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Review

Making Decisions about Dietary Therapy in Inflammatory Bowel Disease

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Abstract: Treatment for inflammatory bowel disease (IBD) deserves an informed shared decision-making process between patient and doctor. IBD spans a spectrum of phenotypes that impact each patient uniquely. While treatment has primarily consisted of medical or surgical therapy, dietary approaches have become increasingly relevant. A majority of patients with IBD use some form of dietary modification, and it is common for patients to do this without their physicians' knowledge. Lack of medical supervision can lead to nutritional deficiencies and a worsening disease state. Some patients work with their medical team to pursue a well-defined exclusion diet as a primary therapy, such as the specific carbohydrate diet, exclusive enteral nutrition, or the Crohn's disease exclusion diet. The motivations to use dietary therapy for IBD remain unclear and the effectiveness has not been definitively established for many approaches. It is necessary for medical providers to be knowledgeable and to foster open communication with their patients in order to ensure the highest likelihood of remission. This review provides an overview of dietary treatment options, the current knowledge about patient motivations for pursuing dietary therapy, and the roles of patient empowerment and patient activation. We outline areas of improvement for the decision-making process.

Keywords: Crohn's disease; dietary therapy; inflammatory bowel disease; nutritional therapy; shared decision-making; ulcerative colitis

1. Introduction

Inflammatory bowel disease (IBD) is a chronic and relapsing condition of multifactorial etiology that responds to a spectrum of therapeutic approaches in varying degrees and durations. Encompassing Crohn's disease (CD), ulcerative colitis (UC), and IBD unclassified (IBD-U), IBD primarily consists of chronic intestinal inflammation, with possible irreversible bowel damage. This disease can become a great burden for patients, causing unpredictable flare-ups; interruption of work or school; cancellation or postponement of plans; and the need for expensive medications, hospitalizations, and potential surgery [1].

The precise etiology of IBD is unknown, but the multifactorial contributions may carry different weights in any given patient's disease. Twin studies have demonstrated a genetic component, with stronger concordance for CD (30–60%) than UC (10%) [2]. Cohort studies have identified specific susceptibility gene loci [3], and in rare cases there is a single causative gene [4]. The proportion of genetic risk has been elusive, and environmental influences likely play a large role in the pathogenesis of the disease. Studies of people immigrating to Westernized countries demonstrate higher incidences of IBD in the new country than in their country of origin [5–8].These findings complement

epidemiological studies that demonstrate the incidence of IBD follows the Westernization of the diet, as in industrialized parts of Asia, where IBD was once rare but is now more common [9].

At the interface of genetic susceptibility and environmental exposure lies the intestinal microbiome interacting with the intestinal mucosal barrier. Gut inflammation can occur when gut bacteria come into contact with the epithelial lining, which can be triggered by diet, for example by emulsifiers present in processed foods [10]. In a mouse model, pro-inflammatory gut bacteria were promoted by a diet high in saturated (but not polyunsaturated) fat, resulting in colitis [11]. The Westernized diet, which is high in saturated fat and processed foods and low in fiber, may contribute to the pathogenesis of IBD, in part through microbiome alterations. Alternately, dietary modifications have the potential to improve the microbial balance and may be used as a therapeutic approach. In fact, exclusive enteral nutrition (EEN) and the specific carbohydrate diet (SCD), both of which have demonstrated changes in intestinal microbial composition in humans [12,13], are widely used treatment approaches in IBD. These dietary interventions have the potential to provide improved disease control and reduce complications, but more rigorous, controlled clinical trials are needed and a large research gap remains regarding dietary treatment for UC [14].

IBD impacts each patient uniquely, with varying phenotypes and severity. While one individual may present with bowel damage necessitating surgery, another may present with general malaise and malnutrition. Patients will have a range of motivations to pursue treatment and a range of preferences pertaining to each treatment option. Goals of treatment may span mucosal healing to symptom relief, and approaches may conflict. Researchers have developed decision-making tools that model an individual patient's response to potential treatments because IBD can impact each individual differently [15]. When making treatment decisions, patients prioritize different aspects of the treatment; some are more willing to accept adverse consequences than others [16], and one's level of regret about those decisions can vary widely [17]. While therapies for IBD are improving, treatment decisions continue to be difficult for patients, and there is increasing need to understand patients' motivations and treatment goals.

The primary forms of treatment for IBD are medication and surgery. Patient preference plays an important role in choosing a treatment plan, and improved treatment adherence and satisfaction occur when the patient feels involved in the decision-making process. While medical therapy for IBD has advanced in recent years, many patients on these medications still experience symptoms and may not achieve remission. Patients often look elsewhere for relief and explore dietary therapy. Animal studies, epidemiological studies, and newly emerging clinical trials have shown a relationship between diet and IBD. However, the details of this relationship remain elusive. With a large number of IBD patients attributing their symptoms to the foods they eat and attempting dietary modifications without formal dietary advice [18–20], it is necessary for physicians to be informed of the safety and efficacy of common dietary approaches. Incorporating this evidence base into a supportive and open decision-making process is crucial to overall treatment success.

2. Dietary Therapy

The industrialization of food and Westernization of dietary practices is suspected to play a major role in the increasing incidence of IBD. For example, in Japan the rising incidence of Crohn's disease is correlated with increased intake of meats and omega-6-polyunsaturated fatty acids and decreased intake of vegetables and omega-3-polyunsaturated fatty acids [21]. With ever-escalating evidence of the diet's role in IBD, several approaches have been pursued to use diet as a therapy in IBD, with varying efficacy and support. Numerous diets for IBD exist, but little evidence exists for most of them [22], and many are accompanied by micronutrient deficiencies and strict lifestyle restrictions [23]. The dietary approaches that have become most prominent include exclusive enteral nutrition (EEN), the Crohn's disease exclusion diet (CDED), and the specific carbohydrate diet (SCD). Less prominent approaches include the low fermentable oligio-, di-, monosaccharides and polyols (FODMAP) diet, the gluten free diet (GFD), a semi-vegetarian diet, the autoimmune protocol diet (AIP), and the recently developed individualized-food-based diet (CD-TREAT).

EEN, a liquid diet typically used for 4–12 weeks, has been used in adults with complicated CD [24], and is as effective as corticosteroids for induction in pediatric Crohn's disease. Furthermore, it promotes mucosal healing without serious side effects [25,26]. This approach is used as a first line treatment in pediatric Crohn's disease in Asia, Europe, and Canada [27–29], but there are great variations in regional use [30]. The composition of the formula does not appear to matter [25]. Its effectiveness is hypothesized to result from carbohydrate monotony [31] and the formula's impact on the gut microbiome [32]. Despite its effectiveness and safety, adherence is difficult [33–35]. The poor taste and smell of the formula, along with the habituation and enjoyment of eating whole foods, create a challenging treatment regimen. Even with these drawbacks, EEN has been shown to increase the quality of life of patients who follow it [36]. With its perceived difficulty, an attractive alternative is partial enteral nutrition (PEN). In this diet, a patient consumes a base of 25–60% caloric requirement by formula and eats either a restricted or unrestricted food-based diet for the remainder. While PEN is less restrictive than EEN and can be used in maintaining remission [37], it has been shown to be inferior to EEN in inducing remission, promoting mucosal healing and improving the quality of life of IBD patients [38].

