Microbiome, Gut and Systemic Health: New Frontiers in Personalised Nutrition

Benjamin Brown

Therapeutic Diets and Food for Gut Health: Benefits, Risks and Personalisation

4:15-5:00pm

An event by: Nutritional Medicine Institute

Platinum sponsors: regenerus labs VIRIDIAN Effective | Ethical | Pure pure encapsulations

1

Therapeutic Diets and Food for Gut Health: *Benefits, Risks* and *Personalisation*

Nutritional Medicine Institute

2

Affiliations and disclosures

Director, the Nutritional Medicine Institute

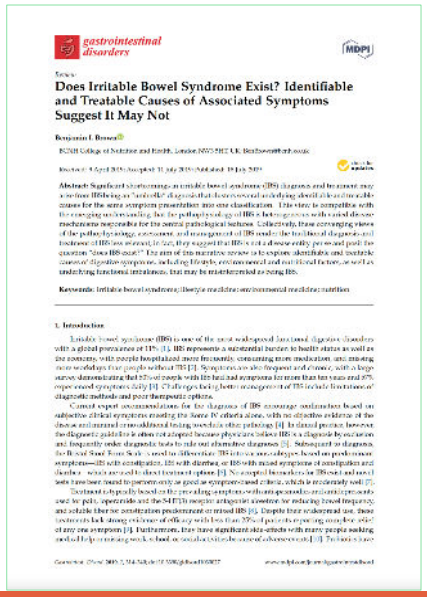
I am a consultant for Pure Encapsulations. I have no other relevant conflicts of interest to disclose.

3

One disease, or many?

"Significant shortcomings in irritable bowel syndrome (IBS) diagnosis and treatment may arise from **IBS being an "umbrella" diagnosis that clusters several underlying identifiable and treatable causes** for the same symptom presentation into one classification."

Gastrointest. Disord. 2019, *1*(3), 314-340


gastrointestinal disorders

MDPI

Review

Does Irritable Bowel Syndrome Exist? Identifiable and Treatable Causes of Associated Symptoms Suggest It May Not

Benjamin I. Brown

4

One diet, or many?

"Up to date, **dietary treatments of the IBS have neither been personalized nor diagnosed with sufficient scientific evidence**. They have mostly been treated using 'one-size-fits-all' approaches."

Clin Nutr ESPEN. 2023 Oct;57:96-105.


Clinical Nutrition ESPEN

A personalized management approach in disorders of the irritable bowel syndrome spectrum

Wolfgang J. Schnedl, Simon Michaelis, Harald Mangge, Dietmar Enko

ARTICLE INFO

SUMMARY

1. Introduction

Footer

5

One way to personalise, or many?

"Identifying predictors of response to dietary therapy is an important goal as **management could be tailored to the individual to target specific dietary components**, and thereby reduce the level of dietary restriction necessary."

Neurogastroenterol Motil. 2018 Jan;30(1). doi: 10.1111/nmo.13238.


WILEY

REVIEW ARTICLE

Dietary therapies for functional bowel symptoms: Recent advances, challenges, and future directions

C. J. Tuck | S. J. Vanner

Abstract

1 | INTRODUCTION

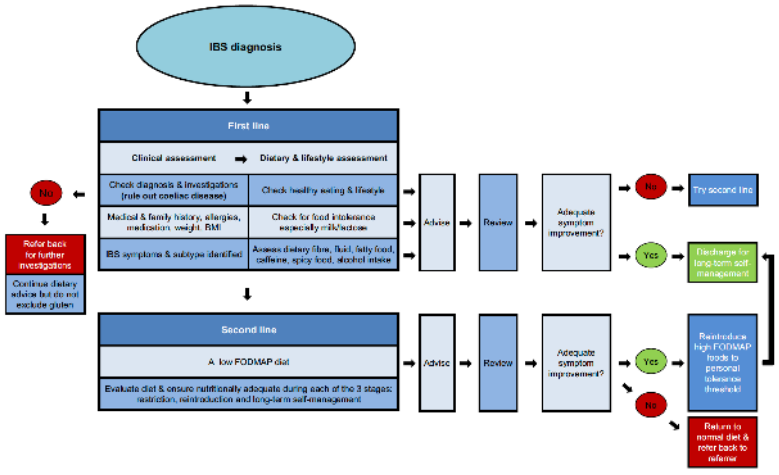
Footer

6

TRADITIONAL DIET

7

Irritable bowel syndrome dietary algorithm



J Hum Nutr Diet. 2016 Oct;29(5):549-75.

8

Key studies evaluating dietary therapies head-to-head

Lead author	Year	Study design	Study duration	Total number of participants	Comparator diets	Outcome
Bohn.	2015	RCT	4 weeks	75 IBS patients (Rome III)	TDA and LFD	No difference in clinical responders between TDA and LFD (50% vs 46%, $p = 0.72$)
Eswaran.	2016	RCT	4 weeks	92 IBS-D patients (Rome III)	mNICE and LFD	No difference in adequate symptom relief between mNICE and LFD (41% vs 52%, $p = 0.31$)
Zahedi.	2017	RCT	6 weeks	110 IBS-D patients (Rome III)	General dietary advice and LFD	LFD significantly improved overall gastrointestinal symptom scores, stool frequency and consistency compared to generalised dietary advice ($p < 0.001$, $p < 0.001$ and $p = 0.003$, respectively)
Paduano.	2019	Prospective study	4 weeks	42 IBS patients (Rome IV)	LFD, GFD and Mediterranean diet	LFD, GFD and Mediterranean diet showed the same efficacy in reducing disease severity ($p < 0.01$)
Goyal.	2021	RCT	16 weeks	101 IBS-D patients (Rome IV)	TDA and LFD	Higher proportion of responders on LFD compared to TDA at both week 4 (63% vs 41%, $p = 0.0448$) and week 16 (53% vs 31%, $p = 0.0274$)
Rej.	2022	RCT	4 weeks	101 IBS patients (Rome IV)	TDA, LFD and GFD	No difference in clinical response between TDA, LFD and GFD (42% vs 55% vs 58%, $p = 0.43$)

BMC Med. 2022 Sep 13;20(1):287.

