Review

A posteriori dietary patterns and risk of inflammatory bowel disease: a meta-analysis of observational studies

Editor's Choice

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Abstract: Inflammatory bowel disease (IBD) is a chronic inflammatory disorder which affects the gastrointestinal tract. Many factors, such as genetics, stress, and dietary patterns have been related to the risk of this disease. Adherence to a prudent/healthy dietary pattern, due to its antioxidant and anti-inflammatory properties, help to reduce the risk of many chronic diseases such as IBD. The results from previous studies regarding the association between dietary patterns and risk of IBD, including Crohn's disease (CD) and ulcerative colitis (UC), are inconsistent. This meta-analysis was performed to evaluate the potential relations between dietary patterns and risk of CD and UC. PubMed and Scopus were searched up to October 2017 for eligible studies. Random-effects or fixed-effects models were used to pool the estimated risks for the highest versus the lowest category of extracted dietary patterns. A total of six studies, including four case-control and two cohort studies with 1099 cases and 263112 controls/participants were included in the meta-analysis. A decreased risk of CD was seen for the highest compared with the lowest categories of healthy dietary pattern (OR/RR = 0.39, 95%CI = 0.16–0.62), while no significant association with western dietary pattern was observed (OR/RR = 0.78, 95% CI: 0.51–1.04). Furthermore, no significant relationship was found between healthy (OR/RR = 0.61, 95%CI = 0.04–1.18, random effects) and western/unhealthy (OR/RR = 0.97, 95% CI: 0.67–1.26) dietary patterns and risk of UC. The results of the current meta-analysis showed that a healthy dietary pattern is associated with a lower risk of CD. Further studies are warranted to confirm these findings.

Keywords: Dietary patterns, inflammatory bowel disease, Crohn's disease, ulcerative colitis, meta-analysis

Introduction

Inflammatory bowel disease (IBD) comprise a group of heterogeneous disorders affecting the gastrointestinal tract of which Crohn's disease (CD) and ulcerative colitis (UC) are the two main clinical forms, which are characterized by idiopathic chronic intestinal inflammation [1, 2]. However, extensive efforts have been made to reveal the etiology and pathogenesis of this disease, but its underlying molecular mechanisms remains vague [3]. The most possible factors involving in the onset and continuation of intestinal inflammation in IBD are the individual genetic tendency and the influence of the host microbiome [2, 4]. Furthermore, some environmental influences, such as geographic location, tobacco use, alcohol consumption [5], appendectomy, stress and depression [6], physical activity, and sleep patterns have been related to the risk of this disease [7].

The IBD incidence is highest in westernized countries, with the highest reported incidence rates in Northern Europe, North America, Australia and the United Kingdom [8]. This shows that the westernization of lifestyle, in particular westernization of diet [9], may be related to the incidence of IBD [10]. Traditionally, the relationship between single nutrients and foods with IBD has been widely studied. Observational studies have found that consumption of fruit [11, 12], vegetable [13, 14], whole grain and fish is associated with reduced risk while higher dietary fat [15], margarine [16], sugars [17], alcoholic beverage [18], animal protein, and meat [19] intake are associated with higher risk, and nutrients, such as fiber [20], vitamin D [17], antioxidant vitamins [21], and dietary anti-inflammatory components, such as omega-3 polyunsaturated fatty acids [22] are associated with reduced risk of IBD. Among the components of the healthy diet, fruits and vegetables, due to the

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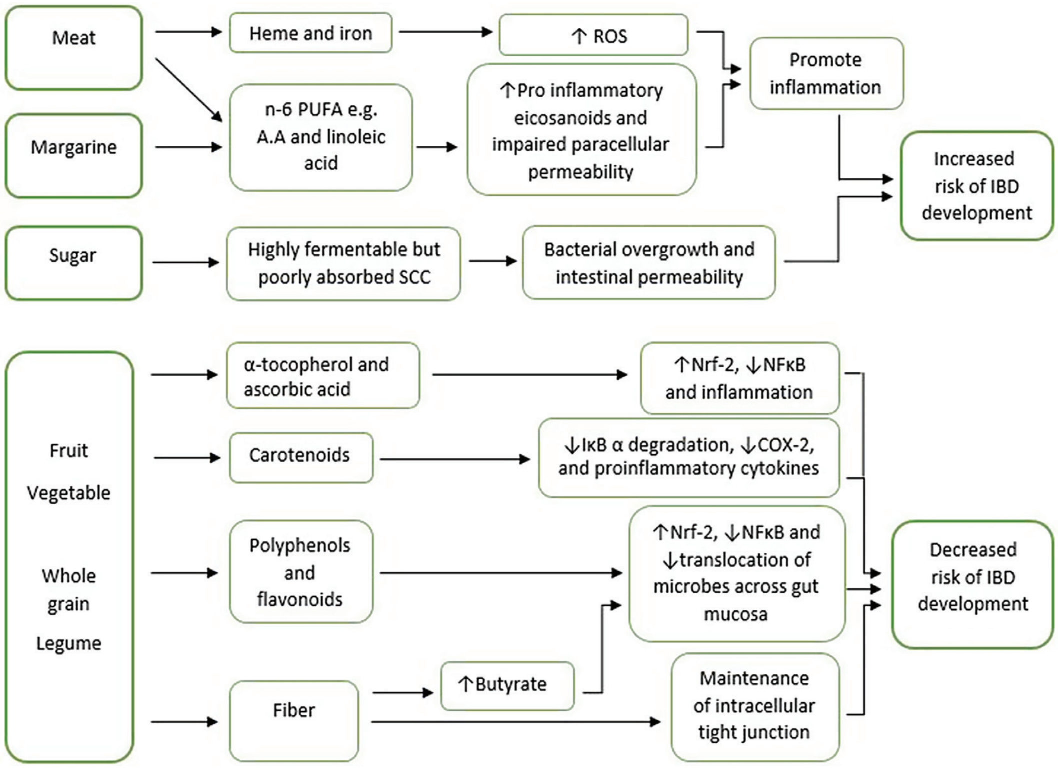

