Published in final edited form as:
Nutr Cancer. 2009 ; 61(4): 427–436. doi:10.1080/01635580802710725.

Associations between *Trans* Fatty Acid Consumption and Colon Cancer among Whites and African Americans in the North Carolina Colon Cancer Study I

Lisa C Vinikoor[1,2], **Jessie A Satia**[1,2,3], **Jane C Schroeder**[1], **Robert C Millikan**[1], **Christopher F Martin**[2], **Joseph Ibrahim**[4], and **Robert S Sandler**[2]

[1]Department of Epidemiology, School of Public Health, University of North Carolina, Chapel Hill, North Carolina

[2]Center for Gastrointestinal Biology and Disease, School of Medicine, University of North Carolina, Chapel Hill, North Carolina

[3]Department of Nutrition, School of Public Health, University of North Carolina, Chapel Hill, North Carolina

[4]Department of Biostatistics, School of Public Health, University of North Carolina, Chapel Hill, North Carolina

Abstract

Disparities in incidence and mortality rates of colon cancer exist between Whites and African Americans. Prior studies examined the association between *trans* fatty acid consumption and colorectal cancer, but none assessed this possible relationship within a large study population of African Americans and Whites. Using data from a population-based case-control study in North Carolina, we investigated this association with attention to possible racial differences. Cases and matched controls were queried on demographic characteristics, lifestyle factors, medical history, and diet. Cases reported higher daily consumption (grams/day) of *trans* fatty acids [mean 5.9 (SD 2.9) and median 5.5 (IQR 3.8-7.5)] compared to controls [mean 5.2 (SD 2.4) and median 4.7 (IQR 3.5-6.4)]. Energy-adjusted *trans* fatty acid consumption was not associated with colon cancer. Compared to participants in the lowest quartile of consumption, those in the highest quartile had an adjusted odds ratio of 1.01 (95% confidence interval 0.69, 1.49) for Whites and 0.99 (95% confidence interval 0.61, 1.62) for African Americans. No association was found between increased consumption of *trans* fatty acid and specific tumor location (proximal or distal colon). In conclusion, *trans* fatty acid consumption is not associated with colon cancer and does not contribute to disparities in colon cancer rates.

Introduction

Colorectal cancer is one of the most common cancers in the United States. There are appreciable disparities in incidence and mortality rates by race, with a higher burden of disease among African Americans. In the United States, the age-adjusted incidence rate for colorectal cancer is 70.2/100,000 for African American men compared to 63.7/100,000 for White men. The disparity is also seen among women, with African American women having an age-adjusted incidence rate of 53.5/100,000 compared to 45.9/100,000 in White women (1).

The etiology of colorectal cancer is thought to be due largely to environmental factors, such as physical activity and diet. Migrant studies have shown that, with increasing duration of residence, migrants have rates of colorectal cancer similar to those of their adopted country (2,3). Diet is thought to be one of the strongest environmental risk factors for colorectal cancer

(4,5). In a recent report from the World Cancer Research Fund/American Institute for Cancer Research, a panel concluded that consumption of red and processed meats and alcohol are likely to increase the risk of colorectal cancer (6).

Although socioeconomic factors and differential screening rates between African Americans and Whites may partly explain the disparity in colorectal cancer incidence, diet may play a role as well. Previous research using the North Carolina Colon Cancer Study I found that African Americans and Whites have different consumption patterns for various groups of foods (7). One of the components of diet that differed between these races was “fats, oils, and snacks,” with African Americans having a higher mean daily intake than Whites. This category included unsaturated, saturated, and *trans* fatty acids. Other reports from this study showed similar mean daily intakes of total fat and saturated fatty acids for Whites and African Americans (8).

Total dietary fat has previously been postulated to affect the risk of developing colorectal cancer but the majority of studies have shown no association (9,10). It is possible, however, that it is not overall fatty acid consumption but perhaps specific fatty acid subgroups that may be relevant to the etiology of colon cancer. For example, some studies have found consumption of n-3 polyunsaturated fatty acids to be inversely associated with colorectal cancer (11,12), although the results are inconsistent (11-14). Recently there has been concern over the health effects of *trans* fatty acid consumption. *Trans* fatty acids have been linked to increased risk of heart disease (15) and potentially type II diabetes (16). A few studies examined the association between colorectal cancer and *trans* fatty acid consumption (11-13,17) and reported inconsistent results. None of these studies has looked at this relationship within a large population of African Americans and Whites. If *trans* fatty acid consumption does play an etiological role in colon cancer, it is possible that differential consumption patterns between Whites and African Americans may account for some of the disparity in colorectal cancer incidence rates. In North Carolina, for instance, White men have an age-adjusted colorectal cancer incidence rate of 52.3/100,000 compared with a rate of 64.6/100,000 among African American men. For women in North Carolina, the incidence rates are 38.7 and 51.4/100,000 respectively (18).

The objectives of this study were to examine the associations of *trans* fatty acid consumption and colon cancer both overall and by location, as certain factors may affect the risk of colon cancer differently for the proximal and distal colon. This study contributes to the existing body of knowledge by exploring possible differences in the association by race using a large population-based sample.

