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Determining Common Patterns of Gastrointestinal Health in Emerging Adults: A Latent Class Analysis Approach

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DETERMINING COMMON PATTERNS OF GASTROINTESTINAL HEALTH IN EMERGING ADULTS: A LATENT CLASS ANALYSIS APPROACH

by

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Abstract

Background

Emerging adulthood is often-overlooked in current gastrointestinal (GI) health research; however, epidemiological evidence suggests that GI disorders are increasing in this population. The Rome IV criteria have taken a biopsychosocial approach to better understand the etiology of functional gastrointestinal disorders (FGID). Therefore, exploring biopsychosocial factors associated with GI functioning in emerging adults is warranted. The purpose of this study was to first define common GI symptom subgroups within emerging adults and then to characterize these group differences with key biopsychosocial factors encompassing diet, depression and anxiety symptoms, as well as physical and social functioning related to quality of life.

Methods

A total of 956 emerging adults from a southeastern US university were recruited. Participants completed a comprehensive survey on GI symptoms, psychosocial factors and demographics. Scores derived from the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS®) GI symptoms scales were used for latent class analyses. The most parsimonious number of classes were identified using Bayesian Information Criterion. A multivariate analysis of variance (MANOVA) was conducted comparing the differences in latent classes to key biopsychosocial factors.

Results

Latent class analysis uncovered three statistically significant GI symptom patterns within the sample identified by the degree of severity: Normal (649 individuals, 64.15% of the sample),

Mild (257 individuals, 30.30% of the sample), and Moderate (50 individuals, 5.55% of the sample). Chi-square analysis indicated that the groups differed in biological sex. Next, results from the MANOVA indicated that the 3 latent classes were significantly different on most of the biopsychosocial factors, $F(8, 1896) = 25.909$, $p < .001$, Pillai's V = .155, partial $\eta^2 = .077$.

Conclusions

The majority of this study's sample had low scores on the various PROMIS GI measures and thus were considered to have healthy GI functioning. However, a surprisingly large proportion of the sample reported mild and moderate GI symptom severity. Latent classes identified 3 groups: Normal (n=649), Mild (n=257), and Moderate (n=50). These groups were different based on symptom levels but also biopsychosocial factors. Notably, the anxiety and depression levels increased with GI symptom levels. In fact, the Moderate group met clinical cutoffs on several measures. This study demonstrated that significant impairment in GI functioning emerges at much earlier ages that is commonly assumed. In addition, these GI symptom levels were associated with important biopsychosocial factors. Assessing GI functioning in emerging adults may provide important insights into understanding the development of FGIDs.

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Introduction

There are few studies assessing the prevalence of functional gastrointestinal disorders (FGIDs) in the general population. According to the data available, between 10% and 25% of the general US population meet the diagnostic criteria for an FGID (Agréus, Svärdsudd, Nyrén, & Tibblin, 1995; Drossman et al., 1993; Jones & Lydeard, 1992; Wilson, Roberts, Roalfe, Bridge, & Singh, 2004). Thirty percent of individuals experiencing a GI symptom will seek primary medical care (Drossman et al., 1993; Hungin, Chang, Locke, Dennis, & Barghout, 2005) and of those patients, 80% will be diagnosed with a FGID (Hungin et al., 2005). As of 2017, over 40% of patients consulting a gastroenterology specialist do so in reference to functional gastrointestinal disorders (Lacy & Patel, 2017).

Generally, emerging adults (age 18-25) are viewed as a physically healthy cohort (Institute of Medicine and National Research Council, 2015) and consequently often-overlooked in current gastrointestinal (GI) health research. Newer epidemiological studies suggest that FGIDs are increasing in emerging adults (Harris, 2010; Kappelman, 2013; Trivedi & Keefer, 2015; Urlep, Blagus, & Orel, 2015). As many as 65% of emerging adults are experiencing symptoms (Lee, Mun, Lee, & Cho, 2011) and approximately one third are seeking medical care (Jafri, Yakoob, Jafri, Islam, & Ali, 2005).

Emerging adulthood marks the shift from being dependent on a care provider to taking independent responsibility for seeking medical care (Institute of Medicine and National Research Council, 2013). Research indicate this population have decreased adherence to medication and attend fewer physician appointments (Harris, Gordon-Larsen, Chantala, & Udry, 2006; Trivedi

& Keefer, 2015). Furthermore, this period establishes fundamental health and self-care behaviors that carry forward into adulthood (Auerbach, Admon, & Pizzagalli, 2014; Dalton & Hammen, 2018; Harris, 2010). Adverse health behaviors have been observed in the amount of sleep, cigarette use, drinking, exercise, and eating habits of emerging adults (Dalton & Hammen, 2018; Harris et al., 2006; Olson, Hummer, & Harris, 2017).

The current understanding of FGIDs is supported with evidence that multidimensional interactions between biological, psychological, and social/environmental distress are involved in the onset and severity of FGIDs (Drossman, 2016; Engel, 1977). These associations have led to the adoption of a biopsychosocial model in the study of FGIDs (Drossman, 2016). Interestingly, a culmination of biopsychosocial changes occurs in the emerging adult population (Arnett, 2000; Trivedi & Keefer, 2015). However, detailed observations of GI and biopsychosocial functioning in emerging adults have not yet been investigated.

The purpose of this study was to first define homogenous GI symptom subgroups within emerging adults and then to characterize their differences using key biopsychosocial factors encompassing diet, mood and anxiety disorders, and health related quality of life.

Background

The following literature highlights current theories and research on functional gastrointestinal disorders, diet and psychosocial factors within the emerging adult population.

Functional Gastrointestinal Disorders: A Brief Overview

History of FGIDs.

The study of GI disorders was heavily impacted by the 17th century Cartesian beliefs that the mind and body are separate. Mind-body dualism deemphasized the importance of psychological variables to the etiology of many illnesses such as FGID. Those experiencing psychological distress about physical symptoms without any apparent morphological signs were quickly dismissed as exaggerating or psychosomatic. It wasn't until the early 19th century when observations of emotions affecting gastric function were documented (Drossman, 2016). By the mid 20th century, several scientific studies had uncovered a direct relationship between emotions and changes in bowel function (Alvarez, 1949; Drossman, 1998; Drossman, 2016). Nevertheless, the 1960s re-emphasized the presence of biological markers in classifying GI illnesses and psychosocial factors were again discounted. This approach resulted in many gastrointestinal symptoms such as IBS to be classified as a "psychosomatic" disorder (Drossman, 2016).

The emergence of the biopsychosocial model in the study of FGIDs. It wasn't until the late 1970's that a unified theory of biological and psychological interactions was offered: The biopsychosocial model (Engel, 1977). The biopsychosocial model defines illness as the combined "…product of biological, psychological, and social subsystems interacting at multiple levels" (Drossman, 2016, p. 1265). This approach leads researchers to not only measure

biological markers, but to also include variables such as health-related quality of life, patient perceptions and behaviors, symptom severity and daily function. Another transformation in understanding GI disorders occurred through the development of the field of neurogastroenterology in the 1990s (Drossman, 2016). Neurogastroenterology employed the latest technology to provide scientific evidence of the physiological interactions between the gut and brain, setting the foundation for the gut-brain axis model (Drossman, 2016). The gut-brain axis can be described as the system of "bidirectional communication between the central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions" (Carabotti, Scirocco, Maselli, & Severi, 2015, p. 203).

The 21st century marked a paradigm shift in defining the gut-brain axis with the emphasis on the role of the gut microbiota as a key physiological element in the development of FGIDs. Gut microbiota are the populations of microorganisms present in the body's gastrointestinal tract (Evrensel & Ceylan, 2015, p. 239) and "engage in bidirectional communication with the brain via neural, endocrine, and immune pathways" (Van Oudenhove et al., 2016, p. 1362). These microorganisms have been associated with both the presentation of IBS symptoms and psychological disorders including anxiety and depression (Cryan, & Dinan, 2012; Van Oudenhove et al., 2016). The extent of these interactions has resulted in the emergence of the term microbiome-gut-brain axis (Van Oudenhove et al., 2016) thus expanding the conceptual framework of the gut-brain axis. Just as the field of gastroenterology expanded and evolved, so did the criteria for classifying and diagnosing GI disorders.