Figure 1. Function of dietary components in development of IBD.

presence of carotenoids, ascorbic acid and alpha tocopherol and their anti-inflammatory properties, may reduce the risk of IBD [23, 24]. Moreover, whole grains and legumes, due to their fiber and polyphenols, reduce colonic permeability and production of proinflammatory cytokines, and subsequently decrease the risk of IBD [25]. Figure 1 briefly shows the mechanism which dietary components affect IBD. Since individuals are exposed to a variety of foods with complex interactions of nutrients, dietary patterns are more appropriate to evaluate the overall effects of dietary factors than isolated nutrients or food items [26, 27]. More recently, a substantial attention has been drawn to the study of the association between overall dietary patterns and the risk of IBD. However, the results are inconsistent and varied considerably. Thus, the present meta-analysis was conducted to further clarify the potential relations between dietary patterns and the risk of Crohn's disease and ulcerative colitis.

Materials and methods

Data sources and searches

To find the relevant studies, we systematically searched Scopus and PubMed databases up to October 2017 to identify all published observational studies exploring the relationship between dietary patterns and the risk of incidence of CD or UC. The following search terms were used: (Dietary patterns OR dietary pattern OR food patterns OR food pattern OR eating patterns OR dietary habits OR food habits) AND (Crohn disease OR ulcerative colitis OR IBD OR inflammatory bowel disease). The search was restricted to search terms located in the title/abstract, and language was restricted to English. Furthermore, a manual search of references from eligible studies and review articles was conducted to obtain relevant studies. Our systematic review was performed based on the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [28].

Inclusion and exclusion criteria

Pertinent articles were eligible to be included in the present meta-analysis if the following criteria were met: (a) there were case–control studies or prospective cohorts studies that explored the relationship between dietary patterns as exposure and CD or UC as the main outcome; (b) the estimated risk (relative risk or odds ratios) and the corresponding 95% confidence interval (CI) was extractable; and (c) dietary patterns were evaluated by principal component analysis or factor analysis. Dietary patterns are defined by a combination of food groups, and can be different somewhat among various studies. To reduce the error and combine the results accurately, only the dietary patterns, sharing most foods with same factor loadings were analyzed. Accordingly, two most common dietary patterns were obtained from the included studies. The first pattern, named as a healthy dietary pattern, had a higher loading of vegetables, fruits, legumes, low-fat dairy products, dietary fiber, poultry, fish, nuts, and whole-grain foods, and low in fat dairy, processed food and red meat. The second pattern was named as unhealthy pattern, which had a higher loading of red meat and processed meat, refined grains, sugary desserts, soft drinks, high-fat foods, processed food, fried food items, snacks, and fast foods, and lower loading of fruits, vegetables, and dietary fibers. For meta-analysis, relative risks (RRs) and odds ratios (ORs) were considered the same and are referred to as OR estimates. Studies that were focused on single foods or nutrients were excluded. In addition, experimental studies, unpublished studies, reviews, editorials, and comments were excluded, but abstracts were included. Identified articles were independently reviewed by two authors for eligibility based on predefined criteria and discrepancies were resolved by discussion with a third reviewer.

Data Extraction and Quality assessment

We collected the following data from each included study, with the use of a standardized data extraction form: the first author's name, the design of the study, year of publication, country, sex, mean or range of age, the method of dietary assessment, the method of dietary pattern identification, sample size of cases and controls, follow-up duration, and odds ratios (ORs) or relative risks (RRs) with their corresponding 95% confidence intervals (CIs), and confounders adjusted for in the analysis. When a study reported different adjustment variables, we extracted the results from the most complete multivariable model that included the maximum number of adjusted covariates. Data were extracted independently by two authors, and the discrepancies during the data extraction were resolved by the involvement of a third reviewer. The quality of eligible articles was calculated using the Newcastle–Ottawa scale, which is generally applied in evaluating the quality of nonrandomized studies [29]. Concisely, each study was allocated a maximum of 9 stars for items of selection, comparability, and assessment of outcomes or exposures, and studies were classified as low quality (0–3), moderate quality (4–6), and high quality (7–9) in terms of the total scores.

Statistical analysis

The results in the original studies were reported in terms of tertiles, quartiles or quintiles of adherence to the dietary patterns. We used multivariable adjusted hazard ratios and odds ratios with 95% CI from individual studies for a comparison of the highest versus the lowest category of extracted dietary patterns (healthy and unhealthy). Heterogeneity across studies was calculated with the use of the Q and I^2 statistics [30]. Studies with an I^2 statistic of 25–50% are known as low heterogeneity, those with an I^2 statistic of 50–75% are as moderate heterogeneity, and those with an I^2 statistic of > 75% are considered to have a high heterogeneity. When heterogeneity was significant, the random-effects model was done; Otherwise, the fixed-effects model was applied [31]. Subgroup analysis was conducted to determine whether differences in study design (case-control or cohort) affected the study results. Publication bias was evaluated visually by a funnel plot and formally using Begg's test [32, 33]; $P < 0.05$ was considered as significant. All statistical tests for current meta-analysis were performed using statistical software of STATA (version 13.0; Stata Corporation, College Station, TX).

