United European Gastroenterology Journal

WILEY

UNITED EUROPEAN GASTROENTEROLOGY
ueg journal

GUIDELINE OPEN ACCESS

European Consensus on Functional Bloating and Abdominal Distension—An ESNM/UEG Recommendations for Clinical Management

Chloé Melchior[1] | Heinz Hammer[2] | Serhat Bor[3] | Elizabeth Barba Orozco[4] | Indira Benjak Horvat[5] | Altay Celebi[6] | Vasile Drug[7] | Dan Dumitrascu[8,9] | Ismail Hakki Kalkan[10] | Goran Hauser[11] | Christos Lionis[12] | Dan Livovsky[13] | Amir Mari[14,15] | Agata Mulak[16] | Teodora Surdea-Blaga[8,9] | Jan Tack[17] | Tim Vanuytsel[17] | Edoardo Vincenzo Savarino[18,19] | Natalia Zarate-Lopez[20] | Johann Hammer[21] | Ram Dickman[22,23]

[1]Department of Gastroenterology, INSERM, ADEN UMR1073, "Nutrition, Inflammation and Microbiota-Gut-Brain Axis", CHU Rouen, CIC-CRB 1404, University Rouen Normandie, Rouen, France | [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Medical University Graz, Graz, Austria | [3]Division of Gastroenterology, Department of Internal Medicine, Ege University School of Medicine, Izmir, Turkiye | [4]Neurogastroenterology and Motility Unit, Gastroenterology Department, Hospital Clínic de Barcelona, University of Barcelona, Barcelona, Spain | [5]Department of Gastroenterology, General Hospital Varaždin, Varaždin, Croatia | [6]Division of Gastroenterology, Department of Internal Medicine, Kocaeli University Faculty of Medicine, Kocaeli, Turkiye | [7]Digestive Endoscopy and Functional Measurements Unit, "Grigore T. Popa" University of Medicine and Pharmacy, "St. Spiridon" University Hospital, Iasi, Romania | [8]2nd Department of Internal Medicine, Cluj County Clinical Emergency Hospital, Cluj-Napoca, Romania | [9]"Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania | [10]Department of Gastroenterology, TOBB University of Economics and Technology, School of Medicine, Ankara, Turkey | [11]Faculty of Medicine, University of Rijeka, Centre for Digestive and Metabolic Medicine, Clinical Hospital Center Rijeka, Rijeka, Croatia | [12]Department of Social Medicine and Laboratory of Health and Society, School of Medicine, University of Crete, Heraklion, Greece | [13]Faculty of Medicine, Digestive Diseases Institute, Shaare Zedek Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel | [14]Gastroenterology Department, Nazareth Hospital, Nazareth, Israel | [15]The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel | [16]Department of Gastroenterology and Hepatology, Wroclaw Medical University, Wroclaw, Poland | [17]Department of Chronic Diseases and Metabolism (CHROMETA), Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium | [18]Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy | [19]Gastroenterology Unit, Azienda Ospedale Università Padova, Padua, Italy | [20]Division of Surgery and Interventional Science, University College London, London, UK | [21]Department of Gastroenterology and Hepatology, University Hospital for Internal Medicine III, Medical University of Vienna, Vienna, Austria | [22]Division of Gastroenterology, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel | [23]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Correspondence: Chloé Melchior (chloe.melchior@chu-rouen.fr)

Received: 15 January 2025 | **Revised:** 29 June 2025 | **Accepted:** 10 July 2025

Funding: This project was funded by The United European Gastroenterology Activity Grant in Support of Standards & Guidelines initiatives.

Keywords: abdominal distension | consensus | Delphi | disorders of gut-brain interaction | ESNM | European guidelines | functional bloating | microbiota | Rome criteria | UEG

ABSTRACT

Introduction: Abdominal distension is an objective visible sign of increased abdominal girth. Bloating is a feeling of abdominal fullness and discomfort. Bloating may be associated or not with abdominal distension. Bloating and abdominal distension are among the most commonly reported gastrointestinal symptoms and may be associated with both organic and functional disorders. Nevertheless, specific consensus and recommendations on diagnosis, underlying mechanisms, assessment and

Abbreviations: aCPQ, adult Carbohydrate Perception Questionnaire; CBT, cognitive behaviour therapy; CIC, chronic idiopathic constipation; CIPO, chronic intestinal pseudo-obstruction; CPO, colonic pseudo-obstruction; CT, computed tomography; DGBI, disorders of gut-brain interaction; ED, enteric dysmotility; EMG, electromyography; FD, functional dyspepsia; FEL-1, faecal pancreatic elastase 1; FODMAPs, fermentable oligo-, di-, and monosaccharides and polyols; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-C, IBS constipation-predominant; IBS-D, IBS diarrhoea-predominant; IMO, intestinal methanogenic overgrowth; NCGS, non-coeliac gluten sensitivity; NNT, number needed to treat; OR, odds ratio; PCOS, polycystic ovary syndrome; PEI, pancreatic exocrine insufficiency; PROM, patient-reported outcome measure; RCT, randomised controlled trial; SBM, small bowel manometry; SIBO, small intestinal bacterial overgrowth; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TSH, thyroid-stimulating hormone.

management of functional bloating and abdominal distension are still lacking. The aim of this European consensus, then, is to provide expert opinions and recommendations on the epidemiology, diagnosis, pathophysiology and treatment of functional bloating and abdominal distension.

Methods: A multidisciplinary team of experts in the field, including European specialists and national societies, participated in the development of this consensus. Relevant questions were formulated and addressed through a literature review and statements were developed and voted using a Delphi process.

Results: Functional bloating and abdominal distension are common and frequently overlap with other disorders of gut-brain interaction. Diagnosis is made according to the Rome IV criteria after the exclusion of organic disease, based on the physical examination and assessment of the patient's medical history and alarming signs. In the absence of alarming signs or any relevant finding, clinical laboratory, imaging or endoscopic tests are unnecessary. The pathophysiology of functional bloating and abdominal distension is multifactorial and involves visceral hypersensitivity, abdomino-phrenic dyssynergia, intestinal dysmotility and dysbiosis. Treatment may include dietary modifications (e.g. lactose-limiting diet and low FODMAP diet), probiotics, antispasmodics (e.g., otilonium bromide, peppermint oil), rifaximin, secretagogues (e.g., linaclotide), neuromodulators (e.g., serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, buspirone), and plethysmography-based biofeedback. Moreover, cognitive behaviour therapy and hypnotherapy can be used in case of functional bloating associated with irritable bowel syndrome.

Conclusion: This consensus provides an evidence-based framework for the evaluation and treatment of patients with functional bloating and abdominal distension.

1 | Introduction

Abdominal distension is an objective visible sign of increased abdominal girth. Bloating refers to a sensation of abdominal fullness and discomfort, which may or may not be accompanied by abdominal distension. Bloating and abdominal distension are prevalent gastrointestinal (GI) complaints, occurring in 19% and 9% of the general population, respectively, and was confirmed by a recent worldwide study with a global prevalence of 18% [1, 2]. Prevalence increases to 66%–90% in irritable bowel syndrome (IBS) and up to 60% in functional dyspepsia (FD) [3]. Bloating is also a frequent complaint among patients with other disorders of gut-brain interaction (DGBI) [3]. According to Rome IV criteria [4], functional bloating and abdominal distension can be diagnosed when they are recurrent and the predominant symptoms, in the absence of overlap with other DGBI such as IBS, FD, functional diarrhoea and functional constipation. Functional bloating and abdominal distension affect 3.5% of the global population, with a higher prevalence in women (4.6%) and between the age of 40–60 years [5].

Risk factors for functional bloating and abdominal distension include female sex, older age, lower education level, associated symptoms such as abdominal pain, early satiety and somatic symptoms [3, 6, 7]. Assessment of bloating is challenging due to its non-specific nature, but validated questionnaires now exist to evaluate its severity and impact (e.g., Mayo bloating questionnaire) [8, 9]. Bloating and abdominal distension can also indicate small intestinal bacterial overgrowth, carbohydrate intolerance, chronic intestinal pseudo-obstruction or diseases such as coeliac disease, inflammatory bowel disease, pancreatic insufficiency, or even incomplete mechanical obstruction due to gastrointestinal or gynaecological malignancies [10]. The pathophysiology of functional bloating is multifactorial, involving visceral hypersensitivity, abdomino-phrenic dyssynergia, intestinal dysmotility (slow transit) and dysbiosis inducing excessive gas production as well [10–12]. Treatment remains challenging and involves targeting these mechanisms through dietary modifications, medications, and biofeedback [10]. In this guideline, we will focus on the evaluation and evidence-based management of functional bloating and abdominal distension.

2 | Methods

2.1 | General Framework

A total of 21 experts (authors of article), recommended by ESNM, The European Association for Gastroenterology, Endoscopy and Nutrition (EAGEN) and The European Society for Primary Care Gastroenterology (ESPCG), from different countries agreed to participate as the International Working Group for the European Consensus on Bloating to vote on the Delphi statements. All participants have significant experience and expertise in general clinical practice, gastroenterology, and neurogastroenterology. The United European Gastroenterology (UEG) provided financial support and Medical Statistic Consulting (MS-C) provided technical support. Four distinct core working groups, made up of five to nine experts in the field were selected. The four working groups covered the following topics: Group 1 ‘pathophysiology’, Group 2 ‘epidemiology and diagnosis’, Group 3 ‘diagnostic procedures and evaluation’ and Group 4 ‘treatments’. Each core group framed and answered clinical questions according to a PICO framework (Table S1). A core group leader coordinated the various steps with his/her group. The consensus coordinators (RD, CM) harmonised and supervised each step. Multiple online and face-to-face meeting were held during the entire period needed to complete the consensus.

2.2 | Literature Search and Questions

A comprehensive literature review was conducted to address each question based on experts' knowledge, followed by the

drafting of statements summarising the evidence. Each expert conducted a structured review of the literature based on specific search terms, using databases such as MEDLINE (accessed via PubMed), EMBASE, and the Cochrane Database of Systematic Reviews (Cochrane Library) until April 17, 2024. The types of studies included were systematic reviews with or without meta-analysis, randomised or non-randomised clinical trials, cohort studies, and observational studies. Documents with low-quality evidence, such as expert opinion articles, case reports, or pre-clinical studies, were excluded (Table S1).

2.3 | Consensus/Modified Delphi Process

We used the adapted RAND/UCLA modified Delphi panel method [13, 14], which combines the Delphi procedure with the "nominal group" technique [15, 16]. This method integrates current scientific evidence with the collective judgement of a panel of experts and aims to establish a consensus for complex conditions where evidence from controlled trials is limited [17]. The process began with the formulation of 27 clinically relevant questions for our target population (Table S1) [18]. Based on the evidence in the literature, each expert formulated statements related to the assigned questions, which were subsequently reviewed and validated by the expert panel. The evidence supporting the recommendations was evaluated by the expert panel classifying each statement according to four categories (Table S2). Meta-analyses and randomised control trials were considered high-quality studies, while well-designed observational studies received lower consideration.

The process continued with two rounds of blinded voting on these statements, and their strength was graded using accepted criteria. In the first voting round, held in May 2024, the final list of 75 statements was evaluated by all members. Each member indicated their level of agreement with the statements using a 9-point Likert scale (1: totally disagree, 2: disagree, 3: partially disagree, 4: somewhat disagree, 5: neither agree nor disagree, 6: somewhat agree, 7: partially agree, 8: agree, 9: totally agree).

The degree of agreement for each statement was measured using the following criteria [13–16]: Agreement was reached when more than two-thirds of the panelists voted in the same range (either lower [1–3] or upper range [7–9]). Disagreement occurred when the median was in the lower [1–3] or upper range [7–9], but one-third or more of the panel voted in the opposite range; or if the median was 4-6, but one-third or more of the panel voted in the lower [1–3] or upper range [7–9]. A neutral result was defined when the median was 4-6, and less than one-third of the panel voted in the lower [1–3] or upper range [7–9].

Participants were blinded to the votes of other participants and provided suggestions to improve the clarity of the statements. After the first round of voting, the expert panel revised the statements and recommendations. Five statements underwent a second round of blinded voting due to a lack of agreement. Finally, a manuscript was drafted and reviewed by the expert panel for final approval.

2.4 | Final Statements and Brief Explanatory Text

Each final statement was agreed upon by all the participants. Each statement is followed by a brief explanatory text. Since most of our statements are either definition or expert-based recommendations, or good clinical practice recommendations, we could not fully apply to the GRADE methodology for rating the quality of evidence. This is also because the quality of evidence was overall poor.

3 | Results

The results of the Delphi process are depicted in Table 1. There was complete agreement in all the statements related to epidemiology, evaluation, diagnosis and pathophysiology of functional bloating and abdominal distension. However, in the treatment section, there was a lack of agreement in several statements that had to be re-evaluated for modifications and underwent a second voting round. Finally, there was consensus in all recommendations, except in those related to the effect of physical activity and antispasmodic agents for functional bloating. For clarity, the statements not backed up by the expert consensus have been removed from the list of recommendations below, but they are fully disclosed in Table 1. A summary of the main recommendations on functional bloating and abdominal distension is presented in Table 2.

4 | Recommendations

4.1 | Section 1. Pathophysiology

4.1.1 | How Does Gas Get Into the GI Tract and How Is Gas Removed From the GI Tract?

- ➢ Gas enters the human GI tract by swallowing air, by chemical processes that liberate gas, by diffusion from the blood into the lumen of the GI tract and by gas-producing intestinal microorganisms (100% agreement—ungraded: expert opinion)
- ➢ Gas is eliminated from the GI tract by eructation of gas from the upper GI tract, by diffusion from the small and large intestine into the blood, by consumption by microorganisms or by anal evacuation (100% agreement—ungraded: expert opinion)
- ➢ The volume and composition of gas in different GI compartments is the result of the mechanisms which lead to the entry and elimination of gas (95% agreement—ungraded: expert opinion)

Five gases: nitrogen (N2), oxygen (O2), carbon dioxide (CO2), hydrogen (H2), and methane (CH4) make up over 99% of intestinal gas in healthy individuals, as measured by the washout technique. Gas can accumulate throughout the GI tract, including the stomach, small intestine, and colon, depending on mechanisms of gas entry and elimination [19].

TABLE 1 | Statements and recommendations on the bloating consensus.

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
Section 1. Pathophysiology						
Statement 1	Gas enters the human GI tract by swallowing air, by chemical processes that liberate gas, by diffusion from the blood into the lumen of the GI tract, and by gas-producing intestinal microorganisms	Yes		Expert opinion	100	[19]
Statement 2	Gas is eliminated from the GI tract by eructation of gas from the upper GI tract, by diffusion from the small and large intestine into the blood, by consumption by microorganisms or by anal evacuation	Yes		Expert opinion	100	[19–21]
Statement 3	The volume and composition of gas in different gastrointestinal compartments is the result of the mechanisms which lead to the entry and elimination of gas	Yes		Expert opinion	95	[19–21]
Statement 4	DGBI such as IBS, functional dyspepsia or chronic constipation are predisposing factors for the presence of functional bloating and abdominal distension	Yes		Good practice statement	100	[3, 6]
Statement 5	A variety of pathophysiologic consequences which result from organic gastrointestinal or extraintestinal diseases, such as intraluminal accumulation of nutrients, bacterial metabolism, mucosal inflammation or altered visceral motility and perception may predispose to bloating and abdominal distension	Yes		Expert opinion	90	[22–24]
Statement 6	Visceral hypersensitivity, rather than distension of the gastrointestinal tract due to increased intraluminal gas, plays a key role in the pathophysiology of functional bloating and abdominal distension	Yes		Expert opinion	95	[12]
Statement 7	Visceral hypersensitivity may trigger aberrant viscerosomatic reflexes, including abdomino-phrenic dyssynergia causing abdominal distension	Yes		Expert opinion	90	[25]
Statement 8	Physiologically, the accommodation response to any increase in intraluminal volume is achieved by relaxation of the diaphragm and by increasing the postural tone of the abdominal wall	Yes		Expert opinion	100	[10, 26, 27]
Statement 9	During episodes of abdominal distension, a diaphragmatic descent, as a result of an increase in its	Yes	Low-	Expert opinion	100	[26, 28]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
	muscular activity, is coupled with a decrease in abdominal wall postural tone, causing the abdominal wall to bulge; this phenomenon is known as abdomino-phrenic dyssynergia (APD)					
Statement 10	Intestinal dysmotility and intestinal gas retention are uncommon causes of functional bloating and abdominal distension	Yes	Low-	Expert opinion	70	[27]
Statement 11	Intestinal dysmotility can result in a significant retention of gas and non-gaseous contents in the GI tract, leading to pronounced abdominal distension	Yes	Low-	Expert opinion	100	[11, 29]
Statement 12	Patients with disorders of gut brain interaction complaining of functional bloating and abdominal distension might have impaired propulsion and delayed clearance of intraluminal gas, due to abnormal reflex control of gas transit	Yes	Low-	Expert opinion	90	[30, 31]
Statement 13	Bloating and distension may be secondary to organic disorders, which need to be considered and evaluated appropriately	Yes	Low-	Good practice statement	100	[4, 27, 32]
Statement 14	Functional bloating and abdominal distension (i.e., not associated with organic disorders) are highly prevalent symptoms in a variety of DGBI and frequently represent the most troublesome complaint	Yes	Low -	Expert opinion	100	[3, 6, 23, 33–37]
Section 2. Epidemiology and diagnosis criteria						
Statement 15	Functional bloating and abdominal distension are frequent and can overlap with other disorders of gut-brain interaction	Yes	Moderate-	Expert opinion	100	[5]
Statement 16	Rome IV diagnostic criteria are adequate for the diagnosis of functional bloating and abdominal distension	Yes	Low-	Expert opinion	90	[4]
Section 3. Diagnostic procedures and evaluation						
Statement 17	Accurate diagnostic evaluation of bloating and abdominal distension includes on a thorough medical history and comprehensive physical examination	Yes	Very low	Good practice statement	75	NA
Statement 18	The medical history and physical examination serve as the foundation for determining the need for additional investigations	Yes	Very low	Good practice statement	95	NA
Statement 19	Validated patient-reported outcome measures (PROMs) can provide an	Yes	Low	Expert opinion	80	[38, 39]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
	unbiased diagnosis of the presence of bloating and/or abdominal distension					
Statement 20	Upon diagnosis, specific questionnaires may be instrumental in conducting further work-up, evaluating treatment response, and conducting population studies	Yes	Very low	Expert opinion	95	[8, 9]
Statement 21	A normal physical examination conducted during a patient's office visit does not exclude the possibility of excessive bloating and abdominal distension during other times, especially if the patient has a medical history that suggests the presence of such symptoms	Yes	Very low	Good practice statement	100	NA
Statement 22	The combination of physical examination and medical history typically allows differentiation between an abdominal distension caused by ascites and a non-fluid abdominal distension	Yes	Very low	Expert opinion	90	[40]
Statement 23	A detailed medical history related to food intake should be obtained from patients experiencing bloating/ abdominal distension	Yes	Low	Good practice statement	95	[41, 42]
Statement 24	Endoscopic procedures or imaging techniques have limited diagnostic value in assessing functional bloating/abdominal distension but may be required to rule out organic causes	Yes	Low	Good practice statement	100	[43–45]
Statement 25	Maldigestion and malabsorption, as in carbohydrate intolerance, pancreatic exocrine insufficiency, Crohn's disease and coeliac disease, should be considered in the differential diagnosis of bloating and abdominal distension	Yes	Moderate	Good practice statement	90	[10]
Statement 26	Stool elastase may be used to assess exocrine pancreatic insufficiency as a cause of bloating and abdominal distension	Yes	Low	Good practice statement	80	[46]
Statement 27	Hypothyroidism and diabetes mellitus are the most common endocrine disorder that are associated with bloating and abdominal distension	Yes	Very low	Good practice statement	75	[47–50]
Statement 28	In women experiencing bloating and abdominal distension, conditions related to sex hormone fluctuations, that can impact gastrointestinal motility and visceral sensitivity should be considered	Yes	Very low	Good practice statement	80	[51]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
Statement 29	In patients with severe bloating and abdominal distension, the exclusion of chronic intestinal pseudo-obstruction (CIPO), colonic dysmotility (CPO) and enteric dysmotility (ED) is recommended	Yes	Very low	Good practice statement	95	[52]
Statement 30	A trial of elimination diet with meticulous assessment of its effect on bloating and abdominal distension may suggest an association between diet and such symptoms	Yes	Very low	Good practice statement	100	[24, 53]
Statement 31	Diagnosis of carbohydrate intolerance or malabsorption, as potential causes of bloating and abdominal distention, is made by combining results of breath tests (measuring exhaled hydrogen and methane) and reported gastrointestinal symptoms after an oral load of carbohydrate	Yes	Low	Weak	80	[54, 55]
Statement 32	Breath tests used to identify potential causes of bloating and distension should adhere to the procedures outlined in the latest guidelines for breath testing	Yes	Low	Weak	85	[54, 55]
Statement 33	Psychological factors or psychiatric conditions like work-related or social stressors, anxiety, depression, and somatization may aggravate the perception and clinical impact of functional bloating and abdominal distension, and thus must be considered in its clinical evaluation	Yes	Moderate	Good practice statement	100	[56]
Statement 34	Laboratory tests can be useful to diagnose underlying medical conditions associated with bloating and abdominal distension but do not provide useful information for diagnosing functional bloating or abdominal distension	Yes	Low	Good practice statement	100	[27]
Statement 35	Microbiota stool tests do not provide useful information for diagnosing bloating or abdominal distension and should not be used	Yes	Very low	Good practice statement	95	[57]
Statement 36	There is insufficient evidence to recommend measuring gas volume in the bowel in clinical practice; however, it may be useful for research purposes	Yes	Low	Expert opinion	95	[58, 59]
Statement 37	Objective evaluation of abdominal distension with abdominal CT (combined with EMG) or a non-stretch belt with a metric tape is reserved for research	Yes	Very low	Expert opinion	95	[60]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
Statement 38	Studies of gastrointestinal motility or transit have limited clinical yield for both diagnosis and treatment of functional bloating and abdominal distension	Yes	Low	Expert opinion	95	[61]
Statement 39	The term bloating is used to describe the subjective sensation of increased abdominal pressure, fullness or trapped abdominal gas, while the term distension refers to an objective (i.e., measurable) increase in abdominal girth	Yes	Low	Expert opinion	95	[4]
Statement 40	It is frequent for bloating and abdominal distension to present in conjunction; however, this is not always the case	Yes	Moderate	Weak	100	[6, 34, 62]
Statement 41	In patients with functional bloating, with or without abdominal distension, there is no consistent correlation between severity of bloating, increase in abdominal girth and volume of intestinal gas	Yes	Moderate	Weak	95	[29, 63–65]
Section 4. Treatment						
Statement 42	Poor physical activity is one of the risk factors of functional bloating and abdominal distension	No	—	—	65	—
Statement 43	Physical activity, particularly aerobic exercise, seems to have a positive impact on gastrointestinal symptoms, especially in patients with DGBI	Yes	Very low	Expert opinion	80	[35]
Statement 44	All patients with functional bloating and abdominal distention should receive a lactose-limiting diet	No	—	—	10	—
Statement 45	Patients with functional bloating and abdominal distention should receive a lactose-limiting diet based on their self-reported symptoms	No	—	—	55	—
Statement 46	Patients with functional bloating and abdominal distention should receive a lactose-limiting diet based on validated assessment of symptoms (intolerance)	No	—	—	60	—
Statement 47	Patients with functional bloating and abdominal distention should receive a lactose-limiting diet based on the presence of lactose malabsorption [breath test)	No	—	—	50	—
Statement 48	Patients with functional bloating and abdominal distention should receive a lactose-limiting diet trial based on their self-reported symptoms or the presence of intolerance during a	Yes	Very low	Good practice statement	70	[66]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
	breath test after ingestion of a defined lactose load					
Statement 49	Patients with functional bloating and abdominal distention should receive a lactose-limiting diet trial based on the presence of lactose malabsorption (asymptomatic increase of hydrogen in breath test after ingestion of lactose)	No	—	—	55	—
Statement 50	For the general patient population with functional bloating and abdominal distension, a lactose-restrictive diet is of limited efficacy as the symptoms are not related to lactose intolerance, either with or without malabsorption	Yes	Very low	Good practice statement	75	[66]
Statement 51	A low FODMAP diet is effective in reducing functional bloating and abdominal distention	Yes	Moderate	Weak	80	[67]
Statement 52	There is insufficient evidence to recommend a gluten-free diet in patients with functional bloating and abdominal distension, unless they have coeliac disease	Yes	Low	Expert opinion	90	[68]
Statement 53	The use of selected probiotics may improve bloating and abdominal distension	Yes	Low	Good practice statement	80	[69]
Statement 54	Probiotic medications differ greatly from one another, and the outcomes observed from one cannot be generalised to the others	Yes	Low	Expert opinion	90	[69]
Statement 55	There are no encouraging data to recommend the use of prebiotics or symbiotic for the treatment of functional bloating and abdominal distension	Yes	Very low	Expert opinion	75	[70]
Statement 56	Rifaximin may be useful for the treatment of functional bloating and abdominal distention with efficacy	Yes	Low	Good practice statement	80	[71]
Statement 57	We do not recommend the use of other antibiotics for the treatment of functional bloating and abdominal distention	Yes	Very low	Good practice statement	85	NA
Statement 58	As a group, antispasmodic agents are effective in relieving functional bloating and abdominal distention	No	—	—	60	—
Statement 59	Among antispasmodic agents, pinaverium and otilonium bromide have been shown to be the most effective drugs for the treatment of functional bloating and abdominal distension	Yes	Low	Weak	75	[72]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
Statement 60	There is insufficient evidence to recommend simethicone for the treatment of functional bloating and abdominal distension	Yes	Low	Weak	75	[72]
Statement 61	Lubiprostone, plecanatide and linaclotide are effective in improving constipation associated with functional bloating and abdominal distension	Yes	Moderate	Weak	90	[73]
Statement 62	Linaclotide is the most effective secretagogue for functional bloating, although limited data is available for lubiprostone and plecanatide as well	Yes	Low	Good practice statement	85	[73]
Statement 63	There are no prospective data to support the use of prucalopride for functional bloating and abdominal distension. Prucalopride may improve bloating and abdominal distension in patients with constipation, gastroparesis or motility disorders	Yes	Very low	Expert opinion	90	[74]
Statement 64	There is insufficient evidence to recommend neostigmine (IV) or pyridostigmine for patients with functional bloating and abdominal distension	Yes	Very low	Expert opinion	100	[31, 75]
Statement 65	There is insufficient evidence to recommend metoclopramide and acotiamide for the treatment of functional bloating and abdominal distension	Yes	Very low	Expert opinion	100	[76]
Statement 66	Indirect evidence supports tegaserod use for the treatment of functional bloating. However, due to its possible cardiac side effects close cardiac monitoring should be performed	Yes	Very low	Expert opinion	95	[74]
Statement 67	Selective serotonin reuptake inhibitors (SSRI's) are effective in reducing symptoms of functional bloating	Yes	Low	Good practice statement	90	[77]
Statement 68	Tricyclic antidepressants (TCA) such as amitriptyline are effective in reducing symptoms of functional bloating	Yes	Moderate	Good practice statement	90	[78]
Statement 69	Buspirone, a serotonin 5-HT1A receptor agonist, commonly used for treating anxiety, improves postprandial functional bloating	Yes	Low	Expert opinion	75	[79]
Statement 70	In patients with discrete episodes of visible abdominal distension, biofeedback-guided techniques to re-educate abdominothoracic muscular	Yes	Very low	Good practice statement	90	[80]

(Continues)

TABLE 1 | (Continued)

Section and number	Statement/recommendation	Endorsement	Level of evidence	Recommendation	Agreement	References
	activity are safe and effective for correction of abdominal distention and are associated with improvement in the subjective sensation of abdominal bloating					
Statement 71	There are no specific neuromodulatory techniques that have been specifically studied for the treatment of functional bloating and abdominal distension	Yes	Very low	Expert opinion	95	[81]
Statement 72	Although acupuncture and some herbal medicines such as Zataria-Trachyspermum, rikkunshito, STW5, peppermint oil, curcumin and Boswellia extracts have been shown to reduce bloating and abdominal distension in patients with IBS, there is insufficient evidence to recommend them in the treatment of functional bloating and abdominal distention	Yes	Very low	Expert opinion	95	[82–84]
Statement 73	Cognitive behaviour therapy (CBT) can be offered to patients with functional bloating associated with IBS as an alternative treatment in patients refractory to conventional therapies	Yes	Low	Good practice statement	95	[85]
Statement 74	Hypnotherapy improves symptoms of bloating in patients with IBS. However, its effect on functional bloating and abdominal distension was not explored and cannot be recommended	Yes	Very low	Expert opinion	95	[85–90]
Statement 75	There is not enough evidence to recommend other psychological therapies in functional bloating and abdominal distension	Yes	Very low	Expert opinion	95	[91]

In the oesophagus, gas primarily results from inadvertent air swallowing, leading to supragastric belching and potential chronic eructation [92]. Gas in the stomach may cause discomfort, relieved by belching or passing gas into the bowel. In post-fundoplication, this process can be disrupted, leading to gas-bloat syndrome [93]. In the duodenum, CO2 is produced by the reaction of acid and bicarbonate, diffusing into the blood, while N2 diffuses into the intestinal lumen [19].

