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# INTRODUCTION

## Disorders of Gut–Brain Interaction and the Rome V Process



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**Disorders of gut–brain interaction (DGBI) are characterized by gastrointestinal symptoms related to any combination of motility disturbance, visceral hypersensitivity, altered mci function, altered gut microbiota, or altered central nervous system processing. Research on and clinical management of DGBI is based on selective diagnostic criteria, generated through the Rome Foundation. The Rome V process generated a broad overview of the knowledge accumulated since Rome IV was published 10 years ago, with a focus on evidence-based adjustments. It builds on (1) an update of the DGBI definitions based on the latest basic and clinical literature; (2) offering new information on the role of diet, gut microenvironment, gut–brain interactions, pharmacogenomics, biopsychosocial, gender and cross-cultural factors; (3) reducing the use of imprecise or stigmatizing terms; (4) generating updated diagnostic algorithms; (5) incorporating information on the patient illness experience and sociocultural aspects; and (6) updating the therapeutic approaches to DGBI.**

*Keywords:* Disorders of Gut–Brain Interaction; Diagnostic Criteria; Rome Criteria; Brain–Gut Axis; Functional Gastrointestinal Disorders; Functional Dyspepsia; Irritable Bowel Syndrome; Chronic Constipation.

Disorders of gut–brain interaction (DGBI), previously referred to as functional gastrointestinal disorders (FGID), have been poorly understood historically. Although providers have observed these symptoms in their patients for hundreds of years, standard diagnostic capabilities have only emerged in the past several decades through the Rome criteria, moving from a simplistic and reductionist view to a more comprehensive biopsychosocial model.[1,2] Initially viewed primarily as motility disorders, scientific understanding has shifted to encompass broader disturbances in neurogastroenterology,[3] alterations in gastrointestinal (GI) microbiota and immune activation, and reactions to food—all acting through brain–gut interactions.[4] These advancements have validated DGBI for patients and health care providers and have catalyzed research efforts for new treatments. Yet there remains a mismatch between the high prevalence and clinical burden of DGBI, the limited attention DGBI receive in clinical practice, and the poor representation of DGBI in medical school and training curricula.[5,6]

Established in the early 1990s, the Rome Foundation has been instrumental in transforming the understanding and management of DGBI. The Foundation gathered global experts to collaborate on research and education, and to develop criteria and guidelines by consensus (ie, Delphi approach).[7,8] This elevated the status of DGBI within the gastroenterology field, promoting acceptance and legitimacy. A key achievement was the shift from a diagnosis by exclusion to a standardized positive diagnostic approach,[9] which facilitated the development of clinical trials and furthered research efforts. In addition, the Foundation has played a pivotal role in disseminating knowledge through worldwide educational programs and research studies.

Since Rome IV was published in 2016[4,10] science has evolved and now is the time to introduce an enhanced global conceptualization of DGBI with updated diagnostic criteria and guidelines incorporating critical advancements in the pathophysiology of DGBI and detailing new treatment recommendations.

## Definition of Disorders of Gut–Brain Interaction

The older name—functional gastrointestinal disorders—was replaced in 2016 because the term "functional" was

***Abbreviations used in this paper:*** **CNS, central nervous system; DGBI, disorders of gut–brain interaction; ENS, enteric nervous system; FGID, functional gastrointestinal disorders; GI, gastrointestinal; IBS, irritable bowel syndrome; PDS, postprandial distress syndrome.**

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attributed to being "nonorganic" or psychiatric, and even illegitimate. This perception stems from historical dualistic principles that distinguish between "organic" disorders, considered tangible, and "functional" disorders, which are poorly understood and often labeled as psychiatric.[11] The understanding of DGBI has shifted over the years from the absence of organic disease viewed as psychosomatic to disorders of GI function and dysregulation of the gut–brain axis.[11]

Moving from FGID to DGBI relied on a Delphi method,[7,8] which fosters a team effort to produce consensus using iteration and feedback to answer complex questions not easily addressed by traditional inquiry. The Rome Foundation used the Delphi method to develop the original classification more than 35 years ago.[12] This approach was used in 2016 to define DGBI in a positive and nonstigmatizing way, reflective of scientific progress.[4] The agreed-upon definition (Table 1) is consistent with the evolving understanding of multiple pathophysiological processes that determine DGBI. We believe this definition is understood and readily acceptable to clinicians, academicians, regulatory agencies, the pharmaceutical industry, and patients.

## Rome IV Classification and Criteria for Disorders of Gut–Brain Interaction

The classification system of DGBI was originated more than 35 years ago by a committee that reviewed clinical and epidemiologic data from patient and nonpatient populations.[12] Moving from a physiological (motility-based) classification to a symptom-based approach was a paradigm shift for the field. Several factors prompted this change, including the recognition that symptoms are central to patient presentation; the lack of availability of motility laboratories and insufficient explanation of symptoms by motility findings; and the practical reality that symptoms are what drive patients to seek health care providers.

The classification of DGBI according to organ regions assumes these anatomic areas have specific cohesive features underlying diagnosis and management. However, simply localizing symptoms is insufficient, as certain DGBI, particularly those characterized by predominant pain, are less straightforward to localize. These conditions are influenced by broader systemic factors stemming from dysregulation within the central nervous system (CNS)–enteric nervous system (ENS) axis, affecting pathways that control symptom perception and regulation.[13]

Moreover, DGBI exhibit several common physiological features, such as altered motor control, visceral hypersensitivity, changes in mucosal immune and inflammatory function, bacterial dysbiosis, altered reactions to nutrients, and alterations in CNS-ENS regulation influenced by psychosocial and sociocultural factors. The relative importance of these factors may vary depending on the location of symptoms and their duration, and can differ among individuals or within the same individual over time.

Although the classification system remains crucial for categorizing DGBI, effective management necessitates a comprehensive biopsychosocial approach that accommodates the variability and complexity observed in patients with these conditions. These clinical, psychosocial, and physiological modifiers are addressed in the multidimensional clinical profile (see below).

Table 2 lists the 34 adult and 22 pediatric DGBI for Rome V. Some additions and modifications were made based on recent scientific evidence that will be discussed.

**Table 1.** Definition of the Term Disorders of Gut–Brain Interaction

| Term | Definition |
|---|---|
| Disorders of gut–brain interaction | A group of disorders characterized by GI symptoms related to any combination of:<br>Motility disturbance<br>Visceral hypersensitivity<br>Altered mucosal and immune function<br>Altered gut microbiota<br>Altered CNS processing |

## The Rome V Content

The educational materials of Rome V encompass several components, which are produced in printed books and also compiled online. The details of these are summarized in section A of the Supplementary Material. These collectively result in a broad knowledge base and support a comprehensive biopsychosocial approach to understanding, diagnosing, and treating DGBI, ensuring relevance across diverse clinical and cultural contexts.

