Gastroenterology 2026;170:1190–1204

Sociocultural Aspects of the Pathophysiology, Clinical Presentation, and Management of Disorders of Gut–Brain Interaction

Reuben K. Wong,[1] Xiucai Fang,[2] Uday C. Ghoshal,[3] Purna C. Kashyap,[4] Agata Mulak,[5] Yeong Yeh Lee,[6,7] Ami D. Sperber,[8] and Gerald Holtmann[9,10]

[1]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; [2]Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [3]Institute of Gastrosciences & Liver Transplantation, Apollo Multispeciality Hospitals, Kolkata, India; [4]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota; [5]Department of Gastroenterology and Hepatology, Wroclaw Medical University, Wroclaw, Poland; [6]School of Medical Sciences, Universiti Sains Malaysia, Kota Bharu, Malaysia; [7]GI Function and Motility Unit, Hospital Universiti Sains Malaysia, Kota Bharu, Malaysia; [8]Faculty of Health Sciences, Ben-Gurion University of the Negev, Be'er Sheva, Israel; [9]University of Queensland, Faculty of Health, Medicine and Behavioural Science, Queensland, Australia; and [10]Department of Gastroenterology and Hepatology, Princess Alexandra Hospital, Queensland, Australia

Sociocultural determinants such as cultural norms, diet, and environmental factors, along with their effects on the gastrointestinal microbiome, can modify the risk to develop disorders of gut–brain interaction (DGBI). These factors also shape symptom perception and health care–seeking behaviors, and how society and health care providers respond to patients with DGBI. This document summarizes the knowledge about the role of sociocultural factors in the manifestation of DGBI and the management of these patients. Symptom expression and societal response to DGBI varies across different cultural settings, influencing individual patient outcomes and the overall societal burden of disease. Patients with DGBI are often stigmatized, leading to a bias toward conditions with visible abnormalities and underfunded services for DGBI. Recognizing the role of sociocultural factors for DGBI outcomes presents an opportunity to refine pathophysiologic concepts and improve patient outcomes. This calls for greater awareness and equitable resource allocation for DGBI research and treatment.

Keywords: Sociocultural; Environment; Language; Disorders of Gut–Brain Interaction.

For Rome IV, a section addressing multicultural aspects for disorders of gut–brain interaction (DGBI) had been introduced.[1] Although the previous Rome IV document addressed "multicultural" aspects of DGBI, the authors of this article took a broader approach to address "sociocultural" aspects capturing the interplay of social and cultural factors, including societal norms, health attitudes, cultural beliefs, socioeconomic status, and the impact on DGBI manifestations, treatment, and prioritization of health care services to meet the needs of patients with DGBI.

Expanding on these concepts, this article focuses on the interplay among societal, cultural, and environmental factors affecting individuals in relation to the manifestation and the long-term outcomes of DGBI. In general, the influence of social and cultural factors on the manifestation of disease is well established, but in the context of DGBI, it is poorly integrated in contemporary approaches to managing patients with DGBI. For this article, the social determinants of health are the nonmedical factors that influence outcomes, including the conditions in which people are born, grow up, live, work, and age.[2] Not surprisingly, it is now well established that sociocultural factors also play a role in the manifestation and course of DGBI.[3]

Culture comprises the knowledge, behaviors, arts, beliefs, and institutions passed down through generations and influences the manifestation and management of DGBI through practices like dietary habits and health care–seeking behavior.[4] Culture and ethnicity shape human identity and interact with the environment and genes, affecting belief systems and DGBI pathophysiology through epigenetics. In cross-cultural research, "race" and "ethnicity" categorize individuals, impacting perceptions and resource allocation, and lower care quality is observed in racial and ethnic minorities, leading to worse health outcomes.

Social and cultural aspects not only influence disease manifestation but also health care–seeking behavior, contributing to health inequalities. Key factors affecting disease outcomes include environmental, climatic, cultural,

Abbreviations used in this paper: **ATI, amylase trypsin inhibitors; CAM, complementary and alternative medicine; DGBI, disorders of gut–brain interaction; FC, functional constipation; FD, functional dyspepsia; FODMAPs, fermentable oligo-, di-, and monosaccharides and polyols; FP7, Seventh Framework Program for Research and Technological Development of the European Union; GI, gastrointestinal; H2020, Horizon 2020; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; PROM, patient-reported outcome measure; QoL, quality of life; RFGES, Rome Foundation Global Epidemiology Study.**

Most current article

0016-5085
https://doi.org/10.1053/j.gastro.2026.02.006

and socioeconomic aspects such as income, support, health care access, education, and gender.

Dietary habits linked to sociocultural factors, like the Mediterranean diet, can confer health benefits, whereas some lifestyles increase the risk for specific disease such as inflammatory bowel disease (IBD). Social factors are also linked to the risk of food- or waterborne diseases, notably in regions like Africa. There is a notable risk increase for developing irritable bowel syndrome (IBS) after gastrointestinal (GI) infections, with data suggesting a 6-fold increase after acute GI infections[5] and a recent ecologic study revealed compelling evidence for the role of various sociocultural/environmental factors and the prevalence of DGBI in various regions of the world.[6]

Recent ecological studies have shown that sociocultural factors influence specific aspects of the pathophysiology of DGBI, affecting its presentation and, ultimately, the treatment of patients with DGBI. Based on culturally driven belief systems, subjects presenting with GI symptoms may receive appropriate medical management and support and have access to required services. However, defined by cultural belief systems, symptoms in patients without an apparent underlying cause may not be considered legitimate[7] or even trivial, and access to care may be difficult or even denied.

This article addresses relevant aspects related to sociocultural factors influencing the manifestation of DGBI and the subsequent presentation of patients' symptoms to health care providers (health care–seeking behaviors) and sociocultural factors influencing therapeutic preferences and treatment response. See Figure 1.

Methodology

To craft this article, a staged approach was used. Before preparing this article, every author independently reviewed the available literature (or conducted systematic literature reviews with the search terms "social determinants health"; "sociocultural factors"; and "irritable bowel syndrome," "functional gastrointestinal disorders," "functional dyspepsia," or "disorders of gut–brain interaction") and, subsequently, a formal horizon scan was performed. The available information was assessed in a structured fashion that included a modified SWOT (strengths, weaknesses, opportunities, and threats) analysis that aimed to identify themes and emerging trends that represent opportunities or challenges for established concepts concerning sociocultural factors influencing the manifestation and course of DGBI. Subsequently, all working group members identified relevant "themes" for a subsequent analysis of SWOT. Well-established and relevant themes were recorded under "strengths," themes that were considered problematic or insufficiently substantiated under "weaknesses," emerging novel insights under "opportunities," and themes from the literature that were potentially misleading or not aligned with contemporary evidence as "threats." The key themes were identified and short-listed by the team members and allocated to team members for further assessment and inclusion into the various sections of this article (Supplementary Figure 1).

Influence of Social and Cultural Factors on Symptom Prevalence, Perception, Reporting, and Health Care–Seeking Behavior

The diagnosis of DGBI is based primarily on symptoms. Therefore, the accuracy of the assessment of patient-reported symptoms and their severity is essential to diagnose DGBI. An international study on patients with IBS from 8 countries showed that subjects from Italy had significantly higher abdominal pain and bloating scores, subjects from India had the lowest abdominal pain score, and Chinese patients had the highest score for diarrhea.[8] In Asia, experts believe that defecation-associated abdominal discomfort and bloating are sufficient for a diagnosis of IBS.[9] However, abdominal discomfort defined as an "uncomfortable sensation not described as pain" is a potentially vague definition. Spiegel et al[10] found that abdominal discomfort encompasses a wide range of symptoms such as bloating, gas, fullness, flatulence, and urgency in US patients with IBS. However, these data may not be representative of all cultures. Indeed, factors such as language use and symptom interpretation are not simple reflections of sociocultural norms. They are highly relevant for the interpretation of GI symptom perception, whereas currently established DGBI criteria anchor definitions to specific symptoms such as postprandial fullness, abdominal bloating, and distension.

