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NARRATIVE REVIEW

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Effectiveness of adalimumab in severe ulcerative colitis: A systematic review and a meta-analysis

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Abstract

Background and Aim: Ulcerative colitis (UC) causes chronic inflammation in the digestive tract, leading to abdominal pain and diarrhea. Adalimumab, a monoclonal antibody, is used to treat moderate to severe cases. This review and meta-analysis evaluated adalimumab's effectiveness for severe UC, considering patient age, disease duration, and gender.

Methods: This study was designed as a systematic review and a meta-analysis. Articles were searched in PubMed, Scopus, and Web of Science databases based on the keywords of adalimumab and UC. The titles, the abstracts, and, if necessary, the full texts of the articles were read. Then for further review, the full texts of the related articles were carefully examined, and the final articles were selected. Seventy-eight articles were searched based on the keywords, and after reading the articles, 50 articles were related to the topic of the dissertation. The 50 articles were evaluated critically based on a checklist prepared by a statistical consultant and four articles with a score above 70% were selected. In the four articles, the main indicators of the effectiveness of adalimumab, including mucosal healing, clinical remission, and clinical response, were evaluated.

Results: The effectiveness of adalimumab on the mucosal healing index was 75.40%, the clinical remission index was 70.79%, and the clinical response index was 83.02%, based on different doses and treatment durations in the study. In the four meta-analysis studies on adalimumab's effectiveness, 1613 UC patients were treated with varying doses over 8 and 52 weeks. Based on a meta-analysis over 8 and 52 weeks for treating moderate to severe UC, adalimumab's effectiveness was 70%–83%. The highest effectiveness, based on three main indices, was with a 40 mg dose over 52 weeks.

Conclusion: According to the meta-analysis, the effectiveness of adalimumab for treating moderate to severe UC over 8 and 52 weeks was 70%–83%. The highest effectiveness, based on three main indices, was with a 40 mg dose over 52 weeks.

KEYWORDS

abdominal pain, adalimumab, diarrhea, digestive, monoclonal antibody, ulcerative colitis

1 | INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) marked by persistent inflammation in the digestive tract, specifically affecting the innermost layer of the large intestine (colon) and rectum.[1,2] Common symptoms include abdominal pain and diarrhea. In severe cases, UC can be debilitating and even life-threatening.[3]

This condition arises from ongoing inflammation in the colon.[4] While there is no definitive cure for UC, various treatments can alleviate symptoms and extend periods of remission.[5,6] These treatments aim to manage the disease effectively and improve the patient's quality of life.[7]

UC typically manifests in two peak age ranges: from the second to fourth decades and from the seventh to ninth decades of life.[8] It is more frequently observed in urban areas and among populations with higher socioeconomic status, indicating that environmental and lifestyle factors may influence its development.[9]

IBDs do not adhere to Mendelian inheritance patterns.[10] However, genetic factors are implicated, as evidenced by racial differences, familial clustering, increased incidence in twins, chromosomal associations, genetic markers, and related syndromes.[11] First-degree relatives have an approximate 7% risk, with studies indicating a 4 to 20-fold increase in risk. A positive family history is also significant in younger patients.[12]

The pathophysiology of UC involves several critical components: gut dysbiosis, the formation of mucosal lesions, and dysregulated mucosal immunity marked by elevated levels of inflammatory mediators such as TNF-α (tumor necrosis factor-alpha), IL-6 (interleukin-6), and PGE2 (prostaglandin E2).[13] This framework is essential for studying UC's pathophysiological traits and offers new pathways for developing therapeutic strategies.[14]

Biologic drugs are another category of medications currently under investigation that show effectiveness in treating UC.[15] These drugs function by targeting inflammatory proteins that activate the immune system response, thereby reducing inflammation by blocking these receptors.[16] Their primary aim is to alleviate inflammation in the intestine.[17]

Adalimumab, a non-fusion monoclonal antibody, binds to the TNF-α receptor.[18] Elevated levels of TNF-α are associated with pathological pain and joint destruction in conditions such as psoriatic arthritis, rheumatoid arthritis, and ankylosing spondylitis. Adalimumab helps reduce symptoms of these diseases and prevents structural damage.[19] It also improves clinical manifestations of Crohn's disease and UC.[20]

Known for its ability to reduce inflammation and alleviate symptoms in individuals with inflammatory conditions, adalimumab targets TNF-α and mitigates its inflammatory effects, leading to reduced inflammation and symptom relief.[21] The result of most studies indicates that adalimumab has been effective in improving the initial stage of moderate to severe active UC patients.[22,23]

Our study aims to determine the effectiveness of adalimumab in treating severe UC.

2 | METHODS

The current study is a type of systematic review and meta-analysis conducted to investigate the effectiveness of the drug adalimumab in severe UC. The protocol used in this study was based on the recommended guidelines in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist. The search strategy (Supporting Information Methods) involved querying external databases, including PubMed, Scopus, and Web of Science, with carefully selected keywords, thereby ensuring the identification of relevant studies about the effectiveness of adalimumab in treating severe UC.

Search strategy:

The search strategy was constructed using the PICO framework, which consisted of:

- Population: Individuals diagnosed with severe UC.
- Intervention: Adalimumab, a biological drug.
- Comparison: Comparative studies involving adalimumab as the intervention or studies without a direct comparison group.
- Outcome: Main outcomes such as mucosal healing, clinical remission, and clinical response.

The following keywords were employed in combination to create the search strategy:

- Adalimumab: Targeting the specific intervention, the biological drug adalimumab.
- Ulcerative colitis: Focusing on the condition under investigation, severe UC.
- Detailed search strategy for PubMed, Scopus, and Web of Science databases to identify relevant studies for your systematic review and meta-analysis on the effectiveness of adalimumab in severe UC was as follows:
- PubMed search strategy:

((("Ulcerative Colitis"[MeSH Terms]) OR "ulcerative colitis") AND (("Adalimumab"[MeSH Terms]) OR "adalimumab")) AND ("Clinical Trial"[Publication Type] OR "Randomized Controlled Trial"[Publication Type]).

