Precision Medicine in Disorders of Gut-Brain Interaction

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Abstract: Overarching goals for the practice of medicine include preventing disease, making the correct diagnosis, and initiating evidence-based therapy to improve patient symptoms and quality of life. Precision medicine is an emerging field that encompasses these important goals. Precision medicine can be defined as a form of medicine that uses information about a patient's genes, proteins, environment, and lifestyle to prevent, diagnose, or treat disease. Oncologists have effectively used precision medicine for years to improve diagnostic strategies and treatment options; however, precision medicine has not been used to any significant degree in patients with disorders of gut-brain interaction (DGBIs). There is an argument to use precision medicine in DGBIs because these disorders are highly prevalent, affecting approximately 40% of the world's population. Functional dyspepsia, irritable bowel syndrome, and chronic constipation, some of the most prevalent and important DGBIs, are also clinically significant because they impose a negative impact on the health care system and greatly reduce patients' quality of life. This article defines precision medicine, clarifies differences between precision medicine and personalized medicine, discusses the use of precision medicine in the field of DGBIs, reviews its limitations, and outlines a strategy for its use in this field.

Keywords
Chronic constipation, functional dyspepsia, genomics, irritable bowel syndrome, metabolomics, precision medicine

Precision medicine is a form of medicine that uses information about a person's genes, proteins, environment, lifestyle, and psychological profile to prevent, diagnose, or treat disease.[1] The goal of precision medicine is to classify patients with shared characteristics into distinct subgroups based on specific and similar clinical features, prognostic factors, and treatment. Precision medicine is often confused with personalized medicine, although the approaches are quite different. Personalized medicine focuses on the individual patient—a single person at a time. In contrast, precision medicine focuses on subpopulations identified by clinical and molecular characteristics. The value of precision medicine becomes clear when comparing it with the standard (ie, traditional) treatment paradigm (Figure 1). Traditionally, a population of interest (eg, patients with irritable bowel syndrome [IBS]) would be offered a specific treatment (eg, a new medication) to improve their symptoms. In general, there would be 3 main outcomes from that course of therapy—some patients would respond, others would not respond,