Development of the diagnostic manual for FGIDs. The first major unified effort to produce a GI classification and diagnostic manual began in the late 1980s with the publication of

the Rome I criteria in 1994. The Rome I was the first comprehensive book aimed at identifying and describing GI disorders lacking in any visible organic abnormalities, such as IBS. In sync to the scientific community's interpretation of GI disorders, the publishing of the Rome II criteria in 2000 officially coined the term neurogastroenterology, formalizing the field of gut-brain research (Kellow et al., 1999; Wood, Alpers, & Andrews, 1999). The Rome III criteria, published in 2006, utilized more evidence-based data to support GI classifications. The most recent version published in 2016, the Rome IV criteria, has undertaken the task of further redefining FGIDs based on the latest scientific discoveries along with providing the latest diagnostic and classification criteria (Schmulson & Drossman, 2017). According to the latest definition:

> FGIDs are disorders of gut–brain interaction. It is a group of disorders classified by GI symptoms related to any combination of the following: motility disturbance, visceral hypersensitivity, altered mucosal and immune function, altered gut microbiota, and altered central nervous system processing. (Drossman, 2016, p. 1268)

In addition to changing the definition of FGIDs, the Rome IV criteria also added the microbiome, food, and nutrition as important elements in the study of GI function (Barbara et al., 2016). Additionally, genetics and culture have been added to the current list of significant factors (age, gender, and women's health) that impact GI disorders. Another key change in the Rome IV criteria was to officially adopt the biopsychosocial model, thus anchoring the new definition of FGIDs as disorders of gut-brain interaction. The biopsychosocial model emphasizes the interaction between all these diverse elements and their potential role in explaining the heterogeneity of GI disorders.

The six FGID domains.

The Rome IV criteria contains 6 primary FGID domains for adults encompassing over 33 types of FGIDs and two domains dedicated to children. Each FGID is classified based on the patient's report of symptom type and severity. A symptom is "…a noticeable experiential change in the body or its parts that is reported by the patient as being different from normal and may or may not be interpreted as meaningful" (Drossman, 2016, p. 1266). Functional GI disorders consider clusters of symptoms experienced together to describe a syndrome. A syndrome "…relates to the association of several clinically recognizable symptoms or signs that occur together to define a clinical entity" (Drossman, 2016, p. 1266). Therefore, FGIDs can be conceptualized as a "…syndrome based on symptoms that cluster together and are diagnosed by Rome criteria" (Drossman, 2016, p. 1266). Historically, individuals seek out medical support when they experience GI symptoms. Additionally, it is these symptoms that patients use to describe their illness to their clinician. Therefore, although FGIDs can include morphological changes or motility abnormalities, they are not the primary criteria used to classify an FGID (Drossman, 2016; Schmulson & Drossman, 2017).

Notably new to the Rome IV criteria, FGIDs may be thought of as a "spectrum of chronic GI disorders with combinations of symptoms … existing on a continuum rather than as discrete disorders" (Simren, Palsson, & Whitehead, 2017, p. 4). Multiple studies support this new description by the Rome IV criteria providing scientific evidence that patients can transition from one disorder to another and can receive multiple diagnoses (Chey et al., 2015; Lacy et al., 2016; Shah et al., 2018; Whitehead et al., 2002). However, the primary symptoms experienced is used to classify the six domains of FGIDs.

Table 1 *FGID Domains According to the Rome IV Criteria.*

FGID Domains	Primary Symptoms
1. Esophageal Disorders	Heartburn, chest pain, or reflex
2. Gastroduodenal Disorders	Dyspepsia, belching, nausea/vomiting
3. Bowel Disorders	Constipation, diarrhea, and gas/bloating
4. Centrally Mediated Disorders of GI Pain	Abdominal pain
5. Gallbladder and Sphincter of Oddi Disorders	Sudden pain usually experienced during gallstone or gallbladder attacks
6. Anorectal Disorders	Fecal incontinence and anorectal pain

Note. (Drossman, 2016).

One of the most studied FGID domains is Bowel Disorders which can be grouped into 6 main categories. Additionally, four subcategories were created within the IBS category, the most frequently diagnosed GI disorder (Chey, Kurlander, & Eswaran, 2015) covering 11.2% of the world's population (Lacy et al., 2016).

Table 2 *Bowel Disorder Categories.*

Bowel Disorders
1. Irritable Bowel Syndrome (IBS)
a. IBS-C: Predominant in constipation
b. IBS-D: Predominant in diarrhea
c. IBS-M: Mixed bowel habits
d. IBS-U: Unclassified
2. Functional Constipation
3. Functional Diarrhea
4. Functional Abdominal Bloating/Distention
5. Unspecified Functional Bowel Disorders
6. Opioid-induced Constipation

Note. Simren, Palsson, & Whitehead, 2017

Almario et al. evaluated FGID symptom prevalence within the general US adult population (n=71,812, ages 18-65) using the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS®) GI scales (Almario et al.,

2018). Eight overarching FGID symptom domains (abdominal pain, bloating/gas, bowel incontinence, constipation, diarrhea, swallowing, reflux, and nausea/vomiting) were assessed including the occurrence of overlapping symptoms. Over 61% of their study sample endorsed at least one symptom within the past 7 days. Of those, 58.4% indicated they experienced two or more symptoms concurrently. Based on their findings, close to 1/3 of their sample population experienced reflux/heartburn, making it the most prevalent symptom. One quarter reported abdominal pain and a fifth of the participants experienced bloating, diarrhea, and constipation. This study included emerging adults in their population sample, finding that over 54% (n=6,954) reported the occurrence of at least 1 FGID symptom within the past week. However, further descriptions of FGID symptoms within emerging adults were not provided.

The most commonly studied FGID syndrome in emerging adults is IBS. According to the ACHA-National College Health Assessment II national survey for the Fall 2017 semester, 3.2% of the undergraduate students surveyed (n=5,789) had been diagnosed by a healthcare professional of having IBS (American College Health Association, 2017, pg. 3). Another study focused on recurrent abdominal pain (RAP) and IBS prevalence in emerging adults. The study concluded that those individuals who had higher levels of RAP also experienced higher rates of recurrence five years later for RAP and IBS, resulting in higher levels of functional disability, school absence, and clinic visits for abdominal stress (Walker, Guite, Duke, Barnard, & Greene, 1998). A third study evaluated the frequency of IBS in college students demonstrating that 34% of the sample (n=508, mean age: 22+/-2.8yrs) experienced clinical symptoms (Jafri et al., 2005). This previous research demonstrated clinical rates of IBS in the emerging adult population but is

limited in that it does not capture a broader range of general GI distress or subclinical symptomatology.

GI symptoms are usually present before an FGID diagnosis is made and therefore serve as a likely reason for seeking medical care (Almario et al., 2018; Spiegel et al., 2014). However, fewer than 20% of the US population who experience GI symptoms will actually seek medical care (Sandler, Stewart, Liberman, Ricci, & Zorich, 2000). It therefore stands to reason that measuring GI symptoms within a healthy, non-clinical population rather than relying on clinically diagnosed cases may provide additional insight into the overall prevalence of GI distress. Additionally, FGIDs including IBS are considered heterogenous, not only in their diagnostic classification but also in their potential pathogenesis (Adam, Liebregts, & Holtman, 2007; Jones, Van Oudenhove, & Talley, 2012). With that in mind, applying the biopsychosocial model to determine what factors are potentially responsible for FGIDs is needed.

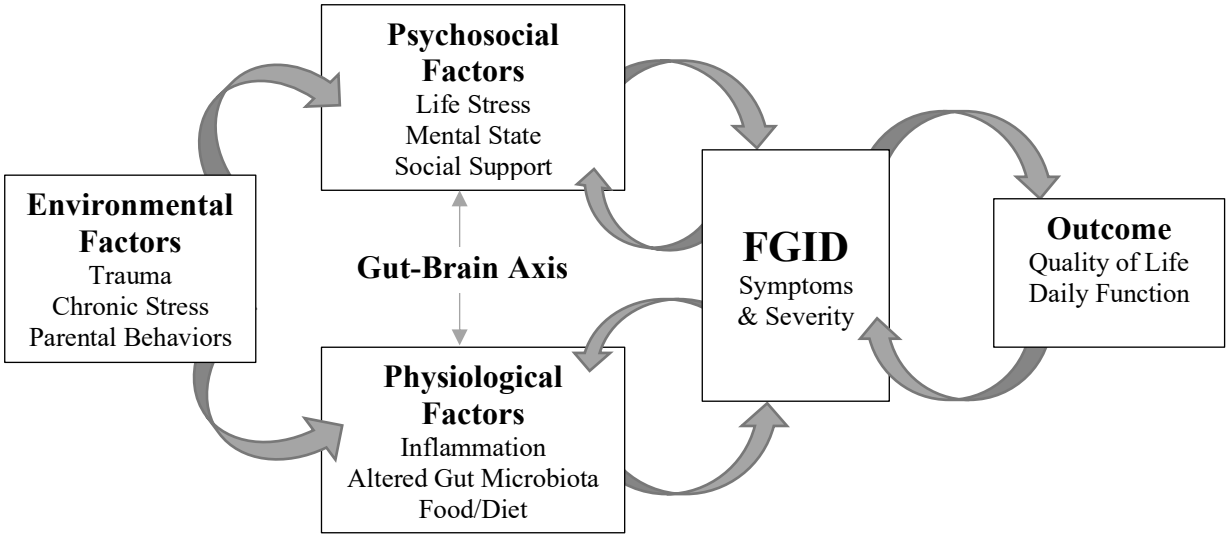
The Biopsychosocial Model of FGIDs

Exploring the etiology of FGIDs expanded with the biopsychosocial model, providing researchers with a new conceptual framework that incorporated research from both psychosocial and biological fields. Specifically, the biopsychosocial model placed equal value in researching the patient's reported experience of illness with the physical indicators of disease (Drossman & Dumitrascu, 2006), resulting in studies of a singular mind-body system. Consequently, researchers identified a bi-directional communication pathway between the mind and GI tract, termed the gut-brain axis (Drossman, 2016; Van Oudenhove et al., 2016). The gut-brain axis provided evidence that changes in either the mind or gut can disrupt the balance of the other. More specifically, biopsychosocial factors impacting the gut-brain axis could be traced to the

risk of developing GI symptoms, symptom severity, and affecting treatment outcomes (Drossman, 2016; Van Oudenhove et al., 2016).