## The Rome V Process

Since the first Rome consensus in the 1980s,[14] availability of, and access to, scientific information on distinct patient groups with DGBI has grown tremendously. With Rome IV (2016),[4,10] there was already a major shift toward requiring evidence-based information to modify or create new criteria, using consensus only where empirical evidence was lacking. With Rome V, an even more stringent process of prospective and retrospective data gathering, synthesis, and presentation was used. Recommendations from support committees and other Rome working teams were reviewed extensively. The development of Rome V spanned 7 years, from 2019 when the Rome Foundation Board of Directors selected Doug Drossman and Jan Tack as co-senior editors, to 2026 when Rome V was published. A detailed overview of the process is found in section B of the Supplementary Material.

**Table 2.** Overview of Rome V Disorders of Gut–Brain Interaction

| Overview |
|---|
| A. Esophageal disorders |
| A1. Functional chest pain |
| A2. Functional heartburn |
| A3. Reflux hypersensitivity |
| A4. Globus |
| A5. Functional dysphagia |
| B. Gastroduodenal disorders |
| B1. Functional dyspepsia |
| B1a. PDS |
| B1b. Epigastric pain syndrome |
| B2. Nausea and vomiting disorders |
| B2a. Chronic nausea vomiting syndrome |
| B2b. Cyclic vomiting syndrome |
| B2c. Cannabinoid hyperemesis syndrome |
| B3. Belching disorders |
| B3a. Supragastric belching |
| B3b. Gastric belching |
| B3c. Inability to belch syndrome |
| B4. Rumination syndrome |
| C. Bowel disorders |
| C1. IBS |
| C1a. IBS with predominant constipation |
| C1b. IBS with predominant diarrhea |
| C1c. IBS with mixed bowel habits |
| C1d. IBS unclassified |
| C2. Chronic constipation |
| C3. Functional diarrhea |
| C4. Functional abdominal bloating |
| C5. Unclassified bowel disorders |
| C6. Opioid-induced constipation |
| D. Centrally mediated disorders of GI pain |
| D1. Centrally mediated abdominal pain syndrome |
| D2. Abdominal migraine |
| D3. Narcotic bowel syndrome/opioid-induced GI hyperalgesia |
| E. Gallbladder and SOD disorders |
| E1. Biliary-type abdominal pain |
| E2. Dysfunctional gallbladder disorder |
| E3. Biliary SOD |
| E4. Pancreatic SOD |
| F. Anorectal disorders |
| F1. Fecal incontinence |
| F2. Anorectal pain disorders |
| F2a. Levator ani syndrome |
| F2b. Unexplained anorectal pain |
| F2c. Proctalgia fugax |
| F3. Dyssynergic defecation |
| F4. Anorectal sensory dysfunction disorders |
| F4a. Rectal hyposensitivity |
| F4b. Rectal hypersensitivity |
| G. Pediatric upper DGBI |
| G1. Esophageal disorders |
| G1a. Reflux hypersensitivity |
| G1b. Reflux-negative esophageal pain disorder |
| G1c. Disorders of esophageal air transit |
| G1c.i. Aerophagia syndrome |
| G1c.ii. Supragastric belching syndrome |
| G2. Functional pediatric feeding disorders |
| G2a. Hypersensitive dysphagia |
| G2b. Anticipatory restrictive feeding |
| G2c. Hunger dysregulation feeding disorder |
| G2d. Medically triggered functional feeding disorder |
| G3. Gastroduodenal disorders |
| G3a. Rumination syndrome |
| G3b. Cyclic vomiting syndrome |
| G3b.i. Cannabanoid hyperemesis syndrome |
| G3c. Chronic nausea syndrome |
| G3d. Functional dyspepsia |
| G3d.i. PDS |
| G3d.ii. Epigastric pain syndrome |
| H. Pediatric lower and biliary DGBI |
| H1. Abdominal pain disorders |
| H1a. Irritable bowel syndrome |
| H1b. Abdominal pain syndrome– not otherwise specified |
| H1c. Biliary pain syndrome |
| H1d. Abdominal migraine |
| H1e. Centrally mediated abdominal pain syndrome |
| H2. Defecation and anorectal disorders |
| H2a. Functional constipation |
| H2b. Nonretentive fecal incontinence |
| H2c. Infant dyschezia |
| H2d. Proctalgia fugax |
| H2e. Functional diarrhea |
| H3. Discomfort disorders |
| H3a. Functional abdominal bloating |
| H3b. Infant distress syndrome |

SOD, Sphincter of Oddi.

## Limitations for Using Standard Rome Criteria for Diagnosis and Management in Clinical Practice and Efforts to Reconcile Them

The Rome classification system relies on criteria allowing a reliable categorical diagnosis. This is of particular value for clinical research and pharmaceutical trials because it provides a clearly defined and sufficiently symptomatic cohort, allowing us to gather new knowledge and evaluate treatments reliably. This diagnostic classification system has been approved by regulatory agencies and used by investigators and pharmaceutical companies for clinical trials around the

world. However, there are limitations to using these criteria in clinical practice, as discussed below.

### Subdiagnostic Groups

Although meeting predefined Rome criteria establishes a legitimate diagnosis to use in patient education and clinical and treatment trials, there are patients in clinical practice who have symptoms but do not fully meet the Rome criteria. These patients may still need to understand what they have and to be treated. An extensive study of a worldwide population of >50,000 individuals found that 41.4% met the Rome criteria for at least 1 DGBI and 33.4% had no GI symptoms.[15] Notably, the remaining one-fourth, categorized as a subdiagnostic group, had GI symptoms but did not meet the Rome criteria for a DGBI diagnosis. This subdiagnostic group had significantly poorer health-related quality of life and higher scores for anxiety, depression, health care utilization, and life and work impairment compared with the population who had no GI symptoms. Thus, there is a sizeable portion of the population with GI symptoms affecting their lives but who are overlooked in research and clinical care because they do not meet standard Rome criteria. These patients must still receive diagnostic evaluation when clinically needed and be appropriately treated based on the symptom burden.

### Symptom Patterns Involving More Than One Anatomic Area

The Rome classification for DGBI comprises diagnostic entities that are attributed to anatomic regions, and this is supported by factor analysis of Rome diagnostic questionnaires.[16,17] However, adding additional questions on the relationship to physiological events, such as food intake or bowel movements, allows us to identify symptomatic entities involving more than 1 anatomic area.[18] In view of the limited available data, the current Rome criteria do not include any of these entities, and clinically they may also be considered as overlapping DGBI.

### Multiple Overlapping Disorders of Gut–Brain Interaction

In clinical practice, patients often present with 2 or more DGBI diagnoses involving different regions of the GI tract. In a cross-sectional general population study of 5931 adults in 3 countries, 35% met the Rome criteria for 1 DGBI, and more than one-third of this group had a co-occurrence of 1 or more other diagnoses involving different anatomic regions.[19] A higher number of co-occurrences was associated with poorer mental and physical quality of life, and more medical treatments and abdominal surgeries. For clinical studies, especially clinical trials, investigators will often exclude these patients so as not to confound the study results. Yet, the number of symptoms has an additive impact on the patient's symptom severity, quality of life, and psychosocial impact, which must be addressed in clinical practice. Patients with multiple overlapping DGBI may require special attention to management using a biopsychosocial approach.