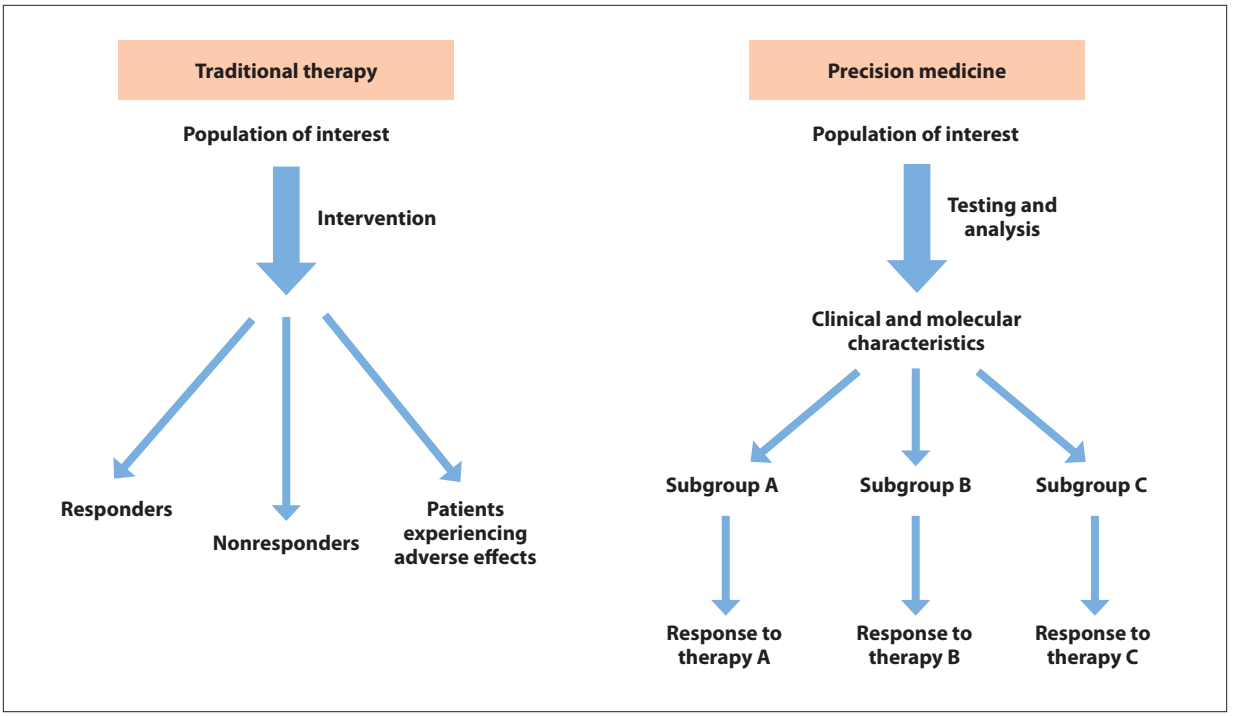

Figure 1. Traditional therapy vs precision medicine. In current practice (traditional therapy), a population of interest is offered an intervention to improve symptoms. Three outcomes typically evolve: some patients respond, others do not respond, and some develop adverse effects. In precision medicine, the use of multiomics helps classify subgroups based on clinical and molecular characteristics to identify the therapy most likely to provide a beneficial response without causing a side effect. Thus, some patients are treated with therapy A, whereas others are treated with therapy B or C, ideally maximizing response rates while minimizing adverse event rates.

and some would develop adverse effects—although there may be some overlap with these potential outcomes. In precision medicine, the population of interest is subgrouped into distinct populations based on genetic factors, demographics, symptoms (eg, severity, frequency, intensity), pharmacogenomics, and comorbid systemic or psychological disorders (see the following paragraph on multiomics). Patients would then be treated with a specific therapy predetermined to provide a positive response with little chance of causing a side effect. Thus, some patients would be treated with therapy A, whereas others would be treated with therapy B or C, depending on their clinical and molecular characteristics. In theory, response rates for each group would approach 100% and adverse event rates would approach 0%. Although not yet used to direct treatment, latent class analysis has been used to group IBS patients into different subpopulations based on symptoms and their psychological state.[2] This subgrouping is a critical first step to advance the use of precision medicine in disorders of gut-brain interaction (DGBIs).

A component critical to the success of precision medicine is multiomics, which involves various biologic data points combining different omics during analysis to provide a holistic understanding of disease.[1] As illustrated in Figure 2 and explained in the figure legend, multiomics is important to understanding disease development and symptom expression. These omics vary in importance from one disease state to another and also vary from individual to individual. Thus, genomic factors combined with past exposure (exposomics) and microbiome factors may be critical to symptom expression in one patient with IBS with diarrhea (IBS-D), whereas genomics, epigenomics, and metabolomics may be more critical in symptom expression in another patient with IBS-D.

Precision medicine is important to the continued progress of treatment of DGBIs for a number of reasons. One, DGBIs are prevalent. The Rome Foundation Global Epidemiology Study determined that 30% to 40% of adults have symptoms of at least 1 DGBI.[3] Two, DGBIs impose a significant economic impact on the health care system.[4,5] A recent study from the Netherlands identified mean direct and indirect costs of IBS (Rome III criteria) at $2444 per quarter or nearly $10,000 per patient per year.[6] Three, DGBIs significantly reduce patients' quality of life, on par with patients who have end-stage renal disease and diabetes.[7,8] Female patients with IBS typically score lower than male patients on most quality-of-life dimensions.[9] Four, precision medicine provides an opportunity to