Materials and Methods

The North Carolina Colon Cancer Study I (NCCCS I) was a large population-based case-control study conducted in central North Carolina. It enrolled subjects from 33 counties, representing urban, suburban, and rural areas of the state. The study was approved by the Institutional Review Board at the University of North Carolina School of Medicine.

Study Population

Cases were identified using the rapid case ascertainment system of the North Carolina Central Cancer Registry. Those patients with a first diagnosis of histologically confirmed adenocarcinoma of the colon between October 1996 and September 2000 were classified as potential cases. Additional eligibility requirements were as follows: aged 40-80 years, residence in one of the 33 study counties, able to give informed consent, able to complete an interview, had a North Carolina driver's license or identification card (if under the age of 65), and had received no denial by their primary physician for us to contact them.

Potential cases received a call from a race-matched enrollment specialist, who explained the study and scheduled an in-person interview with the patient once consent had been obtained. On average, interviews took place within five months of the participant's diagnosis. White cases were under-sampled for recruitment in order to increase the proportion of non-White cases in the study population.

Controls were selected from two sources: the North Carolina Department of Motor Vehicles records (for participants under the age of 65) and the Center for Medicare and Medicaid Services (previously the Health Care Financing Administration) records (for those 65 years and older). Potential controls were contacted in a manner similar to that of the cases. Controls were matched to cases using randomized recruitment strategies (19) with recruitment probabilities defined according to strata of 5-year age, sex, and race groups.

Data Collection

Interviews were conducted by trained nurse interviewers at the participant's residence or another convenient location. Participants were asked questions about demographic information, lifestyle factors, medical history, and diet. Physical activity was measured for occupational, non-occupational, and non-work/weekend activities using a modified version of a seven-day physical activity recall (20-22). Frequency, intensity, and duration was estimated and converted into a variable estimating MET minutes per day. Interviewers also measured the height and weight of each participant. They recorded the participant's self-reported weight for one year prior in order to capture weight prior to illness or cancer therapy for cases. Both cases and controls were offered a $25 incentive for participation in the study.

Dietary Information

Dietary information was collected using a modified version of the 100-item semiquantitiative Block Food Frequency Questionnaire (FFQ) (23). Twenty-nine foods commonly consumed in North Carolina were added to the questionnaire to offer local cuisine choices to participants. Each food item had three choices for portion size (given as “small,” “medium,” and “large”) and nine choices for frequency (ranging from “never or less than once per month” to “2+ times per day”). When estimating frequency and portion size, study participants were asked to use a reference period of the year prior to diagnosis (for cases) or interview (for controls) so that seasonal variations in diet could be captured. Additional questions were asked about the following: types of foods/oils used in cooking and preparation techniques, fats used in cooking, fortified beverage consumption, low-fat food consumption, and restaurant eating.

The version of the Block FFQ that we used did not contain nutritional information on *trans* fatty acids for any of the foods it included. Therefore, with the assistance of the Clinical Nutrition Research Center at the University of North Carolina, we paired each food listed in the Block FFQ with foods listed in the National Cancer Institute's Diet and History Questionnaire (DHQ). We assigned the amount of *trans* fatty acid listed for each food in the DHQ to the corresponding food in the Block FFQ (per 100 grams of food). If more than one DHQ food matched, we applied the mean amount of *trans* fatty acids for those foods to the corresponding Block FFQ food. Of the 201 Block FFQ foods, 176 (87.6%) were matched to foods in the DHQ. For the remaining foods, we searched for *trans* fatty acid values in the USDA National Nutrient Database for Standard Reference (Release 19) and eight more foods were assigned values (4.0% of all foods). We were unable to determine the amount of *trans* fatty acid in 17 foods (8.5%), which were assigned values of 0 grams of *trans* fatty acid. We employed the same methods to estimate energy (i.e. caloric) intake. One hundred percent of the Block FFQ foods were matched and assigned caloric values. The original values for caloric intake present in the Block FFQ and the values determined using the DHQ and USDA databases were highly correlated (correlation was greater than 0.99).

Data Analysis

We excluded participants with extreme or implausible values for energy intake [men: total kcal/day <800 or >5000 (n=10); women: total kcal/day <600 or >4000 (n=21)]. In addition, participants whose self-reported race was "other" were removed from further analyses (n=11).

We energy-adjusted the *trans* fatty acid variable using the residual method with total energy intake as the independent variable and *trans* fatty acid intake as the dependent variable (24, 25). This allowed us to investigate the association between *trans* fatty acid consumption and colon cancer independent of the amount of total energy consumed. In addition, energy adjustment removes potential variation contributed to the association by total energy intake (24). This method is often used for continuous nutrient values but is also an acceptable method of energy adjustment when the nutrient values are categorized (25). Residuals of *trans* fatty acid consumption were then divided into quartiles based on the distribution of consumption in the control population.