## Rome Clinical Criteria

In an effort to address these issues, and with the approval of the Rome Foundation Board of Directors, we revised the standard Rome criteria into clinical criteria for use in practice, as summarized in Table 3. The Rome clinical criteria can be used to diagnose patients and justify treatment of patients with subdiagnostic or co-occurring symptoms.[20]

The clinical criteria presume that the frequency and duration of the GI symptoms are not as relevant in a clinical context as in research studies. In clinical practice, the provider can use interview skills and make judgments as to whether to order diagnostic studies to rule out other disorders. Furthermore, in clinical practice, the criterion of bothersomeness addresses the impact of the symptoms on the patient. Bothersomeness indicates that the symptoms are sufficient to interfere with life activities or affect the decision to seek health care.[20] Thus, clinical criteria for a diagnosis is fulfilled when organic disease is sufficiently ruled out, the patient's symptoms meet the qualitative features of the Rome V criteria (ie, the nature and quality of symptoms), and the patient and provider judge the symptoms to be sufficiently bothersome. In such case, the frequency and duration criteria can be eliminated or reduced. We recommend the use of the Rome clinical criteria over the standard Rome V research criteria in clinical practice, to attend to the larger cohort of patients in need of management.

### Using Diagnostic Algorithms to Achieve Disorders of Gut–Brain Interaction Diagnoses

Although the Rome V diagnostic criteria help to characterize the DGBI diagnosis, the symptoms may not be

**Table 3.** Rome Foundation Clinical Criteria for Disorders of Gut–Brain Interaction

| Criteria | Description |
|---|---|
| Qualitative symptom criteria | The qualitative features of the Rome V Diagnostic Criteria must be met |
| Bothersomeness | Sufficiently bothersome symptoms to seek medical care or interfere with daily activity and quality of life |
| Frequency criteria | A frequency lower than the traditional criteria threshold is permitted provided |
| Duration criteria | The Rome V 6-mo duration is not required. We suggest an 8-wk duration to exclude other diagnoses. Exceptions are:<br><br>When the clinician is satisfied that medical evaluation excludes other disorders or Infrequent symptom episode disorders (eg, cyclical vomiting syndrome and proctalgia fugax) |

specific enough to exclude other diagnoses. To address this issue, all Rome V clinical criteria chapter committees have generated diagnostic algorithms for each DGBI. These provide a pathway of evaluation based on a stepwise assessment of the symptom profile, consideration of associated symptoms or conditions, and selected technical examinations that guide the clinician to a Rome V DGBI diagnosis, while excluding other disorders with similar symptoms. This is published in the 3rd edition of *Rome V Diagnostic Algorithms for Common GI Symptoms*.

### *Multidimensional Clinical Profile*

We also recognize that a diagnosis *per se* does not capture the full dimensionality of the patient's clinical condition to adequately determine treatment. The severity and impact of a DGBI involve multidimensional constructs.[21,22] To address these limitations in classification, the Rome Foundation developed the Multidimensional Clinical Profile approach for clinicians to individualize management based on identifying and integrating the multiple components (ie, psychosocial, clinical, physiological, quality of life, and impact aspects) of the symptom experience.[23,24] The Multidimensional Clinical Profile concept is published separately in its 4th edition, and it allows us to capture the full dimensionality of the patient's illness and to better target biopsychosocial treatment.

## Changes for Rome V

What follows are some of the important changes in the content and classification of DGBI for Rome V since the publication of Rome IV. Due to its rapid acceptance, the term "disorders of gut–brain interaction" entirely replaced "functional gastrointestinal disorder" for Rome V. The additions and changes that follow were made on the basis of new evidence and by means of consensus when evidence alone was insufficient.

1. Replacement of "functional gastrointestinal disorder" with "disorders of gut–brain interaction" and removal of "functional" in Rome diagnoses. When Rome IV was published in 2016,[4,10] we introduced "disorders of gut–brain interaction" to replace "functional gastrointestinal disorder," making it more scientifically accurate and reducing stigma, although both terms were acceptable. Due to the wide acceptance of DGBI, we recommend that the term "functional gastrointestinal disorder" no longer be used. Furthermore, the Rome V committees sought to remove the term "functional" in the Rome V diagnoses when possible, but some diagnoses retained the term "functional" because the committees were unable to find suitable alternatives. We believe these changes help to facilitate the legitimacy, understanding, and acceptance of DGBI in medicine.

2. The addition of new diagnoses. With each new Rome edition, the chapter committees add new disorders through clinical experience, review of the literature, and consensus. These recommendations are submitted to the Editorial Board for approval. The new adult diagnoses for Rome V include:

   a. Inability to belch syndrome (category B3c) has been added to the gastroduodenal disorders based on epidemiologic, mechanistic, and treatment studies. several recent studies have established that this disorder, also referred to as "retrograde cricopharyngeal dysfunction," is commonly encountered in clinical practice, with a variable symptom presentation. In addition, the diagnosis can be confirmed by esophageal impedance manometry with sparkling prowater provocation, and successful treatment with botulinum toxin injection in the upper sphincter has been demonstrated.[25]

   b. Abdominal migraine (category D2) is added to the centrally mediated disorders of GI pain. This diagnosis, initially described in the pediatric population and with Rome pediatric criteria existing since Rome II, is increasingly recognized in adults. The rationale for adding this diagnosis to the centrally mediated pain chapter rather than the bowel chapter relates to its well-recognized feature of episodic abdominal pain with symptom-free intervals and no bowel dysfunction.

   c. Anorectal sensory dysfunction disorders (F4), which include rectal hyposensitivity (F4a) and rectal hypersensitivity (F4b) has been added to the anorectal disorders. Although previous Rome anorectal diagnoses focused on rectal pain and motility disturbances, including fecal incontinence and dyssynergic defecation, these new diagnoses address abnormalities in rectal sensation leading to decreased urge to defecate, straining and digital maneuvers to evacuate, or increased urge to defecate, associated with prolonged or frequent toilet times, respectively. Given that rectal sensitivity testing is available to help in the diagnosis, and biofeedback and balloon sensory training are used in treatment, the inclusion of these categories is rational for clinical practice and research.

3. The pediatric classification system has been revised to include upper DGBI and lower DGBI. In Rome III and IV, the childhood pediatric disorders included neonate/toddler disorders (birth to age 4 years) and child/adolescent disorders (age 5 years through adolescence). However, as more epidemiologic, mechanistic, and intervention studies were conducted using Rome IV pediatric criteria, it became apparent that DGBI in children follow a pattern based on an anatomic division, similar to that in adults. The initial classification of pediatric disorders based on age, although anchored in developmental characteristics, was arbitrary and not based on physiological or pathophysiological evidence.

After careful consideration, iteration, and consensus, the committees decided to reclassify pediatric DGBI based on anatomic regions, incorporating necessary developmental aspects within each proposed criterion. The new classification includes many new diagnoses for upper GI DGBI (category G) and lower GI and biliary DGBI (category H), as shown in Table 2.