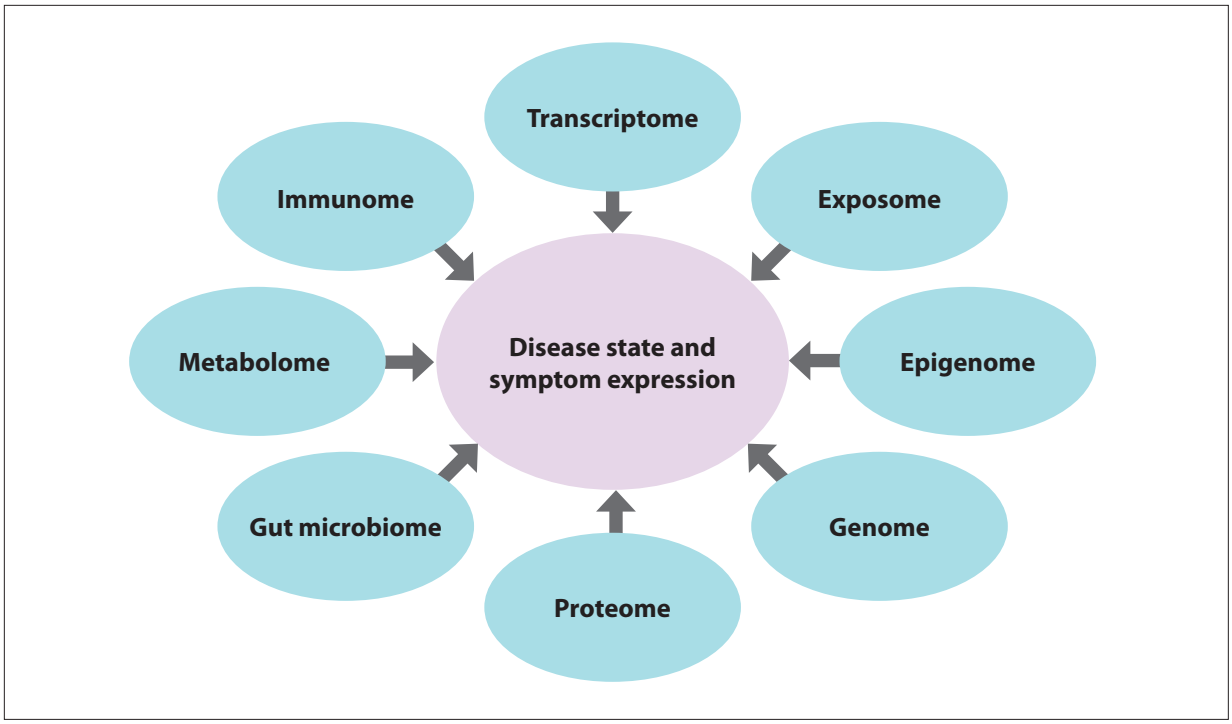

Figure 2. Multiomics is the interplay of various omics. These various processes are critical to the development of a specific disease state and symptom expression. The type and extent of omic process differs from patient to patient. The genome is the complete set of DNA that contains all genetic instructions for an organism. The exposome is the measure of all the environmental exposures of an individual in a lifetime. The epigenome refers to modifications to the genome that do not affect the DNA sequence. For example, environmental factors cause alterations in DNA methylation, histone modifications, and messenger RNA (mRNA) synthesis, thus changing phenotypic expression of genes. The transcriptome refers to the full range of mRNA expressed, whereas the proteome refers to the complete set of proteins expressed by an organism. The gut microbiome includes not just bacteria and their genes but also fungi and viruses. The metabolome represents the collection of small molecules and metabolites present in living tissue and biosamples, whereas the immunome refers to all the genes and proteins that constitute the immune system.

boost diagnostic accuracy, minimize or eliminate diagnostic uncertainty, and help predict treatment response. For example, measuring serum interleukin (IL)-22 levels (immunoprofiling) predicts therapeutic response in patients with Crohn's disease treated with anti–IL-23p19 agents.[10] Lastly, precision medicine will improve therapeutic response. For example, in treatment trials of IBS, functional dyspepsia (FD), and gastroparesis, placebo response rates typically range from 30% to 35%, and the therapeutic gains for many medications are limited to the range of 10% to 20%.[11-14] Precisely classifying patients into distinct subgroups (eg, based on genes, proteins, environmental factors, lifestyle, and ideally psychological profile as well) should greatly increase the response rate (ideally to 100%) and slash the placebo response (ideally to 0%). One example of this comes from studies in inflammatory bowel disease (IBD), where transcriptomics found that oncostatin M (OSM) was associated with increased responsiveness to anti–tumor necrosis factor (TNF) therapy in patients with IBD.[15]

This article aims to define precision medicine, distinguish the fields of precision medicine and personalized medicine, and review the importance of how precision medicine can further advance the field of DGBIs while acknowledging some of its limitations.