A closer look at the biopsychosocial factors involved in FGIDs reveal a diverse range of domains. At present, these include but are not limited to environmental, cultural, and psychosocial factors, including the composition of an individual's gut microbiome, diet, and nutrition (Van Oudenhove et al., 2016).

Figure 1 *The Biopsychosocial Model*



Adapted from Functional gastrointestinal disorders: History, pathophysiology, clinical features and Rome IV. *Gastroenterology*. 150, 1262-1279 by D.A. Drossman, 2016.

Environmental factors: childhood, trauma, & chronic stress.

Environmental factors are important contributors to the lifespan development of an individual. The degree of susceptibility to FGIDs can be traced to early childhood development, where children learn to modify their behaviors in response to their parent's reaction to their illness (Levy et al., 2004). Exposure to any form of abuse, whether psychological, physical, or

sexual, will increase the likelihood of experiencing an FGID (Bradford et al., 2012), specifically affecting symptom severity and clinical outcomes (Drossman, 2011). Furthermore, experiencing a major loss can influence the onset of an FGID (Bitton et al., 2008; Lackner & Gurtman, 2004; Sperber, Drossman, & Quigley, 2012). However, an environment with chronic and high levels of life stress has proven to be one of the strongest factors for developing FGIDs (Drossman et al., 2000). Emerging adults are especially susceptible to chronic stress as they transition into adulthood (Cohen, Burt, & Bjorck, 1987; D'Zurilla & Sheedy, 1991). Stress provoking environments for emerging adults include attending college and adjusting to new social settings (Ross, Niebling, & Heckert, 1999). Consequently, the inability to properly cope with chronic stress frequently result in depression and maladaptive eating behaviors in emerging adults (Dalton & Hammen, 2018; McGonagle & Kessler, 1990).

Environmental factors affecting FGIDs can occur at any point in life, ranging from early childhood conditioning, experiencing acute adverse events, to sustaining ongoing periods of stress. Environmental factors illustrate the multidimensional aspect of the biopsychosocial model because they not only influence the susceptibility to FGIDs, they can also foster psychological disorders.

Psychosocial factors: mood disorders, anxiety disorders & quality of life.

In addition to demonstrating the multidimensional aspect of FGIDs, the biopsychosocial model also accounts for the bi-directional communication pathways between domains, such as the gut-brain axis. The gut-brain axis is a defining representation of the relationship between psychosocial factors and FGIDs. Psychosocial disturbances can ignite the exacerbation of GI symptoms or they can be a consequence of experiencing GI symptoms (Van Oudenhove et al.,

2016). Additionally, psychosocial factors have great influence over whether someone will seek medical care and also over the effectiveness of treatment (Drossman, 2016). According to the latest Rome IV overview, psychosocial factors associated with the gut-brain axis that interact with the development and severity of FGIDs include mood disorders (depression and suicide ideation), anxiety disorders, somatization, and cognitive-affective processes (Van Oudenhove et al., 2016).

Based on a systematic review, when patients' GI symptoms are categorized into mild, moderate, or severe levels discrete associations with levels of care and psychosocial variables emerge (Drossman et al., 2011; Drossman, 2016). For example, 40% of patients who endorse mild GI symptoms are commonly treated in primary care settings and psychological disorders are not elevated and the general quality of life is good (Drossman, 2016). In comparison, approximately 30%-35% of patients will meet the criteria for moderate GI symptoms. This segment will experience a stronger association between their social environment, psychological distress and abdominal pain, creating some interference in daily activity. Finally, individuals with severe GI symptom levels make up 20%-25% of patients and are more frequently seen by a gastroenterologist. Individuals experiencing severe GI symptoms also experience high levels of anxiety, depression, and/or personality disorders. Additionally, history of abuse, major loss, and poor social networks are strongly associated with this group. Furthermore, these individuals experience frequent disruptions in their daily activity due to their GI symptoms (Drossman, 2016). These findings need to be replicated in general non-patient populations.

Anxiety disorders are closely associated with the onset and duration of FGIDs. Studies have found that anxiety disorders are directly associated with the biological stress response

processes, and as a result, can alter pain tolerance and motility (Van Oudenhove et al., 2016). In a sample of 604 college students (age= 20.93 ± 1.47 years), 36.9% endorsed IBS symptoms, according to Rome III criteria, with 13.9% presenting with both IBS and GAD (Afridi, Ahmad, Sethi, & Irfan, 2017). Additionally, it's been argued that anxiety disorders have a greater impact on the risk, comorbidity, and outcome of IBS than depression (Roy-Byrne et al., 2008).

Mood disorders are associated with depression and suicide ideation (Van Oudenhove et al., 2016). The prevalence of depression was found in 30% of medical-seeking patients presenting with FGIDs (Addolorato et al., 2008) with 15% to 38% of clinical patients with IBS presenting with suicidal ideation (Miller, Hopkins, & Whorwell, 2004), while anxiety disorders were revealed in 30%-50% of clinical patients with FGIDs (Oudenhove, Levy et al., 2016). However, depression alone, can alter the number of GI symptoms an individual experience including the number of diagnoses made (Bouchoucha et al., 2013; Van Oudenhove et al., 2011). Only a few studies have evaluated GI symptoms and depression in an emerging adult population. One study with emerging adults found that 13.6% (n=773) of their sample reported moderate to major depression (Lisznyai, Vida, Nemeth, & Benczur, 2014).

The comorbidity of depression and anxiety can be associated with poor health outcomes and inferior quality of life (Lackner et al., 2010; Lackner & Gurtman, 2005). Furthermore, experiencing chronic GI symptoms can also result in psychological consequences on overall health-related quality of life (HQoL)., i.e. "…one's general well-being, daily function status, and sense of control over the symptoms." (Drossman, 2016, p. 1273). Studies have shown that HQoL was significantly lower in individuals with IBS than healthy individuals (Badia et al., 2002). Studies concerned with health outcomes in emerging adults were very limited. Nevertheless, one

study evaluating HQoL including a population group of 16 to 23-year old participants concluded that males reported higher scores than females (Jörngården, Wettergen, & Vo Essen, 2006).

Albeit promising, research is currently limited on general emerging adult population samples. The prevalence of depression is found to be higher in emerging adults than other age groups, with 5.8% meeting symptom criteria (Weitzman, 2004). Yet, the presence of depressive symptoms in emerging adults, regardless of meeting a clinical diagnostic level, have shown to have an effect on health behaviors, including diet (Dalton & Hammen, 2018).

Biological factors: microbiome, food, & dietary habits.

The 21st century brought new scientific exploration of the gut microbiota's enigmatic relationship with gut function and brain behavior (Ghoshal & Srivastava, 2014). Gut microbiota are the intestinal microbes located within the GI tract that feed on the undigested components of foods consumed (Barbara et al., 2016). The gut microbiota ecosystem (microbiome) is an ever-present part of the bidirectional interaction between the gut-brain axis (Osadchiy, Martin, & Mayer, 2019) suggesting a microbiome-gut-brain axis (Oudenhove, et al, 2016). Present research has demonstrated the role gut microbiota has in "energy homeostasis, immune function, and the development of certain diseases" (Dong & Gupta, 2019, p. 231). Environmental factors including stages of early life development, drugs, stress, and diet influence the balance and composition of the gut microbiome (Barbara et al., 2016; Evrensel & Ceylan, 2015). Adverse input from these factors result in a dysfunctional gut microbiota ecosystem, termed dysbiosis (Sundin, Öhman, Simrén, & Magnus, 2017). Researchers studying dysbiosis, frequently encounter the presence of anxiety, depression, and IBS, thus concluding that a strong interaction exist between dysbiosis and these factors (O'Mahony et al., 2005).

Research on the relationship between gut microbiota and FGID have employ advanced technological and analytic methods, yet much is still unclear as to the extent of this relationship. A recent study employing new machine learning techniques, found that microbial diversity decreased as IBS symptom severity increased, distinguishing between mild/moderate, and severe levels compared to healthy sample groups, and that these differences were not mediated by diet or medications (Tap et al., 2017).

The gut microbiome is fundamentally established early in life and can remain fairly stable even with interference from drugs, infections, and diet, however, studies have shown that to some degree, diet can modify both microbiota composition and function in adults (Osadchiy et al., 2019, p. 327). Consequently, researchers have begun exploring diet as a potential means to create changes in physiological and psychological symptoms via the gut microbiome (Barbara et al., 2016; Chey, 2013; Evrensel & Ceylon, 2015). Studies of dietary measurements have provided evidence of associations with FGIDs, dysbiosis of the gut microbiome, and psychological disorders (Evrensel & Ceylon, 2015; Francisconi et al., 2016). Importantly, the relationship between GI symptoms and eating behaviors and diet has been marked as significant (Ananthakrishnan et al., 2015; Drossman, 2016; Gibson, Varney, Malakar, & Muir, 2015; Lee et al., 2015).

