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Original Contribution

Consumption of *trans*-Fatty Acid and Its Association with Colorectal Adenomas

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trans-Fatty acid consumption is known to have detrimental effects on cardiovascular health, but little is known about its role in digestive tract neoplasia. To investigate the association between colorectal adenomas and *trans*-fatty acid consumption, the authors utilized data from a cross-sectional study of 622 individuals who underwent complete colonoscopy between 2001 and 2002 at the University of North Carolina Hospitals. Participants were interviewed about demographic, lifestyle, and dietary factors thought to be related to colorectal cancer. *trans*-Fatty acid consumption, energy adjusted by the residual method, was categorized into quartiles based on its distribution in controls. Compared with participants in the lowest quartile of consumption, those in the highest quartile had an increased prevalence of colorectal adenomas, with an adjusted prevalence odds ratio of 1.86 (95% confidence interval: 1.04, 3.33). The authors further investigated the relation between *trans*-fatty acid consumption and colorectal neoplasia by examining the adenoma characteristics, with the adjusted prevalence odds ratios showing little or no difference by adenoma location, size, or number. These results suggest that consumption of high amounts of *trans*-fatty acid may increase the risk of colorectal neoplasia, and they provide additional support to recommendations to limit *trans*-fatty acid consumption.

colonic polyps; colorectal neoplasms; dietary fats; *trans* fatty acids

Abbreviations: CI, confidence interval; NSAID, nonsteroidal antiinflammatory drug; UNC, University of North Carolina.

Colorectal cancer is a major health concern in the United States, with over 150,000 diagnoses and 52,180 deaths expected in the year 2007 (1). It is widely accepted that the majority of colorectal cancers develop from precursor lesions, colorectal adenomatous polyps (2). Recent colonoscopy-based studies have shown that adenomas are very common. Rex and Helbig (3) reported that 66 percent of a study population aged 50 years or more had at least one adenoma, a higher percentage than most previous reports. The rate of adenoma detection in participants who were undergoing screening colonoscopy for the first time was 55 percent (3). An earlier study also detected adenomas in 55 percent of study participants undergoing screening colonoscopies at a Veterans Affairs hospital. Patients with adenomas are more likely to develop additional adenomas in the future, with a reported recurrence rate of 37 percent within 5 years (4). The concern about adenomas stems from the fact that they can progress to cancer (2); therefore, preventing adenomas from developing by modifying diet or lifestyle could decrease the incidence of colorectal cancer.

Currently, there is increasing concern that consumption of *trans*-fatty acids may contribute to disease risk. This is

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TABLE 1. Characteristics of the Diet and Health Study IV population by case status, November 2001–December 2002 ($N = 622$)

Characteristics of participants	Colorectal adenoma ($n = 173$)		No colorectal adenoma ($n = 449$)		p value*
	No.	%	No.	%	
Age, years†					
30–49	28	16.38	98	21.88	0.02
50–59	82	47.95	193	43.08	
60–69	39	22.81	116	25.89	
70–80	22	12.87	41	9.15	
Mean years (SD‡)	56.96 (9.60)		55.95 (9.86)		0.25
Sex					
Men	98	56.65	172	38.31	<0.01
Women	75	43.35	277	61.69	
Race†					
White	133	77.78	349	78.25	0.90
Non-White	38	22.22	97	21.75	
Highest level of education†					
Some high school	24	14.04	40	8.93	0.26
High school	27	15.79	72	16.07	
Some college	30	17.54	95	21.21	
College degree or above	90	52.63	241	53.80	
Body mass index 1 year prior to enrollment†					
Normal (18–24.9 kg/m^2)	53	32.92	174	42.03	0.10
Overweight (25–29.9 kg/m^2)	58	36.02	140	33.82	
Obese ($\geq$30 kg/m^2)	50	31.06	100	24.15	
Mean kg/m^2 (SD)	28.15 (5.82)		27.00 (5.54)		0.03
Current physical activity (MET‡-minutes/day)†					
Quartile 1	41	26.11	106	24.65	0.48
Quartile 2	37	23.57	110	25.58	
Quartile 3	34	21.66	113	26.28	
Quartile 4	45	28.66	101	23.49	
Mean MET-minutes/day (SD)	2,670.47 (845.85)		2,591.08 (754.79)		0.28

