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PROCEEDINGS

# A PERSONALIZED DIET PLAN FOR INFLAMMATORY BOWEL DISEASE. CURRENT EVIDENCE AND FUTURE INSIGHTS

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## ABSTRACT

**The prevalence of inflammatory bowel disease (IBD) has been rising year by year. Crohn's disease (CD) and ulcerative colitis (UC) are increasingly diagnosed in both pediatric and adult populations. Since the early 21st century, IBD has become a global health problem. Despite the advances in medical treatment, clinical remission and mucosal healing are still not achieved in many patients. The cause is likely rooted in the fact that the immune system and microbiome of genetically susceptible, with the environment also playing a role, fail to provide an appropriate response, which subsequently leads to chronic inflammation of the gut. Recently increasing evidence has emerged that one of the major environmental factors that play a role in the onset and course of the disease is the diet. This leads to the conclusion that it can be used as part of the strategy to reduce clinical symptoms and intestinal inflammation.**

**The aim of this article is to analyze the available information in the field of personalized dietary patterns with an accent on their level, focus, and scope. The ever-changing evidence for modifiable dietary approaches will give us the opportunity to walk the path from generic advice on a healthy diet to truly personalized dietary plans tailored to meet the needs of each individual patient with IBD.**

**Keywords:** *personalized diet, IBD, microbiome, precision nutrition*

## INTRODUCTION

Inflammatory bowel diseases (IBDs), a group of diseases of the gastrointestinal tract (GIT), which includes Crohn's disease (CD) and ulcerative colitis (UC), are characterized by significant morbidity and influence negatively the quality of life of the patients due to being unpredictably relapsing-remitting, because of the risk of developing serious complications, the need of frequent hospitalizations, surgical interventions, as well as the application of high-cost therapies. According to the available data, it has been estimated that by 2030 there will be over 7 million individuals suffering from IBD in Europe and the USA (1). Its prevalence by that time will reach more than 0.3% on the territory of North America, Oceania, and various European countries (2,3,4).

The pathogenetic mechanisms of IBD are still not perfectly understood. However, there are presently several hypotheses that focus on the significance of factors related to the environment, such as food antigens, which may impact immune dysregulation and proinflammatory changes in the microbiome of genetically predisposed people. Historically, North America and Europe have been the territories with the highest IBD morbidity rates. A significant increase in IBD in adults as well as childhood IBD has been observed in the last century. In addi-

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tion, IBD has been steadily spreading to the developed countries in the last fifty years.

Inflammatory bowel disease was first described as a separate clinical entity about the end of the 18th century in North America and Western Europe. It was linked to the dawn of the Industrial Revolution. By the beginning of the 20th century, UC was a widely recognized intestinal disorder. The year 1932 saw the publication of a landmark article with a detailed description of regional ileitis while distinguishing it from UC. It was authored by Crohn and his colleagues (6). In the second half of the 20th century, in the industrialized regions in Western Europe and North America, the incidence of CD and UC began to increase rapidly (7,8). According to data from recent studies, the IBD incidence in these endemic areas has become stable unlike the incidence of childhood IBD, which is still increasing (2,4). In the last fifty years, IBD has become a global disease merging erasing the boundaries between the traditional geographic areas and the rest of the world (7–9). In areas historically marked by low IBD incidence, the incidence of UC is rising. It is followed by CD, which, in time, becomes predominant. An identical pattern has been observed in both North America and Northern Europe over the past century.

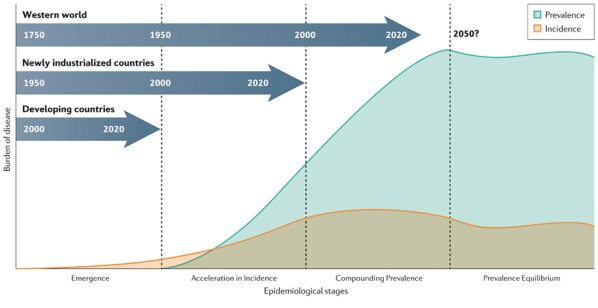


*Fig. 1. Four epidemiological stages in the evolution of IBD. (Source: Kaplan GG, Windsor JW. The four epidemiological stages in the global evolution of inflammatory bowel disease. Nat Rev Gastroenterol Hepatol. 2021;18(1):56-66. doi: 10.1038/s41575-020-00360-x.)*