Assessing dietary intake can be evaluated at the nutrient, food group, and eating pattern levels (Jacobs & Steffen, 2003; Lee et al., 2015). Nutrients such as vitamins and minerals, fats, fibers, carbohydrates, and proteins, characterize diet at the most basic level (Hu, 2002). At a higher level of analysis are food groups. Food groups are defined as grains, vegetables, fruits, diary, and protein, as marked by the food pyramid (Marcoe, Juan, Yamini, Carlson, & Britten,

2006). At the most macro level of analysis are dietary patterns, such as the Mediterranean or Western diet. Dietary patterns are defined as "the quantities, proportions, variety or combination of different foods, drinks, and nutrients in diets, and the frequency with which they are habitually consumed" (2015 Dietary Guidelines Advisory Committee, 2015, p. 8). "Dietary factors that reportedly trigger symptoms include eating patterns as well as specific foods and/or food components" (Barbara et al., 2016, p. 1306).

The Western dietary pattern, also known as the American diet is "characterized by high fat, high sugar, high level of red and processed meat, high levels of refined grains and a lower level of fiber" (Dong & Gupta, 2019, p. 234). Individuals on the Western diet are at moderate risk for developing IBS (Buscail et al., 2017), have low gut microbiota diversity, show higher levels of inflammation, and have an increased risk of obesity, colon cancer, and type 2 diabetes (Dong & Gupta, 2019; Miyoshi et al., 2017; Schulfer et al., 2018; Turnbaugh et al., 2009). The Mediterranean diet, considered the healthiest diet, is "characterized by a beneficial fatty acid profile; higher intake of fiber, vegetables, and fruits; and with lower intake of sugar and red meat" (Dong & Gupta, 2019, p. 234). Individuals on a Mediterranean diet have rich microbial diversity, decreased levels of inflammation and are at lower risk of cardiovascular disease and obesity (Ley et al., 2005; Miyoshi et al., 2017; Rivera et al., 2007).

Evaluating eating habits in an emerging adult population showed that 89% of emerging adults were not meeting healthy dietary recommendations, missing serving level requirements for all standard food groups (Song, Schuette, Huang, & Hoerr, 1996). The amount of carbohydrates consumed exceeded 33% to 46% and they were 53% to 58% of their daily vegetable serving requirements (2015-2020 Dietary Guidelines for Americans - Ch2, p42, 2015).

Current research on diet and FGIDs indicated mixed results. A study found patients diagnosed with FGIDs were more inclined to snack throughout the day, eating fewer meals per week than their non-FGID counterparts (Barbara et al., 2016). A large population study (n=44,350) in France found the Western dietary pattern connected to a moderate risk for IBS (Buscail et al., 2017). Higher levels of constipation were found in Japanese college students who frequently skipped breakfast (Fujiwara, 2012) and another study demonstrated the risk of ulcerative colitis increased with a high consumption of soft drinks (Nie & Zhao, 2017). Further exploring common associations between an individual's diet and gastrointestinal functioning may offer insight into the extent diet plays in the development of FGIDs.

Conceptual Framework: Defining Patterns of FGID Symptoms in Emerging Adults

Emerging adulthood is often-overlooked in current GI health research (Park, Mulye, Adams, Brindis, & Irwin, 2006). However, as a critical period of development it is important to determine the active biopsychosocial factors associated with various GI functioning in emerging adults. The purpose of this study was to define common GI symptom subgroups within emerging adults and characterize their differences based on key biopsychosocial factors. To accomplish this task, the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS®) GI symptom scales was administered (Spiegel et al., 2014). The PROMIS-GI is currently the only PRO that has been validated to measure symptoms of multiple FGID domains in both a general and clinical population group. The use of the NIH PROMIS-GI scales afforded this study with a means to measure a broad range of GI functioning and symptom levels within a general emerging adult population group. To date, there is no comprehensive study exploring general GI functioning in the emerging adult population using the PROMIS-GI

symptom scales. To identify underlying GI symptom patterns, a latent class analysis approach was employed. Latent class analysis (LCA) is a statistical method that allows the researcher to use a set of observed variables to identify hidden but meaningful patterns resulting in a number of homogenous subgroups of participants (latent classes) (Schreiber, 2016). The key biopsychosocial factors measured included dietary patterns, eating behaviors, mood and anxiety disorders, and physical and social functioning related to quality of life. Between class differences were established by these variables using a MANOVA. Currently, this is the only study that sought to identify underlying GI patterns and associated psychosocial factors within a general emerging adult population group.

Method

Participants

Undergraduates enrolled in introductory psychology courses at a large university in the south-eastern United States were recruited to participate in this study for course credit. Introductory psychology is a required course for all programs at this university. Eligibility criteria excluded vulnerable populations and required participants to be between the age of 18 and 25 years and able to complete an online questionnaire in the English language. All measures were administered online. This study was approved by the Institutional Review Board.

Measures

The online survey included 198 questions assessing the following: FGID symptoms, dietary patterns, eating behaviors, depression and anxiety symptoms and emotional and physical functioning. In addition, the survey included demographic items such as age, gender, race/ethnicity, education, income, and living arrangements. The survey took approximately 30 minutes to complete. Nine validity check questions were also included in the questionnaire as a determining variable for respondent data retention or elimination. The data analysis for this paper was generated using Qualtrics software (Qualtrics, Provo, UT).

Functional gastrointestinal assessment.

The NIH PROMIS-GI symptom scales. The National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS®) Gastrointestinal Symptom Scales (PROMIS-GI) were developed in 2014. The PROMIS-GI scales are disease-agnostic, thus allowing for the characterization of a broad range of GI symptoms within the general population

(Shah, Almario, Speigel, & Chey, 2018; Spiegel et al., 2014). These scales have been employed in several GI studies validating its ability to measure GI symptom burden and to characterize GI symptom differences (Shah et al., 2018). Importantly, the PROMIS-GI symptom scales may be effective in identifying clinical thresholds for action (Spiegel et al., 2014). The PROMIS-GI scales were developed using multiple patient focus groups and an extensive systematic literary review. A psychometric evaluation confirmed the internal construct validity of the PROMIS-GI Scales (Spiegel et al., 2014). The PROMIS-GI has been validated in studies as an effective PRO measure to be used in both clinical and general populations (Spiegel et al., 2014). The PROMIS-GI scales evaluate eight GI symptom domains, of which this study focused on six: abdominal pain (6 items), gas/bloating (12 items), diarrhea (5 items), constipation (9 items), gastroesophageal reflux (GER) (13 items), and nausea/vomiting (4 items). Individuals' scores were provided as a T-score metric with 50 representing the U.S. general population mean with a standard deviation (s.d.) of 10 (Spiegel, et al, 2014). The higher the T-score, the greater the severity of the symptom. Scores were calculated by pre-determined algorithms available via the PROMIS website. T-scores were then converted into GI symptom severity levels using the suggested general PROMIS T-Score threshold range of mild (t-scores between 55 and 60), moderate (t-scores between 60 and 70), and severe (t-scores above 80).

Dietary assessments.

14-Item Mediterranean Diet Adherence Screener (MEDAS). The dietary behaviors were evaluated in this study due to their confirmed validity in association with FGIDs (Ananthakrishnan, 2015; Barbara et al., 2016; Chey, 2013; Drossman, 2016; Evrensel & Ceylon, 2015; Francisconi et al., 2016; Gibson, et al., 2015; Lee, 2015). Assessing dietary patterns is one

of the preferred methods used in research (Hu, 2002) as they describe eating behaviors generally consistent over time (Quatromoni et al., 2002). The Mediterranean Diet (MedDiet) is a frequently recommended dietary pattern by nutritional research and the USDA (Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Part D. Chapter 2). This study employed the validated 14-Item (MEDAS) to assess individuals' degree of adherence to the MedDiet. The 14-Item MEDAS is the English version of the original Spanish version, PREvencion con DIetaMEDiterranea (PREDIMED) (Papadaki et al., 2018). It is scored (0-14) based on 14 questions (Martínez-González et al., 2012). This questionnaire has been validated in Spain and the UK for its objective assessment of adherence to the MedDiet (Martínez-González et al., 2012; Papadaki et al., 2018). The main outcome measure was the level of adherence to the Mediterranean diet.

Psychosocial assessments.

Past research has confirmed that anxiety, depression and HQoL is associated with many FGID symptoms and their level of severity (Addolorato et al., 2008; Badia et al., 2002; Lisznyai et al., 2014; Miller et al., 2004; Oudenhove et al., 2016; Roy-Byrne et al., 2008). Specifically, relevant to evaluating FGIDs, the Rome IV committee provided within their supplementary materials their recommended measures for assessing psychosocial factors associated with FGIDs (Oudenhove et al., 2016). These include the GAD-7, PHQ-9 and SF-36.

