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Association Between Body Size and Colorectal Adenoma Recurrence

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Abstract

Background and Aims—Obesity has been associated with increased risk for colorectal adenoma, though its role as a risk factor after polypectomy for successive events is unclear. Therefore, we sought to evaluate the effect of anthropometric measures of obesity on adenoma after polypectomy.

Methods—Subjects with baseline adenomas (n=2465) and follow-up colonoscopy data were drawn from two randomized trials designed to prevent adenoma recurrence.

Results—Presence of a BMI ≥ 30 kg/m² was associated with a non-significant 17% increase in the odds for any adenoma recurrence among all subjects (OR=1.17; 95% CI=0.92–1.48). This result was confined to men (OR= 1.36; 95% CI=1.01–1.83), and not observed for women (OR=0.90; 95% CI= 0.60–1.33). Results for waist circumference did not reach statistical significance, though trends were similar to those for BMI. Analyses of the effects of obesity on more clinically significant lesions demonstrated that high BMI was a slightly stronger risk factor for advanced adenoma recurrences in men (OR=1.62; 95% CI=1.04–2.53) when compared to non-advanced lesions (OR= 1.26; 95% CI= 0.91–1.75). Additionally, we observed an association for obesity and odds of adenoma recurrence among participants reporting a family history of colorectal cancer (OR=2.25; 95% CI= 1.32–3.84), but not for those without (OR=1.00; 95% CI=0.77–1.31; $p_{int} = p=0.008$).

Conclusions—Our results support obesity as a risk factor for subsequent short-interval development of colorectal adenomas, particularly among men and persons with a family history of colorectal cancer. Further, obesity in men appears to be strongly associated with the development of clinically advanced lesions.

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Introduction

The presence of colorectal adenomas at endoscopy identifies a group of individuals at higher risk for future development of colorectal cancer as compared to those without adenomas. Among patients that have had colorectal adenomas, recognized predictors of subsequent lesions include age, adenoma size, histology and multiplicity of the lesions at detection¹. Depending on the age of the population, between 20 and 50% of those patients with adenomas will recur within a 3–5 year period, with 10–20% of recurrent lesions possessing clinically advanced features (larger size, villous histology, and/or high-grade dysplasia)^{2–6}. The current recommendation for patients presenting with small polyps (less than 1 cm) is to have a follow-up colonoscopy 5–10 years after the initial procedure¹. Identification of risk factors that influence the rate of development of adenomas is important in determining and planning subsequent follow-up intervals for screening, and for the identification of modifiable factors for targeted risk reduction in at-risk individuals. One such risk factor may be obesity.

In the United States, obesity has risen to epidemic proportions⁷ making it the most important nutritional disease in our society. Abundance of food and high-energy diets are now common in Western cultures and are reflected in anthropometric population shifts, with significantly higher body fat in children and adults⁷. The evidence for obesity as a common risk factor in a number of human diseases, including colorectal cancer, has led to the hypothesis that the metabolic changes associated with chronic overeating and sedentary behaviors have a role in development of many pathologies⁸. The majority of epidemiologic studies support a role for obesity as a risk factor for colorectal adenomas^{9–18}, cancers^{12, 19–30}, and colon cancer mortality^{31, 32}. These observations suggest a continuous action of the adverse effects of obesity along the adenoma to carcinoma continuum, starting early in colon tumorigenesis. In general, the effect of obesity on colorectal cancer risk has been stronger for cancers arising in the colon as compared to the rectum, and for those occurring in men as compared to women^{33, 24} 27 3435. Recent work has also suggested that a family history of colorectal cancer may render one more susceptible to lifestyle-related risk factors for colorectal adenoma^{36, 37}; therefore, body size may have differential effects in those with a family history as compared to those without.

In addition to body mass index (BMI), measures of central adiposity such as waist circumference and waist-to-hip ratio (WHR) are used to assess disease risk related to body size. Findings from the prospectively-collected Framingham Cohort²⁷, suggest that waist circumference and WHR may be more informative for risk of colon cancer than measures of BMI. Earlier data from the Health Professionals Follow up Study¹² reported similar findings, where stronger associations for colorectal cancer were observed with measures of waist circumference than for BMI. However, the best measure of body size for evaluation of risk for colorectal neoplasia remains equivocal. The primary aim of the current study was to evaluate whether obesity and/or waist circumference are associated with colorectal adenoma recurrence, and to assess which of these measures may better describe the relationship of body size to the development of colorectal neoplasia. The secondary aim was to determine whether the effect of body size varied by gender or a family history of colorectal cancer.

Materials and Methods

The current analyses were conducted with data collected from the combined study populations of two randomized clinical trials, the Wheat Bran Fiber [WBF] Trial² and the Ursodeoxycholic Acid [UDCA] Trial³. Both studies were approved by the University of Arizona Human Subjects Committee and local hospital committees, and written informed consent was obtained from each participant prior to study enrollment.

Briefly, the WBF trial was a randomized, double-blind, controlled trial conducted to compare the effect of a high-fiber vs. a low-fiber cereal supplement on adenoma recurrence among individuals who had undergone colonoscopy and had one or more adenoma(s) removed². A total of 1429 participants were randomized into the trial and 1304 (91.3%) completed the study by undergoing one or more colonoscopies after randomization². The mean follow-up time from randomization to colonoscopy was 3.1 years. No effect of the high-fiber supplement was detected for colorectal adenoma recurrence as compared to the low-fiber supplement².

The UDCA trial was a randomized, double-blind, placebo-controlled trial conducted to compare the effect of UDCA on adenoma recurrence among patients that had a prior polyp removed at colonoscopy³. A total of 1285 participants were randomized to either the treatment or placebo group, with 1192 participants (92.8%) completing the study³. The mean follow-up time from randomization to colonoscopy was 3.2 years. Compared to the placebo group, those in the ursodeoxycholic acid group had no significant difference in risk for colorectal adenoma recurrence³.

