Gastroenterology 2026;170:1205–1223

Biopsychosocial Aspects of Adult and Pediatric Disorders of Gut–Brain Interaction

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This review offers information and practical guidance for professionals who care for patients with disorders of gut–brain interaction (DGBI). It summarizes evidence-based psychosocial approaches for adult and pediatric populations, organized into 4 sections: background, assessment, management, and training. The review begins by establishing a biopsychosocial framework, highlighting the bidirectional influences of biological and psychosocial factors on gut physiology and brain mechanisms. It then outlines key assessment strategies, including targeted patient interview questions and guidance on interpreting responses followed by empirically supported psychosocial treatments suitable for integrated and standalone care settings. The final section presents curriculum recommendations for providers in DGBI-specific psychosocial care. Emphasizing the brain–gut axis and the importance of the patient-provider relationship, this review underscores the need for accurate psychosocial assessment and contextually informed intervention. It concludes with future directions for training and research to enhance clinical outcomes in this complex and multifaceted domain.

Keywords: Psychosocial Assessment; Brain–Gut Behavioral Therapies; Central Neuromodulators; Social Determinants of Health.

This narrative review provides practical background and advice for professionals in disorders of gut–brain interaction (DGBI)–specific care, summarizing approaches recommended for both adult and pediatric clinical intervention. The Background section contains material about the biopsychosocial context of DGBI on which subsequent sections on assessment and management are based. The Assessment section provides specific suggestions on exactly what (and how) to ask patients and how to proceed based on their answers. The Management section explains recommended psychosocial treatments for DGBIs, for integrated care and other practice settings. The Biopsychosocial Training Curriculum section presents curriculum recommendations for gastroenterologists and primary care providers, based on the framework of the biopsychosocial model (Figure 1).[1]

This model shows how biological and psychosocial risk factors affect both gut physiology and psychosocial mechanisms, such as cognitive-affective processes and their underlying brain mechanisms. The bidirectional links between these mechanisms and gut physiology constitute the brain–gut axis. These factors contribute to the clinical presentation of an individual patient. The patient-provider relationship and interactions, in turn, impact psychosocial and brain mechanisms as well as the outcome of treatment. Recognizing the interactive nature of these relationships, indicated by the bidirectional shape of the figure's arrows, is critical to understanding the presentation and maintenance of DGBI and treatment approaches.

Background

Interpersonal and Societal Factors

Key messages:

- **Parents, partners, and others in a patient's life can affect DBGI symptoms.**
- **Adverse and traumatic experiences are linked to DGBI.**

Abbreviations used in this paper: **ACE, adverse childhood event; ANS, autonomic nervous system; BGBT, brain–gut behavior therapies; CBT, cognitive behavioral therapy; DGBI, disorders of gut–brain interaction; GDH, gut-directed hypnotherapy; GI, gastrointestinal; HPA, hypothalamus-pituitary-adrenal; IBS, inflammatory bowel syndrome; PTSD, post-traumatic stress disorder; QoL, quality of life; SES, socioeconomic status; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitor; TCA, Tricyclic antidepressant.**

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0016-5085
https://doi.org/10.1053/j.gastro.2026.02.009

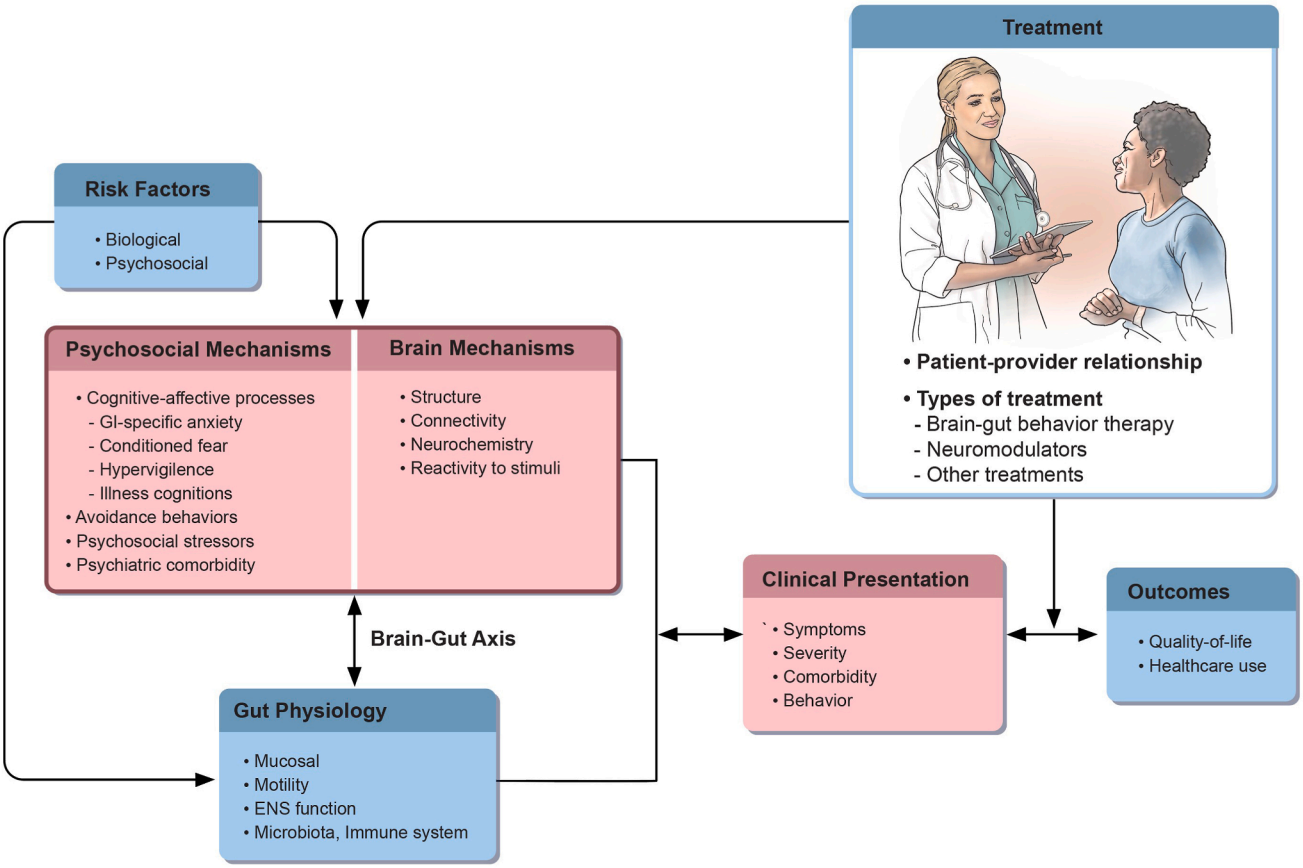

Figure 1. Biopsychosocial model of DGBI. The clinical presentation and treatment outcomes of DGBI is shaped by multiple biological and psychosocial risk factors that impact on psychosocial factors and their underlying brain mechanisms along the gut–brain axis. The patient-provider relationship plays a major role in patient management and treatment outcomes. Adapted from van Oudenhove et al.[1]

- **People with DGBI experience high levels of stigma.**
- **Social determinants of health and social support are important for people with DGBI.**
- **Psychosocial factors should inform treatment plans.**

Interpersonal factors. *Social learning, relationships, and social support.* Pain-related DGBI are known to run in families. There is some evidence that this intergenerational transmission of DGBI is partly genetic, but what children learn from their parents may contribute even more to the risk of developing a DGBI (Supplementary Figure 1).[2,3] In fact, how parents respond to their child's symptoms plays an important role in DGBI outcomes (Figure 2, Supplementary Figure 2).[2]

Parents influence their child's responses to pain in 2 ways: either through the child directly observing how parents respond to their own symptoms (modeling of behaviors), or by the child receiving certain types of feedback from their parents when the child displays illness behaviors (reinforcement). There is widespread evidence that if parents model pain behaviors that increase disability or reinforce child behaviors that increase disability, child outcomes are worse.[2] For example, when a child has irritable bowel syndrome, a parent may worry a child's symptom complaints mean they are seriously ill, leading to actions such as the parent focusing on the symptoms, encouraging the child to avoid activities such as going to school, and seeking healthcare more frequently. These actions over time exacerbate the child's experience of symptoms (child will pay more attention to, worry about, and complain of symptoms), as well as disability.[4]

Parental beliefs and behaviors can be changed through psychoeducation and/or cognitive behavioral therapy (CBT).[5,6] The most important factors explaining child outcomes comprise reductions in parental pain threat perception and catastrophizing (ie, thoughts such as "any symptoms mean my child may be seriously sick") and reductions in parental protective behaviors when a child has symptoms (eg, excusing the child from normal chores; Supplementary Figure 3).

