



Online article and related content  
current as of December 14, 2009.

## Nut, Corn, and Popcorn Consumption and the Incidence of Diverticular Disease

Lisa L. Strate; Yan L. Liu; Sapna Syngal; et al.

*JAMA*. 2008;300(8):907-914 (doi:10.1001/jama.300.8.907)

<http://jama.ama-assn.org/cgi/content/full/300/8/907>

Correction

[Contact me if this article is corrected.](#)

Citations

[This article has been cited 3 times.](#)  
[Contact me when this article is cited.](#)

Topic collections

Men's Health; Men's Health, Other; Diet; Gastroenterology; Gastrointestinal  
Diseases  
[Contact me when new articles are published in these topic areas.](#)

Subscribe

<http://jama.com/subscribe>

Permissions

[permissions@ama-assn.org](mailto:permissions@ama-assn.org)  
<http://pubs.ama-assn.org/misc/permissions.dtl>

Email Alerts

<http://jamaarchives.com/alerts>

Reprints/E-prints

[reprints@ama-assn.org](mailto:reprints@ama-assn.org)

# Nut, Corn, and Popcorn Consumption and the Incidence of Diverticular Disease

Lisa L. Strate, MD, MPH

Yan L. Liu, MS

Sapna Syngal, MD, MPH

Walid H. Aldoori, MD, MPA, ScD

Edward L. Giovannucci, MD, ScD

**D**IVERTICULAR DISEASE IS A COMMON and costly digestive disorder in Western countries. One-third of the US population will develop diverticulosis by the age of 60 years and two-thirds by the age of 85 years.<sup>1-3</sup> Complications, including diverticulitis and diverticular bleeding, occur in an estimated 10% to 35% of persons with diverticulosis.<sup>4,5</sup> Treatment of these complications frequently necessitates hospitalization and invasive procedures, including surgery. At least \$2.4 billion in direct health care costs and 3400 deaths are attributed to diverticular disease in the United States each year,<sup>6,7</sup> and the medical and economic impact of this disorder is likely to increase substantially as the population ages.

Historically, physicians have advised individuals with diverticular disease to avoid nuts, seeds, popcorn, corn, and other high-residue foods.<sup>5,8,9</sup> This recommendation stems from the theory that luminal trauma is a causal mechanism for both diverticulitis and diverticular bleeding.<sup>10-12</sup> Stool may lodge within a diverticulum, obstruct the neck, or abrade the mucosa and precipitate inflammation or bleeding.<sup>1,13</sup> Nuts, seeds, popcorn, and corn are presumed to be particularly likely to abrade the mucosa or to lodge within small diverticula.<sup>5</sup> However, the biological mechanisms responsible for diverticu-

**Context** Patients with diverticular disease are frequently advised to avoid eating nuts, corn, popcorn, and seeds to reduce the risk of complications. However, there is little evidence to support this recommendation.

**Objective** To determine whether nut, corn, or popcorn consumption is associated with diverticulitis and diverticular bleeding.

**Design and Setting** The Health Professionals Follow-up Study is a cohort of US men followed up prospectively from 1986 to 2004 via self-administered questionnaires about medical (biennial) and dietary (every 4 years) information. Men reporting newly diagnosed diverticulosis or diverticulitis were mailed supplemental questionnaires.

**Participants** The study included 47 228 men aged 40 to 75 years who at baseline were free of diverticulosis or its complications, cancer, and inflammatory bowel disease and returned a food-frequency questionnaire.

**Main Outcome Measures** Incident diverticulitis and diverticular bleeding.

**Results** During 18 years of follow-up, there were 801 incident cases of diverticulitis and 383 incident cases of diverticular bleeding. We found inverse associations between nut and popcorn consumption and the risk of diverticulitis. The multivariate hazard ratios for men with the highest intake of each food (at least twice per week) compared with men with the lowest intake (less than once per month) were 0.80 (95% confidence interval, 0.63-1.01; *P* for trend = .04) for nuts and 0.72 (95% confidence interval, 0.56-0.92; *P* for trend = .007) for popcorn. No associations were seen between corn consumption and diverticulitis or between nut, corn, or popcorn consumption and diverticular bleeding or uncomplicated diverticulosis.

**Conclusions** In this large, prospective study of men without known diverticular disease, nut, corn, and popcorn consumption did not increase the risk of diverticulosis or diverticular complications. The recommendation to avoid these foods to prevent diverticular complications should be reconsidered.

*JAMA.* 2008;300(8):907-914

www.jama.com

lar complications remain poorly understood. Aside from luminal trauma, potential inciting factors include elevated colonic pressures, compromised colon wall integrity, and altered bacterial flora.<sup>14-20</sup> To our knowledge, there is no evidence to support consumption of nuts, corn, popcorn, or seeds as a risk factor.

Compelling evidence suggests that nuts are an important part of a healthy diet. Nuts are high in protein, unsaturated fats, fiber, vitamins, minerals, and other micronutrients. A diet high in nuts may protect against many com-

mon diseases, including cardiovascular disease, diabetes, cancer of the colon and prostate, and cholelithiasis.<sup>21-32</sup>

**Author Affiliations:** University of Washington School of Medicine, Seattle (Dr Strate); Division of Gastroenterology, Department of Medicine, Harborview Medical Center, Seattle (Dr Strate); Departments of Nutrition (Ms Liu and Dr Giovannucci) and Epidemiology (Dr Giovannucci), Harvard School of Public Health, Boston, Massachusetts; Harvard Medical School, Boston (Drs Syngal and Giovannucci); Division of Gastroenterology (Dr Syngal) and Channing Laboratory (Dr Giovannucci), Department of Medicine, Brigham and Women's Hospital, Boston; Division of Population Sciences, Dana Farber Cancer Institute, Boston (Dr Syngal); and Wyeth Consumer Healthcare Inc, Mississauga, Ontario, Canada (Dr Aldoori).

