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The Mediterranean Diet and Inflammatory Bowel Disease: A Comprehensive Systematic Review and Meta-Analysis of Efficacy

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Data Availability Statement

All data supporting the findings of this study are included within the manuscript and its supplementary files.

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Ethics Approval Statement

This study did not require ethics approval as it does not involve human participants or animals.

Patient Consent Statement

Patient consent was not applicable to this study.

Permission to Reproduce Material from Other Sources

No copyrighted material or proprietary data requiring permission was included in this study.

Clinical Trial Registration

This study is not a clinical trial and does not require registration.

Introduction:

Environmental and dietary factors significantly influence the development and progression of inflammatory bowel disease (IBD). The Mediterranean diet (MD), characterized by high consumption of fruits, vegetables, healthy fats, and lean proteins and low intake of processed foods and sugars, is frequently recommended as an adjunctive therapy. The American Gastroenterological Association includes MD in its guidelines for managing Crohn's disease (CD); however, the recommendation strength is low due to the DINE-CD trial, which did not demonstrate superiority of MD compared to the specific carbohydrate diet.

This meta-analysis aims to enhance current data by evaluating existing research on dietary management in ulcerative colitis (UC) and assessing the effectiveness of MD in achieving symptomatic remission or improvement in IBD patients compared to other dietary interventions.

Methods:

Following Cochrane and PRISMA guidelines We compared the MD to alternative dietary interventions in IBD patients Randomized controlled trials (RCTs) were identified through comprehensive database searches up to October 2024. Data were analyzed using RevMan Web, employing a random-effects model.

Results:

Four RCTs involving a total of 339 IBD patients were included in this analysis. Among these, 167 patients (including those with UC and CD) received the Mediterranean diet, while 172 followed non-Mediterranean diets (NMD). The MD was associated with a statistically significant improvement in clinical remission compared to NMD (RR 1.18, $P = 0.02$). When compared specifically to a regular diet, MD significantly reduced both CRP levels (MD -2.66, $P < 0.00001$) and fecal calprotectin (MD -229.46, $P = 0.008$). Specifically, within the UC population, MD significantly decreased CRP and fecal calprotectin levels.

Discussion:

Our findings suggest the Mediterranean diet provides significant benefits in managing IBD, particularly for UC patients, demonstrated by notable reductions in CRP and fecal calprotectin levels. However, similar benefits in patients with CD remain less clear despite previous evidence of symptomatic improvement.

Although MD shows superiority over regular diets, its relative advantage compared to other specialized diets, such as the specific carbohydrate diet (SCD), remains uncertain. Variability among studies and adherence challenges complicate these comparisons. Future research should aim to identify specific patient subgroups most likely to benefit from MD and strategies to enhance adherence.

Keywords: Inflammatory Bowel Diseases; Mediterranean Diet; Ulcerative Colitis; Crohn Disease; Remission, Induced; C-Reactive Protein; Calprotectin

Introduction:

Inflammatory Bowel Disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract characterized by a relapsing-remitting course and a heterogeneous clinical presentation. IBD is further divided into two related but distinct disorders, Ulcerative Colitis (UC) and Crohn's Disease (CD). A smaller cohort of unclassified IBD (IBD-U) has also been described [1,2]. There are an estimated 4.9 million people with IBD worldwide, contributing to 1.62 million disability-adjusted life-years (DALYs) and 0.9 million years of life lost (YLLs) in 2019 [3]. Clinical features include abdominal pain, chronic diarrhea, rectal bleeding, and weight loss, often accompanied by systemic signs of inflammation, causing significant morbidity and complications [2,4]. The inflammation is thought to result from a complex interaction between genetic and environmental factors, leading to dysfunction of the mucosal immune system along with defects in the barrier function of the intestinal epithelium [5].

Various environmental factors are thought to play a role in the pathophysiology, clinical course, and management of IBD. These include tobacco smoking, NSAID use, antibiotic use, breastfeeding, and diet [6]. There is a higher prevalence of IBD in high-income countries and the westernized world [3]. The western diet, high in fats and sugars and low in vegetables and fruits, is thought to contribute to the development of IBD [7] and has been linked to changes in the gut microbiome [8]. Another study investigating the increasing incidence of IBD in the East also suggests the role of westernization of diet as one of the probable causes [9]. Diets that have been studied in inflammatory bowel disease include, but are not limited to, the Mediterranean diet (MD), specific carbohydrate diet (SCD), low-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (low-FODMAP diet), gluten-free diet, and Crohn's Disease Exclusive Diet (CDED) [10,11].

The MD appears to be the preferred diet in regions bordering the Mediterranean Sea, including countries such as Greece, Italy, and Spain. It is rich in plant-based foods such as fruits, vegetables, whole grains, and monounsaturated fatty acids such as olive oil, while limiting intake of red meat and processed food [12]. There is a long list of reported health benefits such as lower rates of cardiovascular mortality, metabolic syndrome, cancer, and weight loss [11,12]. The AGA recommends MD as part of the management approach to IBD [11]. In the excellent work by Lewis et al., who conducted a prospective interventional study on patients with Crohn's disease, the MD resulted in improvement of multiple disease-related parameters, including symptomatic remission, decreased fecal calprotectin, and CRP levels [13,14]. Other studies have shown a decrease in inflammatory markers, normalization of gut microbiome [15], decreased disease severity measured through disease activity indices and CRP levels, and increased quality of life in CD [16]. Results from two large prospective cohort studies independently showed that the MD was associated with a significantly lower risk of later-onset CD but not UC [17]. Additionally, work by Lewis et al. indicated that the SCD and MD improve quality of life, with the added benefit that MD is easier to adhere to and may be more sustainable [14].

While individual studies suggest that MD has the potential to decrease disease activity and severity, the available evidence is limited on the role of diet in established IBD [18], especially ulcerative colitis.

This meta-analysis aims to contribute to the existing evidence by systematically evaluating the effectiveness of the MD in achieving symptomatic remission or improvement in IBD patients compared to other dietary interventions and also reviewing specific effects in UC.

Materials and Methods

This meta-analysis was conducted following the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [19]. The study was prospectively registered with PROSPERO (CRD42025642145). The data used were from existing datasets and literature; as such, the Institutional Review Board waived the requirement for ethical approval.

Information Sources

A comprehensive literature search was performed across multiple databases: the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Embase (Elsevier), and Web of Science. The search spanned from each database's inception up to November 2024. Only randomized controlled trials (RCTs) were considered. The search used a combination of medical subject headings (MeSH) and free-text terms, including “Inflammatory Bowel Disease,” “Mediterranean Diet,” “Crohn Disease,” “Ulcerative Colitis,” and “Diet.” The detailed search strategy is in Supplemental File 1.