Findings in adults are often similar to those of child studies. Reinforcement of pain behaviors (such as giving special attention) can increase pain behaviors in adults with chronic pain, whereas reinforcement of wellness

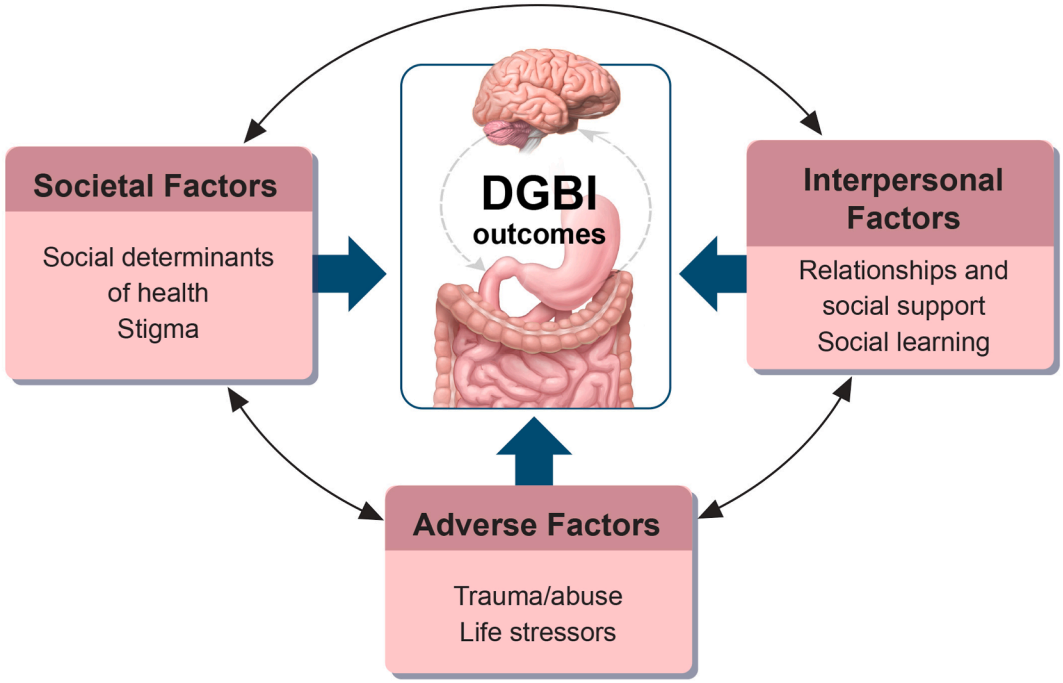

Figure 2. Interpersonal and societal factors in DGBI. Multiple interpersonal and societal factors contribute to the development and maintenance of DGBI.

behaviors (eg, carrying on with normal activities such as work) can decrease pain behaviors.[7]

Adverse experiences. Adverse life events frequently occur in patients with DGBI.[8–10] Adults and children with DGBI are significantly more likely to have a history of trauma, poverty, and bullying compared with those without DGBI.[8,11–13] Although adverse events can happen at any age, children are at the highest risk of experiencing traumatic events, including sexual and physical abuse, and subsequently developing post-traumatic symptoms.[14] Adverse events in children (often not singular, include poverty, parental addiction/mental health issues, parental incarceration, divorce, or death) often precede gastrointestinal (GI) symptoms, including abdominal pain and nausea.[15] The higher number of adverse childhood events (ACEs) experienced increases the risk for negative child and adult health outcomes, including DGBI.[16] ACEs can influence long-term health through several mechanisms, all of which have been identified in the pathophysiology of DGBI as well (including changes in the hypothalamus-pituitary-adrenal [HPA] axis, inflammatory pathways such as elevated interleukin 6 and C-reactive protein, brain circuitry such as the anterior cingulate, and cognitive deficits, emotional difficulties, and ineffective coping mechanisms).[17,18] Many of these mechanisms may explain why ACEs predispose people to developing DGBI. Unfortunately, there is a dearth of studies exploring the impact of protective factors and treatment of ACE trauma on the development of DGBI and/or other negative sequalae. There is a clear need to further investigate these as potential prevention strategies.[19,20]

Societal factors. *Stigma.* Another challenge impacting DGBI patients is a culture of minimizing symptoms experienced by characterizing symptoms as "not real" or "all in their heads." This problematic perspective originates from the biomedical model, with its inappropriate artificial separation of "body" and "mind." Several studies have found that even healthcare providers hold these stigmatizing views (eg, psychological factors are assumed to play a causative role in symptom expression).[21,22] Not surprisingly, patients with DGBI report high levels of stigma. A recent review found that, across studies, patients with irritable bowel syndrome (IBS), compared with inflammatory bowel disease or other organically labeled disorders, report higher stigma from healthcare providers, family, and colleagues.[23] Patients themselves often internalize this stigma; consequently, there is evidence this negative stigmatization spiral can in turn adversely affect quality of life (QoL), mental health, and healthcare use.[23,24]

A broader acceptance of the biopsychosocial over the biomedical model (Figure 1), including training and awareness programs for providers, will be necessary for destigmatization and a better understanding and effective treatment of DGBI.

Social determinants of health. There has been considerable interest in the broad range of social factors that impact health and healthcare, particularly the links between social equity and physical health.[25,26] In addition to dietary factors, poor water, air quality, and other facets characteristic of disadvantaged neighborhoods, racial/ethnic group, and low socioeconomic status (SES) are associated with poorer symptoms and QoL outcomes

because these factors adversely impact health outcomes via stress processes. According to social stress theory, low social status is a type of chronic stressor that is negatively related to a broad range of physical health conditions.[27,28] A number of factors related to SES (age, education, income, and occupation) have been linked to DGBI outcomes, with education consistently emerging as a risk factor across many studies.[29,30] These findings, in addition to transportation and insurance challenges,[31,32] highlight barriers to treatment. SES factors may also be associated with less healthcare access and opportunities for diagnosis,[8] however, there are few studies on SES as a risk factor for DGBI.

Race is, of course, often confounded with a variety of other factors such as SES, potential referral biases, reduced opportunities to access specialist care and differing patterns of healthcare use, but literature regarding associations between race, SES, and DGBI is limited and has produced mixed results.[8] Future research is needed to explore how cultural and SES factors might influence treatment interventions and patient engagement.

Psychological Factors

Key Messages:

- **Comorbid mental and physical health conditions are common in DGBI patients, with negative impact on QoL and treatment outcome.**
- **Psychiatric comorbidity can precede or follow the DGBI diagnosis.**
- **DGBI symptoms and behaviors are shaped by cognitive and emotional processes, which can influence the perception, evaluation, and reporting of symptoms independent of psychological comorbidity.**
- **GI-specific cognitions and emotions are important targets in psychosocial assessment and behavioral treatment approaches.**

Psychiatric and comorbid somatic conditions. Comorbid mental and physical health conditions are common in patients with DGBI. Patients can present with multiple psychiatric disorders,[33] most commonly anxiety disorders, mood disorders, eating disorders, and somatic symptom disorders (for diagnoses and defining symptoms, see Supplementary Table 1). Prospective studies document that a psychiatric diagnosis, especially of an anxiety disorder, often precedes a diagnosis of DGBI.[34] This evidence does not imply a simple cause-effect relationship, as there also exists evidence that GI conditions can precede psychiatric comorbidity.[35,36] Psychiatric comorbidity can affect the outcomes of a DGBI, with negative impacts on consultation seeking,[37,38] symptom severity and symptom course,[39,40] treatment response, and discontinuation as well as medication side effects,[41] direct and indirect healthcare costs,[42] and impairment in work, activities of daily living, and QoL.[43] Reduced QoL may be mainly driven by psychiatric comorbidities rather than GI symptoms.[8]

The overlap of DGBI with somatic conditions (previously described as functional somatic disorders) and other GI conditions is also substantial.[44] Importantly, somatic comorbidities in DGBI are not solely explained by psychiatric comorbidity or high chronic stress burden. The combination of different somatic and psychiatric comorbidities is also associated with more refractory DGBI symptoms,[45] and lower QoL.[46,47]

Common gastrointestinal-specific cognitions and emotions. The subjective experience of DGBI symptoms is only partially determined by peripheral sensory input. Rather, symptom perception emerges from a complex psychobiological process where visceral signaling is modulated in the brain by cognitions and emotions (for an extended summary, see Supplementary Table 2). These processes can influence the perception, evaluation, and reporting of visceral pain and other GI symptoms independent of the presence or absence of psychiatric comorbidity. Modulation by cognitions, emotions, and behaviors can play a role in symptoms even in psychologically healthy individuals with DGBI and are a major focus of brain–gut behavior therapies such as CBT.