Another prominent sociocultural influence on DGBI is the reporting of comorbid psychosocial and stressful events and the acceptance of the explanation of the relationship between GI symptoms and distress. Communicating psychological stressors may be perceived as stigmatizing and ultimately may result in an underreporting of psychological stress during consultations. The Rome Foundation Global Epidemiology Study (RFGES) provides further evidence for the role of cultural differences.[11] While utilizing a combination of face-to-face household interviews and an internet survey, the project revealed important, novel data with substantial variations in the prevalence of DGBI symptoms across various countries. It is important to note that the mode of symptom assessment influenced the proportion of participants who met specific diagnostic criteria. For "any DGBI" the prevalence was 40.3% for the internet surveys as compared with 20.7% for face-to-face household interviews. This disparity related to the mode of data assessment is an important observation. Although the RFGES revealed significant differences in the prevalence of DGBI across different countries, it is also noteworthy that the prevalence rates were highly variable across different regions, although the country ranking (low, intermediate, or high) for the prevalence of "any DGBI" or IBS was similar for most countries (Figure 2). In East and Southeast Asia, where subjects from China, Japan, South Korea, and Singapore have similar food habits, the prevalence in each country of functional dyspepsia (FD) meeting Rome IV criteria is 5.9%, 2.4%, 4.9%, and 5.9%, whereas the prevalence of IBS is 2.3%, 2.2%, 4.7%, and 1.3%, and the

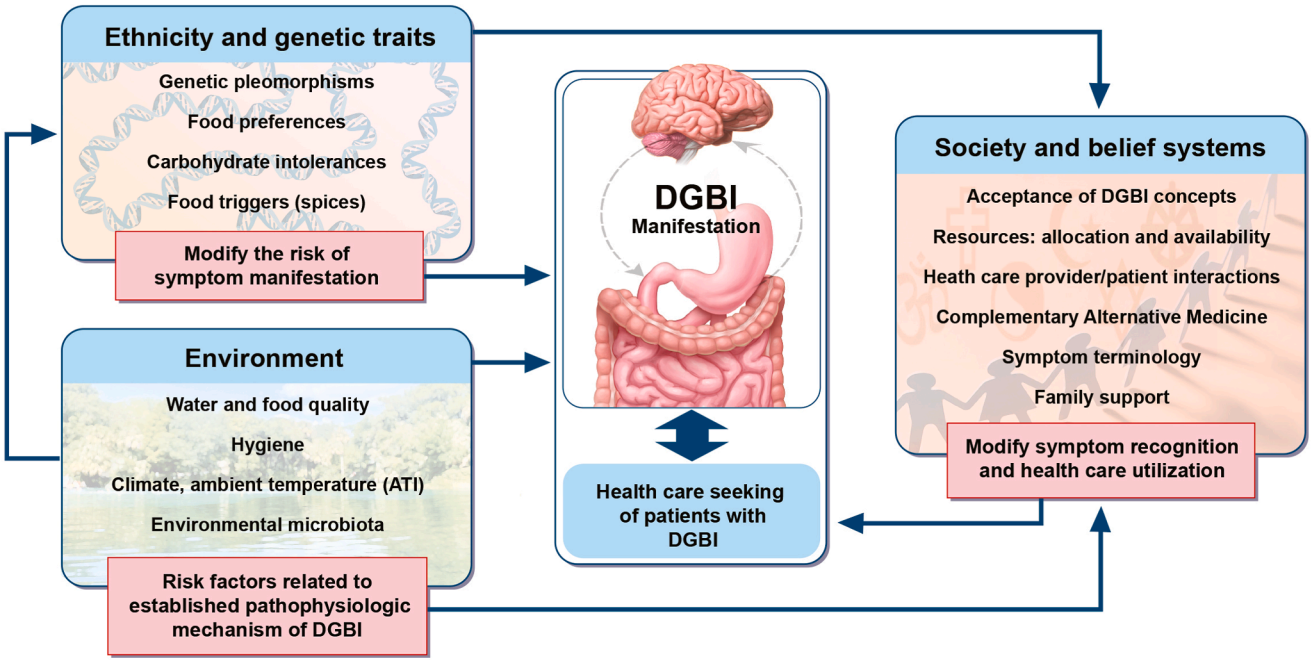

Figure 1. Sociocultural factors influencing the manifestation, reporting of symptoms, and health care utilization by patients with DGBI.

prevalence of functional constipation (FC) is 10.6%, 16.6%, 12.5%, and 9.5%, respectively.[11] This may suggest that sociocultural factors are relevant for these differences. Indeed, in Western Europe, the prevalence of FD ranges from 4.1% (Netherlands) to 8.5% (France), whereas the prevalence of FC ranges from 8.6% (UK) to 14.5% (France).[11] In a large cohort study involving more than 23,000 age- and gender-stratified subjects who were representative of the populations in the respective 13 countries, the prevalence of dyspepsia and other upper GI

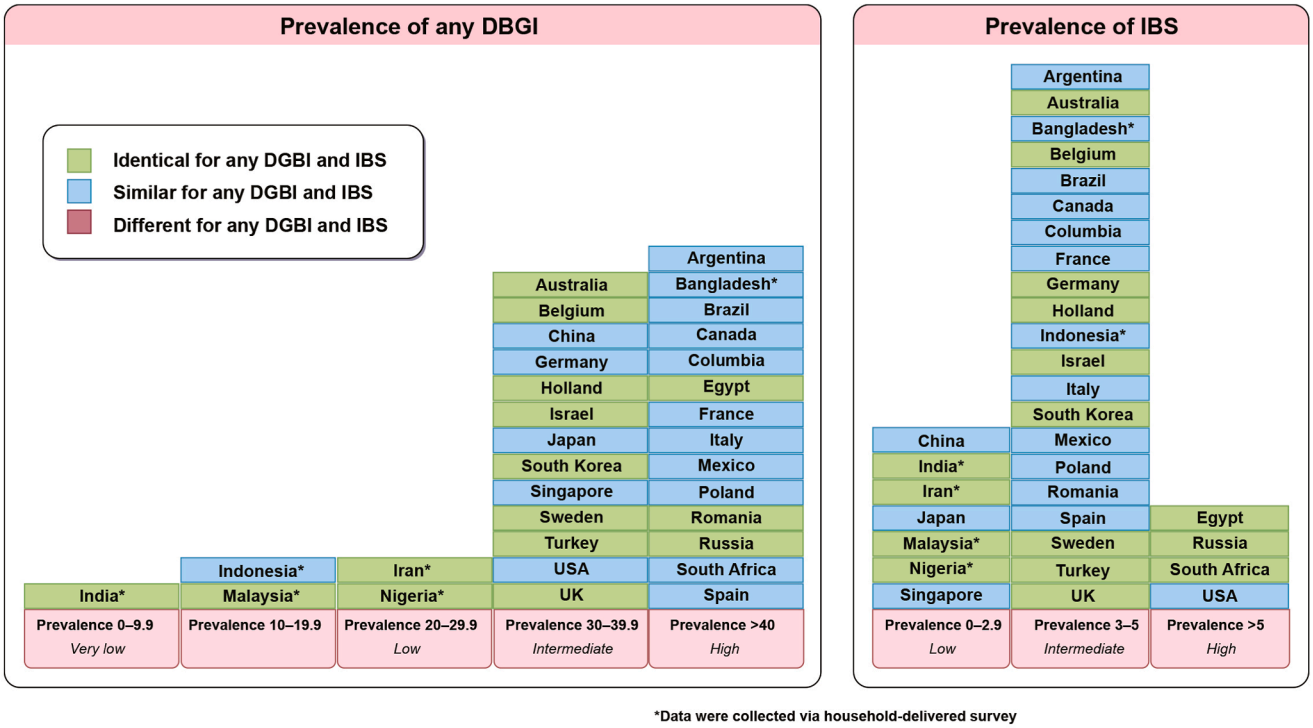

Figure 2. Results of the RFGES presented as frequency of different prevalence ranges. Frequency distribution of the prevalence range (eg, 0%–9.9%, 10%–19.9%) of any DGBI (*left*) or IBS (*right*), of different countries, color-coded is the match or mismatch of the prevalence ranking of DGBI and IBS. *Indicates countries where data were collected via internet-delivered survey.

symptoms were assessed by interview.[12] The prevalence of (mostly functional) upper GI symptoms ranged from 24% to 45%, and further analysis revealed a significant, inverse association between the prevalence of upper GI symptoms and the gross domestic product per capita.[12] Although the precise mechanisms that drive the inverse association between economic development and the manifestation of symptoms remain to be identified, it is reasonable to assume that this reflects environmental factors, including dietary factors, that play a role in the manifestation of DGBI.

The ability to seek medical attention for the treatment of symptoms of DGBI is influenced by sociocultural factors. A study from the United States revealed that 82% of subjects with IBS had sought advice from a health care professional, whereas these rates might be lower in other countries.[12]

Language as a Modifier of Symptom Reporting

In the absence of specific biomarkers of DGBI, language is vital for conveying GI symptoms in patients with DGBI. The complexity of these symptoms can make it difficult for patients to accurately describe their intensity, location, and nature, potentially leading to miscommunication with health care providers and affecting diagnosis and treatment.

Different languages have varying terminologies for pain and discomfort; some may lack precise terms for certain sensations, resulting in vague symptom descriptions. This linguistic variation can lead to differences in how DGBI symptoms are reported across different communities. Moreover, cultural influences can affect patient beliefs about the nature, cause, and treatment of disease. This can impact symptom reporting as patients may use idioms or metaphors based on their educational background and cultural understandings to express their symptoms, potentially interfering with the health care provider's interpretation and understanding of the symptoms (Figure 3).

The use of validated and culturally and linguistically appropriate symptom or pain scales, qualitative interviews, and visual aids could assist to accurately understand and record patients' symptoms, but they still might not be sufficient.[13] This underscores the importance of culturally competent health care providers who can ensure effective cross-cultural communication and care (Figure 4). Assessment of symptoms can be standardized and facilitated with patient-reported outcome measures (PROMs), which directly provide information on different health aspects from subjects, without mediation or interpretation by a physician or other providers. Good data are supporting the use of PROMs that are designed to allow time-efficient and standardized assessment of symptoms while meeting established quality criteria of questionnaires that have been used routinely in large patient cohorts.[14–16] Five main components of superior-quality PROMs include item selection, validity, reliability, responsiveness, and interpretability. Even if PROMs have undergone extensive validation and testing, experimental data suggest that divergent cultural groups may emphasize distinct aspects of their quality of life (QoL). There was evidence of greater emphasis on cognitive functioning for subjects from South Asia and Latin America compared with those from the United Kingdom, whereas in subjects from Islamic countries, the role of physical and social functioning appears to have more influence.[17] This has potential implications for studies using QoL questionnaires to conduct international comparisons.

