

A Diet High in Fruits and Low in Meats Reduces the Risk of Colorectal Adenomas¹

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Abstract

Recent evidence suggests overall dietary patterns, rather than specific dietary components, may be a better predictor of colorectal adenomas or cancers. Using cluster analysis, we aimed to assess the association between dietary patterns and colorectal adenomas and whether adjusting for total energy consumption prior to creating clusters affects this relation. Data from a case-control study of 725 individuals undergoing a colonoscopy were utilized. Cases ($n = 203$) had ≥ 1 adenoma on colonoscopy, and controls ($n = 522$) were those who had no adenomas. Dietary data were obtained from an FFQ. Daily intake for 18 different food groups was calculated. The values were transformed into Z-scores. Participants were first clustered without energy adjustment, then again based on their consumption per 1000 kcal (4187 kJ). There was no association between dietary patterns and colorectal adenomas without energy adjustment prior to creating dietary clusters, as clusters formed as a by-product of energy consumption. After adjusting for energy consumption, 3 distinct clusters emerged: 1) high fruit-low meat cluster; 2) high vegetable-moderate meat cluster; and 3) high meat cluster. After adjusting for potential confounders, the high vegetable-moderate meat cluster (odds ratio [OR] 2.17; [95% CI] 1.20–3.90) and high meat cluster (OR 1.70; [95% CI] 1.04–2.80) were at significantly increased odds of having had an adenoma compared with the high fruit-low meat cluster. A high-fruit, low-meat diet appears to be protective against colorectal adenomas compared with a dietary pattern of increased vegetable and meat consumption. *J. Nutr.* 137: 999–1004, 2007.

Introduction

Increasing BMI (1,2), smoking (3), and alcohol consumption (4) have been linked to the development of colorectal neoplasms (either adenomas or cancers). Although the relation between dietary components and the development of colorectal neoplasms has been explored, individual studies have primarily focused on 1 or only a few food groups or nutrients. Some dietary variables are consistently related to colorectal neoplasms. Red meat consumption, for example, has been shown in multiple studies to be associated with an increased risk of colorectal adenomas and cancers (2,5–8). However, the results for other dietary food groups or items have been conflicting. Several studies have found a protective effect of fruit and vegetable consumption (5,7,9), but multiple other studies have found no association between fruit and vegetable consumption and the risk of having or developing a colorectal neoplasm (10–13). Similar conflicting results exist for the relation among nonred meat consumption (2,6,7), dietary fat (6,9,13,14), and dairy products (15–17).

Because of the indeterminate results of these studies, there has been an interest in evaluating the overall dietary pattern of

an individual for the risk of colorectal neoplasms. Moreover, dietary patterns may be better predictors of disease outcomes, because they capture the complexity of food composition and nutrient interactions and reflect actual eating behaviors. The use of factor (18–20) and cluster (21–24) analyses have helped enrich our knowledge about the relation between diet and complex health outcomes, such as cancer. These analytical techniques allow a complex set of data from FFQ to be aggregated into meaningful groups. The use of cluster analysis, for instance, allows individuals to be separated into nonoverlapping groups based on the distribution of all the foods that they consume, not on the basis of 1 or 2 dietary variables. Factor and cluster analysis of diets have revealed important diet-disease relations. For example, a Mediterranean diet (including fruits, vegetables, olive oils, and lean meats) (25) and a high-dairy, high-fruit, high-vegetable, high-starch, low-alcohol diet (26) have been shown to be protective against colorectal cancers. Conversely, increased risks have been associated with diets consisting of increased pork, processed meat, and potato products (27), as well as a diet that is high in starch but also high in fat and low in fruits (20).

Daily energy intake has been associated with an increased risk of colorectal cancer (1,7). In assessing the relation between dietary patterns and colorectal neoplasms, some adjustment for total energy consumption is necessary, but it is unclear whether the consumption of various food groups or items should be

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adjusted for total energy intake before or after clustering. It is possible that the relative, instead of absolute, constituents of an individual's diet influence the association between dietary components and the risk of a colorectal neoplasm. This was demonstrated for adenocarcinoma of the distal esophagus and stomach (28). The purpose of this study was to identify what dietary patterns were associated with the presence of an adenoma on colonoscopy. Additionally, we hypothesized that energy-adjusting dietary food groups will have an important impact on clustering, and adjusting for total energy intake will lead to more meaningful clusters as it relates to the risk of having a colorectal adenoma.