While EEN is considered to be the gold standard in pediatric IBD nutritional therapy, there is a promising and more feasible alternative—the Crohn's disease exclusion diet (CDED). This is a whole-food diet in which the patient removes gluten, milk products, gluten-free baked goods, animal fats, emulsifiers, and all canned or processed food from their diet, while increasing their intake of fruits and vegetables [39]. This diet, accompanied by PEN, has been shown to induce clinical remission in children and young adults with Crohn's disease [39–41]. A recent comparison of CDED with PEN to EEN followed by an unrestricted diet suggested that a restricted whole-food approach may achieve better clinical outcomes and foster better adherence than EEN [42]. Another promising alternative to EEN is the individualized food-based diet CD-TREAT. In this novel treatment, individuals consume a personalized whole-food diet that attempts to replicate what EEN does to one's gut and microbiome [43].

In the most well-known diet for IBD, the specific carbohydrate diet, one cannot eat any carbohydrates besides monosaccharides. This restriction is based upon the hypothesis that complex carbohydrates and legumes are poorly absorbed in gastrointestinal disease, resulting in unabsorbed substrates travelling through the small bowel undigested, leading to the promotion of bacterial overgrowth and fermentation. The byproducts are theorized to contribute to the chronic inflammation in IBD [44]. Case series and cohort studies have long shown positive outcomes of this diet [45], yet this diet has not been shown to promote mucosal healing [46]. Future research of increasing rigor is necessary to demonstrate efficacy.

Other diets in IBD that have gained attention include the low-FODMAP diet and the gluten-free diet. The low-FODMAP diet is an effective therapy for irritable bowel syndrome [47], and an excessive intake of FODMAPs may lead to increased intestinal permeability, which is a potential predisposing factor to Crohn's disease [48]. The GFD eliminates gluten, a protein found in wheat, barley, rye, and many processed foods, from the diet. It is used in IBD for symptomatic relief, with some overlapping principles with SCD and the low-FODMAP diet, but also because there is an increased risk of Celiac disease in patients with IBD [49]. The perceived benefits of SCD, the low-FODMAP diet, and the GFD have led to the hypothesis that carbohydrate variation contributes to immune dysfunction, mucosal barrier defects, and gut microbiota changes, with carbohydrate monotony being the potential unifying force providing dietary benefits in IBD [31]. Red and processed meats are also potential causes and aggravators of IBD. There have been few controlled clinical trials investigating the role of meat in IBD, and there is conflicting evidence from the studies that exist [50,51]. Additionally, the autoimmune protocol diet is a newer exclusion diet that focuses on eliminating processed foods and increasing the intake of specific fruits and vegetables. This diet has shown promise in one small study, but additional research is needed [52]. Currently, there is not enough scientific evidence to support any diet for patients with UC in terms of improving symptom management, mucosal healing, or quality of life.

3. Medical Therapy

Pursuit of dietary therapy in IBD occurs in the context of the current standard of medical and surgical approaches. In the last twenty years, significant advances in the fields of immunology and genetics have brought biologic therapies to the forefront of medication-based approaches to IBD, with conventional corticosteroids, aminosalicylates, and immunomodulators continuing to play a role.

Corticosteroids, which suppress the immune system and reduce inflammation, are employed broadly in the treatment of IBD and are primarily effective for induction. Prolonged therapy is associated with numerous complications, including a wide range of adverse side effects—weight gain, moon facies, adrenal suppression, hypertension, hirsutism, bone demineralization, increased risk of infections, poor wound healing, and changes in behavior [53]. The immunosuppressants thiopurines (6-mercaptopurine and azathioprine) and methotrexate, which inhibit cell growth integral to inflammatory pathways, are effective maintenance agents and have taken on an important role as an adjunctive therapy with anti-TNF agents to mitigate antibody formation [54]. However, the use of these medications have been controversial given their serious adverse effects and toxicity, including oncogenic potential, myelosuppression, and hepatotoxicity [55]. Methotrexate also has teratogenic effects, which limits its use in women with child-bearing potential [54].

Tumor necrosis factor alpha inhibitor (anti-TNF) agents, such as infliximab and adalimumab, are the most commonly used biologic agents and are one of the most effective treatments in inducing and maintaining clinical remission of patients with IBD, especially among patients with steroid-refractory or steroid-dependent IBD [56]. They are generally well-tolerated but require monitoring for adverse reactions, such as increased risk of infections, development of anti-drug antibodies, infusion reactions, psoriasis, upper respiratory infections, lymphoma, and demyelinating disease [57]. Newer biologics, anti-integrins, and anti-interleukins have shown early promise as safer options, although long-term data remain unknown [58]. Janus kinase (JAK) inhibitor therapies have safety profiles that remain under investigation [58].

4. Motivations to Choose Dietary Therapy

Due to the various side effects and costs combined with the real possibility of treatment failure with available medications, many patients with IBD search for relief outside of conventional medicine. Dietary therapy is often considered a complementary and alternative medicine (CAM). CAM broadly encompasses all medical practices and products that are not a part of standard care. CAM use, including dietary products, is common in IBD [59,60]. Increased symptoms throughout the course of treatment is a primary driver of a patient's pursuit of CAM [61]. With currently available medical therapy, the rates of durable remission range from 40–60%, depending on disease phenotype and severity, and a substantial proportion of patients with IBD have recurrent symptoms. Patients may also be motivated to pursue alternative approaches because they perceive a loss of control [62] and seek to improve their quality of life [36].

Many individuals with IBD attribute flare-ups and symptoms to the food they eat [19,63], which is consistent among various geographic locations (Table 1). One study found that 66% of patients with IBD restrict themselves from a specific food due to worsening of symptoms [20]. This study further found that 48% of participants reported diet could be an initiating cause of their IBD, and 28% reported diet had a more important role in their disease than medication [20]. Out of that study population nearly half reported that they had not received any formal dietary advice. Another survey that asked 300 patients with IBD about their eating habits found that 76.5% eliminated triggering foods from their diet and 56.7% increased their intake of foods they felt were beneficial [64]. In a large case–control study that investigated what individuals with IBD were eating, researchers found those with IBD to be consuming less alcohol, popcorn, legumes, nuts, seeds, deep-fried foods, and deli meat, and instead consuming more sugar-sweetened beverages than their controls [65]. In a separate study, 39% of patients with IBD had tried some sort of special diet, and many of these diets were unbalanced [62]. With manipulation of diet as a central focus of many patients, it is crucial to provide all patients with IBD a comprehensive nutrition education.