The increasing incidence of IBD globally clues to the fact that the tendency to approximate the lifestyle and diet to the so-called Western diet has a key role in the pathogenesis of IBD. The Western diet is famous for its high animal fat content, the increased consumption of red and highly processed meat, and is very poor in terms of fiber intake (2–4). Various observational studies have indicated that the increased CD and UC risk is linked to high consumption of fat, polyunsaturated fatty acids (PUFAs), omega-6 fatty acids, and meat (5).

In recent years, the consumption of over-processed food has increased manifold. According to many epidemiological studies, the occurrence of chronic diseases is related to the presence of ultra-processed food (UPF) in people's diet. In murine studies, carboxymethylcellulose and polysorbate-80 (P-80), common emulsifiers, used in non-high concentrations, have been established to lead to low-grade gut inflammation in susceptible mice by altering the microbiome of their gut (11,12).

Numerous studies have suggested that dietary patterns and nutritional factors influence the etiology of IBD. Dietary strategies are therefore needed for the prevention and reversal of these deleterious effects. They also play a role in the therapies for IBD management and it is preferable to have them customized based on each individual patient.

The aim of this article is to present a discussion with a focus on the currently available information and the future development of personalized diets in the treatment of IBD.

Personalized nutrition is a type of approach where individual characteristics, such as age, gender, the state of gut microbiota, or, for example—insulin sensitivity, are used in order to refine the dietary advice and make it more suitable for the specific person. The aim is to achieve longer-lasting and beneficial changes in the patient's dietary behavior (8). All this is partially based on the idea that personalized nutrition counseling will achieve better results than the available generic approaches, thus leading to long-term lifestyle changes (8). In addition, this personalized advice has been shown to be superior to the conventional approach, even in cases where it is delivered by means of an online consultation (9).

Precision nutrition is a step forward and a way to provide individual nutrition advice, which more beneficial to the individual patient. It shows the relationship between the individual person, their phenotype and specific food consumption (8). In order to apply these ideas, newly developed technologies will

continue to gain significance and aid immensely in the decision-making process.

The two main levers are nutrigenetics, which attempts to understand the various phenotypic responses to a particular diet and how they are related to the individual genotype, and nutrigenomics, whose focus is the way nutrients affect gene expression (8–10).

In personalized dietary patterns, three levels emerge:

1. level of customization;
2. customization focus;
3. scope of customization.

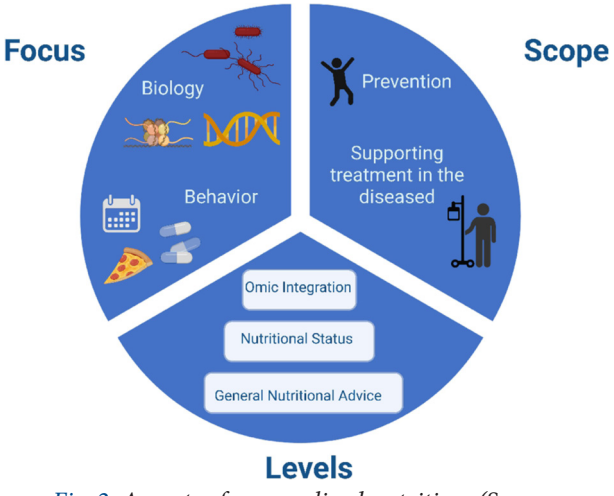


*Fig. 2. Aspects of personalized nutrition. (Source: Wellens J, Vissers E, Matthys C, Vermeire S, Sabino J. Personalized dietary regimens for inflammatory bowel disease: current knowledge and future perspectives. Pharmgenomics Pers Med. 2023;16:15-27. doi: 10.2147/PGPM.S359365.)*

The personalized nutrition model goes through three levels.

