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Association Between Obesity and Weight Change and Risk of Diverticulitis in Women

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CLINICAL AT

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BACKGROUND & AIMS: There is little evidence that adiposity associates with diverticulitis, especially among women. We conducted a comprehensive evaluation of obesity, weight change, and incidence of diverticulitis in a large cohort of women. **METHODS:** We conducted a prospective cohort study of 46,079 women enrolled in the Nurses' Health Study who were 61–89 years old and free of diverticulitis, diverticular bleeding, cancers, or inflammatory bowel disease at baseline (in 2008). We used Cox proportional hazards models to examine the associations among risk of incident diverticulitis and body mass index (BMI), waist circumference, waist to hip ratio, and weight change from age 18 years to the present. The primary end point was first incident diverticulitis requiring antibiotic therapy or hospitalization. **RESULTS:** We documented 1084 incident cases of diverticulitis over 6 years of follow-up, encompassing 248,001 person-years. After adjustment for other risk factors, women with a BMI $\geq$35.0 kg/m^2 had a hazard ratio for diverticulitis of 1.42 (95% confidence interval [CI], 1.08–1.85) compared to women with a BMI $<$22.5 kg/m^2. Compared to women in the lowest quintile, the multivariable hazard ratios among women in the highest quintile were 1.35 (95% CI, 1.02–1.78) for waist circumference and 1.40 (95% CI, 1.07–1.84) for waist to hip ratio; these associations were attenuated with further adjustment for BMI. Compared to women maintaining weight from age 18 years to the present, those who gained $\geq$20 kg had a 73% increased risk of diverticulitis (95% CI, 27%–136%). **CONCLUSIONS:** During a 6-year follow-up period, we observed an association between obesity and risk of diverticulitis among women. Weight gain during adulthood was also associated with increased risk.

Keywords: Overweight; Colon; Inflammation; Risk Factor.

Diverticulitis, or acute inflammation of colonic diverticula, is associated with acute and chronic complications. It is among the leading gastrointestinal indications for hospitalization and outpatient clinical visits in the United States.[1,2] Accumulating evidence suggests an association between dietary and lifestyle factors and disease development.[3–9]

Obesity is one of the major risk factors for a number of gastrointestinal diseases, including gastroesophageal reflux disease,[10] pancreatic disease,[11,12] and colorectal cancer,[13,14] possibly due to chronic inflammation and alterations in gut microbiota, which are proposed drivers in the pathogenesis of diverticulitis.[15] Several studies from our group and others have consistently demonstrated an association between higher body mass index (BMI) and increased risk of diverticulitis[16] or diverticular disease requiring hospitalization or as the cause of death.[4,17,18] However, evidence on obesity and diverticulitis remains sparse for more common and mild presentations of this disease, especially among women. Beyond BMI, limited evidence suggests that visceral fat may be more important in the pathogenesis of diverticulitis,[16,19,20] but it is unclear whether abdominal adiposity, as assessed by waist circumference (WC) and waist to hip ratio (WHR), is also related to diverticulitis in women. Furthermore, the influence of weight change on incidence of diverticulitis remains poorly understood. Compared to studies of adult BMI, investigation of weight change may better capture the effect of excess body fat during adulthood.

To address these knowledge gaps, we conducted a comprehensive evaluation of obesity and incidence of diverticulitis in a large cohort of US women from the Nurses' Health Study.

Abbreviations used in this paper: **BMI, body mass index; CI, confidence interval; HR, hazard ratio; WC, waist circumference; WHR, waist to hip ratio.**

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Accumulating evidence links diet and lifestyle factors to development of diverticulitis. The influence of adiposity and weight change on the etiopathogenesis of the disease remains poorly understood, especially among women.

NEW FINDINGS

The researchers observed an association between higher body mass index and increased risk of diverticulitis in a large prospective cohort of women. Weight gain from early adulthood was also associated with increased risk.

LIMITATIONS

Anthropometric measurements and ascertainment of diverticulitis were based on self-reported or recalled information. Data on central adiposity were only collected over several years, and changes over time would cause measurement error.

IMPACT

Maintaining a healthy weight throughout adulthood may help prevent diverticulitis.

Materials and Methods

Study Population

The Nurses' Health Study began in 1976 with 121,700 US female registered nurses aged 30 to 55 years at enrollment. Participants have been mailed questionnaires every 2 years since inception, querying demographics, lifestyle factors, medical history, and disease outcomes, with a follow-up rate >90% of available person-time. Details of the cohort have been described elsewhere.[21] The study was approved by the Institutional Review Board of Brigham and Women's Hospital.

Assessment of Exposure

Participants were asked to report their height at enrollment and current body weight in biennial questionnaires. Recalled weight at age 18 years was inquired in 1980. BMI was calculated as weight in kilograms divided by height squared in meters. In 1986, participants were asked to measure their waist at the umbilicus and hips at the largest circumference between their waist and thighs, while standing and relaxed. Waist and hip circumference information was updated using the same procedure in 1996 and 2000. Circumference measurements were recorded to the nearest quarter of an inch, and WHR was calculated for each set of circumferences. We assessed weight change from early adulthood (age 18 years) to updated weight as reported in the current questionnaire cycle, which represented long-term weight change from early adulthood.[22,23] To evaluate the effect of recent weight change, in a secondary analysis, we assessed 4-year weight change during follow-up, which was calculated and updated using repeated weight assessments 4 years apart. We suspended updating weight change information when a participant quit smoking or reported a diagnosis of cancer, cardiovascular disease, or inflammatory bowel disease in the past 2 years, to reduce the influence of unintentional weight change and confounding from shared risk factors.[22]

In a validation study among 140 women within the Nurses' Health Study cohort, self-reported weight, waist and hip circumference, and WHR were compared to the average of 2 measurements taken by technicians approximately 6 months apart. Self-reported and measured weight, WC, hip circumference, and WHR were highly correlated (correlation coefficients of 0.97, 0.89, 0.84, and 0.70, respectively).[24] Recalled weight at age 18 years has also shown high validity among 118 women within the parallel Nurses' Health Study II cohort, with a correlation coefficient of 0.87 between recalled and measured weight at age 18 years.[25]

Ascertainment of Outcomes

In 2008 and 2012, participants were asked if they ever had a diagnosis of diverticulitis requiring antibiotic therapy or hospitalization, as well as diverticular bleeding requiring blood transfusion and/or hospitalization. If yes, participants were subsequently asked the year of each episode dating back to 1990. In 2014, participants were asked the same question, but restricted to the last 2 years. In a review of 107 medical records from women reporting incident diverticulitis on the 2008 questionnaire, self-report was confirmed in 88% of cases. Recurrent diverticulitis was defined as cases with more than 1 episode of diverticulitis. In 2012 and 2014, participants were asked to report if they ever had surgery for diverticulitis. The primary end point was diverticulitis requiring antibiotic therapy or hospitalization, and we also included diverticular bleeding, recurrent diverticulitis, and surgery for diverticulitis as secondary outcomes.