**Corresponding Author:** Lisa L. Strate, MD, MPH, Harborview Medical Center, 325 Ninth Ave, Box 359773, Seattle, WA 98104 (lstrate@u.washington.edu).

The potential health benefits of nut consumption paired with the large number of individuals with diverticulosis makes it timely and important to study the long-held belief that eating nuts and other high-residue foods is associated with diverticular complications. We examined the association between nut, corn, and popcorn consumption and complicated diverticular disease in a large prospective cohort.

## METHODS

### Study Population

The Health Professionals Follow-up Study is a prospective cohort study initiated in 1986 when 51 529 male dentists, veterinarians, pharmacists, optometrists, osteopathic physicians, and podiatrists aged 40 to 75 years returned a self-administered questionnaire covering diet, lifestyle, and medical history. Follow-up questionnaires have been mailed biennially to update information on newly diagnosed conditions and potential risk factors for disease and every 4 years to assess diet via a semiquantitative, validated food-frequency questionnaire. The mean follow-up rate is greater than 90%.

Men who reported a diagnosis of diverticulosis or its complications ( $n=224$ ), cancer other than nonmelanoma skin cancer ( $n=2000$ ), or inflammatory bowel disease ( $n=475$ ) at baseline in 1986 were excluded from the analysis. In addition, we excluded men with mean daily intakes of food outside the range of 800 to 4200 kcal ( $n=6$ ) and men who failed to return the food-frequency questionnaire ( $n=1596$ ). After these baseline exclusions, the study cohort consisted of 47 228 men who were followed up from 1986 to 2004.

### Assessment of Diverticular Complications

The primary end points were incident diverticulitis and diverticular bleeding. Beginning in 1990, biennial follow-up questionnaires assessed whether diverticulosis or diverticulitis had been diagnosed in the preceding 2 years. Supplemental questionnaires were sent to all participants reporting diverticular disease. Response rates have been

84% or greater. Five questions pertaining to the diagnosis of diverticular disease were addressed: month and year of diagnosis; procedures done to confirm the diagnosis; symptoms leading to the detection of diverticular disease; diet modification prior to the date of diagnosis as a result of symptoms; and treatment received. Trained abstractors entered data, including information contained in any free text. All questions arising during data abstraction, particularly those pertaining to free text, were reviewed with a study investigator (L.L.S.) who was blinded to exposure status.

End point definitions were based on responses to the supplemental questionnaire and were used to refine the self-report of diverticular complications. Diverticulitis was defined as abdominal pain attributed to diverticular disease and 1 of the following criteria: (1) complicated by fistula, abscess, perforation, or obstruction; (2) treated with antibiotics, hospitalization, or surgery; or (3) described as severe or acute or presenting with fever, requiring medication, or evaluated with computed tomography. Diverticular bleeding was defined as rectal bleeding attributed to diverticular disease and 1 of the following criteria: (1) requiring hospitalization, intravenous fluids, blood transfusion, angiography, nuclear medicine scanning, or surgery; (2) described as profuse; or (3) without other potential gastrointestinal, rectal, or anal sources in men whose bleeding was not evaluated as part of a routine endoscopy or barium study. The first 2 criteria for diverticulitis and diverticular bleeding were considered the most stringent and were used in sensitivity analyses for the end point definitions. These definitions were intended to identify the spectrum of patients with diverticular complications, including those managed in the outpatient setting (which make up a majority of patients with uncomplicated diverticulitis).<sup>8</sup> Men who reported asymptomatic diverticulosis or nonspecific symptoms such as pain or change in bowel habits but did not meet these criteria were categorized as uncomplicated diverticulosis.

A total of 179 medical records from men reporting diverticular disease on the 1990 and 1992 questionnaires were reviewed (by L.L.S.) to assess the validity of self-reporting. The record review was blinded to self-report. Diverticular disease (complicated or uncomplicated) was confirmed in 97%. The diagnosis in the medical record matched the study end point definition in 85% of charts reviewed. Fifty percent of the uncorroborated cases had diverticulitis or diverticular bleeding on chart review but were classified as uncomplicated disease based on self-report.

### Assessment of Nut, Corn, and Popcorn Consumption

Dietary information was ascertained from a semiquantitative food-frequency questionnaire that was validated in this cohort.<sup>33</sup> Participants were asked to indicate how frequently on average they consumed a standard portion of 131 specified food items during the previous year according to 9 response categories (never or less than once a month, 1-3 times per month, once per week, 2-4 times per week, 5-6 times per week, once a day, 2-3 times daily, 4-5 times daily, more than 6 times a day). Nut consumption was ascertained via questions regarding the average frequency of consumption of a 1-ounce serving of peanuts, walnuts, or other nuts. Walnuts were added as a distinct category of nuts in 1998. The food questionnaire also separately assessed consumption of fat-free or light popcorn and regular popcorn (1 standard unit was equivalent to 3 cups). Corn consumption was documented in a single question (a typical serving was equal to 1 ear or one-half cup of kernels). Simple updating was used to assess dietary information such that the food questionnaire immediately preceding the follow-up interval of interest was used in the analysis. The mean time interval between dietary assessment and study end point was 28.4 months. Total nut and popcorn consumption were calculated as the sum of the nut and popcorn items, respectively. Frequency categories for total nut, corn, and popcorn consumption were collapsed into 4 categories: less than once per month, 1 to 3 times per month, once per week,

and 2 or more times per week. Categories were created for missing nut, corn, and popcorn data. Data on consumption was missing at baseline for 412 participants (0.9%) for nuts, 767 participants (1.6%) for corn, and 758 participants (1.6%) for popcorn.

