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The Contribution of Diet and Lifestyle Factors in the Prevalence of Irritable Bowel Syndrome

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***Abstract*—**Irritable Bowel Syndrome (IBS) is a heterogeneous functional bowel disease that is characterized by chronic visceral abdominal pain and abnormal bowel function and habits. Its multifactorial pathophysiology and mechanisms are still largely a mystery to the contemporary biomedical community, although there are many hypotheses to try to explain IBS's presumed physiological, psychosocial, genetic, and environmental etiologies. IBS's symptomatic presentation is varied and divided into four major subtypes: IBS-C, IBS-D, IBS-M, and IBS-U. Given its diverse presentation and unclear mechanisms, diagnosis is done through a combination of positive identification utilizing the "*Rome IV Irritable Bowel Syndrome Criteria*" (Rome IV) diagnostic criteria while also excluding other potential conditions with similar symptoms. Treatment of IBS is focused on the management of symptoms using an assortment of pharmaceuticals, lifestyle changes, and dietary changes, with future potential in microbial treatment and psychotherapy as other therapy methods. Its chronic, heterogeneous nature and disruptive gastrointestinal (GI) symptoms are negatively impactful on patients' daily lives, health systems, and society. However, with a better understanding of the gaps in knowledge and technological advances in IBS's pathophysiology, management, and treatment options, there is optimism for the millions of people worldwide who are suffering from the debilitating effects of IBS.

***Keywords*—**Irritable bowel syndrome, lifestyle, diet, functional gastrointestinal disorder.

I. Introduction

IBS is a chronic functional gastrointestinal disorder characterized by long-term (at least 6 months) mild to recurrent abdominal pain, bloating, and altered bowel habits. It greatly decreases a patient's health-related quality of life, reduces work productivity, and generates significant healthcare costs. IBS symptoms tend to overlap with a variety of other GI and even non-GI symptoms [1]. However, IBS's pathophysiology is not well understood, and it is only hypothesized that IBS is the multifactorial combination of visceral hypersensitivity, issues with gut motility, and abnormal gut secretions [2], [3]. The mechanisms behind these factors are equally poorly understood, but there are a few possible explanations. Symptomatic presentation is insufficient for a diagnosis of IBS; the methodology necessitates the exclusion of other diseases that may cause or mimic these symptoms [1]. Furthermore, the complexity and diversity of IBS's presentation makes treatment difficult. Treatment of IBS involves managing the predominant symptoms utilizing a variety of contemporary methods including pharmacotherapy, lifestyle, dietary, psychotherapy, and microbial therapy [4].

Ultimately, the incomplete knowledge of IBS coupled with the extensive rigor in staying concurrent with the most recent research of IBS can lead to clinical difficulties in understanding IBS as well as complications in diagnosing and managing a patient's IBS. There is a profusion of existing literature that covers a diverse number of topics, hypotheses, and strategies regarding IBS, but these sources are scattered, cover a broad chronological range that includes modern and outdated studies, and are often narrow in scope. Thus, there exists a need for an all-encompassing overview of IBS that provides sufficient, contemporary information. As such, it is the goal of this work to collate contemporary sources to offer some insights on IBS and serve as a resource for clinical practice and future study of IBS.

II. Method

The purpose of this metanalysis is to understand IBS and its history, prevalence, diagnosis, symptoms, effects on body physiology and patient psychology, clinical pathology, treatment options, and current and future research. Peer reviewed articles and journals that contained the keywords 'Irritable Bowel Syndrome' and 'IBS' were found utilizing the California State University East Bay's Library Database system. The articles and journals from a variety of academic sources, journals, or databases were reviewed to evaluate their content and quality. The academic papers deemed useful, well researched, and were published within the past 8 years as of 2023, were then compiled into a list and each was thoroughly reviewed. The information within each source was subsequently categorized in a text document based on the type of information provided and the recency of the article. The data and information gathered were ultimately collated into a comprehensive literature review serving as a current resource on IBS.