Eligibility Criteria

Studies were included if they met the following criteria: they were RCTs; involved any age of diagnosis with UC or CD; compared patients on the Mediterranean diet (intervention group) to those consuming any other diet (control group); and reported at least one of the following outcomes—clinical remission and change in inflammatory markers including CRP and fecal calprotectin from baseline.

Observational studies (prospective or retrospective cohort studies, case-control studies), case reports, case series, single-arm studies, guidelines, duplicate publications, animal studies, unpublished non-peer-reviewed articles, and review articles were excluded. In instances where multiple studies reported overlapping data, the most comprehensive and recent publication was included to avoid duplication.

Selection Process

All articles were imported into Mendeley (version 1.19.8), and duplicates were removed. Two independent reviewers (MS and SKK) screened the titles and abstracts for relevance. Full-text articles of potentially eligible studies were then assessed against the inclusion criteria. Any discrepancies between the reviewers were resolved through discussion or, if necessary, consultation with a third reviewer (FH). The study selection process is illustrated in a PRISMA flowchart (Figure 1).

Data Collection Process

Data extraction was conducted independently by two reviewers (MS and FH), and data were compiled into a predefined Excel template. Extracted information included study characteristics (author, year of publication, country, study design), participant characteristics (age, sex, baseline inflammatory markers, disease severity scoring, use of steroids and biologics), details of the interventions, outcomes measured, and duration of follow-up. Any disagreements were resolved by consensus or by involving a third reviewer (WD) to ensure accuracy and completeness.

Outcomes

The primary outcome of this study was clinical remission, defined using validated scoring systems reported in the included studies. These included the Pediatric Crohn's Disease Activity Index (PCDAI), Pediatric Ulcerative Colitis Activity Index (PUCAI), Simple Clinical Colitis

Activity Index (SCCAI), Partial Mayo Score (PMS), and Short Crohn's Disease Activity Index (sCDAI). Secondary outcomes included changes in inflammatory markers, specifically serum CRP levels and fecal calprotectin (FC) levels from baseline.

Risk of Bias and Quality of Evidence Assessment

The quality of included studies was assessed with the Cochrane Risk of Bias 2.0 tool for RCTs [20]. Each study was independently evaluated by two reviewers (MS and FH) across domains such as selection bias, performance bias, detection bias, attrition bias, and reporting bias. Judgments were categorized as low risk, some concerns, or high risk of bias. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess the certainty of evidence for each outcome [21]. Detailed assessments are in Supplemental File 1.

Statistical Analysis

Statistical analyses were conducted using RevMan Web (The Cochrane Collaboration, Copenhagen, Denmark) with a random-effects model. Dichotomous outcomes were expressed as risk ratios (RRs) with 95% confidence intervals (CIs); continuous outcomes were reported as mean differences with 95% CIs. A p-value <0.05 was considered statistically significant. Subgroup analyses were performed based on IBD type (UC vs. CD) and type of diet.

Heterogeneity among studies was assessed with the Chi-square test ($p<0.10$) and quantified with the Higgins I^2 statistic. I^2 values of 25%, 50%, and 75% represented low, moderate, and high heterogeneity, respectively. For substantial heterogeneity ($I^2>50\%$), sources were explored through subgroup and sensitivity analyses.

Publication bias was evaluated with funnel plots for outcomes reported in more than 10 studies. All analyses adhered to guidelines provided in the Cochrane Handbook and recommendations by Rücker et al. [22,23]. Continuous and dichotomous data were combined following appropriate formulas.

Results:

Literature Search Results and Patients

Out of a total of 1231 records identified from databases such as PubMed, Embase, Cochrane, and Web of Science, along with additional records identified through grey literature and citation searching, 4 studies were included in the final meta-analysis after a rigorous screening process as outlined in the PRISMA flow chart (Figure 1). The final analysis comprised data from four studies [14,24-26], with patient numbers varying across different outcomes.

Baseline Characteristics:

All included RCTs were conducted in the United States and Egypt and had a total of 339 participants: 167 subjects in the Mediterranean Diet (MD) group and 172 in the control group. Age of participants was 31.2 ± 18.9 years, with mean follow-up durations varying between 10 to 12 weeks across the studies. The baseline characteristics of the patients included in the studies are detailed in Tables 1-3.

Quality Assessment & Publication Bias:

The included studies demonstrated excellent methodological rigor, as assessed by the Cochrane Risk of Bias (RoB 2.0) tool. The randomized controlled trials indicated possible bias across some RoB domains. A detailed account is provided in Figure 2.

Primary Outcome:

1. Clinical Remission

When compared to the non-Mediterranean diet (NMD) group, the MD group showed a statistically significant improvement in clinical remission across 4 studies with 342 participants (Risk Ratio [RR] 1.18 [95% CI: 1.03 to 1.36], P = 0.02). Heterogeneity was minimal (I^2 = 0%) (Figure 3). The GRADE assessment indicated moderate-quality evidence due to inconsistencies across studies.

Secondary Outcomes:

1. Change in Serum CRP

Baseline serum CRP levels did not show a statistically significant difference between groups (Mean Difference [MD]: -1.21 [95% CI: -4.64 to 2.22], P = 0.49). Heterogeneity was minimal (I^2 = 0%). However, at the end of the study, the Mediterranean diet group showed a statistically significant reduction in serum CRP compared to the NMD group (MD: -2.60 [95% CI: -3.56 to -1.65], P < 0.0001). Heterogeneity was minimal (I^2 = 0%) (Figure 3). The GRADE assessment indicated moderate-quality evidence due to inconsistencies across studies.

2. Change in Fecal Calprotectin

There was no statistically significant difference in baseline fecal calprotectin between groups (MD: -23.39 [95% CI: -88.88 to 42.10], P = 0.48). Heterogeneity was minimal (I^2 = 0%). By the end of the study, a greater reduction in fecal calprotectin was observed in the Mediterranean diet group, but this difference was not statistically significant (MD: -128.66 [95% CI: -357.45 to 100.14], P = 0.27). Heterogeneity was high (I^2 = 83%) (Figure 4). The GRADE assessment indicated moderate-quality evidence due to inconsistencies across studies.

Subgroup Analyses based on Disease Type

1. Ulcerative Colitis (UC)

Among patients with UC, there was no statistically significant improvement in clinical remission (RR: 1.15 [95% CI: 0.94 to 1.41], P = 0.78). Heterogeneity was minimal (I^2 = 0%). The GRADE assessment indicated moderate-quality evidence due to suspected publication bias. By the end of the study, a statistically significant difference was observed in serum CRP in the MD group compared to the NMD group (MD: -2.66 [95% CI: -3.65 to -1.66], P < 0.0001). Heterogeneity was minimal (I^2 = 0%). The GRADE assessment indicated moderate-quality evidence due to suspected publication bias. Fecal calprotectin levels in this subgroup showed a statistically significant difference in the MD group compared to the NMD group (MD: -229.46 [95% CI: -399.71 to -59.21], P = 0.008). Heterogeneity was substantial (I^2 = 53%) (Figure 4,5). The GRADE assessment indicated moderate-quality evidence due to likely publication bias.