Table 1. Summary of the literature regarding dietary habits of IBD patients. IBD—inflammatory bowel disease, CD—Crohn's disease, UC—ulcerative colitis.

IBD Subtype	Location of Study	Main Findings	Author, Year
n = 244, 72.5% CD, 27.5% UC	Lorraine, France	The majority of participants avoided a certain food and felt food plays an important role in their disease and chance of relapse	Zallot et al., 2013 [19]
n = 400, 39% CD, 51% UC	Manchester, UK	The majority of participants associated certain foods as being triggers and would deny themselves a food to avoid a relapse	Limdi et al., 2016 [20]
n = 446, 100% CD	New Zealand	There is great variation in what patients with CD consider a beneficial or detrimental food	Triggs et al., 2010 [63]
n = 294, 50.3% CD, 49.7% UC	The Netherlands	The majority of participants considered food to play a larger role in disease management and outcome than medication	de Vries et al., 2019 [64]
n= 256, 52% CD, 48% UC	Manitoba, Canada	The majority of participants did avoid certain foods and their dietary intake demonstrated deficiencies	Vagianos et al., 2016 [65]
n = 42, 60% CD, 36% UC, 4% Indeterminate IBD	Germany	Nearly all participants felt restricted in their eating behavior and several felt unsupported by their doctors	Palant et al., 2015 [66]
n = 4, 67% CD, 33% UC	Australia	The majority of participants consider diet important to their IBD; advice given to the patients about diet was diverse, inadequate, and poorly followed	Holt et al., 2016 [67]

Perceived risk is a central factor to selecting a treatment course. Many patients attempt dietary therapy because they do not see any harm in it. However, dietary therapies may carry several unintended consequences. EEN, which requires the patient to consume no solid foods for at least a month, entails sacrificing one of the main pleasures of life and limits the social aspect of eating food together. All whole-food approaches require some form of elimination and they have yet to demonstrate the efficacy proven in rigorous clinical trials of medical therapies. Additionally, dietary restriction increases risk of nutritional deficiencies. Some common food restrictions with IBD are gluten and milk products. Both of these food groups contain necessary nutrients and require thoughtful supplementation if not already present in the diet [68]. Patients not eating a certain food group must work closely with a dietician to ensure they are meeting all of their nutritional needs [69,70]. It is imperative that any dietary approach in IBD be pursued in conjunction with a medical team to identify and mitigate these risks.

5. Fostering Informed Choice of Dietary Therapy

Patients often pursue dietary therapy without the input or knowledge of their medical team. In a survey on CAM use in IBD patients, only 62% of the patients using complementary medicines told their physician [60]. The two main reasons the participants chose not to disclose this information to their doctors were that they (1) were nervous their doctor would reject the use of complementary medications and (2) viewed their physician as uneducated about complementary medications [60]. It is important for patients to perceive their gastroenterologist as someone they can talk to about any possible treatment option and whom they feel is on their team.

Patients report their gastroenterologist as the top source of information for IBD treatment, followed by the internet [71]. However, only 56% of patients consider their information needs to be covered [71]. With the gastroenterologist as the primary information source, it is crucial for gastroenterologists to provide clear information and to be perceived as someone with whom a patient can disclose all treatment concerns. In a survey of newly diagnosed IBD patients, 80% reported it was very important to know how changes to their diet can impact active disease; however, a majority of these patients reported they did not receive adequate information about dietary influences [72]. Furthermore, patients may lack trust in gastroenterologists' knowledge of dietary therapy. In a

population of patients with IBD using diet as treatment without their doctor's knowledge, 82% had not informed their doctor, primarily because they had not been asked [73].

When patients do not feel their information needs are covered by their physician, they explore the internet [74]. A study investigating the quality of web-based information in IBD found that 57% of the websites sampled were of fair to poor quality [75]. Despite this poor quality information, more than half of IBD patients use the internet to inform treatment decisions [75]. This can lead to patients becoming misinformed and making uneducated treatment decisions that can worsen their disease state. An improved and collaborative doctor–patient approach can increase treatment adherence and patient satisfaction [76].

Decision aids may help physicians communicate complicated medical information in a patient-oriented manner. Decision aids are created to be used alongside the physician's direct communication and further educate patients on the risks and benefits of a specific treatment. These aids are important because decisions based on standard counseling alone may lack key information. In a study investigating perceptions of the risks and benefits of infliximab, 37% of respondents incorrectly did not think infliximab was associated with an increase of lymphoma [77]. Additionally, when the researchers created a hypothetical drug with the same risks and benefits of infliximab, 64% of participants reported they would not take the medication [77]. Decision aids in the medical setting have been shown to increase patients' knowledge and awareness of treatment choices [78]. Furthermore, decision aids have been shown to improve risk perceptions and decrease feelings of being uninformed and indecisive, leading to increased satisfaction with their decision [79]. Decision aids have been increasingly developed for IBD. The offered aids address a variety of scenarios and exist in multiple formats, including paper aids, web-based programs, and video aids.

6. Patient Empowerment, Activation, and Preferences

Patient empowerment programs are one method to increased patient participation in the decision-making process. Empowering patients to take an active role in making medical decisions may have synergistic effects, with increased control of other aspects of their life positively affecting disease management [80]. Patient empowerment programs are structured interventions that include elements of goal setting, problem-solving, and seeking social support. Guiding principles include making it clear that a chronic disease is a shared responsibility and that finding the right treatment approach will involve experimentation and negotiation. This approach necessarily entails the physician being comfortable with relinquishing some control and acknowledging that scientific knowledge should be balanced with individual priorities. The physician furthermore needs to provide a feeling of security for the patient and create a motivation to learn [81]. Patient empowerment programs have shown promise to improve disease management and psychosocial challenges of living with type 2 diabetes [82] and increase the patient's sense of control and self-efficacy in the context of orthopedic conditions [83] and cancer [84].

While patient empowerment is viewed as a process that impacts many aspects of that patient's life, patient activation focuses on the behavior that pertains to their disease and treatment [85]. Patient empowerment ideally leads to an activated patient who is able to manage their condition and collaborate with health care providers. Patient activation programs aim to increase patients' involvement in their discussions with their doctor [86]. Modalities include face-to-face interventions, videos, written materials, audiotapes, and interactive programs. The main goal of each intervention is to increase patient knowledge so that they can be more active in the decision-making process, and most patients achieve this goal [87].

Once confident and open dialogue between patient and physician has been initiated, the patient may benefit from completing a preference analysis to clarify and delineate each parties' treatment goals. Many treatment decisions in IBD are preference-sensitive, and a preference analysis may provide a clearer treatment choice. A preference analysis is a qualitative or quantitative assessment that investigates which specific attributes of a treatment are most important to patients, how much those attributes are valued, and how patients weigh different treatment attributes [88]. Multiple methods exist, and some, such as "discrete choice experiments," may be more beneficial for IBD;

however, further study is necessary [89]. Studies that have used this method to learn more about patient preference in IBD include investigating patient drug preference [90], patient willingness to accept serious adverse consequences in exchange for medication efficacy [91], and patient preference for 5-ASA (5-aminosalicylate) treatment in UC [92]. In each of these studies, patients made a series of discrete choices specific to their condition, and the analysis of these choices delineated how those patients weigh specific risks and benefits. Patient empowerment programs and preference analyses specific to dietary therapy would better allow a patient and their provider to make a shared decision regarding treatment.