Unconditional logistic regression models were used to examine the relationship between colorectal cancer and *trans* fatty acid consumption. In all models, we included an offset term to account for the randomized recruitment sampling fractions (19). Highest educational level achieved (dichotomized as high school or less, more than high school), sex, and non-steroidal anti-inflammatory drug (NSAID) use (dichotomized as never/rare use, frequent use) were assessed as potential effect measure modifiers using tests of homogeneity and likelihood ratio tests with an *a priori* p-value cut-off of 0.15. Similar studies found that the relationship between *trans* fatty acid consumption and colon/colorectal cancer varied by sex (12,17) and NSAID use (17). Previous research has shown NSAID use to be inversely associated with colon cancer (26). NSAIDs could affect the association between *trans* fatty acid consumption and colon cancer if inflammation resulting from *trans* fatty acid consumption (27) affects the development of colon cancer. Highest level of education achieved was used as a proxy for socioeconomic status, as individuals with low socioeconomic status may have less access fresh foods (resulting in higher consumption of *trans* fatty acids). None of these were found to be odds ratio modifiers and interaction terms were not retained in the final models. Using the 10% change in estimate criterion with backwards elimination, we assessed the following variables, which have previously been found to be associated with colorectal cancer and which may be associated with *trans* fatty acid consumption, as potential confounding variables: family history of colorectal cancer (yes, no), body mass index (BMI) one year prior (normal, overweight, obese according to the World Health Organization cut-points), physical activity (quartiles based on the control group), NSAID use (never, occasional, regular), smoking status (never, former, current), highest level of education achieved (high school degree or less, some college, college degree or higher) alcohol consumption (none, one or fewer drinks/day, more than 1 drink/day), and total fatty acid consumption, dietary fiber consumption, folate consumption (dietary and supplemental), calcium consumption (dietary and supplemental), red meat consumption, total fruit/fruit juice consumption, and total vegetable consumption (quartiles based on the control groups). All models also included a term for the matching factors (five-year age and sex stratum) as well as total energy intake. We found that the only confounder of the energy-adjusted model was calcium intake; therefore, it was included with total energy intake, the matching factors, and the offset term in the final model.

We further explored the relationship between *trans* fatty acid consumption and colorectal cancer by examining the location of the cancer. Cases were categorized as having proximal tumors if the cancer was present in the cecum, ascending colon, hepatic flexure, or transverse colon. Cancers were considered distal tumors if they were present in the splenic flexure, descending colon, or sigmoid colon. Cases with unspecified tumor locations or overlapping lesions were excluded from this analysis (n=59). We estimated these associations using multinomial logistic regression and reevaluated potential odds ratio modifiers and confounders

using the aforementioned criteria. Due to the limitations of multinomial logistic regression, we were not able to include an offset term with these models. Alcohol consumption and calcium intake were confounders of the energy-adjusted model based on our change-in-estimate criterion and were included in the energy-adjusted model with the matching factors and energy intake.

Results

Among those who were eligible, reasons for not being interviewed were as follows: refusal (14% cases; 36% controls), untraceable (1% cases, 1% controls), not reachable by phone (6% cases, 1% controls), and physician denial (7% cases). Completed interviews were obtained for 1691 participants (643 cases, 1048 controls). The rate of study cooperation (interviewed/(interviewed+refused)) was 84% for cases and 63% for controls. Response rates (interview/eligible) for cases and controls were 72% and 61%, respectively. Excluding the aforementioned participants with implausible dietary values or self-reported “other” race, our final study population included 623 cases (341 Whites and 282 African Americans) and 1020 controls (606 Whites and 414 African Americans).

Characteristics of the study population are given in Table 1. The majority of participants were over 60 years old with less than a college degree. The proportion in both cases and controls of participants with a high school degree or less was greater among African Americans than Whites (cases: 72.3% versus 57.1%; controls: 69.1% versus 48.8%). Overall, cases had a higher mean BMI than controls [29.4 (standard deviation: 6.1) versus 28.4 (standard deviation: 5.8), respectively]. The proportion of African American cases and controls classified as overweight or obese (BMI of 25 kg/m^2 or higher) one year prior to diagnosis/interview was greater than the proportion of White cases and controls, respectively. Cases of both races were more likely to have a family history of colorectal cancer. Both Whites and African American cases reported higher total energy intake than their respective controls, and total energy intake was found to be associated with colon cancer among both races. This was demonstrated using a t-test as well as a logistic regression model adjusted for other potential confounders [p-values <0.01 for t-tests among both Whites and African Americans; logistic regression results for 100 kcal units of total energy intake: Whites, OR=1.05 (95% CI 1.02, 1.08); African Americans, OR=1.05 (95% CI 1.02, 1.07). Also *trans* fatty acid consumption and total energy intake were correlated in the control group (Pearson correlation coefficients greater than 0.79 overall and among Whites and African Americans).

Cases also had a higher mean daily intake of *trans* fatty acid than controls. White cases reported a mean (standard deviation) and median (interquartile range) *trans* fatty acid consumption of 5.9 (2.7) and 5.5 (3.9, 7.3) grams per day compared with 5.2 (2.4) and 4.8 (3.5, 6.4) grams per day for White controls (t-test p<0.01; Wilcoxon rank-sum test p<0.01). The mean (standard deviation) and median for African Americans were 6.1 (3.2) and 5.4 (3.7, 7.5) grams per day among cases and 5.2 (2.6) and 4.7 (3.5, 6.4) grams per day among controls, respectively (t-test p<0.01, Wilcoxon rank-sum test p<0.01). Although African American cases had a higher mean daily intake of *trans* fatty acids compared to White cases, these values were not statistically different (p-value 0.34).