Data Collection

Self-administered questionnaires were used to obtain data on diet, sociodemographic variables, and medical history. The height and weight of each participant were measured at baseline by study personnel. Waist and hip circumference were self-reported; participants repeated both measurements three times and documented the measurements to the nearest 1/16 of an inch. Participants were instructed to measure their waist at the smaller circumference of their natural waist, which is usually just above the belly button. The hip measurement was taken at the maximal protrusion of the buttocks, or at 6 inches below the waist. Participants were classified into one of three weight classifications based on their BMI (kg/m²): normal weight (BMI >18.5 and < 25), overweight (BMI ≥ 25 and <30), and obese (BMI ≥ 30). Baseline waist measurements were used to classify waist size as small, medium, large, and extra-large separately for males and females based the population distribution in order to ensure a more equal distribution of waist sizes by category. For men, the categories were as follows: small waist circumference was < 36.5 inches; medium was 36.5–39.0 inches; large was 39.1–42.0 inches; and extra large was >42.0 inches. For women, the categories for waist circumference were defined as <30.0, 30.0–33.1, 33.2–37.0, and >37.0 inches for small, medium, large, and extra-large, respectively.

Definition of Adenoma Recurrence and Advanced Adenoma Recurrence

As reported previously³⁸, data regarding adenoma characteristics (i.e., number, size, location, and histology) were obtained from the medical record and the pathology report for each subject. Any colorectal adenoma detected at colonoscopy at least six months after randomization to either trial was counted as a recurrent adenoma. Adenomas were classified as advanced if they had a diameter of 1 cm or more and/or tubulovillous or villous histology (at least 25% villous). Additionally, adenocarcinomas were counted as advanced recurrences. All other adenomas were considered non-advanced. In subjects with more than one adenoma, size and characterization of the histologic type were based on the largest and/or most advanced adenoma.

Statistical Analysis

All analyses were conducted using STATA statistical software package [version 9.0, Stata Corporation, College Station, TX]. Summary data for baseline characteristics by study and by category of BMI were calculated using means and standard deviations for the continuous variables and frequencies and percentages for the categorical variables. Statistically significant differences between WBF and UCDA or between BMI categories were tested using the

student's t-test for continuous variables and chi-square analyses for categorical variables. All statistical tests were two-sided and deemed statistically significant at $p \leq 0.05$.

Unconditional logistic regression modeling was used to assess the associations between BMI, waist circumference, and adenoma recurrence. First, regression models were used to determine which baseline variables were associated with both adenoma recurrence and BMI or waist circumference, and as such might be potential confounders. Variables tested for confounding included age, treatment group, dietary intake of fat, energy, fiber, alcohol, calcium, aspirin use, family history of colorectal cancer, gender, race, history of previous polyps, smoking, number of colonoscopies, and baseline adenoma characteristics. If a variable changed the point estimate by 10% or greater, it was considered a potential confounder³⁹ and included in the final multivariate logistic regression analyses of body size and adenoma recurrence. Though not identified as a classical confounder, a variable accounting for study (WBF vs. UDCA) was also added to final model to account for any potential differences between the two study populations. Two multivariate models were then constructed; the first included the confounding variables and the second included the confounding variables plus simultaneous adjustment for BMI and waist circumference.

Multinomial logistic regression was used to evaluate the association between body size and both non-advanced and advanced recurrences. This analysis allowed for assessment of the effect of body size on type of adenoma by comparing non-advanced recurrence to no recurrence while excluding all advanced recurrences, and conversely to compare advanced to no recurrence by excluding all non-advanced recurrences. For the analysis of adenoma recurrence by family history, the final multivariate models for BMI and waist circumference were run separately among those who had no family history of colorectal cancer and those who did report a history.

Results

As shown in Table 1, age, gender, race, smoking, number of colonoscopies, large or villous baseline adenomas, and rates of obesity were not significantly different between the WBF and UDCA trials. Differences between the two studies were observed for a family history of colorectal cancer, with 16.9% of those in the WBF trial reporting a family history as compared to 27.6% in the UDCA trial, and for history of polyps prior to randomization to the trial (39.1% in WBF vs. 47.1% in UDCA). Participants in the UDCA trial were more likely to have had a proximal adenoma at baseline compared to those in the WBF trial (33.9% vs. 27.1%, respectively). Finally, significant differences were observed between the two studies for waist circumference. Those in the UDCA trial were more likely to have an extra-large waist circumference than those in the WBF trial, and less likely to have a small waist circumference. Therefore, we initially assessed the effect of BMI and waist circumference in each of the two studies separately (data not shown). We observed similar relationships between measures of body size and central adiposity in each of the studies, and thus pooled the data to derive a stronger point estimate of these associations. We retained a variable for study (WBF vs. UDCA) in the logistic regression models to control for any differences between the two trials.

Table 2 presents the characteristics of participants in the pooled trials by BMI category (normal, overweight, and obese). In the total population, 45% percent of subjects were categorized as overweight (n= 1120) and 24% obese (n= 606). Those who were categorized as obese were significantly younger than those who were normal weight ($p < 0.001$) and those who were overweight ($p < 0.001$), and were more likely to be male than normal weight individuals ($p < 0.001$). However, the proportion of males classified as obese was lower than the proportion who were overweight ($p < 0.001$). Smoking was significantly less common in those overweight ($p < 0.001$) and obese ($p < 0.001$) compared to normal weight individuals. Those who were

overweight ($p < 0.01$) or obese ($p < 0.05$) were significantly more likely to have had more than one adenoma at baseline than those who were normal weight. With regard to adenoma recurrence rates, those who were obese were significantly more likely to recur with a non-advanced adenoma compared to normal weight participants; while those who were overweight exhibited a greater percentage of advanced adenomas compared to normal weight individuals. In addition, men who were overweight recurred more often with advanced adenomas compared to normal weight men. However, these comparisons are not adjusted for potentially confounding variables as presented using logistic regression modeling in Tables 3, 4, and 5.

The odds ratios and 95% confidence intervals for adenoma recurrence by category of BMI are shown in Table 3. We observed a non-significant 17% increase in odds of recurrence (OR=1.17; 95% CI= 0.92–1.48) associated with obesity (BMI ≥ 30 kg/m²) as compared to normal weight individuals that was completely attenuated by adding waist size to the model (OR=1.08; 95% CI= 0.74–1.57). When stratified by gender, increasing BMI was associated with increased odds of recurrence only in men (OR=1.36; 95% CI= 1.01–1.83; p -trend= 0.04), with the results slightly attenuated after adding waist size to the model (OR =1.29; 95% CI=0.82–2.04, p -trend=0.27). In contrast to men, we observed no associations for overweight or obese women.