Colonic gas mainly originates from the metabolic activity of gut microbiota, which produce CO2, H2, and CH4 from carbohydrates [94, 95]. Significant inter-individual differences exist in gas production, with some gas being consumed by other microorganisms, reducing the net volume produced [96, 97]. H2, CH4, and CO2 can diffuse from the colon into the blood, with the extent depending on gas accumulation rates [98]. Breath tests detecting H2 and CH4 are used to diagnose carbohydrate malabsorption, SIBO, or to measure orocecal transit time [54].

Gas is ultimately evacuated through the anus, with volumes varying by diet. The mean flatus excretion rate is 17 mL/h in fasting conditions, increasing significantly after consuming non-absorbable carbohydrates or high-residue meals [20, 21]. The average number of daily anal gas evacuations is about 10, potentially doubling or tripling with a flatulogenic diet (e.g., plant-based diets rich in fermentable residues) [21]. The volume of gas evacuated is mainly odourless, with the odour of flatus primarily due to sulphur-containing compounds like hydrogen sulphide and methanethiol, resulting from bacterial protein metabolism [99].

TABLE 2 | Summary of the main recommendations on functional bloating and abdominal distension.

Rome IV diagnostic criteria are adequate for the diagnosis of functional bloating and abdominal distension
The medical history and physical examination serve as the foundation for determining the need for additional systemic work-up (laboratory, imaging and endoscopy)
Laboratory tests can be useful to diagnose underlying medical conditions associated with bloating and abdominal distension but do not provide useful information for diagnosing functional bloating or abdominal distension
The term bloating is used to describe the subjective sensation of increased abdominal pressure, fullness or trapped abdominal gas, while the term distension refers to an objective (i.e., measurable) increase in abdominal girth
Patients with functional bloating and abdominal distention should receive a lactose-limiting diet trial based on their self-reported symptoms or the presence of intolerance during a breath test after ingestion of a defined lactose load
A low FODMAP diet is effective in reducing functional bloating and abdominal distention
Rifaximin may be useful for the treatment of functional bloating and abdominal distention with efficacy
Among antispasmodic agents, pinaverium and otilonium bromide have been shown to be the most effective drugs for the treatment of functional bloating and abdominal distension
Lubiprostone, plecanatide and linaclotide are effective in improving constipation associated with functional bloating and abdominal distension
Linaclotide is the most effective secretagogue for functional bloating, although limited data is available for lubiprostone and plecanatide as well
Selective serotonin reuptake inhibitors (SSRI's) are effective in reducing symptoms of functional bloating
Tricyclic antidepressants (TCA) such as amitriptyline are effective in reducing symptoms of functional bloating
In patients with discrete episodes of visible abdominal distension, biofeedback-guided techniques to re-educate abdominothoracic muscular activity are safe and effective for correction of abdominal distention and are associated with improvement in the subjective sensation of abdominal bloating
Hypnotherapy improves symptoms of bloating in patients with IBS. However, its effect on functional bloating and abdominal distension was not explored and cannot be recommended

4.1.2 | Which Diseases Predispose to Abdominal Distension?

- ➢ DGBI such as IBS, functional diarrhoea or functional constipation are predisposing factors for the presence of functional bloating and abdominal distension (100% agreement—ungraded: good practice statement)
- ➢ A variety of pathophysiologic consequences which result from organic GI or extraintestinal diseases, such as intraluminal accumulation of nutrients, bacterial metabolism, mucosal inflammation or altered visceral motility and perception, may predispose to bloating and abdominal distension (90% agreement—ungraded: expert opinion)

DGBI are a major cause of functional bloating and abdominal distension, with approximately 85% of patients with IBS, functional diarrhoea or functional constipation reporting bloating, and 25% experiencing severe symptoms [3, 6]. Positive demographic predictors include female gender, Latin-American race, and age under 60 years [10, 22]. Over 90% of patients with functional constipation and IBS-C report bloating, with greater abdominal distension observed in those with prolonged colonic transit [23, 100].

Carbohydrate intolerance and diseases like coeliac disease and inflammatory bowel disease (IBD) are common causes of bloating [22–24]. Bloating and distension due to malabsorption arise from water accumulation in the small bowel or gas in the colon, particularly with poorly absorbable fermentable carbohydrates like FODMAPs [101]. DGBI also play a significant role in these symptoms [12]. A meta-analysis revealed a higher prevalence of lactose intolerance in patients with IBS compared to healthy controls (OR 3.49; 95% CI, 1.62–7.55) [101, 102].

In coeliac disease, malabsorbed nutrients increase the osmotic load in the small intestine, leading to bloating, distension, and accelerated GI transit [103]. Additionally, 70% of patients with non-coeliac gluten sensitivity (NCGS) report bloating. However, a double-blind crossover challenge [104] found that fructan, rather than gluten, induces symptoms in patients with self-reported NCGS. In clinical practice, in this condition, avoidance of gluten is frequently recommended, as avoidance it is usually accompanied by a parallel avoidance of fructan [105, 106].

4.1.3 | What Is the Role of Visceral Perception (Visceral Sensitivity and Hypersensitivity, Sensitivity to Distension, Sensitivity to Chemical Nociceptors, Etc.) in Functional Bloating and Abdominal Distension?

- ➢ Visceral hypersensitivity, rather than distension of the GI tract due to increased intraluminal gas, plays a key role in the pathophysiology of functional bloating and abdominal distension (95% agreement—ungraded: expert opinion)
- ➢ Visceral hypersensitivity may trigger aberrant viscerosomatic reflexes, including abdomino-phrenic dyssynergia causing abdominal distension (90% agreement—ungraded: expert opinion)

Visceral hypersensitivity, characterised by abnormal pain signalling in response to chemical [107] or mechanical stimuli [108], is central to the pathophysiology of DGBI. It has been documented in conditions such as non-cardiac chest pain, FD, and IBS [109–116]. Visceral pain and discomfort are detected by nociceptors when excessive and potentially noxious thermal, mechanical, or chemical stimuli are present in the GI tract. The peripheral nerve terminals are equipped with various receptors and ion channels that can be pro-nociceptive (excitatory) or anti-nociceptive (inhibitory). Depending on the balance between these signals, neurons will signal discomfort to the brain. Visceral hypersensitivity can occur both at a peripheral level, through mechanisms such as local immune activation, and at a central level, in the spinal cord or the brain through abnormal processing of incoming sensory signals [117, 118].

Research indicates that colonic gas content is similar in patients with IBS and healthy controls in normal conditions and after ingesting non-absorbable carbohydrates like inulin [12, 63, 119]. However, only patients with IBS experience heightened symptoms, suggesting that functional bloating is driven more by visceral hypersensitivity than by actual distension [12]. Similarly, FD patients with gastric hypersensitivity report greater postprandial bloating [120]. In terms of visceral sensitivity, there is a distinction between functional bloating and abdominal distension. Patients with bloating but no abdominal distension exhibit lower pain and urgency thresholds, pointing to visceral hypersensitivity as a key factor [25]. Moreover, the symptom of functional bloating was associated with visceral hypersensitivity in patients with lactose malabsorption, while there was no correlation between the degree of functional bloating and abdominal distension [64].

4.1.4 | What Is the Role of the Abdominal Wall, Including Abdomino-Phrenic Dyssynergia in Bloating and Distension?

- ➢ Physiologically, the accommodation response to any increase in intraluminal volume is achieved by relaxation of the diaphragm and by increasing the postural tone of the abdominal wall (100% agreement—ungraded: expert opinion)
- ➢ During episodes of abdominal distension, a diaphragmatic descent, as a result of an increase in its muscular activity, is coupled with a decrease in abdominal wall postural tone, causing the abdominal wall to bulge; this phenomenon is known as abdomino-phrenic dyssynergia (100% agreement—ungraded: expert opinion)

The normal response to increased intraluminal bowel content, whether experimentally induced by colonic gas infusion [121] or caused by meal ingestion [122], involves diaphragmatic relaxation, allowing the abdominal cavity to expand craniocaudally without visible distension, aided by increased postural tone of the anterior abdominal wall [10, 26, 27]. However, in patients with DGBI, visible abdominal distension is associated with diaphragmatic contraction and anterior abdominal wall relaxation [11, 26, 28, 122, 123]. This response, present during both induced and spontaneous episodes, leads to caudoventral redistribution of abdominal gas content and increased girth, despite only a slight increase in intestinal gas volume [11]. This phenomenon is termed abdomino-phrenic dyssynergia [26, 28].

Intercostal muscles also play a role in this process. Normally, diaphragmatic descent is balanced by relaxation of the intercostals to preserve lung capacity [121]. However, during severe distention, paradoxical chest wall elevation due to intercostal contraction may occur, explaining occasional shortness of breath reported by patients [26, 121, 124]. Understanding these mechanisms has informed the development of therapeutic strategies [124, 125]. The underlying cause of this abnormal viscerosomatic response is not fully understood. A study in healthy volunteers showed that voluntary diaphragmatic contraction after a meal worsened bloating and discomfort, suggesting a pathological muscle response in DGBI [126].

4.1.5 | What Is the Role of Motility Disorders in Functional Bloating and Abdominal Distension?

- ➢ Intestinal dysmotility and intestinal gas retention are uncommon causes of functional bloating and abdominal distension (70% agreement—ungraded: expert opinion)
- ➢ Intestinal dysmotility can result in a significant retention of gas and non-gaseous contents in the GI tract, leading to pronounced abdominal distension (100% agreement—ungraded: expert opinion)
- ➢ Patients with DGBI complaining of bloating and abdominal distension might have impaired propulsion and delayed clearance of intraluminal gas, due to abnormal reflex control of gas transit (90% agreement—ungraded: expert opinion)

Intestinal dysmotility and intestinal gas retention are rare causes of functional bloating and abdominal distension. These symptoms, along with other gas-related conditions, may arise from primary or secondary neuro-myopathic disorders of the small bowel. In such cases, the symptoms are typically severe, including pronounced abdominal distension, pain, and an inability to eat, all resulting from gut dysmotility, as defined by manometric criteria. In certain instances, intestinal dysmotility can lead to significant and painful retention of gas and non-gaseous contents within the small bowel, resulting in nausea, vomiting and prominent abdominal distension, characteristic of intestinal pseudo-obstruction. This is the only condition where small bowel dysmotility directly produces gas-related symptoms, including objective abdominal distension. In these patients, the abdominal distension is caused by an increase in abdominal contents with elevation of the diaphragm [11, 29].

Some studies have indicated that patients with DGBI who experience functional bloating and abdominal distension exhibit impaired propulsion and delayed clearance of intraluminal gas [30, 31], potentially due to abnormal reflex control of gas transit [127, 128]. This motor dysfunction, however, cannot be identified with conventional techniques such as intestinal manometry or scintigraphic measurement of solid/liquid chyme transit, and the relevance of these motor alterations to the symptoms remains unclear. Recent imaging studies using CT and MRI have

meticulously evaluated the relationship between functional bloating, abdominal distension, and flatulence relative to gut contents, but failed to identify any changes in luminal volume or content distribution that could account for the symptoms in patients with DGBI [63, 119, 129].

4.1.6 | What Is the Association With Other Conditions (Organic Disorders, DGBI, Etc.)?

- ➢ Bloating and abdominal distension may be secondary to organic disorders, which need to be considered and evaluated appropriately (100% agreement—ungraded: good practice statement)
- ➢ Functional bloating and abdominal distension (i.e., not associated with organic disorders) are highly prevalent symptoms in a variety of DGBI and frequently represent the most troublesome complaint (100% agreement—ungraded: expert opinion)

Bloating and visible abdominal distension can indicate organic diseases that require specific treatment, and these should be considered in the differential diagnosis. Red flags suggesting organic disorders must be identified in the patient history, physical examination, and laboratory testing, especially for severe conditions like neoplastic, mechanical, or neuromuscular pseudo-obstructions, early ascites in advanced liver disease, or bowel ischaemia [4, 27, 32]. While most patients do not have structural abnormalities, carbohydrate malabsorption due to lactase deficiency is common [130].

Functional bloating and abdominal distension often appear within DGBI, particularly in IBS, where functional bloating is highly prevalent. Studies have shown that 62%–76% of patients with IBS report functional bloating, a consistent finding across Rome I, II, III, and IV criteria [3, 6, 23, 33–37]. Visible abdominal distension is also common in IBS, with a prevalence of 48%–75%, particularly in IBS-C and IBS-M [6, 34, 62, 100].

In FD, upper abdominal bloating is frequently reported, though it is not a diagnostic criterion [6, 32, 131]. The prevalence of functional bloating in FD ranges from 40% to 68% [6, 132, 133], but it can be challenging to distinguish from fullness, a recognised dyspeptic symptom under Rome IV criteria [134]. Notably, treating dyssynergic defecation in FD patients with biofeedback has been shown to improve both fullness and FD symptoms [135].

4.2 | Section 2. Epidemiology and Diagnostic Criteria

- ➢ Functional bloating and abdominal distension are frequent and can overlap with other DGBI (100% agreement—ungraded: expert opinion)

Functional bloating and abdominal distension are among the most frequently reported GI symptoms, often linked to a variety of disorders [1]. These symptoms are more prevalent in women than in men, with an odds ratio (OR) of 2.8 (2.0–3.9). They are also more common in older patients and are frequently associated with psychological disorders, including somatization [2, 3, 6]. Consequently, there is a considerable overlap with other DGBI, as they share similar risk factors. Among these, IBS, functional constipation, functional diarrhoea, and FD are the most commonly reported. In these disorders, the prevalence of gas-related symptoms can range from 66% to 90%, often with a greater overall severity of symptoms [3, 6, 22].

The prevalence of functional bloating is notably higher in patients with constipation-predominant IBS (IBS-C) compared to those with diarrhoea-predominant IBS (IBS-D) [136]. However, the specific prevalence within each DGBI has not yet been well characterised. Functional bloating can also occur as an independent condition. According to the Rome Foundation Global Epidemiology Study, the global prevalence of functional bloating is 3.5% [5]. This extensive multinational survey, which encompassed 33 countries, found a pooled prevalence of 4.6% among females, compared to 2.4% in males. Additionally, the highest prevalence of functional bloating was observed in individuals aged 40–61 years. Geographical variations were also noted, with Italy reporting the highest prevalence at 8.2% [5].

- ➢ Rome IV diagnostic criteria are adequate for the diagnosis of functional bloating and abdominal distension (90% agreement—ungraded: expert opinion)

In patients with functional bloating who self-report abdominal distension, objective distension can be measured by computed tomography (CT) [137]. However, for functional bloating, an objective measure is not feasible as the amount of intraluminal gas is similar to that observed in healthy individuals, indicating that it should be considered a sensation rather than an objective physical phenomenon [63]. Diagnosis based on the ROME IV criteria has been proven to be reliable and consistent with previous epidemiological studies [4]. However, it is crucial to differentiate between functional bloating and abdominal distension and other DGBI. Therefore, if a patient meets the ROME IV criteria for functional bloating and abdominal distension, it is essential to ensure they do not also meet the criteria for other DGBI such as IBS, functional constipation, functional diarrhoea, or FD [134, 138]. Adhering to the ROME IV criteria enables a standardised clinical approach and provides clear guidance for further diagnostic procedures and therapy [139].

4.3 | Section 3. Diagnostic Procedures and Evaluation

4.3.1 | Detailed Medical History and Physical Examination

- ➢ Accurate diagnostic evaluation of bloating and abdominal distension as symptoms includes a thorough medical history and comprehensive physical examination (75% agreement—very low level of evidence—ungraded: good practice statement)
- ➢ The medical history and physical examination serve as the foundation for determining the need for additional

investigations (95% agreement—very low level of evidence—ungraded: good practice statement)

- ➢ Validated patient-reported outcome measures (PROMs) can provide an unbiased diagnosis of the presence of functional bloating and/or abdominal distension (80% agreement—low level of evidence—ungraded: expert opinion)
- ➢ Upon diagnosis, specific questionnaires may be instrumental in conducting further work-up, evaluating treatment response, and conducting population studies (95% agreement—very low level of evidence—ungraded: expert opinion)
- ➢ A normal physical examination conducted during a patient's office visit does not exclude the possibility of excessive functional bloating and abdominal distension during other times, especially if the patient has a medical history that suggests the presence of such symptoms (100% agreement—very low level of evidence—ungraded: good practice statement)
- ➢ The combination of physical examination and medical history typically allows differentiation between an abdominal distension caused by ascites and a non-fluid abdominal distension (90% agreement—very low level of evidence—ungraded: expert opinion)

The diagnosis of bloating and abdominal distension, as symptoms, is based on a thorough medical history and physical examination. Key aspects include the timing of symptoms, diurnal patterns, triggers and associated signs. Factors like diet, lifestyle, stress, underlying conditions and bowel habits should also be evaluated as well as treatment affecting transit such as opioids (delaying gastric transit for example). Comprehensive evaluation is necessary for patients with alarming signs, while younger patients with stable symptoms over 6 months often need minimal further investigation. If bloating is confirmed as a symptom, the physician should always focus on ruling out any related-organic pathology (see chapter exclusion of organic causes below). A systematic initial work-up is recommended (Figure 1).

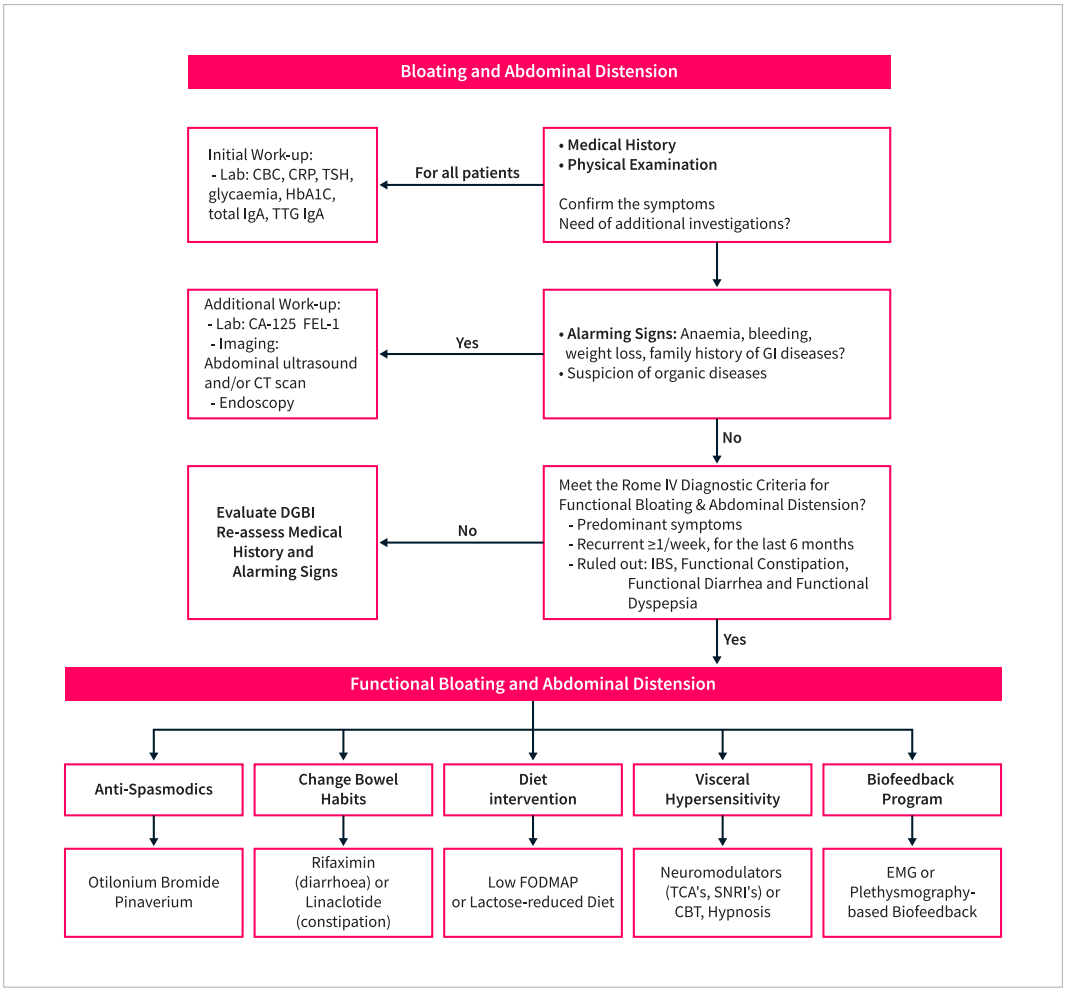

FIGURE 1 | Algorithm of recommendations for the optimal management of functional bloating and abdominal distension. CBC, Cell Blood Count; CBT, cognitive behaviour treatment; CRP, C-Reactive Protein; CT, Computed Tomography; DGBI, disorders of gut-brain interaction; EMG, Electromyography; FEL, Faecal Elastase; FODMAP, Fermentable; GI, Gastrointestinal; HbA1C, Haemoglobin A1C; IBS, Irritable bowel syndrome; Oligosaccharides; Disaccharides; Monosaccharides and Polyols; IBS, irritable bowel syndrome; GI, gastrointestinal; TCA, tricyclic antidepressant; TSH, Thyroid Stimulating Hormone; TTG, Tissue Transglutaminase Antibody; SNRI, Serotonin-norepinephrine reuptake inhibitors. #: biofeedback has been shown to be effective especially in patients exhibiting visible abdominal distention.

Assessing GI symptoms is subjective and prone to bias. Validated patient-reported outcome measures (PROMs) aid in accurately diagnosing bloating and distension, reducing assessment time. These tools are available for both adults and children (e.g., pSAGIS) [38, 39]. After diagnosis, specific questionnaires can further evaluate symptom impact and treatment response, and are useful in population studies [8, 9].

Functional bloating and abdominal distension, especially the latter, often follow a circadian rhythm, worsening later in the day and subsiding overnight. Continuous measurement of abdominal girth via abdominal inductance plethysmography is possible, though its clinical value is unproven [40]. Other causes for a distended abdomen, such as ascites, organ enlargement, or pregnancy, should be considered. Ascites is typically detected through physical examination signs, such as a positive fluid wave, shifting dullness or the presence of a puddle sign [40].

Baseline gas analysis can identify the origin of GI gas, with elevated nitrogen suggesting aerophagia, and increased carbon dioxide, hydrogen, or methane indicating colonic metabolism of food residue [140]. However, gas analysis is rarely used clinically; instead, symptoms like belching, excessive salivation, or stress-related onset may indicate aerophagia. Bloating associated with meals, occurring at night or producing foul odours suggests intestinal gas formation rather than air swallowing [141]. Functional bloating is often linked to altered bowel movements, as seen in IBS or other DGBI [142]. Some patients may confuse bloating with postprandial epigastric distension [10].

Retrograde cricopharyngeal dysfunction (inability to belch) can cause significant bloating/distension in some patients [143, 144]. Asking about belching ability or rumbling retrosternal noises may help identify this disorder.

➢ A detailed medical history related to food intake should be obtained from patients experiencing functional bloating/abdominal distension (95% agreement—low level of evidence—ungraded: good practice statement)

Patients with DGBI, particularly IBS with bloating/abdominal distension, frequently report food-related symptoms [41, 42]. The osmotic activity of incompletely absorbed carbohydrates can cause fluid accumulation in the small bowel [145]. In the colon, these carbohydrates are metabolised by bacteria into gases, contributing to symptoms of malabsorption [24, 53, 98]. Notably, carbohydrate-induced symptoms may occur even without detectable malabsorption [12, 146].

In a study of 330 patients with IBS and 80 healthy volunteers [41], two-thirds of patients with IBS reported meal-related symptoms, gas being the most common (25%), linked to foods like cabbage, onions, peas/beans, raw vegetables, and peppers. Abdominal distension, accounting for 10% of symptoms, was associated with pizza, cabbage, peas/beans, deep-fried food, and onions, all foods rich in FODMAPs (fermentable oligo-, di-, and monosaccharides and polyols).

Fried and fatty foods are also common IBS triggers, affecting 50% of patients [42]. Lipids can exacerbate symptoms by inhibiting gut motility, inducing hypersensitivity and increasing gas retention [127, 147, 148]. High-calorie meals have been shown to increase abdominal girth in healthy individuals [149]. Fat intake has also been linked to upper abdominal bloating in 18% of FD patients [150, 151]. High sodium intake and protein-rich diets have also been associated with increased bloating [152, 153].

