

Nutritional Interventions and Dietary Supplements for Patients with Rheumatoid Arthritis: A Systematic Study for Clinical Use, Part 1: Diet

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease involving local and systemic inflammation, resulting in chronic pain and limited physical function that can negatively impact the quality of life (QOL). Despite advances in pharmacological therapy, currently, available treatment options can be associated with side effects and be expensive. Therefore, research efforts have focused on nutritional interventions to support pharmacological therapies, reduce inflammation, and improve quality of life.

Goal: In this systematic review, data were collected on the most recent non-pharmacological interventions used in the treatment of RA. The effectiveness and potential practical applications of various nutritional interventions used in the management of RA will be discussed. The diets discussed in this article include the anti-inflammatory diet in the RA diet, the elemental and elimination diet, weight loss, and the Mediterranean diet (MD). For more information on other aspects of this systematic review, you can refer to Section 2; Supplement, and Section 3; Fruits and Herbs.

Method: A literature review was performed to identify nutritional interventions during RA progression and management. Eligible study designs included meta-analyses, systematic reviews, randomized controlled trials (RCTs), and prospective/retrospective studies.

Result: Initially, 334 articles were identified. After excluding studies for lack of relevance, exclusion criteria, and duplication, 22 articles remained. Eligible articles were divided into five groups based on design meta-analysis, systematic review, RCT, literature review, and prospective study. Five articles were classified as dietary, including one systematic review, two RCTs, and two literature reviews.

Conclusion: Dietary interventions can be an effective method to reduce inflammation and symptoms associated with RA. Significant improvements in PR scores, such as DAS-28 and HAQ, were observed when the MD, vegan, and vegetarian diets were used together with exercise and weight loss. However, previous research has identified high-immune foods that can trigger symptoms. Therefore, clinicians should familiarize themselves with these agents to educate their patients.

Keywords: Rheumatoid arthritis; Mediterranean diet; Losing weight; Randomized controlled trial

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease involving local and systemic inflammation, resulting in chronic pain and limited physical function that can negatively impact the quality of life (QOL). This localized inflammation mediated (mediated by inflammatory cytokines and some host cells) manifests as joint swelling and cartilage erosion leading to pain, which can be severe and debilitating and leads to limitation of joint pain. functional mode [1]. Therefore, pain relief is the first priority in treatment. Pharmaceutical disease-modifying agents have been commonly used to manage RA. However, the high price and serious side effect profile associated with these drugs can lead to compliance problems and serious complications. Research efforts have revealed that environmental and lifestyle factors, including diet, may play a role in the expression and progression of RA, and that altering these factors can play a role may be associated with improved pain and quality of life. Therefore, the use of non-pharmaceutical interventions to support pharmacological therapies and/or to target the underlying mechanisms of disease action could be of considerable value to patients. 2].

In particular, previous studies have shown that the Mediterranean diet (DM), including increased consumption of monounsaturated and polyunsaturated fatty acids, has been shown to improve disease status in GO OUT. The dietary supplements that have been studied include plant-based, anti-inflammatory, elimination, and elemental diets, as well as general weight loss that can be achieved through a number of diets. this diet [3]. This article provides a systematic review of the existing evidence on the use of non-pharmaceutical interventions for the management of RA, published between 2017 and 2020. The aim is to provide clinicians with information on the safety and effectiveness of non-pharmaceutical interventions in the management of RA to help them make recommendations. These recommendations include whether these non-pharmaceutical methods can be used in combination with or in place of pharmaceutical agents.