Assessment of Covariates

Since baseline, and updated biennially, information on smoking status, menopausal status and menopausal hormone use, physical examination, and use of multivitamin, aspirin, and other nonsteroidal anti-inflammatory drug or acetaminophen was obtained. Physical activity was assessed every 2–4 years using validated questionnaires.[26] Hypertension and hypercholesterolemia were self-reported, with their validity confirmed previously.[27] Usual dietary habits were assessed every 4 years using validated semi-quantitative food frequency questionnaires.[28]

Statistical Analysis

We restricted the analysis to participants who returned 2008, 2012, or 2014 questionnaires, and restricted follow-up from 2008 to 2014 to ensure the cases were ascertained prospectively. We also excluded those who reported a diagnosis of diverticulitis, diverticular bleeding, non-melanoma cancers, or inflammatory bowel disease before 2008, or those with missing exposure information. Person-time was calculated from the date of return of the 2008 questionnaire until the date of diagnosis of diverticulitis or diverticular bleeding, death, last return of a valid follow-up questionnaire, or the end of follow-up (June 2014), whichever came first. We censored women who reported a new diagnosis of gastrointestinal cancer or inflammatory bowel disease at the date of diagnosis.

Cox proportional hazards models were applied to assess the hazard ratio (HR) and 95% confidence interval (CI). To control for confounding by age, calendar time, and any possible 2-way interactions between these 2 timescales, we stratified the analysis jointly by age in years at start of follow-up and calendar time of the current questionnaire cycle. Proportional hazards assumption was tested by including the product term between exposure variable and age, and testing significance by Wald test. No deviation from proportional hazards assumption was detected. We discretized BMI into 6 categories routinely used in clinical practice to define subgroups for overweight and obese subjects.[29] Quintiles were created to categorize WC and WHR, with the lowest quintile as a reference. We also created 6 categories of weight change from early adulthood to the present, based on the observed distribution (median weight change: 12.7 kg): weight loss ≥2.0 kg; loss or gain <2.0 kg (reference); gain 2.0–5.9 kg; gain 6.0–9.9 kg; gain 10.0–19.9 kg; and gain ≥20.0 kg. These cutoffs were comparable with those used in prior studies.[23] Test for trend was assessed by assigning the median value for the sample to each category and modeling this as a continuous variable. We allowed exposures and covariates to be time-varying by updating and using the most recent information before the questionnaire cycle of interest to account for changes in these exposures and covariates over time. For example, BMI and covariates from the 2008 questionnaire was used to calculate the risk for the period from 2008 to 2010.

In multivariate analysis, we adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, use of aspirin, other nonsteroidal anti-inflammatory drug, or acetaminophen, multivitamin use, physical examination, hypertension, hypercholesterolemia, calorie intake, dietary fiber intake, and red meat intake. In analysis of weight change, we additionally controlled for height and baseline weight. In our analysis of WC and WHR, we further controlled for height and BMI to explore the potential association independent of overall adiposity. We also classified participants jointly by BMI and WHR and assessed the association with diverticulitis. We conducted stratified analyses to evaluate whether the associations of BMI and weight change with diverticulitis varied by subgroups defined by age, physical activity, and smoking status. Test for interaction was performed by including the product term between BMI/weight change and the stratified variable into the model and testing the statistical significance using Wald test.

Finally, we performed a sensitivity analysis by utilizing the full follow-up from 1990 to 2014, with the inclusion of cases that were reported on the 2008, 2012, and 2014 questionnaires with dates of the episode between 1990 and 2008. Statistical analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC). All *P* values are 2-sided and <.05 was considered statistically significant.

Results

In 2008, the baseline characteristics associated with categories of BMI, WC, and WHR in the study participants are shown in Table 1. Women with higher BMI, WC, and WHR were more likely to be physically inactive, past smokers, use aspirin and acetaminophen, and have higher BMI at early adulthood, but less likely to be current smokers and use menopausal hormone. They were more frequently diagnosed with hypertension, hypercholesterolemia, and diabetes, and also tended to consume more red meat but less fiber, resulting in lower scores on the healthy eating index.[30]

Over 6 years encompassing 248,001 person-years of follow-up, we documented a total of 1084 incident cases of diverticulitis. We found a linear association between BMI and increasing risk of diverticulitis (Table 2). After adjustment for various lifestyle and dietary risk factors, compared to women in the reference group with a BMI <22.5 kg/m^2, the HRs were 1.31 (95% CI, 1.09–1.59), 1.35 (95% CI, 1.09–1.68), 1.51 (95% CI, 1.23–1.86), and 1.42 (95% CI, 1.08–1.85; *P* trend <.001) for those with a BMI 25.0–27.4, 27.5–29.9, 30.0–34.9, and ≥35.0 kg/m^2, respectively. The association of BMI with diverticulitis did not appear to differ according to subgroups defined by age, smoking status, or physical activity (Supplementary Table 1). Findings were similar in the sensitivity analysis using follow-up from 1990 to 2014, which included 5,377 incident diverticulitis cases during 1,391,633 person-years (Supplementary Table 2). Compared to women with a BMI <22.5 kg/m^2, those with a BMI 30.0–34.9 had a HR of 1.45 (95% CI, 1.32–1.60), and those with a BMI ≥35.0 kg/m^2 had a HR of 1.58 (95% CI, 1.41–1.78; *P* trend <.001). Higher BMI was also associated with increased risk of diverticular bleeding (Table 2). Compared to women with a BMI <22.5 kg/m^2, the HRs (95% CIs) were 1.98 (95% CI, 1.32–2.98), 1.97 (95% CI, 1.24–3.13), and 1.56 (95% CI, 1.01–2.41; *P* trend = .02) for those with a BMI 25.0–27.4, 27.5–29.9, and ≥30.0 kg/m^2, respectively.