4.3.2 | Exclusion of Organic Causes

➢ Endoscopic procedures or imaging techniques have limited diagnostic value in assessing functional bloating and abdominal distension but may be required to rule out organic causes (100% agreement—low level of evidence—ungraded: good practice statement)

Organic diseases can disrupt normal intestinal gas handling, including absorption, propulsion, and evacuation [20, 98]. Endoscopic procedures or imaging may be necessary to exclude GI or extraintestinal conditions that impair gas propulsion and evacuation, such as bowel obstruction or pseudo-obstruction, ascites, and abdominal tumours [43–45]. Non-invasive tests, such as abdominal ultrasound and radiologic examination, can provide information on gas retention and accumulation [154, 155]. CT or MRI scans offer more specific insights into diseases that impair gas transport by compressing or obstructing the GI lumen.

Endoscopy is used to diagnose upper or lower GI diseases that cause distension by obstructing gas passage. Clinical guidelines suggest using alarming signs, such as new-onset anaemia, nocturnal pain, weight loss, bloody stools, severe tenderness, succussion splash, fever, vomiting, steatorrhoea, family history of GI malignancy and new-onset diarrhoea, to guide advanced imaging or endoscopic tests [27, 43, 156]. However, except for anaemia, the scientific validation of this approach is limited. The role of impaired gas absorption, potentially due to inflammatory or vascular disorders, contributing to gas accumulation, remains uncertain.

➢ Maldigestion and malabsorption, as in carbohydrate intolerance, pancreatic exocrine insufficiency (PEI), Crohn's disease and coeliac disease, should be considered in the differential diagnosis of bloating and abdominal distension (90% agreement—moderate level of evidence—ungraded: good practice statement)

➢ Stool elastase may be used to assess exocrine pancreatic insufficiency as a cause of bloating and abdominal distension (80% agreement—low level of evidence—ungraded: good practice statement)

Maldigestion and malabsorption, such as in carbohydrate intolerance, pancreatic exocrine insufficiency (PEI), Crohn's disease and coeliac disease, should be considered when diagnosing severe or refractory bloating and abdominal distension. Indicators of malnutrition, including unintentional weight loss, chronic diarrhoea, steatorrhoea, low BMI, and nutrient deficiencies, support the suspicion of malabsorption syndrome [10].

The faecal pancreatic elastase (FEL-1) test is a preferred first-line test for PEI due to its cost-effectiveness, convenience, and availability [46]. FEL-1 is a stable pancreatic enzyme, unaffected by gut passage or temperature for up to 72 h, reflecting overall pancreatic secretion [157, 158]. However, liquid stool can cause false positive results, necessitating adjustment for stool water content [46, 159]. FEL-1 levels < 200 μg/g have a sensitivity of 25%–100% for PEI, with specificity over 90% [46].

Coeliac disease screening involves serologic testing with anti-tissue transglutaminase antibodies and IgA while on a gluten-containing diet [160, 161]. Total IgA measurement is crucial to exclude IgA deficiency, affecting 2%–3% of coeliac patients [162]. Duodenal biopsies are still mostly suggested for confirmation in all situations, though no-biopsy approach has been suggested to be the future way by large international prospective studies and meta-analysis [163]. Obtaining a single biopsy per pass improves specimen quality [164]. For detailed diagnostic guidelines, we refer to the European Society for the Study of Coeliac Disease guidelines [160].

➢ Hypothyroidism and diabetes mellitus are the most common endocrine disorder that are associated with bloating and abdominal distension (75% agreement –very low level of evidence—ungraded: good practice statement)

Certain endocrine conditions, including hypothyroidism and diabetes, present with digestive symptoms, such as bloating and abdominal distension. Hypothyroidism often leads to reduced GI motility, which promotes small intestinal bacterial overgrowth [165]. This gut dysbiosis can further impair GI tract function, worsening chronic symptoms [47, 166]. Slower gas evacuation combined with increased gas production exacerbates bloating and abdominal distension. Screening for thyroid dysfunction involves serum thyroid-stimulating hormone (TSH) evaluation; risk factors include female sex, age, low iodine intake, family history of thyroid disease, and intake of iodine-containing drugs such as amiodarone [48].

Long-term and uncontrolled diabetes causes structural and functional changes throughout the brain-gut axis, affecting the enteric, autonomic, and central nervous systems [49, 50]. Factors such as hyperglycaemia, hypoglycaemia, oxidative stress, inflammation and gut dysbiosis contribute to chronic enteric neuron damage [167]. Autonomic neuropathy, particularly affecting the vagus nerve, reduces GI function, while abnormal central sensory processing can intensify bloating [49]. Blood glucose and glycated haemoglobin (HbA1C) tests, reflecting average levels over the past 3 months, are essential for diagnosing and monitoring diabetes [168].

➢ In women experiencing bloating and abdominal distension, conditions related to sex hormone fluctuations, that can impact GI motility, and visceral sensitivity should be considered (80% agreement—very low level of evidence—ungraded: good practice statement)

Bloating commonly occurs during sex hormone fluctuations that are known to affect GI motility and visceral sensitivity. Fluctuations typically occur during the menstrual cycle, pregnancy, menopause and in gynaecological disorders like endometriosis, polycystic ovary syndrome (PCOS) and ovarian cancer [169]. Hormonal imbalances involving oestrogen and progesterone lead to GI dysmotility, gut dysbiosis and water retention, exacerbating bloating and abdominal distension [51]. Premenstrual bloating is typically observed in healthy women; however, a consistent monthly pattern of worsening symptoms before and during menstruation may indicate endometriosis [170]. Endometriotic lesions (areas of endometrial tissue growth) do not necessarily have to originate from the gut to cause inflammation, bloating, and related symptoms [171].

Bloating is also frequently reported in PCOS (74%–80%) [172]. While the pathogenesis of PCOS remains unclear, insulin resistance and elevated androgen levels are key factors, while gut microbiota alterations also play a significant role [173]. PCOS should be considered in the differential diagnosis of bloating when accompanied by symptoms like hirsutism, hyperandrogenism, ovulatory dysfunction, menstrual disorders, and infertility [174]. Bloating with or without ascites may also be the only symptoms of ovarian cancer, with advancing age and a family history of ovarian and breast cancers being the primary risk factors [175, 176]. The CA125 protein is widely used in ovarian cancer screening or follow-up and should be paired with specific imaging techniques [177].

➢ In patients with severe bloating and abdominal distension, the exclusion of chronic intestinal pseudo-obstruction (CIPO), colonic pseudo-obstruction (CPO) and enteric dysmotility (ED) is recommended (95% agreement—very low level of evidence—ungraded: good practice statement)

CIPO, CPO and ED are severe motility disorders caused by neuromuscular abnormalities [178]. CIPO is diagnosed based on clinical features, natural history, and radiological findings, characterised by bowel obstruction symptoms without a fixed narrowing lesion. Prominent abdominal distension in these patients results from large volumes of gas retention, particularly in the small bowel, with reported gas volumes ranging from 400 to 800 mL [29, 179]. Symptoms such as persistent abdominal distension, intestinal dilation, episodes of occlusion, vomiting, malnutrition and bladder dysmotility strongly suggest CIPO [52]. Intestinal dilation and slow transit often lead to small intestinal bacterial overgrowth (SIBO), contributing to further malabsorption and diarrhoea [180].

A CT scan is recommended for patients with symptoms mimicking mechanical obstruction to exclude organic causes. Small bowel manometry (SBM) indirectly assesses the propriate functioning of the enteric nervous and muscular system activity, refining the understanding of CIPO [137]. Normal neuromuscular function is indicated by a proper fasting pattern and conversion to a fed pattern after a meal; however, it should be mentioned that SBM may not detect distal small bowel dysfunction [181]. Normally, abdominal walls adapt to content changes through abdominal accommodation, with minimal impact on the anterior wall [182]. In CIPO and ED patients, abdominal distension arises from impaired gas transit despite normal abdomino-thoracic accommodation [29].

4.3.3 | Dietary Factors and Breath Tests

➢ A trial of elimination diet with meticulous assessment of its effect on bloating and abdominal distension may suggest an association between diet and such symptoms (100% agreement—very low level of evidence—ungraded: good practice statement)

A survey of symptoms is best achieved by a dedicated dietician and should be conducted following the consumption of poorly absorbable carbohydrates using a validated, standardised questionnaire to ensure the reliability of the results [24, 53]. Validated versions of the aCPQ are now available in the following 10 languages: Bulgarian, English, French, German, Hungarian, Italian, Polish, Romanian, Russian, and Slovenian [183]. In some countries, mobile applications (Carboception [184], currently available only in German-speaking countries) are also available for this purpose.

➢ Diagnosis of carbohydrate intolerance or malabsorption, as potential causes of bloating and abdominal distention, is made by combining results of breath tests (measuring exhaled hydrogen and methane) and reported GI symptoms after an oral load of carbohydrate (80% agreement—low level of evidence -ungraded: weak)

➢ Breath tests used to identify potential causes of functional bloating and abdominal distension should adhere to the procedures outlined in the latest guidelines for breath testing (85% agreement—low level of evidence -ungraded: weak)

Non-invasive breath tests serve to monitor various GI functions or conditions, whose practical application in DGBI has been summarised [185]. The general principle underlying breath tests involves the oral ingestion of a test substance, the metabolism of which results in a substrate that can be measured in expiratory air [185]. Tests available in clinical practice usually employ either carbohydrates or ^{13}C-enriched substrates. Carbohydrates, when metabolised by bacteria in the GI tract, result in hydrogen and methane being exhaled [54], whereas ^{13}C-enriched substrates are metabolised into $^{13}CO_2$, which can be measured in exhaled air [55].

Recently published guidelines provided a comprehensive overview of the background and methodology of breath tests used in clinical medicine in detail [54, 55]. Different carbohydrates are chosen depending on the specific question to be addressed. If the aim is to evaluate malabsorption of a specific carbohydrate, like lactose or fructose, the respective carbohydrate is utilised. However, it is important to note that a causal link between carbohydrate malabsorption and the symptom of bloating (which is part of the spectrum of carbohydrate intolerance symptoms) can only be confirmed by an appropriate measurement of symptoms using validated questionnaires [24, 53]. We recognise that the role of SIBO for symptoms in IBS has been questioned for good reasons on the basis of misinterpretation of hydrogen-based breath tests in the past. In fact, hydrogen-based breath tests only, have poor sensitivity and specificity. The most recent guidelines (on the indications of breath tests and on the diagnosis of malabsorption) do not support the use of breath testing for diagnosing SIBO [54, 186].

4.3.4 | Psychological factors

➢ Psychological factors or psychiatric conditions like work-related or social stressors, anxiety, depression, and somatization may aggravate the perception and clinical impact of functional bloating and abdominal distension, and thus must be considered in its clinical evaluation (100% agreement—moderate level of evidence—ungraded: good practice statement)

Functional GI diseases like IBS are strongly influenced by gut-brain signalling [187]. Psychological distress (especially depression and somatization) can increase postprandial functional bloating and abdominal distension [56]. Research by Van Oudenhove et al. [188] has revealed a significant link between GI symptoms and psychiatric disorders. Psychosocial factors heavily impact the modulation of the central processing of visceral sensory signals, with patients with IBS experiencing higher rates of psychological comorbidities and somatic symptoms, such as fibromyalgia and chronic fatigue syndrome, affecting their quality of life and healthcare utilisation [189–192].

The relationship between anxiety and depression with functional bloating is particularly noteworthy. Anxiety and depression are prevalent in 40% and 30% of patients with IBS, respectively [193]. GI symptoms and persistent bloating are strongly associated with higher anxiety levels [194–196], which can even reduce the effectiveness of a low FODMAP diet [106]. High anxiety levels are closely associated with feelings of fullness and bloating, while depression is linked to abdominal pain and symptoms like nausea and gas that become evident over time.

Stress correlates with daily functional bloating and abdominal pain in patients with IBS, though this link is less apparent after controlling for depression and anxiety [197]. Work-related stress is also associated with bloating, particularly in high-stress professions like aviation, where it is the most frequent GI complaint among commercial aircrew [198, 199]. Additionally, a study of urban working women, including various professionals, found a strong connection between work-related stress and somatic symptoms, such as nausea, gas, indigestion, and bloating [200]. The study highlighted that work stress, particularly effort-reward imbalance, significantly increased the likelihood of experiencing these symptoms [201].

4.3.5 | Laboratory Evaluation, Microbiome

➢ Laboratory tests can be useful to diagnose underlying medical conditions associated with bloating and abdominal distension but do not provide useful information for diagnosing functional bloating or abdominal distension (100% agreement—low level of evidence—ungraded: good practice statement)

➢ Microbiota stool tests do not provide useful information for diagnosing functional bloating or abdominal distension and should not be used (95% agreement—very low level of evidence—ungraded: good practice statement)

Bloating and abdominal distension can indicate underlying medical conditions that can be identified by laboratory testing. In DGBI, limited lab tests are recommended to exclude organic disorders, although the probability of abnormal findings is low. Common tests include complete blood count, C-reactive protein, serum albumin, prothrombin time, and iron levels [27, 202, 203]. IgA anti-tissue transglutaminase is advised for symptoms or lab values suggesting malabsorption [27, 160, 204]. Faecal calprotectin helps differentiate GI symptoms of organic versus functional origin, especially in patients with diarrhoea [57, 205, 206]. The above-mentioned tests and additional tests like TSH, liver enzymes, glycaemia, CA125 protein and HbA1C may be relevant depending on the clinical context. In primary care, a Helicobacter pylori test can be used as an alternative to endoscopy in patients with functional bloating and dyspeptic symptoms but no alarm symptoms [131].

Currently, no studies have focused on the role of gut microbiome composition in the pathogenesis of functional bloating and abdominal distension [57]. While gut microbiota may influence GI symptoms, microbiota tests do not provide definitive diagnostic or therapeutic information for functional bloating or abdominal distension and therefore are not recommended in managing functional bloating. Further research is needed to determine their clinical utility.

4.3.6 | Role of Functional Testing

➢ There is insufficient evidence to recommend measuring gas volume in the bowel in clinical practice; however, it may be useful for research purposes (95% agreement—low level of evidence—ungraded: expert opinion)

Various techniques have been used to estimate bowel gas volume, including intestinal gas overloading, plain abdominal radiographs, gas volume scoring, and abdominal CT scans. Measuring abdominal gas volume and distribution is valuable for understanding bloating and distension mechanisms, but no consensus exists on the best method. The intestinal gas overloading (or washout) technique, which involves infusing labelled gas into the jejunum, has shown that patients with functional bloating and IBS retain more gas than healthy individuals, correlating with increased symptoms and abdominal girth [31, 207].

On plain abdominal radiographs, bowel gas is estimated by measuring gas bubble areas or calculating gas volume scores from digitalised images [208–211]. However, a study utilising CT scan scout views to measure abdominal gas found no difference in gas volume between active distension and asymptomatic periods [65].

Recent research using helical abdominal CT scans has estimated abdominal gas volume without disrupting gas homoeostasis [58, 59]. A model measured abdominal and air volume using rectal insufflation of known volumes, showing gas distribution across the small bowel and colon [58]. After meal ingestion, gas primarily accumulated in the distal colon, increasing total abdominal volume by 700 mL and girth by 2 cm [58]. GI ultrasonography is also used in DGBI patients, but its efficacy in estimating functional bloating remains undocumented, aside from identifying meteorism [212].

➢ Objective evaluation of abdominal distension with abdominal CT (combined with EMG) or a non-stretch belt with a metric tape is reserved for research (95% agreement—very low level of evidence—ungraded: expert opinion)

➢ Studies of GI motility or transit have limited clinical yield for both diagnosis and treatment of functional bloating and abdominal distension (95% agreement—low level of evidence—ungraded: expert opinion)

Abdomino-phrenic dyssynergia, a key mechanism of functional bloating and abdominal distension, requires electromyography (EMG) for assessment, as it cannot be adequately evaluated by CT [65]. Abdominal girth can be measured using a non-stretch belt with a metric tape, positioned over the umbilicus, with the average of inspiratory and expiratory measurements recorded during quiet breathing [60]. The sensation of abdominal distension typically corresponds with an increase in abdominal girth, but not with increased gas volume [60]. Abdominal inductance plethysmography offers a 24-h ambulatory measure of abdominal girth. Studies indicate that patients with distension display an abnormal viscerosomatic reflex, where diaphragmatic contraction and abdominal muscle relaxation occur in response to intestinal stretch [25].

Disordered GI transit, due to stasis or reflex activity, contributes to functional bloating and abdominal distension symptoms. However, in most patients, transit tests, unless severely impaired, do not significantly impact diagnosis or treatment. In cases of suspected retrograde cricopharyngeal dysfunction (inability to belch), combined oesophageal impedance manometry with sparkling water provocation may confirm the diagnosis and guide treatment, such as botulinum toxin injection [143, 144]. Gastric emptying tests are useful for dyspeptic symptoms with a negative endoscopy, though they are consistently linked only to nausea or vomiting, not to upper abdominal bloating or distension [213, 214]. Thus, routine gastric emptying assessment is unnecessary for functional bloating.

Colonic transit time, measurable via radiopaque markers, scintigraphy, or a wireless capsule, is generally unrelated to functional bloating and abdominal distension in IBS and similar disorders, and is more associated with stool patterns [61]. Therefore, it is not typically indicated for functional bloating assessment. Rectal evacuation disorders, like dyssynergic defecation, may cause retention of colonic content, including gas, contributing to severe bloating/distension [215]. Anorectal manometry with balloon expulsion testing can confirm this, with biofeedback therapy as a potential treatment if abnormalities are detected [216].

4.3.7 | Terminology: What Is Meant by the Term 'Bloating' and What Is Meant by 'Distension'? What Is the Relation Between Volume of Luminal Gas and Symptoms?

- ➢ The term bloating is used to describe the subjective sensation of increased abdominal pressure, fullness or trapped abdominal gas, while the term distension refers to an objective (i.e., measurable) increase in abdominal girth (95% agreement—low level of evidence—ungraded: expert opinion)
- ➢ It is frequent for bloating and abdominal distension to present in conjunction; however, this is not always the case (100% agreement—moderate level of evidence -ungraded: weak)
- ➢ In patients with functional bloating, with or without abdominal distension, there is no consistent correlation between severity of bloating, increase in abdominal girth and volume of intestinal gas (95% agreement—moderate level of evidence -ungraded: weak)

Symptoms attributed to an excess in abdominal gas, such as bloating and abdominal distension, are nearly universal among patients with DGBI [27, 217]. The Rome IV consensus in 2016 classified functional bloating and abdominal distension as a single entity; however, it is recognised that these represent two distinct symptoms with different underlying mechanisms [4]. While functional bloating and abdominal distension often occur together, not all patients who experience bloating also exhibit visible distension [6, 34, 62]. This suggests that separate mechanisms may drive each phenomenon [32, 34, 62, 203].

In contrast to patients with proven dysmotility [29, 75], those with functional gut disorders do not consistently demonstrate a correlation between the severity of bloating, abdominal girth increase and intestinal gas volume, as measured by CT scans [29, 63–65]. However, there appears to be a positive correlation between the severity of abdominal pain and the intensity of bloating [37]. Although bloating and abdominal distension are often used interchangeably, patients clearly distinguish between these two symptoms, a distinction crucial for both understanding and management [137]. Bloating, defined as the sensation of abdominal pressure or trapped gas, should be recognised as a symptom, whereas distension, characterised by a measurable increase in abdominal girth, should be understood as a sign observable during physical examination. Consequently, the term "visible abdominal distension" has been suggested as more appropriate [32].

4.4 | Section 4. Treatments

4.4.1 | Physical activity

- ➢ Physical activity, particularly aerobic exercise, seems to have a positive impact on GI symptoms (including functional bloating and abdominal distension), especially in patients with DGBI (80% agreement—very low level of evidence—ungraded: expert opinion)

There is no strong evidence directly linking functional bloating and abdominal distension with poor physical activity. A multivariate analysis identified female gender, medical student status, non-vegetarian diet, junk food consumption, tea/coffee intake, poor physical activity, anxiety, and insomnia as independent predictors of DGBI. However, data on the association between poor physical activity and functional bloating/abdominal distension remains inconclusive, though there may be an indirect link through IBS, as poor physical activity is associated with a higher risk of IBS, which co-occurs with functional bloating and abdominal distension [35].

Another study by Ohlsson and Manjer [218] concluded that higher physical activity levels were associated with a lower risk of GI complaints, while physical inactivity correlated strongly with functional GI symptoms, including bloating.

Although there is no substantial evidence from meta-analyses or RCTs supporting the efficacy of physical exercise for functional bloating, some observational studies suggest potential benefits. Villoria et al. [219] reported that exercise reduced gas retention and improved abdominal symptoms compared to rest. Another study found that both prokinetic medications and postprandial walking significantly improved abdominal symptoms, including bloating [220]. Moderate-intensity aerobic exercise, such as walking, has been shown to improve GI symptoms and psychological well-being in patients with IBS, serving as a complementary non-pharmacological therapy [221].

4.4.2 | Diet

- ➢ Patients with functional bloating and abdominal distention should receive a lactose-limiting diet trial based on their self-reported symptoms or the presence of intolerance during a breath test after ingestion of a defined lactose load (70% agreement—very low level of evidence—ungraded: good practice statement)
- ➢ For the general patient population with functional bloating and abdominal distension, a lactose-restrictive diet is of limited efficacy, as symptoms are not related to lactose intolerance, either with or without malabsorption (75% agreement—very low level of evidence—ungraded: good practice statement)

Lactose malabsorption, which affects up to 70% of the global population, is primarily caused by the non-persistence of the lactase brush border enzyme after infancy. However, a genetic mutation prevalent in individuals from Northwestern Europe allows for the persistence of active lactase into adulthood, enabling continued lactose digestion and absorption [222]. Although there are no specific data linking lactose malabsorption to an increased prevalence of functional bloating and abdominal distension, it is noteworthy that patients with IBS often exhibit more pronounced symptoms following a lactose challenge, despite not having a higher prevalence of lactose malabsorption compared to the general population [64, 223].

In uncontrolled studies involving patients with IBS, some variability in symptom improvement following a reduction in

lactose intake has been reported, though the quality of these studies is generally low. Consequently, a lactose-restricted diet cannot be universally recommended for unselected patients with IBS [224]. Additionally, no studies specifically targeting patients with functional bloating and abdominal distention are available. The therapeutic application of a lactose-limiting diet should be based on validated evidence of symptom onset after a lactose challenge, rather than solely on the presence of lactose malabsorption, as indicated by elevated hydrogen levels during a breath test following lactose ingestion [66]. This approach is also applicable to other carbohydrate intolerances such as fructose intolerance [66].

➢ A low FODMAP diet is effective in reducing functional bloating and abdominal distention (80% agreement—moderate level of evidence -ungraded: weak)

The low FODMAP diet involves initially restricting fermentable carbohydrates, including fructose and lactose, followed by a reintroduction phase to identify specific intolerances. FODMAPs cause symptoms by increasing osmolar load in the small bowel and the colon, attracting water, and through fermentation by gut microorganisms, producing gases like methane, CO2, and H2, which lead to bloating, abdominal distension, abdominal pain, and changes in stool pattern [101].

In a single-blind study involving 30 patients with IBS, it was found that a low FODMAP diet led to a significant reduction in overall IBS symptoms and bloating when compared to a typical Australian diet [225]. Approximately 70% of the participants experienced positive outcomes. A systematic review of 13 randomised controlled trials (RCTs) with a total of 944 patients identified the low FODMAP diet as the most effective intervention for IBS-related symptoms, particularly bloating and abdominal distension [67]. This diet proved significantly more effective than the traditional NICE diet in reducing these symptoms, though it did not show a notable difference when compared to a habitual diet. While specific studies on functional bloating and abdominal distension in patients without IBS are lacking, the success of the low FODMAP diet in IBS suggests it could be beneficial for these conditions as well. Limitations of a low FODMAP diet are possible reduction of natural prebiotics, which may negatively impact gut microbiota and metabolome, increasing the risk of nutritional deficiencies and the development of eating disorder behaviour [226]. Thus, we would like to highlight the importance of a dietician follow-up of patients with documented carbohydrate intolerances on carbohydrate reduced diets.

➢ There is insufficient evidence to recommend a gluten-free diet in patients with functional bloating and abdominal distension, unless they have coeliac disease (90% agreement—low level of evidence—ungraded: expert opinion)

Most patients on a gluten-free diet for medical reasons do not have coeliac disease but rather experience symptom improvement when avoiding gluten, a condition known as non-coeliac gluten sensitivity (NCGS) [227, 228]. However, there is a considerable heterogeneity among those patients [229]. About 70% of NCGS patients report bothersome bloating [230]. However, gluten proteins are unlikely the primary triggers; other components like amylase trypsin inhibitors (ATI) are potential culprits, leading to a shift in terminology to non-coeliac wheat sensitivity (NCWS) [231].

Biesiekierski et al. [232] found lower scores for bloating, pain, and fatigue in NCWS patients consuming gluten-free muffins compared to gluten-containing ones. However, a follow-up study found no effects of gluten in patients with self-reported NCWS after low FODMAP diet [68]. Another study found that fructans, not gluten, increased bloating severity [104]. Nonetheless, an Italian study showed worse bloating and other symptoms during a gluten challenge in NCGS patients [233]. It seems that the expectancy of gluten intake rather than gluten itself, have an important nocebo effect on patients [234, 235].

4.4.3 | Pro-Prebiotics

➢ The use of selected probiotics may improve bloating and abdominal distension (80% agreement—low level of evidence—ungraded: good practice statement)

➢ Probiotic medications differ greatly from one another, and the outcomes observed from one cannot be generalised to the others (90% agreement—low level of evidence—ungraded: expert opinion)

The gut microbiota plays a crucial role in the GI tract, given its involvement in the processing of luminal content and various metabolic functions [203, 236–239]. Due to its significant role, it has been proposed that the composition of gut microbiota could be a pathogenic factor in the development of functional bloating and abdominal distension [240, 241]. Specific microbiota profiles have also been associated with functional bloating in individuals with IBS [242], suggesting that modifying the gut microbiota could potentially alleviate these symptoms [142, 243].

Probiotics offer a sophisticated approach to manipulating gut microbiota. They work not only by altering the abundance and diversity of gut microbiota but also through their own metabolic activities [244]. Faecal microbial transplantation has also shown promise in this regard [245]. However, most of the existing data on the effects of gut microbiota manipulation on functional bloating primarily focuses on IBS rather than on functional bloating and abdominal distension.

There is evidence supporting the use of selected probiotics for treating functional bloating and abdominal distension [240, 243]. The gut microbiota spectrum, linked to these symptoms, was the basis for trials with probiotics looking for symptom relief [239, 246]. In a double-blind trial, a combination of *Lactobacillus acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 improved bloating in non-constipated patients with DGBI [247]. A more recent trial using a blend of five *Bifidobacterium* and *Lactobacillus* strains also showed symptom improvement in two-thirds of patients with functional gastrointestinal symptoms [248]. VSL#3, *Lactobacillus plantarum*, *Bifidobacterium infantis* 35,624, and *Bifidobacterium animalis* DN-173 010 have also been effective in reducing bloating [249–252].

