Animal Protein Intake and Risk of Inflammatory Bowel Disease: The E3N Prospective Study

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OBJECTIVES: **Diet composition has long been suspected to contribute to inflammatory bowel disease (IBD), but has not been thoroughly assessed, and has been assessed only in retrospective studies that are prone to recall bias. The aim of the present study was to evaluate the role of dietary macronutrients in the etiology of IBD in a large prospective cohort.**

METHODS: **The Etude Épidémiologique des femmes de la Mutuelle Générale de l'Education Nationale cohort consists of women living in France, aged 40–65 years, and free of major diseases at inclusion. A self-administered questionnaire was used to record dietary habits at baseline. Questionnaires on disease occurrence and lifestyle factors were completed every 24 months. IBDs were assessed in each questionnaire until June 2005, and subsequently validated using clinical and pathological criteria. We estimated the association between nutrients or foods and IBD using Cox proportional hazards models adjusted for energy intake.**

RESULTS: **Among 67,581 participants (705,445 person-years, mean follow-up since completion of the baseline dietary questionnaire 10.4 years), we validated 77 incident IBD cases. High total protein intake, specifically animal protein, was associated with a significantly increased risk of IBD, (hazards ratio for the third vs. first tertile and 95% confidence interval being 3.31 and 1.41–7.77 (*P* trend=0.007), and 3.03 and 1.45–6.34 (*P* trend=0.005) for total and animal protein, respectively). Among sources of animal protein, high consumption of meat or fish but not of eggs or dairy products was associated with IBD risk.**

CONCLUSIONS: **High protein intake is associated with an increased risk of incident IBD in French middle-aged women.**

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg.

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INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory disorders of the gastrointestinal tract. The pathogenic mechanisms involve epithelial cell barrier dysfunction, defects in the innate immune system that affect its interaction with commensal bacteria, abnormal composition of the bowel microbiota, and dysregulated T-cell function promoting chronic intestinal inflammation (1,2). Genetic predisposition is well documented, particularly in CD, in which several susceptibility genes affecting bacterial clearance, the IL23 pathway, and T-cell function have been identified (3,4). There is also some evidence that environmental factors may have a role in the pathogenesis of inflammatory bowel disease (IBD). First, the incidence of IBD has increased dramatically since World War II, which is inconsistent with a purely genetic disease (5). Second, migrants who move from a low-incidence area to a high-incidence area have a high risk of IBD (6,7). Few environmental factors have been linked reproducibly with susceptibility in IBD (8). Among them, smoking is the best documented; quitting smoking is a risk factor for UC, whereas continuing smoking is a risk factor for CD (9). Diet composition has long been suspected to contribute to IBD and has been assessed in many studies. With respect to macronutrients, several retrospective case–control studies have found that high intakes of sucrose and fat were associated with CD and/or UC (10–12). However, these associations were prone to recall bias, because of the retrospective design of the studies (13).

In the present prospective study, we tested the hypothesis that the composition of the macronutrient content of the diet is

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associated with IBD risk. Thus, we investigated the relationship between pre-illness diet composition and risk of incident IBD in a large prospective cohort of women who were free of major diseases at enrollment.

METHODS

The Etude Épidémiologique des femmes de la Mutuelle Générale de l'Education Nationale (E3N) is a prospective cohort study conducted in France to study hormonal and dietary risk factors for the most common diseases, especially cancer, in women. The cohort was established in 1990 and consisted of 98,995 women living in France, aged 40–65 years at baseline and insured with the Mutuelle Générale de l'Éducation Nationale, which is a national health insurance scheme for teachers and co-workers (14). E3N is also the French counterpart of the EPIC (European Prospective Investigation into Cancer and Nutrition) study.

Physical activity, reproductive factors, use of hormonal treatments, tobacco consumption, anthropometric measurements, personal history of disease, family history of cancer, and other factors were recorded in self-administered questionnaires that were completed approximately every 24 months. Each questionnaire inquired about the occurrence of personal medical events, and there were specific questions about CD and UC occurrence in each questionnaire until July 2005. All study subjects signed an informed consent form, in compliance with the rules of the French National Commission for Computed Data and Individual Freedom (Commission Nationale Informatique et Libertés), from which we obtained approval.