Prior to adjustment for total energy intake, colon cancer was positively associated with high *trans* fatty acid consumption. Odds ratios adjusted for confounding factors other than energy intake comparing the fourth quartile with the first quartile of *trans* fatty acid consumption were 2.01 (95% CI: 1.22, 3.30) for Whites and 2.50 (95% CI: 1.40, 4.47) for African Americans (Table 2). This relationship did not persist in energy-adjusted analyses. The adjusted odds ratios for the fourth quartiles of consumption compared with the lowest quartiles were 1.01 (95% CI:

0.69, 1.49) and 0.99 (95% CI: 0.61, 1.62) for Whites and African Americans, respectively (Table 2).

In addition, we investigated whether the relationship between *trans* fatty acid consumption and cancer differed by tumor location (Table 3). There was no association present for proximal or distal colon cancer in relation to *trans* fatty acid consumption. Among Whites, the adjusted odds ratios (95% confidence intervals) for the highest quartile compared to the lowest quartile of intake were 1.05 (95% CI: 0.60, 1.83) and 0.92 (95% CI: 0.55, 1.56) for the proximal and distal colon, respectively. Adjusted odds ratios (95% confidence intervals) were 1.35 (95% CI: 0.71, 2.55) and 0.69 (95% CI: 0.36, 1.31), respectively, among African Americans.

Discussion

In this population-based case-control study of colon cancer in North Carolina, *trans* fatty acid consumption was not associated with colon cancer in either Whites or African Americans. In addition, the association did not differ between proximal or distal colon cancer locations. The point estimate for the highest quartile of *trans* fatty acid was greater for the proximal colon compared with the distal colon among African Americans, but due to a lack of precision we were unable to establish whether high *trans* fatty acid consumption was truly associated with cancer in this section of the colon. Without energy-adjustment there was a modest positive association between *trans* fatty acid consumption and colon cancer but because this association was not present in the energy-adjusted model, we conclude that it was likely due to confounding.

The greater consumption of “fats, oils, and snacks” by African Americans in comparison to the consumption by Whites previously illustrated in our research (7) does not appear to be due to *trans* fatty acid consumption, as Whites and African Americans had similar daily intakes of *trans* fatty acids in the present analyses. Moreover, the absence of an association between *trans* fatty acid consumption and colon cancer in energy-adjusted analyses, combined with the similarity in *trans* fatty acid consumption between the races, makes it unlikely that *trans* fatty acid consumption contributes to the disparity in colon cancer rates observed between Whites and African Americans.

To date, results of studies examining the association between colorectal cancer and *trans* fatty acid consumption have been mixed. Three previous case-control studies investigated at the association between *trans* fatty acid consumption and colon (17) and colorectal cancer (11, 12). One demonstrated that higher consumption was positively associated with colon cancer for post-menopausal women not on hormone replacement therapy (17) and another found an elevated relative risk among women, in general (12). There was no association among men in either study (12,17). The other case-control study also showed no association between colorectal cancer and *trans* fatty acid consumption (11). A cohort study, the Women's Health Study, also examined *trans* fatty acid consumption but found no association (13). No previous studies to which we could compare our results have examined the relationship between *trans* fatty acid consumption and colon cancer in a large population of African Americans. Among these studies, gram amounts of *trans* fatty acids consumption have varied. The levels seen in our study population are among the highest, but still are not very different than levels of consumption reported for other study populations. Therefore, differences in levels of consumption are unlikely to explain the discrepancies in study results.

We have previously shown that high consumption of *trans* fatty acid is associated with higher prevalence of colorectal adenomas (28). Other studies of adenomas have found no association (29,30). *Trans* fatty acids may work to increase the risk of colorectal adenomas by altering the concentration of fat and bile normally found in the colon (31), thereby irritating the colonic

mucosa and resulting in increased oxidative stress (32) and inflammation (27,32). In addition, some studies have shown that colonic bacteria metabolize bile acids to form compounds that are carcinogenic and increase cellular proliferation (9,33-35). *Trans* fatty acids may also affect insulin resistance (16,36,37), which could lead to increased cellular proliferation (38,39). It is plausible that these mechanisms bring about changes in the mucosa that result in the formation of adenomas but that *trans* fatty acid consumption does not affect the transition from adenoma to cancer in the colon. Other studies have also found certain exposures to be associated with colorectal adenomas but not with cancer. Despite the lack of association between *trans* fatty acid consumption and colon cancer in our study, if *trans* fatty acids have even a moderate effect on colorectal adenoma development, it can be expected that the current reductions in the amount of *trans* fatty acids in the food supply, through voluntary removal from food products and bans in the commercial food outlets of certain localities, will favorably affect the rates of colon cancer.