To ensure that verbal symptom descriptors in PROM tools are clearly understood, they must mitigate bias from cultural, educational, social, and linguistic differences. This involves a rigorous cross-cultural adaptation process, including forward and backward translation, and review by linguists, native speakers, and local health care professionals. In addition, cognitive debriefing with representatives of the target population is necessary to confirm the clarity and consistency of the PROM. Because of the complexity and often vague nature of DGBI symptoms, verbal descriptors may not always precisely convey their characteristics.

Moreover, the lack of equivalent words across various languages may result in ambiguity or misunderstanding, as in the case of "bloating" or "discomfort" in some non–English-speaking populations.[18] Validated translations, enabling uniform research methodology, constitute a cardinal step in successful cross-cultural epidemiological studies, as recently shown by the RFGES.[11]

Pictorial Descriptors of Symptoms as an Approach to Overcoming Language Barriers

A potential solution to language barriers in health care is the use of image-based representations or pictograms. These can be beneficial for certain ethnic minorities or patients needing cultural and language education. Pictogram questionnaires, like the Bristol Stool Form Scale[19] and GERD Analyzer (GERDlyzer),[20] have improved communication of symptoms between patients and providers, enhancing symptom reporting accuracy. This is supported by several other studies. Pictorial representations can be very useful among individuals where the written or spoken language may not be well understood, for example in children or individuals with linguistic disabilities.

Although pictograms can convey simple information effectively, they require rigorous validation to ensure they are appropriate for diverse populations and are not without problems.[21] Factors like color choice and image realism also affect their efficacy. Overall, although pictograms can aid in communication for patients with digestive issues, thorough validation across different cultural groups is critical, and many factors need to be considered before they add value (Supplementary Table 1, Supplementary Figure 2).

Socioenvironmental Determinants: Hygiene and Climate

Climate change is considered the largest global health threat of the 21st century. Hygiene, on the other hand, is

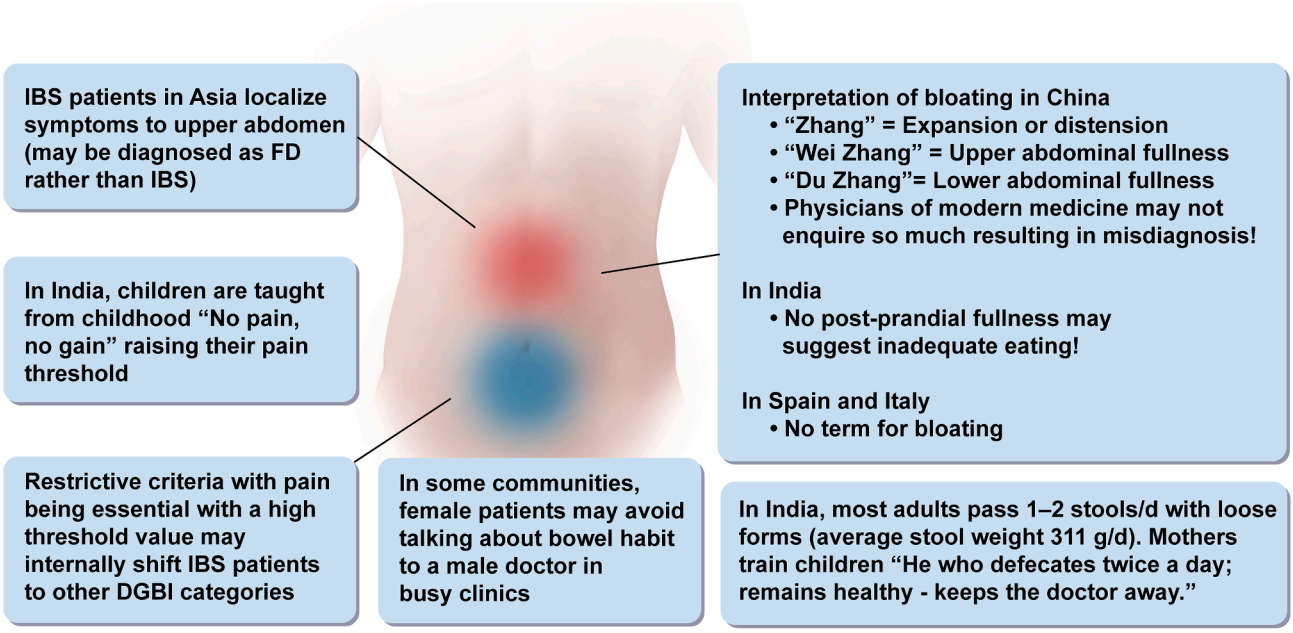

Figure 3. Sociocultural factors influencing reporting of symptoms and diagnosis of DGBI. This figure illustrates a range of sociocultural factors that may affect the reporting of gastrointestinal symptoms. The factors presented are derived from the authors' insights and collective experience. Key influences also include cultural beliefs about health and illness, family dynamics, social stigma associated with GI issues, varying levels of health literacy, and the accessibility of health care resources.

closely correlated with socioeconomic development, and improving hygiene over the past few decades of economic boom may have been the primary reason for the decline in *Helicobacter pylori* and other infections.

Climate change and hygiene may partly explain the variations in frequency and spectrum of DGBI observed across different countries in the RFGES.[11] The major factors underlying variability may include the frequency of GI infections, the prevalence of *H pylori* infections, and variations in gut T-regulatory or other immune responses.[22,23] These effects are modified by "pain tolerance" due to variations in sociocultural characteristics. This is evidenced by studies showing that pain is reported more frequently and is more severe in developed nations than in developing countries. The frequency of GI infections and infestations is variable across distinct parts of the world and linked to hygiene and climate. It is well recognized that extreme precipitation and temperature are linked to waterborne GI infections.[24] Whereas acute infectious gastroenteritis is common in tropical and developing countries, it occurs less

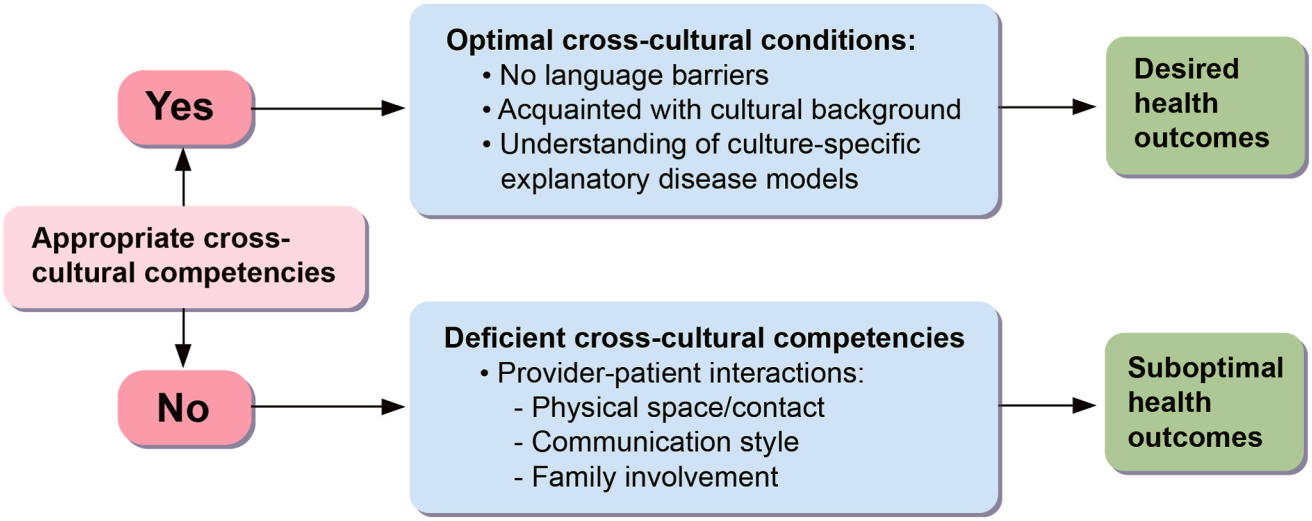

Figure 4. Influence of cross-cultural competencies on health outcomes.

commonly in temperate areas and the developed world. Water hygiene is related to the frequency of GI infection, which may influence the development of long-term consequences such as postinfection IBS and dyspepsia.

In a study from Australia using the microsimulation model, the risk of salmonellosis, which is also known to result in postinfection IBS, was projected to increase under the influence of climate change.[25] In another study from Malaysia after a major flood, exposure to environmental microbiota (including *Plesiominas* and *Trabulsiella*) due to poor water hygiene explained prevalent and persistent abdominal pain and IBS.[26]

Another factor might be changes in the composition of food ingredients. It is well established that amylase trypsin inhibitors (ATIs) in wheat and similar products activate the GI immune system.[27] Temperature and precipitation influence ATI concentrations in wheat products,[28] and increased temperatures and periods of drought are linked to increased ATI concentrations. Thus, climate change, with a rise in ambient temperature, may not only increase the risk of GI infections but also cause subtle changes of the composition of our food (Table 1).