- Scopus search strategy

  TITLE-ABS-KEY("Ulcerative Colitis") AND TITLE-ABS-KEY ("Adalimumab") AND DOCTYPE(ar) AND (LIMIT-TO(SUBJAREA, "MEDI") OR LIMIT-TO(SUBJAREA, "PHAR")) AND (LIMIT-TO (DOCTYPE, "ar")).
- Web of Science search strategy

  TS = ("Ulcerative Colitis") AND TS = ("Adalimumab") AND DT = (Article) AND (LIMIT-TO(SUBJECT, "Medicine, General & Internal") OR LIMIT-TO(SUBJECT, "Pharmacology & Pharmacy")).
- In the search strategy above

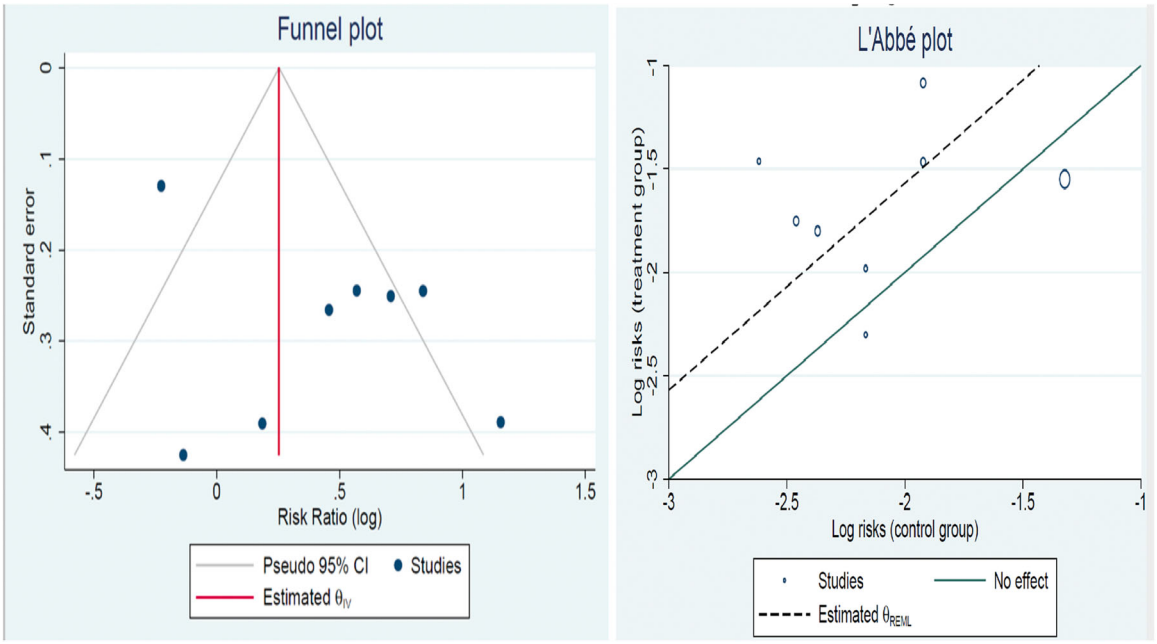

FIGURE 1 Funnel and L Abbe plot or heterogeneity measurement to check publication bias publication of included studies.

- "Ulcerative Colitis" and "Adalimumab" are the main keywords that focus on the condition and the intervention under study.
- "MeSH Terms" in PubMed and "TITLE-ABS-KEY" in Scopus and Web of Science are used to ensure that the search includes both controlled vocabulary terms and terms present in the title and abstract of the articles.
- "Clinical Trial" [Publication Type] and "Randomized Controlled Trial" [Publication Type] are used to narrow down the search to clinical trials, which are relevant to assessing the effectiveness of interventions.
- "DOCTYPE(ar)" in Scopus is used to limit the results to articles.
- LIMIT-TO(SUBJAREA, "MEDI") or LIMIT-TO(SUBJECT, "Medicine, General & Internal") in Scopus and Web of Science, respectively, is used to focus the search on medical-related articles.
- LIMIT-TO(SUBJAREA, "PHAR") in Scopus and LIMIT-TO (SUBJECT, "Pharmacology & Pharmacy") in Web of Science are used to further refine the focus on pharmacology and pharmacy-related articles.

The search commenced with the review of titles and abstracts of the identified articles. If necessary, the full texts of these articles were scrutinized. Then, for deeper investigation, the full texts of relevant articles were carefully examined, and the final articles were selected. In addition to electronic searches, the reference lists of the related articles were manually explored. Initially, 78 articles were searched based on the keywords, and after reading the articles, 50 articles were found to be related to the thesis topic. These articles were included in the next stage of the study for further examination.

2.1 | Data extraction

Data extraction was performed based on a checklist prepared by a statistical consultant (attachment1). The texts of 50 selected articles were studied, and they were critically evaluated according to the checklist questions. Articles scoring over 70% were selected, resulting in the selection of four articles.

In these four articles, the main effectiveness indicators of adalimumab, which include the following three indicators, were evaluated:

1. Mucosal healing
2. Clinical remission
3. Clinical response

Then, in these articles, secondary indicators such as patient gender, duration of illness from diagnosis, and use of other therapeutic drugs were evaluated.

Inclusion criteria:

Each original article in the PubMed, Scopus, and Web of Science databases should have the keywords "severe ulcerative colitis" and "adalimumab" present in the title or abstract based on the search strategy.

Exclusion criteria:

Case reports, letters to the editor, and other irrelevant articles were excluded from the study process. Observational studies were removed. Articles that were determined to be irrelevant to the research question based on the study's title and abstract were excluded from the analysis. Articles that did not meet the threshold score in the critical evaluation were also excluded from the study.