Generalized Anxiety Disorder Screener (GAD-7). This study evaluated generalized anxiety disorder (GAD) using the Generalized Anxiety Disorder Screener (GAD-7) instrument, which recorded the level of general anxiety experienced within the past two weeks using a set of 7 questions (Spitzer, Kroenke, Williams, & Lowe, 2006). The GAD-7 scored each question from

0 (not at all) to 3 (nearly every day) with a total score of 21. Summary scores of 5, 10, and 15 were used as threshold values for mild, moderate and severe anxiety (Spitzer et al., 2006). The GAD-7 was constructed using existing GAD criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) (Spitzer et al., 2006). It has been validated by multiple studies (Löwe et al., 2008).

Patient Health Questionnaire (PHQ-9). The Rome IV committee recommends screening for suicide ideation when depression is severe and accompanied with feelings of hopelessness and severe/persistent abdominal pain (Oudenhove et al., 2016). To evaluate depressive symptoms, the Patient Health Questionnaire (PHQ-9) was administered. In keeping to the diagnostic criteria of the DMS-IV, the PHQ-9 measures the level of depression, including suicide ideation (Kroenke, Spitzer, & Williams, 2001). This instrument consists of 9 items, scored 0 (not at all) to 3 (nearly every day), with a total summary score of 27. The severity of depression can be calculated using validated cut-off points with scores above 10 qualifying as a form of depression, and scores of 15 or greater indicating major depression (Kroenke et al., 2001). The PHQ-9 is a simplified version of the 3-page Patient Health Questionnaire used by clinicians to diagnose their patients for depression. The PHQ-9 has been validated and replicated by mental health professionals conducting patient interviews and comparing the PHQ-9 with current measurement tools in place (Kroenke et al., 2001).

RAND 36-Item Health Survey 1.0 (SF-36). Studies have concluded that GI symptoms correlate negatively with HQoL (Halder et al., 2003). This study employed the RAND 36-Item Health Survey 1.0 (SF-36) measuring eight separate domains along with two summary scores on mental and physical health (Hays, Sherbourne, & Hazel, 1993). A mental summary score was

calculated using the four domains: emotional wellbeing, social functioning, energy/fatigue, and role limitations due to emotional problems. The physical health summary score was derived from the remaining four domains: physical functioning, pain, role limitations based on physical health, and general health perception (Cunningham, Nakozono, Tsai, & Hays, 2003). Of note, the version of the SF-36 used in this study was based on the RAND-36 scoring algorithms rather than the original SF-36 scoring method. The key difference is that the RAND-36 summary scores were calculated based on the assumption that physical and mental health is correlated (Cunningham et al., 2003). The original SF-36 was constructed in 1992 during the Medical Outcome Study from longer patient-completed forms (Ware & Sherbourne, 1992). The RAND-36 uses the exact same items as the SF-36 (Cunningham et al., 2003). It has been validated in numerous studies for accurately measuring health-related quality of life (Oudenhove et al., 2016).

Demographic assessments.

Demographic information collected in this study can be grouped by: (i) general standard items (age, gender, race/ethnicity, marital status); (ii) socioeconomic (ii) birth profile (birth mode, breastfed); (iii) current housing; (iv) and physiological profile (BMI, allergies, taking antibiotics, probiotics, or multivitamins). See Table A1 for detailed list of question items.

Statistical Analysis

Data from the PROMIS-GI symptoms scales were analyzed in LatGold v5.1.0.18311 (Statistical Innovations Inc.), a latent class analysis software package. LCA methods have the same goal as traditional cluster analysis, in that both attempt to create the largest between-cluster

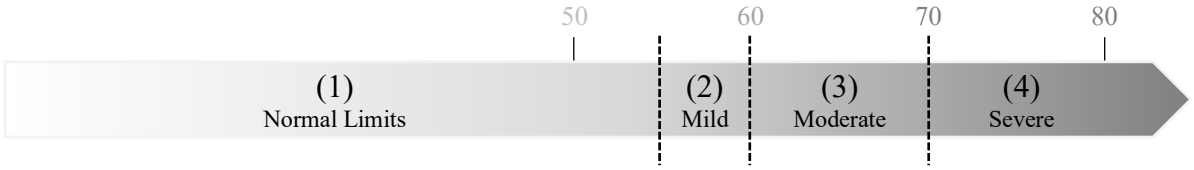
and smallest within-cluster differences. However, unlike standard cluster methods, LCA uses a probabilistic model-based approach rather than distance measures of dissimilarity (Kent, Jensen, & Kongstad, 2014). Additional advantages for using the LCA includes: (i) greater control of the criteria used to determine clusters, (ii) normal distribution of variables are not required, and (iii) mixed measurement levels can exist between variables in the same test (Schreiber, 2016; Vermunt & Magidson, 2002). The ideal model was based on appropriate model fit, the number of individuals per class, the certainty of being assigned to one class (membership probability), and significant difference between classes (Kongsted & Nielsen, 2017).

Class differences based on biopsychosocial factors were then explored using multivariate analysis of variance (MANOVA) analysis. Subgroups that differed significantly were compared at a pair level using the least significant difference (LSD) test. A p value of < 0.05 was considered statistically significant. Both MANOVA and LSD tests were conducted in SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

Results

The final study sample totaled 956 emerging adults between the age range of 18 and 25 (M=18.97, SD = 1.47) with 58.3% identifying as female, and 57.3% identified as Caucasian. To evaluate the presence of GI symptoms within the emerging adult sample group, the T-scores derived from the PROMIS-GI symptoms scales were assigned a rating of 1 through 4, as illustrated in Figure 2, marking symptom severity.

Figure 2 *PROMIS Symptom Severity Range*



Note. Symptom severity ratings were based on the recommended PROMIS T-Score ranges, using the mean of 50 and standard deviation (SD) of 10. Normal limits (1) = t-scores < 55; Mild (2) = t-scores between 55 – 60; Moderate (3) = t-scores between 60 – 70; Severe (4) = t-scores > 70. Adapted from http://www.healthmeasures.net/score-and-interpret/interpret-scores/promis

Symptom prevalence was assessed using the severity scores. As presented in Table 3, 25.8% of the emerging adult sample group did present at least one GI symptom.

Table 3 *Overall GI Symptom Severity Found in Participants (n=956)*

GI Symptom Severity	Belly Pain	Constipation	Diarrhea	Gas/ Bloating	Nausea/ Vomiting	Reflux/ Heartburn
Within Normal Limits (1)	750 (78.5%)	845 (88.4%)	870 (91%)	608 (63.6%)	699 (73.1%)	891 (93.2%)
Mild (2)	99 (10.4%)	77 (8.1%)	53 (5.5%)	247 (25.8%)	142 (14.9%)	49 (5.1%)
Moderate (3)	91 (9.5%)	34 (3.6%)	32 (3.3%)	99 (10.4%)	105 (11%)	15 (1.6%)
Severe (4)	16 (1.7%)	-	1 (0.1%)	2 (0.2%)	10 (1%)	1 (0.1%)

Note. Levels of severity were interpreted using the threshold range guidelines developed by the NIH to be used with their PROMIS measures. Within Normal Limits = T-scores < 55; Mild = T-Scores between 55 and 60; Moderate = T-Scores between 60 and 70; Severe = T-scores > 70. There was no endorsement for severe constipation within the sample group.

Having confirmed the presence of GI symptoms in this emerging adult sample group, latent class analysis (LCA) was explored using the assigned symptom severity scores 1-4.

A baseline model was created using a 1-Class (latent) cluster model (Myrseth & Notelaers, 2018). Classes were subsequently added and compared to the baseline 1-Class model. Model sizes with up to 7 classes were calculated as there were no previous studies that suggested the number of classes for conducting a latent class analysis using the PROMIS-GI scales. Each estimation model was replicated 10 times to determine the most frequently occurring Bayesian Information Criterion results per model (Nielsen, Vach, Kent, & Kongsted, 2016). By selecting the most common solution, the evaluations will be using the most likely scenario.

Model Selection

Table 4 provides an overview of the various information criteria considered in determining the best model fit. The information criteria consisted of the likelihood ratio chi-squared statistic (L^2) and Bayes Information Criterion (BIC) with lower values indicating improved model prediction of the data (Vermunt & Magidson, 2016, p.69). The L^2 statistic calculates the similarity between model-based estimated frequencies and observed frequencies with smaller values indicating better model fit. The BIC accounts for model complexity and endorses model parsimony of the latent classes, and when using sample sizes larger than 500, proves to be a superior indicator to model fit compared to all other information criteria (Nylund, Asparouhov, & Muthen, 2007, p. 563). A more formal assessment of the model holding true for the population is determined by the p-value with $p < 0.05$ indicating a poor model fit. Due to some of the GI symptom severity levels containing small group sizes, a bootstrapping method was used to better assess the global fit of the model (Nylund et al., 2007). Additionally, entropy R-squared was evaluated for quality of membership classification with values closest to 1 indicating improved probability of an individual belonging to just one class (Schreiber, 2016).