Dietary data collection

Dietary data were collected once, between June 1993 and July 1995, using a two-part questionnaire. The first part contained questions on the usual amounts and frequency of consumption of foods from the various food groups, while the second included qualitative questions specifying individual foods within the food groups. The questionnaire was used to assess the consumption of 208 food items, beverages, and the recipes used to prepare them. It was accompanied by a booklet of photographs illustrating portion sizes. Both the questionnaire and the booklet were validated (15). A high proportion of subjects (76% for foods and 72% for nutrients) were classified in the same or adjacent quintile for the dietary questionnaire and the mean of 12-monthly 24-h recalls. The reproducibility of the dietary questionnaire was tested after 1 year. The Spearman correlation coefficient for reproducibility was 0.69 for dietary protein, 0.59 for carbohydrates, and 0.73 for fat. The diet history questionnaire was sent to 95,644 women, with two reminders to non-responders. In all, 77,613 completed questionnaires (81.1%) were received. After exclusion of 978 questionnaires because of absence of consent to external health follow-up by the health insurer in case of dropout, 2,050 questionnaires because of miscoded answers, 8 blank questionnaires, and 46 duplicates, 74,531 questionnaires were available for analysis.

Women with extreme values (in the top or bottom 1%) for the energy intake/energy requirement ratio (calculated by taking age, weight, and height into account) were excluded. The mean daily intake of nutrients was assessed using a food composition table derived from the French national database.

Validation of cases and non-cases

Cases were first identified through the questionnaires, in which the women checked the item "Crohn's disease" or "ulcerative colitis." After exclusion of miscoded answers, a letter was sent to the potential cases in order to confirm their answers and to obtain the names of their physicians. Then a brief questionnaire was sent to the gastroenterologist or general practitioner, requesting for information about diagnostic procedures, final IBD diagnosis after follow-up, location, number of flares, and medical and surgical treatments.

All cases of IBD were reviewed by two of the authors (P.J. and F.C.), in order to confirm or rule out the diagnosis. Definition of IBD was based on clinical, radiological, endoscopic, and histological criteria. We classified cases as certain or possible. Possible IBD cases were those of women, which were considered and treated as IBD, but did not meet all inclusion criteria after a careful review. IBD cases for which radiological or endoscopic data did not enable us to classify them as CD or UC were considered as indeterminate colitis (IC). As IBD presentation, and thus classification, may vary with time, we retained the diagnosis at the latest follow-up.

Non-cases were defined as subjects who never reported a personal history of IBD and were free of cancer at baseline. Because of potential major changes, especially in diet, subjects with incident cancer were censored at the date of cancer diagnosis. Thus, subjects contributed person-time up to the date of IBD diagnosis, date of cancer at any site (other than basal cell skin carcinoma or *in situ* colorectal cancer), date of last completed questionnaire, or July 2005, whichever occurred first.

Among the 74,531 women with available dietary questionnaires, we excluded 4,654 women because of prevalent cancer, 810 who were lost to follow-up after replying to the dietary questionnaire, 1,364 with extreme values of energy intake, and 5 with no information available.

Statistical analysis

The association between dietary factors and IBD was estimated using Cox proportional hazards models with age as the time scale. Age at diagnosis of IBD or at censoring date was used as the end-of-study time variable. Dietary factors that were considered included the macronutrients (carbohydrates, proteins, animal and vegetal proteins, and lipids) and food sources of animal protein: meat (red and white meat), eggs, dairy products (milk and cheese), and fish (fish and seafood). Dietary intake was analyzed in tertiles. To calculate *P* values for trends across tertiles, participants were assigned a score ranging from 1 to 3 according to their tertile of intake and this variable was entered as a continuous term in the Cox regression models. Power calculations indicated that for a bilateral test and alpha risk set at the 5% level, we had a 78%, 93%, and 98% power to detect a hazards ratio (HR) of 2.5, 3.0, or 3.5, respectively, in our main sample using tertiles for

the exposure variable; the corresponding figures were 38%, 54%, and 69%, respectively, for the CD group, and 59%, 78%, and 90%, respectively, for the UC group.