Fear, hypervigilance, and avoidance. Many GI symptoms, such as pain, nausea, diarrhea, and vomiting, have an inherently high threat value. They are, in essence, a warning signal that physical harm or even injury is imminent. Fear in the face of threat is a healthy and important response. However, excessive or unfounded fear can fuel hypervigilance (to symptoms) as well as excessive safety-seeking and maladaptive avoidance behaviors, a vicious cycle captured by the fear-avoidance model[48–50] (Supplementary Figure 4) that is highly relevant to the generation and treatment of DGBI.[51–53] Conditioned fear of nonpainful sensations can generalize,[54] inducing a perception bias where visceral sensations feel more intense, aversive, or painful.[55] Brain imaging studies support involvement of the amygdala (central fear network) and hippocampus (memory processes),[56,57] and even benign visceral stimuli activate fear responses[58] and subsequently avoidance of food or situations expected to increase symptoms.[58] Pain-related fear, hypervigilance, and avoidance behaviors are key treatment targets of behavioral therapies in DGBI.[59,60] CBT focuses on reducing the threat value of the symptoms and aims at reducing maladaptive avoidance behavior.

Catastrophizing and gastrointestinal-specific anxiety. Catastrophizing is a cognitive process in which an individual magnifies the seriousness of symptoms and consequences while simultaneously viewing themself as helpless. Catastrophizing in DGBI can exert a negative impact on QoL, contributing to greater worry, suffering, and disability.[40,61] Parental catastrophizing also predicts negative outcomes in children with DGBI.[62] Catastrophizing is one of the major treatment targets and has been shown to predict symptom and disability reduction with CBT.[63–65] Pain catastrophizing, together with GI-specific anxiety (the excessive worry, fear, and concern about

current or future GI symptoms, the situations in which they may occur, and their consequences), has also been found to be one of the main mechanisms by which CBT affects pain outcomes.[64–67]

GI-specific anxiety is associated with increased symptom reporting,[68] as well as health care use.[68,69] Changes in GI-specific anxiety may be one of the main mechanisms by which exposure-based CBT approaches reduce symptoms.[70]

Expectation effects: placebo and nocebo. Placebo and nocebo effects are examples of the powerful effect of cognitive processes in (visceral) pain perception and treatment outcomes.[71,72] Positive (placebo) and negative (nocebo) suggestions can decrease and increase pain ratings as well as brain responses to visceral pain, respectively. When used as a treatment, open-labeled placebos work just as well as blinded placebo in treating IBS symptoms,[73,74] indicating treatment expectations can be harnessed to the benefit of patients.

Stress and mood. DGBI symptoms can be influenced or exacerbated by chronic and acute stress. Traumatizing stressors or stressful life events (eg, ACE) are obvious reasons that patients experience chronic stress. However, chronic stress can also be a response to daily hassles or long-term difficulties (ie, divorce, job loss). DGBI symptoms themselves can become major long-term stressors, as symptoms can be unpredictable and largely uncontrollable. In children, school can be a chronic stressor, yet school (or in adults: work) avoidance may bring additional stressors such as isolation and loss of self-efficacy. Emerging from this knowledge comes recent interest in understanding how patients cope with their symptoms. Although the relationship between stress, coping, and resilience is important for brain–gut behavior therapies (BGBTs),[75] this has not been thoroughly studied thus far in DGBI.

Besides chronic stress, different types of acute stressors and negative mood states can alter visceral sensorimotor functions in healthy individuals as well as in patients with DGBI.[76,77] Collectively, existing laboratory studies document that acute stress and negative emotional states can alter visceral perception and gut motility, engaging multiple pathways of the brain–gut axis. In patients with DGBI, adaptive modulation of perception during stress or negative emotional states appears to be altered. Changes in ratings of pain intensity, autonomic, as well as neuroendocrine and brain responses, appear to be more pronounced in DGBI than healthy controls.[76–79]

Mechanisms: The Microbiota-Brain–Gut Axis as Mechanistic Basis of the Biopsychosocial Model

Key messages:

- **Various signals reflecting the physiological condition of the gut are continuously transmitted to the brain through brain–gut (ie, bottom-up) pathways.**
- **The brain does not only passively process these signals, but cognitive and affective networks profoundly modulate them to shape the symptom experience.**
- **The result of this process in the brain is impacting gut function through brain–gut (ie, top-down) pathways, which in turn alter brain–gut signaling.**

Brain–gut: bottom-up pathways transmitting gastrointestinal signals to the brain. The (microbiota-) brain–gut axis is the bidirectional communication system between the gut microbiota and the brain, including neural and humoral (ie, through the systemic circulation) pathways, visualized in Figure 3.[80] The bottom-up limb of the brain–gut axis is continuously signaling information about the physiological condition of the GI tract to the brain through neural and humoral pathways.[81]

Neural brain–gut pathways originate in the enteric nervous system, which then transmits sensory information to the central nervous system through vagal (transmitting mostly physiological signals) and spinal (transmitting mostly salient, including noxious, signals requiring a behavioral response).[82] Importantly, those sensory neurons do not only respond to mechanical signals (eg, gut distension), but also to endocrine (eg, GI hormones) and immune (eg, cytokines) mediators as well as bacterial metabolites (eg, short-chain fatty acids, tryptophan metabolites) and/or neurotransmitters (eg, serotonin (5-HT)).[81] However, the previously mentioned mediators may also exert direct effects on the brain after absorption into the systemic circulation and passing the blood-brain barrier.[81] These highly integrated bottom-up pathways explain why and how many of the peripheral alterations identified in DGBI are sensed by the brain.[83–86]

Brain: brain mechanisms shaping visceral sensation. Under normal physiological conditions, most of the previously mentioned brain–gut signals are not consciously perceived. However, the subjective experience of GI symptoms (particularly visceral pain) results from the conscious perception of brain–gut signals induced by salient stimuli indicating a potential threat to the body, shaped by memories of such signals, emotional, cognitive, and motivational processes, and factors. In other words, translation of "objective" gut signals into subjective symptoms is highly nonlinear.

The generation of GI symptoms results from the interaction between distinct yet partially overlapping and highly intertwined brain networks involved in various aspects of processing and modulation of visceral signals as well as shaping bodily and behavioral responses to them.[87] There are multiple steps of integration (for a visualization, see Supplementary Figure 5). Sensory brain–gut signals are first processed in a sensorimotor network primarily including the posterior insula, which can be considered the "primary viscerosensory cortex." In a second step, the salience of the information is assessed in the salience network, with an integration of inputs at the level of the anterior insula. A positive outcome of this salience assessment may then shift activity from the default mode network to the central executive network, directing attention toward the salient visceral stimulus. As a result of this shift, the emotional arousal network is activated, triggering affective-motivational responses to the sensory input,