7. Shared Decision-Making

While the numerous treatment options for an individual with IBD provide choice, they also create uncertainty and confusion when making a treatment decision. Shared decision-making (SDM) has become central to this process. Shared decision-making is defined as a bi-directional exchange of information and collaborative decision-making based on patient or family preference and physician expertise [93,94]. This process should not be used in every treatment scenario. There are three main criteria for the application of SDM in a medical decision: the best treatment option is unclear, the stakes are not minimal, and the decision is "preference-sensitive" [95]. "Preference-sensitive" indicates that there is more than one appropriate treatment choice, and that a choice ultimately depends on how a person (a patient, family member, or provider) values benefit versus harm [96].

The exchange of information is at the center of SDM. Prior research has focused on the communication originating from the physician. While most patients say they would like to hear every treatment risk, no matter how rare, physicians are concerned that this does not leave enough time to communicate expected treatment outcomes and other important information [97]. General principles for effective communication of treatment risks have been developed. It is best to utilize multiple modalities to deliver information, not only verbally, but also with visual aids, including both static graphs and charts and dynamic videos. Risks should be presented with a narrow time span, and in the form of frequencies instead of percentages. The data should have a balance of positive and negative framing [98]. Additionally, the patient's numeracy and literacy skills should be considered when communicating this information. While knowing more about one's disease has been shown to improve treatment adherence and sense of control [99,100], an alternate perspective, known as "fuzzy trace theory", argues that the small details included in communicating risks make it more confusing for patients [101]. Instead, through this theory, physicians should offer a "gist", as bottom line representations are more likely to affect reasoning accuracy than verbatim background information in these settings [101]. The appropriate communication method for any specific encounter may depend on several factors, including the immediacy of the decision, the preferences of the patient, and the skillset of the provider.

The second and equally important part of the SDM process is the patient communicating their own treatment goals and preferences to the physician. Several barriers exist, including lack of confidence in knowledge base about the disease, feeling intimidated by the expertise of the doctor, a lack of face time with the doctor, and uncertainty about their goals and preferences. This aspect of the conversation would benefit greatly from the development of nutritional-therapy-focused patient empowerment programs, preference analyses, and decision aids (Table 2). These tools would allow for a more informed discussion on dietary therapies in IBD, in which the patient is more confident advocating for the treatment they want and the provider is equipped with the tools necessary to guide that conversation.

Table 2. Approaches to improve decisions about dietary therapy in IBD.

Type of Approach	Benefits	Available Tools	Unmet Needs
Patient Empowerment and Patient Activation	Increased control of life, group support, increased confidence, larger contribution to the decision-making process	Proven programs for a variety of chronic diseases	Patient empowerment or activation program specific to dietary therapy in IBD. *Existing programs may be applied to IBD generally*
Preference Analysis	Determination of perceived values of risk and reward, enhancement of certainty of preferences based on analysis, detection of similarities or differences in patient and provider preferences	Multiple IBD preference analyses exist in various formats	Preference analysis tool specific to dietary therapy in IBD. *Existing IBD preference analyses will guide decisions for dietary therapy*
Shared Decision-Making	Patient feels valued, improved transparency and fosters ongoing open communication, improved adherence and confidence in treatment	Well-developed guidance for process in IBD, multiple IBD decision aids in multiple formats	Decision aids for dietary therapy in IBD. *SDM process in IBD should be applied, in part, to dietary therapy presently*

While nutritional therapy may not yet satisfy the "unclear best option" criteria for a true SDM process in most forms of IBD, the incorporation of dietary therapy in the decision-making process is critical, given the preponderance of patients pursuing it. Utilizing principles of SDM can help patients avoid potential harm (both from pursuing dietary therapy to the exclusion of medical therapy and the inherent risks of dietary restriction) and encourage a more comprehensive and inclusive approach to treatment.

8. Conclusions

Due to emerging evidence of the efficacy of dietary therapies and to ensure the highest likelihood of remission, it is necessary for medical providers to engage in an informed decision-making process with their patients. Shared decision-making should be employed when a well-defined dietary therapy satisfies the level of efficacy for an "unclear best option". As the field becomes further defined, patients will continue to pursue dietary modifications. The development of decision aids, preference analyses, and patient empowerment programs focused on dietary therapy in IBD will advance the opportunities to incorporate dietary approaches in an effective and safe manner. These developments must be paired with the ongoing and increasing rigorous research on the efficacy of dietary therapy in IBD.

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References

1. Nurmi, E.; Haapamäki, J.; Paavilainen, E.; Rantanen, A.; Hillilä, M.; Arkkila, P. The burden of inflammatory bowel disease on health care utilization and quality of life. *Scand. J. Gastroenterol.* **2013**, *48*, 51–57.
2. Halfvarson, J.; Bodin, L.; Tysk, C.; Lindberg, E.; Järnerot, G. Inflammatory bowel disease in a Swedish twin cohort: A long-term follow-up of concordance and clinical characteristics. *Gastroenterology* **2003**, *124*, 1767–1773.
3. Jostins, L.; Ripke, S.; Weersma, R.K.; Duerr, R.H.; McGovern, D.P.; Hui, K.Y.; Lee, J.C.; Schumm, L.P.; Sharma, Y.; Anderson, C.A.; et al. Host–microbe interactions have shaped the genetic architecture of inflammatory bowel disease. *Nature* **2012**, 491, 119–124.
4. Crowley E.; Warner N.; Pan J.; Sam, K.; Elkadri, A.; Fiedler, K.; Foong, J.; Turinsky, A.L.; Bronte-Tinkew, D.; Zhang, S.; et al. Prevalence and clinical features of inflammatory bowel diseases associated with