Nevertheless, many of these trials have shown mixed results as the efficacy varies between different microbial strains [253]. A meta-analysis of 24 trials found that combinations of bacterial strains showed a trend toward improving in functional bloating, but individual strains like *Bifidobacterium*, *Lactobacillus*, and *Saccharomyces* were not significantly effective [69]. For example, *Bacillus subtilis* BS50 reduced bloating in healthy participants, but *Bacillus clausii* did not impact IBS-related symptoms in children [254, 255]. *Bacillus subtilis* BS50 reduced a composite score of bloating, belching, and flatulence after six weeks of administration in half of the healthy participants in a placebo-controlled trial [256]. In a multicenter study, *Bacillus subtilis* MB40 given for four weeks to healthy volunteers reduced bloating and abdominal discomfort only in males [257]. In another multicenter study, administration of *Bifidobacterium infantis* 35,624 for four weeks (after a 2-week run-in period) showed no benefit in the general population [258]. A recent meta-analysis showed that *Bifidobacterium animalis* subspecies did not improve functional bloating [259]. Scepticism remains regarding the overall benefit of probiotics in managing bloating in IBS [260], although probiotics have also been suggested to prevent unpleasant bloating and abdominal discomfort after colonoscopy [261].

In summary, while some probiotics may improve functional bloating and abdominal distension, their effects are modest and vary among individuals. More robust studies are needed, particularly focusing on functional bloating and abdominal distension outside the context of IBS.

➢ There are no encouraging data to recommend the use of prebiotics or symbiotic for the treatment of functional bloating and abdominal distension (75% agreement—very low level of evidence—ungraded: expert opinion)

Attempts to use prebiotics like fructooligosaccharides for treating functional bloating have shown mixed results [262]. While fructooligosaccharides can temporarily worsen flatulence, a *trans*-galactooligosaccharide mixture improved bloating at 3.5 g/day but worsened it at higher doses [263]. A combination of inulin, choline, and silymarin improved bloating in patients with IBS over 8 weeks [264]. Similarly, soluble fibre-enriched snacks and copra meal hydrolysate improved bloating and bowel movements in small trials [265, 266]. In another trial, a compound including not only oligosaccharides but also xyloglucan, proteins, and tannins for 4 weeks, improved IBS-D related symptoms, including bloating [267]. However, a recent meta-analysis concluded that prebiotics are not effective for DGBI, including functional bloating, and may even exacerbate symptoms [70].

Symbiotics, combining probiotics and prebiotics, have also been studied with limited success. A symbiotic with *Bifidobacterium longum* BB536 and partially hydrolysed guar gum improved constipation and bloating in haemodialysis patients, but a different symbiotic showed no effect on bloating in elderly patients with IBS [268, 269]. Overall, there is insufficient evidence to recommend prebiotics or symbiotic for treating functional bloating and abdominal distension, as results have been inconsistent, and studies often have methodological limitations.

4.4.4 | Antibiotics

➢ Rifaximin may be useful for the treatment of functional bloating and abdominal distention (80% agreement—low level of evidence—ungraded: good practice statement)

➢ We do not recommend the use of other antibiotics for the treatment of functional bloating and abdominal distention (85% agreement—very low level of evidence—ungraded: good practice statement)

Rifaximin is a semisynthetic, broad-spectrum antibiotic based on the rifamycin antibiotics family that has minimal systemic absorption (< 0.4%). It is effective against Gram-negative bacteria in the small intestine, where its concentration is highest due to the presence of bile [270]. Since symptoms associated with gas production are linked to bacterial fermentation and SIBO, rifaximin has been tested in treating bloating and abdominal distension [271]. In two Phase 3 trials (TARGET 1 and 2), rifaximin (550 mg t.i.d. for 2 weeks) significantly improved IBS-D-related bloating compared to placebo, with sustained effects for up to 3 months [272]. A 2012 meta-analysis found rifaximin more likely to improve bloating than placebo (OR 1.55; 95% CI: 1.23–1.96), with a therapeutic gain of 9.9% and number needed to treat (NNT) of 10.1 [71]. A more recent meta-analysis of 10 trials found a higher likelihood of symptom improvement, confirming these findings, especially at doses ≥ 1200 mg/day [273].

Neomycin, an aminoglycoside with minimal absorption, was initially studied for IBS treatment. In a randomised trial, neomycin (500 mg twice daily for 10 days) was superior to placebo in improving IBS symptoms [274]. However, its use is limited by risks of ototoxicity and clinical resistance [275].

A retrospective chart review comparing rifaximin and neomycin found rifaximin more effective in both initial treatment and re-treatment of IBS, with a 69% clinical response rate compared to 38% for neomycin [276]. These results suggest that rifaximin may be more effective than other antibiotics in the initial treatment and re-treatment of IBS [276].

4.4.5 | Antispasmodics

➢ Among antispasmodic agents, pinaverium and otilonium bromide have been shown to be the most effective drugs for the treatment of functional bloating and abdominal distension (75% agreement—low level of evidence -ungraded: weak)

➢ There is insufficient evidence to recommend simethicone for the treatment of functional bloating and abdominal distension (75% agreement—low level of evidence -ungraded: weak)

Antispasmodic agents are used to reduce increased contractility in IBS, particularly in diarrhoea-predominant cases. Several meta-analyses have evaluated their effectiveness in IBS [277]. A Cochrane review found antispasmodics effective in improving IBS-global symptoms, with 57% of patients showing improvement compared to 39% with placebo (NNT = 5). Specific agents

like cimetropium, dicyclomine, peppermint oil, and pinaverium showed statistically significant benefits, though the review did not assess their impact on functional bloating and abdominal distension [278]. Another meta-analysis found that otilonium bromide, pinaverium, and hyoscine significantly improved IBS symptoms, with a consistent trend toward relieving bloating and abdominal distension (OR: 1.455; 95% CI 1.17–1.81) [279]. A recent network meta-analysis of 57 RCTs (8869 patients) confirmed the efficacy of otilonium bromide, cimetropium, and pinaverium in providing relief from IBS symptoms [280]. Pooled analysis of three RCTs showed that otilonium bromide significantly reduced bloating severity, with high responder rates (71.8% at week 10% and 77.2% at week 15) [72]. A meta-analysis of eight studies found that pinaverium significantly relieved IBS symptoms (NNT = 4), with notable improvements in bloating (RR 1.52; $p = 0.0033$) [281]. These findings support the use of specific antispasmodics in managing IBS associated with functional bloating and abdominal distension.

4.4.6 | Secretagogues

- ➢ Lubiprostone, plecanatide and linaclotide are effective in improving constipation associated with functional bloating and abdominal distension (90% agreement—moderate level of evidence -ungraded: weak)
- ➢ Linaclotide is the most effective secretagogue for functional bloating, although limited data is available for lubiprostone and plecanatide as well (85% agreement—low level of evidence—ungraded: good practice statement)

Secretagogues increase water retention in the bowel lumen and decrease visceral hypersensitivity, making them effective for treating bloating associated with constipation. Lubiprostone, a type 2 chloride channel activator, accelerates intestinal transit and improves constipation and bloating [282]. In a randomised trial with 1171 IBS-C patients, lubiprostone (8 mg twice daily) significantly improved global IBS symptoms, including bloating [283]. Another 48-week open-label study in chronic idiopathic constipation (CIC) patients showed significant improvement in bloating, though without a placebo group [284]. Lubiprostone is approved for CIC and has shown long-term safety and efficacy for IBS-C [285].

Plecanatide, a guanylate cyclase-C receptor agonist, improves stool frequency and reduces visceral hypersensitivity in constipation but is not specifically recommended for bloating due to lack of targeted data and a 1.2% withdrawal rate attributed to diarrhoea [286].

Linaclotide, another guanylate cyclase-C agonist, is widely used for IBS-C and improves symptoms like pain, bloating, and abdominal distension [287]. A systematic review found linaclotide (290 mg daily) to be the most effective secretagogue for bloating in IBS-C, outperforming lubiprostone, tenapanor, and tegaserod [73].

The mechanisms by which secretagogues alleviate bloating may involve improved GI transit and modulation of visceral sensation, though this varies among patients. Further studies are needed to better understand these processes and optimise treatment for IBS-C-related bloating [57]. Secretagogues are generally well-tolerated, with diarrhoea being the most common side effect, and linaclotide remains the most widely used globally.

4.4.7 | Prokinetic Agents

- ➢ There are no prospective data to support the use of prucalopride for functional bloating and abdominal distension. Prucalopride may improve bloating and abdominal distension in patients with constipation, gastroparesis or motility disorders (90% agreement—very low level of evidence—ungraded: expert opinion)

Prucalopride is a selective serotonin type 4 receptor agonist primarily used in the treatment of functional constipation and for enhancing gastric emptying. In 2022, Staller et al. [74] published a post-hoc analysis of data from six clinical trials involving 1931 patients with CIC and moderate to severe bloating. The analysis focused on the effects of prucalopride on abdominal bloating and health-related quality of life (HRQOL). The study found a positive impact starting as early as week 2, with 62.1% of patients treated with prucalopride showing a ≥ 1 point improvement in abdominal bloating score by week 12, compared to 49.6% in the placebo group.

Additionally, a recent randomised placebo-controlled study involving 34 patients with gastroparesis treated with prucalopride (2 mg four times a day for four weeks) demonstrated improvements in bloating and other gastroparesis-related symptoms [288]. Another study, employing a double-blind, placebo-controlled, crossover multiple $n = 1$ design with a small patient cohort, showed that prucalopride improved bloating in all patients with CIPO [289].

- ➢ There is insufficient evidence to recommend neostigmine (IV) or pyridostigmine for patients with functional bloating and abdominal distension (100% agreement—very low level of evidence—ungraded: expert opinion)

Cholinesterase inhibitors, which increase acetylcholine levels by blocking the cholinesterase enzyme, are primarily used in neurodegenerative diseases, myasthenia gravis, and glaucoma [290–293]. While these agents have a prokinetic effect on the GI tract, the mechanism is not well understood. The most commonly used cholinesterase inhibitor is neostigmine, primarily used in acute colonic pseudo-obstruction (Ogilvie syndrome) [294]. Some studies suggest neostigmine may improve symptoms; for example, in patients with IBS, neostigmine (0.5 mg IV) was shown to improve abdominal symptoms and abdominal distension compared to saline [31, 75]. Another study involving patients with spinal cord injury found that neostigmine combined with polyethylene glycol for bowel preparation resulted in more bloating and abdominal distension compared to other groups [295].

Pyridostigmine, another cholinesterase inhibitor, showed some efficacy in reducing bloating severity in one study, though the

results did not reach statistical significance across groups [59]. RCTs specifically evaluating its efficacy in functional bloating and abdominal distension are lacking. Therefore, while some studies suggest a potential benefit of cholinesterase inhibitors like neostigmine and pyridostigmine for bloating, the evidence is not strong enough to recommend their use for this indication.

➢ There is insufficient evidence to recommend metoclopramide and acotiamide for the treatment of functional bloating and abdominal distension (100% agreement—very low level of evidence—ungraded: expert opinion)

Acotiamide, a novel acetylcholinesterase inhibitor and muscarinic antagonist, is approved in Japan for treating postprandial fullness, upper abdominal bloating, and early satiation in FD. It works by inhibiting acetylcholinesterase and increasing acetylcholine release at neuromuscular junctions [296]. Although there are no RCTs specifically targeting functional bloating and abdominal distension, studies on FD show promising results [297, 298].

In one RCT, Yamawaki et al. [297] reported significant improvement in meal-related symptoms and epigastric pain in patients with FD treated with acotiamide. Another study by Kusunoki [298] also demonstrated improvement in FD-related symptoms using acotiamide. The effective dose of acotiamide for relieving postprandial fullness, early satiety, and upper abdominal bloating was 100 mg [299, 300]. A phase III trial comparing acotiamide with mosapride found both effective and safe, with significant quality of life improvements in FD patients [296].

Metoclopramide, a dopamine D2-receptor antagonist known for its antiemetic effects, has limited evidence supporting its use in functional bloating and abdominal distension. In a double-blind trial involving diabetic gastroparesis patients, metoclopramide did not significantly improve bloating compared to placebo [76].

➢ Indirect evidence supports tegaserod use for the treatment of functional bloating. However, due to its possible cardiac side effects, close cardiac monitoring should be performed (95% agreement—very low level of evidence—ungraded: expert opinion)

Tegaserod is a selective 5-hydroxytryptamine 4 receptor agonist used for treating constipation in women with IBS, particularly IBS-C. It functions by improving GI motility and visceral sensation. However, the drug was withdrawn from the market in 2007 due to concerns over cardiovascular and cerebrovascular events. In 2018, the FDA re-approved tegaserod for use in women with IBS-C who are ≤ 65 years old and have ≤ 1 cardiovascular risk factor [301]. To date, no RCT has been specifically designed to evaluate the use of tegaserod in patients with functional bloating and abdominal distension alone.

In 2021, Nelson et al. [73] conducted a pairwise and network meta-analysis using a frequentist approach to assess the efficacy of FDA-approved drugs for IBS-C on bloating. The analysis included 5132 patients from four trials investigating the effects of 6 mg tegaserod. The study found that as compared to placebo, tegaserod was significantly more effective in treating bloating, with a relative risk (RR) of 0.85 (95% CI 0.80–0.90) for failure to achieve improvement in bloating, and a NNT of 13 (95% CI 10–20) [73].

4.4.8 | Neuromodulators

➢ Selective serotonin reuptake inhibitors (SSRI's) are effective in reducing symptoms of functional bloating (90% agreement—low level of evidence—ungraded: good practice statement)

➢ Tricyclic antidepressants (TCA) such as amitriptyline are effective in reducing symptoms of functional bloating (90% agreement—moderate level of evidence—ungraded: good practice statement)

➢ Buspirone, a serotonin 5-HT1A receptor agonist, commonly used for treating anxiety, improves postprandial functional bloating (75% agreement—low level of evidence—ungraded: expert opinion)

Neuromodulators, including antidepressants, antipsychotics, antiepileptic drugs and others, target primarily the central nervous system and, to a lesser extent, the peripheral nervous system. These medications are increasingly used to treat DGBI, such as IBS and FD [77]. However, the evidence supporting the use of neuromodulators specifically for treating functional bloating and abdominal distension is limited, with no studies focusing exclusively on this patient population.

A large study comparing the tricyclic antidepressant amitriptyline with the selective serotonin reuptake inhibitor (SSRI) escitalopram and placebo in 292 patients with FD demonstrated a reduction in postprandial bloating with both neuromodulators [302]. However, only amitriptyline, not escitalopram, was superior to placebo in providing adequate relief from FD symptoms, which was the primary endpoint of the study [78].

In a small proof-of-concept crossover study in IBS, citalopram was found to improve abdominal pain and bloating compared to placebo after three and 6 weeks of treatment [303]. Notably, this symptom improvement was independent of any effect on anxiety and depression. Additionally, the 5-HT1A agonist buspirone was evaluated in FD and significantly reduced overall dyspeptic symptoms, including upper abdominal bloating, postprandial fullness, and early satiation [79]. The beneficial effects in FD are likely due to enhanced gastric accommodation [304].

4.4.9 | Biofeedback and Neuromodulatory Techniques

➢ In patients with discrete episodes of visible abdominal distension, biofeedback-guided techniques to re-educate abdomino-thoracic muscular activity are safe and effective for correction of abdominal distention and are associated with improvement in the subjective sensation of functional bloating (90% agreement—very low level of evidence—ungraded: good practice statement)

➢ There are no specific neuromodulatory techniques that have been specifically studied for the treatment of

functional bloating and abdominal distension (95% agreement—very low level of evidence—ungraded: expert opinion)

The pathophysiology of episodic abdominal distension, also termed abdomino-thoracic dyssynergia (diaphragmatic contraction, chest hyperinflation, and abdominal wall relaxation) has been extensively studied [11, 26, 32, 121, 123, 305]. Based on these findings, a specialised EMG-guided biofeedback technique was developed to reverse this abnormal response. In an open-label study of 45 patients, they were taught to voluntarily reduce the activity of intercostal muscles and the diaphragm while simultaneously increasing the activity of the anterior abdominal wall muscles. Biofeedback significantly reduced intercostal muscle and diaphragm activity while increasing internal oblique muscle activity, leading to a decrease in abdominal girth and bloating sensation [124]. These results were confirmed in a randomised placebo-controlled trial [125]. However, EMG-guided biofeedback is technically challenging and has only been studied at a single centre. A recent randomised, placebo-controlled, single-blind study demonstrated similar results using a much simpler plethysmography-based biofeedback technique, which could enable broader validation and more widespread application of this method [80].

The biofeedback technique includes a series of instructions as the key factor in abdomino-phrenic dyssynergia is the blockade of the diaphragm, and the main target of biofeedback is its release. First, patients were taught to relax the diaphragm (diaphragmatic ascent) through combined elevation of the costal wall (chest up) and contraction of the abdominal wall (abdomen in) [80]. Subsequently, they were instructed to mobilise the diaphragm by alternating manoeuvres of diaphragmatic contraction (chest down–abdomen out) and relaxation (chest up–abdomen in) (link of the video http://doi.org/10.1053/j.gastro.2024.03.005). These movements were performed with either an open airway (breathing into the chest and out) or a closed airway (moving air from the chest to the abdomen and back in a pendular movement). After the first session, the patients were instructed to perform the same exercises daily at home for 5 min before and after breakfast, lunch, and dinner during the 4-week intervention period. In a separate randomised trial, biofeedback targeting dyssynergic defecation also improved bloating and abdominal distension in patients with postprandial upper abdominal symptoms [135]. Overall, the effectiveness of the plethysmography-based biofeedback technique indicates that abdomino-thoracic wall motion is an effective signal for guiding the biofeedback. Based on this finding, a non-instrumental biofeedback procedure through manual control of thoraco-abdominal wall movements is being explored. The procedure is still under development, but if proven effective, this technique may become available for widespread application. Nevertheless, application of the method requires proper training, and currently, the training-the-trainer programme is still ongoing and not completely defined.

Since abdominal distension is associated with chronic pain, neuromodulatory interventions that modify brain processes underlying the experience of pain have the potential to provide substantial relief for some of these patients [306]. Interventions like transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have been explored as potential treatments for some patients with abdominal pain [81, 307] and drug-resistant depression [308]. These studies highlight the uncertainties about the clinical use of these neuromodulatory techniques with the current available scientific evidence [81].

4.4.10 | Complementary, Alternative and Herbal Medicine

➢ Although acupuncture and some herbal medicines such as Zataria-Trachyspermum, rikkunshito, STW5, peppermint oil, curcumin and Boswellia extracts have been shown to reduce bloating and abdominal distension in patients with IBS, there is insufficient evidence to recommend them in the treatment of functional bloating and abdominal distention (95% agreement—very low level of evidence—ungraded: expert opinion)

While no specific studies focus on complementary and alternative medicine for functional bloating and abdominal distension, data from IBS and FD studies provide some insights. Simethicone, often added to polyethylene glycol (PEG) for colon preparation, has been shown in meta-analyses of RCTs to improve colon cleanliness and to reduce bloating [309, 310]. However, there is no study showing the effect of simethicone in the treatment of functional bloating and abdominal distension.

In an uncontrolled study of 22 subjects investigating the efficacy of holistic acupuncture points PC6, SP4, and DU20 in patients with idiopathic refractory nausea, abdominal pain, and bloating, abdominal bloating scores improved only in the group treated at acupuncture point PC6 [311].

Limitations of acupuncture may include a considerable placebo effect on perception of distension but it has no effect on distensibility and visceral referral [312].

Regarding herbal medicines, a prospective controlled study compared the administration of ZT capsules (a mixture of *Zataria multiflora and Trachyspermum copticum*) to placebo and mebeverine in 150 patients with IBS. After 4 weeks, the ZT group showed significant reductions in abdominal pain and bloating compared to the other groups [313]. Another herbal medicine (rikkunshito, from Japan) significantly improved postprandial fullness, early satiety, and bloating in FD patients after 8 weeks in a randomised, placebo-controlled study [82]. Another study with a new sustained-release peppermint oil formulation showed significant improvement in bloating and abdominal distension symptoms in patients with IBS [83]. Curcumin and Boswellia extracts, combined with a low FODMAP diet, significantly reduced bloating and pain in patients with IBS with small bowel dysbiosis, outperforming the low FODMAP diet alone [314]. Additionally, the herbal drug STW 5 (Iberogast) has been shown to improve general dyspeptic symptoms, though not specifically targeting bloating [84].

4.4.11 | Psychological Therapies and Hypnotherapy

➢ Cognitive behaviour therapy (CBT) can be offered to patients with functional bloating associated with IBS as an alternative treatment in patient's refractory to conventional therapies (95% agreement—low level of evidence—ungraded: good practice statement)

As with many other chronic diseases, especially DGBI, patients with functional bloating could benefit from psychotherapy, regardless of whether it occurs alone as functional bloating and abdominal distension or with IBS, chronic constipation, or eating disorders [315–320]. These therapies are often used alongside pharmacotherapy, especially in severe cases with psychiatric symptoms [321]. The most effective psychological therapies are CBT and hypnotherapy [322].

Although CBT is commonly employed, there are few quality trials specifically for functional bloating, and only marginal efficacy has been reported. Due to the complexity and need for specialised therapists, some authors do not recommend CBT for functional bloating [27, 32, 203, 323]. However, online CBT, especially during the COVID-19 pandemic, has shown improvements in IBS symptoms, including bloating [85].

In conclusion, while CBT has shown positive results for functional bloating and abdominal distension, it is not suitable for every patient. It is best reserved for individuals open to psychotherapy, patients with psychiatric comorbidities, or those unresponsive to standard treatments.

➢ Hypnotherapy improves symptoms of bloating in patients with IBS. However, its effect on functional bloating and abdominal distension was not explored and cannot be recommended (95% agreement—very low level of evidence—ungraded: expert opinion)

Hypnotherapy has been shown to improve IBS symptoms in several trials, including bloating, though it was often assessed as an accompanying symptom [10]. Early studies, such as one involving 12 hypnotherapy sessions over three months, reported significant improvements in IBS symptoms, including bloating, with long-term benefits [86–90]. Hypnotherapy is more effective when performed by experienced therapists and is thought to work by reducing anxiety, potentially altering gut microbiota [324–326].

In the large multicentre IMAGINE trial, individual and group hypnotherapy significantly outperformed educational supportive therapy in relieving IBS symptoms. After 3 months, the response rate was 41% in the individual hypnotherapy group and 33% in the group hypnotherapy vs. 17% in the control group. At 12 months, relief was reported by 41% of patients in the individual hypnotherapy group, 49.5% in the hypnotherapy group, and 23% in the control group [327]. However, the assessment of GI symptoms was not rigorous.

➢ There is not enough evidence to recommend other psychological therapies in functional bloating and abdominal distension (95% agreement—very low level of evidence—ungraded: expert opinion)

Various psychological therapies, including brief psychoanalytic psychotherapy (psychodynamic therapy), have been tested for bloating in patients with IBS, with some improvement noted, although these results often pertain to FD [91]. A larger study showed benefits with psychodynamic and solution-focused therapies for psychiatric symptoms in IBS, but bloating was not analysed [328]. Yoga has been explored for IBS symptom management, but evidence on its effectiveness for bloating is limited and not specific [329, 330]. We suggest therefore that it may work in patients with an interest and belief in alternative medicine and if delivered by experienced yogis. Recent research

TABLE 3 | Medical treatment for functional bloating and abdominal distension.

Generic Medication	Maximal Daily Dosage	Associated Conditions
Antibiotics		
Rifaximin	550 mg three times a day for 2 weeks	Diarrhoea
Antispasmodics		
Pinaverium	50 mg three times a day	Abdominal pain
Otilonium bromide	40–80 mg three times a day	Abdominal pain
Hyoscine	10–20 mg four times a day	Abdominal pain
Secretagogues		
Linaclotide	290 mcg once daily	Constipation
Lubiprostone	24 mcg twice a day	Constipation
Prokinetic agents		
Prucalopride	1–4 mg a day	Constipation, gastroparesis, dysmotility
Neuromodulators		
Amitriptyline/Nortriptyline	100 mg daily	Abdominal pain, diarrhoea
Buspirone	15 mg three times a day	Dyspepsia, anxiety
Citalopram	10–15 mg daily	Anxiety, depression

indicates that combining guided imagery with progressive muscle relaxation can alleviate functional bloating [331]. Mind-body techniques, including these, have been shown to improve functional bloating. Additionally, simple structured education, whether direct or online, has been effective in improving IBS symptoms, including bloating [332].

4.5 | Future Research

Most of the guidelines were based on literature of patients with IBS with functional bloating and abdominal distension. It is important to have data from studies that enroled patients with functional bloating and abdominal distension not combined with other DGBI. Further research should also focus on personalised medicine for functional bloating and abdominal distension as well as on microbiota modulation. The complex link between psychological factors and functional bloating and abdominal distension should be evaluated as well. Future research and consensus might also implicate patients' opinion.

5 | Conclusion

Functional bloating and abdominal distension are common medical conditions diagnosed according to the Rome IV criteria, after organic causes have been excluded (Figure 1). Pathophysiology is multifactorial and treatment focuses on addressing the main underlying pathophysiological mechanisms. Recommended treatments include dietary modifications, medical therapies (Table 3) targeting dysbiosis, pain or transit disorders, psychological interventions and a specifically designed biofeedback programme. Despite these treatment options, functional bloating and abdominal distension remain a challenging target to treat. Certain recommendations received high agreement and are supported by high evidence grading, and they can assist generalists and specialists in their patients' clinical management. We hope that our guidelines will assist practitioners in managing functional bloating and abdominal distension.

Acknowledgements

The UEG research administration funded and supported this project. Prof. Fernando Azpiroz, Prof. Jordi Serra and Prof. Henriette Heinrich provided support in designing and planning this study. Dr Beatriz Albuixech-Crespo and Dr Anchel González Barriga, from Medical Science Consulting (Spain), provided editorial support, in the form of medical writing, assembling tables based on authors' detailed directions, collating author comments, copyediting, fact-checking, and referencing. This work is dedicated to the memory of Dr. Radislav Nakov, who passed away during the completion of these guidelines. The authors would like to acknowledge his contribution to this work.