Table continues

especially true for heart disease (5), but higher intakes have also been found to be detrimentally associated with other health outcomes, such as type II diabetes (6). Consequently, all nutritional labels in the United States were required to include information on *trans*-fat content by January 1, 2006 (7). In addition, some localities, including New York City, have banned *trans*-fatty acids from commercial food outlets (8).

There is little published information on *trans*-fatty acid consumption and colorectal neoplasia, but there are several mechanisms by which *trans*-fatty acids could influence the risk of colorectal neoplasia. For example, *trans*-fatty acid consumption may lead to elevated risk of developing colorectal adenomas by altering the concentration of fatty acids or bile acids normally found in the colon (9–12). This may result in irritation of the colonic mucosa, increasing oxidative stress (13) and inflammation (14). Studies in humans have shown *trans*-fatty acid intake to be associated with markers of oxidative stress (13) and systemic inflammation (14). Another possible mechanism is through the increase of insulin resistance. Studies in humans are inconsistent, although a few studies have shown that *trans*-fatty acid consumption is associated with insulin resistance in diabetics (6, 15). This insulin resistance may lead to increased cellular proliferation (16, 17), which is associated with colorectal cancer.

We used data from a cross-sectional study of subjects attending University of North Carolina (UNC) Hospitals for a colonoscopy to investigate the association between colorectal adenomas and *trans*-fatty acid consumption. We also examined the relation between *trans*-fatty acid consumption and the location, number, and size of adenomas. In contrast to prior publications (18, 19), the present study reports the relation between energy-adjusted *trans*-fatty acid consumption

TABLE 1. Continued

Characteristics of participants	Colorectal adenoma ($n = 173$)		No colorectal adenoma ($n = 449$)		*p* value*
	No.	%	No.	%	
Smoking status†					
Never	80	47.06	229	51.12	0.21
Former	63	37.06	171	38.17	
Current	27	15.88	48	10.71	
Family history					
Yes	27	15.61	59	13.14	0.43
No	146	84.39	390	86.86	
NSAID‡ use over the past 5 years†					
Regular user§	50	29.76	124	28.51	0.76
Nonregular user§	118	70.24	311	71.49	
Postmenopausal hormone replacement therapy use $\geq$1 year†					
Yes	35	48.61	141	52.03	0.61
No	37	51.39	130	47.97	
Not applicable	98		172		
Diabetes†					
Yes	25	14.71	41	9.17	0.05
No	145	85.29	406	90.83	
trans-Fatty acid intake, mean g/day (SD)	4.97 (3.20)		4.42 (3.16)		0.05
Total energy intake, mean kcal/day (SD)	2,084.74 (1,037.18)		1,958.67 (917.30)		0.14
Total fat intake, mean g/day (SD)	76.41 (41.72)		72.10 (38.17)		0.22
Saturated fat intake, mean g/day (SD)	24.04 (14.39)		22.15 (12.49)		0.11
Calcium consumption, mean mg/day (SD)	796.42 (442.11)		820.72 (467.44)		0.56
Alcohol consumption, mean g/day (SD)†	12.49 (20.98)		8.03 (14.23)		$<$0.01
Red meat consumption, mean ounces¶/day (SD)	1.88 (1.57)		1.57 (1.44)		0.02
Vegetable consumption, mean vegetable servings/day (SD)	4.34 (2.40)		4.32 (2.46)		0.94

* Calculated with chi-square tests for categorical variables and *t* tests for continuous variables.