III. Literature Review

IBS Symptoms

The defining symptoms of IBS are chronic abdominal pain as well as altered bowel habits with constipation, diarrhea, or both [5]. Additionally, depending on the presence of constipation, diarrhea, a mix of both, or an indeterminable

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pattern of altered bowel habits, an IBS subtyping can be given to the patient, which includes IBS-D, IBS-C, IBS-M, or IBS-U. Features that further support a diagnosis of IBS include pain relieved or worsened by bowel movements, bloating, distention, flatulence, migraine, interstitial cystitis, dyspareunia, lethargy, dysphagia, early satiety, intermittent dyspepsia, nausea, non-cardiac chest pain, and comorbidity with other functional GI disorders [5], [6]. Additionally, psychiatric disorders such as major depression and anxiety occur frequently in IBS patients, and it is assumed that these disorders are linked to IBS via an underlying yet undiscovered pathophysiological mechanism [7].

Reference [8] reports that patients describe episodic moderate symptoms of pain and bloating present in about half of the days over a period of 21 days in untreated patients. When taking into account episodes of constipation and diarrhea, IBS symptom episodes occur for approximately two-thirds of the time out of 21 days. As a result of its high episodic frequency, chronic nature, and varying signs and symptoms that also vary in severity, patients report often suffering significantly negative effects on their quality of life.

Pathophysiology

IBS is categorized as a functional GI disorder under the Rome IV diagnostic criteria, and thus there are no detectable structural or biochemical abnormalities that clinicians can attribute the symptoms of IBS to [4], [7]. The assumed etiology of IBS is multifactorial and involves genetic, physiological, psychosocial, and environmental origins [9]. Most studies agree however that IBS's central and traditional pathophysiological presentations include abnormal GI motility, impaired immune function of the intestinal mucosa, a dysregulated central nervous system, and visceral hypersensitivity [10]. These pathophysiological factors involve endocrine, neuronal and immune system mechanisms that link the brain and gut, and are modified by the intestinal microbiota, allowing IBS to be further defined as gut-brain disorder [10]. However, even in contemporary studies, the traditional pathophysiological presentations and its mechanisms are not well understood or illustrated, and there exists a plethora of proposed hypotheses that either attempt to unify the multifactorial origins into a cohesive umbrella hypothesis, or only partially explain one or several facets of IBS separately [2], [9], [10]. Overall, studies have highlighted the potential importance of serotonin, GI endocrine cells, neuroendocrine systems, mucosal immune function, inflammation, intestinal microbiota, and early life stressors such as psychosocial stressors and abuse in the pathophysiology of IBS, but once again there are a diverse variety of hypotheses that attempt to explain these factors while a proven mechanism remains elusive [1], [2], [9]-[13].

A major hypothesized component of IBS's pathophysiology is its relation to psychosocial triggers and effectors such as depression, with an emphasis on early life psychosocial stressors and abuse [1], [9], [12]. It has been found that IBS symptom severity was significantly worse in IBS patients with abuse histories compared to patients lacking a history of abuse [14]. Similarly, a study by [14] indicated that mood disorders such as depression and anxiety have greater influences on IBS symptoms and health related quality of life (HRQOL). The study also noted that women have a higher incidence of having a history of mood disorder or abuse, which can explain why women have higher prevalence of IBS. Reference [14] further describes how childhood abuse or trauma increases the hypothalamic-pituitary-adrenal (HPA) axis activation as seen through neuroimaging, with similar HPA changes identified in those with major depressive disorder. In addition to HPA abnormalities, limbic structure abnormalities related to abuse and depression are also seen, and the combination of the two leads to more severe symptoms and poorer outcomes in regard to chronic pain symptoms, such as IBS. Another study by [12] found that there is overlap in multiple pathways in IBS and depression, including: (a) change in microbe characteristics attributable to immune system dysfunction; (b) alterations in the HPA axis mediated by CRF in response to stress, altered cytokines, and immune function; and (c) other factors involved in neuroplasticity that are attributable to comorbidities of depression and IBS.