Results

Characteristics of included studies

A total of 599 studies were identified by the literature search. The flow diagram describing the process of screening and excluded articles with specific reasons is shown in Figure 2. Among the all excluded studies, 49 were duplicated publications; 492 were not relevant to dietary patterns and CD or UC risk; 28 were focused on the single nutrients or foods; ten were reviews; and one used dietary index method. The primary eligibility process yielded five studies and crosscheck of the references of included studies and other databases yielded one further study [16]. A total of six studies [16, 34–38] were finally included based on the inclusion criteria for the association between dietary patterns and risk of IBD; they included four case-control studies [16, 34, 35, 38] and two cohort studies [36, 37]. Among these studies, two were from the USA [36, 37], one from Italy [16], one from Australia [34], one from Canada [35], and one was a multinational study [38]. All studies assessed dietary intakes using a food frequency questionnaire. All of six included studies had medium-to-high quality scores, with ranges from 5 to 8 of 9 possible points, and no study met all requirements for a high-quality study free of bias. The results in all the studies were adjusted for the most potential confounders, including age, gender and total energy intake. The included studies labeled as healthy pattern were reported originally as "Prudent" [16, 35–37], "vegetables" [38], and in one study, a healthy pattern was not investigated [34]. In contrast the unhealthy pattern included "Fast foods" [34], "western" [35–37], "Refined"

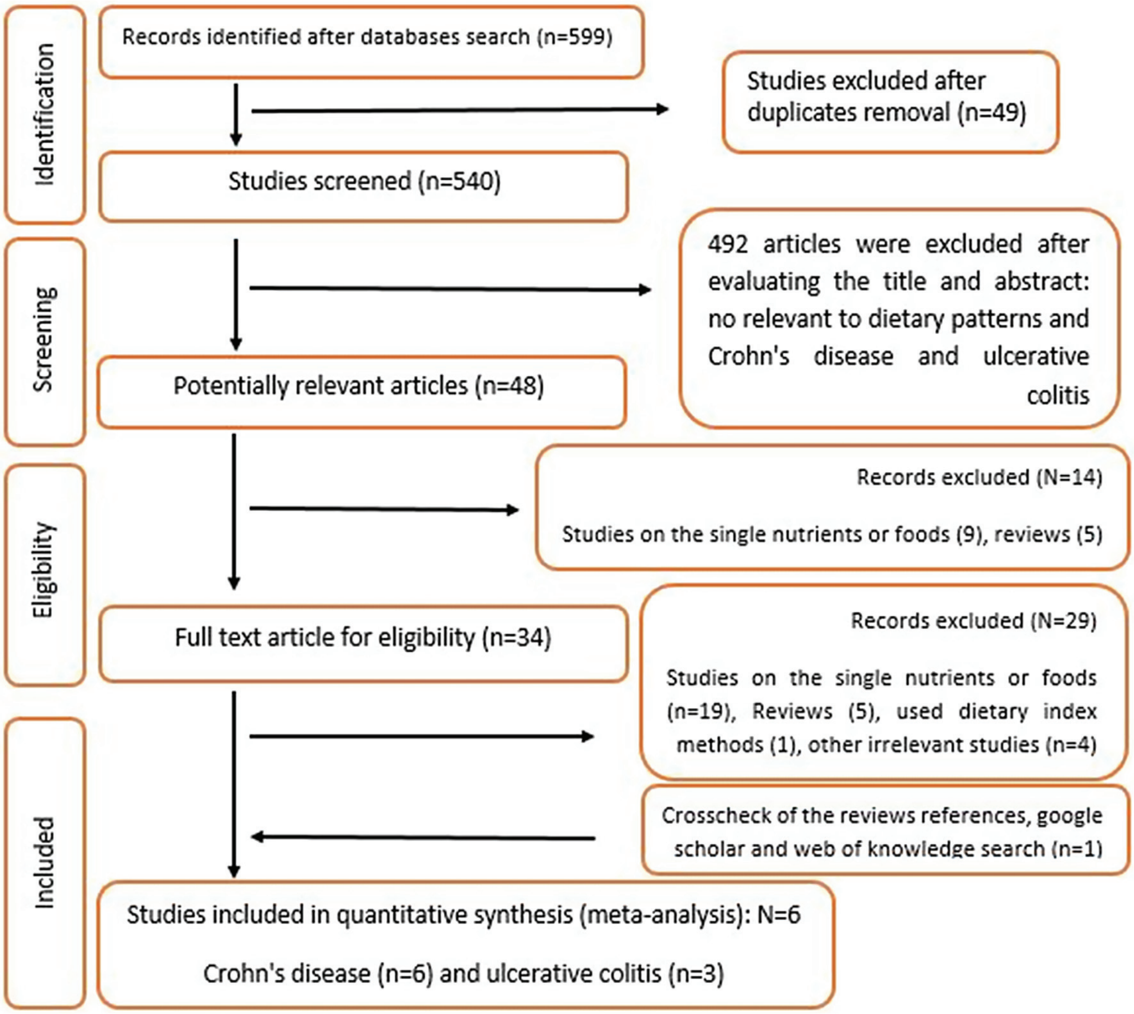

Figure 2. The flow diagram describing the process of screening and excluded articles, as a result of searching Scopus and PubMed Central databases from the beginning until October 2017 in English.

[16], "Alcohol, Animal Fat, Potatoes, Seafood" [38], and "Sugar and Soft Drinks" [38] dietary patterns. Table 1 shows detailed information about the studies included in the meta-analysis.