Methods

Study population. The Diet and Health Study IV is a case-control study of 725 outpatients who underwent a colonoscopy between November 2001 and December 2002 at the University of North Carolina Hospitals (Chapel Hill, NC). Eligible participants were enrolled if they gave informed consent and agreed to participate in a telephone interview. All subjects were between 30 and 80 y old and both men and women were eligible to participate. Exclusion criteria included a personal history of colon cancer (or adenoma), inflammatory bowel disease, or history of previous colon resection. Patients were also excluded if they were unable to give informed consent, had a polyposis (>100 polyps) syndrome, or had an incomplete examination (cecum not reached). Cases were defined as participants who had 1 or more adenomatous polyps. Control subjects had no adenomatous polyps. The institutional review board at the University of North Carolina School of Medicine approved this study. A total of 725 subjects were enrolled, with 203 cases and 522 controls. The indications for colonoscopy were as follows: 1) average risk colorectal cancer screening ($n = 448$); 2) colorectal cancer screening with positive family history of colorectal cancer or polyps ($n = 120$); 3) occult blood in stool ($n = 40$); 4) diarrhea ($n = 38$); 5) abdominal pain or bloating ($n = 31$); 6) anemia ($n = 25$); and 7) constipation ($n = 23$). Participants who had incomplete data ($n = 80$) were excluded from final analyses, leaving a total of 645 participants (466 controls and 179 cases) eligible for analysis.

Data collection. Participants were contacted within 12 wk after their colonoscopy for assessment of dietary and lifestyle variables by a trained interviewer. A lifestyle questionnaire was used to collect information about demographics, personal and family medical history, physical activity, smoking, alcohol consumption, and utilization of certain medications, including nonsteroidal antiinflammatory drugs (NSAID)⁴. Dietary data were collected using a validated FFQ developed by the National Cancer Institute (NCI) (29,30). The NCI FFQ collects information on portion sizes for 124 food items as well as data for dietary supplements. Data reported represent consumption patterns over the year prior to the colonoscopy. Answers to the FFQ were converted into nutrient estimates and then aggregated into food groups using software specifically designed by the NCI to use with its FFQ.

Dietary cluster analysis. Dietary clusters were derived from a set of 18 food groups. These included the number of daily servings of whole grains, total vegetables, green vegetables, yellow vegetables, beans/peas, potatoes, other starchy vegetables, tomatoes, other vegetables, total fruit, citrus/melon/berry, other fruit, and total dairy. Daily consumption (in grams) of poultry/fish, beef/pork/lamb, and frankfurters/luncheon meats was also calculated. Additionally, daily values for the number of grams of discretionary fat and the number of grams of added sugar were also included as separate variables from which 3 distinct clusters were produced. Because there were significant differences in the orders of magnitude of some of these dietary variables, all dietary variables were transformed by creating Z-scores for each variable. The clusters were

produced using the "cluster kmeans" command in Stata 8.2 (StataCorp). This produced 3 nonoverlapping clusters. To adjust for total energy (caloric) consumption, the 18 dietary variables were divided by the participants' total calculated daily energy intake (based on the FFQ) and multiplied by 1000. This generated the number of servings (or grams of meat, or grams of discretionary fat, or teaspoons of added sugar) per 1000 kcal (4187 kJ) for each dietary variable. Because there were still significant differences in the orders of magnitude of some of the dietary variables, the energy-adjusted variables were also transformed by creating Z-scores for each variable. Three nonoverlapping dietary patterns emerged from this analysis with energy-adjusted food variables.

Covariates. Demographic data were obtained from all study participants at the time of colonoscopy. We recorded sex, race, age, smoking history, and NSAID use. Weight and height were recorded at the time of colonoscopy and used to calculate BMI. Smoking history (recorded as number of years smoked) and alcohol consumption (recorded as number of drinks per week) were obtained with the lifestyle questionnaire that was administered as part of the same telephone interview during which the FFQ was completed. One alcoholic drink was considered to be 355 mL of beer, 148 mL of wine, or 44 mL of spirits, with each drink representing ~14 g of alcohol. The relation between alcohol consumption and colorectal adenomas was not linear, so appropriate dummy variables for a 4-category alcohol variable were created and utilized in logistic regression models. These 4 categories were: 1) abstainers (0 drinks/wk); 2) light drinkers (>0 and <7 drinks/wk); 3) moderate drinkers (7 to <14 drinks/wk); and 4) heavy drinkers (≥ 14 drinks/wk).

Statistical analyses. The Student's *t* test and the chi-square test were performed for the statistical comparison of means and proportions among groups, respectively. Multivariate analyses were performed using logistic regression to assess the relation between dietary patterns (by cluster) and case-control status, while adjusting for covariates age, race, sex, BMI, NSAID use, smoking, and alcohol consumption. All data were entered into and analyzed using Stata 8.2 statistical software (STATA). A *P*-value of <0.05 was considered significant for all situations.