We also examined the association of WC and WHR as measures of central adiposity with risk of diverticulitis (Table 3). Compared to women in the lowest quintile, the multivariable HRs were 1.35 (95% CI, 1.02–1.78; *P* trend = .06) among those in the highest quintile of WC and 1.40 (95% CI, 1.07–1.84; *P* trend = .04) among those in the highest quintile of WHR. With additional adjustment for BMI, the associations for WC (multivariable HR, 1.16; 95% CI, 0.82–1.63; *P* trend = .57) and WHR (multivariable HR, 1.31; 95% CI, 0.99–1.73; *P* trend = .15) were attenuated and became not significant when comparing extreme quintiles. We further classified participants according to combined categories of BMI (<25 vs ≥25 kg/m^2) and WHR (≤0.85 vs >0.85), with the group with BMI <25 kg/m^2 and WHR ≤0.85 as the reference (Figure 1). Women who had a BMI ≥25 kg/m^2 and WHR >0.85 showed the highest risk of diverticulitis compared to the reference group (multivariable HR, 1.38; 95% CI, 1.11–1.72). Moreover, the association between WHR and diverticulitis appeared to be more evident among women who were overweight or obese. In the sensitivity analysis using follow-up from 1990 to 2014, WC and WHR were significantly associated with risk of diverticulitis even after adjusting for BMI (Supplementary Table 3). After accounting for BMI in addition to potential confounders, compared to women in the lowest quintile, the HRs among those in the highest quintile were 1.26 (95% CI, 1.10–1.44; *P* trend <.001) for WC and 1.23 (95% CI, 1.10–1.37; *P* trend <.001) for WHR.

Table 4 shows the weight change from early adulthood at age 18 years to present age in relation to incident diverticulitis. In the analysis controlling for age, height, and weight at 18 years of age, women who gained 2.0–5.9 kg from age 18 years to the present had a 39% increased risk of diverticulitis (95% CI, 0%–96%), and women who gained 20 kg or more had an 80% increased risk (95% CI, 33%–144%; *P* trend <.001), compared to those maintaining their weight with loss or gain no greater than 2.0 kg. The association was robust despite additional adjustment for

Table 1. Baseline Age-Adjusted Characteristics According to Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio in Nurses' Health Study Participants (2008)[a]

	BMI			WC			WHR		
Characteristics	<25.0 kg/m^2	25.0–30.0 kg/m^2	≥30.0 kg/m^2	Q1	Q3	Q5	Q1	Q3	Q5
Age, *y*[b], mean (SD)	73.2 (6.9)	71.9 (6.5)	70.4 (6.0)	71.5 (6.6)	72.9 (6.7)	73.4 (6.8)	71.0 (6.4)	72.8 (6.7)	74.6 (6.8)
White race, %	97.4	97.4	97.0	97.6	97.6	98.1	97.6	97.6	97.7
BMI, *kg/m^2*, mean (SD)	22.2 (1.9)	27.3 (1.4)	34.2 (4.1)	21.6 (2.8)	25.2 (3.4)	30.8 (5.4)	23.6 (4.1)	25.8 (5.1)	27.5 (5.0)
BMI at age 18 y, *kg/m^2*, mean (SD)	20.4 (2.3)	21.3 (2.6)	22.7 (3.4)	20.4 (2.1)	20.8 (2.4)	22.2 (3.3)	21.0 (2.5)	21.0 (2.8)	21.3 (2.8)
WC, *cm*, mean (SD)	79.5 (9.6)	90.2 (10.4)	101.8 (12.6)	70.3 (3.7)	85.1 (1.7)	106.7 (8.3)	73.5 (7.5)	86.1 (9.3)	101.0 (11.1)
WHR, mean (SD)	0.8 (0.1)	0.8 (0.1)	0.9 (0.1)	0.7 (0.1)	0.8 (0.1)	0.9 (0.1)	0.7 (0.0)	0.8 (0.0)	0.9 (0.0)
Alcohol, *g/d*, mean (SD)	7.8 (11.8)	6.0 (10.6)	3.7 (8.2)	7.8 (11.1)	6.9 (11.0)	4.5 (9.7)	6.8 (10.0)	6.7 (11.0)	5.8 (11.7)
Vigorous activity, *MET-h/wk*, mean (SD)	11.3 (19.7)	8.6 (15.1)	5.9 (11.8)	13.2 (20.5)	9.7 (16.4)	6.8 (13.1)	11.7 (18.3)	9.6 (16.1)	8.2 (16.2)
Past smoker, %	45.4	48.4	49.7	45.1	46.1	49.3	44	47.5	48.3
Current smoker, %	6.8	4.6	3.5	6.0	4.2	3.7	4.8	4.6	4.5
Current postmenopausal hormone user, %	16.7	13.2	9.4	18.3	16.4	10.7	17.6	14.7	12.5
Past postmenopausal hormone user, %	60.4	61.2	60.3	60.9	62.0	62.6	61.9	61.9	62.0
Multivitamin use, %	76.1	74.3	71.0	78.1	76.7	75.3	78.3	75.4	76.1
Aspirin use, %	51.4	54.9	55.5	51.7	55.7	58.0	53.3	56.5	59.0
Other NSAID use, %	21.3	24.0	22.9	21.1	23.7	22.3	22.6	23.2	21.8
Acetaminophen use, %	25.0	29.1	33.1	23.3	28.9	34.5	26.2	29.9	31.8
History of hypertension, %	40.3	52.6	63.7	36.3	49.2	62.1	38.8	50.0	57.5
History of hypercholesterolemia, %	41.9	51.6	54.6	38.1	51.0	55.5	38.8	49.0	55.8
History of diabetes, %	4.2	9.2	20.0	2.1	5.7	18.0	3.1	6.5	15.3
Physical examination, %	82.8	83.5	81.5	84.5	86.0	84.3	85.5	85.0	85.1
Total energy intake, *kcal/d*, mean (SD)	1663 (524)	1661 (532)	1643 (545)	1667 (524)	1683 (517)	1687 (541)	1676 (524)	1699 (526)	1684 (547)
Protein intake, *g/d*, mean (SD)	70.9 (9.0)	73.1 (9.3)	75.1 (9.7)	71.2 (9.1)	71.9 (8.7)	73.7 (9.4)	72.5 (9.2)	71.9 (8.8)	72.4 (9.3)
Cholesterol intake, *g/d*, mean (SD)	221.5 (55.8)	233.6 (52.7)	248.2 (59.3)	216.6 (53.8)	226.6 (51.4)	240.9 (55.0)	224.0 (54.2)	226.8 (53.1)	231.9 (53.8)
Fiber intake, *g/d*, mean (SD)	18.9 (4.7)	18.5 (4.2)	18.1 (4.1)	19.7 (4.9)	18.7 (4.1)	18.1 (4.0)	19.6 (4.6)	18.7 (4.4)	18.2 (4.2)
Red meat intake, *serving/d*, mean (SD)	0.8 (0.5)	0.9 (0.5)	0.9 (0.5)	0.8 (0.5)	0.9 (0.5)	1.0 (0.5)	0.8 (0.5)	0.9 (0.5)	0.9 (0.5)
Alternate Healthy Eating Index score, mean (SD)	48.7 (8.7)	47.8 (8.3)	47.0 (8.2)	50.2 (8.8)	48.1 (8.2)	46.8 (8.2)	49.8 (8.5)	48.0 (8.4)	47.2 (8.2)