4. Chapter modifications. To address the new scientific data since Rome IV, we have modified several chapters.

   a. Patient Experience, Gender, Age, Race, and Social Determinants of Health now replaces the previous Age, Gender, and Women's Health and the Patient, putting the patient at the forefront. This update includes additional content and data on the impact of DGBI on the lesbian, gay, bisexual, transgender, and queer community and offers considerations for clinicians treating lesbian, gay, bisexual, transgender, and queer patients. It also provides a more in-depth analysis of life stages and aging, including pregnancy, menopause, and the effects of gender hormones on symptom severity and quality of life. Updated information is presented on how stigma, trauma, age, race, and income inequality affect DGBI symptom severity, health care–seeking behavior, and access to care.

   b. The committee for Esophageal Disorders has synchronized the Rome and Lyon consensuses to provide a modern definition of gastroesophageal reflux disease and DGBI in the esophagus. It also introduces the mean nocturnal baseline impedance as a metric for mucosal permeability alterations in gastroesophageal reflux disease and uses the Chicago Classification, Version 4.0, with criteria for esophagogastric junction outflow obstruction. Finally, it introduces the concept that the functional lumen image probe may uncover abnormalities not identified with manometry.

   c. The committee for Gastroduodenal Disorders has continued to build on the concepts of postprandial distress syndrome (PDS) and epigastric pain syndrome that were launched with Rome III and expanded in Rome IV. In Rome V, the committee aimed to define these conditions as well as the nausea and vomiting disorders more distinctly to obtain clearer, separated entities. The postprandial symptom pattern of PDS is now more explicitly defined, and using a hierarchical stepwise diagnostic approach algorithm, PDS is separated from both epigastric pain syndrome and nausea and vomiting disorders. For cyclic vomiting syndrome and cannabinoid hyperemesis syndrome, timing of symptoms and intervals was specified based on more recent cohort studies. The entities of rumination syndrome and supragastric and gastric belching were maintained and, as indicated above, the inability to belch syndrome was added.

   d. The committee for Bowel Disorders has made the following changes:

      i. Irritable bowel syndrome (IBS):

         1. Abdominal discomfort is reincluded in the diagnostic criteria after having been removed in Rome IV. This inclusion relates to the evidence that patients in certain countries can experience discomfort without pain when diagnosing IBS.

         2. Regarding the time frame, abdominal pain or discomfort must be present at least 3 days per month in the last 3 months compared with 1 day per week during the previous 3 months for Rome IV. This change relates to the drop in prevalence of IBS from approximately 10% to 4%. The Rome Foundation global epidemiology study found that this drop related to a higher frequency threshold for pain, thereby defining a population that is more severe and not consistent with what is seen in clinical practice.

         3. Abdominal pain and discomfort should not be continuous. The addition of this criterion differentiates IBS from centrally mediated abdominal pain, where the pain is continuous.

      ii. "Chronic constipation" has replaced "functional constipation" from Rome IV, as discussed above, to remove "functional."

      iii. "Functional abdominal bloating" has replaced "functional abdominal bloating and distention" from Rome IV because bloating is the DGBI symptom, and distention co-occurs with bloating without adding further diagnostic value.

      iv. "Unclassified bowel disorders" has replaced "unspecified bowel disorders" from Rome IV because it more accurately reflects that these individuals do not meet other diagnoses.

   e. The committee for Centrally Mediated Disorders of Gastrointestinal Pain

      i. Has added "abdominal migraine" as a new diagnosis (see above).

      ii. Modified centrally mediated abdominal pain syndrome to include 2 subcategories that are associated with continuous pain. Category A is retained from Rome IV where the pain is not associated with physiological events, and category B defines that the pain may be modified by physiological events (worsening pain after eating or relief with defecation) but the pain still retains its continuity, thereby differentiating it from other disorders, like IBS, where pain is intermittent. This was determined by evidence that category B is 5 times more common in epidemiologic and clinical

studies, and yet the diagnostic and treatment approaches are the same as with category A. Therefore the new category B identifies a new cohort of patients not previously categorized but much more common than Rome IV centrally mediated abdominal pain syndrome.

f. The committee for Gallbladder and Sphincter of Oddi Disorders has clarified and simplified the definition of typical biliary pain, making it easier to diagnose. For dysfunctional gallbladder disorder, the new definition of typical biliary pain is considered specific enough to preclude the previous recommendation for performing cholescintigraphy to identify a low gallbladder ejection fraction. The committee believed that typical biliary pain strongly outperforms cholescintigraphy as a predictor of response to surgical resection. Furthermore, they recommended a period of watchful waiting rather than surgery to reduce unneeded cholecystectomy when symptoms are transient. Finally, for the biliary and pancreatic sphincter of Oddi disorders, sphincter manometry is now omitted from the supportive criteria due to its lack of sensitivity and reproducibility.

g. The committee for Anorectal Disorders has made the following changes:

1. The fecal incontinence criteria, compared with Rome IV, has added "Two or more episodes of uncontrolled passage of fecal material" rather than "recurrent uncontrolled passage" to have a threshold frequency for diagnosis.

2. The functional defecation disorders category was removed because it was thought to be too broad in scope, as it can also include structural abnormalities such as rectal prolapse and perineal descent.

3. Dyssynergic defecation is now listed separately. The criteria now require difficult evacuation symptoms (eg, straining and digital maneuvers) and only 1 of 3 abnormal tests (ie, balloon expulsion, manometry, and imaging) compared with previously requiring 2 tests in Rome IV. In addition, electromyography testing has been dropped as a criterion because of its infrequency of use; diagnosis now relies on more specific manometric patterns of abnormal evacuation, including the rectoanal gradient.

4. As discussed above, anorectal sensory dysfunction disorders: rectal hypersensitivity, and rectal hyposensitivity are added as new criteria.

## Biopsychosocial Model of Disorders of Gut–Brain Interaction

The optimal treatment management of patients with DGBI requires a biopsychosocial approach. Figure 1 illustrates the biopsychosocial conceptual model for DGBI.[4] Figure 1 illustrates DGBI's biopsychosocial predeterminants, brain–gut influences, and clinical presentation, leading to the outcome. Early in life, genetics, sociocultural influences, and environmental factors may affect psychosocial development in terms of personality traits, susceptibility to life stresses, psychological state, and cognitive and coping skills. In addition, these factors also influence the susceptibility to gut dysfunction, such as abnormal motility or sensitivity, altered mucosal immune dysfunction or inflammation, and the microbial environment, as well as the effect of food and nutritional substances. Furthermore, these brain–gut variables reciprocally influence CNS expression. Therefore, a DGBI is the product of interactions of these psychosocial factors and altered gut physiology via the brain–gut axis.[26–31] Furthermore, the clinical outcome will, in turn, affect the severity of the disorder.[32] When the provider acknowledges the reality of the patient's symptoms, provides empathy, and engages in an effective patient–provider interaction, symptom severity and health care seeking are reduced.[33,34] But a provider who does not engage in these skills and who repeatedly performs unnecessary diagnostic studies to rule out pathologic disease, dismisses the patient's concerns, or does not effectively collaborate in the patient's care is likely to promote a vicious cycle of symptom anxiety and health care seeking.[33,34]

Using Figure 1 as a template, we provide a brief introduction to these concepts and associations, which are covered in more detail in the Rome V chapters.