### Assessment of Other Potential Risk Factors

We also assessed a number of dietary, lifestyle, and medical factors that have been implicated as risk factors for complicated or symptomatic diverticular disease in this cohort and/or in other studies.<sup>20,34-40</sup> These included red meat and total dietary fiber and fat intake, which were assessed on the semi-quantitative food-frequency questionnaires. Dietary fat and fiber amounts were calculated by multiplying the consumption frequency of a specified serving size by the corresponding nutrient content derived from food composition tables. Total fat and fiber consumption were adjusted for total energy intake using regression analysis.

We also considered physical activity as a potential risk factor. On biennial questionnaires, men were asked to indicate the average time spent each week engaged in any of 10 moderate to vigorous activities in addition to the number of flights of stairs climbed each day. Physical activity was summed and expressed in metabolic equivalent (MET) hours per week. (One MET is equivalent to 1 kcal of energy expended per kilogram of body weight per hour while at rest.) Current weight as reported on biennial questionnaires and height reported at baseline were used to calculate body mass index (weight in kilograms divided by height in meters squared). Current, regular use of nonsteroidal anti-inflammatory drugs including aspirin and acetaminophen was also assessed and updated every 2 years, as was cigarette smoking.

### Statistical Analysis

Person-years of follow-up accrued from the date of return of the 1986 baseline questionnaire to the month of the first diagnosis of diverticular disease (di-

verticulosis or a complication), death, or the end of follow-up (December 31, 2004). Men who reported a new diagnosis of diverticulitis, diverticular bleeding, uncomplicated diverticulosis, gastrointestinal cancer, or inflammatory bowel disease were censored at the date of diagnosis.

Cox proportional hazards models were employed to estimate the hazard ratio (HR) and 95% confidence interval (CI) for each study end point (diverticulitis and diverticular bleeding) adjusted for age (1-year intervals) and study period (2-year intervals).<sup>41</sup> Men in the highest intake category of nuts, corn, and popcorn were compared with men in the lowest category. Multivariate models were also developed to adjust for other known or potential risk factors for diverticular complications. Covariates included in the models included age, study period, total energy-adjusted fat intake (quintiles), total energy-adjusted fiber intake (quintiles), red meat intake (quintiles), physical activity level (quintiles), body mass index (6 categories), current use of nonsteroidal anti-inflammatory drugs (yes/no), current use of acetaminophen (yes/no), and current cigarette smoking (never, past, <15 cigarettes/d, ≥15 cigarettes/d). The Wald test was used to test for linear trend using the median value of each of the 4 intake categories as a continuous variable. The proportional hazards assumption was tested for nut, corn, and popcorn intake by creating interaction terms between the exposure and the time period and participant age; there were no significant departures ( $P > .05$  for all interaction terms).

All analyses were performed using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina). All analyses were 2-sided, and a  $P$  value of less than .05 was considered statistically significant. Return of the self-administered study questionnaire was regarded as informed consent. The institutional review boards of the Harvard School of Public Health and the Brigham and Women's Hospital approved the study protocol.

### RESULTS

We identified 801 incident cases of diverticulitis and 383 incident cases of diverticular bleeding during 730 446 person-years of follow-up. Baseline characteristics of the cohort categorized by nut, corn, and popcorn consumption and standardized for age are shown in TABLE 1. Twenty-seven percent of participants reported eating nuts at least twice per week. Corn and popcorn each were consumed at least twice a week in 15%. Consumption of less than 1 serving per month of nuts, corn, and popcorn was noted in 25%, 12%, and 36% of men, respectively. Participants in the highest category of nut consumption tended to be older and to consume more alcohol but were slightly more physically active than those in the lowest category. Compared with men with the lowest intake of corn, men with the highest intake generally consumed more fiber and red meat but less alcohol. Men who ate popcorn at least twice per week were, in general, younger, more likely to use analgesics, and more likely to be non-smokers than those who ate popcorn less than once per month.

Nut, corn, and popcorn consumption was not associated with an increased risk of complicated diverticular disease. Instead, we observed inverse relationships between nut and popcorn consumption and the risk of diverticulitis (TABLE 2). After adjustment for other known and potential risk factors for diverticular complications, the multivariate HRs for men with the highest intake of each food (at least twice per week) compared with men with the lowest intake (less than once per month) were 0.80 (95% CI, 0.63-1.01;  $P$  for trend = .04) for nuts and 0.72 (95% CI, 0.56-0.92;  $P$  for trend = .007) for popcorn. The population-attributable risks of developing incident diverticulitis associated with low consumption (less than 2 times per week compared with more than 2 times per week) were 6005 per 100 000 men for nuts and 6558 per 100 000 men for popcorn. Although the  $P$  for trends for the associations between increasing consumption of nuts and popcorn and the risk of diverticulitis were significant, the

patterns of the HRs across consumption categories did not indicate dose-response relationships (Table 2). No association was seen between corn consumption and diverticulitis. For diverticular bleeding, there were no significant associations observed for nut, corn, or popcorn consumption (TABLE 3). Compared with men with the lowest intake, the multivariate HRs for men with the highest intake were 1.08 for nuts

(95% CI, 0.77-1.49; *P* for trend = .89), 1.07 for corn (95% CI, 0.67-1.71; *P* for trend = .97), and 0.82 for popcorn (95% CI, 0.59-1.15; *P* for trend = .63).