H pylori infections, which are more common in tropical than temperate countries, are considered a potential cause of dyspeptic symptoms, even without peptic lesions, that can be prevented by *H pylori* eradication. Although *H pylori* eradication therapy is suggested to improve FD symptoms, a recent systematic review and meta-analysis found no association between the eradication rate and the relative risk for improvement or cure of FD.[29] This would be consistent with the contention that the benefits of antibiotic therapy are unrelated to *H pylori* infection. In addition, helminthic infection and certain dietary ingredients such as curcumin, onion, and others, may influence the degree of *H pylori*–associated gastritis, a potential factor in the pathogenesis of dyspeptic symptoms.[30]

Culture and Social Factors Influencing Gut Microbiota Profiles

The gut microbiome is a potential unifying factor that could explain the variability of DGBI across different geographic regions. In this section, we focus on the gut microbiome as a potential unifying factor that links these differences in the variance in DGBI.[31]

The gut microbiome contributes to myriad aspects of host biology that are implicated in DGBI, such as alteration in intestinal permeability, GI transit, secretion and sensation, immune function, and brain–gut communication. An individual's gut microbiome is shaped by the total of an individual's exposures (exposome) during their lifetime, and their genetic makeup. This is supported by the significant similarities in microbiome composition observed among genetically unrelated individuals who live in the same house; 20% of microbiome variability is associated with factors related to an individual's environment.[32] Furthermore, in genetically similar Himalayan populations that live within the same geographic region, differences in gut microbiome were found to be driven by differences in dietary habits.[33] Collectively, there is good evidence that sociocultural factors are linked via the microbiome to prevalence, pathogenesis, and outcomes of DGBI[6,31] that is driven at least in part by differences in the gut microbiome. Although it may be challenging to delineate the effect of genetics, sociocultural influences, and the environment, this approach is suitable to generate hypotheses that subsequently can be tested. Indeed, in a large study of adults living in the Netherlands, ethnic origin was an important determinant of an individual's gut microbiota composition, with *Prevotella* being dominant among Moroccan, Turkish, and Ghanaian individuals; *Bacteroides* among African and South-Asian Surinamese individuals; and *Clostridiales* among Dutch individuals.[34] Although individuals with different ethnic backgrounds migrated as adults and shared a common postmigration environment (eg, diet, lifestyle, or environmental exposure), they exhibited a distinct microbial composition, suggesting that ethnicity may impart a certain degree of resiliency. The differences, however, were only partly explained by ethnicity-related factors and included sociodemographics, lifestyle, and diet. On the other hand, a large multiethnic, multigenerational cohort study found that the gut microbiome is strongly impacted by migration from a non-Western to a Western country, even in the short term. This effect was only partially

Table 1. Effects of Climate and Climate Change on Factors That May Influence the Manifestation of DGBI

Environmental change	Mediator	Consequences in relation to DGBI
Increase of ambient temperature	Increased water temperature in supply pipes	Risk of contaminated water
Increase of risk of severe weather events, floods, hurricanes	Interruptions of normal services, electricity and temporary lack of access to clean water	Increased rates of gastrointestinal infections
Increase of ambient temperature and increased sun exposure	Increased concentration of ATI in wheat and similar grains	Stimulated gastrointestinal immune system due to higher ATI concentrations

explained by dietary variation, suggesting that environmental exposure beyond diet played a significant role following migration.[35] It is important to note that dietary history often does not account for dietary components such as food additives (eg, emulsifiers, preservatives) and artificial sweeteners,[36] which vary among developed and developing countries, or the use of antibiotics in animal products, which can vary even among developed countries.

Social factors contribute to health care disparities and also affect the gut microbiome. Differences in gut microbiome due to social circumstances may influence outcomes in DGBI. Socioeconomic status is linked to gut microbiome variability across populations, affecting both adults and children. Factors such as cesarean births, early formula feeding, poor hygiene, limited medical access, reliance on low-fiber high-fat diets, and disrupted sleep patterns, which are more common in low socioeconomic and minority groups,[37] can lead to altered microbial composition and reduced diversity. Although studies suggest a role for the gut microbiome in mediating sociocultural factors in DGBI, further research is needed.

The gut microbiome, unlike the host genome, is dynamic and potentially modifiable. Thus, targeted modulation of the microbiome can potentially surmount sociocultural-driven differences among groups. As an example, consumption of a low-fiber diet in the Western world, resulting in decreased butyrate production by gut microbiota, can contribute to the development of IBS with constipation, but a targeted increase in butyrate-producing bacteria can overcome this.[38] Similarly, a low microbial diversity in infants because of lack of breastfeeding or antibiotic use has been associated with DGBI later in life.[39] A coordinated global approach would offer an opportunity to characterize the effect of distinct sociocultural factors on the gut microbiome and then to determine whether changes in the gut microbiome are causally linked or just correlated with variance in DGBI.

Sociocultural Differences in Dietary Triggers and Eating Behavior

Food and diet are intricately intertwined with the society and culture of any population. Food and diet are also frequently implicated as triggers for DGBI. For instance, Chinese and Iranian populations believe that specific diseases can be explained by an imbalance between hot and cold principles and, consequently, categorize diseases and foods in terms of their hot and cold characteristics. These classifications are unrelated to the actual temperature but rather to related properties. For example, Puerto Rican individuals in New York attribute “cold diseases” to “cold foods,” such as avocados, bananas, coconut, and white beans, believing them to provoke a cooling of the stomach. Consequently, doctors should not prescribe “cold” remedies, such as sodium bicarbonate, milk of magnesia, or belladonna, for these diseases.

Culture influences one’s dietary preferences and patterns, which in turn have ramifications for DGBI symptoms. The best example is the Mediterranean diet, which has been shown in several studies to have cardiovascular benefits. Although this diet does have health benefits, specific food components (in particular, fermentable oligo-, di-, and monosaccharides and polyols [FODMAPs]) in fruits and vegetables are considered potential triggers of digestive symptoms in patients with DGBI. The daily intake of FODMAPs is variable among different age groups and geographic regions.[40] This is based on the locally available food supplies and local preferences defined by traditions and cultural, environmental, and economic factors.

In many parts of East Asia, including China, Japan, and Korea, staple foods frequently include legumes, garlic, onion, cauliflower, and cabbage—all considered high in FODMAPs; however, the prevalence of DGBI is no higher than in Australia. Although a reduction of FODMAPs intake is advocated as a therapy for IBS, in one cohort study, patients with IBS had lower FODMAP intake as compared with controls.[41] This may indicate that the relationship between DGBI and food or diet in a society is not always unidirectional; and although specific foods such as FODMAPs may cause or aggravate GI symptoms (in a dose-dependent fashion), consumption of staple foods that cause or aggravate GI symptoms are avoided by patients with DGBI. Therefore, simple cohort studies may not be sufficient to unravel the role of nutritional factors and the manifestation of DGBI. This indeed would require careful food challenges and control of dietary intake.

Specific foods, for example spices, have been implicated as a cause of GI symptoms across diverse cultural groups. A cross-sectional study of adults in Iran demonstrated that spicy food was significantly associated with IBS. However, although chili causes symptoms in patients with IBS and in controls, symptoms following the ingestion of chili were more severe in patients with IBS.[42] Notably, diverse cultures are known to vary in their tolerance to hot chili peppers, and cultural upbringing may change the sensitivity to capsaicin contained in chili. Interestingly, the ingestion of chili enhanced gastric accommodation in patients with nonerosive reflux disease (NERD) but did not affect controls.[42] These findings point toward the possibility that specific spices, such as chili, interact with receptors and physiologic mechanisms that are involved in conditions such as NERD and IBS, but that certain individuals express greater tolerance to capsaicin, not because of differences in peripheral sensitivity, but due to behavioral mechanisms.

Wheat is a staple food in most Western countries, including those of North America and Europe. In recent years, it has been recognized that a considerable proportion of patients with DGBI report symptoms that are triggered or aggravated by the consumption of wheat products, and that symptoms improve when wheat-containing foods are avoided, even in cases in which celiac disease has been excluded. These patients with DGBI who also have intolerance to wheat products (without celiac disease as the cause of their symptoms) are now frequently referred to as patients with self-reported non-celiac wheat sensitivity,[43] and there is considerable overlap between self-reported non-celiac wheat sensitivity and DGBI. Like other food

components that potentially trigger symptoms in susceptible subjects, the consumption of wheat products that cause symptoms may subsequently change the dietary intake of wheat and gluten products, whereas previous data also suggest that a low-gluten diet alters the GI (stool) microbiome.[44] Thus, changes in the dietary intake of gluten-containing foods may result in alterations of the gut microbiome, and conceptually it might be important to compare differences in the microbiome in patients with DGBI and in controls, stratified for subjects with and without wheat-related symptoms. Recent work also has highlighted the possibility that specific wheat proteins such as ATI can cause immune activation.[45] Previously, it has been shown that in patients with DGBI, alterations in the duodenal mucosa-associated microbiome, GI symptoms, and meal-related QoL scores are linked.[46] Recent data demonstrate that the manifestation of non-celiac wheat sensitivity is strongly associated with an immune activation reflected by an increase of circulating gut-homing T cells, whereas patients with self-reported non-celiac wheat sensitivity have a distinctive duodenal mucosa-associated microbiome.[47] This is akin to the immune activation already reported in patients with DGBI and altered gut function FD.[23] It is essential to note that immune activation in patients with DGBI may be associated with intolerance to specific foods, such as wheat.[47] Although reduction of specific foods such as FODMAPs may improve symptoms in some patients with DGBI, some populations with high FODMAP intake may experience low prevalence rates of DGBI. This suggests that the oversimplification of links between specific foods and symptoms should be avoided.