Precision Medicine in Other Disciplines

Oncology is at the forefront of precision medicine. Significant achievements have been made in the area of molecular testing dating back to the late 1900s, spanning both hematologic and solid tumor malignancies, through the combined efforts of oncologists and pathologists.[16] The identification of oncogenes, tumor suppressor genes, protein expression, and receptor activity through various laboratory methods, including Southern blotting, immunohistochemistry, and flow cytometry, prompted research in genome sequencing in oncology, which began more than a decade ago.[17] Genome sequencing has continued to evolve with the identification of systemic mutations

and gene alterations through next-generation sequencing, a large parallel sequencing technique to efficiently assess entire cancer genomes.[18] As a result, cancers can now be grouped based on phenotypes or genotypes, such as receptor or gene expression subgroups, allowing for more targeted therapies that treat patients effectively while minimizing side effects and improving outcomes. This cancer profiling has improved prognostication of cancers, as witnessed in the identification of human epidermal growth factor receptor 2 (HER2) mutations for breast cancer, *BRAF* gene mutations in melanoma, *KRAS* gene mutations in colorectal cancer, and many other instances.[19,20] One example of precision therapy in oncology involves cetuximab (Erbitux, Lilly), a monoclonal antibody that targets colorectal cancers expressing epidermal growth factor receptor. When used in this targeted population, cetuximab significantly improves survival benefit with enhanced quality of life.[21] Other well-known precision therapies include imatinib, a tyrosine kinase inhibitor targeting the *BCR-ABL1* fusion gene in chronic myeloid leukemia, and trastuzumab for HER2-positive breast cancer.[16] Ongoing strategies to classify cancers based on molecular markers and genes have changed the therapeutic playing field and improved the safety profiles of currently available agents. The valuable insights from precision oncology diagnostics and therapeutics provide a framework that can be used to guide precision medicine in DGBIs.

Using precision medicine in the evaluation and treatment of patients with IBD is much needed, as IBD can be a debilitating and lifelong condition associated with a long list of potential complications, including cancer.[22] Approaches to precision medicine in IBD have adopted similar structures to oncology, although they are less developed at this point in time. Currently, several biomarkers are routinely used to monitor patients with IBD. C-reactive protein (CRP), fecal calprotectin, and albumin are commonly used to evaluate and monitor inflammatory and nutritional status in patients with IBD.[23] Thiopurine methyltransferase genotype testing is utilized to assess thiopurine metabolism, thereby improving its efficacy and safety in IBD.[24] Monitoring serum drug levels of biologic therapies, particularly anti-TNF therapy, is also widely used to help guide treatment.

Many factors have been shown to correlate with IBD severity or response to therapy, and these can be incorporated into a precision medicine treatment plan. On a genetic level, factors associated with disease activity include phagocyte pathways (nucleotide-binding oligomerization domain containing 2 [NOD2]), intestinal barrier function (hepatocyte nuclear factor 4 alpha), immune signaling, fibrosis (OSM receptor and SMAD3), and cellular homeostasis.[22,25] For example, the genetic NOD2 mutation is associated with more severe disease.[26] Genetic testing of transcripts in serum or intestinal biopsies can help differentiate responders from nonresponders to anti-TNF therapy and anti-integrin therapy.[22] Similarly, identification of phenotypic expression of the OSM receptor can help distinguish the response profile to anti-TNF therapy.[27] Variations in the gut microbiome, such as *Clostridium* and *Bacteroides* populations, and insights from metagenomic sequencing, metabolomic analysis (secondary bile acid production), and proteome profiles (serum proteins caspase 8, interferon lambda receptor 1) have been studied to identify a greater likelihood to respond to anti-integrin and anticytokine therapy.[28]

Recent studies have focused on the identification of biomarkers that could aid in the diagnosis and disease monitoring of patients with IBD. These biomarkers include αvβ6 integrin antibody, microRNA (miRNA), the OSM receptor, B-cell–activating factor (BAFF), and prostaglandin E-major urinary metabolite (PGE-MUM).[29] Importantly, the αvβ6 integrin antibody demonstrates greater than 90% sensitivity and specificity in diagnosing ulcerative colitis, whereas PGE-MUM shows stronger correlation with IBD endoscopic activity than CRP.[30,31] Recent studies demonstrate that miRNA dysregulation correlates with intestinal inflammation, and increased OSM receptor or BAFF cytokine expression correlates with disease severity and inflammation.[29,32-34]

The aforementioned findings demonstrate that the future of precision medicine in IBD likely involves adopting a comprehensive multiomics model to effectively stratify patient populations for targeted treatments. Ideally, readily available and inexpensive biomarkers would facilitate diagnosis, guide therapy, and predict severity of disease or the risk of relapse. However, despite recent advances in IBD, the clinical use of precision medicine biomarkers remains limited. Future efforts should focus on validating these evidence-based tests, establishing standardized protocols, and educating providers on how to readily incorporate them into their practice paradigm.