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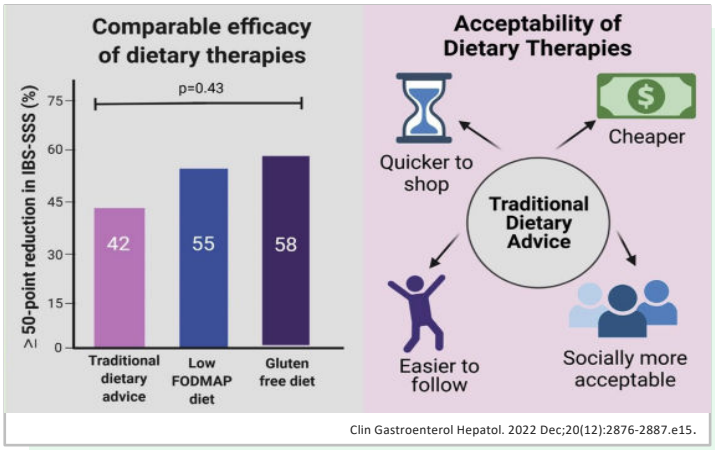
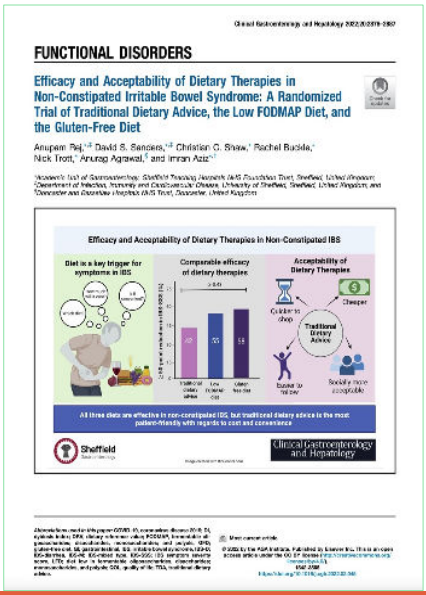
9

Traditional vs. Low FODMAP vs. gluten free



Clin Gastroenterol Hepatol. 2022 Dec;20(12):2876-2887.e15.


FUNCTIONAL DISORDERS

Efficacy and Acceptability of Dietary Therapies in Non-Constipated Irritable Bowel Syndrome: A Randomized Trial of Traditional Dietary Advice, the Low FODMAP Diet, and the Gluten-Free Diet

Anupam Rej, David S. Sanders, Christian C. Shaw, Rachel Buckle, Nick Trott, Anurag Agrawal, and Imran Aziz

Efficacy and Acceptability of Dietary Therapies in Non-Constipated IBS

Sheffield

Clinical Gastroenterology and Hepatology

National Medicine Institute

10

Traditional dietary advice

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Traditional dietary advice	Recommendations include regular meals, adequate fluids, restrict caffeine, alcohol, fizzy drinks, limit fat, gas producing foods (e.g., onions, beans), fiber, resistant starch, spicy foods, and fruit, increase soluble fiber.	Head-to-head comparisons suggest similar efficacy to other dietary approaches (GFD, LFD) with better acceptance.	N/A	N/A

See supplementary file for references.

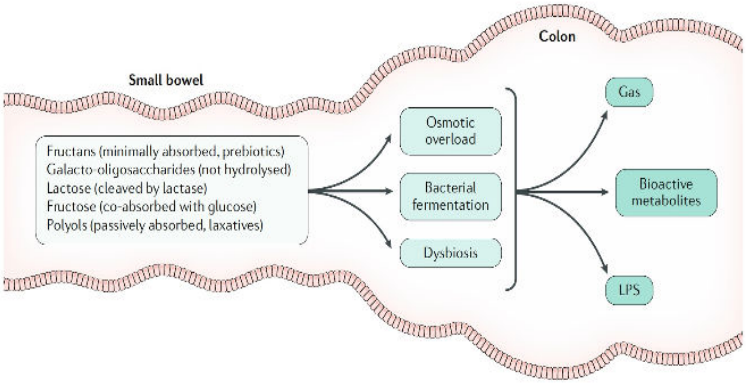
11

LOW FODMAP DIET

12

Mechanisms by which FODMAPs might cause IBS symptoms

Fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) might cause irritable bowel syndrome (IBS) symptoms via osmotic overload, bacterial fermentation or dysbiosis. LPS, lipopolysaccharide.



Nat Rev Gastroenterol Hepatol. 2020 Jul;17(7):406-413.

13

Predicting who will benefit

"Due to the complexity of the low FODMAP diet and knowing that **approximately a third of people with IBS will be non-responders,** it is pertinent to identify whether a certain symptom profile or a biomarker can predict response."

Proc Nutr Soc. 2023 Jul 7:1-11.


Proceedings of the Nutrition Society

Conference on 'Architecture of food: Processing, structure and health'
Symposium two: Changing dietary patterns and health

The low FODMAP diet in clinical practice: where are we and what are the long-term considerations?

Miranda C. E. Lomer

14

Low FODMAP diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Low FODMAP diet	A diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) present in foods including certain grains, fruit, vegetables, legumes and sweeteners. The diet consists of three phases: a period of FODMAP restriction, reintroduction of individual food items to determine tolerance, and personalisation to create a modified FODMAP-containing diet based on individual tolerance.	The LFD reduces global symptoms and has been found to be generally more effective than traditional dietary advice.	Microbiome	Microbiome signatures, including a 'pathogenic' profile and 'dysbiosis index,' may predict response to diet in some, but not all studies. Relationships between dysbiosis and symptom improvement are contradictory.
			Faecal and urine metabolites	Pattern of 15 volatile organic compounds predicted response to diet with good accuracy, while faecal propionate, cyclohexanecarboxylic acid esters, and urine metabolite profile also predicted clinical response.

See supplementary file for references.

15

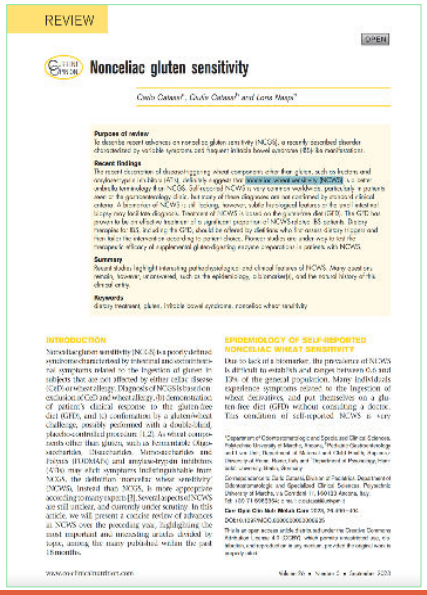
GLUTEN FREE DIET

16

Nonceliac wheat sensitivity

"From a clinical point of view, the overlap with IBS is a challenging feature of nonceliac wheat sensitivity (NCWS) that is currently the focus of intense clinical research. **The possibility to personalize the dietary treatment of IBS can improve the quality of life of a large number of patients** affected with this common disorder."