Dietary patterns and Crohn's disease (CD)

There were six studies including four case–control studies [16, 34, 35, 38] and two prospective cohort study [36, 37] with 699 cases and 222419 participants/controls concerning dietary patterns and CD risk. In five studies, the association between the highest compared to the lowest adherence to healthy dietary pattern intake and the risk of CD is shown in Figure 3. When all studies were pooled, there was a strong association between the healthy dietary pattern and reduced risk of CD (OR/RR = 0.39, 95% confidence interval (CI) = 0.16, 0.62), with evidence of heterogeneity (I^2 = 67.9%, P = 0.014). In the stratified analysis by study type, case-control studies also showed a significant negative association with CD incidence (OR = 0.25, 95%CI = 0.05, 0.45), but prospective cohort studies revealed no such association (RR = 0.68, 95%CI = 0.18–1.18). Figure 4 shows the associations between the "unhealthy" dietary pattern and CD risk. The pooled results indicated that there was no evidence of a difference in the risk of CD in the highest category compared to the lowest category of unhealthy dietary pattern (OR/RR = 0.78, 95% CI: 0.51, 1.04 (fixed effects)), and a moderate variability was detected (P-value for heterogeneity = 0.201, I^2 = 31.3%). Similar results were seen in both case-control (unhealthy pattern, OR = 0.95, 95%CI = 0.50–1.39, P for heterogeneity = 0.255) and cohort (unhealthy pattern,

Table 1. Characteristics of studies included in the meta-analysis on the association between healthy dietary pattern and inflammatory bowel disease.

Author and year	Country	Study design	Age (range or mean ± sd)/Sex	Cases	Control/ cohort size	Dietary Assessment	Dietary Patterns Identification Method	Dietary Patterns Identified	Adjusted Variables in analyses	Outcome	Quality[1]
Bencke et al. 2002	Australia	Case-control	NR/NR	65	186	FFQ	Principal Components Analysis (PCA)	"Fast foods" "Teetotal, sugar & cakes"	Oral contraceptive use, breast fed less than 6 weeks & past smoking.	CD	5
D'Souza et al. 2008	Canada	Case-control	2.6–20/Both	149	251	validated self-administered FFQ	Factor analyses (FA)	"Prudent" "Western" "Meat" "Cheese-snacks" "Beverages" "Miscellaneous"	energy intake, age at diagnosis, gender, body mass index [BMI], and study center	CD	8
Maconi et al. 2010	Italy	Case-control	39.4 + 15/Both	CD = 42 UC = 41	160	validated FFQ	Factor analysis	"Prudent" "healthy" "Refined"	Age, sex, years of education, tobacco consumption (never, smoker, current smoker of < 15, 15–24, ≥ 25 cigarettes/d) and body mass index	CD UD	7
Khalili et al. 2014	USA	Prospective cohort (24 years follow up)	NR/F	256	181843	validated FFQ	Principal component analysis	"Prudent" "Western"	Age, smoking, body mass index, physical activity, history of appendectomy, and use of oral contraceptives, menopausal hormone therapy, or non-steroidal anti-inflammatory drugs.	CD	7
Ananthakrishnan et al. 2015	USA	Prospective cohort (20 years follow up)	13–17/F	CD = 70 UC = 103	39511	High school dietary food frequency questionnaire (HS-FFQ), validated, 124-item.	Factor analysis	"Prudent" "Western"	smoking, oral contraceptive use, menopausal status, and postmenopausal hormone use, body mass index, non-steroidal anti-inflammatory drug use, physical activity, and adult dietary fiber and vitamin D intake	CD UC	8
Racine et al. 2015	Multinational	Case-control	20–80/Both	CD = 171 UC = 256	CD = 468 UC = 1022	validated FFQ, 200-item	factor analysis	"Drinks, Vegetables, and Legumes" "Vegetables" "Sugar and Soft Drinks" "Potatoes, Coffee, and Alcohol" "Animal Fat, Seafood, Potatoes, and Alcohol"	Age, sex, center and date of recruitment into study and adjusted for daily energy intake (kcal/day), body mass index (kg/m2), and smoking status (never/past/current smoker).	CD UC	8

[1]The Newcastle-Ottawa Scale was utilized to assess the quality of each study [29]. Abbreviations: NR, not reported; F, female; FFQ, food frequency questionnaire; CD, Crohn's disease; UC, ulcerative colitis.