NOTE. Values are standardized to the age distribution of the study population.
MET, metabolic equivalent; NSAID, nonsteroidal anti-inflammatory drug; Q, quintile.
[a]BMI was assessed in 2008; WC and WHR were assessed in 2000.
[b]Value is not adjusted for age.

Table 2. Body Mass Index and Risk of Diverticulitis and Diverticular Bleeding (2008–2014)[a]

Variable	BMI <22.5 kg/m^2	BMI 22.5–24.9 kg/m^2	BMI 25.0–27.4 kg/m^2	BMI 27.5–29.9 kg/m^2	BMI 30.0–34.9 kg/m^2	BMI ≥35.0 kg/m^2	*P* for trend
Diverticulitis							
No. of cases	207	199	238	159	196	85	
Person-years	58,787	52,515	50,683	32,632	36,288	17,096	
Age, HR (95% CI)	1 (ref)	1.08 (0.89–1.32)	1.34 (1.11–1.62)	1.39 (1.13–1.71)	1.55 (1.27–1.89)	1.42 (1.10–1.84)	<.001
Multivariate,[b] HR (95% CI)	1 (ref)	1.07 (0.88–.31)	1.32 (1.09–1.59)	1.36 (1.10–1.69)	1.52 (1.24–1.87)	1.43 (1.10–1.87)	<.001
Multivariate+diet, HR (95% CI)[c]	1 (ref)	1.07 (0.88–1.30)	1.31 (1.09–1.59)	1.35 (1.09–1.68)	1.51 (1.23–1.86)	1.42 (1.08–1.85)	<.001
Diverticular bleeding[d]							
No. of cases	61	55	73	41	61		
Person-years	58,278	51,929	50,061	32,187	52,600		
Age, HR (95% CI)	1 (ref)	1.22 (0.82–1.81)	1.79 (1.22–2.64)	1.65 (1.07–2.55)	1.31 (0.88–1.96)		.10
Multivariate,[c] HR (95% CI)	1 (ref)	1.26 (0.84–1.90)	1.95 (1.30–2.93)	1.87 (1.18–2.96)	1.52 (0.99–2.34)		.03
Multivariate+diet,[d] HR (95% CI)	1 (ref)	1.30 (0.86–1.95)	1.98 (1.32–2.98)	1.97 (1.24–3.13)	1.56 (1.01–2.41)		.02

[a]BMI was updated every 2 y from 2008 to 2012.
[b]Adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.
[d]Categories of BMI 30.0–34.9 and ≥35.0 were combined for diverticular bleeding because of limited case number in single categories.

potential confounders. A weight loss of 2.0 kg or more was not significantly associated with diverticulitis. The association of weight change from age 18 years to current with diverticulitis did not appear to differ according to early adulthood BMI, age, smoking status, or physical activity (Supplementary Table 4).

In a secondary analysis, we assessed 4-year weight change during follow-up and risk of diverticulitis (Supplementary Table 5). Compared to women who maintained their weight (loss or gain <1.0 kg), 4-year weight gain or weight loss was not significantly associated with risk of diverticulitis. The association was not significantly different between underweight/normal weight and overweight/obese people (Supplementary Table 6).

Among the 1,084 incident diverticulitis cases occurring during 2008 to 2014, we documented 240 incident recurrent cases with more than one episode. The association of BMI with an episode of recurrent diverticulitis seemed to be slightly stronger than that with non-recurrent diverticulitis cases (Supplementary Table 7). As compared to women with a BMI <22.5 kg/m^2, those with a BMI ≥30.0 kg/m^2 had a multivariable HR of 1.66 (95% CI, 1.09–2.51; *P* trend = .002) for recurrent diverticulitis and 1.44 (95% CI, 1.16–1.79; *P* trend <.001) for non-recurrent diverticulitis. We also utilized the full cohort with follow-up from 1992 to 2014 and identified 559 incident cases of surgery for diverticulitis. After adjusting for other risk factors, the HRs were 1.71 (95% CI, 1.30–2.24), 1.65 (95% CI, 1.22–2.24), 1.67 (95% CI, 1.24–2.26), and 1.56 (1.06–2.30; *P* trend = .002) for women with a BMI 25.0–27.4, 27.5–29.9, 30.0–34.9, and ≥35.0 kg/m^2, respectively, compared with those with a BMI <22.5 kg/m^2 (Supplementary Table 8).

Discussion

In this large prospective cohort of women, we found a consistent association between BMI and risk of diverticulitis, independent of other dietary and lifestyle risk factors. Weight gain from early adulthood was also associated with increased risk. Our findings provide an additional rationale for maintaining a healthy weight throughout adulthood.