Precision Medicine Tools Available for Disorders of Gut-Brain Interaction

A single highly sensitive and specific biomarker for the diagnosis of IBS does not currently exist, although anti-vinculin and anticytolethal distending toxin B antibodies appear to be valid markers of postinfectious IBS and can help distinguish IBS-D from IBD.[35-37] However, it is worth noting that a positive test may not lead to a change in treatment. A variant in the IL-6 gene was associated with an increased risk for postinfectious IBS in people involved in the Walkerton, Canada water contamination incident in May 2000.[38] An accurate prognostic marker for predicting a therapeutic response in all IBS patients

does not exist. Some experts currently promote the concept that the best biomarker for the diagnosis of IBS is a combination of individual elements, including a thoughtful history and physical examination, a careful review of potential warning signs, the Rome IV criteria, and limited diagnostic testing.[14,39] The Rome criteria were originally designed primarily for research, although a modified version can be easily used in clinical practice.[40] Validated patient-reported outcomes for IBS are available and should be used to ensure that patient-centric therapeutic outcomes are addressed.[41] The severity of gastrointestinal symptoms and the presence of extraintestinal symptoms, along with ongoing psychological distress (if present), can be combined to phenotype IBS patients into distinct subgroups using latent class analysis, although the utility of this for predicting therapeutic response has not yet been evaluated.[2,42] Pharmacogenomic testing can determine whether a patient is a hyper- or hypometabolizer of different drug classes, thus predicting the need for dose adjustments, although this is not routinely employed in clinical practice.[43] For example, 7% of Swedes are poor metabolizers of CYP2D6, meaning that they may have enhanced effects to nortriptyline.[44] The long variant of SERT (5-HTTLPR), the serotonin transport protein, is associated with increased efficacy of alosetron in IBS-D patients, whereas the short variant (5HTT) is associated with a reduced response rate to tegaserod.[45,46] A positive lactulose breath test has been shown to predict a higher likelihood of response to rifaximin in patients with IBS-D, whereas elevated methane levels are associated with IBS with constipation (IBS-C) and chronic constipation.[47,48] Despite these options, diagnostic and therapeutic uncertainty persists for many health care providers as they evaluate patients with IBS symptoms, thus highlighting the need for precision medicine. Although data are limited, metabolomics (see Figure 2) has the potential to address this dilemma. For example, a genome-wide association study from the United Kingdom involving more than 53,000 adults with IBS identified 6 susceptibility loci.[49] All of these loci were identified on autosomal chromosomes; none were present on the X chromosome. There was a strong genome-wide correlation with IBS and anxiety, depression, and neuroticism. Point-of-care blood testing could identify these loci in patients with IBS symptoms, thereby improving diagnostic accuracy. Identifying epigenomic changes, modifications to the genome that do not affect the DNA sequence, may also improve diagnostic accuracy, and one study in IBS patients uncovered changes in methylated DNA and miRNA.[50] The clinical utility of this is currently unknown. Transcriptomic changes, reflecting the full range of messenger RNA expressed, were detected in one study focusing on patients with IBS-D.[51] Proteomic changes, defined as the complete set of proteins expressed by an organism, were identified in patients with IBS-D after dietary changes.[52] Finally, research involving the gut microbiome has consistently demonstrated that IBS patients are different from healthy controls and patients with IBD. Although a specific signature for individual IBS subtypes has not been identified, reduced levels of *Bifidobacterium* and *Bacteroidetes* appear to be a common theme across studies.[53-55]

A precision medicine–based approach would appear particularly well suited for patients with FD, given the complex pathophysiology of this condition, its wide prevalence (roughly 10% in the United States), and the fact that there is currently no treatment approved by the US Food and Drug Administration for the condition despite its prevalence.[3] FD is divided into 2 subtypes, epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS). Numerous physiologic mechanisms are thought to contribute to symptoms, including impaired gastric accommodation, delayed gastric emptying, visceral hypersensitivity, abnormalities in intestinal permeability, duodenal immune alterations, and changes in the gut microbiome.[56,57] Thus, FD represents a heterogeneous disorder in which precision medicine would provide welcome guidance to subclassify patients and direct treatment, particularly as there is currently no universally accepted treatment algorithm.