2. Crohn's Disease (CD)

Comparing MD to NMD among patients with CD, there was no statistically significant improvement in clinical remission (RR: 1.20 [95% CI: 0.99 to 1.46], P = 0.06). Heterogeneity was minimal (I^2 = 0%) (Figure 5). The GRADE assessment indicated moderate-quality evidence due to possible publication bias.

Subgroup Analyses based on Comparator groups

1. Specific Carbohydrate Diet (SCD)

When the MD group was compared to the SCD group, there was no statistically significant improvement in clinical remission (RR: 0.97 [95% CI: 0.69 to 1.34], P = 0.84). This is similar to reported results in the DINE-CD study. Heterogeneity was minimal (I^2 = 0%). The GRADE assessment indicated moderate-quality evidence due to suspected publication bias. Similarly,

changes in IBDQ scores did not show a statistically significant difference (MD: -1.05 [95% CI: -2.82 to 0.71], P = 0.24). Heterogeneity was minimal (I^2 = 0%) (Figure 5). The GRADE assessment indicated moderate-quality evidence due to possible publication bias.

2. Regular Diet

When MD was compared to regular diet, there was a statistically significant improvement in clinical remission (RR: 1.18 [95% CI: 1.01 to 1.38], P = 0.03). Heterogeneity was minimal (I^2 = 0%). The GRADE assessment indicated high-quality evidence as there were no major concerns regarding bias or inconsistency. By the end of the study, serum CRP (MD: -2.66 [95% CI: -3.65 to -1.66], P < 0.00001) and fecal calprotectin (MD: -229.46 [95% CI: -399.71 to -59.21], P = 0.008) demonstrated statistically significant differences between groups. Heterogeneity was minimal (I^2 = 0%) for serum CRP; the GRADE assessment indicated moderate-quality evidence due to possible publication bias. Heterogeneity was substantial (I^2 = 53%) for fecal calprotectin (Figure 6); the GRADE assessment indicated moderate-quality evidence due to possible publication bias.

Discussion:

Our meta-analysis suggests that the MD demonstrates statistically significant symptomatic improvement in the IBD population (UC and CD combined). However, when analyzed separately, neither UC nor CD patients exhibited statistically significant improvements in symptomatic remission. Notably, statistically significant reductions in inflammatory biomarkers, including serum CRP and fecal calprotectin, were observed in UC patients on MD. Statistically significant reductions in inflammatory markers were observed when MD was compared to a regular diet but not when MD was compared to SCD.

Inflammatory markers such as fecal calprotectin and CRP are widely recognized tools for monitoring responses to dietary interventions in IBD patients. A systematic review by Barros et al. confirmed that dietary interventions influence these biomarkers [27]. The AGA acknowledges fecal calprotectin as a key marker for tracking CD disease activity. Results from the CALM study indicated that integrating biomarker-based evaluations resulted in superior disease control compared to symptom-based monitoring alone [28,29]. Wagner et al. found that normalization of fecal calprotectin strongly predicted full treatment response [30].

Several studies have explored dietary interventions to modulate disease activity in IBD, including MD efficacy [23,31]. Comeche et al. found that adherence to MD improved quality of life and reduced fecal calprotectin levels [30]. MD's anti-inflammatory potential is often attributed to its rich antioxidants and anti-inflammatory compounds, enhancing gut health and modulating immune response, consequently decreasing inflammation markers such as CRP [32,33]. Khavandegar et al. described MD positively influencing gut microbiome composition [34]. Similarly, Haskey et al. demonstrated MD's association with reduced intestinal inflammation and favorable gut microbiome modulation [23].

Despite these promising findings, the lack of significant clinical improvement in CD patients observed in our meta-analysis suggests that the MD's anti-inflammatory effects may not be universally robust across all IBD populations. This raises questions as to whether its benefits are more disease phenotype-specific or dependent on individual patient characteristics.

The differences between our findings and prior studies could be attributed to several factors. These include differences in study design, patient populations, and patient adherence to dietary interventions, all of which may influence outcomes. Patient compliance with dietary interventions can be influenced by cultural, economic, and individual preferences. High

adherence to the MD has been associated with improved quality of life and reduced disease activity in observational studies [35]. However, adherence was not consistently reported or measured across the studies included in this meta-analysis. The study by Lewis et al. reported high adherence only during the first six weeks when meals were provided to participants. Similarly, in the study by Chen et al., despite conservative measures to standardize control (e.g., preparing meals in hospital kitchens), persistent adherence issues remained [14,26].

Additionally, variations in the definition of the MD across studies likely contribute to inconsistent results. For example, the degree to which ultra-processed foods and sugars were restricted varied, and populations accustomed to Western dietary patterns might find adherence challenging, potentially affecting outcomes.

Another consideration is the duration of the intervention. Many studies reporting positive outcomes emphasized long-term adherence to the MD [36], whereas our meta-analysis included studies with shorter follow-up periods. Given that dietary changes may exert gradual effects on gut microbiota composition and systemic inflammation, the lack of significant benefits in shorter-term studies may not fully capture the MD's potential. Moreover, differences in control diets across studies make direct comparisons difficult. Some trials compared the MD to highly processed Western diets [23], while others used more nutritionally balanced alternatives [24].

There are several limitations to our meta-analysis. No standardized Western diet control groups were used consistently across studies. The lack of a consistently defined comparator diet makes it difficult to determine whether dietary interventions like the MD or SCD are equally effective or ineffective relative to typical Western dietary patterns [37]. Furthermore, the study by El Amrousy et al., which was included, focused on a pediatric population. Their results may not be generalizable to adult patients with IBD due to differences in disease progression, dietary needs,

and metabolic responses [25]. Sample sizes across studies were relatively small, and the inclusion of CD and UC patients in the same analysis could introduce some heterogeneity in responses to dietary interventions. We attempted to mitigate these limitations by analyzing data specific to UC and CD separately.

Despite these limitations, the MD remains a promising option within a holistic approach to IBD management, particularly for UC patients. Its potential to enhance quality of life, reduce inflammation in specific subgroups, and promote sustainable eating habits positions it as a beneficial dietary strategy. Compared to restrictive diets such as the SCD, the MD's less restrictive nature may enhance its practicality and acceptability among patients.

CONCLUSION

The MD shows promise as part of a comprehensive IBD management plan. This meta-analysis indicates that its role in patients with CD regarding clinical remission remains unclear and requires additional studies.

Future larger, controlled randomized trials with standardized comparator diet protocols are still required to better understand the role of the MD and identify specific patient populations most likely to benefit. Tailoring dietary interventions to individual patient profiles, disease characteristics, and lifestyle factors will be critical for optimizing outcomes and effectively integrating dietary strategies into clinical practice.