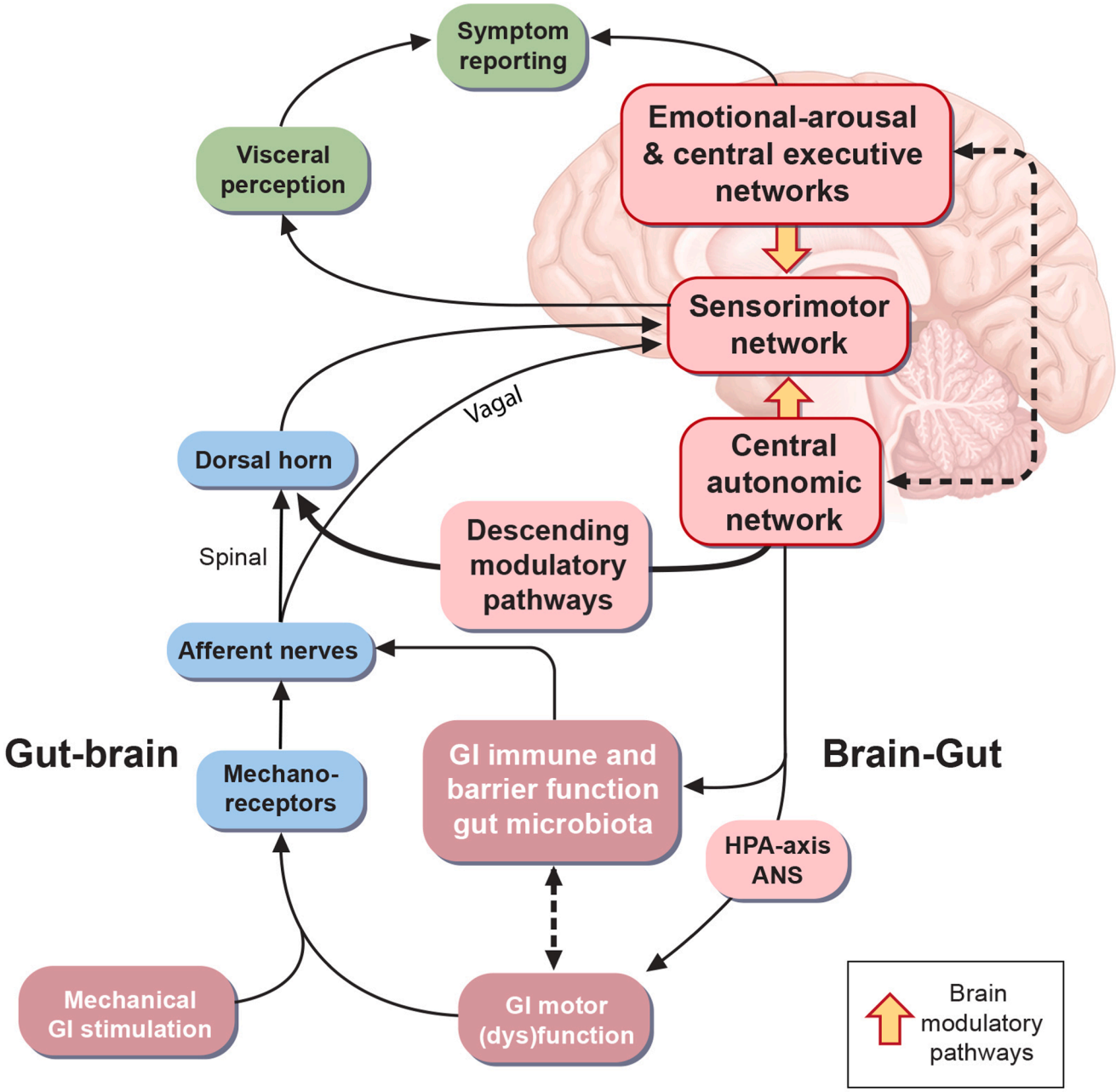

Figure 3. Bottom-up and top-down pathways of the brain–gut axis involved in DGBI symptom generation. Symptom perception and reporting in DGBI is strongly modulated by psychosocial factors, involving the central executive, emotional arousal, and central autonomic networks modulating visceral input processes in the sensorimotor network. Those brain processes impact peripheral gut functions and vice versa, involving a loop of top-down and bottom-up pathways. Adapted from Levy et al.[80]

which form an integral part of the symptom experience, thereby profoundly shaping it. Finally, the emotional-arousal network activates the partially overlapping central autonomic network, including top-down projections from key emotional-arousal and salience network regions to subcortical nuclei regulating autonomic output through the HPA-axis and the sympathetic and parasympathetic branches of the autonomic nervous system (ANS). Through these pathways, it profoundly impacts on a plethora of GI functions which may in turn impact bottom-up signaling, thereby closing the bidirectional brain–gut loop underlying symptom generation.

It should be noted that abnormalities in the structure and/or function of many, if not all of the regions constituting these networks, have been observed in DGBI using various brain imaging approaches.[87] Task-based functional magnetic resonance imaging studies have elucidated the specific neural mechanisms underlying the impact of several of the cognitive-affective processes and psychiatric comorbidities including comorbid anxiety and depressive

symptoms, stress, pain-related fear and anxiety, and expectancy/placebo effects.

Brain–gut: top-down pathways impacting gut function. *The descending modulatory system: the neural basis of cognitive and affective pain modulation.* Brain-Brainstem areas send descending projections to the dorsal horn of the spinal cord, where bottom-up pain transmission is modulated (descending modulatory system). These circuits represent the biological basis of cognitive and emotional modulation of (visceral) pain perception. Dysfunction of this modulatory system may allow physiological (non-noxious) stimuli to be perceived as painful or unpleasant and/or the amplification of the perception of noxious stimuli (ie, visceral hypersensitivity). There is indeed behavioral evidence for impaired descending modulatory system function in DGBI,[88] as well as brain imaging evidence confirming a role of central autonomic network regions.[87]

The autonomic nervous system and the stress hormone system impact on gastrointestinal function. Psychological processes and psychiatric comorbidity have modulatory influences on the processing of input from brain–gut pathways through the descending modulatory systems within the central nervous system. They can also influence various aspects of GI function through neural (ANS) and humoral (the HPA-axis, the main hormonal stress response system) brain–gut pathways. The corticotrophin-releasing factor transmitter system, both centrally (at the level of the hypothalamus and amygdala, among others) and peripherally (at the level of the GI tract/enteric nervous system), is of major importance here,[89] especially via the principal human stress hormone, cortisol, which exerts a plethora of effects on bodily systems, including the immune system and the GI tract. Finally, there is an important bidirectional crosstalk between the ANS (through the so-called "cholinergic anti-inflammatory pathway"),[90] the HPA-axis, and the peripheral immune responses,[91] but the exact role of these complex mechanisms remain to be elucidated in human health and DGBI.[76]

Psychosocial Assessments in Clinic: A Primer for Healthcare Professionals

Key messages:

- **Psychosocial assessment should be a part of routine care and should drive referrals to multidisciplinary treatment.**
- **Including psychosocial assessment into DGBI clinical encounters can improve patient outcomes and patient satisfaction.**
- **The primary domains of psychosocial assessment for DGBI include health- and symptom-specific anxiety, cognitions, and behaviors; psychiatric comorbidity; and sleep and stress (Supplementary Figure 6).**

Proper psychosocial assessment is a critical component of patient care in DGBI because it has the potential to improve patient satisfaction and trust, to improve the provider's understanding of a patient's experience with symptoms of DGBI, and to identify patients who may be at risk for refractory symptoms and/or low QoL due to psychosocial issues. Additionally, understanding the patient's healthcare beliefs and considering social and cultural factors are important parts of the biopsychosocial assessment to work toward a collaborative management plan, especially when considering second-line interventions and BGBTs.

Psychosocial assessment, which can be as simple as asking about QoL or as involved as administering and scoring validated questionnaires (for a list of validated questionnaires, see Supplementary Table 3), should be a part of routine care and should drive referrals to multidisciplinary treatment, but a comprehensive assessment does not need to be conducted in a single visit. Questions about psychosocial issues can fit seamlessly into the provider's routine questions about how the DGBI impacts the patient's life. In addition, the provider should provide feedback regarding the results of the entire evaluation and discuss treatment plans, which may involve both medical and psychosocial treatment strategies. Note that we do not recommend symptom tracking with all DGBI patients and instead suggest that this be used specifically with patients who express interest in symptom tracking or who seem to be having trouble recognizing their progress.