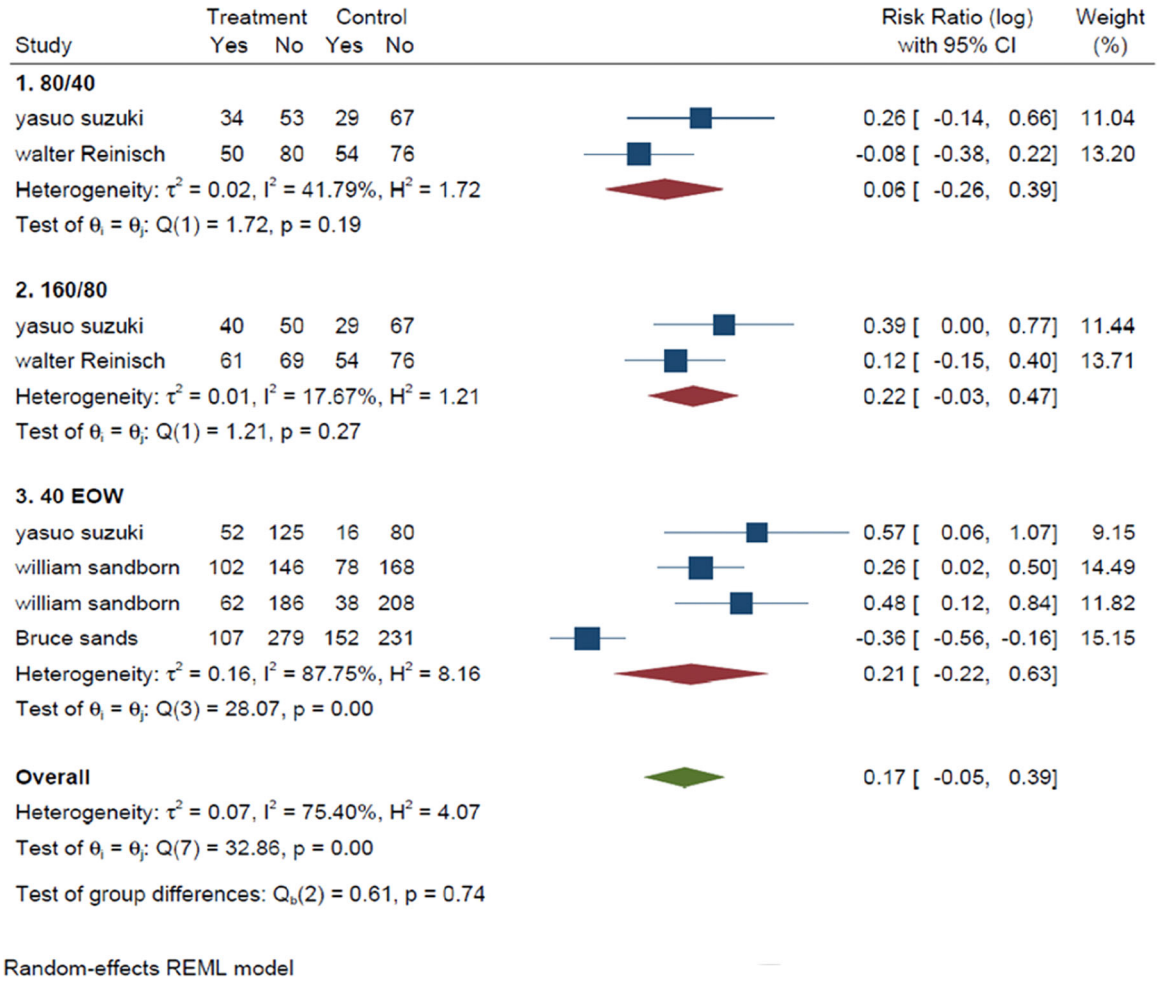

FIGURE 2 Mucosal healing according to different doses of adalimumab treatment.

2.2 | Data analysis method

The heterogeneity among studies was evaluated using Cochran's *Q* test. The degree and quantity of heterogeneity were determined using the I^2 statistic. Pooled estimates were calculated using random-effects and fixed-effects models and presented in Forest plots. All analyses were performed using Stata software version 14. Despite the limited quantitative variables encountered in the study, a dose–response meta-analysis was conducted. The recent analysis was performed using R software version 3.6.0. The best model was selected based on Egger and Begg's criteria.[24,25] Additionally, to assess publication bias, BIC and AIC tests were conducted, and a funnel plot was generated. Finally, to determine the effect of different factors such as gender, age, and drug dosage on heterogeneity, as well as to determine the direction of these effects (increase or decrease), meta-regression analysis was performed.

Lorestan University of Medical Sciences with the code IR.LUMS.REC.1400.195, the following points were considered research ethics and were observed.

3 | RESULTS

3.1 | Study process and selection

In the first stage of the study, which is a Systematic Review, all articles were searched using the main keywords, namely UC and adalimumab. In the second stage, after reviewing the articles, which amounted to 78, the relevant ones related to the thesis topic were selected and filtered, resulting in 50 articles. The 50 filtered articles underwent critical evaluation using a checklist, and those scoring over 70% on this checklist were chosen, totaling four articles.

3.2 | Navigating through indicators

In the four filtered articles, the three main effectiveness indicators, namely clinical remission, clinical response, and mucosal healing were examined. Articles that addressed all three main indicators were selected. All selected articles are Randomized Controlled Trials.

The selected articles, based on the three main indicators, consist of four articles. In these articles, secondary indicators such as age, gender, duration of adalimumab treatment, and duration of the disease were considered.

3.3 | Unveiling insights: Publication bias and heterogeneity

Given that the studies entered on both the left and right sides of the indicator are under examination and are almost symmetrical, the graphical result indicates the absence of publication bias (Figure 1).

3.4 | Diverse but coherent: Heterogeneity assessment

According to the results of the meta-analysis and quantitative assessment of heterogeneity (I^2) reported for the mucosal healing indicator in the group treated with adalimumab:

For the dose of 40/80 mg, RR = 1.06 with a confidence interval (CI) (1.47 and 0.77). Since the CI includes both a value below 1 and a value above 1, the point estimate (RR) is not statistically significant.

The value of heterogeneity quantity (I^2) is 41.79%, which is acceptable.