† Data were missing for age ($n = 3$), race ($n = 5$), education ($n = 3$), body mass index ($n = 47$), physical activity ($n = 35$), smoking ($n = 4$), nonsteroidal antiinflammatory drug use ($n = 19$), postmenopausal hormone replacement therapy ($n = 9$), diabetes ($n = 5$), and alcohol consumption ($n = 1$).

‡ SD, standard deviation; MET, metabolic equivalent; NSAID, nonsteroidal antiinflammatory drug.

§ Regular user is defined as using nonsteroidal antiinflammatory drugs at least 15 times/month.

¶ One ounce = 28.35 g.

and colorectal adenomas among participants who had their entire colon examined by complete colonoscopy.

MATERIALS AND METHODS

Study population

The Diet and Health Study IV recruited consecutive patients undergoing an outpatient colonoscopy at the UNC Hospitals in Chapel Hill, North Carolina, from November 2001 to December 2002. The study received human subjects approval from the UNC School of Medicine Institutional Review Board, and research assistants obtained written informed consent from individuals prior to their colonoscopy. Eligibility requirements were as follows: age 30–80 years; proficient in English; ability to give informed consent; a satisfactory preparation for colonoscopy and a complete examination to the cecum; no previous colonoscopies; not an inpatient; and no history of familial polyposis, colitis, previous colonic resection, or previous colon cancer or polyps. For this study, cases were defined as subjects who had a colorectal adenoma (a polyp with tubular, villoglandular, or villous histology) detected during complete colonoscopy. Controls were defined as those subjects with no adenomas present. A single study pathologist examined all tissue samples collected from participants and reported the diameter, location, and histologic type of each polyp detected. In addition, a 10 percent random sample of all biopsies collected

TABLE 2. Adjusted prevalence odds ratios for colorectal adenoma prevalence by quartiles of *trans*-fatty acid intake, Diet and Health Study IV, November 2001–December 2002

Quartiles of *trans*-fatty acid consumption	Median energy-adjusted *trans*-fatty acid consumption, g/day (interquartile range)	Minimally adjusted model ($N = 614$)*				Fully adjusted model ($N = 546$)†			
		No. of controls ($n = 445$)	No. of cases ($n = 169$)	Prevalence odds ratio	95% confidence interval	No. of controls ($n = 401$)	No. of cases ($n = 145$)	Prevalence odds ratio	95% confidence interval
1	3.63 (3.09–3.91)	111	40	1.00		99	35	1.00	
2	4.58 (4.39–4.80)	111	36	1.01	0.58, 1,75	101	31	0.98	0.53, 1.79
3	5.34 (5.14–5.58)	111	32	0.95	0.54, 1.67	98	29	1.07	0.57, 2.00
4	6.54 (6.13–7.08)	112	61	1.74	1.06, 2.86	103	50	1.86	1.04, 3.33

* Adjusted for age, sex, race, and caloric intake.
† Adjusted for caloric intake, alcohol consumption, physical activity, race, age, sex, and body mass index.

from the study participants was blindly resubmitted for pathology review to determine the reliability of the case-control classification; 99 percent of classifications were concordant.

Data collection

Within 12 weeks of their colonoscopy, consenting subjects were followed up with a phone call from a trained interviewer who was blinded to case-control status, although participants themselves were aware of their status. Interviewers collected information on participants' age, sex, educational background, race, smoking history, nonsteroidal antiinflammatory drug (NSAID) use, and physical activity. Physical activity was measured for occupational, nonoccupational, and non-work/weekend activities by use of a modified version of a validated 7-day physical activity recall (20–22). Height and weight were measured at the time of colonoscopy.

