



Multicultural Aspects in Functional Gastrointestinal Disorders (FGIDs)

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Cross-cultural factors are important in functional gastrointestinal disorders (FGIDs). In the setting of FGIDs, the aims of this review were as follows: (1) to engender interest in global aspects; (2) to gain a clearer understanding of culture, race, and ethnicity, and their effect on patient care and research; (3) to facilitate cross-cultural clinical and research competency; and (4) to improve and foster the quality and conduct of cross-cultural, multinational research. Cultural variables inevitably are present in the physician-patient context. Food and diets, which differ among cultural groups, are perceived globally as related to or blamed for symptoms. From an individual perspective, biological aspects, such as genetics, the microbiome, environmental hygiene, cytokines, and the nervous system, which are affected by cultural differences, all are relevant. Of equal importance are issues related to sex, symptom reporting and interpretation, and family systems. From the physician's viewpoint, understanding the patient's explanatory model of illness, especially in a cultural context, affects patient care and patient education in a multicultural environment. Differences in the definition and use of complementary and alternative medicine and other issues related to health care services for FGIDs are also a relevant cross-cultural issue. This article highlights the importance of cross-cultural competence in clinical medicine and research.

Keywords: Culture; Explanatory Model; Cross-Cultural Competence; Cross-Cultural Research.

The inclusion of a new chapter in the Rome IV book devoted to multicultural aspects in functional gastrointestinal disorders (FGIDs) attests to the growing recognition of the importance and value of a global perspective in addressing these disorders. The Rome Foundation has expanded its scope and global outreach greatly in the past decade. Various initiatives undertaken in recent years, collectively called the Rome Foundation Global Initiative, show this concern for the dissemination of

knowledge on and appreciation of the relevance of FGIDs at a global level (Figure 1).

The aims of this review were as follows: (1) to engender greater interest in the global aspects of FGIDs; (2) to gain a clearer understanding of culture, race, and ethnicity, and their effect on patient care and research in FGIDs; (3) to facilitate cross-cultural clinical and research competency in FGIDs; and (4) to improve the quality of multinational research in FGIDs and foster collaborative international research networks for the conduct of cross-cultural, multinational research in this area.

Figure 2 presents a conceptual model of the interaction of factors that have been identified as central to understanding the influence of multicultural factors on FGIDs. Obviously, reality entails greater complexity than any model can capture, but Figure 2 attempts to incorporate salient factors and the interactions between them, as discussed in text later. The model highlights the following: (1) the centrality of the patient, the physician, food and eating, and culture in symptom interpretation and clinical manifestations; and (2) the other factors that feed into these central aspects. These other factors are shown in association with the central items to which they would seem most linked, although in reality there are multiple avenues of interaction and mutual influence. This article focuses on individual factors and the interactions between them.

Definitions

Culture has been defined as the values, beliefs, norms, and practices of a particular group that are learned and

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Abbreviations used in this paper: CAM, complementary and alternative medicine; FD, functional dyspepsia; FGID, functional gastrointestinal disorders; 5-HTT, hydroxytryptamine transporter; IL, interleukin; IBS, irritable bowel syndrome; PI-IBS, postinfection irritable bowel syndrome; TCM, traditional Chinese medicine; TNF, tumor necrosis factor.

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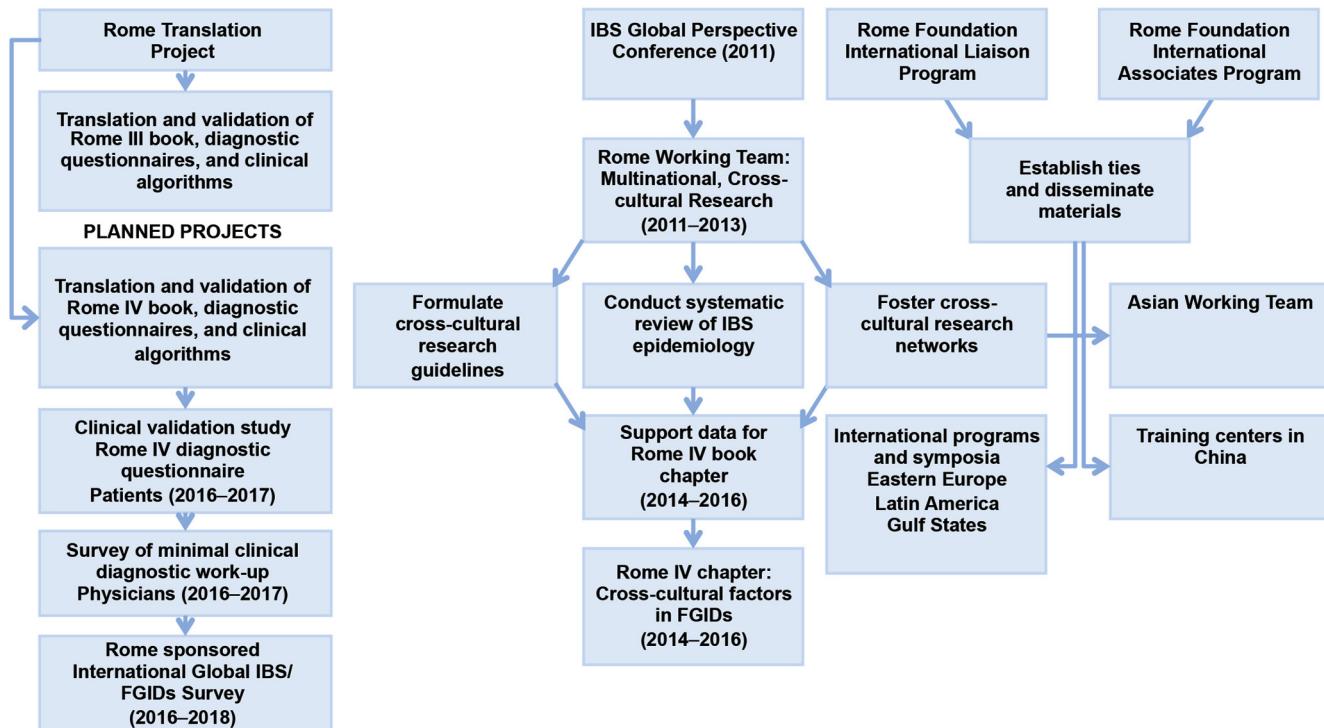