Conflicts of Interest

C.M. has served as a consultant or advisory board member for Kyowa Kirin, Norgine, Biocodex, Mayoly Spindler, Tillotts, Ipsen, and Nestlé Health Science. E.V.S. has received speaker fees, served as a consultant, or received research support from Abbvie, Abivax, Agave, AG Pharma, Alfasigma, Apoteca, Biosline, Bonollo, Bristol-Myers Squibb, CaDiGroup, Celltrion, Difass, Dr. Falk Pharma, EG Stada Group, Eli Lilly, Fenix Pharma, Ferring, Galapagos, Giuliani, Grünenthal, Innovamedica/Adacyte, JB Pharmaceuticals, Johnson & Johnson, Malesci, Mayoly Biohealth, Merck & Co., Nestlé Health Science, Novartis, Omega Pharma, Pfizer, Rafa, Reckitt Benckiser, Sandoz, Sanofi/Regeneron, SILA, Sofar, Takeda, Tillotts, Unifarco, and Zeta Farmaceutici. T.V. has received lecturing fees from Abbott, Baxter, Biocodex, BMS, Dr. Falk Pharma, Ipsen, Menarini, Microbiotica, MyHealth, Schwabe, Takeda, Truvion. T.V. has served as a consultant for Biocodex, BMS, Dr. Falk Pharma, EcoR1, Promed, Ipsen, Norgine, Takeda and Truvion. T.V. has received research grants from Danone, Dr. Falk Pharma, MyHealth and Takeda. All other authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

References

1. C. V. Almario, M. L. Ballal, W. D. Chey, C. Nordstrom, D. Khanna, and B. M. R. Spiegel, "Burden of Gastrointestinal Symptoms in the United States: Results of a Nationally Representative Survey of Over 71,000 Americans," *American Journal of Gastroenterology* 113, no. 11 (2018): 1701–1710, https://doi.org/10.1038/s41395-018-0256-8.

2. S. Ballou, P. Singh, J. Nee, et al., "Prevalence and Associated Factors of Bloating: Results From the Rome Foundation Global Epidemiology Study," *Gastroenterology* 165, no. 3 (2023): 647–655, https://doi.org/10.1053/j.gastro.2023.05.049.

3. C. P. Gardiner, P. Singh, S. Ballou, et al., "Symptom Severity and Clinical Characteristics of Patients With Bloating," *Neurogastroenterology and Motility* 34, no. 3 (2022): e14229, https://doi.org/10.1111/nmo.14229.

4. B. E. Lacy, F. Mearin, L. Chang, et al., "Bowel Disorders," *Gastroenterology* 150, no. 6 (2016): 1393–1407, https://doi.org/10.1053/j.gastro.2016.02.031.

5. A. D. Sperber, S. I. Bangdiwala, D. A. Drossman, et al., "Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study," *Gastroenterology* 160, no. 1 (2021): 99–114, https://doi.org/10.1053/j.gastro.2020.04.014.

6. X. Jiang, G. R. Locke 3rd, R. S. Choung, A. R. Zinsmeister, C. D. Schleck, and N. J. Talley, "Prevalence and Risk Factors for Abdominal Bloating and Visible Distention: A Population-Based Study," *Gut* 57, no. 6 (2008): 756–763, https://doi.org/10.1136/gut.2007.142810.

7. X. Jiang, G. R. Locke, A. R. Zinsmeister, C. D. Schleck, and N. J. Talley, "Health Care Seeking for Abdominal Bloating and Visible Distention," *Alimentary Pharmacology & Therapeutics* 30, no. 7 (2009): 775–783, https://doi.org/10.1111/j.1365-2036.2009.04080.x.

8. M. Duracinsky, S. Archbold, B. Lobo, et al., "The Intestinal Gas Questionnaire (IGQ): Psychometric Validation of a New Instrument for Measuring Gas-Related Symptoms and Their Impact on Daily Life Among General Population and Irritable Bowel Syndrome," *Neurogastroenterology and Motility* 34, no. 3 (2022): e14202, https://doi.org/10.1111/nmo.14202.

9. B. E. Lacy, D. J. Cangemi, J. L. Wise, and M. D. Crowell, "Development and Validation of a Novel Scoring System for Bloating and Distension: The Mayo Bloating Questionnaire," *Neuro-Gastroenterology and Motility* 34, no. 8 (2022): e14330, https://doi.org/10.1111/nmo.14330.

10. B. E. Lacy, D. Cangemi, and M. Vazquez-Roque, "Management of Chronic Abdominal Distension and Bloating," *Clinical Gastroenterology and Hepatology* 19, no. 2 (2021): 219–231, https://doi.org/10.1016/j.cgh.2020.03.056.

11. A. Accarino, F. Perez, F. Azpiroz, S. Quiroga, and J. R. Malagelada, "Abdominal Distention Results From Caudo-Ventral Redistribution of

Contents," *Gastroenterology* 136, no. 5 (2009): 1544–1551, https://doi.org/10.1053/j.gastro.2009.01.067.

12. G. Major, S. Pritchard, K. Murray, et al., "Colon Hypersensitivity to Distension, Rather than Excessive Gas Production, Produces Carbohydrate-Related Symptoms in Individuals With Irritable Bowel Syndrome," *Gastroenterology* 152, no. 1 (2017): 124–133, https://doi.org/10.1053/j.gastro.2016.09.062.

13. A. Fink, J. Kosecoff, M. Chassin, and R. H. Brook, "Consensus Methods: Characteristics and Guidelines for Use," *American Journal of Public Health* 74, no. 9 (1984): 979–983, https://doi.org/10.2105/ajph.74.9.979.

14. K. Fitch, S. J. Bernstein, M. D. Aguilar, et al., *RAND/UCLA Appropriateness Method User's Manual* (RAND corporation, 2000).

15. A. Hutchings, R. Raine, C. Sanderson, and N. Black, "A Comparison of Formal Consensus Methods Used for Developing Clinical Guidelines," *Journal of Health Services Research & Policy* 11, no. 4 (2006): 218–224, https://doi.org/10.1258/135581906778476553.

16. S. S. McMillan, M. King, and M. P. Tully, "How to Use the Nominal Group and Delphi Techniques," *International Journal of Clinical Pharmacy* 38, no. 3 (2016): 655–662, https://doi.org/10.1007/s11096-016-0257-x.

17. P. M. Mullen, "Delphi: Myths and Reality," *Journal of Health, Organisation and Management* 17, no. 1 (2003): 37–52, https://doi.org/10.1108/14777260310469319.

18. W. S. Richardson, M. C. Wilson, J. Nishikawa, and R. S. Hayward, "The Well-Built Clinical Question: A Key to Evidence-based Decisions," *ACP Journal Club* 123, no. 3 (1995): A12–A13.

19. F. Azpiroz, "Intestinal Gas," in *Sleisenger and Fordtran's Gastrointestinal and Liver Disease. Pathophysiology, Diagnosis, Management*, M. Feldman, L. Friedman, and L. Brandt, eds. 11th ed. (Elsevier, 2021).

20. H. Hammer and M. Sheikh, "Colonic Gas Excretion in Induced Carbohydrate Malabsorption—Effect of Simethicone," *European Journal of Gastroenterology and Hepatology* 4, no. 2 (1992): 141–145.

21. C. Manichanh, A. Eck, E. Varela, et al., "Anal Gas Evacuation and Colonic Microbiota in Patients With Flatulence: Effect of Diet," *Gut* 63, no. 3 (2014): 401–408, https://doi.org/10.1136/gutjnl-2012-303013.

22. J. E. Oh, W. D. Chey, and B. Spiegel, "Abdominal Bloating in the United States: Results of a Survey of 88,795 Americans Examining Prevalence and Healthcare Seeking," *Clinical Gastroenterology and Hepatology* 21, no. 9 (2023): 2370–2377, https://doi.org/10.1016/j.cgh.2022.10.031.

23. L. Neri, P. Iovino, and tL. I. R. S. Group, "Bloating Is Associated With Worse Quality of Life, Treatment Satisfaction, and Treatment Responsiveness Among Patients With Constipation-Predominant Irritable Bowel Syndrome and Functional Constipation," *Neurogastroenterology and Motility* 28, no. 4 (2016): 581–591, https://doi.org/10.1111/nmo.12758.

24. J. Hammer, M. Sonyi, K. M. Engeßer, G. Riedl, S. Luong, and H. F. Hammer, "Carbohydrate-Induced Gastrointestinal Symptoms: Development and Validation of a Test-specific Symptom Questionnaire for an Adult Population, the Adult Carbohydrate Perception Questionnaire," *European Journal of Gastroenterology and Hepatology* 32, no. 2 (2021): 171–177, https://doi.org/10.1097/MEG.0000000000001880.

25. A. Agrawal, L. A. Houghton, R. Lea, J. Morris, B. Reilly, and P. J. Whorwell, "Bloating and Distention in Irritable Bowel Syndrome: The Role of Visceral Sensation," *Gastroenterology* 134, no. 7 (2008): 1882–1889, https://doi.org/10.1053/j.gastro.2008.02.096.

26. J. A. Damianos, S. K. Tomar, F. Azpiroz, and E. Barba, "Abdomino-Phrenic Dyssynergia: A Narrative Review," *American Journal of Gastroenterology* 118, no. 1 (2022): 41–45, https://doi.org/10.14309/ajg.0000000000002044.

27. A. Mari, F. Abu Backer, M. Mahamid, et al., "Bloating and Abdominal Distension: Clinical Approach and Management," *Advances in Therapy* 36, no. 5 (2019): 1075–1084, https://doi.org/10.1007/s12325-019-00924-7.

28. A. Villoria, F. Azpiroz, E. Burri, D. Cisternas, A. Soldevilla, and J. R. Malagelada, "Abdomino-Phrenic Dyssynergia in Patients With Abdominal Bloating and Distension," *American Journal of Gastroenterology* 106, no. 5 (2011): 815–819, https://doi.org/10.1038/ajg.2010.408.

29. E. Barba, S. Quiroga, A. Accarino, et al., "Mechanisms of Abdominal Distension in Severe Intestinal Dysmotility: Abdomino-Thoracic Response to Gut Retention," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 25, no. 6 (2013): e389–e394, https://doi.org/10.1111/nmo.12128.

30. B. Salvioli, J. Serra, F. Azpiroz, et al., "Origin of Gas Retention and Symptoms in Patients With Bloating," *Gastroenterology* 128, no. 3 (2005): 574–579, https://doi.org/10.1053/j.gastro.2004.12.047.

31. M. P. Caldarella, J. Serra, F. Azpiroz, and J. R. Malagelada, "Prokinetic Effects in Patients With Intestinal Gas Retention," *Gastroenterology* 122, no. 7 (2002): 1748–1755, https://doi.org/10.1053/gast.2002.33658.

32. J. R. Malagelada, A. Accarino, and F. Azpiroz, "Bloating and Abdominal Distension: Old Misconceptions and Current Knowledge," *Official journal of the American College of Gastroenterology | ACG.* 112, no. 8 (2017): 1221–1231, https://doi.org/10.1038/ajg.2017.129.

33. W. G. Thompson, "Gender Differences in Irritable Bowel Symptoms," *European Journal of Gastroenterology and Hepatology* 9, no. 3 (1997): 299–302, https://doi.org/10.1097/00042737-199703000-00015.

34. L. Chang, O. Y. Lee, B. Naliboff, M. Schmulson, and E. A. Mayer, "Sensation of Bloating and Visible Abdominal Distension in Patients With Irritable Bowel Syndrome," *American Journal of Gastroenterology* 96, no. 12 (2001): 3341–3347, https://doi.org/10.1111/j.1572-0241.2001.05336.x.

35. A. K. Tuteja, N. J. Talley, S. K. Joos, K. G. Tolman, and D. H. Hickam, "Abdominal Bloating in Employed Adults: Prevalence, Risk Factors, and Association With Other Bowel Disorders," *American Journal of Gastroenterology* 103, no. 5 (2008): 1241–1248, https://doi.org/10.1111/j.1572-0241.2007.01755.x.

36. D. A. Drossman, C. B. Morris, S. Schneck, et al., "International Survey of Patients With IBS: Symptom Features and their Severity, Health Status, Treatments, and Risk Taking to Achieve Clinical Benefit," *Journal of Clinical Gastroenterology* 43, no. 6 (2009): 541–550, https://doi.org/10.1097/mcg.0b013e318189a7f9.

37. D. Deutsch, M. Bouchoucha, J. Uzan, J.-J. Raynaud, J.-M. Sabate, and R. Benamouzig, "Abdominal Pain Severity is Mainly Associated With Bloating Severity in Patients With Functional Bowel Disorders and Functional Abdominal Pain," *Digestive Diseases and Sciences* 67, no. 7 (2022): 3026–3035, https://doi.org/10.1007/s10620-021-07175-z.

38. N. A. Koloski, M. Jones, J. Hammer, et al., "The Validity of a New Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS) for Evaluating Symptoms in the Clinical Setting," *Digestive Diseases and Sciences* 62, no. 8 (2017): 1913–1922, https://doi.org/10.1007/s10620-017-4599-6.

39. J. Hammer, G. Holtmann, and K. Hammer, "Validation of the Structured Assessment of Gastrointestinal Symptoms Scale to Support Standardized Evaluation and Follow-up," *Journal of Pediatric Gastroenterology and Nutrition* 77, no. 2 (2023): 178–183, https://doi.org/10.1097/mpg.0000000000003821.

40. M. J. Lewis, B. Reilly, L. A. Houghton, and P. J. Whorwell, "Ambulatory Abdominal Inductance Plethysmography: Towards Objective Assessment of Abdominal Distension in Irritable Bowel Syndrome," *Gut* 48, no. 2 (2001): 216–220, https://doi.org/10.1136/gut.48.2.216.

41. M. Simrén, A. Månsson, A. M. Langkilde, et al., "Food-Related Gastrointestinal Symptoms in the Irritable Bowel Syndrome," *Digestion* 63, no. 2 (2001): 108–115, https://doi.org/10.1159/000051878.

42. L. Böhn, S. Störsrud, H. Törnblom, U. Bengtsson, and M. Simrén, "Self-Reported food-related Gastrointestinal Symptoms in IBS Are Common and Associated With More Severe Symptoms and Reduced Quality of Life," *American Journal of Gastroenterology* 108, no. 5 (2013): 634–641, https://doi.org/10.1038/ajg.2013.105.

43. D. J. Cangemi and B. E. Lacy, "A Practical Approach to the Diagnosis and Treatment of Abdominal Bloating and Distension," *Gastroenterol Hepatol (N Y).* 18, no. 2 (2022): 75–84.

44. L. Park, K. O'Connell, K. Herzog, et al., "Clinical Features of Young Onset Colorectal Cancer Patients From a Large Cohort at a Single Cancer Center," *International Journal of Colorectal Disease* 37, no. 12 (2022): 2511–2516, https://doi.org/10.1007/s00384-022-04286-5.

45. B. E. Lacy and D. J. Cangemi, "A Pragmatic Approach to the Evaluation and Treatment of Abdominal Bloating," *American Journal of Gastroenterology* 117, no. 5 (2022): 701–705, https://doi.org/10.14309/ajg.0000000000001665.

46. M. E. Phillips, A. D. Hopper, J. S. Leeds, et al., "Consensus for the Management of Pancreatic Exocrine Insufficiency: UK Practical Guidelines," *BMJ Open Gastroenterol* 8, no. 1 (2021): e000643, https://doi.org/10.1136/bmjgast-2021-000643.

47. E. C. Ebert, "The Thyroid and the Gut," *Journal of Clinical Gastroenterology* 44, no. 6 (2010): 402–406, https://doi.org/10.1097/mcg.0b013e3181d6bc3e.

48. G. E. Bekkering, T. Agoritsas, L. Lytvyn, et al., "Thyroid Hormones Treatment for Subclinical Hypothyroidism: A Clinical Practice Guideline," *BMJ* 365 (2019): l2006, https://doi.org/10.1136/bmj.l2006.

49. T. Meldgaard, J. Keller, A. E. Olesen, et al., "Pathophysiology and Management of Diabetic Gastroenteropathy," *Therap Adv Gastroenterol* 12 (2019): 1756284819852047, https://doi.org/10.1177/1756284819852047.

50. M. J. Concepción Zavaleta, J. G. Gonzáles Yovera, D. M. Moreno Marreros, et al., "Diabetic Gastroenteropathy: An Underdiagnosed Complication," *World Journal of Diabetes* 12, no. 6 (2021): 794–809, https://doi.org/10.4239/wjd.v12.i6.794.

51. X. Qi, C. Yun, Y. Pang, and J. Qiao, "The Impact of the Gut Microbiota on the Reproductive and Metabolic Endocrine System," *Gut Microbes* 13, no. 1 (2021): 1–21, https://doi.org/10.1080/19490976.2021.1894070.

52. L. Zenzeri, R. Tambucci, P. Quitadamo, V. Giorgio, R. De Giorgio, and G. Di Nardo, "Update on Chronic Intestinal Pseudo-obstruction," *Current Opinion in Gastroenterology* 36, no. 3 (2020): 230–237, https://doi.org/10.1097/mog.0000000000000630.

53. J. Hammer, N. Memaran, W. D. Huber, and K. Hammer, "Development and Validation of the Paediatric Carbohydrate Perception Questionnaire (Pcpq), an Instrument for the Assessment of Carbohydrate-Induced Gastrointestinal Symptoms in the Paediatric Population," *Neuro-Gastroenterology and Motility* 32, no. 12 (2020): e13934, https://doi.org/10.1111/nmo.13934.

54. H. F. Hammer, M. R. Fox, J. Keller, et al., "European Guideline on Indications, Performance, and Clinical Impact of Hydrogen and Methane Breath Tests in Adult and Pediatric Patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition Consensus," *United European Gastroenterol J* 10, no. 1 (2022): 15–40, https://doi.org/10.1002/ueg2.12133.

55. J. Keller, H. F. Hammer, P. R. Afolabi, et al., "European Guideline on Indications, Performance and Clinical Impact of (13) C-Breath Tests in Adult and Pediatric Patients: An EAGEN, ESNM, and ESPGHAN Consensus, Supported by EPC," *United European Gastroenterol J* 9, no. 5 (2021): 598–625, https://doi.org/10.1002/ueg2.12099.

56. N. A. Koloski, M. Jones, J. Kalantar, M. Weltman, J. Zaguirre, and N. J. Talley, "The Brain--Gut Pathway in Functional Gastrointestinal Disorders Is Bidirectional: A 12-year Prospective Population-Based Study," *Gut* 61, no. 9 (2012): 1284–1290, https://doi.org/10.1136/gutjnl-2011-300474.

57. B. E. Lacy, M. Pimentel, D. M. Brenner, et al., "ACG Clinical Guideline: Management of Irritable Bowel Syndrome," *American Journal of Gastroenterology* 116, no. 1 (2021): 17–44, https://doi.org/10.14309/ajg.0000000000001036.

58. F. Perez, A. Accarino, F. Azpiroz, S. Quiroga, and J. R. Malagelada, "Gas Distribution Within the Human Gut: Effect of Meals," *American Journal of Gastroenterology* 102, no. 4 (2007): 842–849, https://doi.org/10.1111/j.1572-0241.2007.01071.x.

59. A. Accarino, F. Perez, F. Azpiroz, S. Quiroga, and J. R. Malagelada, "Intestinal Gas and Bloating: Effect of Prokinetic Stimulation," *American Journal of Gastroenterology* 103, no. 8 (2008): 2036–2042, https://doi.org/10.1111/j.1572-0241.2008.01866.x.

60. E. Barba, B. Sánchez, E. Burri, et al., "Abdominal Distension After Eating Lettuce: The Role of Intestinal Gas Evaluated in Vitro and by Abdominal CT Imaging," *Neuro-Gastroenterology and Motility* 31, no. 12 (2019): e13703, https://doi.org/10.1111/nmo.13703.

61. H. Törnblom, L. Van Oudenhove, R. Sadik, H. Abrahamsson, J. Tack, and M. Simrén, "Colonic Transit Time and IBS Symptoms: What's the Link?," *American Journal of Gastroenterology* 107, no. 5 (2012): 754–760, https://doi.org/10.1038/ajg.2012.5.

62. L. A. Houghton, R. Lea, A. Agrawal, A. Agrawal, B. Reilly, and P. J. Whorwell, "Relationship of Abdominal Bloating to Distention in Irritable Bowel Syndrome and Effect of Bowel Habit," *Gastroenterology* 131, no. 4 (2006): 1003–1010, https://doi.org/10.1053/j.gastro.2006.07.015.

63. R. A. Bendezu, E. Barba, E. Burri, et al., "Intestinal Gas Content and Distribution in Health and in Patients With Functional Gut Symptoms," *Neuro-Gastroenterology and Motility* 27, no. 9 (2015): 1249–1257, https://doi.org/10.1111/nmo.12618.

64. Y. Zhu, X. Zheng, Y. Cong, et al., "Bloating and Distention in Irritable Bowel Syndrome: The Role of Gas Production and Visceral Sensation After Lactose Ingestion in a Population With Lactase Deficiency," *American Journal of Gastroenterology* 108, no. 9 (2013): 1516–1525, https://doi.org/10.1038/ajg.2013.198.

65. E. Barba, D. M. Livovsky, L. Relea, et al., "Evaluation of Abdominal Gas by Plain Abdominal Radiographs," *Neuro-Gastroenterology and Motility* 35, no. 2 (2023): e14485, https://doi.org/10.1111/nmo.14485.

66. C. Klare, J. Hammer, and H. F. Hammer, "The Adult Carbohydrate Perception Questionnaire Identifies Patients With Lactose or Fructose Intolerance Who Respond to Diet," *Digestive Diseases* 42, no. 3 (2024): 276–284, https://doi.org/10.1159/000538419.

67. C. J. Black, H. M. Staudacher, and A. C. Ford, "Efficacy of a Low FODMAP Diet in Irritable Bowel Syndrome: Systematic Review and Network Meta-Analysis," *Gut* 71, no. 6 (2022): 1117–1126, https://doi.org/10.1136/gutjnl-2021-325214.

68. J. R. Biesiekierski, S. L. Peters, E. D. Newnham, O. Rosella, J. G. Muir, and P. R. Gibson, "No Effects of Gluten in Patients With Self-Reported Non-Celiac Gluten Sensitivity After Dietary Reduction of Fermentable, Poorly Absorbed, Short-Chain Carbohydrates," *Gastroenterology* 145, no. 2 (2013): 320–8.e1-3, https://doi.org/10.1053/j.gastro.2013.04.051.

69. A. C. Ford, L. A. Harris, B. E. Lacy, E. M. M. Quigley, and P. Moayyedi, "Systematic Review With Meta-Analysis: The Efficacy of Prebiotics, Probiotics, Synbiotics and Antibiotics in Irritable Bowel Syndrome," *Alimentary Pharmacology & Therapeutics* 48, no. 10 (2018): 1044–1060, https://doi.org/10.1111/apt.15001.

70. J. Tsuchiya, R. Barreto, R. Okura, S. Kawakita, E. Fesce, and F. Marotta, "Single-Blind Follow-Up Study on the Effectiveness of a Symbiotic Preparation in Irritable Bowel Syndrome," *Chinese Journal of Digestive Diseases* 5, no. 4 (2004): 169–174, https://doi.org/10.1111/j.1443-9573.2004.00176.x.

71. S. B. Menees, M. Maneerattannaporn, H. M. Kim, and W. D. Chey, "The Efficacy and Safety of Rifaximin for the Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis," *American Journal of Gastroenterology* 107, no. 1 (2012): 28–35: quiz 6, https://doi.org/10.1038/ajg.2011.355.

72. P. Clavé and J. Tack, "Efficacy of Otilonium Bromide in Irritable Bowel Syndrome: A Pooled Analysis," *Therap Adv Gastroenterol* 10, no. 3 (2017): 311–322, https://doi.org/10.1177/1756283x16681708.

73. A. D. Nelson, C. J. Black, L. A. Houghton, N. S. Lugo-Fagundo, B. E. Lacy, and A. C. Ford, "Systematic Review and Network Meta-Analysis: Efficacy of Licensed Drugs for Abdominal Bloating in Irritable Bowel Syndrome With Constipation," *Alimentary Pharmacology & Therapeutics* 54, no. 2 (2021): 98–108, https://doi.org/10.1111/apt.16437.

74. K. Staller, J. Hinson, R. Kerstens, W. Spalding, and A. Lembo, "Efficacy of Prucalopride for Chronic Idiopathic Constipation: An Analysis of Participants With Moderate to Very Severe Abdominal Bloating," *American Journal of Gastroenterology* 117, no. 1 (2022): 184–188, https://doi.org/10.14309/ajg.0000000000001521.

75. J. Serra, A. Villoria, F. Azpiroz, et al., "Impaired Intestinal Gas Propulsion in Manometrically Proven Dysmotility and in Irritable Bowel Syndrome," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 22, no. 4 (2010): 401–e92, https://doi.org/10.1111/j.1365-2982.2009.01447.x.

76. W. J. Snape Jr., W. M. Battle, S. S. Schwartz, S. N. Braunstein, H. A. Goldstein, and A. Alavi, "Metoclopramide to Treat Gastroparesis due to Diabetes Mellitus: A Double-Blind, Controlled Trial," *Annals of Internal Medicine* 96, no. 4 (1982): 444–446, https://doi.org/10.7326/0003-4819-96-4-444.

77. D. A. Drossman, J. Tack, A. C. Ford, E. Szigethy, H. Tornblom, and L. Van Oudenhove, "Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction): A Rome Foundation Working Team Report," *Gastroenterology* 154, no. 4 (2018): 1140–71.e1, https://doi.org/10.1053/j.gastro.2017.11.279.

78. N. J. Talley, G. R. Locke, Y. A. Saito, et al., "Effect of Amitriptyline and Escitalopram on Functional Dyspepsia: A Multicenter, Randomized Controlled Study," *Gastroenterology* 149, no. 2 (2015): 340–9.e2, https://doi.org/10.1053/j.gastro.2015.04.020.

79. J. Tack, P. Janssen, T. Masaoka, R. Farre, and L. Van Oudenhove, "Efficacy of Buspirone, A Fundus-Relaxing Drug, in Patients With Functional Dyspepsia," *Clinical Gastroenterology and Hepatology* 10, no. 11 (2012): 1239–1245, https://doi.org/10.1016/j.cgh.2012.06.036.

80. E. Barba, D. M. Livovsky, A. Accarino, and F. Azpiroz, "Thoracoabdominal Wall Motion-Guided Biofeedback Treatment of Abdominal Distention: A Randomized Placebo-Controlled Trial," *Gastroenterology* 167, no. 3 (2024): 538–46.e1, https://doi.org/10.1053/j.gastro.2024.03.005.

81. M. P. Jensen, M. A. Day, and J. Miró, "Neuromodulatory Treatments for Chronic Pain: Efficacy and Mechanisms," *Nature Reviews Neurology* 10, no. 3 (2014): 167–178, https://doi.org/10.1038/nrneurol.2014.12.

82. K. Tominaga, Y. Sakata, H. Kusunoki, et al., "Rikkunshito Simultaneously Improves Dyspepsia Correlated With Anxiety in Patients With Functional Dyspepsia: A Randomized Clinical Trial (The DREAM Study)," *Neuro-Gastroenterology and Motility* 30, no. 7 (2018): e13319, https://doi.org/10.1111/nmo.13319.

83. B. D. Cash, M. S. Epstein, and S. M. Shah, "A Novel Delivery System of Peppermint Oil Is an Effective Therapy for Irritable Bowel Syndrome Symptoms," *Digestive Diseases and Sciences* 61, no. 2 (2016): 560–571, https://doi.org/10.1007/s10620-015-3858-7.