In this effort, standardized assessments have been developed to identify subjective and objective clinical improvements in disease performance [4]. The 28-joint disease activity score (DAS-28) was used to monitor disease progression and evaluate the number of tender joints (TJC), the number of swollen joints (SJC), the erythrocyte sedimentation rate (RBC) ESR) and global health assessment. The 36-item Short Form Health Survey (SF 36) is a subjective questionnaire used to assess the quality of life. The Image Analogue Scale (VAS) is a tool used to measure subjective pain by choosing a value from 0 (no pain) to 100 (severe pain). The Health Assessment Questionnaire (HAQ) is a tool used to self-assess functional status. Additionally, the Ritchie score is a tool used to monitor disease severity. This score assesses the pain level of the general group and ranks them on a scale of 0 to 3 [5]. These indicators will be used because they emphasize

the role of pain and function and can provide clinicians with a way to understand the impact of these treatments on disease status. Our initial search consisted of 22 articles that were then divided into three sections, Diets, Supplements, and Fruits and Herbs. In the first of our 3-part series, we will discuss more formally structured dietary interventions and their clinical impact on patients with RA. The diets discussed in this article include the anti-inflammatory diet in the RA diet, the elemental and elimination diet, weight loss, and MD. For more information on other aspects of this systematic review, you can refer to Section 2: Supplement and Part 3 Fruits and Herbs [6].

Method

Search strategy

A systematic computer-aided literature review was performed using PubMed for research articles examining nutritional interventions in the progression and management of RA. Searches from PubMed include "Rheumatoid Arthritis Nutrition", filtering articles published between 2017 and 2020. The reference list of retrieved articles is also reviewed as deemed relevant. and if they match the search criteria, but have not been discovered by individual searches [7]. The relevance of these articles was assessed using a hierarchical approach, first by title review, followed by abstract and full manuscript. For articles that are not freely available, access is obtained through the use of Nova Southeast University (NSU) library resources. Selection Criteria (Figure 1).

Studies were considered eligible if they addressed specific nutritional interventions to assess the management or progression of active RA as determined by the American College of Rheumatology criteria. United States (ACR) or European League Against Rheumatism (EULAR). . Eligible study designs included meta-analyses, systematic reviews, randomized controlled trials (RCTs), and prospective/retrospective studies [8].

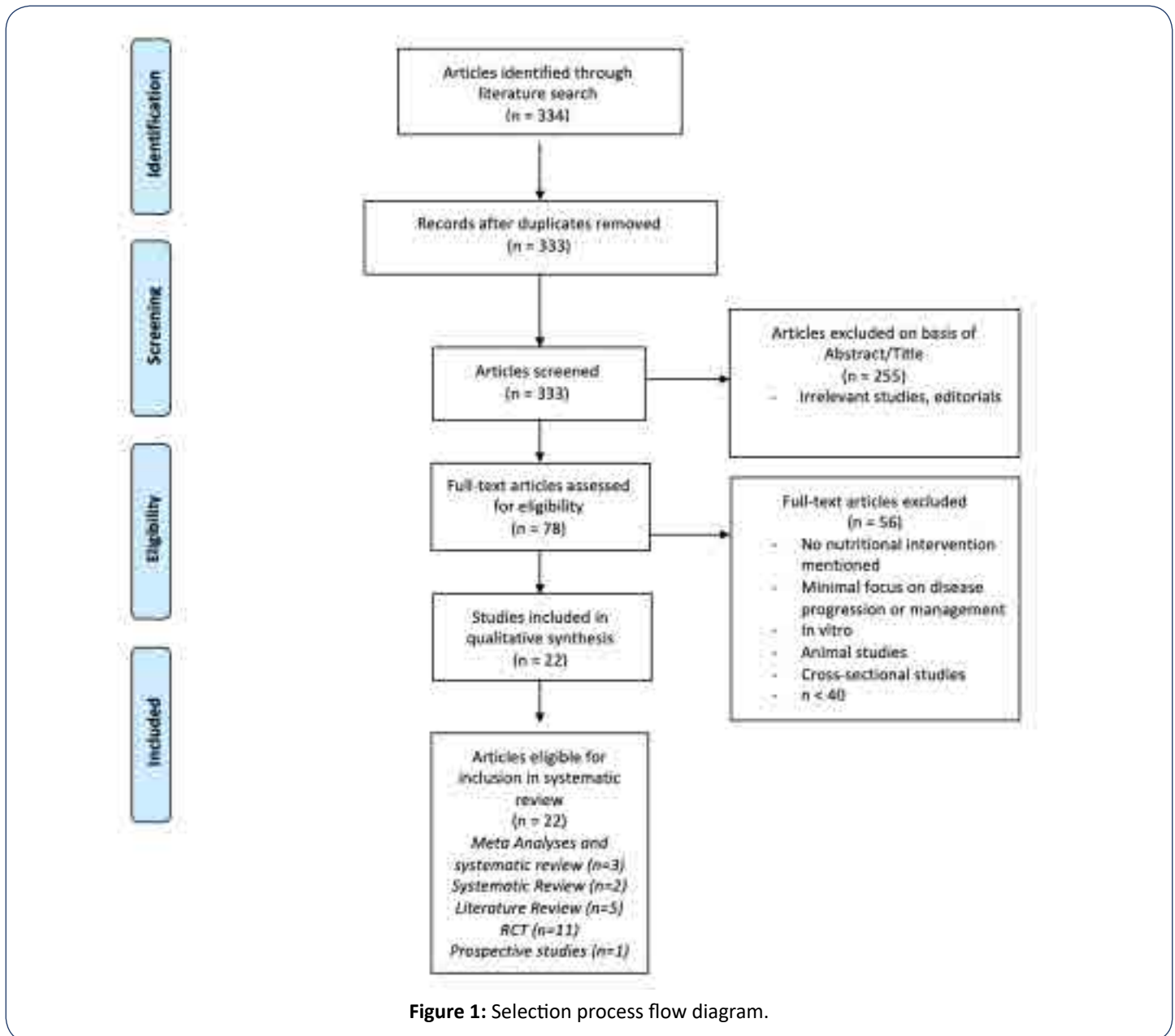
A total of 334 articles were identified from the initial search of the electronic database. Two hundred and fifty-five articles were disqualified for lack of relevance when selecting titles and abstracts, and one duplicate was removed. Out of the remaining 78 articles, 56 articles were excluded for the following reasons. There were no in vivo human models, $n < 40$, and no significant intervention studies.