The relationship between BMI and diverticulitis was consistent with findings from previous studies.[4,16–18] In a prior prospective study, Rosemar et al[17] observed that a BMI of ≥25 kg/m^2 was associated with a 2- to 3-fold increase in the risk of hospitalization with a discharge diagnosis of diverticular disease among middle-aged men in Sweden. However, data were not available on several potential confounders, including physical activity, diet, and nonsteroidal anti-inflammatory drug use. In several subsequent studies,[4,18] the association between BMI and diverticular disease requiring hospitalization was shown to be independent of other risk factors. Moreover, BMI was strongly associated with risk for complicated diverticulitis.[18] However, because all of these studies have been based on registry-level data and included only hospitalized patients, their results may not be readily generalizable to the larger group of patients with less severe disease managed in the outpatient setting.[31] Our prior analysis

Table 3. Waist Circumference, Waist-to-Hip Ratio, and Risk of Diverticulitis (2008–2014)[a]

Variable	Q1	Q2	Q3	Q4	Q5	*P* for trend
WC						
No. of cases	99	132	89	148	129	—
Person-years	29,443	29,226	26,210	31,483	28,552	—
Age, HR (95% CI)	1 (ref)	1.35 (1.04–1.76)	1.03 (0.77–1.38)	1.43 (1.11–1.85)	1.34 (1.03–1.75)	.04
Multivariate,[b] HR (95% CI)	1 (ref)	1.35 (1.04–1.76)	1.03 (0.77–1.37)	1.42 (1.09–1.85)	1.35 (1.02–1.79)	.05
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.35 (1.03–1.76)	1.02 (0.76–1.37)	1.42 (1.09–1.85)	1.35 (1.02–1.78)	.06
Multivariate+diet+BMI, HR (95% CI)	1 (ref)	1.28 (0.98–1.69)	0.93 (0.68–1.27)	1.25 (0.92–1.68)	1.16 (0.82–1.63)	.57
WHR						
No. of cases	98	127	116	116	134	—
Person-years	28,846	29,196	28,504	28,777	28,736	—
Age, HR (95% CI)	1 (ref)	1.28 (0.99–1.67)	1.22 (0.93–1.59)	1.22 (0.93–1.60)	1.43 (1.10–1.87)	.02
Multivariate,[b] HR (95% CI)	1 (ref)	1.27 (0.98–1.66)	1.21 (0.92–1.58)	1.20 (0.91–1.58)	1.41 (1.08–1.85)	.04
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.27 (0.97–1.66)	1.20 (0.92–1.58)	1.20 (0.91–1.57)	1.40 (1.07–1.84)	.04
Multivariate+diet+BMI, HR (95% CI)	1 (ref)	1.24 (0.95–1.61)	1.16 (0.88–1.53)	1.13 (0.85–1.49)	1.31 (0.99–1.73)	.15

Q, quintile.
[a]WC and WHR were assessed in 2000. For WC, Q1: 50.8–74.9 cm; Q2: 75.6–81.3 cm; Q3: 81.9–88.3 cm; Q4: 88.9–96.5 cm; Q5: 97.2-168.9 cm. For WHR, Q1: 0.43–0.76; Q2: 0.76–0.80; Q3: 0.80–0.85; Q4: 0.85–0.90; Q5: 0.90–1.93.
[b]Adjusted for height, menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.

among men in the Health Professionals Follow-up Study showed an association of obesity with diverticulitis that included both less severe forms of the disease treated with antibiotics in the outpatient setting and more severe cases that led to hospitalization or surgery.[16] The current study extends those prior findings by offering evidence that obesity and weight change are associated with an increased risk of both mild and severe diverticulitis in women, and the associations did not differ according to age, smoking, physical activity, or BMI at early adulthood.

Unlike the previous study, in which we reported that the associations of WC and WHR with diverticulitis remained largely unchanged with further adjustment of BMI in men,[16] we showed these associations might not be independent of BMI in this cohort of women. Yet, when BMI and WHR were jointly assessed, WHR appeared to play a role in determining diverticulitis among women who were overweight or obese. Accumulating evidence indicates that WC and WHR are positively associated with risk of chronic diseases, such as cardiovascular disease and cancer, as well as mortality beyond overall adiposity.[32] Although WC and WHR indirectly measure total abdominal fat, they may be better markers of visceral fat than BMI. Visceral fat is metabolically more active than subcutaneous fat[33] and has been suggested

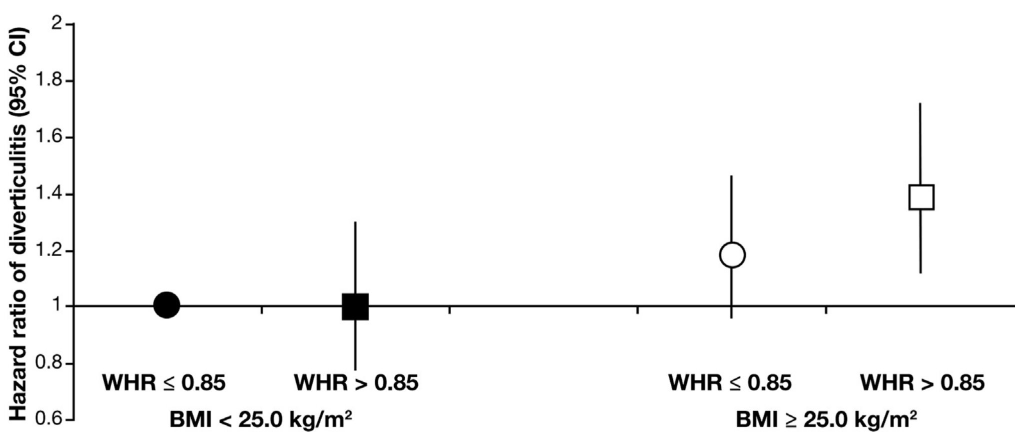

Figure 1. Risk of diverticulitis according to joint categories of BMI and WHR (2008–2014), with women who had a BMI <25 kg/m^2 and WHR ≤ 0.85 as the reference group. BMI was updated every 2 years from 2008 to 2012, and WHR was assessed in 2000. Model was adjusted for age, menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, fiber intake, and red meat intake.