Dietary assessment

Dietary information was collected during the interview by use of the Diet History Questionnaire, a food frequency questionnaire with 124 food items developed at the National Cancer Institute (23–25). Participants were asked to use a reference period of 1 year prior to their colonoscopy, allowing us to capture usual diet across seasons. The Diet History Questionnaire included questions on portion size and frequency of consumption for each food. The Diet History Questionnaire also accounted for the cooking methods that individuals used. Determination of the nutrient intake that individuals consumed was calculated by the Diet*Calc program provided by the National Cancer Institute (http://riskfactor.cancer.gov/DHQ/dietcalc/). Further details on the processes used to create the nutrient database for the Diet*Calc program are given elsewhere (25, 26). Briefly, foods were assigned mean nutrient values by portion size and gender. The original database used values from the 1994–1996 Continuing Survey of Food Intakes by Individuals (CSFII) food codes, but *trans*-fatty acid values were added later by use of the Nutrition Data System for Research (NDS-R) from the University of Minnesota.

Data analysis

trans-Fatty acid consumption was energy adjusted by the residuals method from a regression model, where the independent and dependent variables were energy intake and *trans*-fatty acid intake, respectively (27). This method results in *trans*-fatty acid values that are independent of an individual's overall amount of energy consumed. Although the residual method of energy adjustment is most often used for continuous values of nutrient intake, it is also appropriate when categorizing nutrient intake (28). The residuals of *trans*-fatty acid consumption were categorized into quartiles based on consumption in the adenoma-free (i.e., control) population.

We used logistic regression modeling to explore the associations between colorectal adenomas and energy-adjusted *trans*-fatty acid consumption. Adenomas are more common in men, older individuals, and African Americans, and *trans*-fatty acid consumption was associated with age, sex, and race among the controls; therefore, we adjusted for these variables a priori. In addition, we evaluated family history of colorectal cancer, body mass index, physical activity, NSAID use, smoking status, alcohol consumption, calcium consumption, red meat consumption, and total vegetable serving consumption as potential confounders according to a 10 percent change-in-estimate criterion (29). Analysis was performed with complete case analysis, excluding individuals with missing observations for the variables included in the final models. Sex and NSAID use were assessed as potential prevalence odds ratio modifiers by tests of homogeneity and likelihood ratio tests with a p value cutoff of 0.15. One of the reasons that these two variables were selected as potential effect measure modifiers was that a study of colon cancer and *trans*-fatty acid consumption demonstrated differences within strata of similar variables (30). In addition, NSAIDs have shown an inverse association with adenoma prevalence and recurrence (31–33) and could alter the effects of *trans*-fatty acids on the colon/rectum if *trans*-fatty acids create irritation and inflammation of the colonic mucosa.

We also investigated associations between *trans*-fatty acid consumption and adenomas classified according to

TABLE 3. Adjusted prevalence odds ratios* for location, number, and size of adenomas by quartiles of *trans*-fatty acid consumption, Diet and Health Study IV, November 2001–December 2002

Quartiles of *trans*-fatty acid consumption†	No. of controls ($n = 401$)	Location of adenomas‡					
		Proximal adenomas			Distal adenomas		
		No. of cases ($n = 55$)	Prevalence odds ratio	95% confidence interval	No. of cases ($n = 63$)	Prevalence odds ratio	95% confidence interval
1	99	11	1.00		15	1.00	
2	101	14	1.23	0.50, 3.07	14	1.13	0.49, 2.61
3	98	9	0.94	0.34, 2.59	13	1.16	0.49, 2.75
4	103	21	2.80	1.14, 6.87	21	1.51	0.68, 3.35
		No. of adenomas					
	No. of controls ($n = 401$)	1 adenoma			>1 adenoma		
		No. of cases ($n = 99$)	Prevalence odds ratio	95% confidence interval	No. of cases ($n = 46$)	Prevalence odds ratio	95% confidence interval
1	99	22	1.00		13	1.00	
2	101	23	1.09	0.55, 2.19	8	0.74	0.28, 1.97
3	98	20	1.08	0.52, 2.23	9	1.04	0.39, 2.77
4	103	34	1.79	0.91, 3.53	16	2.01	0.83, 4.87
		Size of adenomas§					
	No. of controls ($n = 401$)	<1 cm			≥1 cm		
		No. of cases ($n = 114$)	Prevalence odds ratio	95% confidence interval	No. of cases ($n = 30$)	Prevalence odds ratio	95% confidence interval
1	99	27	1.00		7	1.00	
2	101	26	1.08	0.56, 2.07	5	0.69	0.20, 2.36
3	98	24	1.16	0.58, 2.28	5	0.79	0.22, 2.80
4	103	37	1.81	0.96, 3.44	13	2.01	0.69, 5.81