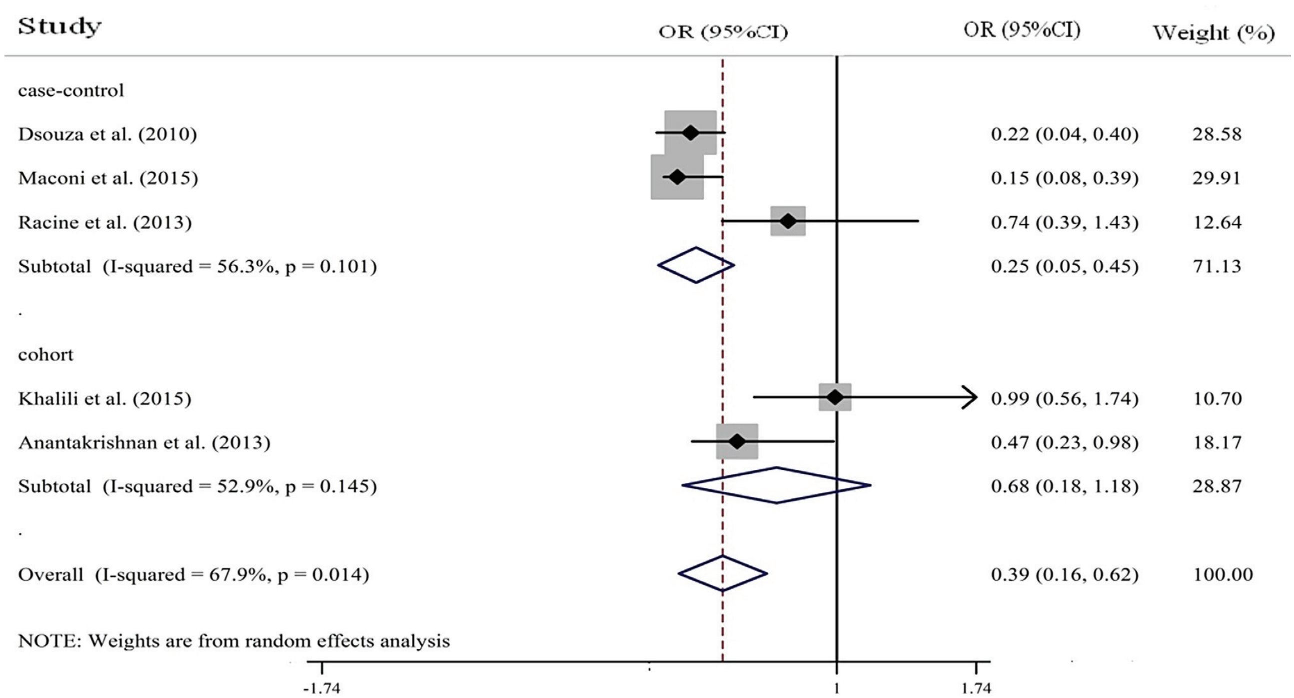

Figure 3. Forest plot of the highest compared with the lowest categories of intake of the healthy/prudent dietary patterns and Crohn's disease risk.

RR = 0.69, 95%CI = 0.36–1.02, P for heterogeneity = 0.121) studies in the subgroup analysis.

Dietary patterns and ulcerative colitis (UC)

There were three studies [16, 37, 38], including two case-control studies [16, 38] and one prospective cohort study [37] with 400 cases and 40693 participants/controls concerning dietary patterns and risk of UC. The pooled results indicated that there was no significant relationship between the healthy dietary pattern and reduced risk of UC (OR/RR = 0.61, 95%CI = 0.04, 1.18) with evidence of high heterogeneity (I^2 = 82.8%, P = 0.003). Furthermore, there was no evidence of a difference in the risk of UC in the highest category compared with the lowest category of unhealthy pattern (OR/RR = 0.97, 95% CI: 0.67–1.26). No considerable heterogeneity was seen between studies (P-value for heterogeneity = 0.591, I^2 = 0%) (Figure 4). Similar results were found in both case-control and cohort studies in the subgroup analysis (data not shown).

Publication bias

Funnel plot did not reveal asymmetry for studies that have investigated the association between dietary patterns and CD (not shown). Moreover, the corresponding statistical tests did not show publication bias for healthy pattern (Begg's test, P = 0.142) and unhealthy pattern (Begg's test, P = 0.091).

Discussion

Compared with investigating single food or nutrient effects, an assessment of whole diet using dietary patterns might be a more appropriate method to explore the combinatorial effects of dietary factors on health outcomes. Studying the effect of dietary patterns on CD and UC is an emerging field; however, the results from published studies are not entirely conclusive. The current meta-analysis was conducted to comprehensively elucidate these associations. A total of six studies, involving 1099 cases and 263112 controls/participants, which identified the healthy and unhealthy dietary patterns as the most common a posteriori dietary patterns were included in this meta-analysis. The results indicated that a healthy dietary pattern may reduce the risk of CD, whereas unhealthy-style dietary pattern was not associated with the risk of CD. Furthermore, the healthy and unhealthy dietary patterns were not related to the risk of UC.

This meta-analysis showed that a healthy dietary pattern is associated with a decreased risk of CD. This dietary pattern was described by a higher intake of vegetables and fruits, legumes, low-fat dairy products, dietary fiber, poultry, fish, nuts, and whole-grain foods. Amre et al.