Based on the lack of an observable influence of BMI on adenoma recurrence in women and findings of published studies suggesting that body composition is poorly captured in women by BMI measures⁴⁰ we evaluated whether waist circumference (Table 3) was independently associated with recurrence separately for women and men. When categorized into four waist sizes (small, medium, large and extra large), waist circumference was not significantly associated with colorectal adenoma recurrence in the total population, or among men and women separately. An analysis of waist-to-hip ratio contributed no added information on associations in our population (data not shown).

To assess whether or not BMI had a specific effect on more advanced adenomas, we tested associations between BMI and waist size on the recurrence of the clinically advanced adenomas (*i.e.*, adenomas ≥ 1 cm and/or with villous histology). In the total population and among women, we observed no significant effect of body size measured as BMI on non-advanced or advanced recurrences (Table 4). In contrast, men who were overweight or obese were at significantly increased odds for advanced recurrence (OR 1.60; 95% CI=1.09–2.33 and OR=1.62; 95% CI=1.04–2.53, respectively; p -trend=0.03) when compared to results for non-advanced lesions in overweight (OR=0.97; 95% CI=0.73–1.29) and obese (OR =1.26; 95% CI=0.91–1.75; p -trend=0.17) men. No significant associations were observed for waist circumference and either non-advanced or advanced recurrence in the total population or in the gender-specific analyses.

Following reports that a positive family history of colon cancer enhances individual susceptibility to lifestyle factors for colon cancer^{36, 37} we conducted stratified analyses to evaluate the association between body size and adenoma recurrence by a family history of colorectal cancer (Table 5). Subjects that reported a positive family history had a higher odds of recurrence if they were overweight (OR 1.35; 95% CI=0.86–2.12), and were more than twice as likely to have an adenoma recurrence if they were obese compared to normal weight individuals (OR 2.25; 95% CI=1.32–3.84; p -trend=0.006); whereas subjects reporting no family history had no elevated odds of recurrence if obese when compared to normal weight individuals (OR=1.00; 95% CI= 0.77–1.31). The interaction between family history and obesity was statistically significant ($p=0.008$). No marked associations were observed between waist size and any type of recurrence, regardless of family history.

Discussion

In this pooled analysis of two large clinical trials of adenoma recurrence, we found that a high BMI is a risk factor for recurrent adenomas after polypectomy. Similar to what has been observed for the association between BMI and colon cancer^{24, 27, 34}, when we stratified by gender, we found that a high BMI was associated with adenoma recurrence in men, but not women. A separate analysis for waist circumference did not appreciably alter the direction or magnitude of the association between BMI category and odds of recurrence. Our results do not support similar studies of colon cancers that suggest that the measurement of waist size may be a better predictor of risk in women than BMI^{27, 41}, as we detected no significant results with either measure.

The magnitude of the association between body size and colorectal adenomas remains equivocal. Our results are in agreement with epidemiological studies showing a relationship between body mass index and risk for colorectal adenomas^{9–18}. Further support for this association was provided in a small study by Almendingen et al.⁴², who reported a direct relationship between obesity and the growth rate of adenomas. In that study, a strongly positive association between obesity and growth of unresected adenomas in patients followed for three years was observed⁴². However, other studies have failed to demonstrate an association between body size and colorectal adenoma recurrence^{43–48}, including secondary analyses conducted in randomized trials of chemopreventive agents for adenoma recurrence similar to our own^{47, 48}. One possible explanation for the failure of these studies to detect an effect of obesity on recurrence under similar study conditions could be the use of combined analyses of men and women and/or smaller sample sizes.

Our study supports a gender-specific effect of obesity on adenoma recurrence following polypectomy. The consistently weaker association between obesity and colon cancer risk in women has been explained in part by the protective action of female sex hormones, particularly estrogen elevated in overweight/obese women³³. Among premenopausal women, the direct relationship between increasing body size and odds of colorectal neoplasia has been observed consistently, while for older women, the effect is attenuated⁴⁹. Whether sex hormones act differentially in the colonic epithelium as growth regulators⁵⁰ or if they differentially influence risk through action on body fat disposition and adverse biochemical changes^{51–54} is currently unclear. Efforts are ongoing to abstract information on the use of hormone replacement therapy in our two trials along with collecting data on serum biochemical markers (hormone, insulin, IGF levels) to explore these issues in subsequent analyses to address potential explanations for our findings.

For advanced adenoma recurrence in the current study, BMI was strongly associated with risk in men, but not women. In several studies of colorectal adenomas reported to date, high BMI has been shown to be associated with the development of advanced, larger adenomas of the colon^{9, 11, 15, 16}. Unlike the results for any adenoma recurrence, an association between body size and large or advanced adenoma recurrence has been demonstrated in both women and men in the literature, generally in mixed populations^{9, 15, 16}. The current results do not show such an association, possibly because heavier women in our population showed a modest, non-significant trend for protection from advanced recurrence with increasing body size. As mentioned above, there may be effect-modification of body size by estrogen in these women.

Our results also demonstrated that BMI was positively associated with adenoma recurrence in subjects with a family history of colorectal cancer in at least one first degree relative, but not for those without a family history. This is consistent with previous studies suggesting a stronger effect of lifestyle factors and risk for colon cancer in patients with a family history^{36, 37}. BMI again appeared to be a better estimator of the association between body size and adenoma

recurrence than waist circumference, which may help in deciding which estimate of body size is optimal for large epidemiological studies of colorectal neoplasia.

A further advantage to the use of BMI to measure body size is that it accounts for the height of the individual. Though it did not achieve statistical significance, exploratory analyses revealed a modest positive association between tall height and risk (data not shown), which may explain part of the independent effects of BMI on odds of recurrence. This is consistent with previous positive associations between tall height and colon cancer risk^{12, 45, 55}. Our data support recent findings from MacInnis et al.⁵⁵ that suggest, at least for males, there may be two independently acting effects of body composition on colon cancer risk; one acting through central adiposity and the other acting through higher fat free mass, perhaps mediated by the insulin-like growth factor/growth hormone axis, which in the MacInnis study included height as a component trait of the variable⁵⁵. Given that BMI captures aspects of both height and girth for the majority of men, it can be easily integrated into clinical care in discussing the odds for subsequent adenomas, particularly advanced adenomas, in male patients. Overall, our data further strengthen the hypothesis that adverse biochemical changes such as hyperinsulinemia associated with adiposity may be mechanistically coupled with risk for development and growth of premalignant lesions in the colon⁵⁶. These data strongly support the consideration of BMI as a simple measure for assessing elevated odds for adenoma recurrence, particularly for men or for those with a family history of colorectal cancer.