Figure 1. The Rome Foundation's global initiative began with the Rome Translation Project and the Global Perspective conference held in Milwaukee in 2011. Since then, it has branched out in many directions, encompassing outreach educational programs, Rome-sponsored symposia at international meetings around the world, fostering of cross-cultural research networks, and a planned global epidemiology study.

shared, and that guide thinking, decisions, and actions in a patterned way.¹ Individuals within social networks share ideas and values, which create order and further adaptation to local surroundings.

The terms *culture*, *ethnicity*, and *race* often are used interchangeably, although each has a specific definition and reference. Ethnicity can be thought of as a measure of cultural heritage, in contrast to race, which is based more on phenotype (eg, skin color).^{2,3} The term *race* is considered controversial and may not reflect biologic difference owing to the complexity of the human genome. Although there is some recognized overlap between ethnicity and race in this article, the term *race* will refer to the conventional phenotype definition, and in all other category designations, ethnicity is intended.

Ethnocentrism is defined as judging another culture solely by the values and standards of one's own culture,⁴ which can be an impediment to effective clinical practice and research. Beliefs and definitions may have an impact on symptom interpretation. For example, a doctor may ask a patient if they suffer from bloating, but the patient may think the doctor is asking about abdominal pain.

Ethnic identity can be defined as that part of an individual's self-concept that is derived from his or her knowledge of membership in a social group, together with the value and emotional significance attached to that membership.^{5,6}

A patient's culture is related closely to religious principles, language (implicit expression of symptoms and

feelings), and explanatory models of illness. The effect of culture on health and health care can manifest itself in illness beliefs,⁷ symptom expression, and learned coping patterns. Cultural and ethnic factors also may affect pathophysiology, the patient-physician relationship, the diagnostic process,⁸ openness to treatment modalities such as complementary and alternative medicine (CAM) and psychotherapy,^{8,9} and health outcomes.¹⁰

Gender generally is used to refer to the nonbiological aspects of being a woman or man, such as the social or cultural expectations associated with femininity or masculinity.¹¹ The term *sex* generally is used to refer to a person's biological femaleness or maleness. However, most differences between men and women are known to be a function of the interaction between biology and the environment.¹¹ In this review, the term *sex* will be used as a more inclusive term. The term *sex* will be used for the classification of individuals based on their reproductive organs and function, as assigned by their chromosomal complement. Gender roles are based on sex stereotypes, which are socially shared beliefs that biological sex determines certain qualities.

Symptom Interpretation and Reporting

The manner in which symptoms manifest and are reported varies between groups. Evidence exists that African Americans have lower pain tolerance and higher ratings of suprathreshold stimuli than non-Hispanic whites, with greater symptom severity and increased functional