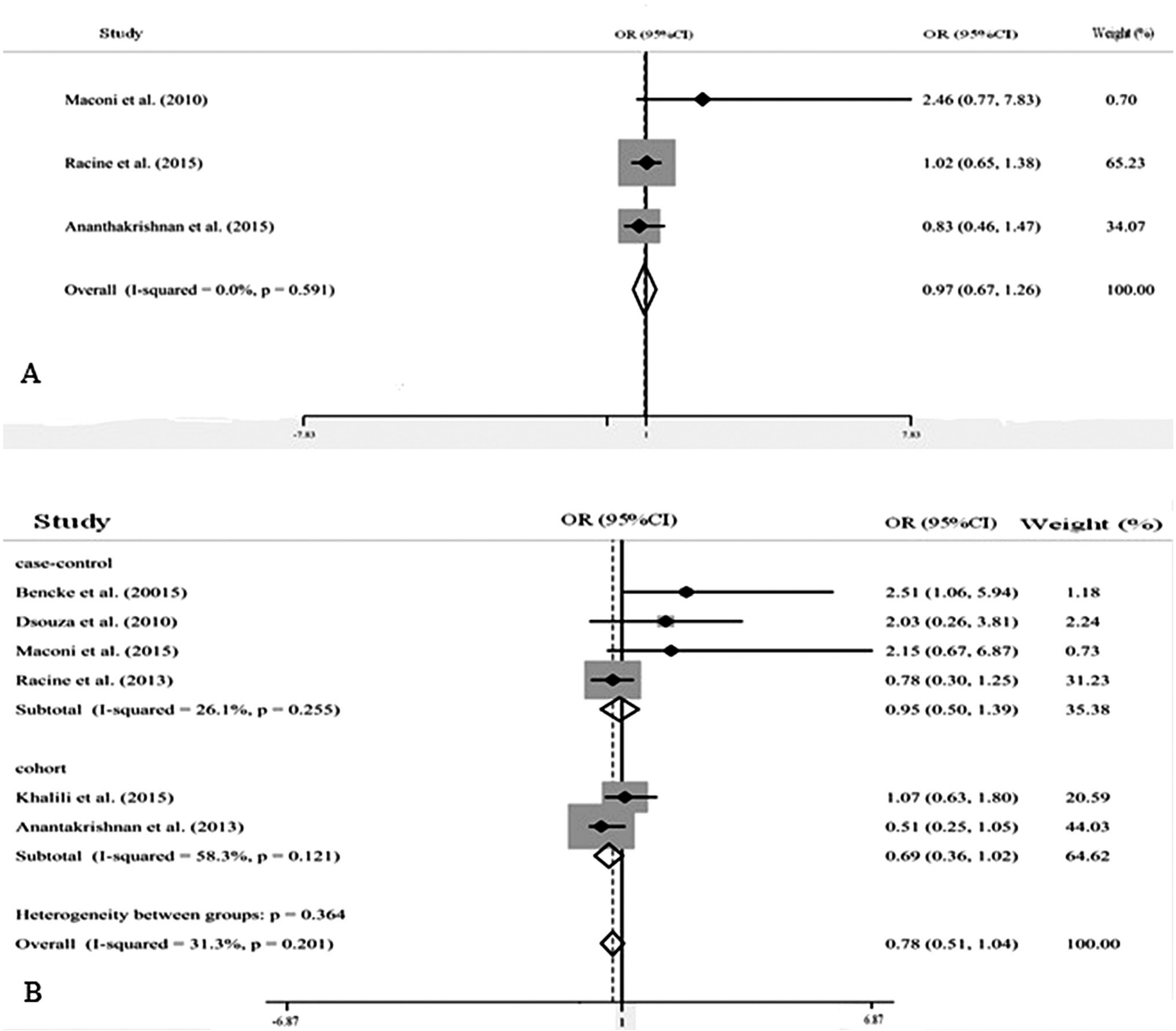

Figure 4. Forest plot of the highest compared with the lowest categories of intake of the Western/unhealthy dietary patterns and ulcerative colitis risk (A) and the highest compared with the lowest categories of intake of the Western/unhealthy dietary patterns and Crohn's disease risk (B).

reported that high intake of vegetables, fruits, and fiber was associated with a reduced risk of CD among Canadian children [13]. Also, in the study of Halfvarson et al. reduction in cancer risk with increased fruit consumption was observed [39]. These results show that the protective effect of the healthy dietary pattern on the risk of CD might be linked to its higher content of minerals, vitamins, polyphenols, antioxidants, and dietary fiber [40]. Polyphenols, some minerals and vitamins, and butyrate derived from fermentation of fibers in the colon have antioxidant and anti-inflammatory properties through activation of Nrf-2 and inhibition of NFκB activity, respectively and could decrease the risk of CD [25, 41, 42]. Carotenoids found in fruits and vegetables reduce the secretion of proinflammatory cytokines from macrophages, which play a crucial role in acute and chronic inflammation in IBD [43]. Moreover, CD is associated with changes in the gut microbiota composition characterized by reducing diversity, increased proportions of *Proteobacteria*, and reduced proportion of *Firmicutes* and *Actinobacteria* [44]. A healthy dietary pattern might also reduce the risk of CD via its effects on the composition of the intestinal microbiota, promotion of the epithelial cell resistance to injury and by suppression of the inflammatory responses to luminal antigens [10].

The unhealthy dietary pattern in included studies was characterized by high intake of red meat and processed meat, refined grains, sugary desserts, soft drinks, high-fat foods, processed food, fried food items, snacks, and fast foods, was not associated with an increased risk of CD and UC in our meta-analysis. Although, the present meta-analysis did not show any relationship between the two major dietary patterns (healthy and western) and the risk of UC, the results need to be interpreted with caution. For evaluation of investigated patterns, there were limited published studies. Due to the relatively small sample size, the findings are not able to come to a firm conclusion. Moreover, most of the included studies involved only Europeans and North Americans and data regarding other ethnicities such as Africans and Asians were not found, and thus the results of the current study could not be expanded to all populations. Therefore, additional studies are necessary to evaluate the effect of healthy and unhealthy dietary patterns on IBD risk in different ethnicities, particularly in Africans and Asians.

To the best of our knowledge, the present study is the first meta-analysis on the associations of dietary patterns with the risk of CD and UC. However, some limitations of our study need to be discussed. First, due to the limited available published articles, the number of studies included in this meta-analysis is relatively small. Second, potential language bias existed because only articles published in the English language were included. Third, most of included studies were adjusted for a wide spectrum of dietary and lifestyle confounders, however, we could not ignore the likelihood that other confounders are relevant to the observed results. Fourth, most included studies were case-control in term of study design, which are more prone to selection bias and recall, particularly dietary recall bias, than a cohort design. Finally, there was substantial heterogeneity across studies that investigated healthy dietary patterns and CD and UC risk. This heterogeneity is expected because the studies included participants who differed by various characteristics, such as gender and age. However, given the insufficient data, subgroup analyses were impossible to be performed to find the source of heterogeneity.