Race, Ethnicity, and Genetic Predisposition

Race and ethnicity are important variables in cross-cultural studies.[48] In fact, the terms "race" and "ethnicity" are frequently used interchangeably, whereas race is based on phenotype, and ethnicity can be considered as a measure of cultural heritage.[49] However, a contradistinction between innate, biological predispositions and environmental influence, which corresponds to the "nature vs nurture" theory, may be a false dichotomy.[50] Interestingly, according to the concept of gene-culture coevolution, race and ethnicity are social constructs that encompass both shared genetic ancestry and environmental exposure. Moreover, both genetic and environmental factors may alter the activity of genes via epigenetic mechanisms that bridge the gap between the nature vs nurture debate.[50]

Although significant differences in prevalence rates of DGBI according to geographical region, race, and ethnicity have been reported,[51] the available data are still limited and inconsistent. For example, in the United States, a higher prevalence of IBS was observed in African American individuals compared with white individuals,[52] whereas there was considerable variability in dyspepsia prevalence rates across 13 distinct countries.[12] Furthermore, in Asian populations, ethnic differences were observed for dyspepsia but not IBS.[53,54] Recently, the results of the RFGES, conducted on an unprecedented scale and using very rigorous and uniform research methodology, confirmed differences in DGBI prevalence rates between countries and regions.[11] The study has opened new avenues for research into the reasons for the observed differences, which may include cultural and ethnic diversity, social reporting sensitivity, genetics, and dietary habits.[55]

Ethnic differences in genetic polymorphisms associated with IBS have been reported, for example, the serotonergic system, the adrenergic system, the voltage-gated sodium channel NaV1.5, the endocannabinoid system, cholecystokinin, interleukins, and tumor necrosis factors.[56] Importantly, the diverse distribution in allele frequency in different ethnic groups may contribute to the observed inconsistency in genetic research results. So far, there have been no data concerning ethnic variations in genome-wide association studies since they were conducted in IBS cohorts in Northern Europe.[57] It is noteworthy that ethnic differences in genetic predisposition for anxiety and depression related to the serotoninergic system may also significantly contribute to the prevalence, manifestation, and severity of DGBI, as well as treatment response.[58]

Given the close interactions between genes and culture, susceptibility to food intolerance may contribute to the pathogenesis and manifestation of DGBI.[59] Lactose intolerance serves as a good example of cultural practices (dairy farming in this case) shaping the human genome,[60] with considerable variability across geographic regions.[61] Although the symptoms of lactose intolerance may mimic IBS, the concern that IBS may be misdiagnosed in populations with a high prevalence of lactose intolerance was not confirmed by a study in a multiethnic population in Scotland.[53]

One of the main limitations of studies exploring the phenomenon of race and ethnic variations in DGBI is the issue of ethnicity as a demographic characteristic, as there are no unified standards of ethnic/racial classification.[56] The quickly evolving structure of modern societies, given their multiethnic and multiracial character, constitutes another challenge. The inclusion of relevant environmental and social exposure in (epi)genetic studies may help to elucidate racial/ethnic disparities in disease prevalence, manifestation, and treatment response.

Culture and Society as Modifiers for Explanatory Models of Disorders of Gut–Brain Interaction

For patients and health care providers, there is often ambiguity between illness (changes to state of being and social function) and disease (abnormalities in bodily structure and function). This challenge is partly a result of the separation of mind and body, a doctrine that has been dominant in medicine since it was popularized in 1641 by the French philosopher René Descartes. Illness behavior, sociocultural differences, and societal needs further widen the mismatch. Patients with DGBI may develop self-explanatory models of illness, especially considering

recurrent or persistent symptoms that are not explained by diagnostic testing and not controlled by ineffective conventional treatments. As a result, they are left to endure and manage their symptoms on their own. Simply put, an explanatory model is how patients and doctors understand the illness or disease experience and is often based on emotions and beliefs. The major interacting factors that lead to explanatory models in patients include sociocultural background, socioeconomic status, educational level, and gender.[48] For patients, illness-related beliefs, including concerns, anxieties, and expectations from the treatment process, are most important. As an example, in a study of chronic pelvic pain among women, patients did not have a clear idea of their disease process but were flexible with disease concepts and had clear ideas of what they wanted from their health care provider. Health care professionals are likely to explain DGBI symptoms based on etiology and pathophysiology and make treatment recommendations based on their own explanatory model of disease mechanisms,[62] oblivious to the patient's sociocultural needs. This obvious mismatch between patients and physicians in their explanatory model can create tension, lead to a therapeutic impasse, and worsen health care–seeking behavior.[63] The funding of health care services, cultural attitudes toward tradition, frequent use of local remedies, variation in health care systems, concerns regarding organic disease, or even religious practices, may influence health care–seeking behavior among patients with DGBI from different geographic regions.[64] Understanding what is most important to the patient (ie, the patient's illness model), addressing the patient's concerns based on his or her explanatory model, and considering emotional, sociocultural, behavioral, and religious aspects can establish a more therapeutic patient-physician relationship and improve outcomes for patients with DGBI.

The Patient-Provider Relationship

The clinical presentation, including health care seeking, of patients with DGBI is linked to cultural and social norms.[65] For example, patient expectations in relation to the treating clinician. Available data show a disconnect between expectations and experiences on both sides.[66] A large survey with >1200 patients with IBS revealed that the 3 most desired qualities of (1) providing information, (2) answering questions, and (3) listening were fulfilled only 38%, 68%, and 63% of the time, respectively, by their physicians. The sense of being supported happened less than half of the time. Specifically, an added dimension is their expectation of cultural and social empathy and the issue of cultural competency of health care providers. This is crucial in DGBI, in which relevant history of subtle stressors and possible previous abuse can be elicited only if the physician understands the cultural context and navigates the social nuances with sensitivity.

It would be too easy to assume that with globalization there is uniformity and homogenization of cultures. Rather, the challenge is that health care providers face patients who hail from different ethnicities and societies. This reality should be considered in patient diagnosis, treatment, and management. Still, physicians are not usually trained to consider their patients' backgrounds or to elicit and understand the patients' explanatory model for their DGBI and their expectations. Thus, working in a multicultural milieu presents a difficult challenge that can be met by fostering clinical cross-cultural competency in medical schools and in ongoing medical education. Published educational material provides further insight into barriers to cross-cultural competence, including personal space, handling language disconnects, handshakes and eye contact, and being of the opposite sex. However, there are significant challenges relating to cultural competencies in the health care environment

The training of providers to understand and manage patients with DGBI is likely inadequate and needs to be significantly strengthened to achieve better patient outcomes. A British study revealed the only DGBI mentioned across all medical training curricula was IBS, whereas the general practitioner and gastroenterology curricula also recognize the outdated term nonulcer dyspepsia (as opposed to FD). The 2010 gastroenterology curriculum also includes FC and disordered defecation, with the incoming 2022 iteration adding functional upper GI syndromes, functional abdominal pain, and opioid-induced GI disturbances. This inequity is perceptible, when one considers the overall prevalence of DGBI in the same country is nearly 40%.[67]

Culture Influences the Management of Patients

Although much progress has been made in relation to therapies for DGBI, they are only helpful if patients are willing to accept and use them. Cultural and societal acceptance plays a pivotal role, and it is important to identify the facilitators and barriers that are at play.

Most cultures use both complementary and alternative medicine (CAM) and conventional Western medicine, but the emphasis is often on one or the other, and individuals may favor one approach over the other. The same issue exists with conventional treatment options. For example, the use of a psychotropic agent as a neuromodulator is often rejected because of the stigma of perceived treatment for a "mental disease," and payers often refuse to fund psychotherapy for DGBI for the same reason.

Identifying the societal barriers and putting facilitators in place for treatment is key. In most settings, a large proportion of patients with DGBI have concomitant anxiety or depression. To provide these patients with the required care addressing the mental health needs can be challenging depending on the resourcing. Other critical issues include the intersections between cultural psychology and cross-cultural psychology with health belief models, or potential explanatory models in DGBI influencing the behavior of patients and clinicians (see Supplementary Table 2). The Rome Foundation provides important guidance for the management of these patients.

Requirements for Providers to Address the Clinical Needs of Diverse, Multicultural Communities

To provide the appropriate care for culturally diverse communities, the appropriate skills are required. DGBI, which have unclear etiologies, are more likely to be influenced by cultural factors than disorders that have defined biological bases and clear-cut diagnostic criteria. To achieve effective communication with patients, doctors must be cognizant of and adjust to the cultural background and perspective through which patients view their illness (Figure 3 and Supplementary Table 2). Explanatory models can facilitate complicated and often frustrating communication between health care providers and patients with unexplained symptoms and chronic conditions.[68] Because the physician-provider relationship is a defining factor for the treatment of patients with DGBI, it is essential to address the patient's explanatory disease model—likely defined by the patient's cultural background—and negotiate a treatment partnership that is suitable within the context of the patient's and the medical team's beliefs and attitudes.

Barriers to the patient-provider relationship are often created by patient beliefs that may make the consulting process difficult. Because of the inherent intricacy and multifaceted aspects of this clinical setting, patients may struggle to convey this issue during the consultation. Supplementary Table 2 provides examples of areas of cultural sensitivity in clinical practice, sets out the potential minefields that exist, and outlines practical steps the clinician can adopt to minimize them.

