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Authors

Bustamante, Marta F
Agustín-Perez, Meritxall
Cedola, Francesca
et al.

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Research paper

Design of an anti-inflammatory diet (ITIS diet) for patients with rheumatoid arthritis

Marta F. Bustamante [a], Meritxall Agustín-Perez [a], Francesca Cedola [a], Roxana Coras [a,c], Rekha Narasimhan [a], Shahrokh Golshan [b], Monica Guma [a,c,*]

[a] Department of Medicine, University of California San Diego, San Diego, CA, USA
[b] Department of Psychiatry, University of California San Diego, San Diego, CA, USA
[c] Department of Medicine, Autonomous University of Barcelona, Plaça Cívica, 08193, Bellaterra, Barcelona, Spain

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that affects synovial joints, leading to inflammation, joint destruction, loss of function, and disability. Although recent pharmaceutical advances have improved treatment of RA, patients with RA often inquire about dietary interventions to improve RA symptoms, as they perceive rapid changes in their symptoms after consumption of certain foods. There is evidence that some ingredients have pro- or anti-inflammatory effects. In addition, recent literature has shown a link between diet and microbiome changes. Both diet and the gut microbiome are linked to circulating metabolites that may modulate inflammation. However, evidence of the effects of an anti-inflammatory and probiotic-rich diet in patients with RA is scarce. There is also a need for biological data to support its anti-inflammatory effects.

Methods: The main goal of this study is to delineate the design process for a diet tailored to our RA population. To achieve this goal, we collected information on diet, supplements, cooking methods, and intake of different ingredients for each patient. Different groups were interviewed, and their feedback was assessed to design a diet that incorporates suggested anti-inflammatory ingredients in a manner that was easy for patients to adopt based on their lifestyles and backgrounds.

Results: We designed a diet that includes a high intake of potential anti-inflammatory ingredients. Feedback from highly motivated patients was critical in constructing an anti-inflammatory diet (ITIS diet) with elevated adherence.

Conclusion: In order to tailor our diet, we surveyed our patients on several different parameters. We obtained important feedback on how feasible our ITIS diet is for RA patients. Using this feedback, we made minor improvements and finalized the design of the ITIS diet. This diet is being used in an on-going pilot study to determine their anti-inflammatory effect in pain and joint swelling in RA patients.

Trial registration: Not applicable.

1. Background

Rheumatoid arthritis (RA) is a systemic, debilitating, chronic inflammatory autoimmune disorder affecting approximately 1% of the world population [1]. RA is a form of arthritis that causes pain, swelling, stiffness, and loss of function in joints. This disease severely impacts quality of life with increased morbidity and mortality. Although recent pharmaceutical advances have improved the treatment of RA, most RA patients need lifelong pharmacological therapy. RA patients often seek additional sources of relief and/or treatments with less side effects, and often inquire about dietary interventions to improve RA symptoms, as they perceive rapid changes in pain and/or swelling after consumption of certain foods [2]. However, rheumatologists lack information to advise RA patients on nutrition.

Diet might modulate RA symptoms by influencing the patient's metabolic profile and increasing antioxidant levels, but also by altering the microflora of the intestine. The gut microbiome is incredibly dynamic and can change rapidly to dietary perturbations [3]. In addition,

* Corresponding author. Division of Rheumatology, Allergy and Immunology, UCSD School of Medicine, 9500 Gilman Drive, La Jolla, CA, 92093-0656, USA.
E-mail address: mguma@health.ucsd.edu (M. Guma).

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the gut microbiome is also involved in the metabolism of some dietary components and has the potential to modify circulating pro- or anti-inflammatory mediators [4]. For example, trimethylamine-*N*-oxide, a pro-inflammatory metabolite that derives from choline and carnitine present in red meat, eggs, and dairy products, is produced by *Prevotella copri* among other bacteria [5,6]. An increased abundance of *Prevotella copri* was found in new-onset untreated RA patients suggesting *P. copri* may be pathogenic [7]. In general, bacteria that have an almost exclusive saccharolytic metabolism, such as lactobacilli and bifidobacterial, are considered potentially beneficial [8]. Both gut microbial species produce a variety of tryptophan catabolites which are critical for intestinal homeostasis by decreasing intestinal permeability [9]. In addition, some of these catabolites enter the bloodstream and have anti-inflammatory and anti-oxidative effects [9]. Various dietary components including miso and yogurt are a source of this beneficial flora. Daily yogurt was shown to reduce biomarkers of chronic inflammation in premenopausal women [10]. Dietary fiber, other complex carbohydrates, and sugar alcohols present in fruits are prebiotics and might also be beneficial by supporting healthy microbiome [11,12]. For instance, microbial degradation of whole-grain complex carbohydrates increases short chain fatty acids (SCFA), which were shown to be beneficial to intestinal immune response [13].