To account for the possibility that symptoms of undiagnosed diverticular disease may have led to a reduction in nut, corn, or popcorn consumption, we performed a 2-year time lag analysis with respect to ascertainment of diet and diagnosis of diverticular

complications (eg, data from the 1986 food-frequency questionnaire were used for the 1990-1992 disease follow-up). The inverse association between frequent nut consumption and the risk of diverticulitis was strengthened (multivariate HR, 0.76; 95% CI, 0.61-0.96; *P* for trend = .03 in a high/low comparison), and the association for popcorn was attenuated (multivariate HR, 0.89; 95% CI, 0.70-1.13; *P* for trend = .21). No

**Table 1.** Baseline Characteristics According to Nut, Corn, and Popcorn Consumption<sup>a</sup>

	Servings, No.					
	Nuts		Corn		Popcorn	
	<1 per mo	≥2 per wk	<1 per mo	≥2 per wk	<1 per mo	≥2 per wk
No. of individuals	11 860	12 928	5784	6973	16 958	7273
Age, mean (SD), y	54 (10.0)	60 (9.6)	56 (9.7)	53 (9.8)	57 (9.8)	51 (9.0)
BMI, mean (SD) <sup>b</sup>	25.0 (3.5)	24.8 (3.3)	24.9 (3.5)	25.0 (3.7)	24.7 (3.4)	25.3 (3.4)
Physical activity, mean (SD), MET h/wk	25 (28.0)	27 (31.0)	27 (29.1)	27 (31.7)	26 (30.6)	26 (31.1)
Current smoking, %	10.1	9.9	9.9	9.8	11.2	7.6
Current use of NSAIDs, %	32	34	33	32	31	36
Daily intake, mean (SD)						
Alcohol, g	9.8 (15.0)	13.3 (16.6)	12.0 (16.5)	9.7 (14.6)	11.5 (16.1)	11.2 (15.1)
Total fat, g <sup>c</sup>	69 (15.3)	74 (15.2)	71 (15.6)	69 (13.8)	71 (14.6)	72 (13.9)
Total fiber, g <sup>c</sup>	21 (7.7)	22 (7.4)	20 (7.9)	24 (7.3)	20 (7.3)	23 (7.2)
Red meat servings, No.	4.0 (3.1)	4.4 (3.3)	3.3 (2.8)	5.3 (3.6)	4.0 (3.0)	4.6 (3.4)

Abbreviations: BMI, body mass index; MET, metabolic equivalents; NSAIDs, nonsteroidal anti-inflammatory drugs.  
<sup>a</sup>All characteristics except for age were age standardized. The total number of individuals differs from the total study population because of missing values for consumption of nuts (n = 412), corn (n = 767), and popcorn (n = 758) at baseline.  
<sup>b</sup>Calculated as weight in kilograms divided by height in meters squared.  
<sup>c</sup>Total fat and fiber were adjusted for total energy intake (kilocalorie).

**Table 2.** Risks for Diverticulitis According to the Frequency of Nut, Corn, and Popcorn Consumption

Variable	Frequency of Consumption, No. of Servings				<i>P</i> Value for Trend
	<1 per mo	1-3 per mo	1 per wk	≥2 per wk	
<b>Nuts</b>					
No. of cases <sup>a</sup>	199	138	221	133	
Person-years	167 825	116 892	171 950	149 354	
Age-adjusted HR (95% CI) <sup>b</sup>	1 [Reference]	1.00 (0.80-1.24)	1.10 (0.91-1.34)	0.77 (0.61-0.95)	.006
Multivariate HR (95% CI) <sup>c</sup>	1 [Reference]	0.97 (0.78-1.21)	1.10 (0.90-1.34)	0.80 (0.63-1.01)	.04
<b>Corn</b>					
No. of cases <sup>a</sup>	85	295	207	94	
Person-years	75 620	241 893	197 299	85 639	
Age-adjusted HR (95% CI) <sup>b</sup>	1 [Reference]	1.09 (0.86-1.39)	0.95 (0.74-1.23)	1.00 (0.75-1.35)	.64
Multivariate HR (95% CI) <sup>c</sup>	1 [Reference]	1.08 (0.85-1.38)	0.98 (0.76-1.27)	1.13 (0.83-1.54)	.44
<b>Popcorn</b>					
No. of cases <sup>a</sup>	242	223	126	92	
Person-years	198 936	179 739	117 400	105 201	
Age-adjusted HR (95% CI) <sup>b</sup>	1 [Reference]	1.01 (0.84-1.22)	0.88 (0.71-1.09)	0.71 (0.56-0.91)	.004
Multivariate HR (95% CI) <sup>c</sup>	1 [Reference]	0.98 (0.82-1.19)	0.87 (0.70-1.09)	0.72 (0.56-0.92)	.007

Abbreviations: CI, confidence interval; HR, hazard ratio.  
<sup>a</sup>The total number of cases varies slightly between nut, corn, and popcorn consumption because of missing information for individual food items. For diverticulitis, information on recent intake (simple updating) was missing for nuts in 110 cases, for corn in 120 cases, and for popcorn in 118 cases. Dietary information was updated every 4 years; age, body mass index, physical activity level, medication use, and cigarette smoking were updated every 2 years.  
<sup>b</sup>Values adjusted for age and study time period.  
<sup>c</sup>Values adjusted for age; study time period; body mass index; physical activity level; total daily caloric intake; intake of nuts, corn, popcorn, total fat, total fiber, and red meat; current use of nonsteroidal anti-inflammatory drugs; current use of acetaminophen; and current cigarette smoking.

significant associations were observed between nut, corn, or popcorn consumption and diverticular bleeding in the time lag analysis.