Significance Statement:

This systematic review and meta-analysis evaluates the efficacy of the Mediterranean diet in achieving clinical remission and reducing inflammation markers in patients with inflammatory bowel disease (IBD). By synthesizing evidence from randomized controlled trials, the findings

provide robust support for dietary intervention, particularly highlighting its potential benefits in ulcerative colitis. These insights offer clinicians and patients evidence-based guidance to enhance dietary management strategies, improve clinical outcomes, and potentially reduce disease-associated inflammation in IBD.

References:

1. Zhang YZ, Li YY. Inflammatory bowel disease: pathogenesis. *World J Gastroenterol.* 2014;20(1):91-99. doi:10.3748/wjg.v20.i1.91
2. Flynn S, Eisenstein S. Inflammatory bowel disease presentation and diagnosis. *Surg Clin North Am.* 2019;99(6):1051-1062. doi:10.1016/j.suc.2019.08.001
3. Wang R, Li Z, Liu S, Zhang D. Global, regional and national burden of inflammatory bowel disease in 204 countries and territories from 1990 to 2019: a systematic analysis. *BMJ Open.* 2023;13(3):e065186. doi:10.1136/bmjopen-2022-065186
4. Faye AS, Colombel JF. Aging and IBD: a new challenge for clinicians and researchers. *Inflamm Bowel Dis.* 2022;28(1):126-132. doi:10.1093/ibd/izab039
5. Podolsky DK. Inflammatory bowel disease. *N Engl J Med.* 2002;347(6):417-429. doi:10.1056/NEJMra020831
6. Ananthakrishnan AN, Bernstein CN, Iliopoulos D, *et al.* Environmental triggers in IBD: a review of progress and evidence. *Nat Rev Gastroenterol Hepatol.* 2018;15(1):39-49. doi:10.1038/nrgastro.2017.136
7. Gentschew L, Ferguson LR. Role of nutrition and microbiota in susceptibility to inflammatory bowel diseases. *Mol Nutr Food Res.* 2012;56(4):524-535. doi:10.1002/mnfr.201100630

8. David LA, Maurice CF, Carmody RN, *et al.* Diet rapidly and reproducibly alters the human gut microbiome. *Nature.* 2014;505(7484):559-563. doi:10.1038/nature12820
9. Mak WY, Zhao M, Ng SC, Burisch J. The epidemiology of inflammatory bowel disease: East meets West. *J Gastroenterol Hepatol.* 2020;35(3):380-389. doi:10.1111/jgh.14872
10. Hashash JG, Elkins J, Lewis JD, Binion DG. AGA clinical practice update on diet and nutritional therapies in patients with IBD: expert review. *Gastroenterology.* 2024;166(3):521-532. doi:10.1053/j.gastro.2023.11.303
11. Herfarth HH, Martin CF, Sandler RS, Kappelman MD, Long MD. Prevalence of a gluten-free diet and symptom improvement in IBD. *Inflamm Bowel Dis.* 2014;20(7):1194-1197. doi:10.1097/MIB.0000000000000077
12. Jiang Y, Jarr K, Layton C, *et al.* Therapeutic implications of diet in IBD and related immune-mediated diseases. *Nutrients.* 2021;13(3):890. doi:10.3390/nu13030890
13. Chicco F, Magrì S, Cingolani A, *et al.* Multidimensional impact of Mediterranean diet on IBD patients. *Inflamm Bowel Dis.* 2021;27(1):1-9. doi:10.1093/ibd/izaa097
14. Lewis JD, Sandler RS, Brotherton C, *et al.* A randomized trial comparing the specific carbohydrate diet with a Mediterranean diet in adults with Crohn's disease. *Gastroenterology.* 2021;161(3):837-852.e9. doi:10.1053/j.gastro.2021.05.047
15. Marlow G, Ellett S, Ferguson IR, *et al.* Transcriptomics of a Mediterranean-inspired diet in Crohn's disease. *Hum Genomics.* 2013;7(1):24. doi:10.1186/1479-7364-7-24
16. Papada E, Amerikanou C, Forbes A, Kaliora AC. Adherence to the Mediterranean diet in Crohn's disease. *Eur J Nutr.* 2020;59(3):1115-1121. doi:10.1007/s00394-019-01972-z

17. Khalili H, Håkansson N, Chan SS, *et al.* Adherence to a Mediterranean diet is associated with lower risk of later-onset Crohn's disease. *Gut.* 2020;69(9):1637-1644. doi:10.1136/gutjnl-2019-319505
18. Ananthakrishnan AN, Gerasimidis K, Ho SM, *et al.* Challenges in IBD research 2024: environmental triggers. *Inflamm Bowel Dis.* 2024;30(Suppl 2):S19-S29. doi:10.1093/ibd/izae085
19. Higgins JPT, Thomas J, Chandler J, *et al*, eds. *Cochrane Handbook for Systematic Reviews of Interventions.* Version 6.5. Cochrane; 2024.
20. Sterne JAC, Savović J, Page MJ, *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* 2019;366:l4898. doi:10.1136/bmj.l4898
21. GRADEpro GDT [software]. McMaster University; 2025. Available from: https://gradepro.org
22. Rücker G, Cates CJ, Schwarzer G. Methods for including information from multi-arm trials in pairwise meta-analysis. *Res Synth Methods.* 2017;8(4):392-403. doi:10.1002/jrsm.1259
23. Rücker G, Carpenter JR, Schwarzer G. Detecting and adjusting for small-study effects in meta-analysis. *Biom J.* 2011;53(2):351-368. doi:10.1002/bimj.201000151
24. Haskey N, Estaki M, Ye J, *et al.* A Mediterranean diet pattern improves intestinal inflammation with bacteriome reshaping in ulcerative colitis: a randomised controlled trial. *J Crohns Colitis.* 2023;17(10):1569-1578. doi:10.1093/ecco-jcc/jjad073
25. El Amrousy D, Elashry H, Salamah A, *et al.* Adherence to the Mediterranean diet improved clinical scores and inflammatory markers in children with active IBD: a randomised trial. *J Inflamm Res.* 2022;15:2075-2086. doi:10.2147/JIR.S349502