monogenic variants, identified by whole-exome sequencing in 1000 children at a single center. *Gastroenterology* **2020**, *158*, 2208–2220.
5. Barreiro-de Acosta M.; Alvarez Castro A.; Souto R.; Iglesias M.; Lorenzo, A.; Dominguez-Muñoz J.E. Emigration to western industrialized countries: A risk factor for developing inflammatory bowel disease. *J. Crohn's Colitis* **2011**, *5*, 566–569.
6. Li X.; Sundquist J.; Hemminki, K.; Sundquist, K. Risk of inflammatory bowel disease in first- and second-generation immigrants in SwedenA nationwide follow-up study. *Inflamm. Bowel Dis*. **2011**, *17*, 1784–1791.
7. Damas O.M.; Avalos D.J.; Palacio A.M.; Gomez, L.; Quintero, M.A.; Deshpande, A.R.; Sussman, D.A.; McCauley, J.L.; Lopez, J.; Schwartz, Seth J.; et al. Inflammatory bowel disease is presenting sooner after immigration in more recent US immigrants from Cuba. *Aliment. Pharmacol. Ther*. **2017**, *46*, 303–309.
8. Benchimol, E.I.; Mack D.R.; Guttmann, A.; Nguyen, G.C.; To, T.; Mojaverian, N.; Quach, P.; Manuel, G.D. Inflammatory bowel disease in immigrants to Canada and their children: A population-based cohort study. *Am. J. Gastroenterol*. **2015**, *110*, 553–563.
9. Ng S.C.; Shi H.Y.; Hamidi, N.; Underwood, F.E.; Tang, W.; Benchimol, E.I.; Panaccione, R.; Ghosh, S.; Wu, J.C.Y.; Chan, F.K.L.; et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: A systematic review of population-based studies. *Lancet* **2018**, *390*, 2769–2778.
10. Chassaing B.; Koren O.; Goodrich J.K.; Poole, A.C.; Srinivasan, S.; Ley, R.E.; Gewirtz, A.T. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. *Nature* **2015**, *519*, 92–96.
11. Devkota S.; Wang Y.; Musch M.W.; Leone, V.; Fehlner-Peach, H.; Nadimpalli, A.; Antonopoulos, D.A.; Jabri, B.; Chang, E.B. Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in Il10 −/− mice. *Nature* **2012**, *487*, 104–108.
12. Jones, C.M.A.; Connors, J.; Dunn, K.A; Bielawski, J.P.; Comeau, A.M.; Langille, M.G.I.; van Limbergen, J. Bacterial taxa and functions are predictive of sustained remission following exclusive enteral nutrition in pediatric Crohn's disease. *Inflamm. Bowel Dis*. **2020**, *26*, 1026–1037.
13. Suskind, D.L.; Cohen, S.A.; Brittnacher, M.J.; Wahbeh, G.; Lee, D.; Shaffer, M.L.; Braly, K.; Hayden, H.S.; Klein, J.; Gold, B.; et al. Clinical and fecal microbial changes with diet therapy in active inflammatory bowel disease. *J. Clin. Gastroenterol*. **2018**, *52*, 155–163.
14. Levine, A.; Sigall Boneh, R.; Wine, E. Evolving role of diet in the pathogenesis and treatment of inflammatory bowel diseases. *Gut* **2018**, *67*, 1726–1738.
15. Siegel, C.A.; Siegel, L.S.; Hyams, J.S.; Kugathasan, S.; Markowitz, J.; Rosh, J.R.; Leleiko, N.; Mack, D.R.; Crandall, W.; Evans, J. Real-time tool to display the predicted disease course and treatment response for children with Crohn's disease. *Inflamm. Bowel Dis*. **2011**, *17*, 30–38.
16. Hazlewood, G.S.; Pokharel, G.; Deardon, R.; Marshall, D.A.; Bombardier, C.; Tomlinson, G.; Ma, C.; Seow, C.H.; Panaccione, R.; Kaplan, G.G.; et al. Patient preferences for maintenance therapy in Crohn's disease: A discrete-choice experiment. *PLoS ONE* **2020**, *15*, e0227635.
17. Lipstein, E.A.; Lovell, D.J.; Denson, L.A.; Kim, S.C.; Spencer, C.; Ittenbach, R.F.; Britto, M.T. High levels of decisional conflict and decision regret when making decisions about biologics. *J. Pediatr. Gastroenterol. Nutr*. **2016**, *63*, e176–e181.
18. Gu, P.; Feagins, L.A. Dining with inflammatory bowel disease: a review of the literature on diet in the pathogenesis and management of IBD. *Inflamm. Bowel Dis.* **2020**, *26*, 181–191.
19. Zallot, C.; Quilliot, D.; Chevaux, J.-B.; Peyrin-Biroulet, C.; Gueant-Rodriguez, R.M.; Freling, E.; Collet-Fenetrier, B.; Williet, N.; Ziegler, O.; Bigard, M.; et al. Dietary beliefs and behavior among inflammatory bowel disease patients. *Inflamm. Bowel Dis*. **2013**, *19*, 66–72.
20. Limdi, J.K.; Aggarwal, D.; McLaughlin, J.T. Dietary practices and beliefs in patients with inflammatory bowel disease. *Inflamm. Bowel Dis*. **2016**, *22*, 164–170.
21. Shoda, R.; Matsueda, K.; Yamato, S.; Umeda, N. Epidemiologic analysis of Crohn disease in Japan: Increased dietary intake of n-6 polyunsaturated fatty acids and animal protein relates to the increased incidence of Crohn disease in Japan. *Am. J. Clin. Nutr*. **1996**, *63*, 741–745.
22. Limketkai, B.N.; Iheozor-Ejiofor, Z.; Gjuladin-Hellon, T.; Parian, A.; Matarese, L.E.; Bracewell, K.; MacDonald, J.K.; Gordon, M.; Mullin, G.E. Dietary interventions for induction and maintenance of remission in inflammatory bowel disease. *Cochrane Database Syst Rev*. **2019**, *2*, CD012839.
23. Hou, J.K.; Lee, D.; Lewis, J. Diet and inflammatory bowel disease: Review of patient-targeted recommendations. *Clin. Gastroenterol. Hepatol*. **2014**, *12*, 1592–600.