The present study has several strengths, one of which is that we performed in-depth in-person interviews. In addition, we had a large number of African Americans in the study population, which permitted us to examine associations separately for Whites and African Americans, a group that has not been examined with respect to *trans* fatty acid consumption and colon cancer. Also, our study was geographically diverse, including individuals from urban, suburban, and rural areas. There are limitations to the study as well. We did not have *trans* fatty acid values for all of the foods options present in the Block FFQ. For example, fried chicken can be classified as homemade or restaurant-made. These may have different amounts of *trans* fatty acid but we assigned them the same value. This is unlikely to have greatly affected our results as it was a potential problem for a small number of foods that contributed to only a minor part of participants' reported diets. Also, the mean grams per day of *trans* fatty acid reported in our study was comparable to that seen in similar studies, thereby supporting our estimates of *trans* fatty acid values. There are always some errors inherent in dietary measurements using food frequency questionnaires. First, participants' recall of their diet over the past year may have been biased by their most recent consumption patterns. In addition, we have no information on brands of food consumed, so we cannot differentiate between an individual who consumed a specific food but chose a brand with low amounts of *trans* fatty acid from an individual who chose the same food and a brand with high amounts of *trans* fatty acid. Nonetheless, ranking individuals into quartiles based on their energy-adjusted *trans* fatty acid consumption allowed us to compare risks according to relative amounts of consumption and avoid bias due to minor misclassification of absolute levels of consumption. As with all case-control analyses, our study was subject to selection and recall biases. However, selection bias is likely to have been minimal because of high response rates among both cases and controls and the randomized recruitment strategies employed. Recall bias is also unlikely to have affected results, as no studies examining *trans* fatty acid consumption and colon/colorectal cancer had been published prior to the completion of our study. In addition, for participants to respond differentially, they would need to know the amount of *trans* fatty acids in each of the foods present in the Block FFQ.

In conclusion, using data from a large case-control study, we found no association of *trans* fatty acid consumption with colon cancer in either Whites or African Americans. Based on these results, it is unlikely that *trans* fatty acid intake contributes to racial disparities in colon cancer incidence.

Acknowledgments

Grant support was received from the following: National Institutes of Health T32DK07634, P30DK34987, R01CA66635, DK56350.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, et al. Cancer statistics, 2007. CA Cancer J Clin 2007;57:43–66. [PubMed: 17237035]
2. McMichael AJ, Giles GG. Cancer in migrants to Australia: extending the descriptive epidemiological data. Cancer Res 1988;48:751–756. [PubMed: 3335035]
3. Wilmink AB. Overview of the epidemiology of colorectal cancer. Dis Colon Rectum 1997;40:483–493. [PubMed: 9106701]
4. Giovannucci, E.; Wu, K. Cancers of the Colon and Rectum. In: Schottenfeld, D.; Fraumeni, JF., editors. Cancer Epidemiology and Prevention. 3. New York: Oxford University Press Inc.; 2006.
5. Potter, JD.; Hunter, D. Colorectal Cancer. In: Adami, HO.; H, D.; Trichopoulos, D., editors. Textbook of Cancer Epidemiology. New York: Oxford University Press; 2002. p. 188-211.
6. World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington DC: AICR; 2007.
7. 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;109:728–736. [PubMed: 14999782]
8. Satia-Abouta J, Galanko JA, Potter JD, Ammerman A, Martin CF, et al. Associations of total energy and macronutrients with colon cancer risk in African Americans and Whites: results from the North Carolina colon cancer study. Am J Epidemiol 2003;158:951–962. [PubMed: 14607803]
9. Giovannucci E, Goldin B. The role of fat, fatty acids, and total energy intake in the etiology of human colon cancer. Am J Clin Nutr 1997;66:1564S–1571S. [PubMed: 9394716]
10. Howe GR, Aronson KJ, Benito E, Castelleto R, Cornee J, et al. The relationship between dietary fat intake and risk of colorectal cancer: evidence from the combined analysis of 13 case-control studies. Cancer Causes Control 1997;8:215–228. [PubMed: 9134246]
11. Nkondjock A, Shatenstein B, Maisonneuve P, Ghadirian P. Assessment of risk associated with specific fatty acids and colorectal cancer among French-Canadians in Montreal: a case-control study. Int J Epidemiol 2003;32:200–209. [PubMed: 12714537]
12. Theodoratou E, McNeill G, Cetnarskyj R, Farrington SM, Tenesa A, et al. Dietary fatty acids and colorectal cancer: a case-control study. Am J Epidemiol 2007;166:181–195. [PubMed: 17493949]
13. Lin J, Zhang SM, Cook NR, Lee IM, Buring JE. Dietary fat and fatty acids and risk of colorectal cancer in women. Am J Epidemiol 2004;160:1011–1022. [PubMed: 15522858]
14. MacLean CH, Newberry SJ, Mojica WA, Khanna P, Issa AM, et al. Effects of omega-3 fatty acids on cancer risk: a systematic review. JAMA 2006;295:403–415. [PubMed: 16434631]
15. Zaloga GP, Harvey KA, Stillwell W, Siddiqui R. *Trans* fatty acids and coronary heart disease. Nutr Clin Pract 2006;21:505–512. [PubMed: 16998148]
16. Odegaard AO, Pereira MA. *Trans* fatty acids, insulin resistance, and type 2 diabetes. Nutr Rev 2006;64:364–372. [PubMed: 16958313]
17. Slattery ML, Benson J, Ma KN, Schaffer D, Potter JD. Trans-fatty acids and colon cancer. Nutr Cancer 2001;39:170–175. [PubMed: 11759276]
18. U.S. Cancer Statistics Working Group. United States Cancer Statistics: 2004 Incidence and Mortality. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2007.
19. Weinberg CR, Sandler DP. Randomized recruitment in case-control studies. Am J Epidemiol 1991;134:421–432. [PubMed: 1877602]
20. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32:S498–S504. [PubMed: 10993420]
21. Blair SN, Haskell WL, Ho P, Paffenbarger RS Jr, Vranizan KM, et al. Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. Am J Epidemiol 1985;122:794–804. [PubMed: 3876763]
22. Richardson MT, Ainsworth BE, Jacobs DR, Leon AS. Validation of the Stanford 7-day recall to assess habitual physical activity. Ann Epidemiol 2001;11:145–153. [PubMed: 11164131]

23. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, et al. A data-based approach to diet questionnaire design and testing. Am J Epidemiol 1986;124:453–469. [PubMed: 3740045]
24. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27. [PubMed: 3521261]
25. Willett, W.; Stampfer, MJ. Implications of total energy intake for epidemiologic analyses. In: Willett, W., editor. Nutritional Epidemiology. 2. New York: Oxford University Press; 1998. p. 273-301.
26. Baron JA, Sandler RS. Nonsteroidal anti-inflammatory drugs and cancer prevention. Annu Rev Med 2000;51:511–523. [PubMed: 10774479]
27. Mozaffarian D, Pischon T, Hankinson SE, Rifai N, Joshipura K, et al. Dietary intake of trans fatty acids and systemic inflammation in women. Am J Clin Nutr 2004;79:606–612. [PubMed: 15051604]
28. Vinikoor LC, Schroeder JC, Millikan RC, Satia JA, Martin CF, et al. Consumption of *trans* fatty acid and its association with colorectal adenomas. Am J Epidemiol 2008;168:289–297. [PubMed: 18587137]
29. McKelvey W, Greenland S, Chen MJ, Longnecker MP, Frankl HD, et al. A case-control study of colorectal adenomatous polyps and consumption of foods containing partially hydrogenated oils. Cancer Epidemiol Biomarkers Prev 1999;8:519–524. [PubMed: 10385142]
30. McKelvey W, Greenland S, Sandler RS. A second look at the relation between colorectal adenomas and consumption of foods containing partially hydrogenated oils. Epidemiology 2000;11:469–473. [PubMed: 10874557]
31. Colandre ME, Diez RS, Bernal CA. Metabolic effects of trans fatty acids on an experimental dietary model. Br J Nutr 2003;89:631–639. [PubMed: 12720583]
32. Kuhnt K, Wagner A, Kraft J, Basu S, Jahreis G. Dietary supplementation with 11trans- and 12trans-18:1 and oxidative stress in humans. Am J Clin Nutr 2006;84:981–988. [PubMed: 17093147]
33. Franco A, Sikalidis AK, Solis Herruzo JA. Colorectal cancer: influence of diet and lifestyle factors. Rev Esp Enferm Dig 2005;97:432–448. [PubMed: 16011418]
34. O'Keefe SJ. Nutrition and colonic health: the critical role of the microbiota. Curr Opin Gastroenterol 2008;24:51–58. [PubMed: 18043233]
35. Reddy BS, Simi B, Patel N, Aliaga C, Rao CV. Effect of amount and types of dietary fat on intestinal bacterial 7 alpha-dehydroxylase and phosphatidylinositol-specific phospholipase C and colonic mucosal diacylglycerol kinase and PKC activities during stages of colon tumor promotion. Cancer Res 1996;56:2314–2320. [PubMed: 8625306]
36. Saravanan N, Haseeb A, Ehtesham NZ, Ghafoorunissa. Differential effects of dietary saturated and trans-fatty acids on expression of genes associated with insulin sensitivity in rat adipose tissue. Eur J Endocrinol 2005;153:159–165. [PubMed: 15998628]
37. Riserus U. Trans fatty acids and insulin resistance. Atheroscler Suppl 2006;7:37–39. [PubMed: 16713388]
38. Bruce WR, Giacca A, Medline A. Possible mechanisms relating diet and risk of colon cancer. Cancer Epidemiol Biomarkers Prev 2000;9:1271–1279. [PubMed: 11142411]
39. Giovannucci E. Insulin, insulin-like growth factors and colon cancer: a review of the evidence. J Nutr 2001;131:3109S–3120S. [PubMed: 11694656]

TABLE 1

Characteristics of the North Carolina Colon Cancer Study I (NCCCS I) population by case status and race, North Carolina, 1996-2000