26. Chen SY, Gray B, Williams KM, *et al.* Specific carbohydrate diet versus Mediterranean diet in adult UC: a randomised controlled-feeding trial. *Gastroenterology.* 2024;166(5 Suppl):S1087-S1088. doi:10.1016/S0016-5085(24)02969-X
27. Barros VJDS, Severo JS, Mendes PHM, *et al.* Dietary interventions and inflammatory biomarkers in IBD: a systematic review. *Nutrition.* 2021;91-92:111457. doi:10.1016/j.nut.2021.111457
28. Colombel JF, Panaccione R, Bossuyt P, *et al.* Tight-control management in Crohn's disease (CALM): a randomised trial. *Lancet.* 2017;390(10114):2779-2789. doi:10.1016/S0140-6736(17)32641-7
29. Ananthakrishnan AN, Adler J, Chachu KA, *et al.* AGA guideline on biomarkers for Crohn's disease management. *Gastroenterology.* 2023;165(6):1367-1399. doi:10.1053/j.gastro.2023.09.029
30. Wagner M, Peterson CG, Ridefelt P, Sangfelt P, Carlson M. Fecal inflammation markers as surrogates for treatment outcome in relapsing IBD. *World J Gastroenterol.* 2008;14(36):5584-5588. doi:10.3748/wjg.14.5584
31. Comeche JM, Gutierrez-Hervás A, Tuells J, *et al.* Predefined diets in IBD: systematic review and meta-analysis. *Nutrients.* 2021;13(1):52. doi:10.3390/nu13010052
32. Neale EP, Batterham MJ, Tapsell LC. Healthy dietary patterns reduce C-reactive protein: meta-analysis. *Nutr Res.* 2016;36(5):391-401. doi:10.1016/j.nutres.2016.02.009
33. Tsigalou C, Konstantinidis T, Paraschaki A, *et al.* Mediterranean diet as a tool to combat inflammation and chronic diseases. *Biomedicines.* 2020;8(7):201. doi:10.3390/biomedicines8070201

34. Khavandegar A, Heidarzadeh A, Angoorani P, *et al.* Adherence to the Mediterranean diet beneficially affects gut microbiota: systematic review. *BMC Med Genomics.* 2024;17(1):24. doi:10.1186/s12920-024-01861-3

35. Çelik K, Güveli H, Erzin Y, *et al.* Mediterranean diet adherence and IBD activity. *Turk J Gastroenterol.* 2023;34(7):714-719. doi:10.5152/tjg.2023.22193

36. Vrdoljak J, Vilović M, Živković PM, *et al.* Mediterranean diet adherence and attitudes in IBD. *Nutrients.* 2020;12(11):3429. doi:10.3390/nu12113429

37. Limketkai BN, Godoy-Brewer G, Parian AM, *et al.* Dietary interventions for IBD: updated systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2023;21(3):690-708.e12. doi:10.1016/j.cgh.2022.11.026

Tables:

Table 1 – Baseline characteristics of patients in the four included studies.

Author	**Study Year**	**Study Design**	**Country**	**Intervention**	**Control**	**Total No. of Patients**		**Females,n (%)**		**Mean age in years (SD)**		**BMI**	
						Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Amrousy et al.	2022	RCT	Egypt	Meditearranean diet	Standard diet	50	50	22 (44)	24 (48)	13.8 (2.6)	13.1 (1.9)	17.7 (2.4)	17.2 (2.6)
Haskey et al.	2023	RCT	Canada	Meditearranean diet	Standard diet	15	13	18 (65)	NR	47	NR	NR	NR
Lewis et al.	2022	RCT	United States	Meditearranean diet	Specific Carbohydrate diet	93	101	63 (68.5)	58 (58.6)	42.8 (20.5)	36.4 (14.3)	25.7 (4.9)	25.7 (4.9)
Chen et al.	2024	RCT	United States	Meditearranean diet	Specific Carbohydrate diet	9	8	4 (44.4)	5 (62.5)	44.2 (18.3)	38.4 (15.8)	28.9 (4.5)	25.1 (4.6)

Abbreviations: MD: Mediterranean Diet; NMD: Non-Mediterranean Diet; UC: Ulcerative Colitis; CD: Crohn's Disease; RCT: Randomized Controlled Trial; SD: Standard Deviation; IBD: Inflammatory Bowel Disease; CRP: C-reactive Protein; FC: Fecal Calprotectin; wks: Weeks.

Table 2 – Laboratory parameters and treatment details at baseline.

Author	**CRP mg/L**		**ESR mm/h**		**Fecal calprotectin(ug/g)**		**Follow up**	**Biologics**	**Steroids**	**Surgery**
	Intervention	Control	Intervention	Control	Intervention	Control				
Amrousy et al.	25.4 (18.1)	27.1 (20.5)	14.3 (12.1)	15.7 (10.9)	622.4 (411.5)	645.8 (435.7)	12 weeks	14/100	35/100	NR
Haskey et al.	1.4 (1.9)	0.93 (0.8)	NR	NR	44.1 (66.6)	50.7 (77.2)	12 weeks	Yes but number not reported	NR	NR
Lewis et al.	5.9 (12.2)	6.1 (7.6)	NR	NR	203.3 (484.5)	115.9 (156)	12 weeks	108/191	25/191	64/191
Chen et al.	NR	NR	NR	NR	NR	NR	10 weeks	8/17	14/17	0/17

Abbreviations: CRP: C-reactive Protein; FC: Fecal Calprotectin; MD: Mediterranean Diet; NMD: Non-Mediterranean Diet; SD: Standard Deviation; mg/L: Milligrams per Liter; µg/g: Micrograms per Gram.

Table 3 – Inclusion criteria for each included study.

Author	**Inclusion Criteria**
Amrousy et al.	One hundred consecutive IBD patients aged 12–18 years old were included.. This study included patients with CD or UC who had mild or moderate disease activity, as measured by a PCDAI score of 10–45 or a PUCAI score of 10 to 60. Before the trial, no changes in IBD medication could be made for at least one monthwith immunosuppressive medicines and two months with biologics.
Haskey et al.	Adult participants [18–65 years] diagnosedwith mild-moderate UC in remission [Partial Mayo score 0–2] were recruited through outpatient gastroenterology clinics from April 2017 to September 2021. Included were those on a stable dose of UC therapy [no dosage adjustments for 2 months before starting the study for participants prescribed oral 5-aminosalicylates, thiopurines, or methotrexate or if taking biologics [infliximab, adalimumab], for 3 months before starting the study.
Lewis et al.	Adult patients (age >18 years) with CD established by usual endoscopic, histologic and radiologic criteria and with mild to moderate symptoms defined as a short Crohn's

	Disease Activity Index (sCDAI) score >175 and <400 were potentially eligible for inclusion.
Chen et al.	Adult patients (18-75 years old) with mild to moderate UC defined by a partial Mayo Clinic score between two to six AND either endoscopic subscore of one to two or a fecal calprotectin > 150 mcg/g were randomly assigned by a 1:1 ratio to either consume the SCD or MeD diets for six weeks, with a four-week post-completion follow-up.

Abbreviations: MD: Mediterranean Diet; NMD: Non-Mediterranean Diet; UC: Ulcerative Colitis; CD: Crohn's Disease; IBD: Inflammatory Bowel Disease; SCD: Specific Carbohydrate Diet; RCT: Randomized Controlled Trial; PUCAI: Pediatric Ulcerative Colitis Activity Index; PCDAI: Pediatric Crohn's Disease Activity Index; SCCAI: Simple Clinical Colitis Activity Index; PMS: Partial Mayo Score; sCDAI: Short Crohn's Disease Activity Index.