In addition, several foods have been identified as pro-inflammatory, including highly refined flours, gluten [14], trans- and saturated-fatty acids (FA) [15–17], dairy products (milk and cheeses) [18], and red meat [19,20]. Some vegetables such as tomatoes, eggplants, and potatoes contain solanine, a glycoalkaloid, which was suggested to increase intestinal permeability and be detrimental for arthritogenic pathologies [21–26]. In contrast, other nutrients have been suggested to offer numerous health benefits [27], including long chain omega-3 polyunsaturated FA (PUFA) (chia seeds, flaxseeds, fatty fish) [28–32], monounsaturated FA (MUFA) (avocado, sesame) [33,34], antioxidants [35], phytochemicals [36], flavonoids [37,38], vitamin D [39], fruits with enzymatic proteins such as papain and bromelain (papaya, mango, pineapple) [40–42], ginger [43], turmeric [44,45], black pepper [46,47], green tea [48–50], and legumes [46,51]. However, only a few randomized double-blind placebo-controlled clinical trials have attempted to determine whether supplementation with these ingredients [31,34,35,37,38,43] or probiotics [52,53] are beneficial in RA patients. So far, most of the studies are pilot studies with small number of patients, studies on animal models, or *in vitro* studies.

Despite a large number of publications on the effect of different ingredients and gut microbiome on inflammation, and reports showing an association between poor dietary quality and inflammation in RA patients [54,55], only a few interventional studies have investigated whether specific diet improves RA symptoms (for review [56,57]). The effects of complete diet intervention (including vegetarian and Mediterranean diets) have shown positive effects in ameliorating RA symptoms. One of the studies showed that fasting first and then eating a vegetarian diet for one year was beneficial in RA, particularly in terms of number of swollen joints, stiffness, and C reactive protein (CRP) [58]. A diet trial with Mediterranean diet (MD) also showed a decrease in disease activity (DAS28) of 0.56 ($p < 0.001$) and in quality of life compared to control diet [59]. Yet, we could not find a trial using a diet that incorporates and combines different potential anti-inflammatory ingredients.

Here, we will describe the steps taken to design our anti-inflammatory diet (ITIS diet) for a complementary therapy in RA patients. In Table 1, we summarized the strategies and ingredients included in the ITIS diet. This diet is an omnivorous diet, based on a Mediterranean diet but with several modifications. Our diet reinforces fast digestions by dissociating grains from proteins, suggests certain cooking methods [60], is a diet low on gluten, and also includes enzymatic fruits, whole grains, a very high consumption of omega 3 PUFA and MUFA, and anti-inflammatory dressings and spices. It introduces green juices in the morning to increase green leafy vegetables and fruit

Table 1
Strategies and recommendations in the ITIS diet.