Discussion

The ADIRA diets

ADIRA-A Randomized, controlled crossover trial showing an effect on disease activity:

In a study conducted on the Swedish population. Conducted a 10-week, single-blind, crossover study in which 50 RA patients were randomly assigned to an anti-inflammatory food diet or an



equivalent control diet common in Sweden. Dietary interventions emphasize increased intake of fruit, fiber, fish, and probiotics. The diet was referred to as a "fiber" diet while the control diet was referred to as a "protein" diet intended to mask the interference. Fiber content, as well as n-3 PUFA (polyunsaturated fatty acids), were higher in the intervention at 24 g/day (5.2 g/MJ) and 4 g/day respectively compared with 8.3 g/day (1.8 g/MJ) and 0.8 g/day (0.6 E%) in the control diet. One concern with this study is the difficulty of blinding a diet where participants are likely to have preconceived ideas about which foods are inherently healthier. In addition, this diet was performed on a local population of Swedes and therefore, the results may not be generalized to other populations with different dietary and genetic backgrounds [9]. Initially, improvements were found in the intervention group compared with the control group, however, during the ANCOVA analysis; The study indicated that

there was no significant difference in DAS28-ESR scores between groups. Overall, given the failure to achieve statistical significance of the intervention after the ANCOVA analysis and the lack of generalizability beyond the Swedish population, we do not believe that this study supports our recommendation.

Elimination and the elemental diet

Treatment of rheumatoid arthritis with dietary interventions:

The basal diet contains hypoallergenic foods with essential nutrients for daily needs and is considered less immunogenic than the average diet. Forty-seven RA patients received either their basal diet or their usual diet. The basal diet is given to induce remission, then gradually adjusted to reintroduce the foods. When reintroduced foods were found to cause symptoms, they were quickly eliminated from the diet [10]. Statistically significant

improvements were seen in grip (GS) ($p=0.008$) and Ritchie score ($p=0.006$), but not with ESR, CRP, thermography, or functional scores. Any improvement seen with baseline diet therapy diminishes rapidly upon discontinuation of use. Limitations of this study included the inability to blind subjects, resulting in an emphasis on subjective measures of improvement in addition to a high dropout rate with only 38% of patients completing the study.