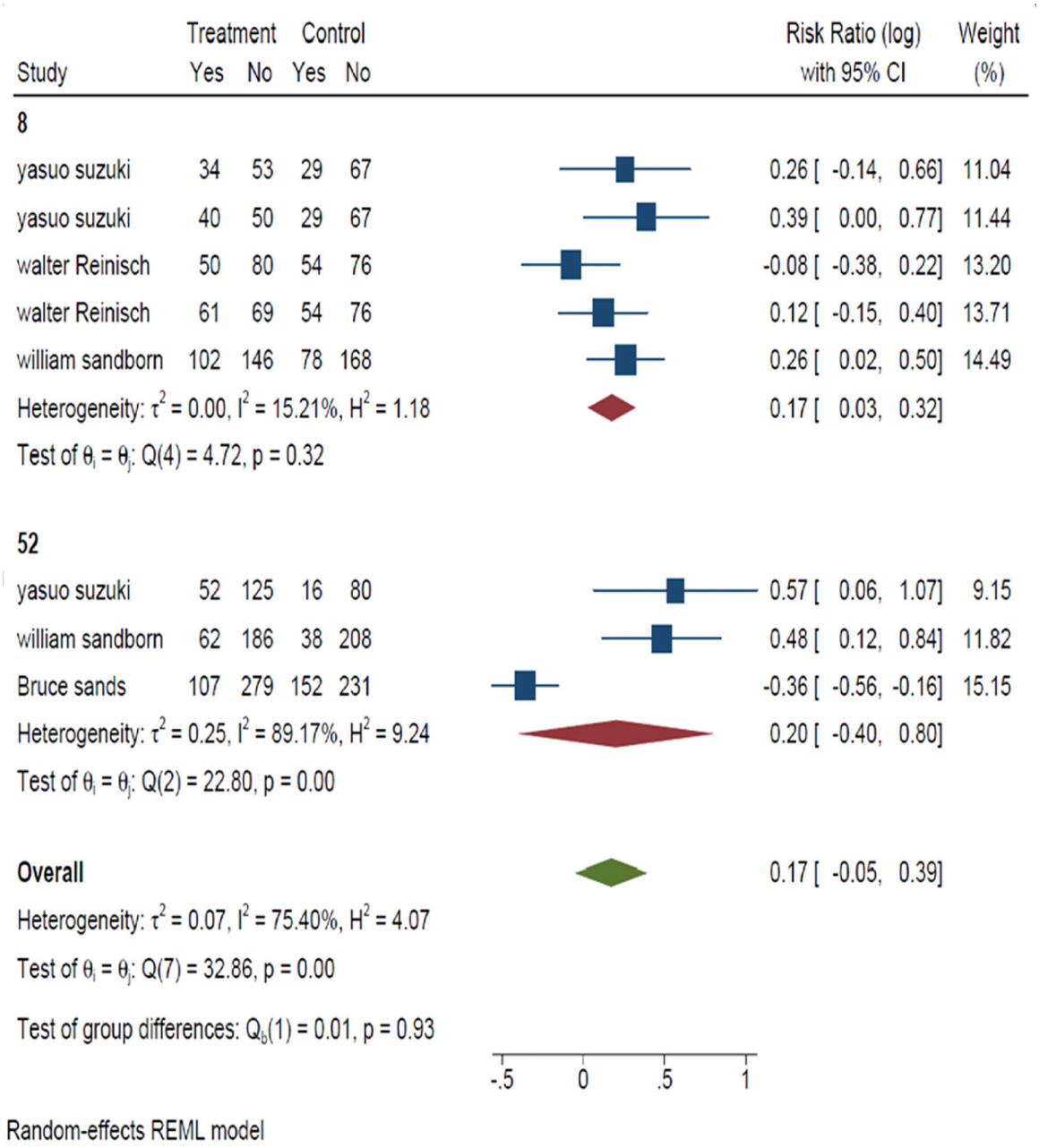

FIGURE 3 Mucosal healing according to different durations of adalimumab treatment.

3.5 | Zooming in on mucosal healing

According to the meta-analysis results for mucosal healing with adalimumab treatment:

For the 40/80 mg dose, RR = 1.06 (CI: 1.47–0.77), with non-significant statistical significance. Heterogeneity (I^2) is 41.79%, acceptable.

For the 80/160 mg dose, RR = 1.24 (CI: 1.59–0.97), also nonsignificant statistically. Heterogeneity (I^2) is 17.67%, acceptable.

For the 40 mg dose, RR = 1.23 (CI: 1.87–0.80), again non-significant statistically. Heterogeneity (I^2) is 87.75%, relatively unacceptable.

Overall, RR = 1.18 (CI: 1.47–0.95), with nonsignificant statistical significance. Heterogeneity (I^2) is 75.40%, relatively acceptable.

According to the meta-analysis results for mucosal healing with adalimumab treatment:

In the 8-week treatment period, RR = 1.18 (CI: 1.37–1.03). The CI above 1 indicates statistical significance. Heterogeneity quantity (I^2) is 15.12%, acceptable.

In the 52-week treatment period, RR = 1.22 (CI: 2.22–0.67). The CI spans both above and below 1, making the point estimate not statistically significant. Heterogeneity quantity (I^2) is 89.17%, relatively acceptable.

Overall, RR = 1.18 (CI: 1.47–0.95). The CI spans both above and below 1, rendering the point estimate not statistically significant. Heterogeneity quantity (I^2) is 75.40%, acceptable (Figures 2 and 3).

3.6 | A glimpse into clinical remission

According to the meta-analysis results and heterogeneity measurement (I^2) for the clinical remission indicator in the adalimumab-treated group:

For the 40/80 mg treatment dose, RR = 1.45 (CI: 2.23–0.94) is not statistically significant as the CI spans both above and below 1. Heterogeneity (I^2) is 0%, indicating acceptable consistency.

For the 80/160 mg treatment dose, RR = 1.50 (CI: 3.90–0.58) is not statistically significant as the CI spans both above and below 1. Heterogeneity (I^2) is 74.75%, relatively acceptable.