Figure Legends

Figure 1. PRISMA flow chart of literature search and study selection.

Figure 2. Risk-of-bias summary (RoB 2.0) for included RCTs.

Figure 3. Forest plot of clinical remission and change in CRP (baseline and end-of-study) comparing MD versus non-MD.

Figure 4. Forest plot of FC change (baseline and end-of-study) comparing MD versus non-MD; subgroup analysis for UC (remission and CRP).

Figure 5. Subgroup analyses: (a) FC change in UC; (b) remission in CD; (c) remission and IBDQ change comparing MD versus SCD.

Figure 6. Subgroup analyses comparing MD versus regular diet for remission, end-of-study CRP, and FC.

Figure 1

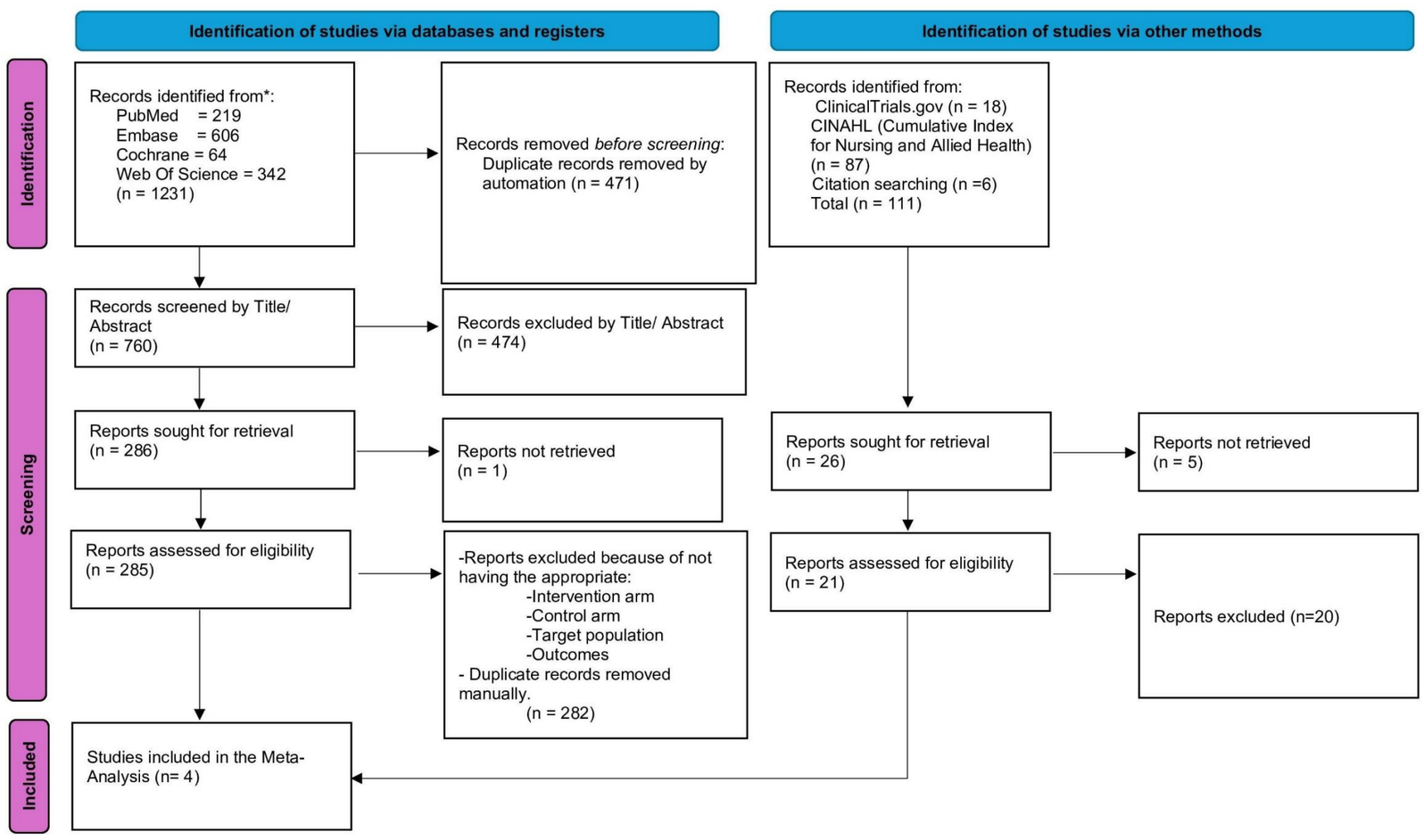


Figure 2

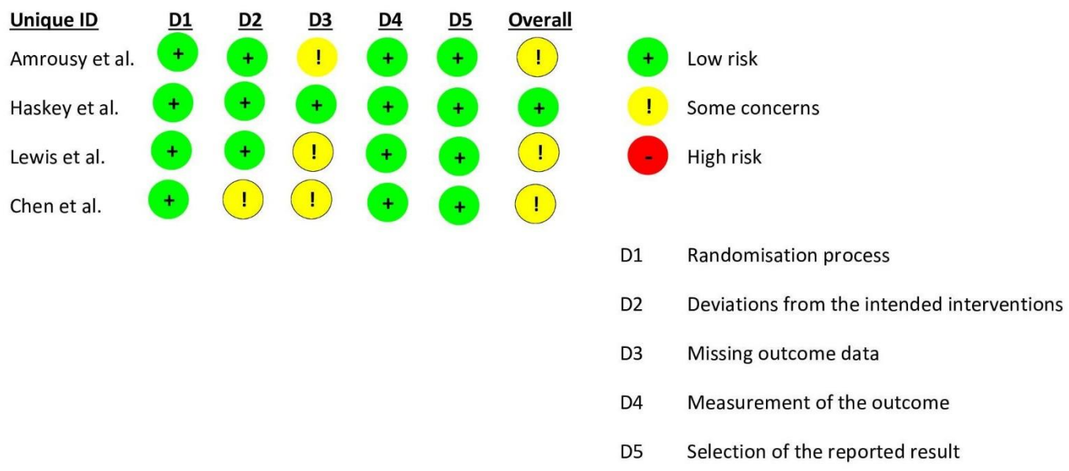
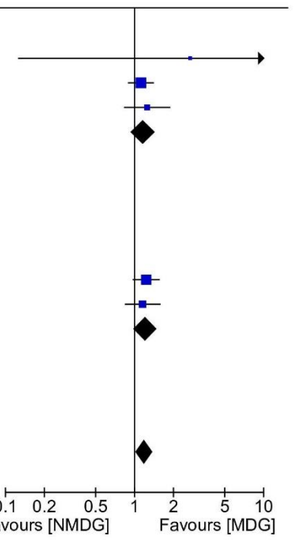