* Adjusted for caloric intake, alcohol consumption, physical activity, race, age, sex, and body mass index.

† Median energy-adjusted *trans*-fatty acid consumption per day: quartile 1 (3.63 g, interquartile range (IQR) = 3.09–3.91); quartile 2 (4.58 g, IQR = 4.39–4.80); quartile 3 (5.34 g, IQR = 5.14–5.58); quartile 4 (6.54 g, IQR = 6.13–7.08).

‡ Adenomas were classified as proximal if they were detected in the cecum, ascending colon, hepatic flexure, or transverse colon and as distal if present in the splenic flexure, descending colon, sigmoid colon, or rectum. Participants with adenomas in both the proximal and distal colon were excluded from this analysis ($n = 30$).

§ The size of adenoma was classified on the basis of the size of the largest adenoma detected.

their location (proximal or distal), size (none, <1 cm, or ≥1 cm based on the size of the largest adenoma), and number (none, one adenoma, more than one adenoma), with controls serving as the referent outcome for all analyses. Location was classified as proximal if an adenoma was detected in the cecum, ascending colon, hepatic flexure, or transverse colon and as distal if an adenoma was present in the splenic flexure, descending colon, sigmoid colon, or rectum. If a participant had an adenoma in both the proximal and distal colon, he or she was excluded from this analysis ($n = 30$). We estimated these associations using multinomial logistic regression.

In addition, we investigated the association between *trans*-fatty acid consumption and two types of polyps. For these analyses, participants with polyps were categorized as having either hyperplastic or adenomatous polyps. Participants were categorized as controls if they had neither hyperplastic polyps nor adenomatous polyps detected during colonoscopy. Participants with both hyperplastic and adenomatous polyps were excluded from this analysis ($n = 50$). The exposure, consumption of *trans*-fatty acids, retained the same categorization despite the change in the control group. If cutpoints had been reformatted for the distribution of consumption present in the specific control group used in these analyses, 99 percent of individuals would have remained in the same exposure category. Multinomial logistic regression was used, and confounding was reassessed with the 10 percent change-in-estimate criterion.

RESULTS

Between November 2001 and December 2002, 1,027 eligible individuals had a colonoscopy performed at the UNC

TABLE 4. Adjusted prevalence odds ratios for hyperplastic and adenomatous polyp* prevalence by quartiles of *trans*-fatty acid intake, Diet and Health Study IV, November 2001–December 2002

Quartiles of *trans*-fatty acid consumption†	Minimally adjusted model‡						Fully adjusted model§					
		Hyperplastic polyps		Adenomatous polyps				Hyperplastic polyps		Adenomatous polyps		
	No. of controls ($n = 373$)	No. of cases ($n = 72$)	Prevalence odds ratio	95% confidence interval	No. of cases ($n = 122$)	Prevalence odds ratio	95% confidence interval	No. of controls ($n = 338$)	No. of cases ($n = 63$)	Prevalence odds ratio	95% confidence interval	No. of cases ($n = 103$)	Prevalence odds ratio	95% confidence interval
1	97	14	1.00		30	1.00		88	11	1.00		26	1.00	
2	91	20	1.49	0.69, 3.22	28	1.05	0.57, 1.95	84	17	1.46	0.60, 3.57	24	1.00	0.49, 2.04
3	93	18	1.37	0.62, 3.03	20	0.79	0.40, 1.53	83	15	1.43	0.55, 3.71	18	0.80	0.36, 1.75
4	92	20	1.60	0.75, 3.44	44	1.74	0.98, 3.06	83	20	1.93	0.77, 4.85	35	1.66	0.80, 3.43