When analyzing macronutrients, adjustment for energy intake was made with the energy partition method, considering energy from carbohydrates, from lipids, and from proteins as three separate mutually adjusted variables (16). Else, when considering subtype of protein intake (vegetable or animal) or food sources of protein intake, covariates were mutually adjusted while adjustment on other sources of energy intake was carried out by adding energy intake from lipids and carbohydrates (non-protein energy) as a covariate in the Cox model. In order to assess the potential impact of dietary changes due to undiagnosed IBD, we carried out sensitivity analyses excluding cases diagnosed within 6 or 12 months after dietary assessment. We further investigated the effect of additional adjustment for body mass index at baseline, total daily alcohol intake (all as continuous variables), physical activity (tertiles of weekly energy expenditure), oral contraceptive intake, menopause hormonal treatment, smoking status at baseline (former/never/current), and the level of education as proxy for the socio-economic status. Analyses were carried out for all IBD cases, as well as separately for CD and UC. A heterogeneity test was performed to compare the HRs associated with CD and UC risk using the Wald statistics (17). Sensitivity analyses were carried out after exclusion of 16 patients for whom IBD diagnosis was considered only possible (5 CD, 10 UC, and 1 IC cases). All analyses were performed using SAS software, version 9 (SAS Institute, Cary, NC); all statistical tests were two-sided. For all analyses, P values <0.05 were considered statistically significant.

Table 1. Baseline characteristics of IBD cases and non-cases in the E3N cohort study

Baseline demographics and lifestyle characteristics	Total incident IBD cases (n=77)[a]	Crohn's disease (n=30)	Ulcerative colitis (n=43)	Non-cases (n=67,504)
Age at dietary questionnaire (year)				
Mean	51.2	50.9	51.4	52.8
Range	43.5–67.6	43.5 – 67.6	44.1–63.6	41.8–72.0
Age at IBD diagnosis				
Mean	56.3	55.6	56.7	—
Range	46.0–72.5	43.5–67.5	46.0–71.0	
Time to diagnostic (years)				
Median	4.5	3.7	5.1	—
Interquartile range	2.2–7.9	1.5–8.1	2.5–7.9	
Anthropometric factors, mean (s.d.)				
Height (cm)	162 (5.4)	163.8 (5.0)	160.6 (5.2)	161 (5.7)
Weight (kg)	60.3 (8.8)	61.2 (9.2)	59.1 (8.4)	60.0 (9.4)
Body mass index (kg/m^2)[b]	23.0 (3.5)	22.8 (3.6)	22.9 (3.5)	23.0 (3.3)
Smoking status, n *(%)*				
Never smoker	39 (50.7)	16 (53.3)	22 (51.2)	37,911 (56.2)
Former smoker	21 (27.3)	8 (26.7)	12 (27.9)	20,325 (30.1)
Current smoker	17 (22.1)	6 (20.0)	9 (20.9)	9,268 (13.7)
Exogenous hormone use, n *(%)*				
Ever used HRT[c]	59 (76.6)	23 (76.7)	33 (76.7)	47,848 (70.9)
Ever used oral contraceptive	49 (63.6)	19 (63.3)	27 (62.7)	41,177 (61.0)
Total physical activity[d], n *(%)*				
Weakly active	28 (36.4)	14 (46.7)	12 (27.9)	22,313 (33.3)
Moderately active	22 (28.6)	9 (30.0)	12 (27.9)	22,384 (33.4)
Active	27 (35.1)	7 (23.3)	19 (44.2)	22,345 (33.4)

HRT, hormone replacement therapy; IBD, inflammatory bowel disease.
[a]Total IBD cases: 30 CD cases, 43 UC cases, and 4 indeterminate colitis.
[b]Weight (kg)/height (m)^2.
[c]HRT: among postmenopausal women only.
[d]Continuous variables are presented as mean (standard deviation). Categorical variables are presented as n (%). Unknown values were excluded from the calculations: physical activity, 0.6%.

RESULTS

A total of 67,581 participants contributed 705,445 person-years in a mean follow-up of 10.4 years since completion of the dietary questionnaire. Among the entire cohort, 458 women checked the item "Crohn's disease" or "ulcerative colitis" on the self-administered questionnaire. After investigation, we validated the diagnosis of IBD in 194 women. Among them, 77 women were diagnosed as having IBD after inclusion in the study (incident cases) with a median of 54.5 months follow-up (interquartile range: 26.5–95.5). The 77 women with incident IBD were compared with the 67,504 non-cases. On the basis of available data, 43 cases were classified as UC, 30 cases as CD, and 4 cases as IC. In all, 16 cases were considered as possible and 61 cases were classified as certain (including 33 UC cases, 25 CD cases and 3 cases with IC). The baseline characteristics of cases and non-cases are reported in **Table 1**.