Strengths of our study include the large sample size and the prospective nature of the data collected for adenoma recurrence using colonoscopy. Additional strengths include the use of measured height and weight in all subjects for BMI calculation and the completeness of the variable data set. A limitation of our study lies in the design that includes only individuals with a recent history of at least one adenoma and for whom the average follow up time was three years. These adenoma patients are a distinct group, and therefore the generalizability of the results is somewhat limited. Our findings apply only to the association of body size with recurrent adenomas, not the formation of a first-time adenoma. The short interval between endoscopy procedures limits our ability to demonstrate associations between obesity and adenoma over longer periods of time in study participants that may not have increased susceptibility to the effects of obesity, such as those without a family history of colorectal cancer. Finally, because of the design of the original clinical trials, it is likely that polyps missed at baseline colonoscopy may be included as recurrences in some cases. The rate for missed polyps at colonoscopy have been estimated to be approximately 13% for adenomas 5–10mm in size and 26% for those 1–5 mm⁵⁷. However, our results support a stronger association between body size and advanced adenomas than smaller, non advanced lesions. This increases the validity of the observed association given that the proportion of missed large/advanced adenomas is far lower (2.1%) than for smaller lesions⁵⁷. In the unlikely event that a significant difference in miss rates by BMI explains more lesions at follow up in our studies in the obese, our finding of an association between obesity and risk for advanced adenoma at polypectomy remain relevant as the association yields a higher risk population regardless of the underlying cause.

In summary, our results support previous studies that suggest that obesity is associated with the growth of adenomas in the colon among men, and is particularly related to the development of advanced lesions. Though these data may not directly impact current screening paradigms in a broad sense, they do lend support to the growing body of evidence that body weight, by whatever causal mechanism, is an important determinant in risk of colonic neoplasia and therefore a valid and important clinical factor to consider in patient and high risk family counseling. Simple measures of obesity offer an additional factor in patient education when emphasizing vigilance to follow up particularly among high-risk family members for which the gastroenterologist can advocate. This aspect of our findings may be most relevant in persons

with lower- risk lesions where screening recommendations are extending to longer and longer intervals in attempts to reduce health care costs. Finally, it may be particularly important to take steps to achieve high compliance with colorectal cancer screening and surveillance recommendations in subjects with high BMI.

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References

1. Winawer SJ, Zauber AG, Fletcher RH, Stillman JS, O'Brien MJ, Levin B, Smith RA, Lieberman DA, Burt RW, Levin TR, Bond JH, Brooks D, Byers T, Hyman N, Kirk L, Thorson A, Simmang C, Johnson D, Rex DK. Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. *CA Cancer J Clin* 2006;56:143–59. [PubMed: 16737947]quiz 184–5
2. Alberts DS, Martinez ME, Roe DJ, Guillen-Rodriguez JM, Marshall JR, van Leeuwen JB, Reid ME, Ritenbaugh C, Vargas PA, Bhattacharyya AB, Earnest DL, Sampliner RE. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. Phoenix Colon Cancer Prevention Physicians' Network. *N Engl J Med* 2000;342:1156–62. [PubMed: 10770980]
3. Alberts DS, Martínez ME, Hess LH, Einspahr JG, Green SB, Bhattacharyya AK, Guillen J, Krutzsch M, Batta AK, Salen G, Fales L, Koonce K, Parish D, Clouser M, Roe D, Lance P. the Phoenix and Tucson Gastroenterologist Networks. Phase III Trial of Ursodeoxycholic Acid to Prevent Colorectal Adenoma Recurrence. *J Natl Cancer Inst*. 2005In Press
4. Bonithon-Kopp C, Piard F, Fenger C, Cabeza E, O'Morain C, Kronborg O, Faivre J. Colorectal adenoma characteristics as predictors of recurrence. *Dis Colon Rectum* 2004;47:323–33. [PubMed: 14991494]
5. Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, Shike M, Weissfeld J, Burt RW, Cooper MR, Kikendall JW, Cahill J. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group. *N Engl J Med* 2000;342:1149–55. [PubMed: 10770979]
6. Wallace K, Baron JA, Cole BF, Sandler RS, Karagas MR, Beach MA, Haile RW, Burke CA, Pearson LH, Mandel JS, Rothstein R, Snover DC. Effect of calcium supplementation on the risk of large bowel polyps. *J Natl Cancer Inst* 2004;96:921–5. [PubMed: 15199111]
7. Hedley AOCL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of Overweight and Obesity Among US Children, Adolescents, and Adults, 1999–2002. *JAMA* 2004;291:2840–2846. [PubMed: 15199034]
8. Moller DE, Kaufman KD. Metabolic syndrome: a clinical and molecular perspective. *Annu Rev Med* 2005;56:45–62. [PubMed: 15660501]
9. Bird CL, Frankl HD, Lee ER, Haile RW. Obesity, weight gain, large weight changes, and adenomatous polyps of the left colon and rectum. *Am J Epidemiol* 1998;147:670–80. [PubMed: 9554606]
10. Kono S, Handa K, Hayabuchi H, Kiyohara C, Inoue H, Marugame T, Shinomiya S, Hamada H, Onuma K, Koga H. Obesity, weight gain and risk of colon adenomas in Japanese men. *Jpn J Cancer Res* 1999;90:805–11. [PubMed: 10543250]
11. Giovannucci E, Colditz GA, Stampfer MJ, Willett WC. Physical activity, obesity, and risk of colorectal adenoma in women (United States). *Cancer Causes Control* 1996;7:253–63. [PubMed: 8740738]
12. Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Physical activity, obesity, and risk of colon cancer and adenoma in men. *Ann Intern Med* 1995;122:327–334. [PubMed: 7847643]
13. Larsen IGT, Almendingen K, Hoff G. Lifestyle as a predictor for colonic neoplasia in asymptomatic individuals. *BMC Gastroenterol* 2006;13:5. [PubMed: 16412216]