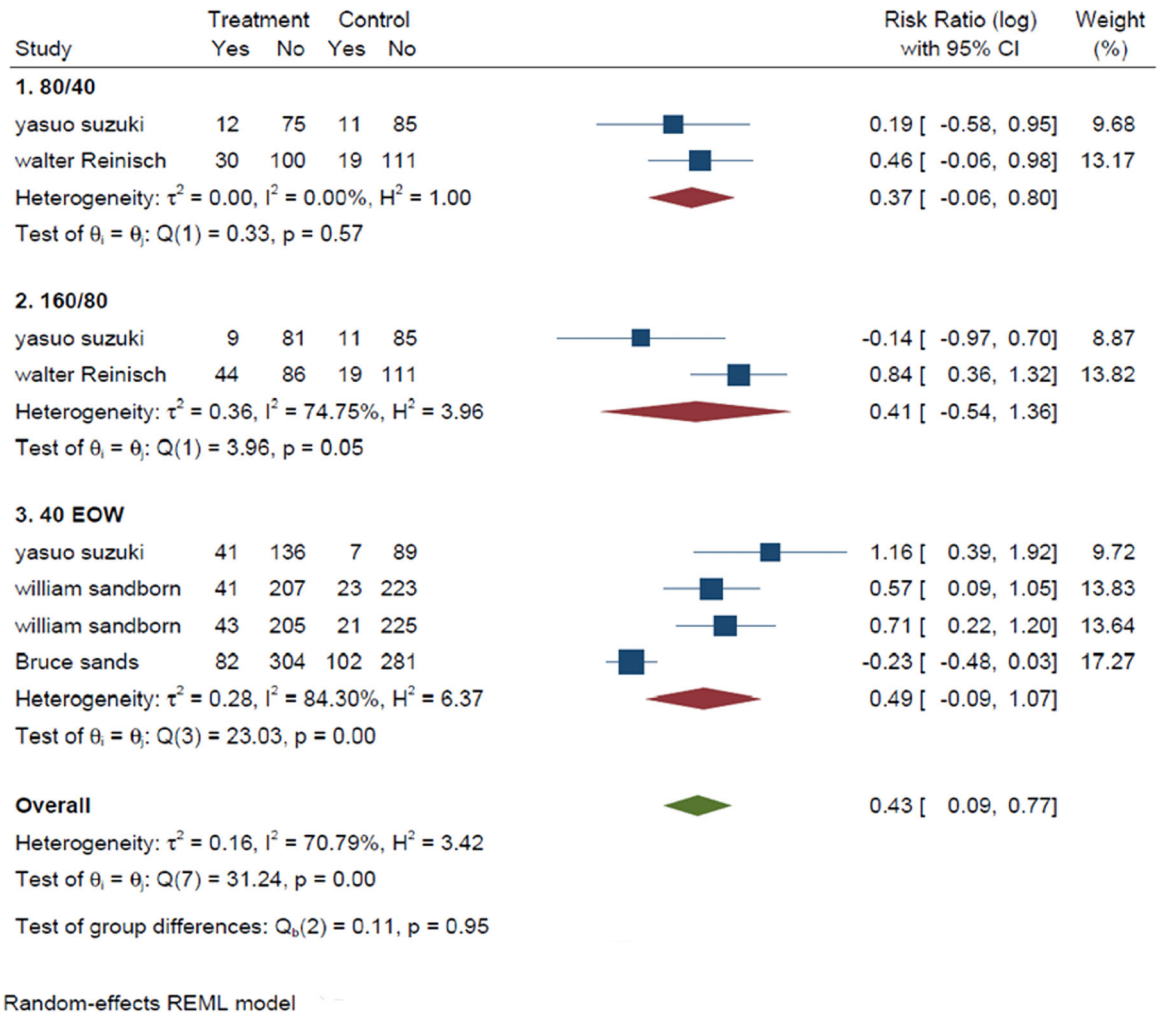

FIGURE 4 Remission rates according to different doses of adalimumab treatment.

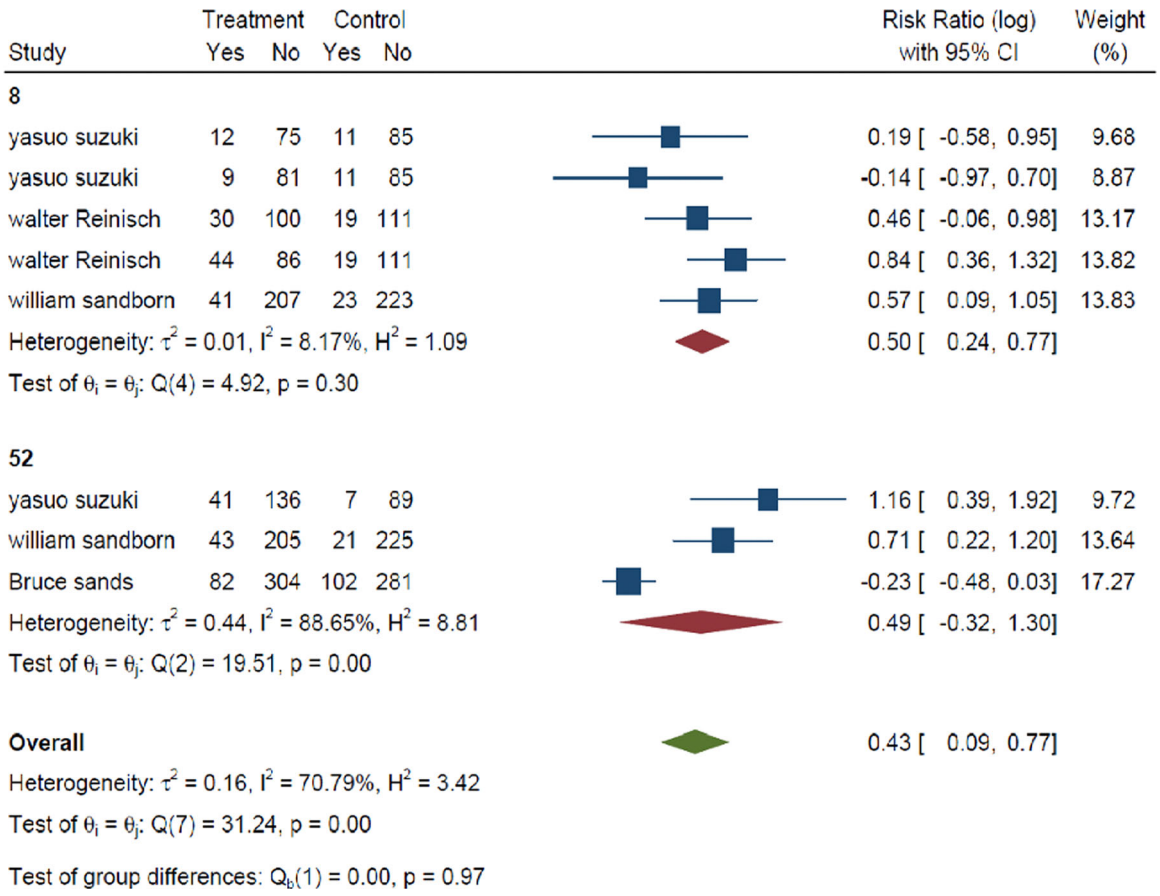

FIGURE 5 Remission rates according to different durations of adalimumab treatment.

For the 40 mg treatment dose, RR = 1.63 (CI: 2.91–0.91) is not statistically significant as the CI spans both above and below 1. Heterogeneity (I^2) is 84.30%, relatively acceptable.

Overall, RR = 1.53 (CI: 2.15–1.09), statistically significant as the CI includes values above 1. Heterogeneity (I^2) is 70.79%, which is acceptable.

According to the meta-analysis results for the clinical remission indicator in the adalimumab-treated group:

RR = 1.64 (CI: 2.15–1.27) at 8 weeks, statistically significant (CI above 1), with I^2 = 8.17%, acceptable heterogeneity.

RR = 1.63 (CI: 3.66–0.72) at 52 weeks, not statistically significant (CI spans both above and below 1), with I^2 = 88.65%, relatively acceptable heterogeneity.

Overall RR = 1.53 (CI: 2.15–1.09), statistically significant (CI above 1), with I^2 = 70.79%, acceptable heterogeneity (Figures 4 and 5).