Individual class sizes below 3% were considered to be too small for this study. Accordingly, the class sizes in the 4-Class model and higher did not meet the minimum distribution requirement and was thus eliminated. Of note, the 3-Class model indicated a small sample group (n=50) for their 3rd class which would be acceptable if the cluster/class was describing an element that is uncommon in the sampled emerging adults.

The 2-Class model had the lowest BIC, however, both the L^2 and *p*-value were not ideal. Additionally, according to the conditional bootstrap analysis, the 3-Class model showed a statistically significant improvement over the 2-Class model ($p < 0.05$, 0.00 s.e.) for overall model fit, thus the 3-Class model was selected.

Table 4 *Summary of Statistical Model Fit Statistics Used for Model Selection*

Model	BIC	L^2	*df*	*p*[a]	Entropy	Class. Err.
Baseline 1-Class Model	6798.2738	1185.6210	940	1.00	1.00	0.0000
2-Class Model	**6339.2847**	603.0833	922	0.0020	**0.7033**	**0.0621**
3-Class Model	6344.9257	**485.1760**	904	**0.0980**	0.6426	0.1101
4-Class Model	6426.8327	443.5345	886	0.0640	0.6548	0.1139
5-Class Model	6518.9844	412.1377	868	0.0119	0.6022	0.1637
6-Class Model	6624.2116	393.8164	850	0.0142	0.6939	0.1347
7-Class Model	6722.1687	368.2251	832	0.0103	0.7045	0.1332

Note. Comparison between the 2-Class and 3-Class are shown with values in bold indicating optimal values. The 4-Class and higher models did not meet the minimum group size criteria. BI = Bayesian information criterion; L^2 = Likelihood-ratio; *df* = degrees of freedom; *p* = p-value; Entropy = quality of predicting model classification with values closer to 1 preferred; Class. Err. = classification errors.

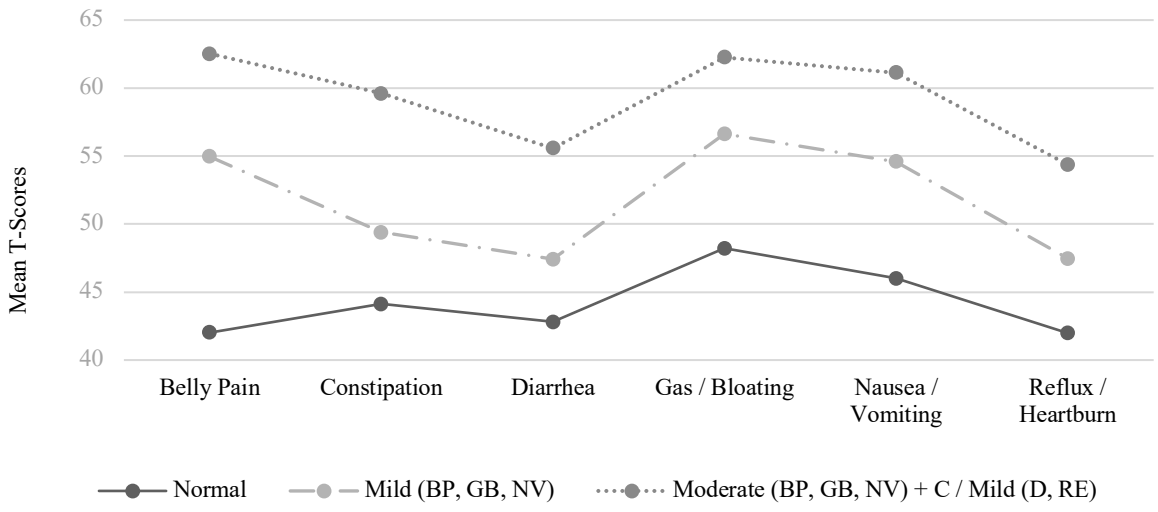
[a] *p* value calculated using bootstrap method.

Describing the Latent Classes

Between-class differences were described based on the high conditional probabilities (values > 0.5) for class assignment, available in Table A2. Additionally, differences between classes are graphically illustrated in Figure 2 based on the T-Score means for each class. The differences between these classes are statistically significant ($p < .001$) for each symptom domain, as shown in Table A3. It was concluded that the 3-Class model adequately identified

three unique latent classes that were informative to the study and could be defined based on their GI symptom patterns. The three classes were described as Normal (649 individuals, 64.15%), Mild (257 individuals, 30.30%), and Moderate (50 individuals, 5.55%). Symptom severity marked the main difference between these classes. The differences between the Mild, and Moderate groups was found in the increased symptom severity of belly pain, gas/bloating, and nausea/vomiting with the Moderate class also endorsing moderate constipation along with mild diarrhea and reflux/heartburn. A comparison of the demographic information among the three latent classes are provided in Table A5.

Figure 3 *3-Class Model Profile Plot Using Conditional Mean T-Scores per Class*



Note. PROMIS T-Score ranges for GI symptoms include Normal limits = < 55; Mild = between 55 – 60; Moderate = between 60 – 70; Severe = > 70.

Comparisons of Biopsychosocial Factors

Based on previous literature, this study hypothesized that the three latent classes will differ on biopsychosocial factors with a decrease in psychosocial functioning as levels of GI

symptoms increase (Mild and Moderate classes). Demographic analyses revealed differences between the three groups in the proportion of men and women ($\chi^2(2) = 75.431$, $p < .001$) with females dominating both the Mild and Moderate groups (Normal = 48.8%, Mild = 77.1%, Moderate = 84%). Therefore, it was also hypothesized that the scores for biopsychosocial factors for each of the GI groups would depend on sex. A two-way MANOVA was run with two independent variables – sex and GI symptom groups – and five dependent variables - Mediterranean diet (MEDAS) score, anxiety (GAD-7) score, depression (PHQ-9) score, and the overall emotional (SF-36 MH) and physical functioning (SF-36 PF) scores. The combined dependent variables were used to assess biopsychosocial functioning.

Evidence of multicollinearity was found, as assessed by Pearson correlation ($|r| > 0.9$) between the SF-36 MH and PHQ-9, therefore, the mental health summary score for the SF-36 was removed. Univariate outliers were present in the data (n=25), as assessed by inspection of a boxplot, and multivariate outliers (n=25), as assessed by Mahalanobis distance ($p < .001$). Outliers were retained because analysis with and without these cases proved to have a statistically trivial effect. The interaction effect between sex and GI symptom groups on the combined dependent variables was statistically significant, $F(8, 1896) = 2.638$, $p = .007$, Pillai's V = .022, partial $\eta^2 = .011$. Follow up univariate two-way ANOVAs were run for each dependent variable.

Analysis showed a statistically significant interaction effect between sex and GI group for physical functioning scores, $F(2, 950) = 8.301$, $p < .001$, partial $\eta^2 = .017$, but not for the Mediterranean diet score, $F(2, 950) = 10.677$, $p = .069$, partial $\eta^2 = .006$, depression, $F(2, 950) = 1.561$, $p = .210$, partial $\eta^2 = .003$, or anxiety, $F(2, 950) = 1.388$, $p = .250$, partial $\eta^2 = .003$. As

such, a simple main effects analysis for physical functioning was conducted. A statistical difference was observed between GI groups and males for physical functioning, $F(2, 950) = 36.837$, $p < .001$, partial $\eta^2 = .072$, and for females, $F(2, 950) = 27.026$, $p < .001$, partial $\eta^2 = .054$. Table A6 shows simple comparisons for differences in mean physical functioning scores between GI groups for males and females demonstrating a statistically significant difference between all three GI groups for both males and females. Thus, it could be concluded that GI symptom groups and physical functioning scores vary by sex. However, the main interaction effect between GI groups and sex was considered trivial due to the small effect size (partial $\eta^2 = .011$), warranting a separate evaluation of the main effects for GI groups and sex on biopsychosocial factors.

There was a statistically significant main effect of GI symptom groups on the combined dependent variables, $F(8, 1896) = 23.322$, $p < .001$, Pillai's V = .179, partial $\eta^2 = .090$. Follow up univariate two-way ANOVAs were run, showing a statistically significant main effect of GI groups on physical functioning, $F(2, 950) = 61.194$, $p < .001$, partial $\eta^2 = .114$, depression, $F(2, 950) = 47.924$, $p < .001$, partial $\eta^2 = .092$, anxiety, $F(2, 950) = 54.438$, $p < .001$, partial $\eta^2 = .103$, but not for the Mediterranean diet, $F(2, 950) = 1.922$, $p = .147$, partial $\eta^2 = .004$. Additionally, there was a statistically significant main effect of sex on the combined dependent variables, $F(4, 947) = 5.95$, $p < .001$, Pillai's V = .025, partial $\eta^2 = .025$. Follow up univariate two-way ANOVAs were run showing a statistically significant main effect of sex for the Mediterranean diet, $F(1, 950) = 16.794$, $p < .001$, partial $\eta^2 = .017$, and physical functioning, $F(1, 950) = 6.707$, $p = .010$, partial $\eta^2 = .007$, but not for anxiety, $F(1, 950) = .873$, $p = .350$, partial $\eta^2 = .001$, or depression, $F(1, 950) = .017$, $p = .897$, partial $\eta^2 = < .001$.