Racial/ethnic differences in response to various treatment modalities represent another important aspect of DGBI management. Culturally determined beliefs and behavioral patterns may influence patient expectations for treatment response, treatment adherence, and clinician interactions (eg, conventional treatment vs CAM). In addition, differences in pharmacotherapeutic responses can be determined by different pharmacokinetics and pharmacodynamics.[69]

Care Provision, Resource Allocation, Health Care Equity

Patients with DGBI frequently undergo extensive and repeated examinations that, per definition, are normal. In some societies, repeated consultations and tests may result in these patients being dismissed as "attention seekers" or malingerers. Even with the diagnosis of DGBI, the perception of being a "nonorganic and functional disorder" creates a stigma in some societies, preventing the patient from getting proper recognition for their disease, let alone the good and proper treatment they deserve.[70] There may be additional factors that feed this discrepancy in care; for example, ethnic and cultural discrimination, which then set up a vicious cycle in which patients feel that their concerns are not being addressed, resulting in a loss of faith in the health care system and the use of unproven and suboptimal remedies and therapeutics.[65] It is also noteworthy that socially disadvantaged groups (African American or Asian) are less likely to receive care for their IBS by a specialist.[71] This may be because of a variety of factors, including social disparities as well as conscious and unconscious biases in some health care workers and health care systems that influence health care access.

Often, there is a marked discrepancy in funding for "real" organic pathology over functional disorders in resource availability and prioritization of health care services. DGBI have functional disease-related group codes, which attract much lower resource allocation and funding. Insurance companies frequently deny reimbursement and payment for investigation and treatment of patients with DGBI. This is particularly prevalent in certain parts of the world (eg, Asia) where there is poor recognition of these disorders. In contrast, treatments that aim to improve QoL in organic conditions are a globally well-accepted concept across many cultures, whereas the needs of patients with DGBI and the "requirement" to manage these patients effectively are frequently questioned. Indeed, it is speculated that patients with DGBI may stop consulting because of disenchantment with the inadequacies of current therapies. Consequently, the indirect and intangible costs of the disorder may increase, but these burdens do not directly impact those responsible for purchasing and providing health care for people with DGBI. A cultural bias against DGBI has also been noted in relation to the allocation of funding for research. For example, in the Seventh Framework Program for Research and Technological Development of the European Union (FP7), the breakdown by type of GI disease shows that the most significant amount of funding was allocated to IBD (34.9% of funding in FP7, 38.8% in Horizon 2020 [H2020]) and GI cancers (15.2% in FP7, 34.9% in H2020). Despite being among the most common diagnoses in gastroenterology, funding for IBS projects represented only 0.8% of the contributions by the European Union in FP7 and 0.2% of contributions to date in H2020. In comparison, celiac disease, with a prevalence of 0.17% to 2.9% in Europe, received 11% of the funding in FP7 and 4.3% of the funding in H2020. Over a 10-year period between 2007 and 2017, DGBI, such as FD and functional bowel disorders, did not receive any funding from FP7 or H2020.[72]

The bias toward organic disease is also reflected by the fact that a patient with concomitant IBS symptoms who is also affected by an organic condition (eg, IBD in complete remission), is managed differently compared with a patient with only a severe manifestation of a DGBI. In the patient with IBD, the health care provider may suspect "residual inflammation" or undiagnosed structural abnormalities as the cause of symptoms and subsequently will order additional tests or escalate therapy, whereas in patients with IBS, clinicians see limited need and opportunities to escalate therapy because after lifestyle interventions, specific dietary interventions, or medications, therapeutic options are limited, and multidisciplinary treatments are not widely available. Recent data from the Netherlands (with a publicly funded health system) reveal annual mean (direct and

indirect) cost per patient per year with DGBI (eg, IBS) of €8624.[73] Although in many developing countries this excess spending would exceed the average spending per capita, this highlights that there is not only considerable pressure on public health care systems, but that for patients with DGBI in health systems that provide comprehensive services to communities, there might be considerable inequalities in relation to the care patients receive.

Society and Culture Affecting Outcomes

Support networks play a key role in patient outcomes, beyond the efficacy of medication and therapies. Negative family dynamics, such as spousal and generational conflicts, can affect the manifestation of DGBI. Family structures also can determine how much support is given to a patient, affecting the treatment outcome. For example, tightly knit, extended multigenerational families have been shown to provide dedicated support for patients with IBS, resulting in a more positive response to therapy.[74]

It is well established that in patients with "organic disease" such as acute coronary effects of stress can be buffered by social support structures. Social support can be provided, not only by direct human interactions, but also through technology. A study explored the effects of a computer-mediated bulletin board for individuals affected by IBS, regarding the communication of informational support, symptom interpretation, illness management, and interaction with health care professionals.[75] The flip side of this is the rise of unregulated websites, especially those that are unmoderated by a medically trained professional that occasionally may offer advice that could result in adverse health outcomes.

An interesting concept asks whether we can control the opposing effects of support and strain. A Norwegian twin study[76] revealed that genetic effects explained between 30% and 40% of the variation. Surprisingly, all the genetic variation underlying the liability to develop IBS was shared with genetic influences underlying social strain and low support.

The advent and availability of digital media has made it a major determinant of health outcomes. One aspect of relevance has been the rise of social media and the outsized role played by social media influencers. Content generated by influencers is readily accessible and can have both helpful and negative benefits. One area of relevance to the sociocultural aspects of DGBIs has been the effect on diet. A study of influencers on Instagram showed the significant effect they had in changing dietary intake of their young followers, in this case to consume an "unhealthy" marketed food product.[77] Along the same lines of influence, there have also been chat rooms dedicated to managing a whole plethora of DGBI such as IBS, where the discussion ranges from suggested changes to cooking practices to even stooling habits, for example the use of squatting vs sitting toilets, in the hope of alleviating symptoms. The challenge therefore is for health care practitioners not to shun this deluge of unfiltered information in cyberspace, but rather to act as a guide to their patients, helping them to navigate and separate fact from myth to achieve desired health outcomes.

Globalization: The Great Social Equalizer or Threat to Cultural Uniqueness?

Globalization in the form of the physical migration of peoples or the movement and morphing of cultures has resulted in the formation of multicultural communities and the ideological blending of societies. Globalization tends to extend cultures across all civilizations of the world and thus provides, across cultures and geographic boundaries, access to knowledge, resources, and products including products or behaviors that influence gut health, and subsequently DGBI.

In the field of DGBI, this presents both opportunities and challenges. First, with urbanization, we see the decline of indigenous eating habits and a widespread use of processed food diets. This has resulted in shifts in microbial composition and an increase in food intolerances, potentially explaining the increase in the prevalence of DGBI such as IBS. Second, the traditional customs of "modern societies," such as prolonged breastfeeding, have been abandoned and replaced by early formula and food feeding, also with potential downstream effects for DGBI later in life. In the opposite direction, we see how hitherto questionable practices such as Moxibustion have made their way into the CAM options available to patients with DGBI in places where they were never considered in the past. Although these trends may be perceived as an enrichment of culture, and the opportunities to address consumer needs might be welcomed, this also challenges established concepts that "regulate" access to therapies.

Herbal medicines are widely used for the treatment of patients with DGBI,[78] although there are differences between countries in relation to the regulatory requirements for these treatments.[79] Conventional drugs are typically preferred for DGBI; CAM and dietary changes are common adjuncts and can be effective, but the use varies markedly by region.

Cross-Cultural Research

Research comparing the prevalence of DGBI in various geographic regions is frequently alluded to as "cross-cultural" research. These studies compare prevalence in different geographic regions (or countries) with distinct climates and cultural features and may provide information in relation to ethnicity. A recent example is the RFGES.[11] Observing considerable variation in the prevalence of DGBI in different regions allows cross-cultural research to be instrumental in delineating the role of specific ethnic (genetic) or psychosocial factors in the disease process by exploring complex data sets from diverse communities.[17]

Furthermore, cross-cultural research may help individuals to better understand symptom presentation and extra-intestinal comorbidities, to appreciate nuanced approaches toward diagnosis and treatment, and to characterize determinants of disease severity, health care utilization, and health-related QoL.

Recommendations for Future Research

Sociocultural factors play a crucial role for DGBI. The available data support the notion that sociocultural factors influence pathophysiology, health care utilization, management strategies, treatment responses, and ultimately societal disease burden. A cohesive research approach is needed to integrate these traits into structured assessments and personalized care plans. Emerging technologies like artificial intelligence can address real-world issues by leveraging machine learning and deep learning to analyze data from diverse sociocultural backgrounds, enhancing DGBI diagnostics and treatment.

Future research should identify the enablers, modifiers, and outcomes of sociocultural influences in DGBI (Supplementary Table 3). Population data from previous studies can help define research hypotheses. Given the global variance in DGBI incidences, prospective and ecologic studies can uncover sociocultural factors affecting prevalence. In addition, the impact of the microbiome on DGBI warrants exploration of how lifestyle and cultural influences interact with gut health.

Recognizing complex interactions among sociocultural factors, including food influences on the microbiome and health outcomes, is essential. Valid methods to measure GI symptoms across culturally diverse communities, including visual aids, must be developed without oversimplifying symptom representation. Patient expectations, often overlooked, significantly affect satisfaction and outcomes. Understanding how diverse populations express symptoms and their health care expectations is critical for patient-centered care.