Curr Opin Clin Nutr Metab Care. 2023 Sep 1;26(5):490-494.


REVIEW

OPEN

Nonceliac gluten sensitivity

Carlo Catassi*, Giulia Catassi* and Lena Maya*

Purpose of review

Recent findings

Summary

Keywords

INTRODUCTION

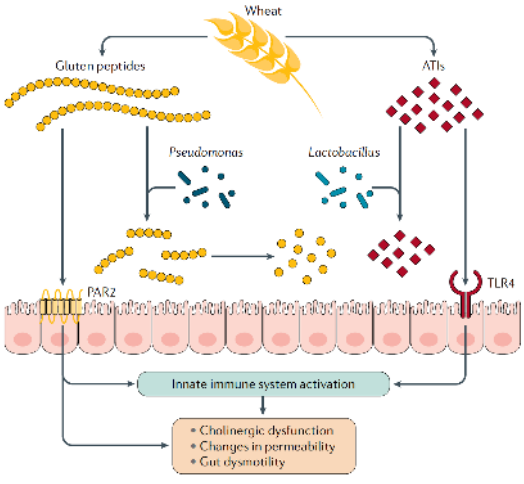
EPIDEMIOLOGY OF SELF-REPORTED NONCELIAC WHEAT SENSITIVITY

Nat Rev Gastroenterol Hepatol. 2020 Jul;17(7):406-413.

17

Mechanisms by which wheat might cause IBS symptoms

Certain small intestinal bacteria, such as Pseudomonas, produce elastases that have proteolytic activity against gluten, which contributes to overall gluten degradation. However, this elastase activity is also associated with gluten- independent, protease-activated receptor 2 (PAR2)- mediated upregulation of inflammatory pathways. Similarly, amylase tryptase inhibitors (ATIs; proteins found in wheat) induce an innate immune response by activation of the Toll- like receptor 4 (TLR4) pathway. Interestingly, ATIs are degraded by Lactobacillus. IBS, irritable bowel syndrome.



18

Gluten-free diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Gluten-free diet	Complete exclusion of wheat, rye, and barley from the diet independent of wheat allergy and celiac disease (non-celiac gluten sensitivity), assessing clinical response and response to gluten challenge.	Gluten elimination has been shown to reduce symptoms, and blinded gluten challenge to aggravate symptoms. A GFD showed comparative efficacy to an LFD or traditional Mediterranean diet.	HLA-DQ2 and HLA-DQ8	Predicted greater reduction in symptoms of depression and improvements in vitality, but not GI symptoms.
			Antigliadin antibodies	Predicted greater reductions in symptoms, particularly diarrhoea.
			Confocal laser endomicroscopy	Poor diagnostic accuracy.

See supplementary file for references.

19

ELIMINATION DIETS

20

I'm on an elimination diet.

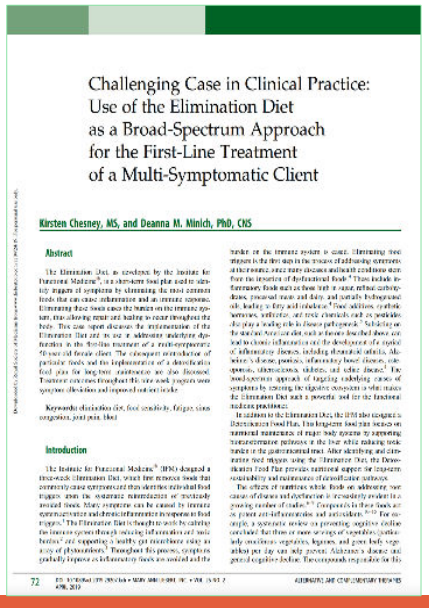
I eat food, then I eliminate it.

21

Empirical elimination diets

"This case report demonstrates the importance of optimal nutrition as the first line of treatment for a client with multiple and severe symptoms. **Upon the elimination of inflammatory and immune-stimulating foods** [Elimination Diet, Institute of Functional Medicine], **this client experienced sudden and lasting improvement in her symptoms**."

Alternative and Complementary Therapies. Apr 2019.72-76.



Challenging Case in Clinical Practice: Use of the Elimination Diet as a Broad-Spectrum Approach for the First-Line Treatment of a Multi-Symptomatic Client

Kirsten Chesney, MS, and Deanna M. Minich, PhD, CNS

Abstract

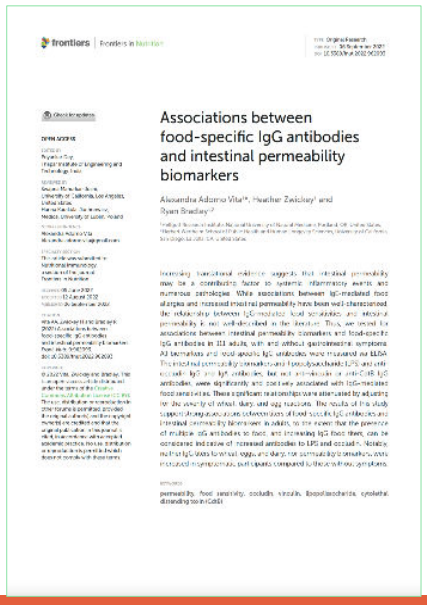
Introduction

22

Testing clinical utility unresolved

"The results of this study support **strong associations between titers of food-specific IgG antibodies and intestinal permeability biomarkers in adults**, to the extent that the presence of multiple IgG antibodies to food, and increasing IgG food titers, can be considered indicative of increased antibodies to LPS and occludin. Notably, neither IgG titers to wheat, eggs, and dairy, nor permeability biomarkers, were increased in symptomatic participants compared to those without symptoms."