* Cases were categorized as having either hyperplastic or adenomatous polyps. Participants with both were excluded from this analysis ($n = 50$).
† Median energy-adjusted *trans*-fatty acid consumption per day: quartile 1 (3.63 g, interquartile range (IQR) = 3.09–3.91); quartile 2 (4.58 g, IQR = 4.39–4.80); quartile 3 (5.34 g, IQR = 5.14–5.58); quartile 4 (6.54 g, IQR = 6.13–7.08).
‡ Adjusted for age, sex, race, and caloric intake.
§ Adjusted for caloric intake, age, sex, race, alcohol consumption, physical activity, body mass index, smoking status, red meat intake, and vegetable intake.

Hospitals. Of these individuals, 91 were not asked to participate because the research assistant was not available, and 123 did not provide consent for participation in the study. An additional 107 were classified as ineligible after the colonoscopy was completed for reasons such as an unsatisfactory preparation or an incomplete examination. The study was completed by 701 individuals, with a response rate (number interviewed/number eligible) of 76 percent.

Complete information on colorectal adenomas and *trans*-fatty acid consumption was available for 622 participants (173 cases and 449 controls). Characteristics of the study participants by case and control status are given in table 1. The mean age at the time of interview was similar for the cases and controls (57 and 56 years, respectively). There were more women than men in the study population, but more men had colorectal adenomas detected. Over 75 percent of study participants were White, and more than half had at least a college degree. As expected, a higher proportion of cases than controls was classified as obese (body mass index, $\geq$30 kg/m^2; 31 vs. 24 percent, respectively). Cases also had a higher mean consumption of alcohol and a slightly higher energy intake than controls did.

Cases reported higher unadjusted *trans*-fatty acid consumption than did controls, with a mean of 4.97 g (standard deviation, 3.20 g) and a median of 4.12 g compared with 4.42 g (standard deviation, 3.16 g) and 3.61 g, respectively, in controls (*t*-test $p = 0.054$). The crude (unadjusted) prevalence odds ratio comparing the highest quartile of *trans*-fatty acid consumption with the lowest quartile was 1.55 (95 percent confidence interval (CI): 0.95, 2.54).

Prevalence odds ratios were homogeneous across strata of sex and NSAID use (likelihood ratio test $p > 0.15$); therefore, multiplicative interaction terms between these covariates and the exposure were not retained. The following variables were entered into the final model as confounders: age (continuous), sex, race (categorized as White, non-White), physical activity (continuous), body mass index (continuous), and alcohol consumption (continuous). In addition to adjusting the exposure, *trans*-fatty acid consumption, for energy intake, we included a continuous variable for energy intake in the final model. For the multinomial model comparing subjects with hyperplastic polyps and adenomatous polyps with controls, smoking status (categorized as never, former, current smoker), consumption of red meat (continuous), and total number of vegetable servings consumed (continuous) were also found to be confounders on the basis of a 10 percent change-in-estimate criterion and they were added to the model in addition to the covariates above.

The fully adjusted prevalence odds ratio comparing those in the lowest quartile of *trans*-fatty acid consumption with those in the highest quartile was 1.86 (95 percent CI: 1.04, 3.33) in the fully adjusted model (table 2). Consumption of *trans*-fatty acid was not associated with the prevalence of colorectal adenomas for those in the second or third quartiles of consumption. Estimates from the minimally adjusted models were similar (table 2).