Main recommendations (WHAT/WHAT FOR)	Based on (WHY)	Diet strategies (HOW)
• Lower the omega6/3 PUFA ratio to 2:1 • Increase intake of MUFA • Decrease intake of pro-inflammatory FA such as trans-FA and saturated FA (present in dairy products, red meat and processed food)	• A low omega 6/3 PUFA ratio reduces inflammation and improves autoimmunity symptoms [28–32]. • MUFA found in nuts, avocado, sesame and olive oil have beneficial effect in RA [33,34] • Industrially produced trans-FA increase inflammatory markers and saturated FA increase inflammation [15–17].	• The diet must contain fatty fish such as sardines, tuna, twice per week, daily intake of chia seeds and flaxseed oil. • Daily intake of nuts, avocado, and/or sesame seeds or tahini • Avoid pre-cooked food, red meat and processed meat. Cook by baking, boiling or vapor. Avoid frying for long periods since it modifies PUFA to trans-FA [60].
• High intake of prebiotics • Daily intake of probiotics	• Dietary fiber, whole-grain complex carbohydrates, and sugar alcohols present in fruits are prebiotics that support healthy microbiome [11,12] and increases SCFA production improving immunity [13]. • Probiotics including yogurt reduce the levels of the pro-inflammatory cytokines and improves disease activity in RA [10,52,53]	• Daily green leafy vegetables (arugula, lettuce, broccoli, zucchini, Green beans) and fruits (prebiotic source). • Daily home-made green juice (made of fruits and green vegetables) (prebiotic source). • Promote whole grains and avoid refined flours (prebiotic source). • Daily yogurt (a brand that contains *Lactobacillus Casei* among other species (Chobani) and miso (probiotic source).
• Help digestion of large proteins in the gut and avoid unnecessary fermentation	• Fiber consumption and enzymatic fruits will reduce colonic transit, and will help protein digestion • Bromelain and papain were shown to have an anti-inflammatory effect as well [40–42]. • Large proteins in dairy products are not completely digested and can feed proteolytic bacteria, resulting in the production of pro-inflammatory metabolites [66].	• Daily enzymatic fruit: pineapple, mango or papaya (source of bromelain, papain and other proteolytic enzymes) • Disassociate consumption of proteins from grains • Increase fiber intake • Substitute plant-based milks (almond, rice, coconut) for dairy.
• Condiment with anti-inflammatory spices • Eliminate salt	• Turmeric, black pepper and ginger have antioxidant and anti-inflammatory actions [43–46] • Black pepper increases bioavailability of curcuma [46,47] • High salt intake is associated with the risk of arthritis and has been related to autoimmunity [67,68].	• Condiment with turmeric, black pepper and ginger. • Turmeric and black pepper should be used at the same time. • Low salt intake by eliminating precooked food
• Substitute vegetables with potential anti-inflammatory	• *Solanaceae* vegetables contain glycoalkaloids. Glycoalkaloids have been reported to affect	• Avoid the consumption of eggplant, tomatoes and potatoes and increase consumption

(*continued on next page*)

Table 1 (*continued*)

Main recommendations (WHAT/WHAT FOR)	Based on (WHY)	Diet strategies (HOW)
properties for *solanaceae* vegetables	intestinal permeability [21–26] • Vegetables with high content of phytochemicals were suggested to have anti-inflammatory properties (garlic, onion, pumpkin, zucchini, carrot, green leafy vegetables) [36]	of garlic, onion, carrot, pumpkin, zucchini or green leafy vegetables.
• Decrease consumption of red meat.	• It contains high levels of choline, which is the precursor of the inflammatory metabolite TMAO [5,6] and saturated FA.	• Introduce legumes (red, white beans, lentils or garbanzo), poultry and white fish, 2–3 days a week each. Avoid red meat.
• Reduce consumption of gluten	• Gluten has been associated with inflammatory states [14]. • Pseudocereals and whole grains reduce inflammation [69,70]	• Substitute whole grains such as rye, corn, oats or quinoa for refined wheat.
• Avoid sugars, sugary foods and sugary beverages	• Sugary foods and beverages are associated to obesity, microbiome changes and low-grade inflammatory state [71].	• Substitute honey for sugar. Avoid soda and juices.
• Substitute green tea for coffee	• Green tea contains polyphenols which decrease pro-inflammatory cytokines in animal models and in *vitro* models of RA) [48–50,72,73] • Some studies suggest that coffee consumption may increase the risk of developing RA [74].	• Daily green tea
• Increase the intake of antioxidants, phytochemicals vitamins and flavonoids	• Antioxidants, phytochemicals, flavonoids and vitamins were suggested to have anti-inflammatory properties [35–39].	• Vegetables, fruits, apple cider vinegar, whole grains contain high amounts of antioxidants, phytochemicals vitamins, and flavonoids. • Daily home-made green juice (made of fruits and green vegetables)

consumption, and daily yogurt and miso as probiotic. It also avoids consumption of processed and red meat, caffeine, dairy products (except yogurt), and vegetables from the solanaceae family. Of note, not all the ingredients and strategies proposed in our ITIS diet are based on interventional diet studies in RA patients. We wanted to introduce ingredients suggested to be beneficial in animal models or other inflammatory diseases as well. Therefore, the design of this diet is intended to give an alternative to non-vegetarian population with higher content of potential anti-inflammatory ingredients than the typical Mediterranean diet.