Front Nutr. 2022 Sep 6;9:962093.



frontiers | Frontiers in Nutrition

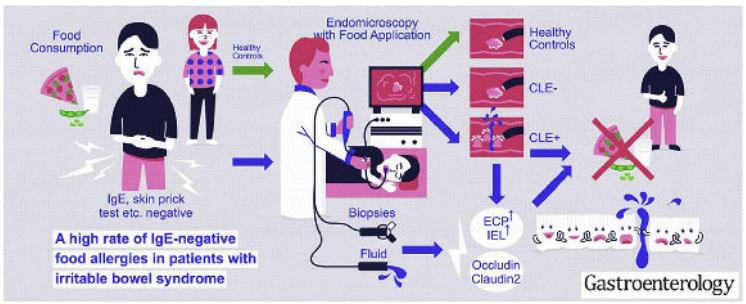
Associations between food-specific IgG antibodies and intestinal permeability biomarkers

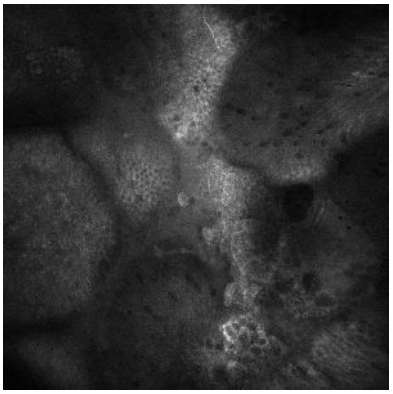
Alexandra Adams Vital*, Heather Zwickey† and Ryan Bradley†

National Medicine Institute

23

Confocal laser endomicroscopy





Gastroenterology. 2019 Jul;157(1):109-118.e5.

National Medicine Institute

24

Elimination diets

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Elimination diets	Empirical elimination diets involve initial short-term restriction followed by re-challenge to assess tolerance to each food. Commonly restricted foods include seafood, wheat, corn, eggs, dairy, soy, nuts, citrus, and yeast. Testing-led elimination diets follow the same procedure, but elimination is personalised based on test results.	There is mixed evidence for empirical elimination re-challenge diets. IgG antibody-led elimination diets reduce symptoms and improve quality of life but suffer from low evidence. An IgG guided diet was superior to a LFD.	IgG antibodies	IgG antibody-led elimination diets result in clinical improvement in symptoms.
			Confocal laser endomicroscopy	Confocal laser endomicroscopy (CLE)-led elimination diets result in significant symptom improvement. CLE is expensive, invasive and may lack accuracy.
			Leukocyte activation assay	Leucocyte activation test-led elimination diets reduce symptoms.

See supplementary file for references.

25

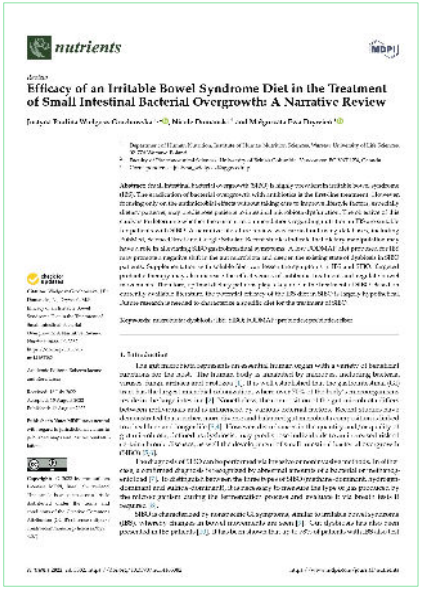
SIBO DIET

26

A SIBO diet?

"Based on the currently available literature, **the potential efficacy of the IBS diet in SIBO is largely hypothetical** and future research is needed to characterize the specific dietary recommendations for the treatment of SIBO."

Nutrients. 2022 Aug 17;14(16):3382.


nutrients

Efficacy of an Irritable Bowel Syndrome Diet in the Treatment of Small Intestinal Bacterial Overgrowth: A Narrative Review

27

SIBO diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
SIBO diet	Small intestinal bacterial overgrowth (SIBO) has controversially been proposed as a cause of IBS. The LFD has been recommended during SIBO management with antibiotic therapy.	A case report described benefit of a LFD and herbal antibiotic therapy, no clinical trials have assessed the LFD for SIBO. A single study examined a short-term elemental diet.	Hydrogen and methane breath testing	Breath testing has important limitations; it may not correlate with bacterial overgrowth (jejunal aspirate culture) or differentiate symptomatic subjects from healthy controls. Breath testing has not yet been studied in relation to dietary management.

See supplementary file for references.

28

HISTAMINE DIET

29

Consider histamine intolerance

"…histamine and, histamine intolerance, should be considered in differential diagnoses of patients with functional, nonspecific, non-allergic gastrointestinal complaints."

Crit Rev Food Sci Nutr. 2021;61(17):2960-2967.

Considering histamine in functional gastrointestinal disorders

30

Histamine diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Histamine diet	Recommendations vary but most often include restriction of cured and semi cured cheese, grated cheese, oily fish, canned and semi preserved oily fish derivatives, dry-fermented meat products, spinach, tomatoes, fermented cabbage, strawberries, citrus, wine, and beer.	Histamine intolerance has been suggested in a subgroup of IBS patients. A histamine diet has been shown to symptoms in patients presenting primarily with functional abdominal symptoms. This is supported by benefit of DOA enzyme intervention on GI symptoms. FODMAPs may favour the production of faecal histamine by Klebsiella aerogenes in a subgroup of IBS patients. A moderate correlation was found between visceral pain severity and urinary histamine with an LFD.	Serum DAO	Does not have reliable diagnostic value. Despite uncertainty, may be useful to complement diagnosis and prediction of clinical response to treatment.
			Urinary histamine	Methylhistamine in urine is emerging as a potential biomarker.
			DAO gene variants	The relevance of gene variants to histamine intolerance is unknown. DAO gene variants were associated with lower serum DAO in a subgroup of people with histamine intolerance, but not with clinical histamine intolerance phenotype.

See supplementary file for references.

31

LOW SUCROSE DIET

32

Back to the future

"Intestinal carbohydrate dyspepsia is one of the commonest abdominal disorders, although in the majority of English books on medicine it is not even mentioned."