Other categorizations were undertaken to further examine the association present in the extreme quartile of *trans*-fatty acid consumption (data not shown). Although it was difficult

to draw definitive conclusions regarding a specific threshold of *trans*-fatty acid consumption because of small numbers, similar trends were seen. In models of the various categorizations (which included deciles and further split of the quartile categories), the highest 20–25 percent of energy-adjusted *trans*-fatty acid consumption had similar point estimates to those seen in the highest quartile of consumption from our original model. These results confirm the appearance of a threshold effect; the prevalence of adenomas was increased only among those with the highest levels of *trans*-fatty acid consumption in our study population.

The results of the minimally and fully adjusted models for the investigation of adenoma location, size, and number were very similar, and therefore only the results of the fully adjusted model are presented (table 3). As seen in the models examining only the presence/absence of colorectal adenomas, the fourth quartile of consumption was associated with the largest increase in prevalence among all categories of location, number, and size of adenomas. Adenomas in the proximal colon were more strongly associated with high consumption of *trans*-fatty acids (prevalence odds ratio = 2.80, 95 percent CI: 1.14, 6.87) than were adenomas of the distal colon (prevalence odds ratio = 1.51, 95 percent CI: 0.68, 3.35); however, for the fourth quartiles, the *p* value for the difference between the two adenoma locations was 0.28. There does not appear to be a difference in the prevalence of multiple or large adenomas versus single or small adenomas with increasing consumption of *trans*-fatty acid.

Minimally adjusted prevalence odds ratios comparing the highest with the lowest consumptions of *trans*-fatty acid were 1.60 (95 percent CI: 0.75, 3.44) for hyperplastic polyps and 1.74 (95 percent CI: 0.98, 3.06) for adenomatous polyps. The estimates from the fully adjusted model were less precise but otherwise similar to the minimally adjusted estimates (table 4).

DISCUSSION

Using data from a large cross-sectional study, we found that the prevalence of colorectal adenomas was positively associated with high *trans*-fatty acid consumption. This association was not evident with lower levels of consumption, suggesting a possible threshold effect. We also identified a stronger association between high *trans*-fatty acid consumption and prevalence of proximal versus distal adenomas when these case subtypes were compared with controls, although a difference between associations with adenomas classified by location could not be firmly established given the precision of our estimates. Associations between *trans*-fatty acid consumption and location, size, and number of adenomas were imprecise but were consistently elevated for the highest versus lowest quartiles of consumption. This supports the conclusion that the association is limited to the highest versus lowest quartiles of consumption without clear differences in the relations by location, size, or number.

It is well established that adenomatous polyps are precursor lesions for colorectal cancer. However, recent evidence suggests that hyperplastic polyps may also have malignant potential (34). In addition, some studies have found that the risk factors for adenomatous polyps and hyperplastic polyps are similar. Smoking (35–37), fiber consumption (37, 38), alcohol intake (37, 38), and hormone replacement therapy use (35) have all been shown to increase the risk of both hyperplastic and adenomatous polyps. To explore the possibility that high *trans*-fatty acid consumption is associated with both types of polyps, we estimated associations with adenomas and hyperplastic polyps separately. The number of subjects within each quartile of consumption for this analysis was small, but point estimates were elevated for the fourth quartile of consumption, without clear differences between histologic subtypes. Further work with larger sample sizes needs to be performed before a definitive conclusion can be drawn.

Previous studies have generally not reported an association between total fat consumption and adenoma development. Randomized trials of a low-fat, high-fiber diet found no association between recurrent colorectal adenomas and total fat intake with intent-to-treat analyses (39, 40). Two earlier observational studies found associations between colorectal adenomas and higher total fat consumption (41, 42), but other observational studies have not confirmed this association. Using data from one of the above randomized trials (40), Cantwell et al. (43) estimated the association between what people actually reported consuming and the risk of recurrent adenomas with the use of food records collected during the intervention. There was no increase in the risk of recurrent colorectal adenomas with increasing consumption of total or saturated fats (43). Another study performed a similar analysis and also found no association between total fat intake and recurrent colorectal adenomas (44).