The biopsychosocial model emphasizes the need for an integrated treatment approach that aligns with cultural aspects, ensuring effective communication between health care providers and patients. Advances in diagnostic approach should incorporate biopsychosocial markers to facilitate personalized treatment strategies, complemented by social pharmacology to account for sociocultural influences on medication use.

Conclusions

Sociocultural factors and their variability across diverse communities significantly influence the manifestation of DGBI in different geographic regions with key findings summarized in Table 2. Although current disease models focus on specific mechanisms, such as sensory or motor function abnormalities and the gut microbiome, integrating sociocultural factors into the disease concept can enhance understanding of symptom manifestation and chronicity (Figure 1). Although often overlooked in clinical practice and research, these factors offer a unique opportunity to create a comprehensive framework within the biopsychosocial model of DGBI. This emerging knowledge enhances established biological models and our understanding of the multifactorial nature of DGBI, potentially leading to more targeted and effective therapies.

Table 2. Key Findings of the Rome V Sociocultural Working Group

1) Sociocultural factors influence the manifestation of DGBI, subsequent health care seeking, and response to therapeutic interventions.
2) The effects of sociocultural factors on DGBI are mediated by socially and culturally defined food preferences, risk of gastrointestinal infections, stress exposure, and adaptive coping strategies, potentially by ethnic differences in genetic variations associated with DGBI.
3) The variation in the incidence and prevalence of DGBI (and subsequent long-term outcomes) across socially and culturally diverse communities is likely also linked to differences in colonization of the gastrointestinal tract by microbes.
4) Social norms in different cultures affect how DGBI symptoms (and extraintestinal or psychological comorbidities that frequently accompany DGBI) are experienced, interpreted, reported to others, and subsequently influence health care utilization.
5) The diagnosis and categorization of DGBI relies on symptoms. Therefore, language is critical for assessing symptoms and categorizing DGBI accurately. This has implications for cross-cultural comparisons of the incidence and prevalence of DGBI.
6) To assess gastrointestinal symptoms in culturally and linguistically diverse communities, appropriate consideration of the impact of language needs to be given. Instruments, including questionnaires that use pictograms alone or in combination with verbal descriptors, ideally should have undergone formal testing of validity and reliability across the intended linguistically diverse communities.
7) Climate change due to sociocultural factors likely influences the manifestation of DGBI via an increased risk of severe weather events and an increased ambient temperature and precipitation. Extreme weather events may increase the risk of gastrointestinal infections because they interrupt access to clean food and drinking water. Increased ambient temperatures and changes in precipitation can also affect our food supply's composition, leading to, for example, increased exposure to ingredients that may cause indigestion (eg, increased exposure to immune-stimulating amylase trypsin inhibitors).
8) Providing care to culturally diverse populations with DGBI requires health care providers to possess appropriate cultural competence, including culture-specific communication skills.
9) The health equity of patients affected by DGBI, as reflected by the ability to access services that address the needs of patients with DGBI, is affected by a sociocultural bias toward diseases with excess mortality and/or structural disease markers.
10) Despite the high prevalence of DGBI, their significant impact on quality of life and the immense economic and societal burden, the inequality in relation to care provided for patients with DGBI is further aggravated by insufficient funding for basic and clinical research.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2026.02.006.

References

1. Francisconi CF, Sperber AD, Fang X, et al. Multicultural aspects in functional gastrointestinal disorders (FGIDs). Gastroenterology 2016;150:1344–54.e2.
2. Braveman P, Gottlieb L. The social determinants of health: it's time to consider the causes of the causes. Public Health Rep 2014;129(Suppl 2):19–31.
3. Chang L, Toner BB, Fukudo S, et al. Gender, age, society, culture, and the patient's perspective in the functional gastrointestinal disorders. Gastroenterology 2006; 130:1435–1446.
4. Heyes C. Culture. Curr Biol 2020;30:R1246–R1250.
5. Thabane M, Kottachchi DT, Marshall JK. Systematic review and meta-analysis: the incidence and prognosis of post-infectious irritable bowel syndrome. Aliment Pharmacol Ther 2007;26:535–544.
6. Fairlie T, Shah A, Wong RK, et al. A multifaceted ecological approach to explore links between environmental factors and the epidemiology of disorders of gut-brain interaction. Neurogastroenterol Motil 2024;36:e14866.
7. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features, and Rome IV. Gastroenterology 2016;150:1262–1279.e2.
8. Gerson MJ, Gerson CD, Awad RA, et al. An international study of irritable bowel syndrome: family relationships and mind-body attributions. Soc Sci Med 2006; 62:2838–2847.
9. Gwee KA, Gonlachanvit S, Ghoshal UC, et al. Second Asian Consensus on Irritable Bowel Syndrome. J Neurogastroenterol Motil 2019;25:343–362.
10. Spiegel BM, Bolus R, Agarwal N, et al. Measuring symptoms in the irritable bowel syndrome: development of a framework for clinical trials. Aliment Pharmacol Ther 2010;32:1275–1291.
11. Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. Gastroenterology 2021;160:99–114.e3.
12. Haag S, Andrews JM, Gapasin J, et al. A 13-nation population survey of upper gastrointestinal symptoms: prevalence of symptoms and socioeconomic factors. Aliment Pharmacol Ther 2011;33:722–729.
13. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. J Clin Epidemiol 1993;46:1417–1432.
14. Koloski NA, Jones M, Hammer J, et al. The validity of a new Structured Assessment of Gastrointestinal Symptoms Scale (SAGIS) for evaluating symptoms in the clinical setting. Dig Dis Sci 2017;62:1913–1922.
15. Alrubaiy L, Hutchings HA, Williams JG. Assessing patient reported outcome measures: A practical guide for gastroenterologists. United European Gastroenterol J 2014;2:463–470.
16. Khanna P, Agarwal N, Khanna D, et al. Development of an online library of patient-reported outcome measures in gastroenterology: the GI-PRO database. Am J Gastroenterol 2014;109:234–248.
17. Scott NW, Fayers PM, Aaronson NK, et al. The relationship between overall quality of life and its subdimensions was influenced by culture: analysis of an international database. J Clin Epidemiol 2008; 61:788–795.
18. Mahd-Ab Lah N, Kueh YC, Kuan G, et al. Validity and reliability of the Malay Versions of Bloating Severity (BSQ-M) and Quality of Life (BLQoL-M) questionnaires. Int J Environ Res Public Health 2021;18:2487.
19. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997; 32:920–924.
20. Holtmann G, Chassany O, Devault KR, et al. International validation of a health-related quality of life questionnaire in patients with erosive gastro-oesophageal reflux disease. Aliment Pharmacol Ther 2009; 29:615–625.
21. Dowse R. Designing and reporting pictogram research: problems, pitfalls and lessons learnt. Res Social Adm Pharm 2021;17:1208–1215.
22. Liebregts T, Adam B, Bredack C, et al. Immune activation in patients with irritable bowel syndrome. Gastroenterology 2007;132:913–920.
23. Liebregts T, Adam B, Bredack C, et al. Small bowel homing T cells are associated with symptoms and delayed gastric emptying in functional dyspepsia. Am J Gastroenterol 2011;106:1089–1098.
24. Guzman Herrador BR, de Blasio BF, MacDonald E, et al. Analytical studies assessing the association between extreme precipitation or temperature and drinking water-related waterborne infections: a review. Environ Health 2015;14:29.
25. Stephen DM, Barnett AG. Using microsimulation to estimate the future health and economic costs of salmonellosis under climate change in Central Queensland, Australia. Environ Health Perspect 2017; 125:127001.
26. Yusof N, Hamid N, Ma ZF, et al. Exposure to environmental microbiota explains persistent abdominal pain and irritable bowel syndrome after a major flood. Gut Pathog 2017;9:75.
27. Pickert G, Wirtz S, Matzner J, et al. Wheat consumption aggravates colitis in mice via amylase trypsin inhibitor-mediated dysbiosis. Gastroenterology 2020;159: 257–272.e17.
28. Simonetti E, Bosi S, Negri L, et al. Amylase trypsin inhibitors (ATIs) in a selection of ancient and modern wheat: effect of genotype and growing environment on inhibitory activities. Plants (Basel) 2022;11:3268.
29. Ford AC, Tsipotis E, Yuan Y, et al. Efficacy of *Helicobacter pylori* eradication therapy for functional dyspepsia: updated systematic review and meta-analysis. Gut 2022;71:1967–1975.