84. U. von Arnim, U. Peitz, B. Vinson, K. J. Gundermann, and P. Malfertheiner, "STW 5, a Phytopharmacon for Patients With Functional Dyspepsia: Results of a Multicenter, Placebo-Controlled Double-Blind Study," *American Journal of Gastroenterology* 102, no. 6 (2007): 1268–1275, https://doi.org/10.1111/j.1572-0241.2006.01183.x.

85. H. Everitt, S. Landau, P. Little, et al., "Therapist Telephone-Delivered CBT and Web-Based CBT Compared With Treatment as Usual in Refractory Irritable Bowel Syndrome: The ACTIB Three-Arm RCT," *Health Technology Assessment* 23, no. 17 (2019): 1–154, https://doi.org/10.3310/hta23170.

86. W. M. Gonsalkorale, L. A. Houghton, and P. J. Whorwell, "Hypnotherapy in Irritable Bowel Syndrome: A Large-Scale Audit of a Clinical Service With Examination of Factors Influencing Responsiveness," *American Journal of Gastroenterology* 97, no. 4 (2002): 954–961, https://doi.org/10.1111/j.1572-0241.2002.05615.x.

87. G. Moser, S. Trägner, E. E. Gajowniczek, et al., "Long-Term Success of GUT-Directed Group Hypnosis for Patients With Refractory Irritable Bowel Syndrome: A Randomized Controlled Trial," *American Journal of Gastroenterology* 108, no. 4 (2013): 602–609, https://doi.org/10.1038/ajg.2013.19.

88. A. N. Webb, R. H. Kukuruzovic, A. G. Catto-Smith, and S. M. Sawyer, "Hypnotherapy for Treatment of Irritable Bowel Syndrome," *Cochrane Database of Systematic Reviews*, no. 4 (2007): Cd005110, https://doi.org/10.1002/14651858.CD005110.pub2.

89. H. Noble, S. S. Hasan, V. Simpson, P. J. Whorwell, and D. H. Vasant, "Patient Satisfaction After Remotely Delivered Gut-Directed Hypnotherapy for Irritable Bowel Syndrome During the COVID-19 Era: Implications for Future Practice," *BMJ Open Gastroenterol* 9, no. 1 (2022): e001039, https://doi.org/10.1136/bmjgast-2022-001039.

90. A. Sasegbon, S. S. Hasan, P. J. Whorwell, and D. H. Vasant, "Experience and Clinical Efficacy of Gut-Directed Hypnotherapy in an Asian Population With Refractory Irritable Bowel Syndrome," *JGH Open* 6, no. 7 (2022): 447–453, https://doi.org/10.1002/jgh3.12770.

91. M. Faramarzi, P. Azadfallah, H. E. Book, K. R. Tabatabaei, H. Taheri, and J. Shokri-shirvani, "A Randomized Controlled Trial of Brief Psychoanalytic Psychotherapy in Patients With Functional Dyspepsia," *Asian J Psychiatr* 6, no. 3 (2013): 228–234, https://doi.org/10.1016/j.ajp.2012.12.012.

92. A. J. Bredenoord, "Management of Belching, Hiccups, and Aerophagia," *Clinical Gastroenterology and Hepatology* 11, no. 1 (2013): 6–12, https://doi.org/10.1016/j.cgh.2012.09.006.

93. B. K. Oelschlager, E. Quiroga, J. D. Parra, M. Cahill, N. Polissar, and C. A. Pellegrini, "Long-Term Outcomes After Laparoscopic Antireflux Surgery," *American Journal of Gastroenterology* 103, no. 2 (2008): 280–287: quiz 8, https://doi.org/10.1111/j.1572-0241.2007.01606.x.

94. M. D. Levitt, "Production and Excretion of Hydrogen Gas in Man," *New England Journal of Medicine* 281, no. 3 (1969): 122–127, https://doi.org/10.1056/nejm196907172810303.

95. C. Hoegenauer, H. F. Hammer, A. Mahnert, and C. Moissl-Eichinger, "Methanogenic Archaea in the Human Gastrointestinal Tract," *Nature Reviews Gastroenterology & Hepatology* 19, no. 12 (2022): 805–813, https://doi.org/10.1038/s41575-022-00673-z.

96. S. U. Christl, G. R. Gibson, and J. H. Cummings, "Role of Dietary Sulphate in the Regulation of Methanogenesis in the Human Large Intestine," *Gut* 33, no. 9 (1992): 1234–1238, https://doi.org/10.1136/gut.33.9.1234.

97. F. Carbonero, A. C. Benefiel, and H. R. Gaskins, "Contributions of the Microbial Hydrogen Economy to Colonic Homeostasis," *Nature Reviews Gastroenterology & Hepatology* 9, no. 9 (2012): 504–518, https://doi.org/10.1038/nrgastro.2012.85.

98. H. F. Hammer, "Colonic Hydrogen Absorption: Quantification of Its Effect on Hydrogen Accumulation Caused by Bacterial Fermentation of Carbohydrates," *Gut* 34, no. 6 (1993): 818–822, https://doi.org/10.1136/gut.34.6.818.

99. F. L. Suarez, J. Springfield, and M. D. Levitt, "Identification of Gases Responsible for the Odour of Human Flatus and Evaluation of a Device Purported to Reduce This Odour," *Gut* 43, no. 1 (1998): 100–104, https://doi.org/10.1136/gut.43.1.100.

100. A. Agrawal, L. A. Houghton, B. Reilly, J. Morris, and P. J. Whorwell, "Bloating and Distension in Irritable Bowel Syndrome: The Role of Gastrointestinal Transit," *American Journal of Gastroenterology* 104, no. 8 (2009): 1998–2004, https://doi.org/10.1038/ajg.2009.251.

101. H. F. Hammer and J. Hammer, "Diarrhea Caused by Carbohydrate Malabsorption," *Gastroenterology Clinics of North America* 41, no. 3 (2012): 611–627, https://doi.org/10.1016/j.gtc.2012.06.003.

102. P. Varjú, N. Gede, Z. Szakács, et al., "Lactose Intolerance But Not Lactose Maldigestion Is More Frequent in Patients With Irritable Bowel Syndrome than in Healthy Controls: A Meta-Analysis," *Neurogastroenterology and Motility* 31, no. 5 (2019): e13527, https://doi.org/10.1111/nmo.13527.

103. M. I. Pinto-Sanchez, P. Bercik, and E. F. Verdu, "Motility Alterations in Celiac Disease and Non-Celiac Gluten Sensitivity," *Digestive Diseases* 33, no. 2 (2015): 200–207, https://doi.org/10.1159/000371400.

104. G. I. Skodje, V. K. Sarna, I. H. Minelle, et al., "Fructan, Rather Than Gluten, Induces Symptoms in Patients With Self-Reported Non-Celiac Gluten Sensitivity," *Gastroenterology* 154, no. 3 (2018): 529–39.e2, https://doi.org/10.1053/j.gastro.2017.10.040.

105. U. Volta and R. De Giorgio, "New Understanding of Gluten Sensitivity," *Nature Reviews Gastroenterology & Hepatology* 9, no. 5 (2012): 295–299, https://doi.org/10.1038/nrgastro.2012.15.

106. E. Colomier, L. Van Oudenhove, J. Tack, et al., "Predictors of Symptom-Specific Treatment Response to Dietary Interventions in Irritable Bowel Syndrome," *Nutrients* 14, no. 2 (2022): 397, https://doi.org/10.3390/nu14020397.

107. B. Schmidt, J. Hammer, P. Holzer, and H. F. Hammer, "Chemical Nociception in the Jejunum Induced by Capsaicin," *Gut* 53, no. 8 (2004): 1109–1116, https://doi.org/10.1136/gut.2003.029793.

108. H. F. Hammer, S. F. Phillips, M. Camilleri, and R. B. Hanson, "Rectal Tone, Distensibility, and Perception: Reproducibility and Response to Different Distensions," *American Journal of Physiology* 274, no. 3 (1998): G584–G590, https://doi.org/10.1152/ajpgi.1998.274.3.g584.

109. S. Sarkar, Q. Aziz, C. J. Woolf, A. R. Hobson, and D. G. Thompson, "Contribution of Central Sensitisation to the Development of Non-Cardiac Chest Pain," *Lancet* 356, no. 9236 (2000): 1154–1159, https://doi.org/10.1016/s0140-6736(00)02758-6.

110. R. Barbera, C. Feinle, and N. W. Read, "Abnormal Sensitivity to Duodenal Lipid Infusion in Patients With Functional Dyspepsia," *European Journal of Gastroenterology and Hepatology* 7, no. 11 (1995): 1051–1057, https://doi.org/10.1097/00042737-199511000-00007.

111. H. Mertz, B. Naliboff, J. Munakata, N. Niazi, and E. A. Mayer, "Altered Rectal Perception Is a Biological Marker of Patients With Irritable Bowel Syndrome," *Gastroenterology* 109, no. 1 (1995): 40–52, https://doi.org/10.1016/0016-5085(95)90267-8.

112. G. E. Boeckxstaens, D. P. Hirsch, B. D. van den Elzen, S. H. Heisterkamp, and G. N. Tytgat, "Impaired Drinking Capacity in Patients With Functional Dyspepsia: Relationship With Proximal Stomach Function," *Gastroenterology* 121, no. 5 (2001): 1054–1063, https://doi.org/10.1053/gast.2001.28656.

113. J. Tack, P. Caenepeel, B. Fischler, H. Piessevaux, and J. Janssens, "Symptoms Associated With Hypersensitivity to Gastric Distention in Functional Dyspepsia," *Gastroenterology* 121, no. 3 (2001): 526–535, https://doi.org/10.1053/gast.2001.27180.

114. J. Hammer, "Identification of Individuals With Functional Dyspepsia With a Simple, Minimally Invasive Test: A Single Center Cohort Study of the Oral Capsaicin Test," *American Journal of Gastroenterology* 113, no. 4 (2018): 584–592, https://doi.org/10.1038/ajg.2018.16.

115. J. Ritchie, "Pain From Distension of the Pelvic Colon by Inflating a Balloon in the Irritable Colon Syndrome," *Gut* 14, no. 2 (1973): 125–132, https://doi.org/10.1136/gut.14.2.125.

116. S. D. Kuiken, R. Lindeboom, G. N. Tytgat, and G. E. Boeckxstaens, "Relationship Between Symptoms and Hypersensitivity to Rectal Distension in Patients With Irritable Bowel Syndrome," *Alimentary Pharmacology & Therapeutics* 22, no. 2 (2005): 157–164, https://doi.org/10.1111/j.1365-2036.2005.02524.x.

117. J. Aguilera-Lizarraga, H. Hussein, and G. E. Boeckxstaens, "Immune Activation in Irritable Bowel Syndrome: What Is the Evidence?," *Nature Reviews Immunology* 22, no. 11 (2022): 674–686, https://doi.org/10.1038/s41577-022-00700-9.

118. M. Ceulemans, I. Jacobs, L. Wauters, and T. Vanuytsel, "Immune Activation in Functional Dyspepsia: Bystander Becoming the Suspect," *Frontiers in Neuroscience* 16 (2022): 831761, https://doi.org/10.3389/fnins.2022.831761.

119. S. E. Pritchard, L. Marciani, K. C. Garsed, et al., "Fasting and Postprandial Volumes of the Undisturbed Colon: Normal Values and Changes in Diarrhea-Predominant Irritable Bowel Syndrome Measured Using Serial MRI," *Neuro-Gastroenterology and Motility* 26, no. 1 (2014): 124–130, https://doi.org/10.1111/nmo.12243.

120. R. Farre, H. Vanheel, T. Vanuytsel, et al., "In Functional Dyspepsia, Hypersensitivity to Postprandial Distention Correlates With Meal-Related Symptom Severity," *Gastroenterology* 145, no. 3 (2013): 566–573, https://doi.org/10.1053/j.gastro.2013.05.018.

121. E. Burri, D. Cisternas, A. Villoria, et al., "Accommodation of the Abdomen to Its Content: Integrated Abdomino-Thoracic Response," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 24, no. 4 (2012): 312-e162, https://doi.org/10.1111/j.1365-2982.2011.01846.x.

122. E. Burri, E. Barba, J. W. Huaman, et al., "Mechanisms of Postprandial Abdominal Bloating and Distension in Functional Dyspepsia," *Gut* 63, no. 3 (2014): 395–400, https://doi.org/10.1136/gutjnl-2013-304574.

123. E. Barba, E. Burri, S. Quiroga, A. Accarino, and F. Azpiroz, "Visible Abdominal Distension in Functional Gut Disorders: Objective Evaluation," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 35, no. 2 (2022): e14466, https://doi.org/10.1111/nmo.14466.

124. E. Barba, E. Burri, A. Accarino, et al., "Abdomino-Thoracic Mechanisms of Functional Abdominal Distension and Correction by Biofeedback," *Gastroenterology* 148, no. 4 (2015): 732–738, https://doi.org/10.1053/j.gastro.2014.12.006.

125. E. Barba, A. Accarino, and F. Azpiroz, "Correction of Abdominal Distention by Biofeedback-Guided Control of Abdominothoracic Muscular Activity in a Randomized, Placebo-Controlled Trial," *Clinical Gastroenterology and Hepatology* 15, no. 12 (2017): 1922–1929, https://doi.org/10.1016/j.cgh.2017.06.052.

126. D. M. Livovsky, C. Barber, E. Barba, A. Accarino, and F. Azpiroz, "Abdominothoracic Postural Tone Influences the Sensations Induced by Meal Ingestion," *Nutrients* 13, no. 2 (2021): 658, https://doi.org/10.3390/nu13020658.

127. J. Serra, B. Salvioli, F. Azpiroz, and J. R. Malagelada, "Lipid-Induced Intestinal Gas Retention in Irritable Bowel Syndrome," *Gastroenterology* 123, no. 3 (2002): 700–706, https://doi.org/10.1053/gast.2002.35394.

128. M. C. Passos, J. Serra, F. Azpiroz, F. Tremolaterra, and J. R. Malagelada, "Impaired Reflex Control of Intestinal Gas Transit in Patients With Abdominal Bloating," *Gut* 54, no. 3 (2005): 344–348, https://doi.org/10.1136/gut.2003.038158.

129. R. A. Bendezu, E. Barba, E. Burri, et al., "Colonic Content in Health and Its Relation to Functional Gut Symptoms," *Neuro-Gastroenterology and Motility* 28, no. 6 (2016): 849–854, https://doi.org/10.1111/nmo.12782.

130. C. L. Storhaug, S. K. Fosse, and L. T. Fadnes, "Country, Regional, and Global Estimates for Lactose Malabsorption in Adults: A Systematic Review and Meta-Analysis," *Lancet Gastroenterology & Hepatology* 2, no. 10 (2017): 738–746, https://doi.org/10.1016/s2468-1253(17)30154-1.

131. L. Wauters, R. Dickman, V. Drug, et al., "United European Gastroenterology (UEG) and European Society for Neurogastroenterology and Motility (ESNM) Consensus on Functional Dyspepsia," *United European Gastroenterology Journal* 9, no. 3 (2021): 307–331, https://doi.org/10.1002/ueg2.12061.

132. M. S. Ryu, H.-K. Jung, J.-i Ryu, J.-S. Kim, and K. A. Kong, "Clinical Dimensions of Bloating in Functional Gastrointestinal Disorders," *J Neurogastroenterol Motil* 22, no. 3 (2016): 509–516, https://doi.org/10.5056/jnm15167.

133. H. Piessevaux, B. De Winter, E. Louis, et al., "Dyspeptic Symptoms in the General Population: A Factor and Cluster Analysis of Symptom Groupings," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 21, no. 4 (2009): 378–388, https://doi.org/10.1111/j.1365-2982.2009.01262.x.

134. V. Stanghellini, F. K. Chan, W. L. Hasler, et al., "Gastroduodenal Disorders," *Gastroenterology* 150, no. 6 (2016): 1380–1392, https://doi.org/10.1053/j.gastro.2016.02.011.

135. J.-W. Huaman, M. Mego, A. Bendezú, et al., "Correction of Dyssynergic Defecation, But Not Fiber Supplementation, Reduces Symptoms of Functional Dyspepsia in Patients With Constipation in a Randomized Trial," *Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association.* 18, no. 11 (2020): 2463–70.e1, https://doi.org/10.1016/j.cgh.2019.11.048.

136. M. Schmulson, O. Y. Lee, L. Chang, B. Naliboff, and E. A. Mayer, "Symptom Differences in Moderate to Severe IBS Patients Based on Predominant Bowel Habit," *American Journal of Gastroenterology* 94, no. 10 (1999): 2929–2935, https://doi.org/10.1111/j.1572-0241.1999.01440.x.

137. E. Barba, E. Burri, S. Quiroga, A. Accarino, and F. Azpiroz, "Visible Abdominal Distension in Functional Gut Disorders: Objective Evaluation," *Neuro-Gastroenterology and Motility* 35, no. 2 (2023): e14466, https://doi.org/10.1111/nmo.14466.

138. V. C. Goodoory, L. A. Houghton, C. J. Black, and A. C. Ford, "Characteristics Of, and Natural History Among, Individuals With Rome IV Functional Bowel Disorders," *Neuro-Gastroenterology and Motility* 34, no. 5 (2022): e14268, https://doi.org/10.1111/nmo.14268.

139. D. A. Drossman, "Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV," *Gastroenterology* 150, no. 6 (2016): 1262–1279.e2, https://doi.org/10.1053/j.gastro.2016.02.032.

140. M. D. Levitt, J. Furne, M. R. Aeolus, and F. L. Suarez, "Evaluation of an Extremely Flatulent Patient: Case Report and Proposed Diagnostic and Therapeutic Approach," *American Journal of Gastroenterology* 93, no. 11 (1998): 2276–2281, https://doi.org/10.1111/j.1572-0241.1998.00635.x.

141. F. L. Suarez and M. D. Levitt, "An Understanding of Excessive Intestinal Gas," *Current Gastroenterology Reports* 2, no. 5 (2000): 413–419, https://doi.org/10.1007/s11894-000-0042-8.

142. L. L. Pop, I. A. Mureşan, and D. L. Dumitraşcu, "How Much Bloating in the Irritable Bowel Syndrome?," *Romanian Journal of Internal Medicine* 56, no. 4 (2018): 221–226, https://doi.org/10.2478/rjim-2018-0017.

143. S. H. Siddiqui, E. S. Sagalow, M. A. Fiorella, N. Jain, and J. R. Spiegel, "Retrograde Cricopharyngeus Dysfunction: The Jefferson Experience," *Laryngoscope* 133, no. 5 (2023): 1081–1085, https://doi.org/10.1002/lary.30346.

144. R. A. B. Oude Nijhuis, J. A. Snelleman, J. M. Oors, et al., "The Inability to Belch Syndrome: A Study Using Concurrent High-Resolution Manometry and Impedance Monitoring," *Neuro-Gastroenterology and Motility* 34, no. 5 (2022): e14250, https://doi.org/10.1111/nmo.14250.

145. H. F. Hammer, A. C. A. Santa, L. R. Schiller, and J. S. Fordtran, "Studies of Osmotic Diarrhea Induced in Normal Subjects by Ingestion of Polyethylene Glycol and Lactulose," *Journal of Clinical Investigation* 84, no. 4 (1989): 1056–1062, https://doi.org/10.1172/jci114267.

146. V. Hammer, K. Hammer, N. Memaran, W. D. Huber, K. Hammer, and J. Hammer, "Relationship Between Abdominal Symptoms and Fructose Ingestion in Children With Chronic Abdominal Pain," *Digestive Diseases and Sciences* 63, no. 5 (2018): 1270–1279, https://doi.org/10.1007/s10620-018-4997-4.

147. M. Simrén, P. Agerforz, E. S. Björnsson, and H. Abrahamsson, "Nutrient-Dependent Enhancement of Rectal Sensitivity in Irritable Bowel Syndrome (IBS)," *Neuro-Gastroenterology and Motility* 19, no. 1 (2007): 20–29, https://doi.org/10.1111/j.1365-2982.2006.00849.x.

148. A. C. Hernando-Harder, J. Serra, F. Azpiroz, and J. R. Malagelada, "Sites of Symptomatic Gas Retention During Intestinal Lipid Perfusion in Healthy Subjects," *Gut* 53, no. 5 (2004): 661–665, https://doi.org/10.1136/gut.2003.026385.

149. H. Harder, A. C. Hernando-Harder, A. Franke, H. J. Krammer, and M. V. Singer, "Effect of High- and Low-Caloric Mixed Liquid Meals on Intestinal Gas Dynamics," *Digestive Diseases and Sciences* 51, no. 1 (2006): 140–146, https://doi.org/10.1007/s10620-006-3099-x.

150. R. Bisschops, G. Karamanolis, J. Arts, et al., "Relationship Between Symptoms and Ingestion of a Meal in Functional Dyspepsia," *Gut* 57, no. 11 (2008): 1495–1503, https://doi.org/10.1136/gut.2007.137125.

151. A. N. Pilichiewicz, M. Horowitz, G. J. Holtmann, N. J. Talley, and C. Feinle-Bisset, "Relationship Between Symptoms and Dietary Patterns in Patients With Functional Dyspepsia," *Clinical Gastroenterology and Hepatology* 7, no. 3 (2009): 317–322, https://doi.org/10.1016/j.cgh.2008.09.007.

152. A. W. Peng, S. P. Juraschek, L. J. Appel, E. R. Miller 3rd, and N. T. Mueller, "Effects of the DASH Diet and Sodium Intake on Bloating: Results From the DASH-Sodium Trial," *American Journal of Gastroenterology* 114, no. 7 (2019): 1109–1115, https://doi.org/10.14309/ajg.0000000000000283.

153. M. Zhang, S. P. Juraschek, L. J. Appel, P. J. Pasricha, E. R. Miller 3rd, and N. T. Mueller, "Effects of High-Fiber Diets and Macronutrient Substitution on Bloating: Findings From the Omniheart Trial," *Clinical and Translational Gastroenterology* 11, no. 1 (2020): e00122, https://doi.org/10.14309/ctg.0000000000000122.

154. S. R. Wilson, P. N. Burns, L. M. Wilkinson, D. H. Simpson, and D. Muradali, "Gas at Abdominal US: Appearance, Relevance, and Analysis of Artifacts," *Radiology* 210, no. 1 (1999): 113–123, https://doi.org/10.1148/radiology.210.1.r99ja12113.

155. J. Jones, J. Yap, and D. Bell, "Abnormal Intra-abdominal Gas," *Reference article. Radiopaedia.org* (2009), https://doi.org/10.53347/rID-6166.

156. W. Chan, *Irritable Bowel Syndrome: Changes You Should Not Ignore* (IFFGD publication): 2472021, https://iffgd.org/wp-content/uploads/247-Changes-You-Should-Not-Ignore.pdf.

157. C. Löser, A. Möllgaard, and U. R. Fölsch, "Faecal Elastase 1: A Novel, Highly Sensitive, and Specific Tubeless Pancreatic Function Test," *Gut* 39, no. 4 (1996): 580–586, https://doi.org/10.1136/gut.39.4.580.

158. S. Lüth, S. Teyssen, K. Forssmann, C. Kölbel, F. Krummenauer, and M. V. Singer, "Fecal elastase-1 Determination: 'Gold Standard' of Indirect

Pancreatic Function Tests?," *Scandinavian Journal of Gastroenterology* 36, no. 10 (2001): 1092–1099, https://doi.org/10.1080/003655201750422729.

159. N. Bush and V. K. Singh, "Pancreatic Exocrine Insufficiency Guidelines: More Questions than Answers," *Hepatobiliary Surgery and Nutrition* 12, no. 3 (2023): 428–430, https://doi.org/10.21037/hbsn-23-214.

160. A. Al-Toma, U. Volta, R. Auricchio, et al., "European Society for the Study of Coeliac Disease (Esscd) Guideline for Coeliac Disease and Other gluten-related Disorders," *United European Gastroenterol J* 7, no. 5 (2019): 583–613, https://doi.org/10.1177/2050640619844125.

161. A. Rubio-Tapia, I. D. Hill, C. Semrad, et al., "American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease," *American Journal of Gastroenterology* 118, no. 1 (2023): 59–76, https://doi.org/10.14309/ajg.0000000000002075.

162. K. E. McGowan, M. E. Lyon, and J. D. Butzner, "Celiac Disease and Iga Deficiency: Complications of Serological Testing Approaches Encountered in the Clinic," *Clinical Chemistry* 54, no. 7 (2008): 1203–1209, https://doi.org/10.1373/clinchem.2008.103606.

163. M. G. Shiha, N. Nandi, S. A. Raju, et al., "Accuracy of the No-Biopsy Approach for the Diagnosis of Celiac Disease in Adults: A Systematic Review and Meta-Analysis," *Gastroenterology* 166, no. 4 (2024): 620–630, https://doi.org/10.1053/j.gastro.2023.12.023.

164. M. Latorre, S. M. Lagana, D. E. Freedberg, et al., "Endoscopic Biopsy Technique in the Diagnosis of Celiac Disease: One Bite or Two?," *Gastrointestinal Endoscopy* 81, no. 5 (2015): 1228–1233, https://doi.org/10.1016/j.gie.2014.10.024.

165. O. Yaylali, S. Kirac, M. Yilmaz, et al., "Does Hypothyroidism Affect Gastrointestinal Motility?," *Gastroenterol Res Pract* 2009 (2009): 529802–529807, https://doi.org/10.1155/2009/529802.

166. W. Jiang, G. Lu, D. Gao, Z. Lv, and D. Li, "The Relationships Between the Gut Microbiota and Its Metabolites With Thyroid Diseases," *Frontiers in Endocrinology* 13 (2022): 943408, https://doi.org/10.3389/fendo.2022.943408.

167. S. S. Yarandi and S. Srinivasan, "Diabetic Gastrointestinal Motility Disorders and the Role of Enteric Nervous System: Current Status and Future Directions," *Neuro-Gastroenterology and Motility* 26, no. 5 (2014): 611–624, https://doi.org/10.1111/nmo.12330.

168. J. H. Sellin and E. B. Chang, "Therapy Insight: Gastrointestinal Complications of Diabetes--Pathophysiology and Management," *Nature Clinical Practice Gastroenterology & Hepatology* 5, no. 3 (2008): 162–171, https://doi.org/10.1038/ncpgasthep1054.

169. X. Nie, R. Xie, and B. Tuo, "Effects of Estrogen on the Gastrointestinal Tract," *Digestive Diseases and Sciences* 63, no. 3 (2018): 583–596, https://doi.org/10.1007/s10620-018-4939-1.

170. S. Mechsner, "Endometriosis, an Ongoing Pain-Step-By-Step Treatment," *Journal of Clinical Medicine* 11, no. 2 (2022): 467, https://doi.org/10.3390/jcm11020467.

171. P. T. K. Saunders and A. W. Horne, "Endometriosis: Etiology, Pathobiology, and Therapeutic Prospects," *Cell* 184, no. 11 (2021): 2807–2824, https://doi.org/10.1016/j.cell.2021.04.041.