Approach to Psychosocial Assessment: Adults and Children

Health and symptom-specific anxiety, cognitions, and behaviors. Assessment of GI-specific anxiety, cognitions, and behaviors is perhaps the most important assessment domain in the treatment of DGBI. Although many patients with DGBI will also meet criteria for comorbid anxiety and/or depression, many more will endorse symptom-specific anxiety and illness behaviors such as avoidance or hypervigilance, all of which can lead to decreased QoL, increased emotional distress, and worse symptom severity.[92]

Evaluation of pediatric health-related anxiety, cognitions, and behaviors will vary depending on the age of the patient. For young patients, evaluation might focus more on the child's behavioral responses to pain or discomfort while also listening for the parent's reported worries or fears about their child's symptoms. In adolescents and young adults, interview topics and questions might be more like what is described already in this article for adults, with less focus on parent worries and behaviors (see Supplementary Table 4 for sample interview questions).

Illness impact, stigma, and quality of life. It is also important to ask patients about the actual impact of their symptoms on their daily lives, as well as their experience of stigma (eg, following up on statements like "This is embarrassing to talk about" and "None of my doctors believe me that my symptoms are real").[24,93] In children and adolescents with DGBI, it is important to understand the impact of DGBI symptoms on daily functioning to help

the patient re-engage in academic and social activities. Here, it is also necessary to address parents' beliefs about whether and how much children can participate in age-appropriate activities to inform potential referral to behavioral therapy or social work intervention. Finally, it can be useful to ask about, and listen for, parent reports of the impact of their child's symptoms on overall family functioning and family QoL (for sample assessment questions, see Supplementary Table 5).

Coping and resilience. The ability to cope with, and respond positively to, stressful situations (ie, "resilience" and "self-efficacy") is associated with lower DGBI symptom severity and improved QoL.[94] It, therefore, is important that providers inquire about, and encourage, resilience in DGBI patients early on in the clinical relationship (Supplementary Table 6). Asking about children's and parents' coping styles in response to DGBI symptoms can identify both strengths and weaknesses that might benefit from further intervention. Capitalizing on healthy coping skills that already exist in a family is a very effective place to start when trying to help patients to increase their sense of self-efficacy. Similarly, identifying unhealthy or unhelpful coping skills can allow the provider to either gently suggest alternatives or to make appropriate, informed referrals to behavioral therapy.

Assessment of psychiatric comorbidity. It can be important to screen for anxiety and depression (Supplementary Table 7). It may not be necessary to screen all patients in a GI clinic for histories of abuse and post-traumatic stress disorder (PTSD; Supplementary Table 8). However, screening for abuse can be useful before performing a rectal examination and/or before referring to a colonoscopy, both of which can be very difficult for patients with abuse histories.[95]

Sleep, stressors, life events, and sociocultural factors. Other important parts of the biopsychosocial assessment to include are: (1) Sleep disturbances (highly prevalent among both adult and pediatric patients with DGBI),[96–99] (2) environmental factors, changes, and stressors, and (3) the patient's healthcare beliefs and social and cultural context (for sample interview questions, see Supplementary Tables 9 and 10). This will facilitate working toward a collaborative, shared, agreed management plan, especially with second-line interventions and BGBTs.

In summary, the provider can likely address many factors contributing to DGBI symptoms through their biopsychosocial assessment. During the encounter, the provider should strive to obtain information from the patient about: (1) unhelpful thoughts, beliefs, feeling stigmatized, and/or emotional responses related to their GI symptoms; (2) significant disruption to their lives because of symptoms (eg, avoidance, restrictive eating habits), chronic stress, and ACEs; (3) clinically significant levels of general mental health issues (eg, anxiety, depression, PTSD); and (4) symptoms consistent with insomnia or poor sleep quality.

Often, but not always, referral to a gastropsychologist or other mental health provider may be indicated if patients endorse any of the above and express psychological insight and interest in behavioral treatment (for guidelines and flags for referring to a mental health provider, see Supplementary Table 11).

Psychosocial Management and the Role of Brain–Gut Behavior Therapies

Key messages:

- **Basic (Level 1) psychosocial care should be provided by all medical professionals involved in DGBI care.**
- **Therapist-delivered BGBTs have a strong evidence base for DGBI either when delivered by trained, non–mental health providers (level 2 psychosocial care), or by a gastropsychologist (level 3 psychosocial care) (Supplementary Figure 7).**
- **Fully integrated level 3 psychosocial care with a gastropsychologist is the gold standard, especially in treatment-refractory and psychologically complex DGBI, allowing case conceptualization and individualization of BGBT.**

Clinical practice guidelines have highlighted the role of evidence-based nonpharmacologic treatments for DGBI. There is now greater understanding of the limitations of a purely biomedical approach to the long-term management of DGBI.[100–102] Contemporary best practice management of DGBI involves a patient-centered, personalized biopsychosocial approach, with sequential first, second-, and third-line treatment options including brain–gut neuromodulators and BGBTs, often in combination, taking into consideration patient preferences.

It is important to explore with patients the acceptability of different pharmacologic and nonpharmacologic interventions so that a personalized treatment framework can be formulated at the outset. These discussions should be open with an initial explanation of potential options. This can improve adherence and avoid misunderstandings at a later stage. Psychoeducation about the brain–gut axis, lifestyle factors, and role of self-management is also important.

An Overview of Commonly Used Brain–Gut Behavioral Therapies

The strongest evidence for BGBTs in DGBI exists for CBT and gut-directed hypnotherapy.[103] This is supported for adult populations by more than 20 randomized controlled trials primarily in IBS,[104] with additional evidence from randomized controlled trials in other painful DGBI, such as functional dyspepsia[105] and noncardiac chest pain.[106] In pediatric abdominal pain–related DGBI, an umbrella term that often includes IBS, there similarly exist more than 25 controlled trials for treatment with CBT or hypnotherapy, including 1 trial on hypnotherapy for functional nausea.[107] Although BGBT have not been studied in every DGBI subtype, these therapies target common

mechanisms of gut–brain dysregulation (eg, visceral hypersensitivity, hypervigilance, fear conditioning, and symptom-specific anxiety) that transcend diagnostic categories[59] and, because of the personalized nature of BGBTs, can be safely executed by trained clinicians. For a comprehensive review of all available BGBTs, please refer to the recently published working team report on BGBTs for DGBI[59] on how to explain BGBTs to a patient. For BGBTs in children and adolescents, see Santucci et al,[108] Reed et al,[109] and van Tilburg et al[110] (see also Supplementary Figure 8).

Briefly, CBT refers to a theoretical framework through which a provider conceptualizes how the interaction between thoughts, feelings, and behaviors influences a patient's experience. In DGBI, CBT focuses on teaching patients to modify styles of thinking and behaving to offer GI symptom relief in addition to improved QoL. CBT for DGBI has multiple forms of delivery, including group-based, phone, internet-delivered, and with minimal therapist contact.[5,59,104]

Gut-directed hypnotherapy (GDH) is a form of medical hypnosis provided by a specially trained provider usually delivered in 6–12 sessions for adults[111] and 3–6 sessions for children.[112–114] In GDH, patients with DGBI are placed into a heightened state of focus and awareness to increase openness to posthypnotic suggestions, which usually focus on broad themes of brain–gut dysregulation. Systematic reviews, meta-analyses, and smaller randomized clinical trials have demonstrated GDH's efficacy in DGBI.[103,107,114–118]

Working With Parents When the Child is the Identified Patient

The extent to which a provider directs management strategies solely at children or their parents will be age dependent, but once underlying medical problems have been ruled out and/or treated, successful treatment of children with some DGBI can often be accomplished without meeting with the child at all![6] A provider may observe and consider addressing, in the same way as with adults, a parent's hypervigilance and/or GI-specific anxiety or cognitions regarding their child's symptoms. For parents, particularly, overprotection of the child when symptomatic is an important target for treatment. Physicians can discuss the difference between acute and chronic pain, and how hurt does not equal harm for the latter. It may also be appropriate to educate a parent about how a child's stress response (toward school, etc.) may exacerbate their symptoms; the parent can learn relaxation techniques that they can then teach their child. Also, if the provider ascertains during assessment that the child is rewarded for expressing symptom complaints and engaging in illness behaviors, the provider could suggest that the parent consider alternative responses to their child that encourage wellness behaviors. Finally, parents should also be informed that responses to their own discomfort (modeling) may influence their child's response to their similar discomfort.