Results

Demographics. Age and racial distribution were similar in the cases and the controls (Table 1). However, there were significant differences in many other baseline characteristics. Men represented 59% of the cases compared with 39% of the controls ($P < 0.001$). Cases had a higher mean BMI ($P = 0.015$) and had significantly more smoking exposure ($P = 0.047$) compared with controls. Regular NSAID use over the past 5 y did not differ between cases and controls. Individuals with adenomas consumed more alcohol compared with controls ($P = 0.002$). Cases tended to consume more total energy than controls ($P = 0.145$).

Dietary patterns without energy adjustment. A comparison of nonenergy-adjusted mean Z-scores for each of the 18 dietary food groups showed little evidence for differences between the cases and controls. Only increased potato ($P < 0.001$) and beef/pork/lamb ($P = 0.011$) consumption were found to be associated with an increase in the odds of having had an adenoma on colonoscopy (Table 2). Decreased odds of having an adenoma was not associated with increased consumption of any of the food groups.

The data were then clustered into 3 nonoverlapping groups based on the Z-scores for the 18 food groups (Fig. 1A). Cluster 1 ($n = 326$) yielded uniformly low consumption of all food groups; Cluster 2 ($n = 49$) yielded uniformly high consumption of all food groups; and Cluster 3 ($n = 270$) yielded uniformly average consumption of all food groups. There was a dramatic difference in mean energy consumption among the 3 clusters. The mean daily energy intake was 1369 kcal (5731 kJ) for

⁴ Abbreviations used: NCI, National Cancer Institute; NSAID, nonsteroidal antiinflammatory drugs; OR, odds ratio.

TABLE 1 Selected characteristics of participants with and without a colorectal adenoma^{1,2}

Characteristic	0 Adenomas, n = 466	≥1 Adenoma, n = 179	P-value
Age, y	55.8 ± 0.5	57.1 ± 0.7	0.134
<39, %	5	3	
40–49, %	18	13	
50–59, %	42	47	
60–69, %	26	24	
>70, %	9	13	
Sex, % male	39.1	59.1	<0.001
Race, % white	79.0	81.2	0.507
BMI, kg/m ²	27.1 ± 0.3	28.3 ± 0.4	0.015
Smoking, y	8.3 ± 0.6	10.8 ± 1.1	0.047
Regular NSAID use in past 5 y, %	53.2	49.7	0.417
Energy consumption, kJ/d	8185 ± 176	8660 ± 323	0.145
Alcohol, ³ %			
Abstainers	30.0	33.0	
>0 and <7 drinks/wk	50.0	36.9	
7 to <14 drinks/wk	12.9	15.1	
≥14 drinks/wk	7.1	15.1	

¹ Results are means ± SE for continuous variables and percent for categorical variables.

² P-values for differences in means were determined by t test and differences in proportions were determined by chi-squared test.

³ One alcoholic drink was considered to be 355 mL of beer, 148 mL of wine, or 44 mL of spirits, with each drink representing ~14 g alcohol.

Cluster 1, 4142 kcal (17,341 kJ) for Cluster 2, and 2328 kcal (9746 kJ) for Cluster 3. The unadjusted proportion of individuals who had an adenoma did not differ among the 3 clusters. The probability of having an adenoma was 25% for Cluster 1, 31% for Cluster 2, and 30% for Cluster 3.

Energy-adjusted dietary patterns. After adjusting for total energy intake, several food groups were related to the presence

TABLE 2 Intake of food items and groups among participants with and without a colorectal adenoma^{1,2}

Variable	Controls, n = 466	Cases, n = 179	P-value
Whole grains, servings/d	1.3 ± 0.9	1.2 ± 0.8	0.251
Vegetables, servings/d	4.3 ± 2.4	4.3 ± 2.4	0.916
Green vegetables, servings/d	0.6 ± 0.8	0.6 ± 0.7	0.542
Yellow vegetables, servings/d	0.3 ± 0.4	0.3 ± 0.4	0.468
Beans/peas, servings/d	0.1 ± 0.2	0.1 ± 0.2	0.853
Potatoes, servings/d	0.6 ± 0.6	0.8 ± 0.7	<0.001
Other starches, servings/d	0.4 ± 0.3	0.4 ± 0.3	0.790
Tomato, servings/d	0.5 ± 0.6	0.5 ± 0.4	0.495
Other vegetables, servings/d	1.6 ± 1.0	1.6 ± 1.0	0.392
Total fruits, servings/d	3.0 ± 2.1	2.8 ± 2.1	0.187
Citrus, melon, and berry, servings/d	1.4 ± 1.3	1.2 ± 1.2	0.170
Other fruits, servings/d	1.6 ± 1.2	1.5 ± 1.3	0.356
Dairy, servings/d	1.4 ± 1.3	1.3 ± 1.1	0.223
Poultry/fish, g/d	112 ± 77	122 ± 73	0.135
Beef/pork/lamb, g/d	44 ± 41	53 ± 44	0.011
Franks/lunchmeats, g/d	17 ± 21	19 ± 17	0.313
Discretionary fat, g/d	56 ± 31	59 ± 34	0.235
Added sugar, g/d	63 ± 67	62 ± 52	0.814

¹ Values are means ± SD.