Figure 3

Analysis 1.1: Clinical Remission

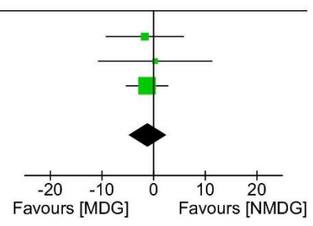
Study or Subgroup	Mediterranean Diet Group Events	Total	Non- Mediterranean Diet Group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Ulcerative Colitis						
Chen et al	1	9	0	8	0.2%	2.70 [0.13 , 58.24]
El Amrousy et al (UC Cohort)	22	24	18	22	36.2%	1.12 [0.89 , 1.41]
Haskey et al	13	15	9	13	11.3%	1.25 [0.83 , 1.89]
Subtotal (Wald [a])		**48**		**43**	**47.7%**	**1.15 [0.94 , 1.41]**
Total events:	36		27			
Test for overall effect: Z = 1.40 (P = 0.16)						
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.51, df = 2 (P = 0.78); I² = 0%						
1.1.2 Crohn's Disease						
El Amrousy et al (CD Cohort)	24	26	21	28	33.2%	1.23 [0.97 , 1.57]
Lewis et al	45	96	41	101	19.1%	1.15 [0.84 , 1.59]
Subtotal (Wald [a])		**122**		**129**	**52.3%**	**1.20 [0.99 , 1.46]**
Total events:	69		62			
Test for overall effect: Z = 1.88 (P = 0.06)						
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%						
Total (Wald [a])		**170**		**172**	**100.0%**	**1.18 [1.03 , 1.36]**
Total events:	105		89			
Test for overall effect: Z = 2.33 (P = 0.02)						
Test for subgroup differences: Chi² = 0.08, df = 1 (P = 0.77), I² = 0%						
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.69, df = 4 (P = 0.95); I² = 0%						



Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 1.2: Serum CRP (Baseline)

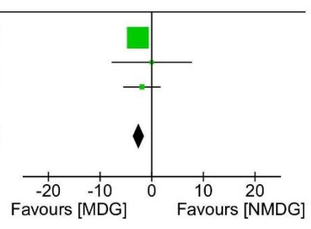
Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	25.4	18.1	50	27.1	20.5	50	20.5%	-1.70 [-9.28 , 5.88]
Haskey et al	9.3	17.564512	11	9	5.854283	9	9.6%	0.30 [-10.76 , 11.36]
Lewis et al	11.7	7.2	28	12.97	9.68	37	69.9%	-1.27 [-5.37 , 2.83]
Total (Wald [a])			**89**			**96**	**100.0%**	**-1.21 [-4.64 , 2.22]**
Test for overall effect: Z = 0.69 (P = 0.49)								
Test for subgroup differences: Not applicable								
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.09, df = 2 (P = 0.96); I² = 0%								



Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 1.3: Serum CRP (At the end of the study)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	3.1	0.9	50	5.8	3.5	50	91.4%	-2.70 [-3.70 , -1.70]
Haskey et al	7	6.847183	11	7	10.147423	9	1.5%	0.00 [-7.77 , 7.77]
Lewis et al	10.67	4.78	28	12.58	9.76	37	7.0%	-1.91 [-5.52 , 1.70]
Total (Wald [a])			**89**			**96**	**100.0%**	**-2.60 [-3.56 , -1.65]**
Test for overall effect: Z = 5.33 (P < 0.00001)								
Test for subgroup differences: Not applicable								
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.61, df = 2 (P = 0.74); I² = 0%								



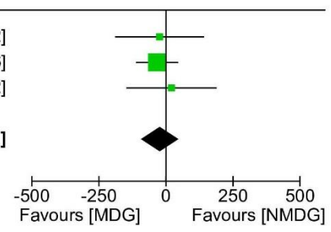
Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Figure 4

Analysis 1.4: Fecal Calprotectin (Baseline)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	622.4	411.5	50	645.8	435.7	50	15.5%	-23.40 [-189.52 , 142.72]
Haskey et al	33	73.494685	15	66	111.832289	10	69.3%	-33.00 [-111.66 , 45.66]
Lewis et al	465.72	260.79	13	445.11	222	23	15.1%	20.61 [-147.70 , 188.92]
Total (Wald [a])			**78**			**83**	**100.0%**	**-23.39 [-88.88 , 42.10]**

Test for overall effect: Z = 0.70 (P = 0.48)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.32, df = 2 (P = 0.85); I² = 0%

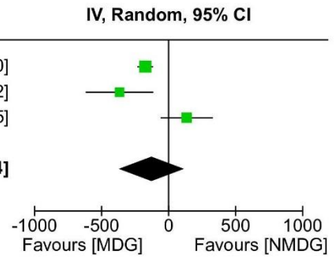


Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 1.5: Fecal Calprotectin (At the end of the study)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	221.5	88.5	50	395.7	194.4	50	40.4%	-174.20 [-233.40 , -115.00]
Haskey et al	27	69.216087	11	393	380.268182	9	27.6%	-366.00 [-617.78 , -114.22]
Lewis et al	478.18	311.45	13	343.65	236.36	23	31.9%	134.53 [-60.39 , 329.45]
Total (Wald [a])			**74**			**82**	**100.0%**	**-128.66 [-357.45 , 100.14]**

Test for overall effect: Z = 1.10 (P = 0.27)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 32791.29; Chi² = 11.56, df = 2 (P = 0.003); I² = 83%

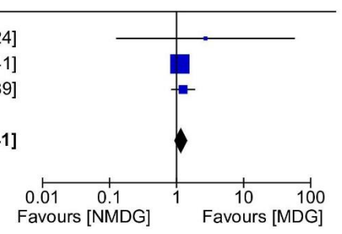


Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 2.1: Clinical Remission (UC Cohort)

Study or Subgroup	Mediterranean Diet Group Events	Total	Non- Mediterranean Diet Group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Chen et al	1	9	0	8	0.4%	2.70 [0.13 , 58.24]
El Amrousy et al (UC Cohort)	22	24	18	22	75.9%	1.12 [0.89 , 1.41]
Haskey et al	13	15	9	13	23.7%	1.25 [0.83 , 1.89]
Total (Wald [a])		**48**		**43**	**100.0%**	**1.15 [0.94 , 1.41]**
Total events:	36		27			

Test for overall effect: Z = 1.40 (P = 0.16)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.51, df = 2 (P = 0.78); I² = 0%