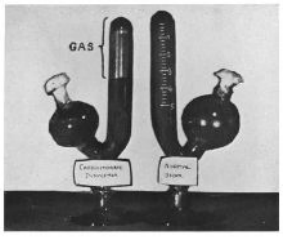


FIG. 9. Carbohydrate dyspepsia (left) compared with normal (right). Faecal fermentation tests applied to similar amounts of faeces. The left hand tube contains much gas, the right hand tube practically none.

QJM. Jan 1931; 94:171–9.

INTESTINAL CARBOHYDRATE DYSPEPSIA[1]

BY ARTHUR F. HURST AND F. A. KNOTT.

With Plates 7 and 8.

INTESTINAL carbohydrate dyspepsia is one of the commonest abdominal disorders, although in the majority of English books on medicine it is not even mentioned. The following account is based on a study of a large number of cases, twenty-four of which have been investigated in great detail at New Lodge Clinic.

Starch Digestion in Man.

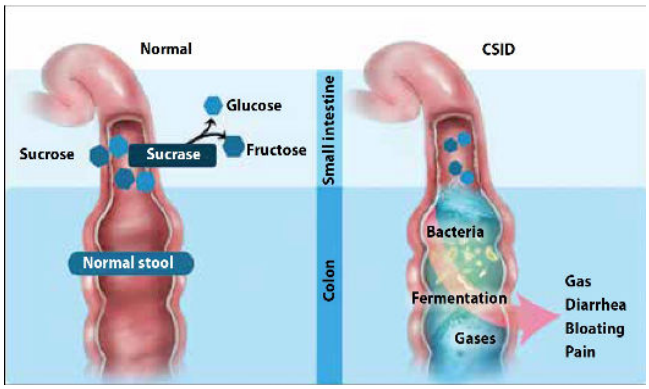
Under normal conditions the starch taken in food is digested by the ptyalin of the saliva, the amylopsin of the pancreatic juice, and the diastase of the juice secreted by the small and large intestines. The ptyalin is least important, as it is destroyed by the first trace of free hydrochloric acid with which it comes in contact in the stomach; consequently salivary digestion of starch only continues in the stomach for any length of time in the centre of lumps of insufficiently chewed food. The amylopsin, which has up to now been held to be solely responsible for the initial break-down of starch in the small intestines, is certainly not the only or even the most important diastatic ferment present. This is proved by the fact that the digestion of starch was unimpaired in all the cases of pancreatic disease we have investigated, though much undigested fat and protein were found in the stools. We have also been able to demonstrate the presence of a diastatic ferment in specimens of the duodenal contents obtained through a Ryle's tube in cases of complete obstructive jaundice in which bile and trypsin were absent and in which a normal quantity of free acid was secreted by the stomach. It is clear, therefore, that the intestinal juice contains an active diastatic ferment. This diastase appears to be essential for the efficient digestion of starch: when for any reason its secretion is deficient, a more or less considerable quantity of unaltered starch reaches the colon. It has hitherto been taught by physiologists that the succus entericus contains no starch-splitting ferment, and there is in fact no direct evidence to the contrary, except for some observations carried out on a single case by Esser in 1908. A patient with polyposis of the colon had a caecostomy performed. After a time a number of polypi projected out of the stoma and the clear, pale

[1] Received November 13, 1930.

[Q. J. M., Jan., 1931.]

Congenital sucrase-isomaltase deficiency

When sucrase isomaltase is absent or deficient, non-absorbed carbohydrates enter the distal small intestine and colon causing excess bacterial fermentation and increased production of short-chain fatty acids and gases, leading to abdominal distension, cramping, pain, excessive flatulence, and osmotic diarrhoea. CSID, congenital sucrase-isomaltase deficiency.



Gastroenterol Hepatol 2020;16(10):1-11.

Sucrase-isomaltase deficiency and IBS

"The classic congenital sucrase-isomaltase deficiency (CSID) manifests itself during infancy when one begins to introduce fruits and juices into the diet and leads to severe diarrhea, poor weight gain, irritability, and diaper rash. The treatment mainly consists of avoiding starch and sucrose, which reverses the symptoms. **Milder forms of mutations can present clinically later in life** with the same symptoms as in other carbohydrate intolerances, especially diarrhoea, **and can be misdiagnosed as IBS** in adults."

Mol Med Rep. 2021 Oct;24(4):732.

MOLECULAR MEDICINE REPORTS 24: 732, 2021

Theories behind the effect of starch- and sucrose-reduced diets on gastrointestinal symptoms in irritable bowel syndrome (Review)

BODIL OHLSSON

Department of Internal Medicine, Lund University, Skåne University Hospital, 20502 Malmö, Sweden

Received July 1, 2021; Accepted July 22, 2021

DOI: 10.3892/mmr.2021.12372

Abstract. Increased amounts of starch and sugar have been added to the diet in the Western world during the last decades. Undigested carbohydrates lead to bacterial fermentation and gas production with diffusion of water, causing abdominal bloating, pain and diarrhea. Therefore, dietary advice is the first line of treatment of irritable bowel syndrome (IBS), a disease characterized by abdominal pain and altered bowel habits without any organic findings. Recently, a diet with a reduction of starch and sucrose led to a marked effect on gastrointestinal (GI) symptoms. The mechanism is unknown, but three possible mechanisms are presented in the present review: First, functional variants of the enzyme sucrase-isomaltase (SI) have been described in IBS. A subgroup of patients with IBS may thus suffer from partial SI deficiency with reduced digestion of starch and sucrose. Second, fructose absorption is less efficient than glucose absorption, which may lead to a physiological fructose malabsorption when ingesting high amounts of sucrose. A third mechanism is that high-sugar diets causing hyperglycemia, hyperinsulinemia and weight gain have led to painful neuropathy in animal models; whereas, improved metabolic control in humans has led to improvement of neuropathy. Starch- and sucrose-reduced diets lead to decreased levels of C-peptide, insulin, gastric inhibitory peptide, leptin and weight reduction. These metabolic changes may reduce the excitability of the hypersensitive nervous system often found in IBS and, thereby, lead to the reduced symptoms found after the diet. In conclusion, further studies are needed to investigate the pathophysiology behind development of symptoms after starch and sucrose intake, and the mechanisms behind symptom relief after reduced intake.