In addition, we performed several analyses to explore the possibility that nut, corn, and popcorn consumption influences the development of diverticulosis. We examined the relationship between consumption of these foods and uncomplicated diverticulosis (restricting the analysis to men who had undergone prior lower endoscopy to minimize detection bias) and found no significant associations. The multivariate HR for nuts was 0.91 (95% CI, 0.78-1.07; *P* for trend = .26), for corn was 0.98 (95% CI, 0.78-1.23; *P* for trend = .83), and for popcorn was 0.93 (95% CI, 0.78-1.10; *P* for trend = .38). To better isolate the independent effect of very recent diet from the long-term effect of past diet, we added baseline consumption of nuts, corn, and popcorn to the multivariate models. The associations between recent intake of these foods and diverticulitis and diverticular bleeding remained unchanged. No significant associations were seen for baseline consumption of nuts, corn, or popcorn and diverticulitis or diverticular bleeding. For diverticulitis, the multivariate HRs for base-

line consumption were 0.95 for nuts (95% CI, 0.77-1.16; *P* for trend = .52), 1.02 for corn (95% CI, 0.75-1.38; *P* for trend = .44), and 0.92 for popcorn (95% CI, 0.73-1.15; *P* for trend = .40) in high to low comparisons. The multivariate HRs for baseline consumption and diverticular bleeding were 0.85 for nuts (95% CI, 0.61-1.18; *P* for trend = .18), 0.97 for corn (95% CI, 0.62-1.52; *P* for trend = .64), and 1.30 for popcorn (95% CI, 0.89-1.92; *P* for trend = .73).

A sensitivity analysis for each end point was performed by including only men with the strongest evidence of diverticular complications. The study end points were restricted to men meeting either of the first 2 end point criteria. For diverticulitis, this included men reporting an abscess, fistula, perforation, obstruction, hospitalization, surgery, or antibiotics (*n* = 235), and for diverticular bleeding men reporting profuse bleeding or bleeding requiring hospitalization, intravenous fluids, blood transfusions, angiography, nuclear medicine scanning, or surgery (*n* = 70). In this analysis, the inverse relationship between frequent vs infrequent nut consumption and diverticulitis was all but lost (multivariate HR, 0.97; 95% CI, 0.63-1.47; *P* for

trend = .88) while that for popcorn was strengthened (multivariate HR, 0.55; 95% CI, 0.34-0.90; *P* for trend = .01). In the sensitivity analyses for diverticular bleeding, there were no significant associations seen for nut, corn, or popcorn consumption.

Finally, although we were unable to assess total seed intake, we did examine the relationship between combined strawberry and blueberry consumption and diverticular complications and found no significant association. (The small seeds found in berries have been implicated in diverticular complications.) The multivariate HRs for consumption of berries at least twice per week compared with less than once a month were 0.87 for diverticulitis (95% CI, 0.65-1.16; *P* for trend = .37) and 0.86 for diverticular bleeding (95% CI, 0.57-1.30; *P* for trend = .54).

## COMMENT

Data from this large prospective cohort of men followed up for 18 years indicate that frequent nut, corn, and popcorn consumption is not associated with an increased risk of diverticular complications. Indeed, nut and popcorn consumption appears to be inversely associated with the risk of diverticulitis

**Table 3.** Risks for Diverticular Bleeding According to the Frequency of Nut, Corn, and Popcorn Consumption

Variable	Frequency of Consumption, No. of Servings				<i>P</i> Value for Trend
	<1 per mo	1-3 per mo	1 per wk	≥2 per wk	
<b>Nuts</b>					
No. of cases <sup>a</sup>	92	64	90	75	
Person-years	167 825	116 892	171 950	149 354	
Age-adjusted HR (95% CI)	1 [Reference]	1.02 (0.74-1.40)	1.00 (0.75-1.33)	0.93 (0.68-1.26)	.56
Multivariate HR (95% CI) <sup>b</sup>	1 [Reference]	1.05 (0.76-1.45)	1.08 (0.80-1.45)	1.08 (0.77-1.49)	.89
<b>Corn</b>					
No. of cases <sup>a</sup>	38	127	116	38	
Person-years	75 620	241 893	197 299	85 639	
Age-adjusted HR (95% CI)	1 [Reference]	1.09 (0.76-1.57)	1.27 (0.88-1.83)	0.95 (0.61-1.49)	.64
Multivariate HR (95% CI) <sup>b</sup>	1 [Reference]	1.16 (0.80-1.67)	1.40 (0.96-2.04)	1.07 (0.67-1.71)	.97
<b>Popcorn</b>					
No. of cases <sup>a</sup>	130	85	50	53	
Person-years	198 936	179 739	117 400	105 201	
Age-adjusted HR (95% CI)	1 [Reference]	0.79 (0.60-1.04)	0.73 (0.53-1.02)	0.86 (0.62-1.19)	.52
Multivariate HR (95% CI) <sup>b</sup>	1 [Reference]	0.75 (0.57-1.00)	0.70 (0.50-0.98)	0.82 (0.59-1.15)	.63

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>The total number of cases varies slightly between nut, corn, and popcorn consumption because of missing information for individual food items. For diverticular bleeding, information on recent intake (simple updating) was missing for nuts in 62 cases, for corn in 64 cases, and for popcorn in 65 cases. Dietary information was updated every 4 years; age, body mass index, physical activity level, medication use, and cigarette smoking were updated every 2 years.

<sup>b</sup>Values adjusted for age; study time period; body mass index; physical activity level; total daily caloric intake; intake of nuts, corn, popcorn, total fat, total fiber, and red meat; current use of nonsteroidal anti-inflammatory drugs; current use of acetaminophen; and current cigarette smoking.

independent of other known or potential risk factors, including age; body mass index; dietary fat, fiber, and red meat consumption; physical activity; cigarette smoking; and the use of nonsteroidal anti-inflammatory drugs and acetaminophen. No associations were found between nut, corn, or popcorn consumption and diverticular bleeding.