Both genomic factors and microbiome alterations have been implicated in FD. In a recent survey of multiple large population-based biobanks involving 10,078 FD patients and 351,282 controls, no genome-wide significant association was identified; however, suggestive signals were detected for 13 independent loci.[58] The heritability of FD was estimated to be 5%, but a significant genetic correlation with other gastrointestinal conditions (eg, hiatal hernia, gastritis, duodenitis), pain-related traits, and personality traits (eg, neuroticism, anxiety, depression) was demonstrated, suggesting that FD can present with other unique symptom and personality traits as a result of genetic factors. In a meta-analysis of 35 case-control studies, minor allele (T) of GNB3 825C>T was associated with increased susceptibility to EPS, but a number of other genes evaluated were not found to be associated with susceptibility to FD at large.[59] However, in a study of 174 Greek patients with FD, significant associations were identified in CD14 rs2569190, GNB3 rs5443, MIF rs755622, and TRPV1 rs 222747 gene polymorphisms compared with controls; furthermore, CD14 CT genotype was associated with higher epigastric burning and nausea scores.[60] Certainly, more investigation is needed, but these data suggest that genomics could play a role in classifying and predicting unique symptom presentations in FD.

With respect to the microbiome, a recent study

compared the duodenal microbiome via analysis of duodenal aspirates among patients with FD, IBS, and healthy controls and found that the α-diversity index was significantly lower in patients with FD and IBS compared with controls.[61] Specifically, the relative abundance of the *Chloroflexota* phylum was lower in patients with FD and IBS compared with controls, and the relative abundance of the *Rhodothermota* and *Thermotogota* phyla was lower in patients with FD compared with controls (but not in patients with IBS). Additionally, in a study of 50 patients with FD, compared with 30 control patients, analysis of the mucosa-associated microbiota obtained via duodenal biopsies revealed that a relative abundance of Firmicutes was associated with increased dyspeptic symptom burden, whereas taxa affiliated with *Bacteroidota* decreased with increasing symptom burden.[62] Moreover, an inverse relationship was identified between gastric emptying time and the relative abundance of *Veillonella* species. Microbiome assessment may be another pathway by which precision medicine can stratify patients and potentially identify novel treatment mechanisms via targeted modulation of the gut microbiome.

Finally, there is evidence that diet may trigger dyspeptic symptoms in some patients. In a study of 50 patients with FD, compared with 23 healthy controls, lamina propria mononuclear cells (LPMCs) were isolated from duodenal biopsies and exposed to gluten and gliadin. In response to gliadin (but not gluten), the effector Th2-like population was increased in LPMCs in patients with FD compared with controls. Furthermore, the gene expression of TRAV26-2, a T-cell receptor variant associated with gliadin processing, was found to be reduced in patients with FD.[63] These findings highlight an interesting interplay between gene expression/immune response and diet, underscoring another area where precision medicine could refine diagnosis and treatment in DGBIs, particularly given the frequent association between DGBIs (such as IBS and FD) and dietary triggers.

Precision medicine in chronic constipation is starting to evolve through a growing understanding of individualized symptom and microbiome profiles. Chronic constipation affects 10% to 15% of the general population, mostly consisting of those with functional constipation, leading to significantly impaired quality of life.[64] There is a need for precision medicine approaches in functional constipation, where treatment is limited and health care resource utilization is sizable.[65] Current efforts in clinical phenotyping include transit testing and anorectal manometry, both used to tailor therapy in medically refractory chronic constipation patients.[66] Microbial dysbiosis has been shown to contribute to the pathogenesis of chronic constipation, raising potential for treatment options such as probiotics, prebiotics, antibiotics, or fecal microbiota transplantation.[67] The use of artificial intelligence to devise a personalized microbiome modulatory diet has been shown to improve constipation and quality of life, further supporting the potential role of individual microbiome-directed therapies.[68]