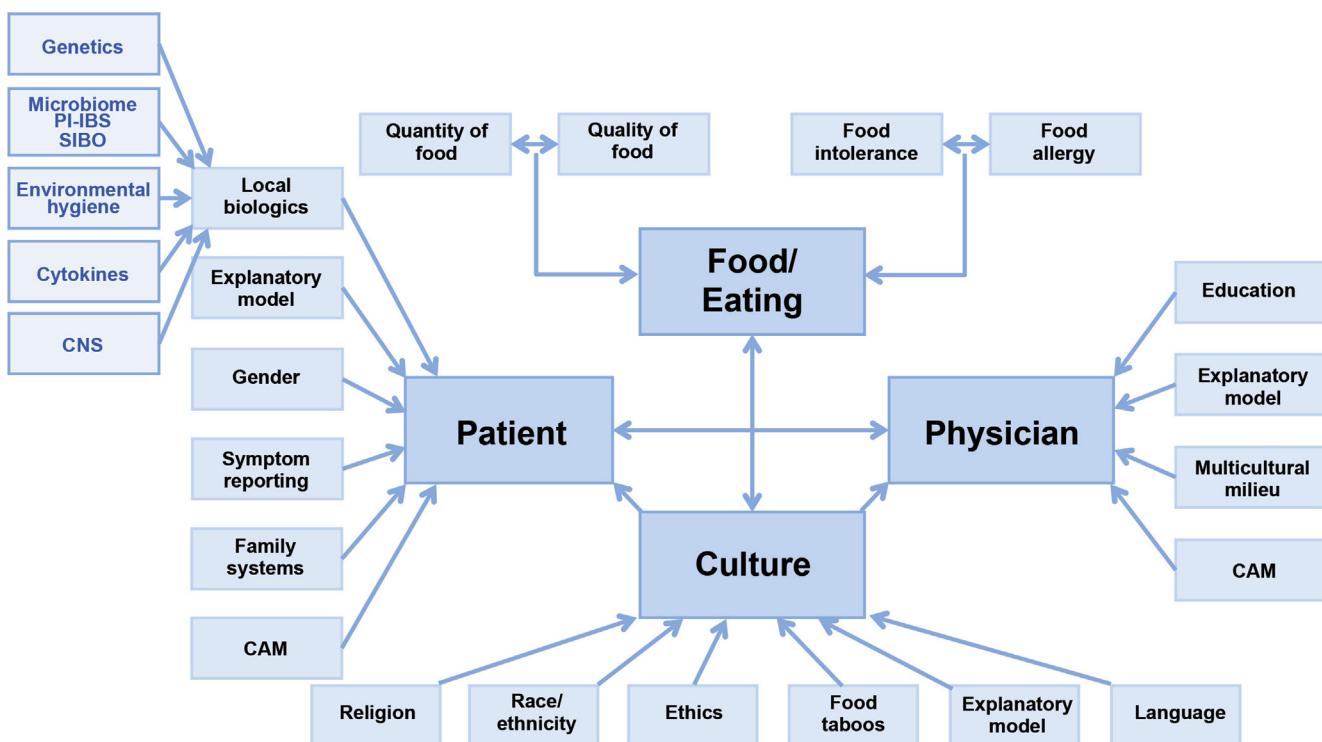


Figure 2. A conceptual model of the interactions between culture and FGIDs. The focus is on patients, physicians, food and eating, and culture in symptom interpretation and clinical manifestations. Although no figure can do justice to all the interactions among factors, the other factors are shown in association with the central factor with which they are most significantly linked. CNS, central nervous system; SIBO, small intestine bacterial overgrowth.

disability related to somatic pain. Similarly, Hispanic individuals have increased sensitivity to pain compared with non-Hispanic whites.^{12,13} Sociocultural, psychological, biological,¹² and ethnic variables can indicate coping styles, which can influence experimental and acute pain response.¹⁴

Some ethnic groups readily describe sensations as painful, whereas others do not complain about pain at all.¹⁵ In much the same way, the sensation of pain may be localized differently in non-Western compared with Western populations (ie, Chinese patients often report pain as occurring in the upper abdominal region, but because it is relieved by a bowel movement, it meets the Rome diagnostic criteria for irritable bowel syndrome [IBS]).

Even if the patient and the physician speak the same language, misunderstandings can take place concerning symptom interpretation and reporting, especially if the symptoms are of a somewhat embarrassing nature. This is particularly the case in FGIDs, in which symptoms are vague and multiple, and in which there are no robust ways of objectively capturing or quantifying them. Furthermore, there are many colloquial ways of describing various symptoms. These can vary greatly from region to region within the same country and may not necessarily be understood by people living outside a particular region.¹⁶ This whole issue becomes even more complex when considering how a word used to describe a symptom is translated into another language, particularly if the exact equivalent does not exist in that language.

For example, “bloating” is a word that is particularly difficult to understand and translate into other languages and adapt into other cultures. Bloating as an English term refers to any abnormal general swelling or any increase in abdominal girth. The most common symptom associated with bloating is a sensation that the abdomen is full or distended. According to Stedman’s Medical Dictionary, bloat or bloating refers to abdominal distension from swallowed air or intestinal gas.¹⁷

Whorwell¹⁸ proposed that bloating is a sensation of increased pressure within the abdomen, whereas distension is a demonstrable increase in abdominal girth. However, putting this distinction into practice is a major challenge because the term *bloating* is confined primarily to English-speaking cultures. The Latin language holds no equivalent word for bloating and the word distension usually is used. In Spain and Latin America, physicians use the term *distension* (a technical medical term) to describe what patients and the public refer to as bloating, often using the words “swelling” and “inflammation.”

Important related issues are whether postprandial fullness is different from bloating and whether bloating and abdominal pain are part of a severity continuum. For example, in China postprandial fullness is limited to the epigastrium, whereas bloating refers to a sensation of gas in most of the abdomen and can reflect abdominal discomfort, another term that does not translate well into other languages. Thus, bloating also may be a component of discomfort in some cultures.

In many languages, including English, Spanish, and Farsi, postprandial fullness is different from bloating. In Chinese, in contrast, patients and physicians may not be able to distinguish between the source of fullness (gastric) and bloating/distension (intestinal).

Bloating, however defined and perceived, is a key symptom among IBS patients in Asia, occurring almost as commonly as abdominal pain, and is an important motive for patient consultation.¹⁹ In this region, phrases such as “feeling blown up like a balloon” are regarded as important features of IBS.^{20,21}

Americans may consider pain and discomfort on a continuum of severity, whereas Europeans perceive them as different types of nociceptive input.^{22,23} Spiegel et al²⁴ conducted a study designed to develop a framework for measuring patient symptoms and inform patient reported outcomes for clinical trials. They concluded that discomfort encompasses a range of symptoms such as bloating, gas, fullness, flatulence, sensation of incomplete evacuation, and urgency, with wide variations in patient understanding. Thus, asking patients about discomfort alone can be nonproductive because the term is nonspecific and covers many symptoms and concepts. It should be noted that this study was conducted in one country and one language alone, and does not necessarily reflect similar symptom experiences in other countries, languages, and cultures.