The Value of Integrated Psychosocial Care for Disorders of Gut–Brain Interaction

Integrated care has become synonymous with a multidisciplinary approach to IBS and has implications across the spectrum of DGBI, especially with respect to the outcomes of improved symptom control, QoL, and, in some cases, cost of illness. Involvement of other professionals who can focus more holistically on the range of biological, psychological, and social factors impacting health has been shown to be efficient, cost-effective, and associated with improved outcomes.[109,119]

The United States and Australia have seen an explosion of integrated care models in GI settings, with prominent trials such as the MANTRA Trial,[120] to support efficacy and cost effectiveness even longer-term. Multidisciplinary care for children with refractory Functional Abdominal Pain Disorder has also been shown to lead to more use of psychological care[121] and to significantly decrease acute healthcare use.[122,123]

Unlike multidisciplinary models, in which a group of professionals from different backgrounds help a patient with one aspect of their overall condition (eg, diet, exercise, sleep, behavior), integrated care models usually require a specific approach or methodology guiding how the members of the multidisciplinary team interact with each other, prioritize recommended treatments, track progress, and alter care plans over time based on input from the professionals and the patient.

Levels of integrated psychosocial care. Integrated biopsychosocial care can be achieved even when a gastropsychologist is not available. Here we describe the levels of integration from Level 1, in which the patient is responsible for learning self-management skills with little to no guidance, to Level 3 in which a licensed mental health professional is available (Figure 4).

Along with concurrent diagnosis and first-line medical treatments in Level 1, the first step would be for the physician to provide psychoeducation about the brain–gut axis and self-management strategies (eg, stress-management techniques, modifications to exercise, diet, and lifestyle).[124] In Level 2, patients receive second-line medical therapies along with psychosocial interventions (provided by a nurse or other advance practice provider trained to deliver psychosocial interventions such as self-management and BGBT) as part of their GI treatment. These interventions can be delivered in groups, over the phone, or even digitally via smart phone.[125–128] An infrequently used, but potentially valuable, Level 2 integration of psychosocial care includes the option for the physician to prescribe psychotropic medications to patients with mild anxiety or depression. Although some patients will do very well with Level 1 or Level 2 care, many patients (especially those nonresponsive to treatment and/or psychologically complex) will require a higher level of treatment. Level 3 describes what should be considered the gold standard of integrated psychosocial care, with a mental health professional (such as a gastropsychologist) augmenting treatment. At this level, personalization of therapeutic content

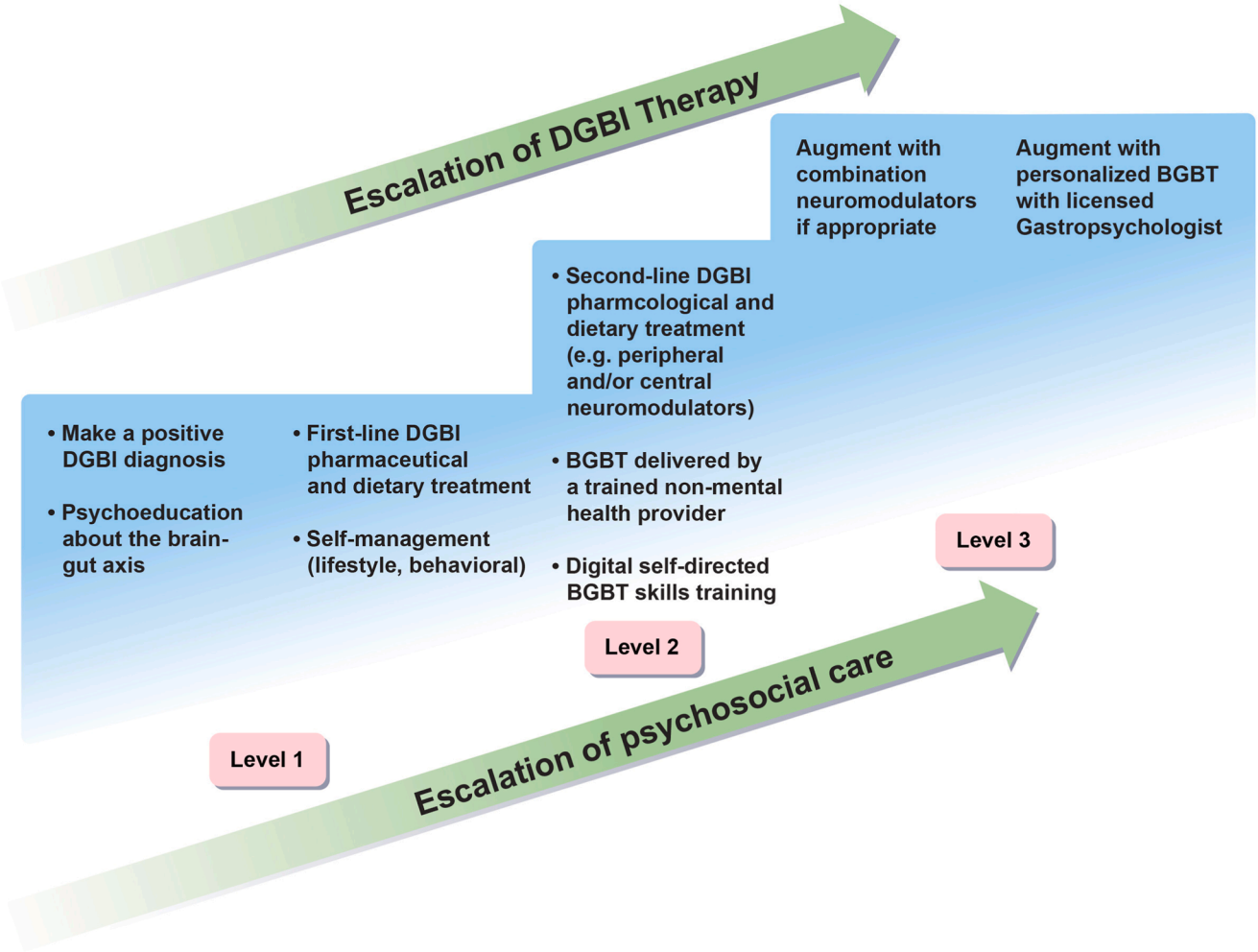

Figure 4. Stepwise approach to biopsychosocial DGBI care. Medical and psychosocial therapy for DGBI are complementary. This figure depicts a stepwise approach to the patient with DGBI.

will be based on the patient's primary symptom concern and functional impairment, context in which symptoms present, and consideration of physical and mental health comorbidities. The aspirational level of integrated psychosocial care, including a fully integrated gastropsychology practice, has many benefits (Figure 5), but there are advantages and limitations (Supplementary Table 12).

Central Neuromodulators in the Treatment of DGBI

Key messages:

- **The choice of neuromodulator is determined by a patient's predominant symptoms, disease severity, psychiatric comorbidity, and prior experience with medications in the same class as well as by patient and provider preference.**
- **Tricyclic antidepressants (TCAs) are preferred over selective serotonin reuptake inhibitors (SSRIs) for treating chronic GI pain in adults, particularly when constipation is not a concern, and are used at doses lower than those for psychiatric indications.**
- **Serotonin-norepinephrine reuptake inhibitors (SNRIs) are more potent analgesics than the SSRIs and have an advantage over TCAs in that they have fewer anticholinergic effects, but their evidence base in DGBI is more limited.**

Despite increasing evidence base for their efficacy,[129–132] until recently the value and utility of central neuromodulators in treating patients with DGBI have not been well understood by many gastroenterologists.[133] This issue was addressed by a Rome Foundation Working Team Report that redefined centrally acting pharmacologic treatments working both in the brain and gut as gut–brain neuromodulators[129] and summarized the major clinical trials evaluating the use of centrally acting agents in DGBI. This term includes the primarily central neuromodulators (eg, central neuromodulators and antipsychotics or other centrally acting agents, such as buspirone) and the $\alpha 2\delta$ (delta) ligand agents. This new terminology was introduced to improve understanding of their pharmacologic value and the rationale for their use in DGBI, reduce stigma, and improve treatment adherence. For a rationale and mechanisms of action of central