Bile acid diarrhea (BAD) is another area where precision medicine is gaining momentum, as deeper insights into bile acid metabolism and regulatory pathways may guide diagnostic and therapeutic approaches. BAD affects one-fourth of patients presenting with chronic diarrhea as a consequence of dysregulation of enterohepatic circulation through either excessive synthesis or reduced absorption.[69] Molecular mediators such as fibroblast growth factor 19 (FGF19), farnesoid X receptor (FXR), and Takeda G protein–coupled receptor 5 all play key roles in bile acid homeostasis.[70] Alterations in gut microbiome have been correlated with BAD, indicating interplay with colonic bacteria and metabolism of bile acids.[71] Emerging studies suggest that serum and fecal biomarkers, including reduced serum FGF19 levels, increased 7α-hydroxy-4-cholesten-3-one, or the selenium homotaurocholic acid test (75SeHCAT), may allow for more accurate diagnosis and stratification of patients with BAD who could benefit from specific therapies.[72] Such insights have opened the door to individualized treatment strategies, including bile acid sequestrants and FXR agonists, based on a patient's biochemical profile.[73] These developments support an effort to shift from standard therapies toward more guided interventions in BAD, although further research is needed to validate diagnostic and therapeutic methods.

Pathway for Precision Medicine in Disorders of Gut-Brain Interaction

Adopting a precision medicine–based model to diagnose and treat DGBIs should help propel this important field of medicine forward and lead to improved patient care. A basic model of how such a model could fit into future clinical practice is proposed in Figure 3. The first step would be to analyze a patient's unique predefined risk factors with genome sequencing, as well as analysis of one's transcriptome, proteome, and immunome, to identify specific inheritable factors that put an individual at risk for a specific DGBI. Next, assessment of environmental factors, acquired as a result of an individual's unique exposures in life, such as one's epigenome, metabolome, and, importantly, microbiome characterization, would also be necessary to further risk stratify and classify patients. This information, combined with an individual's unique symptom presentation, could then be incorporated into a large database, which when integrated with artificial intelligence, could ultimately yield not only a diagnosis but identify a specific subclassification of DGBI presentation.

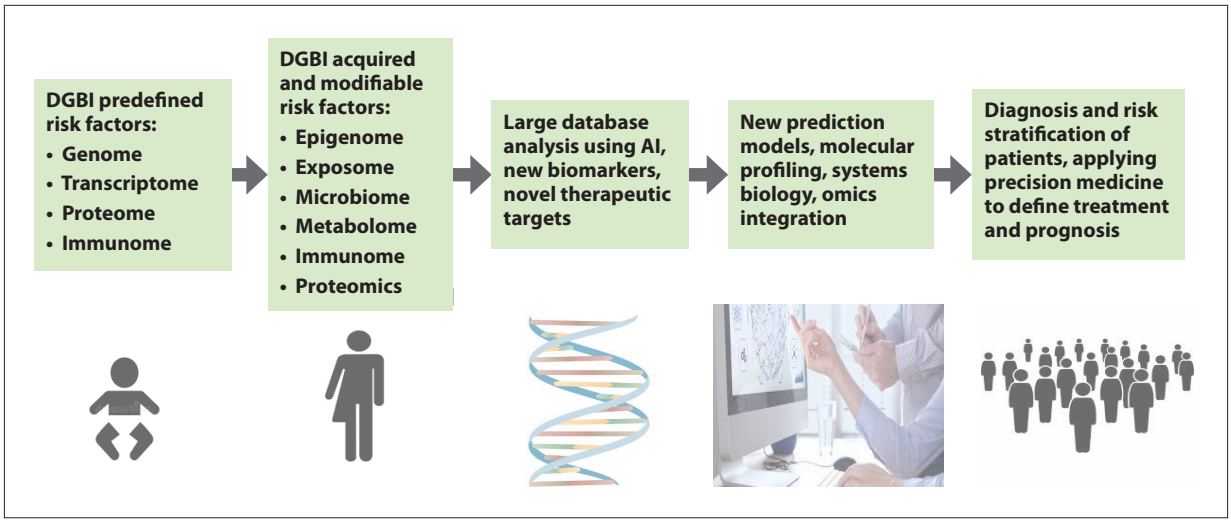

Figure 3. A proposed pathway for precision medicine in DGBIs.

AI, artificial intelligence; DGBIs, disorders of gut-brain interaction.