Contents

1. Introduction

Gastrointestinal (GI) symptoms without any organic changes are called functional gastrointestinal disorders (FGID). The most common of these disorders is irritable bowel syndrome (IBS) (1). The pathophysiology behind FGID is unknown, but visceral hypersensitivity, psychological factors, low-grade inflammation, alterations in gut microbiota composition, or hormonal profile have been discussed (2).

IBS symptoms are frequently experienced during food intake, and as such, dietary interventions are usually prescribed to improve the symptoms (3). Also, patients with IBS have been found to have altered expression of endocrine cells in the GI tract and different levels of circulating hormones (4-6).

Dietary changes may influence the production of gut hormones since the production is predominantly influenced by food ingestion and food nutrient content (7). Hormones such as C-peptide, gastric inhibitory peptide (GIP), glucagon, glucagon-like peptide-1 (GLP-1), and insulin are key hormones in regulation of glucose homeostasis. These hormones control energy and glucose metabolism by acting on the function of the digestive system in glucose regulation, motility, and pancreatic function (8,9). Leptin controls appetite and food intake, thereby regulating energy intake (10). Thus, the improvement of IBS symptoms with dietary changes may possibly be linked to the effect of changes in gut hormones (11).

The first line of dietary advice is the National Institute for Health and Care Excellence (NICE) guidelines, which recommend regular meal patterns and decreased intake of mineral water, caffeine, fat, and spicy foods (12), or the low FODMAP diet, which advocates exclusion of fermentable oligo-, di- and monosaccharides and polyols (13). These diets have an effect in 20-50% of IBS patients (14).

Correspondence to: Professor Bodil Ohlsson, Department of Internal Medicine, Lund University, Skåne University Hospital, 13 Jan Waldenströms Street, Floor 5, 20502 Malmö, Sweden
E-mail: bodil.ohlsson@med.lu.se

Key words: fructose malabsorption, neuropathy, starch, sucrose, sucrase-isomaltase deficiency

35

Low sucrose diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Low sucrose diet	Modified dietary guidelines for patients with congenital sucrase-isomaltase deficiency including avoiding sucrose containing foods, foods with added sugars, and replacing refined grain product with high fiber alternatives.	Low sucrose diets have been shown to reduce symptoms. Congenital sucrase-isomaltase deficiency may also masquerade as adult IBS and respond to diet.	Sucrase-isomaltase gene variants	Predict a moderately better response to a low sucrose diet in IBS-D. May predict poor response to a LFD. Positive test does not rule out congenital deficiency as not all gene variants have been identified.

See supplementary file for references.

36

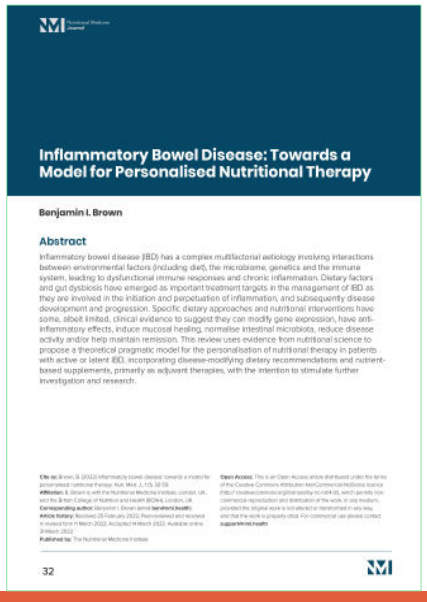
SPECIFIC CARBOHYDRATE DIET

37

Specific carbohydrate diet

"Originally developed for the management of coeliac disease symptoms in the 1950s, the specific carbohydrate diet (SCD) was popularised with the book 'Breaking the Vicious Cycle' in the 1980s for the management of IBD. The original premise for the diet was that restriction of complex carbohydrates and refined sugar from the diet would prevent malabsorption and symptom development, later **the hypothesis was expanded to include the idea that malabsorbed carbohydrates could cause bacterial dysbiosis and contribute to the intestinal inflammation** of IBD."

Nutr. Med. J. 2022., 1 (1), 32-59.



Inflammatory Bowel Disease: Towards a Model for Personalised Nutritional Therapy

Benjamin I. Brown

Abstract

32

38

Specific carbohydrate diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Specific carbohydrate diet	The SCD restricts grains, refined sugars except for honey, processed foods, and most milk products except for fully fermented yogurt and some hard cheeses.	The SCD has primarily been studied in IBD. A clinical trial found no significant improvement in IBS symptoms with a SCD.	N/A	N/A

See supplementary file for references.

39

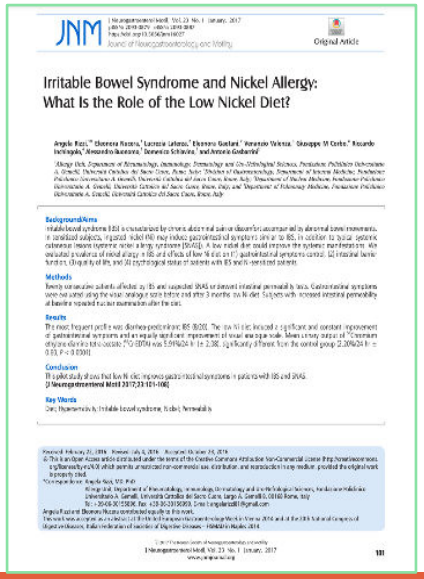
LOW NICKLE DIET

40

Low-nickel diet for IBS

"The most frequent profile was diarrhoea-predominant IBS (8/20). **The low nickel diet induced a significant and constant improvement of gastrointestinal symptoms and an equally significant improvement of visual analogue scale.** Mean urinary output of chromium ethylene-diamine-tetra-acetate was 5.91%/24 hr, significantly different from the control group."

J Neurogastroenterol Motil. 2017 Jan 30;23(1):101-108.


JNM
Original Article

Irritable Bowel Syndrome and Nickel Allergy: What Is the Role of the Low Nickel Diet?

41

Low nickel diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Low nickel diet	The low nickel diet was constructed to manage adverse reactions to nickel containing foods and restricts foods high in nickel such as oats, almonds, chickpeas, tomato, cocoa, peanuts, walnuts and many others.	A low nickel diet improves gastrointestinal symptoms in patients with nickel sensitivity and IBS or IBS-like symptoms.	Oral mucosa patch test	The oral mucosa patch test complements clinical diagnosis of nickel sensitivity and predicts treatment response.