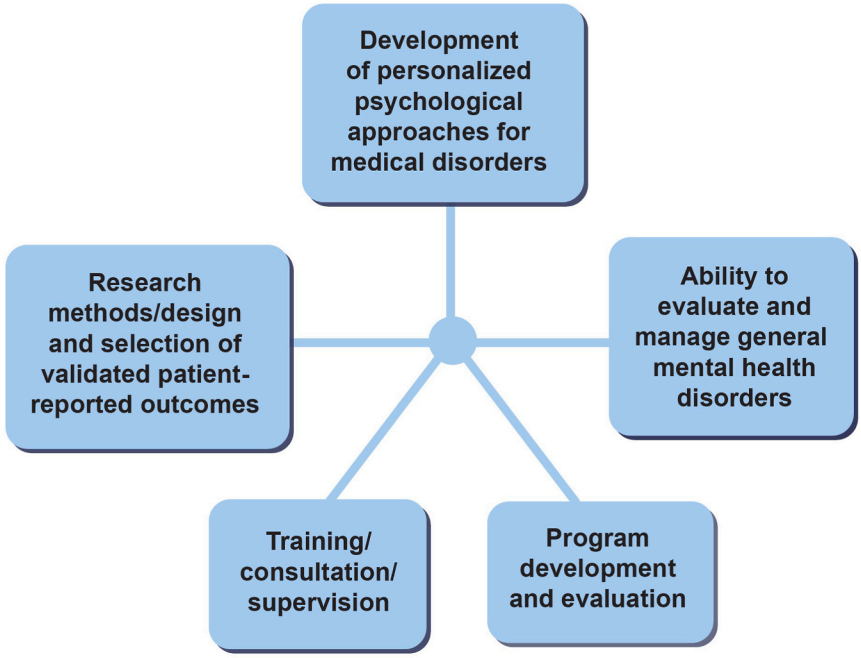

Figure 5. The benefits of integrating a gastropsychologist into a DGBI clinic. The role of a gastropsychologist in an integrated DGBI clinic extends beyond providing BGBT to patients, although the behavioral conceptualization and provision of individualized behavioral approaches for DGBI are likely to be among their primary contributions. Other important roles of a gastropsychologist in an integrated clinic include their training in research methods and design, their ability to coordinate and evaluate program development, their contributions to training and supervision, and their experience in evaluation and treatment of general mental health conditions.

neuromodulators in DGBI, see Supplementary Figure 9 and Supplementary Table 13.

Clinical considerations for the use of neuromodulators in DGBI. In general, neuromodulators should be reserved for patients with moderate-to-severe disease severity and with significant impairment of QoL and in whom other first-line treatments have not been sufficiently effective.

The choice of agent. In patients with painful DGBI, a brain–gut neuromodulator can be considered as a first-line option.[129] The choice of central neuromodulator is based on the patient's predominant symptoms, disease severity, psychiatric comorbidity, and prior experience with medications in the same class, and on patient and prescriber preference (Supplementary Figure 10).

In general, TCAs are the first choice for pain in nonconstipated adult IBS patients.[134–137] Given the limited evidence base and conflicting information in pediatric studies, a 2021 Cochrane review concluded that there is currently very little evidence to support clinical decision-making regarding the use of neuromodulators in children for painful DGBI.[138]

Nortriptyline or desipramine is generally better tolerated than amitriptyline or imipramine due to fewer antihistaminergic and anticholinergic effects.[137] Similar to the safety considerations in pediatric populations, caution may be required in the dosing of tricyclic medications in the elderly due to potential sedating and anticholinergic side effects, particularly in patients at risk of polypharmacy. Because SSRIs are less effective for pain, they are not commonly used as monotherapy; rather, SSRIs are a useful augmentation agent (see later in this article), or when the patient has a high level of anxiety that is contributing directly to their clinical presentation.

The SSRIs and SNRIs have a narrower therapeutic range. SNRIs (duloxetine, venlafaxine, or milnacipran) may have similar benefit as TCAs for treating chronic GI pain although they have not been specifically evaluated in chronic GI pain.[129,139]

If nausea and weight loss are of concern, and in functional dyspepsia, the addition of a low dose of mirtazapine can also be helpful in adults.[140] There are no studies evaluating effectiveness of mirtazapine in children with functional dyspepsia. Atypical antipsychotics such as quetiapine are recommended only for adult patients with severe, refractory IBS, especially if severe anxiety and sleep disturbances are also present and the patients have failed to respond to other centrally acting agents.[141]

Buspirone, an anxiolytic azapirone, may be used for functional dyspepsia in adults when early satiety, fullness, and nausea predominate. It has relatively few side effects and no potential for physical dependence and the mode of action involves 5-HT_{1A} agonism, which may improve receptive relaxation of the gastric fundus.[142] There are limited data on its use for functional dyspepsia in children and adolescents, but it is generally well tolerated in children and adolescents with anxiety.[143]

Delta ligand agents treat neuropathic pain, and may be of help in adults with chronic GI pain, although studies have not adequately addressed their benefits in DGBI. Pregabalin or gabapentin may reduce visceral hypersensitivity and improve pain in DGBI.[129] Due to lack of available data, these agents are not currently recommended for children and adolescents with DGBI.

Augmentation. In the patient with anxiety or multiple somatic symptoms or where there are incomplete benefits from TCAs or SNRIs, adding an augmenting agent is the recommended next option for treating chronic GI pain.[129]

Augmentation therapy refers to the use of a combination of drugs from different classes at low doses instead of 1 drug at a maximal dose. Examples of augmentation include: (1) adding buspirone to an SSRI, TCA, or SNRI to enhance the therapeutic effects; (2) adding buspirone to mirtazapine to improve dyspeptic symptoms, such as early satiety, epigastric discomfort, or nausea (especially associated with weight loss) and to reduce anxiety and depression; and (3) adding a low-dose antipsychotic (eg, quetiapine) to a TCA or SNRI to augment pain benefit, reduce anxiety, and improve sleep. In addition, combining centrally acting agents and behavioral treatments is recommended when the DGBI is severe and associated with psychological comorbidity, such as anxiety, depression, or PTSD.[144,145]

Due to the potential adverse effects of neuromodulators, BGBT are often used before tricyclics in children and adolescents, however, in children with refractory symptoms, there may be a synergistic role for augmentation with a neuromodulator in conjunction with BGBT.

When combining medications, it is important to have a familiarity with each agent's side effect profile, and be aware of potential hazardous side effects, such as serotonin syndrome.[129]

Adherence to medications. Attention to strategies to enhance patient adherence to any prescribed medications is critical, including eliciting patient concerns or barriers to taking neuromodulators. For further information on best prescribing practices there are several recommended review articles.[129,132,133,141,146]

Centrally acting pharmacologic agents vs brain–gut behavioral treatments. Central neuromodulators and BGBTs are often used together for their complementary and synergistic effects. Patient preferences, the availability of behavioral therapists, and medication tolerances may be important considerations when selecting treatment. In patients with significant psychiatric comorbidity, medications are often needed before patients are able or willing to engage in BGBTs. Although medications work faster and are more accepted and readily available, behavioral treatments have several advantages over pharmacologic approaches: they are safe and effective, their effects persist beyond the duration of the treatment, and they may be more cost effective.[147–149] Limitations of using behavioral treatments include the longer treatment duration and the need for patient motivation, as well as availability of and access to a professional trained in BGBT for DGBI.

Given the limited evidence-base for using central neuromodulators in pediatric DGBI, the potential for adverse effects with medications, and the excellent response to BGBT in children and adolescents with DGBI,[6,100,109,116,150,151] behavioral interventions are often preferred at an earlier stage in pediatrics.

Racial, Cultural, Gender, and Patient Preferences Specific to Treatment

Key messages:

- **Patient demographics, sociocultural factors, dietary preferences, availability of medications, resources, and religion are likely to influence the choice of treatment for DGBI.**
- **Patients should be provided with choice with respectful, shared decision making, striving toward equitable access to evidence-based treatment for patients from all different backgrounds.**

There is increasing recognition of the need to make healthcare accessible and equitable, and improving the diversity of the workforce with the aim to reduce disparities in the approach to delivering care, particularly in countries with multiethnic populations.[152] Effective patient-provider communication is one of the key foundations of treatment to achieve positive outcomes. Minority groups are more likely to experience difficult patient-provider communication, to feel disrespected by the healthcare system, and to experience barriers in obtaining healthcare insurance, with language and cultural barriers creating additional inequalities and limitations.[153]

Communicating a positive diagnosis helps improve patient acceptance, promotes shared understanding, prevents exhaustive, noncontributory, invasive investigations, may reduce stigma, and sets the scene for treatment.[24,154] Multicenter cohort data from the United States suggest that adoption of an evidence-based approach to DGBI may differ toward patients from different ethnic groups.[155,156] Patients from ethnic minority groups may receive unnecessary delays in commencing effective treatment, which may affect outcomes including adherence, healthcare use, QoL, and costs.