Nutritional interventions in rheumatoid arthritis

Potential uses of plant-based diets. Evaluate:

A 2019 review of the potential use of a plant-based diet discussed research efforts on elimination and elemental diets in the management of RA. As new research efforts point to a possible link between the gastrointestinal tract and the etiology of RA, attention has begun to turn to food sensitivities and the involvement of certain antigens as discussed above. found in other autoimmune diseases. The basal diet removes specific ingredients from a person's diet to determine if they play a role in the symptoms of concern, while the basal diet involves specific food choices involving eliminating all antigenic proteins from his diet. The review refers to a 2001 clinical trial involving 66 RA patients following a gluten-free vegan diet for a period of 9 months [11]. The study results showed a 40.5% improvement in the ACR20 improvement criterion, compared with 4% in the non-vegan group. Meanwhile, Alwarith's review indicates that responses to these methods can vary widely and that any improvement can quickly wear off with the continuation of the previous diet. However, determining individual food sensitivities has also been described as a challenge for these treatments. Typically, skin tests are used to identify immunoglobulin-mediated responses to an irritant, although this does not always correlate with offending foods.

Another study was performed by eliminating and stimulating eating in 48 RA patients to identify foods that were likely to cause symptoms in this population. Participants followed a six-week diet that identified 20 different foods. Of these foods, corn and wheat were the most common causes of symptoms, for 57% and 54% of the participants, respectively. These results are summarized. In addition, a 2009 systematic review evaluated the efficacy and safety of dietary interventions in the treatment of RA. Two clinical trials evaluating the effects of vegan diets and diets were included [12]. Both trials evaluated the effect of improving RA symptoms using a baseline diet for four weeks compared with controls, but due to underreporting, the results were inconclusive. Overall, there are reported data on non-pharmaceutical interventions and further research is needed to determine the effectiveness of these dietary modifications in identifying RA and improving symptoms. Many of these studies have resulted in high dropout rates and regressions of disease severity upon treatment discontinuation, which raises questions about the efficacy of their application in the clinical setting. Meanwhile, for foods commonly known to induce immune responses, clinicians should encourage

patients to be aware of the components of their diet to minimize these effects. exacerbations and symptom control.

Mediterranean diet and exercise

Effects of the Mediterranean diet on the prevention and treatment of RA:

Among the various interventions discussed, DM has received a lot of attention in recent years. A 2017 systematic review assessed the impact of DM on the prevention and management of RA. For this review, we will focus on the processing aspect of the Forsynth article. DM is characterized by the consumption of olive oil, unrefined grains, fresh or dried fruits and vegetables, and moderate amounts of fish, dairy products, and meat in addition to spices and wine. The reason this diet has gained so much interest is because of its potential anti-inflammatory effects, which, for the reasons discussed earlier, may be beneficial for RA patients. In 2003, an RCT was conducted to evaluate the effectiveness of Cretan MD compared with a typical Western diet in suppressing disease activity in patients with newly diagnosed RA over a period of time. three months. The first three-week phase of the study was conducted in a hospital setting, in which participants received desired diet-like meals along with six lessons on cooking and Mediterranean cuisine. Hai in an effort to maintain compliance for the next nine weeks outside the hospital. setting. The control group received no recommendations [13].

Adherence was determined by questionnaire, interview and measurement of biomarkers. Compared with the control group, the MD group demonstrated improvements in disease activity ($p<0.001$), physical activity ($p=0.006$) and inflammatory biomarkers ($p=0.006$). However, no significant changes were noted in morning stiffness or drug dosage changes. At week 12, the intervention group reported a significant decrease in the DAS28 score ($p<0.001$), while no change was observed in the control group. The other study included in the review was a controlled clinical trial (CCT). This study included 130 patients diagnosed with RA assigned to either the intervention group ($n=75$) or the control group ($n=55$). The intervention group completed a six-week cooking course in addition to receiving information on diabetes and related cooking practices, while the control group received literature on general principles of eating healthy. Dietary adherence was determined using a food frequency questionnaire and laboratory markers were measured at baseline and follow-up visits. The results showed a significant improvement in the measured parameters after 3 months of follow-up, including pain ($p=0.011$) and physical activity ($p=0.03$) as well as after 6 months of follow-up on the scale. similar measures of overall image ($p = 0.002$) and morning stiffness ($p = 0.041$) compared with controls. However, no changes were reported in DAS28 scores for either group. In addition, both the Sköldstam and McKellar interventions showed a decrease in the HAQ score of the MD group after 6 months of follow-up ($p<0.05$).