A multinational study involving the United States, Mexico, Canada, England, Italy, Israel, India, and China showed significant positive correlations between pain and bloating in the 6 Western-culture countries and India.²⁵ The only exception was China, where this relationship was significantly negative. One possible explanation is that the 2 symptoms in China may be conceptualized as being on a continuum, where bloating may be considered a milder form of pain. Investigators also found differences in symptom expression in different parts of Europe. Pain, discomfort, and bloating scores were consistently higher in Italy than in England, so the relative influence of sociocultural norms, language, and symptom interpretation may be significant.²⁵

The observation that Chinese physicians and patients may attribute the origin of abdominal symptoms to a problem in the upper abdomen rather than to bowel dysfunction might lead to diagnostic confusion in some cases and even to misdiagnosis in others, such as IBS being diagnosed as functional dyspepsia (FD).^{20,21} This may explain the lower rates of IBS in these populations, with a concomitant higher prevalence of FD.²⁰ In a study from Taipei, Taiwan, 50% of patients initially diagnosed with FD actually had pure IBS, based on the Rome I criteria, because their upper abdominal pain or discomfort was relieved with defecation.²⁶ A study from Guangzhou, China, observed that postprandial fullness was the only independent predictor of FD in patients with overlapping IBS according to the Rome III criteria.²⁶ Thus, postprandial fullness is defined as originating from the gastroduodenal region, whereas abdominal discomfort, possibly including bloating (but not pain) relieved by defecation, is considered a symptom of IBS.

In summary, there is no consistent understanding of the term *bloating* across cultures and languages. It is interesting

to note that although the term *bloating* presents no linguistic problems to English-language authors or the general English-speaking public, non-English scholars have had to adapt words, or groups of words, from their own language to describe this term.

Pictograms have been developed in an attempt to overcome difficulties in clinical research and improve understanding of what is reported by patients. The pictorial version of the Bristol Stool Form Scale²⁷ is a good example of how patients easily can communicate the appearance of their stools, without having to choose from verbal response options that may be difficult to understand or translate from one language to another and between cultures. The success of this scale is underlined by the fact that it is now used widely in both clinical and research settings. However, a picture-only version has not, to our knowledge, been validated in any formal study.

Carruthers et al²⁸ asked patients to describe the images they had of their condition and a medical artist then painted these in watercolor. The images subsequently were verified or modified according to the wishes of the patient to ensure they represented the perspective of the patient, not the artist. The investigators reported that 90% of the patients in the study who had bloating as their principal symptom chose 1 of 3 images representative of bloating as the image that most reflected their worst symptom. Thus, the use of symptom images might be an ideal way of crossing the language and cultural barriers that currently prevent accurate comparison of symptoms from different parts of the world.

However, the use of pictograms does entail potential problems that should be weighed in terms of benefit vs possible harm: (1) overly realistic images may be offensive in some cultures; (2) colors have significance in some cultures, so one should use caution in the choice of colors; (3) should the body be depicted in full anatomic detail or covered by clothes, (4) should pictograms be accompanied by text, and (5) pictograms should be adapted and validated for specific cultures.

Food and Food Taboos

Food in most cultures plays a prominent role in FGID patient symptom attribution and reporting. This is especially true of IBS and FD, clinical entities for which there is a large body of research concerning the association of eating and food with gastrointestinal symptoms.

The act of eating involves 3 elements: the person, the circumstances under which food intake occurs, and the nature of the ingested food. These 3 elements are all subject to culture-related influences. Other relevant regional issues related to food can be linked to its scarcity (hunger stemming from low socioeconomic status), overabundance, intolerance, and cultural taboos. Food is reported to be associated with symptom onset or exacerbation in a significant proportion of patients with FGIDs.

Cultural factors can impart positive or negative meanings to food (placebo or nocebo properties, respectively). There are several cultural aspects to food and eating, and

potential internal conflicts related to food ingestion that can lead to functional symptoms based on activation of neural circuits in the central nervous system.²⁹

Certain food types have religious connotations in some cultures and their consumption may be seen as sacrilegious, such as the eating of pork in Islam and Judaism.

Ethical issues related to food are relevant to some groups of patients. For example, there are strong advocates for the avoidance of meat consumption because of the cruelty of animal slaughter or procurement of food in ways that can damage the ecosystem.³⁰ Vegans avoid the use of animal or animal-derived products for nourishment, clothing, or any other purpose. Physicians should respect the ethical and religious beliefs of their patients when providing counsel on food and diet, and understand how potential breaches of these ethical and religious values may lead to the development of functional abdominal symptoms.

The Rome Foundation Working Group on the Role of Food in FGIDs recently published a series of evidence-based comprehensive reviews on the physiological changes associated with nutrient intake related to carbohydrates,³¹ fiber,³² protein,³³ and fats,³⁴ but information relating to cultural, ethnic and geographic differences still is lacking.

Food can be classified according to how it is perceived within culture groups, so physicians should be aware of the significance of different food types to individual patients. Often patients provide information on perceived associations between types of food and their digestive symptoms, leading physicians to prescribe a particular diet as part of the treatment.

Chinese, Hispanic, and Iranian populations³⁵ believe that diseases can be caused by an imbalance between hot and cold principles and, as such, classify diseases and foods in terms of their hot and cold characteristics. These classifications bear no relation to the actual temperature, but rather to related properties. For example, Puerto Ricans 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, and belladonna, for these diseases.^{36,37}

Traditional Chinese medicine (TCM) is completely different from Western medicine as we know it. Illnesses in TCM are categorized into 4 main syndromes (ie, cold syndrome, heat syndrome, deficiency syndrome, and excess syndrome). They then are differentiated further along the lines of yin and yang, qi and blood, and the viscera where the symptoms originate. Viscera, for example, the spleen or spleen-qi, is not the anatomic spleen, but rather an indication of digestive function. This is the case for the terms *liver* and *blood*, as well. TCM emphasizes diagnosis and treatment based on an overall analysis of the illness and the patient's condition, mostly based on the practitioner's experience over a long time in practice, so the diagnosis for one disease in TCM might be more than 10 syndromes.^{38,39} For example, the common distinguishing pattern for IBS with diarrhea is liver-qi stagnation and spleen-qi deficiency, which is considered a cold and deficiency syndrome. Ginger, one of the common subsidiary foods in Asian countries, is

considered to have a warm efficacy in TCM and usually is used to supplement prescription medicine. One survey found that 28% of Chinese IBS patients drink ginger soup (cooked with brown sugar and red dates) when their bowel symptoms get worse and 43.5% of them reported this to be effective in reducing symptoms.⁴⁰