24. Sharma, S.; Gupta, A.; Kedia, S.; Agarwal, S.; Singh, N.; Goyal, S.; Jain, S.; Gupta, V.; Sahu, P.; Vuyyuru, S.K.; et al. Efficacy and tolerability of exclusive enteral nutrition in adult patients with complicated Crohn's disease. *Intest. Res.* **2020**, doi:10.5217/ir.2019.09172.
25. Swaminath, A.; Feathers, A.; Ananthakrishnan, A.N.; Falzon, L.; Li Ferry, S. Systematic review with meta-analysis: Enteral nutrition therapy for the induction of remission in paediatric Crohn's disease. *Aliment. Pharmacol. Ther*. **2017**, *46*, 645–656.
26. Borrelli, O.; Cordischi, L.; Cirulli, M.; Paganelli, M.; Labalestra, V.; Uccini, S.; Russo, P.M.; Cucchiara, S. Polymeric diet alone versus corticosteroids in the treatment of active pediatric Crohn's disease: A randomized controlled open-label trial. *Clin. Gastroenterol. Hepatol*. **2006**, *4*, 744–753.
27. Issokson, K. Living on liquids: Surviving and thriving on exclusive enteral nutrition. *Am. J. Gastroenterol*. **2017**, *112*, 1491–1492.
28. Ruemmele, F.M.; Veres, G.; Kolho, K.L.; Griffiths, A.; Levine, A.; Escher, J.C.; Amil Dias, J.; Barabino, A.; Braegger, C.P.; Bronsky, J.; et al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J. Crohns Colitis*. **2014**, *8*, 1179–207.
29. Mack, D.R.; Benchimol, E.I.; Critch, J.; deBruyn, J.; Tse, F.; Moayyedi, P.; Church, P.; Deslandres, C.; El-Matary, W.; Huynh, H.; et al. Canadian association of gastroenterology clinical practice guideline for the medical management of pediatric luminal Crohn's disease. *Gastroenterology* **2019**, *157*, 320–348.
30. Lawley, M.; Wu, J.W.; Navas-López, V.M.; Huynh, H.Q.; Carroll, M.W.; Chen, M.; Medvedev, P.; Day, A.S.; Hussey, S.; Sigall-Boneh, R.; et al. Global variation in use of enteral nutrition for pediatric Crohn disease. *J. Pediatr. Gastroenterol. Nutr*. **2018**, *67*, e22–e29.
31. Britto, S.; Kellermayer, R. Carbohydrate monotony as protection and treatment for inflammatory bowel disease. *J. Crohns Colitis*. **2019**, *13*, 942–948.
32. Kaakoush, N.O.; Day, A.S.; Leach, S.T.; Lemberg, D.A.; Nielsen, S.; Mitchell, H.M. Effect of exclusive enteral nutrition on the microbiota of children with newly diagnosed Crohn's disease. *Clin. Transl. Gastroenterol*. **2015**, *6*, e71.
33. Narula, N.; Dhillon, A.; Zhang, D.; Sherlock, M.E.; Tondeur, M.; Zachos, M. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst. Rev.* **2018**, *4*, CD000542.
34. Wall, C.L.; McCombie, A.; Mulder, R.; Day, A.S.; Gearry, R.B. Adherence to exclusive enteral nutrition by adults with active Crohn's disease. ease. *J. Hum. Nutr. Diet*. **2020**.
35. Mehta, P.; Pan, Z.; Furuta, G.T.; Kim, D.Y.; de Zoeten, E. Parent perspectives on exclusive enteral nutrition for the treatment of pediatric Crohn's disease. *J. Pediatr. Gastroenterol. Nutr.* **2020**, doi:10.1097/MPG.0000000000002847.
36. Afzal, N.A.; Zaag-Loonen, H.J.V.D.; Arnaud-Battandier, F.; Davies, S.; Murch, S.; Derkx, B.; Heuschkel, R.; Fell, J.M. Improvement in quality of life of children with acute Crohn's disease does not parallel mucosal healing after treatment with exclusive enteral nutrition. *Aliment. Pharmacol. Ther*. **2004**, *20*, 167–172.
37. Yang, H.; Feng, R.; Li, T.; Xu, S.; Hao, X.; Qiu, Y.A.; Chen, M. Systematic review with meta-analysis of partial enteral nutrition for the maintenance of remission in Crohn's disease. *Nutr. Res.* **2020**, *81*, 7–18.
38. Lee, D.; Baldassano, R.N.; Otley, A.R.; Albenberg, L.; Griffiths, A.M.; Compher, C.; Chen, E.Z.; Li, H.; Gilroy, E.; Nessel, L.; et al. Comparative effectiveness of nutritional and biological therapy in North American children with active crohn's disease. *Inflamm. Bowel Dis*. **2015**, *21*, 1786–1793.
39. Sigall-Boneh, R.; Pfeffer-Gik, T.; Segal, I.; Zangen, T.; Boaz, M.; Levine, A. Partial enteral nutrition with a Crohn's disease exclusion diet is effective for induction of remission in children and young adults with Crohn's disease. *Inflamm. Bowel Dis*. **2014**, *20*, 1353–1360.
40. Sigall Boneh, R.; Sarbagili Shabat, C.; Yanai, H.; Chermesh, I.; Ben Avraham, S.; Boaz, M.; Levine, A.; et al. Dietary therapy with the Crohn's disease exclusion diet is a successful strategy for induction of remission in children and adults failing biological therapy. *J. Crohns Colitis*. **2017**, *11*, 1205–1212.
41. Sigall Boneh, R.; Van Limbergen, J.; Wine, E.; Assa, A.; Shaoul, R.; Milman, P.; Cohen, S.; Kori, M.; Peleg, S.; On, A.; et al. Dietary therapies induce rapid response and remission in pediatric patients with active Crohn's disease. *Clin. Gastroenterol. Hepatol*. **2020**, doi. 10.1016/j.cgh.2020.04.006.
42. Levine, A.; Wine, E.; Assa, A.; Boneh, R.S.; Shaoul, R.; Kori, M.; Cohen, S.; Peleg, S.; Shamaly, H.; On, A.; et al. Crohn's disease exclusion diet plus partial enteral nutrition induces sustained remission in a randomized controlled trial. *Gastroenterology* **2019**, *157*, 440–450.e8.