30. Kumar S, Patel GK, Ghoshal UC. *Helicobacter pylori*-induced inflammation: possible factors modulating the risk of gastric cancer. Pathogens 2021;10:1099.
31. Shah A, Lee YY, Suzuki H, et al. A pathophysiologic framework for the overlap of disorders of gut-brain interaction and the role of the gut microbiome. Gut Microbes 2024;16:2413367.
32. Rothschild D, Weissbrod O, Barkan E, et al. Environment dominates over host genetics in shaping human gut microbiota. Nature 2018;555:210–215.
33. Jha AR, Davenport ER, Gautam Y, et al. Gut microbiome transition across a lifestyle gradient in Himalaya. PLoS Biol 2018;16:e2005396.
34. Deschasaux M, Bouter KE, Prodan A, et al. Depicting the composition of gut microbiota in a population with varied ethnic origins but shared geography. Nat Med 2018; 24:1526–1531.
35. Vangay P, Johnson AJ, Ward TL, et al. US immigration westernizes the human gut microbiome. Cell 2018; 175:962–972.e10.
36. Suez J, Korem T, Zeevi D, et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature 2014;514:181–186.
37. Amato KR, Arrieta MC, Azad MB, et al. The human gut microbiome and health inequities. Proc Natl Acad Sci U S A 2021;118:e2017947118.
38. Chu JR, Kang SY, Kim SE, et al. Prebiotic UG1601 mitigates constipation-related events in association with gut microbiota: a randomized placebo-controlled intervention study. World J Gastroenterol 2019;25:6129–6144.
39. Saffouri GB, Shields-Cutler RR, Chen J, et al. Small intestinal microbial dysbiosis underlies symptoms associated with functional gastrointestinal disorders. Nat Commun 2019;10:2012.
40. Drossman DA, Weinland SR. Commentary: sociocultural factors in medicine and gastrointestinal research. Eur J Gastroenterol Hepatol 2008;20:593–595.
41. Schneider E, Sabaté JM, Bouchoucha M, et al. Fermentable oligo-, di-, and mono-saccharides and polyols (FODMAPs) consumption and irritable bowel syndrome in the French NutriNet-Santé Cohort. Nutrients 2021;13:4513.
42. Gonlachanvit S, Mahayosnond A, Kullavanijaya P. Effects of chili on postprandial gastrointestinal symptoms in diarrhoea predominant irritable bowel syndrome: evidence for capsaicin-sensitive visceral nociception hypersensitivity. Neurogastroenterol Motil 2009;21:23–32.
43. Sergi C, Villanacci V, Carroccio A. Non-celiac wheat sensitivity: rationality and irrationality of a gluten-free diet in individuals affected with non-celiac disease: a review. BMC Gastroenterology 2021;21:5.
44. Hansen LBS, Roager HM, Søndertoft NB, et al. A low-gluten diet induces changes in the intestinal microbiome of healthy Danish adults. Nat Commun 2018;9:4630.
45. Bellinghausen I, Weigmann B, Zevallos V, et al. Wheat amylase-trypsin inhibitors exacerbate intestinal and airway allergic immune responses in humanized mice. J Allergy Clin Immunol 2019;143:201–212.e4.
46. Zhong L, Shanahan ER, Raj A, et al. Dyspepsia and the microbiome: time to focus on the small intestine. Gut 2017;66:1168–1169.
47. Shah A, Kang S, Talley NJ, et al. The duodenal mucosa associated microbiome, visceral sensory function, immune activation and psychological comorbidities in functional gastrointestinal disorders with and without self-reported non-celiac wheat sensitivity. Gut Microbes 2022;14:2132078.
48. Francisconi CF, Sperber AD, Fang X, et al. Multicultural aspects in functional gastrointestinal disorders (FGIDs). Gastroenterology 2016;150:1344–1354.e2.
49. Ross PT, Hart-Johnson T, Santen SA, et al. Considerations for using race and ethnicity as quantitative variables in medical education research. Perspect Med Educ 2020;9:318–323.
50. Crews D, Gillette R, Miller-Crews I, et al. Nature, nurture and epigenetics. Mol Cell Endocrinol 2014;398:42–52.
51. Sperber AD, Dumitrascu D, Fukudo S, et al. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. Gut 2017;66:1075–1082.
52. Kang JY. Systematic review: the influence of geography and ethnicity in irritable bowel syndrome. Aliment Pharmacol Ther 2005;21:663–676.
53. Bhopal RS, Cezard G, Bansal N, et al. Ethnic variations in five lower gastrointestinal diseases: Scottish health and ethnicity linkage study. BMJ Open 2014;4:e006120.
54. Ho KY, Kang JY, Seow A. Prevalence of gastrointestinal symptoms in a multiracial Asian population, with particular reference to reflux-type symptoms. Am J Gastroenterol 1998;93:1816–1822.
55. Enck P, Azpiroz F, Boeckxstaens G, et al. Functional dyspepsia. Nat Rev Dis Primers 2017;3:17081.
56. Xiao QY, Fang XC, Li XQ, et al. Ethnic differences in genetic polymorphism associated with irritable bowel syndrome. World J Gastroenterol 2020; 26:2049–2063.
57. Ek WE, Reznichenko A, Ripke S, et al. Exploring the genetics of irritable bowel syndrome: a GWA study in the general population and replication in multinational case-control cohorts. Gut 2015;64:1774–1782.
58. Hawes AM, Axinn WG, Ghimire DJ. Ethnicity and psychiatric disorders. Ann Psychiatry Ment Health 2016; 4:1072.
59. Duncanson K, Burns G, Pryor J, et al. Mechanisms of food-induced symptom induction and dietary management in functional dyspepsia. Nutrients 2021;13:1109.
60. Jellema P, Schellevis FG, van der Windt DA, et al. Lactose malabsorption and intolerance: a systematic review on the diagnostic value of gastrointestinal symptoms and self-reported milk intolerance. QJM 2010;103:555–572.
61. Storhaug CL, Fosse SK, Fadnes LT. Country, regional, and global estimates for lactose malabsorption in adults: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2017;2:738–746.
62. Eisenberg L. Disease and illness. Distinctions between professional and popular ideas of sickness. Cult Med Psychiatry 1977;1:9–23.
63. Collins J, Farrall E, Turnbull DA, et al. Do we know what patients want? The doctor-patient communication gap in functional gastrointestinal disorders. Clin Gastroenterol Hepatol 2009;7:1252–1254; e1–2.

64. Chuah KH, Mahadeva S. Cultural factors influencing functional gastrointestinal disorders in the east. J Neurogastroenterol Motil 2018;24:536–543.
65. Yap P, Mahadeva S, Goh KL. The influence of cultural habits on the changing pattern of functional dyspepsia. Dig Dis 2014;32:217–221.
66. Halpert A, Dalton CB, Palsson O, et al. Irritable bowel syndrome patients' ideal expectations and recent experiences with healthcare providers: a national survey. Dig Dis Sci 2010;55:375–383.
67. Simons J, Shajee U, Palsson O, et al. Disorders of gut-brain interaction: highly prevalent and burdensome yet under-taught within medical education. United European Gastroenterol J 2022;10:736–744.
68. Drossman DA, Chang L, Deutsch JK, et al. a review of the evidence and recommendations on communication skills and the patient-provider relationship: a Rome Foundation Working Team Report. Gastroenterology 2021;161:1670–1688.e7.
69. Halawi H, Camilleri M. Pharmacogenetics and the treatment of functional gastrointestinal disorders. Pharmacogenomics 2017;18:1085–1094.
70. Hearn M, Whorwell PJ, Vasant DH. Stigma and irritable bowel syndrome: a taboo subject? Lancet Gastroenterol Hepatol 2020;5:607–615.
71. Silvernale C, Kuo B, Staller K. Racial disparity in healthcare utilization among patients with irritable bowel syndrome: results from a multicenter cohort. Neurogastroenterol Motil 2021;33:e14039.
72. Törnblom H, Simrén M, Barbara G, et al. Funding for gastrointestinal disease research in the European Union. Lancet Gastroenterol Hepatol 2018;3:593–595.
73. Bosman M, Weerts Z, Snijkers JTW, et al. The socio-economic impact of irritable bowel syndrome: an analysis of direct and indirect health care costs. Clin Gastroenterol Hepatol 2023;21:2660–2669.
74. Lackner JM, Brasel AM, Quigley BM, et al. The ties that bind: perceived social support, stress, and IBS in severely affected patients. Neurogastroenterol Motil 2010;22:893–900.
75. Coulson NS. Receiving social support online: an analysis of a computer-mediated support group for individuals living with irritable bowel syndrome. Cyberpsychol Behav 2005;8:580–584.
76. Kutschke J, Harris JR, Bengtson MB. How are perceptions of social strain and low support related to irritable bowel syndrome? A Norwegian twin study. Neurogastroenterol Motil 2021;33:e14007.
77. Coates AE, Hardman CA, Halford JCG, et al. Social media influencer marketing and children's food intake: a randomized trial. Pediatrics 2019;143:e20182554.
78. Holtmann G, Talley NJ. Herbal medicines for the treatment of functional and inflammatory bowel disorders. Clin Gastroenterol Hepatol 2015;13:422–432.
79. Holtmann G, Schrenk D, Madisch A, et al. Use of evidence-based herbal medicines for patients with functional gastrointestinal disorders: a conceptual framework for risk-benefit assessment and regulatory approaches. Dig Dis 2020;38:269–279.

Received December 3, 2025. Accepted February 9, 2026.

Correspondence
Address correspondence to: Gerald J. Holtmann, MD, PhD, MBA, FRACP, FRCP, FAHMS, Princess Alexandra Hospital, Brisbane, Department of Gastroenterology and Hepatology & University of Queensland, Ipswich Road, Woolloongabba, Queensland 4102, Australia. e-mail: g.holtmann@uq.edu.au.

Conflicts of interest
These authors disclose the following: Uday C. Ghoshal has received patents for indigenous radio-opaque markers for colon transit study, and double-lumen catheter for upper gut aspirate culture. Purna C. Kashyap is a member of the scientific advisory board of the International Observatory of Biocodex Microbiota Institute, advisory board member for Pendulum and 32 Biosciences, and has stock options in 32 Biosciences. The remaining authors disclose no conflicts.

Funding
The Rome Foundation provided organizational and editorial support.