Indeed, diet plays a crucial role in any treatment program in Chinese medicine. The Chinese verbs for "to eat" and "to take" (medicine) are the same. All food is believed to have medicinal value, and in ancient times court chefs were considered physicians. This primacy of nutrition in Chinese society may create a preferential labeling of adverse sensations as arising through meals rather than caused by bowel dysfunction.

Dietary habits in Asia vary widely between the different countries and analyses of possible associations between specific foods and IBS symptoms are lacking. There would appear to be a trend in Asian countries to Westernization, with increasing consumption of milk and dairy products. These may give rise to symptoms often associated with lactose intolerance, which ranges from 12.6% in Bangladesh to 70%–100% in other countries.^{41,42} IBS patients in the Middle East often are convinced that their abdominal symptoms are related to food and eating, whereas diet in Israel is associated with a prevalence of bloating and flatulence.

Italian patients with FGIDs often report food avoidance. Many patients avoid lactose or gluten in the belief they are intolerant of these food components.⁴³ This conduct is reinforced by the fact that General Practitioners also consider food allergies and/or food intolerance to be a probable cause of IBS.⁴⁴

In Eastern Europe, diarrhea and constipation in FGIDs are attributed to the type of food consumed, food intolerances and allergies, as well as nonfunctional conditions such as lactose intolerance and celiac disease, but epidemiologic data exist only for FD.⁴⁵

Recently, a blood test for food intolerance has become very popular in many South American countries. Patients are furnished with a list of foods to which they are intolerant, based on antibodies, and follow very strict elimination diets in accordance with the results, but without a documented reduction in gastrointestinal symptoms.

Physicians should be aware of the importance of cultural associations with food and eating because these play a central role in the patient's explanatory model of illness from the patient perspective. Cultural competency in the clinical setting should include recognition of the role of food and eating, including cultural aspects, and nutritional counseling should consider these factors.

Explanatory Models of Illness

Patients

Patients have symptom- or disease-related beliefs that affect their concerns, anxieties, and expectations of the health care process. This set of beliefs has been called the "explanatory model."⁴⁶ Cultural background, socioeconomic status, educational level, and sex are major factors that

contribute to the development of explanatory models.⁴⁷ These models provide a way of understanding patient perspectives in a health care setting. FGIDs, which have unclear etiologies, are more likely to be influenced by cultural factors than disorders that have a defined biological basis with clear-cut diagnostic criteria.⁴⁸ To achieve effective communication with patients, the physician should be cognizant of and adjust to the cultural background and perspective through which the patient views their illness. Elicitation of the patient's explanatory model can facilitate the complicated and often frustrating communication process between physicians and patients who have unexplained symptoms and chronic conditions.

Because the physician–patient relationship is a critical part of therapy in FGIDs it is important to understand the cultural background in which the patient's explanatory model developed and to negotiate a treatment partnership that will be effective within the context of patient and medical team beliefs and attitudes.⁴⁹

Barriers to the physician–patient relationship often are created by patient beliefs that may make the consulting process difficult. The inherent intricacy and multifaceted nature of the physician–patient encounter in this clinical setting may make it difficult for patients to convey their concerns during the consultation.⁵⁰ Some relevant questions from the patient's perspective are important to address: (1) What caused my sickness? (2) Why did I become sick at this time? (3) How does the illness work inside me? (4) What will happen to me? What will it do to me? and (5) How should it be treated?

Physicians

Physicians also develop explanatory models, primarily based on pathophysiology and the need to expedite the diagnostic process and provide effective therapy, as taught in medical school. These models also include several important elements: (1) etiology, (2) time and mode of onset, (3) pathophysiology, (4) course (including symptom severity and trajectory, ie, acute, chronic, impaired), and (5) recommended treatment.

There is an almost inevitable discrepancy or disconnect between the explanatory models of the physician and the patient. The physician is driven by the therapeutic imperative, that is, something has to be performed (tests, treatment, education, and reassurance), and the sooner the better.

An important culture-related skill for physicians is cultural competency, which is gaining in importance owing to the multicultural backgrounds of patients in clinical practices. Cultural competency includes overcoming any language barrier (linguistic competency) and an understanding of the cultural background from which the patient comes and within which he/she develops explanatory models of illness. All physician–patient encounters have the potential for cross-cultural misunderstanding. Issues that may lead to these misunderstandings and their unwanted consequences include differing or even conflicting attitudes relating to authority, physical contact, communication style, sex, sexuality, and family.⁴⁹ Important cultural issues related to the

religious significance involved in the contact and context of clinical encounters between doctors and patients must be considered. For example, male physicians should act with caution when examining Muslim female patients and, likewise, non-Muslim female physicians must be careful when examining Muslim men.

Clinicians should ask themselves whether cultural factors are liable to lead them to misunderstand a patient's history? By eliciting a patient's explanatory model, physicians have a better chance of understanding where the patient is coming from and how to foster and therapeutic relationship.