2. Methods

Patients: Thirty-four adult patients with RA fulfilling the 2010 ACR/EULAR classification criteria for RA, were recruited from the Arthritis Clinics at the University of California at San Diego (UCSD). The study was approved by the UCSD Institutional Review Board. We recruited patients from the two most prevalent populations in our Arthritis Clinics: Hispanic and Caucasian RA patients. For one year, we worked with a total of 20 Hispanic and 14 Caucasian RA patients in collaboration with a nutritionist to put together a 14-day ITIS diet that was feasible and that included our proposed anti-inflammatory/probiotic components (Table 1).

Initial design of the diet: In order to design this first draft, we examined the bibliography relating ingredients and inflammation, and diet intervention in RA patient. Once we decided the strategies and ingredients we wanted to introduce, we designed a Mediterranean-based 7-day draft diet, which also included the main strategies described in Table 1, and was structured as followed: daily green juices in the morning, 3 main meals and 2 snacks.

Diet modifications with RA patients was conducted in four phases: Since our main goal was to design a feasible diet, we worked with several small groups of patients to tailor the diet for higher adherence. The information gathered in the four phases of the study contributed to modify the draft until we built the final diet and instructions. Different patients were recruited for each phase. In Phase I, we evaluated the dietary habits of each patient in the last year in order to gather information about their current diet habits. In Phase II, we gathered information about patient knowledge, accessibility, affordability, and taste preferences of our proposed ingredients. In phase III, we designed a first draft of the diet with patient instructions and asked for patient feedback to assess how accurately patients were able to understand and follow the diet. In phase IV, we conducted a 7-day trial with patient feedback for final adjustments on the diet (Fig. 1). Macro and micro-nutrient composition as well as more details of our ITIS diet is available for interested parties.

3. Results

3.1. Phase I

A representative sample of 5 Hispanic and 5 Caucasian patients were included in this phase. We constructed and distributed a diet habit questionnaire (Additional file 1) in order to elucidate dietary habits of the patients in the last year. The questionnaire contained questions about how frequently (how many times per week) our patients had

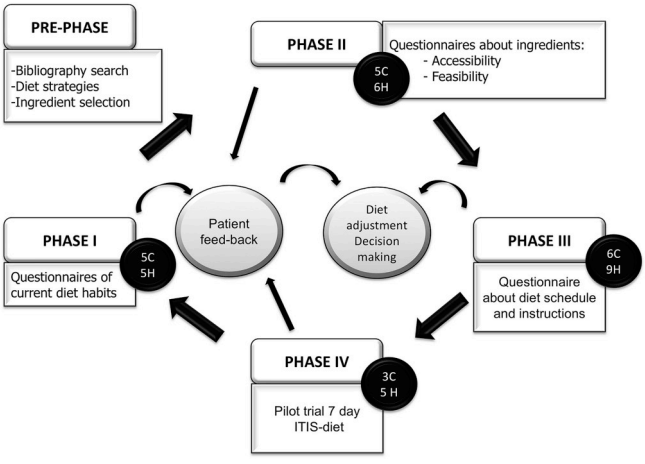

Fig. 1. Flow chart showing the different phases of the design of the ITIS diet. From a draft that included potential anti-inflammatory ingredients described in the scientific literature, in phase I, we got information of current dietary habits, in phase II, we collected information about the ingredients that we wanted to include, in phase III, we requested feedback about the instructions and strategies of our ITIS diet, and in phase IV, a few patients followed the ITIS diet for 7 days. The continuous feedback from our patients helped us make adjustments to the diet and build our final version of the ITIS diet.

consumed meat, eggs, fish, bread, grains, vegetables, mushrooms, legumes, nuts, fruits, sauces, sweets, snacks, soups, and dairy products in the last year. In addition, patients were asked about their drinking habits and food preparation practices, including time invested in cooking. The questionnaire took approximately 1 h to complete, and RA patients filled the questionnaires individually in a designated room at the clinical facilities.

Average frequency of consumption of the ingredients (times per week) of these 10 RA patients are shown in additional file 2. Patient consumption of vegetables, fruits, meat, eggs, fish, grains, legumes and nuts did not differ from our ITIS diet. Of note, red meat was consumed less than once a week among these RA patients. Leeks, onion, peppers, and lettuce were the most consumed vegetables; berries and avocados were the most consumed fruits followed by peaches, nectarines, apricots, oranges, apples, and pears. Enzymatic fruits and ginger were not frequently consumed. Alcohol consumption was low, but they had daily coffee. Patients also reported a high consumption of simple carbohydrates such as cookies and cakes, added sugar, and consumed dairy products almost daily. They did consume yogurt but not miso. They did not frequently add seeds, anti-inflammatory dressings or anti-inflammatory spices in their food. They used olive oil followed by canola oil. Patients mainly steamed or boiled their food, but also fried for longer than 5 min. Though patients mainly prepared their meals at home, pre-cooked food was used frequently.