### *Early Life*

At or perhaps even before birth, a person's genetic composition and interactions with the environment begin to affect later susceptibility to disease, phenotypic expression, and patient attitudes and behaviors (including health care seeking). Regarding genetic susceptibility, family and twin studies indicate a genetic component to IBS and likely other DGBI, and there have been several polymorphisms and candidate genes reported,[35] which can affect physiological functioning, including motor function, membrane permeability, and visceral sensitivity.[36] However, Mendelian single-gene susceptibility is unlikely; rather, multiple genes likely interact with environmental risk factors to produce the clinical heterogeneity among individuals with DGBI,[37] and psychophysiological factors such as stress may affect the epigenetic expression of these genes, leading to visceral hypersensitivity and other functions associated with these disorders.[38]

Sociocultural factors and family interactions can shape later reporting of symptoms, the development of DGBI, and health care seeking. The expression of pain varies across cultures, from denial to stoicism to dramatic expression.[39–43] Environmental exposures, such as childhood salmonella infection, can be a risk factor for IBS in adulthood.[44,45]

Early learning difficulties or emotionally challenging interactions that occur early in life may predispose individuals to DGBI.[46–48] Early family attention toward GI

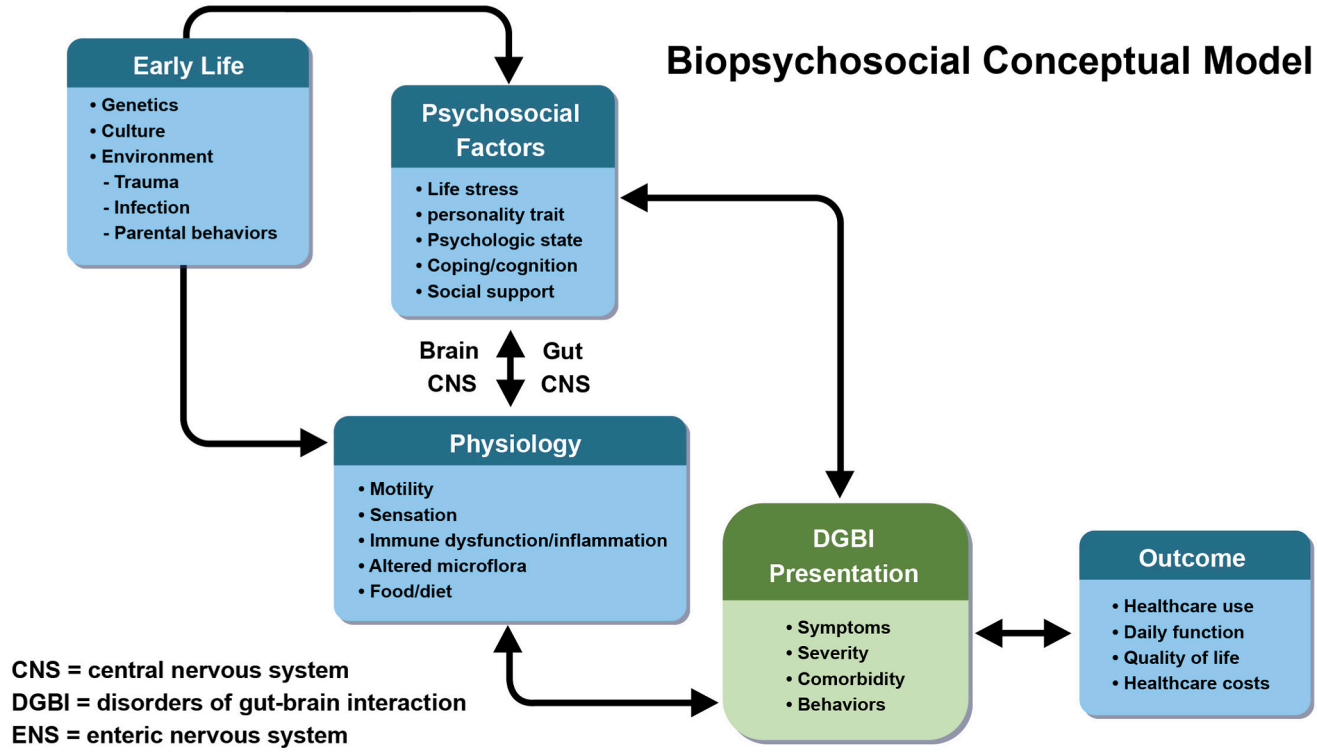


**Figure 1.** Biopsychosocial conceptual model. A biopsychosocial conceptualization of the pathogenesis, clinical experience, and effects of functional GI disorders. There is a relationship between early-life factors that can influence the psychosocial milieu of the individual, the individual's physiological functioning, and their mutual interaction (brain–gut axis). These factors influence the clinical presentation of the disorder and the clinical outcome. Consistent with this biopsychosocial conceptualization is that the influences on these factors are bidirectional and mutually interactive. Adapted with permission from Drossman DA. The functional gastrointestinal disorders and the Rome III process. Gastroenterology 2006;130:1377–1390.

symptoms and other illnesses can influence later symptom reporting, health behaviors, and health care costs.[31]

### *Psychosocial Factors*

Although psychosocial disturbances are not required for diagnosis, they influence the physiological functioning of the GI tract via the brain–gut axis (ie, motility, sensitivity, and barrier function), are modulators of the patient's experience and behavior, and ultimately affect treatment selection and the clinical outcome. When evaluating the patient for psychosocial factors, the clinician should consider the following 4 general observations:

1. Psychological stress or one's emotional response to stress exacerbates GI symptoms and may contribute to DGBI development. This symptom development or exacerbation occurs among healthy people or patients with structural diagnoses, respectively, but notably, it is well demonstrated in patients who have a DGBI, a common example being postinfection IBS or dyspepsia.[26,49,50] We also see a high association of psychosocial comorbidities, life stress, and abuse among patients with DGBI, which leads to poorer outcomes.[26]
2. Psychosocial factors, including psychological distress and comorbidity, are strongly associated with DGBI and modify the illness experience, increase health care seeking, and reduce quality of life. In a global epidemiologic study involving >54,000 participants, psychological distress and somatic symptom severity were reported in 37.5% of the sample. These individuals had 4.45 times higher odds of having at least 1 DGBI than those without psychological distress or symptoms. Those with DGBI and psychological distress or somatic symptoms, compared with those with psychological distress and no DGBI, also had increased health care and medication utilization and reduced mental and physical quality of life.[51] Thus, psychological distress, somatic symptoms, and DGBI coexistence are detrimental to quality of life and are associated with increased health care utilization.
3. A DGBI may have psychosocial consequences. Any chronic illness has psychosocial consequences on a patient's general well-being, daily function status, and sense of control over the symptoms, as well as implications for future functioning at work and at home. If a patient dismisses the role of stress in their illness, it should be noted that just having the illness is a stressor leading to psychosocial consequences, affecting emotional well-being and quality of life. When this is understood and accepted, patients are more willing to consider brain–gut treatments.