To our knowledge, no prior study has examined the association between nut, corn, or popcorn consumption and diverticular complications. Nonetheless, in a recent survey of colorectal surgeons, 47% felt that patients with diverticular disease should avoid these foods.<sup>8</sup> The commonly held belief that these foods can incite complications of diverticulosis and the recommendation that individuals with this condition avoid them apparently evolved from the theory that luminal trauma is a causal mechanism.<sup>5</sup> In this model, inflammation or bleeding is precipitated when a fecalith or particulate fecal material lodges within a diverticulum and erodes the mucosa.<sup>1,13</sup> Foods with poorly digested particles, such as nuts, corn, and seeds, are presumed to be particularly abrasive or apt to lodge within diverticula. Although fecal matter is commonly found within wide-necked diverticula, the relationship between the ingestion of a particular food and subsequent trauma to a diverticulum is largely speculative, and the exact mechanisms leading to diverticular complications are not known.

The differences in our results with respect to diverticulitis and diverticular bleeding may be explained by potentially distinct mechanisms underlying these complications. A histological study of bleeding colonic diverticula found an absence of mucosal inflammation or evidence of diverticulitis at the bleeding sites.<sup>42,43</sup> Abnormalities were confined to the vasa rectum and included eccentric intimal thickening near the site of bleeding and asymmetric rupture toward the lumen, findings consistent with a nonspecific vascular response to injury.

There are several plausible mechanisms by which nut intake may pro-

tect against diverticulitis, although our data did not enable us to make causal inferences. Nuts are rich in nutrients with anti-inflammatory properties such as vitamin E,  $\alpha$ -linolenic acid and other unsaturated fatty acids, and phytochemicals. Nut consumption is inversely correlated with levels of inflammatory markers including C-reactive protein and IL-6<sup>24</sup> and is protective against certain inflammatory disease states.<sup>22,27,28</sup> The high mineral content in nuts, including zinc and magnesium, may also favorably influence the colon. Alterations in the structure and content of collagen in the colon have been noted in diverticular disease, which may in part be due to decreased expression of zinc-containing endopeptidases.<sup>44,45</sup> Magnesium may reduce oxidative stress in the colon, a mechanism that is also postulated for the inverse association seen between magnesium intake and colon cancer.<sup>46,47</sup> Popcorn is less nutrient dense than nuts but does contain lutein, a micronutrient with anti-inflammatory and chemoprotective properties that is also found in nuts, as well as modest amounts of magnesium.

The high fiber content of nuts and popcorn does not appear to provide adequate explanation for the observed inverse associations between nuts and popcorn and diverticulitis. The multivariate analyses adjusted for total dietary fiber intake, and the consistency between the age-adjusted and multivariate models does not imply significant confounding by fiber or the other covariates. Nor do nuts and popcorn appear to be markers for generally healthy habits because the data on other lifestyle and dietary factors such as physical activity and red meat consumption do not suggest a health-conscious pattern in men with frequent nut and popcorn consumption. Notably, the majority of our data were acquired during a time period when nuts were not perceived as a healthy food. Nonetheless, given the observational nature of the study, we cannot exclude the possibility of residual confounding by a lifestyle or other unmeasured factor.

We were unable to specifically study the effect of nut, corn, and popcorn consumption in men with established diverticulosis because the presence of diverticulosis was not known at baseline in all individuals. Men with known asymptomatic diverticulosis likely represent a biased subset of men who have undergone lower endoscopy or colon imaging, and men with known diverticulosis are likely to alter their behaviors, including decreasing the consumption of nuts, corn, and popcorn. However, the prevalence of undiagnosed asymptomatic diverticulosis was presumably quite high in this cohort of middle-aged and elderly men, and therefore, our findings likely apply to patients with established diverticular disease.

A long-term influence of nut and popcorn consumption on the development of diverticulosis does not appear to account for the inverse associations with diverticulitis observed in this study. We did not find significant associations between nut and popcorn consumption and incident uncomplicated diverticulosis. Furthermore, our results remained unchanged after adjustment for baseline consumption. The later analysis aims to distinguish the independent effect of very recent diet (relevant to the risk of diverticular complications) from past diet (relevant to the development of diverticulosis).

In the 2-year time lag analysis, the inverse relationship between nuts and diverticulitis was strengthened, but the results for popcorn were attenuated. Some men may have reduced their consumption of popcorn in response to symptoms of undiagnosed diverticulitis under the assumption that popcorn is harmful. However, if recent popcorn consumption is protective, their subsequent risk of diverticulitis would increase. This would enhance the inverse relationship seen between popcorn consumption and diverticulitis in the standard analysis and attenuate it in the time lag analysis. Overall, there was no evidence from the time lag analysis that consumption of nuts, popcorn, or corn was positively associated with diverticular complications. Lastly, we had not hy-

pothesized that these foods would decrease the incidence of diverticular complications, and it is possible that this finding is the result of chance alone.

Our study has certain limitations. As noted earlier, it is possible that the associations found between nuts and popcorn were the result of residual confounding. In addition, diverticular complications and dietary intake were based on self-report. However, several factors limit the possibility of misclassification bias. Study participants were health professionals, review of 179 medical records endorsed the validity of self-report, and secondary analyses supported our findings. Food consumption was assessed prior to the development of diverticular complications using a validated food-frequency questionnaire. On the whole, any misclassification bias would likely be random and thus would weaken any true association. The generalizability of our results to younger patients and women may be limited. However, diverticulosis is rare before the age of 40 years,<sup>1</sup> and there are no clear sex differences in diverticular disease.<sup>1,48</sup> Lastly, we were unable to directly examine the relationship between seed consumption and diverticular complications. However, consumption of strawberries and blueberries (fruits with small seeds) was not associated with diverticular complications.