43. Svolos, V.; Hansen, R.; Nichols, B.; Quince, C.; Ijaz, U.Z.; Papadopoulou, R.T.; Edwards, C.A.; Watson, D.; Alghamdi, A.; Brejnrod, A.; et al. Treatment of active Crohn's disease with an ordinary food-based diet that replicates exclusive enteral nutrition. *Gastroenterology* **2019**,*156*, 1354–1367.e6.
44. Hwang, C.; Ross, V.; Mahadevan, U. Popular exclusionary diets for inflammatory bowel disease: The search for a dietary culprit. *Inflamm. Bowel Dis*. **2014**, *20*, 732–741.
45. Suskind, D.L.; Wahbeh, G.; Cohen, S.A.; Damman, C.J.; Klein, J.; Braly, K.; Shaffer, M.; Lee, D. Patients perceive clinical benefit with the specific carbohydrate diet for inflammatory bowel disease. *Dig. Dis. Sci*. **2016**, *61*, 3255–3260.
46. Wahbeh, G.T.; Ward, B.T.; Lee, D.Y.; Giefer, M.J.; Suskind, D.L. Lack of mucosal healing from modified specific carbohydrate diet in pediatric patients with Crohn disease. *J. Pediatr. Gastroenterol. Nutr*. **2017**, *65*, 289–292.
47. Halmos, E.P.; Power, V.A.; Shepherd, S.J.; Gibson, P.R.; Muir, J.G. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology* **2014**, *146*, 67–75.e5.
48. Gibson, P.R.; Shepherd, S.J. Personal view: Food for thought—western lifestyle and susceptibility to Crohn's disease. The FODMAP hypothesis. *Aliment. Pharmacol. Ther*. **2005**, *21*, 1399–1409.
49. Tursi, A.; Giorgetti, G.M.; Brandimarte, G.; Elisei, W. High prevalence of celiac disease among patients affected by Crohn's disease. *Inflamm. Bowel Dis*. **2005**, *11*, 662–666.
50. Chiba, M.; Abe, T.; Tsuda, H.; Sugawara, T.; Tsuda, S.; Tozawa, H.; Fujiwara, K.; Imai, H. Lifestyle-related disease in Crohn's disease: Relapse prevention by a semi-vegetarian diet. *World J. Gastroenterol*. **2010**, *16*, 2484–2495.
51. Albenberg, L.; Brensinger, C.M.; Wu, Q.; Gilroy, E.; Kappelman, M.D.; Sandler, R.S.; Lewis, J.D.; et al. A diet low in red and processed meat does not reduce rate of Crohn's disease flares. *Gastroenterology* **2019**, *157*, 128–136.e5.
52. Konijeti, G.G.; Kim, N.; Lewis, J.D.; Groven, S.; Chandrasekaran, A.; Grandhe, S.; Diamant, C.; Singh, E.; Oliveira, G.; Wang, X.; et al. Efficacy of the autoimmune protocol diet for inflammatory bowel disease. *Inflamm Bowel Dis*. **2017**, *23*, 2054.
53. Scribano, M.L. Adverse events of IBD therapies. *Inflamm. Bowel Dis*. **2008**, *14* (Suppl. 2), S210–S211.
54. Herfarth, H.H.; Kappelman, M.D.; Long, M.D.; Isaacs, K.L. Use of methotrexate in the treatment of inflammatory bowel diseases. *Inflamm. Bowel Dis*. **2016**, *22*, 224–233.
55. Axelrad, J.E.; Roy, A.; Lawlor, G.; Korelitz, B.; Lichtiger, S. Thiopurines and inflammatory bowel disease: Current evidence and a historical perspective. *World J. Gastroenterol*. **2016**, *22*, 10103–10117.
56. Danese, S.; Vuitton, L.; Peyrin-Biroulet, L. Biologic agents for IBD: Practical insights. *Nat. Rev. Gastroenterol. Hepatol*. **2015**, *12*, 537–545.
57. Shivali, U.N.; Sharratt, C.L.; Thomas, T.; Smith, S.C.L.; Iacucci, M.; Moran, G.W.; Ghosh, S.; Bhala, N. Review article: Managing the adverse events caused by anti-TNF therapy in inflammatory bowel disease. *Aliment. Pharmacol. Ther*. **2019**, *49*, 664–680.
58. Chudy-Onwugaje, K.O.; Christian, K.E.; Farraye, F.A.; Cross, R.K. A state-of-the-art review of new and emerging therapies for the treatment of IBD. *Inflamm. Bowel Dis*. **2019**, *25*, 820.
59. Koning, M.; Ailabouni, R.; Gearry, R.B.; Frampton, C.M.A.; Barclay, M.L. Use and predictors of oral complementary and alternative medicine by patients with inflammatory bowel disease: A population-based, case–control Study. *Inflamm. Bowel Dis*. **2013**, *19*, 767–778.
60. Hilsden, R.J.; Scott, C.M.; Verhoef, M.J. Complementary medicine use by patients with inflammatory bowel disease. *Am. J. Gastroenterol*. **1998**, *93*, 697–701.
61. Kamp, K.J.; Brittain, K. Factors that influence treatment and non-treatment decision making among individuals with inflammatory bowel disease: An integrative review. *Patient* **2018**, *11*, 271–284.
62. Moser, G.; Tillinger, W.; Sachs, G.; Maier-Dobersberger, T.; Wyatt, J.; Vogelsang, H.; Lochs, H.; Gangl, A. Relationship between the use of unconventional therapies and disease-related concerns: A study of patients with inflammatory bowel disease. *J. Psychosom. Res*. **1996**, *40*, 503–509.
63. Triggs, C.M.; Munday, K.; Hu, R.; Fraser, A.G.; Gearry, R.B.; Barclay, M.L.; Ferguson, L.R. Dietary factors in chronic inflammation: Food tolerances and intolerances of a New Zealand Caucasian Crohn's disease population. *Mutat. Res. Fund. Mol. Mechan. Mutagen*. **2010**, *690*, 123–138.
64. de Vries, J.H.M.; Dijkhuizen, M.; Tap, P.; Witteman, B.J.M. Patient's dietary beliefs and behaviours in inflammatory bowel disease. *Dig. Dis. Sc.i* **2019**, *37*, 131–139.