3.7 | Diving into clinical response

In the meta-analysis of clinical response to adalimumab treatment:

For the 8 weeks, RR = 1.29 (CI: 1.46–1.15), statistically significant with 0% heterogeneity.

For the 52 weeks, RR = 1.22 (CI: 1.52–0.65), not statistically significant with 92.46% heterogeneity.

Overall, RR = 1.24 (CI: 1.55–0.99), not statistically significant with 83.02% heterogeneity.

In the analysis of clinical response to adalimumab treatment:

For the 8 weeks, RR = 1.29 (CI: 1.46–1.15), statistically significant with 0% heterogeneity.

For the 52 weeks, RR = 1.22 (CI: 1.52–0.65), not statistically significant with 92.46% heterogeneity.

Overall, RR = 1.24 (CI: 1.55–0.99), not statistically significant with 83.02% heterogeneity (Figures 6 and 7).

4 | DISCUSSION

Four articles were chosen based on achieving a critical evaluation score of over 70%. These selected articles, published between 2011 and 2019, were examined for both primary and secondary indicators. The study assessed the effectiveness of adalimumab across various therapeutic doses and treatment periods for different indicators. Results revealed that the mucosal healing indicator exhibited an effectiveness rate of 75.40%. The clinical remission indicator showed a 70.79% effectiveness rate, while the clinical response indicator revealed an effectiveness rate of 83.02%. These findings shed light on the efficacy of adalimumab across diverse treatment regimens, highlighting its potential in managing the conditions under investigation.

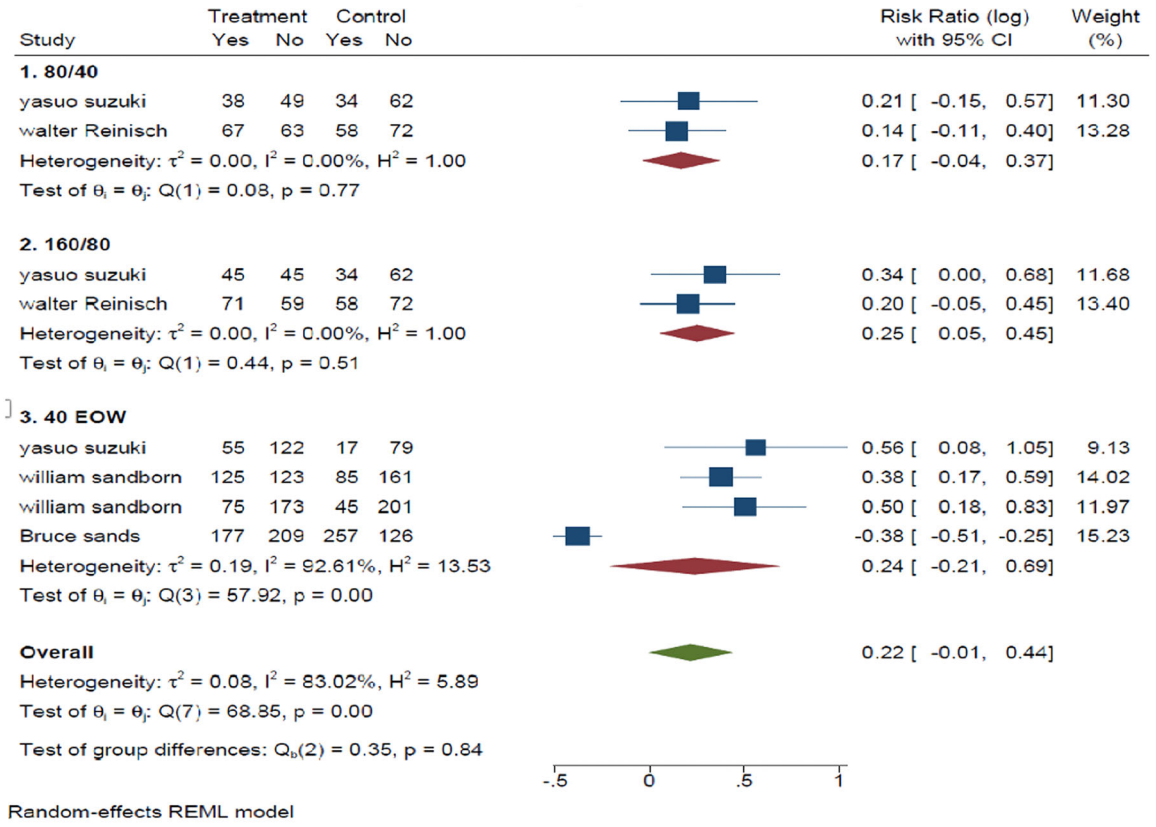

FIGURE 6 Treatment response according to different doses of adalimumab.

According to the findings of Abbas et al., no conclusive evidence regarding the adverse effects of adalimumab on Crohn's disease could be established. Additional research is necessary to explore the long-term advantages and disadvantages of adalimumab in individuals with Crohn's disease.[26]

Watanabe et al. aimed to demonstrate the efficacy and tolerability of adalimumab in Western patients with Crohn's disease. The results of this study showed that adalimumab is effective and well-tolerated for inducing and maintaining clinical improvement in Japanese patients with moderate to severe Crohn's disease.[27]

Sandborn et al. conducted studies to investigate the fact that adalimumab is a fully human monoclonal antibody that binds to TNF-α. The results of this study revealed that adalimumab is safer and more effective than placebo in inducing and maintaining clinical improvement in patients with moderate to severe UC who had an inadequate response to conventional treatment with steroids or immunosuppressants.[28]

In the study conducted by Barberio et al., 1-year endoscopic response to adalimumab treatment in patients with UC showed excellent results, with a reported treatment response of approximately 44%.[1]

In a study conducted by Angelison et al., it has been revealed that pharmacological treatment with anti-TNF drugs such as adalimumab has shown effective preliminary and maintenance responses in improving mucosal conditions in patients. Furthermore, changing the route of drug administration from subcutaneous to intravenous has been associated with a more favorable response.[2]

Han et al. revealed that treatment with infliximab and adalimumab had a significant impact on the management of patients with UC. The results of the studies indicate that treatment with these biological drugs can be considered a priority in the therapeutic approach for patients with UC.[8]

In the research conducted by Chen et al., through a systematic review and meta-analysis, it was determined that adalimumab at a dose of 161/81 mg has been effective in the initial treatment of moderate to severe UC.[29]

Gies et al. reported a treatment response of 81% in the initial stage for adalimumab. The outcome of this study indicates that the patients under investigation who experienced treatment failure with corticosteroids and immunosuppressants achieved a favorable treatment response in the initial and maintenance stages when starting treatment with adalimumab.[30]

In our study, the effectiveness of adalimumab in achieving mucosal healing, considering different therapeutic doses and treatment durations, was examined in the above-mentioned study.