One significant proposed hypothesis behind the pathophysiology of IBS includes the dysregulation of the HPA axis; chronic, low-grade subclinical mucosal inflammation; and colonic mucosal abnormalities [13]. Reference [13] found evidence that supports the inflammation-immunological etiopathogenesis hypothesis of IBS, where elevated proinflammatory plasma cytokines IL-6 and IL-8 have been found. These elevated cytokines indicate a dysregulated HPA axis and abnormal serotonergic 5-HT function, leading to visceral hypersensitivity, altered gut motility, and enhanced pain sensitivity, all features within IBS's umbrella of pathophysiological presentations. Further examination also found that posttraumatic stress disorder, childhood, abuse, depression, and anxiety also are contributory towards the proinflammatory phenotype leading to the elevated levels, which is consistent with the accepted brain-gut axis and psychosocial links of IBS. This culminates in a hypothesis that neuroinflammation is involved in the gut-brain axis, leading to altered neuroendocrine pathways and glucocorticoid receptor genes that in turn promotes an overall proinflammatory phenotype with a dysregulated HPA axis and serotonergic function which accounts for the symptoms of IBS [13].

Another proposed hypothesis explaining the pathophysiology behind IBS by [9] involves alterations in gut microbiota as the unifying factor in all of IBS's pathophysiological etiologies. Reference [9] suggests that given the gut microbiota's importance in development of the host immune system, maintenance of normal GI physiology, and fermentation of undigested carbohydrates along with its propensity to be modulated by stress, host genetics, diet, early childhood experiences, it is a strong candidate for being the unifying factor that ties together all the origins of IBS's etiology. The study further elucidates the effect of gut microbiota on the gut-brain axis, visceral sensation, GI motility, intestinal barrier dysfunction, and immune activation, highlighting many of the hypothesized factors of IBS and the role of gut microbiota in each. However, despite the

connections made, the study recognizes that there are still gaps in research excluding the fact that gut microbiota is indeed the unifying factor. Reference [9], instead, proposes that gut microbiota constitute the framework of future IBS studies using longitudinal study designs, well-annotated clinical metadata, and more targeted approaches to studying microbiota with new technological advances.

Diagnosis Methodology

Under Rome IV, IBS is defined as recurrent abdominal pain that occurs, on average, at least one day per week in the last three months and is also associated with two or more of the following criteria: (a) related to defecation, (b) associated with a change in stool frequency, (c) associated with a change in form or appearance of stool, and (d) the criteria fulfilled for the last three months with symptoms having onset equal or greater than six months before diagnosis [4]. The Rome IV diagnostic criteria are further elaborated, categorizing IBS into four subtypes based on patients' reported predominant bowel habits in conjunction with the standards set by the Bristol Stool Form Scale (BSFS). The four IBS subtypes are: 1) IBS-C, or IBS-constipation dominant, in which greater than 25% of bowel movements are types one or two on the BSFS and less than 25% are BSFS types six or seven; 2) IBS-D, or IBS-diarrhea dominant, where greater than 25% of bowel movements are BSFS types six or seven and less than 25% consists of BSFS types one or two; 3) IBS-M, or IBS-mixed, defined as greater than 25% of bowel movements can be categorized BSFS types one or two, with less than 25% categorized at BSFS types six or seven; (4) and lastly, IBS-U, or IBS-unsubtyped, an unclassified subcategory where the patients meet criteria for IBS, but their bowel movement patterns cannot accurately be categorized into one of the three aforementioned subtypes [4], [15].

However, contemporary methodology for diagnosing IBS dictates that the symptom-based Rome IV criteria and identifying the subtype is not sufficient in affirming IBS as a diagnosis, as there needs to be limited diagnostic testing to distinguish IBS from other GI conditions with similar symptoms, such as celiac disease, inflammatory bowel disease (IBD), or lactose intolerance [5]. Other conditions with significant overlap in symptoms and presentation that also respond similarly to the same treatment plans of IBS include functional diarrhea, functional constipation, and other functional GI disorders, and thus must be also considered during the diagnostic process as they may present as comorbidities [4]. Non-celiac gluten sensitivity is a condition that exhibits the same GI and extra-GI symptoms as those with IBS, and thus is important to identify in a patient and give consideration to during diagnosis [16], [17]. Patients with IBS-like symptoms that also present with atypical symptoms and alarm features such as anemia, weight loss, rectal bleeding, progressive abdominal pain, laboratory abnormalities such as elevated inflammatory markers, and family history of colorectal cancer or celiac disease should be screened to rule out other inflammatory, malignant, or organic disease [6].