HRs of IBD according to the dietary intake of macronutrients (expressed as the absolute amount of energy provided by each macronutrient) are presented in **Table 2**. In a mutually adjusted model, total protein intake, but neither carbohydrates nor lipids, was statistically positively associated with IBD risk (**Table 2**). When protein intake was expressed per kilogram body weight, mean intakes per tertile were 1.08 g/kg (range: 0.30–1.33), 1.52 g/kg (range: 1.34–1.71), and 2.07 g/kg (range: 1.72–4.46). High intake of protein per kilogram body weight was also significantly associated with IBD risk (HR for the third vs. first tertile of intake = 2.63; 95% CI, 1.23–5.59; *P* for linear trend across tertiles = 0.008). The positive association between high protein intake and IBD risk was restricted to animal protein intake, as there was no significant association with vegetable protein (**Table 3**). Although no heterogeneity test was statistically significant when comparing UC and

Table 2. Mutually adjusted HR estimates and 95% confidence intervals for IBD in relation to macronutrient intake in the E3N cohort (*n*=67,581), 1993–2005

Nutrient	Tertile 1	Tertile 2	Tertile 3	*P* trend
IBD				
Protein	1 (—)	2.46 (1.15–5.28)	3.31 (1.41–7.77)	0.007
Carbohydrate	1 (—)	0.76 (0.43–1.37)	0.68 (0.37–1.27)	0.26
Fat	1 (—)	1.41 (0.70–2.84)	1.24 (0.57–2.72)	0.77
UC				
Protein	1 (—)	2.83 (1.07–7.48)	3.24 (1.07–9.84)	0.06
Carbohydrate	1 (—)	0.42 (0.19–0.94)	0.51 (0.24–1.08)	0.12
Fat	1 (—)	1.01 (0.41–2.47)	1.47 (0.56–3.84)	0.34
CD				
Protein	1 (—)	1.96 (0.58–6.68)	3.34 (0.90–12.4)	0.04
Carbohydrate	1 (—)	2.01 (0.70–5.72)	1.31 (0.42–4.14)	0.46
Fat	1 (—)	2.27 (0.69–7.45)	0.98 (0.25–3.88)	0.88

CD, Crohn's disease; IBD, inflammatory bowel disease; HR, hazard ratio; UC, ulcerative colitis.
All nutrient tertiles were calculated from daily intake expressed in absolute amount of energy provided by the nutrient (Kcal/day).

Table 3. HR estimates and 95% confidence intervals for IBD in relation to type of protein in the E3N cohort (*n*=67,581), 1993–2005

Nutrient	Tertile1	Tertile 2	Tertile 3	*P* trend
IBD				
Animal protein	1 (—)	2.62 (1.29–5.30)	3.03 (1.45–6.34)	0.005
Vegetable protein	1 (—)	0.91 (0.47–1.77)	1.31 (0.59–2.88)	0.44
UC				
Animal protein	1 (—)	1.62 (0.65–4.02)	3.29 (1.34–8.04)	0.005
Vegetable protein	1 (—)	0.59 (0.23–1.54)	1.70 (0.59–4.81)	0.33
CD				
Animal protein	1 (—)	4.51 (1.28–15.83)	2.70 (0.69–10.52)	0.33
Vegetable protein	1 (—)	1.15 (0.39–3.35)	1.04 (0.28–3.80)	0.98

CD, Crohn's disease; IBD, inflammatory bowel disease; HR, hazard ratio; UC, ulcerative colitis.
Model including energy from animal protein, energy from vegetable protein, and non-protein energy (i.e., energy from carbohydrates and lipids as ordered tertiles).