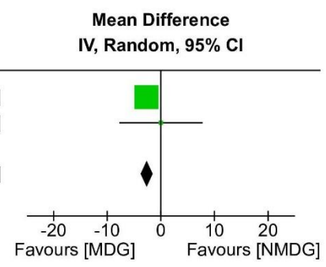


Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 2.2: Serum CRP (At the end of the study) (UC Cohort)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	3.1	0.9	50	5.8	3.5	50	98.4%	-2.70 [-3.70 , -1.70]
Haskey et al	7	6.847183	11	7	10.147423	9	1.6%	0.00 [-7.77 , 7.77]
Total (Wald [a])			**61**			**59**	**100.0%**	**-2.66 [-3.65 , -1.66]**

Test for overall effect: Z = 5.24 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.46, df = 1 (P = 0.50); I² = 0%

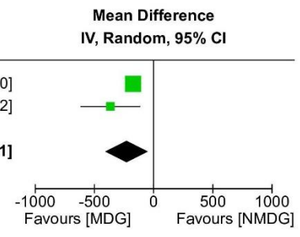


Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Figure 5

Analysis 2.3: Fecal Calprotectin (At the end of the study)(UC Cohort)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Non- Mediterranean Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	221.5	88.5	50	395.7	194.4	50	71.2%	-174.20 [-233.40 , -115.00]
Haskey et al	27	69.216087	11	393	380.268182	9	28.8%	-366.00 [-617.78 , -114.22]
Total (Wald [a])			**61**			**59**	**100.0%**	**-229.46 [-399.71 , -59.21]**



Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 9686.07; Chi² = 2.11, df = 1 (P = 0.15); I² = 53%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 3.1: Clinical Remission (CD Cohort)

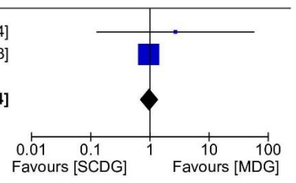
Study or Subgroup	Mediterranean Diet Group Events	Total	Non- Mediterranean Diet Group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Amrousy et al (CD Cohort)	24	26	21	28	63.5%	1.23 [0.97 , 1.57]
Lewis et al	45	96	41	101	36.5%	1.15 [0.84 , 1.59]
Total (Wald [a])		**122**		**129**	**100.0%**	**1.20 [0.99 , 1.46]**
Total events:	69		62			

Test for overall effect: Z = 1.88 (P = 0.06)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.10, df = 1 (P = 0.75); I² = 0%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 4.1: Clinical Remission

Study or Subgroup	Mediterranean Diet Group Events	Total	Specific Carbohydrate Diet Group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Chen et al	1	9	0	8	1.2%	2.70 [0.13 , 58.24]
Lewis et al	39	96	43	101	98.8%	0.95 [0.69 , 1.33]
Total (Wald [a])		**105**		**109**	**100.0%**	**0.97 [0.69 , 1.34]**
Total events:	40		43			

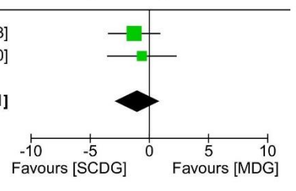


Test for overall effect: Z = 0.21 (P = 0.84)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.44, df = 1 (P = 0.51); I² = 0%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 4.2: Change in IBDQ Score

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Specific Carbohydrate Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chen et al	3.6	2.24	9	4.89	2.4	8	63.8%	-1.29 [-3.51 , 0.93]
Lewis et al	8.21	10.66	92	8.85	10.04	99	36.2%	-0.64 [-3.58 , 2.30]
Total (Wald [a])			**101**			**107**	**100.0%**	**-1.05 [-2.82 , 0.71]**



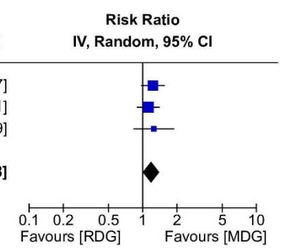
Test for overall effect: Z = 1.17 (P = 0.24)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.12, df = 1 (P = 0.73); I² = 0%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Figure 6

Analysis 4.3: Clinical Remission

Study or Subgroup	Mediterranean Diet Group Events	Total	Regular Diet Group Events	Total	Weight	Risk Ratio IV, Random, 95% CI
El Amrousy et al (CD Cohort)	24	26	21	28	41.2%	1.23 [0.97 , 1.57]
El Amrousy et al (UC Cohort)	22	24	18	22	44.8%	1.12 [0.89 , 1.41]
Haskey et al	13	15	9	13	14.0%	1.25 [0.83 , 1.89]
Total (Wald [a])		**65**		**63**	**100.0%**	**1.18 [1.01 , 1.38]**
Total events:	59		48			

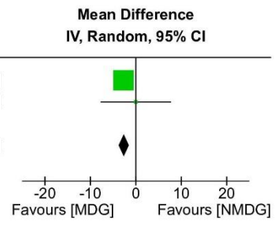


Test for overall effect: Z = 2.13 (P = 0.03)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.39, df = 2 (P = 0.82); I² = 0%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 4.4: Serum CRP (At the end of the study)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Regular Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	3.1	0.9	50	5.8	3.5	50	98.4%	-2.70 [-3.70 , -1.70]
Haskey et al	7	6.847183	11	7	10.147423	9	1.6%	0.00 [-7.77 , 7.77]
Total (Wald [a])			**61**			**59**	**100.0%**	**-2.66 [-3.65 , -1.66]**

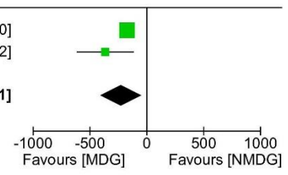


Test for overall effect: Z = 5.24 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 0.00; Chi² = 0.46, df = 1 (P = 0.50); I² = 0%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Analysis 4.5: Fecal Calprotectin (At the end of the study)

Study or Subgroup	Mediterranean Diet Group Mean	SD	Total	Regular Diet Group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
El Amrousy et al (UC Cohort)	221.5	88.5	50	395.7	194.4	50	71.2%	-174.20 [-233.40 , -115.00]
Haskey et al	27	69.216087	11	393	380.268182	9	28.8%	-366.00 [-617.78 , -114.22]
Total (Wald [a])			**61**			**59**	**100.0%**	**-229.46 [-399.71 , -59.21]**



Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL [b]) = 9686.07; Chi² = 2.11, df = 1 (P = 0.15); I² = 53%

Footnotes
[a] CI calculated by Wald-type method.
[b] Tau² calculated by DerSimonian and Laird method.

Supplemental File 1. Appendix

Legend:

- Table 1: Presents detailed search strategies used across MEDLINE (PubMed), Embase, Web of Science, and Cochrane Central, including Boolean terms for identifying relevant studies on the Mediterranean diet and inflammatory bowel disease.
- Table 2: Summarizes the GRADE certainty assessments for clinical remission, serum CRP, and fecal calprotectin across the total IBD population and in subgroup analyses of UC, CD, and comparator diets (specific carbohydrate and regular diet).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalFile1.docx