According to [10], it is recommended that the diagnosis of IBS be made utilizing the Rome IV criteria along with a reliable collection of medical history, physical examination, and necessary laboratory tests in justified situations including the possibility of colonoscopy if justified and the patient is under 50 years old. According to [10] and [5], justified situations with consideration to the patient's presentation of symptoms, demographics, and medical history may include: (a) serum C-reactive protein (CRP) and fecal calprotectin to differentiate between IBS without constipation and IBD, (b) serological tests to rule out celiac disease, (c) breath tests to rule out SIBO, (d) thyroid testing to rule out thyroid disorder, and potentially (e) abdominal ultrasound. Another factor both studies emphasize that must be considered during the diagnostic process is the onset of the symptoms, as for example onset post-gastroenteritis or following an acute episode of diverticulitis would suggest post-infectious IBS.

Treatment

Given that IBS lacks a cure, treatment for IBS is aimed at addressing the patient's symptoms and tailoring the management with regards to the patient's personal goals, predominant symptoms, subtyping, and other comorbidities or personal history [1]. Contemporary treatment involves utilizing one or a combination of these methodologies: dietary and lifestyle recommendations, pharmacotherapy, microbial therapy, and complementary and alternative medicine (CAM). However, regarding exploring CAM as a potential treatment methodology, recent research involving randomized controlled trials is inconclusive of its beneficial effects and further research in this area is needed [18].

Lifestyle

Reference [5] notes that following diagnosis of IBS, patients should be reassured and educated on their condition, ensuring that the patient understands IBS in order to serve as a guide for exploring avenues of IBS treatment, intervention, counseling, and caregiving. This process can include providing a simplified explanation of the presumptive pathophysiology behind IBS. Following education, it is recommended that the provider obtains a detailed understanding of the patient's dietary habits and lifestyle habits, as they are important in identifying a starting point for beginning management. Personal disease triggers play in the presentation of the diseases, and thus gaining a detailed history can allow a more tailored management plan [5]. Beyond education and obtaining a clear personal history however, there are no recommended lifestyle changes to recommend a patient, as studies involving regular exercising via walking, yoga, or personalized exercise routines to reduce IBS symptoms have shown to be inconclusive in any direct benefits [10], [19].

The Role of Diet

Patients often associate their IBS symptoms with eating a meal, as food intolerances or sensitivities are frequently reported, and up to 90% of IBS patients restrict their food to prevent symptoms or reduce their frequency or severity [4]. Current dietary therapies that have shown success in reducing

symptoms include avoiding triggering foods, initiating a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet, and the inclusion of fiber in diet [1], [4]. Patients with IBS often attribute their symptoms to eating specific food items such as milk, milk products, wheat products, cabbage, onion, peas, beans, and fried foods [11]. However, according to [11], there is no evidence of food allergy or intolerance being directly involved in IBS, but it is recommended by the British Dietetic Association to trial the NICE-modified diet that involves: (a) having regular meals; (b) replace wheat products with spelt products; (c) reduce intake of fatty foods, onions, cabbage, and beans; (d) avoid soft drinks, carbonated beverages, chewing gum, and sweeteners that end with "-ol"; and (e) regularly intake of psyllium husk fibers.

Although there is no long-term data, current evidence is supportive of a low FODMAP diet aiding in relieving IBS symptoms that are a result of poorly absorbed carbohydrates and fiber triggering or worsening IBS symptoms [11], [15], [20], [21]. It is hypothesized that a low FODMAP diet restores the density of Peptide YY (PYY) cells located in endocrine cells in the large intestine [20]. The study indicated that PYY plays a role in GI motility, secretion, absorption, and appetite, but IBS patients have low PYY concentration and low density of PYY cells in the large intestine, which contributes to the dysmotility and visceral hypersensitivity seen in IBS patients. However, diet management through a low FODMAP diet appears to restore the PYY cell density within and reduce IBS symptoms. Despite there being evidence supporting beneficial effects from the FODMAP diet, current concerns regarding the efficacy of the FODMAP diet compared to other dietary recommendations and the validity of the studies require further research to be done before the FODMAP can be conclusively recommended [10].