4. Psychosocial effects of illness, namely emotional distress and maladaptive cognitions, may feedback to perpetuate and amplify symptoms. Patients with severe symptoms may develop feelings of pessimism and helplessness (eg, catastrophize), and may selectively attend to and be hypervigilant of their symptoms. This can lead to visceral anxiety, lower sensation thresholds, and produce feelings of poor self-efficacy and self-esteem. These are the conditions for which brain–gut behavioral treatments are needed to help re-establish a psychological substrate of improved health.[52]

## *Physiology*

A variety of physiological processes may lead to GI symptoms and, when more prevalent, to DGBI.

**Abnormal motility.** It is well recognized that vomiting, diarrhea, constipation, acute abdominal pain, incontinence, and many other GI symptoms may be generated by disturbed GI motility. There are several components (ie, muscle contractility and tone, compliance, and transit), all of which can produce symptoms of nausea, vomiting, diarrhea, and constipation. Furthermore, in healthy subjects, and more so in patients with DGBI, strong emotion or environmental stress via the brain–gut axis can lead to dysmotility throughout the GI tract. DGBI are characterized by an even greater motility response to stressors (psychological or physiological) compared with subjects without DGBI.[53] Yet dysmotility is only partially correlated with symptoms; for example, they are not sufficient to explain reports of chronic abdominal pain or nausea, which are more centrally mediated.

**Visceral hypersensitivity.** The poor association of pain with GI motility with many DGBI is explained by studies showing that the pain is related to abnormalities in visceral sensation, called visceral hypersensitivity.[54,55] These patients have a lower pain threshold to balloon distention of the stomach or bowel (visceral hyperalgesia), or they have increased sensitivity even to normal intestinal function (allodynia). There also may be an increased area of somatic referral of visceral pain. Visceral sensitivity may be amplified in patients with DGBI, a process called sensitization or stimulus hyperalgesia. Repetitive balloon inflations in the colon lead to a progressive, although transient, increase in pain intensity in healthy subjects[56] and for a longer period in patients with DGBI.[57] Hypersensitivity and sensitization may be amplified at all levels of the neuraxis, as shown below.

**Immune dysregulation, inflammation, and barrier dysfunction.** Beginning with the work on post-infection IBS and dyspepsia over the past 2 decades, there has been increased interest in mucosal membrane permeability, intestinal flora, and altered mucosal immune function.[53,58,59] These factors lead to the increased access of intraluminal antigens into the submucosa associated with low-grade activation of mast cells and increased inflammatory cytokine release. The effects are to alter receptor sensitivity at the mucosa and myenteric plexus, producing visceral hypersensitivity and hyperreactivity to food and other luminal stimuli. Factors contributing to this occurrence include genetics, psychological stress via mast cell activation, and mucosal and neuronal alterations resulting from mucosal immune dysfunction.[60] This, in turn, is enhanced by alteration of the bacterial environment or outright infection. Mucosal barrier dysfunction is a potential target for treatment of DGBI.[61]

**Microbiome.** The microbiome represents the collection of microbes, including bacteria, fungi, and viruses, that live in the human body. The microbiome is shaped by host factors, such as genetics and nutrients, and is able to influence host biology in health and disease. It has played a crucial role in the bidirectional brain–gut axis that integrates the gut and CNS activities. Thus the concept of microbiome–gut–brain axis is emerging,[62] and there is growing interest in the role of altered bacterial flora composition in the development of certain DGBI.[62] Differences among patients with IBS in the bacterial composition of the gut, and also reduced fecal microbial diversity relative to healthy individuals, have implied a causative role in the onset and maintenance of IBS. The idea that altered bacterial flora composition may influence the development of DGBI may be supported by the modest effect of probiotics, the variable effects of microbiota transplant, and more substantive benefit of periodic antibiotic treatment in improving IBS symptoms.[63,64] The upper GI tract, duodenal microbiota, and *Helicobacter pylori* have been implicated in dyspeptic symptom generation.[65,66] Further research is needed to fully understand the place of the bacterial flora in the pathogenesis of DGBI.

**Food and diet.** The most recent addition to our understanding of DGBI is that of the contribution of food and diet,[67] and also their relationship to intestinal microbiota.[68] Certain specific alterations in diet (eg, low fermentable oligo-, di-, and monosaccharides and polyols, or gluten restriction in some patients) may provide benefit due to reduced osmotic effects or alterations in gut mucosa; however, there will be no one diet that is specific for patients. In addition, the diet provides substrates for microbial fermentation, and as the composition of the intestinal microbiota is altered in IBS, the link between food and diet, microbiota composition, and fermentation products may play an important role in IBS pathogenesis. This is notable because, for decades, there has been a discrepancy between patients' and physicians' attributions to the effect of food on DGBI symptoms, with patients believing the effect was more relevant.[69] In PDS, the role of food as a trigger is well-established, and early research also indicates a potential benefit from dietary interventions.[70] This new area requires further study to help define the subsets of patients who are more likely to respond to alterations in diet.

## *Brain–Gut Axis*

The brain–gut axis is the neuroanatomic pathway through which psychosocial factors influence the GI tract and vice versa. This bidirectional complex connects the CNS and the digestive system, encompassing the brain, spinal cord, and autonomic nervous system (including the sympathetic, parasympathetic, and enteric nervous systems), as

well as the neuroendocrine and neurohumoral systems.[71–73] In addition, the brain–gut axis also interacts with the intestinal microbiota composition and the intestinal barrier permeability. This interaction is referred to as the brain–gut–microbiota axis.[74]

The "hardwiring" between the brain and gut is a complex integrated circuitry that communicates information from emotional and cognitive centers of the brain via neurotransmitters to the peripheral functioning of the GI tract and vice versa.[72] Structurally, there are direct connections between the CNS and the myenteric plexus that extend to the visceral muscles and other end-organ structures. These connections influence sensory, motor, endocrine, autonomic, immune, and inflammatory functions.

Psychological stress can disrupt the gut pain threshold and impair mucosal secretory and barrier functions. This disruption is associated with the transmigration of bacterial cell products, leading to GI pain and diarrhea, as seen in IBS. Conversely, enhanced motility, visceral inflammation, and injury can each amplify ascending visceral pathways and affect brain regions, leading to increased pain and contributing to altered mental states, including anxiety and depression.[75] In effect, the brain–gut axis is the neuroanatomic and neurophysiological substrate for the clinical application of the biopsychosocial model.

Regarding pain regulation, the brain nuclei involved include the nucleus of the solitary tract, parabrachial nucleus, locus coeruleus, rostral ventromedial medulla, anterior cingulate cortex, paraventricular nucleus, and the amygdala.[72] Once these signals are registered centrally, the brain can modify incoming visceral signals through descending modulation via the gate control mechanism. Essentially, the brain's pain control system acts as a "filter" to enhance or block pain by up-regulating or down-regulating the incoming neural signals, thereby affecting symptom perception. Down-regulation, which raises the pain threshold, is often impaired in patients with DGBI.

This gate control mechanism can alter visceral sensitivity and central control of pain perception through the involvement of 2 key neurotransmitters—serotonin and noradrenaline. These neurotransmitters are also the main targets of neuromodulator treatments, such as tricyclic antidepressants or serotonin-noradrenaline reuptake inhibitors.[71,72]

The anterior cingulate cortex, which is involved in the motivational and affective components of the limbic pain control system, tends to be dysfunctional in conditions such as IBS, other DGBI, fibromyalgia, and with other functional somatic symptoms. However, improvement in pain control can be achieved through cognitive or emotional interventions such as focused attention, hypnosis, psychological treatment, and certain neuromodulators. Conversely, when this system is influenced by psychosocial distress, the "gate" remains open, leading to a lowered pain threshold.