Although the exact reasons for disparities in the approach to DGBI toward patients from different ethnic groups are unclear,[157] it is likely to be multifactorial (Figure 6) with contributing factors including patient culture, provider/healthcare professional culture, and culture of health organizations.[25] Potential solutions include raising awareness of sociocultural differences among healthcare professionals and improving diversity within the gastroenterology and mental health workforce. There is an urgent need for further research to measure structural racism and discrimination and implementation of interventions to address this within gastroenterology and other disciplines (see Supplementary Table 14 for examples of diverse DGBI patient interviews).[158]

One important contributing factor may be the lack of inclusivity of males, patients of older age, children, and those from different racial and ethnic groups in DGBI clinical trials, resulting in a lack of a population-specific evidence base.[159] Given the complex contributions of psychosocial factors, the implementation of inclusive future clinical study designs is important to ensure that unbiased findings may be generalized to all population groups.[160] Patient-specific factors (ie, dietary practices and religious beliefs) may also contribute significantly to the choice of treatment. In terms of GI psychology and behavioral interventions for DGBI, uptake among different ethnic and racial groups may also be influenced by sociocultural factors (ie, psychological support may be a taboo subject for some racial and ethnic minority groups and may be

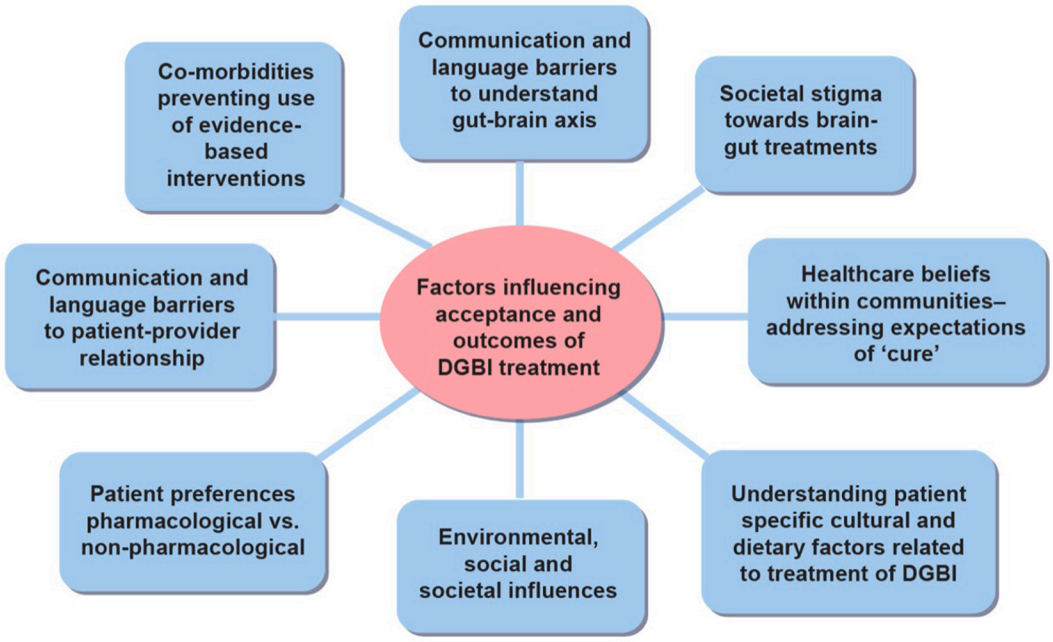

Figure 6. Factors influencing acceptance and outcomes of DGBI treatment. Several factors affect a patient's acceptance and outcomes in DGBI treatment. Among these, in addition to patient preferences, are the environment of communication, the patient's healthcare beliefs, cultural, dietary, and social factors, as well as any existing comorbidities.

influenced by the patient's relationships with their own ethnic group, with other ethnic groups, and with the dominant society, contributing to self-stigma and perceived stigma from others [public stigma] for seeking psychological support).[161]

Recommended Training Curriculum for Biopsychosocial Aspects of Disorders of Gut–Brain Interaction for Gastroenterologists and Primary Care Providers

Key messages:

- **Providers should be trained to understand the biopsychosocial basis of DGBI, the brain–gut axis and the limitations of a purely biomedical model of care for DGBI.**
- **Communication skills training can meaningfully improve the patient-provider relationship.**
- **Other important core competencies include initiation of first- and second-line therapies, initiation and titration of brain–gut neuromodulators, working knowledge of behavioral therapies, and competency in approaching refractory DGBI and the role of integrated multidisciplinary care.**

The Need for a Training Curriculum for Gastroenterologists and Primary Care Providers

Advances in the evidence-based management of some of the most frequently encountered DGBI have led to updated clinical practice guidelines that provide an important practical framework,[100,101] but it is paramount that healthcare professionals receive appropriate training to keep pace with these advances and ensure competency in implementing them in patient care.

Existing undergraduate, primary care, and gastroenterology training curriculums have very limited DGBI requirements,[162] likely resulting in limited levels of subjective competence in neurogastroenterology conditions[163] and the development of biases and negative attitudes toward DGBI.[164] Most primary care providers report uncertainty of the causes and treatment effectiveness for DGBI, leading to varied therapeutic approaches and broad but frequent use of diagnostic tests, despite guidance to limit investigations and use of a positive diagnostic approach.[165] Moreover, neuromodulators can be used effectively by primary care, highlighting the need to improve training for primary care providers. Similarly, many gastroenterologists in secondary care report a lack of confidence in initiating and titrating neuromodulators,[166] which is likely a consequence of limited training.[133]

A 2018 report from a joint task force of The American Neurogastroenterology and Motility Society (ANMS) and the European Society of Neurogastroenterology and Motility (ESNM) recommended that all gastroenterologists need basic training in DGBI.[167]

Defining themes for core DGBI competency (Supplementary Figure 11), with suggested different methods of delivery (Supplementary Table 15), and recommendation of specific skills, including communication training, based on modern understanding and developments in the field, will provide trainees with the skills needed to meet clinical demands.

The Importance of Communication Skills Training

The importance of improving communication training in psychosocial aspects of DGBI and forming a therapeutic patient-provider relationship cannot be overemphasized,[154] and is perhaps even greater in DGBI compared with better-defined chronic conditions. An effective patient-provider relationship (and parent/caregiver-provider relationship for children) is critical for health outcomes and is associated with improved diagnosis and patient adherence to a treatment plan, better self-management, reduced medical costs, improved practice efficiency, reduced risk of malpractice claims, and increased job satisfaction.[168,169]

Recommended Training in the Psychosocial Aspects of Disorders of Gut–Brain Interaction

It is essential for gastroenterology providers caring for patients with DGBI to recognize the role of GI-specific psychological factors in informing treatment decisions. A recently published primer has provided a stepwise, practical guide about how these factors can be assessed during clinical encounters in a time-efficient manner.[92] Providers should also be aware of common verbal and nonverbal behaviors affecting communication (Supplementary Table 16).[170]

Conclusions

This review has outlined for practicing providers the basic psychosocial context in which their DGBI patients develop and maintain their DGBI. This context must be accurately assessed and understood if treatment is to be successful, and we have highlighted the most critical areas where this assessment should occur, as well as optimal strategies to approach treatment, considering the complex multifaceted nature of the DGBI as well as the realities of varied clinical practice settings. We concluded with suggestions for strategies to best train future providers with the knowledge and skills to work with patients with DGBI, and future research directions that are likely to and are recommended to emerge. With the growing recognition of the critical importance of the relationship between social and psychological factors to the understanding and effective prevention and treatment of DGBI, this information is the foundational knowledge base for all providers in this field.

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.2026.02.009.

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Received December 19, 2025. Accepted February 9, 2026.

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Conflicts of interest
This author discloses the following: Laurie Keefer is chief executive officer of the Rome Foundation. The remaining authors disclose no conflicts.

Funding
The Rome Foundation provided organizational and editorial support.