14. Terry MB, Neugut AI, Bostick RM, Sandler R, Haile RW, Jacobson JS, Fenoglio CM, Potter JD. Risk factors for advanced colorectal adenomas: a pooled analysis. *Cancer Epidemiol Biomarkers Prev* 2002;11:622–629. [PubMed: 12101109]
15. Boutron-Ruault MC, Senesse P, Meance S, Belghiti C, Faivre J. Energy intake, body mass index, physical activity, and the colorectal adenoma-carcinoma sequence. *Nutr Cancer* 2001;39:50–7. [PubMed: 11588902]
16. Neugut AI, Lee WC, Garbowski GC, Wayne JD, Forde KA, Treat MR, Fenoglio-Preiser C. Obesity and colorectal adenomatous polyps. *J Natl Cancer Inst* 1991;83:359–61. [PubMed: 1995919]
17. Bayerdorffer E, Mannes GA, Ochsenkuhn T, Kopcke W, Wiebecke B, Paumgartner G. Increased risk of 'high-risk' colorectal adenomas in overweight men. *Gastroenterology* 1993;104:137–44. [PubMed: 8419236]
18. Erhardt JG, Kreichgauer HP, Meisner C, Bode JC, Bode C. Alcohol, cigarette smoking, dietary factors and the risk of colorectal adenomas and hyperplastic polyps—a case control study. *Eur J Nutr* 2002;41:35–43. [PubMed: 11990006]
19. Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women. *J Chronic Dis* 1979;32:563–576. [PubMed: 468958]
20. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents. A follow-up of the Harvard Growth Study of 1922 to 1935. *N Engl J Med* 1992;327:1350–5. [PubMed: 1406836]
21. Le Marchand L, Wilkins LR, Mi MP. Obesity in youth and middle age and risk of colorectal cancer in men. *Cancer Causes Control* 1992;3:349–354. [PubMed: 1617122]
22. Graham S, Marshall J, Haughey B, Mittelman A, Swanson M, Zielezny M, Byers T, Wilkinson G, West D. Dietary epidemiology of cancer of the colon in western New York. *Am J Epidemiol* 1988;128:490–503. [PubMed: 2843038]
23. Bostick RM, Potter JD, Kushi LH, Sellers TA, Steinmetz KA, McKenzie DR, Gapstur SM, Folsom AR. Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes Control* 1994;5:38–52. [PubMed: 8123778]
24. Phillips RL, Snowdon DA. Dietary relationships with fatal colorectal cancer among Seventh-Day Adventists. *JNCI* 1985;74:307–317. [PubMed: 3856044]
25. Martinez ME, Giovannucci E, Spiegelman D, Hunter DJ, Willett WC, Colditz GA. Leisure-time physical activity, body size, and colon cancer in women. Nurses' Health Study Research Group. *J Natl Cancer Inst* 1997;89:948–55. [PubMed: 9214674]
26. Pischon T, Lahmann PH, Boeing H, Friedenreich C, Norat T, Tjonneland A, Halkjaer J, Overvad K, Clavel-Chapelon F, Boutron-Ruault MC, Guerne G, Bergmann MM, Linseisen J, Becker N, Trichopoulos A, Trichopoulos D, Sieri S, Palli D, Tumino R, Vineis P, Panico S, Peeters PH, Bueno-de-Mesquita HB, Boshuizen HC, Van Guelpen B, Palmqvist R, Berglund G, Gonzalez CA, Dorronsoro M, Barricarte A, Navarro C, Martinez C, Quiros JR, Roddam A, Allen N, Bingham S, Khaw KT, Ferrari P, Kaaks R, Slimani N, Riboli E. Body size and risk of colon and rectal cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *J Natl Cancer Inst* 2006;98:920–31. [PubMed: 16818856]
27. Moore LL, Bradlee ML, Singer MR, Splansky GL, Proctor MH, Ellison RC, Kreger BE. BMI and waist circumference as predictors of lifetime colon cancer risk in Framingham Study adults. *Int J Obes Relat Metab Disord* 2004;28:559–67. [PubMed: 14770200]
28. Moller H, Mellemegaard A, Lindvig K, Olsen JH. Obesity and cancer risk: a Danish record-linkage study. *Eur J Cancer* 1994;30A:344–50. [PubMed: 8204357]
29. Lee IM, Paffenbarger RS Jr. Quetelet's index and risk of colon cancer in college alumni. *J Natl Cancer Inst* 1992;84:1326–31. [PubMed: 1495102]
30. Lin J, Zhang SM, Cook NR, Rexrode KM, Lee IM, Buring JE. Body mass index and risk of colorectal cancer in women (United States). *Cancer Causes Control* 2004;15:581–9. [PubMed: 15280637]
31. Haydon AMRJ, English DR, Giles GG. Effect of physical activity and body size on survival after diagnosis with colorectal cancer. *Gut* 2006;55:62–67. [PubMed: 15972299]
32. Murphy TK, Calle EE, Rodriguez C, Kahn HS, Thun MJ. Body mass index and colon cancer mortality in a large prospective study. *Am J Epidemiol* 2000;152:847–54. [PubMed: 11085396]