² Servings for fruit and vegetable intake were based on dietary guidance from the USDA, as specified in the Food Guide Pyramid (35).

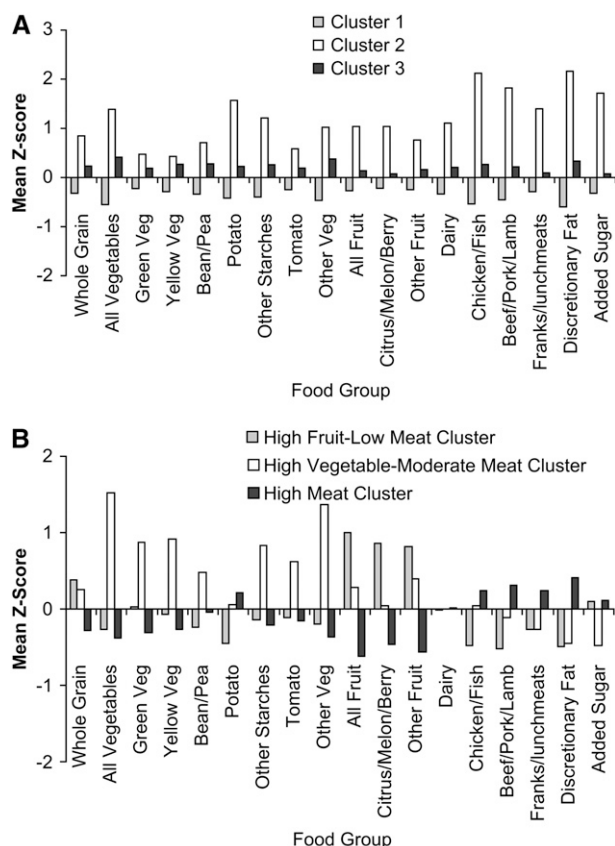


Figure 1 Mean Z-score by dietary cluster for the 18 nonenergy-adjusted food groups (A) and the 18 energy-adjusted food groups (B).

of an adenoma on colonoscopy. Increased consumption of whole grain products ($P = 0.021$), total fruits ($P = 0.014$), citrus/melon/berry fruits ($P = 0.009$), and dairy products ($P = 0.004$) were all associated with a decrease in the odds of having an adenoma. Increased consumption of potatoes ($P < 0.001$) and beef/pork/lamb ($P = 0.005$) were still associated with an increased probability of having an adenoma, whereas increased consumption of poultry/fish tended to be associated ($P = 0.070$) with increased odds of having an adenoma.

Cluster analysis was repeated using the Z-scores of the energy-adjusted food groups to produce 3 nonoverlapping clusters. Differences in mean energy intake among the resulting 3 clusters were much smaller than those observed for the clusters derived from unadjusted intakes (Table 3). These 3 clusters had a much different pattern compared with the clusters produced without adjusting for total energy consumption (Fig. 1B). The high fruit-low meat cluster ($n = 181$) had high consumption of total fruits (including citrus/melon/berry fruits) and whole grain products with slightly below-average vegetable consumption and significantly lower consumption of all animal meats (chicken/fish, beef/pork/lamb, and franks/luncheon meats). The high fruit-low meat cluster also had low intake of discretionary fats (typically items such as salad dressings, mayonnaise, etc.) but added a moderate amount of sugar to their diet. The high vegetable-moderate meat cluster ($n = 119$) consumed high amounts of total vegetables, including both green and yellow vegetables and beans and peas. The high vegetable-moderate meat cluster also consumed above-average amounts of whole grain products and starches, but they consumed an average amount of fruit and meat. This group had low consumption of both discretionary fat and supplemental sugar in their diet.

TABLE 3 Selected characteristics of participants by energy-adjusted dietary cluster^{1,2}

Characteristic	High vegetable-			P-value
	High fruit-low meat cluster, n = 181	moderate meat cluster, n = 119	High meat cluster, n = 345	
Age, y	58.1 ± 0.7	58.2 ± 0.9	54.7 ± 0.5	<0.001
Sex, % male	31	35	54	<0.001
Race, % white	76	90	81	0.004
BMI, kg/m ²	26.9 ± 0.4	26.9 ± 0.5	27.7 ± 0.3	0.169
Smoking, y	6.1 ± 1.0	8.6 ± 1.2	10.6 ± 0.7	<0.001
Regular NSAID use in past 5 y, %	51	50	54	0.620
Energy consumption, kJ/d	7393 ± 284	6938 ± 350	9236 ± 206	<0.001
Daily fiber intake, g/d	21.2 ± 0.7	24.2 ± 0.8	19.5 ± 0.5	<0.001
Alcohol, %				
Abstainers	39	21	30	
>0 and <7 drinks/wk	45	55	44	
7 to <14 drinks/wk	11	21	12	
≥14 drinks/wk	4	3	14	

¹ Results are means ± SE for continuous variables and percent for categorical variables.