Subsequently, testing an individual's pharmacogenomic profile to help predict treatment response and risk of adverse events, as well as assessing one's immune response to dietary factors such as wheat proteins, could help pinpoint the right treatment for the right patient. As an example, a recent randomized, double-blind, sham-controlled multicenter trial found that a novel 18-food serum immunoglobulin G assay could be used to guide dietary therapy for patients with IBS.[74] As it stands, treatment options for many DGBIs are limited and universally accepted treatment algorithms are lacking. Furthermore, patients are placed into large diagnostic categories where few subclassifications exist. Disorders in which subcategories of disease presentation have been defined, such as EPS and PDS for FD and IBS-C, IBS-D, and IBS mixed for IBS, are in the minority. Thus, the clinician is often left with little guidance regarding how to identify the best treatment for each patient. Precision medicine would fundamentally shift the approach to DGBIs by utilizing the multitude of inherited and acquired individual factors, which no doubt influence individual symptom manifestation, to assign patients into precise DGBI subclassifications, which would then guide highly precise treatment pathways that maximize efficacy and limit the potential for adverse effects.

The Future

The future of precision medicine in DGBIs has the potential to transform clinical care. With continued advances in multiomics, patients will be more accurately subclassified into clinically significant phenotypes that build upon traditional generalized disease labels. Much can be learned from the fields of oncology and IBD, where genomic and transcriptomic patterns already guide immunosuppressive and cancer therapy. Cell-free tumor DNA testing is gaining traction for a quick analysis of patient genes, as seen in FoundationOne Liquid CDx, which identifies more than 300 genes to guide solid tumor cancer therapy.[75] Similarly, patient-derived organoids for targeted therapies using biopsied and cultured organ tissue can help delineate the ideal treatment strategy.[76] Biobanks will start to play a larger role in building a foundation of large data stores of patient biospecimens linked to clinical phenotypes. Newly emerging and rapidly transforming technology, including artificial intelligence, could more efficiently interpret the complex data analysis of multiomics, identifying predictive patterns that guide both diagnosis and treatment. Wearable technologies could be refined and utilized, such as a digital symptom tracker or point-of-care testing that works to further classify a disease phenotype, allowing real-time evaluations to personalize patient care.

However, several challenges remain in precision medicine. There is a need for validation of serum biomarkers and multiomics signatures in larger studies. Large data pools raise ethical concerns about maintaining patient privacy and confidentiality. Widespread availability of different testing methods, clinical workflows to interpret complex results, and cost-effective access to diagnostics will be essential for future practice. Research funding will be critical. Although the National Institutes of Health appropriates billions of dollars per year for oncology research, the level of funding for DGBIs is but a fraction of this.

Conclusion

In many ways, precision medicine is the future of DGBI management. Precision medicine is already a part of real practice in other fields of medicine such as oncology and

other subspecialities of gastroenterology such as IBD. DGBIs, in particular, appear ripe for precision medicine given their complex pathophysiology, frequent overlap with other systemic and psychological disorders, variable symptom presentations, and the recognized intricate interplay between environmental factors (such as the microbiome and diet) and genetics/immune response. Furthermore, despite the wide prevalence of DGBIs, generally speaking, treatment options are limited. Adopting precision medicine would allow health care providers to better understand how DGBIs present differently among groups of patients, including those with the same disorder, and would help to identify specific treatments for unique subclassifications of patients, which would maximize efficacy and minimize adverse effects. Importantly, precision-based medicine may change how DGBIs are diagnosed, as the field moves from symptom-based criteria to a classification system based on genetics, biomarkers, and symptoms. By understanding how groups of patients present differently, precision medicine will also open the door for discovery of novel treatments, which are sorely needed for DGBIs, diseases that are frequently difficult to treat in current practice. Certainly, precision medicine is not without limitations. For instance, adopting a precision medicine–based approach may lead to more testing, particularly if genomic profiling, microbiome assessment, and pharmacogenetic testing, among other testing, are required for all patients. This may be burdensome and costly, especially because of the costs associated with computing the vast amounts of data required to classify and risk stratify individual patients. However, with the rise of artificial intelligence, it is likely that such a process will become more efficient and less costly with time. As well, it will be critical to demonstrate that a new biomarker (or genetic test or microbiome profile) leads to a change in treatment or outcome.

In short, precision medicine is already part of current medical practice and appears poised to expand across all fields in the near future. The groundwork for precision medicine has been laid in DGBIs and continues to expand as the field gains more understanding about the complex interplay between inherited traits and environmental exposures, which influence the individual manifestation of symptoms and response to treatment. It is only a matter of time before precision medicine becomes firmly entrenched in the clinical management of DGBIs, a field that remains incompletely understood, where diagnosis and treatment are often uncertain—a field where precision is needed.

Disclosures

The authors do not have any relevant conflicts of interest to disclose.

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