We hypothesized that specific types of fatty acids, rather than the overall amount, may be important in determining disease risk and, therefore, investigated the relation between *trans*-fatty acid intake and colorectal adenomas. Two prior studies (18, 19) also examined the relation between *trans*-fatty acids and colorectal adenomas. In these studies, investigators looked at the association between risk of colorectal adenomas and groups of foods that contain partially hydrogenated vegetable oils. Both studies reported a weak association between colorectal adenomas and high consumption of sweetened baked goods, but the authors concluded that there was no overall association between colorectal adenomas and consumption of partially hydrogenated vegetable oils. Only one of these studies went further and investigated the association between colorectal adenomas and the amount of *trans*-fatty acid (categorized in intervals of 2 g per day); there was no association after adjustment for confounding (18). However, in that study, because cases and controls were classified on the basis of sigmoidoscopy results, it is possible that cases with adenomas in the proximal colon were misclassified as controls. In addition, if *trans*-fatty acids differentially affect the proximal and distal sections of the colon, then results of the studies based on sigmoidoscopy will differ from those investigating adenomas of the entire colon.

Other studies have been performed to examine the association between *trans*-fatty acid consumption and colorectal cancer. Two case-control studies have shown a positive association between colorectal cancer and *trans*-fatty acid

consumption for women but no association for men (30, 45). However, similar studies have not detected any relation (46, 47). One study demonstrated a positive association between *trans*-fatty acid consumption and distal colorectal cancer in Whites (data unpublished).

This study has important strengths. First, every participant underwent complete colonoscopy to the cecum, increasing the likelihood that all visible adenomas were enumerated and that there was no misclassification of case-control status. The study had a high response rate. Dietary data were collected by use of a food frequency questionnaire that has been validated in other study populations. In addition, all colorectal adenoma pathology slides were reviewed by a single experienced gastrointestinal pathologist, and reliability was evaluated and found to be good.

There are some limitations to the present study. First, results may not be generalizable to other populations because the individuals going to UNC Hospitals for screening colonoscopies are not representative of the general population. However, previous reports with data from similar populations have identified associations that are supported by other studies. For example, in the Diet and Health Study III population, NSAID use was inversely associated with colorectal adenomas (33), which is consistent with two randomized control trials that reported associations between recurrent colorectal adenomas and aspirin use (31, 32). Other limitations are the relatively small size of the study population and the possibility that the people who participated in the study are different from those who refused. Also, Diet History Questionnaire-based estimates of *trans*-fatty acid consumption have not been validated. In addition, the Diet History Questionnaire does not ask participants about what brand of food they consumed. Different brands contain varying amounts of *trans*-fatty acids, and we were unable to distinguish participants that consumed brands with high amounts of *trans*-fatty acids from participants eating similar foods with lower amounts of *trans*-fatty acids. Recall bias is unlikely because the interviews were conducted before there was much publicity about the negative health effects of *trans*-fatty acids. Moreover we asked about consumption of specific foods so not only would participants need to have been aware of concerns regarding *trans*-fatty acid consumption, but they would also have needed knowledge of what foods contained *trans*-fatty acids. Moreover, patients may not be able to distinguish between the severity of adenomatous polyps and hyperplastic polyps (controls). Therefore, it is difficult to know whether individuals with hyperplastic polyps would have a more biased recall than those with no polyps at all and whether individuals with an adenomatous polyp would have greater recall bias than individuals with hyperplastic polyps. Finally, *trans*-fatty acid consumption may not be directly related to colorectal adenoma risk but may instead be acting as a proxy for unhealthy behaviors. We attempted to decrease this bias by controlling for other characteristics that are associated with unhealthy behaviors (energy intake, physical activity, and alcohol consumption).

In conclusion, we found that the highest quartile of *trans*-fatty acid consumption in our study population was positively associated with colorectal adenoma prevalence. These results provide further support for recommendations to limit consumption of *trans*-fatty acids.

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