172. T. Jain, O. Negris, D. Brown, I. Galic, R. Salimgaraev, and L. Zhaunova, "Characterization of Polycystic Ovary Syndrome Among Flo App Users Around the World," *Reproductive Biology and Endocrinology* 19, no. 1 (2021): 36, https://doi.org/10.1186/s12958-021-00719-y.

173. Y. Xu and J. Qiao, "Association of Insulin Resistance and Elevated Androgen Levels With Polycystic Ovarian Syndrome (PCOS): A Review of Literature," *Journal of Healthcare Engineering* 2022 (2022): 9240569, https://doi.org/10.1155/2022/9240569.

174. F. F. He and Y. M. Li, "Role of Gut Microbiota in the Development of Insulin Resistance and the Mechanism Underlying Polycystic Ovary Syndrome: A Review," *Journal of Ovarian Research* 13, no. 1 (2020): 73, https://doi.org/10.1186/s13048-020-00670-3.

175. B. Orr and R. P. Edwards, "Diagnosis and Treatment of Ovarian Cancer," *Hematology-Oncology Clinics of North America* 32, no. 6 (2018): 943–964, https://doi.org/10.1016/j.hoc.2018.07.010.

176. C. A. Doubeni, A. R. Doubeni, and A. E. Myers, "Diagnosis and Management of Ovarian Cancer," *American Family Physician* 93, no. 11 (2016): 937–944.

177. Z. Nash and U. Menon, "Ovarian Cancer Screening: Current Status and Future Directions," *Best Practice & Research Clinical Obstetrics & Gynaecology* 65 (2020): 32–45, https://doi.org/10.1016/j.bpobgyn.2020.02.010.

178. D. Gallego, C. Malagelada, A. Accarino, et al., "Functional Neuromuscular Impairment in Severe Intestinal Dysmotility," *Neuro-Gastroenterology and Motility* 30, no. 12 (2018): e13458, https://doi.org/10.1111/nmo.13458.

179. L. G. Alcalá-Gonzalez, C. Malagelada, D. M. Livovsky, and F. Azpiroz, "Effect of Colonic Distension on Small Bowel Motility Measured by Jejunal High-Resolution Manometry," *Neuro-Gastroenterology and Motility* 34, no. 9 (2022): e14351, https://doi.org/10.1111/nmo.14351.

180. V. Stanghellini, R. F. Cogliandro, R. De Giorgio, et al., "Natural History of Chronic Idiopathic Intestinal Pseudo-Obstruction in Adults: A Single Center Study," *Clinical Gastroenterology and Hepatology* 3, no. 5 (2005): 449–458, https://doi.org/10.1016/s1542-3565(04)00675-5.

181. A. Villoria, F. Azpiroz, A. Soldevilla, F. Perez, and J. R. Malagelada, "Abdominal Accommodation: A Coordinated Adaptation of the Abdominal Wall to Its Content," *American Journal of Gastroenterology* 103, no. 11 (2008): 2807–2815, https://doi.org/10.1111/j.1572-0241.2008.02141.x.

182. D. Ang, J. Pannemans, T. Vanuytsel, and J. Tack, "A Single-Center Audit of the Indications and Clinical Impact of Prolonged Ambulatory Small Intestinal Manometry," *Neuro-Gastroenterology and Motility* 30, no. 9 (2018): e13357, https://doi.org/10.1111/nmo.13357.

183. M. Sonyi, J. Hammer, G. Basilisco, et al., "Coordinated Multi-Language Translation of A Validated Symptom Questionnaire for Carbohydrate Intolerances: A Practical Structured Procedure," *J Gastrointestin Liver Dis* 31, no. 3 (2022): 331–335, https://doi.org/10.15403/jgld-4463.

184. Carboception, https://carboception.com/.

185. F. Baumann-Durchschein, S. Fürst, and H. F. Hammer, "Practical Application of Breath Tests in Disorders of Gut-Brain Interaction," *Current Opinion in Pharmacology* 65 (2022): 102244, https://doi.org/10.1016/j.coph.2022.102244.

186. M. V. Lenti, H. F. Hammer, I. Tacheci, et al., "European Consensus on Malabsorption-UEG & SIGE, LGA, SPG, SRGH, CGS, ESPCG, EAGEN, ESPEN, and ESPGHAN. Part 1: Definitions, Clinical Phenotypes, and Diagnostic Testing for Malabsorption," *United European Gastroenterol J* 13, no. 4 (2025): 599–613, https://doi.org/10.1002/ueg2.70012.

187. E. A. Mayer and K. Tillisch, "The Brain-Gut Axis in Abdominal Pain Syndromes," *Annual Review of Medicine* 62, no. 1 (2011): 381–396, https://doi.org/10.1146/annurev-med-012309-103958.

188. L. Van Oudenhove, H. Törnblom, S. Störsrud, J. Tack, and M. Simrén, "Depression and Somatization Are Associated With Increased Postprandial Symptoms in Patients With Irritable Bowel Syndrome," *Gastroenterology* 150, no. 4 (2016): 866–874, https://doi.org/10.1053/j.gastro.2015.11.010.

189. L. Van Oudenhove and Q. Aziz, "The Role of Psychosocial Factors and Psychiatric Disorders in Functional Dyspepsia," *Nature Reviews Gastroenterology & Hepatology* 10, no. 3 (2013): 158–167, https://doi.org/10.1038/nrgastro.2013.10.

190. W. E. Whitehead, O. S. Palsson, R. R. Levy, A. D. Feld, M. Turner, and M. Von Korff, "Comorbidity in Irritable Bowel Syndrome,"

American Journal of Gastroenterology 102, no. 12 (2007): 2767–2776, https://doi.org/10.1111/j.1572-0241.2007.01540.x.

191. I. Aziz, O. S. Palsson, H. Törnblom, A. D. Sperber, W. E. Whitehead, and M. Simrén, "The Prevalence and Impact of Overlapping Rome IV-Diagnosed Functional Gastrointestinal Disorders on Somatization, Quality of Life, and Healthcare Utilization: A Cross-Sectional General Population Study in Three Countries," *American Journal of Gastroenterology* 113, no. 1 (2018): 86–96, https://doi.org/10.1038/ajg.2017.421.

192. A. Riedl, M. Schmidtmann, A. Stengel, et al., "Somatic Comorbidities of Irritable Bowel Syndrome: A Systematic Analysis," *Journal of Psychosomatic Research* 64, no. 6 (2008): 573–582, https://doi.org/10.1016/j.jpsychores.2008.02.021.

193. M. Zamani, S. Alizadeh-Tabari, and V. Zamani, "Systematic Review With Meta-Analysis: The Prevalence of Anxiety and Depression in Patients With Irritable Bowel Syndrome," *Alimentary Pharmacology & Therapeutics* 50, no. 2 (2019): 132–143, https://doi.org/10.1111/apt.15325.

194. M. Mussell, K. Kroenke, R. L. Spitzer, J. B. Williams, W. Herzog, and B. Löwe, "Gastrointestinal Symptoms in Primary Care: Prevalence and Association With Depression and Anxiety," *Journal of Psychosomatic Research* 64, no. 6 (2008): 605–612, https://doi.org/10.1016/j.jpsychores.2008.02.019.

195. N. A. Koloski, N. J. Talley, and P. M. Boyce, "Does Psychological Distress Modulate Functional Gastrointestinal Symptoms and Health Care Seeking? A Prospective, Community Cohort Study," *American Journal of Gastroenterology* 98, no. 4 (2003): 789–797, https://doi.org/10.1111/j.1572-0241.2003.07388.x.

196. M. Bouchoucha, M. Hejnar, G. Devroede, T. Babba, C. Bon, and R. Benamouzig, "Anxiety and Depression as Markers of Multiplicity of Sites of Functional Gastrointestinal Disorders: A Gender Issue?," *Clin Res Hepatol Gastroenterol* 37, no. 4 (2013): 422–430, https://doi.org/10.1016/j.clinre.2012.10.011.

197. V. L. Hertig, K. C. Cain, M. E. Jarrett, R. L. Burr, and M. M. Heitkemper, "Daily Stress and Gastrointestinal Symptoms in Women With Irritable Bowel Syndrome," *Nursing Research* 56, no. 6 (2007): 399–406, https://doi.org/10.1097/01.nnr.0000299855.60053.88.

198. T. Lindgren, R. Runeson, K. Wahlstedt, G. Wieslander, B. G. Dammström, and D. Norbäck, "Digestive Functional Symptoms Among Commercial Pilots in Relation to Diet, Insomnia, and Lifestyle Factors," *Aviation Space & Environmental Medicine* 83, no. 9 (2012): 872–878, https://doi.org/10.3357/asem.3309.2012.

199. M. L. Omholt, T. H. Tveito, and C. Ihlebæk, "Subjective Health Complaints, Work-Related Stress and Self-Efficacy in Norwegian Aircrew," *Occupational Medicine (London)* 67, no. 2 (2017): 135–142, https://doi.org/10.1093/occmed/kqw127.

200. J. Li, H. Ding, W. Han, et al., "The Association of Work Stress With Somatic Symptoms in Chinese Working Women: A Large Cross-Sectional Survey," *Journal of Psychosomatic Research* 89 (2016): 7–10, https://doi.org/10.1016/j.jpsychores.2016.08.001.

201. K. Kroenke, R. L. Spitzer, and J. B. Williams, "The PHQ-15: Validity of a New Measure for Evaluating the Severity of Somatic Symptoms," *Psychosomatic Medicine* 64, no. 2 (2002): 258–266, https://doi.org/10.1097/00006842-200203000-00008.

202. P. Moayyedi, F. Mearin, F. Azpiroz, et al., "Irritable Bowel Syndrome Diagnosis and Management: A Simplified Algorithm for Clinical Practice," *United European Gastroenterology Journal* 5, no. 6 (2017): 773–788, https://doi.org/10.1177/2050640617731968.

203. J. Serra, "Management of Bloating," *Neuro-Gastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society* 34, no. 3 (2022): e14333, https://doi.org/10.1111/nmo.14333.

204. A. Rubio-Tapia, I. D. Hill, C. P. Kelly, A. H. Calderwood, and J. A. Murray, "ACG Clinical Guidelines: Diagnosis and Management of Celiac Disease," *American Journal of Gastroenterology* 108, no. 5 (2013): 656–676, https://doi.org/10.1038/ajg.2013.79.

205. Y. M. Kan, S. Y. Chu, and C. K. Loo, "Diagnostic Accuracy of Fecal Calprotectin in Predicting Significant Gastrointestinal Diseases," *JGH Open* 5, no. 6 (2021): 647–652, https://doi.org/10.1002/jgh3.12548.

206. O. D. Tavabie, S. A. Hughes, and A. Loganayagam, "The Role of Faecal Calprotectin in the Differentiation of Organic From Functional Bowel Disorders," *British Journal of General Practice* 64, no. 628 (2014): 595–596, https://doi.org/10.3399/bjgp14x682525.

207. J. Serra, F. Azpiroz, and J. R. Malagelada, "Impaired Transit and Tolerance of Intestinal Gas in the Irritable Bowel Syndrome," *Gut* 48, no. 1 (2001): 14–19, https://doi.org/10.1136/gut.48.1.14.

208. T. N. Chami, M. M. Schuster, M. E. Bohlman, T. J. Pulliam, N. Kamal, and W. E. Whitehead, "A Simple Radiologic Method to Estimate the Quantity of Bowel Gas," *American Journal of Gastroenterology* 86, no. 5 (1991): 599–602.

209. A. Koide, T. Yamaguchi, T. Odaka, et al., "Quantitative Analysis of Bowel Gas Using Plain Abdominal Radiograph in Patients With Irritable Bowel Syndrome," *American Journal of Gastroenterology* 95, no. 7 (2000): 1735–1741, https://doi.org/10.1016/s0002-9270(00)00981-3.

210. S. Y. Park, H. B. Park, J. M. Lee, et al., "Relevance of Colonic Gas Analysis and Transit Study in Patients With Chronic Constipation," *J Neurogastroenterol Motil* 21, no. 3 (2015): 433–439, https://doi.org/10.5056/jnm14109.

211. M. H. Morken, A. E. Berstad, G. Nysaeter, and A. Berstad, "Intestinal Gas in Plain Abdominal Radiographs Does Not Correlate With Symptoms After Lactulose Challenge," *European Journal of Gastroenterology and Hepatology* 19, no. 7 (2007): 589–593, https://doi.org/10.1097/MEG.0b013e328133f2e7.

212. G. Maconi, T. Hausken, C. F. Dietrich, et al., "Gastrointestinal Ultrasound in Functional Disorders of the Gastrointestinal Tract – EFSUMB Consensus Statement," *Ultrasound Int Open* 7, no. 1 (2021): E14–e24, https://doi.org/10.1055/a-1474-8013.

213. P. Vijayvargiya, S. Jameie-Oskooei, M. Camilleri, V. Chedid, P. J. Erwin, and M. H. Murad, "Association Between Delayed Gastric Emptying and Upper Gastrointestinal Symptoms: A Systematic Review and Meta-Analysis," *Gut* 68, no. 5 (2019): 804–813, https://doi.org/10.1136/gutjnl-2018-316405.

214. F. Carbone, R. De Buysscher, K. Van den Houte, J. Schol, N. Goelen, and J. Tack, "Relationship Between Gastric Emptying Rate and Simultaneously Assessed Symptoms in Functional Dyspepsia," *Clinical Gastroenterology and Hepatology* 20, no. 3 (2022): e429–e437, https://doi.org/10.1016/j.cgh.2021.03.023.

215. P. Iovino, M. C. Neri, L. D'Alba, A. Santonicola, and G. Chiarioni, "Pelvic Floor Biofeedback Is an Effective Treatment for Severe Bloating in Disorders of Gut-Brain Interaction With Outlet Dysfunction," *Neuro-Gastroenterology and Motility* 34, no. 5 (2022): e14264, https://doi.org/10.1111/nmo.14264.

216. J. Brandler and M. Camilleri, "Pretest and Post-Test Probabilities of Diagnoses of Rectal Evacuation Disorders Based on Symptoms, Rectal Exam, and Basic Tests: A Systematic Review," *Clinical Gastroenterology and Hepatology* 18, no. 11 (2020): 2479–2490, https://doi.org/10.1016/j.cgh.2019.11.049.

217. F. Azpiroz, *Intestinal Gas* (Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management, 2020), 224–231.

218. B. Ohlsson and J. Manjer, "Physical Inactivity During Leisure Time and Irregular Meals Are Associated With Functional Gastrointestinal Complaints in Middle-Aged and Elder Subjects," *Scandinavian Journal of Gastroenterology* 51, no. 11 (2016): 1299–1307, https://doi.org/10.1080/00365521.2016.1209786.

219. A. Villoria, J. Serra, F. Azpiroz, and J. R. Malagelada, "Physical Activity and Intestinal Gas Clearance in Patients With Bloating," *American Journal of Gastroenterology* 101, no. 11 (2006): 2552–2557, https://doi.org/10.1111/j.1572-0241.2006.00873.x.

220. M. K. Hosseini-Asl, E. Taherifard, and M. R. Mousavi, "The Effect of a Short-Term Physical Activity After Meals on Gastrointestinal Symptoms in Individuals With Functional Abdominal Bloating: A Randomized Clinical Trial," *Gastroenterol Hepatol Bed Bench* 14, no. 1 (2021): 59–66.

221. G. Riezzo, L. Prospero, B. D'Attoma, et al., "The Impact of a Twelve-Week Moderate Aerobic Exercise Program on Gastrointestinal Symptom Profile and Psychological Well-Being of Irritable Bowel Syndrome Patients: Preliminary Data From a Southern Italy Cohort," *Journal of Clinical Medicine* 12, no. 16 (2023): 5359, https://doi.org/10.3390/jcm12165359.

222. M. C. Lomer, G. C. Parkes, and J. D. Sanderson, "Review Article: Lactose Intolerance in Clinical Practice--Myths and Realities," *Alimentary Pharmacology & Therapeutics* 27, no. 2 (2008): 93–103, https://doi.org/10.1111/j.1365-2036.2007.03557.x.

223. J. S. Barrett, P. M. Irving, S. J. Shepherd, J. G. Muir, and P. R. Gibson, "Comparison of the Prevalence of Fructose and Lactose Malabsorption Across Chronic Intestinal Disorders," *Alimentary Pharmacology & Therapeutics* 30, no. 2 (2009): 165–174, https://doi.org/10.1111/j.1365-2036.2009.04018.x.

224. J. Algera, E. Colomier, and M. Simrén, "The Dietary Management of Patients With Irritable Bowel Syndrome: A Narrative Review of the Existing and Emerging Evidence," *Nutrients* 11, no. 9 (2019): 2162, https://doi.org/10.3390/nu11092162.

225. E. P. Halmos, V. A. Power, S. J. Shepherd, P. R. Gibson, and J. G. Muir, "A Diet Low in Fodmaps Reduces Symptoms of Irritable Bowel Syndrome," *Gastroenterology* 146, no. 1 (2014): 67–75.e5, https://doi.org/10.1053/j.gastro.2013.09.046.

226. M. Bellini, S. Tonarelli, A. G. Nagy, et al., "Low FODMAP Diet: Evidence, Doubts, and Hopes," *Nutrients* 12, no. 1 (2020): 148, https://doi.org/10.3390/nu12010148.

227. C. Catassi, A. Alaedini, C. Bojarski, et al., "The Overlapping Area of Non-Celiac Gluten Sensitivity (NCGS) and Wheat-Sensitive Irritable Bowel Syndrome (IBS): An Update," *Nutrients* 9, no. 11 (2017): 1268, https://doi.org/10.3390/nu9111268.

228. R. De Giorgio, U. Volta, and P. R. Gibson, "Sensitivity to Wheat, Gluten and FODMAPs in IBS: Facts or Fiction?," *Gut* 65, no. 1 (2016): 169–178, https://doi.org/10.1136/gutjnl-2015-309757.

229. J. Molina-Infante and A. Carroccio, "Suspected Nonceliac Gluten Sensitivity Confirmed in Few Patients After Gluten Challenge in Double-Blind, Placebo-Controlled Trials," *Clinical Gastroenterology and Hepatology* 15, no. 3 (2017): 339–348, https://doi.org/10.1016/j.cgh.2016.08.007.

230. A. Khan, M. G. Suarez, and J. A. Murray, "Nonceliac Gluten and Wheat Sensitivity," *Clinical Gastroenterology and Hepatology* 18, no. 9 (2020): 1913–22.e1, https://doi.org/10.1016/j.cgh.2019.04.009.

231. Y. Junker, S. Zeissig, S. J. Kim, et al., "Wheat Amylase Trypsin Inhibitors Drive Intestinal Inflammation via Activation of Toll-Like Receptor 4," *Journal of Experimental Medicine* 209, no. 13 (2012): 2395–2408, https://doi.org/10.1084/jem.20102660.

232. J. R. Biesiekierski, E. D. Newnham, P. M. Irving, et al., "Gluten Causes Gastrointestinal Symptoms in Subjects Without Celiac Disease: A Double-Blind Randomized Placebo-Controlled Trial," *American Journal of Gastroenterology* 106, no. 3 (2011): 508–514: quiz 15, https://doi.org/10.1038/ajg.2010.487.

233. A. Di Sabatino, U. Volta, C. Salvatore, et al., "Small Amounts of Gluten in Subjects With Suspected Nonceliac Gluten Sensitivity: A Randomized, Double-Blind, Placebo-Controlled, Cross-Over Trial," *Clinical Gastroenterology and Hepatology* 13, no. 9 (2015): 1604–12.e3, https://doi.org/10.1016/j.cgh.2015.01.029.

234. M. C. G. de Graaf, C. L. Lawton, F. Croden, et al., "The Effect of Expectancy Versus Actual Gluten Intake on Gastrointestinal and Extra-Intestinal Symptoms in Non-Coeliac Gluten Sensitivity: A Randomised, Double-Blind, Placebo-Controlled, International, Multicentre Study," *Lancet Gastroenterology & Hepatology* 9, no. 2 (2024): 110–123, https://doi.org/10.1016/s2468-1253(23)00317-5.

235. C. Crawley, N. Savino, C. Halby, et al., "The Effect of Gluten in Adolescents and Young Adults With Gastrointestinal Symptoms: A Blinded Randomised Cross-Over Trial," *Alimentary Pharmacology & Therapeutics* 55, no. 9 (2022): 1116–1127, https://doi.org/10.1111/apt.16914.

236. M. Simrén, G. Barbara, H. J. Flint, et al., "Intestinal Microbiota in Functional Bowel Disorders: A Rome Foundation Report," *Gut* 62, no. 1 (2013): 159–176, https://doi.org/10.1136/gutjnl-2012-302167.

237. U. C. Ghoshal, "Gut Microbiota-Brain Axis Modulation by a Healthier Microbiological Microenvironment: Facts and Fictions," *J Neurogastroenterol Motil* 24, no. 1 (2018): 4–6, https://doi.org/10.5056/jnm17150.

238. L. Wei, R. Singh, S. Ro, and U. C. Ghoshal, "Gut Microbiota Dysbiosis in Functional Gastrointestinal Disorders: Underpinning the Symptoms and Pathophysiology," *JGH Open* 5, no. 9 (2021): 976–987, https://doi.org/10.1002/jgh3.12528.

239. M. Di Stefano, E. Miceli, E. Armellini, A. Missanelli, and G. R. Corazza, "Probiotics and Functional Abdominal Bloating," *Journal of Clinical Gastroenterology* 38, no. 6 Suppl (2004): S102–S103, https://doi.org/10.1097/01.mcg.0000128939.40458.25.

240. M. Pimentel, R. Mathur, and C. Chang, "Gas and the Microbiome," *Current Gastroenterology Reports* 15, no. 12 (2013): 356, https://doi.org/10.1007/s11894-013-0356-y.

241. K. Kalantar-Zadeh, K. J. Berean, R. E. Burgell, J. G. Muir, and P. R. Gibson, "Intestinal Gases: Influence on Gut Disorders and the Role of Dietary Manipulations," *Nature Reviews Gastroenterology & Hepatology* 16, no. 12 (2019): 733–747, https://doi.org/10.1038/s41575-019-0193-z.

242. T. Ringel-Kulka, A. K. Benson, I. M. Carroll, J. Kim, R. M. Legge, and Y. Ringel, "Molecular Characterization of the Intestinal Microbiota in Patients With and Without Abdominal Bloating," *American Journal of Physiology - Gastrointestinal and Liver Physiology* 310, no. 6 (2016): G417–G426, https://doi.org/10.1152/ajpgi.00044.2015.

243. B. Issa, N. A. Wafaei, and P. J. Whorwell, "Abdominal Bloating and Distension: What Is the Role of the Microbiota," *Digestive Diseases and Sciences* 57, no. 1 (2012): 4–8, https://doi.org/10.1007/s10620-011-1834-4.

244. T. Bai, Z. Xu, P. Xia, et al., "The Short-Term Efficacy of Bifidobacterium Quadruple Viable Tablet in Patients With Diarrhea-Predominant Irritable Bowel Syndrome: Potentially Mediated by Metabolism Rather Than Diversity Regulation," *American Journal of Gastroenterology* 118, no. 7 (2023): 1256–1267, https://doi.org/10.14309/ajg.0000000000002147.

245. Y. Z. Wang, F. F. Xiao, Y. M. Xiao, et al., "Fecal Microbiota Transplantation Relieves Abdominal Bloating in Children With Functional Gastrointestinal Disorders via Modulating the Gut Microbiome and Metabolome," *J Dig Dis* 23, no. 8–9 (2022): 482–492, https://doi.org/10.1111/1751-2980.13135.

246. P. Ducrotte, "Abdominal Bloating: An Up-To-Date," supplement, *Gastroenterologie Clinique et Biologique* 33, no. S10–S11l (2009): SF94–SF100, https://doi.org/10.1016/j.gcb.2009.08.004.

247. T. Ringel-Kulka, O. S. Palsson, D. Maier, et al., "Probiotic Bacteria Lactobacillus Acidophilus NCFM and Bifidobacterium Lactis Bi-07 Versus Placebo for the Symptoms of Bloating in Patients With Functional Bowel Disorders: A Double-Blind Study," *Journal of Clinical Gastroenterology* 45, no. 6 (2011): 518–525, https://doi.org/10.1097/mcg.0b013e31820ca4d6.

248. L. A. Harris, B. D. Cash, K. Moftah, and H. Franklin, "An Open-Label, Multicenter Study to Assess the Efficacy and Safety of a Novel Probiotic Blend in Patients With Functional Gastrointestinal Symptoms," *Journal of Clinical Gastroenterology* 56, no. 5 (2022): 444–451, https://doi.org/10.1097/mcg.0000000000001567.

249. H. J. Kim, M. I. Vazquez Roque, M. Camilleri, et al., "A Randomized Controlled Trial of a Probiotic Combination VSL# 3 and Placebo in Irritable Bowel Syndrome With Bloating," *Neurogastroenterology and Motility* 17, no. 5 (2005): 687–696, https://doi.org/10.1111/j.1365-2982.2005.00695.x.

250. S. Nobaek, M. L. Johansson, G. Molin, S. Ahrné, and B. Jeppsson, "Alteration of Intestinal Microflora Is Associated With Reduction in Abdominal Bloating and Pain in Patients With Irritable Bowel Syndrome," *American Journal of Gastroenterology* 95, no. 5 (2000): 1231–1238, https://doi.org/10.1111/j.1572-0241.2000.02015.x.

251. L. O'Mahony, J. McCarthy, P. Kelly, et al., "Lactobacillus and Bifidobacterium in Irritable Bowel Syndrome: Symptom Responses and Relationship to Cytokine Profiles," *Gastroenterology* 128, no. 3 (2005): 541–551, https://doi.org/10.1053/j.gastro.2004.11.050.

252. D. Guyonnet, O. Chassany, P. Ducrotte, et al., "Effect of a Fermented Milk Containing Bifidobacterium Animalis DN-173 010 on the Health-Related Quality of Life and Symptoms in Irritable Bowel Syndrome in Adults in Primary Care: A Multicentre, Randomized, Double-Blind, Controlled Trial," *Alimentary Pharmacology & Therapeutics* 26, no. 3 (2007): 475–486, https://doi.org/10.1111/j.1365-2036.2007.03362.x.

253. M. Schmulson and L. Chang, "Review Article: The Treatment of Functional Abdominal Bloating and Distension," *Alimentary Pharmacology & Therapeutics* 33, no. 10 (2011): 1071–1086, https://doi.org/10.1111/j.1365-2036.2011.04637.x.

254. G. Hong, Y. Li, M. Yang, et al., "Baseline Gut Microbial Profiles Are Associated With the Efficacy of Bacillus subtilis and Enterococcus faecium in IBS-D," *Scandinavian Journal of Gastroenterology* 58, no. 4 (2023): 339–348, https://doi.org/10.1080/00365521.2022.2136013.