² P-values for differences in means were determined by *t* test and differences in proportions were determined by chi-squared test.

The high meat cluster ($n = 345$) was the largest of the 3 clusters and represented a more typical American diet. This group had below-average consumption of whole grain products, all vegetables (except potatoes), and fruits. The high meat cluster had above-average consumption of all the major meat categories and this cluster also had above-average consumption of discretionary fat and added sugar. Mean energy intake in the high meat cluster was higher than that of the high fruit-low meat cluster and high vegetable-moderate meat cluster. In an unadjusted analysis, the clusters had a significant effect on the odds of having an adenoma. In the high fruit-low meat cluster, 18% had an adenoma, whereas 30% in the high vegetable-moderate meat cluster had an adenoma, and 32% in the high meat cluster had an adenoma. The overall difference was significant among the 3 clusters ($P = 0.002$).

The 3 dietary clusters differed in other variables that could affect adenoma risk. The high meat cluster was significantly younger than the other 2 clusters and had a greater smoking exposure history (Table 3). Additionally, over one-half of the individuals in the high meat cluster were men, whereas males comprised only one-third of both the high fruit-low meat cluster and the high vegetable-moderate meat cluster. The high meat cluster also had a higher proportion of individuals who consumed 14 or more drinks per week. The clusters were similar with respect to BMI and regular NSAID use over the past 5 y. Although whites made up the vast majority of individuals in all 3 clusters, the high fruit-low meat cluster had a higher proportion of nonwhites (predominantly African-Americans) compared with the high vegetable-moderate meat cluster.

Multivariate analysis. Because there were significant differences in baseline characteristics between the cases and controls, we performed logistic regression to control for these potential confounders. Smoking (years smoked), age, BMI, race (white or nonwhite), NSAID use, sex, and alcohol consumption were

included in the logistic regression model. After adjustment, the high vegetable-moderate meat cluster had significantly increased odds of having an adenoma (odds ratio [OR] 2.17; [95% CI] 1.20–3.90), as did the high meat cluster (OR: 1.70; [95% CI] 1.04–2.80) compared with the high fruit-low meat cluster. These results did not differ from the results of the unadjusted analysis (Table 4). The adjusted probability of having an adenoma was 19% for the high fruit-low meat cluster, 33% for the high vegetable-moderate meat cluster, and 28% for the high meat cluster. The high vegetable-moderate meat cluster and the high meat cluster did not differ.

Discussion

The relation between diet and colorectal neoplasia (cancers or adenomas) has been widely investigated, yet the literature is inconclusive. Until recently, most of the investigation regarding diet and colorectal neoplasia involved the study of 1 or a few specific dietary components. Food groups or items, such as fruit and vegetable consumption, have been investigated. The results have often been conflicting, even in prospective studies (5–7,9–13). The conflicting results likely indicate that this approach (which assumes that only 1 or a few dietary food groups are responsible for a significant change in the risk of developing colorectal adenomas and cancers) may have been too simplistic. Because of the development and acceptance of analytic techniques such as cluster analysis, we are able to make some assessment regarding the role of overall dietary patterns on the risk of various disease outcomes, including colorectal cancers and adenomas. The purpose of this study was to utilize cluster analysis to investigate what dietary patterns were associated with an increased risk of having a colorectal adenoma and to assess the effect of adjusting for total energy intake before creating clusters.

When clusters were created without adjusting for total energy consumption, the individuals essentially clustered by total energy intake. Cluster 1 had the lowest consumption for all 18 food groups, with a mean daily energy intake of 1369 kcal (5731 kJ). Cluster 2 had the highest consumption of all 18 food groups and the mean daily energy intake was 4142 kcal (17,341 kJ). Cluster 3 had an intermediate level of consumption of all 18 food groups and had a mean daily energy intake of 2328 kcal (9746 kJ). It is obvious that that while these 3 clusters clearly represent unique groups, there is essentially no variation in the pattern with the various food groups. Using these clusters in multivariate modeling would be similar to modeling based on 3 categories of total energy intake.