The effectiveness of adalimumab in achieving clinical remission, considering different therapeutic doses and treatment durations, was examined in the above-mentioned study and found to be 71.79%.

The effectiveness of adalimumab in achieving clinical response, considering different therapeutic doses and treatment durations,

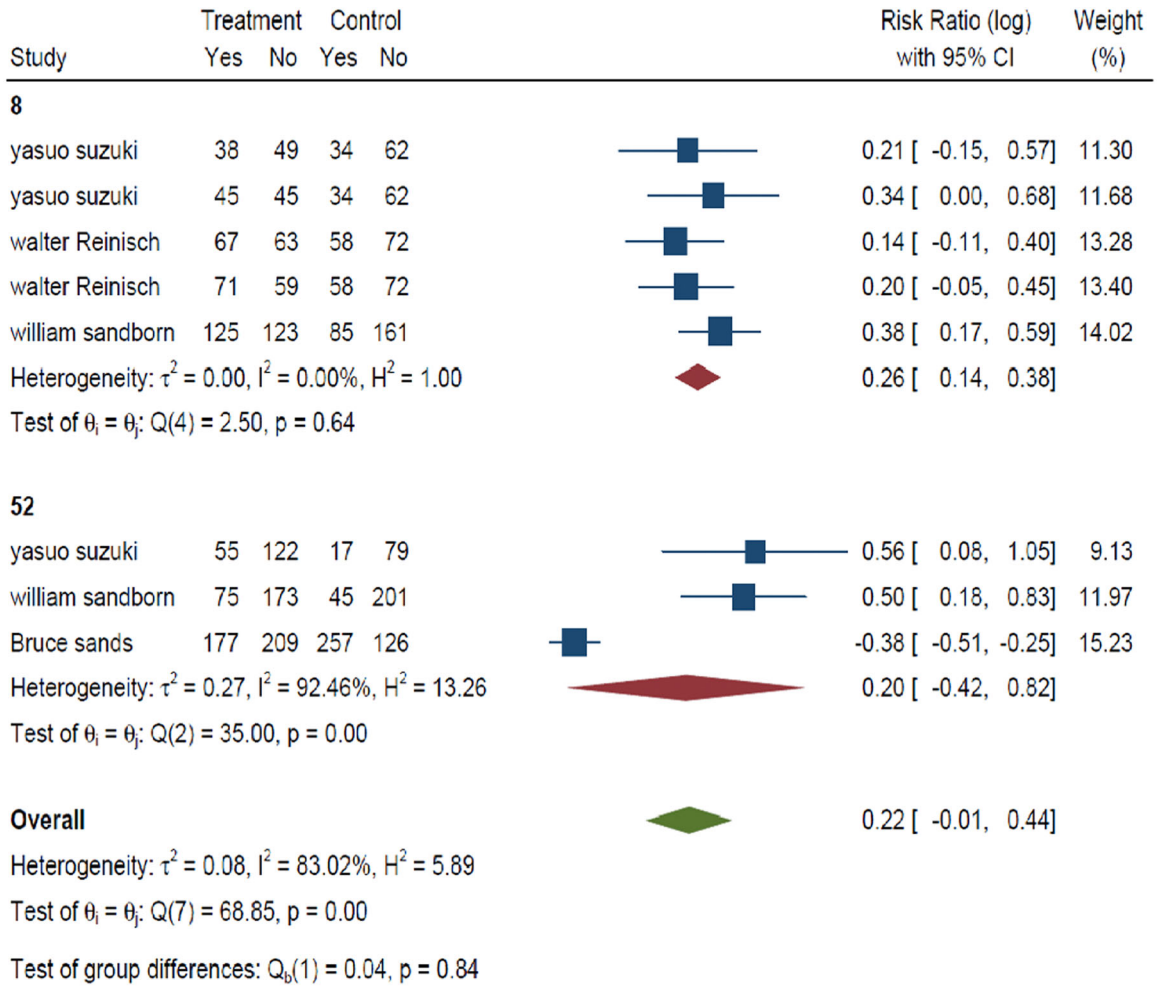

FIGURE 7 Treatment response according to different durations of adalimumab treatment.

was examined in the above-mentioned study and found to be 83.12%.

5 | CONCLUSION

In the four articles included in the study, using the meta-analysis method, the efficacy of adalimumab was investigated in 1613 patients with UC. These patients received adalimumab at different therapeutic doses during two treatment periods of 8 and 52 weeks. The results of the study are presented in the following tables based on three main indicators.

According to the results obtained from the conducted meta-analysis during the two treatment periods of 8 and 52 weeks, the efficacy of adalimumab in treating patients with moderate to severe UC at different therapeutic doses has been reported to be between 71% and 83%.

In comparing the results obtained from the meta-analysis in the above-mentioned study, the highest efficacy of adalimumab based on the three main indicators was observed with a therapeutic dose of 41 mg during the 52-week treatment period.

Our findings contribute valuable insights into the treatment landscape for UC patients and inform clinical decision-making.

AUTHOR CONTRIBUTIONS

Saleh Azadbakht: Conceptualization; investigation; funding acquisition; writing—original draft. **Masomeh Seighali**: Resources; writing—review and editing; software; formal analysis; project administration; data curation. **Salehe Azadbakht**: Visualization; validation; methodology; supervision. **Morteza Azadbakht**: Writing—original draft; funding acquisition; investigation; conceptualization; methodology; validation; visualization; writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. All relevant data and materials are provided in the manuscript.

TRANSPARENCY STATEMENT

The lead author, Morteza Azadbakht, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and if relevant, registered) have been explained.