Inclusion of soluble fiber in diet, particularly psyllium, is strongly recommended as first line therapy and is the most accepted of all dietary therapies as being beneficial in mitigating the symptoms of IBS [10], [11], [15]. The therapeutic benefits of fiber include the lack of side effects; ability to improve stool viscosity and frequency; ability to increasing stool volume; acceleration of peristalsis; stimulation of the colon mucosa; and interaction with intestinal microbiota, immune system, nervous system, and neuroendocrine system. Insoluble fibers such as wheat bran, nuts, beans, grains, and root vegetables are not recommended.

Pharmacotherapy

Medications have been shown to be efficacious in treating the symptoms of IBS, and thus a practical algorithm is created based on the specific predominant symptom of GI dysfunction and the particular subtype of IBS [4]. The typical types of medications and specific medications used in treatment involve: (a) antispasmodics, including drugs with anticholinergic or calcium-channel blocking properties that function to relax gut smooth muscle, or peppermint oil which blocks L-type calcium ion channels; (b) antidepressants, including tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) which affect pain perception, mood, and motility; (c) antidiarrheal medications such as *loperamide* or *eluxadoline* to inhibit peristalsis, prolong gut transit, and reduce fecal volume; (d) serotonin agents such as 5-HT receptor agonists including *ondansetron*, *alosetron*, *ramosetron* which serve to slow colonic transit and reduce visceral pain; (e) bile acid sequestrants, such as *cholestyramine*, to bind intraluminal bile acids; prokinetic agents, for example *prucalopride*, as well as other osmotic laxatives to treat constipation; (f) *lubiprostone*, which has been proven to provide relief from bloating, bowel movement frequency, abdominal pain, straining, constipation, and stool consistency; (g) and *linaclotide*, a guanylate cycle C agonist that reduces constipation and visceral hypersensitivity [1], [4], [5], [10], [15], [22]. Of this list, most have sufficient studies and evidence that support their therapeutic effects, albeit several treatment methods that are used as mainstays of IBS management, including antispasmodics, *loperamide*, and bile acid sequestrants only have low evidence in supporting their usage and need further research to confirm their benefits [4], [10], [13], [15].

Reference [15] notes that pharmacotherapy is specific in treating IBS-C and IBS-D, as there are no approved medications intended to treat IBS-M and IBS-U, given their mixed presentation of symptoms. Reference [5] suggested utilization of medications that reduce diarrhea, bloating, and pain while also firming up loose or liquid stools in IBS-D. As such, recommended pharmacotherapies include *loperamide* or *eluxadoline*, bile acid sequestrants, serotonin agents such as 5-HT, antispasmodics, and antidepressants [5]. If using antidepressant therapy, there is specific mention of using TCAs, as their anticholinergic properties potentially reduce the symptoms of urgency and diarrhea [7], [15]. In IBS-C, it is indicated to trial medications that aim to decrease constipation through improving stool frequency and consistency as well as lessen pain and bloating, and so medications such as antidepressants, antispasmodics, and laxatives and prokinetics [5]. Similarly, it has been noted that in IBS-C, SSRIs are possibly more beneficial as SSRIs have the opposite effect of TCAs in regards of intestinal transit time and can potentially reduce constipation [7].

Psychotherapy

Given the hypothesized nature of IBS's link with the brain-gut axis, the effects of psychosocial stressors on IBS symptom severity, and frequent comorbidities of depression and anxiety, psychological therapies have been investigated and studied to identify the potential therapeutic benefits on IBS symptoms [10], [22]. From the two studies ([10] and [22]), psychological therapies including cognitive behavioral therapy, relaxation therapy, multi-component psychological therapy, hypnotherapy, and dynamic therapy have been trialed to see if they would reduce the effect that psychosocial factors, co-existing mental disorders, or histories of mental disorders have on the presentation of IBS symptoms. The results of these trials differed significantly, and although there was some favorable evidence that supported psychotherapy, the heterogeneity in testing along with methodological concerns preclude psychological therapies from being officially recommended [22].