Practical Approaches to Cultural Issues Related to the Physician–Patient Relationship

Two scenarios can be presented in which cultural issues may become important in the physician–patient relationship: the physician represents the prevailing culture and the patient represents a distinct different culture, or the physician represents a minority culture and the patient represents the prevailing one. Physicians who are unaware of these issues or lack cultural competency might try to impose their values on patients, severely impairing the provider–patient relationship.

Recommendations that can lead to improved cultural competency in the clinical setting include the following: (1) be aware of cultural differences at the onset of the consultation (eg, is the patient from a different culture?), (2) assess whether the patient has or has not assimilated into the prevailing culture, (3) be aware of the patient's cultural beliefs and attitudes relating to physical contact (handshake, hug, touching of the head),⁵¹ (4) have respect for elderly patients and avoid making the consultation too informal at an early stage, and (5) respect cultural principles regarding eye contact.

Family Systems

Family relationships can have a significant effect on the illness experience of the patient. Family structures differ widely among geographic regions and cultural groups, from the extended family structure in developing countries, especially in rural areas, to the more typical nuclear family in developed countries. These differences can have an impact on how patients are supported and how relationships with health care providers are negotiated. Cultural belief systems regarding illness, which can affect the patient with FGIDs, are most clearly enacted and transacted within the family.

The family setting is particularly relevant to multicultural issues because family dynamics are the major site for transmission of cultural values, and family structure may vary considerably in different cultures. As stated by McGoldrick et al,⁵² "It is almost impossible to understand the meaning of behavior unless one knows something of the cultural values of a family." Even the definition of family differs greatly from group to group. The dominant American (Anglo) definition focuses on the intact nuclear family, whereas for Italians, family means a strong, tightly knit,

3- or 4-generational family that also includes godparents and old friends. African American families focus on even wider networks of kin and community and Asian families include all ancestors, going all the way back to the beginning of time, and all descendants, or at least male ancestors and descendants, reflecting a sense of time that is almost inconceivable to others.⁵²

Research has shown the relevance of conflict in intrafamily relationships, with it being among the most important risk factors for a variety of health outcomes and seeming to affect women more than men.⁵³

An international cross-cultural study of patients with IBS encompassing 8 geographic sites examined the relationship of symptom severity with family support or conflict.⁵⁴ Support and conflict were related significantly to symptom severity and the results indicated a global pattern rather than cultural differences in different locations. They also verified that the perception of family support was correlated with lower levels of symptom distress, whereas intrafamily conflict correlated with higher levels.

Within the family setting there are culturally based differences in health care and health care outcomes. For example, evidence from India suggests that men use the health care system more than women and that female subservience in rural areas can result in them being unable to access the health care system as much as the men.⁵⁵ This same form of male dominance also is observed in Pakistan.⁵⁶ In IBS epidemiology studies in Israel involving subpopulations,^{57–59} an attempt to survey the adult Israeli Arab population by telephone was unsuccessful because the women were not permitted to answer telephone calls and, therefore, could not respond to survey questions.

Parental, in particular maternal, attitudes regarding physical distress are likely to vary with culture. Research in Japan showed that Japanese mothers are more attentive to their children's complaints compared with mothers in the United States, so solicitous behavior in Japan would be considered normative and not problematic, while it might be considered contributive to the development of IBS in the United States.⁶⁰

Gerson and Gerson⁶¹ showed that family inclusion in IBS patient treatment programs varied considerably between different cultures, depending on factors such as gender norms, nuclear or extended family structure, and openness to exploration of relationship difficulties. Based on these observations, they incorporated a family systems perspective in a group treatment program for IBS patients.

Physicians should be open to diverse narratives. Patients and families who believe that their doctor attends to and respects their symptoms and complaints are more likely to be open to medical recommendations.

Local Biologics

Complex environmental and biological factors interact with patients' explanatory models of illness, sex, and family systems. These also can affect the way in which patients interpret and report symptoms and adhere to treatment recommendations.

In recent years, biological factors such as low-grade inflammation, immune activation, the gut microbiota, and genetic differences have gained importance in relation to FGIDs and theories as to their pathophysiology. These factors also may be affected by culture, ethnicity, and geographic region. In addition, environmental aspects such as climate, water composition, and psychosocial stressors may affect sociocultural issues in FGIDs.

Genetics

Genes and culture often are thought of as being at opposite ends of the nature-nurture spectrum but there are relevant interactions.⁶² Different genes associated with FGIDs have been studied. Those linked to serotonin metabolism, such as the hydroxytryptamine transporter (*5-HTT*) gene, provide interesting indications for sociocultural issues and gene-environment interactions.

Polymorphisms in the *5-HTT* linked promoter region and their effects on the expression and function of *5-HTT* have been linked to patient emotional behavior and vary in frequency in different races and ethnicities. These polymorphisms also are reflected in the effectiveness of selective serotonin reuptake inhibitors. A high response rate to selective serotonin reuptake inhibitors has been reported in Caucasian and Japanese populations,^{63,64} whereas a higher percentage of nonresponders has been seen in African American people.⁶⁵

Microbiota, Postinfection IBS, and Small Intestine Bacterial Overgrowth

The Rome Foundation Working Team on Intestinal Microbiota reviewed associations between FGIDs and the intestinal microbiome.⁶⁶ The importance ascribed recently to intestinal microbiota comes from a growing recognition of its association with alterations in digestive system function and brain-gut interactions. However, little is known worldwide about variations in the composition and function of the human gut microbiome, and even less in relation to IBS and other FGIDs. Arumugam et al⁶⁷ identified 3 robust clusters of bacteria in individuals from 4 countries, called *enterotypes*. They showed that these enterotypes are neither nation- or continent-specific, nor dependent on individual host properties such as body mass index, age, or sex. Nonetheless, the enteric microbiota may be related to phenotypic manifestations of FGIDs, as well as to the psychological reactions of patients.⁶⁸

De Filippo et al⁶⁹ compared the fecal microbiota composition of children from urban Florence, Italy, and from a rural area of Burkina-Faso in Africa. The investigators detected a significant difference in intestinal microbiota composition for these 2 populations, which was attributed to the marked difference in eating habits, among other factors. These differences can have a significant effect on gut function and brain-gut interaction.