Table 4. Weight Change From Age 18 Years to Current and Risk of Diverticulitis (2008–2014)[a]

Weight change	Median, *kg*	No. of cases	Person-years	Model 1[b], HR (95% CI)	Model 2[c], HR (95% CI)
Loss ≥2.0 kg	–5.9	56	21,434	0.92 (0.62–1.35)	0.90 (0.61–1.33)
Loss or gain <2.0	0	49	16,852	1 (ref)	1 (ref)
Gain 2.0–5.9	4.1	100	24,800	1.39 (0.99–1.96)	1.39 (0.99–1.95)
Gain 6.0–9.9	8.2	111	28,922	1.32 (0.94–1.85)	1.30 (0.93–1.82)
Gain 10.0–19.9	14.5	304	63,511	1.66 (1.23–2.25)	1.62 (1.19–2.19)
Gain ≥20.0	27.2	321	62,664	1.80 (1.33–2.44)	1.73 (1.27–2.36)
P for trend	—	—	—	<.001	<.001

[a]Weight change from age 18 y to current was calculated by subtracting weight at age 18 y from updated weight as reported in current questionnaire cycle.
[b]Model 1 was adjusted for age, weight at age 18 y, and height.
[c]Model 2 was further adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, fiber intake, and red meat intake.

to promote systemic inflammation,[34] through which it may affect the pathogenesis of diverticulitis. Using a matched case-control study design, Yamada et al[19] reported that compared to controls with diverticulosis, the proportion of visceral obesity defined by visceral fat area ≥100 cm^2 in abdominal computed tomography was significantly higher in the patients with left-sided diverticulitis. In another case series, diverticulitis patients with a higher visceral/subcutaneous fat ratio had an increased likelihood of requiring emergency surgery and having complications.[20] However, prospective, population-based data on abdominal adiposity and diverticulitis are lacking. Our data suggest that the clinical impact of slight increase in WC and WHR over time may be low in terms of risk of diverticulitis in women.

Excess adiposity tends to accrue during early and middle adulthood for most people. Based on data from the National Health and Nutritional Examination Survey, the mean weight gain for US women is approximately 0.5 to 1.0 kg per year,[35,36] and this modest annual accumulation typically leads to obesity over time. In a recent analysis,[23] weight gain during adulthood has been associated with increased risk of type 2 diabetes, cardiovascular disease, cholelithiasis, and obesity-related cancers, as well as decreased odds of healthy aging, a composite measure of major chronic diseases and cognitive and physical function. Our results suggest that maintaining a healthy weight throughout adulthood may be important in the prevention of incident diverticulitis. In contrast, 4-year weight change during follow-up was not significantly associated with risk of diverticulitis, indicating that short-term weight change is not a risk factor for diverticulitis compared to current body weight or long-term weight change from early adulthood.

Our study has several strengths. First, we used a well-established cohort with prospective design and minimal loss of follow-up. Second, we had repeated anthropometric measurements, providing a unique opportunity to examine the long-term influence of adiposity and weight change on risk of diverticulitis. Finally, a comprehensive and longitudinal assessment of lifestyle and diet on repeated measurement enabled us to finely control for potential confounders.

Potential limitations of our study should be noted. First, anthropometric measurements were self-reported or recalled. However, robust validity has previously been established.[24,25] Second, the ascertainment of diverticulitis was also based on recalled and self-reported information. Yet, we have restricted follow-up to prospective assessment of diverticulitis from 2008 to 2014 to reduce the potential of recall bias and selection bias. Although the validity of self-reported diverticulitis has been endorsed in the cohort with 88% of self-reported cases confirmed by a review of medical records, we acknowledge that the possibility of misclassification of some reported cases, which would attenuate the association toward the null, could not be excluded. Third, data on WC and WHR were only collected over several years, and changes over time would cause measurement error. However, random errors in exposure assessments generally attenuate true associations towards the null. Last, although the homogeneity of health care access and socioeconomic status of our population helps minimize confounding and enhances the internal validity, the results may not be as generalizable to other populations. Future investigations are needed to determine whether BMI and abdominal adiposity are associated with a similar risk of diverticulitis in a broader, more diverse population.

In conclusion, our results indicate an association between obesity and risk of diverticulitis in a prospective cohort study of women. Weight gain during adulthood was also associated with increased risk. Given the increasing prevalence of diverticulitis, with relatively few known modifiable risk factors, our findings have important clinical implications in the prevention of diverticulitis and provide further scientific rationale for adults to maintain a healthy weight throughout adulthood.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2018.03.057.

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Supplementary Table 1. Body Mass Index and Risk of Diverticulitis Stratified by Age, Smoking Status, and Physical Activity (2008–2014)[a]

Variable	No. of cases	BMI, HR (95% CI) <22.5 kg/m^2	22.5–24.9 kg/m^2	25.0–27.4 kg/m^2	27.5–29.9 kg/m^2	30.0–34.9 kg/m^2	≥35.0 kg/m^2	*P* for interaction
Age								.58
Age <70 y	338	1 (ref)	1.28 (0.86–1.89)	1.24 (0.83–1.84)	1.43 (0.94–2.16)	1.74 (1.18–2.57)	1.63 (1.04–2.57)	
Age ≥70 y	746	1 (ref)	1.00 (0.80–1.26)	1.35 (1.09–1.68)	1.33 (1.04–1.71)	1.40 (1.09–1.79)	1.31 (0.93–1.85)	
Smoking status								.16
Never	468	1 (ref)	0.96 (0.72–1.28)	1.15 (0.87–1.53)	1.33 (0.98–1.82)	1.19 (0.87–1.64)	1.31 (0.87–1.96)	
Ever	608	1 (ref)	1.19 (0.91–1.55)	1.47 (1.14–1.91)	1.41 (1.05–1.89)	1.85 (1.40–2.43)	1.49 (1.04–2.13)	
Physical activity[b]								.62
<12 MET-h/wk	513	1 (ref)	0.98 (0.71–1.34)	1.28 (0.96–1.72)	1.43 (1.05–1.96)	1.41 (1.04–1.91)	1.42 (0.99–2.04)	
≥12 MET-h/wk	477	1 (ref)	1.10 (0.84–1.43)	1.30 (1.00–1.70)	1.22 (0.88–1.69)	1.46 (1.07–2.01)	1.15 (0.69–1.92)	

MET, metabolic equivalent.
[a]BMI was updated every 2 y from 2008 to 2012. Models were adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, dietary fiber intake, and red meat intake.
[b]Dichotomized according to median level of physical activity.