Microbial Therapy

Microbial therapy typically involves utilizing probiotics, prebiotics, synbiotics, postbiotics, antibiotics, or fecal transplants in treatment of IBS symptoms [4]. According to [23] recent trials, probiotic and synbiotic treatment seem to induce inconsistent therapeutic effects in IBS patients. However, the mechanism of these effects is not well understood, and it is unknown how probiotics affect the microbiota of IBS patients. Furthermore, the studies involving probiotic and synbiotic therapies differed in strains, combinations of strains, dosages, duration, involved different populations differing in a variety of demographics, and involved a very small sample size, thus hampering the validity of the studies and trials. Regarding the other two types of microbial therapy, postbiotics and prebiotics, there are very few studies and thus little evidence of therapeutic effects [23]. Given the lack of consensus or harmonious data and results, there are no current formal recommendations to use probiotics as a treatment plan [15]. In addressing antibiotics, *rifaximin* is a poorly absorbed, broad-spectrum antibiotic that has potential to alleviate IBS symptoms, though through an uncertain mechanism [1], [24]. One study indicates that *rifaximin* has proven to have beneficial effects in reducing abdominal pain and improving stool consistency compared to placebo in IBS-D; efficacious in its therapeutic effects; and safe to use, in regard to usage in conjunction with TCAs, as well as having no significant disruption to the gut microbiome of patients [15]. Further research in fecal transplants is needed, as current studies have conflicting results; some studies [28]-[30] report complete ineffectiveness in alleviating IBS symptoms, while other studies report successfully reducing IBS symptoms and improvement of quality of life [25], [11], [13].

Prevalence

In Western countries, the population prevalence of IBS is approximately 10%, although more specifically within the United States of America, the prevalence ranges between 7% and 16%. IBS has been shown to be most prevalent in South America, with a population prevalence of 21% and least prevalent in Southeast Asia at an estimated 7% [4], [8]. Additional studies have suggested a number of trends in regards to the prevalence of IBS within certain demographics: IBS more commonly affects women than men except in Asia; IBS prevalence decreases with age, as it is mainly prevalent in working age individuals under the age of 50; and there is low prevalence of IBS in developing countries, but increasing prevalence in newly developing economies as they undergo "westernization" [1], [8], [13], [15].

Another study [26] examined the prevalence of IBS independently in the United States of America, Canada, and United Kingdom suggested that the population prevalence of IBS in these countries has been halved as a direct result of the change in the diagnostic methodology from the older "*Rome III Irritable Bowel Syndrome Criteria*" (Rome III) to the modern Rome IV in 2016, due to a disqualification from IBS diagnosis under Rome IV than what would have been accepted under Rome III. Furthermore, this change in diagnostic methodology changes the prevalence of the four subtypes of IBS. Under Rome III, the subtype IBS-M represented approximately 60% of cases while IBS-C and IBS-D respectively represented approximately 16% to 19% and 18% to 20% of cases, with IBS-U representing the remaining minimal 1% to 5%. Under Rome IV criteria, IBS-C, IBS-D, and IBS-M each represented approximately 28% to 40% of the cases and IBS-U represented approximately 5% of the cases. The Rome IV diagnostic criteria effectively divide the IBS-M subtype's prevalence into the IBS-C and IBS-D groups, creating a balanced distribution of approximately one third proportions of IBS-M, IBS-C, and IBS-D, with IBS-U remaining the very slim remaining percentile of prevalence [26], [21].

Impact on Patients, Healthcare Systems, and Society

As a result of IBS's chronic, episodic, highly variable, and diverse presentations all whilst lacking a cure or guaranteed way to manage symptoms, patient quality of life (QOL) is often highly negatively impacted [8]. In a study by [27], IBS patients were surveyed to evaluate the areas of their daily life that are impaired because of their IBS symptoms; the study evaluated ten domains of daily life including: job or school performance, social activity, physical activity, physical appearance, household activities, sexual activity, leisure activity, travel, eating alone, and eating in groups. The results showed that the 76% of IBS patient respondents reported impairment in five or more domains of daily living, with the most impacted being social functioning, eating alone, and job functioning. Individuals in this study who also met the questionnaire-based criteria for comorbid depression, anxiety, or panic disorder reported even worse impairment than their peers who only had IBS symptoms. The study associated the degree of impairment to symptom severity and GI-specific anxiety. A survey by [8] found that two-thirds of respondents reported missing an average of over ten activities or social events over a three-month period due to their IBS symptoms. Additional personal impacts on patient QOL that this study reported were financial impact of over-the the counter medicine, private consultation, and complementary medicine; the cost of absenteeism from work; and the burden of IBS on relationships with family, friends, and caretakers [8].