- Dietary advice uses the general guidelines, which divide the different population groups by age and sex. This is consistent with the model of the traditional nutritional sciences, whose basis is the average population response to a particular nutrient or diet and can be defined as a primary preventive intervention.
- The next step is to move toward customization with the addition of phenotypic information on the nutritional status of the patient (biochemical and anthropometric information).
- Subsequently, our aim is to achieve a level of personalized nutrition, or precision nutrition, while taking into consideration different aspects, such as genotype, metabolome, or gut microbiome.

Like drugs, some nutrients may interact with and direct the molecular mechanisms that underlie the physiological functions of the body, and can thus help in the formulation of individually tailored dietary advice (10).

### *What is Personalized Nutrition? Is it Underlying Biology or Dietary Behavioral Changes?*

In precision medicine, we are trying to understand differential responses to diets and nutrients based on genetic, epigenetic, and gut microbial profiles. Thus, the degree of biological understanding can guide us to adequate nutritional advice. Improved understanding of how and which specific nutrients and non-nutrient components can trigger an intestinal inflammatory response when encountered with certain specific strains of gut bacteria and turn this into the key to personal advice in IBD. Dietary pattern changes should be made after a thorough analysis of behaviors, preferences, barriers, and goals.

The goals of personalized nutrition include assessing nutritional status and avoiding nutritional deficiencies.

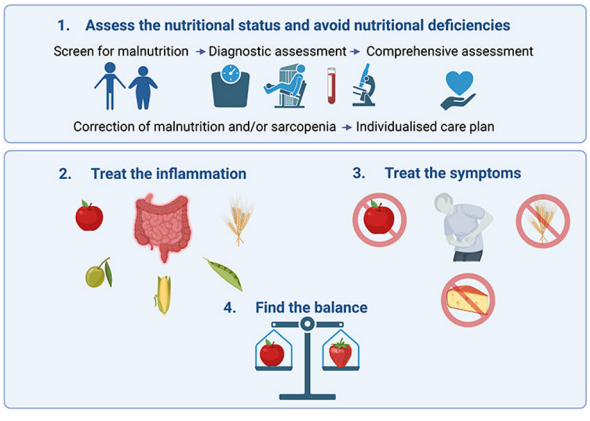


*Fig. 3. Goals of personalized nutrition. (Source: Wellens J, Vissers E, Matthys C, Vermeire S, Sabino J. Personalized dietary regimens for inflammatory bowel disease: current knowledge and future perspectives. Pharmgenomics Pers Med. 2023;16:15-27. doi: 10.2147/PGPM.S359365.)*

Inflammation, in IBD, can lead to malnutrition and loss of weight, which is a result of the decreased food consumption, increased resting energy expenditure, and elevated muscle catabolism. Other factors, including oral ulcers, diarrhea, small bowel resection, or malabsorption, can also result in malnutrition. For this purpose, there are criteria for the assessment of nutritional status summarized by the European Society for Clinical Nutrition and Metabolism (ESPEN) (13).

A large proportion of IBD patients, in addition to manifestations of malnutrition, show a rate of food avoidance (28–89%) and other restrictive dietary behaviors (41–93%), which inevitably impacts their diet-related quality of life (QoL) (11,12).

Despite *lege artis* treatment of intestinal inflammation in IBD, malnutrition leads to very serious and severe complications, such as prolonged hospitalizations, superimposed infections, surgical interventions, venous thromboembolism, and postoperative complications. It appears that a high percentage of patients achieve only partial control of IBD, which poses the question whether changes in the diet can help to control inflammation. The potential to regulate inflammation through alterations to the diet is increasing and is now considered standard of care in the therapy of pediatric CD patients.

Looking back over the years, it appears that various dietary regimens have been tested specifically for IBD patients. These include: Crohn's exclusion diet (CDED), CD-TREAT (dietary treatment for IBD), anti-inflammatory diet (AID), autoimmune protocol diet (AIP), but each still requires further research.

The lack of overlap between diets demonstrated by conflicting ingredients or nutrients is a very good example of how complex dietary interventions are.