33. Slattery ML, Ballard-Barbash R, Edwards S, Caan BJ, Potter JD. Body mass index and colon cancer: an evaluation of the modifying effects of estrogen (United States). *Cancer Causes Control* 2003;14:75–84. [PubMed: 12708728]
34. Russo A, Franceschi S, La Vecchia C, Dal Maso L, Montella M, Conti E, Giacosa A, Falcini F, Negri E. Body size and colorectal-cancer risk. *Int J Cancer* 1998;78:161–5. [PubMed: 9754646]
35. Terry PD, Miller AB, Rohan TE. Obesity and colorectal cancer risk in women. *Gut* 2001;51:191–194. [PubMed: 12117878]
36. Slattery ML, Levin TR, Ma K, Goldgar D, Holubkov R, Edwards S. Family history and colorectal cancer: predictors of risk. *Cancer Causes Control* 2003;14:879–87. [PubMed: 14682445]
37. Le Marchand L, Wilkens LR, Hankin JH, Kolonel LN, Lyu LC. Independent and joint effects of family history and lifestyle on colorectal cancer risk: implications for prevention. *Cancer Epidemiol Biomarkers Prev* 1999;8:45–51. [PubMed: 9950239]
38. Martinez ME, Sampliner R, Marshall JR, Bhattacharyya AB, Reid ME, Alberts DS. Adenoma characteristics as risk factors for recurrence of advanced adenomas. *Gastroenterology* 2001;120:1077–1083. [PubMed: 11266371]
39. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol* 1989;129:125–37. [PubMed: 2910056]
40. Bostick RM, Geisler C, Onur S, Korth O, Selberg O, Schrezenmeier J, Muller MJ. Value of body fat mass vs anthropometric obesity indices in the assessment of metabolic risk factors. *Int J Obes (Lond)* 2006;30:475–83. [PubMed: 16261188]
41. Macinnis RJ, English DR, Hopper JL, Gertig DM, Haydon AM, Giles GG. Body size and composition and colon cancer risk in women. *Int J Cancer* 2006;118:1496–500. [PubMed: 16187280]
42. Almendinger KHB, Vatn MH. Does high body fatness increase the risk of presence and growth of colorectal adenomas followed up in situ for 3 years? *Am J Gastroenterol* 2001;96:2238–46. [PubMed: 11467659]
43. Little J, Logan R, Hawtin P, Hardcastle J, Turner I. Colorectal adenomas and diet: a case-control study of subjects participating in the Nottingham faecal occult blood screening programme. *Br J Cancer* 1993;67:177–184. [PubMed: 8381298]
44. Stemmermann G, Heilbrun L, Nomura A. Association of diet and other factors with adenomatous polyps of the large bowel: a prospective autopsy study. *Am J Clin Nutr* 1988;47:312–317. [PubMed: 3341261]
45. Hauret KG, Bostick RM, Matthews CE, Hussey JR, Fina MF, Geisinger KR, Rouffail WM. Physical activity and reduced risk of incident sporadic colorectal adenomas: observational support for mechanisms involving energy balance and inflammation modulation. *Am J Epidemiol* 2004;159:983–92. [PubMed: 15128611]
46. Davidow AL, Neugut AI, Jacobson JS, Habibul A, Garbowski GC, Forde KA, Treat MR, Wayne JD. Recurrent adenomatous polyps and body mass index. *Cancer Epidemiol, Biomarkers & Prev* 1996;5:313–315.
47. Wallace K, Baron JA, Karagas MR, Cole BF, Byers T, Beach MA, Pearson LH, Burke CA, Silverman WB, Sandler RS. The association of physical activity and body mass index with the risk of large bowel polyps. *Cancer Epidemiol Biomarkers Prev* 2005;14:2082–6. [PubMed: 16172213]
48. Sass DA, Schoen RE, Weissfeld JL, Weissfeld L, Thaete FL, Kuller LH, McAdams M, Lanza E, Schatzkin A. Relationship of visceral adipose tissue to recurrence of adenomatous polyps. *Am J Gastroenterol* 2004;99:687–93. [PubMed: 15089903]
49. Giovannucci E. Obesity, gender, and colon cancer. *Gut* 2002;51:147. [PubMed: 12117867]
50. Gustafsson JA. What pharmacologists can learn from recent advances in estrogen signalling. *Trends in Pharmacological Sciences* 2003;24:479–485. [PubMed: 12967773]
51. Kelley DE, Thaete FL, Troost F, Huwe T, Goodpaster BH. Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance. *Am J Physiol Endocrinol Metab* 2000;278:E941–8. [PubMed: 10780952]
52. Campagnoli C, Biglia N, Altare F, Lanza MG, Lesca L, Cantamessa C, Peris C, Fiorucci GC, Sismondi P. Differential effects of oral conjugated estrogens and transdermal estradiol on insulin-like growth factor 1, growth hormone and sex hormone binding globulin serum levels. *Gynecol Endocrinol* 1993;7:251–8. [PubMed: 8147234]

53. Jorgensen JO, Christensen JJ, Vestergaard E, Fisker S, Ovesen P, Christiansen JS. Sex steroids and the growth hormone/insulin-like growth factor-I axis in adults. *Horm Res* 2005;64 (Suppl 2):37–40. [PubMed: 16286769]
54. Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, Retzlaff BM, Knopp RH, Brunzell JD, Kahn SE. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia* 2003;46:459–69. [PubMed: 12687327]
55. MacInnis RJ, English DR, Hopper JL, Haydon AM, Gertig DM, Giles GG. Body size and composition and colon cancer risk in men. *Cancer Epidemiol Biomarkers Prev* 2004;13:553–9. [PubMed: 15066919]
56. Giovannucci E. Nutrition, insulin, insulin-like growth factors and cancer. *Horm Metab Res* 2003;35:694–704. [PubMed: 14710348]
57. van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E. Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am J Gastroenterol* 2006;101:343–50. [PubMed: 16454841]

Table 1
Baseline characteristics of study participants in the WBF and UDCA Trials

Baseline Characteristics	Pooled	WBF	UDCA	p value
	N=2465	N=1289	N=1176	
Age at baseline (mean ± sd)	66.0 ± 8.7	65.9 ± 8.8	66.2 ± 8.5	0.32 ¹
Male, n (%)	1668 (67.2)	871 (67.0)	797 (67.4)	0.84 ²
White, n (%)	2347 (95.3)	1247 (95.9)	1100 (94.6)	0.12
Family History CRC, n (%) ³	545 (22.0)	219 (16.9)	326 (27.6)	<0.001
Current Smoker (yes), n (%)	315 (12.9)	177 (13.6)	138 (12.0)	0.24
Number of colonoscopies (mean ± sd)	1.8 ± 0.8	1.8 ± 0.9	1.8 ± 0.8	0.27
Previous Polyps (yes), n (%) ⁴	976 (40.3)	450 (39.1)	526 (47.1)	<0.001
Aspirin Use (yes) ⁵	693 (27.9)	366 (28.2)	327 (27.6)	0.78
Baseline Adenoma Characteristics				
Number > 1 (yes), n (%)	1017 (41.0)	559 (43.0)	458 (38.8)	0.03
Large, n (%)	1072 (43.5)	573 (44.7)	499 (42.2)	0.22
Villous histology, n (%)	517 (21.0)	272 (21.2)	245 (20.8)	0.78
Proximal Location, n (%)	747 (30.3)	347 (27.1)	400 (33.9)	<0.001
BMI (kg/m²)				
Normal (% >18.5 & <25 kg/m ²)	739 (30.0)	372 (28.9)	367 (31.2)	
Overweight (% 25 – <30 kg/m ²)	1120 (45.4)	593 (46.0)	527 (44.8)	
Obese (% ≥ 30 kg/m ²)	606 (24.6)	324 (25.1)	282 (24.0)	0.44
Waist (in.)⁶				
Small, n (%)	591 (26.1)	352 (29.5)	239 (22.4)	
Medium, n (%)	563 (24.9)	289 (24.2)	274 (25.7)	
Large, n (%)	569 (25.2)	294 (24.6)	275 (25.8)	
Extra-Large, n (%)	538 (23.8)	259 (21.7)	279 (26.2)	<0.001

¹ Statistical tests for continuous variables comparing participants in WBF to participants in UDCA performed with a student's t-test.