See supplementary file for references.

42

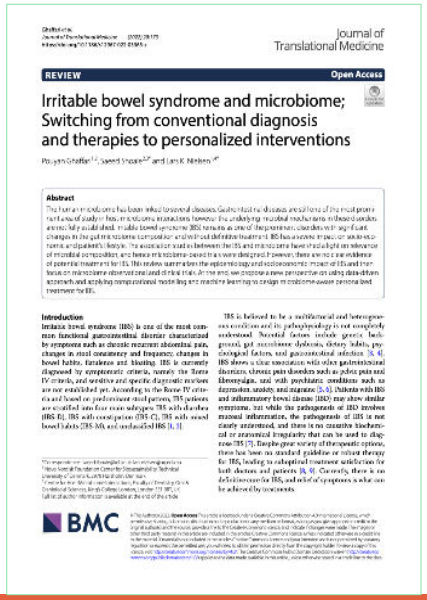
MICROBIOME-TARGETED DIET

43

Microbiome informed nutrition

"There is strong evidence supporting the role of diet and microbiome in the triggering and progression of IBS, and **targeting microbiota appears promising considering positive response of some patients to microbiome-related therapies.** However, the complexity and heterogeneity of IBS and lack of highly predictive diagnostic and prognostic biomarkers resulted in unsatisfactory outcomes."

J Transl Med. 2022 Apr 11;20(1):173.



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IBS-Microbiome-Diet axis

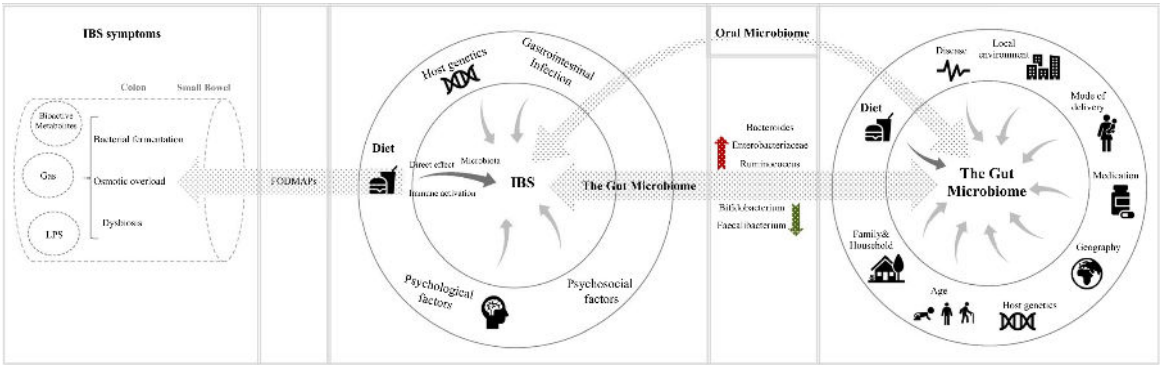


Fig. The gut microbiome might be an important factor with higher degrees of dysbiosis and altered abundance of some species observed in IBS patients. Diet might have a substantial effect on IBS symptoms through mechanisms, such as changing gut microbiota, direct effect of food, and immune activation. Fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) might cause IBS symptoms via microbiome dysbiosis, bacterial fermentation and osmotic overload. Gut microbiota composition and function is shaped by several factors from which, diet might be the key determinant of the microbiota configuration. Oral microbiome may have a potential in diagnosis and patient stratification in IBS. LPS, lipopolysaccharide

J Transl Med. 2022 Apr 11;20(1):173.

45

Phytochemicals and symptom severity

"We found a significant inverse association between dietary phytochemical index (DPI) and IBS severity in the study population (OR: 0.70; 95% CI: 0.51–0.98). Concerning gender, such an association was only found in women (OR: 0.65; 95% CI: 0.44–0.96)."

Clin Nutr ESPEN. 2023 Oct;57:158-165.


Clinical Nutrition ESPEN

Dietary intake of phytochemicals in association with irritable bowel syndrome in adults

46

Microbiome-targeted diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Microbiome-targeted diet	Targeting the gut microbiota with dietary changes such as improving dietary quality, increasing intake of fermented foods, polyphenol rich foods, and reduction of artificial food additives has been proposed but lacks a defined dietary approach.	Intervention studies have found symptom reductions with polyphenol rich food (blueberries), fermented foods (sauerkraut, kimchi), and elimination of artificial sweeteners, and monosodium glutamate. A traditional Mediterranean diet showed comparative efficacy to an LFD or GFD.	Microbiome	Microbiome testing-based dietary advice is limited by considerable inter-individual variability and lack of evidence linking microbiota signatures to disease phenotypes and treatment responses.

See supplementary file for references.

47

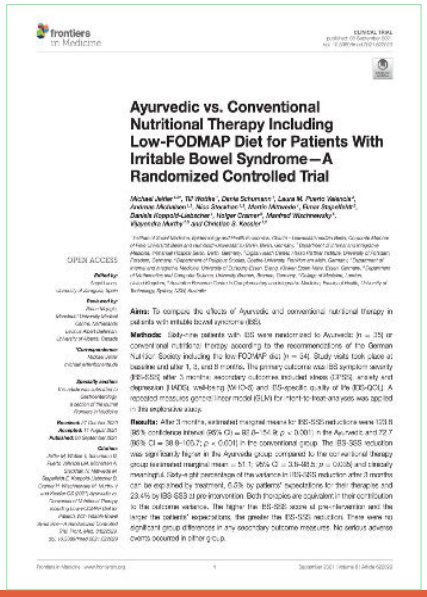
AYURVEDIC DIET

48

Ayurveda vs. 'Traditional' Diet

"Ayurvedic IBS-treatment is based on diagnosing the condition from an Ayurvedic perspective, which takes into consideration inter-person variablity of digestive functions, physio-psychological personality type and variations in the presenting symptoms."

Front Med (Lausanne). 2021 Sep 6;8:622029.



frontiers in Medicine

Ayurvedic vs. Conventional Nutritional Therapy Including Low-FODMAP Diet for Patients With Irritable Bowel Syndrome—A Randomized Controlled Trial

OPEN ACCESS

Aims: To compare the effects of Ayurvedic and conventional nutritional therapy in patients with irritable bowel syndrome (IBS).