Because the exact relation among energy, specific food groups, and specific health outcomes is not known, analysis with either factor or cluster analysis has proceeded in a non-standard manner. Some authors have energy-adjusted dietary variables before clustering (31), whereas others have not done

TABLE 4 OR of having a colorectal adenoma by dietary cluster

Cluster	Unadjusted OR [95% CI]	Adjusted OR [95% CI] ¹
High fruit-low meat cluster	1.00	1.00
High vegetable-moderate meat cluster	2.02 (1.17–3.49)	2.17 (1.20–3.90)
High meat cluster	2.21 (1.42–3.44)	1.70 (1.04–2.80)

¹ OR adjusted for smoking, age, BMI, race (white or nonwhite), NSAID use, sex, and alcohol consumption.

so (22,24). Research using factor analysis is similar, with some authors controlling for energy intake in the modeling stages of their analysis (27), whereas others have not controlled for energy intake (25). Although a recent study suggested that results from a study where clusters are derived from energy-adjusted variables may be less interpretable (32), adjusting for total energy produced more meaningful results in this study. The nonenergy-adjusted clusters produced 3 groups with similar adjusted probabilities of having an adenoma on colonoscopy. However, after energy adjustment, 3 clusters were produced and there was a significant increase in the odds of having an adenoma for both the high meat cluster and the high vegetable-moderate meat cluster compared with the high fruit-low meat cluster. The high fruit-low meat cluster actually had an intermediate energy intake compared with the other 2 groups, despite having the lowest probability of having an adenoma.

The findings in this study indicate that a diet high in fruit consumption and low in meat consumption may be protective against the development of colorectal adenomas, even when compared with a group that consumes a large amount of vegetables. There has been an extensive investigation into the role of fruit, vegetable, and meat consumption on colorectal neoplasms. Although many studies have demonstrated a protective effect of fruit and vegetable consumption (5,7,9), several authors have found no association between fruit and vegetable consumption and the risk of having or developing a colorectal neoplasm (10–13). There is more consistent evidence that red meat consumption is associated with an increased risk of colorectal adenomas and cancers (2,5–8). However, as shown in this study, individuals who eat above-average amounts of red meat are also more likely to consume above-average amounts of other meats and low amounts of fruits, vegetables, and whole grains.

The high vegetable-moderate meat cluster in this study also had a moderate amount of meat consumption. Therefore, the relative increased probability of having an adenoma for the high vegetable-moderate meat cluster may be the result of increased meat intake compared with the high fruit-low meat cluster. The increased consumption of meats (both the chicken/fish and the beef/pork/lamb food groups) by the high vegetable-moderate meat cluster compared with the high fruit-low meat cluster may have obscured a possible protective effect of vegetable consumption. A recent report by Michels et al. (33) supported a significant protective effect of fruit, but not vegetable, consumption in the Nurses' Health Study. The authors highlight the fact that vegetables, particularly potatoes, are often consumed with meat products. Indeed, in simple bivariate analysis for the subjects in this study, energy-adjusted potato consumption was associated with an increased probability of having an adenoma. However, consumption of green vegetables, yellow vegetables, beans, peas, tomatoes, and other vegetables was the highest in the high vegetable-moderate meat cluster. Individuals who primarily consume meats and vegetables appear to represent a distinct group, whose risk of a colorectal adenoma is similar to the individuals in the high meat cluster that consumed low amounts of both fruits and vegetables.

Interestingly, in unadjusted analyses, individuals in the high vegetable-moderate meat cluster and the high meat cluster were twice as likely to have had an adenoma compared with those in high fruit-low meat cluster. After adjusting for known risk factors for colorectal adenomas (sex, race, alcohol, smoking, BMI, and NSAID use), the adjusted OR for the high vegetable-moderate meat cluster was marginally increased, whereas the adjusted OR for the high meat cluster was slightly decreased.

An issue that cannot be resolved in a study of this nature is that of residual confounding, although the change in the OR for the high meat cluster and the high vegetable-moderate meat cluster after adjusting for confounders is small. It is possible that there are other variables that are associated with the dietary clusters and colorectal adenomas that were not measured as part of this study and, therefore, could not be adjusted for in analysis.

The results of this study should be interpreted with some caution because of certain limitations of the study design. First, dietary and lifestyle questionnaires were completed after the colonoscopy had been performed. By this time, participants were aware of their diagnosis of a colorectal adenoma and this may have contributed to recall bias. Although it is reasonable to expect increased recall related to meat intake, it is less clear why recall bias would also lead to increased reporting of vegetable intake. There is also conflicting evidence about whether the NCI FFQ provides good estimates of energy intake, and attenuation of associations may result from this inaccuracy in intake assessment (29,30,34). It is important to highlight that the 3 clusters have other unique characteristics beyond fruit, vegetable, and meat consumption. In addition to being associated with high fruit and low meat consumption, the high fruit-low meat cluster was also associated with low consumption of discretionary fat and potatoes. Although the consumption of fruits, vegetables, and meat was the primary focus of this study, other characteristics of the dietary patterns may affect risk. One final limitation of the study is the use of colorectal adenomas as the primary outcome. Because adenomas are the precursors for the vast majority of colorectal cancers, it is frequently used as the primary outcome when assessing risk factors for colorectal carcinogenesis. However, because carcinogenesis is a multi-step process, it should be noted that the dietary variables that influence the development of colorectal adenomas may differ from those that promote the progression to cancer.