² Statistical tests for categorical variables comparing participants in WBF to participants in UDCA performed with chi-square analyses.

³ History of colorectal cancer in one or more first degree relatives.

⁴ History of polyps prior to baseline

⁵ Aspirin use in the last month at baseline

⁶ Waist cutpoints for men (inches) small <36.5; medium 36.5–39.0; large 39.1–42.0; extra-large >42. Waist cutpoints for women (in) small <30.0; medium 30.0–33.0; large 33.2–37.0; extra-large >37.0. Numbers may not add up to total due to missing data.

Table 2

Characteristics of participants in the WBF and UDCA trials combined, by category of body mass index.

Characteristics	Category of Body Mass Index ¹		
	Normal Weight	Overweight	Obese
	n=739	n=1120	n=606
Age at baseline (mean ± sd)	67.0 ± 9.0	66.5 ± 8.4	63.8 ± 8.4 ^{2,3}
Male, n (%)	418 (56.6)	834 (74.5) ²	411 (67.8) ^{2,3}
White, n (%)	705 (96.1)	1059 (95.2)	566 (94.7)
Family History CRC, n (%) ⁴	151 (20.4)	259 (23.3)	132 (21.8)
Current Smoker (yes), n (%)	131 (18.1)	118 (10.6) ²	60 (10.1) ²
Number of colonoscopies (mean ± sd)	1.8 ± 0.9	1.8 ± 0.8	1.8 ± 0.9
Previous Polyps (yes), n (%) ⁵	279 (41.0)	458 (45.0)	231 (41.8)
Aspirin Use (yes), n (%) ⁶	206 (27.9)	316 (28.2)	170 (28.1)
Baseline Adenoma Characteristics			
Number > 1 (yes), n (%)	272 (36.9)	482 (43.0) ²	256 (42.2) ²
Large, n (%)	323 (43.9)	487 (44.0)	258 (42.7)
Villous histology, n (%)	154 (21.0)	215 (19.4)	146 (24.2)
Proximal Location, n (%)	215 (29.3)	343 (31.0)	186 (30.8)
Adenoma Recurrence Rates, n (%)			
Non-advanced adenoma (Total Population)	211 (28.6)	344 (30.7)	202 (33.3) ²
Men ⁷	134 (32.1)	263 (31.5)	149 (36.3)
Women ⁸	77 (24.0)	81 (28.3)	53 (27.2)
Advanced adenoma ⁹ (Total Population)	105 (14.2)	187 (16.7) ²	85 (14.0)
Men	53 (12.7)	153 (18.3) ²	64 (15.6)
Women	52 (16.2)	34 (11.9)	21 (10.8)

¹ Normal weight is a BMI of greater than 18.5 and less than 25; Overweight is a BMI of greater than or equal to 25 and less than 30; Obese is a BMI of greater than or equal to 30.

² Value significantly different from normal weight, p <0.05.

³ Value significantly different from overweight, p <0.05.

⁴ Family history of colorectal cancer in one or more first degree relatives.

⁵ History of polyps prior to baseline.

⁶ Aspirin use in the last month at baseline.

⁷ The number of men in each category was 418 for normal weight, 834 for overweight, and 411 for obese.

⁸ The number of women in each category was 321 for normal weight, 286 for overweight, and 195 for obese.

⁹ Adenomas were classified as advanced if they had a diameter of 1 cm or more and/or tubulovillous or villous histology (at least 25% villous).

Table 3
Odds ratios (OR) and 95% confidence intervals for colorectal adenoma recurrence according to BMI categories by gender in WBF and UDCA combined.

BMI Category ¹ (recur/total)	Total Population			Men		Women	
	Model 1 ²	Model 2 ³	Model 2 ³	Model 1 ²	Model 2 ³	Model 1 ²	Model 2 ³
Normal Weight (316/739)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Overweight (531/1120)	1.07 (0.87–1.31)	1.05 (0.82–1.35)	1.14 (0.88–1.47)	1.16 (0.85–1.57)	0.98 (0.69–1.40)	0.88 (0.55–1.38)	
Obese (287/606)	1.17 (0.92–1.48)	1.08 (0.74–1.57)	1.36 (1.01–1.83)	1.29 (0.82–2.04)	0.90 (0.60–1.33)	0.78 (0.40–1.51)	
p-trend ⁴	0.20	0.67	0.04	0.27	0.61	0.46	
Waist Category⁵ (recur/total)							
Small (257/591)	1.00	1.00	1.00	1.00	1.00	1.00	
Medium (247/563)	0.94 (0.73–1.21)	0.92 (0.71–1.20)	1.04 (0.77–1.41)	1.03 (0.74–1.42)	0.76 (0.48–1.20)	0.71 (0.44–1.16)	
Large (274/569)	1.07 (0.83–1.37)	1.02 (0.76–1.38)	1.13 (0.84–1.53)	1.11 (0.78–1.59)	0.94 (0.60–1.47)	0.83 (0.48–1.44)	
Extra Large (260/538)	1.18 (0.91–1.52)	1.09 (0.73–1.62)	1.28 (0.93–1.74)	1.23 (0.76–1.99)	1.01 (0.64–1.58)	0.81 (0.39–1.68)	
p-trend ⁴	0.15	0.56	0.11	0.75	0.76	0.54	

¹ BMI categories are normal weight, > 18.5 and <25; overweight >=25.0 and <30; and obese >30.

² Model adjusted for age, gender, previous polyps, number of adenomas at baseline, and study.