In summary, the available data provide evidence of an inverse association between healthy dietary patterns and the risk of the CD but this correlation was not seen for UC. The results of this meta-analysis indicate that dietary patterns influence the development of CD, and emphasize the significance of good dietary practices for the prevention of CD. Overall, the findings of studies support this hypothesis that intake of healthy dietary pattern, rather than unhealthy dietary pattern, can lower the risk of IBD. Due to the paucity of the existing data, additional large, well-designed studies, in particular prospective cohort studies, are warranted to allow a more definitive conclusion.

References

1. Shah, N.D., Parian, A.M., Mullin, G.E., & Limketkai, B.N. (2015) Oral diets and nutrition support for inflammatory bowel disease what is the evidence? Nutr Clin Pract. 30, 462–473.
2. Devkota, S., & Chang, E.B. (2015) Interactions between diet, bile acid metabolism, gut microbiota, and inflammatory bowel diseases. Dig Dis. 33, 351–356.
3. Wang, L., Wang, Z., Hu, J., Fan, R., Zhou, J., & Zhong, J. (2014) Polymorphisms of the vitamin D receptor gene and the risk of inflammatory bowel disease: a meta-analysis. Genet Mol Res. 13, 2598–2610.
4. Herfarth, H.H., Martin, C.F., Sandler, R.S., Kappelman, M.D., & Long, M.D. (2014) Prevalence of a gluten free diet and improvement of clinical symptoms in patients with inflammatory bowel diseases. Inflamm Bowel Dis. 20, 1194.
5. Leone, V.A., Cham, C.M., & Chang, E.B. (2014) Diet, gut microbes, and genetics in immune function: can we leverage our current knowledge to achieve better outcomes in inflammatory bowel diseases? Curr Opin Immunol 31, 16–23.
6. Ananthakrishnan, A.N. (2015) Environmental risk factors for inflammatory bowel diseases: a review. Dig Dis Sci. 60, 290–298.
7. Legaki, E., & Gazouli, M. (2016) Influence of environmental factors in the development of inflammatory bowel diseases. World J Gastrointest Pharmacol Ther. 7, 112.
8. Ng, S.C. (2014) Epidemiology of inflammatory bowel disease: focus on Asia. Best Pract Res Clin Gastroenterol. 28, 363–372.
9. Kakodkar, S., Farooqui, A.J., Mikolaitis, S.L., & Mutlu, E.A. (2015) The specific carbohydrate diet for inflammatory bowel disease: A case series. J Acad Nutr Diet. 115, 1226–1232.
10. Lee, D., Albenberg, L., Compher, C., Baldassano, R., Piccoli, D., & Lewis, J.D., et al. (2015) Diet in the pathogenesis and treatment of inflammatory bowel diseases. Gastroenterology. 148, 1087–1106.
11. Russel, M.G., Engels, L.G., Muris, J.W., Limonard, C.B., Volovics, A., & Brummer, R.-J.M., et al. (1998) "Modern life" in the epidemiology of inflammatory bowel disease: a case-control study with special emphasis on nutritional factors. Eur J Gastroenterol Hepatol. 10, 243–250.
12. Pieczynska, J., Prescha, A., Ilow, R., Kokorska, J., Neubauer, K., & Smereka, A., et al. (2009) Dietary habits of patients with inflammatory bowel disease-a short report. Polish Journal of Food and Nutrition Sciences. 59.
13. Amre, D.K., Dsouza, S., Morgan, K., Seidman, G., Lambrette, P., & Grimard, G., et al. (2007) Imbalances in dietary consumption of fatty acids, vegetables, and fruits are associated with risk for Crohn's disease in children. Am J Gastroenterol. 102, 2016–2025.
14. Tsiountsioura, M., Wong, J.E., Upton, J., McIntyre, K., Dimakou, D., & Buchanan, E., et al. (2014) Detailed assessment of nutritional status and eating patterns in children with gastrointestinal diseases attending an outpatients clinic and contemporary healthy controls. Eur J Clin Nutr. 68.
15. Gentschew, L., & Ferguson, L.R. (2012) Role of nutrition and microbiota in susceptibility to inflammatory bowel diseases. Mol Nutr Food Res. 56, 524–535.
16. Maconi, G., Ardizzone, S., Cucino, C., Bezzio, C., Russo, A.G., & Bianchi Porro, G. (2010) Pre-illness changes in dietary habits and diet as a risk factor for inflammatory bowel disease: a case-control study. World J Gastroenterol. 16, 4297–4304.
17. Gibson, P., & Shepherd, S. (2005) Personal view: food for thought – western lifestyle and susceptibility to Crohn's disease. The FODMAP hypothesis. Aliment Pharmacol Ther. 21, 1399–1409.
18. Jowett, S., Seal, C., Pearce, M., Phillips, E., Gregory, W., & Barton, J., et al. (2004) Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. Gut. 53, 1479–1484.
19. Jantchou, P., Morois, S., Clavel-Chapelon, F., Boutron-Ruault, M.-C., & Carbonnel, F. (2010) Animal protein intake and risk of

