in the associations observed for women and men for both colorectal cancer (48, 49) and adenomas (12, 17). Differences in hormone levels, including the use of exogenous hormones, colorectal epithelial cell proliferation, transit times, fecal mass, and fecal bile acid composition may contribute to these differences in risk between women and men (31–35).

Multiple control groups were included in our analyses to enable comparisons of cases with control groups with inherently different advantages and disadvantages. The primary advantage of the colonoscopy-negative control group is that all colonoscopy-negative controls had received a complete colonoscopy and were determined to be polyp free, thereby reducing misclassification in the outcome. Recall bias also was probably minimized for comparisons of cases with colonoscopy-negative controls, because both sets of participants completed the study questionnaires prior to receiving their colonoscopy and diagnosis. However, because participants in these groups had an indication for receiving a colonoscopy, lifestyle factors, including diet, may have been too similar between the colonoscopy-negative controls and cases, resulting in attenuation of the associations observed. This type of attenuation should not have occurred in comparisons with the community control group. However, because the current polyp status of the community control group participants was unknown, associations may have been attenuated by the inclusion of persons with polyps in this control group. Thus, with either control group, some attenuation of associations is possible but for different reasons.

Most limitations of this study are specific to using a case-control study design. Because the response rate was 65–68 percent across the three study groups, selection bias could affect the validity of our results. Generalizability also is limited because study participants were relatively homogeneous for several sociodemographic variables. In addition, participants may have overestimated their fruit and vegetable consumption as a result of increased awareness of the potential cancer-preventive effects of fruits and vegetables (4–7) or social desirability bias.

In conclusion, our results show that fruit and vegetable intakes generally were not associated with the risk of adenomatous polyps, although we did show a statistically significant inverse association for juice consumption in women in comparisons with each control group. Because previous studies, as well as our study, suggest that fruits and vegetables may be more strongly associated with adenomas with greater malignant potential and because elevated fruit and vegetable consumption has been associated more consistently with a lower risk of colorectal cancer than of adenomas (1, 2, 4, 5, 7), fruits and vegetables may have a stronger role in preventing the progression of adenomas to carcinomas than in preventing the initial appearance of adenomas. Further research aimed at identifying factors that lead to the progression of adenomas may help to clarify the role of fruits and vegetables in colorectal cancer prevention.
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