3.2. Phase II

A total of 6 Hispanic and 5 Caucasian patients were included in this phase. The objective of this phase was to gather information about patient knowledge and assess the affordability and accessibility of the products included in the ITIS diet. We designed a questionnaire that assessed the following categories: familiarity with ingredients, previous consumption of ingredients, knowledge of food and preparation methods, knowledge of where to buy the ingredients, and affordability of the ingredients. The questionnaire took around 30 min to complete and RA patients answered it individually in a designated room at the clinical facilities.

After the questionnaire was administered, we assigned a numeric value based on patient responses: if the response was negative, we assigned 0. If the response was positive, we assigned 100, and if it was doubtful, we assigned 50. Finally, we averaged patient responses for each ingredient and analyzed feasibility of patient use. Responses regarding patient knowledge and accessibility to consumption were averaged for individual ingredients (Additional file 3). We also calculated two final scores: *accessibility* was calculated as the average of the following questions: 'do you know where to buy it?', 'can you buy it near your home?', 'do you know the price?' and 'can you afford it?'. *Knowledge* was calculated as the average of the following questions: 'do you know what it is?', 'do you consume it?' and 'do you know how to cook it?'. If final averages fell below 50 for any category, this was interpreted as poor knowledge or accessibility for that ingredient, and we reconsidered introducing the ingredient and/or reevaluated our strategy for introducing the ingredient.

Additional file 3 shows the results of this questionnaire. Most of the ingredients that we intended to include in our ITIS diet were well-known and easily accepted. All of the fruits, most vegetables, chicken, and nuts, were well-known and accessible. Of note, knowledge and accessibility correlated well for each product; this possibly reflects a relationship between knowing how to use an ingredient and knowing where to buy it at the best price. Notably, products that have been promoted recently in the media, such as ginger and chia seeds, were well-known and accessible to patients.

Several ingredients had a value of <50 in knowledge or accessibility. These ingredients were: rye, tahini, kefir, arugula, turmeric, quinoa, miso, tofu, flaxseed oil, omelets, apple cider vinegar, and sweet potato. Among the ingredients that were poorly accepted, we decided to completely remove kefir, and substituted it with yogurt. Other ingredients such as rye (contained in german bread), sweet potato, arugula shoots, quinoa, apple cider vinegar, and tofu were made optional (but recommended). Ingredient that we deemed critical were left as a mandatory ingredient in the ITIS diet: miso, turmeric, flaxseed oil, and tahini.

We also asked patients if they were willing to avoid some products and/or substitute them for others. Of the patients surveyed, one did not respond to this question, and 9 out of 10 patients agreed to substitute: refined cereals for integral cereals, solanaceae vegetables for green vegetables, trans fatty acids and saturated fatty acids for omega 3 PUFA and MUFA, sugar for stevia or honey, soda drinks for home-made juices, and dairy products for vegetable extracts. 8 out of 10 patients were willing to substitute alcoholic drinks and coffee for green tea, and 6 out of 10 patients agreed to reduce gluten consumption.

Finally, patients were asked if they had access to a blender to determine if they were able to prepare smoothies. All Hispanic patients and 3 of the 4 Caucasian patients had one available at home. Average available time to cook per day was 1.5 h ($\pm$1.03), with a range from 30 min to 3 h. All but one patient responded that they were willing to learn new recipes, and subjects assigned themselves an average of 8.6/10 in their resolution to follow the diet.

3.3. Phase III

9 Hispanic and 6 Caucasian patients were included in phase III. We asked patients for feedback on a final version of the 14-day diet (which included both the diet and pertinent instructions). We focused on whether the diet could be easily understood and completed by patients. Patients were shown the diet and instructions, and after providing necessary clarifications, we asked patients to answer the diet-related questions shown in additional file 4A. Patients responded individually in a designated room at the clinical facilities.