Methods: Sixty-nine patients with IBS were randomized to Ayurvedic (n = 35) or conventional nutritional therapy according to the recommendations of the German Nutrition Society including the low FODMAP diet (n = 34). Study visits took place at baseline and after 1, 3, and 9 months. The primary outcome was IBS symptom severity (IBS-SSS) after 3 months; secondary outcomes included stress (CPSS), anxiety and depression (HADS), well-being (W-HO-5), and IBS-specific quality of life (IBS-QOL). A repeated measures general linear model (GLM) for "intent-to-treat" analyses was applied in this exploratory study.

Results: After 3 months, estimated marginal means for IBS-SSS reductions were 123.8 (95% confidence interval (95% CI) = 82.8–164.8; p < 0.001) in the Ayurveda and 72.7 (95% CI = 38.9–106.7; p < 0.001) in the conventional group. The IBS-SSS reduction was significantly higher in the Ayurveda group compared to the conventional therapy group (estimated marginal mean = 51.1; 95% CI = 3.9–98.3; p = 0.035) and clinically meaningful. Sixty-one percentages of the variance in IBS-SSS reduction after 3 months can be explained by "treatment," 6.0% by patients' expectations for their therapies and 23.4% by IBS-SSS at pre-intervention. Both principles are equivalent in their contribution to the outcome variance. The higher the IBS-SSS score at pre-intervention and the larger the patients' expectations, the greater the IBS-SSS reduction. There were no significant group differences in any secondary outcome measure. No serious adverse events occurred in either group.

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49

Ayurvedic diet

Diet	Diet description	Evidence for efficacy	Biomarkers	Biomarker evidence
Ayurvedic diet	Ayurvedic nutritional therapy based on general concepts to support digestive health including warm food, regular timings of meals, and foods which are generally light on digestion but nourishing with additional personalization based on symptoms.	Personalised Ayurvedic nutritional therapy was as effective as a traditional diet and LFD.	N/A	N/A

See supplementary file for references.

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DISCUSSION

51

Risks related to diet therapy

Nutritional adequacy

- Micronutrients deficiencies and toxic metal excess (arsenic, methylmercury, nickel).[1-3]

Disordered eating

- Eating disorders (orthorexia nervosa and avoidant/restrictive food intake disorder), increased anxiety, and decreases in quality of life.[4-6]

Applicability and acceptability

- Family values, culture, and social challenges.[7]

Alterations in the microbiome

- Reduction in *Bifidobacteria* and an increase in bacteria associated with dysbiosis.[8]

Changes in food tolerance

- Decreases, or increases, in food tolerance related to elimination diets or other therapies.

Overlooking complementary or alternative strategies

- Prebiotics (GOS vs. low FODMAP), probiotics (LGG vs. low FODMAP, + low nickel diet), enzyme therapy (vs. high GOS foods, vs. antigens, vs. histamine), glutamine (+ low FODMAP).[9-15]

52

Risks related to diet therapy

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15. Rastgoo S, et al. Glutamine Supplementation Enhances the Effects of a Low FODMAP Diet in Irritable Bowel Syndrome Management. Front Nutr. 2021 Dec 16;8:746703. **Note: Improvement in IBS-severity score of more than 45% was observed in 22 of 25 participants (88%) in the glutamine group, while it was only 15 of 25 participants (60%) in the control (low FODMAP only) group (p = 0.015).**

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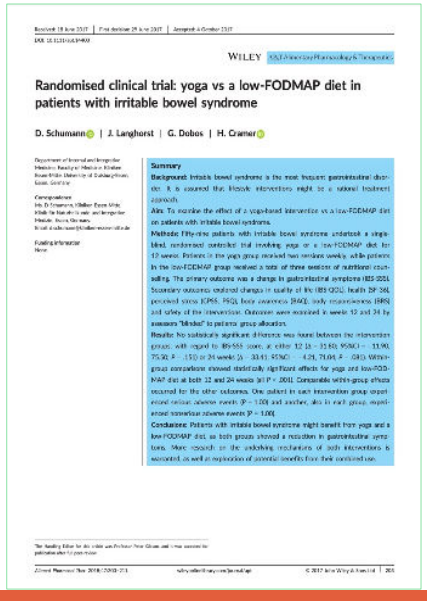
53

Stretching beyond diet

"No statistically significant difference was found between the intervention groups, with regard to IBS-SSS score, at either 12 or 24 weeks. **Within-group comparisons showed statistically significant effects for yoga and low-FODMAP diet at both 12 and 24 weeks.** Comparable within-group effects occurred for the other outcomes."

Aliment Pharmacol Ther. 2018 Jan;47(2):203-211.



WILEY

Randomised clinical trial: yoga vs a low-FODMAP diet in patients with irritable bowel syndrome

D. Schumann | J. Langhorst | G. Dobos | H. Cramer

Summary

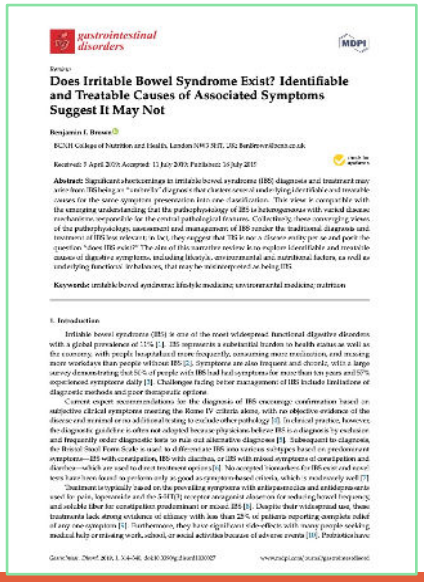
National Medicine Institute

54

Dietary management needs to get personal

"Obtaining a better understanding of each patient's pathophysiology with clinical and molecular assessments could therefore help improve diagnosis and target different therapies to individuals most likely to benefit."

Gastrointest. Disord. 2019, *1*, 314-340.


gastrointestinal disorders

MDPI

Review

Does Irritable Bowel Syndrome Exist? Identifiable and Treatable Causes of Associated Symptoms Suggest It May Not

Benjamin E. Brenner

Nutritional Medicine Institute

55

Microbiome, Gut and Systemic Health: New Frontiers in Personalised Nutrition

Thank you

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56