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REFERENCES

1. Barberio B, Zingone F, D'Incà R, et al. Infliximab originator, infliximab biosimilar, and adalimumab are more effective in Crohn's disease than ulcerative colitis: a real-life cohort study. *Clin Transl Gastroenterol*. 2020;11(5):e00177.
2. Angelison L, Almer S, Davidsdottir L, et al. Short and long-term efficacy of adalimumab in ulcerative colitis: a real-life study. *Scand J Gastroenterol*. 2020;55(2):154-162.
3. Macaluso FS, Ventimiglia M, Fries W, et al. A propensity score weighted comparison of vedolizumab, adalimumab, and golimumab in patients with ulcerative colitis. *Dig Liver Dis*. 2020;52(12):1461-1466.
4. Hibi T, Kamae I, Pinton P, et al. Efficacy of biologic therapies for biologic-naïve Japanese patients with moderately to severely active ulcerative colitis: a network meta-analysis. *Intest Res*. 2021;19(1):53-61.
5. Vitello A, Grova M, Pugliese D, et al. Effectiveness of adalimumab for ulcerative colitis: a multicentre, retrospective study of clinical practice in Italy. *Dig Liver Dis*. 2022;54(3):352-357.
6. Rubin DT, Dotan I, DuVall A, et al. Etrolizumab versus adalimumab or placebo as induction therapy for moderately to severely active ulcerative colitis (HIBISCUS): two phase 3 randomised, controlled trials. *Lancet. Gastroenterol Hepatol*. 2022;7(1):17-27.
7. Numa K, Kakimoto K, Tanaka Y, et al. Efficacy of switching to adalimumab for maintenance of remission following induction therapy with tacrolimus in patients with ulcerative colitis. *J Clin Med*. 2023;12(20):6699.
8. Panés J, Colombel JF, D'Haens GR, et al. Higher vs standard adalimumab induction and maintenance dosing regimens for treatment of ulcerative colitis: SERENE UC trial results. *Gastroenterology*. 2022;162(7):1891-1910.
9. Merza N, Nawras Y, Saab O, et al. Comparing the efficacy and safety of adalimumab and vedolizumab in treating moderate to severe Crohn's disease and ulcerative colitis. *Gastroenterol Res*. 2023;16(6):289-306.
10. Singh S, Allegretti JR, Siddique SM, Terdiman JP. AGA technical review on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158(5):1465-1496.e17.
11. Kim ES. Infliximab versus adalimumab, which one is better for ulcerative colitis? *Gut Liver*. 2021;15(2):149-150.
12. Petryszyn P, Ekk-Cierniakowski P, Zurakowski G. Infliximab, adalimumab, golimumab, vedolizumab and tofacitinib in moderate to severe ulcerative colitis: comparative cost-effectiveness study in Poland. *Therap Adv Gastroenterol*. 2020;13:1756284820941179.
13. Miri SR, Mahmoodzadeh H, Hadjilooei F, et al. An expert opinion regarding the management of lower gastrointestinal cancers during COVID-19 outbreak in Iran: a brief report. *Acta Med Iranica*. 2021;59:249-252.
14. Miri SR, Khalaj A, Jafarlou V, Farahani PK, Bahramian A. Thoracoscopic esophagectomy in prone position: a cross-sectional study. *Acta Med Iranica*. 2021;59:442-446.
15. Loscalzo J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. *Harrison's Principles of Internal Medicine*. McGraw Hill; 2022.
16. Peyrin-Biroulet L, Bossuyt P, Bettenworth D, et al. Comparative efficacy of subcutaneous and intravenous infliximab and vedolizumab for maintenance treatment of TNF-naive adult patients with inflammatory bowel disease: a systematic literature review and network meta-analysis. *Dig Dis Sci*. 2024;69:1-8.
17. Han M, Jung YS, Cheon JH, Park S. Comparison of real-world outcomes of infliximab versus adalimumab in biologic-naïve Korean patients with ulcerative colitis: a population-based study. *Yonsei Med J*. 2020;61(1):48.
18. Patra R, Dey AK, Mukherjee S. Identification of genes critical for inducing ulcerative colitis and exploring their tumorigenic potential in human colorectal carcinoma. *PLoS One*. 2023;18(8):e0289064.
19. Patra R, Padma S, Mukherjee S. An improved method for experimental induction of ulcerative colitis in Sprague Dawley rats. *MethodsX*. 2023;10:102158.
20. Shin SY, Park SJ, Kim Y, et al. Clinical outcomes and predictors of response for adalimumab in patients with moderately to severely active ulcerative colitis: a KASID prospective multicenter cohort study. *Intest Res*. 2022;20(3):350-360.
21. Lu M, Zhang T, Lu Z, Wang W, Chen T, Cao Z. A comparison of the efficacy and safety of complementary and alternative therapies for ulcerative colitis: a protocol for systematic review and meta-analysis. *Medicine*. 2020;99(28):e21219.
22. Armuzzi A, Bouhnik Y, Cummings F, Bettey M, Pieper B, Kang T. Enhancing treatment success in inflammatory bowel disease: optimising the use of anti-TNF agents and utilising their biosimilars in clinical practice. *Dig Liver Dis*. 2020;52(11):1259-1265.
23. Lu X, Jarrett J, Sadler S, Tan M, Dennis J, Jairath V. Comparative efficacy of advanced treatments in biologic-naïve or biologic-experienced patients with ulcerative colitis: a systematic review and network meta-analysis. *Int J Clin Pharmacy*. 2023;45(2):330-341.
24. Nakagawa S, Lagisz M, Jennions MD, et al. Methods for testing publication bias in ecological and evolutionary meta-analyses. *Methods Ecol Evolution*. 2022;13(1):4-21.
25. Mathur MB, VanderWeele TJ. Sensitivity analysis for publication bias in meta-analyses. *J Royal Statistical Soc Series C: Applied Statistics*. 2020;69(5):1091-1119.
26. Abbas R, Ibrahim N, Elawad M, Al-Mudahka F, Abdelrhman H, Akobeng AK. P617 dual biologic therapy in pediatric inflammatory bowel disease. *J Crohn's Colitis*. 2023;17(suppl ment_1):i747.
27. Townsend CM, Nguyen TM, Cepek J, et al. Adalimumab for maintenance of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2020;(5):CD012877.
28. Singh S, Murad MH, Fumery M, Dulai PS, Sandborn WJ. First-and second-line pharmacotherapies for patients with moderate to severely active ulcerative colitis: an updated network meta-analysis. *Clin Gastroenterol Hepatol*. 2020;18(10):2179-2191.e6.
29. Chen X, Hou J, Yuan Y, et al. Adalimumab for moderately to severely active ulcerative colitis: a systematic review and meta-analysis. *BioDrugs*. 2016;30(3):207-217.
30. Gies N, Kroeker KI, Wong K, Fedorak RN. Treatment of ulcerative colitis with adalimumab or infliximab: long-term follow-up of a single-centre cohort. *Aliment Pharmacol Ther*. 2010;32(4):522-528.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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