Effects of an active exercise program combined with MD on quality of life in women with rheumatoid arthritis:

The results of the study indicated that there were statistically significant changes in the global health, global scores, and mental health components of SF-36 compared with controls for the DEP groups, MD and MD + DEP. Improvements in all components were greatest for the MD + PED group, with the exception of the mental component, where the largest change was only in PED. One potential explanation for this could be that sticking to a new diet can cause additional mental stress. Notably, this study also showed statistically significant changes in the physical composition of SF-36 in the DEP and MD+DEP groups, but not only for MD. Limitations of this study include that it involved only the female population and included only patients with hypoglycemia.

It appears that DM in addition to a twice-weekly exercise regimen may help improve the quality of life in women with RA with low DAS-28 scores. In addition, Garcia-Morales emphasizes the importance of the duration of the intervention to achieve and maintain significant improvements as seen in the Bilberg study. In addition, Garcia-Morales points out that a period of at least 24 weeks should be used to observe the benefits of this dual intervention. Overall, this study indicates that the combination of diet and exercise leads to greater improvements than the combination of the disease status of RA patients alone. Information regarding the effectiveness of DM in patients with RA is limited, with the data in this review being the results of two trials that have been published in different publications. In addition, the results of these studies show a high degree of bias and the results should be approached with caution. Meanwhile, the results of these two studies, along with the one conducted by Garcia-Morales, indicate that MD exhibits the ability to improve the disease status of patients with RA. With the greatest concern for compliance, this diet is safe and practical to recommend to clinicians for their patients. The effects of this diet can be maximized by incorporating simultaneous exercise. At this time, we recommend physicians, in addition, to exercise for RA patients, with the caveat that further studies should be performed to strengthen these recommendations and provide additional data. Vegetarian/vegan diet

Treatment of rheumatoid arthritis with dietary interventions:

Khanna's paper discusses a 2001 meta-analysis performed by Müller et al. to determine the effect of fasting followed by a vegetarian diet in patients with RA. Müller's research yielded 31 original papers that were critically analyzed. However, the review focuses mainly on four controlled studies, the work of which will be discussed in detail in the next article of this section. Two of these four controlled trials were randomized. Pooling the p-values from these studies when combined showed significant results ($p < 0.001$). Müller's review indicates that the literature reviewed supports the hypothesis that short periods of fasting followed by

a vegetarian diet can lead to statistically and clinically relevant long-term improvements. available in patients with RA. These improvements are mainly evaluated using VAS. However, they acknowledged limitations in drawing any final conclusions due to the small number of methodologically plausible studies, and potential publication bias that may have limited their exposure. with other articles that may have been included in the study. are popular with the general population as the majority of patients expect to quickly and adhere to these rigorous procedures. Finally, the composition of these fasts was poorly defined in the analysis, making it more difficult to compare results. Other work discussed in this Khanna review includes those discussed in more detail in Nutritional Interventions in Rheumatoid Arthritis.

Potential uses of plant-based diets

Nutritional interventions in RA:

Many studies have linked inflammatory markers, such as C-reactive protein (CRP), IL-6, and homocysteine, with the consumption of red meat and animal products, while others have demonstrated the potential of vegan and plant-based diets to reduce these markers. inflammatory markers. Given that RA is a disease mediated by similar inflammatory markers, it is reasonable to assume that implementing such a treatment regimen should lead to clinical improvement. This study evaluated the effects of fasting for 7 to 10 days, followed by 3.5 months of a gluten-free vegan diet with a gradual transition to a vegetarian diet taking place over the course of a year. Both the intervention and control groups were in nursing homes for the first four weeks of the study. After one month, the diet group began to show improvement in the number of swollen and painful joints, Ritchie joint index, pain score, time of morning stiffness, grip strength (GS), and erythrocyte sedimentation rate (ESR). CRP, white blood cell (WBC) and HAQ scores are maintained after one year. For comparison, after one month, the control group showed a significant improvement in pain scores alone.