Participant Characteristics	Whites (n=947)		African-Americans (n=696)	
	Cases (n=341)	Controls (n=606)	Cases (n=282)	Controls (n=414)
Age (%)				
<50	27 (7.92)	34 (5.61)	37 (13.12)	25 (6.04)
50-59	66 (19.35)	108 (17.82)	73 (25.89)	81 (19.57)
60-69	117 (34.31)	206 (33.99)	92 (32.62)	129 (31.16)
>70 years	131 (38.42)	258 (42.57)	80 (28.37)	179 (43.24)
Mean years (SD)‡	65.06 (9.70)	66.16 (9.30)	62.04 (10.32)	65.94 (9.63)
Sex (%)				
Men	190 (55.72)	328 (54.13)	135 (47.87)	181 (43.72)
Women	151 (44.28)	278 (45.87)	147 (52.13)	233 (56.28)
Education (%)				
≤ High School	194 (57.06)	296 (48.84)	204 (72.34)	286 (69.08)
Some college	69 (20.29)	148 (24.42)	50 (17.73)	73 (17.63)
College graduate/advanced degree	77 (22.65)	162 (26.73)	28 (9.93)	55 (13.29)
Body Mass Index 1 year prior to enrollment (%)*				
Normal (18-24.9 kg/m2)	95 (28.53)	190 (31.99)	44 (15.94)	81 (20.72)
Overweight (25-29.9 kg/m2)	139 (41.74)	250 (42.09)	113 (40.94)	145 (37.08)
Obese (>=30 kg/m2)	99 (29.73)	154 (25.93)	119 (43.12)	165 (42.20)
Mean kg/m^2 (SD)‡	28.37 (5.62)	27.57 (5.15)	30.07 (6.52)	29.73 (6.50)
Physical Activity (MET-minutes/day) (mean, %)*				
1st quartile	64 (18.93)	121 (20.17)	73 (27.24)	131 (32.11)
2nd quartile	87 (25.74)	151 (25.17)	62 (23.13)	102 (25.00)
3rd quartile	95 (28.11)	175 (29.17)	59 (22.01)	76 (18.63)
4th quartile	92 (27.22)	153 (25.50)	74 (27.61)	99 (24.26)
Mean MET-minutes/day (SD)‡	2261.46 (565.66)	2199.71 (450.66)	2229.19 (566.56)	2154.99 (533.56)
Smoking status (%)				
Never	115 (33.92)	243 (40.10)	133 (47.50)	188 (45.41)
Former	180 (53.10)	267 (44.06)	91 (32.50)	143 (34.54)
Current	44 (12.98)	96 (15.84)	56 (20.00)	83 (20.05)
Family History (%)				
Yes	74 (21.83)	57 (9.48)	47 (16.67)	43 (10.41)
No	265 (78.17)	544 (90.52)	235 (83.33)	370 (89.59)
NSAID use over the past 5 years (%)†				
Never	38 (11.18)	43 (7.10)	32 (11.35)	31 (7.49)
Occasionally	128 (37.65)	173 (28.55)	123 (43.62)	133 (32.13)
Regularly	174 (51.18)	390 (64.36)	127 (45.04)	250 (60.39)
Trans Fatty Acid Consumption				

Participant Characteristics	Whites (n=947)		African-Americans (n=696)	
	Cases (n=341)	Controls (n=606)	Cases (n=282)	Controls (n=414)
Mean grams/day (SD)‡	5.85 (2.69)	5.17 (2.35)	6.07 (3.15)	5.20 (2.56)
Total Energy Intake				
Mean kcal/day (SD)‡	1951.58 (689.12)	1784.01 (599.53)	1940.41 (832.11)	1697.62 (652.52)
Calcium Consumption§				
Mean milligrams/day (SD)‡	868.97 (482.36)	980.24 (522.15)	676.62 (392.36)	672.15 (377.45)
Alcohol Consumption				
0 drinks/day	209 (61.29)	361 (59.57)	220 (78.01)	334 (80.68)
>0 and ≤1 drink/day	81 (23.75)	182 (30.03)	38 (13.48)	67 (16.18)
>1 drink/day	51 (14.96)	63 (10.40)	24 (8.41)	13 (3.14)
Fiber Consumption				
Mean grams/day (SD)‡	14.18 (5.83)	13.95 (5.95)	13.89 (6.22)	14.03 (6.00)
Folate Consumption§				
Mean micrograms/day (SD)‡	442.91 (240.16)	393.95 (222.73)	426.31 (252.64)	414.14 (230.36)
Red Meat Consumption				
Mean grams/day (SD)‡	139.00 (94.96)	118.33 (80.06)	122.77 (85.56)	104.14 (77.85)
Red Meat Consumption				
Mean grams/day (SD)‡	139.00 (94.96)	118.33 (80.06)	122.77 (85.56)	104.14 (77.85)
Fruit/Fruit juice Consumption				
Mean grams/day (SD)‡	173.38 (147.34)	171.31 (140.04)	178.43 (169.17)	162.45 (133.40)
Vegetable Consumption				
Mean grams/day (SD)‡	231.99 (107.13)	251.94 (123.00)	188.92 (117.43)	191.40 (105.37)