In conclusion, our results suggest that nut, corn, and popcorn consumption is not associated with an increased risk of incident diverticulitis or diverticular bleeding and may be protective for the former. These findings refute the pervasive but unproven belief that these foods are associated with diverticular complications and suggest that the recommendation to avoid these foods in diverticular disease should be reconsidered.

**Author Contributions:** Dr Giovannucci had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Strate, Giovannucci.

**Acquisition of data:** Strate, Liu, Aldoore, Giovannucci. **Analysis and interpretation of data:** Strate, Liu, Syngal, Aldoore, Giovannucci.

**Drafting of the manuscript:** Strate.

**Critical revision of the manuscript for important intellectual content:** Strate, Liu, Syngal, Aldoore, Giovannucci.

**Statistical analysis:** Strate, Liu, Giovannucci.

**Obtained funding:** Strate, Giovannucci.

**Administrative, technical, or material support:** Giovannucci.

**Study supervision:** Syngal, Aldoore, Giovannucci.

**Financial Disclosures:** None reported.

**Funding/Support:** This study was funded by grant K08 HS14062 from the Agency for Healthcare Research and Quality (Dr Strate); grants P01 CA055075 (Dr Giovannucci) and K24 CA113433 (Dr Syngal) from the National Cancer Institute; and grant R01 HL035464 from the National Heart, Lung, and Blood Institute (Dr Giovannucci).

**Role of the Sponsor:** The funding sources for this study had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

**Disclaimer:** The views expressed in this article are those of the authors and do not necessarily represent the official views of the National Cancer Institute, the National Institutes of Health, or the Agency for Healthcare Research and Quality.

**Previous Presentation:** An abstract based on this manuscript was presented at Digestive Disease Week; May 19-23, 2007; Washington, DC.

**Additional Contributions:** We thank the investigators, staff, and participants of the Health Professionals Follow-up Study, especially the following for their contributions: Luba Bondarenko, MS; Mira Kaufman, MS; Siobhan Saint-Surin, BA; and Elizabeth Frost-Hawes, BA, Harvard School of Public Health, and Shiyu Wei, Harvard University. The acknowledged staff received compensation for their contributions.

## REFERENCES

- Hughes LE. Postmortem survey of diverticular disease of the colon: II, the muscular abnormality of the sigmoid colon. *Gut*. 1969;10(5):344-351.
- Parks TG. Post-mortem studies on the colon with special reference to diverticular disease. *Proc R Soc Med*. 1968;61(9):932-934.
- Welch CE, Allen AW, Donaldson GA. An appraisal of resection of the colon for diverticulitis of the sigmoid. *Ann Surg*. 1953;138(3):332-343.
- McGuire HH Jr. Bleeding colonic diverticula: a reappraisal of natural history and management. *Ann Surg*. 1994;220(5):653-656.
- Horner JL. Natural history of diverticulosis of the colon. *Am J Dig Dis*. 1958;3(5):343-350.
- Sandler RS, Everhart JE, Donowitz M, et al. The burden of selected digestive diseases in the United States. *Gastroenterology*. 2002;122(5):1500-1511.
- Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol*. 2006;101(9):2128-2138.
- Schechter S, Mulvey J, Eisenstat TE. Management of uncomplicated acute diverticulitis: results of a survey. *Dis Colon Rectum*. 1999;42(4):470-475.
- Jacobs DO. Clinical practice: diverticulitis. *N Engl J Med*. 2007;357(20):2057-2066.
- Berman LG, Burdick D, Heitzman ER, Prior JT. A critical reappraisal of sigmoid peridiverticulitis. *Surg Gynecol Obstet*. 1968;127(3):481-491.
- Fleischner FG, Ming SC. Revised concepts on diverticular disease of the colon: II, so-called diverticulitis: diverticular sigmoiditis and perisigmoiditis; diverticular abscess, fistula, and frank peritonitis. *Radiology*. 1965;84:599-609.
- Morson BC. The muscle abnormality in diverticular disease of the colon. *Proc R Soc Med*. 1963;56:798-800.
- Bogardus ST Jr. What do we know about diverticular disease? a brief overview. *J Clin Gastroenterol*. 2006;40(7)(suppl 3):S108-S111.
- Almy TP, Howell DA. Medical progress: diver-

tical disease of the colon. *N Engl J Med*. 1980;302(6):324-331.

15. Floch MH, Bina I. The natural history of diverticulitis: fact and theory. *J Clin Gastroenterol*. 2004;38(5)(suppl):S2-S7.

16. Korzenik JR. Case closed? diverticulitis: epidemiology and fiber. *J Clin Gastroenterol*. 2006;40(7)(suppl 3):S112-S116.

17. Laine L, Connors LG, Reicin A, et al. Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use. *Gastroenterology*. 2003;124(2):288-292.

18. Morris CR, Harvey IM, Stebbings WS, Speakman CT, Kennedy HJ, Hart AR. Epidemiology of perforated colonic diverticular disease. *Postgrad Med J*. 2002;78(925):654-658.

19. Morris CR, Harvey IM, Stebbings WS, Speakman CT, Kennedy HJ, Hart AR. Do calcium channel blockers and antimuscarinics protect against perforated colonic diverticular disease? a case control study. *Gut*. 2003;52(12):1734-1737.