Supplementary Table 2. Body Mass Index and Risk of Diverticulitis Using Follow-Up From 1990 to 2014[a]

Variable	BMI <22.5 kg/m^2	22.5–24.9 kg/m^2	25.0–27.4 kg/m^2	27.5–29.9 kg/m^2	30.0–34.9 kg/m^2	≥35.0 kg/m^2	*P* for trend
No. of cases	942	1107	1194	765	908	461	—
Person-years	314,910	317,389	289,433	179,012	197,472	93,417	—
Age, HR (95% CI)	1 (ref)	1.18 (1.08–1.29)	1.38 (1.27–1.51)	1.42 (1.29–1.56)	1.54 (1.41–1.69)	1.69 (1.51–1.89)	<.001
Multivariate,[b] HR (95% CI)	1 (ref)	1.15 (1.06–1.26)	1.33 (1.22–1.45)	1.34 (1.22–1.48)	1.45 (1.32–1.60)	1.59 (1.41–1.79)	<.001
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.15 (1.05–1.26)	1.32 (1.21–1.44)	1.34 (1.22–1.48)	1.45 (1.32–1.60)	1.58 (1.41–1.78)	<.001

[a]BMI as updated every 2 y from 1990 to 2012.
[b]Adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.

Supplementary Table 3. Waist Circumference, Waist-to-Hip Ratio, and Risk of Diverticulitis Using Follow-Up From 1990 to 2014[a]

Variable	Q1	Q2	Q3	Q4	Q5	*P* for trend
WC						
No. of cases	531	752	935	849	1065	
Person-years	195,964	211,301	220,415	181,467	211,707	
Age, HR (95% CI)	1 (ref)	1.22 (1.09–1.37)	1.39 (1.25–1.55)	1.48 (1.33–1.66)	1.57 (1.41–1.75)	<.001
Multivariate,[b] HR (95% CI)	1 (ref)	1.21 (1.08–1.35)	1.36 (1.21–1.51)	1.43 (1.28–1.60)	1.50 (1.34–1.68)	<.001
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.21 (1.08–1.35)	1.35 (1.21–1.50)	1.42 (1.26–1.59)	1.49 (1.33–1.66)	<.001
Multivariate+diet+BMI, HR (95% CI)	1 (ref)	1.16 (1.03–1.30)	1.24 (1.10–1.39)	1.26 (1.11–1.43)	1.26 (1.10–1.44)	<.001
WHR						
No. of cases	589	715	897	915	1005	
Person-years	203,221	203,512	202,935	203,698	203,711	
Age, HR (95% CI)	1 (ref)	1.14 (1.02–1.27)	1.37 (1.23–1.52)	1.34 (1.21–1.49)	1.43 (1.29–1.59)	<.001
Multivariate,[b] HR (95% CI)	1 (ref)	1.11 (1.00–1.24)	1.32 (1.19–1.47)	1.27 (1.14–1.41)	1.34 (1.20–1.49)	<.001
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.11 (0.99–1.24)	1.31 (1.18–1.46)	1.26 (1.13–1.40)	1.33 (1.19–1.48)	<.001
Multivariate+diet+BMI, HR (95% CI)	1 (ref)	1.08 (0.97–1.21)	1.25 (1.13–1.39)	1.18 (1.06–1.31)	1.23 (1.10–1.37)	<.001

Q, quintile.
[a]Waist circumference and waist-to-hip ratio were assessed in 1986, 1996, and 2000. We updated and used the most recent information prior to the questionnaire cycle of interest.
[b]Adjusted for height, menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.

Supplementary Table 4. Weight Change From age 18 to Current and Risk of Diverticulitis Stratified by Various Characteristics (2008–2014)[a]

		Weight change, HR (95% CI)						
Variable	No. of cases	Loss ≥2.0 kg	Loss or gain <2.0 kg	Gain 2.0-5.9 kg	Gain 6.0–9.9 kg	Gain 10.0–19.9 kg	Gain ≥20.0 kg	*P* for interaction
Age								.50
Age <70 y	290	1.00 (0.42–2.36)	1 (ref)	1.03 (0.49–2.18)	1.62 (0.82–3.17)	1.53 (0.81–2.87)	1.78 (0.95–3.35)	
Age ≥70 y	651	0.88 (0.57–1.36)	1 (ref)	1.50 (1.02–2.21)	1.18 (0.80–1.75)	1.64 (1.16–2.33)	1.70 (1.19–2.43)	
BMI age 18 y								.12
<21 kg/m^2	510	1.10 (0.58–2.09)	1 (ref)	1.60 (0.98–2.62)	1.40 (0.86–2.26)	1.48 (0.95–2.32)	1.66 (1.05–2.61)	
≥21 kg/m^2	431	0.81 (0.50–1.33)	1 (ref)	1.14 (0.70–1.87)	1.17 (0.72–1.90)	1.81 (1.19–2.75)	1.86 (1.22–2.84)	
Smoking status								.09
Never	404	1.05 (0.58–1.90)	1 (ref)	1.65 (0.99–2.75)	1.44 (0.86–2.39)	1.64 (1.03–2.62)	1.68 (1.04–2.70)	
Ever	531	0.88 (0.52–1.48)	1 (ref)	1.27 (0.79–2.05)	1.28 (0.81–2.04)	1.69 (1.11–2.56)	1.87 (1.23–2.85)	
Physical activity[b]								.72
<12 MET-h/wk	454	0.88 (0.50–1.57)	1 (ref)	1.26 (0.74–2.13)	1.17 (0.70–1.96)	1.38 (0.87–2.19)	1.50 (0.95–2.39)	
≥12 MET-h/wk	420	0.98 (0.58–1.68)	1 (ref)	1.48 (0.93–2.36)	1.30 (0.82–2.08)	1.62 (1.06–2.48)	1.71 (1.10–2.66)	

MET, metabolic equivalent.
[a]Weight change from age 18 y to current was calculated by subtracting weight at age 18 y from updated weight in current questionnaire cycle. Models were adjusted for age, weight at age 18 y, height, menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, dietary fiber intake, and red meat intake.
[b]Dichotomized according to median level of physical activity.