In conclusion, this study demonstrated a significant association between dietary patterns and the risk of having an adenoma on colonoscopy using cluster analysis after adjusting for total energy consumption. There appears to be a protective effect of eating a diet high in fruits and low in meat. A diet high in meat consumption is associated with an increased risk of having a colorectal adenoma. The results of this study do not indicate a protective effect of vegetable consumption, although this relation may be affected by the moderate amount of meat consumption seen in the high vegetable-moderate meat cluster. This study also demonstrated the importance of adjusting for total energy intake prior to performing cluster analysis and supports the concept that it is the relative proportion of dietary components that influences the development of colorectal neoplasms.

Literature Cited

1. Boutron-Ruault MC, Senesse P, Meance S, Belghiti C, Faivre J. Energy intake, body mass index, physical activity, and the colorectal adenoma-carcinoma sequence. *Nutr Cancer*. 2001;39:50–7.
2. Singh PN, Fraser GE. Dietary risk factors for colon cancer in a low-risk population. *Am J Epidemiol*. 1998;148:761–74.
3. Erhardt JG, Kreichgauer HP, Meisner C, Bode JC, Bode C. Alcohol, cigarette smoking, dietary factors and the risk of colorectal adenomas and hyperplastic polyps: a case control study. *Eur J Nutr*. 2002;41:35–43.
4. Jedrychowski W, Steindorf K, Popiela T, Wahrendorf J, Tobiasz-Adameczyk B, Kulig J, Penar A. Alcohol consumption and the risk of colorectal cancer at low levels of micronutrient intake. *Med Sci Monit*. 2002;8:CR357–63.