Another critical component of the brain–gut axis is the autonomic nervous system, which includes the ENS. The ENS acts as a mediator of the visceral response to central influences.[76] There is evidence suggesting the presence of autonomic dysfunction in patients with DGBI, indicating either decreased or increased vagal outflow or sympathetic activity. Disturbances in autonomic balance can also alter visceral perception and contribute to pain perception. Therefore, autonomic dysfunction could be a pathophysiological mechanism underlying many symptoms of IBS and associated factors such as sweating, cardiac arrhythmias, and alterations in the respiratory cycle.[77] This dysfunction may also be linked to autonomically driven disorders like postural orthostatic tachycardia syndrome.[78] Newer treatments are emerging to treat IBS and functional dyspepsia using vagal stimulation devices.[79,80]

### *Disorders of Gut–Brain Interaction Symptom Experience Severity and Behavior*

The interaction between the brain and GI tract in any individual with a DGBI relates to the clinical expression of illness, namely, the symptom experience, its severity, and subsequent illness-related behaviors. This includes the meaning of illness, the fears of continued symptoms, the perceived concerns relating to alterations in body image, social acceptability (eg, feeling stigmatized[6]), the degree of functional impairment with its implications at work and at home, the sense of helplessness to effect symptom relief, and the difficulty coping with a disability, which must all be dealt with by the patient. How well the patient adapts based on personal and family resources, in addition to the quality of the physician's involvement, is crucial to the patient's psychological well-being and clinical course. Given the proper biopsychosocial milieu, many patients can adapt to their illness with some support from family, friends, and health care providers. Other patients, possibly shaped by genetics and early experiences, respond by feeling helpless and unable to control their symptoms and the effects on their lives; they regress and become dependent. Their continued symptoms, restricted activity, and health care needs may tax family, friends, and physicians, all of whom may feel helpless to provide enough emotional or medical assistance. In this case, additional efforts by the physician and ancillary personnel (eg, psychological counselors, social workers, and peer support groups) will be required.

### *Outcome*

The outcome of the biopsychosocial model as discussed is what we see in the patient's health and personal care behaviors, and in the impact on the family, the physician, and society. Psychosocial factors are strong determinants of medication use, health care visits, functional ability, loss of work time, and health care costs. All of these factors can be addressed and potentially modified by the physician's ability to listen, engage, and affect good communication skills, as discussed below, regardless of the diagnostic condition.[33,81,82]

## An Approach to the Care of Patients With Disorders of Gut–Brain Interaction

This section provides general care guidelines for patients with DGBI. Additional resources and details are found elsewhere.[33,81]

### 12 Steps to Enhance the Therapeutic Relationship

The basis for implementing an effective patient–provider relationship is supported by growing evidence of improved patient satisfaction, treatment adherence, symptom reduction, reduced health care costs, and other improved health outcomes.[33,34] The following is a series of suggestions designed to help establish a therapeutic relationship.

1. Learn how to improve patient satisfaction and engage the patient in the visit. There is good evidence that patient satisfaction relates to the patient's perception of their physician's humaneness, technical competence, interest in psychosocial factors, and provision of relevant medical information.[82] However, too much focus on biomedical issues can have a negative effect.[83] Engagement when patient and provider work together relies on nonverbal communication such as eye contact, affirmative nods, gentle tone of voice, close interpersonal distance, and creation of a partner-like interaction.[82] In a survey of 173 patients attending a gastroenterology clinic, the items that correlate most with patient satisfaction included the provider being likable, informative, accepting of the patients' feelings, available, responsive to questions and concerns, and trustworthy. Negative factors included the provider seeming rushed, being unconcerned or rude, interrupting, and not doing a physical examination.[84]
2. Obtain the history through a nondirective, nonjudgmental, patient-centered interview. This process involves active listening and using questions based on the patient's thoughts, feelings, and experiences rather than using a preset agenda of questions.
3. Determine the immediate reason for the patient's visit and evaluate the patient's verbal and nonverbal communication. Some possible reasons include
    a. new or exacerbating factors (dietary change, concurrent medical disorder, adverse effects of new medication)
    b. personal concern about a serious disease (eg, recent family death)
    c. personal or family stressors (eg, recent or anniversary of death or other major loss, abuse event, or history)
    d. worsening or development of psychiatric comorbidity (eg, depression and anxiety)
    e. impairment in daily function (eg, recent inability to work or socialize)
    f. a "hidden agenda" such as narcotic or laxative abuse, pending litigation, or disability claims
4. Conduct a careful physical examination and cost-efficient investigation. A well-conducted physical examination has therapeutic value.[85]
5. Determine what the patient understands of the illness and the patient's concerns.
6. Elicit the patient's understanding of the symptoms ("illness schema") and then provide a thorough explanation of the disorder that takes into consideration the patient's beliefs.
7. Identify and respond realistically to the patient's expectations for improvement.
8. When possible, provide a link between stressors and symptoms that are consistent with the patient's beliefs. Many patients are unable to associate stressors with illness but most will understand the stress of the illness on their emotional state.
9. Set consistent limits.
10. Involve the patient in the treatment.
11. Make recommendations consistent with patient interests.
12. Help establish an ongoing relationship with you or in association with a primary care provider.

Finally, 1 evidence-based review identified the following 5 key factors to improve the patient–provider connection[86]: (1) prepare in advance for the visit, (2) listen wholly and intently (eg, sit down, lean forward), (3) agree on what matters most (eg, incorporate what the patient cares about), (4) connect with the patient's story, and (5) explore emotional clues.

### Symptom Severity as a Guide to Treatment

Many condition-specific treatments for DGBI are fully covered in Rome V. Deciding on the best treatment is often influenced by symptom severity. Although mild symptoms may have lifestyle recommendations or no treatments prescribed, more severe symptoms may require combining several types of treatments. From a biopsychosocial perspective, when deciding on treatment, the provider needs to rely on more than the patient's report of the type or intensity of the symptoms. The provider must also consider the patient's personal experiences with proposed treatments (eg, prior adverse experiences or nocebo effects); cognitive and affective interpretations of the symptoms; treatment preferences; the patient's medical, physiological, and psychosocial comorbidities; and the degree of functional impairment, among others. Although illness severity exists on a continuum, a Rome Working Team Report provides a means for separating IBS into mild, moderate, and severe categories (Table 4).[21] The following discussion provides general guidelines for IBS but may also be applied for other DGBI.