With reference to the burden of IBS on healthcare systems, [8] found that IBS is the most frequent functional bowel disorder seen by primary care physicians and accounts for 50% of the consultations with gastroenterologists. Patients are also found to have twice the number of consultations per year in both primary and secondary care as opposed to non-IBS patients; up to 85% of IBS patients will undergo an investigation as well, with the most frequent two being an abdominal ultrasound and a colonoscopy. IBS patients will also have more visits to the emergency room, more episodes of hospitalizations, twice as many appendectomies or hysterectomies, and two to three times as many cholecystectomies. Ultimately, [8] estimated that primary care visits account up to 30% of the total direct healthcare costs for patients with IBS, inpatient care accounts for another 25 to 30%, and that 33% to 91% of IBS patients receive at least one and on average three to seven prescriptions per year. In terms of societal impact, within the United States,

it has been estimated that the annual direct costs associated with IBS exceeds $1 billion dollars, estimated to be as high as between $1.5 billion to $10 billion per year excluding prescription and over-the-counter medication costs [15], [21]. This estimated figure includes high levels of health care resource utilization, testing that can be considered too frequent or unnecessary, and variation in testing and treatment patterns. Reference [8] also estimated that in the US and UK, patients with IBS take an average of between 8.5 and 21.6 days off work in a year, resulting in loss of productivity and negatively affecting the welfare of society. This statistic is not accounting for presenteeism due to IBS, which is a difficult parameter to measure as it is a result of interpretation. However, [8] stated that the severity of IBS has been found to be a significant predictor of work and activity impairment that has an overall negative effect on the productivity of society.

IV. Current and Future Research

Given the major gaps in knowledge regarding the pathophysiology and mechanism behind IBS, current research and future research are similarly focused at searching for an explanation that can adequately describe all the facets of IBS [6], [9], [15]. Reference [9] endorses a replacement of the current approach of single or combination biotherapeutic products to be replaced with more targeted approaches once better characterization of IBS is obtained. Ultimately, [9] advocates optimism in the future for better understanding and developing targeting therapies for IBS. Reference [15] notes that within the four subtypes of IBS, current therapeutic agents are tailored to only treat IBS symptoms of a particular subtype and are inefficient at treating the patient's symptoms or potentially further exacerbating the symptoms if the subtype is misidentified. Furthermore, as previously mentioned, there are no approved medications specifically for the treatment of IBS-M or IBS-U. As a result, [15] identifies this lack of cross-subtype effective therapies as well as lack of effective therapy for IBS-M and IBS-U at areas of critical future research. Furthermore, this study suggests future research to identify biomarkers to better assist in predicting treatment and treatment responses. Additionally, as previously addressed, further study into the efficacy and benefits of the commonly used pharmacotherapies of antispasmodics, *loperamide*, and bile acid sequestrants is needed. Beyond pharmacotherapy, additional investigation into fecal transplants, exercise, the FODMAP diet, and psychotherapies are needed before they are more widely recommended as treatment options for IBS patients [7], [10], [19], [25].

Reference [26] questions the most recent diagnostic criteria methodology (Rome IV) since, in their study, this criterion halved the prevalence of IBS as a diagnosis considering those individuals to be afflicted by other functional GI conditions. Additionally, the shift from Rome III to Rome IV reflects a change in prevalence of the respective IBS subtypes, in which proper identification of the patient's subtype is critical in treatment and management. Thus, [26] suggests further examination of the Rome criteria diagnostic methodology and for future revisions to consider the redistribution of IBS diagnoses and subtype prevalence.

V. Conclusion

In spite of its prevalence and disease burden worldwide, the underlying pathophysiology of IBS remains elusive. The treatment of IBS must involve a multi-dimensional approach encompassing pharmacological (medications) and non-pharmacological (microbial transplants, lifestyle and dietary changes, and psychotherapy) options. Future research emphasizing global collaboration and a multicultural approach is needed to elevate the understanding and treatment of IBS for improved patient care outcomes.

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