Table 4. HR estimates and 95% confidence intervals for IBD in relation to different groups of food protein intake in the E3N cohort (*n*=67,581), 1993–2005

	Tertile 1	Tertile 2	Tertile 3	*P* trend
Meat (g/day)[b]	31.8	83.2	144.4	
Number of IBD	15	25	37	
Energy-adjusted HR[a]	1 (—)	1.45 (0.76–2.75)	1.87 (1.00–3.49)	0.02
Fish/sea products (g/day)[b]	10.7	26.4	59.1	
Number of IBD	16	29	32	
Energy-adjusted HR[a]	1 (—)	1.63 (0.88–3.01)	1.83 (1.00–3.36)	0.05
Eggs (g/day)[b]	6.9	19.5	46.1	
Number of IBD	19	33	25	
Energy-adjusted HR[a]	1 (—)	1.31 (0.74–2.31)	0.97 (0.52–1.78)	0.91
Dairy products (g/day)[b]	131.3	264.6	511.4	
Number of IBD	24	27	26	
Energy-adjusted HR[a]	1 (—)	1.02 (0.58–1.77)	0.94 (0.53–1.67)	0.93

HR, hazard ratio; IBD, inflammatory bowel disease.
[a]Mutually adjusted and adjusted on alcohol-free energy intake.
[b]Mean value of daily consumption for each tertile.

CD, the shapes of associations between total and animal protein and risk of IBD tended to differ slightly between UC and CD (**Tables 2** and **3**). Regarding CD, a dose–effect relationship was observed for total protein ($P=0.04$) but not for animal protein ($P=0.33$). Regarding UC, a strong dose–effect relationship was observed with animal protein ($P=0.005$), whereas there was only a borderline statistically significant association with total protein ($P=0.06$).

Analyses of food sources of animal protein showed that high consumptions of meat or fish, but not of eggs or dairy products, were positively associated with IBD risk (**Table 4**).

Further adjustment on daily alcohol intake, physical activity, body mass index, tobacco smoking, menopause hormone therapy, or socio-economic status did not substantially modify the association between protein intake and IBD (see **Supplementary Appendix 1** and **2** online).

When excluding the eight cases that occurred within 6 months (four UC, three CD, and one IC), the HR for the third vs. first tertile of animal protein intake was 2.77 (95% CI, 1.15–6.68); when excluding the 10 cases that occurred within 1 year (six UC, three CD, and one IC), the corresponding HR became 2.74 (95% CI, 1.30–5.78). Another sensitivity analysis was performed on the 61 certain cases of IBD and provided similar results (HR for the third vs. first tertile of intake, 3.63; 95% CI, 1.32–10.01 (P trend = 0.01); and 3.13; 95% CI, 1.34–7.31 (P trend = 0.01) for total and animal protein, respectively).

DISCUSSION

The main finding of this prospective cohort study is that high protein intake was associated with an increased risk of IBD. The positive association between high protein intake and IBD risk was restricted to animal protein intake. Among animal protein sources, both fish and meat were associated with risk, whereas egg and dairy products were not, potentially because of insufficient power. In this study of women with moderate-to-high consumption of protein, and especially animal protein (99% of women consumed more than the mean nutritional requirement of 0.66 g/kg/day and 90% more than the recommended daily amount of 0.83 g/kg/day) (18), high protein intake was associated with a 3.3-fold increased risk of IBD. This would make high-protein diet a major risk factor of IBD. The observed incidence of CD and UC in this cohort lies within the expected range in this age class: 4.2 per 100,000 for CD and 6.1 per 100,000 for UC (19,20). HRs were similar for UC and CD regarding total protein, although a dose–effect relationship with animal protein was only observed for UC. The lack of statistical significance for animal protein in CD could be due to a lack of power. Future studies should confirm this potential association between CD and protein intake, and investigate whether ileal and colonic CD are equally associated with dietary protein intake.

Our dietary survey has several strengths. Dietary questionnaires were completed several years before the diagnosis of IBD. The questionnaire has been validated and found to be reproducible (15). We adjusted the models for energy intake using the energy partition method, which has been largely used and advocated for the study of macronutrients (16). Using this method, we did not find any significant association between lipid or carbohydrate intakes and the risk of CD or UC. A recent prospective study from EPIC showed a significant positive association between the dietary content in linoleic acid and UC incidence, and a negative one with docosohexaenoic acid intake, but not with total lipid intake, in agreement with our findings (21).