As such, a *post hoc* Tukey pairwise comparison was conducted to evaluate the differences in mean biopsychosocial scores between GI symptom groups and also between sex. Table 6 summarizes the comparison for GI symptom groups and Table 7 the sex differences.

Table 6 *Differences Between Biopsychosocial Factors and GI Symptom Classes*

	Latent classification GI group Mean (SD) or N [%]			MANOVA main effect			Post hoc tests Mean difference significance		
Variables	**Normal (n=648)**	**Mild (n=258)**	**Moderate (n=50)**	**F**	**p**	**η^2**	**Normal (v) Mild**	**Normal (v) Moderate**	**Mild (v) Moderate**
Biological									
Med diet[1]	5.36 (2.05)	5.80 (1.93)	5.50 (1.84)	1.922	.147	.004	**	ns	ns
Psychosocial									
GAD-7	3.95 (4.43)	7.57 (5.58)	10.60 (6.45)	54.438	< 0.001	.103	***	***	***
SF-36 (PF)	85.24 (10.85)	78.12 (13.69)	68.91 (18.37)	61.194	< 0.001	.092	***	***	***
PHQ-9	4.90 (4.57)	8.47 (5.63)	10.30 (6.525)	47.924	< 0.001	.092	***	***	*

Note. post-hoc comparisons were evaluated using Tukey HSD and are marked according to the degree of significant difference. ns = non-significant. The mean difference was significant at the .05 level. GAD-7= Generalized Anxiety Disorder; SF-36 (PF) Social functioning summary score for physical functioning; PHQ-9 = Patient health questionnaire to evaluate depression;
[1]Mediterranean dietary adherence score;
∗ p < .05. ∗∗ p < .01. ∗∗∗ p < .001.

Table 7 *Differences Between Biopsychosocial Factors and Sex*

	Male		Female		MANOVA main effect for sex on Biopsychosocial Factors			Post hoc tests Mean difference significance
Variables	N	Mean (SD)	N	Mean (SD)	*F*	*p*	η^2	*Male (v) Female*
Med diet								
Normal GI	332	5.13 (2.07)	316	5.59 (2.01)	8.779	.003	.009	**
Mild GI	59	5.12 (2.00)	199	6.00 (1.87)	8.886	.003	.009	**
Moderate GI	8	3.75 (1.39)	42	5.83 (1.84)	7.397	.007	.008	**
GAD-7								
Normal GI	332	3.07 (3.68)	316	4.88 (4.93)	22.815	.000	.023	***
Mild GI	59	6.56 (5.23)	199	7.86 (5.65)	3.332	.068	.003	ns
Moderate GI	8	11.63 (5.66)	42	10.40 (6.63)	.430	.512	.000	ns
SF-36 (PF)								
Normal GI	332	86.62 (9.44)	316	83.78 (12.00)	8.996	.003	.009	**
Mild GI	59	77.8 (13.62)	199	78.22 (13.75)	.056	.813	.000	ns
Moderate GI	8	55.85 (22.24)	42	71.4 (16.72)	11.185	.001	.012	**
PHQ-9								
Normal GI	332	4.23 (4.13)	316	5.60 (4.90)	12.248	.000	.013	***
Mild GI	59	8.10 (4.79)	199	8.58 (5.87)	.427	.514	.000	ns
Moderate GI	8	11.63 (5.48)	42	10.05 (6.74)	.678	.411	.001	ns

Note. post-hoc comparisons were evaluated using Tukey HSD and are marked according to the degree of significant difference. ns = non-significant. The mean difference was significant at the .05 level. GAD-7= Generalized Anxiety Disorder; SF-36 (PF) Social functioning summary score for physical functioning; PHQ-9 = Patient health questionnaire to evaluate depression;
[1]Mediterranean dietary adherence score;
∗ p < .05. ∗∗ p < .01. ∗∗∗ p < .001.

Discussion

Research on GI health has generally focused on adults who seek out medical treatment for their GI symptoms. Indeed, the recent literature has demonstrated that GI symptoms are common in the general population, however, there is very limited information on GI symptoms and associated factors in emerging adults, those between the ages of 18 and 25. Identifying patterns of GI symptoms in emerging adults along with associated biopsychosocial factors may provide valuable information about the etiology of FGIDs and suggest the most effective treatment strategies for these symptoms. Therefore, this study assessed both GI symptoms and key biopsychosocial variables in a group of 956 emerging adults to determine if meaningful patterns would emerge. Furthermore, this is the first study to evaluate a range of GI symptoms within an emerging adult population using PROMIS-GI measures. Latent class analyses revealed that 30% of the emerging adults surveyed experienced one or more GI symptom, with 5.5% of the sample reaching levels of GI symptom severity associated with clinical diagnoses. Three latent GI classes were identified, Normal (n=649, 64.15%), Mild (n=257, 30.30%), and Moderate (n=49, 5.55%). GI symptom severity marked the main difference between these classes. Additionally, differences were observed between men and women. The Mild and Moderate groups were predominantly female.

Previous general U.S. population studies have indicated that between 35% and 69% of the general population presents with at least one GI symptom (Almario et al., 2018; Camilleri et al., 2005; Drossman et al, 1993). That rate is higher than the 30% that was obtained here in a sample of emerging adults. Breaking down the data into specific GI symptom domains also reveals differences across studies. For example, lower levels of heartburn/reflux and higher

levels of gas/bloating were obtained in the current study as compared to the National GI Survey in 2015 (Almario et al., 2018).

Studies on GI symptoms in emerging adults are limited, however one indicated 51.2% of Canadian-based university students endorsed at least one GI symptom (Norton et al., 1999) and in another 65% of Korean-based nursing students reported more than one GI symptom (Lee et al., 2011). The high incidence of GI symptoms in emerging adults given that this age range should be of optimal health is surprising. One commonality between these studies is that all used convenience samples of emerging adults that were college or professional students. Student populations are under high stress (D'Zurilla & Sheedy, 1991) and these findings may reflect a relationship between GI functioning and stress among the other factors described above.

A review of the literature indicates that GI symptoms are frequently associated with anxiety and depression (Addolorato et al., 2008; Badia et al., 2002; Lisznyai et al., 2014; Miller et al., 2004; Van Oudenhove et al., 2016; Roy-Byrne et al., 2008). For example, previous studies showed 13.9% of their sample presenting with both IBS and anxiety (Afridi et al., 2017) and another found depression in 30% of medical-seeking patients presenting with FGIDs (Addolorato et al., 2008). In the current study, the Moderate GI symptom group met the GAD-7 threshold for moderate anxiety levels and the Moderate GI symptom group also met the PHQ-9 threshold score of 10 or higher for moderate or severe depression.

The gut-brain axis is the proposed communication pathway for psychosocial and GI functioning to interact. The GI symptoms and associated psychosocial measures found in this study are consistent with the existence of a gut-brain axis communication pathway. The bi-directional communication between the gut and brain is integral in maintaining homeostasis and

an imbalance in either can have adverse consequences (Foster, Rinaman, & Cryan, 2017). Following this theory, psychosocial functioning can excite or suppress the GI system, or GI functioning can excite or suppress psychosocial functioning (Van Oudenhove et al., 2016). This study observed that mood, anxiety, and GI symptom severity were strongly correlated and therefore clearly interacting.

Diet was examined in relation to GI symptom groups and the results were not in the direction that was expected. Generally psychosocial functioning was predicted to decrease as GI symptom severity increased and diet was considered one aspect of psychosocial functioning. Results suggest that the Mild GI symptom group actually exhibited higher levels of adherence to the Mediterranean diet than either the Normal GI symptom group or the Moderate GI symptom group. This finding may reveal an early response by individuals to eat a healthy diet in response to GI symptoms. Alternatively, the particular diet examined here; the Mediterranean Diet is high in legumes and vegetables. This diet may lead to higher levels of gas and bloating and may result in mild GI symptoms.

Additionally, evidence of the regulation of the gut-brain axis via microbiota was discussed, including how diet may influence this relationship. Although diet did present as a differentiating factor between the three subgroups, it was not associated with GI health and its effect was very small. It could be suggested that adherence to a healthy diet at this stage in life may be limited in keeping the gut-brain axis in balance. The composition of the microbiota is fundamentally established during childhood (Foster et al., 2017) and therefore, diets intended to alter the microbiota may need to be more targeted and aggressive to achieve meaningful results.

Limitations. The emerging adult population used here was drawn from a university sample, thus generalizing results to the population of emerging adults remains to be determined. However, it should be noted that the sample drawn were from a general psychology class, required by all students, regardless of their major. This study was a cross-sectional study and thus causation could not be determined. When GI and psychosocial symptoms emerged in relation to one another could not be determined. Two PROMIS-GI scales were excluded from the survey measures; one focused on disrupted swallowing and the other on bowel incontinence. Furthermore, evidence suggest that GI symptom severity increase during menstruation (Bernstein et al., 2014), however, this study did not account for this possible interaction between menses and belly pain.