5. Giovannucci E, Stampfer MJ, Colditz G, Rimm EB, Willett WC. Relationship of diet to risk of colorectal adenoma in men. *J Natl Cancer Inst.* 1992;84:91-8.
6. Flood A, Velie EM, Sinha R, Chatterjee N, Lacey JV Jr, Schairer C, Schatzkin A. Meat, fat, and their subtypes as risk factors for colorectal cancer in a prospective cohort of women. *Am J Epidemiol.* 2003;158:59-68.
7. Mathew A, Peters U, Chatterjee N, Kulldorff M, Sinha R. Fat, fiber, fruits, vegetables, and risk of colorectal adenomas. *Int J Cancer.* 2004;108:287-92.
8. Seow A, Quah SR, Nyam D, Straughan PT, Chua T, Aw TC. Food groups and the risk of colorectal carcinoma in an Asian population. *Cancer.* 2002;95:2390-6.
9. Sandler RS, Lyles CM, Peipins LA, McAuliffe CA, Woosley JT, Kupper LL. Diet and risk of colorectal adenomas: macronutrients, cholesterol, and fiber. *J Natl Cancer Inst.* 1993;85:884-91.
10. Flood A, Velie EM, Chatterjee N, Subar AF, Thompson FE, Lacey JV Jr, Schairer C, Troisi R, Schatzkin A. Fruit and vegetable intakes and the risk of colorectal cancer in the Breast Cancer Detection Demonstration Project follow-up cohort. *Am J Clin Nutr.* 2002;75:936-43.
11. Hung HC, Joshipura KJ, Jiang R, Hu FB, Hunter D, Smith-Warner SA, Colditz GA, Rosner B, Spiegelman D, et al. Fruit and vegetable intake and risk of major chronic disease. *J Natl Cancer Inst.* 2004;96:1577-84.
12. Michels KB, Edward G, Joshipura KJ, Rosner BA, Stampfer MJ, Fuchs CS, Colditz GA, Speizer FE, Willett WC. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *J Natl Cancer Inst.* 2000;92:1740-52.
13. Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt R, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *N Engl J Med.* 2000;342:1149-55.
14. Cantwell MM, Forman MR, Albert PS, Snyder K, Schatzkin A, Lanza E. No association between fatty acid intake and adenomatous polyp recurrence in the polyp prevention trial. *Cancer Epidemiol Biomarkers Prev.* 2005;14:2059-60.
15. Larsson SC, Bergkvist L, Wolk A. High-fat dairy food and conjugated linoleic acid intakes in relation to colorectal cancer incidence in the Swedish Mammography Cohort. *Am J Clin Nutr.* 2005;82:894-900.
16. Kampman E, Slattery ML, Caan B, Potter JD. Calcium, vitamin D, sunshine exposure, dairy products and colon cancer risk (United States). *Cancer Causes Control.* 2000;11:459-66.
17. Satia-Abouta J, Galanko JA, Martin CF, Ammerman A, Sandler RS. Food groups and colon cancer risk in African-Americans and Caucasians. *Int J Cancer.* 2004;109:728-36.
18. Fung T, Hu FB, Fuchs C, Giovannucci E, Hunter DJ, Stampfer MJ, Colditz GA, Willett WC. Major dietary patterns and the risk of colorectal cancer in women. *Arch Intern Med.* 2003;163:309-14.
19. Kim MK, Sasaki S, Otani T, Tsugane S. Dietary patterns and subsequent colorectal cancer risk by subsite: a prospective cohort study. *Int J Cancer.* 2005;115:790-8.
20. Terry P, Hu FB, Hansen H, Wolk A. Prospective study of major dietary patterns and colorectal cancer risk in women. *Am J Epidemiol.* 2001;154:1143-9.
21. Millen BE, Quatromoni PA, Copenhafer DL, Demissie S, O'Horo CE, D'Agostino RB. Validation of a dietary pattern approach for evaluating nutritional risk: the Framingham Nutrition Studies. *J Am Diet Assoc.* 2001;101:187-94.
22. Newby PK, Muller D, Tucker KL. Associations of empirically derived eating patterns with plasma lipid biomarkers: a comparison of factor and cluster analysis methods. *Am J Clin Nutr.* 2004;80:759-67.
23. Monda KL, Popkin BM. Cluster analysis methods help to clarify the activity-BMI relationship of Chinese youth. *Obes Res.* 2005;13:1042-51.
24. Villegas R, Salim A, Collins MM, Flynn A, Perry IJ. Dietary patterns in middle-aged Irish men and women defined by cluster analysis. *Public Health Nutr.* 2004;7:1017-24.
25. Cottet V, Bonithon-Kopp C, Kronborg O, Santos L, Andreatta R, Boutron-Ruault MC, Faivre J. Dietary patterns and the risk of colorectal adenoma recurrence in a European intervention trial. *Eur J Cancer Prev.* 2005;14:21-9.
26. Mizoue T, Yamaji T, Tabata S, Yamaguchi K, Shimizu E, Mineshita M, Ogawa S, Kono S. Dietary patterns and colorectal adenomas in Japanese men: the Self-Defense Forces Health Study. *Am J Epidemiol.* 2005;161:338-45.
27. Dixon LB, Balder HF, Virtanen MJ, Rashidkhani B, Mannisto S, Krogh V, van Den Brandt PA, Hartman AM, Pietinen P, et al. Dietary patterns associated with colon and rectal cancer: results from the Dietary Patterns and Cancer (DIETSCAN) Project. *Am J Clin Nutr.* 2004;80:1003-11.
28. Chen H, Ward MH, Graubard BI, Heineman EF, Markin RM, Potischman NA, Russell RM, Weisenburger DD, Tucker KL. Dietary patterns and adenocarcinoma of the esophagus and distal stomach. *Am J Clin Nutr.* 2002;75:137-44.
29. Subar AF, Thompson FE, Kipnis V, Midthune D, Hurwitz P, McNutt S, McIntosh A, Rosenfeld S. Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires: the Eating at America's Table Study. *Am J Epidemiol.* 2001;154:1089-99.
30. Thompson FE, Subar AF, Brown CC, Smith AF, Sharbaugh CO, Jobe JB, Mittl B, Gibson JT, Ziegler RG. Cognitive research enhances accuracy of food frequency questionnaire reports: results of an experimental validation study. *J Am Diet Assoc.* 2002;102:212-25.
31. Millen BE, Quatromoni PA, Pencina M, Kimokoti R, Nam BH, Cobain S, Kozak W, Appugliese DP, Ordovas J, et al. Unique dietary patterns and chronic disease risk profiles of adult men: the Framingham nutrition studies. *J Am Diet Assoc.* 2005;105:1723-34.
32. Bailey RL, Gutschall MD, Mitchell DC, Miller CK, Lawrence FR, Smiciklas-Wright H. Comparative strategies for using cluster analysis to assess dietary patterns. *J Am Diet Assoc.* 2006;106:1194-200.
33. Michels KB, Giovannucci E, Chan AT, Singhania R, Fuchs CS, Willett WC. Fruit and vegetable consumption and colorectal adenomas in the Nurses' Health Study. *Cancer Res.* 2006;66:3942-53.
34. Kipnis V, Subar AF, Midthune D, Freedman LS, Ballard-Barbash R, Troiano RP, Bingham S, Schoeller DA, Schatzkin A, et al. Structure of dietary measurement error: results of the OPEN biomarker study. *Am J Epidemiol.* 2003;158:14-21.
35. USDA Center for Nutrition Policy and Promotion. Alexandria (VA): [cited 2000 Sept]. Available from: <http://mypyramid.gov>.