Our study has some limitations. First, it can be argued that the potential interval between the acquisition of the dietary data and the onset of disease is long enough for substantial changes to occur in dietary habits. However, it has been shown that dietary

habits change very little over time in middle-aged adults (22); in addition, changes in dietary habits would result in non-differential misclassification of dietary exposure, and thus in diluting the effect rather than increasing it. Some misclassification of dietary exposure is a constant feature of dietary surveys, and our moderately high correlation coefficients for reproducibility after 1 year are in favor of some degree of errors in assessing the diet. Again, this would rather dilute the true association. Second, this study included women aged 40–65 years, whereas IBD typically peaks between 20–35 years; further prospective studies should determine whether the results of this study could be reproduced in younger and male subjects. Third, the restricted sample size had limited power to detect effects below a relative risk of 2.5, especially when considering separately CD and UC. Finally, because of the limited number of cases, we could not perform analyses based on quartiles or quintiles, which would have better captured a true dose–effect relationship.

Our results are consistent with the hypothesis formulated by Shoda *et al.* (23), who found a temporal relationship between the rising incidence of CD in Japan and increasing dietary intake of animal protein ($r = 0.908$). Since World War II, animal protein intake has increased not only in Japan but also in all developed countries (24); as an example, a 50% increase has been reported in Belgium between the mid-1950s to 1978, with a per capita meat consumption from 60.8 to 98.0 kg/year (25). The increase in animal protein consumption may therefore explain some of the increased incidence of IBD since World War II. Some (but not all) retrospective case–control studies have described a higher consumption of meat (26) and fish (12) in CD patients as compared with controls. Moreover, a follow-up study in 191 UC patients showed a significant association between high meat intake and risk of relapse of UC (27). On the contrary, a prospective study that included some centers from the EPIC study failed to find any association between any type of macronutrient and UC risk (28). However, there were several differences between that study and ours, including a nested case–control design, intake of protein considered as a percentage of total energy including alcohol, heterogeneity between centers and dietary questionnaires, and the inclusion of both men and women. It needs to be further investigated as to what extent these features would explain the different findings. From our results and those of other studies, it may be speculated that reducing protein intake to the first tertile (< 67 g/day) could decrease both the incidence and activity of IBD. A prospective randomized study should be undertaken to test this hypothesis.

There is biological plausibility for a positive association between animal protein intake and IBD. A variable proportion of heme and amino acids, contained in animal proteins, are not absorbed by the small bowel and reach the colonic lumen, where they are metabolized by the microflora (29). This results in a number of end products, which include hydrogen sulfide, phenolic compounds, and amines and ammonia, some of which are potentially toxic to the colon (29). For instance, it has been suggested that sulfide, in the presence of nitric oxide produced by anaerobic bacteria, may alter the cell membrane of the colonocyte, and lead to the loss of barrier function and the immune cascade as observed in UC (30). It has been shown that, in healthy volunteers, an increase in dietary protein leads to changes in the colonic metabolism of proteins, which is mainly reflected by an increase in fecal ammonia, fecal volatile sulfur substances, and urinary *p*-cresol (31). Thus, high animal protein consumption might increase IBD risk through accrued formation of end products by the colonic microflora, such as hydrogen sulfide, which are toxic for the colon. Additional mechanisms, such as the impact of animal protein intake upon dysbiosis or inflammatory response, can also be suspected (32).

In summary, our results may help better understand the role of diet in IBD risk. If confirmed, they can lead to protective strategies, especially in families at risk of IBD, and possibly to advice for preventing relapse.

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CONFLICT OF INTEREST

Guarantor of the article: Franck Carbonnel, MD, PhD.

Specific author contributions: Prévost Jantchou contributed to study design and implementation, data collection, design and implementation of the statistical analysis, interpretation of results, and drafting and review of the manuscript. Sophie Morois contributed to design and implementation of the statistical analysis, interpretation of results, and drafting and review of the manuscript. Marie-Christine Boutron-Ruault and Franck Carbonnel contributed to design and implementation of the study, data collection, design and implementation of the statistical analysis, interpretation of results, and drafting and review of the manuscript. Françoise Clavel-Chapelon contributed to enrollment and follow-up of patients, design and implementation of the study, and review of the manuscript. All authors have seen the final submitted manuscript and agree with its contents.

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Diet composition has long been suspected to contribute to inflammatory bowel disease (IBD), but has been assessed in retrospective studies.
- ✓ The associations described are prone to recall bias.

WHAT IS NEW HERE

- ✓ High protein intake is associated with an increased risk of incident IBD in middle-aged women.
- ✓ Limiting animal protein intake to the recommended daily amount might reduce the risk of IBD, and possibly, the risk of relapse.

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