Future directions. This study demonstrated that over a third of emerging adults attending college are experiencing at least one GI symptom and that these symptoms form unique patterns, distinguishable by levels of severity in GI symptoms. Anxiety and depression varied by severity of GI symptoms. Including all PROMIS-GI measures in future research would provide a broader scope of GI functioning. Furthermore, additional insight will be gained by comparing the GI symptom groups on other demographic and psychosocial measures. Future studies should consider measuring GI and psychosocial variables over repeated intervals with a time-series design. That way possible cause and effect relationships may be determined. Future research evaluating GI symptoms in emerging adults should include healthcare seeking measures to determine the likelihood that this population accesses medical support. Based on this study's findings, it is recommended that university health service providers evaluate patterns of GI

health when students present with anxiety and depression, and conversely they should assess anxiety and depression when students present with GI complaints.

Appendix

Abbreviations	**Definitions**
CVD	Cardiovascular disease
FGID	Functional Gastrointestinal Disorder
GER	Gastroesophageal Reflux
GI	Gastrointestinal
HQoL	Health-related quality of life
IBS	Irritable Bowel Syndrome
LCA	Latent Class Analysis
NIH	National Institute of Health
PRO	Patient-Reported Outcome
PROMIS	Patient-Reported Outcomes Measurement Information System
RAP	Recurrent abdominal pain
MedDiet	Mediterranean Diet
PREDIMED	PREvencion con DIetaMEDiterranea
MEDAS	Mediterranean Diet Adherence Screener
STC	Starting the Conversation

A1 Descriptive Characteristics of Participants

Variable	n	%
Age		
18	515	53.9%
19	222	23.2%
20	94	9.8%
21	52	5.4%
22	33	3.5%
23	19	2.0%
24	10	1.0%
25	11	1.2%
Sex		
Male	399	41.7%
Female	557	58.3%
Race/ethnicity		
Non-Hispanic white	548	57.3%
Non-Hispanic black	114	11.9%
Puerto Rican	51	5.3%
Mexican-American	14	1.5%
Other Hispanic	108	11.3%
Asians	92	9.6%
American Indian	10	1.0%
Other	19	2.0%
Identified with 2+ ethnicities	81	8.5%
Living Arrangements		
On campus	474	49.6%
Off campus	482	50.4%
Total Household Income		
0-50,000	362	37.9%
50,001-100,000	295	30.9%
100,001-150,000	166	17.4%
≥ 150,001	133	13.9%
Health		
Allergies	300	31.4%
Currently taking antibiotics	48	5.0%
Taking antibiotics past 2 months	197	20.6%
Taking probiotics	89	9.3%
Taking multivitamins	356	37.2%
Currently a smoker	130	13.6%
Body Mass Index (BMI)		
Underweight ≤ 18.5	47	7.9%
Normal weight = 18.5 – 24.9	629	65.8%
Overweight = 25 – 29.9	168	17.6%
Obesity = BMI of 30 or greater	112	11.7%

A2 *Class Membership Probabilities of the 3-Class Model*

	Distribution of the three GI latent classes		
	Normal	**Mild**	**Moderate**
PROMIS-GI Symptom Indicators	**64.15%**	**30.30%**	**5.55%**
Belly Pain			
Within Normal Limits	**0.7992**	0.1864	0.0144
Mild	0.1213	**0.8392**	0.0394
Moderate	0.0149	**0.6836**	0.3015
Severe	0.0349	0.2848	**0.6802**
Constipation			
Within Normal Limits	**0.7013**	0.2897	0.0090
Mild	0.1874	**0.5434**	0.2691
Moderate	0.1852	0.0874	**0.7274**
Severe			
Diarrhea			
Within Normal Limits	**0.6994**	0.2726	0.0280
Mild	0.0717	**0.7942**	0.1342
Moderate	0.0321	0.3254	**0.6425**
Severe	0	0	**1.0000**
Gas / Bloating			
Within Normal Limits	**0.8377**	0.1543	0.0081
Mild	0.3973	**0.5677**	0.0350
Moderate	0.0587	**0.5626**	0.3788
Severe	0	0	**1.0000**
Nausea / Vomiting			
Within Normal Limits	**0.7843**	0.2050	0.0107
Mild	0.2777	**0.6172**	0.1051
Moderate	0.2249	**0.5381**	0.2370
Severe	0.1953	0.2248	**0.5799**
Reflux / Heartburn			
Within Normal Limits	**0.6793**	0.2888	0.0319
Mild	0.1347	**0.6011**	0.2642
Moderate	0.0968	0.1918	**0.7114**
Severe	0	0	**1.0000**

Note. Items in bold indicate high conditional probabilities that characterize each class. Percent values represent the class size based on the overall sample population.

A3 *Paired Comparisons Between Classes Within the 3-Class Model*

Models for Indicators			p-value	Models for Indicators			p-value
Belly Pain				**Constipation**			
Class	1	2	5.1e-6	Class	1	2	0.00017
Class	1	3	0.00040	Class	1	3	5.8e-14
Class	2	3	3.5e-5	Class	2	3	3.5e-6
Diarrhea				**Gas / Bloating**			
Class	1	2	0.0031	Class	1	2	6.8e-15
Class	1	3	7.9e-5	Class	1	3	1.1e-7
Class	2	3	6.3e-6	Class	2	3	2.6e-6
Nausea / Vomiting				**Reflux / Heartburn**			
Class	1	2	7.4e-15	Class	1	2	0.0011
Class	1	3	1.5e-14	Class	1	3	2.6e-10
Class	2	3	0.00011	Class	2	3	0.00053

Note. P-values reveal that all latent classes are statistically significantly different between the groups for GI symptoms.

A5 Descriptive Statistics of the Classes within the 3-Class model

	Normal[1] (n=647)	**Mild[2]** (n=257)	**Moderate[3]** (n=49)
Age (years)			
Mean	18.94 (SD = 1.437)	19.03 (SD = 1.536)	19.08 (SD = 1.592)
Gender			
Male	332 (51.2%)	59 (22.9%)	8 (16%)
Female	316 (48.8%)	199 (77.1%)	42 (84%)
Race/ethnicity			
Non-Hispanic whites	360 (55.6%)	157 (60.9%)	31 (62%)
Non-Hispanic blacks	96 (14.8%)	13 (5%)	5 (10%)
Latinos	111 (17.1%)	53 (20.5%)	14 (28%)
Asians	63 (9.7%)	27 (10.5%)	2 (4%)
Other	18 (2.8%)	8 (3.1%)	3 (6%)
Identified with 2+ ethnicities			
Foreign born persons			
Living Arrangements			
On campus	330 (50.93%)	121 (46.90%)	23 (46%)
Off campus	318 (49.07%)	137 (53.10%)	27 (54%)
Total Household Income			
0-50,000	245 (37.8%)	100 (38.76%)	17 (34%)
50,001-100,000	200 (30.86%)	110 (42.64%)	15 (30%)
100,001-150,000	119 (18.36%)	39 (15.12%)	8 (16%)
≥ 150,001	84 (12.96%)	39 (15.12%)	10 (20%)
Health			
Allergies	185 (28.5%)	92 (35.7%)	20 (40%)
Currently taking antibiotics	25 (3.9%)	16 (6.2%)	7 (14%)
Taking probiotics	52 (8%)	28 (10.9%)	9 (18%)
Taking multivitamins	227 (35%)	102 (39.5%)	27 (54%)
Currently a smoker	81 (12.5%)	41 (15.9%)	8 (16%)
Body Mass Index (BMI)			
Underweight ≤ 18.5	52 (8.02%)	20 (7.75%)	4 (8%)
Normal weight = 18.5 – 24.9	424 (65.43%)	171 (66.28%)	34 (68%)
Overweight = 25 – 29.9	115 (17.75%)	35 (13.57%)	9 (18%)
Obesity = BMI of 30 or greater	57 (8.8%)	23 (8.91%)	3 (6%)

Note. Percent values indicate the percent within the subgroup.

A6 *Simple Comparisons for Physical Functioning Differences According to GI Group and Sex Interaction*

	Latent classification GI group			MANOVA main effect			Post hoc tests mean difference significance		
Sex	**Normal**	**Mild**	**Moderate**	**F**	**p**	**η^2**	**Normal (v) Mild**	**Normal (v) Moderate**	**Mild (v) Moderate**
Male									
N	332	59	8						
Mean (SD)	86.62 (.66)	77.8 (1.57)	55.85 (4.26)	36.837	< 0.001	.072	***	***	***
Female									
N	316	199	42						
Mean (SD)	83.78 (.68)	78.22 (.85)	71.4 (1.86)	27.026	< 0.001	.054	***	***	**

Note. post-hoc comparisons were evaluated using Tukey HSD and are marked according to the degree of significant difference. The mean difference was significant at the .05 level.
∗ p < .05. ∗∗ p < .01. ∗∗∗ p < .001.

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