In addition, the so-called "allowed" foods are reduced to a short list, which makes it even more challenging for patients to stick to the prescribed diets for a prolonged period of time for a number of reasons such as "taste fatigue" or such linked to certain social aspects. Evaluating patients who responded well to the diet and such who did not would be an interesting ground for conducting a study. As with trials involving drugs, the reason behind the lack of response may remain unresolved and might be related to the phenotypes of a severe disease or previous use of biologics. However, revealing the underlying mechanisms might provide us with clues to offer better personalized dietary advice. Until then, it will remain unclear whether a universal approach is a realistic goal, as a variety of potentially effective diets gives the opportunity to customize a nutrition strategy, which takes into consideration the preferences of the patient and the biological causes once they are fully established.

The genes and molecular pathways, which play a role in nutrient absorption, the daily dietary requirements, and the substance metabolism differ between people. In theory, they can be used in predicting the efficacy of the dietary intervention or nutritional deficiencies. Key in the development of personalized dietary approaches in IBD patients will be the knowledge of different -omic levels, for example genomics or metabolomics (which covers the host's metabolic response to the environment, considering the impact of the gut microbiota).

For example, the PUFA intake may lead to gut inflammation or worsen the CD course, as shown in murine models, and in two cohort studies in humans (14). It is interesting to note that elevated interleukin-8 and TNF expression was observed only in CD patients with impaired glutathione peroxidase 4 (GPX4) expression. This, combined with contradictory information from prospective and randomized control trials, proposes that the inflammatory potential of PUFAs is linked not only to their intake but also to the host's genetic profile (15).

The aforementioned hypothesis is in need of further investigation and, so far, no trial of genetic makeup-based dietary intervention has been conducted.

Along with dietary therapy of inflammation, gastrointestinal symptoms sometimes take a back seat.

A large number of patients with IBD mention that they avoid specific foods or stick to an exclusive diet, thinking that this will alleviate symptoms and reduce the inflammatory episodes. Unfortunately, such dietary choices, which lead to new dietary patterns, are based on personal experience, advice received from other patients, published diet books, even the Internet. This can lead to nutritional defi-

ciencies or compound already significant ones (16–18). Without diminishing the importance of symptoms and QoL, the responsibility of clinicians should be focused on adhering patients toward safe therapy that results in disease control while at best also addressing persistent gastrointestinal complaints. Thus, personalized and patient-centered dietary regimens in IBD should aim to improve disease-related symptoms and (diet-related) QoL while maintaining an anti-inflammatory, disease-controlling effect.

### *Personalized Dietary Regimens. Achievable Strategies in the 21st Century*

A patient's individual response to a specific diet is the result of the interaction between metabolic, environmental, social and genetic factors, which means that different people will have a different response to the same interventions (10). A recent randomized controlled trial including 600 individuals, where the participants adhered to a low-fat diet for 12 months, resulted in weight loss of over 30 kg for some, but others gained over 10 kg. This shows that there is no universal diet, which is effective for everyone, confirming the need of personalized nutrition.

### *Can We Predict the Result of Personalized Diet Regimens?*

Zeevi et al. believe that personalized nutrition is possible if the following combination exists: robust trial designs, appropriate patient data (if necessary, incl. several –omic layers), and sophisticated bioinformatics tools (20).

The role of genetics in IBD has been widely recognized and more than 240 common susceptibility loci have been identified. The importance of these findings is strongly reflected in translational clinical applications (21).

The environmental influences to which an individual is exposed throughout life may be able to complement the genome and explain the difference in heritability that occurs in IBD (22–23).

The gut microbiota has been identified as another important player in the IBD pathogenesis. It is well known that diet is a powerful factor in gut microbial composition and function, and the response of the gut microbiota to dietary therapy is quite different from patient to patient. It is safe to say that despite the small number of clinical trials, most of which are still in their infancy, there are already promising results (19). Research in this area suggests that the microbiome may serve as a predictor of dietary response in IBD and pave the way towards a more individualized approach. More research is certainly needed but, based on these data, the combination of phenotypic data, (epi)genomic data, metabolomics and the gut microbiota will be essential in achieving personalized nutrition in IBD.

## CONCLUSION

The ability to design an ideal diet plan for an individual patient is likely to be more effective in treatment. It would increase compliance as personalized strategies are better perceived by patients and are less restrictive. Significant advances in personalized nutrition and its incorporation into precision health assessments in IBD are expected in the future.

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