Disease activity was measured using the DAS-28 index as well as the European Union against Rheumatoid Arthritis (EULAR) response criteria at 3 and 12 months. DAS-28 was found to be higher in the control group ($p=0.047$), while the HAQ score was not significantly different. Additionally, the vegan group was shown to have lost weight and body mass index (BMI) of 4.2 kg and 1.4, respectively. In addition, CRP levels decreased from 13 to 5 to 12 months ($p=0.008$). No serious side effects were reported in these studies. However, in Elkan's study, participants were given vitamin B12 supplements to prevent any deficiency. The studies discussed in this section are limited to and incorporate a mixture of vegetarian, vegan, and vegetarian diets. For these reasons, it is difficult to separate each aspect to determine how applying one or the other could benefit patients with RA. However, available data indicate that vegan and vegetarian diets can significantly improve clinical parameters such as DAS-28 and

VAS. Although the Kjeldsen-Kragh study demonstrated several other significant improvements over the Elkan study, it remains unclear whether this is due to the addition of the fasting period. Currently, we believe that there is sufficient data to recommend the incorporation of a vegan or vegetarian diet to improve clinical symptoms. However, future research should aim to determine the role of fasting and compare the benefits of a vegan versus vegetarian diet to better understand the effects.

Losing weight

Nutritional interventions in RA:

Although adipose tissue was previously thought to be inert, it is understood that adipose tissue as an organ itself can lead to the production of proinflammatory cytokines that may contribute to the inflammation seen in many disease conditions. When considering that the inflammatory process in RA leads to diffuse joint erosion, it is important to consider that additional weight gain may exacerbate this lesion. Several studies have shown that overweight RA patients have worse outcomes than those with a normal BMI.

This study used DAS28 and concluded that each kg of weight loss was associated with an improvement in the clinical disease activity index of 1.15 ($p=0.0026$). Similar results were observed by Sparks et al. in the study of weight loss in 53 patients with rheumatoid arthritis after bariatric surgery. Twelve months after surgery, six percent of patients were considered to have moderate to high disease activity, up from 57 percent previously. Follow-up 5.8 years after surgery showed that 74% of patients were considered to be in remission, compared with 26% before surgery. Additional data were collected from inflammatory markers, measured at 6 months, 12 months, and 5.8 years and found to be significantly lower.

With evidence showing a correlation between healthy BMI, weight loss, and the ability to achieve and maintain remission, it is imperative that clinicians emphasize this aspect of management with their patients. As disease activity worsens, daily activities become more difficult, and therefore, nutritional goals describing the desired weight and BMI should be included regularly as part of the treatment plan. clinical practice in more pharmacological therapy.

Conclusion

The purpose of this review is to evaluate recent dietary interventions for clinical improvement and to summarize recommendations that can serve as tools for clinicians to confidently inform updates for their patients. Among the various complementary approaches that can be taken in patients with RA, various diets have been suggested to improve symptoms and general well-being. Most diets focus on eliminating "inflammatory" foods and eating a diet that helps reduce inflammation. There is not enough evidence to support the effectiveness of ADRIA and elimination diets. However, improvements were seen in MD and plant-based

diets. There is a strong relationship between a healthy weight and symptom severity. Evidence suggests that maintaining a healthy weight and getting regular physical activity correlates with lower disease activity. When used in conjunction with an individual's current treatment, evidence supports dietary habits that encourage the consumption of vegetables, n-3 PUFAs, and minimally processed foods. These patterns are suitable for DM. In addition to diet, clinicians should encourage patients to exercise regularly and maintain a healthy weight to further improve clinical outcomes in patients with RA.

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