The feedback from this phase is shown in additional file 4B. All patients understood the instructions and overall were not worried about satiety and time to prepare the meals. When patients were asked about the diet schedule, all but 3 indicated that they could adhere to it. 12 patients reported that they would be satiated with the diet, while three patients expressed doubt. We also observed that most patients had sufficient time to prepare breakfast correctly. Though most of the questioned patients did not indicate their cooking habits, those who did, indicated that they often steam, bake, or grill. We did encounter a few complaints on certain aspects of the diet plan. Some patients complained about elimination of dairy products, coffee, and alcohol. Yet, we strongly believe that these products would detrimentally affect inflammation and decided to eliminate them from the 14-day diet. We suggested substituting dairy products with nut extracts like almond milk, and coffee with green tea. Finally, patients asked for more recipe examples to facilitate diet completion.

3.4. Phase IV

We conducted a pilot trial of a 7-day ITIS diet on 5 Hispanic and 3 Caucasian patients in order to get their feedback about following the diet. Patients were provided with turmeric, black pepper, powder ginger, flaxseed oil, apple vinegar, tahini, sesame seeds, miso, chai seeds, flaxseeds, rye bread, oatmeal, almond milk, and olive oil to facilitate their consumption. We had 1-h session with groups of two to three patients to explain the diet and instructions in detail. Sessions were conducted in English or Spanish depending on patient preferences. Patients were instructed to keep a diet diary and were given instructions on how to contact us in case of questions.

We obtained feedback from 4 Hispanic patients; one patient dropped out of the trial. All 3 Caucasian patients completed the 7-diet trial. The Hispanic patients surveyed, except for some exceptions attributed to personal tastes, were able to follow the diet and had no critical

difficulties. Among Caucasian patients, two patients asked for a shopping list to help with the menu and struggled to accomplish the timings and the cooking expectations for the diet. We plan to give more flexibility in the diet schedule for the interventional study.

Final diet design: Table 2 shows the final version of the ITIS diet. For lunch and dinner, three recommended options were given, and patients were able to distribute those throughout the week. These options and guidelines for the patient are described in additional file 5. Macro and micro-nutrient composition as well as more details of our ITIS diet is available to interested parties.

4. Discussion

Though there is some evidence that several foods might be pro-inflammatory while other foods might have anti-inflammatory properties, there are few interventional studies to show their effect in patients affected with diseases whose main symptoms are pain and swelling such as RA. Although Mediterranean and vegetarian diets are beneficial for those suffering from RA, these diets do not include several ingredients shown to be anti-inflammatory in some randomized clinical trials or animal models of arthritis or *in vitro* experiments. Given the complexity and severity of RA, it seems doubtful that a single change in diet, by adding or eliminating one ingredient, would be sufficient to diminish systemic inflammation. Some metanalyses of individual ingredients or probiotics in RA reflect contradictory results or mild effects of those supplements [44,45,61,62]. Instead, a diet that combines several of the suggested strategies to decrease inflammation may represent a more realistic dietician approach for those suffering from the disease. Yet, the patients might adhere better to a small change or addition of just supplements than a complete change in their diet. Thus, our goal was to design a diet that introduced patient's feedback to increase their adherence and feasibility for a future interventional trial.

Patient feedback in the different phases helped us adjust the diet based on knowledge and accessibility of ingredients, and to improve the quality of the instructions. In phase I, we learned that the strategies our ITIS diet contemplated did not differ drastically from the current diet habits of our patients. Our patients mentioned that they had adjusted their habits since they had been diagnosed, either after getting information from nutrition websites, or eliminating some foods they thought were triggering their symptoms. We hope that this will increase the patient adherence to the ITIS diet. Of note, one study showed an association between specific foods and symptoms in RA patients, and they reported that blueberries, fish, and spinach improved RA symptoms, while soda containing sugar and desserts aggravated their symptoms [2].

In phase II, we collected patient feedback about the ingredients that were part of the ITIS diet. To increase the feasibility of our diets, the ingredients that were poorly known or too expensive were either removed, made optional, given more information or provided. Interestingly, some studies have suggested that low socio-economic status has been associated with increased RA morbidity, poorer clinical outcomes, decreased functional ability and reduced quality of life [63]. Although people from lower socio-economic are more likely to smoke, which is a known environmental risk factor for RA, they are also more deficient in certain micronutrients. Of interest, a study from Harvard School of Public Health found that eating a healthy diet (rich in fruits, vegetables, fish, and nuts) cost about $1.50 more per day per person than eating an unhealthy diet (the kind full of processed foods and refined grains) [64]. In phase III, we received feedback about our diet instructions and guideline, and we improved the text for clarity and included more recipes. Finally, in phase IV, a 7-day feasibility trial helped us with the last version of our ITIS diet. Overall, patients were highly motivated and open to trying most of the suggested ingredients. Managing chronic diseases in self-motivated patients with diet and lifestyle changes was shown to be critical to achieve treatment goals in other diseases [65].