255. R. Vázquez-Frias, A. Consuelo-Sánchez, C. P. Acosta-Rodríguez-Bueno, et al., "Efficacy and Safety of the Adjuvant Use of Probiotic Bacillus clausii Strains in Pediatric Irritable Bowel Syndrome: A Randomized, Double-Blind, Placebo-Controlled Study," *Paediatr Drugs* 25, no. 1 (2023): 115–126, https://doi.org/10.1007/s40272-022-00536-9.

256. S. M. Garvey, E. Mah, T. M. Blonquist, V. N. Kaden, and J. L. Spears, "The Probiotic Bacillus Subtilis BS50 Decreases Gastrointestinal Symptoms in Healthy Adults: A Randomized, Double-Blind, placebo-controlled Trial," *Gut Microbes* 14, no. 1 (2022): 2122668, https://doi.org/10.1080/19490976.2022.2122668.

257. C. Penet, R. Kramer, R. Little, et al., "A Randomized, Double-Blind, Placebo-Controlled, Parallel Study Evaluating the Efficacy of Bacillus subtilis MB40 to Reduce Abdominal Discomfort, Gas, and Bloating," supplement, *Alternative Therapies in Health & Medicine* 27, no. S1 (2021): S146–S157.

258. T. Ringel-Kulka, J. McRorie, and Y. Ringel, "Multi-Center, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study to Evaluate the Benefit of the Probiotic Bifidobacterium infantis 35624 in Non-Patients With Symptoms of Abdominal Discomfort and Bloating," *American Journal of Gastroenterology* 112, no. 1 (2017): 145–151, https://doi.org/10.1038/ajg.2016.511.

259. M. M. Araújo, C. O. Vogado, M. M. Mendes, V. S. S. Gonçalves, and P. B. Botelho, "Effects of Bifidobacterium Animalis Subspecies Lactis Supplementation on Gastrointestinal Symptoms: Systematic Review With Meta-Analysis," *Nutrition Reviews* 80, no. 6 (2022): 1619–1633, https://doi.org/10.1093/nutrit/nuab109.

260. M. Olesen and E. Gudmand-Hoyer, "Efficacy, Safety, and Tolerability of Fructooligosaccharides in the Treatment of Irritable Bowel Syndrome," *American Journal of Clinical Nutrition* 72, no. 6 (2000): 1570–1575, https://doi.org/10.1093/ajcn/72.6.1570.

261. J. Labenz, D. P. Borkenstein, F. J. Heil, et al., "Application of a Multispecies Probiotic Reduces Gastro-Intestinal Discomfort and Induces Microbial Changes After Colonoscopy," *Frontiers in Oncology* 12 (2022): 1078315, https://doi.org/10.3389/fonc.2022.1078315.

262. D. B. Silk, A. Davis, J. Vulevic, G. Tzortzis, and G. R. Gibson, "Clinical Trial: The Effects of a Trans-galactooligosaccharide Prebiotic on Faecal Microbiota and Symptoms in Irritable Bowel Syndrome," *Alimentary Pharmacology & Therapeutics* 29, no. 5 (2009): 508–518, https://doi.org/10.1111/j.1365-2036.2008.03911.x.

263. O. B. Bărboi, I. Chirilă, I. Ciortescu, C. Anton, and V. L. Drug, "Inulin, Choline and Silymarin in the Treatment of Irritable Bowel Syndrome With Constipation-Randomized Case-Control Study," *Journal of Clinical Medicine* 11, no. 8 (2022): 2248, https://doi.org/10.3390/jcm11082248.

264. E. Stachowska, D. Maciejewska, J. Palma, et al., "Improvement of Bowel Movements Among People With a Sedentary Lifestyle After Prebiotic Snack Supply – Preliminary Study," *Przegląd Gastroenterologiczny* 17, no. 1 (2022): 73–80, https://doi.org/10.5114/pg.2021.108985.

265. W. Sathitkowitchai, N. Suratannon, S. Keawsompong, et al., "A Randomized Trial to Evaluate the Impact of Copra Meal Hydrolysate on Gastrointestinal Symptoms and Gut Microbiome," *PeerJ* 9 (2021): e12158, https://doi.org/10.7717/peerj.12158.

266. A. Trifan, O. Burta, N. Tiuca, D. C. Petrisor, A. Lenghel, and J. Santos, "Efficacy and Safety of Gelsectan for Diarrhoea-Predominant Irritable Bowel Syndrome: A Randomised, Crossover Clinical Trial," *United European Gastroenterol J* 7, no. 8 (2019): 1093–1101, https://doi.org/10.1177/2050640619862721.

267. B. Wilson, M. Rossi, E. Dimidi, and K. Whelan, "Prebiotics in Irritable Bowel Syndrome and Other Functional Bowel Disorders in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials," *American Journal of Clinical Nutrition* 109, no. 4 (2019): 1098–1111, https://doi.org/10.1093/ajcn/nqy376.

268. M. Miyoshi, H. Kadoguchi, M. Usami, and Y. Hori, "Synbiotics Improved Stool Form via Changes in the Microbiota and Short-Chain Fatty Acids in Hemodialysis Patients," *Kobe Journal of Medical Sciences* 67, no. 3 (2021): E112–e8.

269. J. H. Oh, Y. S. Jang, D. Kang, et al., "Efficacy of a Synbiotic Containing Lactobacillus paracasei DKGF1 and Opuntia humifusa in Elderly Patients With Irritable Bowel Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial," *Gut Liver* 17, no. 1 (2023): 100–107, https://doi.org/10.5009/gnl210478.

270. K. Gupta, H. S. Ghuman, and S. V. Handa, "Review of Rifaximin: Latest Treatment Frontier for Irritable Bowel Syndrome Mechanism of Action and Clinical Profile," *Clinical Medicine Insights: Gastroenterology* 10 (2017): 1179552217728905, https://doi.org/10.1177/1179552217728905.

271. S. Zar, M. J. Benson, and D. Kumar, "Review Article: Bloating in Functional Bowel Disorders," *Alimentary Pharmacology & Therapeutics* 16, no. 11 (2002): 1867–1876, https://doi.org/10.1046/j.1365-2036.2002.01369.x.

272. M. Pimentel, A. Lembo, W. D. Chey, et al., "Rifaximin Therapy for Patients With Irritable Bowel Syndrome Without Constipation," *New England Journal of Medicine* 364, no. 1 (2011): 22–32, https://doi.org/10.1056/nejmoa1004409.

273. U. Arora, K. Sachdeva, P. Garg, et al., "Efficacy of Rifaximin in Patients With Abdominal Bloating or Distension: A Systematic Review and Meta-Analysis," *Journal of Clinical Gastroenterology* 58, no. 4 (2024): 360–369, https://doi.org/10.1097/mcg.0000000000001872.

274. M. Pimentel, S. Chatterjee, E. J. Chow, S. Park, and Y. Kong, "Neomycin Improves constipation-predominant Irritable Bowel Syndrome in a Fashion That Is Dependent on the Presence of Methane Gas: Subanalysis of a Double-Blind Randomized Controlled Study," *Digestive*

Diseases and Sciences 51, no. 8 (2006): 1297–1301, https://doi.org/10.1007/s10620-006-9104-6.

275. B. D. Cash, "Emerging Role of Probiotics and Antimicrobials in the Management of Irritable Bowel Syndrome," *Current Medical Research and Opinion* 30, no. 7 (2014): 1405–1415, https://doi.org/10.1185/03007995.2014.908278.

276. J. Yang, H. R. Lee, K. Low, S. Chatterjee, and M. Pimentel, "Rifaximin Versus Other Antibiotics in the Primary Treatment and Retreatment of Bacterial Overgrowth in IBS," *Digestive Diseases and Sciences* 53, no. 1 (2008): 169–174, https://doi.org/10.1007/s10620-007-9839-8.

277. R. Spiller, Q. Aziz, F. Creed, et al., "Guidelines on the Irritable Bowel Syndrome: Mechanisms and Practical Management," *Gut* 56, no. 12 (2007): 1770–1798, https://doi.org/10.1136/gut.2007.119446.

278. L. Ruepert, A. O. Quartero, N. J. de Wit, G. J. van der Heijden, G. Rubin, and J. W. Muris, "Bulking Agents, Antispasmodics and Antidepressants for the Treatment of Irritable Bowel Syndrome," *Cochrane Database of Systematic Reviews* 2011, no. 8 (2011): Cd003460, https://doi.org/10.1002/14651858.CD003460.pub3.

279. M. A. Martínez-Vázquez, G. Vázquez-Elizondo, J. A. González-González, R. Gutiérrez-Udave, H. J. Maldonado-Garza, and F. J. Bosques-Padilla, "Effect of Antispasmodic Agents, Alone or in Combination, in the Treatment of Irritable Bowel Syndrome: Systematic Review and Meta-Analysis," *Revista de Gastroenterología de México* 77, no. 2 (2012): 82–90, https://doi.org/10.1016/j.rgmx.2012.04.002.

280. M. Chen, D. Qin, S. L. Huang, T. C. Tang, and H. Zheng, "Chinese Herbal Medicine Versus Antispasmodics in the Treatment of Irritable Bowel Syndrome: A Network meta-analysis," *Neuro-Gastroenterology and Motility* 33, no. 8 (2021): e14107, https://doi.org/10.1111/nmo.14107.

281. S. Bor, P. Lehert, A. Chalbaud, and J. Tack, "Efficacy of Pinaverium Bromide in the Treatment of Irritable Bowel Syndrome: A Systematic Review and Meta-Analysis," *Therap Adv Gastroenterol* 14 (2021): 17562848211033740, https://doi.org/10.1177/17562848211033740.

282. M. Camilleri, A. E. Bharucha, R. Ueno, et al., "Effect of a Selective Chloride Channel Activator, Lubiprostone, on Gastrointestinal Transit, Gastric Sensory, and Motor Functions in Healthy Volunteers," *American Journal of Physiology - Gastrointestinal and Liver Physiology* 290, no. 5 (2006): G942–G947, https://doi.org/10.1152/ajpgi.00264.2005.

283. D. A. Drossman, W. D. Chey, J. F. Johanson, et al., "Clinical Trial: Lubiprostone in Patients With Constipation-Associated Irritable Bowel Syndrome--Results of Two Randomized, Placebo-Controlled Studies," *Alimentary Pharmacology & Therapeutics* 29, no. 3 (2009): 329–341, https://doi.org/10.1111/j.1365-2036.2008.03881.x.

284. A. J. Lembo, J. F. Johanson, H. P. Parkman, S. S. Rao, P. B. Miner Jr, and R. Ueno, "Long-Term Safety and Effectiveness of Lubiprostone, a Chloride Channel (ClC-2) Activator, in Patients With Chronic Idiopathic Constipation," *Digestive Diseases and Sciences* 56, no. 9 (2011): 2639–2645, https://doi.org/10.1007/s10620-011-1801-0.

285. W. D. Chey, D. A. Drossman, J. F. Johanson, C. Scott, R. M. Panas, and R. Ueno, "Safety and Patient Outcomes With Lubiprostone for up to 52 Weeks in Patients With Irritable Bowel Syndrome With Constipation," *Alimentary Pharmacology & Therapeutics* 35, no. 5 (2012): 587–599, https://doi.org/10.1111/j.1365-2036.2011.04983.x.

286. D. M. Brenner, R. Fogel, S. D. Dorn, et al., "Efficacy, Safety, and Tolerability of Plecanatide in Patients With Irritable Bowel Syndrome With Constipation: Results of Two Phase 3 Randomized Clinical Trials," *American Journal of Gastroenterology* 113, no. 5 (2018): 735–745, https://doi.org/10.1038/s41395-018-0026-7.

287. E. N. Mohammadi, C. O. Ligon, A. Silos-Santiago, et al., "Linaclotide Attenuates Visceral Organ Crosstalk: Role of Guanylate Cyclase-C Activation in Reversing Bladder-Colon Cross-Sensitization," *Journal of Pharmacology and Experimental Therapeutics* 366, no. 2 (2018): 274–281, https://doi.org/10.1124/jpet.118.248567.

288. F. Carbone, K. Van den Houte, E. Clevers, et al., "Prucalopride in Gastroparesis: A Randomized Placebo-Controlled Crossover Study," *American Journal of Gastroenterology* 114, no. 8 (2019): 1265–1274, https://doi.org/10.14309/ajg.0000000000000304.

289. A. Emmanuel, M. Cools, L. Vandeplassche, and R. Kerstens, "Prucalopride Improves Bowel Function and Colonic Transit Time in Patients With Chronic Constipation: An Integrated Analysis," *American Journal of Gastroenterology* 109, no. 6 (2014): 887–894, https://doi.org/10.1038/ajg.2014.74.

290. M. B. Colović, D. Z. Krstić, T. D. Lazarević-Pašti, A. M. Bondžić, and V. M. Vasić, "Acetylcholinesterase Inhibitors: Pharmacology and Toxicology," *Current Neuropharmacology* 11, no. 3 (2013): 315–335, https://doi.org/10.2174/1570159x11311030006.

291. N. Balázs, D. Bereczki, and T. Kovács, "Cholinesterase Inhibitors and Memantine for the Treatment of Alzheimer and Non-Alzheimer Dementias," *Ideggyogyaszati Szemle* 74, no. 11–12 (2021): 379–387, https://doi.org/10.18071/isz.74.0379.

292. M. M. Mehndiratta, S. Pandey, and T. Kuntzer, "Acetylcholinesterase Inhibitor Treatment for Myasthenia Gravis," *Cochrane Database of Systematic Reviews* 2014, no. 10 (2014): Cd006986, https://doi.org/10.1002/14651858.cd006986.pub3.

293. R. Singh and N. M. Sadiq, *Cholinesterase Inhibitors. Statpearls. Treasure Island (FL): Statpearls Publishing Copyright © 2024* (StatPearls Publishing LLC., 2024).

294. R. G. Valle and F. L. Godoy, "Neostigmine for Acute Colonic Pseudo-obstruction: A Meta-Analysis," *Annals of Medicine and Surgery* 3, no. 3 (2014): 60–64, https://doi.org/10.1016/j.amsu.2014.04.002.

295. M. A. Korsten, A. M. Spungen, M. Radulovic, et al., "Neostigmine Administered With Moviprep Improves Bowel Preparation for Elective Colonoscopy in Patients With Spinal Cord Injury: A Randomized Study," *Journal of Clinical Gastroenterology* 49, no. 9 (2015): 751–756, https://doi.org/10.1097/mcg.0000000000000284.

296. S. Sinha, S. Chary, P. Thakur, et al., "Efficacy and Safety of Acotiamide Versus Mosapride in Patients With Functional Dyspepsia Associated With Meal-Induced Postprandial Distress Syndrome: A Phase III Randomized Clinical Trial," *Cureus* 13, no. 9 (2021): e18109, https://doi.org/10.7759/cureus.18109.

297. H. Yamawaki, S. Futagami, T. Kawagoe, et al., "Improvement of Meal-Related Symptoms and Epigastric Pain in Patients With Functional Dyspepsia Treated With Acotiamide Was Associated With Acylated Ghrelin Levels in Japan," *Neuro-Gastroenterology and Motility* 28, no. 7 (2016): 1037–1047, https://doi.org/10.1111/nmo.12805.

298. H. Kusunoki, K. Haruma, N. Manabe, et al., "Therapeutic Efficacy of Acotiamide in Patients With Functional Dyspepsia Based on Enhanced Postprandial Gastric Accommodation and Emptying: Randomized Controlled Study Evaluation by Real-Time Ultrasonography," *Neuro-Gastroenterology and Motility* 24, no. 6 (2012): 540, https://doi.org/10.1111/j.1365-2982.2012.01897.x.

299. J. Tack and P. Janssen, "Acotiamide (Z-338, YM443), a New Drug for the Treatment of Functional Dyspepsia," *Expert Opinion on Investigational Drugs* 20, no. 5 (2011): 701–712, https://doi.org/10.1517/13543784.2011.562890.

300. K. Matsueda, M. Hongo, J. Tack, H. Aoki, Y. Saito, and H. Kato, "Clinical Trial: Dose-Dependent Therapeutic Efficacy of Acotiamide Hydrochloride (Z-338) in Patients With Functional Dyspepsia – 100 Mg T.I.D. Is an Optimal Dosage," *Neuro-Gastroenterology and Motility* 22, no. 6 (2010): 618-e173–e173, https://doi.org/10.1111/j.1365-2982.2009.01449.x.

301. FDA, "Sloan Pharma UW. ZELNORM™ (Tegaserod Maleate) for the Treatment of Irritable Bowel Syndrome with Constipation (IBS-C): FDA Joint Meeting of the Gastrointestinal Drugs Advisory Committee

and Drug Safety and Risk Management Advisory Committee Briefing Document, https://www.fda.gov/media/119013.

302. B. E. Lacy, Y. A. Saito, M. Camilleri, et al., "Effects of Antidepressants on Gastric Function in Patients With Functional Dyspepsia," *American Journal of Gastroenterology* 113, no. 2 (2018): 216–224, https://doi.org/10.1038/ajg.2017.458.

303. J. Tack, D. Broekaert, B. Fischler, L. Van Oudenhove, A. M. Gevers, and J. Janssens, "A Controlled Crossover Study of the Selective Serotonin Reuptake Inhibitor Citalopram in Irritable Bowel Syndrome," *Gut* 55, no. 8 (2006): 1095–1103, https://doi.org/10.1136/gut.2005.077503.

304. L. Van Oudenhove, S. Kindt, R. Vos, B. Coulie, and J. Tack, "Influence of Buspirone on Gastric Sensorimotor Function in Man," *Alimentary Pharmacology & Therapeutics* 28, no. 11–12 (2008): 1326–1333, https://doi.org/10.1111/j.1365-2036.2008.03849.x.

305. E. Burri, D. Cisternas, A. Villoria, et al., "Abdominal Accommodation Induced by Meal Ingestion: Differential Responses to Gastric and Colonic Volume Loads," *Neuro-Gastroenterology and Motility* 25, no. 4 (2013): 339–e253, https://doi.org/10.1111/nmo.12068.

306. B. D. Naliboff, S. R. Smith, J. G. Serpa, et al., "Mindfulness-Based Stress Reduction Improves Irritable Bowel Syndrome (IBS) Symptoms via Specific Aspects of Mindfulness," *Neuro-Gastroenterology and Motility* 32, no. 9 (2020): e13828, https://doi.org/10.1111/nmo.13828.

307. T. Algladi, M. Harris, P. J. Whorwell, P. Paine, and S. Hamdy, "Modulation of Human Visceral Sensitivity by Noninvasive Magneto-electrical Neural Stimulation in Health and Irritable Bowel Syndrome," *Pain* 156, no. 7 (2015): 1348–1356, https://doi.org/10.1097/j.pain.0000000000000187.

308. A. Iannone, A. P. Cruz, J. P. Brasil-Neto, and R. Boechat-Barros, "Transcranial Magnetic Stimulation and Transcranial Direct Current Stimulation Appear to be Safe Neuromodulatory Techniques Useful in the Treatment of Anxiety Disorders and Other Neuropsychiatric Disorders," *Arquivos de Neuro-Psiquiatria* 74, no. 10 (2016): 829–835, https://doi.org/10.1590/0004-282x20160115.

309. X. Liu, M. Yuan, Z. Li, S. Fei, and G. Zhao, "The Efficacy of Simethicone With Polyethylene Glycol for Bowel Preparation: A Systematic Review and Meta-Analysis," *Journal of Clinical Gastroenterology* 55, no. 6 (2021): e46–e55, https://doi.org/10.1097/mcg.0000000000001527.

310. M. Moolla, J. T. Dang, A. Shaw, et al., "Simethicone Decreases Bloating and Improves Bowel Preparation Effectiveness: A Systematic Review and Meta-Analysis," *Surgical Endoscopy* 33, no. 12 (2019): 3899–3909, https://doi.org/10.1007/s00464-019-07066-5.

311. A. Ouyang and L. Xu, "Holistic Acupuncture Approach to Idiopathic Refractory Nausea, Abdominal Pain and Bloating," *World Journal of Gastroenterology* 13, no. 40 (2007): 5360–5366, https://doi.org/10.3748/wjg.v13.i40.5360.

312. R. B. Rohrböck, J. Hammer, H. Vogelsang, N. J. Talley, and H. F. Hammer, "Acupuncture Has a Placebo Effect on Rectal Perception But Not on Distensibility and Spatial Summation: A Study in Health and IBS," *American Journal of Gastroenterology* 99, no. 10 (2004): 1990–1997, https://doi.org/10.1111/j.1572-0241.2004.30028.x.

313. H. Jamalizadeh, B. Ahmadi, F. Shariffar, et al., "Clinical Evaluation of the Effect of Zataria Multiflora Boiss and Trachyspermum Copticum (L.) on the Patients With Irritable Bowel Syndrome," *Explore (NY)* 18, no. 3 (2022): 342–346, https://doi.org/10.1016/j.explore.2021.12.004.

314. A. Giacosa, A. Riva, G. Petrangolini, et al., "Beneficial Effects on Abdominal Bloating With an Innovative Food-Grade Formulation of Curcuma Longa and Boswellia Serrata Extracts in Subjects With Irritable Bowel Syndrome and Small Bowel Dysbiosis," *Nutrients* 14, no. 3 (2022): 416, https://doi.org/10.3390/nu14030416.

315. S. S. Rao, "Belching, Bloating, and Flatulence. How to Help Patients Who Have Troublesome Abdominal Gas," *Postgraduate Medical Journal* 101, no. 4 (1997): 263–278, https://doi.org/10.3810/pgm.1997.04.208.

316. M. P. Jones, "Bloating and Intestinal Gas," *Current Treatment Options in Gastroenterology* 8, no. 4 (2005): 311–318, https://doi.org/10.1007/s11938-005-0024-x.

317. J. M. Wilkinson, E. W. Cozine, and C. G. Loftus, "Gas, Bloating, and Belching: Approach to Evaluation and Management," *American Family Physician* 99, no. 5 (2019): 301–309.

318. D. L. Dumitrascu, A. Baban, I. Bancila, et al., "Romanian Guidelines for Nonpharmacological Therapy of IBS," *J Gastrointestin Liver Dis* 30, no. 2 (2021): 291–306, https://doi.org/10.15403/jgld-3581.

319. J. M. Lackner, "Skills Over Pills? A Clinical Gastroenterologist's Primer in Cognitive Behavioral Therapy for Irritable Bowel Syndrome," *Expert Review of Gastroenterology & Hepatology* 14, no. 7 (2020): 601–618, https://doi.org/10.1080/17474124.2020.1780118.

320. S. H. W. Mares, J. Burger, L. Lemmens, A. A. van Elburg, and M. S. Vroling, "Evaluation of the Cognitive Behavioural Theory of Eating Disorders: A Network Analysis Investigation," *Eating Behaviors* 44 (2022): 101590, https://doi.org/10.1016/j.eatbeh.2021.101590.

321. M. Fadgyas Stanculete, D. L. Dumitrascu, and D. Drossman, "Neuromodulators in the Brain-Gut Axis: Their Role in the Therapy of the Irritable Bowel Syndrome," *J Gastrointestin Liver Dis* 30, no. 4 (2021): 517–525, https://doi.org/10.15403/jgld-4090.

322. C. J. Black, E. R. Thakur, L. A. Houghton, E. M. M. Quigley, P. Moayyedi, and A. C. Ford, "Efficacy of Psychological Therapies for Irritable Bowel Syndrome: Systematic Review and Network Meta-Analysis," *Gut* 69, no. 8 (2020): 1441–1451, https://doi.org/10.1136/gutjnl-2020-321191.

323. P. Iovino, C. Bucci, F. Tremolaterra, A. Santonicola, and G. Chiarioni, "Bloating and Functional Gastro-Intestinal Disorders: Where Are We and Where Are We Going?," *World Journal of Gastroenterology* 20, no. 39 (2014): 14407–14419, https://doi.org/10.3748/wjg.v20.i39.14407.

324. L. Pemberton, L. Kita, and K. Andrews, "Practitioners' Experiences of Using Gut Directed Hypnosis for Irritable Bowel Syndrome: Perceived Impact Upon Client Wellbeing: A Qualitative Study," *Complementary Therapies in Medicine* 55 (2020): 102605, https://doi.org/10.1016/j.ctim.2020.102605.

325. M. G. Craske, K. B. Wolitzky-Taylor, J. Labus, et al., "A cognitive-behavioral Treatment for Irritable Bowel Syndrome Using Interoceptive Exposure to Visceral Sensations," *Behaviour Research and Therapy* 49, no. 6–7 (2011): 413–421, https://doi.org/10.1016/j.brat.2011.04.001.

326. J. Peter, C. Fournier, B. Keip, et al., "Intestinal Microbiome in Irritable Bowel Syndrome Before and After Gut-Directed Hypnotherapy," *International Journal of Molecular Sciences* 19, no. 11 (2018): 3619, https://doi.org/10.3390/ijms19113619.

327. C. E. Flik, W. Laan, N. P. A. Zuithoff, et al., "Efficacy of Individual and Group Hypnotherapy in Irritable Bowel Syndrome (IMAGINE): A Multicentre Randomised Controlled Trial," *Lancet Gastroenterology & Hepatology* 4, no. 1 (2019): 20–31, https://doi.org/10.1016/s2468-1253(18)30310-8.

328. P. Knekt, O. Lindfors, T. Härkänen, et al., "Randomized Trial on the Effectiveness of Long-and Short-Term Psychodynamic Psychotherapy and Solution-Focused Therapy on Psychiatric Symptoms During a 3-year follow-up," *Psychological Medicine* 38, no. 5 (2008): 689–703, https://doi.org/10.1017/s003329170700164x.

329. D. Schumann, D. Anheyer, R. Lauche, G. Dobos, J. Langhorst, and H. Cramer, "Effect of Yoga in the Therapy of Irritable Bowel Syndrome: A Systematic Review," *Clinical Gastroenterology and Hepatology* 14, no. 12 (2016): 1720–1731, https://doi.org/10.1016/j.cgh.2016.04.026.

330. V. Kavuri, N. Raghuram, A. Malamud, and S. R. Selvan, "Irritable Bowel Syndrome: Yoga as Remedial Therapy," *Evid Based Complement Alternat Med* 2015 (2015): 398156, https://doi.org/10.1155/2015/398156.

331. V. Tee, G. Kuan, Y. C. Kueh, et al., "Development and Validation of Audio-Based Guided Imagery and Progressive Muscle Relaxation Tools for Functional Bloating," *PLoS One* 17, no. 9 (2022): e0268491, https://doi.org/10.1371/journal.pone.0268491.

332. P. Lindfors, E. Axelsson, K. Engstrand, et al., "Online Education is Non-Inferior to Group Education for Irritable Bowel Syndrome: A Randomized Trial and Patient Preference Trial," *Clinical Gastroenterology and Hepatology* 19, no. 4 (2021): 743–51.e1, https://doi.org/10.1016/j.cgh.2020.04.005.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Supporting Information S1: ueg270098-sup-0001-suppl-data.doc.