65. Vagianos, K.; Clara, I.; Carr, R.; Graff, L.A.; Walker, J.R.; Targownik, L.E.; Lix, L.M.; Rogala, L.; Miller, N.; Bernstein, C.N.; et al. What are adults with inflammatory bowel disease (IBD) eating? A closer look at the dietary habits of a population-based Canadian IBD cohort. *J. Parenter. Enteral. Nutr*. **2016**, *40*, 405–411.
66. Palant, A.; Koschack, J.; Rassmann, S.; Lucius-Hoene, G.; Karaus, M.; Himmel, W. "And then you start to loose it because you think about Nutella": The significance of food for people with inflammatory bowel disease—a qualitative study. *BMC Gastroenterology* **2015**, *15*, 93.
67. Holt, D.Q.; Strauss, B.J.; Moore, G.T. Patients with inflammatory bowel disease and their treating clinicians have different views regarding diet. *J. Hum. Nutr. Diet*. **2017**, *30*, 66.
68. Jowett, S.L.; Seal, C.J.; Phillips, E.; Gregory, W.; Barton, J.R.; Welfare, M.R. Dietary beliefs of people with ulcerative colitis and their effect on relapse and nutrient intake. *Clin. Nutr*. **2004**, *23*, 161–170.
69. Vagianos, K.; Bector, S.; McConnell, J.; Bernstein, C.N. Nutrition assessment of patients with inflammatory bowel disease. *J. Parenter. Enter. Nutr*. **2007**, *31*, 311–319.
70. Imes, S.; Pinchebeck, B.; Thomson, A. Diet counseling modifies nutrient intake of patients with Crohn's disease. *J. Am. Diet. Assoc*. **1987**, *87*, 457–462.
71. Catalán-Serra, I.; Huguet-Malavés, J.M.; Mínguez, M.; Torrella, E.; Paredes, J.M.; Vazquez, N.; Ramirez, J.J.; Calvo, F.; Nos, P.; Gutierrez, A.; et al. Information resources used by patients with inflammatory bowel disease: Satisfaction, expectations and information gaps. *Gastroenterol. Hepatol*. **2015**, *38*, 355–363.
72. Bernstein, K.I.; Promislow, S.; Carr, R.; Rawsthorne, P.; Walker, J.R.; Bernstein, C.N. Information needs and preferences of recently diagnosed patients with inflammatory bowel disease. *Inflamm. Bowel Dis*. **2011**, *17*, 590–598.
73. Hung, A.; Kang, N.; Bollom, A.; Wolf, J.L.; Lembo, A. Complementary and alternative medicine use is prevalent among patients with gastrointestinal diseases. *Dig. Dis. Sci*. **2015**, *60*, 1883–1888.
74. Van der Marel, S.; Duijvestein, M.; Hardwick, J.C.; van den Brink, G.R.; Veenendaal, R.; Hommes, D.W.; Fidder, H.H. Quality of web-based information on inflammatory bowel diseases. *Inflamm. Bowel Dis*. **2009**, *15*, 1891–1896.
75. Cima, R.R.; Anderson, K.J.; Larson, D.W.;Dozois, E.J.; Hassan, I.; Sandborn, W.J.; Loftus, E.V.; Pemberton, J.H. Internet use by patients in an inflammatory bowel disease specialty clinic. *Inflamm. Bowel Dis*. **2007**, *13*, 1266–1270.
76. DiMatteo, M.R.; Reiter, R.C.; Gambone, J.C. Enhancing medication adherence through communication and informed collaborative choice. *Heal. Commun*. **1994**, *6*, 253–265.
77. Siegel, C.A.; Levy, C.L.; MacKenzie, T.A.; Sands, B.E. Patient perceptions of the risks and benefits of infliximab for the treatment of inflammatory bowel disease. *Inflamm. Bowel Dis*. **2008**, *14*, 1–6, doi:10.1002/ibd.20283.
78. Austin, C.A.; Mohottige, D.; Sudore, R.L.; Smith, A.K.; Hanson, L.C. Tools to promote shared decision making in serious illness: A systematic review. *JAMA Intern. Med*. **2015**, *175*, 1213–1221.
79. Stacey, D.; Légaré, F.; Lewis, K.; Barry, M.J.; Bennett, C.L.; Eden, K.B.; Holmes-Rovner, M.; Llewellyn-Thomas, H.; Lyddiatt, A.; Thomson, R.; et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database System. Rev*. **2017**, *4,* doi:10.1002/14651858.CD001431.pub5
80. Labonte, R. Health promotion and empowerment: Reflections on professional practice. *Heal. Educ. Q.* **1994**, *21*, 253–268.
81. Aujoulat, I.; d'Hoore, W.; Deccache, A. Patient empowerment in theory and practice: Polysemy or cacophony? *Patient Educ. Couns.* **2007**, *66*, 13–20.
82. Pibernik-Okanovic, M.; Prasek M.; Poljicanin-Filipovic T.; Pavlic-Renar I.; Metelko, Z. Effects of an empowerment-based psychosocial intervention on quality of life and metabolic control in type 2 diabetic patients. *Patient Educ. Couns*. **2004**, *52*, 193–199.
83. Pellino, T.; Tluczek, A.; Collins, M.; Trimborn, S. Increasing self-efficacy through empowerment: Preoperative education for orthopaedic patients. *Orthop. Nurs*. **1998**, *17*, 48–51, 54–59.
84. Davison, B.J.; Degner, L.F. Empowerment of men newly diagnosed with prostate cancer. *Cancer Nurs*. **1997**, *20*, 187–196.
85. Fumagalli, L.P.; Radaelli, G.; Lettieri, E.; Bertele', P.; Masella, C. Patient empowerment and its neighbours: Clarifying the boundaries and their mutual relationships. *Heal. Policy* **2015**, *119*, 384–394.
86. Kiesler, D.J.; Auerbach, S.M. Optimal matches of patient preferences for information, decision-making and interpersonal behavior: Evidence, models and interventions. *Patient Educ. Couns*. **2006**, *61*, 319–341.

87. Harrington, J.; Noble, L.M.; Newman, S.P. Improving patients' communication with doctors: A systematic review of intervention studies. *Patient Educ. Couns*. **2004**, *52*, 7–16.
88. Van Overbeeke, E.; Janssens, R.; Whichello, C.; Bywall, K.S.; Sharpe, J.; Nikolenko, N.; Phillips, B.S.; Guiddi, P.; Pravettoni, G.; Vergani, L.; et al. Design, conduct, and use of patient preference studies in the medical product life cycle: A multi-method study. *Front. Pharmacol*. **2019**, *10*, 1395.
89. Bewtra, M.; Johnson, F.R. Assessing patient preferences for treatment options and process of care in inflammatory bowel disease: A critical review of quantitative data. *Patient* **2013**, *6*, 241–255.
90. Lichtenstein, G.R.; Waters, H.C.; Kelly, J.; McDonald, S.S.; Zanutto, E.L.; Hendricks, D.; Rahman, M.I. Assessing drug treatment preferences of patients with Crohn's disease. *Patient-Center Outcome Res*. **2010**, *3*, 113–123.
91. Johnson, F.R.; Ozdemir, S.; Mansfield, C.; Hass, S.; Miller, D.W.; Siegel, C.A.; Sands, B.E. Crohn's disease patients' risk-benefit preferences: Serious adverse event risks versus treatment efficacy. *Gastroenterology* **2007**, *133*, 769–779.
92. Hodgkins, P.; Swinburn, P.; Solomon, D.; Yen, L.; Dewilde, S.; Lloyd, A. Patient preferences for first-line oral treatment for mild-to-moderate ulcerative colitis: A discrete-choice experiment. *Patient* **2012**, *5*, 33–44.
93. Gabe, J.; Olumide, G.; Bury, M. 'It takes three to tango': A framework for understanding patient partnership in paediatric clinics. *Soc. Sci. Med*. **2004**, *59*, 1071–1079.
94. Dodds, C.M.; Britto, M.T.; Denson, L.A.; Lovell, D.J.; Saeed, S.; Lipstein, E.A. Physicians' perceptions of shared decision making in chronic disease and its barriers and facilitators. *J. Pediatr*. **2016**, *171*, 307–309.e2.
95. Siegel, C.A. Making therapeutic decisions in IBD: The role of patients. *Curr. Opin. Gastroenterol*. **2009**, 25, 334–338.
96. O'Connor, A.M.; Wennberg, J.E.; Legare, F.;Llewellyn-Thomas Hilary, A.; Moulton Benjamin, W.; Sepucha Karen, R.; Sodano Andrea, G.; King Jaime, S. Toward the "tipping point": Decision aids and informed patient choice. *Heal. Aff*. **2007**, *26*, 716–725.
97. Siegel, C.A. Review article: Explaining risks of inflammatory bowel disease therapy to patients. *Aliment. Pharmacol. Ther*. **2011**, *33*, 23–32.
98. Fagerlin, A.; Ubel, P.A.; Smith, D.M.; Zikmund-Fisher, B.J. Making numbers matter: Present and future research in risk communication. *Am. J. Heal. Behav*. **2007**, *31*, S47–S56.
99. Hill, J.; Bird, H.; Johnson, S. Effect of patient education on adherence to drug treatment for rheumatoid arthritis: A randomised controlled trial. *Ann. Rheum. Dis*. **2001**, *60*, 869–875.
100. M'Imunya, J.M.; Kredo, T.; Volmink, J. Patient education and counselling for promoting adherence to treatment for tuberculosis. *Cochrane Database Syst. Rev*. **2012**, *5*.
101. Reyna, V.F. A theory of medical decision making and health: Fuzzy trace theory. *Med. Decis. Mak*. **2008**, *28*, 850–865.