inflammatory bowel disease: The E3 N prospective study. Am J Gastroenterol. 105, 2195–2201.
20. Liu, X., Wu, Y., Li, F., & Zhang, D. (2015) Dietary fiber intake reduces risk of inflammatory bowel disease: result from a meta-analysis. Nutrition Research. 35, 753–758.
21. Lomer, M.C., Kodjabashia, K., Hutchinson, C., Greenfield, S. M., Thompson, R.P., & Powell, J.J. (2004) Intake of dietary iron is low in patients with Crohn's disease: a case-control study. Br J Nutr. 91, 141–148.
22. Sung, M.-K., & Park, M.-Y. (2013) Nutritional modulators of ulcerative colitis: clinical efficacies and mechanistic view. World J Gastroenterol. 19, 994–1004.
23. Hansen, T.S., Jess, T., Vind, I., Elkjaer, M., Nielsen, M.F., & Gamborg, M., et al. (2011) Environmental factors in inflammatory bowel disease: a case-control study based on a Danish inception cohort. J Crohns Colitis. 5, 577–584.
24. Moura, F.A., de Andrade, K.Q., dos Santos, J.C.F., Araújo, O.R.P., & Goulart, M.O.F. (2015) Antioxidant therapy for treatment of inflammatory bowel disease: Does it work? Redox Biol 6, 617–639.
25. Chapman-Kiddell, C.A., Davies, P.S., Gillen, L., & Radford-Smith, G.L. (2010) Role of diet in the development of inflammatory bowel disease. Inflamm Bowel Dis. 16, 137–151.
26. Melkonian, S.C., Daniel, C.R., Hildebrandt, M.A., Tannir, N.M., Ye, Y., & Chow, W.-H., et al. (2014) Joint association of genome-wide association study – identified susceptibility loci and dietary patterns in risk of renal cell carcinoma among non-Hispanic whites. Am J Epidemiol. 180, 499–507.
27. Liu, X., Wang, X., Lin, S., Yuan, J., & Yu, I. (2014) Dietary patterns and oesophageal squamous cell carcinoma: a systematic review and meta-analysis. Br J Cancer. 110, 2785–2795.
28. Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., & Rennie, D., et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA. 283, 2008–2012.
29. Wells, G., Shea, B., O'connell, D., Peterson, J., Welch, V., & Losos, M., et al. (2000) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses.
30. Higgins, J., & Thompson, S.G. (2002) Quantifying heterogeneity in a meta-analysis. Stat Med. 21, 1539–1558.
31. Wei, B., Xu, Z., Ruan, J., Zhu, M., Jin, K., & Zhou, D., et al. (2012) MTHFR 677C > T and 1298A > C polymorphisms and male infertility risk: a meta-analysis. Mol Biol Rep. 39, 1997–2002.
32. Begg, C.B., & Mazumdar, M. (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics. 1088–1101.
33. Egger, M., Smith, G.D., Schneider, M., & Minder, C. (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ. 315, 629–634.
34. Bencke, A., Roberts, D., & Batey, R. (2002). Western refined dietary pattern is associated with risk of Inflammatory Bowel Disease.
35. D'Souza, S., Levy, E., Mack, D., Israel, D., Lambrette, P., & Ghadirian, P., et al. (2008) Dietary patterns and risk for Crohn's disease in children. Inflamm Bowel Dis. 14, 367–373.
36. Hamed, K., Ashwin, A., Jenny, S., Leslie, H., James, R., & Andrew, C. (2014) P-028 dietary patterns and risk of Crohn's disease and ulcerative colitis. Inflamm Bowel Dis. 20, S36–S37.
37. Ananthakrishnan, A.N., Khalili, H., Song, M., Higuchi, L.M., Richter, J.M., & Nimptsch, K., et al. (2015) High school diet and risk of Crohn's disease and ulcerative colitis. Inflamm Bowel Dis. 21, 2311–2319.
38. Racine, A., Carbonnel, F., Chan, S.S., Hart, A.R., Bueno-de-Mesquita, H.B., & Oldenburg, B., et al. (2016) Dietary patterns and risk of inflammatory bowel disease in Europe: Results from the EPIC study. Inflamm Bowel Dis. 22, 345–354.
39. Halfvarson, J., Jess, T., Magnuson, A., Montgomery, S.M., Orholm, M., & Tysk, C., et al. (2006) Environmental factors in inflammatory bowel disease: a co-twin control study of a Swedish-Danish twin population. Inflamm Bowel Dis. 12, 925–933.
40. Rosman-Urbach, M., Niv, Y., Birk, Y., Morgenstern, S., & Schwartz, B. (2006) Relationship between nutritional habits adopted by ulcerative colitis relevant to cancer development patients at clinical remission stages and molecular-genetic parameters. Br J Nutr. 95, 188–195.
41. Kaulmann, A., & Bohn, T. (2016) Bioactivity of polyphenols: preventive and adjuvant strategies toward reducing inflammatory bowel diseases – promises, perspectives, and pitfalls. Oxid Med Cell Longev. 2016.
42. Wedlake, L., Slack, N., Andreyev, H.J.N., & Whelan, K. (2014) Fiber in the treatment and maintenance of inflammatory bowel disease: a systematic review of randomized controlled trials. Inflamm Bowel Dis. 20, 576–586.
43. Zhang, H., Fan, M., & Paliyath, G. (2011) Effects of carotenoids and retinoids on immune-mediated chronic inflammation in inflammatory bowel disease. Functional Foods, Nutraceuticals, and Degenerative Disease Prevention. 213–233.
44. Sartor, R.B. (2008) Microbial influences in inflammatory bowel diseases. Gastroenterology. 134, 577–594.

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Conflict of interest
The authors declare that there are no conflicts of interest.

Publication ethics
This study is a systematic review and meta analysis which was performed based on the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.

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