**Mild symptoms.** Patients with mild or infrequent symptoms comprise approximately 40% of patients, are

**Table 4.** Proposed Clinical Profile for Patient-Rated Severity in Irritable Bowel Syndrome

| Clinical feature | Mild | Moderate | Severe |
|---|---|---|---|
| Estimated proportion, % | 40 | 35 | 25 |
| Psychometric correlate<br>FBDSI<br>IBS-SSS | <36<br>75–175 | 36–109<br>176-300 | >109<br>>300 |
| Physiological factors | Primarily bowel dysfunction | Bowel dysfunction and CNS pain dysregulation | Primarily CNS pain dysregulation |
| Psychosocial difficulties | None or mild psychological distress | Moderate psychological distress | Severe: high psychological distress, psychological comorbidity, catastrophizing, trauma history |
| Gender | Equal numbers of men and women | More women than men | Many more women than men |
| Abdominal pain | Mild/intermittent | Moderate, frequent | Severe/very frequent |
| No. of other symptoms | Low (1–3) | Medium (4–6) | High (7 or more) |
| Health-related quality of life | Good | Fair | Poor |
| Health care utilization | 0–1/y | 2–4/y | 5 or more/y |
| Activity restriction | Occasional (0–15 d) | More often (15–50 d) | Frequent/constant (more than 50 d) |
| Work disability, % | <5 | 6–10 | ≥11 |

Based on Drossman et al.[22]
FBDSI, Functional Bowel Disorder Severity Scale[87]; IBS-SSS, IBS Symptom Severity Scale.[88]

seen more in primary care than in gastroenterology practices, and do not have significant impairment in function or psychological distress. Symptoms relate primarily to GI dysfunction, and pain is minimal or mild and without other comorbid physical symptoms. Patients with mild symptoms do not usually have dominant psychiatric diagnoses, and quality of life is good. Still, they may report concerns about the implications of their symptoms on their life. These patients do not make frequent medical visits and usually maintain normal activity levels. Here, treatment is directed toward the following:

1. Education. Education has therapeutic value. The clinician should indicate that IBS is a genuine disorder where the GI system is overly responsive to a variety of stimuli such as food, hormonal changes, medication, and stress. Pain resulting from spasm or stretching of the gut, from a sensitive gut, or from both can be experienced anywhere in the abdomen. Both physiological and psychological factors interact to influence the symptoms.
2. Reassurance. The provider should provide appropriate reassurance based on the patient's vocalized concerns. Reassurance should not be communicated in a perfunctory manner or before necessary tests are completed.
3. Diet and medication. Offending dietary substances and medications that adversely cause symptoms should be identified and reduced or eliminated. Referral to a dietitian may be considered to provide continuity of care when specific dietary interventions are prescribed.

### Moderate symptoms.

1. A smaller proportion of patients, approximately 30%–35%, seen in primary or secondary care report moderate symptoms with intermittent disruptions. They may identify a close relationship between symptoms and inciting events such as dietary indiscretion, travel, or distressing experiences. They may have more moderate abdominal pain and be more psychologically distressed. There may be several other medical or psychological comorbidities, and these patients may lose time from work or need to curtail their usual functioning. For this group, additional treatment options are recommended.
2. Symptom monitoring. The patient can keep a symptom diary for 1–3 weeks to record the time, severity, and presence of associated factors. This may help to identify inciting factors such as dietary indiscretions or specific stressors not previously considered. The physician can then review possible dietary, lifestyle, or behavioral

influences with the patient. This encourages the patient's participation in treatment and, as symptoms improve, increases their sense of control over the illness.

3. Pharmacotherapy directed at specific symptoms. Medication can be considered for symptom episodes that are distressing or that impair daily function. The choice of medication depends on the predominant symptoms. In general, prescription medications are ancillary to dietary or lifestyle modifications for milder symptoms. Using IBS as an example, additional medications may be used during periods of acute symptom exacerbation (eg, antispasmodic and loperamide), and others may be prescribed on a continuous basis (eg, secretagogue and neuromodulator) for more frequent or chronic symptoms of moderate intensity.

4. Brain–gut behavioral treatments. Brain–gut behavioral treatments are recommended to help manage pain for motivated patients with moderate-to-severe GI symptoms. It is helpful if the provider can educate the patient on the benefits of the treatment as a means to improve symptom management, and if the patient can make connections between stress, anxiety, and thoughts with the symptoms. Treatments may include cognitive behavior therapy, hypnosis, mindfulness, and other combinations to help reduce anxiety and depression levels, encourage health-promoting behaviors, improve pain tolerance, and give the patient greater responsibility and control in the treatment.[52]

**Severe symptoms.** Approximately 20%–25% of patients with DGBI, often seen in referral practices, have severe symptoms, and a smaller proportion have very severe and refractory symptoms. These patients also have a high frequency of associated psychosocial difficulties, including anxiety, depression, or somatic symptom disorder, personality disturbance, and chronically impaired daily functioning, and approximately 10% or more will have work disability. There may be a history of major loss or early trauma, poor social networks or coping skills, and "catastrophizing" behaviors. These patients may see gastroenterology consultants frequently and hold unrealistic expectations of being "cured." Perhaps due to earlier experiences in the health care system, they may feel stigmatized with their condition and deny or not consider a role for psychosocial factors in the illness. As a result they may be unwilling to engage in psychological or psychopharmacologic treatment. Still, they will more often seek further diagnostic studies to legitimize their symptoms and choose pharmacologic treatments directed at the gut. For this group, the following treatment options are recommended:

1. The physician's approach. These patients need an ongoing relationship with a physician who provides psychosocial support through repeated brief visits. In general, the physician should

   a. perform diagnostic and therapeutic measures based on objective findings rather than in response to patient demands,

   b. set realistic treatment goals, such as improved quality of life rather than complete pain relief or cure,

   c. shift the responsibility for treatment to the patient by giving therapeutic options, and

   d. change the focus of care from treatment of disease to adjustment to and management of chronic illness.[82]

2. Central neuromodulator treatment. If pain is a dominant feature, tricyclic antidepressants and, more recently, the serotonin-noradrenaline reuptake inhibitor, have a role in controlling pain via central analgesia, as well as relief of associated depressive symptoms.[71,72] The selective serotonin reuptake inhibitors may have an ancillary role, as they are less effective for pain but can help reduce anxiety and associated depression. Neuromodulators are recommended for patients with chronic pain and impaired daily functioning, coexistent symptoms of major or atypical depression, symptom anxiety, or panic attacks. Even without depressive symptoms, these agents may help when the pain is dominant and consuming. A poor clinical response may be due to insufficient doses or failure to adjust the dosage based on therapeutic response or adverse effects.

3. DGBI treatment center referral. There are several GI programs and possibly pain treatment centers that provide an integrated multidisciplinary approach to DGBI management.[89] Here, the team approach is directed toward pain management, improved coping skills, and overall rehabilitation of patients who have become disabled.

## Concluding Comments

Rome V is the culmination of a 7-year effort of 144 internationally recognized investigators and clinicians representing 27 countries participating in 25 committees. We believe this new information will help the reader gain a better understanding of these disorders and improve the diagnosis and care of their patients. As we look back on the process, the information obtained is comprehensive, although there is still more to learn. The next 10 years will likely bring considerably more advances in our understanding and treatment of these disorders. When that occurs, we will revise the information again as we advance to Rome VI. Our mission is to help patients with DGBI, and we are moving closer to that goal. The Rome process is dynamic, and we look forward to future activities designed to help improve the science of DGBI and the care of the patients.

## 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.2026.02.014.

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