The strength of this study is the continuous feedback we got from the community we are planning to treat to build our ITIS diet. Although we expected differences between Hispanic and Caucasian patients given their different socioeconomic status, lifestyle, and accessibility to some stores, our perception was that the diet habits of Hispanic and Caucasian patients were very similar. Additionally, both Caucasians and Hispanics had similar knowledge about ingredients included in the diet. Unfortunately, we were unable to conduct statistical analyses given the small

Table 2
Final version of the ITIS diet.

		Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
7–8 am	SMOOTHIE	Coconut milk, mango, papaya, pineapple	Pear, lemon, yogurt, vanilla, water	Grapes, celery, spinach, cucumber, lime, water	Almond or oat milk, spinach, strawberries, pear, ginger, chia seeds, cinnamon	Spinach, ginger, turmeric, papaya, flaxseeds, banana, water	Papaya, spinach, almond milk, turmeric, chia seeds, honey	Parsley, pineapple, strawberries, water
7–8 am	BREAKFAST	1-2 spoonful of oats with non-dairy milk (oat milk, almond milk or rice milk). Add berries (optional). Green tea infusion.	1-2 corn tortillas, spread with avocado, sesame seeds, and flaxseed oil. Green tea infusion.	1 -2 corn tortillas with tahini (sesame seed extract) with ¼ teaspoon of honey. Green tea infusion	1-2 spoons of oat with non-dairy milk (oat, almond or rice milk. Add berries (optional). Green tea infusion.	1-2 corn tortillas, spread with avocado, sesame seeds, and flaxseed oil. Green tea infusion.	1 -2 corn tortillas with tahini (sesame seed extract) with ¼ teaspoon of honey. Green tea infusion	1-2 corn tortillas, spread with avocado, sesame seeds, and linseed oil. Green tea infusion.
10–11 a.m.	SNACK	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)	Plain yogurt (Chobani Brand, no sugar added)
12-1 pm	LUNCH	OPTION 1: Salad (generous plate) OPTION 2: Grains with vegetables OPTION 3: Legumes with vegetables						
4 p.m.	SNACK	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts	Mango, papaya, pineapple, apple, pear or banana +4 walnuts
6–7 pm	DINNER	OPTION 1: Vegetable soup/cream + protein OPTION 2: Miso soup + baked/steamed/grilled vegetables + protein OPTION 3: Salad + protein						

number or patients in each phase. Second, we provided groceries. Participants received around $100 in specific ingredients that help their consumption. Finally, we also provided detailed instructions and dietary counseling for the participants at the phase IV which together with groceries being provided increased adherence and positive feedback in this pilot phase. This diet is being used in an on-going pilot study to determine their anti-inflammatory effect in pain and joint swelling in RA patients.

Ethical approval and consent to participate

Ethical approval was granted by the Institutional Review Board (IRB) at University of California at San Diego.

Consent for publication

Not applicable.

Availability of supporting data

Not applicable.

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Authors' contributors

Study conception and design: MFB, MAP, RN, SG, and MG. Patients recruitment: FC, RC and MG. Analysis and interpretation of data. MFB, MAP, RC, SG and FC. MG supervised the overall project.

Authors' information

MFB, MAP, FC, RC, RN and MG are of the Department of Medicine University of California San Diego, San Diego, CA, USA; RC and MG are also of the Department of Medicine, Autonomous University of Barcelona, Plaça Cívica, Spain; SG is of the Department of Psychiatry University of California San Diego, San Diego, CA, USA.

Declaration of competing interest

The authors report no conflict of interest.

Acknowledgments

Not applicable.

List of abbreviations

RA	Rheumatoid arthritis
SCFA	Short chain fatty acids
CRP	C reactive protein
FA	Fatty acids
PUFA	polyunsaturated FA
MUFA	monounsaturated FA

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2020.100524.

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