20. Morris CR, Harvey IM, Stebbings WS, Speakman CT, Kennedy HJ, Hart AR. Anti-inflammatory drugs, analgesics and the risk of perforated colonic diverticular disease. *Br J Surg*. 2003;90(10):1267-1272.

21. Albert CM, Gaziano JM, Willett WC, Manson JE. Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study. *Arch Intern Med*. 2002;162(12):1382-1387.

22. Hu FB, Stampfer MJ, Manson JE, et al. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. *BMJ*. 1998;317(7169):1341-1345.

23. Jenab M, Ferrari P, Slimani N, et al. Association of nut and seed intake with colorectal cancer risk in the European Prospective Investigation into Cancer and Nutrition. *Cancer Epidemiol Biomarkers Prev*. 2004;13(10):1595-1603.

24. Jiang R, Jacobs DR Jr, Mayer-Davis E, et al. Nut and seed consumption and inflammatory markers in the multi-ethnic study of atherosclerosis. *Am J Epidemiol*. 2006;163(3):222-231.

25. Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and peanut butter consumption and risk of type 2 diabetes in women. *JAMA*. 2002;288(20):2554-2560.

26. Tsai CJ, Leitzmann MF, Hu FB, Willett WC, Giovannucci EL. A prospective cohort study of nut consumption and the risk of gallstone disease in men. *Am J Epidemiol*. 2004;160(10):961-968.

27. Hu FB, Stampfer MJ. Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence. *Curr Atheroscler Rep*. 1999;1(3):204-209.

28. Sabate J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. *Am J Clin Nutr*. 1999;70(3)(suppl):500S-503S.

29. Hebert JR, Hurley TG, Olendzki BC, Teas J, Ma Y, Hampl JS. Nutritional and socioeconomic factors in relation to prostate cancer mortality: a cross-national study. *J Natl Cancer Inst*. 1998;90(21):1637-1647.

30. Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. *Nutr Cancer*. 1999;34(2):173-184.

31. Mills PK, Beeson WL, Phillips RL, Fraser GE. Cohort study of diet, lifestyle, and prostate cancer in Adventist men. *Cancer*. 1989;64(3):598-604.

32. Qualified health claims: letter of enforcement discretion—nuts and coronary heart disease (July 14, 2003). US Food and Drug Administration Center for Food Safety and Applied Nutrition. <http://www.cfsan.fda.gov/~dms/qhcnuts2.html>. Accessed July 24, 2008.

33. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health

- professionals. *Am J Epidemiol.* 1992;135(10):1114-1126.
34. Aldoori WH, Giovannucci EL, Rimm EB, et al. Prospective study of physical activity and the risk of symptomatic diverticular disease in men. *Gut.* 1995;36(2):276-282.
35. Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Trichopoulos DV, Willett WC. A prospective study of diet and the risk of symptomatic diverticular disease in men. *Am J Clin Nutr.* 1994;60(5):757-764.
36. Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Willett WC. Use of acetaminophen and nonsteroidal anti-inflammatory drugs: a prospective study and the risk of symptomatic diverticular disease in men. *Arch Fam Med.* 1998;7(3):255-260.
37. Aldoori WH, Giovannucci EL, Rockett HR, Sampson L, Rimm EB, Willett WC. A prospective study of dietary fiber types and symptomatic diverticular disease in men. *J Nutr.* 1998;128(4):714-719.
38. Dobbins C, Defontgalland D, Duthie G, Wattchow DA. The relationship of obesity to the complications of diverticular disease. *Colorectal Dis.* 2006;8(1):37-40.
39. Laine L, Smith R, Min K, Chen C, Dubois RW. Systematic review: the lower gastrointestinal adverse effects of non-steroidal anti-inflammatory drugs. *Aliment Pharmacol Ther.* 2006;24(5):751-767.
40. Rosemar A, Angeras U, Rosengren A. Body mass index and diverticular disease: a 28-year follow-up study in men. *Dis Colon Rectum.* 2008;51(4):450-455.
41. Cox DR. Regression models and life tables. *J R Stat Soc (B).* 1972;34:187-220.
42. Meyers MA, Alonso DR, Baer JW. Pathogenesis of massively bleeding colonic diverticulosis: new observations. *AJR Am J Roentgenol.* 1976;127(6):901-908.
43. Meyers MA, Alonso DR, Gray GF, Baer JW. Pathogenesis of bleeding colonic diverticulosis. *Gastroenterology.* 1976;71(4):577-583.
44. Mimura T, Bateman AC, Lee RL, et al. Up-regulation of collagen and tissue inhibitors of matrix metalloproteinase in colonic diverticular disease. *Dis Colon Rectum.* 2004;47(3):371-378.
45. Stumpf M, Cao W, Klinge U, Klosterhalfen B, Kasperk R, Schumpelick V. Increased distribution of collagen type III and reduced expression of matrix metalloproteinase 1 in patients with diverticular disease. *Int J Colorectal Dis.* 2001;16(5):271-275.
46. Folsom AR, Hong CP. Magnesium intake and reduced risk of colon cancer in a prospective study of women. *Am J Epidemiol.* 2006;163(3):232-235.
47. van den Brandt PA, Smits KM, Goldbohm RA, Weijnenberg MP. Magnesium intake and colorectal cancer risk in the Netherlands Cohort Study. *Br J Cancer.* 2007;96(3):510-513.
48. Stollman NH, Raskin JB. Diagnosis and management of diverticular disease of the colon in adults: Ad Hoc Practice Parameters Committee of the American College of Gastroenterology. *Am J Gastroenterol.* 1999;94(11):3110-3121.

We want the facts to fit the preconceptions. When they don't, it is easier to ignore the facts than to change the preconceptions.

—Jessamyn West (1902-1984)