Supplementary Table 5. Four-Year Weight Change During Follow-Up and Risk of Diverticulitis (2008–2014)[a]

Weight change	Median, *kg*	No. of cases	Person-years	Model 1,[b] HR (95% CI)	Model 2,[c] HR (95% CI)
Loss ≥5.0 kg	–8.2	126	30,911	0.86 (0.70–1.07)	0.85 (0.68–1.05)
Loss 4.9–1.0 kg	–2.7	271	60,844	1.02 (0.86–1.20)	1.01 (0.86–1.20)
Loss or gain <1.0 kg	0	300	69,363	1 (ref)	1 (ref)
Gain 1.0–4.9 kg	2.3	240	54,838	1.03 (0.86–1.22)	1.02 (0.86–1.21)
Gain ≥5.0 kg	7.7	90	19,562	1.06 (0.84–1.35)	1.04 (0.82–1.32)
P for trend	—	—	—	.14	.14

[a]4-year weight change during follow-up was calculated and updated using repeated weight assessments 4 years apart. We suspended updating weight change information when a participant quit smoking or reported a diagnosis of cancer, cardiovascular disease, or inflammatory bowel disease in the past 2 years. Results were essentially unchanged if we did not suspend updating.
[b]Model 1 was adjusted for age, body weight at the start of each time period, and height.
[c]Model 2 was further adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, fiber intake, and red meat intake.

Supplementary Table 6. Four-Year Weight Change During Follow-Up and Risk of Diverticulitis Stratified by Body Mass Index (2008–2014)[a]

		BMI <25 kg/m^2		BMI ≥25 kg/m^2	
Weight change	Median, *kg*	No. of cases	HR (95% CI)	No. of cases	HR (95% CI)
Loss ≥5.0 kg	-8.2	18	0.73 (0.44–1.20)	108	0.85 (0.66–1.08)
Loss 4.9–1.0 kg	-2.7	111	1.17 (0.91–1.51)	160	0.92 (0.74–1.14)
Loss or gain <1.0 kg	0	131	1 (ref)	169	1 (ref)
Gain 1.0–4.9 kg	2.3	95	1.10 (0.84–1.44)	145	0.95 (0.76–1.19)
Gain ≥5.0 kg	7.7	24	1.15 (0.74–1.78)	66	0.97 (0.73–1.29)
P for trend	—	—	.36	—	.27
P for interaction	—		.95		

[a]Four-year weight change during follow-up was calculated and updated using repeated weight assessments 4 y apart. We suspended updating weight change information when a participant quit smoking or reported a diagnosis of cancer, cardiovascular disease, or inflammatory bowel disease in the past 2 y. Models were adjusted for age, height, menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, calorie intake, fiber intake, and red meat intake.

Supplementary Table 7. Body Mass Index and Risk of Recurrent and Non-Recurrent Diverticulitis (2008–2014)[a]

Variable	BMI					
	<22.5 kg/m^2	22.5–24.9 kg/m^2	25.0–27.4 kg/m^2	27.5–29.9 kg/m^2	≥30.0 kg/m^2	*P* for trend
Recurrent diverticulitis						
No. of cases	41	37	53	42	67	
Age, HR (95% CI)	1 (ref)	0.94 (0.60–1.47)	1.37 (0.91–2.06)	1.67 (1.08–2.57)	1.58 (1.07–2.35)	.003
Multivariate,[b] HR (95% CI)	1 (ref)	0.94 (0.60–1.47)	1.36 (0.90–2.06)	1.67 (1.08–2.60)	1.62 (1.07–2.44)	.003
Multivariate+diet,[c] HR (95% CI)	1 (ref)	0.95 (0.60–1.48)	1.38 (0.91–2.10)	1.71 (1.10–2.66)	1.66 (1.09–2.51)	.002
Non-recurrent diverticulitis						
No. of cases	166	162	186	117	215	
Age, HR (95% CI)	1 (ref)	1.12 (0.90–1.40)	1.34 (1.09–1.65)	1.31 (1.03–1.66)	1.49 (1.22–1.84)	<.001
Multivariate,[b] HR (95% CI)	1 (ref)	1.11 (0.89–1.38)	1.31 (1.06–1.62)	1.28 (1.00–1.63)	1.47 (1.18–1.82)	<.001
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.10 (0.89–1.37)	1.30 (1.05–1.61)	1.26 (0.99–1.61)	1.44 (1.16–1.79)	<.001

[a]BMI was updated every 2 y from 2008 to 2012.
[b]Adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.

Supplementary Table 8. Body Mass Index and Risk of Surgery for Diverticulitis (1992–2014)[a]

Variable	BMI						
	<22.5 kg/m^2	22.5–24.9 kg/m^2	25.0–27.4 kg/m^2	27.5–29.9 kg/m^2	30.0–34.9 kg/m^2	≥35.0 kg/m^2	*P* for trend
No. of cases	90	107	139	86	95	42	—
Person-years	285,971	292,088	272,705	171,239	190,502	90,852	—
Age, HR (95% CI)	1 (ref)	1.21 (0.92–1.61)	1.67 (1.28–2.18)	1.60 (1.19–2.16)	1.61 (1.20–2.15)	1.47 (1.02–2.13)	.002
Multivariate,[b] HR (95% CI)	1 (ref)	1.23 (0.93–1.63)	1.71 (1.30–2.23)	1.65 (1.22–2.24)	1.67 (1.24–2.26)	1.56 (1.06–2.30)	.001
Multivariate+diet,[c] HR (95% CI)	1 (ref)	1.23 (0.93–1.63)	1.71 (1.30–2.24)	1.65 (1.22–2.24)	1.67 (1.24–2.26)	1.56 (1.06–2.30)	.002

[a]In 2012 and 2014 questionnaires, participants were asked if they had surgery for diverticulitis which dated back to 1992. BMI was updated every 2 years from 1992 to 2012.
[b]Adjusted for menopausal status and menopausal hormone use, vigorous activity, alcohol intake, smoking, aspirin use, other nonsteroidal anti-inflammatory drug use, multivitamin use, acetaminophen use, physical examination, hypertension, hypercholesterolemia, and calorie intake.
[c]Further adjusted for dietary intake of fiber and red meat.