Postinfection IBS (PI-IBS) is a typical example of how one episode of intestinal infection, with its alteration of intestinal microbiota, can bring about lasting changes in both

intestinal function and central mechanisms of pain perception. Nevertheless, no evidence exists to indicate that developing countries with higher rates of intestinal infection have a higher incidence of PI-IBS. For instance, the population-based prevalence of IBS in Mexico is 16%, whereas the prevalence of PI-IBS is 5%, which is low compared with other parts of the world.⁷⁰

Environmental Hygiene

The hygiene hypothesis contends that the high prevalence of IBS in the West may be related, at least in part, to a lack of exposure to enteric pathogens in early life, whereas early exposure in underdeveloped countries may protect in adulthood against the development of this disease.²¹ This does not explain the high prevalence of IBS in countries where infections remain common.²¹ Hygienic conditions across regions, often associated with socioeconomic status, may have a differential impact on the risk of developing PI-IBS.⁷¹

Immunologic Factors: Cytokines

Recent evidence has supported abnormalities in immune regulation and/or immune activation in IBS.⁷² Proinflammatory (tumor necrosis factor [TNF]- α , interleukin [IL] 1 β , IL6, and IL8) and anti-inflammatory (IL10) cytokines are among those most studied, but findings on their association with IBS are inconsistent.⁷³ Serum/plasma levels of TNF- α tended to be higher in IBS vs controls and reached significance in IBS subtypes vs controls and in female IBS patients in different countries, such as Sweden, Turkey, China, India, Mexico, and the United States. However, studies from Ireland reported either no difference or even a decrease in TNF- α circulating levels in IBS patients, resulting in considerable heterogeneity in the meta-analysis of TNF- α levels.⁷⁴

Cytokines are determined genetically. A recent systematic review and meta-analysis assessing TNF- α (-308 G/A) polymorphisms, IL10 (-1082 G/A), and transforming growth factor- β 1 (+869 T/C and +915 G/C) in IBS patients and controls in 5 studies from Holland, Turkey, Iran, India, and Korea,⁷⁴ found no overall associations between TNF- α (-308 G/A) genotypes in IBS. Conversely, a study in Asia showed an association between TNF- α genotypes (-308 G/A and G/G) and IBS, whereas results from a Mexican study were negative.⁷⁵ However, low producers of IL10 were more frequent in diarrhea-predominant IBS vs constipation-predominant IBS and IBS-mixed in this population.⁷⁵

These results from around the world suggest once again that biological factors, such as genetic characteristics, may influence differences in cytokine levels between IBS patients and controls in different populations. At the moment these impressions should be qualified by 2 other possible explanations for the conflicting results: (1) most studies are not large scale and may be relatively small to determine genotype differences, and (2) genetic allele frequency for some genes show that the major allele in one race (eg, Caucasians) is the minor allele in another race (eg, Asian).

Treatment

Some treatment modalities are affected significantly by region and culture. One example is CAM. The National Center for Complementary and Alternative Medicine⁷⁶ in the United States defines CAM as health care approaches developed outside of mainstream Western or conventional medicine. CAM use is widespread throughout the world and possibly increasing over time. The type and prevalence of CAM use varies greatly from country to country. In Western countries, CAM use is generally more common among females, young and middle-aged adults, and patients with a higher educational attainment and larger household income.⁷⁷⁻⁷⁹ In urban Nigeria, by contrast, males and patients with lower income are more likely to use CAM.⁸⁰ Patients generally use CAM in conjunction with conventional medicines, but many people fail to inform their conventional health care providers about this use.

Intercountry comparisons are hindered by definitions. What is defined as CAM in one country may be considered relatively mainstream in another. Most studies on CAM relate to its use in holistic medical care. Only a few specifically addressed gastroenterologic conditions, and even fewer considered FGIDs.

Research in the United States showed that the most commonly used CAM methods include the consumption of ginger, and use of massage therapy and yoga. CAM use was associated with female sex, younger age, college education, anxiety, depression, somatization, and impaired quality of life. Satisfaction with physician care was not a predictive factor for its use, and patient willingness to use conventional medical care was not reduced.⁸¹

Recommendations for CAM by health care providers reflect their belief in the efficacy of this treatment modality and its place in the social environment in which they live. Physicians in Western societies should become more familiar with the various types of CAM, their effectiveness, and side effects. It should be noted that different cultures and countries have different perspectives as to what comprises CAM treatment. For example, probiotics and prebiotics may be considered a component of conventional care in one country or culture, and a CAM treatment in another.