³ Model adjusted for all factors in Model 1, plus waist category for the model of BMI category, and BMI category for the model of waist category.

⁴ P-trend calculated with logistic regression modeling with the categorical variable for body size as the independent variable.

⁵ Waist cutpoints for men (inches) small <36.5; medium 36.5–39.0; large 39.1–42.0; extra-large >42. Waist cutpoints for women (inches) small <30.0; medium 30.0–33.0; large 33.2–37.0; extra-large >37.0.

Table 4
Odds ratios (95% CI)¹ for non-advanced and advanced recurrence by weight category, using multinomial regression.

BMI Category ²	Total Population			Men		Women	
	Non-advanced Recurrence	Advanced Recurrence ³	Advanced Recurrence	Non-advanced Recurrence	Advanced Recurrence	Non-advanced Recurrence	Advanced Recurrence
Normal Weight	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Overweight	1.00 (0.80–1.27)	1.21 (0.90–1.63)	1.60 (1.09–2.33)	0.97 (0.73–1.29)	1.62 (1.04–2.55)	1.12 (0.74–1.68)	0.79 (0.47–1.31)
Obese	1.22 (0.94–1.58)	1.07 (0.90–1.51)	1.62 (1.04–2.55)	1.26 (0.91–1.75)	1.62 (1.04–2.55)	1.15 (0.73–1.79)	0.53 (0.29–1.31)
p-trend ⁴	0.15	0.61	0.03	0.17	0.03	0.49	0.06
Waist Category⁵							
Small ⁶	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Medium ⁷	0.99 (0.75–1.32)	0.85 (0.59–1.22)	0.91 (0.58–1.42)	1.10 (0.79–1.54)	0.77 (0.45–1.32)	0.77 (0.45–1.32)	0.75 (0.39–1.42)
Large ⁸	1.05 (0.79–1.39)	1.10 (0.77–1.56)	1.32 (0.87–2.01)	1.04 (0.74–1.46)	1.32 (0.87–2.01)	1.09 (0.65–1.82)	0.70 (0.36–1.36)
Extra Large ⁹	1.25 (0.94–1.66)	1.03 (0.71–1.50)	1.30 (0.83–2.03)	1.27 (0.90–1.79)	1.30 (0.83–2.03)	1.26 (0.76–2.10)	0.62 (0.31–1.23)
p-trend ⁵	0.12	0.54	0.10	0.24	0.10	0.20	0.17

¹ Models adjusted for age, gender, previous polyps, number of adenomas at baseline, and study.

² BMI categories are normal weight, > 18.5 and <25; overweight ≥25.0 and <30; and obese >30 inches.

³ Advanced recurrence is a recurrence of an adenoma ≥ 1 cm and/or with at least 25% villous histology.

⁴ P-trend calculated with multinomial logistic regression modeling with the categorical variable for body size as the independent variable.

⁵ Waist cutpoints for men (inches) small <36.5; medium 36.5–39.0; large 39.1–42.0; extra-large >42. Waist cutpoints for women (in) small <30.0; medium 30.0–33.0; large 33.2–37.0; extra-large >37.0.

⁶ The number of recurrences/number of participants per cell for small waist size were as follows: Total Population, non-advanced recurrence (167/591); Total Population, advanced recurrence (90/591); Men, non-advanced recurrence (121/400); Men, advanced recurrence (62/400); Women, non-advanced recurrence (46/191); Women, advanced recurrence (28/191).

⁷ The number of recurrences/number of participants per cell for medium waist size were as follows: Total Population, non-advanced recurrence (170/563); Total Population, advanced recurrence (77/563); Men, non-advanced recurrence (131/386); Men, advanced recurrence (54/386); Women, non-advanced recurrence (39/177); Women, advanced recurrence (23/177).

⁸ The number of recurrences/number of participants per cell for large waist size were as follows: Total Population, non-advanced recurrence (176/569); Total Population, advanced recurrence (98/569); Men, non-advanced recurrence (123/387); Men, advanced recurrence (75/387); Women, non-advanced recurrence (53/182); Women, advanced recurrence (23/182).

⁹ The number of recurrences/number of participants per cell for extra-large waist size were as follows: Total Population, non-advanced recurrence (184/538); Total Population, advanced recurrence (76/538); Men, non-advanced recurrence (129/355); Men, advanced recurrence (57/355); Women, non-advanced recurrence (55/183); Women, advanced recurrence (19/183).

Odds ratios (95% CI)¹ for colorectal adenoma recurrence, by obesity and waist circumference stratified by family history of colorectal cancer.

Table 5

BMI Category ³	Family History of Colorectal Cancer ²					
	No			Yes		
	No. recur/ total	Recurrence	No. recur/ total	Advanced Recurrence	No. recur/ total	Advanced Recurrence
Normal Weight	257/588	1.00	81/412	1.00	59/151	1.00
Overweight	407/861	1.01 (0.80–1.27)	143/597	1.13 (0.81–1.58)	124/259	1.35 (0.86–2.12)
Obese	210/474	1.00 (0.77–1.31)	60/324	0.91 (0.61–1.36)	77/132	2.25 (1.32–3.84)
p-trend ⁴		0.78		0.77		0.006
Waist Category⁵						
Small	208/475	1.00	72/339	1.00	49/116	1.00
Medium	189/433	0.92 (0.69–1.22)	51/295	0.73 (0.48–1.12)	58/130	1.00 (0.57–1.74)
Large	206/446	0.95 (0.72–1.26)	73/313	0.96 (0.64–1.42)	68/123	1.67 (0.95–2.94)
Extra Large	197/409	1.10 (0.82–1.46)	59/271	0.98 (0.65–1.49)	63/129	1.56 (0.88–2.77)
p-trend ⁴		0.5		0.81		0.04

¹ Models adjusted for age, gender, previous polyps, number of adenomas at baseline, and study.

² Family history of colorectal cancer in one or more first degree relative.

³ BMI categories are normal weight, > 18.5 and <25; overweight ≥25.0 and <30; and obese >30 inches.

⁴ P-trend calculated with logistic regression modeling with the categorical variable for body size as the independent variable.

⁵ Waist cutpoints for men (inches) small <36.5; medium 36.5–39.0; large 39.1–42.0; extra-large >42. Waist cutpoints for women (in) small <30.0; medium 30.0–33.0; large 33.2–37.0; extra-large >37.0.