*Data were missing for: Education (n=1), BMI (n=49), physical activity (n=29), smoking status (n=4) and family history (n=8), NSAID use (n=1)

†Non-steroidal anti-inflammatory drug (NSAID) use is defined as Never for subjects who reported no use, Occasional for subjects who reported some use but use less than 15 times/month, and Frequent for subjects who reported use at least 15 times/month

‡Standard deviation: SD

§Combined dietary and supplemental intake

TABLE 2

Odds ratios (95% confidence intervals)* of quartiles of non-energy adjusted and energy adjusted *trans* fatty acid intake with colon cancer risk by race, NCCCS I, 1996-2000

NON-ENERGY ADJUSTED†

		WHITES				AFRICAN AMERICANS			
Quartiles of *trans* fatty acid consumption	**Median grams trans fatty acid/day (IQR)**	**N cases**	**N controls**	**OR**	**95% CI**	**N cases**	**N controls**	**OR**	**95% CI**
1	2.70 (2.22, 3.11)	62	140	1.00		57	96	1.00	
2	4.07 (3.76, 4.41)	66	136	1.02	0.65, 1.60	52	104	0.87	0.52, 1.45
3	5.50 (5.11, 5.91)	77	154	1.10	0.69, 1.77	57	85	1.36	0.79, 2.33
4	8.04 (7.20, 9.79)	122	144	2.01	1.22, 3.30	105	96	2.50	1.40, 4.47

ENERGY ADJUSTED‡

		WHITES				AFRICAN AMERICANS			
Quartiles of *trans* fatty acid consumption	Median grams energy-adjusted trans fatty acid/day (IQR)	N cases	N controls	OR	95% CI	N cases	N controls	OR	95% CI
1	4.26 (3.66, 4.59)	92	173	1.00		53	70	1.00	
2	5.24 (5.07, 5.44)	79	138	1.10	0.74, 1.63	57	108	0.80	0.47, 1.34
3	5.99 (5.81, 6.19)	69	137	0.87	0.58, 1.32	75	111	1.02	0.62, 1.68
4	7.12 (6.71, 7.84)	94	138	1.01	0.69, 1.49	91	114	0.99	0.61, 1.62

*Odds ratio: OR; 95% confidence interval (95%CI); Interquartile Range: IQR

†Adjusted for age, sex, vegetable consumption, meat consumption, calcium intake, and BMI

‡Adjusted for age, sex, energy intake, and calcium intake

TABLE 3

Odds ratios (95% confidence intervals)* of quartiles of non-energy adjusted and energy adjusted *trans* fatty acid intake with colon cancer risk by location and race, NCCCS I, 1996-2000

Quartiles of trans fatty acid consumption§	WHITES								AFRICAN AMERICANS							
	Non-Energy Adjusted†				Energy Adjusted‡				Non-Energy Adjusted†				Energy Adjusted‡			
	N cases	N controls	OR	95% CI	N cases	N controls	OR	95% CI	N cases	N controls	OR	95% CI	N cases	N controls	OR	95% CI
	PROXIMAL COLON															
1	26	140	1.00		42	173	1.00		23	96	1.00		22	70	1.00	
2	34	134	1.15	0.62, 2.15	40	138	1.40	0.83, 2.37	25	104	1.08	0.55, 2.14	29	108	0.97	0.49, 1.90
3	33	153	1.22	0.63, 2.35	23	137	0.73	0.40, 1.35	26	84	1.72	0.84, 3.55	24	111	0.77	0.39, 1.55
4	44	144	1.96	0.98, 3.96	35	138	1.05	0.60, 1.83	46	96	3.10	1.45, 6.63	48	114	1.35	0.71, 2.55
	DISTAL COLON															
1	32	140	1.00		43	173	1.00		31	96	1.00		31	70	1.00	
2	28	134	0.79	0.43, 1.46	35	138	0.96	0.56, 1.63	24	104	0.69	0.36, 1.33	26	108	0.77	0.39, 1.50
3	37	153	0.96	0.51, 1.80	35	137	0.90	0.52, 1.56	25	84	0.93	0.46, 1.85	38	111	1.26	0.68, 2.33
4	58	144	1.55	0.81, 2.99	46	138	0.92	0.55, 1.56	49	96	1.72	0.82, 3.59	28	114	0.69	0.36, 1.31

*Odds ratio: OR; 95% confidence interval (95%CI)

†Adjusted for age, sex, calcium intake, meat consumption, alcohol consumption, BMI one year prior, and family history of colorectal cancer

‡Adjusted for age, sex, energy intake, calcium intake, and alcohol intake

§Median grams trans fatty acid/day (IQR): Non-energy adjusted quartiles: Q1) 2.70 (2.22, 3.11); Q2) 4.07 (3.76, 4.41); Q3) 5.50 (5.11, 5.91); Q4) 8.04 (7.20, 9.79); Energy adjusted quartiles: Q1) 4.26 (3.66, 4.59); Q2) 5.24 (5.07, 5.44); Q3) 5.99 (5.81, 6.19); Q4) 7.12 (6.71, 7.84)