Culture, Ethnicity, and Health Care Outcomes

Belief refers to the attitude we have whenever we take something to be the case or regard it as true. The interaction between culture, beliefs, and health affects the quality of health care and health outcomes. Often the importance of cultural factors goes unrecognized, and in clinical practice this can result in poor health outcomes. Culture and ethnicity may affect the diagnostic process and health outcomes. Patient ethnicity exerts an enormous effect on both diagnostic studies and medications prescribed by doctors.⁸ The social circumstances of the doctor and patient cast a large shadow on treatment. Notions about the patient's needs for medication may be tied more to ethnicity than to illness per se.^{8,9}

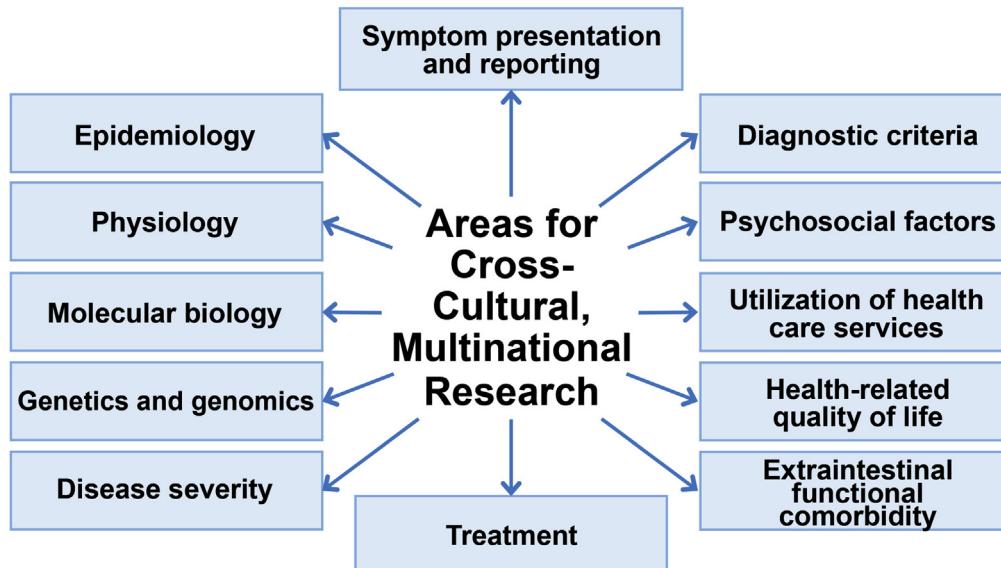


Figure 3. Cross-cultural, multinational research has tremendous potential and can be applied to almost all aspects of FGIDs from basic research to epidemiology to psychosocial comorbidity to drug trials. In all cases, cross-cultural research competence is of the essence.

Some population subgroups, including ethnic groups, are more likely to receive suboptimal health care than others.¹⁰ The concept of health literacy has been coined to describe the skills required to function in the health care environment.⁸² Many individuals from some cultural subgroups do not have these skills and function with a handicap within the health care system. Limited literacy ability, particularly in a second language, may lead to difficulty in understanding diagnoses, discharge instructions, and treatment recommendations.

Differences in Health Care Services and Their Impact on FGIDs

Variations in health care provision around the world may affect how patients with FGIDs are investigated, diagnosed, and managed. Prompted by the lack of global information, the Rome Foundation's Working Team on multinational, cross-cultural research in FGIDs recently addressed this issue. It identified 7 key elements in this regard: (1) coverage afforded by the different health care systems/providers; (2) level of the health care system where patients with FGIDs are treated; (3) extent and types of diagnostic procedures typically undertaken to diagnose FGIDs; (4) physician familiarity with implementation of the Rome diagnostic criteria in clinical practice; (5) range of medications approved for use in FGIDs and the approval process for new agents; (6) costs involved in treating FGIDs; and (7) prevalence and role of CAM in FGIDs. The study was conducted in 4 countries (Italy, India, Mexico, and South Korea), and resulted in the following findings: (1) large variations exist between different countries in access to good quality medical care; (2) it would appear that although the Rome diagnostic criteria are well accepted in Italy, Mexico, and South Korea, a substantial number of physicians, especially general practitioners, do not use them in clinical practice; (3) antispasmodics, osmotic agents, and

laxatives are universally available and regularly prescribed in the 4 countries; (4) CAM is used in many places for FGIDs—in some regions it is part of the accepted health care system (eg, India); and (5) there are differences in the health care burden of FGIDs because medications for FGIDs are not covered by public health care services.⁸³

The Conduct of Cross-Cultural, Multinational Research on FGIDs

Cross-cultural, multinational research has the potential to advance the field of FGIDs at many levels. In addition to FGID prevalence studies, cross-cultural comparative research can make a significant contribution in genetics, psychosocial modulators, symptom reporting, symptom interpretation and symptom presentation, extraintestinal comorbidity, diagnosis and treatment, determinants of disease severity, health care infrastructures, health care utilization, and health-related quality of life, all issues that can be affected by culture, ethnicity, and race.

Establishing Cross-Cultural Research Networks and Fostering Cross-Cultural Research

Appropriate strategies should be established that allow researchers from different nations and cultures to work together on common projects. A recent publication of the Rome Foundation Working Team discussed ways of fostering multinational research networks.⁸⁴

Conclusions and Suggestions for Future Directions

Cross-cultural factors in FGIDs are of great importance, but remain mostly under-recognized in clinical practice and research. The development of cross-cultural competency in

clinical practice is of particular importance in the treatment of disorders such as FGIDs because they are poorly understood and have an unclear etiology, prognosis, and clinical course. The development of cross-cultural competency in basic, clinical, and translational research and the conduct of fruitful multinational, cross-cultural research can make a major contribution to our understanding of biological and psychosocial factors that underlie these disorders, and can facilitate their effective management (Figure 3).

Supplementary Material

Note: The first 50 references associated with this article are available below in print. The remaining references accompanying this article are available online only with the electronic version of the article. To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <http://dx.doi.org/10.1053/j.gastro.2016.02.013>.

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Conflicts of interest

The authors disclose no conflicts.

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